Dietary index scores and invasive breast cancer risk among women with a family history of breast cancer

Joshua Petimar,[1,2] *Yong-Moon Mark Park,*[3] *Stephanie A Smith-Warner,*[1,2] *Teresa T Fung,*[1,4] *and Dale P Sandler*[3]

[1]Department of Nutrition and; [2]Department of Epidemiology, Harvard TH Chan School of Public Health, Boston, MA; [3]Epidemiology Branch, National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, NC; and [4]Department of Nutrition, Simmons University, Boston, MA

ABSTRACT

Background: Many epidemiologic studies have analyzed the relations of individual foods and nutrients and breast cancer risk with inconsistent results. Few studies have examined recommendation-based dietary indices and breast cancer risk.

Objective: The aim of this study was to determine associations between recommendation-based dietary index scores and incident invasive breast cancer.

Methods: The Sister Study is a prospective cohort of 50,884 US women (baseline: 2003–2009) who had a sister with breast cancer but no prior breast cancer themselves. We created scores for the Dietary Approaches to Stop Hypertension (DASH) diet, Alternative Mediterranean Diet (AMED), and Alternative Healthy Eating Index–2010 (AHEI-2010) from dietary intakes estimated by a baseline-validated Block food-frequency questionnaire (FFQ). We used Cox regression to estimate multivariable-adjusted HRs and 95% CIs for total invasive breast cancer risk and by estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor-2 (HER2) status.

Results: We documented 1,700 invasive breast cancer cases through 2015 (mean follow-up, 7.6 y). Individuals in the highest quartile of DASH scores had a lower risk of invasive breast cancer compared with those in the lowest quartile (HR: 0.78; 95% CI: 0.67, 0.90; *P*-trend = 0.001), with stronger associations for ER– (HR: 0.61; 95% CI: 0.40, 0.94; *P*-trend = 0.006) as well as ER–/PR– and ER–/PR–/HER2– subtypes. AHEI-2010 (HR for highest compared with lowest quartile: 0.90; 95% CI: 0.78, 1.03; *P*-trend = 0.15) and AMED (HR for highest compared with lowest quartile: 0.90; 95% CI: 0.77, 1.06; *P*-trend = 0.07) were weakly and nonsignificantly associated with breast cancer risk, but after excluding alcohol, AHEI-2010 was inversely associated with risk of ER–/PR– (HR: 0.64; 95% CI: 0.42, 0.98; *P*-trend = 0.04) and ER–/PR–/HER2– subtypes. We did not observe any significant interactions by menopausal status or other participant characteristics.

Conclusions: DASH scores were inversely associated with breast cancer risk; DASH and AHEI-2010 scores excluding alcohol were particularly inversely associated with risk of ER–/PR– and ER–/PR–/HER2– breast cancers. This trial was registered at clinicaltrials.gov as NCT00047970. *Am J Clin Nutr* 2019;109:1393–1401.

Keywords: breast cancer, dietary index, cohort studies, DASH diet, Mediterranean diet, Alternative Healthy Eating Index

Introduction

Relations between dietary factors and breast cancer incidence have been studied in many settings (1). Although these investigations have identified alcohol as a strong risk factor for breast cancer (2, 3) and fruit and vegetable intake as a probable protective factor for estrogen receptor–negative (ER–) breast cancers specifically (4, 5), there is limited evidence for a role of most individual nutrients and foods in breast cancer risk (1).

Recommendation-based dietary indices offer an alternative approach for assessing the impact of diet on breast cancer. Studying entire dietary patterns may account for the combined effects of and synergy between single dietary components, possibly increasing the power to detect important associations (6). Findings across prospective studies that have investigated these relations are inconsistent (7–15), however, and most studies have only considered the Mediterranean diet. Evidence for hormonal and molecular subtypes of breast cancer is additionally

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Address correspondence to DPS (e-mail: sandler@niehs.nih.gov) or Y-MMP (e-mail: mark.park@nih.gov).

Abbreviations used: AHEI-2010, Alternative Health Eating Index–2010; AMED, Alternative Mediterranean Diet; DASH, Dietary Approaches to Stop Hypertension; ER, estrogen receptor; FFQ, food-frequency questionnaire; FPED, Food Patterns Equivalent Database; HER2, human epidermal growth factor receptor-2; PR, progesterone receptor.

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lacking, despite subtypes having potentially distinct etiologies (16–18).

To elucidate these relations, we evaluated associations between three recommendation-based dietary index scores and risk of invasive breast cancer in a nationwide prospective cohort of women with a family history of breast cancer. We considered the Dietary Approaches to Stop Hypertension (DASH) diet, the Alternative Healthy Eating Index–2010 (AHEI-2010), and the Alternative Mediterranean Diet (AMED), all of which have been inversely associated with risk of cardiovascular disease (19, 20), diabetes (21, 22), and other cancers (23, 24).

Methods

Study population

This analysis was conducted within the Sister Study (25), an ongoing prospective cohort of 50,884 women aged 35–74 y who had never been diagnosed with breast cancer but had a full or half-sister who had previously been diagnosed with breast cancer at the time of enrollment between 2003 and 2009 (26). Participants completed in-person examinations and baseline telephone interviews to obtain medical, lifestyle, and reproductive history. Participants are followed annually with brief health updates, and they are sent comprehensive biennial or triennial follow-up questionnaires to update health and lifestyle data. Response rates for follow-up have been >92% (26). The Sister Study was approved by the institutional review board of the National Institute of Environmental Health Sciences, NIH, and the Copernicus Group Independent Review Board. All participants provided informed consent.

For the present analysis, we excluded participants who had a history of cancer at baseline (except nonmelanoma skin cancer) and those who were pregnant or breastfeeding at baseline. We also excluded women who were missing dietary intake data or who had extreme caloric intake (<500 or >3,500 kcal/d) because these individuals may have filled out their food-frequency questionnaires (FFQ) improperly. We additionally excluded all cases diagnosed within the first year of follow-up, because worry or symptoms of latent breast cancer could affect dietary intake, and those missing covariate data (<10% of participants). After exclusions, there were 45,626 women in the final analysis (**Supplemental Figure 1**).

Dietary assessment

Dietary intake was measured using a modified 1998 Block 110-item FFQ at baseline. Modified versions of the Block FFQ have previously been validated in women (27), and observed correlation coefficients for nutrients ranged from 0.37 (vitamin A) to 0.67 (% calories from fat), with a mean correlation coefficient of 0.55. Participants were instructed to recall their intake of foods and beverages during the past 12 mo, including how often they consumed each item (9 possible frequencies, ranging from "never" to "every day"), as well as the quantity consumed (3 or 4 quantity choices per item). Nutrient intake was estimated using the USDA Food and Nutrient Database for Dietary Studies for US women, and the intake of 37 food groups was estimated using the USDA Food Patterns Equivalents Database (FPED) (28). Briefly, FPED was used to determine the cup (~237 mL) and ounce (~28 g) equivalents for intake of each line item on the FFQ. Total daily FPED food group intakes were generated for each participant by summing over all line items in that food group. Low-fat dairy was the only food group not available in FPED, but it was determined by summing total servings per day of skim milk, 1% milk, low-fat cheese, low-fat yogurt, and low-fat ice cream.

We created a DASH index using the approach operationalized by Fung et al. (29). For 5 of the 8 components (fruits, vegetables, whole grains, nuts and legumes, and low-fat dairy), participants in the lowest quintile of intake were given 1 point, and an additional point was awarded for each increasing quintile. For 3 components (red and processed meat, sugar-sweetened beverages, and sodium), participants in the highest quintile of intake were given 1 point, and an additional point was awarded for each decreasing quintile. The component scores were summed for a total DASH score ranging from 8 to 40. We operationalized the AHEI-2010 score as developed by Chiuve et al. (30). This score measured intake of 11 foods and nutrients. Higher intake was rewarded for 6 components (vegetables, fruits, whole grains, nuts and legumes, polyunsaturated fatty acids, and omega-3 fatty acids), lower intake was rewarded for 4 components (sugar-sweetened beverages, red and processed meats, trans fatty acids, and sodium), and moderate intake was rewarded for alcohol (0.5–1.5 drinks/d). Each component received a score from 0 (least favorable) to 10 (most favorable), with partial scores ranging between 0 and 10 proportional to intake. Component scores were summed for a total AHEI-2010 score ranging from 0 to 110. We operationalized the AMED scores as developed by Fung et al. (7). This score consisted of 9 components. For 7 of these components (vegetables, fruits, legumes, nuts, whole grains, fish, and monounsaturated to saturated fatty acid ratio), intake above the median was given 1 point; for red and processed meats, 1 point was awarded to those with intake below the median; and for alcohol, 1 point was awarded for moderate intake. The component scores were summed for a total AMED score ranging from 0 to 9 points.

Case ascertainment

Participants self-reported incident breast cancer diagnosed between baseline and August 2015 (Sister Study Data Release 5.0.2) on annual questionnaires. We requested permission to obtain medical records for any participant who self-reported a diagnosis of breast cancer, and complete medical records were obtained for more than 80% of cases included in this analysis. There was very high agreement between self-reports and medical records in this cohort (positive predictive value ~99.3% for both invasive breast cancer and estrogen receptor [ER]–positive breast cancer specifically) (31), so we acquired information about diagnosis and hormone receptor status through self-report when medical records were unavailable. We defined cancer subtypes according to ER, progesterone receptor (PR), and human epidermal growth factor-2 (HER2) status. For this study, invasive breast cancer was the primary outcome, and 5 specific hormonal and molecular subtype combinations (ER+, ER–, ER+/PR+, ER–/PR–, and ER–/PR–/HER2–) were secondary outcomes.

Statistical analysis

Person-time was calculated for each participant from age (years) 1 y after enrollment in the study until age at death, invasive breast cancer diagnosis, loss to follow-up, or end of follow-up on August 14, 2015. We additionally censored individuals diagnosed with in situ breast cancer but did not consider them to be cases in our analyses because diagnosis of in situ breast cancer is highly dependent on screening, which may be correlated with lifestyle behaviors including diet. Time-varying menopausal status was calculated for all participants, and postmenopausal time was considered to begin at the age of the last menstrual period prior to a 12-mo period with no menses.

We used Cox proportional hazards regression (32) to obtain HRs and 95% CIs for associations between quartiles of the diet index scores and risk of invasive breast cancer. For all analyses, we used age as the timescale and stratified the baseline hazard by birth cohort. Multivariable models were adjusted for race/ethnicity, education, income, BMI (in kg/m^2), height, physical activity, smoking, total energy intake, number of first-degree relatives with a history of breast cancer, parity, age at first live birth, age at menarche, age at menopause, oral contraceptive use, hormone replacement therapy use, lifetime duration of breastfeeding, time since most recent mammogram, and alcohol intake (for analyses of the DASH diet only). Details of how covariates were modeled can be found in **Table 1**(footnote 3). We tested for trends by modeling the index scores continuously, and we checked for evidence of nonlinearity by running models with restricted cubic splines, with 7 knots placed at prespecified percentiles of each exposure distribution (33). Tests for nonlinearity used the likelihood ratio test, comparing the model with only the linear term to the model with the linear and the cubic spline terms. We tested the proportional hazards assumption by evaluating the P value of an interaction term between each continuous dietary index score and age in multivariable models for total invasive breast cancer risk, and we did not find violations for any exposure ($P > 0.05$ for all).

We ran separate models for the following subtypes: ER+, ER–, ER+/PR+, ER–/PR–, and ER–/PR–/HER2–. Participants were censored when they were diagnosed with breast cancer with the hormone status that was not of interest for each analysis. For each dietary index, we ran an additional Cox model using a data augmentation method to perform a test of heterogeneity comparing a model that assumes separate associations between ER+ and ER– subtypes with a model that assumes a common association using the likelihood ratio test (34). These models constrained each covariate other than the dietary indices to a single effect estimate for both subtypes of breast cancer. We repeated this test to compare ER+/PR+ and ER–/PR– subtypes.

For each dietary index, we explored potential effect modification by menopausal status (pre- compared with postmenopausal) obesity (BMI ≥30 compared with <30), race/ethnicity (non-Hispanic white compared with other), strong family history of breast cancer (>1 compared with 1 first-degree relative with breast cancer), physical activity (above compared with below median physical activity), and alcohol intake (drinkers compared with nondrinkers) by running models with an interaction term between continuous dietary index scores and each potential effect modifier and evaluating the P value of this interaction.

In sensitivity analyses, we removed alcohol from the AHEI-2010 and AMED indices because alcohol is an established risk factor for breast cancer and is generally uncorrelated with energy intake (35). We also repeated our main analyses after removing BMI from all models because BMI may be both a confounder and a mediator of associations between diet and breast cancer risk, and we added a 3-y lag to further reduce the probability of reverse causation among women with undiagnosed breast cancer.

All statistical analysis was done using SAS software (version 9.3; SAS Institute).

Results

We documented 1,700 incident cases of invasive breast cancer during 1–12 y of follow-up (mean: 7.6 y) and a total of 346,361 person-years. Across each of the DASH, AMED, and AHEI-2010 scores at baseline, individuals in the highest quartile of the dietary scores were more likely to be older, white, college educated, and physically active, have a lower BMI, and have breastfed in the past compared to those in the lowest quartile (**Table 2**). All three dietary patterns were moderately correlated, with pairwise Spearman correlation coefficients ranging from 0.52 to 0.66.

We observed a statistically significant inverse association between DASH score and risk of invasive breast cancer when comparing women in the highest quartile of DASH score to those in the lowest quartile after multivariable adjustment (HR: 0.78; 95% CI: 0.67, 0.90; P-trend = 0.001) (Table 1). Results were similar for ER+ breast cancer (HR: 0.81; 95% CI: 0.68, 0.96; P-trend = 0.03) but stronger for ER– breast cancer (HR: 0.61; 95% CI: 0.40, 0.94; P-trend = 0.006), and there was a suggestion of heterogeneity in associations between the DASH diet and ER+ and ER– breast cancers (P-heterogeneity = 0.07). Results for ER+/PR+ and ER–/PR– breast cancers were similar to those for ER+ and ER– breast cancers, respectively; results for ER–/PR–/HER2– were slightly stronger (HR: 0.56; 95% CI: 0.33, 0.95; P-trend = 0.01).

We observed weaker associations for invasive breast cancer risk with the AHEI-2010 (HR: 0.90; 95% CI: 0.78, 1.03; P-trend = 0.15) (**Table 3**) and AMED diets (HR: 0.90; 95% CI: 0.77, 1.06; P-trend = 0.07) (**Table 4**) comparing the highest with the lowest quartile. For the AHEI-2010 diet, we observed inverse but statistically nonsignificant associations for most breast cancer subtypes; however, associations for breast cancer subtypes were stronger after excluding alcohol from the index (e.g., ER–/PR– breast cancer: HR: 0.64; 95% CI: 0.42, 0.98; P-trend = 0.04). We found inverse but statistically nonsignificant associations for most breast cancer subtypes and the AMED diet. Results for the AMED diet excluding alcohol were similar in magnitude to results when including alcohol. We did not observe any statistically significant heterogeneity between ER+ and ER– breast cancer for either the AHEI-2010 diet (P-heterogeneity = 0.36) or the AMED diet (P-heterogeneity = 0.83), with similar results when comparing ER+/PR+ with ER–/PR– breast cancer.

For all dietary indices, results were similar when BMI was removed from the model, as well as when we used a 3-y lag rather than a 1-y lag. We did not find any evidence of nonlinearity for any dietary index and any outcome when comparing the restricted cubic spline models to the model with just the linear

TABLE 1 Associations (HRs and 95% CIs) between quartiles of the Dietary Approaches to Stop Hypertension (DASH) diet and risk of breast cancer outcomes in the Sister Study[1]

	Q1	Q2	Q3	Q4	*P*-trend[2]
Total invasive breast cancer					
Cases, *n*	388	486	409	417	
Age-adjusted	1.00 (reference)	0.92 (0.80, 1.05)	0.95 (0.83, 1.10)	0.83 (0.72, 0.96)	0.02
MV-adjusted[3]	1.00 (reference)	0.88 (0.77, 1.01)	0.89 (0.77, 1.03)	0.78 (0.67, 0.90)	0.001
ER+ breast cancer					
Cases, *n*	274	360	314	321	
Age-adjusted	1.00 (reference)	0.96 (0.82, 1.12)	1.02 (0.87, 1.20)	0.89 (0.76, 1.05)	0.30
MV-adjusted[3]	1.00 (reference)	0.90 (0.76, 1.05)	0.92 (0.78, 1.09)	0.81 (0.68, 0.96)	0.03
ER– breast cancer					
Cases, *n*	56	68	47	46	
Age-adjusted	1.00 (reference)	0.91 (0.64, 1.30)	0.78 (0.53, 1.16)	0.67 (0.45, 1.00)	0.02
MV-adjusted[3]	1.00 (reference)	0.89 (0.62, 1.28)	0.75 (0.50, 1.12)	0.61 (0.40, 0.94)	0.006
ER+/PR+ breast cancer					
Cases, *n*	231	314	257	259	
Age-adjusted	1.00 (reference)	1.00 (0.84, 1.19)	1.01 (0.84, 1.21)	0.88 (0.73, 1.05)	0.20
MV-adjusted[3]	1.00 (reference)	0.94 (0.79, 1.11)	0.91 (0.76, 1.10)	0.80 (0.66, 0.96)	0.03
ER–/PR– breast cancer					
Cases, *n*	52	61	43	43	
Age-adjusted	1.00 (reference)	0.88 (0.61, 1.27)	0.77 (0.51, 1.16)	0.68 (0.45, 1.03)	0.02
MV-adjusted[3]	1.00 (reference)	0.86 (0.59, 1.25)	0.73 (0.48, 1.11)	0.61 (0.39, 0.94)	0.006
ER–/PR–/HER2– breast cancer					
Cases, *n*	37	45	31	27	
Age-adjusted	1.00 (reference)	0.92 (0.59, 1.43)	0.79 (0.49, 1.29)	0.61 (0.37, 1.02)	0.02
MV-adjusted[3]	1.00 (reference)	0.90 (0.57, 1.39)	0.75 (0.46, 1.24)	0.56 (0.33, 0.95)	0.01

[1] Values are HRs (95% CIs) unless otherwise indicated. ER, estrogen receptor; HER2, human epidermal growth factor receptor-2; MET, metabolic equivalent of task; MV, multivariable; PR, progesterone receptor.

[2] *P* value for the continuous DASH score (Wald test).

[3] Adjusted for total energy intake (kcal/d, continuous), race/ethnicity (white [reference], black, other), income (<$50,000 [reference], $50,000 to <$100,000, ≥$100,000/y), smoking (0, >0 to <10, 10 to <20, 20 to <30, ≥30 pack-years), BMI (<18.5, 18.5 to <25 [reference], 25 to <30, 30 to <35, ≥35), physical activity (MET-h/wk, continuous), height (inches, continuous), education (high school or less [reference], some college, college graduate or more), alcohol intake (none [reference], <0.5, ≥0.5 to 1, ≥1 to 2, ≥2 drinks/d), mother diagnosed with breast cancer (yes vs. no [reference]), age at first live birth (nulliparous [reference], <21, 21 to <25, 25 to <29, 29–32, >32 y), parity (0 or 1 [reference], 2 or 3, 4 or more), hormone replacement therapy (none [reference], estrogen only, estrogen and progesterone, both estrogen and progesterone), age at menopause (premenopausal [reference], <40, 40 to <50, 50 to <55, ≥55 y), oral contraception use (yes [reference] vs. no), age at menarche (<12 [reference], 12 to <12.5, 12.5 to <13.5, 13.5 to <14.5, ≥14.5 y), lifetime duration of breastfeeding (0 [reference], >0 to <50, 50 to <100, ≥100 wk), and time of last mammogram (<1 [reference], 1 to <2, ≥2 y ago).

term using the likelihood ratio test ($P > 0.20$ for all). We did not observe statistically significant interactions for any potential effect modifier (P-interaction ≥ 0.12 for all).

Discussion

In this nationwide, prospective cohort study of women with a family history of breast cancer, we found that higher DASH scores were associated with a lower risk of invasive breast cancer, especially hormone receptor–negative subtypes. The AHEI-2010 diet excluding the alcohol component was also statistically significantly inversely associated with risk of ER–/PR– and ER–/PR–/HER2– breast cancer subtypes, whereas the AHEI-2010 including alcohol and the AMED diet (with or without alcohol) were not significantly inversely associated with risk of invasive breast cancer or breast cancer subtypes.

Our findings for both the DASH diet and the AHEI-2010 diet are in contrast with those from the Nurses' Health Study, which to our knowledge is the only other cohort to have considered these diets in relation to breast cancer risk. The Nurses' Health Study reported null results for total breast cancer and all molecular subtypes except for inverse associations between the DASH diet and ER– and HER2 type breast cancers (13, 14). Many prospective studies have examined relations between the Mediterranean diet and breast cancer risk, with most (7–12) but not all (13, 15) studies observing inverse associations, especially among those diagnosed with ER– or ER–/PR– cancers. The suggestive inverse trend we observed for AMED and breast cancer risk is consistent with these previous findings, even though this study was conducted in a US population, in which even participants with the highest quartile of AMED scores may not be following a true Mediterranean diet. Indeed, previous studies with the strongest inverse associations for breast cancer risk were conducted in Spain (10), Greece (12), and Europe as a whole (9).

All 3 dietary indices consist of dietary factors that have been independently associated with reduced breast cancer risk (although with varying degrees of evidence). All reward intake of fruits, vegetables, whole grains, and nuts and legumes, which have been associated with reduced risk of breast cancer, especially ER– breast cancer (5, 36–38). Proposed mechanisms for these associations include the antioxidant, anti-inflammatory, and immunological benefits of carotenoids (39–41) and flavonoids (42–44), as well as possible reductions in circulating estrogen and androstenedione levels with increasing fiber intake (45,

TABLE 2 Baseline characteristics and dietary intake in lowest and highest quintiles of Dietary Approaches to Stop Hypertension (DASH), Alternative Healthy Eating Index–2010 (AHEI-2010), and Alternative Mediterranean Diet (AMED) scores among women in the Sister Study ($n = 45{,}081$)[1]

	DASH (range: 8–40)		AHEI-2010 (range: 0–110)		AMED (range: 0–9)	
	Q1 ($n = 10{,}573$)	Q4 ($n = 11{,}370$)	Q1 ($n = 11{,}604$)	Q4 ($n = 11{,}394$)	Q1 ($n = 10{,}012$)	Q4 ($n = 12{,}530$)
Score	17.7 ± 2.1	30.1 ± 2.0	40.8 ± 4.4	64.4 ± 4.7	1.5 ± 0.6	6.7 ± 0.8
Baseline characteristics						
Age, y	52.5 ± 8.6	58.2 ± 8.6	53.4 ± 9.1	57.3 ± 8.4	53.5 ± 9.0	57.1 ± 8.6
Non-Hispanic white, %	23	10	19	14	19	13
College graduate, %	39	61	44	59	40	62
BMI, kg/m^2	29.1 ± 6.8	26.2 ± 5.4	28.3 ± 6.5	26.9 ± 5.7	28.6 ± 6.5	26.6 ± 5.7
Height, inches	64.6 ± 2.6	64.7 ± 2.5	64.7 ± 2.5	64.6 ± 2.5	64.6 ± 2.5	64.8 ± 2.5
Physical activity, MET-h/wk	44.5 ± 28.7	57.7 ± 33.2	46.9 ± 29.5	55.5 ± 32.8	44.6 ± 28.7	56.7 ± 32.3
Ever smoker, %	46	41	45	43	44	42
Postmenopausal, %	54	75	57	72	57	71
Parous, %	83	81	83	80	84	80
Age at menarche, y	12.7 ± 1.6	12.6 ± 1.5	12.7 ± 1.6	12.6 ± 1.65	12.7 ± 1.5	12.6 ± 1.5
Age at first live birth, y[2]	24.2 ± 5.4	25.1 ± 5.1	24.6 ± 5.4	24.9 ± 5.1	24.3 ± 5.3	25.2 ± 5.2
OC use, %	86	82	86	83	85	83
Hormone replacement therapy, %	34	49	36	47	36	46
Ever breastfed, %	63	75	66	74	63	76
>1 first-degree relative diagnosed with breast cancer, %	24	27	24	26	24	26
Baseline dietary intake						
Energy, kcal/d	1,540 ± 567	1,715 ± 529	1,697 ± 553	1,563 ± 553	1,299 ± 465	1,917 ± 532
Drinkers, %	80	81	81	83	78	85
Alcohol among drinkers, g/d	5.7 ± 10.8	5.2 ± 8.3	7.1 ± 11.2	4.1 ± 7.3	5.0 ± 10.5	6.1 ± 8.3
Total vegetables, servings/d	1.9 ± 1.2	4.0 ± 2.1	2.0 ± 1.3	3.9 ± 2.2	1.5 ± 0.9	4.2 ± 2.0
Total fruits, servings/d	0.5 ± 0.5	1.5 ± 0.8	0.7 ± 0.6	1.3 ± 0.9	0.5 ± 0.5	1.4 ± 0.8
Whole grains, oz/d	0.6 ± 0.4	1.2 ± 0.7	0.8 ± 0.5	1.0 ± 0.7	0.5 ± 0.4	1.2 ± 0.6
Nuts, oz/d	0.7 ± 1.0	2.1 ± 1.7	0.8 ± 1.0	1.9 ± 1.7	0.5 ± 0.7	2.2 ± 1.8
Legumes, oz/d	0.2 ± 0.2	0.4 ± 0.5	0.2 ± 0.2	0.4 ± 0.4	0.1 ± 0.2	0.5 ± 0.5
Low-fat dairy, cups/d	0.2 ± 0.4	1.1 ± 1.0	0.5 ± 0.8	0.7 ± 0.9	0.4 ± 0.7	0.8 ± 0.9
Fish, oz/d	0.5 ± 0.5	0.7 ± 0.7	0.4 ± 0.4	0.8 ± 0.8	0.3 ± 0.3	0.9 ± 0.8
Saturated fat, % energy	12.0 ± 2.6	9.4 ± 2.0	11.1 ± 2.5	10.1 ± 2.3	11.9 ± 2.9	9.8 ± 2.0
Monounsaturated fat, % energy	14.9 ± 3.2	14.1 ± 3.3	13.7 ± 2.9	15.4 ± 3.6	14.0 ± 3.2	15.1 ± 3.1
Polyunsaturated fat, % energy	8.8 ± 2.3	8.8 ± 2.2	7.9 ± 2.1	9.7 ± 2.3	8.2 ± 2.3	9.4 ± 2.1
Omega-3 fatty acids, mg/d	94.3 ± 90.3	139.1 ± 136.3	79.0 ± 67.7	170.2 ± 155.4	60.6 ± 54.3	178.2 ± 146.2
Red and processed meat, oz/d	0.8 ± 0.5	0.4 ± 0.3	0.8 ± 0.5	0.4 ± 0.3	0.6 ± 0.4	0.6 ± 0.4
Sugar-sweetened beverages, drinks/d	0.8 ± 1.3	0.1 ± 0.3	0.8 ± 1.3	0.1 ± 0.2	0.6 ± 1.1	0.2 ± 0.5
Sodium, mg/d	2364 ± 936	2574 ± 926	2527 ± 932	2441 ± 957	1929 ± 729	2984 ± 947
Trans fat, g/d	5.3 ± 3.1	4.1 ± 2.3	5.6 ± 2.9	3.7 ± 2.4	4.3 ± 2.5	5.0 ± 2.7

[1]Means ± SDs or % presented. AMED, Alternative Mediterranean Diet; AHEI-2010, Alternative Healthy Eating Index–2010; DASH, Dietary Approaches to Stop Hypertension; MET, metabolic equivalent of task; OC, oral contraceptive; Q, quartile.

[2]Among parous women.

46). All 3 dietary scores are also negatively impacted by red and processed meat intake, which has been positively associated with breast cancer risk in some (47) but not all (48, 49) epidemiologic investigations. Furthermore, the stronger associations we observed for the DASH diet compared to the other diets may be partially due to the DASH diet's inclusion of low-fat dairy, which has been associated with decreased risk of breast cancer in several studies (50). Proposed mechanisms for observed inverse associations between dairy intake and breast cancer include calcium's antiproliferation, prodifferentiation, and proapoptotic effects on mammary gland cells (51–54). Importantly, alcohol is an established risk factor for breast cancer (1), which may also explain the stronger associations we observed for the DASH diet, which was the only diet that did not reward moderate alcohol intake. This is supported by the fact that inverse associations between the AHEI-2010 and hormone receptor–negative breast cancers were strengthened after excluding alcohol intake from the score, although the same did not occur for the AMED diet.

The stronger associations we observed for the DASH diet and the AHEI-2010 (excluding alcohol) for hormone receptor–negative compared to hormone receptor–positive breast cancers are consistent with evidence from studies of individual foods and nutrients. These differences may be due to the fact that hormone receptor–positive breast cancers are primarily hormone-driven and are more strongly associated with reproductive factors, such as parity, age at first live birth, age at menarche, and hormone replacement therapy, compared with hormone receptor–negative breast cancers (18).

Strengths of this study include its large sample size, prospective nature, low attrition rate, and standardized collection of data on dietary, demographic, lifestyle, and clinical characteristics of participants, allowing us to adjust for all widely recognized confounders of associations between diet and breast cancer

TABLE 3 Associations (HRs, 95% CIs) between quartiles of the Alternative Healthy Eating Index–2010 (AHEI-2010) and risk of breast cancer outcomes in the Sister Study[1]

	Q1	Q2	Q3	Q4	*P*-trend[2]
Total invasive breast cancer					
Cases, *n*	424	416	437	423	
Age-adjusted	1.00 (reference)	0.99 (0.86, 1.13)	0.94 (0.82, 1.08)	0.91 (0.79, 1.04)	0.17
MV-adjusted[3]	1.00 (reference)	0.98 (0.86, 1.13)	0.94 (0.82, 1.07)	0.90 (0.78, 1.03)	0.15
MV-adjusted excluding alcohol[3,4]	1.00 (reference)	0.98 (0.86, 1.12)	0.87 (0.76, 1.00)	0.91 (0.79, 1.05)	0.28
ER+ breast cancer					
Cases, *n*	311	313	326	319	
Age-adjusted	1.00 (reference)	1.00 (0.86, 1.17)	0.95 (0.81, 1.11)	0.92 (0.79, 1.08)	0.35
MV-adjusted[3]	1.00 (reference)	0.99 (0.84, 1.16)	0.93 (0.80, 1.09)	0.90 (0.76, 1.06)	0.23
MV-adjusted excluding alcohol[3,4]	1.00 (reference)	0.98 (0.84, 1.15)	0.90 (0.77, 1.06)	0.93 (0.79, 1.09)	0.58
ER– breast cancer					
Cases, *n*	59	50	60	48	
Age-adjusted	1.00 (reference)	0.86 (0.59, 1.25)	0.94 (0.66, 1.35)	0.75 (0.51, 1.10)	0.18
MV-adjusted[3]	1.00 (reference)	0.88 (0.60, 1.29)	0.96 (0.67, 1.39)	0.77 (0.52, 1.14)	0.25
MV-adjusted excluding alcohol[3,4]	1.00 (reference)	0.93 (0.65, 1.32)	0.72 (0.49, 1.06)	0.69 (0.47, 1.03)	0.06
ER+/PR+ breast cancer					
Cases, *n*	276	264	260	261	
Age-adjusted	1.00 (reference)	0.96 (0.81, 1.14)	0.86 (0.73, 1.02)	0.86 (0.73, 1.02)	0.11
MV-adjusted[3]	1.00 (reference)	0.94 (0.80, 1.12)	0.85 (0.71, 1.01)	0.85 (0.71, 1.01)	0.09
MV-adjusted excluding alcohol[3,4]	1.00 (reference)	0.91 (0.77, 1.08)	0.86 (0.73, 1.03)	0.89 (0.74, 1.06)	0.31
ER–/PR– breast cancer					
Cases, *n*	54	48	56	41	
Age-adjusted	1.00 (reference)	0.90 (0.61, 1.33)	0.96 (0.66, 1.40)	0.70 (0.46, 1.05)	0.16
MV-adjusted[3]	1.00 (reference)	0.93 (0.63, 1.37)	0.99 (0.68, 1.45)	0.72 (0.47, 1.10)	0.24
MV-adjusted excluding alcohol[3,4]	1.00 (reference)	0.97 (0.67, 1.40)	0.75 (0.51, 1.12)	0.64 (0.42, 0.98)	0.04
ER–/PR–/HER2– breast cancer					
Cases, *n*	38	38	37	27	
Age-adjusted	1.00 (reference)	1.02 (0.65, 1.60)	0.91 (0.58, 1.44)	0.66 (0.40, 1.09)	0.06
MV-adjusted[3]	1.00 (reference)	1.04 (0.66, 1.64)	0.93 (0.58, 1.47)	0.68 (0.41, 1.13)	0.08
MV-adjusted excluding alcohol[3,4]	1.00 (reference)	1.21 (0.79, 1.85)	0.73 (0.45, 1.19)	0.65 (0.38, 1.09)	0.02

[1] Values are HRs (95% CIs) unless otherwise indicated. ER, estrogen receptor; HER2, human epidermal growth factor receptor-2; MET, metabolic equivalent of task; MV, multivariable; PR, progesterone receptor.

[2] *P* value for the continuous AHEI-2010 score (Wald test).

[3] Adjusted for total energy intake (kcal/d, continuous), race/ethnicity (white [reference], black, other), income (<$50,000 [reference], $50,000 to <$100,000, ≥$100,000/y), smoking (0, >0 to <10, 10 to <20, 20 to <30, ≥30 pack-years), BMI (<18.5, 18.5 to <25 [reference], 25 to <30, 30 to <35, ≥35), physical activity (MET-h/wk, continuous), height (inches, continuous), education (high school or less [reference], some college, college graduate or more), mother diagnosed with breast cancer (yes vs. no [reference]), age at first live birth (nulliparous [reference], <21, 21 to <25, 25 to <29, 29–32, >32 y), parity (0 or 1 [reference], 2 or 3, 4 or more), hormone replacement therapy (none [reference], estrogen only, estrogen and progesterone, both estrogen and progesterone), age at menopause (premenopausal [reference], <40, 40 to <50, 50 to <55, ≥55 y), oral contraception use (yes [reference] vs. no), age at menarche (<12 [reference], 12 to <12.5, 12.5 to <13.5, 13.5 to <14.5, ≥14.5 y), lifetime duration of breastfeeding (0 [reference], >0 to <50, 50 to <100, ≥100 wk), and time of last mammogram (<1 [reference], 1 to <2, ≥2 y ago).

[4] Additionally adjusted for alcohol intake (none [reference], <0.5, ≥0.5 to 1, ≥1 to 2, ≥2 drinks/d).

incidence. However, this study has several limitations. Diet is measured with error, which can lead to biased results. Moreover, because we only collected dietary information at baseline, we may misclassify participants' diets if they changed over time. However, the FFQ used in this study has been validated previously and shown to have moderate to good correlations with dietary intake by weighed diet records (27). Moreover, due to the prospective nature of the study, we anticipate any measurement error to be nondifferential and thus biased toward the null, suggesting possibly stronger associations of these dietary indices on breast cancer risk than our results imply. Although there is potential for reverse causation if participants with undiagnosed breast cancer change their eating habits, we incorporated a 1-y lag to reduce this probability, and results were similar when using a 3-y lag in sensitivity analyses. Last, this study was conducted within a cohort of women with a family history of breast cancer, which could potentially reduce the generalizability of our findings. However, Sister Study participants are largely similar to the general population in terms of nonfamilial breast cancer risk factors (25), have only modestly elevated average risk of breast cancer given their family histories (55), and are no more likely than women in the general population to engage in healthy lifestyle behaviors (56). Furthermore, we do not expect dietary index scores to be differentially associated with breast cancer risk between those with and without family histories, especially given demonstrated heterogeneity in breast cancer risk among individuals with a family history (57).

In summary, this study of a nationwide, prospective cohort of women with a family history of breast cancer supports an inverse association between the DASH diet and breast cancer risk, as well as inverse associations between the DASH diet and the AHEI-2010 (excluding alcohol) and risk of hormone receptor–negative

TABLE 4 Associations (HRs and 95% CIs) between quartiles of the Alternative Mediterranean Diet (AMED) and risk of breast cancer outcomes in the Sister Study[1]

	Q1	Q2	Q3	Q4	*P* for trend[2]
Total invasive breast cancer					
Cases, *n*	346	579	285	490	
Age-adjusted	1.00 (reference)	1.03 (0.90, 1.17)	1.00 (0.85, 1.17)	1.02 (0.88, 1.17)	0.84
MV-adjusted[3]	1.00 (reference)	0.98 (0.86, 1.13)	0.92 (0.78, 1.08)	0.90 (0.77, 1.06)	0.07
MV-adjusted excluding alcohol[3,4]	1.00 (reference)	1.03 (0.88, 1.19)	0.91 (0.80, 1.05)	0.89 (0.76, 1.05)	0.02
ER+ breast cancer					
Cases, *n*	259	426	211	373	
Age-adjusted	1.00 (reference)	1.00 (0.86, 1.17)	0.98 (0.81, 1.17)	1.02 (0.87, 1.20)	0.98
MV-adjusted[2]	1.00 (reference)	0.95 (0.81, 1.11)	0.88 (0.73, 1.06)	0.87 (0.73, 1.05)	0.05
MV-adjusted excluding alcohol[3,4]	1.00 (reference)	0.95 (0.79, 1.13)	0.86 (0.74, 1.01)	0.86 (0.71, 1.03)	0.02
ER– breast cancer					
Cases, *n*	46	73	37	61	
Age-adjusted	1.00 (reference)	0.99 (0.68, 1.43)	1.01 (0.65, 1.55)	0.97 (0.66, 1.43)	0.82
MV-adjusted[3]	1.00 (reference)	0.93 (0.64, 1.36)	0.90 (0.57, 1.42)	0.83 (0.54, 1.29)	0.33
MV-adjusted excluding alcohol[3,4]	1.00 (reference)	1.07 (0.69, 1.64)	0.99 (0.68, 1.45)	0.86 (0.55, 1.35)	0.24
ER+/PR+ breast cancer					
Cases, *n*	214	366	175	306	
Age-adjusted	1.00 (reference)	1.05 (0.89, 1.25)	1.00 (0.81, 1.22)	1.03 (0.87, 1.23)	0.98
MV-adjusted[3]	1.00 (reference)	1.00 (0.84, 1.19)	0.90 (0.73, 1.11)	0.90 (0.73, 1.10)	0.12
MV-adjusted excluding alcohol[3,4]	1.00 (reference)	1.01 (0.83, 1.23)	0.91 (0.76, 1.08)	0.87 (0.72, 1.07)	0.06
ER–/PR– breast cancer					
Cases, *n*	42	64	36	57	
Age-adjusted	1.00 (reference)	0.95 (0.64, 1.40)	1.07 (0.69, 1.68)	1.00 (0.67, 1.49)	0.92
MV-adjusted[3]	1.00 (reference)	0.88 (0.59, 1.30)	0.92 (0.58, 1.48)	0.80 (0.51, 1.27)	0.25
MV-adjusted excluding alcohol[3,4]	1.00 (reference)	1.05 (0.67, 1.65)	0.94 (0.63, 1.41)	0.80 (0.50, 1.29)	0.18
ER–/PR–/HER2– breast cancer					
Cases, *n*	28	51	28	33	
Age-adjusted	1.00 (reference)	1.14 (0.72, 1.82)	1.27 (0.75, 2.14)	0.88 (0.53, 1.46)	0.51
MV-adjusted[3]	1.00 (reference)	1.03 (0.64, 1.66)	1.05 (0.60, 1.82)	0.68 (0.38, 1.20)	0.11
MV-adjusted excluding alcohol[3,4]	1.00 (reference)	1.28 (0.76, 2.16)	1.03 (0.64, 1.66)	0.66 (0.37, 1.19)	0.07

[1] Values are HRs (95% CIs) unless otherwise indicated. ER, estrogen receptor; HER2, human epidermal growth factor receptor-2; MET, metabolic equivalent of task; MV, multivariable; PR, progesterone receptor.

[2] *P* value for the continuous AMED score (Wald test).

[3] Adjusted for total energy intake (kcal/d, continuous), race/ethnicity (white [reference], black, other), income (<$50,000 [reference], $50,000 to <$100,000, ≥$100,000/y), smoking (0, >0 to <10, 10 to <20, 20 to <30, ≥30 pack-years), BMI (<18.5, 18.5 to <25 [reference], 25 to <30, 30 to <35, ≥35 kg/m^2), physical activity (MET-h/wk, continuous), height (inches, continuous), education (high school or less [reference], some college, college graduate or more), mother diagnosed with breast cancer (yes vs. no [reference]), age at first live birth (nulliparous [reference], <21, 21 to <25, 25 to <29, 29–32, >32 y), parity (0 or 1 [reference], 2 or 3, 4 or more), hormone replacement therapy (none [reference], estrogen only, estrogen and progesterone, both estrogen and progesterone), age at menopause (premenopausal [reference], <40, 40 to <50, 50 to <55, ≥55 y), oral contraception use (yes [reference] vs. no), age at menarche (<12 [reference], 12 to <12.5, 12.5 to <13.5, 13.5 to <14.5, ≥14.5 y), lifetime duration of breastfeeding (0 [reference], >0 to <50, 50 to <100, ≥100 wk), and time of last mammogram (<1 [reference], 1 to <2, ≥2 y ago).

[4] Additionally adjusted for alcohol intake (none [reference], <0.5, ≥0.5 to 1, ≥1 to 2, ≥2 drinks/d).

breast cancers in particular. We observed generally inverse but nonsignificant associations for the AMED diet and breast cancer risk, but may have been limited by the fact that few US individuals truly follow a Mediterranean diet; this relation therefore deserves further investigation.

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References

1. World Cancer Research Fund International/American Institute for Cancer Research. Continuous Update Project report: diet, nutrition, physical activity and breast cancer. [Internet.] 2017. Available from: http://www.aicr.org/continuous-update-project.
2. Jung S, Wang M, Anderson K, Baglietto L, Bergkvist L, Bernstein L, van den Brandt PA, Brinton L, Buring JE, Eliassen AH, et al. Alcohol consumption and breast cancer risk by estrogen receptor status: in a pooled analysis of 20 studies. Int J Epidemiol 2016;45(3):916–28.
3. Choi YJ, Myung SK, Lee JH. Light alcohol drinking and risk of cancer: a meta-analysis of cohort studies. Cancer Res Treat 2018;50(2):474–87.

4. Emaus MJ, Peeters PH, Bakker MF, Overvad K, Tjonneland A, Olsen A, Romieu I, Ferrari P, Dossus L, Boutron-Ruault MC, et al. Vegetable and fruit consumption and the risk of hormone receptor-defined breast cancer in the EPIC cohort. Am J Clin Nutr 2016;103(1):168–77.
5. Jung S, Spiegelman D, Baglietto L, Bernstein L, Boggs DA, van den Brandt PA, Buring JE, Cerhan JR, Gaudet MM, Giles GG, et al. Fruit and vegetable intake and risk of breast cancer by hormone receptor status. J Natl Cancer Inst 2013;105(3):219–36.
6. Hu FB. Dietary pattern analysis: a new direction in nutritional epidemiology. Curr Opin Lipidol 2002;13(1):3–9.
7. Fung TT, Hu FB, McCullough ML, Newby PK, Willett WC, Holmes MD. Diet quality is associated with the risk of estrogen receptor-negative breast cancer in postmenopausal women. J Nutr 2006;136(2):466–72.
8. van den Brandt PA, Schulpen M. Mediterranean diet adherence and risk of postmenopausal breast cancer: results of a cohort study and meta-analysis. Int J Cancer 2017;140(10):2220–31.
9. Buckland G, Travier N, Cottet V, Gonzalez CA, Lujan-Barroso L, Agudo A, Trichopoulou A, Lagiou P, Trichopoulos D, Peeters PH, et al. Adherence to the Mediterranean diet and risk of breast cancer in the European prospective investigation into cancer and nutrition cohort study. Int J Cancer 2013;132(12):2918–27.
10. Toledo E, Salas-Salvado J, Donat-Vargas C, Buil-Cosiales P, Estruch R, Ros E, Corella D, Fito M, Hu FB, Aros F, et al. Mediterranean diet and invasive breast cancer risk among women at high cardiovascular risk in the PREDIMED Trial: a randomized clinical trial. JAMA Intern Med 2015;175(11):1752–60.
11. Cade JE, Taylor EF, Burley VJ, Greenwood DC. Does the Mediterranean dietary pattern or the Healthy Diet Index influence the risk of breast cancer in a large British cohort of women? Eur J Clin Nutr 2011;65(8):920–8.
12. Trichopoulou A, Bamia C, Lagiou P, Trichopoulos D. Conformity to traditional Mediterranean diet and breast cancer risk in the Greek EPIC (European Prospective Investigation into Cancer and Nutrition) cohort. Am J Clin Nutr 2010;92(3):620–5.
13. Hirko KA, Willett WC, Hankinson SE, Rosner BA, Beck AH, Tamimi RM, Eliassen AH. Healthy dietary patterns and risk of breast cancer by molecular subtype. Breast Cancer Res Treat 2016;155(3):579–88.
14. Fung TT, Hu FB, Hankinson SE, Willett WC, Holmes MD. Low-carbohydrate diets, dietary approaches to stop hypertension-style diets, and the risk of postmenopausal breast cancer. Am J Epidemiol 2011;174(6):652–60.
15. Couto E, Sandin S, Lof M, Ursin G, Adami HO, Weiderpass E. Mediterranean dietary pattern and risk of breast cancer. PLoS One 2013;8(2):e55374.
16. Russnes HG, Lingjaerde OC, Borresen-Dale AL, Caldas C. Breast cancer molecular stratification: from intrinsic subtypes to integrative clusters. Am J Pathol 2017;187(10):2152–62.
17. Anderson KN, Schwab RB, Martinez ME. Reproductive risk factors and breast cancer subtypes: a review of the literature. Breast Cancer Res Treat 2014;144(1):1–10.
18. Althuis MD, Fergenbaum JH, Garcia-Closas M, Brinton LA, Madigan MP, Sherman ME. Etiology of hormone receptor-defined breast cancer: a systematic review of the literature. Cancer Epidemiol Biomarkers Prev 2004;13(10):1558–68.
19. Reedy J, Krebs-Smith SM, Miller PE, Liese AD, Kahle LL, Park Y, Subar AF. Higher diet quality is associated with decreased risk of all-cause, cardiovascular disease, and cancer mortality among older adults. J Nutr 2014;144(6):881–9.
20. Bai G, Zhang J, Zhao C, Wang Y, Qi Y, Zhang B. Adherence to a healthy lifestyle and a DASH-style diet and risk of hypertension in Chinese individuals. Hypertens Res 2017;40(2):196–202.
21. Jacobs S, Harmon BE, Boushey CJ, Morimoto Y, Wilkens LR, Le Marchand L, Kroger J, Schulze MB, Kolonel LN, Maskarinec G. A priori-defined diet quality indexes and risk of type 2 diabetes: the multiethnic cohort. Diabetologia 2015;58(1):98–112.
22. de Koning L, Chiuve SE, Fung TT, Willett WC, Rimm EB, Hu FB. Diet-quality scores and the risk of type 2 diabetes in men. Diabetes Care 2011;34(5):1150–6.
23. Tabung FK, Brown LS, Fung TT. Dietary patterns and colorectal cancer risk: a review of 17 years of evidence (2000–2016). Curr Colorectal Cancer Rep 2017;13(6):440–54.
24. Buckland G, Agudo A, Lujan L, Jakszyn P, Bueno-de-Mesquita HB, Palli D, Boeing H, Carneiro F, Krogh V, Sacerdote C, et al. Adherence to a Mediterranean diet and risk of gastric adenocarcinoma within the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort study. Am J Clin Nutr 2010;91(2):381–90.
25. Weinberg CR, Shore DL, Umbach DM, Sandler DP. Using risk-based sampling to enrich cohorts for endpoints, genes, and exposures. Am J Epidemiol 2007;166(4):447–55.
26. Sandler DP, Hodgson ME, Deming-Halverson SL, Juras PS, D'Aloisio AA, Suarez LM, Kleeberger CA, Shore DL, DeRoo LA, Taylor JA, et al. The Sister Study cohort: baseline methods and participant characteristics. Environ Health Perspect 2017;125(12):127003.
27. Block G, Woods M, Potosky A, Clifford C. Validation of a self-administered diet history questionnaire using multiple diet records. J Clin Epidemiol 1990;43(12):1327–35.
28. Bowman SA, Clemens JC, Friday JE, Thoerig RC, Moshfegh AJ. Food Patterns Equivalents Database 2011–12: Methodology and User Guide. Beltsville, MD: Food Surveys Research Group, Beltsville Human Nutrition Research Center, Agricultural Research Service, US Department of Agriculture; 2014.
29. Fung TT, Chiuve SE, McCullough ML, Rexrode KM, Logroscino G, Hu FB. Adherence to a DASH-style diet and risk of coronary heart disease and stroke in women. Arch Intern Med 2008;168(7):713–20.
30. Chiuve SE, Fung TT, Rimm EB, Hu FB, McCullough ML, Wang M, Stampfer MJ, Willett WC. Alternative dietary indices both strongly predict risk of chronic disease. J Nutr 2012;142(6):1009–18.
31. D'Aloisio AA, Nichols HB, Hodgson ME, Deming-Halverson SL, Sandler DP. Validity of self-reported breast cancer characteristics in a nationwide cohort of women with a family history of breast cancer. BMC Cancer 2017;17(1):692.
32. Cox DR. Regression models and life-tables. Journal of the Royal Statistical Society B 1972;34(2):187–220.
33. Durrleman S, Simon R. Flexible regression models with cubic splines. Stat Med 1989;8(5):551–61.
34. Wang M, Spiegelman D, Kuchiba A, Lochhead P, Kim S, Chan AT, Poole EM, Tamimi R, Tworoger SS, Giovannucci E, et al. Statistical methods for studying disease subtype heterogeneity. Stat Med 2016;35(5):782–800.
35. Willett W. Nutritional Epidemiology. 3rd ed. Oxford, UK: Oxford University Press; 2013.
36. Aune D, Chan DS, Vieira AR, Rosenblatt DA, Vieira R, Greenwood DC, Norat T. Fruits, vegetables and breast cancer risk: a systematic review and meta-analysis of prospective studies. Breast Cancer Res Treat 2012;134(2):479–93.
37. Farvid MS, Cho E, Eliassen AH, Chen WY, Willett WC. Lifetime grain consumption and breast cancer risk. Breast Cancer Res Treat 2016;159(2):335–45.
38. van den Brandt PA, Nieuwenhuis L. Tree nut, peanut, and peanut butter intake and risk of postmenopausal breast cancer: the Netherlands Cohort Study. Cancer Causes Control 2018;29(1):63–75.
39. Eliassen AH, Hendrickson SJ, Brinton LA, Buring JE, Campos H, Dai Q, Dorgan JF, Franke AA, Gao YT, Goodman MT, et al. Circulating carotenoids and risk of breast cancer: pooled analysis of eight prospective studies. J Natl Cancer Inst 2012;104(24):1905–16.
40. Sies H, Stahl W. Vitamins E and C, beta-carotene, and other carotenoids as antioxidants. Am J Clin Nutr 1995;62(6 Suppl):1315s–21s.
41. Krinsky NI. Actions of carotenoids in biological systems. Annu Rev Nutr 1993;13:561–87.
42. Hui C, Qi X, Qianyong Z, Xiaoli P, Jundong Z, Mantian M. Flavonoids, flavonoid subclasses and breast cancer risk: a meta-analysis of epidemiologic studies. PLoS One 2013;8(1):e54318.
43. Thomas CM, Wood RC, 3rd, Wyatt JE, Pendleton MH, Torrenegra RD, Rodriguez OE, Harirforoosh S, Ballester M, Lightner J, Krishnan K, et al. Anti-neoplastic activity of two flavone isomers derived from *Gnaphalium elegans* and *Achyrocline bogotensis*. PLoS One 2012;7(6):e39806.
44. Russo M, Spagnuolo C, Tedesco I, Bilotto S, Russo GL. The flavonoid quercetin in disease prevention and therapy: facts and fancies. Biochem Pharmacol 2012;83(1):6–15.
45. Aune D, Chan DS, Greenwood DC, Vieira AR, Rosenblatt DA, Vieira R, Norat T. Dietary fiber and breast cancer risk: a systematic review and meta-analysis of prospective studies. Ann Oncol 2012;23(6):1394–402.

46. Rose DP, Goldman M, Connolly JM, Strong LE. High-fiber diet reduces serum estrogen concentrations in premenopausal women. Am J Clin Nutr 1991;54(3):520–5.
47. Guo J, Wei W, Zhan L. Red and processed meat intake and risk of breast cancer: a meta-analysis of prospective studies. Breast Cancer Res Treat 2015;151(1):191–8.
48. Missmer SA, Smith-Warner SA, Spiegelman D, Yaun SS, Adami HO, Beeson WL, van den Brandt PA, Fraser GE, Freudenheim JL, Goldbohm RA, et al. Meat and dairy food consumption and breast cancer: a pooled analysis of cohort studies. Int J Epidemiol 2002;31(1):78–85.
49. Pala V, Krogh V, Berrino F, Sieri S, Grioni S, Tjonneland A, Olsen A, Jakobsen MU, Overvad K, Clavel-Chapelon F, et al. Meat, eggs, dairy products, and risk of breast cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort. Am J Clin Nutr 2009;90(3):602–12.
50. Dong JY, Zhang L, He K, Qin LQ. Dairy consumption and risk of breast cancer: a meta-analysis of prospective cohort studies. Breast Cancer Res Treat 2011;127(1):23–31.
51. Hidayat K, Chen GC, Zhang R, Du X, Zou SY, Shi BM, Qin LQ. Calcium intake and breast cancer risk: meta-analysis of prospective cohort studies. Br J Nutr 2016;116(1):158–66.
52. Wulaningsih W, Sagoo HK, Hamza M, Melvin J, Holmberg L, Garmo H, Malmstrom H, Lambe M, Hammar N, Walldius G, et al. Serum calcium and the risk of breast cancer: findings from the Swedish AMORIS study and a meta-analysis of prospective studies. Int J Mol Sci 2016;17(9). doi:10.3390/ijms17091487.
53. Jacobson EA, James KA, Newmark HL, Carroll KK. Effects of dietary fat, calcium, and vitamin D on growth and mammary tumorigenesis induced by 7,12-dimethylbenz(a)anthracene in female Sprague–Dawley rats. Cancer Res 1989;49(22): 6300–3.
54. Kumar B, Kumar A, Ghosh S, Pandey BN, Mishra KP, Hazra B. Diospyrin derivative, an anticancer quinonoid, regulates apoptosis at endoplasmic reticulum as well as mitochondria by modulating cytosolic calcium in human breast carcinoma cells. Biochem Biophys Res Commun 2012;417(2):903–9.
55. Sandler DP, Hodgson ME, Deming-Halverson SL, Juras PS, D'Aloisio AA, Suarez LM, Kleeberger CA, Shore DL, DeRoo LA, Taylor JA, et al. The Sister Study cohort: baseline methods and participant characteristics. Environ Health Perspect 2017;125(12): 127003.
56. Spector D, Deroo LA, Sandler DP. Lifestyle behaviors in black and white women with a family history of breast cancer. Prev Med 2011;52(5):394–7.
57. 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(9291): 1389–99.