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Dietary Patterns and Endometrial Cancer Risk in the California Teachers Study Cohort

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Abstract

Purpose—Information on the role of dietary patterns and endometrial cancer risk is limited. We investigated whether dietary patterns are associated with endometrial cancer risk among women in the California Teachers Study cohort.

Methods—Among 75,093 eligible women, 937 developed invasive endometrial cancer between 1995 and 2011. Multivariate Cox regression was performed to estimate relative risks (RR) and 95% confidence intervals (CI) associated with five dietary patterns identified by principal components factor analysis: “plant-based”, “high protein/high fat”, “high carbohydrates”, “ethnic”, and “salad and wine”.

Results—These dietary patterns were not associated with endometrial cancer risk overall (RR=0.91, 95% CI: 0.72, 1.15 for the highest vs. lowest quintile of the “plant-based” dietary pattern) or by menopausal status and hormone therapy use.

Conclusions—Dietary patterns do not seem to be associated with endometrial cancer risk.

Keywords

dietary patterns; endometrial cancer; body mass index; cohort

Introduction

While obesity has been consistently shown to increase risk of endometrial cancer (1), the role of dietary intake, a related and modifiable behavior, is less clear. A number of studies have examined the association between specific foods and nutrients and endometrial cancer risk. There is some evidence from case-control studies suggesting non-starchy vegetables, particularly cruciferous vegetables, may reduce risk and red meat, possibly due to its higher saturated fat content, may increase risk (1-3). However, cohort studies have generally found no associations (4-9) and the 2013 World Cancer Research Fund Continuous Update Project (CUP) found that the data on non-starchy vegetables and red meat were too limited to draw conclusions (10). In addition, examination of individual foods or nutrients does not account

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for the complex interactions that occur between the various nutrients and non-nutritive components of a person's overall diet. These interactions can be captured more fully when overall dietary patterns are analyzed (11).

To date, only three case-control studies have examined dietary patterns and endometrial cancer risk. Two found reduced risk associated with a “healthy” or “plant-based” pattern (12, 13), and one also found some suggestion that a “meat” pattern increased risk among overweight/obese women (12). The third study found no overall association, but observed a statistically non-significant increased risk associated with a “western” diet among women who did not use vitamin supplements (14).

To avoid the biases associated with case-control studies of dietary intake, we evaluated the relationship between dietary patterns and subsequent risk of endometrial cancer in the large prospective California Teachers Study cohort.

Materials and Methods

The California Teachers Study (CTS) cohort, established in 1995-96, includes 133,479 active and retired female teachers and administrators (15). Participants completed a self-administered baseline questionnaire that asked a variety of questions related to health, medical history, and lifestyle and behaviors, including dietary intake. Five and ten years later, follow-up questionnaires collected updated menopausal status and hormone therapy use and current height and weight (ten years only).

The CTS study was approved by the Institutional Review Boards of the Cancer Prevention Institute of California, University of California Irvine, University of Southern California, City of Hope, and California Health and Human Services Agency.

Follow-up

The CTS cohort is followed annually for cancer diagnoses, changes of address, and death. Cancer diagnoses are determined by linkage with the California Cancer Registry (CCR), a population-based cancer registry that covers the entire state of California and is part of the National Cancer Institute's Surveillance, Epidemiology and End Results Program. Since greater than 99% of all cancer diagnoses among California residents are reported to the CCR (16), those cohort members who continue to reside in California are effectively in active follow-up for cancer outcomes. Changes of address are obtained by annual mailings, notifications from participants, and record linkages with multiple sources. California and national mortality files are used to ascertain date of death.

Dietary patterns

Dietary intake assessing consumption in the year prior to baseline was obtained via an early version of the 112 item Block95 food-frequency questionnaire (FFQ) which has been validated in the CTS (17). Principal components factor analysis (PCFA), which is a factor analysis using the principal component method (18, 19), was used to characterize dietary patterns in all cohort members under the age of 85 at baseline who had a valid FFQ (n=118,465). Medium servings per day for all food items and beverages were calculated

based on frequency of consumption and portion size. Vitamin intake was also included in the PCFA (20). An orthogonal varimax rotation was used to minimize correlation and maximize interpretability between the factors. The number of factors (components) retained was based on an eigenvalue criterion >1, scree plot analysis, and interpretability. For each dietary pattern identified, factor scores for each participant were calculated using the loadings for all dietary items by multiplying the standardized scoring coefficient for each item by the standardized servings per day of the item for that individual (21). Thus every participant had a factor score for each dietary pattern, with a higher value representing greater intake of foods associated with that pattern.

We identified five major dietary patterns (Online Resource Table 1) (20, 22). The “plant-based” pattern was characterized by high factor loadings on an array of fruits and vegetables. The “high protein/high fat” pattern included sources of animal protein (e.g., meat and eggs) and added fats (e.g., butter and mayonnaise). The “high carbohydrate” pattern was characterized by convenience foods, pasta, and bread. The “ethnic” pattern was high in legumes, soy-based foods, rice, and dark green leafy vegetables. The “salad and wine” pattern was characterized by salad and low-fat dressing, fish, wine, and coffee/tea. The median factor score (interquartile range; IQR) for these five dietary patterns were, respectively, -0.212 (-0.760 to 0.505); -0.192 (-0.723 to 0.459); 0.004 (-0.561 to 0.675); -0.179 (-0.607 to 0.357); -0.142 (-0.744 to 0.517). Together, these five factors explained 18.6% of the variance in dietary intake in the CTS cohort. Thirty-five percent of the cohort consumed a single dietary pattern (defined as having a score in the top quintile for only one factor), while 28% had diets characterized by a combination of patterns; 37% had diets that were not well characterized by any one of the five patterns.

Study population

For the present analysis, we excluded women, sequentially, who at baseline: did not live in California (N=8,868); chose to participate only in breast cancer research (N=18); had a history of endometrial cancer or whose prior history of cancer was unknown (N=1,619 and 662, respectively); had a hysterectomy (N=27,843); were age 85 years or older (N=1,330); had missing or invalid dietary, alcohol, or vitamin supplement data (N=6,808); had an average daily caloric intake of <600 or >5000 kcal (N=1,361); consumed >50% of calories from alcohol (N=42); or had missing data for one or more adjustment factor or had missing data for menopausal status/hormone therapy (HT) use at baseline, five-year and ten-year follow-up (N=9,835). Of the 75,093 women eligible for this analysis, 937 were diagnosed with invasive endometrial cancer after joining the cohort and before January 1, 2012.

Statistical analyses

Follow-up time was calculated as the number of days between the date the baseline questionnaire was completed and a first diagnosis of endometrial cancer (International Classification of Diseases for Oncology-3 site code C54.1 or C54.9; n=937), death (n=5,858), a permanent (>4 months) move out of California (n=7,194), a hysterectomy (n=6,392), or December 31, 2011, whichever occurred first. The 48 women diagnosed with endometrial sarcoma or lymphoma and 20 women diagnosed with in-situ endometrial cancer were censored on the dates of their diagnosis. Of the n=69,340 and n=61,793 women who

were still under analytic follow-up at the time of completion (responders) or the median completion date (non-responders) of the five and ten years questionnaires, respectively, n=48,342 (70%) and n=37,647 (61%) completed the five-year and ten-year questionnaires, respectively.

Multivariate Cox proportional hazards regression models were fit to estimate relative risks (RR; hazard rate ratio) associated with a diagnosis of invasive endometrial cancer. These models included age (in days) as the time metric, were stratified by age (in years) at baseline, and were adjusted for the following factors measured at baseline: race (white, non-white), age at menarche (single years from ≤9 to ≥17), gravidity (no, yes) and age at last pregnancy (years), oral contraceptive use (never used, used <3 years, used ≥3 years), average annual long-term (high school to age 54 or age at baseline if younger) moderate plus strenuous physical activity (hours per week; <5.5 ≥5.5), smoking status (never, ever), height (inches), and average daily caloric intake (kcal). Models were additionally adjusted for the following time-dependent exposures: body mass index (BMI; kg/m^2) at baseline and updated at the ten-year follow-up, if available; and menopausal status/HT use (premenopausal, peri/postmenopausal not using HT, peri/postmenopausal using HT, missing) at baseline and updated at the five-year and ten-year follow-ups. If the five-year or ten-year questionnaire was not completed or menopausal status/HT use was missing at any questionnaire, the time-dependent menopausal status/HT use variable was set to the missing category at the time of that questionnaire until the next questionnaire or the end of follow-up. Participants with menopausal status/HT use missing at all three questionnaires were excluded from all analyses. Models also included the statistically significant interaction between time-dependent BMI and time-dependent menopausal status/HT use previously reported in this cohort with static exposures (23), and the interactions between race and time-dependent age and between age at last pregnancy and time-dependent age. Variable definitions were chosen that best described the relationship with risk while preserving parsimony. All models included the factor scores for all five dietary patterns.

Likelihood ratio tests for trend across quintiles were conducted using an ordinal variable coded as the median value of each quintile. If the trend test was statistically significant we performed a likelihood ratio test of the non-linearity of the trend, comparing a model with the dietary pattern in quintiles to a model with the dietary pattern as ordinal; a non-significant *P*-value indicated no evidence of a non-linear trend. Effect modification by baseline menopausal status/HT use (premenopausal, peri/postmenopausal not using HT, peri/postmenopausal using HT), baseline BMI (<25, ≥25 kg/m^2), waist circumference (<35, ≥35 in), and waist-to-height ratio (<0.55, ≥0.55) was examined. Likelihood ratio tests of interaction were computed based on cross-product terms. We tested the assumption of proportional hazards for each static adjustment variable and main effect using a likelihood ratio test of interaction with the time metric (continuous age). Race and age at last pregnancy both had a significant interaction with time-dependent age; thus these interactions were included as adjustment factors.

As endometrial cancer risk may differ by tumor type or grade, we performed a competing risk analysis with outcomes of endometrioid adenocarcinoma (International Classification of Diseases for Oncology, 3rd edition [ICD-O-3] codes 8380 and 8382; n=542) split by grade,

and Type II tumors (serous/papillary serous, ICD-O-3 codes 8441, 8460, and 8461, n=42; and mixed cell adenocarcinoma, ICD-O-3 code 8323, n=46)(24). Women who were diagnosed with endometrial cancer not of the type or grade of interest were censored on the dates of their diagnoses.

Results

Among the 75,093 women included in the present analysis, the median age at baseline was 48 years and 88% were non-Hispanic white. At baseline, 54% were premenopausal, 20% were peri/postmenopausal not using HT, 23% were peri/postmenopausal using HT, and 3% had unknown menopausal status/HT use. At baseline, 24% of women were overweight and 14% were obese. The median follow-up was 16.1 years. Among women who were still under analytic follow-up and completed the ten-year questionnaire, 13% were premenopausal, 73% were peri/postmenopausal not using HT, 13% were peri/postmenopausal using HT, and 1% had unknown menopausal status/HT use. In addition, 29% were overweight and 18% were obese at ten years. Later age at menarche, later age at last pregnancy, use of oral contraceptives, and greater physical activity were associated with reduced risk of endometrial cancer, and greater height, greater BMI, and use of HT were associated with increased risk of endometrial cancer (Online Resource Table 2).

Dietary patterns were not associated with endometrial cancer risk overall (Table 1), by menopausal status/HT use (data not shown), or by abdominal adiposity (data not shown). Although the number of cases was small, there did not appear to be an association between dietary patterns and endometrial cancer by tumor type or grade (Table 2).

There was a suggestion that the association between dietary patterns and endometrial cancer risk varied by baseline BMI (Table 3). The “salad and wine” dietary pattern was associated with increased risk of endometrial cancer in women with BMI <25 (RR=1.73, 95% CI: 1.14, 2.61 comparing Q5 to Q1, *P*-trend=0.05, *P*-non-linearity of the trend =0.12), but not among overweight/obese women (RR=0.98, 95% CI: 0.72, 1.33, *P*-trend=0.84; *P*-interaction=0.01). Results were similar when the “salad and wine” factor score was modeled per unit increase (RR=1.11, 95% CI: 1.00, 1.23 for BMI <25 and RR=0.95, 95% CI: 0.87, 1.05 for BMI ≥25; *P* -interaction=0.0003). Further adjustment for total alcohol consumption in the year prior to baseline (none, <20 g/d, ≥20 g/d) did not substantially change the RR associated with this pattern for women with BMI <25 (RR=1.82, 95% CI: 1.18, 2.79, comparing Q5 to Q1, *P*-trend=0.04, *P*-non-linearity of the trend =0.12), or for those with BMI ≥25 (RR=1.06, 95% CI: 0.76, 1.46, *P*-trend=0.74; *P*-interaction=0.01). Results were similar when adjusted for alcohol from wine only and for alcohol from the three types of beverages separately. Alcohol consumption itself was not associated with risk among women with BMI <25 whether dietary patterns were adjusted for (RR=0.90, 95% CI: 0.61, 1.32 ≥20 g/d compared to none) or not (RR=1.12, 95% CI: 0.80, 1.57), or among those with BMI ≥25 (RR=0.74, 95% CI: 0.49, 1.12 and RR=0.75, 95% CI: 0.51, 1.10, respectively). In addition, adjustment for neighborhood-level socioeconomic status (SES) did not change the results for the “salad and wine” dietary pattern (data not shown) nor were there significant interactions between the “salad and wine” dietary pattern and physical activity (data not shown).

When not adjusted for time-dependent BMI, a “high protein/high fat” diet was associated with an increased risk of endometrial cancer among women with a baseline BMI ≥25 (RR=1.48, 95% CI: 1.02, 2.14, comparing Q5 to Q1, *P*-trend=0.02, *P*-non-linearity of the trend =0.91), but not among women with BMI <25 (RR=0.91, 95% CI: 0.62, 1.35, *P*-trend=0.48); the interaction was not statistically significant. However, after further adjusting the baseline BMI ≥25 strata for time-dependent BMI in its continuous form and its interaction with time-dependent menopausal status/HT use, the RR was attenuated (RR=1.29, 95% CI: 0.89, 1.88, *P*-trend=0.14), suggesting residual confounding by BMI.

Discussion

This is the first cohort study to examine the association between dietary patterns and the risk of endometrial cancer; however, even case-control studies evaluating this relationship are limited in number (12-14). As in a previous study (14), we observed no association between dietary patterns and endometrial cancer risk overall; nor did we observe associations by menopausal status/HT use or by abdominal adiposity. However, among women with a normal body weight, the “salad and wine” pattern (characterized by salad and low-fat dressing, fish, wine, and coffee/tea) was associated with an increase in endometrial cancer risk, a finding which is likely due to chance.

While the CUP found that the data were too limited to draw conclusions about the relationship between endometrial cancer risk and specific fruits or vegetables (10), case-control studies have found “plant” (12) and “healthy” (13) dietary patterns and total vegetable consumption (3) to be associated with reduced risk of endometrial cancer. Another study found total vegetables associated with reduced risk predominantly among women with a BMI <25 (25). Contrary to these studies, our prospective analysis found no relationship between a “plant-based” dietary pattern and endometrial cancer risk.

Meta-analyses of individual nutrients have found increased risk with greater meat, red meat, total fat, saturated fat, and animal fat consumption (2, 26), although the recent CUP determined that the evidence was too sparse to draw conclusions (10). Previous studies of dietary patterns have observed statistically non-significant elevations in endometrial cancer risk associated with a “western” diet among women who did not concurrently take vitamin supplements (14) and greater consumption of a “meat” pattern among overweight/obese women (12). Similarly, we observed greater consumption of the “high protein/high fat” dietary pattern associated with increased risk when not adequately adjusting for BMI. Once BMI was adequately taken into account, the diet-disease association was diminished, suggesting that it was the women's obesity, rather than their diet per se, that accounted for the increased risk.

We also observed an increased risk associated with a “salad and wine” dietary pattern among normal weight women; a finding which appears to be unrelated to the alcohol component of this pattern, race or SES. A similar dietary pattern has not emerged in other studies evaluating endometrial cancer risk and dietary patterns. Our “salad and wine” dietary pattern included consumption of fish and coffee/tea. While coffee has been found to reduce endometrial cancer risk (10, 27), few studies have examined the association between fish

consumption and risk. A meta-analysis of case-control studies found greater fish intake increased endometrial cancer risk (2), while a cohort study found no association (8). None of the studies examined this association stratified by body size. It is not clear why greater fish consumption or a “salad and wine” dietary pattern would increase the risk of endometrial cancer. One hypothesis is that fish may contain environmental chemicals including endocrine-disruptors (2). However, if this were the mechanism for the increased risk associated with our “salad and wine” dietary pattern, one would expect the risk to be elevated in heavier, not thinner women as we observed, since endocrine disruptors, such as polychlorinated biphenyls and other organochlorines, are stored in adipose tissue (28). Alternatively, while this association could reflect non-dietary characteristics that increase endometrial cancer risk and which are more prevalent among those women who are primary consumers of this pattern, with the exception of the interaction observed for BMI, we have not identified any such factors (see Online Resource Table 3 for participant characteristics by quintiles of the “salad and wine” dietary pattern). Thus, we consider that the observed association is likely due to chance.

A major strength of this analysis is its basis in a large diverse cohort with dietary intake assessed by a widely used and validated FFQ (17). In addition, reporting of cancer outcomes is essentially complete for cohort members who reside in California, which minimizes bias due to loss to follow-up. Also, while dietary data may suffer from poor recall or the desire to report socially normative values, due to the prospective design, these reporting errors were unlikely to result in bias in this study. We also observed the same relationships between the established risk factors for endometrial cancer in this study as recently reported in a large pooled analysis (24, 29), suggesting that the lack of association for the factors of interest here are not due to bias in our population. Furthermore, to more fully adjust for change over time in two major risk factors for endometrial cancer, BMI and HT use, HT use was updated at five years and both were updated at ten years. BMI did not change much over this time period (median difference from baseline to ten years 0.9 kg/m^2). On the other hand, consistent with the aging of the cohort, while 54% of women were premenopausal at baseline, only 13% remained premenopausal at ten years. In addition, 75% of women using HT at five years in 2000-2001 stopped using it by ten years in 2005-2006, presumably largely due to the results of the Women's Health Initiative trial (30, 31). Finally, we were largely able to rule out possible confounding by BMI, which is related to diet, although not correlated with the dietary patterns in this population (Pearson correlation coefficient $\leq |0.20|$).

A few limitations should also be noted. The dietary intake data were based on a one-year period preceding the baseline assessment. Thus, dietary change and diet during other potentially critical periods of life, such as puberty, were not available for analysis. In addition, several different methods have been proposed for defining dietary patterns, each with strengths and weaknesses (18, 32). *A priori* or hypothesis-driven methods are useful in that previous knowledge of the diet-cancer relationship can be incorporated in the definition of “healthy” and “unhealthy” diets. However, the dietary patterns are then based on current knowledge, so new relationships are not explored, and how the groupings are applied is subjective and can differ between studies. The reduced rank regression method is both

hypothesis-driven and exploratory, but requires an intermediary endpoint, such as a biomarker. We used an *a posteriori* or exploratory approach, PCFA, which is based on observed dietary behavior in our population (19), but does have some drawbacks. Dietary patterns identified with PCFA may not have distinct biological effects on the body, thus, their relationship with health or disease risk may be attenuated (18, 32). Also, the dietary patterns in this study explained only 19% of the variance in dietary intake. While this value may be typical (18, 32), it is still rather low. Also, PCFA has been criticized because it captures dietary patterns that are relatively unique to specific populations (33). However, as the literature on dietary patterns is growing, similar core patterns appear to be present in most populations. Exploring specific dietary patterns from diverse populations may help identify combinations of foods that decrease risk for specific diseases, such as has been observed for heart disease and the Mediterranean diet (34). In addition, while the interpretation for those falling into the lowest and highest quintile for a dietary pattern is likely to represent a clear distinction in the consumption of foods from that pattern, the interpretation in the middle quintiles is less clear. Finally, despite its limitations, the PCFA approach to studying dietary intake reflects the actual combinations of foods that are consumed by the population and the nutrient interactions that occur.

In conclusion, findings from our large cohort study suggest that dietary patterns are not associated with endometrial cancer risk.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Endometrial Cancer Risk by Baseline Dietary Pattern Factor Scores, California Teachers Study Cohort, 1995-2011

		Quintiles					
Dietary pattern	**Per unit increase**	**1**	**2**	**3**	**4**	**5**	***P*-trend[a]**
Plant-based	937	154	170	170	227	216	
Cases[b]	1,033, 141	208, 446	206,646	206,817	206,270	204, 962	
Person-years							
RR	0.97	1.0	0.98	0.88	1.09	0.91	0.68
(95% CI)[c]	(0.89, 1.04)		(0.78, 1.22)	(0.70, 1.10)	(0.87, 1.35)	(0.72, 1.15)	
High protein/fat	937	156	167	175	195	244	
Cases	1,033, 141	208, 408	207, 894	208, 198	205, 974	202, 666	
Person-years							
RR	0.94	1.0	1.01	1.00	1.02	1.09	0.49
(95% CI)	(0.85, 1.05)		(0.81, 1.26)	(0.80, 1.25)	(0.81, 1.28)	(0.84, 1.42)	
High carbohydrate	937	270	219	169	147	132	
Cases	1,033, 141	197, 899	205, 885	208, 490	210, 249	210, 618	
Person-years							
RR	0.90	1.0	1.00	0.89	0.92	0.94	0.54
(95% CI)	(0.80, 1.02)		(0.83, 1.20)	(0.72, 1.10)	(0.73, 1.17)	(0.69, 1.28)	
Ethnic	937	218	168	177	181	193	
Cases	1,033, 141	207, 336	206, 845	206, 814	207, 037	205, 110	
Person-years							
RR	1.02	1.0	0.86	0.95	0.99	1.00	0.64
(95% CI)	(0.95, 1.09)		(0.70, 1.05)	(0.77, 1.16)	(0.81, 1.21)	(0.81, 1.23)	
Salad and wine	937	106	169	175	219	268	
Cases	1,033, 141	209, 211	207, 694	206, 482	205, 970	203, 784	
Person-years							
RR	1.02	1.0	1.27	1.09	1.19	1.23	0.23
(95% CI)	(0.95, 1.09)		(0.99, 1.62)	(0.86, 1.40)	(0.94, 1.52)	(0.96, 1.56)	

CI, confidence interval; RR, relative risk

[a] *P*-trend across quintiles

[b] Number of cases of endometrial cancer

[c] Adjusted for race and its interaction with time-dependent age, age at menarche, gravidity and age at last pregnancy and its interaction with time-dependent age, oral contraceptive use, physical activity, smoking status, height, caloric intake, the other four dietary patterns, and the following time-dependent exposures: body mass index, menopausal status/hormone therapy use, and their interaction; age was the time metric and the model was stratified by age at baseline

Table 2

Association of Dietary Patterns with Endometrial Tumors by Type and Grade, California Teachers Study Cohort, 1995-2011

	Endometrioid Grade 1 & 2 N=446		Endometrioid Grade 3 & 4 N=70		Type II N=88	
Dietary pattern Per unit increase	**RR[a]**	**95% CI**	**RR[a]**	**95% CI**	**RR[a]**	**95% CI**
Plant-based	0.97	0.87, 1.08	0.85	0.63, 1.14	0.85	0.66, 1.09
High protein/high fat	0.90	0.77, 1.05	1.12	0.76, 1.66	0.81	0.58, 1.13
High carbohydrate	0.88	0.74, 1.05	1.39	0.90, 2.14	0.76	0.52, 1.10
Ethnic	0.99	0.90, 1.09	1.17	0.93, 1.48	1.10	0.91, 1.32
Salad and wine	1.03	0.93, 1.15	0.95	0.74, 1.23	0.92	0.74, 1.15

RR, relative risk; CI, confidence interval

[a]Adjusted for race and its interaction with time-dependent age, age at menarche, gravidity and age at last pregnancy and its interaction with time-dependent age, oral contraceptive use, physical activity, smoking status, height, caloric intake, the other four dietary patterns, and the following time-dependent exposures: body mass index, menopausal status/hormone therapy use, and their interaction; age was the time metric and the model was stratified by age at baseline

Table 3

Endometrial Cancer Risk Stratified by Baseline Body Mass Index, California Teachers Study Cohort, 1995-2011

	Per unit increase			RR[a]							
Dietary pattern	**RR[a]**	**95% CI**	***P*-int[b]**	**Q1**	**Q2**	**Q3**	**Q4**	**Q5**	**95%CI[c]**	***P*-trend[d]**	***P*-int[e]**
	BMI <25, 427 cases										
Plant-based	0.93	0.83, 1.05		1.0	0.91	0.73	1.03	0.78	0.56, 1.10	0.35	
High protein/high fat	0.86	0.73, 1.01		1.0	0.97	0.81	0.81	0.90	0.61, 1.33	0.42	
High carbohydrate	0.80	0.67, 0.97		1.0	1.04	0.87	0.80	0.82	0.51, 1.31	0.23	
Ethnic	1.00	0.91, 1.11		1.0	0.94	1.20	1.06	1.07	0.78, 1.46	0.58	
Salad and wine	1.11	1.00, 1.23		1.0	1.70	1.38	1.44	1.73	1.14, 2.61	0.05	
	BMI ≥25, 510 cases										
Plant-based	1.01	0.91, 1.12	0.97	1.0	1.04	1.01	1.14	1.03	0.75, 1.42	0.76	0.69
High protein/high fat	1.03	0.89, 1.18	0.78	1.0	1.05	1.19	1.24	1.29	0.89, 1.88	0.14	0.43
High carbohydrate	0.99	0.84, 1.16	0.80	1.0	0.93	0.88	0.97	1.00	0.67, 1.50	0.96	0.89
Ethnic	1.04	0.95, 1.14	0.37	1.0	0.82	0.79	0.97	0.98	0.75, 1.30	0.78	0.31
Salad and wine	0.95	0.87, 1.05	<0.01	1.0	1.09	0.99	1.11	0.98	0.72, 1.33	0.84	0.01

BMI, body mass index; CI, confidence interval; *P*-int, *P*-interaction; Q, quintile; RR, relative risk

[a] Adjusted for race and its interaction with time-dependent age, age at menarche, gravidity and age at last pregnancy and its interaction with time-dependent age, oral contraceptive use, physical activity, smoking status, height, caloric intake, the other four dietary patterns, and the following time-dependent exposures: BMI, menopausal status/hormone therapy use, and their interaction; age was the time metric and the model was stratified by age at baseline

[b] *P*-interaction for dietary pattern modeled per unit increase

[c] Associated with the highest quintile

[d] *P*-trend across quintiles

[e] *P*-interaction for dietary pattern modeled in quintiles