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Dietary patterns, Mediterranean diet, and endometrial cancer risk

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Abstract This study examines the association between dietary patterns and endometrial cancer risk. A case–control study of endometrial cancer was conducted from 1996 to 1999 in the San Francisco Bay Area in white, African-American, and Latina women age 35–79. Dietary patterns were defined using a principal components analysis; scoring dietary intake based on correspondence to a Mediterranean-style diet; and by jointly categorizing intake of fruits/vegetables and dietary fat. Four dietary patterns were identified and labeled "plant-based," "western," "ethnic," and "phytoestrogen-rich." None of these dietary patterns nor adherence to a Mediterranean diet (to the extent consumed by this population) was associated with endometrial cancer risk. However, among non-users of supplements, greater consumption of the "western" dietary pattern was associated with a 60% increase in risk (95% CI: 0.95–2.7 per unit change; *P*-interaction = 0.10). A diet characterized by high fat consumption increased risk, regardless of fruit and vegetable consumption (OR = 1.4, 95% CI: 0.97–2.1 for high fat, low fruit/vegetable intake and OR = 1.4, 95% CI: 0.95–2.1 for high fat, high fruit/vegetable intake compared to low fat, high fruit/vegetable intake). Thus, while like others we found that dietary fat increases endometrial cancer risk, the evaluation of dietary patterns did not provide any additional information regarding risk.

Keywords Diet · Endometrial neoplasms · Diet Mediterranean · Factor analysis · Risk · Women

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Introduction

Endometrial cancer is the fourth most common cancer in women behind breast, lung, and colon cancer [1]. Cancer of the uterine corpus (mostly endometrial cancer) has an age-adjusted annual incidence of 22.9 per 100,000 in the United States [2]. The known risk factors for endometrial cancer include obesity, early age at menarche, nulliparity, late age at menopause, use of exogenous estrogens without a progesterone component, and being of non-Hispanic white race/ethnicity [3–5].

Most studies addressing the relationship between diet and endometrial cancer risk have focused on individual nutrients, foods or specific groups of foods rather than diet as a whole. Generally, studies examining diet and endometrial cancer risk have found fruit and vegetable intake is associated with reduced risk [6–8], higher dietary fat or energy intake from animal sources is associated with higher risk [6, 8–11], and nutrients, such as fiber and antioxidant vitamins are associated with reduced risk [7, 12, 13], though results have not been entirely consistent. These analyses often have not accounted for the likely additive or synergistic effects of foods and food components in the human body or that in maintaining a consistent caloric intake, people who eat a lot of one class of food (e.g., fruits and vegetables) usually eat less of other types (e.g., red meat) [14–17]. Therefore, it is important to examine dietary patterns that account for the clustering of various foods. Principal components analysis (PCA) is an objective method of data reduction in which individual variables are grouped into components according to how strongly they are correlated; the resulting patterns (or components) are relatively independent and explain the greatest amount of variance [15, 18]. This type of analysis is useful in defining dietary patterns in specific populations and examining diet as a whole [19, 20].

The Mediterranean diet has been identified as a specific dietary pattern associated with reduced risk of cardiovascular disease, certain cancers, and overall mortality [21–24]. It has been noted that Mediterranean countries experience lower incidence of cancer of the colon, breast, endometrium, and prostate [25]. This dietary pattern is characterized by high fruit and vegetable, whole grain, olive oil, and legume intake, moderate dairy, alcohol, and fish intake, and low meat and sweets intake.

Here, we examine several dietary patterns and endometrial cancer risk in the diverse population residing in the San Francisco Bay area.

Materials and methods

Study population

This study utilized data from a population-based case–control study of endometrial cancer among white, African-American, and Latina women in the greater San Francisco-Oakland-San Jose metropolitan area. The methods have been described in detail elsewhere [12]. Briefly, women aged 35–79 were diagnosed with invasive endometrial cancer between 1996 and 1999 were identified using the Greater Bay Area Cancer Registry. This regional population-based registry is part of the California Cancer Registry and the Surveillance, Epidemiology, and End Results (SEER) programs and is estimated to have over 99% complete ascertainment. Controls were identified using random digit dialing and frequency matched to cases on the basis of age (5-year age groups) and self-identified race/ethnicity (white, African American/Black, and Latina/Hispanic). Interviews were conducted in-person in English or Spanish by trained bilingual, bicultural interviewers. Of those eligible, 647 cases and 633 controls were invited to participate and the final study population consisted of 500 interviewed cases (77% of those invited) and 470 interviewed controls (74% of those invited). The present analysis includes the 488 cases (98% of those interviewed) and 461 controls (98%) with valid dietary data (i.e., women with an average daily caloric intake between 600 and 5,000 kcal). At the time of interview, all participants signed informed consent forms approved by the Northern California Cancer Center Institutional Review Board.

Questionnaire data

Reference year is defined as the year preceding diagnosis (cases) or selection (controls). Data were collected on demographics; menstrual, reproductive, and medical histories (through the reference year); physical activity (from menarche through reference year); dietary intake and use of vitamin supplements (for year preceding the reference year); use of oral contraceptives (OC) and hormone therapy (HT) (through the reference year); and body measurements (measured at interview, and self-reported at age 25–30, age 50–55, and in the reference year). Dietary intake was assessed using a food frequency questionnaire (FFQ) adapted from Block's Health History and Habits Questionnaire [26, 28]. This questionnaire contained 103 food and beverage items, as well as summary questions regarding fruit and vegetable intake, and use of low fat food items. Information on frequency of intake and portion size was collected. In-order to improve accuracy of reporting portion sizes, visual aids including abstract models (i.e., various portions of small wood cubes), several meat models, standard size dinner plates, and different size bowls, glasses, and measuring spoons were used.

Statistical analysis

Principal components analysis

Principal components analysis using an orthogonal (varimax) rotation to maximize interpretability and minimize correlation between the factors was used to identify dietary patterns. The frequency of consumption of each of the 103 food and beverage items was adjusted for portion size prior to entering into the PCA. In addition, three vitamin use items were added: single vitamin user, multivitamin user, both single and multivitamin user. PCA was conducted combining both cases and controls. Based on an eigenvalue criterion >1, scree plot analysis, and interpretability, four factors, i.e. dietary patterns, were identified. Factors were labeled descriptively according to the dietary pattern they generally represented: "plant-based," "western," "ethnic," and "phytoestrogen-rich." Scores for each participant were calculated by SAS using the loadings for all 106 items (103 food and beverage items plus three vitamin use items) by multiplying the scoring coefficient (the simple correlation matrix multiplied by the factor loading matrix) for each item by the standardized servings per day of the item for that individual. In order to estimate risk of endometrial cancer associated with the four dietary patterns, the scores were categorized into quintiles according to the control population distribution.

For comparison, a parallel PCA analysis was conducted based on 21 a priori food groups [defined according to botanical classification for fruits and vegetables and other similarities for the other foods (e.g., beef and pork, processed meats, refined grains, etc.)], 13 singleton foods, and three vitamin supplement use patterns. PCA based on these 37 groups identified two dietary patterns consistent with the "plant-based" and "western" patterns that had been identified based on the food-specific analysis and were similarly not associated with endometrial cancer risk (data not shown).

The Mediterranean diet score

Adherence to a Mediterranean diet was measured by three ways. First, using the method established by Trichopoulou et al. [23, 29], individuals were given one point for adherence to each of nine components of the Mediterranean diet (i.e., high monounsaturated-to-saturated fat ratio, high consumption of fish, fruits, vegetables, grains, and legumes, moderate consumption of alcohol, low consumption of dairy products and meat). High versus low intake was defined as above or below the median intake in the control population for each food, with the exception of alcohol, which was given a score of one only if consumption was between 5 g and 25 g of ethanol per day. Second, using the method of Goulet et al. [30] individuals were scored on a scale of 0–4 on each of 11 components of the Mediterranean diet, for a maximum of 44 points. While Goulet was able to score olive oil intake on a scale of 0–4 based on the number of times used per day, the present study only collected information on whether participants used olive oil for cooking (categorized as no olive oil, olive oil and another type of fat, or olive oil only), thus we assigned participants scores of 0–2 on this component of the diet for a maximum of 42 points. The components used by Goulet et al. [30] differed from those used by Trichopoulou et al. [23] in that the ratio of monounsaturated-to-saturated fat and alcohol were not included in the scoring, but the consumption of olive oil, poultry, red meat, eggs, and sweets were included. The third method used was a modified version of Goulet's scoring in which quintiles of the food groups in our control population were used to determine the scoring cutpoints, but following the same pattern as Goulet's scoring method. In addition, alcohol was included in this modified scoring system. Total scores, based on each of the three methods above, were calculated by summing the points for each component. Quintiles of the scores in the control population were used to create categories for evaluating exposure-disease associations.

The joint effects of fruits/vegetables and dietary fat

The joint effects of fruits and vegetables and dietary fat were examined by creating a variable with four levels based on categorizing total fruit and vegetable as above or below median (i.e., <2 vs. ≥2 servings/d), and percent fat based on its association with endometrial cancer risk (i.e., <33% and ≥33% of calories from fat per day).

Unconditional logistic regression

Unconditional multiple logistic regression was used to determine the risk of endometrial cancer associated with each dietary pattern. Odds ratios (OR) and 95% confidence intervals (CI) were calculated for each quintile relative to the lowest quintile. The patterns were also examined using the continuous scores. Confounders included in all final models were age (in years), age^2 (due to the better fit of the model with a polynomial form of this variable), race/ethnicity (white, African American, Latina), age at menarche (in years), use of OC (years of use), parity (continuous), average daily caloric intake (in kilocalories), average weekly physical activity (in hours per week during the period from menarche through the reference year), and the 2-way and 3-way interaction terms defining the joint effects of menopausal status (premenopausal, postmenopausal, and "could not be determined"), use of hormone therapy (years of use), and body mass index (BMI; weight in kilograms/height in meters^2). Menopausal status was classified as "could not be determined" when hormone therapy use preceded the cessation of menstrual periods, and the participant had not reached age 60 prior to diagnosis or selection, i.e., was presumed to still have functioning ovaries. All four factors were included in each model when examining patterns from PCA. Tests for trend were examined over quintiles based on the median value of each quintile. A likelihood ratio test was then used to compare models with and without this ordinal variable.

Subgroup analyses

Associations between each dietary pattern and endometrial cancer risk were evaluated within subgroups defined by use of supplements (i.e., multi-vitamins or single vitamin A, C, E, or beta-carotene supplements) and included 204 cases and 205 controls who did not use supplements in the reference year and 283 cases and 255 controls who did. Of the 538 women taking supplements during the reference year, 132 were taking a multivitamin, 70 were taking at least one single antioxidant vitamin, and 336 were taking both a multivitamin and at least one other single vitamin. In addition we examined the dietary patterns by "high risk" or "low risk" subgroups based on the associations between individual variables and endometrial cancer risk. The "high risk" group included overweight women (BMI ≥ 30) and/or women who had used HT for five or more years (319 cases and 196 controls). All other women were considered low risk. The relative risk of developing endometrial cancer associated with being in the "high risk" subgroup was 2.7 (95% CI: 2.0–3.6). Statistical interaction among subgroups was formally assessed by performing a likelihood ratio test comparing models with and without cross-product terms.

Results

Table 1 presents the distribution of endometrial cancer risk factors for the study participants. Briefly, cases reported consuming fewer calories, had a higher BMI, engaged in fewer hours of physical activity, were more likely to be nulliparous and to use HT, and less likely to have used OCs. Interviewed cases were slightly older and less likely to be Latina than interviewed controls; however, substantial overlap was still observed.

Principal components analysis identified four dietary patterns that we labeled "plant-based," "western," "ethnic," and "phytoestrogen-rich." These four factors accounted for 15.4% of the variance in the 106 food and beverage items (i.e., 4.5%, 3.8%, 3.7%, and 3.4%, respectively). The diet of 28% of the participants was characterized by a single pattern (defined as having a score greater than the median for only one factor); 21% had diets that were characterized by a combination including two or three of the "plant-based", "ethnic", and "phytoestrogen-rich" diets; and 44% by a combination of the western diet and at least one of the other three patterns. The diet of 7% of the participants was not characterized by any of these patterns. The factor loadings for the foods associated with each pattern (loading ≥0.35) are shown in Table 2. The "plant-based" pattern was predominately characterized by consumption of fruits and vegetables and the "western" pattern by convenience and processed foods and sweets. The "ethnic" pattern was composed mostly of tortillas, cornbread, beans, cheese dishes such as macaroni and cheese, and traditional Latino dishes, e.g., tacos and burritos. About 76% of Latina women, 8% of white women,

Table 1 Characteristics of endometrial cases and population controls, San Francisco Bay area, 1996–1999

Characteristic	Cases (n = 488)[a]		Controls (n = 461)[a]		P-value
	Median (IQR)[b]	%	Median (IQR)[b]	%	
Age (years)	62 (54–70)		61 (52–70)		0.13
Average daily caloric intake (kcal)	1,666 (1,278–2,237)		1,743 (1,377–2,292)		0.03
Body mass index	27.0 (23.4–33.1)		26.7 (23.4–30.0)		0.03
Average physical activity (hours/week)	10.0 (5.5–18.6)		13.8 (7.2–24.3)		<0.0001
Age at menarche (years)	13 (12–13)		13 (12–14)		0.13
Parity					
Nulliparous		23.4		14.1	
Parous		76.6		85.9	<0.001
OC use					
Never		49.6		39.5	
Ever		50.4		60.5	0.002
Menopausal status					
Pre-menopausal		19.7		22.3	
Post-menopausal		74.8		73.1	
Can't determine		5.5		4.6	0.51
Hormone therapy (HT) use					
Never		45.5		52.4	
Ever		54.5		47.6	0.03
Race/Ethnicity					
White		78.3		71.6	
African-American		10.0		10.6	
Latina		11.7		17.8	0.02

[a] Sample sizes may vary slightly due to missing values

[b] IQR, Interquartile range

Table 2 Factor loadings of 0.35 and greater based on principal components analysis of average daily intake of 106 food and beverage items

Food	Factor 1 "Plant-based"	Factor 2 "Western"	Factor 3 "Ethnic"	Factor 4 "Phytoestrogen-rich"
Carrots	0.47			
Yellow squash (acorn, winter, butternut)	0.46			
Apples or applesauce	0.44			
Broccoli	0.43			0.37
Oranges, tangerines, grapefruit	0.42			
Strawberries, other berries	0.41			
Sweet potato, yams, pumpkin	0.41			
White/Green squash (zucchini)	0.39			
Pears	0.38			
Cantaloupe	0.37			
Cauliflower, Brussels sprouts	0.37			
Dark green leafy vegetables	0.37			0.39
Bananas or plantains	0.36			
Ham/cheese/turkey burgers		0.46		
French fries, hash browns		0.45		
Lunch Meat (bologna, salami, ham, etc)		0.43		
Ice cream		0.42		
Potatoes (baked, boiled, mashed, etc)		0.41		
Hot dogs		0.40		
Eggs		0.37		
Dressing or mayonnaise		0.36		
Bacon, sausage, chorizo		0.36		
Cake or cookies		0.36		
Beef or pork (steaks, roasts, etc)		0.35		
Corn tortillas, cornbread, corn muffins			0.68	
Frijoles de la olla			0.64	
Pinto or refried beans			0.55	
Jalapeno and hot peppers			0.45	
Tacos/tostadas/enchiladas/empanadas			0.42	
Flour tortilla			0.42	
Cheese dishes (macaroni, quesadillas)			0.39	
Burritos with meat or chicken			0.37	
Donuts, churros, pastries			0.36	
Alfalfa sprouts				0.62
Tofu				0.56
Miso				0.50
Bean sprouts				0.49
Soy sauce				0.44

and 26% of African American women scored in the highest quartile of this factor. The "phytoestrogen-rich" diet included tofu, sprouts, miso soup, and selected vegetables. None of these patterns was associated with overall risk of endometrial cancer (Table 3). However, the western pattern was more strongly associated with risk among women not using supplements (OR = 1.6, 95% CI: 0.95–2.7 per unit change in the factor score) than among users (OR = 0.84, 95% CI: 0.57–1.2), though the difference between these two groups did not reach statistical significance ($P_{\text{interaction}}$ = 0.10). No meaningful variation between "low risk" and "high risk" groups was observed [data not shown].

Regardless of how it was defined in this population, the Mediterranean diet pattern was not associated with endometrial cancer risk in the overall population (OR for

Table 3 Relationship between dietary patterns and endometrial cancer risk

Dietary pattern	Cases	Controls	OR[a]	95% CI[a]	P_{trend}
"Plant-based"					
Q1	85	93	1.0	–	
Q2	97	91	1.1	0.68–1.8	
Q3	103	91	1.2	0.74–1.9	
Q4	109	94	1.1	0.65–1.8	
Q5	94	92	1.2	0.72–2.0	0.51
Per unit change			0.99	0.84–1.2	
"Western"					
Q1	84	94	1.0	–	
Q2	109	90	1.2	0.72–1.8	
Q3	104	92	1.3	0.78–2.1	
Q4	94	93	1.1	0.66–2.0	
Q5	97	92	1.5	0.77–3.0	0.85
Per unit change			1.1	0.82–1.5	
"Ethnic"					
Q1	119	94	1.0	–	
Q2	116	91	1.1	0.74–1.8	
Q3	95	90	0.90	0.57–1.4	
Q4	100	93	1.1	0.68–1.8	
Q5	58	93	0.82	0.41–1.7	0.68
Per unit change			0.80	0.60–1.1	
"Phytoestrogen-rich"					
Q1	104	95	1.0	–	
Q2	121	90	1.2	0.77–1.9	
Q3	84	91	0.83	0.52–1.3	
Q4	98	92	1.0	0.63–1.6	
Q5	81	93	0.99	0.62–1.6	0.68
Per unit change			0.96	0.82–1.1	

[a] Adjusted for age, race/ethnicity, age at menarche, OC use, parity, average daily caloric intake, average weekly physical activity, and the joint effects of menopausal status, HT use, and BMI

modified scoring method = 0.92, 95% CI: 0.59–1.4 for the highest versus lowest quintile; OR = 0.99, 95% CI: 0.97–1.0 for continuous score). Results in subgroups defined by "risk," ethnicity, and supplement use were not significant.

Figure 1 presents the joint effects of dietary fat and fruit and vegetable consumption on endometrial cancer risk. Compared to women consuming a low fat, high fruit and vegetable diet, women consuming a high fat diet were at increased risk of endometrial cancer regardless of fruit and vegetable intake (OR = 1.4, 95% CI: 0.97–2.1 for low fruit/vegetable intake and OR = 1.4, 95% CI: 0.95–2.1 for high fruit/vegetable intake). Women consuming a low fat, low fruit and vegetable diet were at a slightly but not statistically significant increased risk (OR = 1.2, 95% CI: 0.77–1.8). No meaningful differences were observed between the subgroups of interest.

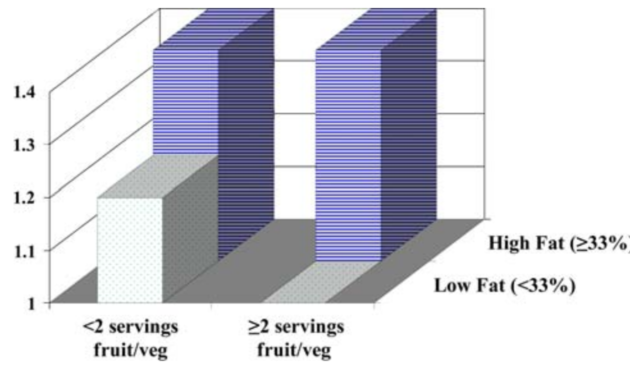

Fig. 1 Joint effects of fruit and vegetable and dietary fat consumption on endometrial cancer risk

Discussion

Out of the four dietary patterns identified using PCA, none was associated with overall endometrial cancer risk. The "western" diet was associated with a nonsignificant increased risk among women who did not use supplements, but not among supplement users. This finding suggests a possible undoing of the negative health effects of a western-style diet by the use of supplemental vitamins. However, the statistical power for detecting an interaction was low and the observed differences did not reach statistical significance. In addition to examining PCA-defined dietary patterns, we looked at the joint effects of dietary fat and fruit and vegetable intake. A high-fat diet was associated with a nonsignificant increase in risk regardless of fruit and vegetable intake, although the intake of fruits and vegetables was relatively low in this population (median intake was two servings per day). This association was not modified by supplement use. Thus, taken together, these findings suggest the possibility that supplements may be modifying a component of the western diet other than dietary fat alone. However, replication is necessary before any conclusions can be drawn.

Various hypotheses exist regarding dietary micronutrients and cancer prevention, including increasing DNA repair, decreasing DNA damage, reduction of cell proliferation, and protection from oxidative damage [31]. The literature on the relationship between antioxidants and endometrial cancer is mixed. Some studies have found risk to be reduced among women consuming greater amounts of various antioxidants from foods and supplements [7, 8], though not all studies share these findings [6, 10, 11, 32]. However, these studies have focused on single nutrients and therefore, may not have appropriately captured the complexity of diet. It is not clear in our study whether the possible modification of the "western" dietary pattern by use of antioxidant supplements is due to their biologic effect or simply reflects behaviors associated with a healthy lifestyle. However, when the patterns were examined by strata of BMI and physical activity, no subgroup differences were observed (data not shown), suggesting that if the effect is not biologic, it is an artifact of some other unmeasured lifestyle factor.

We did not observe any overall association between endometrial cancer risk and the dietary patterns designated as "plant-based," "ethnic," and "phytoestrogen-rich." This is somewhat in contrast to the findings of the smaller Western New York case–control study, which is the only other study to our knowledge that has examined dietary patterns and endometrial cancer risk [33]. This study found two dietary patterns ("healthy" and "high fat") using PCA and reported reduced risk estimates associated with a "healthy" dietary pattern and no association between a 'high fat' dietary pattern and endometrial cancer risk. Subgroup differences were not considered in the New York study. The population in the New York study is very different from our population. For instance, the age adjusted incidence rate of cancer of the corpus uteri the Greater Bay Area from 1999 to 2003 was 22.7 per 100,000 women per year whereas in the state of New York the age adjusted incidence rate was 26.1 per 100,000 women per year [34]. The Western New York study contains a much smaller percentage of women taking hormone therapy (28% of cases and 18% of controls compared to 55% of cases and 48% of controls in our population) [7]. In addition, about 15% of our population were Latina, whereas the study population in the Western New York consists only of white women [35]. Latina women in the U.S. have a lower age-adjusted incidence of endometrial cancer than do non-Hispanic white women [36]. In examining low risk groups where risk is not overwhelmed by stronger risk factors, it may be more readily possible to observe dietary effects which are generally associated only with moderate changes in risk.

While only one study has examined dietary patterns and endometrial cancer risk, there have been quite a few studies that have examined dietary patterns and risk of breast cancer, a cancer that shares many risk factors with endometrial cancer [37–43]. Like our study and the one conducted in Western New York for endometrial cancer, studies on dietary patterns and breast cancer have found differing and potentially contradictory results or results only in specific subgroups [37–43]. Nonetheless, additional low-cost studies using existing data may help to resolve these potential conflicts and provide a more unified body of evidence. When taken together with studies of individual or combinations of specific food components and taking into account population differences and risk in various subgroups, studies of dietary patterns may add to the understanding of cancer risk [15]. In the meantime, they may be useful for making public health recommendations within the specific populations under study.

The Mediterranean diet did not impact endometrial cancer risk in this study. Several authors have hypothesized a lower risk of breast and endometrial cancer associated with this dietary pattern [25, 44, 45]. To our knowledge, this is the first study to examine adherence to a Mediterranean diet and endometrial cancer risk. However, the level at which a Mediterranean-style diet is consumed by our population is low. Compared to control women in our population, Greek women consumed substantially more fruit (median: 356 g/d compared to 171 g/d), vegetables (500 g/d compared to106 g/d), and dairy products (191 g/d compared to 70 g/d), and had a somewhat higher monounsaturated to saturated fat ratio (mean: 1.8 compared to 1.1) [23]. Therefore, women in our study may simply not be consuming enough of a Mediterranean-type diet to see effects.

In our study, grouping foods into 37 a priori groups produced only two dietary patterns, neither of which was associated with endometrial cancer risk, even when subgroups were examined (data not shown). Similarly, in the western New York study [33], patterns based on either 58 or 38 a priori groups diminished the magnitude of effect and produced wider confidence intervals compared to the patterns identified based on 168 individual food items. These authors have concluded that greater specificity is optimal when entering individual food items into PCA [33]. Our findings support this approach, given the identification of an additional two patterns (subsets of the overall plant-based pattern) and a greater percent of variance explained (15.4% vs. 9.2%) when individual foods were used as the basis for the PCA compared to a priori groups.

Several limitations of the present study should be kept in mind when interpreting the findings. First, the four major patterns obtained from the principal components analysis explain a little more than 15% of the variance. While this is comparable to what other diet studies have found [33, 42, 46–48], it depicts the difficulty of reducing a large and complex set of variables such as diet. However, since dietary intake is complex and a wide variety of foods are needed for basic nutrition, more consideration should be placed on the interpretability of the dietary patterns identified rather than a quantitative measure of the amount of explained variance by these factors [7]. Indeed, in the present study only 7% of women did not consume one of these four dietary patterns (i.e., scored below the median value on all four dietary patterns). Second, a limitation in many epidemiologic studies, particularly those of diet, is measurement error. While many nutrients are captured equally well with a FFQ as with other dietary measures (e.g., dietary records) [49], only one study has attempted to validate dietary patterns measured by a FFQ compared with patterns characterized from dietary records. Hu et al. compared PCA-defined "prudent" and "western" dietary patterns based on an FFQ assessment to these patterns estimated from two 1-week diet records among 127 men [50]. Validity coefficients between two FFQ assessments and diet records ranged from 0.45 to 0.74 for the two patterns; the reproducibility coefficients were 0.70 for the "prudent" pattern and 0.67 for the "western" pattern. These correlations are of a similar magnitude to what is seen for various macro- and micronutrients in various validation studies [25, 51–54], suggesting that the methods used in the present study are appropriate for identifying patterns of dietary consumption. A third concern in case–control studies is recall bias. Cases may recall or report diet differently than controls, particularly, since diet and cancer have been linked in the media for many years. However, studies have shown that current diet influences recall of previous diet, but that recalled diet is a better measure of previous diet than is current diet; the shorter the interval between consumption and recall, the better the recall; reports of previous intake are more accurate when food-frequency instruments are administered by trained interviewers than when self-administered; recall is better when complete diet is measured than when only a few items are asked about; and adjusting nutrient intake for portion size results in better estimates of nutrient intake [55–58]. These considerations were incorporated into the design of the present study. A final common limitation when conducting subgroup analyses is insufficient power, thus stratified results must be interpreted with caution. Basing interpretation on the amount of overlap in the confidence intervals between the subgroups of interest and conducting formal tests of statistical interaction help avoid over-interpretation.

In examining complex diseases, a comprehensive approach to diet, such as examining dietary patterns, may be informative, particularly in terms of public health messages. To our knowledge, this is the first study to examine the association between the Mediterranean diet pattern and endometrial cancer risk. Replication of the current study in large, low risk populations is warranted. In addition to various factor analysis methods used to identify dietary patterns, other techniques such as those being developed for microarray and other multidimensional data, may be useful in treating the complex nature of dietary data in future analyses.

In summary, the current study did not find any association between dietary patterns defined using PCA and endometrial cancer risk in the overall population. There was some evidence of an interaction between supplement use and the "Western" pattern, however, results did not reach statistical significance and replication is clearly necessary before appropriate conclusions can be drawn. The Mediterranean diet was not associated with endometrial cancer risk at the level consumed in our population. A diet high in fat was associated with a non-significant increase in endometrial cancer risk, regardless of fruit and vegetable intake. This study adds to the limited data available regarding dietary patterns and endometrial cancer risk.

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