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Dietary patterns and risk of pancreatic cancer in a large population-based case-control study in the San Francisco Bay Area

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Abstract

Pancreatic cancer is highly lethal, and identifying modifiable risk factors could have substantial public health impact. In this population-based case-control study (532 cases, 1701 controls), we used principal component analysis and multivariable unconditional logistic regression models to examine whether a particular dietary pattern was associated with risk of pancreatic cancer, adjusting for other known risk factors. A Prudent dietary pattern, characterized by greater intake of vegetables, fruit, fish, poultry, whole grains, and low-fat dairy, was associated with an approximate 50% reduction in pancreatic cancer risk among men (OR=0.51, 95% CI 0.31-0.84, p-trend=0.001) and women (OR=0.51, 95% CI 0.29-0.90, p-trend=0.04). A Western dietary pattern, characterized by higher intake of red and processed meats, potato chips, sugary beverages, sweets, high fat dairy, eggs, and refined grains, was associated with a 2.4-fold increased risk of pancreatic cancer among men (95% CI 1.3-4.2, p-trend=0.008); but was not associated with risk among women. Among men, those in the upper quintiles of the Western diet and lower quintiles of the Prudent diet had a 3-fold increased risk. Consistent with what has been recommended for several other chronic diseases, consuming a diet rich in plant-based foods, whole grains, and white meat, might reduce risk of pancreatic cancer.

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All authors contributed to the analysis of data and writing of the manuscript, and approved the final manuscript; E.A. Holly and P.M. Bracci also designed the study, and collected the data.

INTRODUCTION

Pancreatic cancer is a highly lethal cancer with more than 37,000 individuals estimated to die from the disease in the USA in 2012.¹ Non-modifiable risk factors such as older age, African American race, family history of pancreatic cancer, and male sex are associated with an elevated risk of pancreatic cancer; whereas a history of allergies has been linked to a decreased risk.² The last decade has ushered in increasing research on potential modifiable risk factors for the disease. Body size, smoking, diabetes, higher insulin levels (or other indices of perturbations in glucose metabolism), heavy alcohol intake, and greater consumption of meat (especially red or processed meat) and fats may also increase risk.²⁻⁶ The literature on the potential benefits of fruits, vegetables, and other plant foods is mixed.⁴

Accumulating data support the study of dietary patterns to help clarify whether and how diet influences disease risk. Dietary pattern analyses allow one to consider several foods and beverages simultaneously, and provide comment on the overall impact of type of diet, rather than the individual effects of single nutrients, foods, or food groups. Assessment of dietary patterns may better estimate the role of diet in disease than evaluation of specific foods or nutrients for several reasons, including: a) the complexity of diets; b) a tendency for dietary patterns to be defined by food preferences and thus less influenced by bias and error that can occur when assessing intake of specific individual foods; c) high co-linearity among foods and nutrients making comprehensive analyses of individual foods frequently impractical and; d) the pattern of consumption is likely to influence absorption and bioavailability of nutrients and other compounds in specific foods.^{7,8} Thus, to expand on our earlier analyses that focused on individual food groups and nutrients and risk of pancreatic cancer,⁹⁻¹³ we examined whether a particular dietary pattern was associated with pancreatic cancer risk in a large population-based case-control study.

SUBJECTS AND METHODS

Study population

Details of the study methods and population characteristics have been described previously.⁹⁻¹⁸ In brief, cases with incident adenocarcinoma of exocrine pancreas who were diagnosed from 1995 to 1999 were identified using rapid case ascertainment conducted by the Northern California Cancer Center. Eligible cases were 21–85 years old, residents of one of six San Francisco Bay Area counties at diagnosis/interview, alive and able to complete an in-person interview in English. Pancreatic cancer diagnoses were confirmed by the patients' physicians and by using abstracts from the Surveillance, Epidemiology and End Results (SEER). Among the 798 eligible cases (717 Bay Area, 81 UCSF out-of-area), 223 refused or were too ill to participate, 23 had moved or could not be located, 20 had physician indicated contraindications to contact and 532 completed the interview for a cooperation rate¹⁹ of 67%. Control participants were frequency-matched to cases by sex, five-year age group and county. Bay Area and out-of area controls were selected using a random-digit-dial (RDD) method that used case participant telephone area-code and 3-digit prefix to randomly generate unscreened telephone numbers that were dialed to identify eligible controls from the target population. In calls to phone numbers that we could establish as residential homes, 2,511 Bay Area and 655 out-of-area homes did not have an eligible control resident, 498

Bay Area and 24 out-of-area eligible controls refused or were too sick to participate, 1,001 Bay Area and 65 out-of-area eligible controls completed interviews for a cooperation rate of 67% among Bay Area RDD controls and of 73% among out-of area RDD controls. Identification of controls greater than 65 years old was supplemented by random sampling of the Health Care Finance Administration (now Center for Medicare and Medicaid Services) lists where 430 eligible controls refused or were too sick to participate, 146 had moved or could not be located and 635 completed interviews for a cooperation rate of 52%. A total of 1,701 controls completed the interview.

Data collection

Detailed data including age, race, education, diabetes status, history of smoking, alcohol consumption, physical activity and anthropometric measures were collected by trained interviewers during in-person interviews. No proxy interviews were conducted. The study was reviewed and approved by the University of California San Francisco Committee on Human Research. Signed informed consent was obtained from each participant prior to interview.

Dietary history was assessed using a 131-item semi-quantitative food-frequency questionnaire (FFQ) developed at Harvard University that has been validated in several populations,²⁰⁻²² and performs similarly to the National Cancer Institute Diet History Questionnaire and the Block food-frequency questionnaire.²² Participants were asked to report their average frequency of consumption of specific foods during the one year before their diagnosis with pancreatic cancer (cases) or interview (controls). Servings per day were computed by multiplying portion size by frequency of consumption of each food and beverage item, and standardized to daily consumption.

Statistical analysis

Principle components factor analysis (PCA), a data reduction method that uses the variable correlation matrix to identify the set of factors or variables that best explain the variation in the data, was used to identify dietary patterns separately for men and women. Food variables were based on the 35 food groups from the FFQ that were predetermined based on the similarity of their nutrient profiles (Table 1). Some individual foods were not combined because of their unique nutrient profile (e.g., eggs, tea and wine). Each food variable was entered into the factor analysis (PROC FACTOR procedure in SAS) and the factors were rotated by an orthogonal transformation that facilitates interpretability by ensuring that the factors are uncorrelated. Criteria used to determine the optimal number of factors included scree plots, eigenvalues (>1.5), and factor interpretability. Factor scores were computed for each study participant by summing the intake of each food group multiplied by its factor loading value where factor loadings were the correlations between the individual food groups and the dietary pattern. The higher the factor loading value the stronger the correlation was between the specific food group and the dietary pattern i.e. the more relevant the food group was to the specific dietary pattern. Two main factors from principal components factor analysis were retained, and we labeled these as Prudent and Western dietary patterns (Table 1).

Unconditional logistic regression models were used to estimate the odds ratios (OR) and 95% confidence intervals (CI) for the association between the dietary pattern factor and pancreatic cancer. In the analysis, dietary pattern factor scores were categorized into quintiles with the lowest quintile as the reference category. The models were fitted for men and women separately and all models were adjusted for age (5-year groups) and total energy intake (in quartiles). Full multivariable models also were fit to adjust for confounders and other known risk factors including race (white, black/African American, Asian/Pacific Islanders, or “other”), education level (less than high school, high school, 1-4 years college, and graduate school), usual adult body mass index (BMI: <25 (normal), 25-30 (overweight), and ≥ 30 kg/m² (obese)), smoking status (never smoker, former cigarette smoker who had quit >15 years previously, former cigarette smoker who had quit 1-15 years previously, current cigarette smoker or former smoker who had quit <1 year previously, and pipe and/or cigar smoker), history of diabetes, frequency of leisure time physical activity (30-minutes: <1/month, 1-4/month, 2-3/week, and ≥ 4 /week), and alcohol consumption (never drinkers, 1-7, 8-14, 15-21, and >21 drinks/week).

We considered an overall dietary pattern score variable that was the sum of two ordinal variables that reflected the quintile assignment for each of the two dietary patterns, i.e. participants were assigned a Prudent ordinal value of -1, -2, -3, -4, or -5, if in quintile 1, 2, 3, 4, or 5 of the Prudent diet respectively; and were assigned a Western ordinal value of 1, 2, 3, 4, or 5 if in quintile 1, 2, 3, 4, or 5 of the Western diet. Thus, a person who might be in the 5th quintile of the Western diet and 3rd quintile of the Prudent diet would have an overall dietary pattern score variable of 2 (=5 minus 3). The overall dietary pattern score variable was examined in the following five groups: -3, -2 or -1, 0, 1 or 2, and ≥ 3 .

Stratified analyses were performed to assess whether BMI (<25 or ≥ 25 kg/m²) and smoking status (never or ever smoking) modified the association between pancreatic cancer risk and diet pattern. Linear trends in odds ratios were based on the chi-square statistic for the factor of interest when included as an ordinal variable in multivariable unconditional logistic regression models.

All statistical tests were two-sided and were considered statistically significant for $p < 0.05$. Statistical analyses were conducted using SAS software V9.2 (SAS Institute, Inc., Cary, NC).

RESULTS

The rotated factor loadings for the individual food groups and the Western and Prudent dietary patterns are shown in Table 1. The Prudent diet pattern was characterized by greater intake of vegetables, fruit, fish, poultry, whole grains, and low-fat dairy. The Western diet pattern reflected higher intake of red and processed meats, potato chips, sugary beverages, sweets, high fat dairy, eggs, and refined grains. There were 6 food items among women that contributed (albeit with different weighting) to both dietary patterns, while this occurred less frequently among the men (2 items). The association between individual social and demographic characteristics of the study population and each dietary pattern is presented in Table 2. Obesity, current smoking, drinking 15+ alcoholic drinks per week, having less

education, and exercising less were associated with being in the highest quintile of Western diet. Having more education and higher physical activity levels tracked with being in the highest quintile of the Prudent diet.

Among both men and women, the Prudent dietary pattern was associated with an approximate 50% reduction in pancreatic cancer risk with statistically significant trends in multivariable-adjusted analyses. There was a two-fold elevated risk of pancreatic cancer associated with being in the highest quintile of the Western diet among men (OR_{Q5 vs Q1}=2.4, 95% CI 1.3-4.2) after adjusting for age, race, education, diabetes, BMI, smoking, alcohol drinking, physical activity, and total energy; and no clear association between the Western dietary pattern and pancreatic cancer risk among women (Table 3).

When we examined the overall dietary pattern score that simultaneously considered an individual's classification for both the Western and the Prudent dietary patterns (described in the Methods above), the results were similar to those in Table 3. For example, among men, the multivariable-adjusted OR for having an overall dietary pattern score of 3+ vs. -3 (i.e. higher the score indicates a more "Western" the diet; lower score indicates a more "Prudent" diet) was associated with an OR of 3.0 (95% CI 1.6-5.5; p-trend=0.002). Among women for the same comparison, the OR was 1.4 (95% CI 0.73-2.6; p-trend=0.26) (data not shown in tables).

In analyses stratified by BMI, overweight men had a higher OR associated with the Western dietary pattern than normal weight men (overweight OR_{Q5 vs Q1}=3.8, 95% CI 1.6-8.8; normal BMI OR_{Q5 vs Q1}=1.8, 95% CI 0.71-4.3), although the interaction was not statistically significant (p-interaction=0.71). There was no statistically significant interaction between BMI and the Western dietary pattern among women, nor for BMI and the Prudent dietary pattern among men or women. Among men, there also was no evidence of interaction between smoking habits and either dietary pattern. However, among women, there was some suggestion that ever-smoking women with a 'stronger' Western dietary pattern had an increased risk of pancreatic cancer (OR_{Q5 vs Q1}=2.3, 95% CI 1.0-5.2; p-trend=0.11), whereas among never-smoking women a 'stronger' Western dietary pattern was inversely associated with pancreatic cancer risk (OR_{Q5 vs Q1}=0.38, 95% CI 0.16-0.90, p-trend=0.05; p-interaction= 0.07).

DISCUSSION

In this large population-based case-control study of pancreatic cancer, eating a more Prudent diet was associated with an approximate 50% relative risk reduction of pancreatic cancer, among both men and women. The Western dietary pattern was positively associated with an approximately doubling in risk of pancreatic cancer among men, but not consistently associated with pancreatic cancer risk among women. There were no statistically significant interactions between dietary patterns, BMI or smoking habits among men or women, although there was also limited power in these stratified analyses. Among women, there were several individual food items that were associated with and contributed to the factor loading for *both* food patterns, whereas among the men this occurred less frequently (Table 1). For example, among women, fish/seafood, poultry, and low-fat dairy contributed both to

the Prudent and Western dietary patterns. This suggests that the Western and Prudent patterns were less contrasting among the women, and may partially explain the less consistent associations observed in the women.

Few studies have reported specifically on dietary patterns and pancreatic cancer risk.²³⁻²⁶ Consistent with our results, a nearly 50% reduction in risk was reported for a dietary pattern characterized by high intake of fresh fruits and cruciferous vegetables in a large Canadian population-based case-control study.²⁴ Also, consistent with our results for women (but not men), the Canadian case-control study observed no association for a Western dietary pattern and pancreatic cancer risk.²⁴ The different associations we observed by sex for the Western dietary pattern and pancreatic cancer warrants further examination.

Reports from cohort studies have also been limited and mixed. Contrary to our results, a large pooled analysis of two cohorts of men and women observed no association between dietary patterns (prudent or western) and the risk of pancreatic cancer.²³ In the Multiethnic Cohort Study, a flavonol food pattern (characterized by intake of the plant-based flavonoids quercetin, kaempferol, and myricetin) was associated with lower pancreatic cancer risk in US smokers²⁵. However, this finding was not replicated in a European cohort, the European Prospective Investigation into Cancer and Nutrition (EPIC).²⁵ Results from the large prospective National Institutes of Health-AARP (NIH-AARP) Diet and Health Study reported that a healthy lifestyle score (characterized by a pre-defined Mediterranean dietary pattern, normal body size (BMI 18-<25), regular physical activity, limited alcohol consumption (1 drink per day for women or 2 drinks for men), and being a never smoker or former smoker who quit 10+ yrs ago) was associated with a greater than 55% reduction in the risk of pancreatic cancer, providing provocative evidence that overall diet along with lifestyle factors may impact pancreatic cancer risk.²⁶ The Mediterranean diet pattern in the NIH-AARP study was similar in quality to the Prudent dietary pattern identified in our results reported here. The Mediterranean diet defined in the NIH-AARP study was based on *a priori* groups rather than from formal statistical quantization using PCA or factor analysis methods as was done in our analyses. The Iowa Women's Health Study reported no association between nutrients, food groups, or dietary patterns among 34,642 women (including 256 cases of pancreatic cancer).²⁷ In the current study, we used PCA to derive the Prudent and Western dietary patterns, and these reflected the actual overall consumption patterns in the study population rather than an optimal or recommended diet, or adherence to *a priori* dietary recommendations. Thus, this may partially explain differences between our results and those of other studies that used dietary score or index approaches to dietary patterns analysis.²⁸ Overall, there are limited and inconsistent data on the topic of dietary patterns and pancreatic cancer, with two cohorts^{25,26} and one case-control study²⁴ reporting a potential benefit of more prudent dietary patterns, and 4 cohort studies^{23,25,27} indicating no association. Thus, our results should be interpreted cautiously and further research may be warranted to clarify this apparent inconsistency.

Our results are consistent with earlier case-control studies that examined individual food groups and risk of pancreatic cancer. We and others previously reported inverse associations between pancreatic cancer risk and greater intake of fruits and vegetables^{9,24,29-39}, whole grains^{10,40}, fiber^{10,30,35,36,41-43}, folate³⁰, antioxidants (e.g. carotenoids, vitamin E, vitamin

C) 12,30,31,35,44-47; and positive associations for increased intake of meat (especially red or processed meat) 11,33,36,37,39,48-51 or dietary fat 11,36,43,52-54. Several cohort studies have reported inverse associations for some aspects of fruit and vegetable intake (e.g. food groups or phytochemicals) 55-61; whereas others have reported no effect with pancreatic cancer 62-70. Similar to case-control studies, cohort studies generally have reported positive associations between greater meat and fat intake and pancreatic cancer risk 64,66,71-75.

Our study also had limitations that should be considered when interpreting the results. Pancreatic cancer is a highly lethal yet relatively rare cancer, and thus it is reasonable to consider results from large well-conducted case-control studies, in addition to cohort data. However, case-control studies may lead to a potential over-estimation of effects due to recall bias, or potential differential reporting of past diet by cases versus controls, and our results should be interpreted cautiously. In this large population-based study we used rapid case ascertainment methods, conducted in-person interviews (no proxy interviews), and used a validated semi-quantitative food-frequency questionnaire, all of which would help to diminish the effects of selection, recall and misclassification bias. We also asked about dietary patterns one year before the cancer diagnosis, or interview for controls, thereby avoiding recent assessment of dietary changes due to pancreatic cancer. Few patients refused to participate (8%), and the primary reason that patients were not interviewed was directly due to the aggressive process of pancreatic cancer and the subsequent high mortality rate. Although effects of recall and survival bias cannot be eliminated, results were similar when analyses were restricted to respondents who indicated that their diet one year prior to diagnosis/interview was the same or similar to their diet 10 years ago. Our data were based on interviews using a validated food-frequency questionnaire that may not be as accurate in capturing usual diet compared to multiple seasonal diet records. However, given the patient population and case-control study design, the latter would have been infeasible.

Our results provide evidence that a Prudent dietary pattern characterized by greater consumption of vegetables, fruit, fish, poultry, whole grains, and low-fat dairy may reduce risk of pancreatic cancer. In contrast, a Western diet comprised heavily of red meat, processed meat, sweets, high-fat dairy, and refined grains may elevate risk, in particular among men. In conclusion, following a diet rich in plant-based foods, whole grains, and white meat may reduce risk of pancreatic cancer.

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Table 1

Rotated factor loadings for the two dietary patterns for men and women in a population-based case-control study, San Francisco Bay Area, California

Food or food group	Dietary pattern			
	Prudent diet		Western diet	
	Men	Women	Men	Women
Vegetables [†]	0.67	0.68	-	-
Yellow vegetables	0.63	0.63	-	-
Cruciferous vegetables	0.57	0.66	-	-
Legumes and products	0.59	0.59	-	-
Green leafy vegetables	0.55	0.59	-	-
Tomatoes	0.60	0.53	-	-
Fruit	0.47	0.57	-	-
Garlic and onions	0.56	0.45	-	0.18
Fish and other seafood	0.43	0.41	-	0.21
Poultry	0.37	0.38	-	0.16
Whole grains	0.26	0.31	-	
Tea	0.20	0.18	-	-
Fruit juice	0.24	0.23	-	-
Low-fat dairy product	-	0.17	-	0.24
Wine	0.15	-	-	-
Processed red meat	-	-	0.67	0.58
Non-processed red meat	-	-	0.59	0.56
Fried potatoes and chips	-	-	0.57	0.60
High-fat dairy products	-	-	0.56	0.47
Eggs	-	0.15	0.45	0.28
Butter	-	-	0.42	0.33
Sweetened grains, dessert	-	-	0.41	0.30
Sweets	-	-	0.39	0.25
Sugar-added beverages	-	-	0.38	0.42
Refined grains	0.17	0.16	0.37	0.50
Pizza	-	-	0.31	0.36
Organ meats	-	-	0.26	0.31
Potatoes	0.17	0.26	0.25	0.15
Nuts	-	0.22	0.22	-
Coffee	-	-	0.21	-
Beer	-	-	0.20	0.18
Margarine	-	-	-	-
Cold breakfast cereals	-	-	-0.16	-

Food or food group	Dietary pattern			
	Prudent diet		Western diet	
	Men	Women	Men	Women
Sugar-free beverages	-	-	-	-
Liquor	-	-	-	-

* For simplicity, factor loadings <0.15 in absolute value are not shown and are indicated by a dash.

† Vegetables other than yellow, green leafy, or cruciferous vegetables.

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Table 2 Demographic, health, and lifestyle characteristics of cases and controls related to dietary pattern factor scores in quintiles (Q1, Q5) among controls in a population-based case-control study for pancreatic cancer, San Francisco Bay Area, California

Characteristics	Cases (n=532) n (%)	Controls (n=1701) n (%)	Factor 1 (Prudent diet)*		Factor 2 (Western diet)*	
			Q1 n (%)	Q5 n (%)	Q1 n (%)	Q5 n (%)
Age (yrs)						
<50	46 (9)	164 (10)	35 (11)	28 (8)	19 (5)	42 (14)
50-59	120 (23)	438 (26)	78 (24)	94 (26)	96 (26)	84 (28)
60-69	172 (32)	473 (28)	83 (26)	103 (29)	105 (29)	74 (25)
70-79	158 (30)	498 (29)	101 (31)	106 (30)	119 (33)	81 (27)
80	36 (7)	128 (8)	24 (8)	25 (7)	27 (7)	17 (6)
Sex						
Male	291 (55)	883 (52)	169 (53)	181 (51)	198 (54)	141 (47)
Female	241 (45)	818 (48)	152 (47)	175 (49)	168 (46)	157 (53)
Race						
White	442 (83)	1471 (86)	279 (87)	300 (84)	331 (90)	247 (83)
Black/African American	46 (9)	78 (5)	13 (4)	17 (5)	12 (3)	20 (7)
Asian or Pacific Islander	35 (7)	119 (7)	19 (6)	34 (10)	20 (6)	20 (7)
Others	9 (2)	33 (2)	10 (3)	5 (1)	3 (1)	11 (4)
Education						
< High-school graduate	71 (13)	162 (10)	46 (14)	27 (8)	24 (7)	52 (17)
High-school graduate	164 (31)	372 (22)	87 (27)	70 (20)	59 (16)	82 (28)
1-4 years college	200 (38)	754 (44)	142 (44)	166 (47)	163 (44)	127 (43)
Graduate school	97 (18)	413 (24)	46 (14)	93 (26)	120 (33)	37 (12)
History of diabetes						
Yes	76 (14)	161 (10)	31 (10)	32 (9)	35 (10)	30 (10)
Body mass index (kg/m ²)						
<25	281 (53)	999 (59)	179 (56)	204 (57)	223 (61)	163 (55)

Characteristics	Cases (n=532) n (%)	Controls (n=1701) n (%)	Factor 1 (Prudent diet)*		Factor 2 (Western diet)*	
			Q1 n (%)	Q5 n (%)	Q1 n (%)	Q5 n (%)
25-30	197 (37)	553 (33)	109 (34)	119 (33)	114 (31)	94 (31)
30	54 (10)	149 (9)	33 (10)	33 (9)	29 (8)	41 (14)
Smoking						
Never-smoker	163 (31)	652 (38)	126 (39)	142 (40)	147 (40)	115 (39)
Former smoker, quit >15 yrs	133 (25)	508 (30)	75 (23)	114 (32)	124 (34)	57 (19)
Former smoker, quit 1-15 yrs	89 (17)	260 (15)	49 (15)	53 (15)	61 (17)	48 (16)
Current smoker & quit <1 yr	131 (25)	208 (12)	56 (18)	31 (9)	18 (5)	67 (22)
Pipe/cigar smoker	16 (3)	73 (4)	15 (5)	16 (4)	16 (4)	11 (4)
Alcohol consumption						
Never	85 (16)	305 (18)	80 (25)	64 (18)	70 (19)	64 (22)
7 drinks/week	231 (43)	804 (47)	152 (47)	155 (43)	188 (51)	122 (41)
8-14 drinks/week	83 (16)	293 (17)	49 (15)	65 (18)	59 (16)	39 (13)
15-21 drinks/week	39 (7)	138 (8)	20 (6)	29 (8)	31 (8)	21 (7)
>21 drinks/wk	91 (17)	161 (9)	20 (6)	43 (12)	18 (5)	52 (17)
Physical activity (30 min.)						
1/month	194 (37)	552 (32)	147 (46)	81 (23)	90 (24)	132 (44)
2-4/month	127 (24)	400 (24)	61 (19)	75 (21)	83 (23)	68 (23)
2-3/week	105 (20)	372 (22)	57 (18)	91 (25)	92 (25)	52 (18)
4/week	99 (19)	377 (22)	56 (17)	109 (31)	101 (28)	46 (5)

* Distribution of demographic, health and lifestyle factors by dietary pattern factor scores for Q1 and Q5 among controls

Table 3

Odds ratios (OR) and 95% confidence intervals (CI) for pancreatic cancer by quintile of Prudent and Western Diet, in a population-based case-control study, San Francisco Bay Area, California

Dietary pattern factor	OR (95% CI), Quintiles (Q)					P for trend
	Q1	Q2	Q3	Q4	Q5	
Men						
Prudent Diet						
Number of cases/controls	64/169	59/175	64/169	48/187	52/181	
Age and total energy-adjusted	1.00	0.84 (0.55-1.3)	0.78 (0.50-1.2)	0.49 (0.31-0.78)	0.45 (0.31-0.78)	<0.0001
Multivariable-adjusted*	1.00	0.92 (0.59-1.4)	0.84 (0.53-1.3)	0.53 (0.33-0.85)	0.51 (0.31-0.84)	0.0001
Western Diet						
Number of cases/controls	35/198	51/183	43/190	65/169	93/141	
Age and total energy-adjusted	1.00	1.6 (1.0-2.7)	1.3 (0.75-2.1)	2.1 (1.2-3.4)	3.0 (1.8-5.2)	0.0001
Multivariable-adjusted*	1.00	1.6 (1.0-2.7)	1.2 (0.69-2.0)	1.8 (1.1-3.1)	2.4 (1.3-4.2)	0.008
Women						
Prudent Diet						
Number of cases/controls	58/152	49/163	45/165	49/162	35/175	
Age and total energy-adjusted	1.00	0.78 (0.50-1.2)	0.66 (0.41-1.1)	0.69 (0.43-1.1)	0.42 (0.25-0.71)	0.002
Multivariable-adjusted*	1.00	0.85 (0.53-1.4)	0.75 (0.46-1.2)	0.84 (0.51-1.4)	0.51 (0.29-0.90)	0.04
Western Diet						
Number of cases/controls	42/168	51/161	35/175	55/156	53/157	
Age and total energy-adjusted	1.00	1.3 (0.82-2.1)	0.83 (0.50-1.4)	1.5 (0.93-2.4)	1.4 (0.80-2.3)	0.22
Multivariable-adjusted*	1.00	1.2 (0.75-2.0)	0.68 (0.40-1.2)	1.2 (0.70-1.9)	0.90 (0.50-1.6)	0.70

* Multivariable model adjusted for age, race, education, diabetes, BMI, smoking, alcohol drinking, physical activity, and total energy