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ARTICLE

The Healthy Eating Index 2005 and Risk for Pancreatic Cancer in the NIH–AARP Study

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Background Dietary pattern analyses characterizing combinations of food intakes offer conceptual and statistical advantages over food- and nutrient-based analyses of disease risk. However, few studies have examined dietary patterns and pancreatic cancer risk and none focused on the 2005 Dietary Guidelines for Americans. We used the Healthy Eating Index 2005 (HEI-2005) to estimate the association between meeting those dietary guidelines and pancreatic cancer risk.

Methods We calculated the HEI-2005 score for 537 218 men and women in the National Institutes of Health–American Association of Retired Persons Diet and Health Study using responses to food frequency questionnaires returned in 1995 and 1996. We used Cox proportional hazards regression to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for risk of pancreatic cancer according to HEI-2005 quintiles and explored effect modification by known risk factors. $P_{interaction}$ values were calculated using the Wald test. All statistical tests were two-sided.

Results We identified 2383 incident, exocrine pancreatic cancer cases (median = 10.5 years follow-up). Comparing participants who met the most dietary guidelines (Q5) with those who met the fewest guidelines (Q1), we observed a reduced risk of pancreatic cancer (HR = 0.85, 95% CI = 0.74 to 0.97). Among men there was an interaction by body mass index ($P_{interaction}$ = .03), with a hazard ratio of 0.72 (95% CI = 0.59 to 0.88) comparing Q5 vs Q1 in overweight/obese men (body mass index ≥25 kg/m^2) but no association among normal weight men.

Conclusions Our findings support the hypothesis that consuming a high-quality diet, as scored by the HEI-2005, may reduce the risk of pancreatic cancer.

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Pancreatic cancer is one of the most rapidly fatal cancers and is the fourth leading cause of cancer death in the United States (1,2). Although most food- and nutrient-based analyses have shown weak or no associations with pancreatic cancer (3,4), dietary pattern analysis may better predict disease risk than individual food or nutrient intakes for several reasons. First, high correlation between nutrients may be difficult to unravel statistically (5). Second, there may be biologic interaction or synergy between different nutrients and/or dietary constituents/components that is not captured when assessing single foods or nutrients (6). Third, diet-related associations with disease may be easier to detect when comparing overall diets of poor or high quality rather than intake of an isolated food or nutrient (6,7).

The few studies on dietary patterns and pancreatic cancer risk have shown inconsistent results (8–13) and used different statistical methods that reflect distinct research questions. All but one of the previous studies examined data-driven, study-specific dietary patterns, preventing comparison between studies. A priori patterns, on the other hand, may be compared between studies because they are characterized based on disease-specific biologic rationale or public health guidance. One such a priori pattern is the Dietary Guidelines for Americans 2005 (14), which can be measured using the Healthy Eating Index 2005 (HEI-2005). These guidelines were the basis of federal nutrition policy and nutrition education activities from 2005 to 2010. Thus, associations between this dietary pattern and disease risk have nationally relevant public health implications.

To our knowledge, no previous studies have assessed the HEI-2005 and pancreatic cancer risk. Also, most previous dietary pattern and pancreatic cancer studies lack sufficient case subjects to fully explore effect modification. Given these identified gaps in the literature, we tested the association between the HEI-2005 score and pancreatic cancer risk in the large, prospective National Institutes of Health (NIH)–AARP (formerly known as the American Association of Retired Persons) Diet and Health Study cohort.

Methods

Study Population

The NIH–AARP Diet and Health Study has been described previously (15). Men and women aged 50 to 71 years who were AARP

members were recruited by mailed questionnaire returned in the period from 1995 to 1996. All participants were residents in one of six US states (California, Florida, Louisiana, New Jersey, North Carolina, or Pennsylvania) or two metropolitan areas (Atlanta, Georgia, or Detroit, Michigan) at baseline. Of the 566 399 participants who satisfactorily completed the baseline questionnaire, we excluded those whose questionnaires were completed by proxy (n = 15 760), those with any prevalent registry-confirmed cancer (except for nonmelanoma skin cancer) at baseline (n = 8587), and participants who moved out of the study area or died at or before processing of the baseline questionnaire (n = 24). We also excluded participants for whom calculated total energy intake exceeded more than two sex-specific interquartile range amounts above the 75th or below the 25th percentile on a logarithmic scale (n = 4810). Our final analytic cohort consisted of 537 218 persons (n = 316 670 men; n = 220 548 women). The NIH–AARP Diet and Health study was approved by the Special Studies Institutional Review Board of the US National Cancer Institute (NCI), and all participants gave informed consent by virtue of completing and returning the questionnaire.

Dietary Assessment

At baseline, participants completed a 124-item food frequency questionnaire (FFQ) developed at the NCI. The FFQ queried the usual frequency of foods and beverages consumed over the previous 12 months (10 categories ranging from never to ≥6 times per day for beverages and never to ≥2 times per day for foods), and usual portion size (less than three-quarters cup, three-quarters to 1 cup, ≥1 cup). Responses to the FFQ were validated for foods and nutrients in a calibration study based on two nonconsecutive telephone-administered 24-hour dietary recalls within a year of the baseline questionnaire (mean days apart = 25) from a stratified random sample of the NIH–AARP participants (n = 2053) (16).

The HEI-2005 was developed jointly by the NCI and the US Department of Agriculture to serve as a measure of overall diet compliance with the 2005 Dietary Guidelines for Americans (14). To calculate the HEI-2005 score, dietary data from the FFQ were merged with the MyPyramid Equivalents Database (MPED) (version 1.0) to generate pyramid equivalents for the 12 components. The MPED disaggregates reported food intakes into component ingredients and combines like ingredients into meaningful groups to generate amounts of each MyPyramid group and subgroup consumed.

Scoring criteria for the HEI-2005 are summarized in Table 1. In short, for the nine "adequacy" components where there was a recommended minimum intake, the highest score was assigned for meeting dietary guidelines. These "adequacy" components included total fruit, nonjuice fruit, total vegetables, dark-green and orange vegetables and legumes, total grains, whole grains, milk products (including soy), healthy oils, and meat and beans (including meat, poultry, fish, and legumes). Only the lowest fat portions of milk and meat were included in respective components. Consumption less than the recommended amount was scored in a linear, prorated fashion. An additional three "moderation" components with maximum recommended intakes (saturated fat, sodium and calories from solid fat, alcohol and added sugars) were reverse scored, whereby lower consumption levels were awarded higher scores. All scores were expressed per 1000 calories to account for differences in energy intake (14). The HEI-2005 score describes 0 as no guidelines met and 100 as all guidelines met.

Table 1. Healthy Eating Index 2005 components and standards for scoring*

Component	Maximum awarded points	Standard for maximum score	Standard for score of zero
Adequacy components			
Total fruit, includes 100% juice	5	≥0.8 cup equivalents per 1000 kcal	No fruit
Whole fruit, not juice	5	≥0.4 cup equivalents per 1000 kcal	No whole fruit
Total vegetables	5	≥1.1 cup equivalents per 1000 kcal	No vegetables
Dark-green and orange vegetables and legumes†	5	≥0.4 cup equivalents per 1000 kcal	No dark-green or orange vegetables or legumes
Total grains	5	≥3.0 oz equivalents per 1000 kcal	No grains
Whole grains	5	≥1.5 oz equivalents per 1000 kcal	No whole grains
Milk‡	10	≥1.3 cup equivalents per 1000 kcal	No milk
Meat and beans†	10	≥2.5 oz equivalents per 1000 kcal	No meat or beans
Oils§	10	≥12 grams per 1000 kcal	No oil
Moderation components			
Saturated fat‖	10	<7% of energy	≥15% of energy
Sodium‖	10	≤0.7 gram per 1000 kcal	≥2.0 grams per 1000 kcal
Calories from solid fat, alcohol, and added sugar (SoFAAS)	20	≤20% of energy	≥50% of energy

* Intakes between the minimum and maximum levels are scored proportionately, except for saturated fat and sodium. Adequacy components include foods with minimum recommended intakes (higher consumption considered better quality diet). Moderation components include foods with maximum recommended intakes (higher consumption considered poorer quality diet). Moderation components are thus reverse scored, with lower consumption levels awarded higher scores.

† Legumes counted as vegetables only after Meat and Beans standard is met. Meat only includes the lowest fat portions.

‡ Includes all milk products, such as fluid milk, yogurt, and cheese, and soy beverages (only lowest fat portions included).

§ Includes nonhydrogenated vegetable oils and oils in fish, nuts, and seeds.

‖ Saturated fat and sodium get a score of 8 for the intake levels that reflect the 2005 Dietary Guidelines, less than 10% of calories from saturated fat, and 1.1 grams of sodium/1000 kcal, respectively.

Identification of Pancreatic Cancer Case Subjects

Incident cancers were ascertained by linking participants to the eight state registries of study enrollment and three additional states (Arizona, Nevada, and Texas). Cancer registry case ascertainment is estimated to be about 90% complete for this cohort (17). Vital status was verified annually by linkage to the Social Security Administration Death Master File and to the US National Death Index, as well as by cancer registry. We included incident exocrine pancreatic cancer case subjects (International Classification of Diseases for Oncology, Third Edition, codes C250–C259) diagnosed during the follow-up period though December 31, 2006, or identified as pancreatic cancer deaths in the US National Death Index. Endocrine pancreatic tumors, sarcomas, and lymphomas (histology types 8150, 8551, 8153, 8155, and 8240) were not counted because the etiologies of these cancers are thought to be different.

Statistical Analysis

We classified individuals into sex-stratified quintiles of HEI-2005 score because previous studies have shown differences in dietary patterns and pancreatic cancer by sex (8,10). We used Cox proportional hazards regression with age as the underlying time metric to test associations between the HEI-2005 score and pancreatic cancer risk. We calculated follow-up time from date of baseline questionnaire to pancreatic cancer diagnosis, death, move from study area, or end of follow-up, whichever came first. The proportional hazards assumption was evaluated by modeling interaction terms of the continuous HEI-2005 score with follow-up time. A cancer diagnosis other than exocrine pancreatic cancer was not treated as a censoring event. We considered all variables in Table 2 as potential confounders during model building and created parsimonious models that included variables that were putative risk factors or changed the log hazard ratio (HR) by more than 10%. Final models were adjusted for smoking status at baseline (never, quit >10 years ago, 5–9 years ago, 1–4 years ago, <1 year ago or current ≤20 cigarettes per day, quit <1 year ago or current >20 cigarettes per day), self-reported diabetes history (yes/no), body mass index (BMI) (15 to <18.5, 18.5 to <25, 25 to <30, 30 to ≤50 kg/m^2, or missing), and sex (for sex-combined models).

In addition to our main hypothesis that there would be a reduced risk comparing extreme HEI-2005 scores, to test whether there was a linear trend, we assigned an ordinal score to the sex-specific median value of each quintile and treated the variable as linear. We also performed continuous analyses scaling the score by the interquartile range. To test whether a linear assumption was

Table 2. Baseline characteristics according to Healthy Eating Index 2005 score among 316 670 men and 220 548 women in the National Institutes of Health–AARP Diet and Health Study*

	Men			Women		
Characteristics	**Quintile 1**	**Quintile 3**	**Quintile 5**	**Quintile 1**	**Quintile 3**	**Quintile 5**
HEI-2005 score, range	20.6–54.7	63.3–69.6	75.6–96.7	19.7–60.4	68.4–73.7	78.6–94.0
Age at baseline, mean, y	61.7	62.3	62.9	61.3	61.9	62.5
Race, % Non-Hispanic white	93.1	92.5	92.4	89.8	89.4	90.0
Education, % college/postgraduate	33.6	45.8	52.7	21.8	31.1	35.9
Body mass index, mean, kg/m^2	27.3	27.4	26.9	26.9	26.8	26.5
Smoking history, %						
Never smoker	19.7	29.9	36.0	35.1	44.8	49.0
Quit >10 years in the past	50.7	56.8	56.1	30.7	38.5	39.6
Quit 1–9 years in the past	25.3	9.4	4.4	30.5	13.2	8.1
Current smoker	4.3	4.0	3.5	3.7	3.5	3.3
Self-reported diabetes, %	6.3	10.1	14.9	5.5	7.3	9.9
Physical activity ≥20 minutes, at least 5 times per week, %	15.5	20.5	28.2	10.5	16.5	21.2
Regular multivitamin use, %	45.4	52.0	58.2	53.5	61.2	66.0
Alcoholic drinks per day, mean	3.3	0.7	0.3	0.9	0.3	0.2
Mean daily nutrient intake						
Calories, kcal/day	2369	1964	1787	1725	1542	1480
Total fat, g/1000 kcal	36.5	34.7	30.0	37.9	32.9	29.3
Saturated fat, g/1000 kcal	12.3	10.4	8.4	13.1	10.0	8.2
Red meat, g/1000 kcal	45.3	39.7	26.6	36.6	29.6	21.6
Total fruit, MPED/1000 kcal	0.7	1.1	1.6	0.7	1.4	1.7
Total vegetables, MPED/1000 kcal	0.5	1.1	1.3	0.9	1.3	1.5
Dark-green/orange vegetables, MPED/1000 kcal	0.1	0.2	0.3	0.2	0.3	0.4
Grains, MPED/1000 kcal	2.3	3.0	3.2	2.5	3.0	3.1
Dairy, MPED/1000 kcal	0.6	0.7	0.9	0.7	0.8	1.1
Solid fat, grams/1000 kcal	21.5	18.0	12.5	22.7	16.4	11.7
Added sugar, tsp/1000 kcal	8.3	5.6	4.0	9.2	5.4	4.2
Percentage of calories from SoFAAS	48.6	30.7	20.3	42.2	26.5	19.0
Folate, ug/ 1000 kcal	111.0	148.5	183.7	123.3	173.8	197.3
Fiber, g/ 1000 kcal	7.1	10.4	13.8	7.8	12.0	14.4

* HEI = Healthy Eating Index; MPED = My Pyramid Equivalents Database, SoFAAS = solid fats, alcoholic beverages, and added sugars.

appropriate, we performed an analysis allowing for a natural spline and also assessed martingale residuals. Both tests indicated that a linear model was sufficient.

We performed sensitivity analyses excluding those who had less than 4 years of follow-up to assess whether results were influenced by undetected disease. We also tested whether the association was driven by specific components of the HEI-2005 score by creating a single model with all 12 components. A previous NIH–AARP study showed that individuals consuming 3 or more drinks per day had an increased risk of pancreatic cancer (18). Therefore, we conducted two sensitivity analyses, first excluding those who consumed 3 or more drinks per day and secondly summing the HEI-2005 score without alcohol, while separately adjusting for alcohol intake. We assessed effect modification by sex, diabetes, smoking (never, former, current), and BMI (18.5 to <25 and ≥25.0 kg/m^2) with stratified analyses and consideration of interactions using the Wald test. Given that 93% of our sample was non-Hispanic white, we were unable to analyze other racial or ethnic groups separately. We used SAS version 9.2 for all analyses (SAS Institute, Cary NC), and all *P* values were two-sided, with those less than .05 considered statistically significant.

Results

Over a median 10.5 years of follow-up, we identified 2383 incident pancreatic cancer cases (n = 1545 men; n = 838 women). Median age at baseline was 63 years for men and 62 for women. The HEI-2005 score range was 20.6 to 96.7 points for men and 19.7 to 94.0 for women (Table 2). For both sexes, compared with those with low scores, participants with high HEI-2005 scores were more likely to be older, be non-Hispanic white, be more educated, be never smokers, be physically active, take multivitamins, consume less alcohol, and report having diabetes.

Hazard ratios and 95% confidence intervals (CIs) for the association between total HEI-2005 score and pancreatic cancer are presented in Table 3 overall and by sex, although interaction by sex was not statistically significant ($P_{interaction}$ = .69). Before adjusting for known risk factors, we calculated that 22.6% (n = 539) of total incident cases occurred in the lowest HEI-2005 quintile, whereas 19.2% (n = 457) of total cases occurred in the highest quintile. In multivariable adjustment, cigarette smoking most affected hazard ratio estimates, whereas other covariables were less influential but still contributed to model estimates. With adjustment, comparing the highest with the lowest quintile of HEI-2005 score, we observed a reduced risk of pancreatic cancer (HR = 0.85, 95% CI = 0.74 to 0.97). In continuous analyses scaled by the interquartile range of the HEI-2005 score, the observed hazard ratio was 0.90 (95% CI = 0.85 to 0.95), whereas comparing more extreme scores and scaling by the difference between the 90th and 10th percentile of HEI-2005 score yielded a hazard ratio of 0.85 (95% CI = 0.76 to 0.94). In analyses stratified by sex, among men we found a lower risk of pancreatic cancer comparing extreme quintiles (HR = 0.83, 95% CI = 0.70 to 0.98). The hazard ratio was of similar magnitude for women but was not statistically significant (HR = 0.87, 95% CI = 0.70 to 1.09).

In exploratory analyses of the 12 components of the HEI-2005 score, higher component scores for milk products, dark-green and

Table 3. Associations between the Healthy Eating Index 2005 (HEI-2005) and pancreatic cancer risk among 537 218 participants in the National Institutes of Health–AARP Diet and Health Study*

HEI-2005	Q1	Q2	Q3	Q4	Q5	P_{trend}§	Continuous†
Total case subjects, No.	539	496	454	437	457		
Energy and sex-adjusted HR (95% CI)	1.00	0.88 (0.78 to 0.99)	0.79 (0.69 to 0.89)	0.74 (0.66 to 0.85)	0.75 (0.66 to 0.86)	<.001	0.84 (0.79 to 0.89)
Multivariable-adjusted HR (95% CI)‡,§¶	1.00	0.94 (0.83 to 1.06)	0.87 (0.76 to 0.98)	0.83 (0.73 to 0.95)	0.85 (0.74 to 0.97)	.003	0.90 (0.85 to 0.95)
Male case subjects, No.	356	317	299	275	298		
Energy adjusted HR (95% CI)	1.00	0.85 (0.73 to 0.99)	0.78 (0.67 to 0.91)	0.71 (0.60 to 0.83)	0.74 (0.63 to 0.87)	<.001	0.85 (0.79 to 0.91)
Multivariable-adjusted HR (95% CI)§¶	1.00	0.91 (0.78 to 1.06)	0.86 (0.73 to 1.00)	0.79 (0.67 to 0.93)	0.83 (0.70 to 0.98)	.008	0.91 (0.84 to 0.98)
Female case subjects, No.	183	179	155	162	159		
Energy adjusted HR (95% CI)	1.00	0.93 (0.76 to 1.14)	0.79 (0.64 to 0.98)	0.82 (0.66 to 1.01)	0.78 (0.63 to 0.96)	.009	0.86 (0.78 to 0.95)
Multivariable-adjusted HR (95% CI)§¶	1.00	0.99 (0.80 to 1.22)	0.87 (0.70 to 1.08)	0.91 (0.73 to 1.13)	0.87 (0.70 to 1.09)	.16	0.92 (0.83 to 1.02)

* Q5 is the highest quintile of scores meeting the most dietary guideline recommendations. CI = confidence interval; HR = hazard ratio.

† Continuous measure is scaled by the interquartile range of the total HEI-2005 score.

‡ $P_{interaction}$ by sex = .69.

§ *P* values (two-sided) for trend and interaction were calculated using the Wald test.

¶ Multivariable models are adjusted for daily caloric intake, sex (where appropriate), diabetes (yes/no), body mass index (15 to <18.5, 18.5 to <25, 25 to <30, 30 to ≤50 kg/m^2, missing) and smoking status (categories describing never, ever, current, and dose).

orange vegetables and legumes, and total grains were nominally associated with lower pancreatic cancer risk (Table 4). The statistical significance of individual components differed by sex; for men, only the milk products were associated with a reduced risk, whereas components representing intake of dark-green and orange vegetables and legumes, total grains, and healthy oils were associated with lower risks for women.

In analyses stratified by BMI (18.5 to <25 or 25 to 50 kg/m^2), we observed a statistically significant interaction with HEI-2005 score in men ($P_{interaction}$ = .03) but not in women ($P_{interaction}$ = .24) (Table 5). Comparing the highest HEI-2005 quintile with the lowest, the hazard ratio was 1.21 (95% CI = 0.88 to 1.67) for normal weight men and 0.72 (95% CI = 0.59 to 0.88) for overweight/obese men.

Tests for interaction between the HEI score and smoking or self-reported diabetes were not statistically significant, and restricting analyses to those who did not smoke or those without diabetes yielded similar results (data not shown). Sensitivity analyses excluding individuals diagnosed within 4 years of baseline or heavy alcohol consumers (≥3 drinks/day) did not change hazard ratios (data not shown). Excluding alcohol from the HEI-2005 score and adjusting for it as a separate variable also did not change results. Additional adjustment for folate, red meat intake, and multivitamin use yielded similar results (data not shown).

Discussion

This study is the first to test the association between the 2005 Dietary Guidelines for Americans, as represented by the HEI-2005 score, and risk of pancreatic cancer. We observed a statistically significantly reduced risk of pancreatic cancer comparing the highest with the lowest HEI-2005 quintiles. We found a statistically significant interaction by BMI among men, and the observed association was stronger among overweight or obese men than among normal weight men.

All but one of the previous studies on dietary patterns and pancreatic cancer were data-driven. Factor analysis was performed in a Canadian case–control study (n = 585 cases) (8), an Italian case–control study (n = 326 cases) (13), and in a combined analysis of the Health Professionals Follow Up Study (HPFS) (n = 355 cases) and Nurses' Health Study (NHS) (n = 185 cases) (10). These studies showed an approximate 50% reduction in risk with high adherence to patterns labeled as prudent (high in fruits, vegetables, whole grains, and lean meats) among men, but in the Canadian and NHS studies no association was observed among women for the "prudent" pattern. Neither the Canadian nor the HPFS/NHS studies showed an association for men or women by quintile of Western dietary pattern (high intake of meat, high-fat dairy, sugar-sweetened beverages, and sweets), but the Italian study showed a twofold increased risk comparing quartiles of diets high in animal products and a 70% increased risk for high-starch diets. The Canadian study characterized an additional "alcohol drinker" dietary pattern but reported no association among men or women (8). A principal components analysis in a California-based case–control study (n = 532 cases) also showed a 50% reduction in pancreatic cancer risk for consumption of a "prudent" dietary pattern among men and women, whereas the Western pattern was associated with a 2.4-fold increase risk among men but not women (12).

Table 4. Hazard ratios and 95% confidence intervals for the 12 components of the Healthy Eating Index 2005 (HEI-2005) and pancreatic cancer risk among 537 218 participants in the National Institutes of Health–AARP Diet and Health Study*

	Total population	Men (n = 316 670)	Women (n = 220 548)
HEI-2005 component	**HR (95% CI)†**	**HR (95% CI)†**	**HR (95% CI)†**
Adequacy components‡			
Total fruit	0.99 (0.95 to 1.04)	0.99 (0.94 to 1.05)	1.00 (0.91 to 1.09)
Whole fruit	1.01 (0.96 to 1.05)	0.99 (0.94 to 1.05)	1.04 (0.96 to 1.14)
Total vegetables	1.03 (0.97 to 1.08)	1.03 (0.96 to 1.10)	1.00 (0.91 to 1.10)
Dark-green and orange vegetables and legumes	0.96 (0.93 to 0.99)‖	0.98 (0.94 to 1.03)	0.92 (0.87 to 0.98)‖
Total grains	0.93 (0.88 to 0.98)‖	0.94 (0.88 to 1.01)	0.91 (0.83 to 0.99)‖
Whole grains	0.99 (0.95 to 1.03)	0.99 (0.95 to 1.04)	0.99 (0.93 to 1.06)
Milk, including soy beverages	0.98 (0.97 to 1.00)‖	0.98 (0.96 to 1.00)‖	0.99 (0.96 to 1.01)
Meat and beans	1.01 (0.98 to 1.03)	1.01 (0.97 to 1.05)	1.01 (0.97 to 1.05)
Oils	0.99 (0.97 to 1.00)	0.99 (0.97 to 1.02)	0.97 (0.94 to 1.00)‖
Moderation components§			
Saturated fat	0.99 (0.97 to 1.00)	0.99 (0.97 to 1.01)	0.98 (0.96 to 1.01)
Sodium	0.98 (0.96 to 1.01)	0.97 (0.94 to 1.00)	1.00 (0.96 to 1.05)
Calories from solid fat, alcohol, and added sugar	1.00 (0.99 to 1.01)	1.00 (0.98 to 1.01)	1.01 (1.00 to 1.03)

* Multivariable models are mutually adjusted for the 12 HEI components and are also adjusted for calories, sex (where appropriate), diabetes (yes/no), body mass index (15 to <18.5, 18.5 to <25, 25 to <30, 30 to <50 kg/m^2, missing), and smoking status (categories describing never, ever, current, and dose). CI = confidence interval; HR = hazard ratio.

† The hazard ratio is based on a one-unit change in the score for the component of interest.

‡ Constitutes food groupings with recommended minimum intakes (regarded as healthful foods). Milk and meat components include only lowest fat portions.

§ Constitutes food groupings with recommended maximum intakes (regarded as unhealthful foods); this component is reverse scored, with lower consumption levels awarded higher scores.

‖ *P* values (two-sided) based on the Wald test were statistically significant at a *P* less than .05 level.

Table 5. Hazard ratios (HRs) and 95% confidence intervals (95% CIs) for quintiles of the Healthy Eating Index 2005 (HEI-2005) and pancreatic cancer risk among 537 218 participants in the National Institutes of Health–AARP Diet and Health Study, stratified by body mass index (BMI)

	Normal weight (BMI 18.5 to <25 kg/m²)		Overweight/obese (BMI 25 to ≤50 kg/m²)		$P_{interaction}$ for BMI and HEI-2005†
HEI-2005 quintile*	Case subjects/total	HR (95% CI)	Case subjects/total	HR (95% CI)	
Total population*					.93
Q1	163/35 605	1.00	352/66 973	1.00	
Q2	157/33 809	1.10 (0.88 to 1.38)	321/69 580	0.88 (0.75 to 1.02)	
Q3	143/35 301	1.00 (0.79 to 1.26)	294/68 379	0.82 (0.70 to 0.95)	
Q4	144/36 735	1.00 (0.79 to 1.27)	275/67 106	0.77 (0.65 to 0.90)	
Q5	155/39 340	0.99 (0.78 to 1.25)	290/64 611	0.81 (0.69 to 0.96)	
P_{trend}†		.66		.004	
Continuous‡		0.99 (0.89 to 1.11)		0.88 (0.82 to 0.95)	
Men					.03
Q1	85/17 915	1.00	263/43 437	1.00	
Q2	75/16 290	1.09 (0.79 to 1.50)	234/45 312	0.85 (0.71 to 1.02)	
Q3	71/17 009	1.02 (0.74 to 1.42)	219/44 701	0.80 (0.67 to 0.96)	
Q4	81/18 114	1.15 (0.83 to 1.59)	186/43 668	0.69 (0.56 to 0.83)	
Q5	98/20 259	1.21 (0.88 to 1.67)	194/41 516	0.72 (0.59 to 0.88)	
P_{trend}†		.23		<.001	
Continuous‡		1.11 (0.96 to 1.28)		0.84 (0.77 to 0.92)	
Women					.24
Q1	78/17 690	1.00	89/23 536	1.00	
Q2	82/17 519	1.12 (0.82 to 1.53)	87/24 268	0.92 (0.68 to 1.24)	
Q3	72/18 292	0.99 (0.71 to 1.37)	75/23 678	0.80 (0.59 to 1.09)	
Q4	63/18 621	0.87 (0.62 to 1.23)	89/23 438	0.94 (0.70 to 1.27)	
Q5	57/19 081	0.76 (0.53 to 1.09)	96/23 095	1.00 (0.74 to 1.34)	
P_{trend}†		.05		.91	
Continuous‡		0.87 (0.74 to 1.02)		1.00 (0.86 to 1.16)	

* Q5 is the highest quintile of scores (meeting the most dietary guideline recommendations). Quintile cutpoints were based on sex-specific HEI-2005 scores. Multivariable models adjusted for calories, sex (where appropriate), diabetes (yes/no), and smoking status (categories describing never, ever, current, and dose).

† P_{trend} and interaction values (two-sided) were based on the Wald test and considered statistically significant at a P less than .05 level

‡ Continuous measure is scaled by the interquartile range of the total HEI-2005 score.

In contrast, also using principal components analysis, the prospective Iowa Women's Health study (n = 256 cases) identified six dietary patterns (high vegetable, low fat, Mediterranean, high fiber, high sweet, high fruit), none of which showed an association with risk of pancreatic cancer (9). Based on findings that flavonol intake was inversely related to pancreatic cancer in the Multiethnic Cohort, researchers used reduced rank regression to generate a dietary pattern predictive of flavonol intake (tea, cabbage, fruit, wine). This flavonol-rich pattern was then tested in relation to pancreatic cancer and showed an inverse P_{trend}, but comparing quintiles, the association was not statistically significant (n = 610 cases), and the flavonol-rich dietary pattern showed no association when applied to data from the European Prospective Investigation into Cancer and Nutrition (n = 517 cases) (19). A previous analysis in NIH–AARP (n = 1057 cases) using a predefined healthy lifestyle score (0–5 points awarded based on dietary pattern, physical activity, smoking status, BMI, and alcohol use) showed no association between a modified Mediterranean diet pattern and pancreatic cancer but did not stratify by sex or compare quartiles/quintiles of the score (11).

Our observed inverse association was not as strong in magnitude as that seen for the data-driven "prudent" diet in previous studies among men. Among women, unlike previous studies that show hazard ratio estimates close to 1.00 (8,10) or that suggest increased risks for women who score high for vegetable- or Mediterranean-pattern adherence (9), our findings suggest a possible inverse association. The lack of statistical significance among women in our study could be because of the smaller sample size of women or biological differences in pancreatic cancer etiology (20,21).

In exploratory analyses in the total population, we observed inverse associations for the following components: dark-green and orange vegetables and legumes, total grains, and milk. These components are not the same as individual foods or food groupings previously associated with pancreatic cancer (3,4) and should not be interpreted as such. Our observed inverse association with vegetables and legumes contrasts with a recent meta-analysis of 14 prospective studies showing no association between fruits and vegetables and pancreatic cancer (4). The inverse association with total grain intake also differs from cohort studies that have shown no association with carbohydrates, glycemic load, or glycemic index (22–26), whereas another cohort suggested a non-statistically significant positive association with glycemic load (27). Our observed inverse association between low-fat milk products and risk may differ from null findings with total dairy intake (28,29)

because of differences in how fat was accounted for. The analysis of individual components is exploratory because it is not conceptually consistent with analyzing dietary patterns because without interaction terms component models assume independent rather than synergistic effects of dietary components (30). Also, the observed associations cannot be attributed to a given food or food group because the HEI-2005 components are not based on individual foods.

Strengths of the HEI-2005 include energy adjustment, which characterizes diet quality controlled for quantity, and consideration of the overall dietary pattern described in the 2005 Dietary Guidelines rather than an isolated dietary component. This pattern was defined a priori and, unlike data-driven patterns, may be compared between study populations. Furthermore, as the basis for federal food and nutrition education programs, evaluating these dietary guidelines in relation to disease risk has general public health relevance. Strengths of our study include the large, prospective nature of the cohort, the greater number of case subjects allowing examination of effect modification by other risk factors, extended follow-up time, and the wide range of dietary intakes to observe associations if they exist.

Study limitations include the measurement error inherent to the FFQ and that the HEI-2005 was not specifically designed for the purpose of overall cancer prevention (eg, requiring that red meat, a suggested cancer risk factor, be separated from other meats). Also, the FFQ measured consumption in categories, thus not capturing specific food intakes beyond the maximum category. However, the HEI-2005 score accounts for total calories and was designed to include limits for moderation components, accounting for excess consumption of foods thought to contribute to poor health outcomes. Another limitation is that self-report of diabetes could result in misclassification of undiagnosed case subjects. Finally, high-quality dietary patterns may be associated with other healthful behaviors or demographics that may not be fully accounted for in the models and that might be associated with risk of disease.

In summary, the inverse association observed with adherence to the 2005 Dietary Guidelines (as measured by the HEI-2005) suggests that a high-quality diet may play a role in reducing pancreatic cancer risk. This finding contrasts with previous studies showing limited associations with specific foods or nutrients. Future studies may seek to replicate this finding in other cohorts or may compare other a priori defined patterns with disease risk.

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