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Original Contribution

Adherence to 5 Diet Quality Indices and Pancreatic Cancer Risk in a Large US Prospective Cohort

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Few prospective studies have examined associations between diet quality and pancreatic ductal adenocarcinoma (PDAC), or comprehensively compared diet quality indices. We conducted a prospective analysis of adherence to the Healthy Eating Index (HEI)-2015, alternative HEI-2010, alternate Mediterranean diet (aMed), and 2 versions of Dietary Approaches to Stop Hypertension (DASH; Fung and Mellen) and PDAC within the National Institutes of Health (NIH)-AARP Diet and Health Study (United States, 1995–2011). The dietary quality indices were calculated using responses from a 124-item food frequency questionnaire completed by 535,824 participants (315,780 men and 220,044 women). We used Cox proportional hazards regression models to calculate adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for each diet quality index and PDAC. During follow-up through 2011 (15.5-year median), 3,137 incident PDAC cases were identified. Compared with those with the lowest adherence quintile, participants with the highest adherence to the HEI-2015 (HR = 0.84, 95% CI: 0.75, 0.94), aMed (HR = 0.82, 95% CI: 0.73, 0.93), DASH-Fung (HR = 0.85, 95% CI: 0.77, 0.95), and DASH-Mellen (HR = 0.86, 95% CI: 0.77, 0.96) had a statistically significant, lower PDAC risk; this was not found for the alternative HEI-2010 (HR = 0.93, 95% CI: 0.83, 1.04). This prospective observational study supports the hypothesis that greater adherence to the HEI-2015, aMed, and DASH dietary recommendations may reduce PDAC.

AHEI-2010; aMed; DASH; diet; HEI-2015; pancreatic cancer

Abbreviations: AHEI-2010, Alternative Healthy Eating Index-2010; aMed, alternate Mediterranean diet; CI, confidence interval; DASH, Dietary Approaches to Stop Hypertension; FFQ, food frequency questionnaire; HEI-2015, Healthy Eating Index-2015; HR, hazard ratio; NCI, National Cancer Institute; NIH, National Institutes of Health; PDAC, pancreatic ductal adenocarcinoma.

Although pancreatic cancer is relatively rare and accounts for only 3% of incident cancer cases in the United States, it is among the most lethal of all major cancers, with a 5-year survival rate of only 10% (1). Pancreatic ductal adenocarcinoma (PDAC) is the most common pancreatic cancer type and accounts for more than 85% of pancreatic cancers (2). Potentially modifiable risk factors for PDAC include cigarette smoking, excess body weight, type 2 diabetes mellitus, and diet (3). In studies of individual nutrients or foods and PDAC risk, the most consistently reported associations have been for higher PDAC risk with heavy alcohol use (4–6) and inconsistent associations for higher consumption of red meat and dietary fat (7–10).

In contrast to individual foods and nutrients, dietary patterns can account for complex correlations and interactions that are not detected when evaluating associations for individual foods or nutrients (11). The Dietary Patterns Methods Project identified the 4 most commonly used a priori–defined US diet quality indices: the Healthy Eating Index (HEI) (12, 13), based on the Dietary Guidelines for Americans (14); Alternative HEI (AHEI) (15), based on Harvard's Healthy Eating Plate (16); alternate Mediterranean diet score (aMed) (17), based on the Mediterranean Diet (18); and Dietary Approaches to Stop Hypertension (DASH) (19), based on the DASH Eating Plan (20–22). These patterns emphasize higher consumption of fruits, vegetables, whole grains, and legumes and limited consumption of refined grains, red and processed meats, sugar-sweetened beverages, added sugars, and saturated fats. Accumulating evidence suggests that greater adherence to these diet quality

indices is associated with lower risk of cancer incidence and mortality (23, 24).

Three prospective studies have evaluated the association between aMed and HEI-2005 indices and pancreatic cancer risk with conflicting results (25–27). Since the publication of the earlier studies of diet and PDAC risk within National Institutes of Health (NIH)-AARP (formerly the American Association of Retired Persons) (26, 28), there has been longer follow-up and more incident PDAC cases. To compare variations between diet indices and PDAC risk, we examined the associations between adherence scores to 5 sets of diet quality index recommendations. To be consistent with the Dietary Patterns Methods Project (24), in this analysis, we considered the HEI-2015 (12, 13), AHEI-2010 (15), aMed (17), and 2 DASH diet indices, one based on food groups (Fung et al.) (19) and the other based on nutrients (Mellen et al.) (29). To the best of our knowledge, HEI-2015, AHEI-2010, and the 2 DASH scores have not previously been examined and compared in relation to PDAC risk. We hypothesized that greater adherence to diet quality indices would be associated with lower PDAC risk.

METHODS

Study population

The NIH-AARP Diet and Health Study is a large prospective cohort of male and female AARP members, aged 50–71 years at baseline, who resided in 1 of 6 states (California, Florida, Louisiana, New Jersey, North Carolina, and Pennsylvania) or 2 metropolitan areas (Atlanta, Georgia, and Detroit, Michigan) (30). During 1995 and 1996, self-administered questionnaires queried participants to provide information about dietary intake during the previous 12 months, demographic characteristics, and health-related behaviors, including physical activity and smoking status (30). In total, 566,398 participants satisfactorily completed and returned the questionnaires. 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.

Participants whose questionnaires were completed by a proxy or who had a prevalent history of cancer (except nonmelanoma skin cancer) based on cancer registry data, end-stage renal disease, or reported extreme energy intake (2 interquartile ranges below the sex-specific 25th percentile or above the 75th percentile of log-transformed energy intake) or with person-years ≤ 0 were excluded. Our analytical sample included 535,824 participants (315,780 men and 220,044 women; Web Figure 1, available at https://doi.org/10.1093/aje/kwac082).

Dietary assessment and index-based dietary quality indices

Participants completed a self-administered semiquantitative 124-item food frequency questionnaire (FFQ) that queried frequency and portion size of foods and beverages over the previous 12 months (30). Further validation of the FFQ was performed within a subset of the NIH-AARP Diet and Health Study, using 2 24-hour dietary recalls (31). Details regarding the FFQ are published elsewhere (31–33).

The dietary data from the FFQ was linked to the MyPyramid Equivalents Database (MPED), version 1.0, to derive guidance-based food group equivalents for whole grains, total grains, total vegetables (including all vegetable subgroups), total fruit, low-fat dairy, protein foods (including poultry, fish, nuts, soy, and legumes), solid fat, added sugars, and alcohol. Additionally, nutrient estimates were generated for saturated fat, monounsaturated fat (MUFA), polyunsaturated fat (PUFA), eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), *trans*-fat, sodium, and alcohol by using the US Department of Agriculture Survey Nutrient Database associated with Continuing Survey for Food Intake by Individuals 1994–1996 and the Nutrition Data System for Research. The MPED and nutrient variables were used to create the dietary quality indices (34) for the HEI-2015, AHEI-2010, aMed, and DASH.

The components for the 5 dietary indices are summarized in Table 1**,** and their scoring is described in the Web Appendix. Briefly, the HEI-2015 consisted of 13 components with a range of 0–100 points (13), the AHEI consisted of 11 components (range, 0–110 points) (15), the aMed consisted of 9 components (range, 0–9 points) (17), the DASH-Fung consisted of 8 components (range, 0–40 points) (19), and the DASH-Mellen consisted of 9 components (range, 0–9 points) (29).

Cohort follow-up and case ascertainment

Cancer cases were identified by linking the cohort participants to 11 state registries (including the 8 states mentioned above plus Arizona, Nevada, and Texas) and the National Death Index from 1995 through 2011 (the final year for which linkage was performed). The cancer registries are estimated to be about 90% complete (35). Vital status was determined via linkage to the Social Security Administration Death Master File.

Our outcome was incident primary adenocarcinoma of the exocrine pancreas (*International Classifications of Diseases for Oncology*, *Third Edition*, codes C250 to C259). Our case definition excluded pancreatic endocrine tumors, sarcomas, and lymphomas (histology types 8150, 8151, 8153, 8155, and 8240), as their etiologies are thought to differ.

Statistical analysis

Spearman correlation coefficients were performed to assess the correspondence between the 5 dietary pattern scores. We calculated follow-up time from date of baseline questionnaire to PDAC diagnosis, death, move from study area, or end of follow-up (December 31, 2011), whichever occurred first. Cox proportional hazards models were used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) for PDAC. We used sex-specific quintiles to categorize each score, with the lowest quintile serving as the referent category and the highest quintile representing the highest diet quality. Continuous HRs (95% CIs) and *P* values

Table 1. Standards for Maximum Scores Across 5 Dietary Quality Indices in the National Institutes of Health–AARP Diet and Health Study, United States, 1995–2011

Diet Quality Component	Diet Quality Indices				
	HEI-2015	AHEI-2010	aMed[a]	DASH-Fung[b]	DASH-Mellen
Adequacy components					
Calcium					≥590 mg/1,000 kcal
Fiber					≥14.8 g/1,000 kcal
Magnesium					≥238 mg/1,000 kcal
Potassium					≥2,238 mg/1,000 kcal
Protein					≥18% kcal/day
MUFA:saturated fat ratio			≥ median: M: 1.2; W: 1.2		
PUFA		≥10% kcal/day			
PUFA+MUFA:saturated fat ratio	≥2.5				
EPA+DHA		250 mg/day			
Fruits	≥0.8 cup eq/1,000 kcal		≥ median (cup eq/day): M: 1.7; W: 1.7	Fifth quintile (cup eq/day): M: ≥3.0; W: ≥2.9	
Fruits, whole	≥0.4 cup eq/1,000 kcal	≥4 servings/day			
Grains, whole	≥1.5 ounce eq/1,000 kcal	M: 90; g/day W: 75 g/day	≥ median (ounce eq/day): M: 0.9; W: 0.7	Fifth quintile (ounce eq/day): M: ≥1.6; W: ≥1.3	
Vegetables	≥1.1 cup eq/1,000 kcal	≥5 servings/day	≥ median (cup eq/day): M: 1.3; W: 1.7	Fifth quintile (cup eq/day): M: ≥2.7; W: ≥2.7	
Greens and beans	≥0.2 cup eq/1,000 kcal				
Total protein foods	≥2.5 ounce eq/1,000 kcal				
Seafood and plant protein	≥0.8 cup eq/1,000 kcal				
Fish			≥ median (ounce eq/day): M: 0.5; W: 0.4		
Legumes			≥ median (cup eq/day): M: 0.1; W: 0.04		
Nuts			≥ median (ounce eq/day): M: 0.3; W: 0.2		
Nuts and legumes		≥1 serving/day		Fifth quintile (ounce eq/day) M: ≥1.0; W: ≥0.6	
Dairy	≥1.3 cup eq/1,000 kcal				
Low-fat dairy				Fifth quintile (cup eq/day) M: ≥2.1; W: ≥1.9	

Table continues

Table 1. Continued

Diet Quality Component	Diet Quality Indices				
	HEI-2015	AHEI-2010	aMed[a]	DASH-Fung[b]	DASH-Mellen
Moderation components					
Total fat					≤27% kcal/day
Saturated fat	≤8% kcal/day				≤6% kcal/day
Trans-fat		≤0.5% kcal/day			
Cholesterol					≤71.4 mg/1,000 kcal
Sodium	≤1.1 g/1,000 kcal	Lowest decile (mg/day): M: ≤1,609; W: ≤1,242		First quintile (mg/day): M: ≤1970; W: ≤1,531	≤1,143 mg/1,000 kcal
Red and processed meats		0 servings/day	< median (ounce eq/day): M: 2.19; W: 1.27	First quintile (ounce eq/day): M: ≤1.1; W: ≤0.6	
SSB and fruit juices		0 servings/day		First quintile (cup eq/day) M: ≤0.2; W: ≤0.1	
Alcohol		drinks/day: M: 0.5–2.0; W: 0.5–1.5	M: 10–25; W: 5–15 g/day		
Grains, refined	≤1.8 ounce eq/1,000 kcal				
Added sugars	≤6.5% kcal/day				

Abbreviations: AHEI-2010, Alternative Healthy Eating Index-2010, aMed, alternate Mediterranean diet; DASH, Dietary Approaches to Stop Hypertension; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; eq, equivalent; HEI-2015, Healthy Eating Index-2015; M, men; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; SSB, sugar-sweetened beverages; W, women.

[a] Sex specific medians.

[b] Sex-specific quintiles.

for trend were based on a 1-standard-deviation increase in dietary quality score. We tested for confounding by the variables in Tables 2 and 3 beyond age and sex. A confounder was associated with both the dietary quality index and PDAC and changed the HRs by 10% or more (36). As none were confounders, all multivariable models adjusted for total energy intake (kcal/day) and putative risk factors for PDAC including for age at baseline (years, continuous), sex (for sex-combined analysis), smoking status (never smoker; quit >10 years ago, 5–9 years ago, 1–4 years ago, or <1 year ago; current smoker ≤20 cigarettes/day or >20 cigarettes/day; or missing), body mass index (calculated as weight (kg)/height $(m)^2$: <25.0, 25.0–29.9, ≥30.0, or missing), and diabetes (yes vs. no). We tested for interactions by sex, race/ethnicity (non-Hispanic White, non-Hispanic Black, and others; others include Hispanics, Asian, Pacific Islander or American Indian, and Alaskan Native), smoking (never/former quit >10 years ago, smoker/quit <10 years ago), body mass index (<25, ≥25), and alcohol consumption (<3 drinks/day, ≥3 drinks/day) (6) using likelihood ratio tests comparing regression models with and without multiplicative term for the continuous score of each diet quality index. Wald tests were used to determine *P* values per 1-standard-deviation score increase and *P* for interaction. We evaluated the proportional hazards assumption by modeling the interaction term for the continuous score of each diet quality index and follow-up time. All proportionality tests showed *P* values of >0.05, meaning insufficient evidence for violations of proportional hazards. We conducted sensitivity analyses including only first primary PDAC and 5-year lagged analyses, excluding cases that developed PDAC within the first 5 years of follow-up by delaying the start of follow-up for all participants, to evaluate potential effects of reverse causation.

To determine whether an association of adherence to diet indices and PDAC was mediated by a specific food or nutrient (37), exploratory analyses were conducted to examine independent associations for individual components. Separate HRs (95% CI) were calculated for each component (component *i*) with adjustment for modified scores that did not include the respective components as follows:

Modified score = total score – component *i* (38).

P values of <0.05 were considered statistically significant; however, to account for multiple comparisons across the 15 associations with the 5 diet quality indices (sex-combined, men, and women), we note associations that were significant below the Bonferroni-corrected *P* value of <0.003 (0.05/15). All statistical analyses were performed with SAS (version 9.4; SAS Institute, Inc., Cary, North Carolina), and statistical tests are 2-sided.

RESULTS

During up to 16 years of follow-up (median 15.5 years), 3,137 (1,988 men and 1,149 women) incident PDAC cases were identified. Sex-specific selected baseline characteristics by diet quality are shown in Table 2 for men and Table 3 for women. Across all indices in both men and women, those in the highest- compared with lowest-quintiles were more likely to be slightly older, a college graduate or postgraduate, leaner, physically active, multivitamin users, never or former smokers having quit ≥10 years ago, and less likely to consume ≥3 drinks/day (except for HEI-2015) (Tables 2 and 3). All the diet quality indices were correlated ($P < 0.0001$; Web Table 1), with the strongest correlations between AHEI-2010 and DASH-Fung ($r = 0.65$).

In sex-combined multivariable-adjusted models, participants with the highest diet quality compared with those with the lowest (quintile 5 vs. quintile 1) had significantly lower PDAC risk (for HEI-2015, HR = 0.84, 95% CI: 0.75, 0.94, *P* for trend = <0.0001; aMed, HR = 0.82, 95% CI: 0.73, 0.93, *P* for trend = 0.0004; DASH-Fung, HR = 0.85, 95% CI: 0.77, 0.95, *P* for trend = 0.004; and DASH-Mellen, HR = 0.86, 95% CI: 0.77, 0.96, *P* for trend = 0.006), except for AHEI-2010: HR = 0.93, 95% CI: 0.83, 1.04 (Table 4). Similar patterns were observed for continuous diet quality indices—per 1-standard-deviation increase for HEI-2015 (HR = 0.99, 95% CI: 0.99, 1.00), aMed (HR = 0.96, 95% CI: 0.94, 0.98), DASH-Fung (HR = 0.99, 95% CI: 0.98, 1.00), and DASH-Mellen (HR = 0.97, 95% CI: 0.95, 0.99). HEI-2015 and aMed diet quality indices remained statistically significant with PDAC risk below the Bonferroni-corrected *P* value of <0.003. As a sensitivity analysis to evaluate potentially unmeasured confounding, we calculated the E-value for the continuous scores of diet quality indices for the significant associations in sex combined analyses (39, 40). The E-value represents the minimum association in terms of relative risk that an unmeasured confounder would need to have per 1-standard-deviation increase of the diet quality index with PDAC to fully explain the observed association (39, 40). The calculated E-values are 1.10 for HEI-2015, 1.24 for aMed, 1.13 for DASH-Fung, and 1.21 for DASH-Mellen. The small E-values suggest small unmeasured confounding could explain our observed associations.

Although interaction by sex was not statistically significant (*P* for interaction > 0.07 for all indices), the pattern of associations for adherence to 4 of the diet quality indices differed by sex (Tables 5 and 6). In men, the highest- compared with the lowest-quintile diet quality scores were statistically significantly associated with a lower PDAC risk for HEI-2015 (HR = 0.78, 95% CI: 0.68, 0.90), aMed (HR = 0.85, 95% CI: 0.74, 0.98), DASH-Fung (HR = 0.77, 95% CI: 0.66, 0.90), and DASH-Mellen (HR = 0.82, 95% CI: 0.71, 0.95), except for AHEI-2010 (HR = 0.89, 95% CI: 0.77, 1.02). Similar patterns were observed for continuous dietary pattern scores per 1-standard-deviation increase (for HEI-2015, HR = 0.99, 95% CI: 0.99, 1.00, *P* for trend < 0.0001; aMed, HR = 0.97, 95% CI: 0.95, 1.00, *P* for trend = 0.04; DASH-Fung, HR = 0.98, 95% CI: 0.97, 0.99, *P* for trend = 0.002; and DASH-Mellen: HR = 0.95, 95% CI: 0.93, 0.98, *P* for trend = 0.0006). The HEI-2015, DASH-Fung, and DASH-Mellen were significantly associated with PDAC risk below the Bonferroni threshold. In women, only aMed diet quality showed a statistically significant association with PDAC, with those in the highest quintile having a lower risk (HR = 0.76, 95% CI: 0.63, 0.92). Similarly, when evaluating the aMed score as a continuous measure, scores were inversely

Table 2. Baseline Characteristics According to Quintile[a] of Dietary Index for Men (n = 315,780), National Institutes of Health–AARP Diet and Health Study, United States 1995–2011

Characteristic	HEI-2015 Quintiles						AHEI-2010 Quintile						aMed Quintile					
	1		3		5		1		3		5		1		3		5	
	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%
Median score	52.5 (5.1)		67.7 (1.5)		79.5 (3.2)		38.5 (4.1)		52.0 (1.5)		66.4 (4.8)		2.5 (0.7)		5.0 (0.0)		7.4 (0.6)	
Age at baseline, years	61.5 (5.5)		62.3 (5.3)		63.1 (5.1)		61.9 (5.5)		62.3 (5.3)		62.6 (5.2)		62.1 (5.4)		62.3 (5.3)		62.5 (5.2)	
Self-reported race[b]																		
Non-Hispanic White		92.8		92.3		93.1		92.9		92.4		92.8		92.9		92.5		92.8
Non-Hispanic Black		2.6		2.6		2.8		3.1		2.8		2.1		2.4		2.8		3.0
Others		3.2		3.9		3.1		2.6		3.7		4.0		3.3		3.7		3.3
College graduate or postgraduate		32.1		45.7		54.6		34.0		44.0		56.2		37.1		45.1		52.1
Body mass index[c]	27.5 (4.7)		27.5 (4.3)		26.6 (3.9)		27.5 (4.5)		27.4 (4.3)		26.7 (4.1)		27.4 (4.4)		27.3 (4.3)		27.0 (4.3)	
Smoking																		
Never smoker		23.3		29.5		33.5		26.5		29.4		31.0		24.0		28.9		34.7
Quit ≥10 years ago		35.5		45.6		49.1		37.5		44.3		49.6		40.5		44.7		46.2
Quit 1–9 years ago		13.2		11.4		8.9		12.6		11.1		9.8		13.0		11.4		9.0
Current smoker or stopped within 1 year		23.7		9.7		4.9		19.4		11.3		6.0		18.2		11.1		6.5
Self-reported diabetes		9.1		11.0		10.1		9.1		10.9		9.9		9.3		10.9		10.2
Physical activity ≥20 minutes, ≥5×/week		14.9		20.5		29.3		15.1		20.1		29.8		15.0		21.5		29.1
Regular multivitamin use		44.3		52.4		58.7		46.5		52.1		57.0		46.5		52.1		57.9
Alcohol intake, ≥3 drinks/day		9.8		11.4		10.2		20.6		10.1		3.0		20.1		9.4		3.2
Mean daily dietary intake																		
Energy, kcals/day	2,243 (999)		1,992 (816)		1,836 (688)		2,104 (903)		1,987 (845)		1,984 (774)		1,730 (808)		2,007 (798)		2,365 (843)	
Red meat, ounce eq/1,000 kcal	1.2 (0.7)		1.0 (0.6)		0.7 (0.4)		1.1 (0.7)		1.0 (0.6)		0.7 (0.5)		1.1 (0.7)		0.9 (0.6)		0.7 (0.5)	
Processed meat, ounce eq/1,000 kcal	1.0 (1.0)		0.7 (0.7)		0.5 (0.5)		1.0 (0.9)		0.7 (0.7)		0.4 (0.6)		0.7 (0.7)		0.7 (0.7)		0.7 (0.7)	

Table continues

Table 2. Continued

Characteristic	DASH-Fung Quintile						DASH-Mellen Quintile					
	1		3		5		1		3		5	
	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%
Median score	18.5 (1.6)		24.0 (0.0)		29.4 (1.6)		1.1 (0.4)		3.2 (0.2)		5.8 (0.8)	
Age at baseline, years	61.5 (5.5)		62.4 (5.3)		62.8 (5.2)		61.8 (5.4)		62.3 (5.3)		62.8 (5.2)	
Self-reported race[b]												
Non-Hispanic White		90.9		93.3		93.5		92.7		92.9		92.4
Non-Hispanic Black		3.6		2.6		2.1		3.6		2.6		2.1
Others		4.1		3.1		3.4		2.6		3.4		4.3
College graduate or postgraduate		35.9		45.0		52.6		36.8		44.1		52.0
Body mass index[c]	27.5 (4.5)		27.4 (4.3)		24.7 (4.2)		27.6 (4.6)		27.5 (4.3)		26.6 (4.0)	
Smoking												
Never smoker		24.0		28.9		34.5		26.4		28.0		32.8
Quit ≥10 years ago		38.3		44.7		47.1		38.0		44.6		47.8
Quit 1–9 years ago		13.5		11.2		8.9		12.3		11.5		9.9
Current smoker or stopped within 1 year		20.0		11.3		5.8		19.6		12.0		5.5
Self-reported diabetes		8.2		10.6		11.6		7.3		11.0		11.5
Physical activity ≥20 minutes, ≥5×/week		14.1		20.0		31.4		15.9		19.4		30.1
Regular multivitamin use		44.8		51.7		58.6		45.4		51.5		58.3
Alcohol intake, ≥3 drinks/day		16.2		10.5		6.4		12.0		12.1		5.6
Mean daily dietary intake												
Energy, kcals/day	1,914 (847)		1,989 (833)		2,181 (829)		2,231 (917)		2,006 (817)		1,745 (711)	
Red meat, ounce eq/1,000 kcal	1.3 (0.7)		0.9 (0.5)		0.6 (0.4)		1.2 (0.6)		1.0 (0.6)		0.6 (0.4)	
Processed meat, ounce eq/1,000 kcal	0.9 (0.9)		0.7 (0.7)		0.5 (0.6)		1.0 (0.9)		0.7 (0.7)		0.5 (0.6)	

Abbreviations: AHEI-2010, Alternative Heathy Eating Index; aMed, alternate Mediterranean diet; DASH, Dietary Approaches to Stop Hypertension; eq, equivalent; HEI-2015, Healthy Eating Index-2015; SD, standard deviation.

[a] Quintile 1, lowest; quintile 3, middle; quintile 5, highest.

[b] Other races/ethnicities include Hispanic, Asian, Pacific Islander or American Indian, and Alaskan Native.

[c] Weight (kg)/height $(m)^2$.

Table 3. Baseline Characteristics According to Quintile[a] of Dietary Index for Women (n = 220,044), National Institutes of Health–AARP Diet and Health Study, United States, 1995–2011

Characteristic	HEI-2015 Quintile						AHEI-2010 Quintile						aMed Quintile					
	1		3		5		1		3		5		1		3		5	
	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%
Median score	54.6 (5.4)		69.7 (1.4)		80.6 (3.0)		39.8 (3.9)		52.4 (1.4)		66.2 (4.5)		2.6 (0.6)		5.0 (0.0)		7.4 (0.6)	
Age at baseline, years	61.3 (5.5)		61.9 (5.4)		62.7 (5.2)		61.7 (5.5)		62.0 (5.4)		62.0 (5.4)		61.8 (5.5)		61.9 (5.4)		62.1 (5.3)	
Self-reported race[b]																		
Non-Hispanic White		90.6		89.5		89.3		89.4		89.4		90.5		91.6		90.0		87.2
Non-Hispanic Black		4.9		5.3		6.1		6.2		5.5		4.4		3.8		5.2		7.4
Others		2.8		3.7		3.3		2.6		3.5		3.7		2.8		3.4		3.9
College graduate or postgraduate		21.1		30.7		37.1		21.7		29.1		39.9		24.3		30.1		35.8
Body mass index[c]	27.6 (6.7)		26.9 (5.9)		26.0 (5.5)		27.4 (6.4)		27.1 (6.3)		25.9 (5.7)		26.9 (6.1)		26.9 (6.0)		26.7 (6.0)	
Smoking																		
Never smoker		37.9		44.5		47.0		44.5		44.6		40.2		38.4		43.6		48.4
Quit ≥10 years ago		19.4		26.5		30.8		19.5		25.1		33.3		22.4		26.3		28.7
Quit 1–9 years ago		11.2		11.0		10.3		10.2		11.3		11.8		11.7		11.4		9.5
Current smoker or stopped within 1 year		27.9		14.4		8.6		22.4		15.6		11.0		23.8		15.4		9.9
Self-reported diabetes		7.3		7.6		7.3		7.8		7.6		6.6		6.9		7.6		7.7
Physical activity ≥20 minutes, ≥5×/week		10.2		15.8		22.7		10.5		15.2		23.9		11.2		15.9		21.6
Regular multivitamin use		52.5		61.4		66.2		55.4		60.6		65.1		55.0		60.5		66.9
Alcohol intake, ≥3 drinks/day		2.8		2.8		2.4		5.9		2.3		0.8		6.0		2.3		0.5
Mean daily dietary intake																		
Energy, kcals/day	1,686 (758)		1,155 (643)		1,485 (565)		1,565 (647)		1,544 (665)		1,643 (655)		1,225 (519)		1,560 (596)		1,960 (695)	
Red meat, ounce eq/1,000 kcal	1.0 (0.6)		0.8 (0.5)		0.5 (0.4)		1.0 (0.6)		0.8 (0.5)		0.5 (0.4)		1.0 (0.6)		0.8 (0.5)		0.6 (0.4)	
Processed meat, ounce eq/1,000 kcal	0.5 (0.6)		0.4 (0.5)		0.3 (0.3)		0.5 (0.6)		0.4 (0.5)		0.3 (0.4)		0.4 (0.5)		0.4 (0.5)		0.4 (0.5)	

Table continues

Table 3. Continued

Characteristic	DASH-Fung Quintile						DASH-Mellen Quintile					
	1		3		5		1		3		5	
	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%
Median score	18.5 (1.2)		23.5 (0.5)		29.4 (1.6)		1.4 (0.6)		3.7 (0.2)		6.7 (0.6)	
Age at baseline, years	61.4 (5.4)		62.0 (5.4)		62.4 (5.3)		61.5 (5.4)		61.9 (5.4)		62.5 (5.3)	
Self-reported race[b]												
Non-Hispanic White		87.8		90.0		90.5		89.1		89.5		90.6
Non-Hispanic Black		7.0		5.2		4.6		6.7		5.6		4.0
Others		3.4		3.3		3.5		2.8		3.3		3.8
College graduate or postgraduate		22.4		29.2		38.0		23.1		29.4		37.4
Body mass index[c]	27.4 (6.4)		27.1 (6.1)		26.1 (5.8)		27.7 (6.6)		27.0 (6.0)		25.8 (5.3)	
Smoking												
Never smoker		38.6		43.5		47.1		40.6		43.7		45.4
Quit ≥10 years ago		20.3		25.9		31.0		20.8		25.8		30.7
Quit 1–9 years ago		11.6		11.3		9.8		11.0		11.2		11.0
Current smoker or stopped within 1 year		25.8		15.7		8.7		24.3		15.7		9.1
Self-reported diabetes		7.1		7.7		7.7		6.8		8.0		7.1
Physical activity ≥20 minutes, ≥5×/week		9.7		14.6		24.6		10.1		14.8		25.2
Regular multivitamin use		52.4		60.4		66.8		54.0		61.0		66.0
Alcohol intake, ≥3 drinks/day		5.1		2.7		1.2		3.7		3.8		0.5
Mean daily dietary intake												
Energy, kcals/day	1,393 (602)		1,528 (629)		1,791 (683)		1,791 (741)		1,570 (648)		1,389 (557)	
Red meat, ounce eq/1,000 kcal	1.1 (0.6)		0.8 (0.5)		0.4 (0.3)		1.0 (0.6)		0.8 (0.5)		0.4 (0.3)	
Processed meat, ounce eq/1,000 kcal	0.5 (0.6)		0.4 (0.5)		0.2 (0.4)		0.5 (0.6)		0.4 (0.5)		0.2 (0.3)	

Abbreviations: AHEI-2010, Alternative Heathy Eating Index; aMed, alternate Mediterranean diet; DASH, Dietary Approaches to Stop Hypertension; eq, equivalent; HEI-2015, Healthy Eating Index-2015.

[a] Quintile 1, lowest; quintile 3, middle; quintile 5, highest.

[b] Other races/ethnicities include Hispanic, Asian, Pacific Islander or American Indian, and Alaskan Native.

[c] Weight (kg)/height $(m)^2$.

Table 4. Sex-Combined Hazard Ratios for Pancreatic Ductal Adenocarcinoma According to Quintile of Dietary Index (n = 535,824) in the National Institutes of Health–AARP Diet and Health Study, United States, 1995–2011

Diet Quality	No.	Person-Years	No. of PDAC Cases	Age- and Sex-Adjusted HR[a]	95% CI	*P* for Trend[b]	Multivariable-Adjusted HR[c]	95% CI	*P* for Trend[b]
HEI-2015									
Quintile 1 (lowest)	107,165	1,408,256	649	1.00	Referent		1.00	Referent	
Quintile 2	107,165	1,429,681	657	0.96	0.86, 1.07		0.97	0.87, 1.09	
Quintile 3	107,165	1,440,965	629	0.89	0.80, 0.99		0.91	0.82, 1.02	
Quintile 4	107,165	1,449,913	598	0.82	0.74, 0.92		0.85	0.76, 0.95	
Quintile 5 (highest)	107,164	1,461,910	604	0.80	0.71, 0.89		0.84	0.75, 0.94	
Continuous[b]				0.99	0.99, 0.99	<0.0001	0.99	0.99, 1.00	<0.0001
AHEI-2010									
Quintile 1 (lowest)	107,165	1,408,789	628	1.00	Referent		1.00	Referent	
Quintile 2	107,165	1,426,679	607	0.93	0.83, 1.04		0.94	0.84, 1.05	
Quintile 3	107,165	1,439,012	633	0.95	0.85, 1.06		0.96	0.86, 1.04	
Quintile 4	107,165	1,448,879	641	0.95	0.85, 1.06		0.96	0.86, 1.08	
Quintile 5 (highest)	107,164	1,467,366	628	0.91	0.82, 1.02		0.93	0.83, 1.04	
Continuous[b]				1.00	0.99, 1.00	0.11	1.00	0.99, 1.00	0.25
aMed									
Quintile 1 (lowest)	121,940	1,605,797	752	1.00	Referent		1.00	Referent	
Quintile 2	101,616	1,357,028	632	0.98	0.88, 1.09		0.98	0.88, 1.09	
Quintile 3	110,164	1,480,186	627	0.89	0.80, 0.99		0.88	0.79, 0.98	
Quintile 4	126,137	1,318,288	548	0.86	0.77, 0.96		0.85	0.77, 0.95	
Quintile 5 (highest)	75,967	1,429,426	578	0.83	0.75, 0.93		0.82	0.73, 0.93	
Continuous[b]				0.96	0.95, 0.98	0.003	0.96	0.94, 0.98	<0.0001
DASH-Fung									
Quintile 1 (lowest)	137,469	1,821,046	836	1.00	Referent		1.00	Referent	
Quintile 2	102,388	1,370,756	585	0.89	0.80, 0.99		0.90	0.81, 1.00	
Quintile 3	110,007	1,478,219	644	0.90	0.81, 0.99		0.90	0.81, 1.00	
Quintile 4	92,204	1,244,921	534	0.87	0.78, 0.97		0.88	0.79, 0.98	
Quintile 5 (highest)	93,756	1,275,784	538	0.84	0.76, 0.94		0.85	0.77, 0.95	
Continuous[b]				0.98	0.98, 0.99	0.001	0.99	0.98, 1.00	0.004
DASH-Mellen									
Quintile 1 (lowest)	145,245	1,926,722	895	1.00	Referent		1.00	Referent	
Quintile 2	112,929	1,508,785	663	0.92	0.84, 1.02		0.92	0.83, 1.02	
Quintile 3	111,671	1,501,068	640	0.88	0.80, 0.97		0.89	0.80, 0.99	
Quintile 4	81,945	1,111,486	468	0.86	0.77, 0.96		0.88	0.79, 0.99	
Quintile 5 (highest)	84,034	1,142,666	471	0.83	0.74, 0.93		0.86	0.77, 0.96	
Continuous[b]				0.96	0.95, 0.98	<0.0001	0.97	0.95, 0.99	0.006

Abbreviations: AHEI-2010, Alternative Heathy Eating Index; aMed, alternate Mediterranean diet; CI, confidence interval; DASH, Dietary Approaches to Stop Hypertension; HEI-2015, Healthy Eating Index-2015; HR, hazard ratio; PDAC, pancreatic ductal adenocarcinoma.

[a] Estimated using Cox proportional hazard regression model with person-years as the underlying time metric. HRs compares the risk of developing PDAC for participants in each quintile of diet quality score compared with participants in the lowest quintile (lower adherence).

[b] HRs (95% CIs) and *P* for trend per 1-standard deviation increase.

[c] Multivariable models adjusted for age at baseline (years, continuous), sex, smoking status (never smoker, quit >10 years ago, quit 5–9 years ago, quit 1–4 years ago, quit <1 year or current smoker ≤20 cigarettes/day, quit <1 year or current smoker >20 cigarettes/day, or missing), body mass index (weight (kg)/height (m)^2: <25.0, 25.0–29.9, ≥30.0, or missing), diabetes (yes vs. no), and total energy intake (kcal/day).

associated with PDAC (HR = 0.94, 95% CI: 0.91, 0.98; *P* for trend = 0.001), which remained statistically significant after Bonferroni correction.

Table 7 shows the results for the exploratory analyses of components separately for each dietary pattern score. With the HEI-2015, greater alignment with the diet quality index recommendations (for whole grains (HR = 0.98, 95% CI: 0.96, 0.99), dairy (HR = 0.99, 95% CI: 0.98, 1.00), and saturated fat (HR = 0.99, 95% CI: 0.97, 1.00) were inversely associated with risk of PDAC, while added sugars (HR = 1.02, 95% CI: 1.00, 1.03) were positively associated with PDAC risk ($P < 0.05$). With the aMed, more optimal alignment with the recommendations for red and processed meat (HR = 0.92, 95% CI: 0.85, 0.99) and alcohol (HR = 0.87, 95% CI: 0.79, 0.96) consumption was associated with lower risk ($P < 0.05$). With the DASH-Fung, greater alignment with recommendations for total fruits (HR = 0.97, 95% CI: 0.95, 1.00) and whole grains (HR = 0.96, 95% CI: 0.94, 0.99) were inversely associated, whereas the sweetened beverages consumption component (HR = 1.04, 95% CI: 1.01, 1.06) was positively associated with PDAC risk ($P < 0.05$). Last, with the DASH-Mellen, more optimal alignment with calcium was associated with reduced risk (HR = 0.89, 95% CI: 0.80, 0.99).

There was a statistically significant interaction (*P* for interaction = 0.01) by smoking for the DASH-Mellen dietary pattern score, where current smokers or those who quit <10 years ago in the highest quintile (quintile 5 vs. quintile 1) had a lower risk (HR = 0.74, 95% CI: 0.58, 0.94, *P* for trend = 0.002) while no association was present in never smokers or those who quit ≥10 years ago (HR = 0.97, 95% CI: 0.85, 1.12; *P* for trend = 0.87) (Web Table 2). There were no other significant interactions by smoking, race, body mass index, or alcohol consumption. All analyses were proportional over time ($P > 0.05$). Overall, in 5-year lagged analyses, the HEI-2015 and aMed remained significantly associated with PDAC but DASH-Fung and DASH-Mellen did not (Web Table 3).

DISCUSSION

In this large cohort of middle-aged and older adults, greater adherence to diet quality indices was associated with lower PDAC risk. Comparing the highest with the lowest quintiles of adherence, 4 diet quality indices—HEI-2015, aMed, and 2 versions of DASH—were associated with a 15%–18% lower risk of PDAC. For women, only aMed adherence remained significant, with a 24% lower PDAC risk.

Previous studies have examined HEI-2005 and various versions of Mediterranean diet scores and PDAC risks (25–27, 41, 42). Consistent with our findings, an earlier analysis in NIH-AARP (n = 2,383 cases) showed a 15% overall lower PDAC risk with higher adherence to HEI-2005 (26). The HEI-2015 differs from the HEI-2005 to reflect evolving dietary guidance and more specific construction of the score, including the addition of the greens and beans component (replacing dark-green and orange vegetables and legumes), total protein foods and seafood and plant protein (replacing meat and beans), fatty acid ratio (replacing oils and saturated fat), refined grains as a moderation component (replacing the adequacy component total grains), and separate components for added sugars and saturated fat (replacing the empty calories from solid fat, alcohol, and added sugars components). Our study showed the most robust association with higher adherence to the aMed score, with an 18% lower PDAC risk overall and significant inverse associations in both men and women. The aMed score uses population-specific medians, and the composition of other Mediterranean diet scores may differ across studies. An Italian hospital-based case-control study showed a statistically significant inverse association with greater adherence to the traditional (Greek) Mediterranean diet score and pancreatic cancer risk (n = 688 cases) (41). These contrast with the nonsignificant inverse associations or null associations observed in earlier analyses, including a pooled analysis of 2 Dutch cohorts examining the aMed and modified Mediterranean diet scores both with and without alcohol (n = 449 cases) (27) and an analysis in the European Prospective Investigation into Cancer and Nutrition cohort examining an adapted Mediterranean diet score without alcohol (n = 865 cases) (25). A recent analysis comparing 4 diet quality indices in the Singapore Chinese Health Study cohort and pancreatic cancer risk (n = 311 cases) suggested inverse associations with higher adherence to the AHEI-2010, aMed, and DASH-Fung, whereas the nutrient-based Healthy Diet Indicator was associated with higher risks (43). In this study of Chinese participants, pancreatic cancer incident cases included PDAC and those of unknown histology (43). Our present study included more PDAC cases than these earlier cohort studies and has more power to observe associations.

Data-driven dietary pattern approaches, including factor and principal components analyses, have shown inconsistent associations with pancreatic cancer (42, 44–46). A limitation of these approaches is that study-specific dietary patterns cannot be compared across studies. Inverse prospective PDAC associations have been observed for a priori–defined dietary pattern scores including total antioxidant capacity (47, 48), 2018 World Cancer Research Fund/American Institute for Cancer Research cancer prevention recommendations (49), and as components within healthy lifestyle scores (28, 50); the last 2 scores include both dietary and lifestyle components, such as body mass index and physical activity. Scores representing the inflammatory potential of diet have been inconsistently associated with pancreatic cancer in prospective studies (51–53).

We observed significant associations in men, but not women, when defining diet quality with the HEI-2015 and the 2 DASH scores, although the interaction by sex was not significant. This could be due to differences in self-reported dietary intake, sex-related biological effects of diet, the larger proportion of male participants in NIH-AARP, or dietary score construction. The aMed showed similar and significant associations in both men and women. The HEI-2015 and DASH-Mellen used the same cutpoints for men and women, and they had food or nutrient components that were energy-density adjusted (Table 1), while the DASH-Fung used sex-specific quintile cutpoints for all components. None of these included the alcohol component in the

Table 5. Hazard Ratios for Pancreatic Ductal Adenocarcinoma According to Quintile of Dietary Index for Men (n = 315,780) in the National Institutes of Health–AARP Diet and Health Study, United States, 1995–2011

Diet Quality	No.	Person-Years	No. of PDAC Cases	Age-Adjusted HR[a]	95% CI	*P* for Trend[b]	Multivariable-Adjusted HR[c]	95% CI	*P* for Trend[b]
HEI-2015									
Quintile 1 (lowest)	63,156	816,953	421	1.00	Referent		1.00	Referent	
Quintile 2	63,156	828,856	422	0.95	0.83, 1.09		0.96	0.83, 1.09	
Quintile 3	63,156	836,086	391	0.85	0.74, 0.98		0.86	0.75, 0.99	
Quintile 4	63,156	841,643	381	0.80	0.70, 0.92		0.82	0.72, 0.95	
Quintile 5 (highest)	63,156	849,410	373	0.75	0.66, 0.87		0.78	0.68, 0.90	
Continuous[b]				0.99	0.99, 0.99	<0.0001	0.99	0.99, 1.00	<0.0001
AHEI-2010									
Quintile 1 (lowest)	63,156	816,127	404	1.00	Referent		1.00	Referent	
Quintile 2	63,156	826,876	390	0.93	0.81, 1.06		0.93	0.81, 1.07	
Quintile 3	63,156	833,982	405	0.94	0.82, 1.08		0.95	0.83, 1.09	
Quintile 4	63,156	841,860	397	0.91	0.79, 1.04		0.92	0.80, 1.05	
Quintile 5 (highest)	63,156	854,104	392	0.87	0.76, 1.00		0.89	0.77, 1.02	
Continuous[b]				1.00	0.99, 1.00	0.03	1.00	0.99, 1.00	0.07
aMed									
Quintile 1 (lowest)	74,653	967,310	480	1.00	Referent		1.00	Referent	
Quintile 2	59,913	787,764	398	1.00	0.88, 1.14		1.00	0.88, 1.14	
Quintile 3	64,601	854,540	391	0.90	0.79, 1.03		0.90	0.78, 1.02	
Quintile 4	56,399	753,150	360	0.94	0.82, 1.07		0.93	0.81, 1.07	
Quintile 5 (highest)	60,214	810,185	359	0.86	0.75, 0.98		0.85	0.74, 0.98	
Continuous[b]				0.97	0.95, 1.00	0.03	0.97	0.95, 1.00	0.04
DASH-Fung									
Quintile 1 (lowest)	55,786	727,251	376	1.00	Referent		1.00	Referent	
Quintile 2	85,120	1,119,633	531	0.88	0.77, 1.00		0.88	0.77, 1.00	
Quintile 3	32,847	434,230	214	0.89	0.76, 1.06		0.89	0.76, 1.06	
Quintile 4	86,892	1,152,784	543	0.84	0.74, 0.96		0.84	0.74, 0.96	
Quintile 5 (highest)	55,135	739,051	324	0.77	0.66, 0.89		0.77	0.66, 0.90	
Continuous[b]				0.98	0.97, 0.99	0.0009	0.98	0.97, 0.99	0.002
DASH-Mellen									
Quintile 1 (lowest)	55,145	720,680	360	1.00	Referent		1.00	Referent	
Quintile 2	61,838	811,813	431	1.04	0.91, 1.20		1.04	0.90, 1.19	
Quintile 3	71,040	937,207	432	0.89	0.77, 1.02		0.89	0.77, 1.02	
Quintile 4	59,862	794,981	371	0.89	0.77, 1.03		0.90	0.77, 1.04	
Quintile 5 (highest)	67,895	908,269	394	0.81	0.70, 0.93		0.82	0.71, 0.95	
Continuous[b]				0.95	0.93, 0.98	0.0002	0.95	0.93, 0.98	0.0006

Abbreviations: AHEI-2010, Alternative Healthy Eating Index-2010; aMed, alternate Mediterranean diet; CI, confidence interval; DASH, Dietary Approaches to Stop Hypertension; HEI-2015, Healthy Eating Index-2015; HR, hazard ratio; PDAC, pancreatic ductal adenocarcinoma.

[a] Estimated using Cox proportional hazard regression model with person-years as the underlying time metric. HRs compares the risk of developing PDAC for participants in each quintile of diet quality score compared with participants in the lowest quintile (lower adherence).

[b] Hazard ratios and *P* for trend per 1-standard deviation increase. *P* for interaction by sex > 0.07 for all scores.

[c] Multivariable models adjusted for age at baseline (years, continuous), smoking status (never smoker, quit >10 years ago, quit 5–9 years ago, quit 1–4 years ago, quit <1 year or current smoker ≤20 cigarettes/day, quit <1 year or current smoker >20 cigarettes/day, or missing), body mass index (weight (kg)/height (m)^2: <25.0, 25.0–29.9, ≥30.0, or missing), diabetes (yes vs. no), and total energy intake (kcal/day).

Table 6. Hazard Ratios for Pancreatic Ductal Adenocarcinoma According to Quintile of Dietary Index for Women (n = 220,044) in the National Institutes of Health–AARP Diet and Health Study, United States, 1995–2011

Diet Quality	No.	Person-Years	No. of PDAC Cases	Age-Adjusted HR[a]	95% CI	*P* for Trend[b]	Multivariable-Adjusted HR[c]	95% CI	*P* for Trend[b]
HEI-2015									
Quintile 1 (lowest)	44,008	591,288	228	1.00	Referent		1.00	Referent	
Quintile 2	44,009	600,825	235	0.98	0.82, 1.17		1.01	0.84, 1.21	
Quintile 3	44,009	604,882	238	0.97	0.81, 1.16		1.02	0.85, 1.22	
Quintile 4	44,009	608,267	217	0.85	0.71, 1.03		0.91	0.75, 1.10	
Quintile 5 (highest)	44,009	612,515	231	0.87	0.73, 1.05		0.94	0.78, 1.13	
Continuous[b]				0.99	0.99, 1.00	0.03	1.00	0.99, 1.00	0.19
AHEI-2010									
Quintile 1 (lowest)	44,008	592,646	224	1.00	Referent		1.00	Referent	
Quintile 2	44,009	599,802	217	0.94	0.78, 1.13		0.95	0.79, 1.14	
Quintile 3	44,009	605,031	228	0.97	0.81, 1.17		0.98	0.82, 1.18	
Quintile 4	44,009	607,019	244	1.03	0.86, 1.24		1.04	0.87, 1.25	
Quintile 5 (highest)	44,009	613,278	236	0.99	0.82, 1.19		1.00	0.83, 1.20	
Continuous[b]				1.00	1.00, 1.01	0.72	1.00	1.00, 1.01	0.67
aMed									
Quintile 1 (lowest)	47,287	638,487	272	1.00	Referent		1.00	Referent	
Quintile 2	41,703	569,264	234	0.95	0.80, 1.13		0.94	0.79, 1.12	
Quintile 3	45,563	625,646	236	0.87	0.73, 1.04		0.85	0.71, 1.02	
Quintile 4	40,898	565,138	188	0.76	0.63, 0.92		0.73	0.61, 0.89	
Quintile 5 (highest)	44,593	619,241	219	0.80	0.67, 0.96		0.76	0.63, 0.92	
Continuous[b]				0.95	0.92, 0.98	0.002	0.94	0.91, 0.98	0.001
DASH-Fung									
Quintile 1 (lowest)	39,796	536,336	206	1.00	Referent		1.00	Referent	
Quintile 2	37,296	509,020	200	0.99	0.81, 1.20		1.00	0.82, 1.22	
Quintile 3	44,623	612,127	218	0.88	0.73, 1.07		0.90	0.74, 1.08	
Quintile 4	59,708	823,561	311	0.92	0.77, 1.10		0.94	0.79, 1.12	
Quintile 5 (highest)	38,621	536,732	214	0.96	0.79, 1.16		0.98	0.80, 1.19	
Continuous[b]				0.99	0.98, 1.01	0.32	0.99	0.98, 1.01	0.47
DASH-Mellen									
Quintile 1 (lowest)	42,346	571,385	215	1.00	Referent		1.00	Referent	
Quintile 2	40,317	548,363	216	1.02	0.85, 1.23		1.04	0.86, 1.26	
Quintile 3	45,248	622,019	230	0.95	0.79, 1.14		0.98	0.82, 1.19	
Quintile 4	54,535	754,910	270	0.90	0.76, 1.08		0.96	0.80, 1.15	
Quintile 5 (highest)	37,598	521,099	218	1.03	0.85, 1.24		1.10	0.91, 1.34	
Continuous[b]				0.99	0.95, 1.02	0.38	1.00	0.97, 1.03	0.92

Abbreviations: AHEI-2010, Alternative Healthy Eating Index-2010; aMed, alternate Mediterranean diet; CI, confidence interval; DASH, Dietary Approaches to Stop Hypertension; HEI-2015, Healthy Eating Index-2015; HR, hazard ratio; PDAC, pancreatic ductal adenocarcinoma.

[a] Estimated using Cox proportional hazard regression model with person-years as the underlying time metric. HRs compares the risk of developing PDAC for participants in each quintile of diet quality score compared with participants in the lowest quintile (lower adherence).

[b] HRs (95% CI) and *P* for trend per 1-standard deviation increase. *P* for interaction by sex $>$ 0.07 for all scores.

[c] Multivariable models adjusted for age at baseline (years, continuous), smoking status (never smoker, quit $>$10 years ago, quit 5–9 years ago, quit 1–4 years ago, quit $<$1 year or current smoker $\leq$20 cigarettes/day, quit $<$1 year or current smoker $>$20 cigarettes/day, or missing), body mass index (weight (kg)/height (m)^2: $<$25.0, 25.0–29.9, $\geq$30.0, and missing), diabetes (yes vs. no), and total energy intake (kcal/day).

Table 7. Multivariable-Adjusted Hazard Ratios for Pancreatic Ductal Adenocarcinoma for Individuals Components of Dietary Index for Men and Women Combined (n = 535,824), National Institutes of Health–AARP Diet and Health Study, United States, 1995–2011

Diet Quality Component	Diet Quality Index									
	HEI-2015		AHEI-2010		aMed		DASH-Fung		DASH-Mellen	
	HR[a,b]	95% CI	HR[a,b]	95% CI	HR[a,b]	95% CI	HR[a,b]	95% CI	HR[a,b]	95% CI
Adequacy Components										
Calcium									0.89	0.80, 0.99[c]
Fiber									0.90	0.79, 1.01
Magnesium									0.99	0.85, 1.16
Potassium									1.03	0.90, 1.18
Protein									1.07	0.98, 1.17
MUFA: saturated fat					0.93	0.87, 1.00				
PUFA			1.01	1.00, 1.02						
PUFA+MUFA: saturated fat	0.99	0.98, 1.00								
EPA+DHA			1.00	0.98, 1.01						
Fruits, total	0.97	0.94, 1.00			0.94	0.87, 1.01	0.97	0.95, 1.00[c]		
Fruits, whole	0.97	0.94, 1.00	0.99	0.98, 1.00						
Grains, whole	0.98	0.96, 0.99[c]	0.95	0.93, 0.98[c]	0.94	0.88, 1.02	0.96	0.94, 0.99[c]		
Vegetables	1.02	0.98, 1.05	0.99	0.98, 1.01	1.00	0.93, 1.08	0.99	0.96, 1.02		
Greens and beans	0.99	0.97, 1.01								
Total protein foods	1.02	0.98, 1.06								
Seafood and plant protein	0.99	0.96, 1.02								
Fish					1.07	1.00, 1.16				
Legumes					0.96	0.89, 1.03				
Nuts					1.00	0.93, 1.07				
Nuts and legumes			0.99	0.98, 1.00[c]			0.98	0.95, 1.00		
Dairy	0.99	0.98, 1.00[c]								
Low-fat dairy							0.98	0.95, 1.00		
Moderation Components										
Total fat									1.01	0.92, 1.12
Saturated fat	0.99	0.97, 1.00[c]							0.97	0.84, 1.11
Trans-fat			1.01	1.00, 1.03						
Cholesterol									0.91	0.82, 1.01
Sodium	1.00	0.98, 1.01	1.01	0.99, 1.03			1.01	0.97, 1.05	0.96	0.81, 1.13
Red and processed meat			0.99	0.97, 1.00	0.92	0.85, 0.99[c]	0.98	0.95, 1.01		
SSB and fruit juices			1.01	1.00, 1.02[c]			1.04	1.01, 1.06[c]		
Alcohol			0.99	0.98, 1.00	0.87	0.79, 0.96[c]				
Grains, refined	1.01	0.99, 1.02								
Added sugars	1.02	1.00, 1.03[c]								

Abbreviations: AHEI-2010, Alternative Healthy Eating Index-2010; aMed, alternate Mediterranean diet; CI, confidence interval; DASH, Dietary Approaches to Stop Hypertension; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; HEI-2015, Healthy Eating Index-2015; HR, hazard ratio; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; SSB, sugar-sweetened beverages.

[a] The HR is based on a 1-unit change in the score for the component of interest (meeting the recommendations vs. not meeting the recommendations).

[b] Multivariable models mutually adjusted for components by each score and also adjusted by age at baseline (years, continuous), sex (for sex-combined analysis), smoking status (never smoker, quit >10 years ago, quit 5–9 years ago, quit 1–4 years ago, quit < 1 year or current smoker ≤ 20 cigarettes/day, quit < 1 year or current smoker > 20 cigarettes/day, or missing), body mass index (weight (kg)/height (m)^2: <25.0, 25.0–29.9, ≥30.0, or missing), diabetes (yes vs. no), and total energy intake (kcal/day).

[c] P values (2-sided) were statistically significant at <0.05

score. In contrast, the aMed's simplified dichotomous scoring approach based on intake above or below sex-specific median intake in NIH-AARP and moderate intake ranges for the alcohol component might have contributed to the significant associations in both men and women. The AHEI-2010 showed no significant associations for both sexes. This may be due to construction of the dietary score, including the scoring approach (e.g., absolute intake and maximum points given for consuming no red or processed meat, sugar sweetened beverages, or fruit juices), fatty acid components (e.g., polyunsaturated fat, eicosapentaenoic acid, docosahexaenoic acid, *trans*-fat), or other differences compared with the HEI-2015, aMed, and DASH-Fung.

In our exploratory by-component analyses, we observed lower PDAC risk with lower consumption of red and processed meats and moderate alcohol consumption as defined by aMed but not as defined by AHEI-2010. Higher intakes of whole grains as defined by HEI-2015, AHEI-2010, and DASH-Fung—but not as defined by aMed—were associated with lower PDAC risk. The dairy and calcium components were inversely associated with PDAC as defined by HEI-2015 and DASH-Mellen, respectively; however, the low-fat dairy DASH-Fung component was not associated with PDAC. The differences in individual associations for components across the dietary scores are likely due to different cutpoints and comparison groups across the indices. For example, the aMed red and processed meat component (based on sex-specific median cutpoints) showed inverse associations. The AHEI-2010 and DASH-Fung red and processed meat component did not show associations. The AHEI-2010 scored optimal red and processed meat consumption as "none" and the DASH-Fung scored optimal red and processed meat consumption as the lowest sex-specific quintile. Compared with the other diet quality indices, the AHEI-2010 gives greater weight to fatty acids that have not been associated with PDAC in the NIH-AARP (10). Individual components of index-based diet quality are not meant to be interpreted independently, as they do not account for synergistic relationships.

Strengths of our study include its large prospective design, with dietary data collected on individuals prior to cancer diagnosis, and long follow-up time; thus, our results are less likely to be influenced by reverse causation and selection or recall biases and have internal validity. In addition to the uniform approach of calculating food components across scores following the Dietary Patterns Methods Project, dietary quality was based on public health guidelines or healthful eating recommendations that reflect a broad range of scientific evidence, including that from epidemiologic studies. Our study includes a large number of PDAC cases, as well as a wide distribution of dietary intake, providing greater power to detect differences and associations.

There are also limitations. Measurement error inherent to dietary assessment using FFQs is likely present and could result in inaccurate risk estimates. Diet was measured only at baseline; repeated measurements would increase the accuracy of the dietary assessment. As score-based dietary patterns are truncated and some individual components are dichotomized, these scores do not reflect the effects of excessive intakes of certain components (e.g., protein, total fruits including juices, or dairy products) and may not capture important information on differences in food and nutrient intake across individuals. Residual confounding and unmeasured exposures associated with both diet quality and PDAC could have influenced our observed associations. Most of the NIH-AARP Study participants are non-Hispanic White persons and our results might not be generalizable to other racial or ethnic groups. Future studies investigating dietary patterns and PDAC should include a more racially and ethnically diverse population.

In conclusion, results from this large prospective cohort support the hypothesis that greater adherence to dietary recommendations based on scientific evidence may reduce the risk of developing PDAC. Higher diet quality index scores have also been associated with lower risks of type 2 diabetes mellitus and body adiposity, known risk factors for PDAC, which could contribute to some of the associations we observe with PDAC. Diet quality represents an important potentially modifiable risk factor that could decrease the burden of pancreatic cancer.

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