Adherence to the Dietary Approaches to Stop Hypertension (DASH) diet and the risk of pancreatic cancer in the Pooling Project of Prospective Studies of Diet and Cancer (DCPP)

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Abstract:

Introduction:

Pancreatic cancer is one of the deadliest cancers on the rise with one of the lowest 5-year survival rates of just 10%. Since early detection is difficult, the identification of modifiable risk factors has been a priority in reducing incidence. Review of the literature shows a gap in research on how dietary patterns can affect pancreatic cancer incidence. This study evaluates the adherence to the Dietary Approach to Stop Hypertension (DASH) diet and the incidence of pancreatic cancer in a pooled consortium of prospective cohort studies.

Methods:

We conducted a pooled analysis from 13 different prospective cohort studies with a total of 820,661 participants. During the follow up period, 3,172 pancreatic cancer cases were identified. Stratified by sex, we used a Cox proportional hazards model to develop multivariable study-specific hazard ratios (HRs) and 95% confidence intervals for each study. The HRs were then combined using a random effects model to get a pooled-estimate HR for each sex. The exposure was examined continuously and in quartiles of DASH diet score. We also conducted one sub-analysis restricted to participants that were diagnosed with adenocarcinoma.

Results:

There were no statistically significant findings when examining the association between adherence to the DASH diet and pancreatic cancer risk in the multi-variable adjusted models, comparing those of highest adherence in Q4 to those of lowest adherence in Q1, for neither males nor females. The results remained null when examining the DASH diet on a continuous scale for both sexes. In a sub-analysis in which we limited the outcome definition to pancreatic adenocarcinoma, the association remained null.

Conclusion:

Our analysis does not provide evidence that adherence to the DASH diet can decrease the risk for pancreatic cancer. This conclusion does not change when evaluating just pancreatic adenocarcinoma risk. Further sensitivity analysis should be conducted on other high-risk factors such as smoking, obesity, and diabetes.

Introduction:

Pancreatic cancer is one of the deadliest cancers in the world. According to the World Cancer Research Fund (WCRF), in 2020, the age-standardized pancreatic cancer incidence rate was 4.9 for every 100,000 people.[22] In 2022, pancreatic cancer was the third most lethal cancer, being responsible for 8% of cancer deaths.[1] In parallel, it also has one of the lowest 5-year relative survival rates of invasive cancers, at 10%.[2] In the early stages, it is usually clinically silent and when symptoms do arise, the cancer has usually progressed to a more severe stage.[3] Thus, due to the delay to diagnose, detection of pancreatic cancer often occurs at the most advanced stage.[3] The combination of being one of the most deadliest cancers, as well as the gap in early detection, stresses the need to focus efforts on identifying factors that can prevent pancreatic cancer incidence.

There are several identified risk factors for pancreatic cancer such as smoking, obesity, genetics, diabetes, and lack of physical activity.[4] There has been inconsistent evidence on how diet can affect pancreatic cancer risk. Conflicting evidence regarding red meat consumption shows in one prospective study that high total and red meat intake were significantly associated with increased pancreatic cancer risk among men but not women[5]. However, in another cohort study, there was no overall association between red and processed meats and pancreatic cancer risk.[6] Regarding other food groups, high nut consumption or high fruit and vegetable intakes respectively show no association or an inverse association with pancreatic cancer risk.[7-8] Considering that certain combinations of food can have synergistic or antagonistic effects on health outcomes, examining dietary patterns that encompass all these food types may be more consistent and a better method to capture the relationship between diet and cancer.[9]

The Dietary Approaches to Stop Hypertension (DASH) diet encourages a diet that is high in the consumption of fruits, vegetables, nuts, low-fat dairy, and whole grains, and low in the consumption of red and processed meats, sweetened beverages, and sodium, originally with the aim to manage hypertension.[23] However, the outline of this dietary pattern is very similar to the dietary guidelines set forth by the WCRF to help prevent cancer.[10] A meta-analyses of prospective cohort studies was conducted using multiple dietary patterns, including DASH, to examine adherence and the effect on various health outcomes; results show that following these diets can lead to a significant reduction in cancer incidence by 16%.[11]

Yet, very few studies have examined the adherence to the DASH diet and pancreatic cancer risk. Two different case-control studies in Iran found an association between adherence to the DASH diet and breast and colorectal cancer risk; those in the highest quantile of the DASH diet score had a 34% reduction in risk of breast cancer and 96% reduction of risk in colorectal cancers compared to those in the lowest quantile.[12-13] However, issues of selection and recall bias can affect the results of case-control studies. To our knowledge, only three studies have been published that directly examined the association of the DASH diet with pancreatic cancer. The studies varied in results and significance of the exposure and outcome in many subgroup

analyses, such as by men (Q4 vs. Q1: 0.36 (0.19–0.66); p-value = 0.002), smoking status (Q4 vs. Q1: Ever smokers = 0.75, (0.61–0.93); p-value = 0.01), and obesity (Q4 vs. Q1: 0.79 (0.65–0.97); p-value = 0.08).[14-16] The number of cases per also varied from 3,137 cases to as low as 311 cases.[14-16] Compared to a pooled-analyses, cohort studies have insufficient statistical power due to fewer cases. A pooled-analyses of individual data has a larger sample and more cases than single prospective cohort studies and it can examine risk of disease with many exposures where previous studies have given inconsistent results.[17] With the urgency to find prevention guidelines for pancreatic cancer and the lack of both research and consistent results in examining for associations between the DASH diet and pancreatic cancer, we used the Pooling Project of Prospective Studies of Diet and Cancer (DCPP), an international consortium of 39 cohort studies examining dietary factors and cancer risk, to elucidate the association of adherence to the DASH diet and risk of pancreatic cancer.

Methods:

Study Population:

The DCPP is an international consortium of prospective cohort studies that have used validated food frequency questionnaires or other diet tools used to gather information on diet and then assess its association with incident cancer. Study participants are from many regions of the world including North America, Asia, Europe, and Oceania.

For this study, we conducted a pooled analysis with 13 cohort studies which had a total of 820,661 participants from the Pooling Project of Prospective Studies of Diet and Cancer (DCPP). To be included in the DCPP, prospective cohorts had to meet the following criteria: 1) have had at least one publication that looked at diet and cancer; 2) used a dietary assessment that satisfactorily recorded nutrient intakes overall and over time; 3) performed validation on the dietary assessment tool; 4) had a minimum of 50 of pancreatic cancer cases.[18] The studies that met this criterion and were included in this analysis were: the Breast Cancer Detection Demonstration Project Follow-up Study (BCDDP); CLUEII: Give us a Clue to Cancer (CLUEII); Cancer Prevention Study-II Nutrition Cohort (CPSII); Melbourne Collaborative Cohort Study (MCCS); Nurses' Health Study b (NHSb); Nurses' Health Study II (NHSII); The Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial USA (PLCO); Swedish Mammography Cohort (SMC); Women's Health Initiative (WHI); Women's Lifestyle and Health Study (WLHS); Vitamins and Lifestyle (VITAL) Study (VITAL); Cohort of Swedish Men (COSM); and Health Professionals Follow-up Study (HPFS) (Table 1).

Exposure Assessment:

All studies used a food frequency questionnaire or other dietary tool that was validated and measured diet intake in the year prior to entry into the cohort. Using harmonized data, we calculated adherence to the DASH diet. The DASH score[24] includes food and nutrients that make

up the 8 following components of the DASH diet: 1) high intake of fruits, 2) vegetables, 3) nuts and legumes, 4) low-fat dairy products, and 5) whole grains and 6) low intake of sodium, 7) sweetened beverages, and 8) red and processed meats. Participants were grouped into quintiles for each component based on intake ranking. For the first five components, participants were assigned a value based on the quintile they are in (e.g., the lowest intake quintile ranking received a value of 1 and the highest intake quintile ranking received a score of 5). The last three components are inversely related to a healthy diet and were assigned into quintiles ranked from 5 to 1 (e.g., the lowest intake quintile ranking received a value of 5 and the highest intake quintile ranking received a score of 1).[19] A participant's overall DASH score is the sum of the quintile rankings across the components. Scores range from 8-40 with 8 representing lowest adherence and 40 representing highest adherence to the DASH diet. Data on sodium intake was not available during the time of this analysis so the sodium component of the DASH diet score was excluded when calculating the DASH diet score **(Supplemental Table 1)**.

Outcome Assessment:

The outcome of interest was invasive pancreatic cancer that was defined by ICD-9 code 157.0 or ICD-10 code C25. Case ascertainment was identified by follow-up questionnaires followed by medical record review, cancer registry linkage, or both. Some studies also used mortality registries to confirm cases.[18] information regarding cancer histology to classify by subtypes were collected by ICD-O code or from patient medical records. Of the 3,172 total pancreatic cancer cases, 2,762 were classified as adenocarcinoma. The 410 non-adenocarcinoma cancer cases were of other histology.

Exclusions:

For this analysis, we applied additional exclusion criteria to participants. We excluded participants who had a history of cancer, except for non-melanoma skin cancer at baseline and participants who had energy intakes that were beyond three standard deviations of the respective study-specific log-e transformed mean energy intake. After applying these exclusions our total study population included 820,661 participants and of those participants, 3,172 were diagnosed with pancreatic cancer during the follow up periods.

Statistical Analysis:

We analyzed the association between adherence to the DASH diet and risk of pancreatic cancer. We assigned participants into quartiles, with those in the highest quartile having the highest adherence to the DASH diet and comparing them to those with the lowest adherence in the lowest quartile (reference group). We also assessed the association on a continuous scale. Summary estimates were calculated using a 2-stage approach. In the first stage, study-specific hazard ratios (HR) and 95% confidence intervals (CI) were calculated using a Cox Proportional Hazard model for each study. Person-years were calculated starting from the date of the baseline questionnaire to the date of pancreatic cancer diagnosis, date of death, date the

participant exited the study, or the date of the end of the study, whichever came first. The models were stratified by age in years at baseline and the calendar year at the start of follow-up. The follow-up time scale was in days. The Multivariable (MV) HR models were adjusted for smoking, diabetes, body mass index (BMI), and energy intake. In the second stage, the study- and sex- specific HRs were pooled together, weighted by the inverse of the sum of their variance and the estimated between study variance component, using a random effects model. We also calculated the I^2 and Q statistic to examine between study heterogeneity. Since subtypes of pancreatic cancer can be associated with different etiologies, we also examined the association limiting the outcome definition to pancreatic adenocarcinoma, the predominant sub-type, with the studies that have available data.[25] We used SAS software, version 9.1, for our analysis.

Results:

The analytic sample contained data from 13 different prospective cohort studies from the DCPP that examined dietary intake and cancer. Data from 11 studies contributed to the analyses for females and 7 studies for males. There was a total of 3,172 incident pancreatic cancer cases identified during follow-up. Participants were between the ages of 18 and 93 years and followed for between 1-18 years. The mean (SD) DASH diet score ranged from as high as 21.61 (5) in WHI to as low as 17.52 (4.17) in WLHS **(Table 1)**.

Before adjusting for covariates, the age-adjusted model showed null results for females in the association of adherence to the DASH diet and pancreatic cancer risk when comparing those in the highest quartile of adherence (Quartile 4, Q4) to those in the lowest quartile of adherence (Q1, reference group) (pooled age-adjusted HR = 0.92, 95% CI = (0.81, 1.05), p-value test for trend = 0.23). However, in males, the age-adjusted model showed statistically significant results comparing Q4 to Q1 (pooled age-adjusted HR = 0.82, 95% CI = (0.70, 0.97), p-value test for trend = 0.03). After adjusting for covariates, the same comparison was null in both females (pooled multivariable-adjusted HR = 1.02, 95% CI = (0.89, 1.16), p-value test for trend = 0.69) and males (pooled multivariable-adjusted HR = 0.89, 95% CI = (0.76, 1.05), p-value test for trend = 0.24) **(Table 2)**. We also analyzed the association with adherence to the DASH diet score as a continuous exposure. When examining the age-adjusted model for females, the results were null. However, for males, there are statistically significant results (pooled age-adjusted HR = 0.99, 95% CI = (0.97, 1.00), p-value test for trend = 0.01); for every one score increase in the DASH diet score, the risk of pancreatic cancer decreased by 1%. After adjusting for covariates, associations were null for both females and males **(Table 2)**.

The results remained null for males and females when limiting the outcome to pancreatic adenocarcinoma and examining the DASH diet score by quantiles or continuously **(Table 3)**.

Discussion:

No statistically significant results for adherence to the DASH diet and pancreatic cancer risk were observed in our pooled analysis of 13 prospective cohort studies; results were similarly null regardless of how the exposure was modeled. Risks also did not differ by studies as all I^2 values were 0% or less than 40%, and there were no significant p-values that tested for heterogeneity between studies. Results also remained null when cases were limited to adenocarcinoma.

Our results were not consistent with findings from other prospective cohort studies. A large US prospective cohort study by the NIH-AARP examined adherence to the DASH-Feng and the DASH-Mellen diets. In sex-combined multivariable-adjusted models, participants with the highest diet quality compared with those with the lowest (Q5 vs. Q1) had significantly lower PDAC risk (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).[20] Furthermore, they found that associations differed by sex but there was only a significant association for men (DASH-Fung (HR = 0.77, 95% CI: 0.66, 0.90), and DASH-Mellen (HR = 0.82, 95% CI: 0.71, 0.95).[20] The DASH-Mellen score is comprised of 9 components which is not comparable to the 8 component DASH diet score structure used in this analysis.[20] In addition, global age-standardized incidence rates of pancreatic cancer show that rates are overall much higher in the Western world (Europe and North America) compared to the rest of the world.[26] Higher incidence rates in a given population can contribute to more cases to detect an association. Another prospective study from a cohort of Chinese participants in Singapore also found that overall, higher levels of adherence to Quality Diet Indexes (QDIs), including the DASH diet, were inversely associated with the risk of pancreatic cancer (HR = 0.66, 95% CI: 0.46–0.95, P-trend < 0.05).[21] In addition, the associations between all four QDIs and risk of pancreatic cancer were more apparent in men compared to women.[21] Singapore and other South-East Asian countries have a one of the lowest age-standardized incidence rates of pancreatic cancer compared to other regions of the world [26] In addition, this study adjusted for additional factors such as educational level, coffee consumption, and Chinese dialect.[21] A study with a population of a specific demographic produces results that make generalizability to the general population more difficult. Our study utilizes a sample of diverse international cohorts with a range of incidence rates, so the results mirror the overall effect of the exposure on the outcome.

Our study has some limitations. This analysis used data from food frequency questionnaires that were collected at baseline; this doesn't allow us to measure the impact of dietary changes over time on cancer risk. In addition, since data on sodium intake was not available at the time of this analysis, we did not include the sodium component of the DASH diet; the resulting score used for analysis is incomplete in its depiction of adherence to the DASH diet which could affect the association seen between the DASH diet and pancreatic cancer risk. Lastly unmeasured confounders left can bias the results.

Our study has many strengths. A pooled analysis of individual data creates a very large sample size, usually much larger than a typical prospective cohort study, which ultimately allows a higher power to detect statistical significance. In addition, this method allows the investigator to harmonize the data and reduce between study heterogeneity. With all I^2 values equal to 0% or less than 40%, our data was harmonized well and any differences between studies are due to chance as opposed to variances in the studies. Publication bias is not a concern compared to a meta-analysis of published studies as the inclusion of studies are not contingent on if a study has published findings on the association. A prospective study design establishes temporality of exposure and outcome, and it can help eliminate selection and recall biases.

In conclusion, we found null results in reference to the association between adherence to the DASH diet and overall pancreatic cancer risk, as well as limiting the outcome to adenocarcinoma. Further sensitivity analysis looking at if risk differs among strata of risk factors such as diabetes, obesity, and smoking would be beneficial.

Table 1. Characteristics of the cohorts in the pooled analysis of DASH diet score and pancreatic cancer risk in the Pooling Project of Prospective Studies on Diet and Cancer (DCPP)

Sex	Cohort[1]	Follow-up years	Median follow-up time (yrs)	Baseline cohort size	Cases (n)	Age range (yrs)	DASH diet score			
							Mean	Standard Deviation	Min.	Max.
Female	BCDDP	1987-1999	10.3	42,146	107	40-93	21.11	4.6	7	35
	CLUEII	1989	17.5	8,046	50	18-93	20.77	4.93	7	35
	CPSII	1992-2001	20.5	74,604	305	40-87	21.04	4.74	7	35
	MCCS	1998-2005	20.5	21,921	77	31-72	21.35	4.78	7	35
	NHSb	1986-2002	28.6	70,094	423	40-67	21.2	5.05	6	35
	NHSII	1986-2002	22.5	93,822	66	26-46	21.18	4.98	6	35
	PLCO	1993-2004	9.3	52,227	161	54-83	21.18	4.53	7	35
	SMC	1997-2004	19.3	34,982	171	48-83	21.14	4.55	2	35
	WHI	1993-1998	18.5	86,427	388	49-81	21.61	5	7	35
	WLHS	1991-1992	21.3	47,539	57	30-50	17.52	4.17	6	30
	VITAL	2010-2018	9.9	30,158	88	50-76	21.48	5	7	35
Male	CLUEII	1989	15.7	5,737	43	18-89	20.67	4.94	7	35
	COSM	1998-2005	19	45,220	212	45-79	21.34	4.48	3	35
	CPSII	1992-2001	18.2	65,897	320	42-89	20.99	4.76	7	35
	HPFS	1986-2002	25.9	47,774	329	32-79	20.96	5.08	6	35
	MCCS	1990-1994	20.3	14,458	58	27-72	20.92	4.99	7	35
	PLCO	1993-2004	9.1	49,436	215	54-83	21.19	4.33	7	35
	VITAL	2010-2018	9.9	30,173	102	50-76	21.08	4.89	7	35
Total				820,661	3172					

[1]BCDDP, Breast Cancer Detection Demonstration Project Follow-up Study; CLUEII, CLUEII: Give us a Clue to Cancer; CPSII, Cancer Prevention Study-II Nutrition Cohort; MCCS, Melbourne Collaborative Cohort Study; NHSb, Nurses' Health Study b; NHSII, Nurses' Health Study II; PLCO, The Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial USA; SMC, Swedish Mammography Cohort; WHI, Women's Health Initiative; WLHS, Women's Lifestyle and Health Study; VITAL, Vitamins and Lifestyle (VITAL) Study; COSM, Cohort of Swedish Men; HPFS, Health Professionals Follow-up Study

Supplemental Table 1. DASH diet components scoring critera and corresponding DCPP data

No.	Component	Unit	Description	Scoring Criteria
1	Fruits	servings/d	All fruits and fruit juices	**Normal Scoring:** Q1 = 1 point Q2 = 2 points Q3 = 3 points Q4 = 4 points Q5 = 5 points
2	Vegetables	servings/d	All vegetables except potatoes and legumes	
3	Nuts and Legumes	servings/d	Nuts and peanut butter, dried beans, peas, tofu	
4	Low-fat dairy products	servings/d	Skim milk, yogurt, cottage cheese	
5	Whole grains	servings/d	cereal, whole grain cereal, other grains, popcorn, wheat germ, bran	
6	Sodium[1]	mg/d	Sum of sodium content of all foods in FFQ	**Reverse scoring:** Q1 = 5 points Q2 = 4 points Q3 = 3 points Q4 = 2 points Q5 = 1 point
7	Sweetened beverages	servings/d	Carbonated and noncarbonated sw	
8	Red and processed meats	servings/d	Beef, pork, lamb, deli meats, organ meats, hot dogs, bacon	

[1]Data on sodium intake for cohort participants were not available at the time of this analysis so the sodium component was excluded

Supplemental Table 2. Mean (SD) in grams/day for each DASH diet score component, by study

Sex	Cohort[1]	Fruits	Vegetables	Nuts and Legumes	Low-fat dairy	Whole grains	Red and processessed meats
Female	BCDDP	167.1(0.8)	161.8(0.7)	12.2(0.1)	1.0(0)	36.9(0.3)	43.0(0.2)
	CLUEII	154.9(1.5)	151.4(1.1)	12.8(0.2)	0.5(0)	24.1(0.4)	43.3(0.4)
	CPSII	174.6(0.4)	185.6(0.4)	12.9(0.1)	1.3(0)	30.7(0.1)	41.1(0.1)
	MCCS	416.4(2.1)	241.2(0.9)	30.4(0.3)	0.3(0)	53.8(0.4)	110.7(0.5)
	NHSb	293.0(0.7)	285.3(0.6)	18.4(0.1)	0.9(0)	36.2(0.2)	75.0(0.2)
	NHSII	208.9(0.5)	238.2(0.4)	18.9(0.1)	1.1(0)	44.3(0.2)	89.0(0.2)
	PLCO	217.0(0.7)	212.6(0.7)	23.7(0.1)	0.6(0)	3.5(0)	54.8(0.2)
	SMC	224.6(0.8)	200.0(0.7)	25.4(0.2)	1.1(0)	43.7(0.3)	63.5(0.2)
	WHI	256.8(0.6)	215.8(0.5)	40.5(0.2)	0.3(0)	38.4(0.2)	46.7(0.1)
	WLHS	142.1(0.5)	73.3(0.2)	13.0(0.1)	1.0(0)	29.1(0.2)	52.8(0.1)
	VITAL	169.5(0.8)	188.8(0.7)	26.1(0.2)	0.5(0)	36.2(0.3)	50.7(0.2)
Male	CLUEII	161.2(2.0)	173.5(1.5)	21.7(0.3)	0.5(0)	30.5(0.7)	71.7(0.7)
	COSM	189.0(0.7)	153.2(0.5)	35.2(0.2)	1.4(0)	152.9(0.6)	105.4(0.3)
	CPSII	163.0(0.5)	224.4(0.5)	20.1(0.1)	1.2(0)	37.7(0.2)	72.6(0.2)
	HPFS	268.6(0.9)	260.3(0.7)	27.2(0.1)	0.8(0)	49.3(0.3)	79.4(0.2)
	MCCS	393.4(2.7)	223.3(1.2)	38.2(0.4)	0.1(0)	53.1(0.6)	157.7(0.9)
	PLCO	200.2(0.7)	200.8(0.7)	31.2(0.2)	0.6(0)	4.8(0)	92.1(0.3)
	VITAL	174.9(0.9)	256.8(0.9)	50.4(0.3)	0.5(0)	49.8(0.5)	85.9(0.4)

[1]BCDDP, Breast Cancer Detection Demonstration Project Follow-up Study; CLUEII, CLUEII: Give us a Clue to Cancer; CPSII, Cancer Prevention Study-II Nutrition Cohort; MCCS, Melbourne Collaborative Cohort Study; NHSb, Nurses' Health Study b; NHSII, Nurses' Health Study II; PLCO, The Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial USA; SMC, Swedish Mammography Cohort; WHI, Women's Health Initiative; WLHS, Women's Lifestyle and Health Study; VITAL, Vitamins and Lifestyle (VITAL) Study; COSM, Cohort of Swedish Men; HPFS, Health Professionals Follow-up Study

Table 2. Pooled Age-adjusted and Multivariable Hazard Ratios (HRs) and 95% Confidence Intervals of Pancreatic Cancer for DASH diet score

	Categories of DASH diet score				I^{2b}	P-value, test for trend[c]	P-value, test for heterogeneity between studies[d]		Continuous per 1 score increment	I^{2b}	P-value, test for trend[c]	P-value, test for heterogeneity between studies[d]
	Q1	Q2	Q3	Q4								
No. of Cases												
Total	724	639	1208	601					3172			
Females	534	350	630	379					1893			
Males	190	289	578	222					1279			
Age-adjusted HR (95% CI)												
Females	REF	0.94 (0.80, 1.11)	0.96 (0.81, 1.13)	0.92 (0.81, 1.05)	0%	0.227	0.528		0.99 (0.98, 1.00)	0%	0.075	0.471
Males	REF	0.90 (0.74, 1.09)	0.93 (0.78, 1.11)	0.82 (0.70, 0.97)	0%	0.026	0.616		0.99 (0.97, 1.00)	0%	0.014	0.828
Multivariable HR (95% CI)[a]												
Females	REF	1.00 (0.85, 1.16)	1.04 (0.89, 1.21	1.02 (0.89, 1.16)	0%	0.692	0.625		1.00 (0.99, 1.01)	0%	0.94	0.539
Males	REF	0.92 (0.76, 1.12)	0.97 (0.81, 1.17)	0.89 (0.76, 1.05)	0%	0.236	0.426		0.99 (0.98, 1.00)	0%	0.184	0.571

[a]Multivariable HR's were adjusted for continuous calories, multiple vitamin use, smoking status (never smoker; past smoker, packs-year <15; past smoker, packs-year 15+; current smoker, packs-year <40; current smoker, packs-year 40+), diabetes (yes, no, missing)

[b]I^2 statistic, percentage of total variation that is due to heterogeneity rather than chance

[c]P-value, test for trend

[d]P-value, test for between study heterogeneity

Table 3. Pooled Age-adjusted and Multivariable Hazard Ratios (HRs) and 95% Confidence Intervals of Pancreatic Adenocarcinoma for DASH diet score

	Categories of DASH diet score				I^{2b}	P-value, test for trend[c]	P-value, test for heterogeneity between studies[d]		Continuous per 1 score increment	I^{2b}	P-value, test for trend[c]	P-value, test for heterogeneity between studies[d]
	Q1	**Q2**	**Q3**	**Q4**								
No. of Cases												
Total	600	552	1073	537					2762			
Females	442	299	563	335					1639			
Males	158	253	510	202					1123			
Age-adjusted HR (95% CI)												
Females	REF	0.95 (0.79, 1.14)	0.99 (0.83, 1.18)	0.91 (0.76, 1.08)	28.80%	0.272	0.191		0.99 (0.98, 1.00)	35%	0.188	0.141
Males	REF	0.91 (0.72, 1.15)	0.95 (0.81, 1.12)	0.86 (0.73, 1.02)	0%	0.109	0.951		0.99 (0.98, 1.00)	0%	0.062	0.94
Multivariable HR (95% CI)												
Females	REF	1.00 (0.84, 1.19)	1.07 (0.90, 1.27)	1.01 (0.84, 1.20)	26.30%	0.974	0.213		1.00 (0.98, 1.01)	36.30%	0.898	0.131
Males	REF	0.94 (0.74, 1.19)	1.00 (0.85, 1.18)	0.94 (0.79, 1.11)	0%	0.61	0.83		1.00 (0.98, 1.01)	0%	0.495	0.667

[a]Multivariable HR's were adjusted for continuous calories, multiple vitamin use, smoking status (never smoker; past smoker, packs-year <15; past smoker, packs-year 15+; current smoker, packs-year <40; current smoker, packs-year 40+), diabetes (yes, no, missing)

[b]I^2 statistic, percentage of total variation that is due to heterogeneity rather than chance

[c]P-value, test for trend

[d]P-value, test for between study heterogeneity

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