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A Combined Healthy Lifestyle Score and Risk of Pancreatic Cancer - A Large Cohort Study

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Abstract

Background—Smoking, alcohol use, diet, body mass index (BMI), and physical activity have been studied independently in relation to pancreatic cancer. We generated a healthy lifestyle score to investigate their joint effect on pancreatic cancer risk.

Methods—In the prospective National Institutes of Health-AARP Diet and Health Study, a total of 450,416 participants aged 50–71 years completed the baseline food frequency questionnaire (1995–1996) eliciting diet and lifestyle information and were followed up through December 2003. We identified 1,057 eligible incident pancreatic cancer cases. Participants were scored for five modifiable lifestyle factors as “unhealthy” (0 points) or “healthy” (1 point) based on current epidemiologic evidence. Participants received 1 point for each respective lifestyle factor: nonsmoking, limited alcohol use, adherence to the Mediterranean dietary pattern, 18 ≤ BMI <25 kg/m^2, or regular physical activity. A combined score (0–5 points) was calculated by summing the scores from the five factors. Cox proportional hazards regression models were used to estimate relative risks (RRs) and 95% confidence intervals (CIs) for pancreatic cancer.

Results—Compared to the lowest combined score (0 points), the highest score (5 points) was associated with a 58% reduction in risk of developing pancreatic cancer in all participants (RR,

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Author Contributions:

Dr. Jiao had full access to all of the data in the study and takes full responsibility for the integrity of the data and the accuracy of the data analysis.

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0.42; 95% CI, 0.26–0.66, *P* trend < .001). Scores of less than 5 points explained 27% of pancreatic cancer cases in our population.

Conclusion—This large study suggests that having a high, as opposed to a low, score on an index combining five modifiable lifestyle factors substantially reduces one's risk of pancreatic cancer.

According to the SEER Surveillance Epidemiology and End Results 2000–2003 statistics, the incidence of pancreatic cancer ranks 10th in men and 9th in women in the United States (US). However, the mortality ranks 4th in both men and women. Since pancreatic cancer is difficult to detect at a potentially resectable stage and remains therapeutically intractable, prevention remains the major hope for reducing the burden of this disease. Cigarette smoking and obesity have been consistently associated with increased risk of pancreatic cancer. Findings on dietary intake and physical activity have been inconsistent.[1, 2]

Typically, in epidemiologic studies of individual health behaviors or exposures, other factors are treated as covariates in statistical models. Several studies identified patterns of health behavior in the US adults and suggested that a multidimensional lifestyle approach would be informative in exploring disease etiology.[3, 4] In this vein, we scored study participants according to their conformity to a healthy lifestyle using five potentially modifiable factors including cigarette smoking, alcohol use, dietary quality, body mass index (BMI), and physical activity. We examined how the combined lifestyle score was associated with pancreatic cancer risk in the National Institutes of Health (NIH)-AARP Diet and Health Study. We hypothesized that a higher healthy lifestyle score would be associated with a lower risk for pancreatic cancer.

METHODS

STUDY POPULATION

The NIH-AARP Diet and Health Study is a large prospective cohort study of AARP members established in 1995–1996. Details of the study design and questionnaire have been described previously.[5] Briefly, a self-administered baseline Food Frequency Questionnaire (FFQ) was mailed to 3.5 million AARP members aged 50–71 years who resided in six US states (California, Florida, Louisiana, New Jersey, North Carolina, and Pennsylvania) and two metropolitan areas (Atlanta, GA, and Detroit, MI). The questionnaire was returned by 617,119 members and 567,169 of them completed the questionnaire satisfactorily.[5] The study was approved by the National Cancer Institute Special Studies Institutional Review Board. Informed consent was obtained from all participants by virtue of completing the questionnaire.

We excluded the participants with duplicate responses (n = 179), who moved out of the study areas before returning the baseline questionnaire (n = 321), died before study entry (n = 261), or withdrew (n = 6). In the remaining 566,402 participants, we further excluded the participants who had questionnaires completed by proxy respondents (n = 15,760), prevalent cancer at baseline as identified by cancer registry match (n = 8,583), extreme energy intake (i.e., more than two interquartile ranges above the 75th or below the 25th percentile of Box-Cox log-transformed intake, n = 4,792), missing smoking information (n = 20,169), less than one year follow-up (n = 6,417), missing weight and height data (n = 11,770), and participants with a BMI of less than 18 kg/m^2 (n = 3,609). We further excluded 44,886 participants with self-reported diabetes because they might modify their diet and health behaviors and diabetes has been linked to a greater risk of pancreatic cancer. Our final analytic cohort consisted of 450,416 members, including 263,398 men and 187,018 women.

COHORT FOLLOW-UP AND CASE ASCERTAINMENT

Person-year of follow-up was calculated from one year after the response to the FFQ to the date of pancreatic cancer diagnosis, death, moving out of the study areas, or December 2003. The participants who moved to Texas, Nevada, and Arizona were followed up. Vital status was ascertained by linkage to the Social Security Administration Death Master File. Pancreatic cancer cases were identified by linkage between the NIH-AARP cohort membership to eleven state cancer registries and the National Death Index. We included adenocarcinoma of the exocrine pancreas (ICD-O-3 code C25.0-C25.3 and C25.7-C25.9) and excluded histology code 8150-8155, 8240, 8246, and 8502. In addition to 922 cases identified from cancer registries, we included 135 cases identified from the National Death Index. We estimated a minimum sensitivity of 89.2% for case ascertainment from the cancer registries.[6]

EXPOSURE ASSESSMENT

A self-administered FFQ was used to elicit information on smoking, dietary intake, anthropometry, and physical activity, as well as demographic factors and medical history.[5] The FFQ was a grid-based version of National Cancer Institute's Diet History Questionnaire (DHQ) that assessed the frequency of consumption and usual portion size of 124 food items including alcohol use over the past year.[7] The DHQ was validated using two 24-hour dietary recalls that were administered to 2,053 randomly chosen NIH-AARP participants.[5] MyPyramid equivalents of all food items were generated by linking the FFQ data with the MyPyramid Equivalents Database (version 1.0, US Department of Agriculture, Washington, DC), which disaggregates all food mixtures into the appropriate food groups using standardized servings.[8, 9]

Participants reported whether they smoked ≥ 100 cigarettes during their entire lifetime to define ever smokers and never smokers. Ever smokers were asked to report whether they currently smoked or whether they stopped smoking within the last year, 1–4, 5–9, or ≥ 10 year ago. BMI was calculated from self-reported weight and height information (kg/m^2). Participants reported how often (never, rarely, 1 to 3 times per month, 1 to 2 times per week, 3 to 4 times per week, 5 or more times per week) they had engaged in physical activity that lasted at least 20 minutes and caused increased breathing or heart rate, or worked up a sweat at work or home.

SCORES FOR SMOKING, ALCOHOL USE, BMI, AND PHYSICAL ACTIVITY

We generated a healthy lifestyle score based on *a priori* knowledge of risk factors for pancreatic cancer and current public health recommendations.[1, 10, 11] We used a binary score for each factor so as to allow the adequate sample size for the pattern analysis. The participants received 1 point for each factor if they: were "nonsmoking" (never smoked or quit smoking 10 or more years ago); had limited daily alcohol use (≤ 1 drink for women or ≤ 2 drinks for men);[10] normal weight ($18 \leq BMI < 25\ kg/m^2$);[11] or regular physical activity. Otherwise they received 0 points for each corresponding factor (Table 1). We combined ever smokers who quit smoking for 10 years or more with never smokers into a "nonsmoking" group because their risk of developing pancreatic cancer was similar with that of never smokers as observed in the current study and in previous studies.[12] We generated a score for alcohol use based on the Dietary Guidelines for Americans 2005.[10] We considered maintaining a BMI ≥18 and <25 kg/m^2 as a healthy behavior.[11] Regular physical activity was defined as activity that lasted at least 20 minutes and caused increase in breathing or heart rate, or worked up a sweat for at least 3–4 times per week.

SCORE FOR DIETARY QUALITY

Dietary quality was evaluated based on an alternate Mediterranean diet score (aMDS). aMDS was derived from the traditional MDS and it evaluated adherence to the Mediterranean dietary pattern in the US population.[13–15] We further modified aMDS by removing the alcohol component[16] (we evaluated alcohol use as a separate factor). This modified score (no-alcohol-aMDS) included 8 components (vegetables not including white potato, legumes, fruits, nuts, whole-grains, red and processed meat, fish, and the ratio of monounsaturated to saturated fat) and took values from 0 to 8 points (minimum to maximum adherence) with a median value of 4 points. Study participants who scored 5 to 8 points were categorized as having a "healthy dietary quality" and received 1 point for the dietary intake component on the combined healthy lifestyle score, while those who scored 0 to 4 points received 0 points (Table 1).

SCORE FOR THE COMBINED HEALTHY LIFESTYLE

We assigned the "healthy lifestyle score" to each participant by summing the binary score for each of the five lifestyle factors as described above, including smoking, alcohol use, dietary quality, BMI and physical activity. The healthy lifestyle score ranges from 0 (the least healthy) to 5 points (the healthiest). Alternatively, we generated "a weighted lifestyle score" by using the proportion of the beta coefficient of each factor to the sum of the beta coefficients of each factor in the Cox proportional hazards regression model with all five factors included. This score ranges 0 to 100 points and takes into consideration magnitudes of the adjusted RRs of each factor in each lifestyle pattern as a combination of five factors. We categorized the weighted lifestyle score to six levels, where the distribution of the categories is similar with that of the six categories of the combined healthy lifestyle score.

STATISTICAL ANALYSES

Cox proportional hazards regression models using age as the underlying time metric were used to calculate (sex-specific or sex-combined) relative risks (RRs) and 95% confidence intervals (CIs) for pancreatic cancer. Age (continuous), sex (in the sex combined model), race (non-Hispanic whites, non-Hispanic African American, Hispanic, and others), educational level (less than high school or unknown, high school, some college, and college graduate), marital status (married or living as married versus other), and total energy intake (log-transformed) were the variables included in the multivariate models. Firstly, we evaluated the association of each binary lifestyle factor with pancreatic cancer risk, adjusting for the other factors including smoking, alcohol use, dietary quality, BMI, and physical activity. Participants with 0 points were the reference group. Secondly, we examined the agreement of the combined score and the weighted score in categorizing participants according to their health lifestyles. We evaluated the associations of two scores with pancreatic cancer risk separately. We calculated the *P*-value for the linear trend using the Wald test treating the lifestyle score as a continuous variable. Thirdly, in order to investigate how risk differs by adding each factor to the combined score, we presented the risk estimate for the most common lifestyle pattern in each score category. In this case, the factors not included in the pattern were adjusted in the models. Fourthly, we evaluated whether the associations between the score and the risk varied significantly by age of enrollment (<62 versus ≥ 62 years) and sex by generating a cross-product term in the multivariate model and using the likelihood ratio test. Last, we performed a lag analysis excluding those who died or censored within the second year of follow-up in order to reduce the influence of sub-clinical disease on the lifestyle factor score. We performed sensitivity analyses by excluding participants with self-reported cancer history or including only pancreatic cancer cases identified from cancer registries.

We calculated the age- and energy-adjusted population attributable risk (PAR) to estimate the percentage of cases that would have been eliminated had all participants adopted the healthiest lifestyle (5 points) or a healthier lifestyle (4 or 5 points), assuming a causal relationship between the score and risk of pancreatic cancer. The PAR of pancreatic cancer according to each of five factors was also calculated.

Statistical analyses were carried out using SAS 9.0 software (SAS Institute, Cary, NC). All *P*-values were based on two-sided tests, and a *P* value of < 0.05 was considered statistically significant.

RESULTS

During an average of 7.2 years of follow-up, a total of 1,057 (675 men and 382 women) pancreatic cancer cases were identified. We found no deviations from the proportional hazards assumption for our main exposures and covariates using Grambsch and Therneau's test.

In the analyses using the combined lifestyle score and the weighted lifestyle score, we found the two scoring algorithms had high agreement (88% overall) in categorizing the participants into the respective score category. The distribution of participants by the combined lifestyle score (0 to 5 points) was 1.5%, 10.7%, 27.8%, 31.3%, 21.1%, and 7.6%, respectively, and the corresponding distribution for the weighted lifestyle score was 1.5%, 9.3%, 36.3%, 26.4%, 19.0%, and 7.6%. Since the risk estimates based on both algorithms were essentially the same (data not shown), we present the results based on the combined healthy lifestyle score only.

In our study population, 74.6% were nonsmoking, 84.5% had limited alcohol use, 38.8% had healthy dietary quality, 36.9% had normal weight, and 47.5% had regular physical activity (Table 1). Table 2 shows the baseline characteristics of the study participants according to the combined healthy lifestyle score in men and women. Women had a statistically significant higher mean score than men (2.86 *versus* 2.81 points, $P < .001$). Participants who received a higher score were older, less likely to be African Americans, and more educated. A higher combined lifestyle score was related to a lower age-adjusted incident rate, less total energy intake, less total fat and red meat intake, more fruit and vegetable intake, and more folate intake. Family history of any cancer was unrelated to the score.

Table 3 shows the main effect of each factor on pancreatic cancer risk. In all participants, after adjusting for the other risk factors, nonsmoking and normal BMI were associated with statistically significant reduced risk, whereas healthy dietary quality, limited alcohol use, and regular physical activity were related to a non-significant reduced risk. We observed a 27% reduced risk when a high no-alcohol-aMDS (7–8 points) compared to a low no-alcohol-aMDS (0–1 points) ($P = 0.055$). The PAR for pancreatic cancer explained by smoking, i.e., current smoking and smoking cessation for less than 10 years, was 14%, which was the largest PAR among the five single lifestyle factors.

Table 4 shows the combined healthy lifestyle score in relation to pancreatic cancer risk. Compared to the least healthy score (0 points), the combination of the five healthy lifestyle factors (5 points) was statistically significantly associated with a 58% risk reduction in men (RR, 0.42; 95% CI, 0.24–0.71, *P*-trend < .001), a non-significant 53% risk reduction in women (RR, 0.47; 95% CI, 0.19–1.15, *P*-trend < .001), and a 58% risk reduction in all participants (RR, 0.42; 95% CI, 0.26–0.66, *P*-trend < .001). The PAR for pancreatic cancer was 27% for having a combined lifestyle score of < 5 points. Since there was a relatively smaller number of cases in the lowest and highest score, we combined the lower (0–1

points) and higher score (4–5 points). The RR for having a higher compared to a lower score was 0.64 (95% CI, 0.45–0.91, *P*-trend = 0.003) among women. The associations between the score and risk of pancreatic cancer did not vary significantly by sex ($P_{interaction}$= .49) or age ($P_{interaction}$= .89).

We identified 32 healthy lifestyle patterns derived from different combinations of the lifestyle score factors. For simplicity, we present the most common pattern in each score category (Table 5). The risk decreased with the addition of each lifestyle factor in the following order: limited alcohol use, nonsmoking, regular physical activity, healthy dietary quality, and normal BMI, when the other factors in the pattern were adjusted in the respective models. The addition of normal BMI to the most common 4-factor pattern (nonsmoking, limited alcohol use, healthy diet quality, and being physically active) reduced the risk in women, but not in men. However, the association between the lifestyle pattern and risk of pancreatic cancer did not differ by sex (*P* value for Wald test: 0.09 ~ 0.72).

In sensitivity analyses, when 5 points compared to 0 points, the RR was 0.39 (95% CI, 0.24–0.62) in a two-year lag analysis based on 925 cases, 0.40 (95% CI, 0.24–0.64) in an analyses based on 922 cases identified from cancer registries only, and 0.41 (95% CI, 0.25–0.66) in the participants without self-reported cancer history, based on 947 cases.

COMMENT

In this large prospective US cohort of older Americans, we found that the risk of pancreatic cancer was significantly lower in those participants who had the highest combined lifestyle score compared to the participants who had the lowest score. Approximately 14% of cases may have been prevented if all participants were nonsmoking, whereas 27% of cases may have been prevented if all participants were nonsmoking, had limited alcohol use, healthy dietary quality, normal weight and regular physical activity. There was a significant trend of risk reduction with increment in the number of healthy lifestyle factors.

In the analyses of single lifestyle factors, consistent with previous studies,[1, 17] nonsmoking and normal BMI had inverse associations with pancreatic cancer. Although nonsmoking showed the strongest effect, the combination with other factors rendered a further risk reduction. We found that the lack of further risk reduction by adding normal BMI to the most common 4-factor pattern was solely driven by the risk estimate in men who were 62 years or older. For example, we did not observe a risk reduction in older men when normal BMI was added to the less common 3-factor pattern (including nonsmoking, limited alcohol use, and healthy dietary quality), whereas the risk reduction was apparently observed in younger men and women regardless of age. We examined alcohol use as a separate factor because we found that limited alcohol use was a significant protective factor for pancreatic cancer in men. Most epidemiologic studies have not shown an association between physical activity and pancreatic cancer.[2] We found that the addition of regular physical activity to the most common 2-factor pattern (nonsmoking and limited alcohol use) did further reduce the risk. If these observations were true, it may reflect the interactions among these lifestyle factors.

Two studies have examined the association between risk of pancreatic cancer and dietary patterns as determined by data-driven factor analysis. A population based study including 585 cases and 4,779 controls showed a significant inverse association with a high fruit and vegetable dietary pattern in men but not in women.[18] A pooled prospective analysis including 366 cases found no association of either a western (high fat and meat intake) or prudent (high fruit and vegetable intake) dietary pattern with incident pancreatic cancer.[19] We used adherence to the no-alcohol-aMDS to evaluate the diet quality because the Mediterranean dietary pattern has been linked to reduced risk of colorectal adenoma in

men[20, 21] and reduced all-cause and cancer mortality[15] in three US studies. We also observed a reduced risk associated with a high no-alcohol-aMDS. Among the food groups in Mediterranean diet, fruits and vegetables have been linked to a reduced risk,[18] whereas red meat intake[22] has been linked to an increased risk of pancreatic cancer.

Several studies have emerged to show the beneficial effects of adopting a healthy lifestyle on total mortality[16] and coronary heart disease.[23] To our knowledge, no study has evaluated the combined lifestyle factors in relation to cancer incidence. The mechanism by which the combined factors reducing risk of pancreatic cancer likely involves multiple pathways. For example, lifestyle with nonsmoking would mean less exposure to tobacco carcinogens.[24] Inflammation may be a common etiologic factor for chronic diseases, which may create a microenvironment that fosters pancreatic tumor growth.[25] Alternatively, the combined healthy lifestyle could influence pancreatic cancer risk *via* energy balance.[26, 27]

The strengths of the current study included the large sample size, the prospective study design, and a wide range of dietary intake and detailed exposure information. Health behaviors are complex and consist of multiple dimensions; thus, using a lifestyle pattern analysis may capture the influence of multiple health behaviors better than an analysis based on single health behaviors. We observed a stronger risk reduction in the lifestyle pattern-based analysis than that observed in a single risk factor-based analysis, which would support the use of lifestyle pattern in risk assessment. The use of the simple score algorithm facilitated study interpretation and provided equivalent risk estimates as compared with the weighted lifestyle score, which takes into account the unequal contribution of each factors in risk reduction in different lifestyle patterns. Finally, our study findings may be generalizable to other study settings and could have implications for the prevention of other lifestyle related cancers.

The current study had some limitations. Firstly, in order to allow adequate number of participants in each of 32 lifestyle patterns, we dichotomized five factors to maintain a lower data dimension. However, the dichotomization could result in lose of study power. Along the same line, the cut-points we used were based on public health recommendations rather than pancreatic cancer specific cut-points. This could further reduce the magnitude of associations and result in lose of study power. Secondly, we only had one baseline measure of the factors that contributed to our healthy lifestyle score which did not take into account lifestyle changes before or after assessment. Thirdly, the combined score did not include all possible lifestyles, occupational exposure, or medical history that could be risk factors for pancreatic cancer. With these additional factors, the PAR might be larger and the prediction of pancreatic cancer might be stronger. Our study findings should be confirmed in other studies with refined exposure information in order to give a comprehensive evaluation on lifestyle patterns and pancreatic cancer risk.

In summary, we showed that the combined healthy lifestyle factors, including nonsmoking, adherence to US alcohol use recommendation, healthy dietary quality as defined by adherence to the Mediterranean diet pattern excluding alcohol consumption, normal weight, and regular physical activity, may have direct implications for pancreatic cancer prevention among older Americans. Although further searching for cancer-causing factors or mechanisms may contribute to innovative preventive strategies, the examination of combined known modifiable factors in cancer risk assessment is an appropriate way to translate analytic epidemiologic findings to primary cancer prevention, especially for the prevention of pancreatic cancer for which both early diagnosis and effective treatment modality remain challenging.

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Table 1

Five Factors of the Combined Healthy Lifestyle Score in the NIH-AARP Diet and Healthy Study

Healthy lifestyle factor	Score	Interpretation of the score	Proportion (%)
Smoking	0	Smoking: current smokers or quit for less than 10 years	
	1	Nonsmoking: never smoked or quit for 10 or more years	74.6
Alcohol use[a]	0	Heavy alcohol use - not adherent to alcohol use recommendation in the US: Daily consumption > 2 drinks for men or > 1 drink for women	
	1	Limited alcohol use - adherent to alcohol use recommendation in the US: Daily consumption ≤ 2 drink for men or ≤ 1 drink for women	84.5
Dietary quality[b]	0	Unhealthy diet quality: 0–4 points for alternate Mediterranean diet score (excluding alcohol)	
	1	Healthy diet quality: 5–8 points for alternate Mediterranean diet score (excluding alcohol)	38.8
BMI[c]	0	Overweight or obese: body mass index ≥ 25 kg/m^2	
	1	Normal weight: body mass index 18–24.99 kg/m^2	36.9
Physical activity[d]	0	Sedentary: never, rarely or less than 3–4 times per week	
	1	Regular: 3–4 times per week	47.5

Abbreviation: BMI, body mass index.

[a] Recommendation on daily alcohol consumption in US.[10]

[b] Adherence to the no-alcohol-alternate Mediterranean diet pattern.[13–15]

[c] According to World Health Organization standard.[11]

[d] At least 20 minutes that caused increase in breathing or heart rate, or worked up a sweat.

Table 2

Mean and Proportion of Baseline Characteristics of Participants According to the Combined Healthy Lifestyle Score[a]

Characteristics	Men Healthy lifestyle score							Women Healthy lifestyle score						
	All	0	1	2	3	4	5	All	0	1	2	3	4	5
Number of participants	263398	4767	29157	72228	82591	55640	19015	187018	2195	18776	52801	58525	39580	15141
Age-adjusted incidence rate	41.8	294.3	59.8	53.1	40.8	25.9	34.3	32.8	68.8	43.3	37.8	33.2	29.0	19.1
Age at entry, mean (year)	62.2	61.0	61.2	61.7	62.3	62.8	63.1	61.8	60.9	61.0	61.6	62.0	62.2	62.3
Race, % white	93.4	95.0	94.4	93.7	93.1	92.9	93.8	90.9	93.0	91.8	91.1	90.5	90.4	91.9
Race, % African American	2.3	2.7	2.5	2.5	2.4	2.3	1.2	4.7	5.4	5.2	5.1	4.9	4.2	2.5
Never smoker, %	30.8	0	7.1	25.8	34.4	41.2	47.6	45.2	0	7.20	39.3	51.4	57.5	62.3
Education, % college or post college	46.1	35.2	34.6	39.9	46.3	54.4	64.6	31.0	26.7	22.9	25.8	30.8	37.2	44.3
Being married, %	85.4	78.7	81.6	85.2	86.3	86.9	86.1	44.9	37.6	39.1	42.4	45.7	47.7	50.8
Family history of any cancer, % yes	48.4	47.8	48.0	48.1	48.6	48.7	49.1	52.8	51.0	52.2	53.0	52.9	52.7	52.5
Dietary intake per day														
Alcohol use, g	17.4	94.5	44.2	19.2	11.0	7.8	6.6	6.2	41.8	16.1	6.4	4.4	3.3	2.4
Total energy intake, kcal	2020	2690	2307	2073	1967	1885	1831	1567	1797	1664	1607	1551	1511	1481
Total fruits, cup/1000 kcal	1.1	0.5	0.7	0.9	1.1	1.4	1.5	1.3	0.7	0.9	1.1	1.4	1.6	1.8
Total vegetables, cup/1000 kcal	1.0	0.7	0.8	0.9	1.1	1.2	1.3	1.3	1.0	1.1	1.1	1.3	1.4	1.6
Total fat, g/1000 kcal	33.5	30.1	34.3	35.4	34.0	31.7	29.0	33.1	33.0	35.6	35.3	33.2	30.8	28.5
Saturated fat, g/1000 kcal	10.5	9.9	11.3	11.4	10.6	9.4	8.2	10.3	10.6	11.5	11.3	10.2	9.2	8.1
Red meat, g/1000 kcal	37.2	42.5	45.3	43.7	37.4	29.4	21.6	29.1	37.7	37.5	34.5	28.6	22.6	17.2
Total folate, μg/1000 kcal	288	197	226	258	294	333	366	364	275	299	328	371	408	440
Fiber, g/1000 kcal	10.3	6.42	7.63	8.87	10.4	12.3	13.9	11.5	7.74	8.87	10.0	11.6	13.3	15.2

[a]Healthy lifestyle score (ranges from 0 to 5 points) was calculated by adding up the binary exposure factors (0, 1) including smoking, alcohol use, dietary quality, body mass index, and physical activity. People received 1 point if they had any of the following behaviors: being never smokers or quit smoking for more than 10 years or more, limited alcohol use, adherence to an alternate Mediterranean dietary pattern (excluding alcohol), 18 ≤ body mass index <25 kg/m^2, or regular physical activity.

Table 3

Relative Risks of Pancreatic Cancer in Relation to Single Lifestyle Factors in Men and Women

		Men			Women			Men and women			
Healthy lifestyle factor	**Score**	**Case**	**RR[a] (95% CI)**	**RR[b] (95% CI)**	**Case**	**RR[a] (95% CI)**	**RR[b] (95% CI)**	**Case**	**RR[a] (95% CI)**	**RR[b] (95% CI)**	**PAR (%)[c]**
Smoking	0	216	1 [Reference]	1 [Reference]	145	1 [Reference]	1 [Reference]	361	1 [Reference]	1 [Reference]	14%
	1	459	0.57 (0.48–0.67)	0.60 (0.51–0.71)	237	0.56 (0.46–0.69)	0.56 (0.45–0.69)	696	0.57 (0.50–0.65)	0.59 (0.51–0.67)	
Alcohol use	0	147	1 [Reference]	1 [Reference]	51	1 [Reference]	1 [Reference]	198	1 [Reference]	1 [Reference]	3%
	1	528	0.69 (0.57–0.83)	0.78 (0.64–0.95)	331	1.02 (0.76–1.38)	1.11 (0.82–1.51)	859	0.78 (0.67–0.91)	0.86 (0.73–1.01)	
Dietary quality	0	437	1 [Reference]	1 [Reference]	239	1 [Reference]	1 [Reference]	676	1 [Reference]	1 [Reference]	5%
	1	238	0.78 (0.67–0.93)	0.89 (0.76–1.05)	143	0.92 (0.75–1.14)	0.98 (0.79–1.21)	381	0.84 (0.74–0.95)	0.92 (0.81–1.05)	
BMI	0	488	1 [Reference]	1 [Reference]	210	1 [Reference]	1 [Reference]	698	1 [Reference]	1 [Reference]	8%
	1	187	0.84 (0.70–0.99)	0.84 (0.71–0.99)	172	0.96 (0.78–1.18)	0.95 (0.77–1.17)	359	0.88 (0.78–1.00)	0.88 (0.77–0.99)	
Physical activity	0	342	1 [Reference]	1 [Reference]	224	1 [Reference]	1 [Reference]	566	1 [Reference]	1 [Reference]	3%
	1	333	0.87 (0.74–1.01)	0.93 (0.80–1.08)	158	0.89 (0.73–1.10)	0.94 (0.77–1.16)	491	0.88 (0.78–0.99)	0.94 (0.83–1.06)	

Abbreviation: BMI, body mass index; CI: confidence interval; PAR, population attributable risk; and RR, relative risk.

[a]Adjusted for age, race, educational level, and marital status. For men and women combined model, adjusted also for sex.

[b]Adjusted for age, race, educational level, marital status, total energy intake (log transformed), and other lifestyle factors including smoking status, alcohol use, dietary quality, body mass index and physical activity (binary variable). For men and women combined model, adjusted also for sex.

[c]Population attributable risk of pancreatic cancer according to each single factor in all participants, adjusted for age, total energy intake (log-transformed), and other risk factors including smoking status, alcohol use, dietary quality, body mass index and physical activity (binary variable).

Table 4

Relative Risks of Pancreatic Cancer in Relation to the Combined Healthy Lifestyle Score

	Men			Women			Men and Women		
Healthy lifestyle score[a]	**Case**	**personyear**	**RR[b] (95% CI)**	**Case**	**personyear**	**RR[b] (95% CI)**	**Case**	**personyear**	**RR[b] (95% CI)**
0	20	29034	1 [Reference]	6	13576	1 [Reference]	26	42610	1 [Reference]
1	88	179315	0.72 (0.44–1.16)	43	116734	0.82 (0.35–1.92)	131	296053	0.73 (0.48–1.12)
2	219	450132	0.69 (0.43–1.09)	119	333804	0.75 (0.33–1.70)	338	783937	0.69 (0.46–1.03)
3	213	519575	0.55 (0.35–0.88)	119	372156	0.65 (0.28–1.47)	332	891731	0.57 (0.38–0.85)
4	95	352406	0.34 (0.21–0.56)	72	253226	0.56 (0.24–1.29)	167	700528	0.40 (0.27–0.61)
5	40	120516	0.41 (0.24–0.71)	23	97035	0.47 (0.19–1.15)	63	217551	0.42 (0.26–0.66)
P trend[c]			< .001			< .001			< .001
0–1	108	208349	1 [Reference]	50	130310	1 [Reference]	157	338663	1 [Reference]
2–3	432	969707	0.81 (0.66–1.01)	238	705960	0.83 (0.61–1.13)	670	1675668	0.81 (0.68–0.97)
4–5	135	472922	0.48 (0.37–0.63)	95	350261	0.64 (0.45–0.91)	230	918079	0.54 (0.44–0.66)
P trend[c]			< .001			.003			< .001

Abbreviation: CI: confidence interval; RR, relative risk.

[a] Healthy lifestyle score (ranges from 0 to 5 points) was calculated by adding up the binary exposure factors (0, 1) including smoking, alcohol use, dietary quality, body mass index, and physical activity. People received 1 point if they had any of the following behaviors: being never smokers or quit smoking for more than 10 years or more, limited alcohol use, healthy dietary quality, 18 ≤ body mass index <25 kg/m^2, or regular physical activity.

[b] Adjusted for age, race, educational level, marital status, and total energy intake (log-transformed). For men and women combined model, adjust also for sex.

[c] P values for linear trend of RR.

Table 5

Relative Risk of Pancreatic Cancer for the Most Common Lifestyle Pattern in Each Score Category

Healthy Lifestyle Score	Proportion (%)	No. of Cases	Score for healthy lifestyle factor [a]					Men RR[b] (95% CI)	Women RR[b] (95% CI)	Men and women RR[c] (95% CI)
			Smoking	Alcohol use	Dietary quality	Body mass index	Physical activity			
0	1.5	26	0	0	0	0	0	1 [Reference]	1 [Reference]	1 [Reference]
1	6.0	73	0	1	0	0	0	0.63 (0.36–1.11)	1.04 (0.43–2.51)	0.77 (0.49–1.24)
2	14.6	151	1	1	0	0	0	0.57 (0.34–0.95)	0.68 (0.29–1.60)	0.61 (0.40–0.94)
3	9.9	106	1	1	0	0	1	0.46 (0.27–0.76)	0.62 (0.25–1.54)	0.50 (0.32–0.78)
4	9.1	80	1	1	1	0	1	0.28 (0.16–0.50)	0.70 (0.28–1.73)	0.40 (0.25–0.64)
5	7.6	63	1	1	1	1	1	0.35 (0.19–0.66)	0.53 (0.21–1.35)	0.41 (0.25–0.69)
Total	48.7	499								

Abbreviation: CI: confidence interval; RR, relative risk.

[a]The score of 1 point indicated nonsmoking, limited alcohol use, healthy dietary quality, normal body weight, and regular physical activity for the respective factors.

[b]For healthy lifestyle score equals 1 point, the RR was adjusted for age, race, educational level, marital status, total energy intake (log-transformed), scores for smoking, dietary quality, body mass index, and physical activity; for healthy lifestyle score equals 2 points, the RR was adjusted for age, race, educational level, marital status, total energy intake (log transformed), scores for dietary quality, body mass index, and physical activity; for Healthy lifestyle score equals 3 points, the RR was adjusted for age, race, educational level, marital status, total energy intake (log transformed), scores for dietary quality, and body mass index; for Healthy lifestyle score equals 4 points, the RR was adjusted for age, race, educational level, marital status, total energy intake (log transformed), and body mass index score; healthy lifestyle score equals 5 points, the RR was adjusted for age, race, educational level, marital status, and total energy intake (log transformed).

[c]For men and women combined model, the RRs were adjusted for sex.