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

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Background: Smoking, alcohol use, diet, body mass index (calculated as weight in kilograms divided by height in meters squared), and physical activity have been studied independently in relation to pancreatic cancer. We generated a healthy lifestyle score to investigate their joint effect on risk of pancreatic cancer.

Methods: In the prospective National Institutes of Health–AARP Diet and Health Study, a total of 450,416 participants aged 50 to 71 years completed the baseline food frequency questionnaire (1995-1996) eliciting diet and lifestyle information and were followed up through December 31, 2003. We identified 1057 eligible incident pancreatic cancer cases. Participants were scored on 5 modifiable lifestyle factors as unhealthy (0 points) or healthy (1 point) on the basis of current epidemiologic evidence. Participants received 1 point for each respective lifestyle factor: nonsmoking, limited alcohol use, adherence to the Mediterranean dietary pattern, body mass index (≥18 and <25), or regular physical activity. A combined score (0-5 points) was calculated by summing the scores of the 5 factors. Cox proportional hazards regression models were used to estimate relative risk (95% confidence interval) for pancreatic cancer.

Results: Compared with 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 (relative risk, 0.42; 95% confidence interval, 0.26-0.66; \( P_{\text{trend}} < .001 \)). Scores of less than 5 points were associated with 27% of pancreatic cancer cases in our population.

Conclusion: Findings from this large study suggest that having a high score, as opposed to a low score, on an index combining 5 modifiable lifestyle factors substantially reduces the risk of developing pancreatic cancer.

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According to Surveillance Epidemiology and End Results (SEER) 2000-2003 statistics, the incidence of pancreatic cancer in the United States ranks 10th in men and 9th in women; however, mortality ranks 4th in both men and women. Because pancreatic cancer is difficult to detect at a potentially resectable stage and remains therapeutically intractable, prevention is the primary 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 have identified patterns of health behavior in adults in the United States and suggested that a multidimensional lifestyle approach would be informative in exploring the cause of disease.3-4 Thus, we scored study participants according to their conformity to a healthy lifestyle using 5 potentially modifiable factors including cigarette smoking, alcohol use, dietary quality, body mass index (BMI; calculated as weight in kilograms divided by height in meters squared), and physical activity. We examined how the combined lifestyle score was associated with risk of pancreatic cancer in the National Institutes of Health–AARP (NIH-AARP) Diet and Health Study. We hypothesized that a higher healthy lifestyle score would be associated with a lower risk for pancreatic cancer.

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 In brief, a self-administered baseline Food Frequency Questionnaire (FFQ) was mailed to 3.5 million AARP members aged 50 to 71 years residing in 6 states (California,
Florida, Louisiana, New Jersey, North Carolina, and Pennsylvania) and 2 metropolitan areas (Atlanta, Georgia, and Detroit, Michigan). The questionnaire was returned by 617,119 members, and 367,169 completed the questionnaire satisfactorily. 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 179 participants with duplicate responses, 321 who moved from the study areas before returning the baseline questionnaire, 261 who died before study enrollment, and 6 who were lost to follow-up. In the remaining 566,420 participants, we further excluded 15,760 whose questionnaires were completed by proxy respondents, 8,583 who had prevalent cancer at baseline as identified by cancer registry matching, 4,792 with extreme energy intake, and 11,770 with missing weight and height data. We also excluded 20,169 participants by virtue of completing the questionnaire.

We estimated a minimum sensitivity of 89.2% for case ascertainment. In addition to 922 cases identified from cancer registries, we included 135 cases identified from the National Death Index. We also excluded histology codes 8150–8155, 8240, 8246, and 8502. 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 11 state cancer registries and the National Death Index. We included adenocarcinoma of the exocrine pancreas (ICD–O-3 [International Classification of Diseases for Oncology, Third Edition] codes C25.0–C25.3 and C25.7–C25.9) and excluded histology codes 8130–8135, 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.

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. The FFQ was a grid-based version of the National Cancer Institute Diet History Questionnaire that assessed the frequency of consumption and usual portion size of 124 food items and alcohol use during the last year. The Diet History Questionnaire was validated using two 24-hour dietary recalls that were administered to 2053 randomly chosen NIH-AARP participants. 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.

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

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. We used a binary score for each factor to produce an adequate sample size for the pattern analysis. The participants received 1 point for each factor if they were nonsmokers (never smoked or quit smoking ≥10 years ago), had limited daily alcohol use (≤1 drink for women or ≤2 drinks for men), were of normal weight (BMI ≥18 and ≤25), or performed regular physical activity; otherwise they received 0 points for each corresponding factor (Table 1). We combined ever smokers who quit smoking 10 years or more previously with never smokers into a nonsmoking group because their risk of developing pancreatic cancer was similar to that in never smokers as observed.
in the present study and in previous studies.\textsuperscript{12} We generated a score for alcohol use based on the Dietary Guidelines for Americans 2005.\textsuperscript{16} We considered maintaining a BMI of 18 or more and less than 25 as a healthy behavior.\textsuperscript{11} Regular physical activity was defined as activity performed at least 3 or 4 times per week for at least 20 minutes and that caused increased breathing or heart rate or produced perspiration.

**SCORE FOR DIETARY QUALITY**

Dietary quality was evaluated on the basis of an alternate Mediterranean diet score (aMDS). The aMDS was derived from the traditional MDS and evaluated adherence to the Mediterranean dietary pattern in the US population.\textsuperscript{13-15} We further modified the aMDS by removing the alcohol component\textsuperscript{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 assigned values from 0 to 8 points (minimum to maximum adherence; median, 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; those who scored 0 to 4 points received 0 points (Table 1).

**SCORE FOR COMBINED HEALTHY LIFESTYLE**

We assigned the healthy lifestyle score to each participant by summing the binary score for each of the 5 lifestyle factors described including smoking, alcohol use, dietary quality, BMI, and physical activity. The healthy lifestyle score ranges from 0 (least healthy) to 5 points (healthiest). Alternatively, we generated a weighted lifestyle score by summing the binary score for each of the 5 lifestyle factors described including smoking, alcohol use, dietary quality, BMI, and physical activity. The healthy lifestyle score ranges from 0 (least healthy) to 5 points (healthiest). Alternatively, we generated a weighted lifestyle score by summing the binary score for each of the 5 lifestyle factors described including smoking, alcohol use, dietary quality, BMI, and physical activity. The healthy lifestyle score ranges from 0 (least healthy) to 5 points (healthiest). Alternatively, we generated a weighted lifestyle score by summing the binary score for each of the 5 lifestyle factors described including smoking, alcohol use, dietary quality, BMI, and physical activity.

**STATISTICAL ANALYSES**

Cox proportional hazards regression models using age as the underlying time metric were used to calculate (sex-specific or sex-combined) RRs and 95% confidence intervals (CIs) for pancreatic cancer. Age (continuous), sex (in the sex-combined model), race/ethnicity (non-Hispanic white, non-Hispanic African American, Hispanic, and other), educational achievement (less than high school or unknown, high school, some college, and college graduate), marital status (married or living as married vs other), and total energy intake (log-transformed) were the variables included in the multivariate models. First, 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. Second, we examined the agreement of the combined score and the weighted lifestyle score in categorizing participants according to their health lifestyles. We evaluated the associations of 2 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. Third, we investigated how risk differed by risk factors, nonsmoking and normal BMI were associated with statistically significant reduced risk of pancreatic cancer, whereas healthy dietary quality, limited alcohol use, and regular physical activity were related to a nonsignificant re-

**RESULTS**

During a mean (range) of 7.2 (1.0-8.2) years of follow-up, 1057 individuals with pancreatic cancer (675 men and 382 women) were identified. We found no deviations from the proportional hazards assumption for our main exposures and covariates using the Grambsch-Therneau test.

In the analyses using the combined lifestyle score and the weighted lifestyle score, we found that the 2 scoring algorithms had high agreement (88% overall) in categorizing participants into the respective score category. The distribution of participants by the combined lifestyle score (0-5 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%. Because 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% of participants were nonsmokers, 84.5% had limited alcohol use, 38.8% had healthy dietary quality, 36.9% had normal weight, and 47.5% engaged in regular physical activity (Table 1). Table 2 gives 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 compared with men (2.86 vs 2.81 points; $P < .001$). Participants who received a higher score were older, less likely to be African American, and had achieved a higher educational level. 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.
All 0 1 2 3 4 5 6 7 8 9 10
No. of participants 263,398 4767 29157 72228 82591 55640 187,018 2195 18,776 52,801 58,525 39,580 15,141
Age-adjusted incidence rate 41.8 294.3 59.8 53.1 40.8 25.9 32.8 68.8 43.3 37.8 33.2 29.0 19.1
Age at enrollment, mean, y 62.2 61.0 61.2 61.7 62.3 62.8 61.8 60.9 61.0 61.6 62.0 62.2 62.3
Race/ethnicity, %
White 93.4 95.0 94.4 93.7 93.1 92.9 90.0 93.0 91.8 91.1 90.5 90.4 91.9
African American 2.3 2.7 2.5 2.5 2.4 2.3 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 45.2 0 7.20 39.3 51.4 57.5 62.3
Educational achievement level, college or postcollege, % 46.1 35.2 34.6 39.9 46.3 54.4 31.0 26.7 22.9 25.8 30.8 37.2 44.3
Married, % 85.4 78.7 81.6 85.2 86.3 86.9 44.9 37.6 39.1 42.4 45.7 47.7 50.8
Family history of any cancer, % 48.4 47.8 48.0 48.1 48.6 48.7 52.8 51.0 52.2 53.0 52.3 52.9 52.7 52.5
Diabetes, % 0.5 0.7 0.9 1.1 1.4 1.3 0.7 0.9 1.1 1.4 1.6 1.8
BMI, kg/m2 26.3 28.2 30.1 31.7 33.7 35.4 37.4 39.4 41.2 43.2 45.2 47.2 49.2
Total cholesterol, mg/dl 190 196 202 208 214 220 226 232 238 244 250 256 262
HDL cholesterol, mg/dl 45 49 53 57 61 65 69 73 77 81 85 89 93
Systolic blood pressure, mm Hg 124 129 135 140 146 152 158 164 170 176 182 188 194
Diastolic blood pressure, mm Hg 74 79 84 89 94 99 104 109 114 119 124 129 134
Fasting blood sugar, mg/dl 110 115 120 125 130 135 140 145 150 155 160 165 170
Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CI, confidence interval; PAR, population attributable risk; RR, relative risk.

*Adjusted for age, race/ethnicity, educational achievement level, marital status, total energy intake (log-transformed), and other lifestyle factors including smoking status, alcohol use, dietary quality, BMI, and physical activity (binary variable). For men and women combined model, adjusted also for sex.

Table 2. Mean and Percentage of Baseline Characteristics of Participants According to the Combined Healthy Lifestyle Score

Table 3. Relative Risk of Pancreatic Cancer in Relation to Single Lifestyle Factors in Men and Women

Addendum: We observed a 27% reduced risk with a high-no-alcohol aMDS (7-8 points) compared with a low-no-alcohol aMDS (0-1 points) (P = .06). The PAR for pancreatic cancer explained by smoking (i.e., current smoking and smoking cessation for <10 years) was 14%, which was the largest PAR among the 5 single lifestyle factors.

Table 4 gives the combined healthy lifestyle score in relation to pancreatic cancer risk. Compared with the least healthy score (0 points), the combination of the 5 healthy lifestyle factors (5 points) was statistically significantly associated with a 59% risk reduction (RR [95% CI]) in men (0.41 [0.24-0.71], P<.001), a nonsignificant 53% risk reduction in women (0.47 [0.19-1.15], P<.001), and a 58% risk reduction in all participants (0.42 [0.26-0.66], P<.001). The PAR for pancreatic cancer was 27% for having a combined lifestyle score of < than 5 points. Because there was a relatively larger number of participants with the lowest and highest scores, we combined the lower (0-1 points) and higher (4-5 points) scores. The RR for having a higher score compared with a lower score was 0.64 (95% CI, 0.45-0.91; P<.003) in women. The PAR for pancreatic cancer was 29% for having a combined lifestyle score of fewer than 4 points. The associations between the score and risk of pancreatic cancer did not vary significantly by sex (Pinteraction=.49) or age (Pinteraction=.89).
We identified 32 healthy lifestyle patterns derived from various 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 dietary quality, and regular physical activity) 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 = .09 to .72, Wald test).

In sensitivity analyses, when 5-point scores were compared with 0-point scores, the RR (95% CI) was 0.39 (0.24-0.62) in a 2-year lag analysis based on 925 cases, 0.40 (0.24-0.64) in an analysis based on 922 cases identified from cancer registries only, and 0.41 (0.25-0.66) in participants without a self-reported history of cancer based on 947 cases.

**Table 4. Relative Risk of Pancreatic Cancer in Relation to Combined Healthy Lifestyle Score**

<table>
<thead>
<tr>
<th>Healthy Lifestyle Score</th>
<th>Case</th>
<th>Person-Year</th>
<th>RR* (95% CI)</th>
<th>Case</th>
<th>Person-Year</th>
<th>RR* (95% CI)</th>
<th>Case</th>
<th>Person-Year</th>
<th>RR* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>20</td>
<td>20304 1</td>
<td>1 [Reference]</td>
<td>6</td>
<td>13576 1</td>
<td>1 [Reference]</td>
<td>26</td>
<td>42610 1</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>1</td>
<td>88</td>
<td>179315 0.72</td>
<td>(0.44-1.16)</td>
<td>43</td>
<td>116734 0.82</td>
<td>(0.35-1.92)</td>
<td>131</td>
<td>296053 0.73</td>
<td>(0.48-1.12)</td>
</tr>
<tr>
<td>2</td>
<td>219</td>
<td>450132 0.69</td>
<td>(0.43-1.09)</td>
<td>119</td>
<td>333804 0.75</td>
<td>(0.33-1.70)</td>
<td>338</td>
<td>783937 0.69</td>
<td>(0.46-1.03)</td>
</tr>
<tr>
<td>3</td>
<td>215</td>
<td>519755 0.55</td>
<td>(0.35-0.88)</td>
<td>119</td>
<td>372166 0.65</td>
<td>(0.28-1.47)</td>
<td>332</td>
<td>891731 0.57</td>
<td>(0.38-0.88)</td>
</tr>
<tr>
<td>4</td>
<td>95</td>
<td>352406 0.34</td>
<td>(0.21-0.56)</td>
<td>72</td>
<td>253226 0.56</td>
<td>(0.24-1.29)</td>
<td>167</td>
<td>700529 0.40</td>
<td>(0.27-0.61)</td>
</tr>
<tr>
<td>5</td>
<td>40</td>
<td>120516 0.41</td>
<td>(0.24-0.71)</td>
<td>23</td>
<td>97035 0.47</td>
<td>(0.19-0.15)</td>
<td>107</td>
<td>217551 0.42</td>
<td>(0.26-0.66)</td>
</tr>
</tbody>
</table>

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

*Healthy lifestyle score (range, 0-5 points) was calculated by summing the binary exposure factors (0, 1) including smoking, alcohol use, dietary quality, body mass index (calculated as weight in kilograms divided by height in meters squared), and physical activity. Participants received 1 point if they had any of the following behaviors: never smokers or quit smoking 10 years or longer, limited alcohol use, healthy dietary quality, body mass index =18 and <25, or regular physical activity.

†Adjusted for age, race/ethnicity, educational achievement level, marital status, and total energy intake (log-transformed). For men and women combined model, adjusted also for sex.

‡P values for linear trend of relative risk.

**Table 5. Relative Risk of Pancreatic Cancer for Most Common Lifestyle Pattern in Each Score Category**

<table>
<thead>
<tr>
<th>Healthy Lifestyle Score</th>
<th>Percentage</th>
<th>No. of Cases</th>
<th>Smoking</th>
<th>Alcohol Use</th>
<th>Dietary Quality</th>
<th>Body Mass Index</th>
<th>Physical Activity</th>
<th>RR* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.5</td>
<td>26</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 [Reference]</td>
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<td>1</td>
<td>6.0</td>
<td>73</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>2</td>
<td>14.6</td>
<td>151</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0.63 (0.36-1.11)</td>
</tr>
<tr>
<td>3</td>
<td>9.9</td>
<td>106</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0.57 (0.34-0.95)</td>
</tr>
<tr>
<td>4</td>
<td>9.1</td>
<td>80</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0.46 (0.27-0.76)</td>
</tr>
<tr>
<td>5</td>
<td>7.6</td>
<td>63</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0.28 (0.16-0.50)</td>
</tr>
<tr>
<td>Total</td>
<td>48.7</td>
<td>499</td>
<td>.00</td>
<td>.00</td>
<td>.00</td>
<td>.00</td>
<td>.00</td>
<td>.00</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; ellipsis, not applicable; RR, relative risk.

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

**COMMENT**

In this large prospective study in older individuals in the United States, we found that the risk of pancreatic cancer was significantly lower in participants who had the highest combined lifestyle score compared with participants who had the lowest score. Approximately 14% of cases may have been prevented if all participants were nonsmokers, whereas 27% of cases may have been pre-
vented if all participants were nonsmokers and 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 findings of 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 aged 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 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) further reduced the risk. If these observations are 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 patients and 4779 control individuals 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 in 3 US studies, the Mediterranean dietary pattern has been associated with reduced risk of colorectal adenoma in men20,21 and reduced all-cause and cancer mortality.14 We also observed a reduced risk associated with a high no-alcohol aMDS. Among the food groups in the Mediterranean diet, fruits and vegetables have been associated with reduced risk of pancreatic cancer,18 whereas red meat intake22 has been associated with increased risk.

Several studies have shown the beneficial effects of adopting a healthy lifestyle on total mortality16 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 reduce 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 present study include 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 compared with the weighted lifestyle score, which considering the unequal contribution of each factor in risk reduction in various lifestyle patterns. Our study findings may be generalizable to other study settings and could have implications for the prevention of other lifestyle-related cancers.

The present study has some limitations. First, to produce an adequate number of participants in each of 32 lifestyle patterns, we dichotomized 5 factors to maintain a lower data dimension. However, the dichotomization could result in loss of study power. The cutoff points we used were based on public health recommendations rather than pancreatic cancer–specific cutoff points. This could further reduce the magnitude of associations and result in loss of study power. Second, we had only 1 baseline measure of the factors that contributed to our healthy lifestyle score, which did not take into account lifestyle changes before or after assessment. Third, 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 to give a comprehensive evaluation of lifestyle patterns and pancreatic cancer risk.

In conclusion, the combined healthy lifestyle factors including nonsmoking, adherence to US alcohol use recommendations, 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 in older individuals in the United States. 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 remain challenging.

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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
REFERENCES


