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Adherence to World Cancer Research Fund/American Institute for Cancer Research Recommendations and Pancreatic Cancer Risk

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Abstract

Background—Pancreatic cancer is a leading cause of cancer death. A role of dietary factors in pancreatic carcinogenesis has been suggested. The World Cancer Research Fund (WCRF) and the American Institute for Cancer Research (AICR) published 8 recommendations for cancer prevention. We evaluated the effect of adherence to the WCRF/AICR recommendations on pancreatic cancer risk.

Methods—We operationalized 7 of the 8 WCRF/AICR recommendations to generate a WCRF/AICR score. We examined the association of WCRF/AICR score with pancreatic cancer in data from an Italian case-control study of 326 incident cases and 652 controls.

Results—Adherence to WCRF/AICR recommendations was associated with a significantly decreased risk of pancreatic cancer. Using a WCRF/AICR score <3.5 as a reference, the adjusted odds ratio (OR) for a score 3.5 to <4 was 0.80 (95% CI 0.49, 1.28), for a score 4 to <5 0.54 (95% CI 0.35, 0.82), and for score 5 or more 0.41 (95% CI 0.24, 0.68; p-value for trend 0.0002). The OR for a continuous increment of one unit of the WCRF/AICR score was 0.72 (95% CI 0.60, 0.87).

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Conclusion—Adherence to the WCRF/AICR recommendations may reduce pancreatic cancer risk.

Keywords

World Cancer Research Fund; American Institute for Cancer Research; Pancreatic Cancer; Diet; Risk Factors

Introduction

Pancreatic cancer is a leading cause of cancer death in both Europe and the United States.[1–3] While mortality rates are expected to drop for most other malignancies, standardized death rates for pancreatic cancer are projected to rise in both regions.[1, 4] Potential risk factors for pancreatic cancer include tobacco,[5] high levels of alcohol consumption,[6, 7] diabetes,[8, 9] obesity,[10–12] and family history.[13, 14] Tobacco contributes to approximately 15–25% of pancreatic cancer in various populations,[5] although the rise in pancreatic cancer rates persists despite declines in tobacco use.[10, 15] Such a rise has been postulated to be related to obesity, although the underlying mechanisms remain uncertain.

A role of dietary factors in pancreatic carcinogenesis has been suggested, although the evidence is not fully consistent. In a recent comprehensive report, a group of experts convened by the World Cancer Research Fund (WCRF)/American Institute for Cancer Research (AICR) concluded that there was limited suggestive evidence that consumption of red and processed meat, foods and beverages containing fructose, and foods containing saturated fatty acids increase pancreatic cancer risk.[12] Evidence for an association between high levels of alcohol intake, body fatness and greater childhood growth and pancreatic cancer was noted. For vegetables, fruits, and foods containing folate the evidence was less consistent and no conclusions were made, while an association with coffee drinking was unlikely.

A limitation of studies of nutritional cancer epidemiology is that these studies mainly investigated the effect of individual dietary factors, while any etiologic role of diet on human cancer is likely to result from the combined effect of multiple components. For this reason, dietary index scores have been developed (e.g., Healthy Eating Index, Diet Quality Index, Recommended Food Score, Mediterranean Diet Score) and applied to the study of health maintenance and cardiovascular disease prevention as well as cancer. [16–22] Arem et al evaluated data from the American Association of Retired Persons Diet and Health Study and found that subjects in the highest quintile of adherence to the Healthy Eating Index guidelines had a reduced risk of pancreatic cancer compared to those in the lowest quintile of adherence.[23] Others have suggested that particular dietary patterns, such as those characterized by animal products and unsaturated fats, are associated with pancreatic cancer risk.[24] One study found an inverse association with a diet high in flavonoids and pancreatic cancer risk in a United States based population, but not in an European population.[25] In particular, dietary indexes that incorporate not only diet but anthropometric and lifestyle factors have been found to be associated with decreased cancer incidence and mortality, thus stressing the advantages of this approach.[19, 22, 26]

In 2007, the WCRF and the American Institute of Cancer Research (AICR) proposed 8 recommendations for cancer prevention on weight management, physical activity, and diet including alcohol use.[21] Since pancreatic cancer has been associated with alcohol,[6, 7] diabetes,[9] obesity,[11] and possibly other dietary factors, adherence to the WCRF/AICR recommendations may have an impact on pancreatic cancer. Previous studies have suggested adherence to the WCRF/AICR recommendations is associated with a decreased risk of cancers such as breast, colorectal, and gastric cancers.[26–30] However, one large prospective cohort study evaluated the effect of WCRF/AICR recommendations on pancreatic cancer and did not demonstrate that adherence to WCRF/AICR recommendations results in a decrease in pancreatic cancer.[29]

In order to investigate the effect of adherence to the WCRF/AICR recommendations on pancreatic cancer risk, we analyzed data from an Italian case-control study, which included detailed information on diet as well other lifestyle factors.

Materials and Methods

Data derived from a hospital-based case-control study of pancreatic cancer conducted between 1991 and 2008 in the provinces of Milan and Pordenone, Italy. This study included 326 incident cases (174 men, 152 women; median age 63 years, range 34–80 years) and 652 controls (348 men, 304 women) who were frequency-matched by age (± 5 years), sex and study center in a 2:1 ratio.[31] Controls were admitted to the same teaching- or general-hospitals as cases for a variety of non-cancer diagnoses, including acute surgical conditions (28%), traumatic orthopedic conditions (31%), other orthopedic conditions (31%), and other miscellaneous conditions (10%). Over 95% of cases and controls who were approached agreed to study participation.

All subjects were interviewed by centrally trained interviewers using a structured questionnaire that included socio-demographic factors, lifestyle habits such as tobacco smoke, dietary habits and physical activity, anthropometric measures, and personal medical history. Height and average weight at ages 30 and 50, as well as before cancer diagnosis (or hospital admission, for controls) were self-reported at time of study enrollment. Physical activity was self-reported in terms of occupational or leisurely activities at ages 12, 15–19, 30–39, and 50–59. Subjects reported level of occupational physical activity as 1) very heavy (e.g., professional athlete), 2) heavy (e.g., farmer), 3) medium (e.g., childcare giver, waiter), 4) standing (e.g., store clerk) and 5) sedentary (e.g., office clerk). Subjects also self-reported sport and leisure activities as 1) > 7 hours per week, 2) 5–7 hours per week, 3) 2–4 hours per week and 4) <2 hours per week. Subject's usual diet two years prior to cancer diagnosis (cases) or at hospital admission (controls) was assessed through a validated and reproducible food frequency questionnaire (FFQ) which included data on 78 foods and beverages grouped into seven sections: 1) bread and cereal dishes, 2) meat and other main dishes, 3) vegetables, 4) fruit, 5) sweets, desserts and soft drinks, 6) milk and hot beverages, and 7) alcohol.[32, 33] Subjects indicated average weekly consumption of each item. Intake of total energy and selected nutrients was computed using an Italian food composition database.[34]

To develop the WCRF/AICR index score, we operationalized 7 out of the 8 recommendations (i.e., body fatness, physical activity, foods and drinks that promote weight gain, foods of plant origin, red and processed meat, alcohol drinking, salt intake); insufficient data was available on intake of dietary supplements (Table 1). For each recommendation/sub-recommendation, we assigned a value of 1 when the recommendation/sub-recommendation was completely met, 0.5 when it was partially met, and 0 otherwise. For recommendations that had more than one sub-recommendation, we created a composite score by weighting each sub-recommendation score so that each overall recommendation contributed equally to the WCRF/AICR score. For each subject, the WCRF/AICR score was then obtained by summing-up the score for each recommendation. Higher scores indicated greater concordance with WCRF/AICR recommendations. Since there were a few missing values for body fatness (26 cases, 54 controls) and physical activity (2 cases, 3 controls) recommendations, the final analyses for the WCRF/AICR score were based on 299 cases and 596 controls.

We estimated odds ratios (ORs) and the corresponding 95% confidence intervals (CIs) of pancreatic cancer for categories of each single WCRF/AICR recommendations (<0.5, 0.5–<1, 1) and for the WCRF/AICR score into four categories (<3.5, 3.5–<4, 4–<5, 5) as a continuous variable (for one unit increment), as well as by unconditional multiple logistic regression models. Models were adjusted for sex, study center (Milan, Pordenone), age (5-year groups), year of interview (continuous), years of education (<7, 7–11, 12), tobacco use (never smoker, ex-smoker, current smoker <20 and 20 cigarettes per day), and history of diabetes (yes, no). Missing values for a few confounding variables (2 cases and 3 controls for education, and 1 one control for tobacco use) were inputted in the most frequent categories. Chi squared test with two-sided alpha was used to compare categorical variables.

Results

Table 2 shows the distribution of pancreatic cancer cases and corresponding controls according to selected covariables. By design, cases and controls have the same distribution by sex, study center and age. Cases reported more years of education and were more frequently heavy tobacco smokers and diabetic ($p < 0.001$ for both).

Adjusted ORs for each individual WCRF/AICR recommendation are provided in Table 3. Adherence (score = 1) to the recommendation for avoiding foods and drinks that promote weight gain (OR 0.50, 95% CI 0.27, 0.93), eating foods of plant origin (OR 0.35, 95% CI 0.16, 0.76) and limiting alcohol (OR 0.59, 95% CI 0.40, 0.85) were associated with a significant decreased pancreatic cancer risk compared to no adherence (score = 0). Partial adherence (score = 0.5) with the recommendation to limit red meat and processed meat was associated with a decreased risk of pancreatic cancer (OR 0.58, 95% CI 0.41, 0.83). Similarly, adherence with this recommendation was associated with a decrease in pancreatic cancer (OR 0.24, 95% CI 0.05, 1.11) but with only 20 subjects (2 cases, 18 controls) in this category, the association was not statistically significant. Adherence to individual recommendations for body fatness and limiting salt intake were also inversely associated, though not significantly, with pancreatic cancer risk, while adherence to individual recommendation for physical activity was not associated with decreased risk of pancreatic

cancer. When stratified by sex, strong inverse associations were observed in men for avoiding foods that promote weight gain, increasing consumption of plant-based foods, and limiting alcohol consumption (data not shown in Table).

Overall, adherence to WCRF/AICR recommendations was associated with a significantly decreased risk of pancreatic cancer (Table 4). Using a WCRF/AICR score <3.5 as a reference, the adjusted OR for a score 3.5 to <4 was 0.80 (95% CI 0.49, 1.28), for a score 4 to <5 0.54 (95% CI 0.35, 0.82), and for score 5 or more 0.41 (95% CI 0.24, 0.68; p-value for trend 0.0002). The OR for a continuous increment of one unit of the WCRF/AICR score was 0.72 (95% CI 0.60, 0.87). When stratified by sex, the adjusted OR for men with a score 3.5 to <4 was 0.70 (95% CI 0.40, 1.23), for a score 4 to <5 0.43 (95% CI 0.25, 0.74), and for score 5 or more 0.28 (95% CI 0.13, 0.63) (p-value for trend = 0.0002). The adjusted OR for women with a score 3.5 to <4 was 1.15 (95% CI 0.45, 2.93), for a score 4 to <5 0.86 (95% CI 0.40, 1.83), and for score 5 or more 0.64 (95% CI 0.29, 1.43) (p-value for trend = 0.16, data not shown in Table).

The OR estimates for a continuous increment of the WCRF/AICR score were consistent in strata of sex, education, body mass index, tobacco smoking and diabetes, while the inverse association was significantly stronger in subjects those aged 60 years or more (OR 0.62, 95% CI 0.49, 0.79) than in those aged less than 60 years (OR 0.90, 95% CI 0.68, 1.19; Supplementary Table 1).

Discussion

Our study provides evidence of an association between adherence to the WCRF/AICR recommendations and decreased pancreatic cancer risk. While several large studies have evaluated the effect of these recommendations on breast,[28, 35] colon[30] and prostate cancer[36] limited data is available on adherence to these recommendations in pancreatic cancer. The European Prospective Investigation into Nutrition and Cancer (EPIC) study, which included 521,330 subjects in 10 European countries, evaluated the effect of WCRF/AICR dietary adherence on various common cancers.[29] EPIC participants in the highest category of WCRF/AICR adherence were found to be 18% less likely to develop any cancers compared to those in the lowest category of adherence. A decreased risk of tumors such as breast, colorectal and gastric was noted; adherence to the WCRF/AICR recommendations was not found to be associated with a decrease in pancreatic cancer.[29]

Prospective studies have not demonstrated that a diet high in fruits and vegetables decreases pancreatic cancer risk. A pooled analysis of 14 prospective studies suggested that fruit and vegetable consumption was not associated with reduced pancreatic cancer risk.[37] However, one systematic review of dietary intake of fruits suggested higher intake of fruit may be associated with decreased pancreatic cancer risk[38] and others have suggested that a diet rich in folate may also be associated with a decreased risk of pancreatic cancer.[39, 40] The WCRF/AICR Pancreatic Cancer Report in 2012 reviewed existing literature and concluded that the evidence for a diet high in fruits or folate was not consistent and too limited to make recommendations.[12] Our study provides evidence that even moderate adherence to the recommendation on plant foods may be associated with decreased risk of

pancreatic cancer, and the association strengthens with greater adherence. This should be interpreted with caution given the negative data from prospective studies.

Several previous studies have also evaluated the effect of red meat intake on pancreatic cancer.[31, 41–43] Red meat is thought to contribute to pancreatic cancer risk by the production of heterocyclic amines and polycyclic aromatic hydrocarbons that may be produced by cooking meat at high temperatures or heating for prolonged times.[44] These compounds have been associated pancreatic cancer risk.[41, 42, 45] In our study, increasing adherence to this recommendation was associated with decreased pancreatic cancer risk; however, very few subjects were fully adherent to this recommendation which led to a wide confidence interval in the fully adherent group.

Meta-analyses and studies of pooled data have suggested that heavy alcohol consumption is associated with pancreatic cancer; [6, 46, 47] Heavy alcohol use also contributes to the development of chronic pancreatitis, which is associated with an increased risk of pancreatic cancer.[48] Certain metabolites of alcohol, including acetaldehyde, N-nitrosodimethylamine, and ethanol itself may lead to pancreatic inflammation and directly contribute to pancreatic cancer development.[49] Our data demonstrating a protective effect of limiting alcohol use on pancreatic cancer risk agree with this existing literature.

Energy dense foods may predispose to obesity and diabetes, both of which have been associated with pancreatic cancer. [8, 9, 11, 12] Limited data is available on consumption of energy dense foods and risk for pancreatic cancer; a Chinese case-control study suggested that subjects who consumed a diet in the highest quintile of energy density had a greater risk of pancreatic cancer.[50] Our data similarly support this finding. While obesity itself has been associated with pancreatic cancer[11], it is interesting that our study did not demonstrate that adherence to the WCRF/AICR recommendation for body fatness was associated with pancreatic cancer risk. In this study, we operationalized BMI at ages 50 and 30 to evaluate the association between pancreatic cancer risk and BMI. Subjects with pancreatic cancer may lose weight prior to diagnosis; for this reason, we did not use BMI before diagnosis. However, weight at age 30 and 50 was self-reported and this may have led to an underestimation of our estimates. Similarly, no associations were found for the recommendations for physical activity or salt intake.

In the EPIC study, no associations with cancer were noted for body fatness, physical activity, foods that promote weight gain, and salt intake in men.[29] In women, however, cancer risk was inversely related to body fatness as well as physical activity, plant foods, and alcohol intake. Data on the protective effect of physical activity on pancreatic cancer risk are inconsistent; the 2012 WCRF/AICR Pancreatic Cancer Report found existing data was too limited to make recommendations.[12] Our data suggest that men in particular may derive the greatest benefit for adherence to WCRF/AICR recommendations, especially with regard to limiting foods that promote weight gain, increased consumption of plant-based foods, and limiting alcohol consumption. In our study, the only single recommendation associated with decreased risk of pancreatic cancer in women is to limit consumption of red and processed foods. Further studies are required to analyze the sex-dependent effects of WCRF/AICR recommendations on development of cancer.

We attempted to minimize bias in our case-control study by having the same trained interviewers administer the questionnaire to both cases and controls. We recognize that dietary questionnaires were based on diet recall, and this may introduce some bias for those with a recent cancer diagnosis; to minimize this, we asked about diet in the two years before the cancer diagnosis or hospital admission. We additionally excluded control subjects with diagnoses associated with long-term dietary modifications. This was a hospital-based case-control study; as such, dietary habits between the hospitalized population and general populations may be different. At the time of interview, very limited data had emerged on various risk factors and pancreatic cancer; therefore recall bias should be minimal. Strengths of the study include our sample size, ability to control for other known risk factors for pancreatic cancer, and near complete enrollment of both cases and controls. We operationalized the AICR/WCRF score *a priori* and in a similar manner to previous large cohort and case-control studies.[27–29, 35]

Overall, we found that a WCRF/AICR score above 4 was associated with decreased risk of pancreatic cancer, when compared to those with a WCRF/AICR score <3.5. The association was similarly found in continuous analysis for increments of WCRF/AICR score. One of the values of the WCRF/AICR score is that it integrates multiple dietary and anthropometric factors which overall may contribute to the prevention of pancreatic cancer. Notwithstanding the problems in further quantifying its beneficial effect, our study provides evidence that adherence to the WCRF/AICR recommendations may reduce pancreatic cancer risk.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Operationalization of WCRF/AICR Recommendations.

WCRF/AICR Recommendations	Personal Recommendations	Operationalization/Comments	Scoring
1) Body fatness. Be as lean as possible without becoming underweight.	1a) Ensure that body weight throughout childhood and adolescent growth projects toward the lower end of the normal body mass index (BMI) at age 21 years 1b) Maintain body weight within the normal range from age 21 years	At age 12, compared to kids of same sex and age, you were: thinner At age 12, compared to kids of same sex and age, you were: same At age 12, compared to kids of same sex and age, you were: heavier	1 0.5 0
2) Physical activity. Be physically active as part of your everyday life.	1c) Avoid weight gain and increases in waist circumference throughout adulthood 2a) Be moderately physically active, equivalent to brisk walking, for 30 min every day. 2b) As fitness improves, aim for 60 min of moderate or for 30 min of vigorous physical activity every day. 2c) Limit sedentary habits such as watching television.	Insufficient data Very Heavy/Heavy job or >5 hours/week of leisure time physical activity (age 30–39) Medium job or 2–4 hours/week of leisure time physical activity (age 30–39) Standing/Sedentary job or <2 hours/week of leisure time physical activity (age 30–39) Insufficient data	1 0.5 0
3) Foods and drinks that promote weight gain. Limit consumption of energy-dense foods; avoid sugary drinks.	3a) Consume energy-dense foods sparingly. 3b) Avoid sugary drinks.	Insufficient data Energy density: 125 kcal/100 g/day Energy density: >125 to <175 kcal/100 g/day Energy density: >175 kcal/100 g/day	1 0.5 0
4) Plant foods. Eat mostly foods of plant origin	3c) Consume fast foods sparingly, if at all. 4a) Eat 5 portions/servings (400 g) of a variety of non-starchy vegetables and of fruit every day.	Sugary drink intake (sweetened fruit juice and soft drinks): 0 g/day Sugary drink intake: 0<250 g/day Sugary drink intake: >250 g/day Insufficient data	1 0.5 0
		Fruit and vegetable intake: 5 servings/day	1

WCRF/AICR Recommendations	Personal Recommendations	Operationalization/Comments	Scoring
		Fruit and vegetable intake: 3–4 servings/day	0.5
		Fruit and vegetable intake: 2 servings/day	0
	4b) Eat relatively unprocessed cereals (grains) and/or pulses (legumes) with every meal.	Dietary fiber intake: 25 g/day	1
		Dietary fiber intake: 12.5 to <25 g/day	0.5
		Dietary fiber intake: <12.5 g/day	0
	4c) Limit refined starchy foods.	Starch: <200 gr/day	1
		Starch: 200 to 300 gr/day	0.5
		Starch: 300 gr/day	0
	4d) People who consume starchy roots or tubers as staples should also ensure sufficient intake of non-starchy vegetables, fruit, and pulses (legumes).	Insufficient data	
5) Animal foods. Limit intake of red meat and avoid processed meat	5a) People who eat red meat should consume <500 g/week and very few, if any, processed meats.	Red and processed meat: <500 g/week and processed meat intake <3 g/day	1
		Red and processed meat: <500 g/week and processed meat intake 3 to <50 g/day	0.5
		Red and processed meat: 500 g/week or processed meat intake 50 g/day	0
6) Alcoholic drinks. Limit alcoholic drinks.	6a) If alcoholic drinks are consumed, limit consumption to 2 drinks/day for men and 1 drink/day for women.	Drinks/day: 2 (men)	1
		Drinks/day: 1 (women)	1
		Drinks/day: >2 to 3 (men)	0.5
		Drinks/day: >1 to 2 (women)	0.5
		Drinks/day: >3 (men)	0
		Drinks/day: >2 (women)	0
7) Preservation, processing, preparation. Limit consumption of salt. Avoid moldy cereals (grains) or pulses (legumes).	7a) Avoid salt-preserved, salted, or salty foods; preserve foods without using salt.	Insufficient data	
	7b) Limit consumption of processed foods with added salt to ensure an intake of <6 g (2.4 g sodium)/day.	Sodium from foods: <2.4 g/day	1
		Sodium from foods: 2.4 to 4 g/day	0.5
		Sodium from foods: >4 g/day	0
8) Dietary supplements. Aim to meet nutritional needs through diet alone.	7c) Do not eat moldy cereals (grains) or pulses (legumes). 8a) Dietary supplements are not recommended for cancer prevention.	Insufficient data	
		Insufficient data	

AICR: American Institute of Cancer Research; WCRF: World Cancer Research Fund.

When BMI at age 50 was unavailable we used BMI at age 30.

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Table 2

Distribution of 326 pancreatic cancer cases and 652 controls by selected covariates, Italy 1991–2008.

	Cases (%)	Controls (%)
Sex		
Male	174 (53.4)	348 (53.4)
Female	152 (46.6)	304 (46.6)
Study center		
Milan	151 (46.3)	302 (46.3)
Pordenone	175 (53.7)	350 (53.7)
Age (years)		
<50	32 (9.8)	64 (9.8)
50–59	89 (27.3)	178 (27.3)
60–69	122 (37.4)	244 (37.4)
70	83 (25.5)	166 (25.5)
Education (years) ^a		
<7	166 (51.2)	350 (53.9)
7–11	86 (26.5)	192 (29.5)
12	72 (22.2)	108 (16.5)
Tobacco smoking ^a		
Never Smoker	137 (42.0)	328 (50.4)
Ex-Smoker	86 (26.4)	189 (29.0)
Current Smoker <20 cigarettes/day	58 (17.8)	84 (12.9)
Current smoker 20 cigarettes/day	45 (13.8)	50 (7.7)
History of diabetes		
No	279 (85.6)	615 (94.3)
Yes	47 (14.4)	37 (5.7)

^aThe sum is not the total number of subjects due to missing values. Two cases and two controls were missing data on education. One control was missing data on tobacco use.

Table 3
Adjusted ORs for pancreatic cancer for each WCRF/AICR Recommendation. Italy 1991–2008.

WCRF/AICR Recommendation	WCRF/AICR Score										p-value for trend
	< 0.5			0.5–1			1			Adjusted OR (95% CI) ^a	
	Cases (%)	Controls (%)	Adjusted OR (95% CI) ^a	Cases (%)	Controls (%)	Adjusted OR (95% CI) ^a	Cases (%)	Controls (%)	Adjusted OR (95% CI) ^a		
1. Body Fatness ^b	87 (29.00)	143 (23.91)	0.95 (0.65, 1.38)	166 (55.33)	339 (56.69)	0.95 (0.65, 1.38)	47 (15.67)	116 (19.40)	0.87 (0.53, 1.42)	0.59	
2. Physical activity ^b	53 (16.36)	124 (19.11)	1.29 (0.83, 2.01)	105 (32.41)	238 (36.67)	1.29 (0.83, 2.01)	166 (51.23)	287 (44.22)	1.54 (0.99, 2.93)	0.057	
3. Food and drinks that promote weight gain	48 (14.72)	77 (11.81)	0.72 (0.46, 1.23)	244 (74.85)	487 (74.69)	0.72 (0.46, 1.23)	34 (10.43)	88 (13.50)	0.50 (0.27, 0.93)	0.029	
4. Eat mostly foods of plant origin	21 (6.44)	21 (3.22)	0.60 (0.30, 1.20)	267 (81.90)	519 (79.60)	0.60 (0.30, 1.20)	38 (11.66)	112 (17.18)	0.35 (0.16, 0.76)	0.003	
5. Limit red meat and processed meat	256 (78.53)	437 (67.02)	0.58 (0.41, 0.83)	68 (20.86)	197 (30.21)	0.58 (0.41, 0.83)	2 (0.61)	18 (2.76)	0.24 (0.05, 1.11)	0.0005	
6. Limit alcohol	133 (40.80)	227 (34.82)	0.87 (0.56, 1.36)	56 (17.18)	110 (16.87)	0.87 (0.56, 1.36)	137 (42.02)	315 (48.31)	0.59 (0.40, 0.85)	0.004	
7. Limit salt	9 (2.76)	13 (1.99)	0.88 (0.33, 2.37)	118 (36.20)	195 (29.91)	0.88 (0.33, 2.37)	199 (61.04)	444 (68.10)	0.59 (0.22, 1.57)	0.012	

AICR: American Institute of Cancer Research; OR: odds ratio; CI: confidence interval; WCRF: World Cancer Research Fund.

^aCovariates include: sex, study center, year of interview, age, education, tobacco smoking, and history of diabetes. A score of <0.5 was used as the reference category.

^bThe sum is not the total number of subjects due to missing values.

Table 4

Adjusted ORs for pancreatic cancer for categories of WCRF/AICR score and for a unit increment. Italy 1991–2008.

WCRF/AICR Score ^a	Cases (%)	Controls (%)	Adjusted OR (95% CI) ^b
<3.5	86 (28.8)	112 (18.8)	1 ^c
3.5–<4	58 (19.4)	107 (18.0)	0.80 (0.49, 1.28)
4–<5	110 (36.8)	238 (39.9)	0.54 (0.35, 0.82)
5	45 (15.1)	139 (23.3)	0.41 (0.24, 0.68)
p-value for trend			0.0002
Adjusted OR for a unit increment			0.72 (0.60, 0.87)

AICR: American Institute of Cancer Research; OR: odds ratio; CI: confidence interval; WCRF: World Cancer Research Fund.

^aThe sum is not the total number of subjects due to missing values.

^bCovariates include: sex, study center, year of interview, age, education, tobacco smoking, and history of diabetes. A score of <3.5 was used as the reference.

^cReference category.