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Physical Activity, Diet, and Pancreatic Cancer: A Population-Based Case-Control Study in Minnesota

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Abstract

Although mounting evidence suggests that insulin resistance is involved in pancreatic carcinogenesis, few epidemiologic studies have comprehensively investigated the role of lifestyle factors influencing this metabolic disorder in the etiology of pancreatic cancer. We sought to examine this problem in a case-control study conducted in 1994-1998 in Minnesota. Cases (n=186), aged 20 years or older, were ascertained from all hospitals in the metropolitan area of the Twin Cities and the Mayo Clinic; from the latter, only cases residing in the Upper Midwest of the US were recruited. Controls (n=554) were randomly selected from the general population and frequency matched to cases by age (within 5 years) and sex. Odds ratios (OR) and 95% confidence intervals (95% CI) were estimated using unconditional logistic regression. After adjustment for confounders, physical activity was associated with a reduced risk but this protective effect was confined to light activity and moderate activity only [OR (95% CI) for highest vs. lowest quartile: 0.55 (0.30-0.97), P_{trend} = 0.038 and 0.51 (0.28-0.93), P_{trend} = 0.07, respectively]. An increased risk was found for dietary intakes of energy and fat but was statistically significant for saturated and polyunsaturated fat only. Of note, no appreciable difference in the magnitude of the associations existed between saturated, monounsaturated, and polyunsaturated fat. Compared with individuals in the lowest quartile of fiber intake, the risk was approximately halved for those in the third [OR (95% CI): 0.49 (0.26-0.94)] and the highest quartile [OR (95% CI): 0.52 (0.21-1.30)]. Our study lends support to the hypothesis that dietary and other lifestyle factors influencing insulin resistance modulate pancreatic cancer risk.

Introduction

Pancreatic cancer is one of the leading causes of cancer death in developed and some developing countries (1). In the US, pancreatic cancer mortality ranks fourth among all

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cancers in 2007 (2). There are no screening tests to detect cases at an early stage of the disease and most cases are diagnosed when the cancer is advanced. In addition, because pancreatic cancer progresses rapidly and most therapies have limited benefit, most patients have an extremely poor prognosis, with a five-year survival of 4% or less (1,3). A major challenge for the primary prevention of this disease is its largely unknown etiology. Cigarette smoking is one of the few established risk factors (1,3).

The worldwide pattern of pancreatic cancer incidence is similar to that of prostate, colorectal, and breast cancer (1), major malignancies in developed countries. These cancers have been associated with a Western lifestyle which is characterized by a diet high in energy and fat and low in fiber, coupled with low levels of physical activity (4). A striking variation in pancreatic cancer incidence exists among populations across the world, with high rates seen in North America, Europe, and some South-American countries (*e.g.*, Argentina) and low rates in most Asian countries and Africa (1,3). Pancreatic cancer incidence has remarkably increased over the last few decades in Japan, most eastern European countries (*e.g.*, Hungary), and some former Soviet Republics (1,3), where nutrition transition towards a typical western diet has taken place during the same time period (5). Collectively, these descriptive epidemiologic data suggest that energy imbalance, fat, and fiber play a critical role in the etiology of pancreatic cancer.

Several lines of evidence indicate that insulin resistance is implicated in pancreatic carcinogenesis. Insulin resistance refers to a condition in which fat, muscle, and liver cells have decreased sensitivity to the action of insulin (6,7). Pancreatic cancer predominately originates from the exocrine pancreas, which is physiologically exposed to high levels of insulin due to its anatomical proximity to the endocrine pancreas (8). Cell culture studies have revealed that insulin stimulated proliferation of pancreatic cancer cells in a dose-response manner (9). The promoting effect of high fat intake on pancreatic carcinogenesis in hamsters fed *N*-nitrosobis-(2-oxopropyl)amine disappeared when metformin, an insulin sensitizer, was administered to the animals (10). Epidemiologic studies have shown that individuals with high serum levels of insulin and glucose (biomarkers of insulin resistance) (11,12) and patients with diabetes (a condition linked to insulin resistance) (13) are associated with an increased risk of developing pancreatic cancer.

Substantial data from animal and human studies indicate that lifestyle factors influence insulin resistance. Energy imbalance results from excess energy intake, physical inactivity, or both and is a well-established risk factor for insulin resistance (14). In most human studies, saturated fat and simple sugars (*e.g.*, glucose, sucrose) promote insulin resistance, whereas monounsaturated fat, n-3 polyunsaturated fat, fiber, fruits, and vegetables improve insulin resistance (6,7). Therefore, it is biologically plausible that physical activity and dietary practices may affect pancreatic cancer risk through modulating insulin resistance. To date, however, few epidemiologic studies have comprehensively evaluated these factors in relation to pancreatic cancer risk. We sought to investigate this question in a population-based, case-control study in Minnesota.

Materials and Methods

Study Population

The design and methods of the case-control study of pancreatic cancer that was conducted from April 1994 to September 1998 in Minnesota have been described in detail elsewhere (15,16). Briefly, cases were subjects with newly diagnosed cancer of the exocrine pancreas confirmed by pathological examinations (International Classification of Disease for Oncology, third edition, code C25). Cases were ascertained from two sources: all hospitals in the seven-county metropolitan area of the Twin Cities, Minneapolis and St. Paul,

Minnesota and the Mayo Clinic; from the latter, only cases residing in the Upper Midwest of the US were recruited. Given the rapid fatality of pancreatic cancer, a rapid case-ascertainment system was adopted to enroll cases. As a result, the median number of days between diagnosis and first contact for the study was only 13 days for the cases recruited in the study. To be eligible for the study, subjects had to be 20 years of age or older, English-speaking, and mentally competent. Of 460 eligible cases identified, 202 failed to participate in the study because of occurrence of death before contact or interview (n = 85), refusal of cases (n = 79), refusal of physicians (n = 31), and inability to contact cases (n = 7). After these exclusions, 258 cases completed the study, yielding a response rate of 56%.

Controls were randomly selected from population of the seven-county metropolitan area of the Twin Cities. Potential controls were identified from the drivers' license and State identity card database for subjects aged 20-64 years and from US Health Care Financing Administration (now Centers for Medicare & Medicaid Services) records for those aged 65 years or older. Controls were frequency matched to cases by age (within 5 years) and sex. Inclusion criteria for controls were the same as those for cases, disallowing diagnosis of pancreatic cancer. Of 1,141 eligible controls identified, 676 participated in the study, giving a response rate of 59%. Data on diet and alcohol consumption were missing for 72 cases and 122 controls primarily because cases were too frail to withstand the entire interview or because controls refused to complete the food frequency questionnaire. Finally, data from a total of 186 cases and 554 controls were available for the present analysis.

Data Collection

The study protocols were approved by the institutional review boards of the University of Minnesota and the Mayo Clinic. Written, informed consent was obtained from each participant prior to interview. In-person interview with all subjects were conducted using a basic questionnaire and a food frequency questionnaire (FFQ) that also covered questions on alcohol use. The basic questionnaire was designed to elicit information on demographics, socioeconomics, physical activity, medical history, family history, and cigarette smoking. Physical activity evaluated in the interview comprised occupational and leisure-time activities and the latter type of activities included walks or hikes, home exercises or dances, home maintenance, and sports. To assess physical activity, all activities were divided into three levels: light (*e.g.*, sitting, strolling), moderate (*e.g.*, carpentry, brisk walking, mopping floors, ice skating), and heavy (*e.g.*, lumberjack, running, heavy shoveling, basketball). During the interview, the participants were asked to report the number of hours per week they usually spent on each of the three levels of activities during the year before pancreatic cancer diagnosis for cases or the past year for controls. The three cards displaying common examples of light, moderate, and heavy activities, respectively, were used to increase the recall accuracy of the participants. A study was conducted to validate the physical activity questionnaire used in the present study by asking the participants to recall activity patterns for the year prior to 2 to 3 years ago and comparing recalled activity patterns with those reported 2 to 3 years ago. This validation study demonstrated that people could reliably recall their activity patterns of the recent past (17).

The diet of all participants was assessed using a slightly modified version of the Willett FFQ (18). This validated instrument contained 153 items of food or food groups commonly eaten in the US diet. In the dietary survey, subjects were asked to recall the average frequency of consumption of each food item included in the questionnaire during the year before pancreatic cancer diagnosis for cases or the past year for controls. Dietary intakes of energy and nutrients were computed by multiplying the amount in a pre-specified portion size of each food item by the reported frequency of consumption and summing over all food items. The estimates of the amounts of energy and nutrients for the portion size of each food item

were based on a nutrient database developed for the Minnesota Colon Cancer Prevention Research Unit studies.

Statistical Analysis

The risk of pancreatic cancer in relation to physical activity and dietary factors of interest was estimated as odds ratios (OR) and 95% confidence intervals (95% CI) by unconditional logistic regression analysis. Total physical activity and each of the three levels of physical activity (light, moderate, and heavy) were divided into quartiles. Similarly, dietary intakes of energy, total fat, types of fat (saturated, monounsaturated, and polyunsaturated fat), fiber, fruits, and vegetables were each classified into quartiles as well. Cutoffs for quartiles were created on the basis of the distribution of each of these variables among controls. The lowest quartile of physical activity and each of the dietary factors examined was used as the reference category to calculate the risk of pancreatic cancer in the three upper quartiles. Potential confounders adjusted for in the initial multivariable models included age, sex, race, education (three levels), cigarette smoking (never, former, and current), and alcohol drinking (serving/week). Body mass index was not entered into the models because anthropometric parameters were not measured to encourage the participation of the patients who were generally physically frail. Also included in the initial models were interaction terms between age, sex, total physical activity (quartiles), and each of dietary factors considered (quartiles). Statistical significance of these potential interactions was tested by the likelihood ratio test. None of the interaction terms constructed was found to be statistically significant and were thus removed from the regression models. Separate analyses were performed for saturated, monounsaturated, and polyunsaturated fat because animal studies have shown that different types of fat have differential effects on pancreatic carcinogenesis (19).

To evaluate whether physical activity and the dietary factors of interest were independently associated with pancreatic cancer risk, the initial multivariable models established for each variable were further adjusted for all other variables considered in this study. Saturated fat, monounsaturated fat, and polyunsaturated fat were not adjusted for each other to avoid potential multicollinearity in multivariable models because strong correlations existed among these three types of fat ($r = 0.69$ to $r = 0.94$, all $p < 0.0001$). Linear trends of risk estimates across quartiles of physical activity and dietary factors were tested by weighting each quartile by its median value. All statistical tests were two-sided and a p-value of less than 0.05 was considered statistically significant. All statistical analyses were performed using the SAS (version 9.1; SAS Institute Inc., Cary, NC).

Results

The mean ages of cases and controls were 65.8 years and 66.5 years, respectively (Table 1.). The study subjects were predominately Caucasians (94.0% for cases and 98.2% for controls). Cases generally had a lower education attainment, were more likely to be former or current smokers, and were less physically active than controls. More cases (27.0%) than controls (7.0%) reported a history of diabetes. Cases tended to have a higher intake of total fat but a lower intake of fiber than controls (Table 2).

After adjustment for age, sex, race, education, cigarette smoking, and alcohol intake, physical activity was significantly inversely associated with the risk of pancreatic cancer (Table 3). Compared with the lowest quartile of physical activity, ORs (95% CIs) were 0.51 (0.30-0.85), 0.53 (0.31-0.90), and 0.60 (0.35-1.04) for the second, third, and highest quartile, respectively. This protective effect appeared to be confined to light and moderate activities, with a similar magnitude of risk reduction for each. In considering a decrease in risk across quartiles of increasing physical activity, the linear trends reached statistical significance only for light activity ($p = 0.026$) while they were of borderline significance for moderate ($p =$

0.058) and total (p = 0.071) physical activity. The risk estimates obtained from the aforementioned analyses were only slightly attenuated after additional adjustment for dietary intakes of energy, fat, fiber, fruits, and vegetables.

Energy intake was weakly inversely associated with pancreatic cancer risk after adjustment for age, sex, race, education, cigarette smoking, and alcohol intake (Table 4). After further adjustment for physical activity and dietary intake of fat, fiber, fruits, and vegetables, a non-significant positive association was found between energy intake and pancreatic cancer. A non-significant positive association also existed between total fat intake and pancreatic cancer. The multivariate-adjusted ORs (95% CIs) for the highest compared with lowest quartile were statistically significant for both saturated fat [2.47 (1.07-5.86), $P_{trend} = 0.061$] and polyunsaturated fat [2.56 (1.19-5.58), $P_{trend} = 0.024$]. Of note, no appreciable differences in the magnitude of risk estimates were observed among saturated, monounsaturated, and polyunsaturated fat (Table 4).

Individuals in the third quartile [OR (95% CI): 0.49 (0.26-0.94)] and highest quartile [OR (95% CI): 0.52 (0.21-1.30)] of fiber intake experienced approximately half the risk of those in the lowest quartile, after adjustment for all confounders mentioned previously. Inverse associations were generally found for dietary intakes of fruits and vegetables, however, none of the risk estimates were statistically significant in the models adjusting for all confounders considered (Table 4). Because diabetes may be in the causal pathway between the lifestyle and dietary factors of interest and pancreatic cancer, it was not included as a confounder in the fully adjusted models. Nevertheless, additional adjustment for diabetes did not materially alter all the results described above.

Discussion

In this study, we demonstrated that physical activity was associated with a reduced risk of pancreatic cancer but this protective effect was limited to light and moderate physical activities. After adjustment for physical activity, alcohol consumption and the dietary factors considered, energy intake was positively associated with risk but this association was not statistically significant. An elevated risk was also observed for fat intake and attained statistical significance for saturated fat and polyunsaturated fat. Dietary intake of fiber significantly decreased the risk of pancreatic cancer.

Although substantial evidence from animal and human studies indicates that insulin resistance plays a role in pancreatic carcinogenesis, few studies have comprehensively evaluated the associations of lifestyle and dietary factors that promote or improve insulin resistance with pancreatic cancer risk. In most epidemiologic studies (20,21), these factors were not evaluated together, which failed to consider that they may be implicated in the etiology of this malignancy through a shared biochemical mechanism (*i.e.*, modulating insulin resistance). In this study, we demonstrated that light physical activity and moderate physical activity were inversely associated with the risk of pancreatic cancer after adjustment for energy intake. Our results were consistent with those of some (22-24), although not all (25,26), previous studies. This protective effect of physical activity could be ascribed to its improvement of insulin sensitivity in skeletal muscles and fat tissue (6,27). We also found that heavy physical activity was associated with elevated risk estimates but this positive association was statistically significant only for individuals in the second quartile. Interestingly, similar increased risks were seen in a Norwegian cohort study (28) and the Iowa Women's Health Study (29). It has been suggested that this potential detrimental effect may be partially related to an increased chance of occupational exposure to carcinogens among subjects who performed heavy physical activity (28).

Little conclusive evidence exists about the relationship between diet and pancreatic cancer (3). Overall, evidence from case-control studies on the associations of energy and specific nutrients with pancreatic cancer risk is limited and inconsistent (3). Of the 10 studies evaluating energy intake in relation to the risk of pancreatic cancer (20,30-38), the relation was positive in seven studies (20,30-34,37), inverse in two studies (36,38), and mixed in one study (35). We found a positive but insignificant association between energy intake and pancreatic cancer risk, which is in agreement with the results of most previous studies (20,30-34,37). Physical activity is a major determinant of energy expenditure in free-living subjects (39). Unlike all of the 10 studies mentioned above (20,30-38), our observed positive relation between energy intake and pancreatic cancer risk was obtained after adjustment for physical activity in multivariable models. Therefore, our results suggest that, for an individual with a given amount of energy expenditure, excess energy intake confers an elevated risk for pancreatic cancer.

Many (40-42), but not all (36,43,44), epidemiologic studies reported that fat intake increased pancreatic cancer risk, and that this positive association was overall stronger for saturated fat than for monounsaturated and polyunsaturated fat (38,40,45). However, opposite findings have generally been observed in animal studies (19). There are no definitive explanations for the discrepancies between human and animal studies. Our study showed elevated odds ratios for energy-adjusted intake of total fat and all three types of fat associated with pancreatic cancer risk. In addition, there were no remarkable differences in the magnitude of the associations among the three types of fat. Fat is a major source of energy intake in the Western diet. Therefore, a habitual high intake of fat may promote pancreatic carcinogenesis by enhancing energy imbalance and, in turn, insulin resistance. As meat contains fat, it is also possible that mutagens and carcinogens derived from meat cooked at high temperature (*e.g.*, heterocyclic amines and benzo(a)pyrene) account for the observed positive association of fat with pancreatic cancer risk (15). However, our risk estimates obtained from the multivariable models adjusted for these mutagenic compounds did not support this alternative explanation.

Of all the dietary factors analyzed in this study, most consistent results have been reported for fiber. An inverse association between fiber intake and pancreatic cancer risk has been identified in all nine case-control studies conducted to date that have tested this hypothesis (30-36,41,42), except for a subgroup analysis of men in a study conducted in Utah (41). ORs for six (31,33-35,41,42) of the nine studies that showed a statistically significant association ranged from 0.26 in an Australian study (33) to 0.65 in a large study conducted in the San Francisco Bay Area (42). Our study revealed an approximately 50% reduction in risk for subjects in the third and highest quartiles of fiber intake as compared with those in the lowest quartile, which provides further support for the beneficial effect of fiber consumption on the development of pancreatic cancer. The only cohort study to date that has examined fiber intake and pancreatic cancer reported null results (38). However, the participants of that study were Finnish male cigarette smokers, a group of persons with high risk for pancreatic cancer (38). Therefore, caution should be exercised when the findings from this prospective study are extrapolated to the general population.

The associations of dietary intakes of fruits and vegetables with pancreatic cancer risk were inconsistent and not statistically significant in the present study. These results are consistent with those of most cohort studies (21,46,47). However, case-control studies have generally shown a modest, inverse relation with intakes of fruits and vegetables (41,48-50). Proxy interviews were performed in some case-control studies of pancreatic cancer due to its rapid fatality (34,51,52) and this could increase the possibility of recall bias, a major threat to the validity of data collected in case-control studies.

There are several advantages in our study. All cases were identified through a rapid case-ascertainment system and interviewed in person by a trained interviewer. Avoidance of proxy interviews minimized recall bias in our study. Food models were used to assist subjects in accurately reporting frequency of consumption for a particular serving size. The dietary and lifestyle factors selected were evaluated in relation to pancreatic cancer under *a priori*, biologically plausible hypotheses. The results of this study were obtained after control for almost all established and potential risk factors for pancreatic cancer. All these factors strengthen the validity and reliability of our findings.

The present study is also subject to a few limitations. Although direct interview was performed for all cases, recall bias is still an issue for consideration. The recall of usual dietary habits during the year before pancreatic cancer diagnosis among cases might be affected by changes in dietary intake after diagnosis and/or treatment of the disease. Dietary measurement error that resulted from the treatment of pancreatic cancer should not be substantial since cases were invited to participate in the study within, on average, approximately one month after diagnosis. However, dietary changes due to the presence of clinical symptoms (*e.g.*, anorexia and indigestion) might have still influenced the accuracy of dietary recall. Dietary measurement error inherent in food frequency questionnaire might have attenuated our risk estimates to some extent. The response rate for both cases and controls was relatively low (<60%), although a rate of this size is not uncommon in case-control studies of pancreatic cancer (34,40,53). It is possible that the subjects who participated in the study were different from those who did not with regard to demographic and socioeconomic factors. In this study, cigarette smoking was adjusted as a categorical variable (*i.e.*, never, former, and current). Such an adjustment might be insufficient and thus likely resulted in residual confounding of smoking. However, no appreciable differences in risk estimates were observed when number of pack-years of cigarette smoking (a combined measure of the amount and duration of tobacco use) was adjusted instead in multivariable models.

A wealth of evidence supports that obesity, especially central obesity, enhances insulin resistance (6,7). Because of lack of data on body mass index, waist circumference, and hip circumference, we could not investigate the associations of these indicators of obesity with pancreatic cancer risk. However, our risk estimates remained virtually unchanged after further adjustment for diabetes, a condition for which obesity is a strong risk factor (13). Intake of carbohydrates, particularly simple sugars, may also influence the risk of pancreatic cancer since they have been linked to insulin resistance (6,7). We found an inverse but insignificant association between carbohydrate intake and pancreatic cancer risk. Limited data on sources and amounts of intakes of simple sugars precluded us from evaluating these nutrients in relation to pancreatic cancer. Notwithstanding these weaknesses, our study is among the first to systematically evaluate the role of lifestyle and dietary factors modulating insulin resistance in the etiology of pancreatic cancer.

In a population-based case-control study in Minnesota, we found that dietary intake of fat was associated with an increased risk of pancreatic cancer, whereas light and moderate physical activities and dietary intake of fiber were associated with a reduced risk. Although physical activity and the nutritional factors we assessed may affect the development of pancreatic cancer through a number of biochemical mechanisms, all have been reported to influence insulin resistance. Therefore, the present study offers additional evidence for a role of this metabolic disorder in pancreatic carcinogenesis. Future studies that can probe the biochemical mechanisms underlying these observations are warranted. Our data give further support to the recommendations for primary prevention of this malignancy by maintaining an active lifestyle and consuming a diet low in fat and high in fiber.

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Table 1

Characteristics of cases and controls in a population-based case-control study of pancreatic cancer in Minnesota, 1994-1998[a]

Characteristic	Cases (n=186)	Controls (n=554)	*P* Value
Age (years)	65.8 (10.9)	66.5 (12.0)	0.47
Sex			
Male	109 (59.2%)	314 (56.7%)	
Female	75 (40.8%)	240 (43.3%)	0.54
Race			
Caucasian	173 (94.0%)	544 (98.2%)	
African-American	7 (3.8%)	4 (0.7%)	
Other	4 (2.2%)	6 (1.1%)	0.006
Education			
Some high school or less	31 (16.8%)	64 (11.6%)	
High school graduate	69 (37.5%)	146 (26.3%)	
Some college or more	84 (45.7%)	344 (62.1%)	0.0005
Cigarette smoking			
Never smoker	67 (37.9%)	263 (47.5%)	
Former smoker	83 (46.9%)	233 (42.0%)	
Current smoker	27 (15.2%)	58 (10.5%)	0.047
Alcohol intake (serving/week)	3.4 (6.8)	4.6 (8.4)	0.057
Physical activity (hrs/week)			
Light	23.0 (16.6)	27.1 (16.4)	0.007
Moderate	14.9 (12.7)	17.6 (12.6)	0.019
Heavy	5.0 (11.1)	3.7 (5.3)	0.16
Total	42.9 (27.3)	48.5 (25.4)	0.020
Diabetes mellitus			
Yes	44 (27.0%)	39 (7.0%)	
No	119 (73.0%)	515 (93.0%)	<0.0001

Data shown are mean (SD) or n (%).

[a]Data for some variables were missing for some cases.

Table 2

Dietary intake of cases and controls in a population-based case-control study of pancreatic cancer in Minnesota, 1994-1998

Nutrient/Food	Cases (n=186) Mean (SD)	Controls (n=554) Mean (SD)	*P* Value
Energy (kcal/day)	2,079 (931)	2,076 (811)	0.97
Total fat (gram/day)	71.7 (33.1)	70.4 (36.5)	0.66
Saturated fat	24.7 (12.5)	24.0 (13.0)	0.58
Monounsaturated fat	27.7 (13.1)	27.2 (14.5)	0.66
Polyunsaturated fat	13.0 (6.1)	13.1 (7.9)	0.97
Fiber (gram/day)	22.4 (11.3)	24.0 (10.4)	0.082
Fruit (serving/week)	22.8 (36.4)	20.4 (13.6)	0.37
Vegetable (serving/week)	18.6 (12.1)	22.1 (14.5)	0.001

Table 3

Risk of pancreatic cancer in relation to physical activity in a population-based case-control study of pancreatic cancer in Minnesota, 1994-1998

	Quartile				*P* trend[a]
Physical activity (hrs/week)	**First**	**Second**	**Third**	**Fourth**	
Light					
Median	10	20	30	45	
Cases/controls	53/122	45/184	28/132	25/115	
OR1 (95% CI)[b]	1.00	0.60 (0.37, 0.97)	0.52 (0.30, 0.89)	0.53 (0.30, 0.93)	0.026
OR2 (95% CI)[c]	1.00	0.64 (0.39, 1.03)	0.55 (0.32, 0.95)	0.55 (0.30, 0.97)	0.038
Moderate					
Median	3	12	20	31	
Cases/controls	53/128	36/169	36/124	26/132	
OR1 (95% CI)[b]	1.00	0.50 (0.30, 0.83)	0.72 (0.42, 1.23)	0.50 (0.28, 0.90)	0.058
OR2 (95% CI)[c]	1.00	0.51 (0.31, 0.86)	0.75 (0.43, 1.28)	0.51 (0.28, 0.93)	0.073
Heavy					
Median	0	1	3	10	
Cases/controls	57/232	16/32	45/163	33/126	
OR1 (95% CI)[b]	1.00	2.04 (1.00, 4.06)	1.22 (0.74, 1.99)	1.07 (0.60, 1.90)	0.81
OR2 (95% CI)[c]	1.00	2.16 (1.05, 4.33)	1.29 (0.78, 2.13)	1.18 (0.66, 2.11)	0.97
Total					
Median	18	35	57	77	
Cases/controls	55/133	32/143	30/138	34/139	
OR1 (95% CI)[b]	1.00	0.51 (0.30, 0.85)	0.53 (0.31, 0.90)	0.60 (0.35, 1.04)	0.071
OR2 (95% CI)[c]	1.00	0.54 (0.32, 0.91)	0.56 (0.32, 0.95)	0.62 (0.35, 1.09)	0.09

[a] Linear trend across quartiles.

[b] Adjusted for age, sex, race, education, cigarette smoking, and alcohol intake.

[c] Additionally adjusted for intakes of energy, fat, fiber, fruits, and vegetables.

Table 4

Risk of pancreatic cancer in relation to intake of nutritional factors in a population-based case-control study of pancreatic cancer in Minnesota, 1994-1998

	Quartile				*P* trend[a]
Nutrient/food	**First**	**Second**	**Third**	**Fourth**	
Energy (kcal/day)					
Median	1,291	1,779	2,160	2,818	
Cases/controls	48/138	47/139	43/139	48/138	
OR1 (95% CI)[b]	1.00	0.93 (0.58, 1.51)	0.81 (0.49, 1.33)	0.89 (0.54, 1.46)	0.59
OR2 (95% CI)[c]	1.00	1.16 (0.65, 2.06)	1.26 (0.64, 2.52)	1.89 (0.72, 5.10)	0.23
Saturated fat (gram/day)					
Median	12.3	18.3	24.8	36.6	
Cases/controls	38/138	50/139	40/139	58/138	
OR1 (95% CI)[b]	1.00	1.27 (0.77, 2.10)	0.99 (0.59, 1.69)	1.27 (0.77, 2.11)	0.51
OR2 (95% CI)[c]	1.00	1.67 (0.93, 3.03)	1.56 (0.80, 3.09)	2.47 (1.07, 5.86)	0.061
Monounsaturated fat (gram/day)					
Median	13.8	21.0	28.5	40.7	
Cases/controls	45/138	41/139	43/139	57/138	
OR1 (95% CI)[b]	1.00	0.81 (0.49, 1.34)	0.89 (0.54, 1.46)	1.05 (0.65, 1.72)	0.65
OR2 (95% CI)[c]	1.00	0.92 (0.51, 1.65)	1.27 (0.66, 2.44)	2.00 (0.87, 4.68)	0.073
Polyunsaturated fat (gram/day)					
Median	6.7	10.0	13.4	19.4	
Cases/controls	39/138	50/139	42/139	55/138	
OR1 (95% CI)[b]	1.00	1.24 (0.75, 2.05)	1.00 (0.59, 1.68)	1.31 (0.80, 2.16)	0.41
OR2 (95% CI)[c]	1.00	1.55 (0.88, 2.76)	1.58 (0.83, 3.03)	2.56 (1.19, 5.58)	0.024
Total fat (gram/day)					
Median	37.5	55.0	73.0	102.0	
Cases/controls	45/138	40/139	44/139	57/138	

	Quartile				*P* trend[a]
Nutrient/food	**First**	**Second**	**Third**	**Fourth**	
OR1 (95% CI)[b]	1.00	0.78 (0.47, 1.29)	0.90 (0.55, 1.48)	1.04 (0.64, 1.70)	0.64
OR2 (95% CI)[c]	1.00	1.02 (0.57, 1.84)	1.42 (0.74, 2.78)	2.16 (0.91, 5.27)	0.059
Fiber (gram/day)					
Median	14.0	20.0	25.0	35.0	
Cases/controls	64/137	45/140	40/139	37/138	
OR1 (95% CI)[b]	1.00	0.69 (0.43, 1.10)	0.54 (0.33, 0.87)	0.58 (0.35, 0.94)	0.021
OR2 (95% CI)[c]	1.00	0.71 (0.41, 1.20)	0.49 (0.26, 0.94)	0.52 (0.21, 1.30)	0.11
Fruit (serving/week)					
Median	8.0	14.5	21.5	33.5	
Cases/controls	62/139	38/139	33/138	53/138	
OR1 (95% CI)[b]	1.00	0.71 (0.43, 1.16)	0.56 (0.33, 0.94)	0.91 (0.57, 1.47)	0.83
OR2 (95% CI)[c]	1.00	0.86 (0.50, 1.47)	0.68 (0.37, 1.23)	1.30 (0.67, 2.52)	0.47
Vegetable (serving/week)					
Median	9.0	15.0	23.0	36.3	
Cases/controls	63/136	55/136	32/140	36/142	
OR1 (95% CI)[b]	1.00	0.93 (0.59, 1.46)	0.49 (0.29, 0.82)	0.64 (0.38, 1.05)	0.026
OR2 (95% CI)[c]	1.00	0.94 (0.57, 1.55)	0.57 (0.31, 1.04)	0.84 (0.41, 1.72)	0.47

[a] Linear trend across quartiles.

[b] Adjusted for age, sex, race, education, cigarette smoking, and alcohol intake.

[c] Additionally adjusted for physical activity and intakes of all other dietary factors; saturated fat, monounsaturated fat, polyunsaturated fat, and total fat were not adjusted for each other.