American Journal of Epidemiology
Vol. 157, No. 12
Printed in U.S.A.
DOI: 10.1093/aje/kwg098

Dietary Meat, Dairy Products, Fat, and Cholesterol and Pancreatic Cancer Risk in a Prospective Study

Dominique S. Michaud[1], Edward Giovannucci[2,3,4], Walter C. Willett[2,3,4], Graham A. Colditz[2,4], and Charles S. Fuchs[2,5]

[1] Nutritional Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, Rockville, MD.
[2] Channing Laboratory, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA.
[3] Department of Nutrition, Harvard School of Public Health, Boston, MA.
[4] Department of Epidemiology, Harvard School of Public Health, Boston, MA.
[5] Department of Adult Oncology, Dana-Farber Cancer Institute, Boston, MA.

Received for publication August 1, 2002; accepted for publication January 8, 2003.

Case-control studies suggest that meat and cholesterol intakes may be related to elevated risks of pancreatic cancer. Few prospective studies have examined associations between diet and pancreatic cancer, although in one recent study saturated fat consumption was related to higher risk. In a cohort of US women, the authors confirmed 178 pancreatic cancer cases over 18 years of follow-up. A mailed 61-item food frequency questionnaire was self-administered at baseline, and health and lifestyle variables were updated biennially. Analyses were performed using Cox proportional hazards models to adjust for potential confounders. Intakes of total fat, different types of fats, and cholesterol were not associated with pancreatic cancer risk. Similarly, total meat, red meat, and dairy products were not related to risk. Individual food items contributing to intakes of total meat and dairy products, as well as fish and eggs, did not reveal any specific association. Updating dietary exposures by using questionnaires from 1980, 1984, 1986, and 1990 produced similar findings. The authors' data do not support previous findings that meat or saturated fat intakes are related to pancreatic cancer risk. Future prospective studies should examine the influence of cooking practices as well as other dietary habits on the risk of pancreatic cancer.

cholesterol; dairy products; fats; meat; pancreatic neoplasms

Abbreviation: ATBC, Alpha-Tocopherol, Beta-Carotene.

Fatality rates for pancreatic cancer are extremely high, and advances in medicine have not improved survival rates for this cancer. In 2002, about 29,000 US men and women were projected to die from pancreatic cancer (1). Consequently, understanding the etiology of pancreatic cancer is of utmost importance as it may lead to prevention opportunities. One of the few accepted modifiable risk factors for pancreatic cancer is cigarette smoking, but smoking may explain only 25 percent of the cases (2). Other factors, including diabetes mellitus, obesity, and chronic pancreatitis, may also play a role in the etiology of pancreatic cancer (3).

Ecologic studies examining international variations in rates suggested that per capita intakes of egg, animal protein, and sugar were related to pancreatic cancer rates (4, 5). Many case-control studies have since examined how intakes of meat, egg, and dairy products and different types of fat are related to the risk of pancreatic cancer. At least six case-control studies have reported positive associations for meat intake and pancreatic cancer risk (6, 7). Consistent positive findings have also been observed for cholesterol intake (6, 7). However, case-control studies of pancreatic cancer are especially prone to biases due to the high and rapid fatality rates. As a result, these studies have frequently relied on next-of-kin interviews to determine exposures, and they tend to have poor response rates among cases. Dietary data from these types of studies should therefore be interpreted with caution (6).

Reprint requests to Dr. Dominique Michaud, National Cancer Institute, 6120 Executive Boulevard, EPS/320 MSC 7232, Rockville, MD 20892 (e-mail: michaudd@mail.nih.gov).

Prospective studies offer unique advantages in the study of dietary factors and pancreatic cancer risk. In these studies, diet is measured prior to cancer and, consequently, they are not prone to recall bias and do not include any proxy interviews. To date, six cohort studies have reported associations between diet and pancreatic cancer risk (8–13); however, many of these studies included fewer than 100 cases (9–11), and only one examined total or different types of fat intakes (13). A significant, positive association between total meat intake and pancreatic cancer risk was reported in one prospective analysis (10), and saturated fat was associated with a significant increase in risk in another cohort (13).

Rodent models of pancreatic cancer indicate that dietary fat can enhance or promote tumor development (14). Certain compounds found in meats with known carcinogenic properties, such as *N*-nitroso compounds, may increase the risk of pancreatic cancer.

We examined consumption of meat, dairy products, types of fat, and cholesterol in relation to pancreatic cancer risk in a large cohort of women with detailed and updated dietary information with 18 years of follow-up.

MATERIALS AND METHODS

Study population

The Nurses' Health Study was initiated in 1976 when 121,700 female registered nurses aged 30–55 years responded to a mailed questionnaire with detailed information on individual characteristics and habits. Questionnaires were mailed biennially to all living participants to update information on certain behaviors (e.g., smoking), weight, menopausal status, medication use, and newly diagnosed medical conditions. In 1980, 98,462 (81 percent) of the participants returned a dietary questionnaire. In 1980, about 800 women from the baseline cohort had died. Most of the deaths in this cohort were reported by family members or by the postal service in response to the follow-up questionnaires. In addition, we used the National Death Index to search for nonrespondents; this method has been shown to have a sensitivity of 98 percent for death (15). This study was approved by the Human Research Committee at the Brigham and Women's Hospital.

After exclusion of participants with 10 or more blank items on the dietary questionnaire, implausibly high or low caloric intake (<500 or >3,500 kcal per day) (6.1 percent), or a cancer diagnosis (other than nonmelanoma skin cancer) prior to baseline (3.7 percent), 88,802 women were eligible for analysis.

Dietary assessment

Dietary intake was assessed in 1980, 1984, 1986, and 1990 by using a standard semiquantitative food frequency questionnaire. A 61-item food frequency questionnaire was mailed to all participants of the study in 1980, whereas the food frequency questionnaire used in 1984, 1986, and 1990 was expanded to include 131 foods. About 80 percent of the women completed the food frequency questionnaires during follow-up. Participants were asked to report their average frequency of intake over the previous year for a specified serving size of each food. Individual nutrient intakes were calculated by multiplying the frequency of each food consumed by the nutrient content of the specified portion size (obtained from the US Department of Agriculture and supplemented by other publications) and then summing the contributions from all foods.

Intakes of red meat, total meat, and dairy products were calculated by multiplying the intake frequency of individual items in those food categories by their weights, estimated from the specified portion size, and summing over those items. Total meat consisted of the following items: chicken with skin; chicken without skin; processed meats; bacon; hot dogs; hamburger; beef, pork, or lamb as a sandwich or mixed dish; and beef, pork, or lamb as a main dish. Red meat consisted of the total meat items minus the chicken items. Dairy products consisted of skim or low fat milk, whole milk, ice cream, yogurt, cottage cheese, hard cheese, and butter. For dairy products, dry weights were used for the calculations instead of total weight.

We used the food intake information on the food frequency questionnaire to calculate each participant's total fat intake as well as her intake of specific types of fat. These included animal, vegetable, saturated, monounsaturated, polyunsaturated, and *trans*-fatty acids and cholesterol. In addition, we measured intakes of stearic, oleic, linoleic, and α-linolenic acids.

In a validity study of 173 women, the 61-item food frequency questionnaire was compared with four 1-week diet records. Correlation coefficients between the average intake assessed by two 1-week diet records completed 6 months apart and our food frequency questionnaire (corrected for within-person variation in the diet records) were as follows: 0.41 for processed meats, 0.43 for meat (from a main dish or mixed dish), 0.69 for skim milk, 0.56 for whole milk, 0.72 for butter, and 0.72 for eggs (16). Correlation coefficients for total fat, saturated fat, and cholesterol were 0.48, 0.49, and 0.61, respectively, comparing two 1-week diet records and one food frequency questionnaire in the same validation study of women (17). In addition, in a study of 185 women, the percentage of calories from fat as measured by the 1984 food frequency questionnaire predicted serum triglyceride levels (18).

Assessment of nondietary factors

Height, current weight, and smoking history (including time since quitting for past smokers) were initially reported at baseline. During follow-up, data on current weight and smoking status were obtained from the biennial mailed questionnaires. We estimated body mass index from weight and height (weight (kg)/height (m)^2) as a measure of total adiposity. Participants were asked about history of diabetes at baseline and in all subsequent questionnaires. In 1982 and biennially thereafter, participants were asked about their history of cholecystectomy. For physical activity, we derived a score based on questions asked in the 1980 questionnaire ("At least once a week, do you engage in any regular activity similar to brisk walking, jogging, bicycling,

TABLE 1. Baseline characteristics among women in the cohort by quintile of total meat intake, Nurses' Health Study, 1980*

	Quintiles of total meat intake				
	1	2	3	4	5
Median (g/day)	62	95	126	156	210
Age (years)	48	47	46	46	47
Body mass index (kg/m^2)†	23	24	24	24	24
Height (inches‡)	64.4	64.4	64.5	64.5	64.4
Diabetes mellitus (%)	1.7	2.0	2.2	2.5	3.1
Cholecystectomy (%)	6.6	7.1	6.8	7.4	7.8
Current smokers (%)	29	29	29	29	29
Pack-years of cigarettes§	10.6	10.5	10.7	10.6	10.8
Race (%)¶					
Caucasian	87	89	89	89	88
African American	6	6	7	7	6
Asian	2	1	1	1	2
Hispanic	1	1	1	1	1
Other	1	<1	<1	<1	<1
Missing	3	3	2	2	3
Daily intakes					
Calories (kcal)	1,180	1,362	1,529	1,703	2,049
Total fat (% calories)	33	36	39	41	45
Carbohydrates (% calories)	46	42	39	36	33
Glycemic load#	143	130	121	114	103
Alcohol (g)	5.9	6.4	6.4	6.6	6.5
Coffee (cups**)	2.1	2.3	2.3	2.3	2.4

* All variables (except age) are age standardized.
† Body mass index in 1976.
‡ One inch = 2.54 cm.
§ Among past and current smokers.
¶ Among women who responded to the 1992 questionnaire.
\# Energy adjusted using residual method.
** One cup = 0.24 liter.

etc., long enough to break a sweat?" "If yes, how many times per week?" "What activity is this?").

Identification of pancreatic cancer cases

Participants were asked to report specified medical conditions including cancers that were diagnosed in the 2-year period between each follow-up questionnaire. Whenever a participant (or next-of-kin for decedents) reported a diagnosis of pancreatic cancer, we asked for permission to obtain related medical records or pathology reports. If permission to obtain records was denied, we attempted to confirm the self-reported cancer with an additional letter or phone call to the participant. If the primary cause (or secondary cause) of death as reported by a death certificate was a previously unreported pancreatic cancer case, we contacted a family member to obtain permission to retrieve medical records or at least to confirm the diagnosis of pancreatic cancer. Less than 4 percent of the total cases of pancreatic cancer initially identified were subsequently rejected as not being pancreatic cancer. We confirmed 178 incident pancreatic cancer cases, diagnosed between 1980 and 1998. We had medical records for 161 (90 percent) of the cases and confirmed 12 cases using death certificates, and the remaining five cases were confirmed by telephone contact.

Statistical analysis

We computed person-time of follow-up for each participant from the return date of the baseline questionnaire to the date of pancreatic cancer diagnosis, death from any cause, or the end of follow-up (May 31, 1998), whichever came first. Incidence rates of pancreatic cancer were calculated by dividing the number of incident cases by the number of person-years in each category of dietary exposure. We computed the relative risk for each of the upper categories by dividing the rates in these categories by the rate in the lowest category.

We examined the relative risk of pancreatic cancer according to intake on the baseline 1980 food frequency

TABLE 2. Baseline intakes of total fat and type of fats and the risk of pancreatic cancer, Nurses' Health Study, 1980*

	Quintiles of intake					Trend test *p* value
	1	2	3	4	5	
Total fat						
Median (g/day)	52	63	70	77	87	
No. of cases	38	41	31	34	34	
Person-years	313,325	303,929	318,505	312,104	297,918	
Age-adjusted relative risk	1.0	1.20	0.89	1.02	1.07	0.99
Multivariate relative risk†	1.0	1.31	1.03	1.22	1.24	0.52
95% confidence interval	Referent	0.83, 2.05	0.63, 1.71	0.73, 2.06	0.70, 2.20	
Saturated fat						
Median (g/day)	20	25	28	31	36	
No. of cases	39	49	26	32	32	
Person-years	294,702	341,246	298,900	322,659	288,275	
Age-adjusted relative risk	1.0	1.18	0.72	0.84	0.94	0.39
Multivariate relative risk†	1.0	1.25	0.78	0.90	0.95	0.55
95% confidence interval	Referent	0.81, 1.93	0.46, 1.31	0.54, 1.51	0.54, 1.66	
Polyunsaturated fat						
Median (g/day)	6.2	7.7	9.0	10.4	12.9	
No. of cases	48	29	30	42	29	
Person-years	308,650	302,161	315,248	304,476	315,246	
Age-adjusted relative risk	1.0	0.67	0.70	1.07	0.74	0.63
Multivariate relative risk†	1.0	0.71	0.76	1.12	0.77	0.71
95% confidence interval	Referent	0.45, 1.13	0.48, 1.20	0.73, 1.70	0.48, 1.22	
Monounsaturated fat						
Median (g/day)	20	25	29	32	38	
No. of cases	33	40	42	33	30	
Person-years	275,597	312,093	364,664	299,391	294,037	
Age-adjusted relative risk	1.0	1.17	1.08	1.05	0.97	0.77
Multivariate relative risk†	1.0	1.25	1.22	1.18	1.10	0.78
95% confidence interval	Referent	0.78, 1.99	0.76, 1.97	0.69, 2.01	0.62, 1.97	
trans-Fat						
Median (g/day)	2.5	3.3	3.9	4.6	5.7	
No. of cases	45	34	40	25	34	
Person-years	324,601	274,606	343,022	301,741	301,813	
Age-adjusted relative risk	1.0	0.96	0.94	0.68	0.92	0.43
Multivariate relative risk†	1.0	0.97	0.98	0.72	0.91	0.44
95% confidence interval	Referent	0.62, 1.52	0.64, 1.50	0.44, 1.18	0.58, 1.43	
Cholesterol						
Median (g/day)	212	275	322	371	466	
No. of cases	36	29	34	43	36	
Person-years	309,975	307,136	308,218	312,024	308,429	
Age-adjusted relative risk	1.0	0.85	0.97	1.21	1.01	0.57
Multivariate relative risk†	1.0	0.95	1.15	1.40	1.11	0.41
95% confidence interval	Referent	0.58, 1.57	0.71, 1.87	0.88, 2.24	0.67, 1.83	

Table continues

questionnaire. In addition, we repeated our analyses using cumulative updating of the dietary exposures with follow-up data in 1984, 1986, and 1990 (19).

Relative risks adjusted for potential confounders were estimated using Cox proportional hazards models stratified on age in years. In these models, cigarette smoking was catego-

TABLE 2. Continued

	Quintiles of intake					Trend test *p* value
	1	2	3	4	5	
Vegetable fat						
Median (g/day)	7	12	16	21	29	
No. of cases	39	42	25	35	37	
Person-years	280,768	362,549	284,828	319,312	298,325	
Age-adjusted relative risk	1.0	0.91	0.71	0.89	0.99	0.96
Multivariate relative risk†	1.0	0.94	0.74	0.91	1.02	0.87
95% confidence interval	Referent	0.61, 1.46	0.44, 1.22	0.57, 1.46	0.65, 1.62	
Animal fat						
Median (g/day)	33	44	51	60	72	
No. of cases	38	35	44	25	36	
Person-years	310,452	295,159	324,667	302,974	312,529	
Age-adjusted relative risk	1.0	1.04	1.21	0.74	1.03	0.70
Multivariate relative risk†	1.0	1.08	1.31	0.78	1.13	0.97
95% confidence interval	Referent	0.68, 1.73	0.82, 2.08	0.45, 1.37	0.64, 1.98	
Stearic acid (18:0)						
Median (g/day)	4.9	6.2	7.2	8.1	9.6	
No. of cases	39	36	39	31	33	
Person-years	307,437	307,541	312,657	308,402	309,031	
Age-adjusted relative risk	1.0	1.00	1.09	0.88	0.94	0.67
Multivariate relative risk†	1.0	1.05	1.16	0.97	1.01	0.96
95% confidence interval	Referent	0.67, 1.67	0.73, 1.85	0.58, 1.60	0.59, 1.71	
Oleic acid (18:1)						
Median (g/day)	18	22	25	28	33	
No. of cases	43	29	37	39	30	
Person-years	323,013	276,241	316,524	350,886	278,405	
Age-adjusted relative risk	1.0	0.85	0.98	0.94	0.91	0.78
Multivariate relative risk†	1.0	0.91	1.10	1.05	1.03	0.78
95% confidence interval	Referent	0.57, 1.47	0.69, 1.74	0.65, 1.70	0.60, 1.79	
Linoleic acid (18:2)						
Median (g/day)	4.5	6	7.2	8.6	11.1	
No. of cases	45	29	33	42	29	
Person-years	308,104	311,072	296,644	325,236	304,015	
Age-adjusted relative risk	1.0	0.70	0.88	1.06	0.82	0.90
Multivariate relative risk†	1.0	0.72	0.94	1.09	0.83	0.91
95% confidence interval	Referent	0.45, 1.15	0.60, 1.47	0.71, 1.67	0.52, 1.33	
α-Linolenic acid (18:3)						
Median (g/day)	0.7	0.8	0.9	1.0	1.1	
No. of cases	42	40	39	29	28	
Person-years	303,896	304,791	315,822	318,512	302,048	
Age-adjusted relative risk	1.0	1.03	1.00	0.75	0.76	0.12
Multivariate relative risk†	1.0	1.08	1.03	0.80	0.77	0.16
95% confidence interval	Referent	0.70, 1.67	0.66, 1.61	0.49, 1.30	0.47, 1.26	

* Analyses are based on dietary intake as measured on the baseline questionnaire in 1980.

† Adjusted for pack-years of smoking (past 15 years; current and past smokers separately), body mass index (quintiles in 1976), history of diabetes mellitus, caloric intake (quintiles), height (quintiles), physical activity (continuous), menopausal status, and glycemic load intake.

rized as follows (based on a previous analysis of these cohorts (2)): never smoker, quit ≥15 years ago, quit <15 years ago and smoked ≤25 pack-years in the past 15 years, quit <15 years ago and smoked >25 pack-years in the past 15 years, current smoker with ≤25 pack-years in the past 15 years, and current smoker with >25 pack-years in the past 15 years. Women with missing smoking data were excluded (there were no cases with missing data on smoking). In addition, we controlled for body mass index (<23, 23–24.9, 25–26.9, 27–29.9, ≥30, missing), height (≤62.0, 62.1–63.0, 63.1–64.5, 64.6–66.0, >66.0 inches; 1 inch = 2.54 cm) (20), total energy intake (quintiles: <1,139, 1,139–1,392, 1,393–1,634, 1,635–1,954, >1,954 kcal), physical activity (hours of activity, continuous variable), menopausal status (pre-, post-, and dubious), and history of diabetes (21, 22) (less than 4 percent of the women in this cohort were type I diabetics). Women who did not indicate that they had diabetes were categorized as nondiabetics. History of diabetes was updated every other year with data from the follow-up questionnaires; for women who did not complete follow-up questionnaires, we used the data from the previous questionnaire. Body mass index was not updated in the main analyses because pancreatic cancer is frequently associated with profound weight loss, and our previous findings showed the strongest associations for body mass index in 1976 (Nurses' Health Study cohort baseline) (20). In addition, we adjusted for glycemic load, shown in separate analyses, as we previously reported an association between this variable and pancreatic cancer risk in this population (23). All p values are based on two-sided tests. We performed tests for trend by assigning the median value to each category and modeling this variable as a continuous variable.

RESULTS

In 1980, women in the Nurses' Health Study consumed, on average, between 25 and 340 g of total meat per day (1–99th percentile) and between 3 and 170 g (dry weight) of dairy products per day (1–99th percentile). Age, body mass index, height, smoking status, lifetime smoking patterns, and ethnicity were similar across the different quintiles of total meat intake (table 1). The percentage of women with a history of diabetes or cholecystectomy both increased with total meat intake. Similarly, total fat, alcohol, coffee, and total caloric intakes increased with total meat intake. In contrast, intakes of carbohydrate and glycemic load decreased with higher meat intakes. Similar patterns were observed when we examined baseline characteristics across quintiles of energy-adjusted total fat intake (data not shown), although the proportion of current smokers increased across quintiles of total fat intake (32 percent in the highest quintile of total fat).

We examined the influence of fat intake as measured on the baseline 1980 questionnaire on the risk of pancreatic cancer during the subsequent 18 years of follow-up. We observed no relation between the intakes of total, saturated, polyunsaturated, monounsaturated, or *trans*-fat and the risk of pancreatic cancer in age-adjusted analyses (table 2). Further control for potential confounders, including pack-years of smoking, body mass index, and history of diabetes, did not affect the associations for the different fat intakes. Similarly, associations remained null after additional control for glycemic load. Dietary cholesterol was also not associated with pancreatic cancer risk in this cohort. In addition, we did not observe any associations for fat when classified by its source (animal vs. vegetable) or for the specific fatty acids examined. We repeated our analyses using cumulative updated measures of fat intake as assessed in 1980, 1984, 1986, and 1990. Results from these analyses were not substantially different from those in table 2. Associations between fat intakes and pancreatic cancer risk were not modified by body mass index or physical activity.

In age-adjusted models, intakes of red and total meat were associated with small, nonsignificant decreases in the risk of pancreatic cancer, but no appreciable association remained after controlling for potential confounders (table 3). Adjusting for glycemic load further attenuated the association. No association was observed for total dairy product intake and pancreatic cancer risk (table 3). Intakes of total or animal protein were not associated with the risk of pancreatic cancer either (data not shown). When we repeated our analyses using updated measures of meat, dairy product, and protein intakes, we continued to observe no significant associations with pancreatic cancer risk (data not shown).

Because red meat is the main source of iron and because serum iron levels were directly related to pancreatic cancer in an exploratory case-control study (24), we examined total iron intake (diet plus supplements). However, we did not observe any association for iron intake and pancreatic cancer risk (data not shown).

Individual dietary items contributing to meat intake were examined separately using the items and frequencies offered on the food frequency questionnaire (table 4). After controlling for potential confounders, we found that none of the meat items appeared to be related to the risk of pancreatic cancer (table 4). Similarly, individual items contributing to dairy product intake, as well as intakes of egg and fish (one item on the food frequency questionnaire), were not associated with the risk of pancreatic cancer (table 5).

DISCUSSION

In this large cohort of women, intakes of meat, dairy products, fat, and cholesterol were not related to the risk of pancreatic cancer. No associations were observed for different types of dietary fat or for different types of meats. Analyses using data on recent dietary intake (simple updating) or cumulative updating yielded results similar to those using baseline dietary measures.

Rodents fed high-fat diets experienced a greater incidence of pancreatic tumors than did rodents fed low-fat diets with a similar caloric content (25, 26). In one study, rodents fed diets rich in saturated fat and also linoleic acid had the greatest increase in pancreatic tumorigenesis (26). Fats and fatty acids in the duodenum stimulate the release of cholecystokinin, and chronic cholecystokininemia in rodents stimulates pancreatic hyperplasia and increases susceptibility of the pancreas to carcinogens (27, 28). Among humans, a large, collaborative, population-based, case-control report on pancreatic cancer comprising five studies

TABLE 3. Baseline intakes of total meat and red meat and the risk of pancreatic cancer, Nurses' Health Study, 1980*

	Quintiles of intake					Trend test *p* value
	1	2	3	4	5	
Total meat						
Median (g/day)	62	95	126	156	210	
No. of cases	42	46	34	27	29	
Person-years	307,472	309,059	309,937	310,233	309,082	
Age-adjusted relative risk	1.0	1.15	0.88	0.71	0.75	0.06
Multivariate relative risk†	1.0	1.21	0.99	0.80	0.81	0.26
Multivariate relative risk‡	1.0	1.27	1.08	0.90	0.94	0.57
95% confidence interval	Referent	0.83, 1.97	0.65, 1.79	0.51, 1.58	0.50, 1.79	
Red meat						
Median (g/day)	34	58	88	117	167	
No. of cases	42	45	30	36	25	
Person-years	304,457	311,786	308,880	311,706	308,953	
Age-adjusted relative risk	1.0	1.19	0.82	0.97	0.67	0.06
Multivariate relative risk†	1.0	1.24	0.91	1.07	0.76	0.27
Multivariate relative risk‡	1.0	1.29	0.98	1.19	0.87	0.59
95% confidence interval	Referent	0.83, 1.98	0.59, 1.64	0.70, 2.03	0.46, 1.65	
Dairy products						
Median (g/day)	13	27	40	57	91	
No. of cases	39	38	30	39	32	
Person-years	308,294	309,523	309,937	309,366	308,662	
Age-adjusted relative risk	1.0	0.95	0.73	0.93	0.78	0.37
Multivariate relative risk†	1.0	1.05	0.87	1.19	1.02	0.81
Multivariate relative risk‡	1.0	1.06	0.88	1.21	1.04	0.75
95% confidence interval	Referent	0.68, 1.67	0.54, 1.43	0.75, 1.94	0.62, 1.77	

* Analyses are based on dietary intake as measured on the baseline questionnaire in 1980.

† Adjusted for pack-years of smoking (past 15 years; current and past smokers separately), body mass index (quintiles in 1976), history of diabetes mellitus, caloric intake (quintiles), height (quintiles), physical activity (continuous), and menopausal status.

‡ Additional control for glycemic load intake.

(SEARCH programme; International Agency for Research on Cancer, Lyon, France) observed elevated risks of pancreatic cancer for higher cholesterol intake but not for total or saturated fat (29). However, only two of the SEARCH studies had dose-dependent associations for cholesterol intake (30, 31), and two separate case-control studies reported no statistically significant associations (32, 33). In addition, four other case-control studies found no association with total or saturated fat intake (32–35). Altogether, only two studies have reported elevated risks of pancreatic cancer with higher total fat intake (36, 37). In addition, the majority of case-control studies have reported no association with dairy products and pancreatic cancer risk (7, 33, 38)

Only one prospective cohort study has previously examined the relation between fat intake and pancreatic cancer (13). Analyzing a cohort of male smokers (the Alpha-Tocopherol, Beta-Carotene (ATBC) Cancer Prevention Study cohort) in Finland, investigators reported elevated pancreatic cancer risks with higher intakes of butter and saturated fat. In contrast to the ATBC cohort, the current study consisted of women who were predominantly former or never smokers. Notably, levels of saturated fat and butter consumption were substantially higher in the ATBC cohort; for example, the median saturated fat intake in the ATBC cohort was 58.5 g/day compared with 28 g/day in our study.

Meat intake has been associated with elevated risk of pancreatic cancer in seven case-control studies (35, 38–43). However, associations from these studies were rarely observed for total meat intake. Results were often based on specific food items, including the following: beef (39); beef and pork (42); pork products (41); fried, grilled, and smoked meats (40); and fat from meat (43). No positive associations for meat items were found in six other case-control studies (33, 34, 44–47). To date, only four cohort studies have reported associations between meat intake and pancreatic cancer risk. For three of these studies, dietary information

TABLE 4. Baseline intakes of individual meat items in relation to the risk of pancreatic cancer, Nurses' Health Study, 1980*

	Categories of intake				Trend test *p* value
	<3/month	1/week	2–4/week	≥5/week	
Beef, pork, or lamb (main dish)					
No. of cases	29	60	67	22	
Person-years	199,925	474,140	634,151	237,565	
Multivariate relative risk†	1.0	0.97	0.89	0.75	0.33
95% confidence interval	Referent	0.62, 1.51	0.56, 1.42	0.41, 1.40	
	0	1–3/month	1/week	≥2/week	
Beef, pork, or lamb (sandwich or mixed dish)					
No. of cases	21	57	55	45	
Person-years	151,568	396,042	524,477	473,695	
Multivariate relative risk†	1.0	1.13	0.91	0.95	0.60
95% confidence interval	Referent	0.68, 1.86	0.55, 1.52	0.55, 1.62	
Processed meats‡					
No. of cases	71	38	27	42	
Person-years	492,722	420,609	314,711	317,740	
Multivariate relative risk†	1.0	0.72	0.78	1.28	0.10
95% confidence interval	Referent	0.48, 1.07	0.50, 1.22	0.86, 1.92	
Bacon					
No. of cases	59	64	34	21	
Person-years	492,106	504,522	371,865	177,290	
Multivariate relative risk†	1.0	1.21	0.85	1.05	0.85
95% confidence interval	Referent	0.84, 1.72	0.55, 1.30	0.63, 1.75	
Hamburger					
No. of cases	12	40	87	39	
Person-years	85,764	291,092	800,900	368,026	
Multivariate relative risk†	1.0	1.10	1.02	1.03	0.92
95% confidence interval	Referent	0.57, 2.09	0.55, 1.87	0.53, 1.99	
Hot dogs					
No. of cases	68	56	46	6	
Person-years	479,404	569,971	417,359	79,048	
Multivariate relative risk†	1.0	0.83	1.02	0.69	0.55
95% confidence interval	Referent	0.58, 1.18	0.69, 1.49	0.30, 1.61	
Chicken without skin					
No. of cases	54	31	56	37	
Person-years	508,962	225,429	509,600	301,791	
Multivariate relative risk†	1.0	1.26	0.99	1.05	0.98
95% confidence interval	Referent	0.81, 1.96	0.68, 1.44	0.68, 1.60	
Chicken with skin					
No. of cases	79	28	50	21	
Person-years	641,714	234,829	500,298	168,942	
Multivariate relative risk†	1.0	1.02	0.99	1.27	0.39
95% confidence interval	Referent	0.66, 1.57	0.69, 1.41	0.78, 2.08	

* Analyses are based on dietary intake as measured on the baseline questionnaire in 1980.

† Multivariate relative risks adjusted for pack-years of smoking (past 15 years; current and past smokers separately), body mass index (quintiles in 1976), history of diabetes mellitus, caloric intake (quintiles), height (quintiles), physical activity (continuous), and menopausal status.

‡ For example, sausage, salami, and bologna.

TABLE 5. Baseline intakes of whole milk, skim milk, butter, hard cheese, eggs, and fish in relation to the risk of pancreatic cancer, Nurses' Health Study, 1980*

	Categories of intake				Trend test *p* value
	<4/month	1/week	2–4/week	≥5/week	
Skim milk					
No. of cases	77	20	26	55	
Person-years	714,449	94,444	177,745	559,144	
Multivariate relative risk†	1.0	2.02	1.42	1.00	0.74
95% confidence interval	Referent	1.22, 3.35	0.91, 2.22	0.70, 1.42	
Hard cheese					
No. of cases	36	31	57	54	
Person-years	264,886	300,718	551,589	428,589	
Multivariate relative risk†	1.0	0.83	0.87	1.08	0.46
95% confidence interval	Referent	0.51, 1.35	0.57, 1.32	0.69, 1.67	
	0	1/month–1/week	≥2/week		
Whole milk					
No. of cases	111	23	44		
Person-years	987,699	207,356	350,727		
Multivariate relative risk†	1.0	0.98	1.17		0.39
95% confidence interval	Referent	0.63, 1.54	0.81, 1.68		
	0	1/month–4/week	≥5/week		
Butter					
No. of cases	117	20	41		
Person-years	930,297	233,652	381,834		
Multivariate relative risk†	1.0	0.72	0.89		0.58
95% confidence interval	Referent	0.45, 1.16	0.62, 1.28		
	<2/week	2–4/week	≥5/week		
Eggs					
No. of cases	62	81	35		
Person-years	540,713	730,141	274,928		
Multivariate relative risk†	1.0	1.09	1.25		0.33
95% confidence interval	Referent	0.78, 1.52	0.81, 1.92		
	<4/month	1/week	≥2/week		
Fish					
No. of cases	59	81	38		
Person-years	661,455	605,371	278,957		
Multivariate relative risk†	1.0	1.42	1.30		0.36
95% confidence interval	Referent	1.01, 1.98	0.86, 1.98		

* Analyses are based on dietary intake as measured on the baseline questionnaire in 1980.

† Multivariate relative risks adjusted for pack-years of smoking (past 15 years; current and past smokers separately), body mass index (quintiles in 1976), history of diabetes mellitus, caloric intake (quintiles), height (quintiles), physical activity (continuous), and menopausal status.

was based on 35 or fewer food items (8, 10, 12). In a fourth study (9), which included more detailed dietary data, associations with diet were based on 40 or fewer cases of pancreatic cancer deaths. Zheng et al. (10) did report a strong association between total meat intake and pancreatic cancer risk (relative risk = 3.0, 95 percent confidence interval: 1.2, 7.5; top to bottom quartile comparison); however, their study was based on only 60 cases and utilized a limited dietary assessment.

It has been suggested that the different practices of cooking or processing meat may be related to the risk of pancreatic cancer. Cooking meat at high temperatures can result in the formation of heterocyclic amines, and processing meats (e.g., curing or smoking) increases *N*-nitroso compounds. In a case-control study in China, intake of deep-fried foods was not associated with pancreatic cancer risk, but smoked and cured foods increased the risk of pancreatic cancer (34). Other findings on cooking and processing practices have been mixed (7). In our cohort, information on cooking practices was not collected until 1990, and thus, we had insufficient statistical power to examine cooking practices in the current study. Future studies with data on cooking methods will have to examine this issue in detail.

The strengths of our study include its large size, the prospective design with 18 years of follow-up, and multiple assessments of diet. This is the largest prospective study to examine diet and pancreatic cancer, and it thus provided greater power for the detection of differences in risk factors. It is also one of the few prospective studies of diet and pancreatic cancer to use a complete food frequency questionnaire to assess nutrient intake, allowing us to adjust for the effects of total energy intake. Control for calorie intake can limit misclassification in nutrient intake caused by differences in body size and physical activity level (48). In addition, repeated dietary assessment over the follow-up period minimized random within-person variation in the measurement of food and nutrient intake (49).

We cannot exclude measurement error as an explanation for the lack of any significant associations in the current study. Misclassification of dietary intake as measured by the food frequency questionnaire may have attenuated the results to some degree; however, this is an unlikely explanation for the lack of any association over extreme levels of intake, because it is improbable that many participants were misclassified from one extreme category to the other. Moreover, previous studies in this cohort have observed a significant positive association between red meat intake and the risk of colon cancer (50). In addition, utilizing the same food frequency questionnaire, we observed significant positive associations for dairy product and meat consumption and the risks of prostate and colon cancers in a large cohort of male health professionals (51–53). Thus, the food frequency questionnaire does appear to capture etiologically relevant variation in these factors for a number of conditions.

In conclusion, we observed no association between meat, dairy product, cholesterol, or fat intakes and the risk of pancreatic cancer in this large prospective cohort of women. We cannot exclude the possibility that different methods of cooking or processing meats may be related to the risk of pancreatic cancer. Moreover, we cannot exclude the possibility that these dietary factors may influence risk among men. Future prospective studies should examine the influence of cooking practices as well as other potential dietary habits on the risk of pancreatic cancer.

ACKNOWLEDGMENTS

Supported by research grants CA 87969 and CA 86102.

REFERENCES

1. Cancer facts & figures 2002. Atlanta, GA: American Cancer Society, Inc, 2002.
2. Fuchs C, Colditz G, Stampfer M, et al. A prospective study of cigarette smoking and the risk of pancreatic cancer. Arch Intern Med 1996;156:2255–60.
3. Michaud DS. The epidemiology of pancreatic, gallbladder, and other biliary tract cancers. Gastrointest Endosc 2002;56(6 suppl):S195–200.
4. Armstrong B, Doll R. Environmental factors and cancer incidence and mortality in different countries, with special reference to dietary practices. Int J Cancer 1975;15:617–31.
5. Ghadirian P, Thouez JP, PetitClerc C. International comparisons of nutrition and mortality from pancreatic cancer. Cancer Detect Prev 1991;15:357–62.
6. Howe GR, Burch JD. Nutrition and pancreatic cancer. Cancer Causes Control 1996;7:69–82.
7. World Cancer Research Fund, American Institute for Cancer Research. Food, nutrition and the prevention of cancer: a global perspective. Washington, DC: American Institute for Cancer Research, 1997.
8. Hirayama T. Epidemiology of pancreatic cancer in Japan. Jpn J Clin Oncol 1989;19:208–15.
9. Mills PK, Beeson WL, Abbey DE, et al. Dietary habits and past medical history as related to fatal pancreas cancer risk among Adventists. Cancer 1988;61:2578–85.
10. Zheng W, McLaughlin JK, Gridley G, et al. A cohort study of smoking, alcohol consumption, and dietary factors for pancreatic cancer (United States). Cancer Causes Control 1993;4: 477–82.
11. Shibata A, Mack TM, Paganini-Hill A, et al. A prospective study of pancreatic cancer in the elderly. Int J Cancer 1994;58: 46–9.
12. Isaksson B, Jonsson F, Pedersen NL, et al. Lifestyle factors and pancreatic cancer risk: a cohort study from the Swedish Twin Registry. Int J Cancer 2002;98:480–2.
13. Stolzenberg-Solomon RZ, Pietinen P, Taylor PR, et al. Prospective study of diet and pancreatic cancer in male smokers. Am J Epidemiol 2002;155:783–92.
14. Roebuck BD. Dietary fat and the development of pancreatic cancer. Lipids 1992;27:804–6.
15. Rich-Edwards JW, Corsano KA, Stampfer MJ. Test of the National Death Index and Equifax nationwide death search. Am J Epidemiol 1994;140:1016–19.
16. Salvini S, Hunter DJ, Sampson L, et al. Food-based validation of a dietary questionnaire: the effects of week-to-week variation in food consumption. Int J Epidemiol 1989;18:858–67.
17. Willett WC, Sampson L, Stampfer MJ, et al. Reproducibility and validity of a semiquantitative food frequency questionnaire. Am J Epidemiol 1985;122:51–65.
18. Holmes MD, Spiegelman D, Willett WC, et al. Dietary fat intake and endogenous sex steroid hormone levels in postmenopausal women. J Clin Oncol 2000;18:3668–76.
19. Willett WC. Issues in analysis and presentation of dietary data. In: Willett WC, ed. Nutritional epidemiology. 2nd ed. New York, NY: Oxford University Press, 1998:321–46.
20. Michaud DS, Giovannucci E, Willett WC, et al. Physical activity, obesity, height and the risk of pancreatic cancer. JAMA 2001;286:921–9.
21. Everhart J, Wright D. Diabetes mellitus as a risk factor for pancreatic cancer: a meta- analysis. JAMA 1995;273:1605–9.
22. Silverman D, Schiffman M, Everhart J, et al. Diabetes mellitus, other medical conditions and familial history of cancer as risk factors for pancreatic cancer. Br J Cancer 1999;80:1830–7.
23. Michaud DS, Liu S, Giovannucci E, et al. Dietary sugar, glycemic load, and pancreatic cancer risk in a prospective study. J Natl Cancer Inst 2002;94:1293–300.
24. Friedman GD, van den Eeden SK. Risk factors for pancreatic cancer: an exploratory study. Int J Epidemiol 1993;22:30–7.
25. Woutersen RA, Appel MJ, van Garderen-Hoetmer A, et al.

Dietary fat and carcinogenesis. Mutat Res 1999;443:111–27.
26. Appel MJ, nan Garderen-Hoetmer A, Woutersen RA. Azaserine-induced pancreatic carcinogenesis in rats: promotion by a diet rich in saturated fat and inhibition by a standard laboratory chow. Cancer Lett 1990;55:239–48.
27. Chu M, Rehfeld JF, Borch K. Chronic endogenous hypercholecystokininemia promotes pancreatic carcinogenesis in the hamster. Carcinogenesis 1997;18:315–20.
28. Roebuck BD, Kaplita PV, Edwards BR, et al. Effects of dietary fats and soybean protein on azaserine-induced pancreatic carcinogenesis and plasma cholecystokinin in the rat. Cancer Res 1987;47:1333–8.
29. Howe GR, Ghadirian P, Bueno de Mesquita HB, et al. A collaborative case-control study of nutrient intake and pancreatic cancer within the search programme. Int J Cancer 1992;51:365–72.
30. Baghurst PA, McMichael AJ, Slavotinek AH, et al. A case-control study of diet and cancer of the pancreas. Am J Epidemiol 1991;134:167–79.
31. Zatonski W, Przewozniak K, Howe GR, et al. Nutritional factors and pancreatic cancer: a case-control study from south-west Poland. Int J Cancer 1991;48:390–4.
32. Kalapothaki V, Tzonou A, Hsieh CC, et al. Nutrient intake and cancer of the pancreas: a case-control study in Athens, Greece. Cancer Causes Control 1993;4:383–9.
33. Silverman DT, Swanson CA, Gridley G, et al. Dietary and nutritional factors and pancreatic cancer: a case-control study based on direct interviews. J Natl Cancer Inst 1998;90:1710–19.
34. Ji BT, Chow WH, Gridley G, et al. Dietary factors and the risk of pancreatic cancer: a case-control study in Shanghai, China. Cancer Epidemiol Biomarkers Prev 1995;4:885–93.
35. Farrow DC, Davis S. Diet and the risk of pancreatic cancer in men. Am J Epidemiol 1990;132:423–31.
36. Ghadirian P, Simard A, Baillargeon J, et al. Nutritional factors and pancreatic cancer in the Francophone community in Montreal, Canada. Int J Cancer 1991;47:1–6.
37. Durbec JP, Chevillotte G, Bidart JM, et al. Diet, alcohol, tobacco and risk of cancer of the pancreas: a case-control study. Br J Cancer 1983;47:463–70.
38. Soler M, Chatenoud L, La Vecchia C, et al. Diet, alcohol, coffee and pancreatic cancer: final results from an Italian study. Eur J Cancer Prev 1998;7:455–60.
39. Mack TM, Yu MC, Hanisch R, et al. Pancreas cancer and smoking, beverage consumption, and past medical history. J Natl Cancer Inst 1986;76:49–60.
40. Norell SE, Ahlbom A, Erwald R, et al. Diet and pancreatic cancer: a case-control study. Am J Epidemiol 1986;124:894–902.
41. Falk RT, Pickle LW, Fontham ET, et al. Life-style risk factors for pancreatic cancer in Louisiana: a case-control study. Am J Epidemiol 1988;128:324–36.
42. Olsen GW, Mandel JS, Gibson RW, et al. A case-control study of pancreatic cancer and cigarettes, alcohol, coffee and diet. Am J Public Health 1989;79:1016–19.
43. Goto R, Masuoka H, Yoshida K, et al. A case control study of cancer of the pancreas. (In Japanese). Gan No Rinsho 1990; spec no.:344–50.
44. Gold EB, Gordis L, Diener MD, et al. Diet and other risk factors for cancer of the pancreas. Cancer 1985;55:460–7.
45. La Vecchia C, Negri E, D'Avanzo B, et al. Medical history, diet and pancreatic cancer. Oncology 1990;47:463–6.
46. Bueno de Mesquita HB, Maisonneuve P, Runia S, et al. Intake of foods and nutrients and cancer of the exocrine pancreas: a population-based case-control study in the Netherlands. Int J Cancer 1991;48:540–9.
47. Raymond L, Infante F, Tuyns AJ, et al. Diet and cancer of the pancreas. (In French). Gastroenterol Clin Biol 1987;11:488–92.
48. Willett WC, Stampfer MJ. Total energy intake: implications for epidemiologic analyses. Am J Epidemiol 1986;124:17–27.
49. Willett WC. Nutritional epidemiology. In: Rothman KJ, Greenland S, eds. Modern epidemiology. Philadelphia, PA: Lippincott-Raven Publishers, 1998.
50. Willett WC, Stampfer MJ, Colditz GA, et al. Relation of meat, fat, and fiber intake to the risk of colon cancer in a prospective study among women. N Engl J Med 1990;323:1664–72.
51. Michaud DS, Augustsson K, Rimm EB, et al. A prospective study on intake of animal products and risk of prostate cancer. Cancer Causes Control 2001;12:557–67.
52. Giovannucci E, Rimm EB, Stampfer MJ, et al. Intake of fat, meat, and fiber in relation to risk of colon cancer in men. Cancer Res 1994;54:2390–7.
53. Giovannucci E, Rimm EB, Wolk A, et al. Calcium and fructose intake in relation to risk of prostate cancer. Cancer Res 1998; 58:442–7.