A Prospective Analysis of Intake of Red and Processed Meat in Relation to Pancreatic Cancer among African American Women

Jessica L. Petrick[1], Nelsy Castro-Webb[1], Hanna Gerlovin[1], Traci N. Bethea[2], Shanshan Li[1], Edward A. Ruiz-Narváez[3], Lynn Rosenberg[1], and Julie R. Palmer[1]

ABSTRACT

Background: African Americans have the highest incidence of pancreatic cancer of any racial/ethnic group in the United States. There is evidence that consumption of red or processed meat and foods containing saturated fats may increase the risk of pancreatic cancer, but there is limited evidence in African Americans.

Methods: Utilizing the Black Women's Health Study (1995–2018), we prospectively investigated the associations of red and processed meat and saturated fats with incidence of pancreatic adenocarcinoma ($n = 168$). A food frequency questionnaire was completed by 52,706 participants in 1995 and 2001. Multivariable-adjusted HRs and 95% confidence intervals (CI) were estimated using Cox proportional hazards regression. We observed interactions with age ($P_{interaction} = 0.01$). Thus, results were stratified at age 50 (<50, ≥50).

Results: Based on 148 cases among women aged ≥50 years, total red meat intake was associated with a 65% increased pancreatic cancer risk ($HR_{Q4\ vs.\ Q1} = 1.65$; 95% CI, 0.98–2.78; $P_{trend} = 0.05$), primarily due to unprocessed red meat. There was also a nonsignificant association between total saturated fat and pancreatic cancer ($HR_{Q4\ vs.\ Q1} = 1.85$; 95% CI, 0.92–3.72; $P_{trend} = 0.08$). Red meat and saturated fat intakes were not associated with pancreatic cancer risk in younger women, and there was no association with processed meat in either age group.

Conclusions: Red meat—specifically, unprocessed red meat—and saturated fat intakes were associated with an increased risk of pancreatic cancer in African-American women aged 50 and older, but not among younger women.

Impact: The accumulating evidence—including now in African-American women—suggests that diet, a modifiable factor, plays a role in the etiology of pancreatic cancer, suggesting opportunities for prevention.

Introduction

African Americans have the highest pancreatic cancer incidence and mortality rate of any racial/ethnic group in the United States, with 5-year survival of only 9.0% (1). As most pancreatic cancers present at an advanced stage with poor survival, etiologic research on pancreatic cancer is limited. Thus, there are few established modifiable risk factors for pancreatic cancer; they include cigarette smoking, high alcohol intake, and metabolic factors (type 2 diabetes and obesity). Due to the rarity of pancreatic cancer (11.7/100,000 persons), research on this disease in prospective cohorts has been limited to date, and there have been few African Americans in those studies.

A number of mechanisms linking red or processed meat to pancreatic carcinogenesis have been postulated, including saturated fat content (2–4), by-products of cooking methods (i.e., polycyclic aromatic hydrocarbons, heterocyclic amines, *N*-nitroso compounds, and advanced glycation endproducts; ref. 5), and increased insulin resistance (6). However, the epidemiologic literature has been inconsistent, which led the World Cancer Research Fund (WCRF)/American Institute for Cancer Research (AICR) Continuous Update Project to conclude that there was limited evidence suggesting consumption of red or processed meat and foods containing saturated fatty acids increased the risk of pancreatic cancer (7). Further, the WCRF/AICR Continuous Update Project reported evidence of modification by sex for red and processed meat intake, with men having a significant 21% to 43% increased risk of pancreatic cancer and women a nonsignificant 6% to 9% increased risk (7). Among the prospective cohorts, only one examined these possible associations in African Americans and reported that red meat consumption was associated with increased risk (8). These results were not stratified by sex, and processed meat or saturated fats were not examined. Until recently, African Americans have consumed the highest quantities of processed meat of any racial/ethnic group in the United States (9, 10). Thus, the relation between intake of red and processed meat and pancreatic cancer risk is of particular concern in this population. In the present study, we prospectively assessed the association of total red meat, unprocessed red meat, processed meat, and saturated fatty acids with pancreatic risk among African American women.

Materials and Methods

Study population

The Black Women's Health Study (BWHS) is an ongoing prospective cohort study, which was designed to assess risk factors for disease outcomes in African-American women (11). In 1995, 59,000 women ages 21 to 69 years were recruited by mailing questionnaires, largely to subscribers of *Essence* magazine. At study baseline, participants completed a self-administered questionnaire on demographics, medical history, lifestyle factors, and diet. Follow-up has been ongoing for over 20 years, and participants complete a questionnaire every 2 years either

[1]Slone Epidemiology Center at Boston University, Boston, Massachusetts. [2]School of Medicine, Georgetown University, Washington, DC. [3]Department of Nutritional Sciences, University of Michigan School of Public Health, Ann Arbor, Michigan.

Note: Supplementary data for this article are available at Cancer Epidemiology, Biomarkers & Prevention Online (http://cebp.aacrjournals.org/).

Corresponding Author: Jessica L. Petrick, Boston University, 72 East Concord Street, L-7, Boston, MA 02118. Phone: 617-206-6179; Fax: 617-738-5119; E-mail: jpetrick@bu.edu

Cancer Epidemiol Biomarkers Prev 2020;29:1775–83

doi: 10.1158/1055-9965.EPI-20-0048

online or by mail. Follow-up is complete for 85% of potential person-years. The Institutional Review Board of Boston University (Boston, MA) approved the BWHS protocol and reviews the study annually.

Outcome

Cases for this analysis were women diagnosed with primary pancreatic adenocarcinoma (consistent with the International Classification of Diseases 10 topography codes C25.0–25.9 and morphology code 8140) from July 1, 1997 (2 years after the baseline questionnaire) through December 31, 2018. Cases were ascertained by self-report on follow-up questionnaires and linkage with cancer registries in 24 states (covering 95% of participants) and the National Death Index (NDI). The majority of pancreatic cancer cases were identified by cancer registries or NDI, as many cases were presumably too ill or had died prior to reporting the disease. Self-reported cancers were confirmed by review of hospital and cancer registry data. Four self-reported cases without available cancer registry data were also included. Participants who reported prevalent pancreatic cancer at baseline in 1995 or a diagnosis within the first 2 years were excluded ($n = 5$). To date, BWHS has identified 191 incident pancreatic cancer cases.

Exposure

Dietary data were collected in 1995 using the National Cancer Institute-Block short-form food frequency questionnaire (FFQ; 68 line items) and again in 2001 (85 line items; refs. 12, 13), modified slightly to include food items commonly eaten by African Americans but not previously included on the Block FFQ. The BWHS FFQ has been validated using three 24-hour recalls as criterion instruments (14). The energy-adjusted and deattenuated Pearson correlation coefficients between the FFQ and 24-hour recalls for protein and saturated fat were 0.78 and 0.63, respectively. Study participants were asked to report usual dietary intake over the past year. Of the 59,000 BWHS participants at baseline, women were excluded due to incomplete or implausible FFQs ($n = 6{,}110$, including 23 pancreatic cancer cases), prevalent pancreatic cancer or diagnosis within the first 2 years ($n = 5$), nonadenocarcinoma pancreatic cancer ($n = 5$), and death within the first 2 years ($n = 174$). Complete (i.e., <10 blank items) and plausible (i.e., intake ≥500 kcal/day and ≤3,800 kcal/day) FFQs were obtained for over 89% of participants ($n = 52{,}706$) in 1995. Of eligible participants that responded to the 2001 questionnaire ($n = 43{,}114$), complete and plausible FFQs were obtained for over 76% of participants ($n = 33{,}151$).

For each food, a common portion size was specified and the participant was asked to report how often she had consumed the food in the past year and the portion size of the food. The portion sizes used were small, medium, and large; in 2001, super-size was also included. A small serving was defined as half or less of the medium serving, a large serving was one and a half times the medium serving, and a super-size was twice the medium serving size. The responses for frequency of consumption ranged from "never or <1 per month" to "2 or more per day." To calculate grams per day of red or processed meat participants consumed, serving size–adjusted frequency of intake was multiplied by the number of grams in a medium serving. One serving was estimated as 85 g, or approximately three ounces. To calculate saturated fat intake, the serving size–adjusted grams per day for each specific food was multiplied by its saturated fat content (in grams) per 100 g fresh weight edible portion of food, using DIETCALC software, version 1.4.1 (National Cancer Institute, Bethesda, MD).

Intake of processed meat included bacon, sausage, hot dogs, and lunchmeats (e.g., turkey, ham, bologna, and salami). Total red meat intake included processed and unprocessed red meat—beef (e.g., hamburgers, steak, roast, and stew) and pork (e.g., chops, roasts, and dinner ham). Total dietary saturated fat intake included butyric acid (4:0), caproic acid (6:0), caprylic acid (8:0), capric acid (10:0), lauric acid (12:0), myristic acid (14:0), palmitic acid (16:0), and stearic acid (18:0).

Meat and saturated fat intake were categorized into quartiles of grams per day, based on the distribution of intake among the complete analytic study population. Tests of linear trend were performed based on the quartile-specific medians of meat or fat intake. We calculated HRs for every 100 g per day of total and unprocessed red meat intake, 50 g per day of processed meat intake, and 10 g per day of total saturated fat intake (7). We also examined modeling total red meat intake using restricted cubic splines, to allow for a nonlinear relationship (15). However, there was a lack of evidence of nonlinearity ($P \geq 0.05$). Dietary intake was examined using the cumulative average approach; thus, beginning in 2001, dietary data were averaged over 1995 and 2001 FFQ reports. This method reduces measurement error and provides a statistically more powerful test of diet–disease associations (16). For participants that did not complete the 2001 FFQ, the 1995 dietary values were carried forward.

Statistical analysis

Cox proportional hazards models, with follow-up time as the underlying time metric, were used to estimate HRs, as an approximation of the incidence ratio, and 95% confidence intervals (CI) for the associations between total red meat, unprocessed red meat, processed meat, and saturated fat intake with incidence of pancreatic cancer. Follow-up began at time of baseline questionnaire and continued until diagnosis of pancreatic cancer, death, or the end of study follow-up, whichever occurred first. Analyses were lagged by excluding the first 2 years of follow-up as women diagnosed with pancreatic cancer during that period may have already altered their dietary habits due to underlying disease. The proportional hazards assumption was tested using an interaction term between meat and saturated fat intakes (defined as quartiles) and age. We observed interaction between total red meat and age (whether continuous or dichotomized at age 50, $P < 0.05$). Thus, we stratified the analyses by age (<50, ≥50), based on prior literature suggesting etiologic differences in earlier versus later-onset pancreatic cancer (17–19). Women <50 years at baseline contributed person-time to the <50 years of age stratum until they reached age 50, at which time they contributed person-time to the ≥50 years of age stratum. The sample size of women <50 years of age was quite limited ($n = 20$ cases; ref. 20); thus, results for women <50 years of age are presented in Supplementary Tables S1 and S2.

All models were stratified by continuous age and time-period (2-year questionnaire cycle), assuming that the baseline hazard differed by age and period of follow-up; total energy intake (kcal/day) was included as an *a priori* confounder. Additional potential covariates included body mass index (BMI; <25, 25–29.9, ≥30 kg/m^2), history of type 2 diabetes, alcohol intake (never, past, current), cigarette smoking (never, current, former; pack-years), vigorous physical activity (none, <5 hours/week, ≥5 hours/week), and education (≤12, 13–15, 16, ≥17 years). If the log(HR) changed by ≥10% due to variable elimination, the variable was considered a confounder and remained in the model (21); only cigarette smoking met this criterion and was included in final models. Models were adjusted for total energy intake utilizing the standard multivariate approach for ease of interpretation. In a sensitivity analysis that utilized the residual and nutrient density models, results did not differ (16).

Effect measure modification by BMI, diabetes, alcohol intake, cigarette smoking, and vigorous physical activity was assessed using

likelihood ratio tests comparing regression models with and without a multiplicative term (22). We found no evidence of effect measure modification ($P \geq 0.05$). All P values are two-sided. Statistical analyses were conducted using SAS version 9.4 (SAS Institute).

Results

After exclusions, the analysis included 168 incident pancreatic cancer cases, with an average of 13.0 years of follow-up. Women with the highest intake of total red meat (Quartile 4) consumed an average of 91.0 g/day, whereas women with the lowest intake (Quartile 1) consumed an average of 9.0 g/day (**Table 1**). Compared with women consuming the lowest amount, women consuming the highest amount of total red meat were more likely at baseline to be younger, have a higher BMI, smoke cigarettes, drink alcohol, have lower educational attainment, be inactive, have a history of type 2 diabetes, and have higher total energy intake.

Overall, there was no association between total red meat intake and pancreatic cancer risk ($HR_{Q4\ vs.\ Q1} = 1.19$; 95% CI, 0.73–1.92; $P_{trend} = 0.3$; **Table 2**). Among women aged ≥50 years, an age group that included 88% of the cases, the highest intake of total red meat was associated with a 65% increased risk of pancreatic cancer ($HR_{Q4\ vs.\ Q1} = 1.65$; 95% CI, 0.98–2.78; $P_{trend} = 0.05$). For every 100 g increase of total red meat intake, risk of pancreatic cancer increased by 49% (HR = 1.49; 95% CI; 0.88–2.53). In terms of servings, consuming more than three servings of total red meat per week was associated with a 36% increased risk of pancreatic cancer (HR = 1.36; 95% CI, 0.83–2.23), compared with less than once a week. Among women <50 years of age, based on 20 cases, there was no association between total red meat intake and pancreatic cancer ($HR_{Q3\text{-}4\ vs.\ Q1\text{-}2} = 0.48$; 95% CI, 0.18–1.28; $P_{trend} = 0.1$; Supplementary Table S1).

Results were similar for unprocessed red meat as for total red meat (**Table 2** and Supplementary Table S1). For women 50 years

Table 1. Baseline characteristics[a] of study participants by quartiles of total red meat consumption, BWHS.

	Total red meat quartiles (g/day)			
	0–16.80 (*n* = 13,175)	**16.81–32.38 (*n* = 13,179)**	**32.39–55.84 (*n* = 13,176)**	**55.84–516.59 (*n* = 13,176)**
Age, years (mean ± SD)	40.3 ± 11.0	39.6 ± 10.8	38.6 ± 10.5	37.0 ± 10.2
BMI, kg/m^2 (mean ± SD)	26.6 ± 5.6	27.6 ± 6.3	28.3 ± 6.7	29.4 ± 7.6
Smoking status (%)				
Current	10	14	17	21
Past	21	20	20	19
Never	69	66	64	60
Smoking,[b] pack-years (mean ± SD)	3.4 ± 8.2	4.0 ± 9.1	4.5 ± 9.6	5.2 ± 10.4
Alcohol intake (%)				
Never	61	58	54	51
Past	14	14	15	15
Current	24	28	31	34
Missing	1	1	1	1
Education, years (%)				
≤12	13	17	20	23
13–15	32	35	37	40
16	27	26	23	22
≥17	28	23	20	16
Vigorous activity, hours/week (%)				
None	24	30	34	39
<5	53	53	51	48
≥5	19	13	11	10
Missing	4	3	4	3
Ever diagnosed with diabetes (%)				
Yes	3	4	4	6
No	97	96	96	94
Energy, kcal/day (mean ± SD)	1,146 ± 495	1,262 ± 531	1,478 ± 563	2,009 ± 670
Total red meat intake, g/day (mean ± SD)	9.0 ± 4.8	24.4 ± 4.5	42.8 ± 6.7	91.0 ± 37.1
Unprocessed red meat intake, g/day (mean ± SD)	7.1 ± 4.3	18.6 ± 5.6	32.3 ± 9.0	69.7 ± 34.0
Processed meat intake, g/day (mean ± SD)	2.1 ± 2.5	6.4 ± 5.2	11.9 ± 8.6	23.9 ± 20.2
Total saturated fat, g/day (mean ± SD)	11.8 ± 6.4	14.2 ± 6.8	18.0 ± 7.5	26.8 ± 10.0
Butyric acid (4:0)	0.2 ± 0.2	0.2 ± 0.2	0.3 ± 0.2	0.4 ± 0.3
Caproic acid (6:0)	0.1 ± 0.1	0.1 ± 0.1	0.1 ± 0.1	0.2 ± 0.1
Caprylic acid (8:0)	0.1 ± 0.1	0.1 ± 0.1	0.1 ± 0.1	0.1 ± 0.1
Capric acid (10:0)	0.2 ± 0.1	0.2 ± 0.2	0.2 ± 0.2	0.3 ± 0.2
Lauric acid (12:0)	0.3 ± 0.2	0.3 ± 0.3	0.4 ± 0.3	0.6 ± 0.3
Myristic acid (14:0)	0.9 ± 0.7	1.1 ± 0.7	1.3 ± 0.8	1.9 ± 0.9
Palmitic acid (16:0)	6.7 ± 3.4	8.0 ± 3.5	10.1 ± 3.9	15.2 ± 5.3
Stearic acid (18:0)	3.0 ± 1.6	3.7 ± 1.7	4.8 ± 1.9	7.2 ± 2.6

[a]Values are standardized to the age distribution of the study population.
[b]Among current and past smokers.

Table 2. Adjusted[a] HRs and 95% CIs for associations of red and processed meat intake with risk of pancreatic cancer overall and among women aged ≥50 years.

	All ages			Age ≥50 years		
Intake	Number of cases	Person-years	HR (95% CI)	Number of cases	Person-years	HR (95% CI)
Total red meat, g/day						
Quartile 1	44	254,838	1.00	34	134,494	1.00
Quartile 2	37	255,015	0.85 (0.55–1.31)	36	126,295	1.10 (0.69–1.76)
Quartile 3	42	254,154	1.03 (0.67–1.60)	37	116,015	1.27 (0.79–2.05)
Quartile 4	45	253,078	1.19 (0.73–1.92)	41	100,147	1.65 (0.98–2.78)
P_{trend}[b]			0.3			0.05
Continuous (per 100 g/day)			1.06 (0.63–1.79)			1.49 (0.88–2.53)
Frequency, servings per week (1 serving = 85 g ≈ 3 ounces)						
<1/week	33	161,537	1.00	24	85,053	1.00
≥1/week–≤3/week	52	393,753	0.65 (0.42–1.01)	49	196,307	0.87 (0.53–1.42)
>3/week	83	461,794	0.97 (0.63–1.51)	75	195,592	1.36 (0.83–2.23)
Unprocessed red meat, g/day						
Quartile 1	48	254,552	1.00	38	134,834	1.00
Quartile 2	35	254,457	0.74 (0.48–1.14)	34	126,099	0.93 (0.59–1.49)
Quartile 3	43	254,606	0.96 (0.63–1.46)	37	115,828	1.12 (0.70–1.78)
Quartile 4	42	253,470	1.01 (0.63–1.61)	39	100,191	1.38 (0.83–2.28)
P_{trend}[b]			0.7			0.6
Continuous (per 100 g/day)			1.20 (0.66–2.19)			1.67 (0.92–3.02)
Frequency, servings per week (1 serving = 85 g ≈ 3 ounces)						
<1/week	46	245,854	1.00	36	129,528	1.00
≥1/week–≤3/week	70	457,038	0.83 (0.57–1.21)	65	221,284	1.03 (0.68–1.55)
>3/week	52	314,192	0.99 (0.64–1.55)	47	126,140	1.31 (0.81–2.13)
Processed meat, g/day						
Quartile 1	46	254,552	1.00	39	126,862	1.00
Quartile 2	45	254,774	0.95 (0.63–1.44)	40	124,611	1.02 (0.66–1.59)
Quartile 3	39	254,650	0.83 (0.54–1.28)	32	118,041	0.85 (0.53–1.36)
Quartile 4	38	253,109	0.79 (0.49–1.25)	37	107,437	1.01 (0.62–1.64)
P_{trend}[b]			0.3			1.0
Continuous (per 50 g/day)			0.74 (0.39–1.44)			0.99 (0.52–1.90)
Frequency, servings per week (1 serving = 85 g ≈ 3 ounces)						
<1/week	107	646,682	1.00	92	310,085	1.00
≥1/week–≤3/week	55	315,504	0.99 (0.70–1.39)	50	144,780	1.09 (0.76–1.56)
>3/week	6	54,899	0.59 (0.25–1.38)	6	22,087	0.77 (0.32–1.82)

[a]Adjusted for age (continuous), cigarette smoking (never, former, current; pack-years), and total energy intake (kcals).
[b]Tests for linear trend were calculated by assigning the median of each quartile as scores.

and older, the highest intake of unprocessed red meat was associated with a 38% increased risk of pancreatic cancer ($HR_{Q4\ vs.\ Q1} = 1.38$; 95% CI, 0.83–2.28), but there was little evidence of an association at lower levels of intake ($P_{trend} = 0.6$). For every 100 g increase of unprocessed red meat intake, risk of pancreatic cancer increased by 67% (HR = 1.67; 95% CI, 0.92–3.02).

No association was observed between processed meat intake and risk of pancreatic cancer in the full cohort ($HR_{Q4\ vs.\ Q1} = 0.79$; 95% CI, 0.49–1.25; $P_{trend} = 0.3$; **Table 2**), and there was no evidence of interaction with age ($P_{interaction} = 0.2$; Supplementary Table S1).

The HR for highest versus lowest quartile of total saturated fat intake in the overall sample was 1.56 (95% CI, 0.82–2.99, $P_{trend} = 0.2$; **Table 3**). There was not a statistically significant interaction by age ($P_{interaction} = 0.4$), but HRs were higher among women ≥50 years of age ($HR_{Q4\ vs.\ Q1} = 1.85$; 95% CI, 0.92–3.72; $P_{trend} = 0.08$) than among women <50 years ($HR_{Q3\text{-}4\ vs.\ Q1\text{-}2} = 0.61$; 95% CI, 0.18–2.06; $P_{trend} = 0.4$). For saturated fats that have primary food sources of red meat (i.e., myristic, palmitic, and stearic acids), there was consistent, but not significant, increased pancreatic cancer risk (e.g., palmitic acid $HR_{Q4\ vs.\ Q1} = 1.54$; 95% CI, 0.74–3.21; $P_{trend} = 0.3$). There was little to no association between saturated fats and pancreatic cancer for women <50 years of age (Supplementary Table S2).

Discussion

In this large prospective study of African-American women, the highest consumption of total red meat intake compared with lowest was associated with a 65% increased risk of pancreatic cancer among women aged 50 and older. Little to no association was observed with processed meat. Total saturated fat was associated with increased risk of pancreatic cancer in the women aged 50 and older, but the findings were not statistically significant.

Our findings are consistent with the WCRF/AICR Continuous Update Project, which found that red meat was associated with an increased risk of pancreatic cancer (7). Specifically, the WCRF recommends limiting red meat consumption to no more than 350 to 500 g per week and eating a minimal amount of processed meats for cancer prevention. In our study, women in the highest quartile of total red meat consumption consumed a median of 558 g per week in 1995. Of note, most of the literature to date indicates that the increased risk

Table 3. Adjusted[a] HRs and 95% CIs for associations of saturated fatty acid intake with risk of pancreatic cancer overall and among women aged ≥50 years.

	All ages			Age ≥50 years		
Intake (g/day)	**Number of cases**	**Person-years**	**HR (95% CI)**	**Number of cases**	**Person-years**	**HR (95% CI)**
Total saturated fat						
Quartile 1	39	253,786	1.00	33	133,634	1.00
Quartile 2	39	254,511	1.07 (0.67–1.69)	36	125,652	1.22 (0.74–1.99)
Quartile 3	42	253,859	1.23 (0.75–2.04)	39	115,595	1.49 (0.87–2.54)
Quartile 4	48	253,489	1.56 (0.82–2.99)	40	101,650	1.85 (0.92–3.72)
P_{trend}[b]			0.2			0.08
Continuous (per 10 g/day)			0.93 (0.69–1.25)			1.04 (0.76–1.42)
Fatty acid 4:0 (butyric acid)						
Quartile 1	42	247,181	1.00	37	137,178	1.00
Quartile 2	34	254,551	0.91 (0.57–1.44)	31	122,764	0.97 (0.60–1.58)
Quartile 3	51	256,278	1.39 (0.90–2.15)	48	114,813	1.57 (1.00–2.47)
Quartile 4	40	250,292	1.13 (0.68–1.89)	31	99,485	1.09 (0.63–1.90)
P_{trend}[b]			0.4			0.6
Continuous (per 1 g/day)			1.21 (0.52–2.81)			1.24 (0.50–3.07)
Fatty acid 6:0 (caproic acid)						
Quartile 1	37	246,535	1.00	33	133,757	1.00
Quartile 2	43	256,730	1.27 (0.81–1.98)	38	124,606	1.30 (0.81–2.08)
Quartile 3	42	253,682	1.30 (0.82–2.07)	38	113,100	1.41 (0.87–2.29)
Quartile 4	45	249,610	1.40 (0.85–2.31)	38	101,951	1.46 (0.85–2.49)
P_{trend}[b]			0.3			0.2
Continuous (per 1 g/day)			1.66 (0.36–7.64)			2.10 (0.41–10.69)
Fatty acid 8:0 (caprylic acid)						
Quartile 1	46	262,815	1.00	41	143,567	1.00
Quartile 2	31	236,417	0.88 (0.56–1.40)	27	110,470	0.90 (0.55–1.47)
Quartile 3	47	260,409	1.18 (0.77–1.81)	45	119,214	1.32 (0.84–2.06)
Quartile 4	44	250,820	1.13 (0.69–1.86)	35	101,567	1.09 (0.64–1.87)
P_{trend}[b]			0.5			0.6
Continuous (per 1 g/day)			1.50 (0.16–14.11)			1.80 (0.16–19.90)
Fatty acid 10:0 (capric acid)						
Quartile 1	44	250,201	1.00	38	136,345	1.00
Quartile 2	33	251,086	0.86 (0.54–1.35)	31	120,626	0.97 (0.60–1.57)
Quartile 3	50	257,858	1.25 (0.81–1.92)	46	116,336	1.41 (0.89–2.23)
Quartile 4	40	250,508	1.00 (0.59–1.67)	32	101,133	1.02 (0.58–1.79)
P_{trend}[b]			0.8			0.8
Continuous (per 1 g/day)			1.18 (0.40–3.49)			1.35 (0.42–4.28)
Fatty acid 12:0 (lauric acid)						
Quartile 1	38	252,089	1.00	34	138,978	1.00
Quartile 2	43	249,861	1.34 (0.86–2.08)	37	119,700	1.33 (0.83–2.15)
Quartile 3	44	258,676	1.33 (0.84–2.13)	43	115,631	1.55 (0.96–2.51)
Quartile 4	43	249,811	1.34 (0.78–2.29)	34	100,311	1.30 (0.73–2.33)
P_{trend}[b]			0.4			0.5
Continuous (per 1 g/day)			0.88 (0.44–1.77)			0.96 (0.46–2.03)
Fatty acid 14:0 (myristic acid)						
Quartile 1	40	250,653	1.00	34	137,943	1.00
Quartile 2	41	253,663	1.15 (0.74–1.80)	37	124,127	1.28 (0.79–2.06)
Quartile 3	41	254,591	1.19 (0.74–1.92)	40	114,411	1.48 (0.90–2.44)
Quartile 4	46	252,700	1.43 (0.82–2.49)	37	98,715	1.56 (0.86–2.83)
P_{trend}[b]			0.2			0.2
Continuous (per 1 g/day)			1.07 (0.83–1.37)			1.13 (0.87–1.47)
Fatty acid 16:0 (palmitic acid)						
Quartile 1	38	253,826	1.00	32	132,820	1.00
Quartile 2	41	254,648	1.11 (0.70–1.76)	38	125,199	1.26 (0.77–2.07)
Quartile 3	43	254,164	1.23 (0.74–2.04)	41	116,351	1.48 (0.86–2.55)
Quartile 4	46	253,565	1.40 (0.71–2.76)	37	102,327	1.54 (0.74–3.21)
P_{trend}[b]			0.3			0.3
Continuous (per 1 g/day)			0.98 (0.93–1.04)			1.00 (0.94–1.07)
Fatty acid 18:0 (stearic acid)						
Quartile 1	42	254,106	1.00	35	133,107	1.00
Quartile 2	39	253,998	0.97 (0.61–1.52)	37	124,865	1.15 (0.71–1.86)
Quartile 3	39	254,435	1.00 (0.61–1.66)	36	115,677	1.22 (0.71–2.09)

(Continued on the following page)

Table 3. Adjusted[a] HRs and 95% CIs for associations of saturated fatty acid intake with risk of pancreatic cancer overall and among women aged ≥50 years. (Cont'd)

	All ages			Age ≥50 years		
Intake (g/day)	**Number of cases**	**Person-years**	**HR (95% CI)**	**Number of cases**	**Person-years**	**HR (95% CI)**
Quartile 4	47	253,341	1.26 (0.66–2.42)	39	102,924	1.52 (0.76–3.06)
P_{trend}[b]			0.4			0.2
Continuous (per 1 g/day)			0.95 (0.85–1.06)			1.00 (0.88–1.12)

[a]Adjusted for age (continuous), cigarette smoking (never, former, current; pack-years), and total energy intake (kcals).
[b]Tests for linear trend were calculated by assigning the median of each quartile as scores.

associated with red meat is primarily confined to men. In the Continuous Update Project, red meat (per 100 g/day) was associated with a 19% increased risk of pancreatic cancer (43% in men, 6% in women; ref. 2). Only four studies in the Continuous Update Project examined the association between red meat and pancreatic cancer in women (23–26), and none of the studies stratified by race or ethnicity. Another recent study, based in the Cancer Prevention Study-II Nutrition Cohort, found no association between red or processed meat and pancreatic cancer risk in men or women (27). In our study, we report that total red meat consumption per 100 g in women aged 50 or older was associated with a 49% increased risk of pancreatic cancer, with unprocessed red meat associated with a 67% increased risk.

Since the Continuous Update Project, one study has examined the association of red meat and pancreatic cancer by race—the Multiethnic Cohort Study (8). This study reported little to no association between red meat and pancreatic cancer among European Americans, Native Hawaiians, or Japanese Americans, but an increased risk among African Americans and Latino Americans. For African Americans —men and women together—the highest consumption of red meat intake compared with lowest was associated with a 48% increased risk of pancreatic cancer (8), which is similar to findings in our study of African-American women aged 50 and older.

None of the prior cohort studies have published on the association at ages <50 years, as most cohort studies begin recruitment at or near age 50. A consortium of case–control studies examined risk factors, albeit not diet, for pancreatic cancer diagnosed before age 45 and reported some differences, primarily for alcohol (17). Thus, it is plausible that there may be different associations between diet and pancreatic cancer by age. However, the small number of early-onset pancreatic cancer cases in the BWHS (age <50 years $n = 20$) limits interpretation of results in that age group.

A number of mechanisms have been proposed linking red and processed meat intake to pancreatic cancer, including mutagens which are by-products of cooking methods (i.e., polycyclic aromatic hydrocarbons, heterocyclic amines, *N*-nitroso compounds, and advanced glycation endproducts; ref. 5), heme iron intake (28), increased insulin resistance (6), and saturated fat intake (2–4). The majority of studies to date examining mutagens formed in meats, due to grilling, barbequing, or cooking at high temperatures, have reported that increased mutagenic activity is associated with an increased pancreatic cancer risk (29–31). *N*-nitroso compounds are known to be a potent carcinogen in experimental models (32, 33), and exposure through tobacco smoking is an established pancreatic cancer risk factor (28). Apart from tobacco smoking, humans are exposed to *N*-nitroso compounds via diet. Specifically, *N*-nitrosamines form in meat which has been preserved with nitrate (e.g., cured, smoked, or pickled) or dried at high temperatures. In addition, *N*-nitroso compounds can be formed endogenously by nitrate in the stomach and amides ingested from meat (34, 35). Both the ingested or endogenously produced *N*-nitroso compounds can reach the pancreas through the blood stream (36). Heme iron has been hypothesized to increase pancreatic cancer risk through promoting oxidative stress or catalyzing formation of *N*-nitroso (37). However, epidemiologic studies to date of dietary heme iron and pancreatic cancer risk have been largely null (25, 38–46). Red and processed meat (6) and saturated fat (47–49) are associated with increasing insulin resistance, which can lead to hyperinsulinemia and subsequent type 2 diabetes. Pre-existing type 2 diabetes has consistently been associated with an increased risk of pancreatic cancer (50).

In the current study, processed meat and saturated fats were not significantly associated with increased pancreatic cancer risk, although HRs for saturated fats were of a similar magnitude to those for red meat. The Continuous Update Project deemed there to be limited suggestive evidence that processed meat and saturated fat intake increase pancreatic cancer risk (7). Processed meat (per 50 g/day) was associated with a 17% increased risk (21% in men, 9% in women), but only four studies reported on the association in women (23–25, 51). Further, the majority of studies examining saturated fat intake did not stratify by sex (7). The one study of this association in women (the Nurses' Health Study) observed no association between saturated fat and pancreatic cancer risk (25).

In animal models, diets rich in saturated fats promote pancreatic carcinogenesis through augmented lipid metabolism (52, 53). Saturated fat may promote pancreatic cancer through other mechanisms as well. For instance, palmitic acid reduces proliferation and induces apoptosis of β-cells, which could lead to a reduction in β-cell mass and decreased functional activity (54). Decreased β-cell mass and function can lead to type 2 diabetes (55), which is an established risk factor for pancreatic cancer. High levels of dietary fat can also cause pancreatic hypertrophy or hyperplasia, which may increase the vulnerability of the pancreas to other carcinogenic insults (56, 57). Bile acids are also hypothesized to promote pancreatic cancer, as bile acids stimulate the tumor promoter cyclooxygenase-2 in cell lines (4, 58–61). Primary bile acids are derived from cholesterol, synthesized in the liver, and stored in the gallbladder. After food ingestion, they are moved into the gut to facilitate lipid absorption (62, 63). However, higher fat intake may induce bile acid reflux into the pancreatic duct, potentially leading to cancer (58).

In our study, we examined saturated fats, as beef and processed meat are primary contributors to saturated fat intake in the United States. Approximately 9% of total saturated fat in a typical U.S. diet is derived from beef, whereas 7% is from processed meat (64). The main dietary sources of butyric, caproic, caprylic, capric, and lauric acids are dairy products (e.g., milk, cheese, butter), whereas the main dietary sources of myristic, palmitic, and stearic acids are red and processed meats. A nonsignificant increased risk of pancreatic cancer was associated with total saturated fat. Increasing levels of intake of individual fatty acids derived primarily from red and processed meats were associated with

increased, but not statistically significant risks in women aged 50 and older. Conversely, among the fatty acids derived from dairy products, there was evidence of an association with pancreatic cancer risk for caproic acid only.

Strengths of the current study include the prospective design; thus, error in reporting of dietary data is unlikely to be associated with disease outcome. As pancreatic cancer can be rapidly fatal and thus potentially susceptible to reverse causation, we excluded cases occurring within 2 years of completing the baseline FFQ about usual diet over the past year. However, whether such time period—versus cumulative lifetime exposure—reflects intakes during the time relevant to pancreatic cancer development is unknown. The cases were identified through self-report and through repeated linkage with cancer registries and the NDI, and over 97% were confirmed through hospital, registry, and death records. Finally, this study was able to assess a wide range of potential confounders.

Limitations of the current study include potential measurement error and generalizability. FFQs have known measurement errors, but they are nevertheless useful for ranking individuals' dietary intake relative to one another, which was our primary objective (16). The BWHS FFQ was validated with criterion instruments (i.e., 3-day food records and three 24-hour recalls) and showed high correlations (14), which are within the range of acceptable validity and comparable with other dietary validation studies (65–68). The BWHS population is more highly educated than the general U.S. population. However, the estimated fat intake from the FFQs are consistent estimates from nationally representative African-American adult populations (69). Thus, these results are likely generalizable to other African-American women.

In conclusion, higher consumption of red meat—specifically, unprocessed red meat—was associated with an increased risk of pancreatic cancer among African-American women aged 50 or older; based on small numbers, there was no association at younger ages. There was a possible association between saturated fat and increased risk of pancreatic cancer in the women aged 50 and older, but the findings were not statistically significant. There is no evidence of an association between processed meat and pancreatic cancer risk. Further research is needed to elucidate the association between red meat—and possibly saturated fat—and pancreatic cancer risk in African-American populations, particularly examining these associations by age.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Authors' Contributions

Conception and design: J.L. Petrick, J.R. Palmer
Development of methodology: J.L. Petrick, J.R. Palmer
Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): T.N. Bethea, L. Rosenberg, J.R. Palmer
Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): J.L. Petrick, N. Castro-Webb, H. Gerlovin, E.A. Ruiz-Narváez
Writing, review, and/or revision of the manuscript: J.L. Petrick, N. Castro-Webb, H. Gerlovin, T.N. Bethea, S. Li, E.A. Ruiz-Narváez, L. Rosenberg, J.R. Palmer

Acknowledgments

Pathology data were obtained from the following state cancer registries: AZ, CA, CO, CT, DE, DC, FL, GA, IL, IN, KY, LA, MD, MA, MI, NJ, NY, NC, OK, PA, SC, TN, TX, and VA, and results reported do not necessarily represent their views.

This research was funded by NIH grants U01 CA164974 (L. Rosenberg and J.R. Palmer), U01 CA187508 (J.R. Palmer), and R01 CA058420 (L. Rosenberg), and the Karin Grunebaum Cancer Research Foundation (J.R. Palmer).

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Received January 13, 2020; revised April 7, 2020; accepted June 24, 2020; published first July 1, 2020.

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