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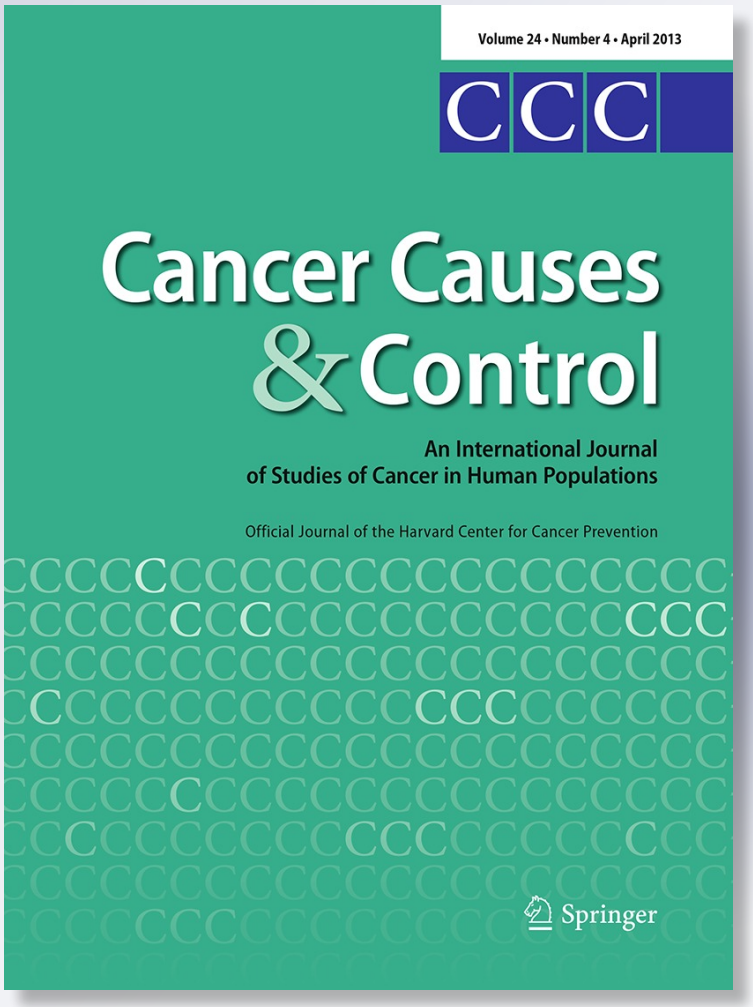

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ORIGINAL PAPER

Diet impacts mortality from cancer: results from the multiethnic cohort study

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Abstract
Purpose Cancer is the second leading cause of death in the United States and mortality varies by ethnicity. The objective of this study was to examine the association between cancer mortality and dietary intake among a large multiethnic population.
Methods A prospective cohort design was used to examine cancer mortality among 146,389 participants. Multiethnic cohort study participants represent five ethnic groups: African American, Native Hawaiian, Japanese American, Latino, and Caucasian. Hazard ratios for cancer mortality by intake levels of five food groups and discretionary fat were calculated using Cox proportional hazards models stratified by sex and ethnicity.
Results There were a total of 2,028 male and 1,464 female fatal cancer cases at the end of follow-up. Among Japanese American men only, there was a significant protective effect seen in those reporting a high grain intake (HR = 0.49, 95 % CI 0.35–0.69); there was no effect of grain consumption in any other ethnic-sex group. There was no evidence that ethnicity modified associations between fruit, vegetable, meat, dairy, or discretionary fat intake and cancer mortality among men. Associations between food group consumption and risk for cancer mortality among women were similar across ethnic groups.
Conclusions The considerable reduction in cancer risk associated with high grain consumption among a specific ethnic-sex group, Japanese American men, warrants further investigation. Additional research is needed to validate this observation and determine whether this was a chance finding, or possibly due to differential intake of specific grain subtypes, and/or related to a sex-specific cancer type.

Keywords Cancer mortality · Diet · Ethnicity · Cohort study

Abbreviations

95 % CI	95 % Confidence interval
FCT	Food composition table
HR	Hazard ratio
ICD	International classifications of diseases
MEC	Multiethnic cohort
NIH-AARP	National Institutes of Health-American Association of Retired Persons
QFFQ	Quantitative food frequency questionnaire
USDA	United States Department of Agriculture

Introduction

In 2010, cancer was the second leading cause of death in the United States, accounting for 573,855 deaths [1]. The age-adjusted death rate from cancer of all sites was estimated to be 185.9 per 100,000 in 2010 [1], with higher rates for men than women [2]. Although total cancer mortality has continued to decline since 1990, there are still major disparities in cancer death rates between different ethnic groups. Ethnic-specific, age-adjusted cancer mortality rates (per 100,000) in the United States were 293.7 and 179.6 for African American men and women, respectively, compared to 222.3 and 159.1 for Caucasians, 152.7

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and 101.9 for Hispanics or Latinos, and 133.0 and 94.5 for Asians or Pacific Islanders in 2005 [2]. In 2010, Hispanics, Blacks, and Asians comprised nearly 35 % of the US population [3], an increase of nearly 5 % from 2007 statistics [2]. Thus, it is important to determine possible reasons for these disparities in disease rates among different ethnic groups and in particular to evaluate the potential modifiable risk factors, such as diet. It has been shown that food group intake also differs between ethnic groups, and this could, at least in part, provide an explanation for these disparities [4, 5].

Risk factors for cancer, such as family history, diet, physical inactivity, and genetic susceptibility, have been extensively investigated [6–8]. While there is clear evidence for genetic predisposition, the key determinants of cancer incidence are largely environmental factors, including diet [9]. It was estimated that 365,000 deaths in the United States in 2000 were due to a poor diet and physical inactivity [10] and that one-third of all cancers in Western countries are associated with dietary factors [11]. In an expert report published in 1997, it was estimated approximately four million cases of cancer per year could be prevented globally by diet and other lifestyle changes [9].

There is substantial evidence that increased intake of fruits and vegetables lowers cancer risk and mortality [12–14] although national surveys have repeatedly found that individuals consume much lower levels of fruits and vegetables than recommended [15]. Key et al. [12] found a higher incidence of cancers of the breast, colon, rectum, and prostate in developed countries compared to developing countries and hypothesized that this may be due to the greater consumption of animal fats, total fat, and sugar.

There are a lack of data on the relationship between diet and total cancer mortality in minority populations in the United States. The aim of this study was to examine the associations of food group intake with total cancer mortality in the large multiethnic cohort (MEC). We examined the associations between risk of total cancer deaths and standardized food group servings (as defined by the USDA), by sex and ethnicity. Additionally, the effect of discretionary fat on cancer mortality was examined.

Methods

Study population

The MEC was established in Hawaii and California (primarily Los Angeles County) to investigate lifestyle exposures in relation to cancer. Study design, recruitment procedures, and baseline characteristics have been reported previously [16]. In brief, 201,257 men and women aged 45–75 years from five different ethnic backgrounds (African American, Native Hawaiian, Japanese American, Latino, and Caucasian) entered the cohort by completing a self-administered comprehensive questionnaire, including a quantitative food frequency questionnaire (QFFQ), between 1993 and 1996. The MEC yielded a highly representative group when comparing the cohort distributions across educational levels and marital status with corresponding census data. The question "Has your doctor ever told you that you had any of the following conditions?" was used to determine the history of medical conditions at baseline. The cancer-related answers were on eight specific types of cancer (colon or rectal cancer, stomach cancer, melanoma, other skin cancer, breast cancer, prostate cancer, cervix cancer, and uterine cancer). Participants who provided a positive response to any of these cancer-related question were excluded ($n = 19{,}571$).

Other exclusions included those individuals with missing smoking information ($n = 6{,}080$), implausible diets based on energy and macronutrient intakes as well as daily food group consumption ($n = 12{,}346$), implausible or missing anthropometric information ($n = 3{,}251$), missing data for hormone replacement therapy for women ($n = 8{,}163$), and other missing covariates ($n = 6{,}234$), leaving a total of 70,333 men and 76,056 women in the present analyses.

All participants provided informed consent. The study protocol was approved by the institutional review boards of the University of Hawaii and the University of Southern California.

Dietary assessment

Dietary intake was assessed using a self-administered QFFQ that collected consumption data of more than 180 food items over the past 12 months [16]. The QFFQ, a modified version of a validated and extensively used face-to-face interview method, was developed from three-day measured dietary records from 60 men and 60 women of each main ethnic group. The QFFQ inquired about the amount of food consumed based on a choice of three portion sizes specific to each food item, which were also shown in representative photographs, and the usual intake frequency based on eight categories ranging from "Never or hardly ever" to "2 or more times a day." A validation and calibration sub-study based on three 24-h dietary recalls collected in each sex-ethnic group revealed that the average correlation coefficients for all nutrients were lowest in African American women (0.26) and highest in Caucasian men (0.57) [17]. However, the average correlations were about twice as high as for absolute intakes when nutrients were expressed as densities (0.57–0.74 across ethnic-sex strata).

Standardized food group servings were computed from the QFFQ for each individual using a food composition table (FCT) developed by the Cancer Research Center of Hawaii. This FCT includes many unique foods consumed by the different ethnic groups in the MEC [16]. All mixed dishes were broken down into their ingredients. The servings of each food group were computed by adding the servings across the appropriate food items on the QFFQ for each individual. The 2000 U.S. dietary guidelines were used to determine the servings of the following food groups: fruits (citrus, melons, berries, and other fruits), vegetables (dark green, deep yellow, potato, starchy, tomato, other vegetables), meat (red meat, poultry, and fish), grains (whole grain, non-whole grain), and dairy products (milk, yogurt, cheese) [18]. The effects of consumption of discretionary fats, defined by the U.S. Department of Agriculture (USDA) as the excess fat consumed if the lowest fat food items were not consumed, and fats used in preparation, were also examined [19].

Identification of total cancer deaths

For this analysis, total cancer deaths were identified through 31 December 2001 via linkages to the Hawaii Tumor Registry, the Cancer Surveillance Program for Los Angeles County, and the California State Cancer Registry, all three of which are part of the U.S. National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program, as well as the U.S. National Death Index. Total cancer deaths were identified using the International Classification of Diseases for Oncology, Second Edition (ICD-O-2) [20].

Statistical analysis

Cox proportional hazards models, with age as the time metric, were used to calculate hazard ratios (HR) and 95 % confidence intervals (95 % CI). We investigated the intake of each food group as quartiles based on sex-specific consumption patterns and assessed dose–response using trend variables, which had the median of the appropriate quartile assigned. Models were adjusted for ethnicity when appropriate, time on study ($\leq$2, 3–5 and >5 years, as a strata variable), maximum years of education, energy intake (logarithmically transformed), smoking behavior (including current smoking, past smoking, and pack-years), alcohol consumption, body mass index, physical activity (defined as average hours of moderate or vigorous physical activity per day), family history of cancer, marital status, and number of children. The models were mutually adjusted for all food groups. Use of hormone replacement therapy and history of oophorectomy were additional adjustment variables for women. A sensitivity analyses were also conducted to examine stability of results without early follow-up cases. Models were examined using two outcome definitions: (1) all follow-up cancer cases and (2) only cases that occurred at least 2 years after the baseline dietary assessment. Results were similar and would not have impacted conclusions; thus, models are presented for all follow-up cases.

Tests based on Schoenfeld residuals showed no evidence that any models violated the proportional hazards assumptions. All tests were two-sided, and a $p < 0.05$ was considered statistically significant.

Potential variations in the effects of diet on cancer mortality were examined using ethnic-sex stratified models, considering direction of point estimates, extent of confidence interval overlap, dose response effects, as well as the plausibility of non-uniform effects based on supporting literature [21].

Results

By 31 December 2001, 2,082 cancer deaths in men and 1,464 in women occurred in the MEC. The entire cohort and fatal cases are described in Table 1. Energy intake, percent contribution to energy from fat, saturated fat, and alcohol, as well as the mean daily servings of the five food groups and dietary components, were similar between fatal cases and all participants. Compared to the entire cohort, cases for both men and women reported a higher number of pack-years of cigarettes smoked, a higher percentage of current smokers, and were slightly older.

Models stratified by ethnicity for male participants are presented in Table 2. There was a significant association (HR = 0.49, 95 % CI 0.35–0.69) and decreasing trend ($p_{\text{trend}} = 0.0009$) in cancer risk with higher levels of grain consumption among Japanese American men only. Comparison of confidence intervals across strata for fruit, vegetable, meat, dairy, and discretionary fat intake did not provide evidence that associations with these food groups and risk of cancer mortality among men varied by ethnicity; thus, results for all ethnicities combined are presented in the final column of Table 2. For the food groups where data were combined, high vegetable consumption had a protective effect for all levels of consumption above the reference, and the association was statistically significant among men with the highest intake (HR = 0.82, 95 % CI 0.71–0.95).

Among women (Table 3), a statistically significant protective effect on risk for cancer mortality was observed among African Americans (HR = 0.76, 95 % CI 0.59–0.99) and Caucasians (HR = 0.73, 95 % CI 0.54–0.99) with vegetable intake in the second quartile. The results for

Table 1 Characteristics of the total participants and fatal cases from all cancers

Characteristics	Men		Women	
	Fatal cases (n = 2,082)	Total participants (n = 70,333)	Fatal cases (n = 1,464)	Total participants (n = 76,056)
Age at cohort entry (years)	65 ± 7	60 ± 9	64 ± 8	59 ± 9
Energy intake (kcal)	2,275 ± 1,015	2,308 ± 979	1,886 ± 887	1,890 ± 844
% energy from fat	30.6 ± 7.6	30.2 ± 7.1	30.8 ± 7.4	29.8 ± 7.1
% energy from saturated fat	9.2 ± 2.8	8.9 ± 2.6	9.2 ± 2.8	8.7 ± 2.6
% energy from alcohol	5.1 ± 9.2	4.1 ± 7.3	2.0 ± 6.0	1.6 ± 4.5
Food group intake (servings/day)				
Fruits	3.1 ± 2.7	3.0 ± 2.7	3.5 ± 2.9	3.5 ± 2.9
Vegetables	4.2 ± 2.7	4.5 ± 2.8	4.5 ± 2.9	4.6 ± 2.9
Meat	4.9 ± 3.2	5.1 ± 3.3	4.0 ± 2.9	4.0 ± 2.8
Dairy	1.2 ± 1.0	1.2 ± 1.0	1.2 ± 1.0	1.2 ± 1.0
Grains	7.9 ± 3.9	8.4 ± 3.8	6.7 ± 3.5	7.0 ± 3.5
Dietary component intake				
Alcohol (drinks/day)	1.4 ± 3.1	1.1 ± 2.4	0.4 ± 1.5	0.3 ± 1.1
Added sugar (teaspoons/day)	13.4 ± 13.3	13.4 ± 12.7	10.9 ± 10.8	10.8 ± 10.3
Discretionary fat (g/day)	63.4 ± 35.6	63.6 ± 34.6	53.3 ± 31.6	51.7 ± 30.0
Hours in moderate or vigorous activity per day	0.7 ± 1.0	0.8 ± 1.0	0.9 ± 1.0	0.9 ± 1.1
Body Mass Index (kg/m^2)	25.7 ± 4.0	26.1 ± 4.0	26.2 ± 5.7	25.8 ± 5.4
Pack-years (number of cigarettes per day × years smoked/20)	23.3 ± 19.8	14.1 ± 16.6	12.3 ± 16.5	6.5 ± 12.0
Number of children	2.8 ± 2.0	2.6 ± 1.9	2.9 ± 2.1	2.8 ± 1.9
Ethnicity (%)				
Caucasian	23	25	24	24
African American	22	13	33	20
Native Hawaiian	7	7	7	7
Japanese American	27	31	19	28
Latino	21	24	17	21
Smoking status (%)				
Never smoked	17	31	42	57
Past smoker	51	51	31	29
Current smoker	32	18	27	14
Currently married (%)	74	77	50	60

the Native Hawaiian women suggested an elevated risk with intake in the second and fourth quartiles, but these results were not statistically significant. As there were a relatively small number of cases among Hawaiian women compared to other groups, and overlap of the stratum-specific confidence intervals was observed across the ethnic groups, a combined measure of effect is presented for vegetable intake. Similarly, there was no evidence that ethnicity modified any of the associations between dietary intake and risk of cancer for any other food groups, and the final associations between food group and risk for cancer death among women are presented for all ethnic groups combined in the final column of Table 3. Similar to men, higher vegetable intake was associated with a protective effect among women (Table 3, last column). Although the results were statistically significant only among women reporting vegetable intake in the second quartile and men reporting intake in the highest quartile, the point estimates suggest that any level of vegetable intake above the reference may have a beneficial effect on risk for cancer mortality. Fruit intake was also associated with a lower risk of cancer mortality among women. There was no evidence of an effect of meat or dairy product consumption on total cancer mortality among the women. Although not statistically significant (HR = 1.23, 95 % CI 0.97–1.56), a higher risk of cancer mortality was also observed among women with consumption of discretionary fat >64.9 g per day, compared to those with intake in the lowest quartile.

Table 2 The associations of food groups and discretionary fat intake with the risk of cancer mortality among men, by ethnicity

Ethnic group Cases/controls	African American 432/8,304 HR (95 % CI)[a]	Native Hawaiian 139/4,764 HR (95 % CI)[a]	Japanese American 594/21,736 HR (95 % CI)[a]	Latino 417/15,798 HR (95 % CI)[a]	Caucasian 500/17,649 HR (95 % CI)[a]	All ethnic groups 2,082/68,251 HR (95 % CI)[a]
Food group (servings/day)						
Fruits						
Q1 (≤1.2)	1.00	1.00	1.00	1.00	1.00	1.00
Q2 (1.3–2.3)	0.91 (0.70–1.18)	1.10 (0.65–1.86)	0.69 (0.54–0.88)[b]	0.94 (0.70–1.27)	1.04 (0.80–1.33)	0.88 (0.78–1.00)
Q3 (2.4–4.0)	0.84 (0.63–1.12)	1.45 (0.87–2.43)	0.88 (0.70–1.12)	1.00 (0.74–1.35)	0.91 (0.70–1.19)	0.93 (0.82–1.05)
Q4 (>4.0)	0.81 (0.60–1.09)	1.46 (0.86–2.48)	0.84 (0.65–1.08)	1.02 (0.75–1.39)	1.01 (0.76–1.34)	0.96 (0.84–1.09)
p for trend	0.27	0.29	0.76	0.70	0.27	0.53
Vegetables						
Q1 (≤2.6)	1.00	1.00	1.00	1.00	1.00	1.00
Q2 (2.7–3.9)	0.83 (0.64–1.09)	1.42 (0.82–2.46)	0.96 (0.76–1.21)	0.95 (0.72–1.25)	0.98 (0.77–1.26)	0.94 (0.84–1.06)
Q3 (4.0–5.8)	0.96 (0.71–1.29)	1.15 (0.65–2.04)	0.86 (0.67–1.10)	0.91 (0.67–1.23)	0.81 (0.62–1.07)	0.88 (0.77–1.01)
Q4 (>5.8)	0.96 (0.68–1.35)	1.15 (0.62–2.15)	0.74 (0.56–0.98)[b]	0.71 (0.50–1.01)	0.89 (0.66–1.20)	0.82 (0.71–0.95)[b]
p for trend	0.89	0.19	0.10	0.03	0.36	0.01
Meat						
Q1 (≤2.8)	1.00	1.00	1.00	1.00	1.00	1.00
Q2 (2.9–4.3)	1.15 (0.86–1.53)	1.43 (0.82–2.51)	1.10 (0.89–1.37)	1.09 (0.81–1.45)	1.01 (0.79–1.29)	1.09 (0.97–1.24)
Q3 (4.4–6.4)	1.20 (0.88–1.64)	1.10 (0.60–1.20)	0.91 (0.71–1.17)	1.05 (0.73–1.38)	1.13 (0.86–1.47)	1.06 (0.92–1.21)
Q4 (>6.4)	1.20 (0.83–1.72)	1.02 (0.52–2.10)	0.89 (0.64–1.20)	0.96 (0.67–1.38)	1.30 (0.94–1.80)	1.11 (0.94–1.30)
p for trend	0.31	0.38	0.35	0.54	0.22	0.47
Grains						
Q1 (≤5.6)	1.00	1.00	1.00	1.00	1.00	N/A
Q2 (5.7–7.8)	0.88 (0.66–1.17)	1.37 (0.76–2.47)	0.84 (0.64–1.10)	1.10 (0.82–1.45)	0.86 (0.68–1.10)	
Q3 (7.9–10.8)	1.18 (0.85–1.65)	0.78 (0.40–1.53)	0.63 (0.47–0.84)[b]	0.92 (0.66–1.30)	0.82 (0.61–1.10)	
Q4 (>10.8)	1.24 (0.83–1.85)	1.27 (0.62–2.58)	0.49 (0.35–0.69)[b]	0.95 (0.63–1.42)	1.17 (0.81–1.68)	
p for trend	0.49	0.41	0.0009	0.86	0.94	
Dairy products						
Q1 (≤0.5)	1.00	1.00	1.00	1.00	1.00	1.00
Q2 (0.6–1.0)	0.89 (0.68–1.15)	0.68 (0.41–1.14)	1.05 (0.86–1.29)	0.82 (0.58–1.15)	0.99 (0.72–1.36)	0.96 (0.84–1.08)
Q3 (1.1–1.7)	0.86 (0.64–1.14)	1.08 (0.67–1.76)	1.00 (0.80–1.26)	0.72 (0.51–1.02)	1.09 (0.80–1.47)	0.96 (0.84–1.09)
Q4 (>1.7)	0.82 (0.58–1.16)	1.12 (0.67–1.89)	1.11 (0.81–1.52)	0.86 (0.60–1.22)	0.96 (0.70–1.32)	0.96 (0.83–1.11)
p for trend	0.81	0.42	0.33	0.18	0.16	0.51
Discretionary fat (g/day)						
Q1 (≤38.8)	1.00	1.00	1.00	1.00	1.00	1.00
Q2 (38.9–56.3)	1.03 (0.76–1.41)	0.84 (0.48–1.48)	0.89 (0.71–1.12)	1.24 (0.89–1.73)	0.94 (0.72–1.24)	0.99 (0.87–1.13)
Q3 (56.4–80.5)	1.07 (0.74–1.55)	0.65 (0.35–1.21)	0.90 (0.69–1.18)	1.32 (0.90–1.92)	1.09 (0.80–1.49)	1.03 (0.89–1.20)
Q4 (>80.5)	1.47 (0.93–2.31)	0.83 (0.39–1.76)	0.85 (0.59–1.23)	1.37 (0.85–2.22)	1.02 (0.68–1.52)	1.08 (0.89–1.32)
p for trend	0.23	1.00	0.38	0.19	0.95	0.51

[a] *HR* hazards ratio; *95 % CI* 95 % confidence interval; Cox regression using age as the time metric, and adjusting for time on study, years of education, energy intake (logarithmically transformed), smoking behaviors (including current smoking, past smoking, and pack-years), body mass index, physical activity (defined as average hours of moderate or vigorous physical activity per day), history of diabetes, and alcohol intake (grams per day)

[b] $p < 0.05$

Discussion

The American Cancer Society's goal for 2015 is to reduce total cancer mortality by 50 % and total cancer incidence by 25 % [22]. Many investigators have focused on all-cause mortality or single site cancer mortality rather than total cancer mortality [23–26], but to our knowledge, none have examined the effects of food group consumption on cancer mortality by ethnicity. In the present study, we examined the effects of dietary intake of various food

Table 3 The associations of food groups and discretionary fat intake with the risk of cancer mortality among women, by ethnicity

Ethnic group Case/control	African American 460/13,646 HR (95 % CI)[a]	Native Hawaiian 101/5,414 HR (95 % CI)[a]	Japanese American 297/21,843 HR (95 % CI)[a]	Latino 246/14,715 HR (95 % CI)[a]	Caucasian 360/18,974 HR (95 % CI)[a]	All ethnic groups 1,464/74,592 HR (95 % CI)[a]
Food group (servings/day)						
Fruits						
Q1 (≤1.5)	1.00	1.00	1.00	1.00	1.00	1.00
Q2 (1.6–2.8)	0.82 (0.63–1.07)	0.96 (0.54–1.71)	0.81 (0.58–1.13)	0.69 (0.48–1.01)	1.04 (0.77–1.39)	0.83 (0.72–0.97)[b]
Q3 (2.9–4.7)	0.94 (0.72–1.23)	1.20 (0.66–2.18)	0.74 (0.52–1.05)	0.79 (0.54–1.14)	0.96 (0.71–1.31)	0.87 (0.75–1.01)
Q4 (>4.8)	0.78 (0.58–1.05)	0.65 (0.32–1.31)	0.90 (0.62–1.31)	0.71 (0.48–1.05)	1.04 (0.74–1.46)	0.82 (0.69–0.92)[b]
p for trend	0.91	0.27	0.97	0.15	0.93	0.15
Vegetables						
Q1 (≤2.6)	1.00	1.00	1.00	1.00	1.00	1.00
Q2 (2.7–3.9)	0.76 (0.59–0.99)[b]	1.71 (0.90–3.25)	1.05 (0.75–1.48)	1.00 (0.69–1.44)	0.73 (0.54–0.99)[b]	0.87 (0.75–1.01)
Q3 (4.0–5.9)	0.78 (0.59–1.04)	0.91 (0.45–1.86)	0.96 (0.67–1.39)	0.94 (0.63–1.40)	0.81 (0.59–1.10)	0.84 (0.71–0.98)[b]
Q4 (>5.9)	0.84 (0.61–1.16)	1.52 (0.73–3.16)	1.01 (0.67–1.53)	1.04 (0.67–1.60)	1.04 (0.74–1.46)	0.93 (0.78–1.11)
p for trend	0.87	0.13	0.84	0.71	0.45	0.51
Meat						
Q1 (≤2.1)	1.00	1.00	1.00	1.00	1.00	1.00
Q2 (2.2–3.3)	0.95 (0.71–1.28)	0.97 (0.50–1.88)	1.13 (0.81–1.59)	1.05 (0.72–1.53)	0.95 (0.72–1.26)	1.04 (0.90–1.21)
Q3 (3.4–5.1)	1.05 (0.77–1.42)	0.89 (0.43–1.82)	1.00 (0.69–1.43)	1.12 0.75–1.67)	1.00 (0.73–1.35)	1.06 (0.90–1.24)
Q4 (>5.1)	0.88 (0.63–1.24)	1.17 (0.54–2.52)	1.29 (0.84–2.00)	1.02 (0.64–1.63)	1.13 (0.78–1.64)	1.15 (0.95–1.38)
p for trend	0.99	0.62	0.99	0.97	0.29	0.04
Grains						
Q1 (≤4.5)	1.00	1.00	1.00	1.00	1.00	1.00
Q2 (4.6–6.4)	0.98 (0.75–1.28)	0.92 (0.47–1.82)	0.62 (0.41–0.92)[b]	1.02 (0.68–1.52)	0.84 (0.63–1.12)	0.87 (0.75–1.02)
Q3 (6.5–8.9)	0.82 (0.59–1.13)	1.07 (0.51–2.23)	0.86(0.56–1.32)	1.17 (0.74–1.84)	0.79 (0.56–1.12)	0.89 (0.74–1.06)
Q4 (>8.9)	0.91 (0.62–1.34)	1.31 (0.54–3.15)	1.03 (0.60–1.77)	1.33 (0.77–2.28)	0.92 (0.59–1.43)	0.97 (0.78–1.22)
p for trend	0.52	0.03	0.77	0.56	0.75	0.97
Dairy products						
Q1 (≤0.5)	1.00	1.00	1.00	1.00	1.00	1.00
Q2 (0.6–1.0)	0.91 (0.70–1.19)	0.85 (0.48–1.48)	0.89 (0.66–1.21)	1.13 (0.74–1.73)	1.11 (0.77–1.60)	0.98 (0.84–1.14)
Q3 (1.1–1.6)	0.98 (0.74–1.29)	0.90 (0.50–1.62)	1.16 (0.85–1.59)	0.91 (0.58–1.42)	1.09 (0.76–1.57)	1.00 (0.86–1.18)
Q4 (>1.6)	1.14 (0.83–1.57)	0.89 (0.46–1.71)	1.30 (0.87–1.95)	0.94 (0.58–1.52)	1.18 (0.81–1.72)	1.08 (0.91–1.29)
p for trend	0.21	0.92	0.06	0.45	0.79	0.01
Discretionary fat (g/day)						
Q1 (≤30.8)	1.00	1.00	1.00	1.00	1.00	1.00
Q2 (30.9–44.9)	1.29 (0.96–1.73)	0.67 (0.33–1.37)	0.80 (0.58–1.11)	1.34 (0.88–2.03)	1.17 (0.85–1.62)	1.09 (0.93–1.28)
Q3 (45.0–64.9)	1.01 (0.71–1.44)	0.98 (0.47–2.03)	0.92 (0.62–1.35)	1.27 (0.78–2.06)	1.25 (0.87–1.80)	1.10 (0.91–1.32)
Q4 (>64.9)	1.38 (0.90–2.12)	0.67 (0.26–1.72)	0.86 (0.50–1.46)	1.60 (0.86–2.95)	1.35 (0.85–2.16)	1.23 (0.97–1.56)
p for trend	0.05	0.54	0.96	0.08	0.35	0.01

[a] *HR* hazards ratio; *95 % CI* 95 % confidence interval; Cox regression using age as the time metric, and adjusting for time on study, years of education, energy intake (logarithmically transformed), smoking behaviors (including current smoking, past smoking, and pack-years), body mass index, physical activity (defined as average hours of moderate or vigorous physical activity per day), history of diabetes, alcohol intake (grams per day), history of hormone replacement therapy, and history of oophorectomy

[b] $p < 0.05$

groups on the risk of cancer mortality among five ethnic groups participating in a large cohort study.

Our findings suggest that the effects of diet on risk for cancer mortality vary by ethnicity, as well as by sex. The most pronounced effect on cancer mortality risk was observed for high dietary grain intake among Japanese American men. Among this group, high grain intake was associated with a considerable protective effect, reducing the risk of cancer mortality by 50 %. No effect of grain intake was observed in any other ethnic group, and nor was

this effect apparent among Japanese American women. Examination of specific grain and food subgroups (e.g., whole vs. non-whole, food sources) and specific cancer types was outside the scope of the current study, but this information would be valuable for further evaluation of these associations. Interestingly, Vlajinac recently reported the finding that high dietary intake of rice was associated with a significant reduction in risk for prostate cancer [27]. Even though the large majority of the Japanese Americans (>90 %) were born in the United States, the baseline data from the MEC study did indeed find that rice intake was considerably higher among the Japanese American participants [16]. However, the observation of a strong, dose-dependent effect among the Japanese men that differed considerably from the effects observed in other ethnic groups, and findings from a previous observational report [27] suggest that additional research to examine the effects of grain subgroups on specific cancer types is warranted to clarify these findings.

Summary effect measures were reported for all other food groups, by sex, with the ethnic-specific data combined. A significant reduction in total cancer mortality was associated with vegetable intake in men overall. Similar effects of vegetable consumption were seen among women. Fruit intake also appeared to have a beneficial effect in both sexes, although the findings were not statistically significant for men. It has been proposed that antioxidants in fruits and vegetables may contribute to beneficial effects of this food group against cancer development, and other bioactive components, such as phytochemicals, may act synergistically in reducing the risk of total cancer risk [12]. Consequently, although each model was adjusted for dietary intake of other food groups, it is also possible that overall dietary patterns that contribute to beneficial synergistic reactions between food types may have a greater impact on cancer risk. The type of fruit consumed, rather than total fruit intake, might also be important, and this may explain some of the relatively weak effects observed in our study. Unfortunately, data on fruit subtypes were not available for this present analysis.

Dietary fat has been shown to be a promoter of cancer development in animal models, although the underlying mechanisms are still unknown, and thus, it is considered a risk factor for cancer development [28]. In the current study, the point estimates indicated a slightly elevated risk for cancer mortality among women with higher discretionary fat intake, although no significant associations were observed among either sex. These observations could be due to the types and quantities of discretionary fat consumed as well as due to undetermined biochemical differences, such as percent body fat or hormonal effects. For example, in the MEC cohort, red meat dishes that were among the top ten sources of saturated fat contributed 3–10 % more to fat intake among men compared to women in all ethnic groups except Latinos, while women tended to have a higher percentage of dairy products contributing to saturated fat intake [29]. Although avoiding a high-fat diet is still recommended to reduce cancer risk [30], a recent review of the literature on diet and cancer risk indicates that the epidemiological evidence for an association between dietary fat intake and cancer risk is inconclusive at this time [31].

In the present study, there was no significant association between dairy product intake and total cancer mortality. A similar null finding was reported by Park et al. [32] on risk of all-site cancer in the National Institute of Health-American Association of Retired Persons (NIH-AARP) Diet and Health Study, although in the same study, dairy food intake was reported to have inverse associations with some specific cancers, such as esophagus and stomach cancer in men and colorectal cancer in women, and a positive association with prostate cancer in men. This suggests that the effect of dairy products may differ based on cancer type.

In this analysis, we did not observe any significant associations with total cancer mortality for intake of meat consumption in either sex group, or with grain intake among women. As previously discussed, the null effects observed associations between grain intake and cancer mortality among most ethnic-sex groups could be attributed to food subtypes (whole vs. refined grains), which may have different effects on cancer mortality, or cancer type [33]. However, among Caucasian men, the sensitivity analyses (i.e., excluding cases occurring in the first 2 years of follow-up) showed slightly stronger associations between high meat intake (i.e., highest quartile) and cancer risk (HR = 1.45; 95 % CI 1.02–2.06) compared to the analysis including all cases (HR = 1.30; 95 % CI 0.94–1.80). A similar pattern was observed for African American men. These observations suggest that very high meat intake may increase cancer mortality among these ethnic groups. These patterns were not observed for other ethnic-sex groups and could be related to the types of meats (e.g., red meat, poultry, fish) preferentially consumed by different ethnic groups [29]. There is a lack of literature on the effect of meat subgroups on total cancer mortality, but evidence from the NIH-AARP study suggests that intake of red and processed meats may elevate risk for some specific cancer types [34].

It is likely that interactions between many factors can influence risk for cancer. Stratified analyses (data not shown) suggest that the preventive association between vegetable intake and cancer may be slightly stronger among women with lower BMI as well as those with higher levels of physical activity, while the associations with dietary intake and cancer mortality appear to be similar regardless of smoking history. Further research examining

the impact of diet in relation to these and other lifestyle and environmental exposures, and the impact on risk for cancer is needed to elucidate the complex interplay between modifiable risk factors.

Several limitations warrant discussion. The multiple statistical comparisons may have led to some significant findings resulting from chance. Nonetheless, even using a conservative method to account for multiple tests of significance (Bonferroni corrected p value = 0.00083), the observed association between grain intake and cancer risk remained highly significant ($p < 0.0001$). Recall bias, including overreporting, associated with the accuracy of dietary data from the QFFQ may also have influenced the results. However, differential recall bias between cases and controls is unlikely as this was a prospective study; thus, any impact on results would be expected to have attenuated associations (i.e., biased results toward the null). Although the self-administered QFFQ used in this present study was validated and has been shown to capture total intake relatively well [15, 16], it is possible that use of face-to-face interview methods may have improved data quality and limited the exclusions due to missing dietary information. There was also a relatively large number of other exclusions, primarily due to missing smoking information and hormone replacement therapy data for women, and the proportion of exclusions varied among the ethnic-sex groups, ranging from 17 to 32 % among men (for Japanese and African Americans, respectively) and from 26 to 39 % among women (Japanese Americans and Latinos, respectively). In addition, the average age of the excluded participants was slightly older (average of 61 years for both men and women among exclusions, compared to 60 and 59 years of age in the current study), and the proportion of married women was lower among the exclusions (57 vs. 60 % among included participants). Although selection bias is a concern, relatively large sample sizes were still maintained in this analysis for each ethnic-sex group, and hence, considerable differences would have to be presented between those excluded and included in the analyses in order to impact the results. Further, the assessment of food consumption over a short period of time, which may not be reflective of historic dietary patterns, would likely have attenuated associations between diet and cancer mortality. Data for non-fatal cancer and specific cancer types would also be useful in further investigations to validate the current findings and elucidate the possible mechanisms for the observed associations.

The strengths of this study include the use of standardized food groupings developed by the USDA and a food composition table which included ethnic-specific food items and recipes. Furthermore, the dietary data were collected using a common QFFQ, which allowed for meaningful comparison of results across the ethnic groups. Information on a variety of covariates allowed for adjustment of a wide range of potential confounders. The MEC participants have also been shown to be representative of the general population with respect to several demographic characteristics, which supports the generalizability of these findings [15]. In addition, the validity of the findings are supported by the similarity of results obtained even when early follow-up cases (i.e., within 2 years of the study baseline) are excluded.

To conclude, the differential association between grain intake and cancer risk observed among the ethnic-sex groups warrants further investigation. These results also support the importance of dietary risk factors for total cancer mortality as well as the need to implement dietary prevention strategies and to tailor public health messages accordingly to reduce cancer deaths. Our research also adds to the limited literature on diet and total cancer mortality in different ethnic groups. The precise role and mechanism of each food group, their subgroups, and dietary compounds in relation to cancer development or prevention remain to be further elucidated and confirmed by additional longitudinal studies.

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References

1. Murphy SL, Xu J, Kochanek KD (2012) Deaths: preliminary data for 2010. National Vital Statistics Reports. National Centre for Health Statistics, Hyattsville, MD
2. National Center for Health Statistics (2009) Health, United States, 2008 with chartbook. National Center for Health Statistics, Hyattsville, MD
3. Humes KR, Jones NA, Ramirez RR (2011) Overview of race and Hispanic origin, 2010. 2010 census briefs. U.S. Census Bureau, Washington, DC
4. Sharma S, Murphy SP, Wilkens LR, Shen L, Hankin JH, Henderson B, Kolonel LN (2003) Adherence to the food guide pyramid recommendations among Japanese Americans, Native Hawaiians, and whites: results from the Multiethnic Cohort Study. J Am Diet Assoc 103:1195–1198
5. Sharma S, Murphy SP, Wilkens LR, Shen L, Hankin JH, Monroe KR, Kolonel LN (2004) Adherence to the food guide pyramid recommendations among African Americans and Latinos: results from the multiethnic cohort. J Am Diet Assoc 104:1873–1877
6. Anand P, Kunnumakkara AB, Sundaram C, Harikumar KB, Tharakan ST, Lai OS, Sung B, Aggarwal BB (2008) Cancer is a preventable disease that requires major lifestyle changes. Pharm Res 25:2097–2116
7. Fair AM, Montgomery K (2009) Energy balance, physical activity, and cancer risk. Methods Mol Biol 472:57–88

8. Stratton MR, Campbell PJ, Futreal PA (2009) The cancer genome. Nature 458:719–724
9. World Cancer Research Fund (1997) Food, nutrition, physical activity, and the prevention of cancer: a global perspective. American Institute for Cancer Research, Washington, DC
10. Mokdad AH, Marks JS, Stroup DF, Gerberding JL (2004) Actual causes of death in the United States, 2000. J Am Med Assoc 291:1238–1245
11. Doll R, Peto R (1981) The causes of cancer: quantitative estimates of avoidable risks of cancer in the United States today. J Natl Cancer Inst 66:1191–1308
12. Key TJ, Allen NE, Spencer EA, Travis RC (2002) The effect of diet on risk of cancer. Lancet 360:861–868
13. Genkinger JM, Platz EA, Hoffman SC, Comstock GW, Helzlsouer KJ (2004) Fruit, vegetable, and antioxidant intake and all-cause, cancer, and cardiovascular disease mortality in a community-dwelling population in Washington County, Maryland. Am J Epidemiol 160:1223–1233
14. Demark-Wahnefried W, Rock CL, Patrick K, Byers T (2008) Lifestyle interventions to reduce cancer risk and improve outcomes. Am Fam Physician 77:1573–1578
15. Kimmons J, Gillespie C, Seymour J, Serdula M, Blanck HM (2009) Fruit and vegetable intake among adolescents and adults in the United States: percentage meeting individualized recommendations. Medscape J Med 11:26
16. Kolonel LN, Henderson BE, Hankin JH, Nomura AM, Wilkens LR, Pike MC, Stram DO, Monroe KR, Earle ME, Nagamine FS (2000) A multiethnic cohort in Hawaii and Los Angeles: baseline characteristics. Am J Epidemiol 151:346–357
17. Stram DO, Hankin JH, Wilkens LR, Pike MC, Monroe KR, Park S, Henderson BE, Nomura AM, Earle ME, Nagamine FS, Kolonel LN (2000) Calibration of the dietary questionnaire for a multiethnic cohort in Hawaii and Los Angeles. Am J Epidemiol 151:358–370
18. U.S. Department of Agriculture and U.S. Department of Health and Human Services (2000) Dietary guidelines for Americans, 5th edn. U.S. Department of Agriculture Center for Nutrition Policy and Promotion, Washington, DC
19. U.S. Department of Agriculture (1992) Food guide pyramid: a guide to daily food choices. U.S. Department of Agriculture, Human Nutrition Information Service, Washington, DC
20. Fritz A, Jack A, Parkin DM, Percy C, Shanmugarathan S, Sobin L, Whelan S (2005) International classification of diseases for oncology (ICD-O), 3rd edn. World Health Organization, Geneva
21. Rothman K, Greenland S (2001) Introduction to stratified analysis. In: Rothman K, Greenland S (eds) Modern epidemiology, 2nd edn. Lippincott Williams and Wilkins, Philadelphia, pp 259–264
22. American Cancer Society (2011) American cancer society stewardship report 2011. American Cancer Society, Atlanta
23. Steffen LM, Jacobs DR Jr, Stevens J, Shahar E, Carithers T, Folsom AR (2003) Associations of whole-grain, refined-grain, and fruit and vegetable consumption with risks of all-cause mortality and incident coronary artery disease and ischemic stroke: the Atherosclerosis Risk in Communities (ARIC) Study. Am J Clin Nutr 78:383–390
24. Fink BN, Gaudet MM, Britton JA, Abrahamson PE, Teitelbaum SL, Jacobson J, Bell P, Thomas JA, Kabat GC, Neugut AI, Gammon MD (2006) Fruits, vegetables, and micronutrient intake in relation to breast cancer survival. Breast Cancer Res Treat 98:199–208
25. Kojima M, Wakai K, Tamakoshi K, Tokudome S, Toyoshima H, Watanabe Y, Hayakawa N, Suzuki K, Hashimoto S, Ito Y, Tamakoshi A, Japan Collaborative Cohort Study Group (2004) Diet and colorectal cancer mortality: results from the Japan Collaborative Cohort Study. Nutr Cancer 50:23–32
26. Vanamala J, Tarver CC, Murano PS (2008) Obesity-enhanced colon cancer: functional food compounds and their mechanisms of action. Curr Cancer Drug Targets 8:611–633
27. Vlajinac H, Ilic M, Marinkovic J, Sipetic S (2010) Nutrition and prostate cancer. J BUON 15(4):698–703
28. Carroll KK, Braden LM, Bell JA, Kalamegham R (1986) Fat and cancer. Cancer 58(8 Suppl):1818–1825
29. Sharma S, Wilkens LR, Shen L, Kolonel LN (2012) Dietary sources of five nutrients in ethnic groups represented in the multiethnic cohort. BJN 5:1–11 [Epub ahead of print]
30. Mead MN (2008) Diet & nutrition: expert panel weighs in on global cancer control. Environ Health Perspect 116(1):A22–A23
31. Key TJ, Schatzkin A, Willet WC, Allen NE, Spencer EA, Travis RC (2004) Diet, nutrition and the prevention of cancer. Public Health Nutr 7(1A):187–200
32. Park Y, Leitzmann MF, Subar AF, Hollenbeck A, Schatzkin A (2009) Dairy food, calcium, and risk of cancer in the NIH-AARP Diet and Health Study. Arch Intern Med 169:391–401
33. Levi F, Pasche C, Lucchini F, Chatenoud L, Jacobs DR Jr, La Vecchia C (2000) Refined and whole grain cereals and the risk of oral, oesophageal and laryngeal cancer. Eur J Clin Nutr 54(6): 487–489
34. Cross AJ, Leitzmann MF, Gail MH, Hollenbeck AR, Schatzkin A, Sinha R (2007) A prospective study of red and processed meat intake in relation to cancer risk. PLoS Med 4(12):e325