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Racial/ethnic differences in lifestyle-related factors and prostate cancer risk: the Multiethnic Cohort Study

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Abstract

Purpose—Older age, African ancestry, and family history of prostate cancer are well-established risk factors for prostate cancer and all are non-modifiable. Various lifestyle factors have been examined in relation to prostate cancer risk, including diet, obesity, and physical activity; however, none of them has been consistently related to risk. In the Multiethnic Cohort Study, we investigated whether lifestyle-related factors are associated with prostate cancer risk and whether such factors explain the racial/ethnic differences in risk.

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Methods—During a mean follow-up of 13.9 years, 7,115 incident cases were identified among 75,216 white, African American, Native Hawaiian, Japanese American, and Latino men. Cox proportional hazards models were used to calculate relative risks (RR) and 95% confidence intervals (95% CI) for prostate cancer.

Results—Among selected lifestyle-related factors including body mass index, height, education, physical activity, and intakes of alcohol, calcium, legumes, lycopene, and selenium, only smoking (RR for current (> 20 cigarettes/day) vs. never smoking = 0.72; 95% CI: 0.63-0.83) and history of diabetes (RR for yes vs. no = 0.78; 95% CI: 0.72-0.85) were significantly associated with prostate cancer risk. Compared to whites, the risk of incident prostate cancer was two-fold higher in African Americans and 16% higher in Latinos. Additional adjustment for a history of PSA testing did not change the results.

Conclusions—The findings suggest that racial/ethnic differences in prostate cancer risk are not explained by the lifestyle factors examined, and that underlying genetic factors may be involved.

Keywords

cohort; lifestyle factors; multiethnic population; prostate cancer; racial/ethnic difference

Introduction

Prostate cancer is the most common cancer other than skin cancer among men in the United States [1]. The risk of prostate cancer increases rapidly after age 50. African Americans experience the highest incidence rate of prostate cancer in the United States and have more than a two-fold higher mortality rate of this cancer than whites. Family history of prostate cancer is also an important risk factor for prostate cancer [2-4]. Thus, the well-established risk factors for prostate cancer - age, African ancestry, and family history - are all non-modifiable. Various lifestyle factors have been examined in relation to prostate cancer risk, including diet, anthropometry, and physical activity. However, they have not been consistently related to prostate cancer risk [5,6].

The Multiethnic Cohort (MEC) is an ongoing study to prospectively investigate the associations between lifestyle and genetic factors and cancer risk in more than 215,000 participants of various racial/ethnic backgrounds [7]. Given that previous studies have been conducted in relatively homogeneous populations in terms of racial/ethnic composition, the MEC provides a unique opportunity to examine racial/ethnic differences in cancer risk. In the current study, we investigated the association between lifestyle-related factors and prostate cancer risk and whether such factors explain the racial/ethnic differences in risk.

Materials and methods

Study population

The Multiethnic Cohort was assembled in Hawaii and California between 1993 and 1996 [7]. Sampling sources of this population-based cohort were drivers' license files in both states, the voters' registration file in Hawaii, and the Health Care Financing Administration files in California. The cohort mainly consists of African Americans, Native Hawaiians,

Japanese Americans, Latinos, and whites aged 45-75 years at baseline, 96,896 of whom are male. For the current analyses, we excluded men who did not belong to one of the five racial/ethnic groups (n=5,941), men with a prior prostate cancer either identified by report on the questionnaire (n=2,725) or through tumor registries (n=284), men with implausible dietary data based on total energy intake (greater than three times a robust standard deviation (RSD) from the mean) or its components (greater than 3.5 RDS from the mean) (n=3,530) [8], and men with missing or incomplete data on height, weight, education, smoking, and physical activity (n=9,200), leaving a total of 75,216 men for the analysis.

Risk factor assessment

All cohort members completed a 26-page self-administered questionnaire at baseline that included information regarding demographics, medical history, family history of cancer, cigarette smoking, dietary habits, height/weight, and physical activity. Dietary intake was assessed by a quantitative food frequency questionnaire (QFFQ) asking about the frequency and amount of consumption for more than 180 food items during the previous year. A calibration study showed satisfactory correlations between the QFFQ and three 24-hour recalls for all ethnic and sex groups being studied [9]. In 1999-2002, information regarding any prior PSA screening utilization was obtained from approximately 80% of the surviving males in the cohort in a shorter follow-up (second) questionnaire.

Case identification

Incident cases of prostate cancer were identified by linkage to the Surveillance, Epidemiology, and End Results (SEER) cancer registries covering the states of Hawaii and California. Case ascertainment was complete through December 31, 2010. The cohort was also linked to the state death files and to the National Death Index file through December 31, 2010. In this analysis, we considered all prostate cancer cases as events except *in situ* cases, which were considered as non-cases. During the mean follow-up period of 13.9 years, a total of 7,115 incident cases among the 75,216 eligible men were identified including 5,726 localized, 969 advanced (regional or metastatic), 4,113 low-grade (Gleason score of 6), 2,710 high-grade (Gleason score of 7), and 564 fatal cases.

Statistical analysis

We estimated relative risks (RR) and 95% confidence intervals (CI) for prostate cancer using Cox proportional hazard models with age as the time metric. The proportionality assumption was tested by Schoenfeld residuals [10] and found to be met. RRs were calculated for each of the following 11 lifestyle-related factors in all men combined and in each racial/ethnic group, with adjustment for ethnicity and family history of prostate cancer (yes, no) as strata variables, and age at cohort entry and the remaining risk factors as covariates: body mass index (BMI; <25, 25-29.9, 30-34.9, 35 kg/m²), height (65, 66-67, 68-69, 70-71, 72 inches), cigarette smoking (never smoker; former smoker: <10, 10-19, 20 cigarettes/day; current smoker: <10, 10-19, 20 cigarettes/day), education (8th grade, 9th-12th grade, vocational school/some college, graduated college or higher), history of diabetes (yes, no), physical activity (quintile cutpoints: 1.41, 1.58, 1.71, 1.87 METs/day), and daily intakes of alcohol (0, >0-4.9, 5-14.9, 15-34.9, 35 g), calcium (quintile cutpoints:

241, 301, 360, 436 mg/1000kcal), legume (quintile cutpoints: 6.4, 10.8, 16.5, 28.2 g/1000kcal), lycopene (quintile cutpoints: 748, 1073, 1435, 2022 $\mu\text{g}/1000\text{kcal}$), and selenium (quintile cutpoints: 44.0, 49.5, 54.4, 60.1 $\mu\text{g}/1000\text{kcal}$). These factors were selected among all lifestyle-related variables available at baseline because they were associated with prostate cancer risk in our data, or because they were suspected to be risk factors for prostate cancer in the literature. Linear trends were tested by entering into the models continuous variables assigned the racial/ethnic-specific median values within the appropriate categories or ordinal variables. Tests for interaction between risk factors and race/ethnicity were based on the Wald statistics for cross-product terms. RRs were calculated for African Americans, Native Hawaiians, Japanese Americans, and Latinos, with whites as the referent group, in age-adjusted and multivariate models including the above known/potential confounders. To further adjust for PSA screening history (ever/never), we repeated the analysis limited to men who completed the follow-up questionnaire (1999-2002) and had no prior prostate cancer ($n=56,903$), using the date of follow-up questionnaire completion as the start date of follow-up. All statistical tests were 2-sided, and $P < 0.05$ was considered statistically significant. Data analyses were performed using SAS, version 9.2 statistical software (SAS Institute, Cary, NC).

Results

The associations between the selected lifestyle-related factors and prostate cancer are presented for all men and by race/ethnicity in Table 1. Among all men combined, smoking (RR for current smoking 20 cigarettes/day vs. never smoking = 0.72; 95% CI: 0.63-0.83; P for trend <0.001) and history of diabetes (RR for yes vs. no = 0.78; 95% CI: 0.72-0.85) were associated with a decreased risk, while education was related to an increase in risk (RR for graduated college or higher vs. 8th grade or less = 1.20; 95% CI: 1.08-1.32; P for trend = 0.0019). A modest inverse trend was observed for physical activity and legume intake. The observed associations were also found for localized prostate cancer, but not for advanced tumors, other than history of diabetes that was related to a decreased risk of both localized and advanced tumors (data not shown). The associations were not statistically different across the racial/ethnic groups.

Table 2 presents the incidence rates and age-adjusted and multivariate-adjusted RRs of prostate cancer by racial/ethnic group. Compared to whites, the age-adjusted RR for total prostate cancer was twice as great in African Americans, while it was close to 1 in Native Hawaiians, Japanese Americans, and Latinos. Higher risk in African American men was not limited to aggressive tumors, but was observed across all stages and grades of tumor, while there were some variations in the rank order of the other three non-white racial/ethnic groups. With multivariate adjustment, RRs were slightly increased in all four racial/ethnic groups, with the greatest increase for Latinos (RR = 1.16; 95% CI: 1.07-1.26, compared to whites). This increase was mainly attributed to adjustment for education. The elevated risk in Latino men was limited to localized (16%) and low-grade (33%) cases.

We repeated the analysis limited to men who had completed the follow-up survey, when information on PSA screening was first collected in the cohort (Supplementary Tables). The majority (64%) of the participants who reported that they ever had a PSA test had the test

within two years. With additional adjustment for PSA screening history, the inverse associations were still present for smoking and history of diabetes (Supplementary Table 1). The risk of incident prostate cancer remained twice as high in African American men and was 17% higher in Latino men, compared to white men (Supplementary Table 2). A significant inverse association with smoking was limited to men who had not reported past PSA screening, although the interaction test was not statistically significant ($P = 0.24$). Other smoking variables, pack years and smoking duration, also showed a similar inverse association with prostate cancer risk.

Discussion

In this large multiethnic cohort, we found that smoking status and history of diabetes were related to a decreased risk of prostate cancer after adjustment for PSA screening history and many other factors. The risk of incident prostate cancer was twice as high in African American men as in white men. The risk in Japanese Americans, Native Hawaiians, and Latinos was similar to or modestly increased, compared to whites. However, the lifestyle-related factors we examined did not appear to explain the racial/ethnic differences in prostate cancer risk in this cohort.

Although lifestyle factors have been extensively examined in relation to prostate cancer risk, none of them have been convincingly established. According to the recent (2014) update of the World Cancer Research Fund (WCRF) / American Institute for Cancer Research (AICR) Second Report from 2007, there was no convincing evidence that diet, obesity, or physical activity are associated with prostate cancer risk [6]. There was limited evidence suggesting an increased risk of prostate cancer associated with dairy products, diets high in calcium, low plasma α -tocopherol concentrations, and low plasma selenium concentrations.

In previous studies in the MEC and consistent with our current findings, a weak inverse association for legumes was found with prostate cancer risk, based on both the questionnaire [11] and biomarkers (urinary isoflavones) [12]. Other dietary components were not related to prostate cancer risk, including calcium, vitamin D, dairy products [13], meat, fat [14], fruit, vegetables [15], and multivitamin supplements [16], and nutritional biomarkers [17-20].

Past studies have provided strong (but not convincing) evidence that body fatness marked by BMI, waist circumference, and waist-hip ratio is associated with an increased risk of advanced prostate cancer, and that adult height, as a marker of genetic, environmental, hormonal, and nutritional factors affecting growth, is linked to an increased risk of prostate cancer [6]. However, in the MEC, BMI at baseline and adult height did not show a significant association with either overall or advanced prostate cancer risk [8]. On the other hand, diabetes was associated with a decreased risk of prostate cancer in all racial/ethnic groups in this cohort, suggesting that the two diseases share risk factors that may influence a common mechanism [21]. Findings for physical activity and prostate cancer are not consistent across studies [22,23]. Our data suggested a weak inverse association which may be due to chance, given the number of tests performed in our analysis.

Although smoking has been linked to a possible increase in the risk of death from prostate cancer [24], some studies have found an inverse association [25-27]. In particular, a large prospective study in Europe found that current smokers had a reduced risk of prostate cancer for localized and low-grade disease, but not for advanced or high-grade disease [27], which was also observed in the current study. This inverse association might reflect a detection bias; smokers tend to be less health-conscious and to seek medical tests less frequently, making them less likely to be diagnosed with non-aggressive prostate cancer through screening; conversely, non-smokers may be more prone to seek medical attention and be diagnosed with non-aggressive prostate cancer. In addition, smokers in our study tended to be younger than nonsmokers, which might also contribute to the inverse association through incomplete adjustment. Another possibility is that the effects of smoking on lowering circulating levels of insulin-like growth factor-I and sex hormone binding globulin might partly explain the inverse association between smoking and prostate cancer incidence [27-29]. Further research is needed to clarify the association between smoking and non-aggressive prostate cancer.

There was little difference in the associations between lifestyle factors and prostate cancer risk across the five racial/ethnic groups. Although the interaction tests suggested that the associations between prostate cancer and diabetes history might vary across the ethnic groups, the associations were in the same direction among all groups. Nevertheless, accounting for all known/suspected risk factors did not reduce, but rather increased, the racial/ethnic differences in prostate cancer risk, suggesting that other factors, including genetic susceptibility, are important contributors to the racial/ethnic variation in incidence. For instance, previous studies in the MEC indicated that specific genetic variation at 8q24 may contribute to the higher incidence rate of prostate cancer in African Americans [30,31]. Unlike the SEER data showing a lower incidence rate in Latino than in white men [1], we found a higher risk in Latino men, mainly for non-aggressive forms, after adjustment for the potential confounders, especially education. This finding is unexpected, since the PSA screening rate adjusted for education and other factors was lower in Latinos than in whites in the MEC [32].

Strengths of our study include a prospective design minimizing differential recall bias, a large number of subjects with diverse racial/ethnic backgrounds, a comprehensive and validated QFFQ, and an ability to control for various confounding factors. However, there are limitations to consider. Although detailed information was collected, there may be other unsuspected lifestyle factors related to prostate cancer risk than those investigated in the current study. In addition, our study may not have included all factors that potentially confound associations between risk factors and prostate cancer. For instance, income was not collected at baseline and thus could not be accounted for in the analysis. Instead, education levels were used as a proxy for socioeconomic status. Also, specific information was not collected on PSA screening practices at baseline. Therefore, additional analyses including PSA screening history (ever/never) were conducted among men who completed the first follow-up questionnaire. More refined analyses will be possible in the future with the information collected in later follow-up questionnaires. Lastly, some risk factors, especially dietary intake, are subject to measurement error which may have led to an

underestimation of their association with prostate cancer risk and of their contribution to racial/ethnic differences.

In summary, in this large multiethnic population, cigarette smoking and diabetes history were inversely associated with prostate cancer risk, while other lifestyle-related factors including dietary components were not related, even in analyses restricted to aggressive cases. We also found no evidence that suspected lifestyle factors can explain the two-fold greater risk in African American men than in white men.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Table 1
Relative risks (RR) with 95% confidence intervals (95% CI) for prostate cancer risk according to risk factors by race/ethnicity in the MEC, 1993-2010

	All men (n=75,216)	White (n = 19,833)	African American (n = 9,284)	Native Hawaiian (n = 5,454)	Japanese American (n = 23,687)	Latino (n = 16,958)	P for interaction ^c
	RR (95% CI) ^a	RR (95% CI) ^a	RR (95% CI) ^a	RR (95% CI) ^a	RR (95% CI) ^a	RR (95% CI) ^a	
No. of cases	7,115	1,594	1,486	367	2,056	1,612	
BMI, kg/m ²							
<25	reference	reference	reference	reference	reference	reference	0.13
25-29.9	1.04 (0.99-1.10)	1.03 (0.93-1.15)	1.20 (1.06-1.35)	1.22 (0.92-1.63)	0.98 (0.90-1.08)	0.97 (0.87-1.09)	
30-34.9	0.98 (0.91-1.06)	1.02 (0.87-1.21)	1.00 (0.85-1.18)	1.05 (0.74-1.47)	0.98 (0.80-1.20)	0.97 (0.83-1.14)	
35	0.90 (0.78-1.04)	0.74 (0.53-1.04)	1.05 (0.81-1.36)	1.30 (0.87-1.93)	0.86 (0.50-1.50)	0.76 (0.56-1.03)	
P for trend	0.34	0.44	0.85	0.51	0.54	0.20	
Height, inches							
65	reference	reference	reference	reference	reference	reference	0.99
66-67	0.98 (0.91-1.05)	0.95 (0.73-1.23)	1.05 (0.80-1.38)	1.06 (0.69-1.64)	0.95 (0.86-1.05)	0.98 (0.85-1.13)	
68-69	0.99 (0.92-1.07)	1.04 (0.81-1.33)	1.05 (0.80-1.36)	1.12 (0.74-1.71)	0.93 (0.81-1.05)	0.93 (0.80-1.08)	
70-71	1.03 (0.95-1.12)	1.00 (0.78-1.28)	1.08 (0.83-1.40)	1.08 (0.70-1.65)	1.08 (0.89-1.31)	1.02 (0.87-1.20)	
72	0.99 (0.90-1.09)	0.97 (0.75-1.24)	1.05 (0.81-1.37)	1.05 (0.67-1.66)	1.16 (0.81-1.66)	0.97 (0.79-1.20)	
P for trend	0.74	0.75	0.75	0.88	0.95	0.97	
Smoking status							
Never	reference	reference	reference	reference	reference	reference	0.12
Former: <10 cigarettes/d	0.97 (0.91-1.04)	0.86 (0.73-1.02)	0.96 (0.83-1.11)	1.11 (0.81-1.54)	1.01 (0.88-1.16)	1.02 (0.90-1.15)	
Former: 10-19 cigarettes/d	0.86 (0.80-0.92)	0.86 (0.74-0.99)	0.79 (0.67-0.92)	1.00 (0.74-1.34)	0.89 (0.79-1.00)	0.84 (0.71-1.00)	
Former: 20 cigarettes/d	0.84 (0.78-0.91)	0.77 (0.67-0.89)	0.92 (0.75-1.12)	0.96 (0.70-1.31)	0.80 (0.70-0.91)	1.03 (0.84-1.26)	
Current: <10 cigarettes/d	0.86 (0.77-0.96)	0.68 (0.47-0.99)	0.92 (0.76-1.12)	1.02 (0.59-1.76)	0.74 (0.55-1.00)	0.93 (0.77-1.13)	
Current: 10-19 cigarettes/d	0.84 (0.65-1.08)	0.96 (0.80-1.17)	0.92 (0.60-1.42)	0.78 (0.63-0.96)	0.84 (0.66-1.07)		
(0.77-0.95)							
Current: 20 cigarettes/d	0.72 (0.63-0.83)	0.73 (0.58-0.92)	0.67 (0.48-0.92)	0.44 (0.24-0.81)	0.72 (0.55-0.93)	0.97 (0.67-1.40)	
P for trend	<0.001	<0.001	0.059	0.039	<0.001	0.14	
Education							
8th	reference	reference	reference	reference	reference	reference	0.73

	All men (n=75,216)		White (n = 19,833)		African American (n = 9,284)		Native Hawaiian (n = 5,454)		Japanese American (n = 23,687)		Latino (n = 16,958)		P for interaction ^c
	RR (95% CI) ^a	RR (95% CI) ^a	RR (95% CI) ^a	RR (95% CI) ^a	RR (95% CI) ^a	RR (95% CI) ^a	RR (95% CI) ^a	RR (95% CI) ^a	RR (95% CI) ^a	RR (95% CI) ^a	RR (95% CI) ^a	RR (95% CI) ^a	
9th-12th	1.13 (1.03-1.24)	1.14 (0.83-1.58)	1.14 (0.83-1.58)	1.24 (0.98-1.56)	0.76 (0.50-1.17)	1.12 (0.85-1.46)	1.14 (1.00-1.30)						
Vocational school /some college	1.13 (1.03-1.24)	1.21 (0.88-1.67)	1.21 (0.88-1.67)	1.27 (1.01-1.60)	0.74 (0.47-1.16)	1.07 (0.82-1.42)	1.05 (0.91-1.22)						
Graduated college	1.20 (1.08-1.32)	1.21 (0.88-1.66)	1.21 (0.88-1.66)	1.31 (1.03-1.66)	0.72 (0.44-1.17)	1.16 (0.88-1.54)	1.18 (0.99-1.40)						
P for trend	0.0019	0.22	0.22	0.10	0.34	0.36	0.16						
History of diabetes													
No	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	0.087
Yes	0.78 (0.72-0.85)	0.61 (0.47-0.80)	0.61 (0.47-0.80)	0.81 (0.69-0.96)	0.90 (0.67-1.22)	0.85 (0.74-0.99)	0.72 (0.61-0.84)						
Physical activity, METs/d ^b													
<1.41	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	0.92
1.41-1.57	1.00 (0.93-1.08)	1.03 (0.89-1.20)	1.03 (0.89-1.20)	0.99 (0.85-1.16)	1.05 (0.75-1.48)	1.00 (0.87-1.15)	0.97 (0.82-1.15)						
1.58-1.70	1.01 (0.94-1.08)	0.96 (0.82-1.11)	0.96 (0.82-1.11)	1.04 (0.89-1.21)	1.06 (0.76-1.50)	1.06 (0.93-1.22)	0.96 (0.81-1.13)						
1.71-1.86	0.93 (0.86-1.00)	0.84 (0.71-0.99)	0.84 (0.71-0.99)	1.00 (0.85-1.17)	0.98 (0.70-1.38)	1.00 (0.87-1.15)	0.88 (0.75-1.04)						
1.87	0.92 (0.86-1.00)	0.89 (0.76-1.05)	0.89 (0.76-1.05)	1.01 (0.85-1.20)	0.95 (0.69-1.32)	0.93 (0.80-1.09)	0.88 (0.75-1.04)						
P for trend	0.014	0.033	0.033	0.71	0.61	0.43	0.066						
Alcohol, g/d													
0	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	0.12
>0-4.9	0.98 (0.92-1.05)	1.02 (0.88-1.19)	1.02 (0.88-1.19)	0.91 (0.80-1.05)	1.07 (0.80-1.44)	0.97 (0.86-1.09)	1.02 (0.90-1.17)						
5-14.9	1.09 (1.02-1.17)	1.11 (0.95-1.30)	1.11 (0.95-1.30)	0.97 (0.83-1.14)	1.18 (0.87-1.61)	1.13 (0.99-1.29)	1.15 (0.99-1.33)						
15-34.9	1.10 (1.03-1.19)	1.28 (1.10-1.48)	1.28 (1.10-1.48)	0.93 (0.78-1.11)	0.98 (0.71-1.36)	1.08 (0.95-1.24)	1.13 (0.96-1.34)						
35	1.02 (0.93-1.10)	1.10 (0.94-1.30)	1.10 (0.94-1.30)	0.99 (0.82-1.20)	0.98 (0.69-1.41)	0.82 (0.68-0.98)	1.21 (1.02-1.45)						
P for trend	0.20	0.086	0.086	0.97	0.74	0.19	0.027						
Calcium, mg/1000kcal/d													
<241	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	reference	0.24
241-300	1.00 (0.92-1.08)	0.82 (0.67-1.02)	0.82 (0.67-1.02)	0.95 (0.81-1.12)	1.10 (0.83-1.45)	1.06 (0.95-1.19)	0.94 (0.71-1.23)						
301-359	1.00 (0.92-1.08)	0.84 (0.69-1.03)	0.84 (0.69-1.03)	0.97 (0.81-1.15)	1.08 (0.79-1.46)	1.01 (0.88-1.15)	1.04 (0.80-1.34)						
360-435	0.99 (0.91-1.07)	0.81 (0.66-0.99)	0.81 (0.66-0.99)	0.94 (0.79-1.13)	0.82 (0.57-1.19)	1.10 (0.95-1.28)	1.03 (0.79-1.33)						
436	1.06 (0.97-1.15)	0.98 (0.81-1.19)	0.98 (0.81-1.19)	0.92 (0.76-1.11)	0.93 (0.63-1.37)	1.08 (0.90-1.29)	1.08 (0.84-1.39)						
P for trend	0.12	0.082	0.082	0.46	0.53	0.28	0.22						
Legume, g/1000kcal/d													

	All men (n=75,216)	White (n = 19,833)	African American (n = 9,284)	Native Hawaiian (n = 5,454)	Japanese American (n = 23,687)	Latino (n = 16,958)	P for interaction ^c
	RR (95% CI) ^a	RR (95% CI) ^a	RR (95% CI) ^a	RR (95% CI) ^a	RR (95% CI) ^a	RR (95% CI) ^a	
<6.4	reference	reference	reference	reference	reference	reference	0.59
6.4-10.7	1.01 (0.94-1.09)	0.98 (0.85-1.12)	1.05 (0.90-1.22)	1.13 (0.85-1.50)	1.02 (0.86-1.20)	1.03 (0.84-1.27)	
10.8-16.4	1.02 (0.95-1.10)	0.97 (0.84-1.12)	1.06 (0.91-1.24)	1.06 (0.78-1.45)	1.11 (0.95-1.31)	0.88 (0.72-1.08)	
16.5-28.1	0.99 (0.92-1.07)	1.00 (0.86-1.17)	1.00 (0.86-1.17)	1.06 (0.75-1.49)	1.04 (0.88-1.23)	0.93 (0.77-1.12)	
28.2	0.94 (0.86-1.02)	0.96 (0.79-1.17)	0.98 (0.81-1.19)	1.42 (0.92-2.20)	1.03 (0.87-1.23)	0.82 (0.69-0.99)	
P for trend	0.015	0.53	0.65	0.15	0.94	0.0064	
Lycopene, µg/1000kcal/d							
<748	reference	reference	reference	reference	reference	reference	0.65
748-1072	1.12 (0.94-1.34)	1.15 (0.98-1.35)	1.01 (0.74-1.39)	0.98 (0.87-1.11)	0.99 (0.83-1.19)	1.12 (0.94-1.34)	
1073-1434	1.10 (0.92-1.31)	1.24 (1.06-1.45)	1.01 (0.74-1.39)	1.02 (0.90-1.16)	1.06 (0.89-1.26)	1.10 (0.92-1.31)	
1435-2021	1.06 (0.89-1.27)	1.03 (0.87-1.23)	1.19 (0.86-1.63)	1.01 (0.88-1.15)	1.05 (0.88-1.25)	1.06 (0.89-1.27)	
2022	1.10 (0.93-1.31)	1.09 (0.93-1.29)	0.77 (0.53-1.12)	0.93 (0.79-1.09)	0.98 (0.82-1.17)	1.10 (0.93-1.31)	
P for trend	0.83	0.61	0.82	0.33	0.54	0.73	
Selenium, µg/1000kcal/d							
<44.0	reference	reference	reference	reference	reference	reference	0.92
44.0-49.4	1.10 (0.96-1.26)	0.94 (0.80-1.09)	1.16 (0.78-1.72)	0.94 (0.77-1.14)	1.06 (0.93-1.21)	1.10 (0.96-1.26)	
49.5-54.3	1.10 (0.95-1.27)	0.97 (0.83-1.14)	1.25 (0.87-1.81)	0.93 (0.77-1.12)	1.08 (0.94-1.25)	1.10 (0.95-1.27)	
54.4-60.0	0.98 (0.84-1.16)	0.94 (0.79-1.10)	0.92 (0.62-1.34)	0.92 (0.77-1.11)	1.02 (0.87-1.20)	0.98 (0.84-1.16)	
60.1	1.01 (0.84-1.20)	1.03 (0.87-1.21)	1.01 (0.69-1.47)	0.92 (0.76-1.10)	1.09 (0.90-1.31)	1.01 (0.84-1.20)	
P for trend	0.71	0.87	0.81	0.61	0.66	0.36	

^a Adjusted for age at cohort entry, race/ethnicity (for all men combined only), family history of prostate cancer, and the other risk factors in the table.

^b Metabolic equivalent of task.

^c Based on categories of exposure.

Incidence rates and relative risks (RR) with 95% confidence intervals (95% CI) for prostate cancer by race/ethnicity in the MEC, 1993-2010**Table 2**

	White (n = 19,833)	African American (n = 9,284)	Native Hawaiian (n = 5,454)	Japanese American (n = 23,687)	Latino (n = 16,958)	P value ^d
No. of total cases	1,594	1,486	367	2,056	1,612	
Incidence rate ^b	383.8	770.0	376.2	370.0	409.5	
RR (95% CI) ^c	reference	2.01 (1.87-2.15)	0.98 (0.87-1.10)	0.96 (0.90-1.03)	1.07 (1.00-1.14)	<0.001
RR (95% CI) ^d	reference	2.08 (1.93-2.25)	1.06 (0.94-1.20)	1.02 (0.94-1.11)	1.16 (1.07-1.26)	<0.001
No. of localized cases	1,277	1,175	292	1,718	1,264	
Incidence rate ^b	301.3	597.7	293.1	302.8	315.1	
RR (95% CI) ^c	reference	1.98 (1.83-2.15)	0.97 (0.86-1.11)	1.00 (0.93-1.08)	1.05 (0.97-1.13)	<0.001
RR (95% CI) ^d	reference	2.08 (1.91-2.27)	1.07 (0.94-1.22)	1.06 (0.97-1.17)	1.16 (1.06-1.27)	<0.001
No. of advanced cases	248	195	59	255	212	
Incidence rate ^b	62.4	110.0	60.9	50.1	56.9	
RR (95% CI) ^c	reference	1.76 (1.46-2.13)	0.98 (0.73-1.30)	0.80 (0.67-0.96)	0.91 (0.76-1.10)	<0.001
RR (95% CI) ^d	reference	1.75 (1.43-2.14)	0.98 (0.73-1.32)	0.86 (0.69-1.08)	0.96 (0.77-1.19)	<0.001
No. of low-grade cases	893	972	178	1,017	1,053	
Incidence rate ^b	206.9	479.8	173.8	175.6	255.9	
RR (95% CI) ^c	reference	2.32 (2.12-2.54)	0.84 (0.71-0.99)	0.85 (0.78-0.93)	1.24 (1.13-1.35)	<0.001
RR (95% CI) ^d	reference	2.41 (2.19-2.66)	0.93 (0.79-1.10)	0.88 (0.79-0.99)	1.33 (1.20-1.48)	<0.001
No. of high-grade cases	636	424	176	988	486	
Incidence rate ^b	157.9	232.6	187.1	186.2	127.9	
RR (95% CI) ^c	reference	1.47 (1.30-1.67)	1.19 (1.00-1.40)	1.18 (1.07-1.30)	0.81 (0.72-0.91)	<0.001
RR (95% CI) ^d	reference	1.55 (1.36-1.77)	1.27 (1.06-1.52)	1.33 (1.16-1.51)	0.90 (0.79-1.04)	<0.001
No. of fatal cases	148	173	27	93	123	
Incidence rate ^b	40.2	91.3	35.1	16.9	36.8	
RR (95% CI) ^c	reference	2.27 (1.82-2.83)	0.87 (0.58-1.32)	0.42 (0.32-0.54)	0.92 (0.72-1.17)	<0.001
RR (95% CI) ^d	reference	2.03 (1.60-2.58)	0.78 (0.51-1.20)	0.37 (0.27-0.51)	0.86 (0.65-1.14)	<0.001

^d Global test of race/ethnicity from the Cox models.

^b Per 100,000 adjusted to 2000 US Standard Population. This is calculated for whites, and the incidence rates for other groups are computed by multiplying this value by the relative risks^c.

^c Adjusted for age at cohort entry.

Additionally adjusted for family history of prostate cancer, BMI, height, smoking, education, history of diabetes, physical activity, alcohol consumption, calcium intake, legume intake, lycopene intake, and selenium intake.