Published in final edited form as:

Prostate Cancer Prostatic Dis. 2019 March ; 22(1): 91–100. doi:10.1038/s41391-018-0070-9.

Prostate cancer risk factors in black and white men in the NIH-AARP Diet and Health Study

Tracy M. Layne[1], **Barry I. Graubard**[1], **Xiaomei Ma**[2,3], **Susan T. Mayne**[2,4], **Demetrius Albanes**[1]

[1]Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD, USA

[2]Department of Chronic Disease Epidemiology, Yale School of Public Health, New Haven, CT, USA

[3]Yale Comprehensive Cancer Center, Yale University, New Haven, CT, USA

[4]Present address: Center for Food Safety and Applied Nutrition, Food and Drug Administration, College Park, MD, USA

Abstract

Background—There are few prospective studies comparing race-specific associations between diet, nutrients, and health-related parameters, and prostate cancer risk.

Methods—Race-specific prostate cancer risk associations were examined among men in the National Institutes of Health (NIH)-AARP Diet and Health Study. We identified 1417 cases among black men (209 advanced), and 28,845 among white men (3898 advanced). Cox proportional hazards regression models estimated hazard ratios (HRs) and 95% confidence intervals (CIs). We also evaluated the cumulative change in the HR for black race following adjustment for each factor.

Results—Race-specific prostate cancer associations were similar in black and white men across disease subtypes only for history of diabetes (overall : HR = 0.77, 95% CI: 0.65–0.90 and HR = 0.72, 95% CI: 0.69–0.76, respectively; $P_{\text{interaction}} = 0.66$). By contrast, there was a positive risk association with height for white men and inverse for black men ($P_{\text{interaction}}$: non-advanced = 0.01; advanced = 0.04). This difference remained among men with at least 2 years of follow-up for non-advanced ($P_{\text{interaction}} = 0.01$), but not advanced disease ($P_{\text{interaction}} = 0.24$); or after adjustment for prostate cancer screening (non-advanced $P_{\text{interaction}} = 0.53$, advanced $P_{\text{interaction}} = 0.31$). The only other evidence of interaction with race was observed for dietary vitamin D intake and non-advanced disease, but only after adjustment for screening ($P_{\text{interaction}} = 0.02$). Cumulative

✉Tracy M. Layne, tracy.layne@nih.gov.

Author contributions DA, STM, XM, and BIG designed the research; TML conducted and analyzed the data; TML, DA, STM, XM, and BIG wrote the paper; TML and DA have primary responsibility for the final content. All authors read and approved the final manuscript.

Electronic supplementary material The online version of this article (https://doi.org/10.1038/s41391-018-0070-9) contains supplementary material, which is available to authorized users.

The opinions and conclusions expressed in this article are solely the views of the authors and do not necessarily reflect those of the Food and Drug Administration.

Conflict of interest The authors declare that they have no conflict of interest.

adjustment for each factor increased the HR for black race by 32.9% for overall cancer and 12.4% for advanced disease.

Conclusions—Our data suggest few of the dietary, nutrient, and health-related factors associated with prostate cancer risk in predominantly non-Hispanic white men were associated with risk in black men, and adjustment for these factors widen the black-white difference in risk. Larger studies of black men, particularly with prospective data, are needed to help identify risk factors relevant to this population.

Introduction

Prostate cancer is the most commonly diagnosed malignancy and the second leading cause of cancer death in American black and white men [1]. However, black men have a 70% higher incidence and a more than twofold higher mortality rate compared with white men [2], and they are diagnosed at younger ages and with more aggressive disease [3]. The cause (s) of these black-white differences in risk remain unclear [3], but are likely multifactorial [4], including a combination of environmental exposures (e.g., dietary and nutrient intake [5]), delays in disease detection, differential genetic susceptibility (i.e., chromosome 8q24), or tumor biology (i.e., DNA methylation) [6], and socio-economic factors [4]. Examination of race-specific modifiable factors potentially related to prostate cancer risk may therefore provide insights into this racial disparity, and opportunities for risk reduction. To date, our knowledge concerning possible dietary, nutrient, and health-related contributors to prostate cancer risk is based on research in predominantly non-Hispanic white populations. Small sample sizes and number of cases for black men and other racial/ethnic minorities have limited prospective race-specific investigations [7]. As such, most evaluation of these factors in black men have been in case–control [8–15] or retrospective cohort studies [16]. There remains a paucity of data prospectively examining the directionality and magnitude of race-specific associations between diet and health-related risk factors and prostate cancer among black and white men, particularly within individual cohorts.

The present study examines the race-specific relationship between diet and nutrient intakes, and health-related factors in relation to prostate cancer risk in the National Institutes of Health (NIH)-AARP Diet and Health Study. Beyond highlighting black-white differences in prostate cancer risk, this analysis considers whether previously identified risk factor associations are consistent in black and white men, and whether they explain some of the excess risk observed in black men.

Methods

Study population

The NIH-AARP (formerly the American Association of Retired Persons) Study is a large cohort of adults aged 50–69 years who were enrolled between 1995 and 1996. As previously described, [17] the cohort includes individuals residing in six US states (California, Florida, Louisiana, New Jersey, North Carolina, and Pennsylvania), and two metropolitan areas (Atlanta, Georgia and Detroit, Michigan). [17] A baseline questionnaire including a detailed 124-item food frequency instrument and other baseline characteristics was completed satisfactorily by 567,169 respondents [17]. A supplementary Risk Factor Questionnaire (RFQ) was completed by a subset of these individuals (approximately 339,000) [17], providing information on screening with prostate-specific antigen (PSA) and digital rectal examination (DRE) within the 3 years prior to baseline (responses: no; yes, once; yes, more than once; and don't know).

From the 566,398 respondents with sufficient dietary data on the baseline questionnaire, we excluded: all women (n = 225,467), men who had proxy questionnaires (n = 15,760), a prior history of cancer (n = 27,289), self-reported poor health (n = 4958) end-stage renal disease (n = 485), cancers reported by autopsy or death certificate only (n = 2742), zero follow-up time (n = 21), total energy intake beyond twice the interquartile range of Box-Cox log-transformed intake (n = 2218), races other than non-Hispanic black or white (n = 13,976), and first incident cancer other than prostate cancer (n = 45,592). After exclusions, our analytic sample consisted of 227,890 non-Hispanic men: 221,032 white and 6858 black. A subset of these individuals (130,371 white (13,079 cases) and 3217 black (520 cases)) completed the RFQ (Supplementary Fig. 1). To maximize statistical power, our primary analyses used data from the baseline questionnaire.

The NIH-AARP Diet and Health Study was approved by the Special Studies Institutional Review Board of the U.S. National Cancer Institute. All participants provided written informed consent.

Code availability

All computer code used to generate results for this study can be accessed by contacting the corresponding author.

Cancer ascertainment

Cases were identified through linkage with state-based cancer registries as previously described [18]. First primary incident prostate cancer (*International Classification of Diseases for Oncology*, 3rd Edition code C619) and vital status, using the National Death Index, were ascertained through 31 December 2011 and included cases without disease staging information (809 white and 35 black). Advanced prostate cancers were defined as clinical stage T3–T4, N1, or M1 based on the American Joint Committee on Cancer's Tumor-Node-Metastasis (i.e., TNM) classification system, or fatal disease, and all other prostate cancer cases are defined as non-advanced. Information on Gleason grade was unavailable.

Statistical analysis

Bivariate analyses were conducted using chi-square tests for categorical variables and t-tests for continuous variables. Person-years of follow-up were calculated from the date of return of the baseline questionnaire to the earliest of the following dates: prostate cancer diagnosis, moved out the registry area, death, or the end of the follow-up. Cox proportional hazards regression, with person-years of follow-up as the time metric, was used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for the risk of prostate cancer. The proportional hazard assumption was assessed and confirmed by modeling cross-product terms between each factor and time.

Using information assessed from the baseline questionnaire, our analysis included factors identified in stepwise selection ($P \leq 0.25$) for the association with overall prostate cancer risk in all men. Selection models began with the following factors: height (cm); body mass index (BMI): normal weight (18.5–< 25 kg/m^2), overweight (25–< 30 kg/m^2), and obese (≥ 30 kg/m^2)); alcohol consumption: never, < 1, 1–3, >3–<6, and ≥6 drinks per day; smoking status: never/rarely, former, and current; self-reported history of diabetes: yes/no; physical activity (≥20 min causing increased breathing/heart rate/sweating): never/rarely, 1–3 times/ month, or 1–2, 3–4, or ≥5 times/week. Average daily dietary intakes included red meat (g/ day), pyramid servings for all sources of: poultry, fish, dairy, fruit, vegetables, and tomatoes, as well as overall vitamin D (μg), alpha-tocopherol (mg), and, beta-carotene (μg). Quintiles of overall intake were estimated based on the baseline distribution among all men. We also considered use (yes/no) of any individual vitamin or mineral supplements (vitamins A, C, E, beta-carotene, calcium, folic acid, iron, selenium and zinc), and/or multi-vitamins (e.g., therapeutic, stress-tab, or one-a-day) within the year prior to baseline. Estimates of supplemental vitamin D were only available from multivitamin sources.

Based on step-wise selection, the following factors were examined together in race-specific models: history of diabetes; height; BMI; alcohol consumption; smoking status; and average daily dietary intakes of: red meat (g); pyramid servings of tomato [one large tomato or eight ounces of tomato juice] and dairy [one cup (244 ml) milk or yogurt, 1.5 ounces (42.5 g) of natural cheese, or 2 ounces (56.0 g) of processed cheese]; and vitamin D (μg). All models adjusted for the following potential confounders as demonstrated by >10% changes in the parameter estimates: age (continuous plus a 3 knot spline term [19]); family history of prostate cancer (father, brother, or son); attained education (≤11 years, high school graduate and some college, college and post graduate); marital status (married/ living as married, never married, separated, divorced, widowed, unknown); as well as quintiles of total energy intake (kcal/day). Indicator variables were used for missing covariate data; overall, values were missing in 3% of white men and 6% of black men. Confounding by screening with PSA and/or DRE was evaluated in the subset of men who completed the RFQ.

Interaction between each factor and race was examined by adding cross-product terms to the model. Trend tests were evaluated treating medians values for quintile-specific categories as continuous in the model and testing the statistical significance of the corresponding regression coefficient. Sensitivity analyses were conducted excluding the first 2 years of follow-up to examine whether associations differed after exclusion of prevalent cases. To evaluate how each factor influenced the black-white disparity in risk, we examined the change in the HR for race following addition of each factor to the model. Models began with an indicator variable for black vs. white race alone, followed by age and family history. Each diet, nutrient, and health-related factor was then added to the model based on the order identified from forward step-wise selection results.

A high degree of correlation (Pearson $r \geq 0.70$) between certain variables (e.g., vitamin D and dairy), made it challenging to disentangle individual associations. As such, these variables were not included in models together. Models including dietary intakes adjusted for total energy intake by adding it as a covariate. We used the *P*-value for equal or unequal variances where appropriate for all groups being statistically compared.

All statistical tests used a two-sided Type I error of 0.05 for statistical significance, and all analyses were carried out using the Statistical Analysis System version 9.3 (SAS Institute, Inc., Cary, NC).

Results

During a median of 15.5 years of follow-up, 28,845 incident prostate cancers were identified in white men (3898 advanced), and 1417 in black men (209 advanced). The baseline distribution of each factor by race and case status is summarized in Table 1. Among white men, compared with non-cases, cases were older, reported more screening, and were more likely to be college educated, married, and drink ≥ 6 drinks/day, but were less likely to be obese or current smokers. Among black men, height was one of the few factors that differed between cases and non-cases (cases were slightly shorter on average), and was the only factor that did not differ between black and white controls other than family history of prostate cancer. For both racial groups, cases were more likely than non-cases to have a history of diabetes (Table 1).

Statistically significant risk factor-prostate cancer associations for overall disease were mainly evident for white men, with many risk estimates similar in magnitude but nonsignificant for black men (Table 2). This includes inverse associations with BMI, current and former smokers, and tomato consumption, and positive associations with alcohol and red meat consumption ($P_{\text{interaction}} > 0.05$ for all factors) (Table 2). History of diabetes was the only factor statistically significant and similar in magnitude for white men (HR = 0.72, 95% CI: 0.69–0.76) and black men (HR = 0.77, 95% CI: 0.65–0.90, $P_{\text{interaction}} = 0.66$). Whereas, the association with height qualitatively differed between white men (HR = 1.03, 95% CI:1.01–1.04) and black men (HR = 0.91, 95% CI:0.85–097, $P_{\text{interaction}} = 0.003$) (Table 2).

Race-specific estimates were similar for advanced and non-advanced disease in both racial groups; exceptions include the statistically significant associations with height and history of diabetes among black men that were only evident for non-advanced disease (Table 3). Interaction between race and height was evident for both advanced (*Pinteraction* = 0.04) and non-advanced ($P_{\text{interaction}} = 0.01$) disease (Table 3).

In sensitivity analyses restricted to men with at least 2 years of follow-up, race-specific estimates were largely unchanged, including the interaction between race and height for overall ($P_{\text{interaction}} = 0.002$) and non-advanced ($P_{\text{interaction}} = 0.01$), but not advanced disease ($P_{\text{interaction}} = 0.24$) (Supplementary Table 1). The positive trend in the association with frequency of alcohol consumption was, however, evident in both white ($HR_{\geq 6\text{ drinks/day vs. never}} = 1.35$, 95% CI:1.12–1.63, $P_{\text{trend}} = 0.01$) and black men ($\text{HR}_{\geq 6\text{ drinks/day vs. never}} = 2.54$, 95% CI:1.22–5.32, $P_{\text{trend}} = 0.03$; $N = 11$ cases with ≥ 6 drinks/day) (Supplementary Table 1).

Controlling for prostate cancer screening yielded similar race-specific estimates, however, without evidence of interaction between race and height (Supplementary Table 2). Additionally, previously apparent black—white differences in the association with vitamin D intake became statistically significant for non-advanced disease: ($HR_{Q5\ vs.\ Q1}$white men = 1.14, 95% CI:1.06–1.23, P_{trend} = 0.0001; black men HR = 0.73, 95% CI:0.49–1.07, P_{trend} = 0.18; $P_{interaction}$ = 0.02). Tests for interactions between race and supplemental or supplemental plus dietary vitamin D intake did not reach statistical significance (data not shown), nor was there evidence of interaction with any of the other evaluated factors (Supplementary Table 2). Among men with at least 2 years of follow-up and controlling for prostate cancer screening, the racial difference in the association with height was only evident for non-advanced disease ($P_{interaction}$ = 0.05), and no longer statistically significant for vitamin D intake and non-advanced disease ($P_{interaction}$ = 0.06) (data not shown).

In cumulatively adjusted models, adjusting for age, family history of prostate cancer, and each of the factors we examined increased HR for black men compared with white men by 32.9% for overall prostate cancer, and 12.4% for advanced disease, relative to models with race alone. This includes <10% individual changes in the HR associated with adjustment for factors associated with risk in black men (i.e., diabetes, height, and dietary vitamin D) (Fig. 1, HRs and 95% CI are presented in Supplementary Table 3).

Discussion

In this prospective cohort, investigation of race-specific associations between dietary, nutrient, and health-related factors and prostate cancer risk, a history of diabetes was the only factor that was both significantly associated with risk, and of a similar inverse direction and magnitude, in black and white men. We also found evidence of racial variation in the associations with attained height and dietary vitamin D intake. Adjustment for all of the investigated factors, including those associated with risk in both racial groups (i.e., diabetes), substantially increased, rather than decreased, the black-white difference in risk.

The latter observation from our study is consistent with findings from prospective analyses of black and white men in the Multiethnic Cohort (MEC) Study [20] and the Health Professionals Follow-up Study [21]. In both cohorts, adjustment for several hypothesized dietary and lifestyle factors increased, rather than decreased, the relative risk for race/ethnicity [20, 21]. This suggests many of the identified prostate cancer risk factors do not adequately explain risk in black men. Evaluation of whether risk associations are consistent and applicable to a broader at-risk population is important within the context of racial/ethnic disparities, as the assumption of risk factor homogeneity may mask or prevent the discovery of important racial differences that underlie some of the persistent risk differences.

The protective association with a history of diabetes we observed, with a weaker association in black men, has been observed in some [20, 22], but not all studies [23]. In meta-analyses, the overall prostate cancer risk estimate for diabetes is protective, particularly with increasing duration of diabetes [23]. Suspected mechanisms for this association, particularly with type II diabetes, include inhibitory effects of hypoinsulinemia on bioavailable insulin growth factor-I (IGF-I), and alterations in circulating androgens and leptin [24].

The aforementioned MEC study, is similar to the NIH-AARP cohort with respect to average years of follow-up (13.9 vs. 12.7, respectively), number of black prostate cancer cases (1486 vs. 1417, respectively) and some of the examined factors [20]. The MEC study found no evidence of racial variation for any of the evaluated factors, however, which included BMI, smoking status, history of diabetes, alcohol consumption, and height [20]. In both studies, observed associations with BMI, alcohol consumption, and smoking status in white men were not significant in black men. However, our analysis identified racial variation in the prostate cancer risk association with height and dietary vitamin D. Attained height, an indicator of early life nutrition, IGF-I concentrations [25], and heredity, has been associated with increased prostate cancer risk in a dose-response manner [26]. Prior studies evaluating the impact of height by race have found modest increases in overall prostate cancer risk in white men [27], similar to previous reports for white men in the NIH-AARP cohort [28], with either no association [10, 13], or a suggestive protective relationship in black men [29–31], whereas others found no racial difference in the positive [32, 33] or null association [20]. Racial differences in the association with prostate cancer risk, however, may be explained by racial variation in the IGF system [34] and its influence on height [35].

Although dietary vitamin D was not associated with risk in black men in our study, for non-advanced disease we found evidence of racial variation in the association, with a positive association in white men and suggestively inverse relation in black men. However, adjusting for dietary vitamin D did not attenuate the relative risk associated with black race. Our findings for white men are consistent with the current literature indicating a positive association with dietary [36] and circulating [37] vitamin D and prostate cancer risk [36]. Our finding of a suggestive inverse association in black men is consistent with both preclinical studies showing a protective role of vitamin D in prostate cancer carcinogenesis [38] and findings from our prospective analysis of serum 25-hydroxyvitamin D and prostate cancer risk in black men [39]. No association has previously been found between vitamin D intake and prostate cancer risk in the few observational studies evaluating this association in black men [40, 41]. In addition to having lower solar ultraviolet B radiation production of 25-hydroxyvitamin D due to greater skin pigmentation [42], black populations have lower intake of vitamin D relative to white populations [43]. Thus, race may be a proxy for vitamin D insufficiency, and lower circulating vitamin D may contribute to black–white differences in prostate cancer risk. A possible mechanism underlying this difference may be related to black-white differences in vitamin D-mediated immune response and inflammation gene expression in the prostate [44, 45].

The present analysis of a large-scale prospective cohort included more than 10 years of average follow-up and information on multiple potential confounders, including prostate cancer screening practices. However, even with a considerable number of black cases, our analysis was limited in power that may have impacted our ability to detect associations among black men, particularly for advanced disease, and to identify heterogeneity in the associations by race. Additionally, measurement error in the questionnaire data, including the food frequency questionnaire, may have influenced our diet and nutrient risk associations. As such, our results should be interpreted cautiously given the potential for chance findings. Further research is needed to reconcile whether certain risk factor-prostate cancer associations in black men are truly null or missed because of limited statistical power.

Similar to prior studies with race-specific estimates of risk, we found that few of the evaluated dietary, nutrient, and health-related factors were associated with prostate cancer risk in black men. Additionally, adjustment for these factors—which primarily explain risk in non-Hispanic white men—widen the black-white difference in risk. This overall lack of association in black men is in part due to their relatively smaller sample size in these studies, limiting the ability to detect risk associations in this group. Multiple inter-related risk factors, including as-yet determined factors associated with black race, likely contribute to the risk difference. The current challenge of identifying factors that meaningfully contribute to this well-known racial risk disparity underscores the need for large-scale prospective studies of racial/ethnic minority populations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

This research was supported [in part] by the Intramural Research Program of the NIH, National Cancer Institute. Cancer incidence data from the Atlanta metropolitan area were collected by the Georgia Center for Cancer Statistics, Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, Georgia. Cancer incidence data from California were collected by the California Cancer Registry, California Department of Public Health's Cancer Surveillance and Research Branch, Sacramento, California. Cancer incidence data from the Detroit metropolitan area were collected by the Michigan Cancer Surveillance Program, Community Health Administration, Lansing, Michigan. The Florida cancer incidence data used in this report were collected by the Florida Cancer Data System (Miami, Florida) under contract with the Florida Department of Health, Tallahassee, Florida. The views expressed herein are solely those of the authors and do not necessarily reflect those of the FCDC or FDOH. Cancer incidence data from Louisiana were collected by the Louisiana Tumor Registry, Louisiana State University Health Sciences Center School of Public Health, New Orleans, Louisiana. Cancer incidence data from New Jersey were collected by the New Jersey State Cancer Registry, The Rutgers Cancer Institute of New Jersey, New Brunswick, New Jersey. Cancer incidence data from North Carolina were collected by the North Carolina Central Cancer Registry, Raleigh, North Carolina. Cancer incidence data from Pennsylvania were supplied by the Division of Health Statistics and Research, Pennsylvania Department of Health, Harrisburg, Pennsylvania. The Pennsylvania Department of Health specifically disclaims responsibility for any analyses, interpretations or conclusions. Cancer incidence data from Arizona were collected by the Arizona Cancer Registry, Division of Public Health Services, Arizona Department of Health Services, Phoenix, Arizona. Cancer incidence data from Texas were collected by the Texas Cancer Registry, Cancer Epidemiology and Surveillance Branch, Texas Department of State Health Services, Austin, Texas. Cancer incidence data from Nevada were collected by the Nevada Central Cancer Registry, Division of Public and Behavioral Health, State of Nevada Department of Health and Human Services, Carson City, Nevada. We are indebted to the participants in the NIH-AARP Diet and Health Study for their outstanding cooperation. We also thank Sigurd Hermansen and Kerry Grace Morrissey from Westat for study outcomes ascertainment and management and Leslie Carroll at Information Management Services for data support and analysis.

Funding This work was supported by the Yale-NCI pre-doctoral training grant T32 CA105666 to STM and XM, and by the Intramural Research Program of the National Cancer Institute at the National Institutes of Health.

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2017. CA Cancer J Clin. 2017;67:7–30. [PubMed: 28055103]
2. American Cancer Society. Cancer Facts & Figures for African Americans 2016–2018. Atlanta: American Cancer Society, 2016.
3. Chornokur G, Dalton K, Borysova ME, Kumar NB. Disparities at presentation, diagnosis, treatment, and survival in African American men, affected by prostate cancer. Prostate. 2011;71:985–97. [PubMed: 21541975]
4. Freedland SJ, Isaacs WB. Explaining racial differences in prostate cancer in the United States: sociology or biology? Prostate. 2005;62:243–52. [PubMed: 15389726]

5. Jones BA, Liu WL, Araujo AB, Kasl SV, Silvera SN, Soler-Vila H, et al. Explaining the race difference in prostate cancer stage at diagnosis. Cancer Epidemiol Biomark Prev. 2008;17:2825–34.
6. Martin DN, Starks AM, Ambs S. Biological determinants of health disparities in prostate cancer. Curr Opin Oncol. 2013;25:235–41. [PubMed: 23399519]
7. Martin DN, Lam TK, Brignole K, Ashing KT, Blot WJ, Burhansstipanov L, et al. Recommendations for cancer epidemiologic research in understudied populations and implications for future needs. Cancer Epidemiol Biomark Prev. 2016;25:573–80.
8. Kolonel LN, Hankin JH, Whittemore AS, Wu AH, Gallagher RP, Wilkens LR, et al. Vegetables, fruits, legumes and prostate cancer: a multiethnic case-control study. Cancer Epidemiol Biomark Prev. 2000;9:795–804.
9. Vogt TM, Mayne ST, Graubard BI, Swanson CA, Sowell AL, Schoenberg JB, et al. Serum lycopene, other serum carotenoids, and risk of prostate cancer in US Blacks and Whites. Am J Epidemiol. 2002;155:1023–32. [PubMed: 12034581]
10. Whittemore AS, Kolonel LN, Wu AH, John EM, Gallagher RP, Howe GR, et al. Prostate cancer in relation to diet, physical activity, and body size in blacks, whites, and Asians in the United States and Canada. J Natl Cancer Inst. 1995;87:652–61. [PubMed: 7752270]
11. Vogt TM, Ziegler RG, Graubard BI, Swanson CA, Greenberg RS, Schoenberg JB, et al. Serum selenium and risk of prostate cancer in U.S. blacks and whites. Int J Cancer. 2003;103:664–70. [PubMed: 12494476]
12. Jackson M, Tulloch-Reid M, Walker S, McFarlane-Anderson N, Bennett F, Francis D, et al. Dietary patterns as predictors of prostate cancer in Jamaican men. Nutr Cancer. 2013; 65:367–74. [PubMed: 23530635]
13. Hayes RB, Ziegler RG, Gridley G, Swanson C, Greenberg RS, Swanson GM, et al. Dietary factors and risks for prostate cancer among blacks and whites in the United States. Cancer Epidemiol Biomark Prev. 1999;8:25–34.
14. Sanderson M, Coker AL, Logan P, Zheng W, Fadden MK. Lifestyle and prostate cancer among older African-American and Caucasian men in South Carolina. Cancer Causes Control. 2004;15:647–55. [PubMed: 15280622]
15. Rowland GW, Schwartz GG, John EM, Ingles SA. Calcium intake and prostate cancer among African Americans: effect modification by vitamin D receptor calcium absorption genotype. J Bone Miner Res. 2012;27:187–94. [PubMed: 21887707]
16. Ben-Shlomo Y, Evans S, Ibrahim F, Patel B, Anson K, Chinegwundoh F, et al. The risk of prostate cancer amongst black men in the United Kingdom: the PROCESS cohort study. Eur Urol. 2008;53:99–105. [PubMed: 17368710]
17. Schatzkin A, Subar AF, Thompson FE, Harlan LC, Tangrea J, Hollenbeck AR, et al. Design and serendipity in establishing a large cohort with wide dietary intake distributions: the National Institutes of Health-American Association of Retired Persons Diet and Health Study. Am J Epidemiol. 2001;154:1119–25. [PubMed: 11744517]
18. Michaud D, Midthune D, Hermansen S, Leitzmann M, Harlan L, Kipnis V, et al. Comparison of cancer registry case ascertainment with SEER estimates and self-reporting in a subset of the NIH-AARP Diet and Health Study. J Regist Manag. 2005;32:70–75.
19. Durrleman S, Simon R. Flexible regression models with cubic splines. Stat Med. 1989;8:551–61. [PubMed: 2657958]
20. Park SY, Haiman CA, Cheng I, Park SL, Wilkens LR, Kolonel LN, et al. Racial/ethnic differences in lifestyle-related factors and prostate cancer risk: the Multiethnic Cohort Study. Cancer Causes Control. 2015;26:1507–15. [PubMed: 26243447]
21. Platz EA, Rimm EB, Willett WC, Kantoff PW, Giovannucci E. Racial variation in prostate cancer incidence and in hormonal system markers among male health professionals. J Natl Cancer Inst. 2000;92:2009–17. [PubMed: 11121463]
22. Atchison EA, Gridley G, Carreon JD, Leitzmann MF, McGlynn KA. Risk of cancer in a large cohort of U.S. veterans with diabetes. Int J Cancer. 2011;128:635–43. [PubMed: 20473855]
23. Bansal D, Bhansali A, Kapil G, Undela K, Tiwari P. Type 2 diabetes and risk of prostate cancer: a meta-analysis of observational studies. Prostate Cancer Prostatic Dis. 2013;16:151–8. S151 [PubMed: 23032360]

24. Rastmanesh R, Hejazi J, Marotta F, Hara N. Type 2 diabetes: a protective factor for prostate cancer? An overview of proposed mechanisms. Clin Genitourin Cancer. 2014;12:143–8. [PubMed: 24513117]
25. Travis RC, Appleby PN, Martin RM, Holly JMP, Albanes D, Black A, et al. A meta-analysis of individual participant data reveals an association between circulating levels of IGF-I and prostate cancer risk. Cancer Res. 2016;76:2288–300. [PubMed: 26921328]
26. World Cancer Research Fund International/American Institute for Cancer Research Continuous Report Update Project Report. Diet, Nutrition, Physical Acitivity, and Prostate Cancer, 2014.
27. Mordukhovich I, Reiter PL, Backes DM, Family L, McCullough LE, O'Brien KM, et al. A review of African American-white differences in risk factors for cancer: prostate cancer. Cancer Causes Control. 2011;22:341–57. [PubMed: 21184263]
28. Kabat GC, Kim MY, Hollenbeck AR, Rohan TE. Attained height, sex, and risk of cancer at different anatomic sites in the NIH-AARP Diet and Health Study. Cancer Causes Control. 2014;25:1697–706. [PubMed: 25307804]
29. Rodriguez C, Patel AV, Calle EE, Jacobs EJ, Chao A, Thun MJ. Body mass index, height, and prostate cancer mortality in two large cohorts of adult men in the United States. Cancer Epidemiol Biomark Prev. 2001;10:345–53.
30. Habel LA, Van Den Eeden SK, Friedman GD. Body size, age at shaving initiation, and prostate cancer in a large, multiracial cohort. Prostate. 2000;43:136–43. [PubMed: 10754529]
31. Zuccolo L, Harris R, Gunnell D, Oliver S, Lane JA, Davis M, et al. Height and prostate cancer risk: a large nested case-control study (ProtecT) and meta-analysis. Cancer Epidemiol Biomark Prev. 2008;17:2325–36.
32. Ahn J, Moore SC, Albanes D, Huang WY, Leitzmann MF, Hayes RB, et al. Height and risk of prostate cancer in the prostate, lung, colorectal, and ovarian cancer screening trial. Br J Cancer. 2009;101:522–5. [PubMed: 19568244]
33. Freedland SJ, Aronson WJ, Trock B, Cohen P, Kane CJ, Amling CL, et al. Racial differences in prognostic value of adult height for biochemical progression following radical prostatectomy. Clin Cancer Res. 2005;11:7735–42. [PubMed: 16278394]
34. Platz EA, Pollak MN, Rimm EB, Majeed N, Tao Y, Willett WC, et al. Racial variation in insulin-like growth factor-1 and binding protein-3 concentrations in middle-aged men. Cancer Epidemiol Biomark Prev. 1999;8:1107–10.
35. McGreevy K, Hoel B, Lipsitz S, Bissada N, Hoel D. Racial and anthropometric differences in plasma levels of insulin-like growth factor I and insulin-like growth factor binding protein-3. Urology. 2005;66:587–92. [PubMed: 16140083]
36. Gilbert R, Martin RM, Beynon R, Harris R, Savovic J, Zuccolo L, et al. Associations of circulating and dietary vitamin D with prostate cancer risk: a systematic review and dose-response meta-analysis. Cancer Causes Control. 2011;22:319–40. [PubMed: 21203822]
37. Xu Y, Shao X, Yao Y, Xu L, Chang L, Jiang Z, et al. Positive association between circulating 25-hydroxyvitamin D levels and prostate cancer risk: new findings from an updated meta-analysis. J Cancer Res Clin Oncol. 2014;140:1465–77. [PubMed: 24838848]
38. Swami S, Krishnan AV, Feldman D. Vitamin D metabolism and action in the prostate: implications for health and disease. Mol Cell Endocrinol. 2011;347:61–69. [PubMed: 21664249]
39. Layne TM, Weinstein SJ, Graubard BI, Ma X, Mayne ST, Albanes D. Serum 25-hydroxyvitamin D, vitamin D binding protein, and prostate cancer risk in black men. Cancer. 2017;123:2698–704. [PubMed: 28369777]
40. Park SY, Murphy SP, Wilkens LR, Stram DO, Henderson BE, Kolonel LN. Calcium, vitamin D, and dairy product intake and prostate cancer risk: the Multiethnic Cohort Study. Am J Epidemiol. 2007;166:1259–69. [PubMed: 17925283]
41. Tseng M, Breslow RA, Graubard BI, Ziegler RG. Dairy, calcium, and vitamin D intakes and prostate cancer risk in the National Health and Nutrition Examination Epidemiologic Follow-up Study cohort. Am J Clin Nutr. 2005;81:1147–54. [PubMed: 15883441]
42. Holick MF. Vitamin D deficiency. N Engl J Med. 2007;357:266–81. [PubMed: 17634462]

43. O'Neil CE, Nicklas TA, Keast DR, Fulgoni VL. Ethnic disparities among food sources of energy and nutrients of public health concern and nutrients to limit in adults in the United States: NHANES 2003–2006. Food Nutr Res. 2014;58:15784. [PubMed: 25413643]

44. Batai K, Murphy AB, Nonn L, Kittles RA. Vitamin D and immune response: implications for prostate cancer in African Americans. Front Immunol. 2016;7:53. [PubMed: 26941739]

45. Hardiman G, Savage SJ, Hazard ES, Wilson RC, Courtney SM, Smith MT, et al. Systems analysis of the prostate transcriptome in African-American men compared with European-American men. Pharmacogenomics. 2016;17:1129–43. [PubMed: 27359067]

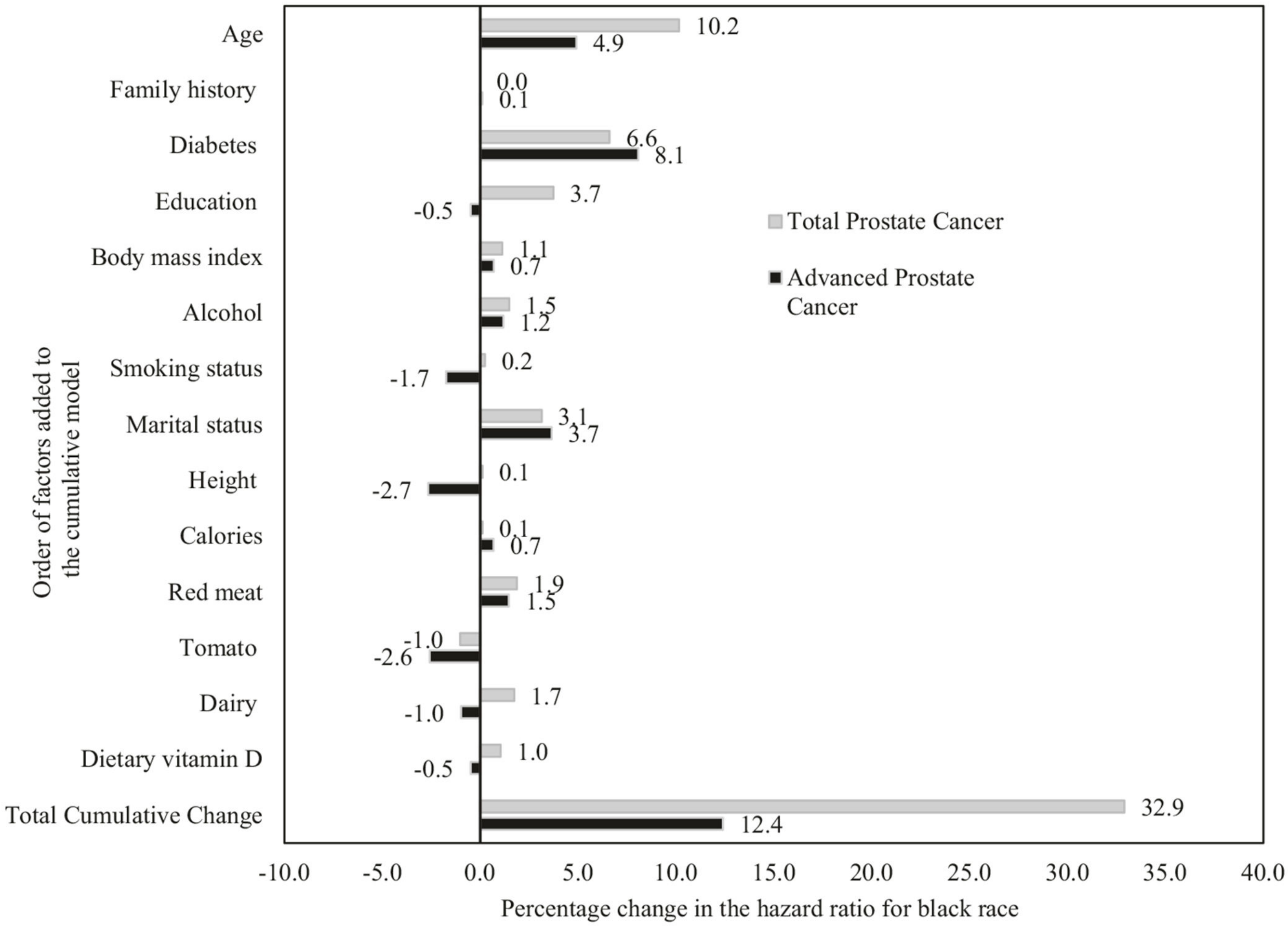

Fig. 1.

The cumulative change in the hazard ratio for the association between black race and risk of overall and advanced prostate cancer after adjustment. The initial model had an indicator variable for black vs. white race alone, followed by adjustment for age, and then family history of prostate cancer. Each diet and health-related factor was subsequently added to the model based on the order identified using forward selection; starting with diabetes and ending with either dairy or dietary vitamin D. Due to high correlation (correlation coefficient ≥0.70), models with dairy and dietary vitamin D are mutually exclusive. The total cumulative change is the percentage change in the hazard ratio between the race alone vs. the final cumulative model (ending with dairy)

Table 1

Distribution of baseline characteristics, mean (SD) or percent

Characteristic	White men (*N* = 221,032)		Black men (*N* = 6858)	
	Cases	Non-cases	Cases	Non-cases
No. of participants	28,845	192,187	1417	5441
Age at entry (years)[a, b]	62.9	61.8	61.2	60.6
Family history of prostate cancer[a,c]	12.3	7.9	11.6	7.7
Prostate cancer screening history[d]				
Prostate-specific antigen test[a,b]	77.9	71.6	69.4	65.1
Digital rectal exam [a,b]	86.6	83.6	81.4	79.8
College or post graduate[a, b]	49.1	45.6	35.6	32.5
Married or living as married[ab]	87.6	85.6	73.6	70.2
History of diabetes[ab,c]	6.1	9.5	13.3	18.8
Height (cm) [c]	178.5 (7.3)	178.5 (7.4)	178.5 (7.7)	178.6 (8.0)
BMI (kg/m^2)[ab]				
Under/normal weight (<25)	32.6	30.6	26.3	25.4
Overweight (25 – <30)	50.1	48.5	49.3	46.5
Obese (≥30)	17.4	20.9	24.5	28.1
Smoking[a, b]				
Never/rarely	33.3	30.4	31.5	28.9
Former	55.5	56.6	50.2	51.6
Current	7.8	9.3	13.0	13.6
Alcohol (drinks/day)[a, b]				
Never	17.9	20.3	28.0	31.6
<1	50.3	49.9	50.8	46.6
1 – 3	20.5	19.3	12.6	12.8
>3 - < 6	6.7	6.2	4.5	5.2
6 or more	4.7	4.3	4.2	3.7

Characteristic	White men (N = 221,032)		Black men (N = 6858)	
	Cases	Non-cases	Cases	Non-cases
Vitamins/minerals supplements[b]	65.2	64.9	59.6	59.9
Daily dietary intake				
Energy (kcal)[a, b]	1993 (804)	2013 (829)	2096 (1143)	2146 (1218)
Red meat (g)[ab]	76.0 (57.9)	78.5 (61.5)	67.3 (65.3)	72.4 (73.4)
Dairy (pyramid servings)[b]	1.5 (1.3)	1.5 (1.4)	1.1 (1.4)	1.2 (1.5)
Tomato (pyramid servings)[a, b]	0.64 (0.52)	0.66 (0.57)	0.51 (0.63)	0.53 (0.66)
Vitamin D (µg)[ab]	5.0 (3.4)	5.0 (3.5)	4.4 (4.1)	4.6 (4.1)

Pyramid serving: tomato = 1 large tomato or eight ounces of tomato juice. Dairy = 1 cup (244 ml) milk or yogurt, 1.5 ounces (42.5 g) of natural cheese, or 2 ounces (56.0 g) of processed cheese

[a] P for difference between white cases and non-cases <0.05

[b] P for difference between black and white non-cases <0.05

[c] P for difference between black cases and non-cases <0.05

[d] Prostate cancer screening in the past 3 years among a subset of men (3217 black and 130,371 white) who responded to the Risk Factor Questionnaire

Table 2

Race-specific hazard ratio (HR) and 95% confidence interval (CI) for the association with overall prostate cancer

No. of cases	White men			Black men			P [a]
	28,845			1417			
Characteristic	**HR** [b]	**95% CI**		**HR** [b]	**95% CI**		
History of diabetes	0.72	0.69	0.76	0.77	0.65	0.90	0.66
Height (10 cm increase)	1.03	1.01	1.04	0.91	0.85	0.97	0.003
BMI (Ref = under/normal weight: <25 kg/m^2)							
Overweight (25 – <30 kg/m^2)	0.99	0.96	1.01	0.998	0.87	1.14	0.93
Obese (≥30 kg/m^2)	0.89	0.85	0.92	0.90	0.77	1.05	
P for trend	<0.0001			0.24			
Smoking (Ref = never)							
Current	0.92	0.88	0.97	1.01	0.83	1.21	0.85
Former	0.92	0.90	0.95	0.95	0.84	1.08	
Unknown	0.90	0.84	0.96	0.88	0.68	1.13	
Alcohol drinks per day (Ref = never)							
Less than a drink/day	1.08	1.04	1.12	1.14	0.998	1.30	0.34
1–3 drinks/day	1.09	1.05	1.14	1.03	0.85	1.24	
>3-<6 drinks/day	1.18	1.12	1.25	0.92	0.69	1.22	
6 or more drinks/ day	1.23	1.15	1.31	1.18	0.88	1.58	
P for trend	<0.0001			0.64			
Red meat (g/day) (Ref = quintile 1: 0–30.7)							
Quintile 2: 30.7–52.2	1.06	1.02	1.10	1.18	1.01	1.37	0.36
Quintile 3: 52.2–77.1	1.07	1.03	1.11	1.12	0.95	1.33	
Quintile 4: 77.1–115.6	1.07	1.03	1.12	1.05	0.87	1.27	
Quintile 5: ≥115.6	1.10	1.05	1.15	0.96	0.78	1.18	
P for trend	0.0003			0.44			
Tomato (pyramid servings/day) (Ref = quintile 1: 0–0.27)							
Quintile 2: 0.28–0.42	1.01	0.97	1.04	0.94	0.81	1.10	0.46
Quintile 3: 0.43–0.60	1.01	0.97	1.05	1.01	0.85	1.21	
Quintile 4: 0.61–0.91	0.99	0.95	1.03	0.85	0.70	1.02	
Quintile 5: ≥0.92	0.97	0.93	1.01	0.94	0.78	1.13	
P for trend	0.02			0.36			
Dairy (pyramid servings/day) (Ref = quintile 1: 0–0.52) [c]							
Quintile 2: 0.53–0.88	1.00	0.97	1.04	1.02	0.88	1.19	0.20
Quintile 3: 0.89–1.32	1.03	0.99	1.07	1.01	0.85	1.19	
Quintile 4: 1.33–2.10	1.06	1.02	1.10	0.87	0.72	1.05	
Quintile 5: ≥2.11	1.05	1.01	1.10	0.96	0.79	1.16	
P for trend	0.005			0.38			
Dietary vitamin D (μg/day) (Ref = quintile 1: 0–2.41) [c]							

No. of cases	White men			Black men			*P* [a]
	28,845			1417			
Characteristic	**HR** [b]	**95% CI**		**HR** [b]	**95% CI**		
Quintile 2: 2.42–3.56	1.04	1.00	1.08	0.93	0.79	1.09	0.19
Quintile 3: 3.57–4.82	1.04	1.00	1.08	0.94	0.79	1.12	
Quintile 4: 4.83–6.87	1.05	1.01	1.09	0.93	0.77	1.12	
Quintile 5: ≥6.88	1.06	1.02	1.11	0.84	0.69	1.02	
P for trend	0.013			0.09			

Pyramid serving: tomato = 1 large tomato or eight ounces of tomato juice. Dairy = 1 cup (244 ml) milk or yogurt, 1.5 ounces (42.5 g) of natural cheese, or 2 ounces (56.0 g) of processed cheese

[a] *P* for interaction between each risk factor and race

[b] Adjusted for all factors presented as well as: age (55–59 years, 60–64 years, 65–69 years, ≥70 years); family history of prostate cancer; marital status (married/living as married, never married, separated, divorced, widowed, unknown); attained education (1< 8 years, 8–11 years, post-high school or some college, college and post graduate); and quintiles of total energy intake

[c] Model excludes either dairy or vitamin D due to high correlation (correlation coefficient ≥0.7) between the three variables

Table 3

Race-specific hazard ratio (HR) and 95% confidence interval (CI) for the association with prostate cancer by disease type

No. of cases	Advanced							Non-advanced						
	White men			Black men			P^a	White men			Black men			P^a
	3898			209				24,138			1173			
	HR[b]	95% CI		HR[b]	95% CI			HR[b]	95% CI		HR[b]	95% CI		
History of diabetes	0.63	0.55	0.73	0.67	0.43	1.06	0.95	0.73	0.69	0.77	0.75	0.63	0.90	0.80
Height (10 cm increase)	1.08	1.04	1.13	0.87	0.72	1.05	0.04	1.02	0.999	1.04	0.91	0.84	0.98	0.01
BMI (Ref = under/normal weight: <25 kg/m^2)														
Overweight (25 <30 kg/m^2)	1.05	0.98	1.13	0.89	0.63	1.25	0.68	0.98	0.95	1.01	1.04	0.90	1.20	0.46
Obese (≥30 kg/m^2)	0.96	0.87	1.06	0.80	0.53	1.20		0.87	0.83	0.90	0.92	0.77	1.09	
P for trend	0.67			0.29				<0.0001			0.30			
Smoking (Ref = never)														
Current	1.06	0.94	1.20	1.27	0.77	2.08	0.27	0.88	0.84	0.93	0.95	0.77	1.16	0.65
Former	0.90	0.84	0.97	1.26	0.88	1.79		0.92	0.90	0.95	0.92	0.80	1.05	
Unknown	1.07	0.90	1.27	1.50	0.82	2.76		0.87	0.81	0.94	0.77	0.58	1.04	
Alcohol drinks per day (Ref = never)														
Less than a drink/day	1.04	0.95	1.14	1.26	0.88	1.81	0.58	1.09	1.05	1.13	1.12	0.97	1.29	0.22
1–3 drinks/day	1.09	0.98	1.21	1.38	0.86	2.21		1.10	1.06	1.15	0.97	0.79	1.20	
>3-<6 drinks/day	1.08	0.93	1.26	0.92	0.43	1.97		1.20	1.13	1.27	0.89	0.65	1.22	
6 or more drinks/day	1.14	0.96	1.36	1.86	0.92	3.74		1.27	1.18	1.36	1.14	0.83	1.58	
P for trend	0.06			0.17				<0.0001			0.99			
Red meat (g/day) (Ref = quintile 1: 0–30.72)														
Quintile 2: 30.7–52.2	0.99	0.90	1.10	0.97	0.63	1.49	0.63	1.06	1.02	1.10	1.23	1.04	1.45	0.39
Quintile 3: 52.2–77.1	1.09	0.98	1.21	1.36	0.89	2.09		1.07	1.02	1.11	1.12	0.93	1.36	
Quintile 4: 77.1–115.6	1.01	0.90	1.13	0.95	0.57	1.57		1.08	1.03	1.12	1.07	0.87	1.31	
Quintile 5: ≥115.6	1.09	0.97	1.23	0.98	0.58	1.68		1.09	1.04	1.15	0.99	0.79	1.23	
P for trend	0.18			0.90				0.0022			0.59			
Tomato (pyramid servings/day) (Ref = quintile 1: 0–0.27)														
Quintile 2: 0.28–0.42	0.93	0.84	1.03	0.76	0.50	1.17	0.80	1.02	0.98	1.06	0.98	0.83	1.16	0.47
Quintile 3: 0.43–0.60	0.97	0.87	1.07	0.94	0.59	1.49		1.02	0.98	1.06	1.03	0.85	1.25	

No. of cases	Advanced							Non-advanced						
	White men			Black men			*P* [a]	White men			Black men			*P* [a]
	3898			209				24,138			1173			
	HR [b]	95% CI		HR [b]	95% CI			HR [b]	95% CI		HR [b]	95% CI		
Quintile 4: 0.61–0.91	0.97	0.87	1.08	0.74	0.45	1.23		0.99	0.95	1.03	0.84	0.68	1.04	
Quintile 5: ≥0.92	0.89	0.80	1.00	1.01	0.63	1.61		0.98	0.93	1.02	0.93	0.76	1.14	
P for trend	0.08			0.97				0.063			0.31			
Dairy (pyramid servings/day) (Ref = quintile 1: 0–0.52) [c]														
Quintile 2: 0.53–0.88	0.95	0.86	1.05	1.14	0.76	1.70	0.32	1.01	0.97	1.05	1.02	0.86	1.20	0.24
Quintile 3: 0.89–1.32	0.98	0.88	1.09	1.44	0.95	2.17		1.03	0.99	1.08	0.97	0.81	1.17	
Quintile 4: 1.33–2.10	1.02	0.92	1.13	0.92	0.56	1.51		1.07	1.02	1.12	0.86	0.71	1.06	
Quintile 5: ≥2.11	0.95	0.85	1.06	0.85	0.50	1.46		1.07	1.02	1.12	0.98	0.80	1.20	
P for trend	0.58			0.46				0.001			0.55			
Dietary vitamin D (μg/day) (Ref = quintile 1: 0–2.41) [c]														
Quintile 2: 2.42–3.56	1.10	0.99	1.21	1.40	0.92	2.13	0.17	1.02	0.98	1.07	0.88	0.74	1.04	0.14
Quintile 3: 3.57–4.82	1.004	0.90	1.12	1.45	0.91	2.30		1.05	1.001	1.09	0.90	0.74	1.09	
Quintile 4: 4.83–6.87	0.99	0.88	1.10	1.55	0.96	2.51		1.05	1.01	1.10	0.88	0.72	1.08	
Quintile 5: ≥6.88	0.99	0.88	1.11	0.90	0.51	1.58		1.07	1.02	1.12	0.83	0.67	1.03	
P for trend	0.34			0.62				0.004			0.13			

Pyramid serving: tomato = 1 large tomato or eight ounces of tomato juice. Dairy = 1 cup (244 ml) milk or yogurt, 1.5 ounces (42.5 g) of natural cheese, or 2 ounces (56.0 g) of processed cheese

[a] *P* for interaction between each risk factor and race

[b] Adjusted for all factors presented as well as: age (55–59 years, 60–64 years, 65–69 years, ≥70 years); family history of prostate cancer; marital status (married/living as married, never married, separated, divorced, widowed, unknown); attained education (1< 8 years, 8–11 years, post-high school or some college, college and post graduate); and quintiles of total energy intake

[c] Model excludes either dairy or vitamin D due to high correlation (correlation coefficient ≥0.7) between the three variables