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High-quality Diets Associate With Reduced Risk of Colorectal Cancer: Analyses of Diet Quality Indexes in the Multiethnic Cohort

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Abstract

Background & Aims—Healthy eating patterns assessed by diet quality indexes (DQIs) have been related to lower risk of colorectal cancer—mostly among whites. We investigated the associations between 4 DQI scores (the Healthy Eating Index 2010 [HEI-2010], the Alternative Healthy Eating Index 2010 [AHEI-2010], the alternate Mediterranean diet score [aMED], and the Dietary Approaches to Stop Hypertension score) and colorectal cancer risk in the Multiethnic Cohort.

Methods—We analyzed data from 190,949 African Americans, Native Hawaiians, Japanese Americans, Latinos and whites, 45–75 years old, who entered the Multiethnic Cohort study from 1993 through 1996. During an average 16 years of follow up, 4770 invasive colorectal cancer cases were identified.

Results—Scores from all 4 DQIs associated inversely with colorectal cancer risk; higher scores associated with decreasing colorectal cancer risk (all P's for trend .003). Associations were not significant for AHEI-2010 and aMED scores in women after adjustment for covariates: for the highest vs lowest quintiles, the hazard ratio for the HEI-2010 score in men was 0.69 (95% CI, 0.59–0.80) and in women was 0.82 (95% CI , 0.70–0.96); for the AHEI-2010 score the hazard ratio in men was 0.75 (95% CI , 0.65–0.85) and in women was 0.90 (95% CI , 0.78–1.04); for the aMED score the hazard ratio in men was 0.84 (95% CI , 0.73–0.97) and in women was 0.96 (95% CI , 0.82–1.13); for the Dietary Approaches to Stop Hypertension score the hazard ratio in men was 0.75 (95% CI , 0.66–0.86) and in women was 0.86 (95% CI , 0.75–1.00). Associations were

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Conclusions—Based on an analysis of data from the Multiethnic Cohort Study, high-quality diets are associated with a lower risk of colorectal cancer in most racial/ethnic subgroups.

Keywords

DASH; food; nutrition; colon cancer

Introduction

Diet quality indexes have been developed to assess overall dietary patterns, in contrast to a single nutrient or food, by using a hypothesis-oriented ('a priori') methodology.^{1–3} Several indexes have been applied to evaluate the role of diet in various health outcomes.^{4–6} Indeed, they have been associated with a lower risk of colorectal cancer,^{7–10} the third most common cancer in the United States.¹¹

The Dietary Patterns Methods Project (DPMP) was initiated as a collaboration of four research groups to strengthen research evidence on dietary indices, dietary patterns, and health.¹² The DPMP selected four indexes with particular relevance for dietary guidance that had been commonly used in US populations: the Healthy Eating Index 2010 (HEI-2010),¹³ the Alternative Healthy Eating Index 2010 (AHEI-2010),¹⁴ the alternate Mediterranean diet score (aMED),¹⁵ and the Dietary Approaches to Stop Hypertension (DASH) score.¹⁶ The DPMP developed a standardized protocol for application in three large cohorts: the Multiethnic Cohort Study (MEC),¹⁷ the NIH-AARP Diet and Health Study,¹⁸ and the Women's Health Initiative Observational Study.¹⁹ All dietary indexes were consistently associated with a reduced risk of all-cause mortality across the three cohorts.¹²

Previous studies on diet quality indexes and colorectal cancer have been performed mostly among whites. Therefore, we investigated the associations between the four diet quality indexes and colorectal cancer risk in the racially heterogeneous MEC population and studied whether associations varied by race/ethnicity, sex, and anatomical subsite.

Materials and Methods

Study Population

The MEC is a prospective cohort study established to investigate lifestyle factors, especially diet, in relation to cancer and other chronic diseases.²⁰ The appropriate institutional review boards of the University of Hawaii and the University of Southern California approved the study protocol. In brief, more than 215,000 adults aged 45–75 years enrolled in MEC between 1993 and 1996 by completing a self-administered, comprehensive questionnaire that included a detailed dietary assessment.²⁰ Study participants were primarily of five major race/ethnicities, African American, Native Hawaiian, Japanese American, Latino and white by design through targeted recruitment. For the current analyses, we excluded participants who were not one of the five racial/ethnic groups (n=13,987), had prior colorectal cancer reported on the baseline questionnaire (n=2,251) or from tumor registries (n=300), and

reported implausible diets based on total energy intake or its components (n=8,137). Specifically, we excluded individuals in the top and bottom 10% tails of the log energy distribution. Then we computed a robust standard deviation (RSD) with an assumption of a truncated normal distribution. Finally, we excluded all individuals with energy values out of the ranges of means \pm 3 RSD. We used a similar approach to exclude individuals with extreme fat, protein, or carbohydrate intakes. ²¹ As a result, a total of 190,949 were included in the current analysis.

Dietary Assessment and Calculation of Dietary Indexes

The baseline questionnaire included a quantitative food frequency questionnaire (QFFQ) with >180 food items, which was developed on the basis of 3-day measured dietary records from approximately 60 men and women of each ethnic group.²⁰ A calibration study showed satisfactory correlations for nutrients and for the MyPyramid Equivalent Database values used in the dietary quality indexes between the QFFQ and three repeated 24-hour recalls for all ethnic-sex groups.²² Daily nutrient intakes from the QFFQ were calculated using the food composition tables developed and maintained at the University of Hawaii Cancer Center for use in the MEC.

As previously described elsewhere,¹² we calculated four dietary indexes for the MEC as part of the DPMP project: HEI-2010, AHEI-2010, aMED, and DASH scores. In brief, the HEI-2010 was developed to quantify adherence to the 2010 Dietary Guidelines for Americans, with higher scores reflecting better quality and adherence.^{13, 23} The HEI-2010 scores 12 components for a total of 100 points. The AHEI-2010 was developed to identify dietary patterns consistently associated with lower risk of chronic disease in clinical and epidemiologic investigations.^{14, 24–26} The AHEI-2010 scores 11 components for a total of 110 points. The aMED score was an adaptation of the Mediterranean diet score, with consideration for eating behaviors consistently associated with lower risks of chronic disease in studies.^{16, 27} The aMED scores 9 components for a total of 9 points. The DASH score was designed to capture the diet tested in 2 DASH feeding trials, which examined the role of dietary patterns on blood pressure.^{28, 29} The DASH, as specified by Fung et al.,¹⁶ scores 8 components for a total of 40 points. The specific dietary components included in the indexes are described in Supplementary Table 1.¹⁷ Some line items in the QFFQ combined or omitted foods, which require modifications to some components. We added foods that became more commonly consumed such as soybeans, fortified drinks and energy drinks. We also added more examples for aggregate food items, such as cream soups.

Case Ascertainment

Invasive incident colorectal cancer cases were identified by linkage to the Surveillance, Epidemiology and End Results Program tumor registries in Hawaii and California. Deaths were identified by linkage to death certificate files in both states and the National Death Index. Case and death ascertainment was complete through December 31, 2012. Cases in the current study were limited to invasive adenocarcinoma of the large bowel and were categorized according to anatomical subsites using International Classification of Disease (ICD)-O2 codes: C18.0–C18.5 for right colon, C18.6–C18.7 for left colon and C19.9 and C20.9 for rectum. During an average follow-up period of 16 years, 3,663 colon and 1,072

rectal cancer cases were identified, while an additional 35 cases had synchronous tumors at both colon and rectum sites.

Statistical Analysis

Cox proportional hazards models of colorectal cancer with age as the time metric were used to calculate hazard ratios (HRs) and 95% confidence intervals (95% CIs). The age period of observation was the age at cohort entry to the earliest of the following ages: age at diagnosis, age at death and age at study close (December 31, 2012). Diet quality indexes were categorized into quintiles based on their distributions across the entire cohort and indicator variables denoting quintile membership were included in the models. Additionally, trend variables for the indexes were assigned the sex- and ethnicity-specific median values for quintiles. The proportional hazards assumption was tested by Schoenfeld residuals and found to be met. Base models for men and women separately were adjusted for race/ ethnicity as a strata variable and age at cohort entry as a covariate. Multivariate models were further adjusted for family history of colorectal cancer (yes/no), history of colorectal polyp (yes/no), BMI (<25, 25-<30 and 30 kg/m²), pack-years of cigarette smoking (continuous), multivitamin use (yes/no), nonsteroidal anti-inflammatory drug use (yes/no), physical activity (hours spent in vigorous work or sports per day), menopausal status and menopausal hormone therapy use (premenopausal; postmenopausal: never; past; current use) for women only and total energy (log transformed kcal/day). For the HEI-2010 and DASH score models, alcohol consumption (g/day) was additionally adjusted. Participants with missing data on covariates (n=23,134) were excluded from the multivariate models, resulting in 167,815 participants. Since subgroup analysis showed similar association patterns in men and women, we present models combining men and women using multivariate adjustment. In supplemental analyses, diet quality indexes were updated as time-dependent variables using data from a follow-up questionnaire (2003–2007) that were available for 77,919 (41%) of the 190,949 participants.

Tests for heterogeneity between subgroups were based on the Wald statistics for crossproduct terms of trend variables and subgroup membership (sex and race/ethnicity). Tests for heterogeneity by anatomical subsite were based on the Wald statistics using competing risk methodology.³⁰ All statistical tests were two-sided. All analyses were performed by using SAS statistical software, version 9.4 (SAS Institute, Inc., Cary, NC).

Results

Mean HEI-2010 score was higher in women (72.9) than in men (68.0). Japanese Americans (70.0 in men, 75.4 in women) had the highest, and African Americans (66.7 in men, 71.9 in women) and Latinos (66.9 in men, 71.7 in women) had the lowest HEI-2010 scores. For the AHEI-2010, mean scores were highest in Japanese Americans and lowest in Latinos. Differences in other two indexes between men and women were smaller.

Across the indexes, men and women in the highest quintiles (Q5) were more likely to be older, never smokers, and more physically active, to have family history of colorectal cancer, history of intestinal polyps, and lower BMI, and to use multivitamin supplements, compared with those in the lowest quintiles (Q1) (Table 1). Men and women in Q5 had higher energy

intakes than in Q1, with the exception of the HEI-2010. The proportions of Japanese Americans were higher in Q5 than in Q1 for all indexes except for the DASH score. The proportions of Latinos and whites were higher in Q5 than in Q1 for the DASH score. Women in Q5 of the indexes tended to be more often menopausal hormone therapy users, compared with those in Q1. Although the HEI-2010 and DASH scores do not include alcohol as a component, participants in Q5 had lower alcohol intakes than did those in Q1 for all indexes.

In both men and women, all four scores were inversely associated with risk of colorectal cancer adjusting for age and race/ethnicity (Table 2). In multivariate models, further adjustment for covariates slightly weakened the associations, especially in women, and the associations with the AHEI-2010 and aMED score were no longer statistically significant. However, tests for heterogeneity did not show statistically significant differences in the associations between men and women (P's for heterogeneity > .13). In men, the risk reductions were greater for the HEI-2010, AHEI-2010, and DASH score than for the aMED score.

In anatomical subsite-specific analyses in men and women combined (Table 3), all four dietary scores were inversely associated with risk of tumors of the rectum and left colon, but not of the right colon and the difference was statistically significant. Overall, the inverse associations for rectum and left colon tumors were stronger with the HEI-2010, AHEI-2010, and DASH score than with the aMED score. These patterns were seen in men and women.

The HEI-2010 was inversely associated with risk of colorectal cancer in all five racial/ethnic groups (Table 4), although the associations were not statistically significant in African Americans and Native Hawaiians (P for heterogeneity = .03). Latinos and whites showed inverse associations with all four indexes. When we further stratified Latinos by place of birth (Supplementary Table 2), the associations were observed among US-born Latinos, especially for HEI-2010 (P for heterogeneity = .05) and AHIE-2010 (P for heterogeneity = .07). For Japanese Americans, the aMED score was not associated, while the other three indexes were significantly inversely associated with colorectal cancer risk. Overall, for African Americans, the association was weakest or null between dietary indexes and colorectal cancer risk (P for heterogeneity between African Americans vs. the other four groups combined = .02 for HEI-2010 and DASH score). The associations did not differ between ever vs. never users of menopausal hormone therapy among women (P's for heterogeneity > .40, data not shown).

Discussion

In this large multiethnic population, all four diet quality indexes examined were inversely associated with colorectal cancer risk in both men and women, although the associations for the AHEI-2010 and aMED score after adjustment for potential confounding factors did not remain statistically significant in women. Associations were limited to the left colon and rectum for all indexes. Inverse associations were less strong in African Americans than in the other four racial/ethnic groups for all four indexes.

Several meta- or pooled analyses and systematic literature reviews have supported the relationship between higher diet quality indexes and a lower risk of colorectal cancer. A meta-analysis of two cohort studies showed an inverse association of the HEI, AHEI, and DASH scores with colorectal cancer risk (RR=0.77, 95% CI: 0.70–0.84 for the highest vs. lowest quintile), but the MED score was not investigated.⁴ All but one of the reports from the eight individual studies investigating the association between a diet quality index and colorectal cancer reported an inverse relationship.⁵ Of these seven studies, three used a variation of the Mediterranean diet score, two used adaptations of the DASH index, and two used HEI variants.⁵ A pooled analysis of nine cohort studies studying adherence to a Mediterranean diet showed a 9% reduction (95% CI for HR: 0.84–0.98) in colorectal cancer incidence for the highest vs. lowest quantile.⁶ A systematic literature review of five case-control and seven cohort studies also supported the association between a higher overall diet quality, including Mediterranean diet score and HEI, and a lower risk of colorectal cancer, and suggested similar associations for men and women.⁸

In the Women's Health Initiative Observation Study, one of the three large cohorts where the four indexes are applied, the HEI-2010 and DASH, but not AHEI-2010 and aMED, scores were inversely associated with colorectal cancer risk in postmenopausal women.³¹ Among MEC female participants in this study, we also observed weaker association with AHEI-2010 and aMED than with HEI-2010 and DASH scores. The former two indexes consider alcohol consumption, while the latter two indexes do not. However, additionally adjusting for alcohol consumption in the models for AHEI-2010 and aMED score did not change the results.

Previous studies had limited statistical power to investigate associations with diet quality indexes in racial/ethnic groups other than whites. In the present study, overall risk reduction was suggested for, but smaller in, African Americans than in the other four racial/ethnic groups, i.e., Native Hawaiians, Japanese Americans, Latinos, and whites. In past analysis of individual dietary components examined in the MEC, however, we found no racial/ethnic difference in relation to colorectal cancer risk, including dietary fiber,^{32, 33} meat,³⁴ calcium and vitamin D,³⁵ carotenoids,³⁶ plasma levels of B vitamins³⁷ and vitamin D.³⁸ Since the incidence rate of colorectal cancer is higher among African Americans than any other racial group in the MEC females³⁹ and in the US,¹¹ the possibility that overall diet quality may play less of a role in colorectal cancer in African Americans warrants further investigation. It is notable that the associations of the HEI-2010 and AHEI-2010 with colorectal cancer were observed only in US-born and not in foreign-born Latinos in the MEC. We speculate that the dietary indexes predict risk of colorectal cancer better in US-born Latinos because of their more Americanized diet and a higher incidence of the disease compared to foreign-born Latinos.

In our previous studies in the MEC, all four indexes were inversely associated with mortality from all causes, cardiovascular disease mortality, and cancer mortality in men and women.¹⁷ The aMED score, but not the HEI-2010, AHEI-2010, or DASH score, was inversely associated with colorectal cancer-specific death among colorectal cancer cases.⁴⁰ The inverse relationship with colorectal cancer survival for the aMED score was limited to African Americans and to colon (compared with rectal) tumors.⁴⁰ In the Hawaii component

of the MEC, high scores for the DASH were related to a 10–30% lower risk of Type 2 diabetes, whereas the AHEI-2010 and aMED score showed weaker associations, and the HEI-2010 was not related to the risk of Type 2 diabetes.⁴¹ When looking into individual components for the HEI-2010, which had stronger associations compared with the other three indexes in the current study, 4 components, greens and beans, dairy, sodium, and empty calories, among the 12 components showed a statistically significant association with colorectal cancer risk. The associations with the aMED score were less strong than those with the other three indexes. The aMED score does not consider sodium, dairy, and empty calories, which were related to colorectal cancer risk among the HEI-2010 components. On the contrary, it is speculated that these components may have different roles in colorectal cancer survival so that the aMED score was associated with colorectal cancer survival.⁴⁰

Strengths of the study include its prospective design, large number of participants from various racial/ethnic backgrounds, a long follow-up period, and comprehensive information on a wide range of potential confounding factors. However, dietary measurements based on a self-administered QFFQ are subject to measurement error, which is most likely nondifferential (uncorrelated with disease) in a cohort study resulting in attenuated risk estimates.⁴² Despite of a large overall sample size, some subgroup analyses might still have limited statistical power. Dietary habits may vary during the follow-up period. When analyzing data updated with a follow-up QFFQ administered approximately 10 years after the baseline among the 41% of the participants who returned this questionnaire, the results did not change. However, participants who completed the follow-up QFFQ were somewhat different than non-respondents: more likely to be younger (57.9 vs. 61.3 years), Japanese American (33.9% vs. 24.4%), white (29.5% vs. 21.3%), never smokers (47.2% vs. 41.9), more educated (graduated college 35.4% vs. 19.6%), and less obese (17.1% vs. 31.8%), although the proportions of females were similar between the two groups (55.4% vs. 54.8%).

In conclusion, in a multiethnic population, we found that higher HEI-2010, AHEI-2010, aMED, and DASH scores were associated with a lower risk of colorectal cancer both in men and women. The inverse associations were stronger for the left colon and rectum and were suggested for all racial/ethnic groups.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Abbreviations

| AHEI | Alternative Healthy Eating Index |
|------|------------------------------------|
| aMED | alternate Mediterranean diet score |

| CI | confidence interval |
|------|---|
| DASH | Dietary Approaches to Stop Hypertension |
| DQI | Dietary Quality Index |
| HEI | Healthy Eating Index |
| HR | hazard ratio |
| MEC | Multiethnic Cohort |
| QFFQ | quantitative food frequency questionnaire |

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Table 1

Baseline characteristics of 190,949 participants by lowest (Q1) and highest (Q5) quintiles of the four diet quality indexes in the Multiethnic Cohort Study

| | QI | Q5 | QI | Q5 | Q1 | Q5 | QI | Q5 |
|--|--------------|----------------|--------------|--------------|--------------|--------------|--------------|--------------|
| Men | n=23,802 | n=11,215 | n=19,024 | n=16,565 | n=16,987 | n=21,414 | n=18,912 | n=19,830 |
| Age at cohort entry, y, mean (SD) | 58.6 (8.8) | 62.6 (8.4) | 58.2 (8.8) | 61.7 (8.8) | 59.4 (8.8) | 60.7 (8.9) | 57.4 (8.6) | 62.2 (8.6) |
| Race/ethnicity, n (%) ^a | | | | | | | | |
| African American | 4030 (16.9) | 1585 (14.1) | 2895 (15.2) | 1862 (11.2) | 2799 (16.5) | 2719 (12.7) | 2816 (14.9) | 2399 (12.1) |
| Native Hawaiian | 1657 (7.0) | 706 (6.3) | 1366 (7.2) | 1091 (6.6) | 1081 (6.4) | 1681 (7.9) | 1916 (10.1) | 983 (5.0) |
| Japanese American | 5033 (21.1) | 3885 (34.6) | 4639 (24.4) | 6257 (37.8) | 4411 (26.0) | 7015 (32.8) | 7639 (40.4) | 4550 (22.9) |
| Latino | 6442 (27.1) | 2005 (17.9) | 5424 (28.5) | 2447 (14.8) | 4599 (27.1) | 4170 (19.5) | 3576 (18.9) | 4830 (24.4) |
| White | 6640 (27.9) | 3034 (27.1) | 4700 (24.7) | 4908 (29.6) | 4097 (24.1) | 5829 (27.2) | 2965 (15.7) | 7068 (35.6) |
| Family history of colorectal cancer, n (%) | 1607 (6.8) | (6.7) 168 | 1266 (6.7) | 1332 (8.0) | 1157 (6.8) | 1685 (7.9) | 1351 (7.1) | 1463 (7.4) |
| History of intestinal polyps, n (%) | 1326 (5.6) | 943 (8.4) | 1007 (5.3) | 1411 (8.5) | 980 (5.8) | 1712 (8.0) | 1090 (5.8) | 1465 (7.4) |
| Body mass index, kg/m ² , mean (SD) | 26.7 (4.3) | 26.1 (3.9) | 26.8 (4.3) | 26.0 (4.0) | 26.8 (4.3) | 26.4 (4.2) | 26.8 (4.4) | 26.2 (4.0) |
| Ever smokers, n (%) | 18512 (78.7) | 6766 (60.9) | 13980 (74.3) | 11037 (67.2) | 12318 (73.4) | 14168 (66.8) | 14326 (76.5) | 12478 (63.6) |
| Pack-years among ever smokers, mean (SD) | 23.9 (17.5) | 17.8 (15.6) | 23.2 (17.3) | 19.0 (15.8) | 22.7 (17.3) | 18.8 (15.9) | 23.5 (16.9) | 18.1 (16.0) |
| Multivitamin use, n (%) | 9641 (41.3) | 6160 (55.9) | 7564 (40.5) | 8884 (54.5) | 6838 (41.2) | 11476 (54.4) | 7070 (38.1) | 10971 (56.2) |
| NSAID use, n (%) | 11936 (51.2) | 5651 (51.3) | 9212 (49.4) | 8235 (50.6) | 8307 (50.2) | 11042 (52.3) | 8483 (45.8) | 10492 (54.0) |
| Physical activity, hours/day, mean $(SD)^b$ | 0.61 (1.10) | $0.54\ (0.93)$ | 0.59~(1.09) | 0.60 (0.97) | 0.48 (0.95) | 0.68 (1.08) | 0.57 (1.06) | 0.63(1.01) |
| Energy intake, kcal/day, mean (SD) | 2533 (1219) | 2188 (914) | 2280 (1088) | 2439 (986) | 1746 (757) | 3010 (1205) | 2129 (906) | 2622 (1180) |
| Alcohol intake, g/day, mean (SD) | 33.9 (53.6) | 3.3 (6.6) | 24.6 (52.8) | 10.7 (14.0) | 16.0(40.2) | 13.3 (24.8) | 18.5 (39.9) | 11.3 (24.4) |
| Women | n=14,387 | n=26,975 | n=19,165 | n=21,625 | n=22,237 | n=24,921 | n=22,756 | n=23,815 |
| Age at cohort entry, y, mean (SD) | 57.4 (8.8) | 61.7 (8.5) | 57.5 (8.8) | 61.2 (8.7) | 58.6 (8.9) | 60.7 (8.7) | 57.1 (8.7) | 61.7 (8.5) |
| Race/ethnicity, n $(\%)^{a}$ | | | | | | | | |
| African American | 3778 (26.3) | 5459 (20.2) | 4170 (21.8) | 3838 (17.7) | 4616 (20.8) | 4918 (19.7) | 5276 (23.2) | 3974 (16.7) |
| Native Hawaiian | 1139 (7.9) | 1770 (6.6) | 1511 (7.9) | 1582 (7.3) | 1431 (6.4) | 2267 (9.1) | 2373 (10.4) | 1385 (5.8) |
| Japanese American | 1692 (11.8) | 8801 (32.6) | 3938 (20.5) | 7836 (36.2) | 5179 (23.3) | 7614 (30.6) | 7405 (32.5) | 5476 (23.0) |
| Latino | 3516 (24.4) | 4511 (16.7) | 4971 (25.9) | 2531 (11.7) | 5315 (23.9) | 4284 (17.2) | 4238 (18.6) | 5268 (22.1) |
| White | 4262 (29.6) | 6434 (23.9) | 4575 (23.9) | 5838 (27.0) | 5696 (25.6) | 5838 (23.4) | 3464 (15.2) | 7712 (32.4) |

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| | HEI-2010 | 2010 | AHEI-2010 | -2010 | aMED | ED | DA | DASH |
|--|-------------|--------------|--------------|--------------|---------------------------|---|--------------|--------------|
| | Q1 | Q5 | QI | Q5 | Q1 | Q5 | QI | Q5 |
| Family history of colorectal cancer, n (%) | 1104 (7.7) | 2543 (9.4) | 1431 (7.5) | 2123 (9.8) | 1703 (7.7) | 2335 (9.4) | 1817 (8.0) | 2171 (9.1) |
| History of intestinal polyps, n (%) | 493 (3.4) | 1356 (5.0) | 666 (3.5) | 1089 (5.0) | 841 (3.8) | 1190 (4.8) | 885 (3.9) | 1147 (4.8) |
| Body mass index, kg/m ² , mean (SD) | 27.3 (6.4) | 25.9 (5.3) | 27.3 (6.2) | 25.5 (5.5) | 26.9 (5.9) | 26.1 (5.7) | 27.2 (6.2) | 25.7 (5.3) |
| Ever smokers, n (%) | 8463 (59.9) | 9845 (37.1) | 9259 (49.2) | 9185 (43.1) | 10525 (48.1) | 10525 (48.1) 10097 (41.3) 11341 (50.6) | 11341 (50.6) | 9368 (40.2) |
| Pack-years among ever smokers, mean (SD) | 19.8 (16.1) | 13.0 (13.0) | 17.9 (15.6) | 14.2 (13.6) | 17.2 (15.3) | 13.6 (13.4) | 17.4 (14.7) | 13.5 (13.7) |
| Multivitamin use, n (%) | 6376 (45.6) | 15801 (59.9) | 8483 (45.6) | 12701 (60.1) | 10045 (46.5) 14871 (60.9) | 14871 (60.9) | 9607 (43.4) | 14544 (62.5) |
| NSAID use, n (%) | 8555 (61.2) | 13007 (49.3) | 10557 (56.8) | 10353 (49.0) | 11805 (54.8) | 13007 (49.3) 10557 (56.8) 10353 (49.0) 11805 (54.8) 12899 (52.9) 11827 (53.5) | 11827 (53.5) | 12265 (52.9) |
| MHT ever use among postmenopausal women, n (%) | 5489 (50.1) | 13786 (58.7) | 7344 (50.5) | 10761 (58.4) | 9105 (52.3) | 11910 (56.7) | 8362 (49.7) | 12017 (58.4) |
| Physical activity, hours/day, mean $(\mathrm{SD})^b$ | 0.20 (0.58) | 0.22 (0.52) | 0.18 (0.54) | 0.25 (0.56) | 0.16~(0.49) | 0.27 (0.61) | 0.17 (0.51) | 0.27 (0.61) |
| Energy intake, kcal/day, mean (SD) | 2068 (1092) | 1858 (812) | 1726 (874) | 2097 (861) | 1362 (570) | 2572 (1076) | 1644 (721) | 2255 (1043) |
| Alcohol intake, g/day, mean (SD) | 13.9 (33.5) | 1.4 (4.2) | 6.4 (24.2) | 4.2 (8.8) | 4.5 (17.2) | 4.1 (12.4) | 4.8 (18.3) | 3.9 (12.6) |

opausal hormone therapy; NSAID, nonsteroidal anti-inflammatory drug.

^aColumn percentages.

 $b_{\mbox{Hours}}$ spent in vigorous work or sports per day.

Table 2

Dietary quality indexes and colorectal cancer risk in the Multiethnic Cohort Study, 1993–2012

| | | Men (n : | Men (n = 85,905) | | | Women (n | Women (n = 105,044) | (1 | P for heterogeneity ^d |
|------------------------------|-------|--------------------------|--------------------|--------------------------|-------|--------------------------|---------------------|--------------------------|----------------------------------|
| | Cases | HR (95% CI) ^a | Cases ^b | HR (95% CI) ^c | Cases | HR (95% CI) ^a | Cases ^b | HR (95% CI) ^c | |
| HEI-2010 | | | | | | | | | |
| 1 (21.1–62.4) | 769 | 1.00 (ref) | 702 | 1.00 (ref) | 337 | 1.00 (ref) | 279 | 1.00 (ref) | |
| 2 (62.5–69.5) | 547 | $0.76\ (0.68-0.85)$ | 496 | 0.81 (0.72–0.91) | 377 | 0.82 (0.71–0.95) | 312 | 0.87 (0.74–1.03) | |
| 3 (69.6–74.7) | 488 | 0.75 (0.67–0.84) | 434 | 0.80 (0.70-0.91) | 454 | 0.78 (0.67–0.89) | 389 | 0.86 (0.73–1.01) | |
| 4 (74.8–79.4) | 372 | 0.64 (0.57–0.73) | 339 | 0.72 (0.62–0.82) | 512 | 0.72 (0.62–0.82) | 421 | 0.78 (0.66–0.91) | |
| 5 (79.5–98.8) | 300 | 0.62 (0.54–0;71: | 267 | $0.69\ (0.59-0.80)$ | 614 | $0.70\ (0.61{-}0.81)$ | 536 | 0.82 (0.70–0.96) | |
| P for trend $^{\mathcal{C}}$ | | <.001 | | < .001 | | <.001 | | .008 | .14 |
| AHEI-2010 | | | | | | | | | |
| 1 (25.1–56.6) | 571 | 1.00 (ref) | 522 | 1.00 (ref) | 424 | 1.00 (ref) | 354 | 1.00 (ref) | |
| 2 (56.7–62.3) | 483 | 0.83 (0.74–0.94) | 429 | 0.84 (0.73–0.95) | 440 | 0.88 (0.77–1.00) | 367 | 0.92 (0.79–1.06) | |
| 3 (62.4–67.1) | 455 | 0.79 (0.70–0.90) | 410 | 0.82 (0.72–0.93) | 433 | 0.78 (0.68–0.89) | 370 | 0.84 (0.73–0.98) | |
| 4 (67.2–72.6) | 516 | $0.89\ (0.79{-}1.00)$ | 465 | 0.92 (0.81–1.04) | 490 | 0.82 (0.71–0.93) | 415 | 0.89 (0.77–1.03) | |
| 5 (72.7–104.5) | 451 | 0.70 (0.62–0.80) | 412 | 0.75 (0.65–0.85) | 507 | 0.81 (0.71–0.92) | 431 | 0.90 (0.78–1.04) | |
| P for trend $^{\mathcal{C}}$ | | < .001 | | < .001 | | .002 | | .18 | .32 |
| aMED | | | | | | | | | |
| 1 (0–2) | 487 | 1.00 (ref) | 432 | 1.00 (ref) | 493 | 1.00 (ref) | 398 | 1.00 (ref) | |
| 2 (3) | 455 | 0.99 (0.87–1.12) | 405 | 0.98 (0.85–1.12) | 418 | 0.94 (0.82–1.07) | 362 | 1.03 (0.89–1.19) | |
| 3 (4) | 522 | 1.02 (0.90–1.15) | 468 | 0.99 (0.87–1.14) | 428 | 0.87 (0.77–0.99) | 375 | 0.99 (0.85–1.15) | |
| 4 (5) | 414 | 0.85 (0.74–0.96) | 380 | 0.84 (0.72–0.97) | 407 | 0.86 (0.76–0.98) | 342 | 0.97 (0.83–1.13) | |
| 5 (6-9) | 598 | 0.85 (0.75–0.96) | 553 | 0.84 (0.73–0.97) | 548 | 0.84 (0.74–0.95) | 460 | 0.96 (0.82–1.13) | |
| P for trend $^{\mathcal{C}}$ | | < .001 | | .004 | | .003 | | .45 | .91 |
| DASH | | | | | | | | | |
| 1 (8-20) | 606 | 1.00 (ref) | 556 | 1.00 (ref) | 528 | 1.00 (ref) | 435 | 1.00 (ref) | |
| 2 (21–22) | 363 | 0.84 (0.73–0.95) | 328 | 0.85 (0.74–0.97) | 346 | 0.89 (0.78–1.02) | 298 | 0.98 (0.85–1.14) | |
| 3 (23–25) | 594 | 0.78 (0.70–0.88) | 535 | 0.81 (0.72–0.92) | 553 | 0.78 (0.69–0.88) | 469 | 0.86 (0.75–0.99) | |
| 4 (26–27) | 376 | $0.78\ (0.68-0.89)$ | 340 | 0.82 (0.71–0.95) | 361 | 0.79 (0.69–0.91) | 304 | 0.90 (0.77–1.05) | |

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| | | Men (n : | Men (n = 85,905) | | | Women (n | Women (n = 105,044) | (1 | P for heterogeneity d |
|--------------------------|-------|--------------------------|------------------|--|-------|--|---------------------|--------------------------|--------------------------|
| | Cases | HR (95% CI) ^a | Casesb | HR $(95\% \text{ CI})^{d}$ Cases ^b HR $(95\% \text{ CI})^{c}$ | Cases | HR $(95\% \text{ CI})^a$ Cases^b HR $(95\% \text{ CI})^c$ | Cases ^b | HR (95% CI) ^c | |
| 5 (28-40) | 537 | 0.70 (0.62–0.79) 479 | 479 | 0.75 (0.66–0.86) 506 | 506 | 0.73 (0.64–0.83) 431 | 431 | 0.86 (0.75–1.00) | |
| P for trend ^e | | < .001 | | < .001 | | < .001 | | .04 | .32 |

AHEI-2010, Alternative Healthy Eating Index 2010; aMED, alternate Mediternanean diet; DASH, Dietary Approaches to Stop Hypertension; HEI-2010, Healthy Eating Index 2010.

 a djusted in Cox regression model of colorectal cancer for age at cohort entry and ethnicity as strata variables.

 $\boldsymbol{b}_{\text{Excluding participants with missing data on any of the covariates.$

vigorous physical activity, menopausal status and menopausal hormone therapy use for women only, and total energy. For HEI-2010 and DASH, the models were further adjusted for alcohol consumption. c Additionally adjusted for family history of colorectal cancer, history of colorectal polyp, body mass index, pack-years of cigarette smoking, multivitamin use, nonsteroidal anti-inflammatory drug use,

d based on Wald test of cross-product terms of sex and the trend variable for the dietary index, adjusting for the covariates in the multivariate models.

 e^{2} Trend variables were assigned the sex- and ethnicity-specific median values for quintiles.

Table 3

Dietary quality indexes and colorectal cancer risk by anatomic subsite in the Multiethnic Cohort Study, 1993–2012

| | Right c | Right colon (1,958 cases) | Left co | Left colon (1,178 cases) | Rect | Rectum (960 cases) | P for heterogeneity between subsites b |
|------------------------------|---------|---------------------------|---------|--------------------------|-------|--------------------------|---|
| | Cases | HR (95% CI) ^a | Cases | HR (95% CI) ^a | Cases | HR (95% CI) ^a | |
| HEI-2010 | | | | | | | |
| 1 (21.1–62.4) | 396 | 1.00 (ref) | 301 | 1.00 (ref) | 272 | 1.00 (ref) | |
| 2 (62.5–69.5) | 372 | 0.93 (0.80–1.07) | 227 | 0.76 (0.63–0.91) | 192 | $0.73\ (0.61{-}0.89)$ | |
| 3 (69.6–74.7) | 380 | 0.90 (0.78–1.05) | 235 | 0.76 (0.64–0.92) | 191 | 0.73 (0.60 - 0.89) | |
| 4 (74.8–79.4) | 371 | 0.84 (0.72–0.98) | 194 | 0.62 (0.51–0.75) | 175 | 0.67 (0.54–0.82) | |
| 5 (79.5–98.8) | 439 | 0.92 (0.79–1.07) | 221 | 0.71 (0.58–0.86) | 130 | 0.51 (0.40 - 0.64) | |
| P for trend $^{\mathcal{C}}$ | | .15 | | <.001 | | <.001 | <.001 |
| AHEI-2010 | | | | | | | |
| 1 (25.1–56.6) | 370 | 1.00 (ref) | 263 | 1.00 (ref) | 230 | 1.00 (ref) | |
| 2 (56.7–62.3) | 366 | 0.92 (0.79–1.06) | 212 | 0.78 (0.65–0.94) | 200 | 0.87 (0.72–1.05) | |
| 3 (62.4–67.1) | 357 | $0.86\ (0.74-0.99)$ | 235 | 0.85 (0.71–1.01) | 171 | 0.72 (0.59–0.88) | |
| 4 (67.2–72.6) | 437 | 1.01 (0.87–1.16) | 246 | 0.86 (0.72–1.03) | 186 | 0.76 (0.63–0.93) | |
| 5 (72.7–104.5) | 428 | $0.94\ (0.81{-}1.08)$ | 222 | 0.73 (0.61–0.89) | 173 | 0.66(0.54 - 0.81) | |
| P for trend $^{\mathcal{C}}$ | | .74 | | .008 | | <.001 | <.001 |
| aMED | | | | | | | |
| 1 (0–2) | 376 | 1.00 (ref) | 246 | 1.00 (ref) | 191 | 1.00 (ref) | |
| 2 (3) | 344 | 0.99 (0.86–1.15) | 216 | 0.96 (0.80–1.15) | 194 | 1.08 (0.88–1.32) | |
| 3 (4) | 384 | 1.00(0.87 - 1.16) | 239 | 0.96 (0.80–1.15) | 207 | 1.02 (0.84–1.26) | |
| 4 (5) | 356 | 0.98 (0.84–1.14) | 206 | 0.88 (0.72–1.07) | 143 | 0.74 (0.59–0.93) | |
| 5 (6–9) | 498 | 0.98 (0.84–1.14) | 271 | 0.83 (0.68–1.02) | 225 | 0.81 (0.65–1.02) | |
| P for trend $^{\mathcal{C}}$ | | .73 | | .05 | | .004 | .07 |
| DASH | | | | | | | |
| 1 (8-20) | 390 | 1.00 (ref) | 307 | 1.00 (ref) | 274 | 1.00 (ref) | |
| 2 (21–22) | 281 | 0.99 (0.84–1.15) | 175 | 0.85 (0.71–1.03) | 157 | 0.85 (0.70–1.04) | |
| 3 (23–25) | 506 | 0.99 (0.87–1.14) | 278 | 0.80 (0.68–0.95) | 201 | 0.64 (0.53–0.77) | |
| 4 (26–27) | 305 | $0.94\ (0.81{-}1.10)$ | 191 | 0.91 (0.75–1.09) | 142 | 0.72 (0.59–0.90) | |

| | Right c | Right colon (1,958 cases) Left colon (1,178 cases) Rectum (960 cases) | Left co | lon (1,178 cases) | Rect | um (960 cases) | P for heterogeneity between subsites b |
|------------------------------|---------|--|---------|--------------------------|-------|--------------------------|--|
| | Cases | Cases HR (95% CI) ^d Cases HR (95% CI) ^d Cases HR (95% CI) ^d | Cases | HR (95% CI) ^a | Cases | HR (95% CI) ^a | |
| 5 (28-40) | 476 | 476 0.96 (0.83–1.11) 227 0.73 (0.61–0.89) 186 0.63 (0.51–0.77) | 227 | 0.73 (0.61–0.89) | 186 | 0.63 (0.51–0.77) | |
| P for trend $^{\mathcal{C}}$ | | .46 | | .004 | | < .001 | < .001 |

AHEI-2010, Altemative Healthy Eating Index 2010; aMED, altemate Mediterranean diet; DASH, Dietary Approaches to Stop Hypertension; HEI-2010, Healthy Eating Index 2010.

^a Adjusted for age at cohort entry, sex, ethnicity, family history of colorectal cancer, history of colorectal polyp, body mass index, pack-years of cigarette smoking, multivitamin use, nonsteroidal anti-inflammatory drug use, vigorous physical activity, menopausal status and menopausal hormone therapy use, and total energy. for HEL-2010 and DASH Additionally adjusted for alcohol consumption.

b based on Wald test comparing subsite-specific associations in a competing risk model, adjusting for the covariates in the multivariate model.

 $^{\mathcal{C}}$ Trend variables were assigned the sex- and ethnicity-specific median values for quintiles.

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Table 4

Dietary quality indexes and colorectal cancer risk by race/ethnicity in the Multiethnic Cohort Study, 1993–2012

| | Author |
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| , | script |

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|------------------------------|-------|--------------------------|-------|--------------------------|-------|--------------------------|-------|--------------------------|-------|--------------------------|----------------------------|
| | Cases | HR (95% CI) ^a | Cases | HR (95% CI) ^a | Cases | HR (95% CI) ^a | Cases | HR (95% CI) ^d | Cases | HR (95% CI) ^a | |
| HEI-2010 | | | | | | | | | | | |
| 1 (21.1–62.4) | 196 | 1.00 (ref) | 67 | 1.00 (ref) | 246 | 1.00 (ref) | 233 | 1.00 (ref) | 239 | 1.00 (ref) | |
| 2 (62.5–69.5) | 131 | 0.75 (0.60–0.95) | 65 | $0.98\ (0.69{-}1.40)$ | 257 | 0.81 (0.67–0.98) | 180 | 0.80 (0.65–0.97) | 175 | 0.90 (0.74–1.11) | |
| 3 (69.6–74.7) | 129 | 0.79 (0.63–1.00) | 48 | $0.80\ (0.54{-}1.19)$ | 331 | 0.83 (0.69–0.99) | 148 | 0.74 (0.60–0.92) | 167 | 0.91 (0.73–1.12) | |
| 4 (74.8–79.4) | 136 | 0.82 (0.65–1.04) | 49 | $0.84\ (0.56{-}1.25)$ | 333 | 0.72 (0.60–0.87) | 110 | 0.62 (0.49–0.79) | 132 | 0.78 (0.62–0.98) | |
| 5 (79.5–98.8) | 181 | 0.81 (0.65–1.01) | 39 | 0.71 (0.46–1.09) | 331 | 0.76 (0.62–0.92) | 102 | 0.69~(0.54-0.89) | 150 | 0.75 (0.60–0.94) | |
| P for trend $^{\mathcal{C}}$ | | .10 | | 60. | | .003 | | < .001 | | .007 | .03 |
| AHEI-2010 | | | | | | | | | | | |
| 1 (25.1–56.6) | 167 | 1.00 (ref) | 61 | 1.00 (ref) | 253 | 1.00 (ref) | 205 | 1.00 (ref) | 190 | 1.00 (ref) | |
| 2 (56.7–62.3) | 160 | 0.95 (0.76–1.18) | 48 | 0.78 (0.53–1.15) | 231 | 0.81 (0.68–0.97) | 201 | 0.93 (0.76–1.13) | 156 | 0.84 (0.68–1.03) | |
| 3 (62.4–67.1) | 144 | 0.84 (0.67–1.06) | 54 | 0.82 (0.56–1.19) | 266 | 0.80 (0.67–0.95) | 154 | 0.81 (0.65–1.00) | 162 | $0.85\ (0.68{-}1.04)$ | |
| 4 (67.2–72.6) | 147 | $0.86\ (0.69{-}1.08)$ | 54 | 0.78 (0.53–1.14) | 367 | 0.93 (0.79–1.10) | 135 | 0.87 (0.70–1.09) | 177 | 0.89 (0.72–1.10) | |
| 5 (72.7–104.5) | 155 | 1.00 (0.80–1.26) | 51 | 0.77 (0.52–1.13) | 381 | 0.79 (0.67–0.94) | 78 | 0.73 (0.56–0.95) | 178 | 0.76 (0.62–0.94) | |
| P for trend $^{\mathcal{C}}$ | | .75 | | .21 | | .07 | | .01 | | .03 | .59 |
| aMED | | | | | | | | | | | |
| 1 (0-2) | 170 | 1.00 (ref) | 42 | 1.00 (ref) | 246 | 1.00 (ref) | 185 | 1.00 (ref) | 187 | 1.00 (ref) | |
| 2 (3) | 143 | 0.99 (0.79–1.24) | 48 | 1.16 (0.76–1.76) | 258 | 1.04 (0.88–1.24) | 166 | 0.98 (0.80–1.22) | 152 | 0.93 (0.75–1.15) | |
| 3 (4) | 146 | 1.00 (0.79–1.26) | 51 | 0.95 (0.62–1.45) | 314 | 1.07 (0.90–1.27) | 158 | 0.92 (0.74–1.15) | 174 | 0.96 (0.78–1.19) | |
| 4 (5) | 112 | 0.84 (0.65–1.09) | 50 | 0.86 (0.55–1.34) | 273 | 0.96 (0.80–1.16) | 136 | 0.86 (0.67–1.09) | 151 | $0.87\ (0.69{-}1.09)$ | |
| 5 (6-9) | 202 | 1.09 (0.85–1.39) | ΤT | 0.78 (0.50–1.21) | 407 | 0.94 (0.78–1.13) | 128 | 0.75 (0.58–0.97) | 199 | $0.83\ (0.66{-}1.03)$ | |
| P for trend $^{\mathcal{C}}$ | .81 | | 11. | | .28 | | .02 | | 60. | | .63 |
| DASH | | | | | | | | | | | |
| 1 (8-20) | 183 | 1.00 (ref) | 87 | 1.00 (ref) | 420 | 1.00 (ref) | 163 | 1.00 (ref) | 138 | 1.00 (ref) | |
| 2 (21–22) | 120 | 0.94 (0.75–1.19) | 37 | 0.85 (0.57–1.25) | 251 | 1.00 (0.85–1.17) | 113 | 0.76 (0.60–0.97) | 105 | 0.81 (0.63–1.04) | |
| 3 (23–25) | 178 | 0.86 (0.70–1.06) | 67 | 0.90 (0.65–1.26) | 344 | 0.87 (0.75–1.01) | 198 | 0.72 (0.58–0.89) | 217 | 0.77 (0.62–0.96) | |
| 4 (26–27) | 129 | 1.04 (0.82–1.31) | 36 | 0.78 (0.52–1.18) | 210 | 0.92 (0.77–1.09) | 123 | 0.71 (0.55–0.91) | 146 | 0.72 (0.57–0.92) | |

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| | African / | African American (n=26,719) Nat | Native H | awaiian (n=12,338) | Japanese | ive Hawaiian (n=12,338) Japanese American (n=49,443) Latino (n=35,997) | Lati | no (n=35,997) | Whi | White (n=43,318) | P for heterogeneity b |
|---------------------|-----------|---------------------------------|----------|--------------------------|----------|--|-------|---|-------|--------------------------|----------------------------|
| | Cases | Cases HR (95% CI) ^d | Cases | Cases HR (95% CI)a Cases | Cases | HR (95% CI) ^a | Cases | Cases HR (95% CI) ^a Cases HR (95% CI) ^a | Cases | HR (95% CI) ^a | |
| 5 (28–40) 163 | 163 | 0.91 (0.73–1.15) | 41 | 0.70 (0.46–1.05) 273 | 273 | 0.86 (0.73–1.01) | 176 | 176 0.71 (0.56–0.89) 257 0.69 (0.56–0.86) | 257 | $0.69\ (0.56-0.86)$ | |
| P for trend c .60 | .60 | | 60. | | .04 | | .006 | | .002 | | .44 |

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AHEI-2010, Alternative Healthy Eating Index 2010; aMED, alternate Mediterranean diet; DASH, Dietary Approaches to Stop Hypertension; HEI-2010, Healthy Eating Index 2010.

^a Adjusted for age at cohort entry, sex, family history of colorectal cancer, history of colorectal polyp, body mass index, pack-years of cigarette smoking, multivitamin use, nonsteroidal anti-inflammatory drug use, vigorous physical activity, menopausal status and menopausal hormone therapy use, and total energy. Additionally adjusted for alcohol consumption for HEI-2010 and DASH.

b based on Wald test of cross-product terms of race/ethnicity and the trend variable for the dietary index, adjusting for the covariates in the multivariate models.

 $c_{\rm T}$ rend variables were assigned the sex- and ethnicity-specific median values for quintiles.