International Epidemiological Association

International Journal of Epidemiology, 2023, 96–106
https://doi.org/10.1093/ije/dyac230
Advance Access Publication Date: 14 December 2022
Original article

OXFORD

Cancer

Dietary patterns and risk of colorectal cancer: a comparative analysis

Peilu Wang [1,2]* Mingyang Song,[1,3,4,5] A Heather Eliassen,[1,3,6] Molin Wang,[1,6,7] and Edward L Giovannucci [1,3]

[1]Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, MA, USA, [2]Department of Nutrition and Food Hygiene, School of Public Health, Institute of Nutrition, Fudan University, Shanghai, China, [3]Department of Nutrition, Harvard T.H. Chan School of Public Health, Boston, MA, USA, [4]Clinical and Translational Epidemiology Unit, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA, [5]Division of Gastroenterology, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA, [6]Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA and [7]Department of Biostatistics, Harvard T.H. Chan School of Public Health, Boston, MA, USA

*Corresponding author. Department of Nutrition and Food Hygiene, School of Public Health, Institute of Nutrition, Fudan University, 130 Dongan Road, Shanghai 200032, China. E-mail: peiluwang@fudan.edu.cn

Received 20 July 2022; Editorial decision 10 November 2022; Accepted 29 November 2022

Abstract

Background: Although several dietary patterns have been associated with incident colorectal cancer (CRC), it is unclear which diet is optimal.

Methods: Participants included 48 409 men and 169 772 women from three USA-based prospective cohort studies. We compared the associations of 18 dietary patterns with CRC risk, including two reference scores. The reference scores were derived based on the dietary recommendations for cancer prevention and CRC-specific dietary risk factors mentioned in the 2018 World Cancer Research Fund/American Institute of Cancer Research (WCRF/AICR) Third Expert Report. Multivariable Cox proportional hazards models were fitted to estimate hazard ratios (HRs) and 95% CIs.

Results: Most dietary patterns showed moderate correlations with the WCRF dietary score (absolute values of Spearman correlation coefficients: 0.45–0.63), except the Plant-based diet index, low-carbohydrate diets, the Empirical dietary index for hyperinsulinemia (EDIH) and Empirical dietary inflammation pattern (EDIP). HR for the 10th–90th percentile difference in the score was 0.86 (95% CI: 0.78–0.94) for the Dietary Approaches to Stop Hypertension score (DASH), 1.15 (1.06–1.26) for Western dietary pattern, 1.20 (1.10–1.31) for EDIH and 1.23 (1.13–1.34) for EDIP. These associations between patterns and CRC risk persisted after adjusting for the two reference scores.

Conclusions: Although further research is needed to improve the WCRF/AICR dietary recommendations, our comprehensive assessment of dietary patterns revealed that the DASH, Western dietary pattern, EDIH and EDIP may be the most relevant diets for preventing CRC.

Key words: Dietary patterns, colorectal cancer, prevention, comparative analysis

Key Messages

- In a comprehensive analysis of 18 dietary patterns, we attempted to identify the optimal diet associated with lower colorectal cancer (CRC) risk in participants of three large cohorts.
- The diets reflecting hyperinsulinemia, chronic inflammation, Western style and adherence to the Dietary Approaches to Stop Hypertension (inversely) were associated with CRC.
- These associations remained after adjusting for the reference scores based on dietary recommendations for cancer prevention and CRC dietary risk factors.

Introduction

Diet is estimated to account for >40% of incident cases of and deaths from colorectal cancer (CRC).[1] Many dietary patterns have been derived to capture overall diet quality and quantity. Considering the additive and interactive effects among dietary components, dietary patterns can better reflect the composite dietary intake. Although several dietary components have been established as CRC risk factors, evidence on dietary patterns was judged as 'limited–no conclusion' for preventing CRC in the 2018 World Cancer Research Fund/American Institute of Cancer Research (WCRF/AICR) Third Expert Report.[2] Comprehensive assessment of dietary patterns within the same context is lacking; therefore, the optimal diet for CRC prevention has not been identified.

It is unclear whether existing dietary patterns might offer more insight into CRC prevention beyond the dietary recommendations and established CRC dietary risk factors mentioned in the WCRF/AICR report. Although not specifically targeted at CRC, the score based on WCRF/AICR dietary recommendations (WCRF) is associated with a lower CRC risk, particularly in men.[3] Several empirically derived patterns such as the Western pattern,[4,5] Empirical dietary index for hyperinsulinemia (EDIH)[6] and Empirical dietary inflammation pattern (EDIP) demonstrated consistent positive associations with CRC risk.[7] Moreover, Alternative Healthy Eating Index-2010 (AHEI-2010), Alternate Mediterranean Diet (AMED) score and Dietary Approaches to Stop Hypertension (DASH) score were inversely associated with CRC risk, especially in men.[8,9] Most existing dietary scores are not cancer-oriented; rather, they were created to characterize diets associated with cardiometabolic risk or specific biological pathways.[10–16] Comparing existing dietary patterns with scores based on dietary recommendations for cancer prevention or CRC-specific risk factors (CRC dietary score) may help pinpoint dietary modification targets to improve CRC prevention.

Leveraging data from three large prospective cohort studies, we performed a comprehensive evaluation of 18 dietary patterns including two reference dietary scores (the WCRF and CRC dietary score) regarding CRC risk overall and according to anatomical locations. Further, we assessed whether these dietary patterns were associated with CRC risk after adjusting for the reference dietary scores.

Methods

Study population

The analyses were based on three ongoing prospective cohorts including the Health Professionals Follow-up Study (HPFS), the Nurses' Health Study (NHS) and the NHSII. The HPFS enrolled 51 529 male health professionals aged 40–75 years in 1986, the NHS enrolled 121 700 female nurses aged 30–55 years in 1976 and the NHSII enrolled 116 429 female nurses aged 25–42 years in 1989. Updated lifestyle and medical history information was collected from participants of all three cohorts using biennial questionnaires. Dietary information during the preceding year was collected using expanded semi-quantitative food frequency questionnaires (SFFQs) every 4 years. The follow-up rates in these cohorts were >90% and we estimate having ascertained ≥98% of the cancers. Institutional review boards at the Brigham and Women's Hospital, Harvard T.H. Chan School of Public Health and participating registries approved the study protocol.

Dietary assessment

We included dietary information extracted from expanded SFFQs, which were initially developed in 1984. Participants recorded consumption frequency for each food item with

standard portion size, ranging from 'never, or less than once per month' to '6 or more times per day'. The total nutrient intake and calorie intake were computed by summing up the nutrient content of each contributing food item multiplied by its consumption frequency. We computed scores as described in the literature for 4 empirically derived and 14 recommendation-based dietary patterns. Details of pattern assessment can be found in the Supplementary Methods and Supplementary Table S1 (available as Supplementary data at *IJE* online). The validity and reproducibility of dietary patterns and food consumption assessed in the SFFQ have been documented previously.[17–19]

Outcome ascertainment

CRC diagnoses were self-reported by participants through biennial questionnaires. Deaths from CRC were identified by next-of-kin or postal system in response to follow-up questionnaires and by active searching of the National Death Index for non-respondents. Permission was obtained from respondents or their family members to access medical records and pathology reports. Physicians who were blinded to the research goals reviewed medical records or death certificates to confirm the diagnoses and extracted information on tumour stage, anatomical location and histologic features.

Covariates assessment

Information from questionnaires and SFFQs were obtained at baseline and updated every 2–4 years for age, cigarette smoking, alcohol intake, bodyweight and height, physical activity, regular aspirin use, regular non-steroidal anti-inflammatory drugs use, post-menopausal hormone use (for NHS and NHSII participants), history of colonoscopy or sigmoidoscopy, family history of CRC in any first-degree relatives, multivitamin use and total energy intake. We replaced the missing values with the cohort-specific median for physical activity, pack-years of smoking and body mass index (missing in 1.4–2.5% of participants).

Statistical analysis

We excluded individuals with a prior diagnosis of cancer (except for non-melanoma skin cancer) or inflammatory bowel disease at baseline, those with implausible energy intake (<600 or >3500 kcal/d for women, <800 or >4200 kcal/d for men) and those with missing data on dietary patterns. Following these exclusions, a total of 169 772 women and 48 409 men were included in the final analysis (Supplementary Figure S1, available as Supplementary data at *IJE* online). Person-months of follow-up accrued from the first questionnaire cycle after the first available SFFQ (1988 for the HPFS, 1986 for the NHS and 1993 for the NHSII) until the diagnosis of CRC, death or the end of the follow-up (2016 for the HPFS and NHS, and 2017 for the NHSII), whichever occurred first.

We calculated cumulative averages of pattern scores to capture long-term dietary intake and reduce random within-person variability; the non-missing exposure values from previous cycles were carried forward to questionnaire cycles without SFFQs. We used the residual method to compute energy-adjusted pattern scores.[20] Specifically, the residuals were obtained from regression models, where the total caloric intake was the independent variable and the scores were the dependent variable. A 2-year lag was applied to pattern scores to reduce potential reverse causation. To facilitate comparison, we used the 10th–90th percentile difference of each continuous score as the increment unit. We calculated the Spearman correlation coefficients (r) between baseline pattern scores and between selected pattern scores and energy-adjusted food components. Correlations with an absolute value of $r \geq 0.35$ were considered as 'moderate'.

Cox proportional hazards models with time-varying covariates were fitted to estimate hazard ratios (HRs) and 95% CIs. All models were stratified by age in months and calendar year of the questionnaire cycle. For the main analysis, we adjusted for pack-years of cigarette smoking, alcohol intake, physical activity, regular aspirin use, regular non-steroidal anti-inflammatory drugs use, post-menopausal hormone use for women, history of colonoscopy or sigmoidoscopy, family history of CRC in any first-degree relatives, multivitamin use and total energy intake as time-varying covariates.

Analyses were first performed in each cohort. We assessed whether associations differed across cohorts or between sexes using Chi-square tests based on Cochran Q statistic.[21] Because no appreciable difference was observed ($P > 0.05$ for all), we combined data from three cohorts and conducted pooled Cox regressions stratified by cohort. Restricted cubic splines were adopted to model the association of continuous exposures and CRC; potential non-linearity was examined by comparing the model with and without the non-linear spline terms using likelihood ratio tests.[22] We performed likelihood ratio tests based on a duplication method to examine whether associations vary by CRC subtypes according to anatomical locations.[23] Proportional hazard assumption was tested by including an interaction term between each exposure variable and age in the multivariable models, and no violation was observed ($P > 0.05$ for all).

We ran two models to evaluate the associations of dietary patterns with CRC risk independent of the reference

dietary scores. In Model 1, we used energy-adjusted scores as exposures and adjusted for the reference dietary score as a covariate. In Model 2, we first computed pattern scores adjusted for both reference dietary score and total energy via the residual method.[20] Then the associations of patterns with CRC were assessed using the reference-adjusted pattern scores as exposures.

Since the model adjusted for alcohol whereas some patterns include alcohol components, we tested whether removing or adjusting for different definitions of alcohol intake affects the results. We further evaluated the associations in subgroups defined by the reference scores and alcohol intake. Potential mediation by body mass index (BMI) and diabetes was also examined. To identify important dietary components, we re-evaluated patterns associated with CRC by adjusting for individual components.

Statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, NC). We reported unadjusted *P*-values based on two-sided statistical tests.

Results

We documented 3428 CRC cases among 218 181 participants with a median follow-up of 24 years. The distribution of dietary patterns was similar across the three cohorts (Supplementary Figure S2, available as Supplementary data at *IJE* online). Participants with higher scores for WCRF, CRC score, Prudent pattern, AHEI-2010, AMED, DASH, Global diet quality score (GDQS), Healthful GDQS (hGDQS), Unhealthful GDQS (uGDQS), Plant-based diet index (PDI) and Healthful PDI (hPDI) were more likely to be older, undergo a lower endoscopy, take multivitamins, smoke fewer cigarettes and be physically active (Table 1). Opposite trends were observed for unhealthful PDI (uPDI), low-carbohydrate diets (LCDs), Western diet, EDIH and EDIP. Prevalence of regular aspirin, regular non-steroidal anti-inflammatory drugs use, average alcohol intake and BMI also varied considerably with a pattern-specific direction. The inter-relationships between patterns were similar in each cohort and combined data (Figure 1 and Supplementary Figure S3, available as Supplementary data at *IJE* online). Most dietary patterns showed moderate correlations with the WCRF dietary score (absolute values of r: 0.45–0.63), except the PDI, LCDs, EDIH and EDIP. The correlations of dietary patterns with CRC dietary score were weaker than those with WCRF but generally in the same direction.

Participants who scored highly for Western pattern (HR for the 10th–90th percentile difference: 1.15; 95% CI: 1.06–1.26; $P = 0.001$), EDIH (HR: 1.20; 95% CI: 1.10–1.31; $P < 0.0001$) or EDIP (HR: 1.23; 95% CI: 1.13–1.34; $P < 0.0001$) experienced higher CRC risk, whereas those who scored highly for DASH had lower CRC risk (HR: 0.86; 95% CI: 0.78–0.94; $P = 0.001$) (Figure 2 and Supplementary Table S2, available as Supplementary data at *IJE* online). Both WCRF and CRC dietary scores were not associated with CRC risk when adjusted for alcohol, but they were inversely associated with CRC risk when not adjusted for alcohol (HR for WCRF: 0.88; 95% CI: 0.80–0.96; $P = 0.004$; HR for CRC score: 0.87; 95% CI: 0.80–0.95; $P = 0.002$) (Supplementary Table S3, available as Supplementary data at *IJE* online). Although results for other patterns were generally null, LCDs and uPDI appeared to be positively associated, whereas Prudent, AHEI-2010, AMED, GDQSs and hPDI appeared to be inversely associated with CRC risk. We did not find any heterogeneity across cohorts or between the sexes even though some estimates were stronger in the NHSII (Supplementary Table S2, available as Supplementary data at *IJE* online). No non-linear associations were detected ($P > 0.05$ for all, not shown).

We ascertained 1420 proximal colon, 931 distal colon and 720 rectal cancer cases. The associations across different anatomical sites showed little statistical heterogeneity (Figure 3 and Supplementary Table S4, available as Supplementary data at *IJE* online). The DASH, Western pattern, EDIH and EDIP showed slightly stronger associations with distal colon cancer than other subtypes, but the overall magnitude and direction were similar.

We examined whether these associations held with additional adjustment for WCRF or CRC dietary score (Table 2). Using energy-adjusted scores as exposure (Model 1), point estimates barely changed for DASH, Western pattern, EDIH and EDIP when WCRF was included in the model. The CIs for Prudent pattern, AHEI-2010, AMED, GDQSs, PDIs and LCDs included one. Similar results were observed using the reference-adjusted dietary scores as the exposure (Model 2).

For WCRF, CRC score, DASH and Western pattern, correlations with established CRC risk factors, such as processed meats, red meats, low-fat dairy products, whole grains, calcium and fibre, were comparable in magnitudes, although slightly greater for the latter three (Supplementary Figure S4, available as Supplementary data at *IJE* online). Most dietary components had weak correlations (absolute values of $r < 0.35$) with the EDIH and EDIP; red meats, processed meats and French fries were positively correlated with the EDIH, whereas coffee was inversely correlated with the EDIP. After adjusting for the aforementioned components, the associations of DASH, Western pattern, EDIH and EDIP with CRC risk changed slightly (absolute change in HR >2%) (Supplementary Table S5, available as Supplementary data at *IJE* online).

Table 1 Age-standardized baseline characteristics of the study population in the lowest and highest quintiles of energy-adjusted dietary patterns

	Quintile	Age[a] (years)	CRC family history (%)	Lower endoscopy history (%)	Multivitamin use (%)	BMI (kg/m^2)	Alcohol intake (g/day)	Physical activity (METS-h/week)	Cigarette smoking (pack-years)	Regular aspirin use[b] (%)	Regular NSAIDs use[c] (%)
Reference dietary patterns											
WCRF	Q1	45.8 (9.7)	6.4	3.7	35.8	24.5 (4.5)	9.7 (13.1)	15.9 (19.8)	11.5 (17.4)	26.7	10.9
	Q5	48.8 (11.0)	6.8	4.3	46.8	24.7 (4.6)	3.2 (7.3)	25.3 (30.1)	7.6 (13.7)	23.6	10.4
CRC score	Q1	47.0 (10.0)	6.6	3.7	34.0	25.1 (4.8)	11.2 (16.2)	16.4 (20.6)	12.7 (18.2)	26.1	10.9
	Q5	47.8 (11.0)	6.6	4.3	47.5	24.2 (4.3)	3.7 (5.9)	24.7 (29.4)	7.2 (13.4)	24.2	9.8
Potentially healthy dietary patterns											
Prudent	Q1	45.4 (9.8)	6.2	3.6	34.4	24.8 (4.9)	7.6 (14.4)	14.7 (20.3)	12.0 (18.6)	26.2	10.7
	Q5	48.6 (10.7)	7.1	4.5	46.7	24.9 (4.6)	5.7 (9.3)	27.1 (30.6)	8.2 (13.8)	25.1	11.2
AHEI-2010	Q1	46.0 (10.1)	6.4	3.6	35.0	25.1 (5.0)	6.5 (14.4)	14.4 (18.8)	10.9 (17.8)	25.8	10.6
	Q5	48.6 (10.7)	6.9	4.5	47.0	24.2 (4.1)	6.4 (7.9)	27.0 (30.1)	8.4 (13.7)	25.2	10.9
AMED	Q1	45.8 (10.0)	6.2	3.6	34.9	25.1 (5.0)	6.8 (14.0)	15.3 (20.1)	11.6 (18.2)	25.6	10.7
	Q5	48.5 (10.7)	6.8	4.4	46.7	24.2 (4.1)	6.3 (8.2)	25.1 (28.1)	7.8 (13.3)	25.4	10.8
DASH	Q1	45.6 (9.4)	6.3	3.4	31.6	25.1 (5.1)	7.2 (13.2)	14.4 (19.4)	12.6 (18.5)	26.0	11.0
	Q5	48.8 (11.1)	6.8	4.3	49.5	24.2 (4.2)	5.0 (8.5)	26.9 (30.3)	7.1 (12.9)	24.2	10.1
GDQS	Q1	45.7 (9.9)	6.3	3.5	33.6	24.9 (4.9)	6.0 (12.0)	14.6 (20.0)	11.0 (17.6)	25.6	10.4
	Q5	48.6 (10.7)	6.8	4.4	47.3	24.6 (4.4)	6.1 (9.8)	25.8 (29.1)	8.3 (14.0)	25.0	11.0
hGDQS	Q1	46.0 (10.2)	6.4	3.5	34.3	24.9 (4.9)	7.0 (13.8)	15.1 (20.9)	11.7 (18.2)	25.5	10.6
	Q5	48.4 (10.6)	6.9	4.3	46.8	24.7 (4.4)	5.5 (8.5)	24.9 (28.1)	7.9 (13.5)	25.3	10.9
uGDQS	Q1	46.0 (9.9)	6.6	3.8	36.0	25.0 (4.8)	4.7 (8.6)	16.1 (20.5)	9.1 (15.5)	25.9	10.3
	Q5	48.3 (10.8)	6.7	4.2	45.5	24.6 (4.4)	7.7 (13.2)	24.0 (28.5)	9.7 (15.8)	24.8	11.0
PDI	Q1	46.4 (10.3)	6.5	4.0	38.7	25.5 (5.1)	8.3 (14.3)	17.7 (22.7)	11.5 (17.8)	25.8	10.7
	Q5	48.2 (10.6)	6.7	4.1	42.2	24.1 (4.1)	4.8 (8.1)	22.3 (26.4)	8.0 (13.8)	25.5	10.8
hPDI	Q1	45.6 (10.0)	6.5	3.8	35.6	25.0 (4.9)	5.5 (9.9)	15.9 (20.4)	9.7 (16.5)	25.5	9.9
	Q5	48.9 (10.7)	6.8	4.3	45.8	24.5 (4.3)	6.6 (11.5)	25.4 (29.6)	9.1 (14.7)	25.2	11.6
Potentially unhealthy dietary patterns											
uPDI	Q1	48.4 (10.4)	7.0	4.4	45.4	25.2 (4.5)	6.7 (10.5)	23.2 (26.6)	10.1 (15.5)	25.9	11.7
	Q5	45.9 (10.4)	6.4	3.5	35.5	24.5 (4.7)	5.3 (11.1)	16.4 (21.9)	8.8 (15.9)	24.9	10.0
LCD	Q1	47.3 (10.8)	6.6	3.9	43.2	23.8 (4.1)	5.1 (9.7)	22.6 (28.6)	8.0 (14.3)	24.4	10.0
	Q5	47.1 (10.1)	6.4	4.1	37.3	25.9 (5.1)	5.4 (8.6)	17.1 (21.2)	11.3 (17.1)	26.7	11.6
Animal-rich LCD	Q1	47.5 (10.7)	6.7	4.0	43.5	23.8 (4.1)	4.5 (8.3)	22.8 (28.5)	7.7 (13.8)	24.4	10.0
	Q5	47.1 (10.2)	6.3	4.0	37.5	25.8 (5.1)	6.4 (10.5)	17.3 (21.5)	11.5 (17.4)	26.3	11.4
Plant-rich LCD	Q1	47.1 (10.9)	6.5	3.8	41.8	24.5 (4.5)	5.5 (11.2)	20.5 (26.1)	9.3 (15.8)	24.4	10.0
	Q5	47.4 (10.1)	6.6	4.2	38.9	25.1 (4.8)	6.1 (9.7)	18.6 (22.7)	10.3 (16.0)	26.5	11.8
Western	Q1	48.5 (11.1)	7.0	4.4	49.5	24.1 (4.1)	6.8 (11.8)	27.5 (31.5)	7.3 (13.4)	23.7	9.8
	Q5	46.1 (9.8)	6.5	3.6	33.5	25.5 (5.2)	5.9 (11.0)	15.2 (19.8)	12.3 (18.3)	27.4	11.9
EDIH	Q1	48.3 (10.6)	6.8	4.2	45.3	23.5 (3.7)	9.7 (13.9)	24.8 (29.3)	9.8 (15.5)	25.1	10.3
	Q5	46.0 (9.9)	6.5	3.9	36.4	26.2 (5.4)	4.8 (9.6)	16.6 (20.9)	9.9 (16.7)	26.8	11.6
EDIP	Q1	47.4 (9.7)	6.8	4.1	43.1	24.0 (4.0)	12.2 (15.8)	22.3 (26.9)	11.8 (16.8)	26.9	11.5
	Q5	46.6 (10.7)	6.3	4.0	36.9	26.0 (5.4)	3.4 (8.0)	17.8 (23.2)	8.6 (15.5)	25.7	11.1

[a]All variables are standardized to the age distribution of the study population, except for age.

[b]Regular users are defined as participants who take at least two tablets of aspirin (325 mg/tablet) per week in the NHS and at least two times per week in the HPFS and NHSII.

[c]Regular users are defined as participants who take at least two times per week.

AHEI-2010, Alternative Healthy Eating Index-2010; AMED, Alternate Mediterranean Diet score; Animal-rich LCD, Animal-rich low-carbohydrate diet score; BMI, body mass index; CRC, colorectal cancer; CRC score, Colorectal cancer dietary score; DASH, Dietary Approaches to Stop Hypertension score; EDIH, Empirical dietary index for hyperinsulinemia; EDIP, Empirical dietary inflammation pattern; GDQS, Global diet quality score; hGDQS, Healthful global diet quality score; hPDI, Healthful plant-based diet index; LCD, overall low-carbohydrate diet score; METS, metabolic equivalent for task score; NSAIDs, non-steroidal anti-inflammatory drugs; PDI, Plant-based diet index; Plant-rich LCD, Plant-rich low-carbohydrate diet score; Prudent, Prudent dietary pattern; uGDQS, Unhealthful global diet quality score; uPDI, Unhealthful plant-based diet index; WCRF, World Cancer Research Fund/American Institute for Cancer Research dietary score; Western, Western dietary pattern. Values are means (standard deviations) for continuous variables and percentages for categorical variables if not specified otherwise.

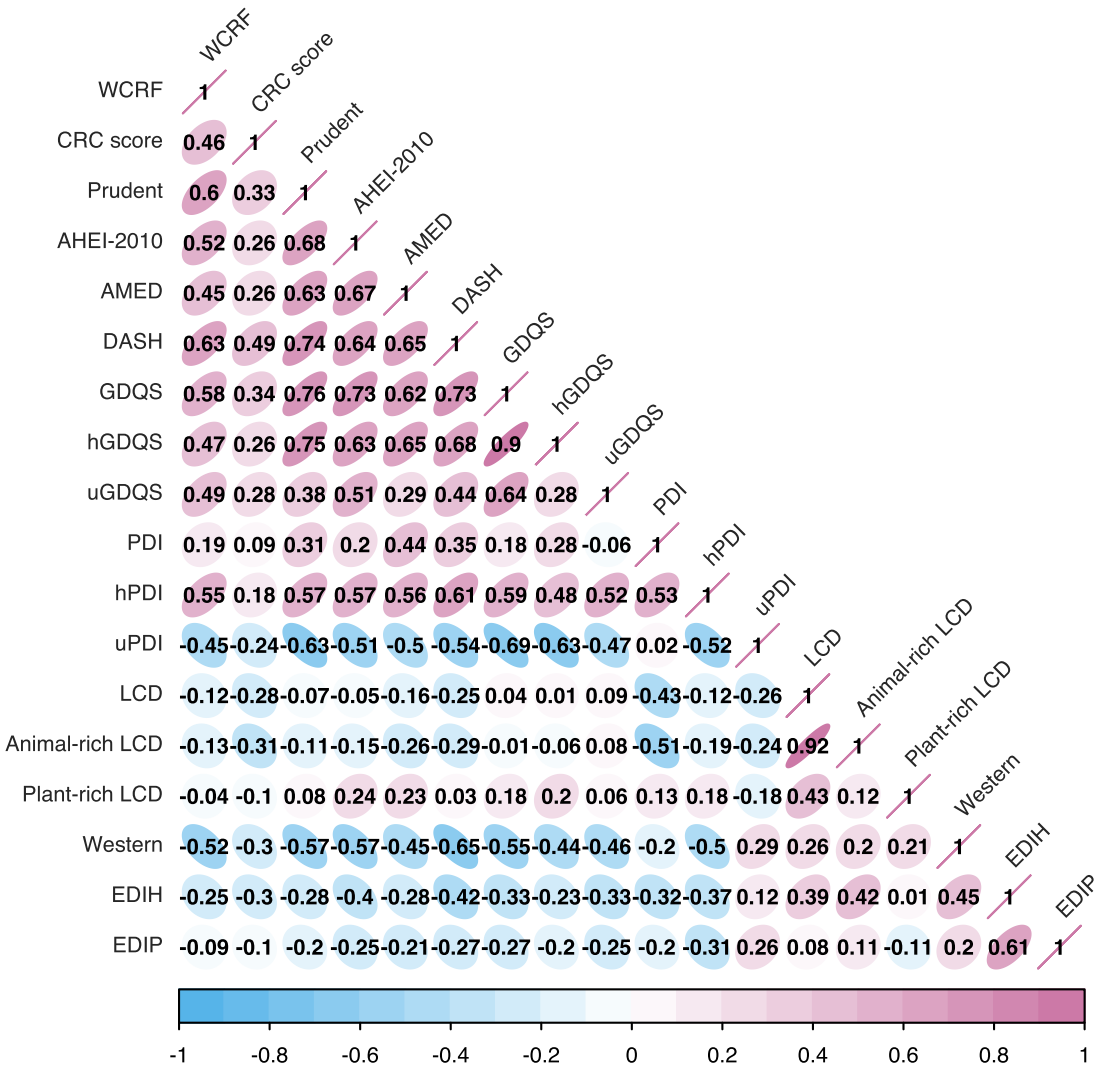

Figure 1 Spearman correlation coefficients between energy-adjusted dietary patterns at baseline in the combined data. The values of coefficients are shown in the lower triangular matrix. The correlation direction is reflected by the major axis of each ellipse, and the correlation magnitude is reflected by the ellipse area and colour shade. *P*-values for all correlations were <0.05. AHEI-2010, Alternative Healthy Eating Index-2010; AMED, Alternate Mediterranean Diet score; Animal-rich LCD, Animal-rich low-carbohydrate diet score; CRC score, Colorectal cancer dietary score; DASH, Dietary Approaches to Stop Hypertension score; EDIH, Empirical dietary index for hyperinsulinemia; EDIP, Empirical dietary inflammation pattern; GDQS, Global diet quality score; hGDQS, Healthful global diet quality score; hPDI, Healthful plant-based diet index; LCD, overall low-carbohydrate diet score; PDI, Plant-based diet index; Plant-rich LCD, Plant-rich low-carbohydrate diet score; Prudent, Prudent dietary pattern; uGDQS, Unhealthful global diet quality score; uPDI, Unhealthful plant-based diet index; WCRF, World Cancer Research Fund/American Institute for Cancer Research dietary score; Western, Western dietary pattern

The overall findings remained the same after adjusting for various definitions of alcohol intake (Supplementary Table S3, available as Supplementary data at *IJE* online). The association for WCRF or CRC dietary score was stronger, whereas the associations were attenuated for EDIH and EDIP when not adjusted for alcohol intake. We did not observe interactions between patterns and WCRF, CRC score or alcohol intake, albeit the point estimates differed between subgroups (Supplementary Table S6, available as Supplementary data at *IJE* online). Noticeable attenuation was observed for the associations of the EDIH and EDIP when BMI was adjusted for in the model (Supplementary Table S7, available as Supplementary data at *IJE* online).

Discussion

In this comprehensive evaluation of 18 dietary scores, the DASH (inversely), Western pattern, EDIH and EDIP were associated with CRC risk and these associations were largely independent of the scores based on WCRF/AICR dietary recommendations or known CRC dietary risk factors. This study provides initial evidence that existing dietary patterns may help refine the WCRF/

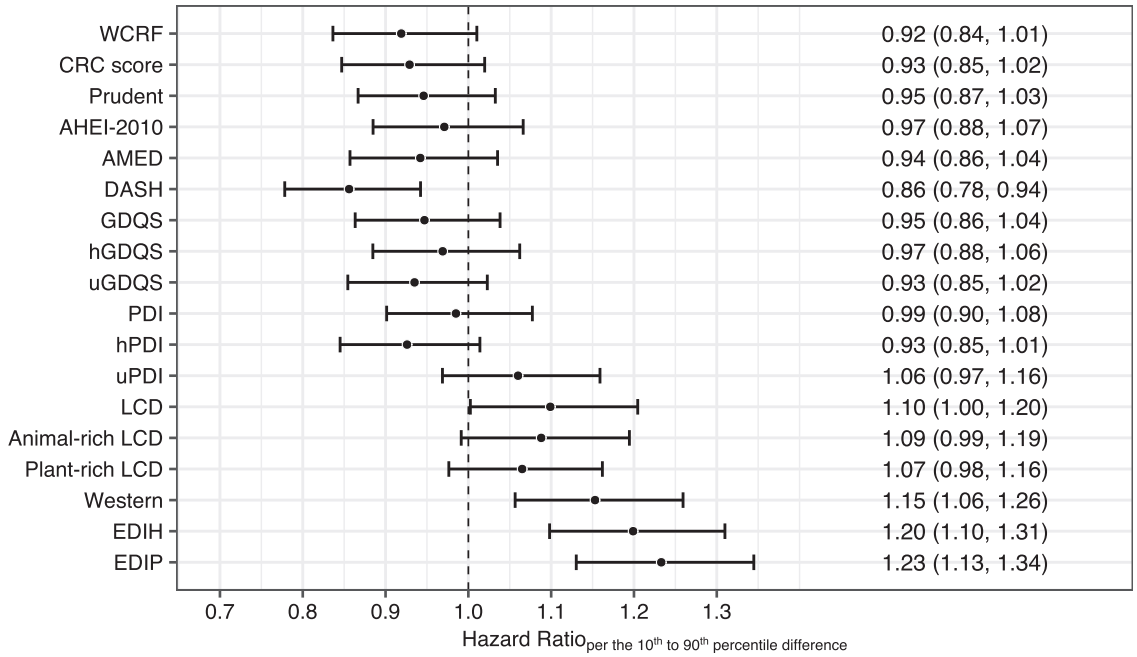

Figure 2 Multivariable-adjusted associations between dietary patterns and colorectal cancer risk in the combined data. Hazard ratios (HRs) for the 10th–90th percentile difference in each score and corresponding 95% CIs are indicated. The models were stratified by age (in month), calendar year, and cohort, and adjusted for cigarette smoking (continuous), alcohol intake (continuous), physical activity (continuous), regular aspirin use (yes or no), regular non-steroidal anti-inflammatory drugs use (yes or no), post-menopausal hormone use (pre-menopausal, never, past, or current use) for women, history of colonoscopy or sigmoidoscopy (yes or no), family history of colorectal cancer in any first-degree relatives (yes or no), multivitamin use (yes or no) and total energy intake (continuous). AHEI-2010, Alternative Healthy Eating Index-2010; AMED, Alternate Mediterranean Diet score; Animal-rich LCD, Animal-rich low-carbohydrate diet score; CRC score, Colorectal cancer dietary score; DASH, Dietary Approaches to Stop Hypertension score; EDIH, Empirical dietary index for hyperinsulinemia; EDIP, Empirical dietary inflammation pattern; GDQS, Global diet quality score; hGDQS, Healthful global diet quality score; hPDI, Healthful plant-based diet index; LCD, overall low-carbohydrate diet score; PDI, Plant-based diet index; Plant-rich LCD, Plant-rich low-carbohydrate diet score; Prudent, Prudent dietary pattern; uGDQS, Unhealthful global diet quality score; uPDI, Unhealthful plant-based diet index; WCRF, World Cancer Research Fund/American Institute for Cancer Research dietary score; Western, Western dietary pattern

AICR dietary recommendations and offer more insights into CRC prevention.

The difference in scoring method and food components may contribute to the varying associations between patterns and CRC risk. Dietary patterns based on actual serving sizes, such as WCRF, CRC score, AHEI-2010, GDQSs, EDIH and EDIP, are more useful for comparison across studies and populations than those determined by the distribution of the study population. Most healthy patterns were moderately correlated with WCRF because they similarly encourage consuming more vegetables, fruits and whole grains; fewer sugar-sweetened drinks; and less fast food and red or processed meat. Dietary risk factors for CRC, such as dairy products and calcium supplements, are left out of the WCRF/AICR recommendations since they may have divergent associations with other important health end points. This partially explains why the CRC-specific score was not strongly correlated with WCRF. The LCDs summarized macronutrients across foods and were weakly correlated with most patterns. They may thus miss food-specific nuances that are etiologically relevant. The moderate correlation between EDIH and EDIP indicates that common pathways may exist between insulin resistance and chronic inflammation, both of which are important mechanisms for CRC.[24]

Our findings are generally consistent with prior studies. As previously found in the HPFS and NHS,[3] the inverse association between WCRF and CRC risk was more pronounced in men than in women. The effect estimate for WCRF in our study was somewhat attenuated because alcohol intake, a component of WCRF, was adjusted for. The EDIH, EDIP, Western, Prudent, AHEI-2010 and AMED also include alcohol intake, but the latter two support moderate drinking. Prior evidence suggests that consuming more than two alcoholic drinks daily is associated with higher CRC risk.[2] Although the associations strengthened for the WCRF but attenuated for EDIH and EDIP, leaving out adjustment for alcohol intake or adjusting for the indicator of moderate drinking did not change the overall finding. A possible explanation is that, whereas total alcohol is positively associated with CRC risk, beer and wine are inversely associated with dietary insulinemic or

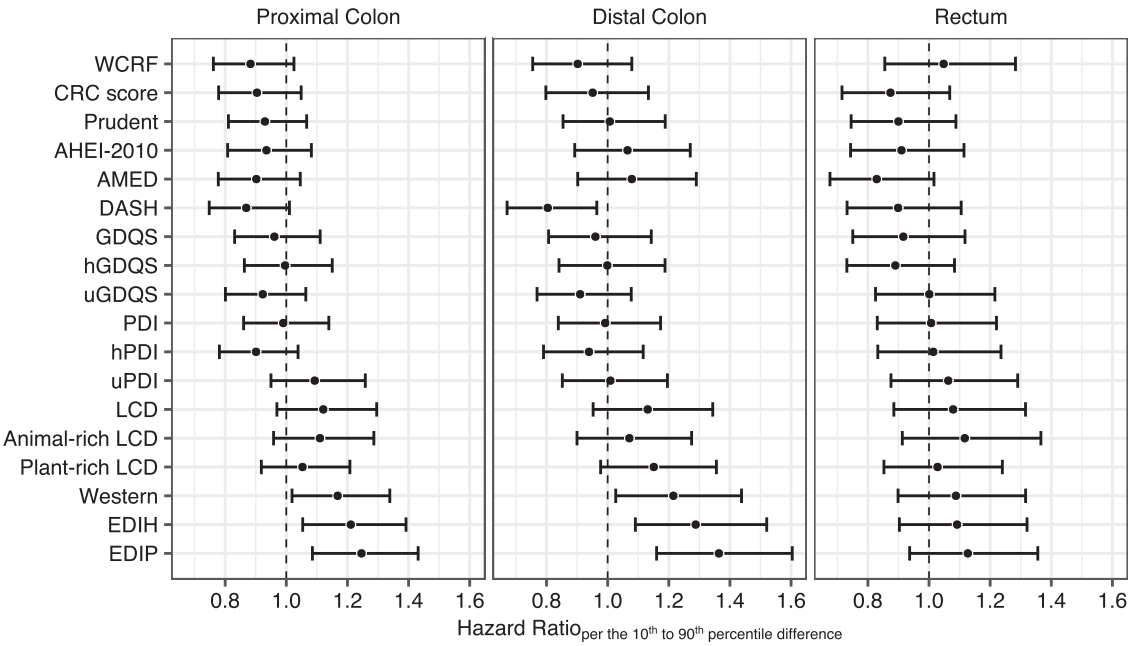

Figure 3 Multivariable-adjusted associations between dietary patterns and risk of colorectal cancer subtypes according to anatomical locations. Hazard ratios (HRs) for the 10th–90th percentile difference in each score and corresponding 95% CIs are indicated. The models were stratified by age (in month), calendar year and cohort, and adjusted for cigarette smoking (continuous), alcohol intake (continuous), physical activity (continuous), regular aspirin use (yes or no), regular non-steroidal anti-inflammatory drugs use (yes or no), post-menopausal hormone use (pre-menopausal, never, past or current use) for women, history of colonoscopy or sigmoidoscopy (yes or no), family history of colorectal cancer in any first-degree relatives (yes or no), multivitamin use (yes or no) and total energy intake (continuous). AHEI-2010, Alternative Healthy Eating Index-2010; AMED, Alternate Mediterranean Diet score; Animal-rich LCD, Animal-rich low-carbohydrate diet score; CRC score, Colorectal cancer dietary score; DASH, Dietary Approaches to Stop Hypertension score; EDIH, Empirical dietary index for hyperinsulinemia; EDIP, Empirical dietary inflammation pattern; GDQS, Global diet quality score; hGDQS, Healthful global diet quality score; hPDI, Healthful plant-based diet index; LCD, overall low-carbohydrate diet score; PDI, Plant-based diet index; Plant-rich LCD, Plant-rich low-carbohydrate diet score; Prudent, Prudent dietary pattern; uGDQS, Unhealthful global diet quality score; uPDI, Unhealthful plant-based diet index; WCRF, World Cancer Research Fund/American Institute for Cancer Research dietary score; Western, Western dietary pattern

inflammatory potential. As a result, adjusting for alcohol intake strengthened the associations of EDIH and EDIP with CRC.

Compared with the estimates using extreme quintiles in previous reports,[6,7] comparable positive associations were observed for EDIH and EDIP using the 10th–90th percentile as the increment unit. Inclusion of the NHSII led to a positive association for Western pattern in the pooled analysis whereas the inverse association for Prudent pattern was restricted to men.[4,5] Results for AHEI-2010, AMED and DASH are compatible with previous reports for CRC risk in men.[8,25] Inverse association was also observed in the pooled analysis for DASH. Compatible with prior null findings,[26,27] we did not observe strong associations for LCDs. In this study, estimates for the association of healthful PDI and unhealthful PDI with CRC demonstrated the opposite direction. Although higher GDQS may be associated with a lower risk of diabetes or obesity,[14,28] the GDQSs appear to provide limited information for preventing CRC.

Additional associations observed for DASH, Western pattern, EDIH and EDIP may provide guidance to optimize dietary recommendations for preventing CRC. The WCRF/AICR dietary recommendations largely target maintaining energy balance and healthy weight to reduce cancer risk. Prior studies showed that high dietary insulinemic potential and inflammatory potential are associated with weight gain.[29,30] Compared with other dietary patterns, EDIH and EDIP showed the largest BMI difference, suggesting that these patterns may better capture elements related to energy balance. Energy balance may be an important mediating mechanism for the associations of EDIH and EDIP with CRC, as seen by the notable attenuation introduced by adjustment for BMI.

Both EDIH and EDIP demonstrated independent associations after adjusting for WCRF dietary score, highlighting their potential for capturing diet linked to CRC-specific biologic pathways.[24] Nevertheless, most foods that were moderately correlated with EDIH or EDIP are not strong CRC risk factors except red or processed meats.[31] The Western pattern and DASH also demonstrated greater correlations with known CRC risk factors, such as red meats, processed meats and low-fat dairy, than the WCRF dietary

Table 2 Multivariable-adjusted association between dietary patterns and colorectal cancer risk adjusting for the reference dietary patterns

	Adjusted for WCRF dietary score				Adjusted for CRC dietary score			
	Model 1[b]		Model 2[c]		Model 1[b]		Model 2[c]	
Patterns[a]	HR (95% CI)	*P*-value[d]	HR (95% CI)	*P*-value[d]	HR (95% CI)	*P*-value[d]	HR (95% CI)	*P*-value[d]
Reference dietary patterns								
WCRF					0.94 (0.84, 1.05)	0.26	0.95 (0.87, 1.04)	0.27
CRC score	0.96 (0.86, 1.07)	0.43	0.96 (0.88, 1.05)	0.40				
Potentially healthy dietary patterns								
Prudent	0.99 (0.88, 1.10)	0.84	0.99 (0.91, 1.08)	0.88	0.96 (0.88, 1.06)	0.43	0.97 (0.88, 1.06)	0.45
AHEI-2010	1.03 (0.92, 1.16)	0.58	1.02 (0.93, 1.12)	0.65	1.00 (0.90, 1.11)	0.96	1.00 (0.91, 1.10)	1.00
AMED	0.98 (0.88, 1.09)	0.69	0.98 (0.89, 1.07)	0.65	0.96 (0.87, 1.06)	0.46	0.96 (0.88, 1.06)	0.44
DASH	0.83 (0.73, 0.95)	0.006	0.88 (0.80, 0.96)	0.006	0.85 (0.76, 0.95)	0.005	0.88 (0.80, 0.96)	0.005
GDQS	0.99 (0.88, 1.12)	0.92	1.00 (0.91, 1.09)	0.96	0.97 (0.88, 1.07)	0.50	0.97 (0.89, 1.07)	0.54
hGDQS	1.01 (0.91, 1.12)	0.83	1.01 (0.93, 1.11)	0.80	0.98 (0.90, 1.08)	0.75	0.99 (0.90, 1.08)	0.76
uGDQS	0.97 (0.87, 1.08)	0.55	0.98 (0.89, 1.07)	0.59	0.95 (0.87, 1.05)	0.34	0.96 (0.87, 1.05)	0.35
PDI	1.00 (0.91, 1.09)	0.97	0.99 (0.91, 1.09)	0.89	1.00 (0.91, 1.09)	0.93	0.99 (0.91, 1.08)	0.84
hPDI	0.96 (0.85, 1.08)	0.48	0.96 (0.88, 1.06)	0.42	0.94 (0.86, 1.04)	0.22	0.94 (0.86, 1.03)	0.21
Potentially unhealthy dietary patterns								
uPDI	1.02 (0.92, 1.14)	0.67	1.02 (0.93, 1.12)	0.72	1.05 (0.96, 1.15)	0.31	1.05 (0.96, 1.15)	0.32
LCD	1.09 (0.99, 1.19)	0.08	1.09 (0.99, 1.20)	0.07	1.08 (0.98, 1.19)	0.11	1.08 (0.98, 1.18)	0.11
Animal-rich LCD	1.07 (0.98, 1.18)	0.14	1.08 (0.98, 1.18)	0.11	1.07 (0.97, 1.18)	0.19	1.07 (0.97, 1.17)	0.17
Plant-rich LCD	1.06 (0.98, 1.16)	0.16	1.07 (0.98, 1.17)	0.15	1.06 (0.97, 1.16)	0.18	1.06 (0.97, 1.16)	0.17
Western	1.15 (1.04, 1.28)	0.008	1.13 (1.03, 1.23)	0.008	1.15 (1.04, 1.27)	0.005	1.13 (1.04, 1.24)	0.005
EDIH	1.19 (1.08, 1.31)	0.0002	1.18 (1.08, 1.28)	0.0003	1.20 (1.09, 1.32)	0.0002	1.18 (1.08, 1.29)	0.0002
EDIP	1.22 (1.12, 1.34)	<0.0001	1.23 (1.13, 1.35)	<0.0001	1.23 (1.12, 1.34)	<0.0001	1.23 (1.13, 1.35)	<0.0001

[a]HRs (95% CI) are for the 10th–90th percentile difference in each score. All analyses were stratified by age (in month), calendar year and cohort, and adjusted for cigarette smoking (continuous), alcohol intake (continuous), physical activity (continuous), regular aspirin use (yes or no), regular non-steroidal anti-inflammatory drugs use (yes or no), post-menopausal hormone use (pre-menopausal, never, past, or current use) for women, history of colonoscopy or sigmoidoscopy (yes or no), family history of colorectal cancer in any first-degree relatives (yes or no), multivitamin use (yes or no) and total energy intake (continuous).

[b]Energy-adjusted dietary pattern scores were fitted as exposure and WCRF dietary score (continuous) or CRC dietary score (continuous) was adjusted for in the model.

[c]WCRF- or CRC-score-adjusted dietary pattern scores were fitted as exposure and WCRF dietary score (continuous) or CRC dietary score (continuous) was adjusted for in the model.

[d]*P*-value for the Wald test.

AHEI-2010, Alternative Healthy Eating Index-2010; AMED, Alternate Mediterranean Diet score; Animal-rich LCD, Animal-rich low-carbohydrate diet score; CI, Confidence interval; CRC score, Colorectal cancer dietary score; DASH, Dietary Approaches to Stop Hypertension score; EDIH, Empirical dietary index for hyperinsulinemia; EDIP, Empirical dietary inflammation pattern; GDQS, Global diet quality score; hGDQS, Healthful global diet quality score; hPDI, Healthful plant-based diet index; HR, Hazard ratio; LCD, overall low-carbohydrate diet score; PDI, Plant-based diet index; Plant-rich LCD, Plant-rich low-carbohydrate diet score; Prudent, Prudent dietary pattern; uGDQS, Unhealthful global diet quality score; uPDI, Unhealthful plant-based diet index; WCRF, World Cancer Research Fund/American Institute for Cancer Research dietary score; Western, Western dietary pattern.

score.[31–33] Given the slight change in the associations of these patterns after adjusting for individual foods, the combined effect of several weak risk factors, such as French fries, coffee, folate and high-energy beverages, may also contribute to the strong associations.

Several limitations should be considered. The self-reported dietary data used in this study are susceptible to measurement error. However, prior validation studies in the HPFS and NHS showed that dietary scores derived from FFQs are highly correlated with those from dietary records.[19] Our study participants are health professionals and predominantly White. The pattern scores, especially those determined by cohort-specific distributions, may not be representative of the general US population. Nonetheless, comparative analysis revealed that the cohort makeup does not always affect the generalizability of the pattern–CRC relationship.[34] Additionally, empirically derived patterns such as EDIH and EDIP are similarly associated with their predictive biomarkers in a multiethnic population.[35] We did not adjust for multiple testing because we intended to systematically compare these patterns, some of which have been examined individually in prior studies. Moreover, the findings remained if a more stringent significant level ($P < 0.0028$) was adopted based on the Bonferroni correction. Strengths of our study include the detailed collection of dietary and covariate data,

long duration of follow-up and reliable outcome ascertainment.

In conclusion, our results suggest that eating a diet with a lower EDIH, EDIP, Western pattern or higher DASH score may help prevent CRC. The independent associations of these patterns with CRC after adjusting for the WCRF or CRC dietary scores indicate that WCRF/AICR dietary recommendations can be further optimized to maximize their effects in preventing CRC. Future research is warranted to understand which additional dietary components and how they might contribute to the associations between dietary patterns and CRC risk. Our findings on EDIH and EDIP, which were developed to predict insulinemic and inflammatory biomarkers, demonstrate the potential for dietary changes that target important biological pathways for cancer prevention.

Ethics approval

This is an observational study. The study protocol was approved by the institutional review boards (IRBs) of the Brigham and Women's Hospital, Harvard T.H. Chan School of Public Health, and participating registries (1999P011117/BWH). The IRBs allowed participants' completion of questionnaires to be considered as implied consent. The study was performed in accordance with the Declaration of Helsinki.

Data availability

Data will be shared at the request of qualified investigators for purposes of replicating procedures and results. Further information including the procedures to obtain and access data from the Nurses' Health Studies and HPFS is described at https://www.nurseshealthstudy.org/researchers (contact e-mail: nhsaccess@channing.harvard.edu) and https://sites.sph.harvard.edu/hpfs/for-collaborators/.

Supplementary data

Supplementary data are available at *IJE* online.

Author contributions

P.W. and E.G. conceived and designed the study. M.S., A.H.E., M.W. and E.G. acquired the data. M.S., A.H.E., M.W. and E.G. obtained funding. P.W. conducted statistical analysis and wrote the first draft of the manuscript. M.S. provided technical review. All authors interpreted the results and revised previous versions of the manuscript. E.G. supervised the study. All authors approved the final manuscript as submitted.

Funding

This work was supported by grants from the National Institutes of Health (UM1 CA186107, P01 CA87969, U01 CA176726, U01 HL145386, U01 CA167552 and U01 CA261961). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Acknowledgements

The authors would like to acknowledge the contribution to this study from central cancer registries supported through the Centers for Disease Control and Prevention's National Program of Cancer Registries (NPCR) and/or the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program. Central registries may also be supported by state agencies, universities and cancer centres. Participating central cancer registries include the following: Alabama, Alaska, Arizona, Arkansas, California, Delaware, Colorado, Connecticut, Florida, Georgia, Hawaii, Idaho, Indiana, Iowa, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Mississippi, Montana, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Carolina, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, Puerto Rico, Rhode Island, Seattle SEER Registry, South Carolina, Tennessee, Texas, Utah, Virginia, West Virginia and Wyoming.

Conflict of interest

None declared.

References

1. Islami F, Goding Sauer A, Miller KD *et al.* Proportion and number of cancer cases and deaths attributable to potentially modifiable risk factors in the United States. *CA Cancer J Clin* 2018;**68**:31–54.
2. World Cancer Research Fund/American Institute for Cancer Research. Continuous Update Project Expert Report 2018. Diet, Nutrition, physical activity and colorectal cancer. 2018. dietandcancerreport.org.
3. Petimar J, Smith-Warner SA, Rosner B, Chan AT, Giovannucci EL, Tabung FK. Adherence to the World Cancer Research Fund/American Institute for Cancer Research 2018 recommendations for cancer prevention and risk of colorectal cancer. *Cancer Epidemiol Biomarkers Prev* 2019;**28**:1469–79.
4. Mehta RS, Song M, Nishihara R *et al.* Dietary patterns and risk of colorectal cancer: analysis by tumor location and molecular subtypes. *Gastroenterology* 2017;**152**:1944–53.e1.
5. Garcia-Larsen V, Morton V, Norat T *et al.* Dietary patterns derived from principal component analysis (PCA) and risk of colorectal cancer: a systematic review and meta-analysis. *Eur J Clin Nutr* 2019;**73**:366–86.
6. Tabung FK, Wang W, Fung TT *et al.* Association of dietary insulinemic potential and colorectal cancer risk in men and women. *Am J Clin Nutr* 2018;**108**:363–70.
7. Tabung FK, Liu L, Wang W *et al.* Association of dietary inflammatory potential with colorectal cancer risk in men and women. *JAMA Oncol* 2018;**4**:366–73.
8. Petimar J, Smith-Warner SA, Fung TT *et al.* Recommendation-based dietary indexes and risk of colorectal cancer in the Nurses' Health Study and Health Professionals Follow-up Study. *Am J Clin Nutr* 2018;**108**:1092–103.

9. Steck SE, Guinter M, Zheng J, Thomson CA. Index-based dietary patterns and colorectal cancer risk: a systematic review. *Adv Nutr* 2015;**6**:763–73.
10. Chiuve SE, Fung TT, Rimm EB *et al.* Alternative dietary indices both strongly predict risk of chronic disease. *J Nutr* 2012;**142**:1009–18.
11. Fung TT, Hu FB, McCullough ML, Newby PK, Willett WC, Holmes MD. Diet quality is associated with the risk of estrogen receptor-negative breast cancer in postmenopausal women. *J Nutr* 2006;**136**:466–72.
12. Satija A, Bhupathiraju SN, Spiegelman D *et al.* Healthful and unhealthful plant-based diets and the risk of coronary heart disease in U.S. adults. *J Am Coll Cardiol* 2017;**70**:411–22.
13. Satija A, Bhupathiraju SN, Rimm EB *et al.* Plant-based dietary patterns and incidence of type 2 diabetes in US men and women: results from three prospective cohort studies. *PLoS Med* 2016;**13**:e1002039.
14. Fung TT, Li Y, Bhupathiraju SN *et al.* Higher global diet quality score is inversely associated with risk of type 2 diabetes in US women. *J Nutr* 2021;**151**:168S–75S.
15. Tabung FK, Wang W, Fung TT *et al.* Development and validation of empirical indices to assess the insulinaemic potential of diet and lifestyle. *Br J Nutr* 2016;**116**:1787–98.
16. Tabung FK, Smith-Warner SA, Chavarro JE *et al.* Development and validation of an empirical dietary inflammatory index. *J Nutr* 2016;**146**:1560–70.
17. Hu FB, Rimm E, Smith-Warner SA *et al.* Reproducibility and validity of dietary patterns assessed with a food-frequency questionnaire. *Am J Clin Nutr* 1999;**69**:243–49.
18. Al-Shaar L, Yuan C, Rosner B *et al.* Reproducibility and validity of a semiquantitative food frequency questionnaire in men assessed by multiple methods. *Am J Epidemiol* 2021;**190**:1122–32.
19. Yue Y, Yuan C, Wang DD *et al.* Reproducibility and validity of diet quality scores derived from food-frequency questionnaires. *Am J Clin Nutr* 2022;**115**:843–53.
20. Willett W, Stampfer MJ. Total energy intake: implications for epidemiologic analyses. *Am J Epidemiol* 1986;**124**:17–27.
21. Smith-Warner SA, Spiegelman D, Ritz J *et al.* Methods for pooling results of epidemiologic studies: the Pooling Project of Prospective Studies of Diet and Cancer. *Am J Epidemiol* 2006;**163**:1053–64.
22. Durrleman S, Simon R. Flexible regression models with cubic splines. *Stat Med* 1989;**8**:551–61.
23. Wang M, Spiegelman D, Kuchiba A *et al.* Statistical methods for studying disease subtype heterogeneity. *Stat Med* 2016;**35**:782–800.
24. Giovannucci E. A framework to understand diet, physical activity, body weight, and cancer risk. *Cancer Causes Control* 2018;**29**:1–6.
25. Moazzen S, van der Sloot KWJ, Bock GH, Alizadeh BZ. Systematic review and meta-analysis of diet quality and colorectal cancer risk: is the evidence of sufficient quality to develop recommendations? *Crit Rev Food Sci Nutr* 2021;**61**:2773–82.
26. Nilsson LM, Winkvist A, Johansson I *et al.* Low-carbohydrate, high-protein diet score and risk of incident cancer; a prospective cohort study. *Nutr J* 2013;**12**:58.
27. Cai H, Sobue T, Kitamura T *et al.* Low-carbohydrate diet and risk of cancer incidence: the Japan Public Health Center-based prospective study. *Cancer Sci* 2022;**113**:744–55.
28. Fung TT, Li Y, Bromage S *et al.* Higher global diet quality score is associated with less 4-year weight gain in US women. *J Nutr* 2021;**151**:162S–67S.
29. Tabung FK, Satija A, Fung TT, Clinton SK, Giovannucci EL. Long-term change in both dietary insulinemic and inflammatory potential is associated with weight gain in adult women and men. *J Nutr* 2019;**149**:804–15.
30. World Cancer Research Fund/American Institute for Cancer Research. Continuous Update Project Expert Report 2018. Diet, nutrition and physical activity: energy balance and body fatness. 2018. dietandcancerreport.org.
31. Vieira AR, Abar L, Chan DSM *et al.* Foods and beverages and colorectal cancer risk: a systematic review and meta-analysis of cohort studies, an update of the evidence of the WCRF-AICR Continuous Update Project. *Ann Oncol* 2017;**28**:1788–802.
32. Cho E, Smith-Warner SA, Spiegelman D *et al.* Dairy foods, calcium, and colorectal cancer: a pooled analysis of 10 cohort studies. *J Natl Cancer Inst* 2004;**96**:1015–22.
33. Huncharek M, Muscat J, Kupelnick B. Colorectal cancer risk and dietary intake of calcium, vitamin D, and dairy products: a meta-analysis of 26,335 cases from 60 observational studies. *Nutr Cancer* 2009;**61**:47–69.
34. Wang P, Giovannucci EL. Are exposure-disease relationships assessed in cohorts of health professionals generalizable? A comparative analysis based on WCRF/AICR systematic literature reviews. *Cancer Causes Control* 2022. doi: 10.1007/s10552-022-01633-3.
35. Shi N, Aroke D, Jin Q *et al.* Proinflammatory and hyperinsulinemic dietary patterns are associated with specific profiles of biomarkers predictive of chronic inflammation, glucose-insulin dysregulation, and dyslipidemia in postmenopausal women. *Front Nutr* 2021;**8**:690428.