The Mediterranean and Dietary Approaches to Stop Hypertension (DASH) diets and colorectal cancer[1–3]

Teresa T Fung, Frank B Hu, Kana Wu, Stephanie E Chiuve, Charles S Fuchs, and Edward Giovannucci

ABSTRACT

Background: Although the Mediterranean diet has been studied for cancer mortality and the Dietary Approaches to Stop Hypertension (DASH) diet shares similarities with the Mediterranean diet, few studies have specifically examined these 2 diets and incident colorectal cancer.

Objective: The objective was to prospectively assess the association between the Alternate Mediterranean Diet (aMed) and the DASH-style diet scores and risk of colorectal cancer in middle-aged men and women.

Design: A total of 87,256 women and 45,490 men (age 30–55 y for women and 40–75 y for men at baseline) without a history of cancer were followed for ≤26 y. The aMed and DASH scores were calculated for each participant by using dietary information that was assessed ≤7 times during follow-up. Relative risks (RRs) for colorectal cancer were computed with adjustment for potential confounders.

Results: We documented 1432 cases of incident colorectal cancer among women and 1032 cases in men. Comparing top with bottom quintiles of the DASH score, the pooled RR for total colorectal cancer was 0.80 (95% CI: 0.70, 0.91; *P* for trend = 0.0001). The corresponding RR for DASH score and colon cancer was 0.81 (95% CI: 0.69, 0.95; *P* for trend = 0.002). There was a suggestion of an inverse association with rectal cancer with a pooled RR of 0.73 (95% CI: 0.55, 0.98; *P* for trend = 0.31) when comparing top with bottom quintiles of DASH score. No association was observed with aMed score.

Conclusion: Adherence to the DASH diet (which involves higher intakes of whole grains, fruit, and vegetables; moderate amounts of low-fat dairy; and lower amounts of red or processed meats, desserts, and sweetened beverages) was associated with a lower risk of colorectal cancer. *Am J Clin Nutr* 2010;92:1429–35.

INTRODUCTION

The traditional Mediterranean diet is characterized by high intakes of fruit, vegetables, fish, and whole grains; moderate amounts of alcohol and dairy products; and low amounts of red or processed meats and sweets (1). Higher intake of whole grains may reduce the risk of colorectal cancer, although results have been inconsistent (2, 3). On the other hand, high red or processed meat intake has been associated consistently with a higher risk of colorectal cancer (4). Therefore, adherence to the traditional Mediterranean diet may confer a reduced risk of colorectal cancer. Various Mediterranean diet scores have been created to measure adherence, with consistent results that this diet is associated with a lower risk of cancer mortality (5) and prevalent colorectal adenoma (6). In one prospective study, adherence to the Mediterranean diet was inversely associated with incidence of colorectal cancer (7).

The Dietary Approaches to Stop Hypertension (DASH) diet features high intakes of fruit, vegetables, legumes, and nuts; moderate amounts of low-fat dairy products; and low amounts of animal protein and sweets; and sodium reduction is now part of the diet (8). Although the DASH diet was originally designed for blood pressure reduction, several characteristics, such as higher intakes of whole grain and lower intakes of red and processed meat, are similar to the Mediterranean diet and may suggest a potential for colorectal cancer risk reduction. Dairy products have been shown to lower the risk of colorectal cancer (9). Although the DASH diet has been previously shown to associate with reduced odds of prevalent colorectal adenomas (6), its association with incident colorectal cancer has not been examined.

We previously developed dietary scores to measure adherence to the Mediterranean diet (10) and the DASH diet (11) in the Nurses' Health Study (NHS) and Health Professionals Follow-Up Study (HPFS). In the current analysis, we prospectively examined the association between diet scores and risk of colorectal cancer in these 2 large ongoing cohorts of men and women. We also separately considered specific anatomic sites of tumor location.

SUBJECTS AND METHODS

Study population

The NHS is a cohort study of 121,700 female nurses aged 30–55 y living in 11 US states at the time of inception in 1976. The first questionnaire regarding medical, lifestyle, and other health-related information was sent at the time of inception (12). Since then, questionnaires have been sent biennially to update this information.

[1] From the Department of Nutrition, Simmons College, Boston, MA (TTF); the Department of Nutrition (TTF, FBH, KW, SEC, and EG) and the Department of Epidemiology (FBH and EG), Harvard School of Public Health, Boston, MA; the Dana Farber Cancer Institute, Boston, MA (CSF); the Channing Laboratory (FBH and EG) and the Division of Preventive Medicine (SEC), Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA.

[2] Supported by the National Institutes of Health (grant nos. CA98859, CA87969, and HL60712).

[3] Address correspondence to TT Fung, Department of Nutrition, Simmons College, 300 The Fenway, Boston, MA 02115. E-mail: fung@simmons.edu.

Received January 20, 2010. Accepted for publication July 9, 2010.
doi: 10.3945/ajcn.2010.29242.

In 1980, participants completed a 61-item food-frequency questionnaire (FFQ). In 1984, the FFQ was expanded to 116 items, and similar FFQs were sent in 1986, 1990, 1994, 1998, and 2002.

The HPFS was established in 1986 with 51,529 male podiatrists, optometrist, pharmacists, dentists, and veterinarians aged 40–75 y. At baseline and every 2 y, a questionnaire on medical, lifestyle, and other health-related information was sent to the cohort members. A validated self-administered FFQ with ≈140 items was sent in 1986 and every 4 y to obtain dietary information (13). Follow-up was complete for >90% in each 2-y cycle for both cohorts.

For this analysis, we used 1980 as baseline for the NHS, because that is the year when the first dietary data were collected. We included women who completed the 1980 FFQ with <10 missing items and who had a realistic total energy intake (as calculated from the FFQ, between 500 and 3500 kcal/d) (14). For the HPFS, we included men with an FFQ with total energy intake (as calculated from the FFQ) between 800 and 4200 kcal/d at baseline and who had <70 missing items. After excluding individuals with a history of cancer (except for nonmelanoma skin cancer) and ulcerative colitis at baseline, we included 87,312 women and 45,080 men in this analysis. This study was approved by the Institutional Review Board of the Brigham and Women's Hospital and the Harvard School of Public Health, Boston, MA.

Dietary assessment

Self-administered, semiquantitative FFQs were designed to assess average food intake over the preceding year. A standard portion size and 9 possible frequency-of-consumption responses, ranging from "never, or less than once per month" to "6 or more times per day" were given for each food. Total energy and nutrient intake was calculated by summing up energy or nutrients from all foods. Previous validation studies in this cohort revealed reasonably good correlations between energy-adjusted nutrients assessed by the FFQ and multiple weeks of food records completed over the preceding year in both the NHS (14) and the HPFS (13). In the NHS, the deattenuated correlation coefficient between diet records and FFQ ranged from 0.48 for polyunsaturated fat to 0.79 for vitamin A. The mean correlation coefficient between frequencies of intake of 55 foods assessed by 2 FFQs 12 mo apart was 0.57 (14, 15). In the HPFS, the deattenuated correlation coefficient between FFQ and diet records ranged from 0.32 for protein to 0.81 for vitamin B-6.

Computation of the Alternate Mediterranean Diet (aMed) (10) and DASH (11) scores has been previously described in detail. We calculated each score for each FFQ and each participant. Briefly, the aMed rewards 1 point if intake is above the cohort-specific median for vegetables, legumes, fruit, nuts, whole-grain cereals, fish, and monounsaturated:saturated fat ratio and 1 point for intake below the cohort-specific median for red and processed meats (10). Alcohol intake of 5–15 g/d for women and 10–25 g/d for men received 1 point. The DASH score rewards points for high intake of fruit, vegetables, nuts and legumes, low-fat dairy products, and whole grains according to quintile rankings (ie, participants in the lowest quintile are assigned 1 point and those in the highest quintile are assigned 5 points). On the other hand, with regard to intake of sodium, sweetened beverages, and red and processed meats, participants with lower quintiles of intake scored higher points (ie, the lowest quintile received a score of 5 and the highest a score of 1) (11). The total possible score range was 8–40.

TABLE 1
Age-standardized baseline (1980) characteristics and 1990 dietary intake according to quintiles (Q) of Alternate Mediterranean Diet (aMed) and Dietary Approaches to Stop Hypertension (DASH) scores among women (n = 87,312)[1]

	aMed			DASH		
	Q1	Q3	Q5	Q1	Q3	Q5
Score	2 (1–2)[2]	4 (4–4)	6 (6–9)	17 (8–19)	24 (23–25)	30 (29–38)
1980 Characteristics						
BMI (kg/m²)	24.5 ± 0.01[3]	24.4 ± 0.01	24.2 ± 0.01	24.5 ± 0.01	24.4 ± 0.01	24.1 ± 0.01
Current smokers (%)	35 ± 0.001	28 ± 0.001	20 ± 0.001	39 ± 0.001	28 ± 0.001	19 ± 0.001
Multivitamin use (%)	28 ± 0.001	34 ± 0.001	41 ± 0.001	26 ± 0.001	34 ± 0.001	42 ± 0.001
Physical activity (METs/wk)	11 ± 0.05	14 ± 0.05	18 ± 0.05	10 ± 0.05	14 ± 0.04	19 ± 0.05
Family history (%)	11 ± 0.001	12 ± 0.001	12 ± 0.001	12 ± 0.001	12 ± 0.001	12 ± 0.001
1990 Dietary intake[4]						
Energy (kcal)	1514 ± 1.1	1740 ± 1.2	2004 ± 1.1	1693 ± 1.3	1740 ± 1.1	1865 ± 1.3
Alcohol (g)	5 ± 0.02	5 ± 0.02	6 ± 0.02	6 ± 0.02	5 ± 0.02	4 ± 0.02
Fiber (g)	14 ± 0.01	18 ± 0.01	22 ± 0.01	13 ± 0.01	18 ± 0.01	24 ± 0.01
Animal protein (g)	56 ± 0.03	56 ± 0.04	55 ± 0.03	54 ± 0.04	56 ± 0.03	56 ± 0.04
Vegetable protein (g)	18 ± 0.01	20 ± 0.01	23 ± 0.01	17 ± 0.01	20 ± 0.01	24 ± 0.01
Glycemic load	102 ± 0.05	106 ± 0.05	109 ± 0.05	102 ± 0.05	105 ± 0.04	112 ± 0.05
Monounsaturated fat (g)	23 ± 0.01	21 ± 0.01	20 ± 0.01	24 ± 0.01	22 ± 0.01	18 ± 0.01
Polyunsaturated fat (g)	10 ± 0.01	11 ± 0.01	11 ± 0.01	11 ± 0.01	11 ± 0.01	10 ± 0.01
Saturated fat (g)	22 ± 0.01	19 ± 0.01	16 ± 0.01	22 ± 0.01	19 ± 0.01	15 ± 0.01
Folate (μg)	370 ± 0.5	432 ± 0.5	488 ± 0.5	331 ± 0.5	434 ± 0.5	527 ± 0.5
Calcium (mg)	951 ± 1.1	988 ± 1.2	1018 ± 1.1	762 ± 1.2	995 ± 1.1	1194 ± 1.2

[1] 1980 scores are for baseline characteristics, and 1990 scores are for dietary intake. METs, metabolic equivalent task hours.
[2] Median; range in parentheses (all such values).
[3] Mean ± SE (all such values).
[4] Energy-adjusted except for alcohol and energy.

TABLE 2

Age-standardized baseline (1986) characteristics according to quintiles (Q) of Alternate Mediterranean Diet (aMed) and Dietary Approaches to Stop Hypertension (DASH) scores among men (n = 45,080)[1]

	aMed			DASH		
	Q1	Q3	Q5	Q1	Q3	Q5
Score	2 (0–2)[2]	4 (4–4)	7 (7–9)	17 (8–19)	24 (23–25)	31 (29–40)
BMI (kg/m^2)	25.9 ± 0.1[3]	25.6 ± 0.1	25.0 ± 0.1	25.9 ± 0.1	25.6 ± 0.1	24.9 ± 0.1
Current smokers (%)	15 ± 0.001	9 ± 0.001	4 ± 0.001	16 ± 0.001	8 ± 0.001	3 ± 0.001
Multivitamin use (%)	35 ± 0.002	40 ± 0.002	50 ± 0.002	34 ± 0.002	41 ± 0.002	50 ± 0.002
Physical activity (METs/wk)	16 ± 0.01	20 ± 0.01	29 ± 0.01	15 ± 0.1	21 ± 0.1	30 ± 0.1
Family history (%)	8 ± 0.001	9 ± 0.001	9 ± 0.001	8 ± 0.001	9 ± 0.001	9 ± 0.001
Dietary intake[4]						
Energy (kcal)	1753 ± 2.1	1946 ± 2.2	2270 ± 2.4	1819 ± 2.0	1993 ± 2.1	2173 ± 2.0
Alcohol (g)	12 ± 0.05	11 ± 0.06	11 ± 0.06	12 ± 0.05	11 ± 0.05	9 ± 0.05
Fiber (g)	15 ± 0.02	20 ± 0.02	27 ± 0.02	15 ± 0.02	21 ± 0.02	28 ± 0.02
Animal protein (g)	68 ± 0.06	68 ± 0.06	66 ± 0.07	67 ± 0.06	68 ± 0.06	66 ± 0.06
Vegetable protein (g)	20 ± 0.02	24 ± 0.02	30 ± 0.02	21 ± 0.02	25 ± 0.02	30 ± 0.02
Glycemic load	116 ± 0.09	123 ± 0.09	133 ± 0.1	117 ± 0.08	123 ± 0.09	136 ± 0.08
Monounsaturated fat (g)	30 ± 0.02	28 ± 0.02	24 ± 0.02	31 ± 0.02	27 ± 0.02	23 ± 0.02
Polyunsaturated fat (g)	12 ± 0.01	13 ± 0.01	14 ± 0.01	13 ± 0.01	13 ± 0.01	13 ± 0.01
Saturated fat (g)	29 ± 0.02	25 ± 0.02	19 ± 0.02	28 ± 0.02	25 ± 0.02	20 ± 0.02
Folate (μg)	391 ± 1.0	463 ± 1.0	584 ± 1.1	370 ± 0.9	481 ± 0.9	598 ± 0.9
Calcium (mg)	872 ± 1.5	892 ± 1.5	922 ± 1.7	723 ± 1.3	900 ± 1.4	1071 ± 1.4

[1] METs, metabolic equivalent task hours.
[2] Median; range in parentheses (all such values).
[3] Mean ± SE (all such values).
[4] Energy-adjusted except for alcohol and energy.

Ascertainment of colorectal cancer

Incident colorectal cancer was ascertained between 1980 and 2006 for the NHS and between 1986 and 2006 for the HPFS. In each biennial questionnaire, participants self-report any diagnosis of colorectal cancer in the previous 2 y. We then sought permission to obtain medical records to confirm the diagnosis. Physicians unaware of dietary and lifestyle data reviewed and recorded information on histology, site, and stage of the cancer. Only adenocarcinomas of the colorectum were included, but we excluded cases associated with ulcerative colitis and familiar polyposis. The follow-up for death in both cohorts is ≥95% complete (16).

Covariate ascertainment

Body mass index (BMI) was calculated from weight reported on each biennial questionnaire and height reported at the first questionnaire. Smoking, history of hypertension, aspirin use, multivitamin intake, menopausal status and use of postmenopausal hormone therapy, parity, and age at first birth were assessed every 2 y. In the NHS, information on hours per week of vigorous activity was collected in 1980, 1982, and 1984. Leisure-time physical activity was measured 7 times beginning in 1986 with validated questions on 10 common activities in the NHS and biennially from baseline in the HPFS. The information was then summed and calculated as metabolic equivalent task hours (METs) (17). In the NHS, we inquired about physical examinations at baseline and in both cohorts every 2 y beginning in 1988. Family history of colorectal cancers and information on lower bowel endoscopy screening were also collected. Deaths were identified from state vital statistics records, the National Death Index, and the postal system and as reported by the families.

Statistical analysis

We used Cox proportional hazard models to assess the association between the DASH and aMed scores and risk of colorectal cancer during follow-up. Proportional hazard assumption was tested with use of interaction terms between the diet scores and age and was found not to be violated ($P > 0.05$). To reduce random within-person variation and to best represent long-term dietary intake, we calculated cumulative averages of the DASH and aMed scores from our repeated FFQs (18). For example, in the NHS, the diet scores in 1980 were used to predict colorectal cancer risk between 1980 and 1984, the average score from 1980 and 1984 was used to predict colorectal cancer from 1984 to 1986, and so forth. The same procedure was used in the HPFS.

In multivariate analyses, we adjusted for age (by stratifying age in months in the Cox model), physical activity (quintiles), BMI (5 categories), energy intake (quintiles), alcohol intake (4 categories, DASH score only), history of colorectal polyps (yes or no), family history of colorectal cancer (yes or no), history of lower bowel endoscopy (yes or no), aspirin use (yes or no), pack-years of smoking (5 categories), and multivitamin use (yes or no) with updated information at each 2-y questionnaire cycle. Test of trend was conducted by fitting continuous terms for the 2 diet scores. We also examined associations separately by tumor location (colon, proximal colon and distal colon, rectum).

To assess the contribution of each of the individual components of the DASH diet, we simultaneously modeled each component individually. In separate models, we also included the

TABLE 3
Relative risks (95% CI) for colorectal cancer according to quintiles (Q) of Alternate Mediterranean Diet score (n = 87,312 for women and 45,080 for men)[1]

	Q1	Q2	Q3	Q4	Q5	*P* for trend
Total colorectal cancer						
Men						
No. of cases	197	188	227	228	192	
Age- and energy-adjusted	1	0.91 (0.74, 1.11)	0.99 (0.82, 1.21)	0.90 (0.74, 1.09)	0.77 (0.62, 0.95)	0.008
Multivariate-adjusted[2]	1	0.94 (0.76, 1.15)	1.04 (0.86, 1.27)	0.98 (0.80, 1.20)	0.88 (0.71, 1.09)	0.25
Women						
No. of cases	285	282	282	279	307	
Age- and energy-adjusted	1	0.92 (0.78, 1.08)	0.79 (0.67, 0.94)	0.79 (0.66, 0.93)	0.79 (0.66, 0.93)	0.002
Multivariate-adjusted[2]	1	0.94 (0.80, 1.12)	0.84 (0.71, 0.99)	0.85 (0.71, 1.01)	0.88 (0.74, 1.05)	0.14
Pooled	1	0.94 (0.83, 1.07)	0.92 (0.75, 1.13)	0.90 (0.79, 1.02)	0.89 (0.77, 1.01)	0.06
Colon cancer						
Men						
No. of cases	130	115	153	152	132	
Age- and energy-adjusted	1	0.83 (0.64, 1.07)	0.99 (0.78, 1.26)	0.88 (0.69, 1.12)	0.77 (0.60, 0.99)	0.07
Multivariate-adjusted[2]	1	0.85 (0.66, 1.09)	1.03 (0.81, 1.31)	0.94 (0.73, 1.20)	0.87 (0.67, 1.13)	0.45
Women						
No. of cases	209	212	224	201	236	
Age- and energy-adjusted	1	0.92 (0.76, 1.12)	0.85 (0.70, 1.03)	0.77 (0.63, 0.94)	0.81 (0.67, 0.99)	0.007
Multivariate-adjusted[2]	1	0.95 (0.78, 1.15)	0.89 (0.74, 1.08)	0.82 (0.67, 1.01)	0.91 (0.74, 1.11)	0.13
Pooled	1	0.91 (0.78, 1.06)	0.94 (0.81, 1.10)	0.87 (0.74, 1.02)	0.89 (0.76, 1.05)	0.11
Rectal cancer						
Men						
No. of cases	42	49	42	53	32	
Age- and energy-adjusted	1	1.18 (0.78, 1.79)	0.88 (0.57, 1.37)	1.03 (0.68, 1.56)	0.63 (0.39, 1.02)	0.03
Multivariate-adjusted[2]	1	1.27 (0.83, 1.94)	0.97 (0.62, 1.51)	1.18 (0.77, 1.82)	0.75 (0.46, 1.23)	0.19
Women						
No. of cases	70	67	53	70	63	
Age- and energy-adjusted	1	0.93 (0.67, 1.31)	0.62 (0.43, 0.90)	0.85 (0.60, 1.20)	0.67 (0.47, 0.96)	0.12
Multivariate-adjusted[2]	1	0.97 (0.69, 1.36)	0.67 (0.47, 0.97)	0.94 (0.66, 1.34)	0.80 (0.55, 1.15)	0.64
Pooled	1	1.08 (0.83, 1.40)	0.79 (0.55, 1.01)	1.03 (0.79, 1.35)	0.78 (0.58, 1.05)	0.21

[1] Relative risks were computed from a Cox proportional hazards model.
[2] Adjusted for age (continuous), BMI (5 categories), alcohol intake (4 categories), family history (yes or no), physical activity (quintiles), aspirin use (4 categories), colonoscopy, history of polyps, multivitamin use (yes or no), pack-years of smoking (5 categories), and energy intake (quintiles).

overall DASH score. The difference in relative risks (RRs) of the DASH score between models with or without the food component can be interpreted as the contribution of the food component on colorectal cancer risk. RRs from each cohort were also pooled to obtain a summary risk estimate by using a random-effects model that allows for between-study heterogeneity (19). *P* values for heterogeneity of study results were calculated by using the Cochran *Q* test. The statistical analysis was conducted with SAS version 9 (SAS Institute, Cary, NC).

RESULTS

In ≤26 y of follow-up in the NHS, we documented 1432 cases of incident colorectal cancer, of which 1082 were colon cancer and 323 were rectal cancer; the rest were not clearly classified for subsite. In the HPFS, with ≤20 y of follow-up, we documented 1032 cases of incident colorectal cancer, of which 682 were colon cancer and 218 were rectal cancer; the rest were not clearly classified for subsite.

The aMed and DASH scores were substantially correlated. Spearman's correlation coefficients for cumulative average aMed and DASH score were 0.74 ($P < 0.0001$) for the NHS and 0.75 ($P < 0.0001$) for the HPFS. As shown in **Tables 1** and **2**, we compared baseline lifestyle characteristics and dietary intake between DASH or aMed. Because of the long follow-up in women, we present the 1990 dietary data, because it is close to the midpoint of follow-up. Men and women who scored higher in either the aMed or DASH were less likely to smoke but more likely to use multivitamins regularly and were more active (Tables 1 and 2). Men with higher aMed and DASH scores tended to be leaner, but this was less apparent among women.

A higher aMed score was associated with a similar magnitude of reduced risk of colorectal cancer in both women and men, but neither reached statistical significance. When data from both cohorts were pooled, we observed an RR of 0.89 (95% CI: 0.77, 1.01; *P* for trend = 0.06) for total colorectal cancer (**Table 3**). The association was slightly weaker for men.

For the DASH score, we observed an RR for total colorectal cancer of 0.80 (95% CI: 0.67, 0.94; *P* for trend = 0.005) when comparing the highest with lowest quintiles in women (**Table 4**). The magnitude of risk reduction was essentially the same among men but marginally significant due to fewer cases. The pooled RR for total colorectal cancer was 0.80 (95% CI: 0.70, 0.91; *P* for trend = 0.001). The association for colon cancer was slightly weaker in both men and women, but the pooled RR remained statistically significant when comparing highest with lowest quintiles (RR: 0.81; 95% CI: 0.69, 0.95; *P* for trend = 0.002). There was also a suggestion of an inverse association with rectal

TABLE 4
Relative risks (95% CI) for colorectal cancer according to quintiles (Q) of Dietary Approaches to Stop Hypertension score (*n* = 87,312 for women and 45,080 for men)[1]

	Q1	Q2	Q3	Q4	Q5	*P* for trend
Total colorectal cancer						
Men						
No. of cases	205	199	212	201	215	
Age- and energy-adjusted	1	0.80 (0.66, 0.98)	0.81 (0.67, 0.99)	0.72 (0.59, 0.87)	0.68 (0.56, 0.83)	0.0003
Multivariate-adjusted[2]	1	0.83 (0.68, 1.08)	0.86 (0.71, 1.05)	0.79 (0.65, 0.97)	0.81 (0.66, 1.00)	0.09
Women						
No. of cases	292	272	294	266	308	
Age- and energy-adjusted	1	0.79 (0.67, 0.94)	0.80 (0.68, 0.94)	0.70 (0.59, 0.83)	0.71 (0.60, 0.83)	<0.0001
Multivariate-adjusted[2]	1	0.81 (0.69, 0.96)	0.84 (0.71, 0.99)	0.76 (0.64, 0.90)	0.80 (0.67, 0.94)	0.005
Pooled	1	0.82 (0.72, 0.93)	0.85 (0.75, 0.96)	0.77 (0.67, 0.88)	0.80 (0.70, 0.91)	0.001
Colon cancer						
Men						
No. of cases	130	137	134	135	146	
Age- and energy-adjusted	1	0.86 (0.67, 1.10)	0.79 (0.62, 1.01)	0.72 (0.56, 0.93)	0.70 (0.55, 0.90)	0.002
Multivariate-adjusted[2]	1	0.88 (0.69, 1.12)	0.82 (0.64, 1.05)	0.78 (0.61, 1.01)	0.82 (0.63, 1.05)	0.10
Women						
No. of cases	216	208	222	195	241	
Age- and energy-adjusted	1	0.82 (0.67, 0.99)	0.80 (0.66, 0.97)	0.68 (0.56, 0.83)	0.73 (0.61, 0.88)	<0.0001
Multivariate-adjusted[2]	1	0.83 (0.68, 1.00)	0.83 (0.69 1.01)	0.73 (0.59, 0.89)	0.81 (0.66, 0.98)	0.007
Pooled	1	0.85 (0.73, 0.99)	0.83 (0.71, 0.96)	0.75 (0.64, 0.87)	0.81 (0.69, 0.95)	0.002
Rectal cancer						
Men						
No. of cases	45	38	54	41	40	
Age- and energy-adjusted	1	0.69 (0.44, 1.07)	1.00 (0.67, 1.50)	0.70 (0.45, 1.08)	0.60 (0.39, 0.94)	0.15
Multivariate-adjusted[2]	1	0.73 (0.47, 1.13)	1.10 (0.73, 1.66)	0.80 (0.51, 1.25)	0.72 (0.45, 1.15)	0.64
Women						
No. of cases	71	62	67	62	61	
Age- and energy-adjusted	1	0.76 (0.54, 1.07)	0.79 (0.56, 1.10)	0.70 (0.49, 0.99)	0.61 (0.43, 0.87)	0.02
Multivariate-adjusted[2]	1	0.79 (0.56, 1.12)	0.86 (0.61, 1.21)	0.80 (0.56, 1.14)	0.74 (0.52, 1.07)	0.34
Pooled	1	0.77 (0.58, 1.00)	0.95 (0.73, 1.24)	0.80 (0.61, 1.06)	0.73 (0.55, 0.98)	0.31

[1] Relative risks were computed from a Cox proportional hazards model.
[2] Adjusted for the same covariates as in Table 3.

cancer with a pooled RR of 0.73 (95% CI: 0.55, 0.98) between top and bottom quintiles, but the *P* value for trend was not significant (*P* = 0.31).

For proximal colon cancer, we observed an inverse association with both DASH (multivariate RR comparing highest to lowest quintiles: 0.81; 95% CI: 0.63, 1.04; *P* for trend = 0.02) and aMed (RR: 0.77; 95% CI: 0.59, 0.96; *P* for trend = 0.01) scores among women only. The aMed score was not associated with distal colon cancer, but a significant inverse association was noted for the DASH score (pooled RR when comparing top with bottom quintile: 0.76; 95% CI: 0.59, 1.01, *P* for trend = 0.02).

We then explored the association of each component of the DASH score and total colorectal cancer. Whole-grain intake was inversely associated with colorectal cancer in the HPFS. The RR for each serving increase was 0.94 (95% CI: 0.88, 0.99) (**Table 5**). On the other hand, each serving increase in sweetened beverages was associated with a 17% increase risk of colorectal cancer in men (RR: 1.17; 95% CI: 1.02, 1.33) but not in women. Among women, low-fat dairy products (RR for 1 serving increase: 0.89; 95% CI: 0.83, 0.96) and fruit (RR: 0.95; 95% CI: 0.90, 0.99) were associated with lower risk of total colorectal cancer. We then tested the contribution of each component by adding them one at a time to the regression model that contains the DASH score and found that the same components (ie, fruit and low-fat dairy for the NHS and sweetened beverages and whole grains for the HPFS) were the strongest contributors for the inverse association observed between the DASH score and colorectal cancer.

TABLE 5
Multivariate relative risks (95% CI) for each serving/d increase in Dietary Approaches to Stop Hypertension food components for total colorectal cancer[1]

	Women (*n* = 87,312)	Men (*n* = 45,080)
Fruit	0.95 (0.90, 0.99)	1.01 (0.96, 1.05)
Nuts	1.02 (0.91, 1.14)	1.04 (0.94, 1.15)
Vegetables	1.01 (0.96, 1.05)	1.00 (0.96, 1.04)
Red/processed meats	1.12 (0.99, 1.26)	1.08 (0.97, 1.21)
Sodium[2]	1.06 (0.93, 1.21)	0.98 (0.90, 1.06)
Low-fat dairy	0.89 (0.83, 0.96)	0.97 (0.90, 1.04)
Sweetened beverages	1.04 (0.94, 1.16)	1.17 (1.02, 1.33)
Whole grains	0.95 (0.89, 1.02)	0.94 (0.88, 0.99)

[1] Values were adjusted for the same variables as in Table 3. Relative risks were computed from a Cox proportional hazards model.
[2] Per 1000-mg increment in sodium intake.

DISCUSSION

In our 2 cohorts of US men and women with ≤20–26 y of follow-up, we observed that a higher DASH score was associated with a lower risk of colorectal cancer. In addition, the DASH score may also be associated with a lower risk of rectal cancer. We found no significant association between the aMed and colorectal, colon, or rectal cancers.

Current data on the association between the Mediterranean diet and colorectal cancer generally pointed toward a reduction of risk, but results were not overwhelmingly consistent. A meta-analysis of prospective studies documented a 6% reduction in cancer mortality for every 2-point increase in Mediterranean diet score (5). However, among members of the Prostate, Lung, Colorectal, and Ovarian Screening (PLCO) Trial, a higher Mediterranean diet score was associated with a lower prevalence of distal colorectal adenomas only in men (6). Similarly, in the NIH-AARP cohort with 5 y of follow-up, adherence to a Mediterranean diet score that was defined similarly to our score was associated with lower risk of colorectal cancer incidence only in men (RR when comparing top with bottom quintiles: 0.72) (7). In addition, significant risk reduction was also observed for distal colon and rectal cancer in men but not in women. We did not observe a sex-specific difference in risk, and our association is less strong than reported in the AARP cohort.

Data on the DASH diet and cancer outcome are sparse. In a population-based cohort of individuals with hypertension with a mean follow-up of 8.2 y, there was a suggestion of an inverse association between those who adhered to a DASH-like diet and cancer mortality (HR: 0.51, 95% CI: 0.23–1.10) (20). To our knowledge, there is only one study on specific colorectal endpoints. A higher score in a 9-point, food group–based DASH diet score was associated with a lower prevalence of distal colorectal adenoma among male participants of the PLCO Trial (6). Our analysis, which specifically focused on incident colorectal cancer, provides stronger data that suggest an inverse association between the DASH diet and risk of colorectal cancer.

Both the Mediterranean and DASH diets emphasize plant foods. However, the possibility of fiber or whole grains being the intermediate factor is uncertain, because current data are equivocal at best (2, 3). On the other hand, both diets award points for low meat consumption. As a number of studies have shown a direct association between red and processed meats and risk of colorectal cancer (4), the inverse association that we observed between the 2 diet scores and colorectal cancer may be mediated through lower red and processed meat intake. The IGF (insulin-like growth factor) axis is a potential pathway for colorectal cancer development (21). Although the association of C-peptide, a marker of insulin secretion, and risk of colorectal cancer is not completely consistent (22) but not all studies (23). Substantial evidence suggests that diabetes is a risk factor for colorectal cancer (24), and versions of the Mediterranean diet (25) and DASH diet (26) have been associated with lower risk of diabetes.

In this analysis, an inverse association with risk of colorectal cancer was observed with the DASH score but not the aMed score. Among components that differ between the DASH and aMed, low-fat dairy products, which are part of the DASH diet, were inversely associated with colorectal cancer (9). In addition, scoring for each food group in the DASH score was based on 5 points instead of 2 in the aMed score. Thus, the DASH score may have more discriminating power.

Our data suggest a potential inverse association between the DASH score and rectal cancer. Although dietary patterns similar to the DASH diet, which is characterized by higher fruit, vegetable, and whole-grain intake, have been associated with a lower risk of rectal cancer risk, the association is not consistent across populations or sex (27, 28). On the other hand, a meta-analysis has shown a positive association with meat consumption (4). Nevertheless, our results suggest that a minimally processed, plant-based diet may lower risk of rectal cancer.

Our long follow-up allowed us to detect the association between diet and slow progressing diseases such as cancer. Our comprehensive and updated information on potential confounders allowed for detailed adjustment and minimized confounding, although we could not completely rule out residual confounding. Because of the large number of cases, we were able to examine tumors at specific anatomical sites. Because lifestyle and dietary data are recorded with some degree of error, a certain amount of misclassification is unavoidable. However, we used a validated questionnaire, so we believe the amount of misclassification is small and random.

Construction of the aMed and DASH scores was based on the literature and our a priori hypotheses. However, it still involved some level of arbitrary decision in the type and number of foods to be included and assignment of points to different amounts of intake. In previous studies on cardiovascular disease, the aMed nevertheless performed similarly with other Mediterranean diet scoring algorithms (5, 29). In a previous study, the DASH score used in this study was inversely associated with cardiovascular mortality (11), which agrees with the results of the original DASH trials on blood pressure reduction (8). Therefore, we believe that our scoring algorithm is successful in capturing the important features of these 2 diets.

Adherence to the DASH diet (which involves higher intake of whole grains, fruits, and vegetables; moderate amounts of low-fat dairy; and lower amounts of red or processed meats, desserts, and sweetened beverages) was associated with a lower risk of colorectal cancer.

The authors' responsibilities were as follows—TTF and FBH: contributed to the design and analysis of the study; and all authors: were involved in the interpretation of the data and review and approval of the manuscript. TTF had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. There were no potential conflicts of interest for any of the authors.

REFERENCES

1. Willett WC, Sacks F, Trichopoulou A, et al. Mediterranean diet pyramid: a cultural model for healthy eating. Am J Clin Nutr 1995;61: S1402–6.
2. Park Y, Hunter DJ, Speigelman D, et al. Dietary fiber intake and risk of colorectal cancer: a pooled analysis of prospective cohort studies. JAMA 2005;294:2849–57.
3. Schatzkin A, Mouw T, Park Y, et al. Dietary fiber and whole-grain consumption in relation to colorectal cancer in the NIH-AARP Diet and Health Study. Am J Clin Nutr 2007;85:1353–60.
4. Larsson SC, Wolk A. Meat consumption and risk of colorectal cancer: a meta-analysis of prospective studies. Int J Cancer 2006;119:2657–64.
5. Sofi F, Cesari F, Abbate R, Gensini GF, Casini A. Adherence to Mediterranean diet and health status: meta-analysis. BMJ 2008;337:a1344.

6. Dixon LB, Subar AF, Peters U, et al. Adherence to the USDA Food Guide, DASH Eating Plan, and Mediterranean dietary pattern reduces risk of colorectal adenoma. J Nutr 2007;137:2443–50.
7. Reedy J, Mitrou PN, Krebs-Smith SM, et al. Index-based dietary patterns and risk of colorectal cancer: the NIH-AARP Diet and Health Study. Am J Epidemiol 2008;168:38–48.
8. Sacks FM, Svetkey LP, Vollmer WM, et al. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. DASH-Sodium Collaborative Research Group. N Engl J Med 2001;344:3–10.
9. 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.
10. Fung TT, Hu FB, McCulloguh ML, Newby PK, Willett WC, Holmes ME. Diet quality is associated with the risk of estrogen receptor–negative breast cancer in postmenopausal women. J Nutr 2006;136:466–72.
11. Fung TT, Chiuve SE, McCulloguh ML, Rexrode KM, Logroscino G, Hu FB. Adherence to a DASH-style diet and risk of coronary heart disease and stroke in women. Arch Intern Med 2008;168:713–20.
12. Colditz GA, Martin P, Stampfer MJ, et al. Validation of questionnaire information on risk factors and disease outcomes in a prospective cohort of women. Am J Epidemiol 1986;123:894–900.
13. Rimm EB, Giovannucci EL, Stampfer MJ, Colditz GA, Litin LB, Willett WC. Reproducibility and validity of an expanded self-administered semiquantitative food frequency questionnaire among male health professionals. Am J Epidemiol 1992;135:1114–26.
14. Willett WC. Nutritional epidemiology. New York, NY: Oxford University Press, 1998.
15. Salvini S, Hunter DJ, Sampson L, et al. Food-based validation of a dietary questionnaire: the effects of week-to-week variation in food consumption. Int J Epidemiol 1989;18:858–67.
16. Rich-Edwards JW, Corsano KA, Stampfer MJ. Test of the National Death Index and Equifax Nationwide Death Search. Am J Epidemiol 1994;140:1016–9.
17. Ainsworth BE, Haskell WL, Whitt MC, et al. Compendium of physical activities: an update of activity codes and MET intensities. Med Sci Sports Exerc 2000;32(9 suppl):S498–504.
18. Hu FB, Stampfer MJ, Rimm E, et al. Dietary fat and coronary heart disease: a comparison of approaches for adjusting for total energy intake and modeling repeated dietary measurements. Am J Epidemiol 1999; 149:531–40.
19. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986;7:177–88.
20. Parikh A, Lipsitz SR, Natarajan S. Association between a DASH-like diet and mortality in adults with hypertension: findings from a population-based follow-up study. Am J Hypertens 2009;22:409–16.
21. Sandhu MS, Dunger DB, Giovannucci EL. Insulin, insulin-like growth factor-I (IGF-I), IGF binding proteins, their biologic interactions, and colorectal cancer. J Natl Cancer Inst 2002;94:972–80.
22. Kaaks R, Toniolo P, Akhmedkhanov A, et al. Serum C-peptide, insulin-like growth factor (IGF)-I, IGF-binding proteins, and colorectal cancer risk in women. J Natl Cancer Inst 2000;92:1592–600.
23. Wei EK, Pollak M, Rifai N, Fuchs CS, Hankinson SE, Giovannucci EL. A prospective study of C-peptide, insulin-like growth factor-I, insulin-like growth factor binding protein-1, and the risk of colorectal cancer in women. Cancer Epidemiol Biomarkers Prev 2005;14:850–5.
24. Larsson SC, Orsini N, Wolk A. Diabetes mellitus and risk of colorectal cancer: a meta-analysis. J Natl Cancer Inst 2005;97:1679–87.
25. Martinez-Gonzalez MA, de la Fuente-Arrillaga C, Nuenz-Cordoba JM, et al. Adherence to Mediterranean diet and risk of developing diabetes: prospective cohort study. BMJ 2008;336:1348–51.
26. Liese AD, Nichols M, Sun X, D'Agostino RBJ, Haffner SM. Adherence to the DASH Diet is inversely associated with incidence of type 2 diabetes: the insulin resistance atherosclerosis study. Diabetes Care 2009; 32:1434–6.
27. Williams CD, Satia JA, Adair LS, et al. Dietary patterns, food groups, and rectal cancer risk in Whites and African-Americans. Cancer Epidemiol Biomarkers Prev 2009;18:1552–61.
28. Wirfalt E, Midthune D, Reedy J, et al. Associations between food patterns defined by cluster analysis and colorectal cancer incidence in the NIH-AARP diet and health study. Eur J Clin Nutr 2009;63:707–17.
29. Mitrou PN, Kipnis V, Thiébaut AC, et al. Mediterranean dietary pattern and prediction of all-cause mortality in a U.S. population: results from the NIH-AARP Diet and Health Study. Arch Intern Med 2007;167:2461–8.