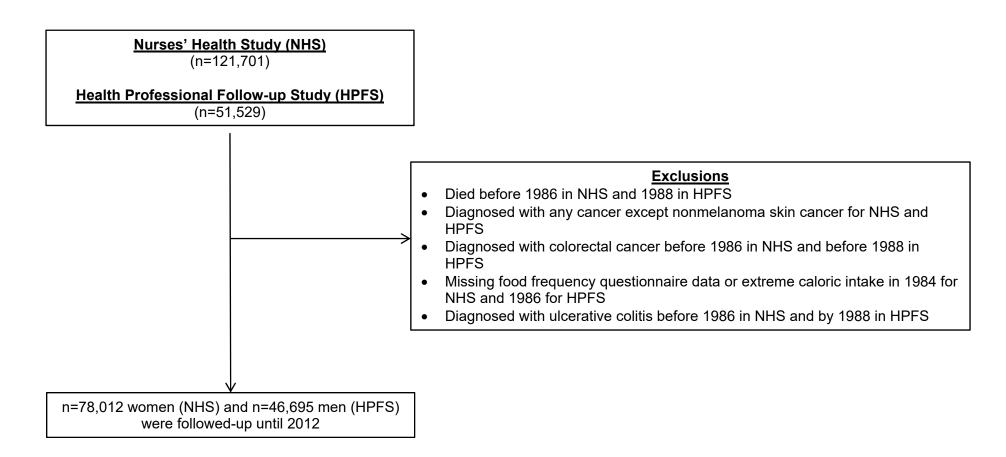
Supplemental Figure 1. Participant flow chart



Supplemental Table 1. Comparison of dietary components included in the Dietary Approaches to Stop Hypertension (DASH, Alternative
Mediterranean Diet (AMED), and Alternative Healthy Eating Index-2010 (AHEI-2010) dietary indices and criteria for minimum and maximum
points

Dietary Component	DASH ¹	AMED ²	AHEI-2010 ³
Fruits	Quintiles (1pt=Q1, 5pt=Q5)	High vs. low (0pt=below median, 1pt=above median)	Absolute cutoffs (0pt=0 serv/day, 10pt=≥4 serv/day)
Vegetables	Quintiles (1pt=Q1, 5pt=Q5)	High vs. low (0pt=below median, 1pt=above median)	Absolute cutoffs (0pt=0 serv/day, 10pt=≥5 serv/day)
Whole grains	Quintiles (1pt=Q1, 5pt=Q5)	High vs. low (0pt=below median, 1pt=above median)	Absolute cutoffs (0pt=0 serv/day, 10pt=≥75 g/day for women and ≥90 g/day for men)
Nuts ⁴ Legumes ⁴	Quintiles (1pt=Q1, 5pt=Q5)	High vs. low (0pt=below median, 1pt=above median) High vs. low (0pt=below median, 1pt=above median)	Absolute cutoffs (0pt=0 serv/day, 10pt=≥1 serv/day)
Low-fat dairy	Quintiles (1pt=Q1, 5pt=Q5)		
Red/processed meat	Quintiles (1pt=Q5, 5pt=Q1)	High vs. low (0pt=below median, 1pt=above median)	Absolute cutoffs (0pt=≥1.5 serv/day, 10pt=0 serv/day)
Sugar-sweetened beverage⁵	Quintiles (1pt=Q5, 5pt=Q1)		Absolute cutoffs (0pt=≥1 serv/day, 10pt=0 serv/day)
Sodium intake	Quintiles (1pt=Q5, 5pt=Q1)		Absolute cutoffs (0pt=highest decile, 10pt=lowest decile)
Alcohol		Moderate vs. not moderate (0pt=not moderate, 1pt=moderate)	Absolute cutoffs (0pt=≥2.5 drinks/day for women and ≥3.5 drinks/day for men, 10pt=0.5-1.5 drinks/day for women and 0.5-2.0 drinks/day for men)
Fish		High vs. low (0pt=below median, 1pt=above median)	
MUFA: SFA ratio		High vs. low (0pt=below median, 1pt=above median)	
Polyunsaturated fat			Absolute cutoffs (0pt=≤2% energy, 10pt=≥10% energy)
Omega-3 fatty acid			Absolute cutoffs (0pt=0mg/day, 10pt=250 mg/day)
Trans fat			Absolute cutoffs (0pt=≥4% energy, 10pt=≤0.5% energy)

DASH, Dietary Approaches to Stop Hypertension; AMED, Alternative Mediterranean Diet; AHEI-2010, Alternative Healthy Eating Index-2010; MUFA, monounsaturated fat; SFA, saturated fat

¹For fruit, vegetable, whole grain, nut and legume, and low-fat dairy intake, the lowest quintile of intake received 1 point and each increasing quintile received an additional point. For red and processed meat, sugar-sweetened beverage, and sodium intake, the highest quintile of intake received 1 point and each decreasing quintile received an additional point.

²For all components except alcohol and red and processed meat intake, individuals with intake below the median received 0 points, and individuals with intake above the median received 1 point. For red and processed meat intake, individuals with intake above the median received 0 points, and individuals with intake below the median received 1 point. For alcohol intake, individuals with 5-15g/day of alcohol intake received 1 point and individuals with intake <5 or >15g/day of alcohol intake received 0 points.

³Intake between the minimum and maximum cutoffs was given a score between 0 and 10 proportional to intake (e.g. for fruit intake, 2 servings/day was given a score 0.5, and 3 servings/day was given a score of 0.75).

⁴Nut and legume intake were combined into one category in the DASH and AHEI-2010 diets, but were separate components in the AMED diet. ⁵Sugar-sweetened beverage intake included fruit juice in the AHEI-2010 diet but not in the DASH diet. Supplemental Table 2. Associations (multivariable hazard ratios, 95% confidence intervals) between quintiles of AMED and AHEI-2010 scores without alcohol and risk of colorectal cancer outcomes in the Nurses' Health Study and Health Professionals Followup Study

	Q1	Q2	Q3	Q4	Q5	P for trend ¹
Total colorectal cancer						
Men ²						
No. cases (AMED/AHEI-2010)	(236/218)	(238/248)	(241/240)	(231/227)	(216/229)	
AMED	1.00 (ref)	0.96 (0.80, 1.15)	0.89 (0.74, 1.08)	0.97 (0.80, 1.17)	0.80 (0.65, 0.98)	0.03
AHEI-2010	1.00 (ref)	1.09 (0.90, 1.31)	1.02 (0.84, 1.23)	0.92 (0.76, 1.12)	0.86 (0.71, 1.05)	0.06
Women ³						
No. cases (AMED/AHEI-2010)	(324/274)	(275/296)	(311/303)	(300/335)	(318/320)	
AMED	1.00 (ref)	0.91 (0.77, 1.07)	0.89 (0.75, 1.04)	0.95 (0.80, 1.12)	0.95 (0.79, 1.13)	0.85
AHEI-2010	1.00 (ref)	1.02 (0.87, 1.19)	1.02 (0.87, 1.19)	1.08 (0.92, 1.27)	1.00 (0.84, 1.20)	0.76
Total colon cancer						
Men ²						
No. cases (AMED/AHEI-2010)	(180/174)	(179/190)	(195/190)	(195/186)	(172/181)	
AMED	1.00 (ref)	0.93 (0.75, 1.15)	0.94 (0.76, 1.17)	1.08 (0.87, 1.33)	0.83 (0.66, 1.04)	0.27
AHEI-2010	1.00 (ref)	1.03 (0.84, 1.27)	0.98 (0.80, 1.22)	0.94 (0.76, 1.17)	0.85 (0.68, 1.06)	0.16
Women ³						
No. cases (AMED/AHEI-2010)	(247/223)	(215/235)	(244/221)	(241/269)	(257/256)	
AMED	1.00 (ref)	0.94 (0.78, 1.13)	0.90 (0.75, 1.09)	1.01 (0.83, 1.22)	1.01 (0.82, 1.23)	0.72
AHEI-2010	1.00 (ref)	0.98 (0.82, 1.16)	0.97 (0.81, 1.16)	1.06 (0.83, 1.27)	1.01 (0.83, 1.23)	0.61
Proximal colon cancer						
Men ²						
No. cases (AMED/AHEI-2010)	(70/71)	(75/83)	(82/66)	(86/95)	(83/81)	
AMED	1.00 (ref)	0.95 (0.68, 1.33)	0.95 (0.67, 1.32)	1.13 (0.82, 1.57)	0.92 (0.65, 1.31)	0.79
AHEI-2010	1.00 (ref)	1.05 (0.76, 1.46)	0.82 (0.58, 1.16)	1.12 (0.81, 1.54)	0.89 (0.64, 1.26)	0.80
Women ³						
No. cases (AMED/AHEI-2010)	(160/145)	(144/143)	(154/144)	(140/155)	(157/168)	
AMED	1.00 (ref)	0.92 (0.73, 1.15)	0.83 (0.66, 1.05)	0.83 (0.65, 1.05)	0.86 (0.67, 1.11)	0.40

AHEI-2010 Distal colon cancer	1.00 (ref)	0.84 (0.67, 1.06)	0.94 (0.75, 1.17)	0.97 (0.77, 1.22)	0.92 (0.72, 1.18)	0.65
Men ²						
No. cases (AMED/AHEI-2010)	(72/65)	(66/70)	(73/84)	(69/51)	(55/65)	
AMED	1.00 (ref)	0.90 (0.64, 1.27)	0.95 (0.67, 1.34)	0.99 (0.70, 1.39)	0.70 (0.48, 1.02)	0.17
AHEI-2010	1.00 (ref)	1.03 (0.73, 1.45)	1.19 (0.85, 1.67)	0.76 (0.52, 1.10)	0.83 (0.57, 1.21)	0.26
Women ³						
No. cases (AMED/AHEI-2010)	(79/73)	(65/89)	(85/72)	(97/102)	(91/81)	
AMED	1.00 (ref)	0.96 (0.69, 1.34)	1.07 (0.77, 1.48)	1.47 (1.07, 2.03)	1.28 (0.90, 1.82)	0.13
AHEI-2010	1.00 (ref)	1.25 (0.93, 1.67)	1.01 (0.73, 1.38)	1.16 (0.84, 1.59)	1.12 (0.79, 1.57)	0.37
Rectal cancer						
Men ²						
No. cases (AMED/AHEI-2010)	(56/44)	(59/58)	(46/50)	(36/41)	(44/48)	
AMED	1.00 (ref)	1.06 (0.73, 1.54)	0.74 (0.49, 1.12)	0.63 (0.41, 0.97)	0.68 (0.44, 1.05)	0.006
AHEI-2010	1.00 (ref)	1.31 (0.87, 1.95)	1.14 (0.75, 1.72)	0.84 (0.54, 1.31)	0.91 (0.58, 1.42)	0.17
Women ³						
No. cases (AMED/AHEI-2010)	(77/51)	(60/61)	(67/82)	(59/66)	(61/64)	
AMED	1.00 (ref)	0.82 (0.58, 1.15)	0.82 (0.59, 1.16)	0.76 (0.53, 1.09)	0.75 (0.50, 1.10)	0.27
AHEI-2010	1.00 (ref)	1.19 (0.85, 1.67)	1.23 (0.87, 1.74)	1.17 (0.81, 1.68)	0.99 (0.66, 1.47)	0.73

AMED, Alternative Mediterranean Diet; AHEI-2010, Alternative Healthy Eating Index-2010

¹P-value for the continuous diet scores determined using the Wald test

²Adjusted for total energy intake (kcal/day, quintiles), alcohol intake (g/day, quintiles), physical activity (MET-hours/wk, quintiles), NSAID use (≥2 NSAID/week vs. <2 NSAID/week [ref]), family history of CRC (yes vs. no [ref]), previous CRC screening via colonscopy or sigmoidoscopy (yes vs. no [ref]), history of polyps (yes vs. no [ref]), smoking (never smoker [ref], 0-<10, 10-<20, 20-<30, 30-<40, 40-<50 ≥50 packyears), multivitamin use (regular use vs. non-use [ref]), supplemental calcium intake (none [ref], >0-200, >200-400, >400-600, >600mg/day), and young adult body mass index (<25 [ref], 25-<27.5, 27.5-<30, ≥30 kg/m²)

³Adjusted for same as multivariable models in men + menopausal status (postmenopausal vs. not [ref]), and postmenopausal hormone use (never use [ref], past use, current use)

<u>Isk stratmed by det</u>	sk stratified by dietary and lifestyle characteristics in the Nurses' Hea DASH ²					AMED ³			AHEI-2010 ³			
	HPFS		NHS		HPFS		NHS		HPFS		NHS	
	HR (95% CI)	P- het⁴	HR (95% CI)	P- het⁵	HR (95% CI)	P- het⁴	HR (95% CI)	P- het⁵	HR (95% CI)	P- het⁴	HR (95% CI)	P- het⁵
Aspirin/NSAID High (n=546 HPFS cases; n=729 NHS cases	0.86 (0.75, 0.98)	0.34	1.04 (0.92, 1.17)	0.30	0.86 (0.74, 1.00)	0.42	1.01 (0.90, 1.14)	0.68	0.87 (0.76, 0.99)	0.12	1.05 (0.93, 1.17)	0.70
Low (n=616 HPFS cases; n=799 NHS cases) Family History of CRC	0.88 (0.78, 0.99)		0.93 (0.83, 1.03)		0.92 (0.81, 1.05)		1.00 (0.90, 1.11)		0.96 0.86, 1.08)		1.00 (0.91, 1.11)	
Yes (n=206 HPFS cases; n=295 NHS cases) No (n=956 HPFS cases; n=1233 NHS	0.89 (0.71, 1.11)	0.67	1.05 (0.87, 1.27)	0.55	0.96 (0.74, 1.24)	0.41	1.19 (0.99, 1.43)	0.05	1.00 (0.81, 1.25)	0.73	1.09 (0.91, 1.31)	0.69
cases)	0.87 (0.79, 0.95)		0.95 (0.87, 1.04)		0.87 (0.78, 0.97)		0.96 (0.88, 1.05)		0.89 (0.81, 0.98)		1.01 (0.93, 1.10)	
Obesity Obese (n=159 HPFS cases; n=320 NHS cases) Not obese (n=1003 HPFS cases; n=1208 NHS cases)	0.70 (0.53, 0.92) 0.91 (0.83, 1.00)	0.06	0.93 (0.78, 1.12) 0.99 (0.90, 1.08)	0.70	0.82 (0.61, 1.11) 0.91 (0.82, 1.01)	0.40	0.90 (0.75, 1.08) 1.03 (0.94, 1.12)	0.33	0.95 (0.73, 1.24) 0.92 (0.84, 1.01)	0.94	0.91 (0.76, 1.09) 1.05 (0.97, 1.15)	0.24
Smoking Ever (n=682 HPFS cases; n=928 NHS cases) Never (n=480 HPFS cases; n=600 NHS cases)	0.89 (0.79, 1.00) 0.86 (0.75, 0.98)	0.90	0.99 (0.89, 1.10) 0.93 (0.82, 1.06)	0.45	0.89 (0.79, 1.01) 0.89 (0.76, 1.04)	0.78	0.99 (0.89, 1.10) 1.01 (0.89, 1.15)	0.99	0.93 (0.83, 1.04) 0.92 (0.80, 1.05)	0.83	1.03 (0.93, 1.14) 1.01 (0.89, 1.14)	0.50
Multivitamin Use Regular use (n=625 HPFS cases; n=524 NHS cases)	0.98 (0.87, 1.10)	0.06	0.91 (0.79, 1.05)	0.32	0.97 (0.84, 1.11)	0.24	0.94 (0.81, 1.08)	0.20	0.96 (0.85, 1.08)	0.40	1.00 (0.87, 1.14)	0.55

Supplemental Table 3. Associations (multivariable hazard ratios, 95% confidence intervals) between continuous DASH, AMED, and AHEI-2010 scores¹ and colorectal cancer <u>risk stratified by dietary and lifestyle characteristics in the Nurses' Health Stu</u>dy and Health Professionals Follow-up Study

Online Supporting	Material
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No regular use (n=537 HPFS cases; n=1004 NHS cases)	0.81 (0.71, 0.91)		0.99 (0.90, 1.09)		0.83 (0.72, 0.96)		1.01 (0.91, 1.11)		0.88 (0.77, 1.00)		1.00 (0.91, 1.10)	
Physical Activity High (n=539 HPFS cases; n=743 NHS cases) Low (n=623 HPFS cases; n=785 NHS cases)	0.90 (0.79, 1.02) 0.86 (0.76, 0.97)	0.58	1.00 (0.89, 1.13) 0.95 (0.85, 1.09)	0.45	0.90 (0.78, 1.05) 0.89 (0.78, 1.02)	0.76	1.05 (0.94, 1.18) 0.96 (0.86, 1.07)	0.17	0.91 (0.80, 1.03) 0.92 (0.82, 1.03)	0.73	1.03 (0.92, 1.14) 1.02 (0.92, 1.14)	0.82
Young overweight Yes (n=254 HPFS cases; n=188 NHS cases) No (n=908 HPFS cases; n=1340 NHS casss)	0.83 (0.68, 1.01)	0.22	0.98 (0.76, 1.26)	0.48	0.79 (0.63, 0.98)	0.08	1.01 (0.79, 1.29) 1.00 (0.92, 1.09)	0.32	0.83 (0.68, 1.01)	0.16	0.91 (0.72, 1.15) 1.04 (0.96, 1.13)	0.24
Screened for CRC Yes (n=581 HPFS cases; n=256 NHS cases) No (n=581 HPFS cases; n=1272 NHS cases)	0.88 (0.77, 1.00) 0.89 (0.79, 1.00)	0.73	0.81 (0.66, 1.00) 1.00 (0.92, 1.09)	0.13	0.89 (0.77, 1.02) 0.89 (0.78, 1.02)	0.59	0.85 (0.69, 1.04) 1.03 (0.94, 1.12)	0.10	0.92 (0.81, 1.04) 0.91 (0.81, 1.02)	0.82	0.89 (0.73, 1.08) 1.05 (0.97, 1.14)	0.22
Supplemental Calcium Use <50 mg/day (n=741 HPFS cases; n=450 NHS cases) ≥50mg/day (n=421	0.84 (0.76, 0.94)	0.18	0.90 (0.78, 1.04)	0.43	0.88 (0.78, 0.99)	0.57	0.95 (0.83, 1.10)	0.55	0.90 (0.81, 1.00)	0.47	0.95 (0.83, 1.10)	0.53
HPFS cases; n=1078 NHS cases) Oral Contraception Use Ever (n=619 NHS cases) Never (n=909 NHS cases)	0.95 (0.82, 1.11) 		1.01 (0.92, 1.12) 0.98 (0.86, 1.11) 0.97 (0.87, 1.07)	0.90	0.95 (0.80, 1.13) 		1.02 (0.93, 1.12) 0.93 (0.82, 1.05) 1.05 (0.95, 1.16)	0.43	0.95 (0.82, 1.09) 		1.06 (0.97, 1.16) 1.02 (0.90, 1.15) 1.03 (0.93, 1.14)	0.48
Postmenopausal Hormone Use											· · ·	

Ever (n=869 NHS cases)	 0.97 (0.87, 1.08) 0.87	 0.99 (0.89, 1.11)	 1.04 (0.94, 1.15) 0.57
Never (n=659 NHS cases)	 0.96 (0.85, 1.08)	 0.99 (0.88, 1.12)	 0.98 (0.87, 1.10)

¹Per a one-unit increase in the interquartile range for each dietary score

²Adjusted for total energy intake (kcal/day, quintiles), alcohol intake (g/day, quintiles), physical activity (MET-hours/wk, quintiles), NSAID use (\geq NSAIDs/week vs. <2 NSAIDs/week [ref]), family history of CRC (yes vs. no [ref]), previous CRC screening via colonscopy or sigmoidoscopy (yes vs. no [ref]), history of polyps (yes vs. no [ref]), smoking (never smoker [ref], 0-<10, 10-<20, 20-<30, 30-<40, 40-<50 \geq 50 packyears), multivitamin use (regular use vs. non-use [ref]), supplemental calcium intake (none [ref], >0-200, >200-400, >400-600, >600mg/day), and young adult body mass index (<25 [ref], 25-<27.5, 27.5-<30, \geq 30 kg/m²); in women, additionally adjusted for menopausal status (postmenopausal vs. not [ref]), and postmenopausal hormone use (never use [ref], past use, current use)

³Adjusted for the same covariates as for the DASH diet but excluding alcohol intake

⁴P value for the interaction term between the potential effect modifier of interest and the continuous diet score in men determined using the Wald test

⁵P value for the interaction term between the potential effect modifier of interest and the continuous diet score in women determined using the Wald test