

Supplementary Materials

Comprehensive Assessment of Diet Quality and Risk of Precursors of Early-Onset Colorectal Cancer

Xiaobin Zheng*, Jinhee Hur*, Long H. Nguyen, Jie Liu, Mingyang Song, Kana Wu, Stephanie A. Smith-Warner, Shuji Ogino, Walter C. Willett, Andrew T. Chan[#], Edward Giovannucci[#], Yin Cao[#]

*Contributed equally as the first authors

[#]Contributed equally as the senior authors

Supplementary Methods

Assessment of dietary pattern

The procedure for deriving dietary patterns using food consumption data from the semiquantitative food-frequency questionnaire (FFQ) was described in detail elsewhere (1). Briefly, food items on the FFQ were categorized into 40 groups and factor analysis was performed to derive two dominant dietary patterns: Western and prudent diet. Factor loadings were then derived from the correlations between food groups and the two derived factors. Each participant was assigned two factor scores, determined by adding the reported frequencies of food group intakes, weighted by the factor loadings for each factor. These factor scores were then standardized with a mean of 0 and standard deviation of 1. Higher scores indicated stronger adherence to that particular pattern. Western dietary pattern was characterized by high intake of red and processed meats, high-fat dairy, refined grains, and desserts, as opposed to prudent dietary pattern rich in fruits, vegetables, whole grains, legumes, and fish (2).

Reference

1. Hu FB, Rimm EB, Stampfer MJ, Ascherio A, Spiegelman D, Willett WC. Prospective study of major dietary patterns and risk of coronary heart disease in men. *The American journal of clinical nutrition*. 2000;72(4):912-921.
2. Hu FB. Dietary pattern analysis: a new direction in nutritional epidemiology. *Current opinion in lipidology*. 2002;13(1):3-9.

Supplementary Table 1. Comparison of dietary components and scoring methods for three recommendation-based dietary indexes*

Dietary Component	Dietary Approaches to Stop Hypertension (DASH)†					Alternative Mediterranean Diet (AMED)‡		Alternative Healthy Eating Index-2010 (AHEI-2010)§	
						Score			
	1	2	3	4	5	0	1	0	10
Fruits	Q1	Q2	Q3	Q4	Q5	≤median	>median	0 svg/day	≥4 svg/day
Vegetables	Q1	Q2	Q3	Q4	Q5	≤median	>median	0 svg/day	≥5 svg/day
Whole grains	Q1	Q2	Q3	Q4	Q5	≤median	>median	0 g/day	75 g/day
Nuts and legumes	Q1	Q2	Q3	Q4	Q5	≤median	>median	0 svg/day	≥1 svg/day
Low-fat dairy	Q1	Q2	Q3	Q4	Q5		–		–
Red and processed meats	Q5	Q4	Q3	Q2	Q1	>median	≤median	≥1.5 svg/day	0 svg/day
Sugar-sweetened beverages	Q5	Q4	Q3	Q2	Q1		–	≥1 svg/day	0 svg/day
Sodium	Q5	Q4	Q3	Q2	Q1		–	Highest decile	Lowest decile
Fish			–			≤median	>median		–
MUFA-to-SFA ratio			–			≤median	>median		–
Alcohol			–			otherwise	5-15 g/day	≥2.5 drinks/day	0.5-1.5 drinks/day
Polyunsaturated fatty acids			–				–	≤2% of energy	≥10% of energy
Omega-3 fatty acids			–				–	0 mg/day	250 mg/day
Trans fatty acids			–				–	≥4% of energy	≤0.5% of energy
Total score			8-40				0-9		0-110

*MUFA = monounsaturated fatty acid; Q1-5 = lowest to highest quintile, respectively; SFA = saturated fatty acid; svg = serving.

†DASH consisted of 8 components and the score ranged from 8 to 40. For 5 components (fruits, vegetables, whole grains, nuts and legumes, and low-fat dairy), 1 point was given to the lowest quintile of intake and an additional point was awarded for each increasing quintile. For 3 components (red and processed meats, sugar-sweetened beverages, and sodium), the highest quintile of intake received 1 point and an additional point was awarded for each decreasing quintile.

‡AMED consisted of 9 components and the score ranged from 0 to 9. Nuts and legumes were considered separate components. For 7 components (fruits, vegetables, whole grains, nuts, legumes, fish, and MUFA-to-SFA ratio), intake above the median received 1 point; for red and processed meats, 1 point was given to intake below the median; and for alcohol, moderate intake (5-15 g/day) received 1 point.

§AHEI-2010, consisted of 11 components and the score ranged from 0 to 110. Higher intake was rewarded for 6 components (fruits, vegetables, whole grains, nuts and legumes, polyunsaturated fatty acids, and omega-3 fatty acids), lower intake was rewarded for 4 components (red and processed meats, sugar-sweetened beverages, trans fatty acids, and sodium), and moderate intake (0.5-1.5 drinks/day) was rewarded for alcohol. Each component received a score from 0 (complete nonadherence) to 10 (complete adherence), with partial adherence scores ranging between 0 and 10 directly proportional to intake.

||Sugar-sweetened beverages included fruit juice in the AHEI-2010 diet but not in the DASH diet.

Supplementary Table 2. Diet quality and risk of early-onset (age<50) adenoma among those who only had a colonoscopy, NHSII, 1991-2011*

Diet quality	Quintile				
	1 (lowest)	2	3	4	5 (highest)
Dietary pattern					
Western Dietary Pattern					
No. of cases	148	173	176	176	238
Unadjusted OR (95% CI)	1[Ref]	1.12 (0.90 to 1.40)	1.05 (0.84 to 1.31)	1.01 (0.81 to 1.26)	1.26 (1.02 to 1.56)
Age-adjusted OR (95% CI)†	1[Ref]	1.10 (0.88 to 1.38)	1.04 (0.83 to 1.30)	1.00 (0.80 to 1.25)	1.31 (1.06 to 1.61)
Multivariable OR (95% CI)‡	1[Ref]	1.09 (0.87 to 1.37)	1.04 (0.82 to 1.30)	0.99 (0.79 to 1.26)	1.28 (1.03 to 1.60)
Prudent Dietary Pattern					
No. of cases	241	202	173	153	142
Unadjusted OR (95% CI)	1[Ref]	0.98 (0.81 to 1.18)	0.92 (0.75 to 1.12)	0.88 (0.72 to 1.09)	0.88 (0.72 to 1.09)
Age-adjusted OR (95% CI)†	1[Ref]	0.93 (0.77 to 1.13)	0.85 (0.70 to 1.04)	0.82 (0.67 to 1.01)	0.83 (0.67 to 1.03)
Multivariable OR (95% CI)‡	1[Ref]	0.93 (0.77 to 1.13)	0.87 (0.70 to 1.07)	0.84 (0.67 to 1.04)	0.85 (0.68 to 1.06)
Recommendation-based dietary indexes					
Dietary Approaches to Stop Hypertension					
No. of cases	214	207	177	150	163
Unadjusted OR (95% CI)	1[Ref]	1.07 (0.88 to 1.30)	0.92 (0.75 to 1.12)	0.86 (0.70 to 1.07)	0.97 (0.79 to 1.20)
Age-adjusted OR (95% CI)†	1[Ref]	1.03 (0.85 to 1.25)	0.87 (0.71 to 1.07)	0.82 (0.66 to 1.02)	0.92 (0.74 to 1.15)
Multivariable OR (95% CI)‡	1[Ref]	1.05 (0.86 to 1.27)	0.90 (0.73 to 1.11)	0.85 (0.68 to 1.07)	0.96 (0.76 to 1.21)
Alternate Mediterranean Diet					
No. of cases	231	197	168	167	148
Unadjusted OR (95% CI)	1[Ref]	0.94 (0.77 to 1.14)	0.82 (0.67 to 1.01)	0.90 (0.73 to 1.10)	0.85 (0.69 to 1.05)
Age-adjusted OR (95% CI)†	1[Ref]	0.91 (0.74 to 1.10)	0.79 (0.65 to 0.97)	0.85 (0.69 to 1.05)	0.80 (0.64 to 1.00)
Multivariable OR (95% CI)‡	1[Ref]	0.92 (0.76 to 1.13)	0.81 (0.66 to 1.00)	0.88 (0.70 to 1.09)	0.83 (0.65 to 1.05)
Alternative Healthy Eating Index-2010					
No. of cases	229	198	192	144	148
Unadjusted OR (95% CI)	1[Ref]	0.95 (0.78 to 1.15)	1.04 (0.86 to 1.27)	0.85 (0.69 to 1.06)	0.98 (0.80 to 1.21)
Age-adjusted OR (95% CI)†	1[Ref]	0.92 (0.76 to 1.12)	1.00 (0.82 to 1.22)	0.80 (0.65 to 1.00)	0.92 (0.74 to 1.14)
Multivariable OR (95% CI)‡	1[Ref]	0.93 (0.76 to 1.13)	1.01 (0.82 to 1.24)	0.83 (0.66 to 1.04)	0.94 (0.75 to 1.18)

*CI = confidence interval; NHSII = Nurses' Health Study II; OR = odds ratio.

†Adjusted for age (continuous), total caloric intake (in quintiles), time period of endoscopy (in 2-year intervals), number of reported endoscopies (continuous), time in years since the most recent endoscopy (continuous), and reason for the current endoscopy (screening, symptoms, missing).

‡Additionally adjusted for height (continuous), body mass index (in quintiles), family history of colorectal cancer (yes, no), menopausal status

(premenopausal, postmenopausal), menopausal hormone use (never, past, current use of menopausal hormones), personal history of type 2 diabetes (yes, no), pack-years of smoking (never, 1-4.9, 5-19.9, 20-39.9, ≥ 40 pack-years), physical activity (in metabolic equivalent of task-hours/week, quintiles), current use of multivitamin (yes, no), regular use of aspirin (yes, no), and regular use of non-steroidal anti-inflammatory drugs (yes, no). For Dietary Approaches to Stop Hypertension, we additionally adjusted for alcohol intake (0, 0.1-14.9, ≥ 15 g/day).

Supplementary Table 3. Diet quality and risk of early-onset (age<50) high-risk adenoma among individuals without or with any symptoms at lower endoscopy, NHSII, 1991-2011*

Diet quality	Quintile					<i>P</i> _{trend} ‡
	1 (lowest)	2	3	4	5 (highest)	
Without any symptoms at lower endoscopy						
Dietary pattern						
Western Dietary Pattern						
No. of cases	26	40	40	30	40	
Unadjusted OR (95% CI)	1 [Ref]	1.55 (0.94 to 2.54)	1.53 (0.93 to 2.51)	1.20 (0.71 to 2.04)	1.59 (0.97 to 2.61)	.23
Multivariable OR (95% CI)†	1 [Ref]	1.50 (0.91 to 2.47)	1.50 (0.91 to 2.47)	1.22 (0.71 to 2.10)	1.69 (1.00 to 2.84)	.16
Prudent Dietary Pattern						
No. of cases	42	41	36	30	27	
Unadjusted OR (95% CI)	1 [Ref]	1.00 (0.65 to 1.54)	0.90 (0.57 to 1.40)	0.75 (0.47 to 1.20)	0.69 (0.42 to 1.12)	.08
Multivariable OR (95% CI)†	1 [Ref]	0.89 (0.57 to 1.39)	0.77 (0.49 to 1.22)	0.65 (0.40 to 1.07)	0.62 (0.37 to 1.03)	.04
Recommendation-based dietary index						
Dietary Approaches to Stop Hypertension						
No. of cases	38	38	42	28	30	
Unadjusted OR (95% CI)	1 [Ref]	0.98 (0.62 to 1.54)	1.01 (0.65 to 1.57)	0.73 (0.45 to 1.20)	0.76 (0.47 to 1.23)	.16
Multivariable OR (95% CI)†	1 [Ref]	0.91 (0.58 to 1.43)	0.91 (0.57 to 1.44)	0.65 (0.39 to 1.08)	0.67 (0.39 to 1.14)	.07
Alternative Mediterranean Diet						
No. of cases	51	28	38	34	25	
Unadjusted OR (95% CI)	1 [Ref]	0.57 (0.36 to 0.90)	0.75 (0.49 to 1.15)	0.74 (0.48 to 1.15)	0.50 (0.31 to 0.81)	.04
Multivariable OR (95% CI)†	1 [Ref]	0.53 (0.33 to 0.85)	0.67 (0.44 to 1.04)	0.63 (0.39 to 1.03)	0.42 (0.24 to 0.73)	.01
Alternative Healthy Eating Index-2010						
No. of cases	44	47	29	26	30	
Unadjusted OR (95% CI)	1 [Ref]	1.06 (0.70 to 1.60)	0.68 (0.42 to 1.08)	0.61 (0.38 to 0.99)	0.72 (0.45 to 1.15)	.04
Multivariable OR (95% CI)†	1 [Ref]	0.96 (0.63 to 1.47)	0.60 (0.37 to 0.96)	0.54 (0.32 to 0.90)	0.62 (0.38 to 1.02)	.01
With any symptoms at lower endoscopy						
Dietary pattern						
Western Dietary Pattern						
No. of cases	24	31	35	39	58	
Unadjusted OR (95% CI)	1 [Ref]	1.23 (0.72 to 2.10)	1.23 (0.73 to 2.08)	1.27 (0.76 to 2.12)	1.72 (1.06 to 2.77)	.03
Multivariable OR (95% CI)†	1 [Ref]	1.20 (0.70 to 2.05)	1.23 (0.72 to 2.10)	1.22 (0.73 to 2.05)	1.58 (0.96 to 2.59)	.08
Prudent Dietary Pattern						

No. of cases	57	39	35	28	28	
Unadjusted OR (95% CI)	1 [Ref]	0.83 (0.55 to 1.25)	0.83 (0.55 to 1.27)	0.73 (0.46 to 1.15)	0.80 (0.51 to 1.26)	.30
Multivariable OR (95% CI)†	1 [Ref]	0.85 (0.56 to 1.29)	0.87 (0.56 to 1.36)	0.76 (0.48 to 1.23)	0.82 (0.50 to 1.34)	.41
Recommendation-based dietary index						
Dietary Approaches to Stop Hypertension						
No. of cases	56	37	40	29	25	
Unadjusted OR (95% CI)	1 [Ref]	0.75 (0.49 to 1.14)	0.86 (0.57 to 1.29)	0.69 (0.44 to 1.08)	0.64 (0.40 to 1.03)	.06
Multivariable OR (95% CI)†	1 [Ref]	0.73 (0.47 to 1.13)	0.83 (0.53 to 1.28)	0.66 (0.41 to 1.07)	0.59 (0.35 to 0.99)	.045
Alternative Mediterranean Diet						
No. of cases	48	41	36	37	25	
Unadjusted OR (95% CI)	1 [Ref]	0.99 (0.65 to 1.50)	0.88 (0.57 to 1.36)	1.03 (0.67 to 1.59)	0.74 (0.45 to 1.20)	.34
Multivariable OR (95% CI)†	1 [Ref]	0.98 (0.63 to 1.50)	0.85 (0.54 to 1.35)	0.97 (0.60 to 1.55)	0.66 (0.39 to 1.11)	.20
Alternative Healthy Eating Index-2010						
No. of cases	56	37	41	27	26	
Unadjusted OR (95% CI)	1 [Ref]	0.76 (0.50 to 1.16)	0.96 (0.64 to 1.44)	0.70 (0.44 to 1.11)	0.77 (0.48 to 1.23)	.20
Multivariable OR (95% CI)†	1 [Ref]	0.78 (0.51 to 1.19)	0.99 (0.65 to 1.51)	0.73 (0.45 to 1.20)	0.80 (0.48 to 1.32)	.32

*High-risk adenoma includes adenoma ≥ 1 cm, or with tubulovillous/villous histology or high-grade dysplasia, or ≥ 3 adenomas. Symptoms include visible blood in stool specimen, positive fecal occult blood test result, abdominal pain, diarrhea or constipation. CI = confidence interval; NHSII = Nurses' Health Study II; OR = odds ratio.

†Adjusted for age (continuous), total caloric intake (in quintiles), time period of endoscopy (in 2-year intervals), number of reported endoscopies (continuous), time in years since the most recent endoscopy (continuous), height (continuous), body mass index (in quintiles), family history of colorectal cancer (yes, no), menopausal status (premenopausal, postmenopausal), menopausal hormone use (never, past, current use of menopausal hormones), personal history of type 2 diabetes (yes, no), pack-years of smoking (never, 1-4.9, 5-19.9, 20-39.9, ≥ 40 pack-years), physical activity (in metabolic equivalent of task-hours/week, quintiles), current use of multivitamin (yes, no), regular use of aspirin (yes, no), and regular use of non-steroidal anti-inflammatory drugs (yes, no). For Dietary Approaches to Stop Hypertension, we additionally adjusted for alcohol intake (0, 0.1-14.9, ≥ 15 g/day).

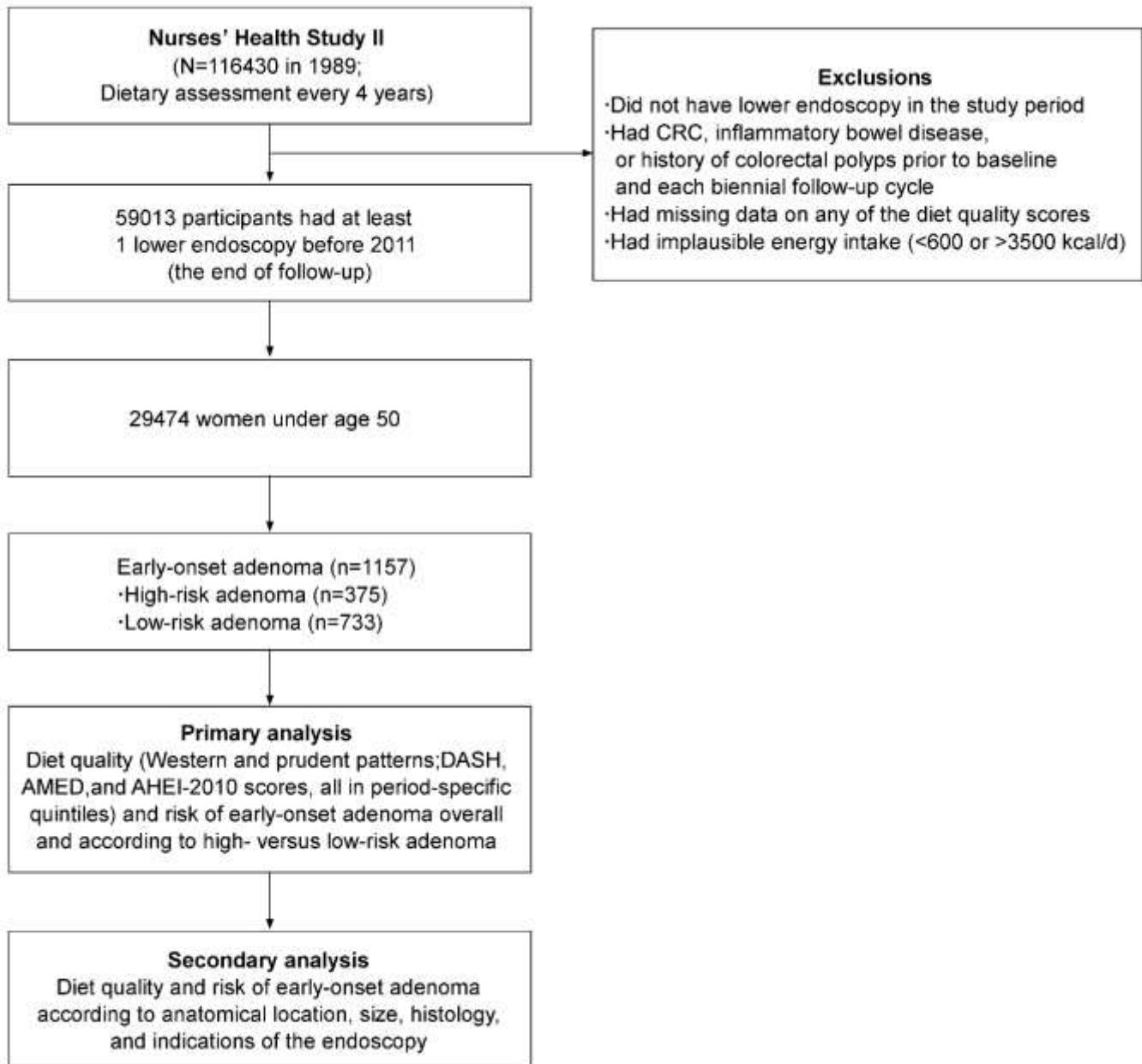
‡Calculated using the median of each quintile as a continuous variable.

Supplementary Table 4. Joint association of Western and prudent dietary patterns with risk of early-onset (age<50) high-risk adenoma, NHSII, 1991-2011*

	Western Dietary Pattern (Q5) & Prudent Dietary Pattern (Q1)	Western Dietary Pattern (Q1) & Prudent Dietary Pattern (Q1)	Western Dietary Pattern (Q5) & Prudent Dietary Pattern (Q5)	Western Dietary Pattern (Q1) & Prudent Dietary Pattern (Q5)
No. of cases	62	1	3	29
Unadjusted OR (95% CI)	1 [Ref]	0.65 (0.09 to 4.74)	1.29 (0.40 to 4.15)	0.59 (0.38 to 0.93)
Multivariable OR (95% CI)†	1 [Ref]	0.82 (0.11 to 6.18)	1.19 (0.37 to 3.80)	0.58 (0.36 to 0.92)

*High-risk adenoma includes adenoma ≥ 1 cm, or with tubulovillous/villous histology or high-grade dysplasia, or ≥ 3 adenomas. CI = confidence interval; NHSII = Nurses' Health Study II; OR = odds ratio; Q1 = lowest quintile; Q5 = highest quintile.

†Adjusted for age (continuous), total caloric intake (in quintiles), time period of endoscopy (in 2-year intervals), number of reported endoscopies (continuous), time in years since the most recent endoscopy (continuous), reason for the current endoscopy (screening, symptoms, missing), height (continuous), body mass index (in quintiles), family history of colorectal cancer (yes, no), menopausal status (premenopausal, postmenopausal), menopausal hormone use (never, past, current use of menopausal hormones), personal history of type 2 diabetes (yes, no), pack-years of smoking (never, 1-4.9, 5-19.9, 20-39.9, ≥ 40 pack-years), physical activity (in metabolic equivalent of task-hours/week, quintiles), current use of multivitamin (yes, no), regular use of aspirin (yes, no), and regular use of non-steroidal anti-inflammatory drugs (yes, no).



Supplementary Figure 1. Flow diagram of the study population.

AHEI, Alternative Healthy Eating Index; AMED, Alternative Mediterranean Diet; CRC, colorectal cancer; DASH, Dietary Approaches to Stop Hypertension.