American Journal of Epidemiology

Vol. 184, No. 1
DOI: 10.1093/aje/kwv304
Advance Access publication:
June 5, 2016

Original Contribution

Diet Quality and Colorectal Cancer Risk in the Women's Health Initiative Observational Study

Ashley J. Vargas, Marian L. Neuhouser, Stephanie M. George, Cynthia A. Thomson, Gloria Y. F. Ho, Thomas E. Rohan, Ikuko Kato, Rami Nassir, Lifang Hou, and JoAnn E. Manson*

* Correspondence to Dr. JoAnn E. Manson, Division of Preventive Medicine, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, 900 Commonwealth Avenue East, Third Floor, Boston, MA 02215 (e-mail: jmanson@rics.bwh.harvard.edu).

Initially submitted July 2, 2015; accepted for publication October 29, 2015.

Diet quality index scores on Healthy Eating Index 2010 (HEI-2010), Alternative HEI-2010, alternative Mediterranean Diet Index, and the Dietary Approaches to Stop Hypertension (DASH) index have been inversely associated with all-cause and cancer-specific death. This study assessed the association between these scores and colorectal cancer (CRC) incidence as well as CRC-specific mortality in the Women's Health Initiative Observational Study (1993–2012), a US study of postmenopausal women. During an average of 12.4 years of follow-up, there were 938 cases of CRC and 238 CRC-specific deaths. We estimated multivariate hazard ratios and 95% confidence intervals for relationships between quintiles of diet scores (from baseline food frequency questionnaires) and outcomes. HEI-2010 score (hazard ratios were 0.81, 0.77, and 0.73 with P values of 0.04, 0.01, and <0.01 for quintiles 3–5 vs. quintile 1, respectively) and DASH score (hazard ratios were 0.72, 0.74, and 0.78 with P values of <0.01, <0.01, and 0.03 for quintiles 3–5 vs. quintile 1, respectively), but not other diet scores, were associated with a lower risk of CRC in adjusted models. No diet scores were significantly associated with CRC-specific mortality. Closer adherence to HEI-2010 and DASH dietary recommendations was inversely associated with risk of CRC in this large cohort of postmenopausal women.

Alternative Healthy Eating Index; Alternative Mediterranean Diet; colorectal cancer; diet; diet quality; Dietary Approaches to Stop Hypertension; dietary patterns; Healthy Eating Index

Abbreviations: aMED, Alternative Mediterranean Diet; AHEI, Alternative Healthy Eating Index 2010; BMI, body mass index; CI, confidence interval; CRC, colorectal cancer; DASH, Dietary Approaches to Stop Hypertension; HEI-2005, Healthy Eating Index 2005; HEI-2010, Healthy Eating Index 2010; HR, hazard ratio; NIH, National Institutes of Health; WHI, Women's Health Initiative.

Colorectal cancer (CRC) is the third most common cancer in the United States, accounting for more than 8% of all US cancer-related deaths (1). Understanding factors that influence development of this disease is a priority. The American Institute of Cancer Research and the World Cancer Research Fund have identified dietary components, such as red meat and fiber, that are associated with increased and decreased CRC risk, respectively (2). However, research evaluating the role of any single dietary component in carcinogenesis is difficult to interpret given the correlations among, and the potential influence of, other nutrients in relation to the total dietary exposure (3). Thus, there has been a concerted effort to strengthen the research evidence on total diet quality and CRC risk (4).

Diet quality measures can be developed using statistical clustering or factor development within a data set or from diet quality index scores defined a priori (5). Of the 2 methods, diet quality index scores are built on emerging evidence from the existing literature on diet and disease risk (5) and have clear algorithms for calculating scores that can be applied across multiple data sets to provide more consistent interpretation of findings. Thus, associations between dietary index scores and disease are translated into public health messages in a more consistent manner than are de novo patterns that vary between studies. The US Department of Agriculture and the National Cancer Institute (6, 7), among others (8, 9), have developed diet quality index scores that use point systems to measure whole diet quality based on the alignment of food choices with recommendations. These and other indices have been used to begin assessing the relationship between overall diet quality and CRC risk (10–16).

Evidence supporting a role for diet quality in CRC risk is accumulating (10–16). Reedy et al. (11) tested associations between scores on 4 diet quality indices—Healthy Eating Index 2005 (HEI-2005) (17), Alternative Healthy Eating Index 2010 (AHEI) (7), Mediterranean Diet Score, and Recommended Food Score (18)—and the risk of CRC in the National Institutes of Health-AARP (NIH-AARP) Diet and Health Study. Results suggested that, in men, higher scores on all 4 indices were associated with a lower risk of CRC, but in women only the HEI-2005 score showed an association (a significant, 17% lower risk of CRC in fully adjusted models). Similarly, Miller et al. (14) evaluated the associations between 4 different methods of indexing adherence to the Dietary Approaches to Stop Hypertension (DASH) diet (19, 20) and the risk of CRC in the same NIH-AARP population. Again, all methods of diet quality indexing were associated with lower risk of CRC in men, but only the DASH indexing methods of Fung et al. (9) and Mellen et al. (21) were associated with a significantly lower risk of CRC in women. With limited analyses published using the updated Healthy Eating Index 2010 (HEI-2010) (6) and emerging evidence supporting a complex but significant relationship between diet quality and CRC in women (11, 14, 15), there is a need to further examine these relationships in diverse study populations.

The aim of this study was to examine the association between scores on 4 common diet quality indices (HEI-2010 (6), AHEI (7), Alternative Mediterranean Diet (aMED) (8), and DASH (9)) and CRC incidence and CRC-specific mortality among more than 80,000 postmenopausal women in the Women's Health Initiative (WHI) Observational Study. Like NIH-AARP, the WHI study was initiated in the 1990s and enrolled older women, but its population is more racially/ethnically diverse, thus providing an ideal cohort in which to further investigate the relationships observed in the NIH-AARP study. We also conducted subgroup analyses to explore risk factors for CRC, including race/ethnicity, age, bowel screening history, and family history of CRC.

METHODS

Study population

Participants were enrolled in the WHI Observational Study, which has been described previously (22–24). In brief, 93,676 postmenopausal women aged 50–79 years enrolled in the Observational Study. The women came from multiple sites across the United States, had a life expectancy of more than 3 years, and were either ineligible for or not interested in the clinical trial arms of the WHI. Women were excluded from the analytical cohort if they had a personal history of any cancer (except nonmelanoma skin cancer; n = 12,075), a CRC event during the first year of observation (n = 105), no clinical follow-up (n = 473), no completed food frequency questionnaire as defined in WHI (25; n = 94), or a self-reported daily energy intake of less than 600 kcal/day or more than 5,000 kcal/day (n = 3,534). The remaining 78,273 participants were followed until September 17, 2012, which included WHI Extension Study 1 (2005–2010) and WHI Extension Study 2 (2010–2015) or were considered censored (if they were lost to follow-up or died during the study) for CRC-event analyses. Average follow-up was 12.4 years; 1.2% of participants were diagnosed with CRC, and 0.3% of participants died as a result of CRC. Institutional review board approval was obtained from all 40 WHI sites across the United States, and written informed consent was obtained from all participants prior to data collection.

Dietary indices and covariates

All estimates of average daily dietary intake were obtained from a self-administered baseline food frequency questionnaire, which included 122 line items, was calibrated against 24-hour dietary recalls and 4-day food records (25), and was modified from the Health Habits and Lifestyle Questionnaire (26) for the diverse WHI cohort. Food frequency questionnaire responses were converted into estimated daily individual nutrient and food serving intakes using the Nutrition Data System for Research, version 2005 (University of Minnesota, Minneapolis, Minnesota) (27), and then further converted into MyPyramid Equivalents using the MyPyramid Equivalents database, version 2.0 (US Department of Agriculture, Beltsville, Maryland; 28), as described elsewhere (29, 30). From these estimates, all diet quality index scores were generated as previously described (HEI-2010 (6), AHEI (7), aMED (8), and DASH (9)), and scores were assigned to each participant such that higher scores indicated a higher-quality diet. (For details on how scores were calculated, see Web Appendix 1, available at http://aje.oxfordjournals.org/.) Contributions of dietary supplements to the diet were not relevant to the algorithms and therefore not included in the calculation of diet quality index scores.

Nondietary covariates and outcomes

Data about participant characteristics (including race/ethnicity, family history of CRC (oneself or first-degree relatives), education, family income, smoking status, postmenopausal hormone therapy, and physical activity) were gathered via questionnaires at baseline (23). Participants' weights and heights were measured at baseline by trained WHI staff, and body mass index (BMI) was calculated as weight (kg)/height (m)^2. Participants were asked annually about incident CRC diagnoses and CRC-specific mortality by mailed questionnaire. CRC events were confirmed through medical records, pathology reports, and trained physician adjudication. CRC-specific deaths were confirmed by death certificates, medical records, and autopsy reports or other records for CRC-specific mortality (31).

Statistical approach

Pearson coefficients for correlations among raw diet quality scores were calculated. For analyses of risk, total diet quality scores, as quintiles, were the independent variables. The follow-up time metric for analyses of incident CRC and CRC-specific mortality was person-years, calculated from the beginning of the observation period (baseline) to censoring ($n = 77,335$, of which 8,976 were non-CRC death censoring) or CRC diagnosis ($n = 938$) and to censoring or CRC-specific death ($n = 238$), respectively.). Cox proportional hazards models were used to generate hazard ratios, 95% confidence intervals, and P values for CRC and CRC-specific mortality outcomes. All models adjusted for confounders identified a priori from the literature. Model 1 adjusted for age and race/ethnicity (African-American/black, non-Hispanic white, and other (32)). Model 2 adjusted for all model 1 covariates plus self-reported physical activity (metabolic equivalent of task (MET)-hours per week (33)), educational level (high school graduate or less, some college, or college graduate or more) as a marker of socioeconomic status (34), smoking status (never smoker, former smoker, or current smoker (35, 36)), and any postmenopausal hormone use (never, former, or current (37)). The addition to model 2 of the use at baseline of aspirin, nonsteroidal antiinflammatory medication, and multivitamins with minerals was considered, but ultimately they were not included because they did not change the hazard ratios by more than 10%. Likelihood-ratio tests were used to determine whether adding diet quality indices as quintiles to the fully adjusted model (model 2) was associated with improved model fit compared with the same model without indices. The Akaike information criterion and Bayesian information criterion were used to determine which index improved model fit the most for each outcome for a given model. Potential effect modification of the relationship between diet quality scores and CRC by race/ethnicity, baseline age (≤65 years or >65 years), family history of CRC, and history of CRC screening at baseline was tested by using a likelihood-ratio test with an interaction term (diet quality score × potential effect modifier) under model 2 conditions. False discovery rates were calculated for effect-modification P values to adjust for multiple testing. We examined these 4 potential effect modifiers because they all modify baseline risk of CRC and, potentially, dietary intake. Dietary energy intake (kcal/day), and alcohol consumption (servings per week) were accounted for in only some diet quality index scores, and BMI may be an intermediate factor on the causal pathway or may be a confounder. Thus, these variables were added to model 2 separately to determine whether associations were significantly altered by their inclusion. Cox proportional hazards assumptions were tested using Schoenfeld residuals and log-minus-log survival plots in models 1 and 2 for CRC outcomes. Proportionality required the addition of age × ln(time) to all models. Component analysis was conducted for each component of each diet score with adjustment for model 2 covariates as previously described (11), to determine which components were the biggest contributors to observed associations for that diet quality index. Specifically, each component for a given diet quality index score (generated as described in the Web Appendix) was added to model 2 simultaneously. Subsequently, we evaluated the association between each component and CRC after adjusting for all other components and model 2 covariates. For each variable in a model, participants with missing data for that variable were not included in that analysis. All tests were 2-sided, and $P < 0.05$ was considered statistically significant. All analyses were conducted using STATA, version 12.1 (StataCorp LP, College Station, Texas).

RESULTS

Study population

Of the 78,273 postmenopausal women enrolled in the WHI Observational Study who met our inclusion criteria, 938 were diagnosed with CRC and 238 died from CRC during a mean follow-up time of 12.4 (standard deviation (SD), 4.0) years. Mean age was 63 (SD, 7) years, and mean BMI was 27.2 (SD, 5.8). The observed diet quality index score ranges were as follows: HEI-2010, 15.7–94.4; AHEI, 12.7–91.6; aMED, 0.0–9.0; and DASH, 8.0–39.0. Compared with participants in quintile 1 (i.e., lower diet quality), participants in quintile 5 (i.e., higher diet quality) more often had a lower BMI and were college graduates, never smokers, from a higher income bracket, more physically active, and non-Hispanic white (Table 1).

Dietary characteristics

Mean diet quality index scores (with standard deviations) were as follows: HEI-2010, 53.8 (SD, 9.5); AHEI, 45.8 (SD, 10.4); aMED, 4.1 (SD, 1.8); and DASH, 25.0 (SD, 4.8). Table 2 shows the contributions of different food groups and dietary components to each diet quality index score. Overall food groups and components associated with CRC (2) varied by quintiles of diet quality index scores. Specifically, intake of fiber, whole grain, fruits, and vegetables was higher in quintile 5 than in quintile 1, whereas intake of saturated fat, red meat, and processed meat was higher in quintile 1. Correlations among the diet quality index scores were within the range of $r = 0.50–0.66$ (all P's < 0.001). DASH and AHEI had the highest correlation, 0.66 ($P < 0.001$).

Associations between diet quality index scores and CRC and CRC-specific mortality

In our fully adjusted model (model 2), quintiles 3–5 of the HEI-2010 diet quality index were significantly associated with a lower risk of CRC compared with quintile 1 (quintile 3: hazard ratio (HR) = 0.81 (95% confidence interval (CI): 0.66, 0.99), $P = 0.04$; quintile 4: HR = 0.77 (95% CI: 0.63, 0.95), $P = 0.01$; and quintile 5: HR = 0.73 (95% CI: 0.59, 0.90), $P < 0.01$; Table 3). Quintiles 3–5 of the DASH diet quality index also were significantly associated with a lower risk of CRC compared with quintile 1 in model 2 (quintile 3: HR = 0.72 (95% CI: 0.59, 0.89), $P < 0.01$; quintile 4: HR = 0.74 (95% CI: 0.60, 0.91), $P < 0.01$; and quintile 5: HR = 0.78 (95% CI: 0.62, 0.97), $P = 0.03$). No diet quality scores were significant predictors of CRC-specific mortality (quintile 5 vs. quintile 1: HR = 0.91 (95% CI: 0.57, 1.47), $P = 0.70$ for HEI-2010; HR = 1.09 (95% CI: 0.67, 1.77), $P = 0.72$ for AHEI; HR = 0.90 (95% CI: 0.57, 1.43), $P = 0.66$ for aMED; and HR = 0.96 (95% CI: 0.58, 1.59), $P = 0.89$ for DASH; data not shown). When CRC-specific mortality outcomes were adjusted for covariates used in the Dietary Patterns Methods Project (38), associations were still not significant.

Table 1. Baseline Characteristics for Selected Quintiles of Diet Quality Index Scores (*n* = 78,273), Women's Health Initiative Observational Study, 1993–2012

Characteristic[a]	Diet Quality Index and Quintile of Score[b]															
	HEI-2010				AHEI				aMED				DASH			
	1		5		1		5		1		5		1		5	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Age, years[c]	62.1 (7.3)		64.6 (7.2)		62.7 (7.4)		63.6 (7.2)		63.2 (7.4)		63.5 (7.3)		62.2 (7.3)		64.1 (7.3)	
Race/ethnicity																
Non-Hispanic white	12,306	18.7	13,321	20.3	12,460	19.0	12,956	19.7	12,923	19.7	15,672	23.9	10,171	15.5	12,848	19.6
African-American/black	1,662	28.1	1,020	17.2	1,808	30.5	825	13.9	1,615	27.3	982	16.6	2,349	39.7	535	9.0
Other	1,650	25.5	1,265	19.6	1,343	20.8	1,228	19.0	1,439	22.3	1,154	17.9	1,683	26.0	727	11.3
First-degree relative with CRC	2,309	19.6	2,281	19.4	2,345	19.9	2,326	19.7	2,406	20.4	2,739	23.2	2,140	18.2	2,168	18.4
Educational level																
High school graduate or less	4,800	29.5	2,410	14.8	4,876	30.0	1,845	11.3	4,991	30.7	2,186	13.4	4,471	29.1	1,645	10.1
Some college	5,841	20.7	5,212	18.5	6,102	21.7	4,864	17.3	6,232	22.1	5,741	20.4	5,505	19.5	4,341	15.4
College graduate or more	4,880	14.7	7,909	23.8	4,534	13.7	8,812	26.6	4,673	14.1	9,788	29.5	3,862	11.6	8,056	24.3
Annual family income, dollars																
<20,000	3,018	27.3	1,915	17.4	3,126	28.3	1,462	13.3	3,091	28.0	1,741	15.8	3,017	27.8	1,443	13.1
20,000–100,000	10,295	19.3	10,710	20.1	10,500	19.7	10,542	19.8	10,659	20.0	12,470	23.4	9,180	17.2	9,876	18.5
>100,000	1,178	14.5	1,874	23.0	858	10.5	2,519	30.9	1,063	13.0	2,418	29.7	873	10.7	1,832	22.5
Smoking status																
Never smoker	7,471	19.0	8,220	20.9	8,434	21.4	7,187	18.2	8,014	20.3	8,986	22.8	6,885	17.5	7,407	18.8
Former smoker	6,303	19.1	6,668	20.2	5,559	16.8	7,721	23.4	6,131	18.6	8,066	24.4	5,348	16.2	6,246	18.9
Current smoker	1,652	35.0	547	11.6	1,442	30.5	492	10.4	1,606	34.0	562	11.9	1,788	37.9	297	6.3
Hormone replacement therapy use																
Never	6,861	22.5	5,872	19.2	6,762	22.1	5,727	18.8	6,873	22.5	6,444	21.1	6,401	21.0	5,211	17.1
Former	2,179	20.4	2,199	20.5	2,267	21.2	2,119	19.8	2,240	20.9	2,469	23.1	1,977	18.5	1,929	18.0
Current	6,602	17.9	7,567	20.5	6,609	17.9	7,791	21.1	6,890	18.7	8,923	24.2	5,847	15.8	6,992	18.9
Estrogen only	3,753	18.8	3,972	19.9	3,906	19.5	3,845	19.2	3,972	19.9	4,576	22.9	3,464	17.3	3,491	17.5
Estrogen-progesterone	2,849	16.8	3,595	21.2	2,703	15.9	3,946	23.3	2,918	17.2	4,347	25.6	2,383	14.1	3,501	20.6
BMI[c,d]	28.8 (6.5)		25.9 (5.2)		28.8 (6.4)		25.6 (4.9)		28.3 (6.2)		26.2 (5.4)		29.0 (6.6)		25.6 (5.0)	
Physical activity, MET-hours/week[c]	9.6 (12.5)		17.3 (15.4)		9.3 (11.8)		19.2 (16.3)		9.8 (12.3)		17.8 (15.4)		8.6 (11.6)		19.5 (16.1)	

Abbreviations: AHEI, Alternative Healthy Eating Index 2010; aMED, Alternative Mediterranean Diet; BMI, body mass index; CRC, colorectal cancer; DASH, Dietary Approaches to Stop Hypertension; HEI-2010, Healthy Eating Index 2010; MET, metabolic equivalent of task.

[a] Participant characteristics at baseline where the total number of participants per variable without missing data is as follows: colorectal cancer during study (*n* = 78,273), age (*n* = 78,273), race/ethnicity (*n* = 78,060), relative with colorectal cancer (*n* = 71,614), educational level (*n* = 77,645), family income (*n* = 72,563), smoking status (*n* = 77,158), hormone replacement therapy (*n* = 78,196), estrogen-only hormone replacement therapy (*n* = 78,215), estrogen-progesterone hormone replacement therapy (*n* = 78,244), BMI (*n* = 77,372), and physical activity (*n* = 77,324).

[b] Quintile of diet quality index score (scores in higher quintiles indicate better diet quality) and the number of participants per quintile by dietary index: HEI-2010 (quintile 1 = 15,655, quintile 2 = 15,655, quintile 3 = 15,654, quintile 4 = 15,655, quintile 5 = 15,654), AHEI (quintile 1 = 15,655, quintile 2 = 15,655, quintile 3 = 15,654, quintile 4 = 15,655, quintile 5 = 15,654), aMED (quintile 1 = 16,018, quintile 2 = 14,450, quintile 3 = 15,742, quintile 4 = 14,211, quintile 5 = 17,852), and DASH (quintile 1 = 14,240, quintile 2 = 14,879, quintile 3 = 18,200, quintile 4 = 16,805, quintile 5 = 14,149).

[c] Values are presented as mean (standard deviation).

[d] BMI was calculated as weight (kg)/height (m)^2.

Table 2. Mean Values (and Standard Deviations) for Estimated Dietary Intake at Baseline in Selected Quintiles of Diet Quality Index Scores, ($n = 78{,}273$), Women's Health Initiative Observational Study, 1993–2012

Dietary Component[a]	Diet Quality Index and Quintile of Score[b]							
	HEI-2010		AHEI		aMED		DASH	
	1	5	1	5	1	5	1	5
Total score	40.5 (4.6)	67.1 (4.8)	31.9 (3.8)	60.9 (5.3)	1.6 (0.6)	6.5 (0.7)	17.8 (2.2)	31.7 (1.6)
Nutrients								
Dietary energy, kcal/day	1,764.1 (729.5)	1,420.6 (478.9)	1,694.9 (627.4)	1,509.7 (544.0)	1,339.8 (521.9)	1,812.7 (594.3)	1,621.6 (658.0)	1,625.4 (525.5)
Dietary carbohydrates, g/day	211.9 (90.2)	196.2 (68.9)	206.9 (79.2)	210.4 (76.8)	160.2 (65.0)	249.8 (76.2)	184.0 (80.4)	242.1 (73.0)
Total fiber, g/day	13.7 (6.3)	19.2 (7.3)	13.3 (5.4)	20.4 (7.6)	10.6 (4.0)	22.8 (6.7)	11.3 (4.7)	23.1 (6.8)
Alcohol, servings/week[c]	2.2 (5.6)	2.7 (4.7)	2.0 (6.3)	3.0 (3.8)	2.2 (5.6)	2.9 (4.6)	2.3 (5.1)	2.3 (4.3)
Dietary total fat, g/day	69.8 (37.1)	42.0 (21.2)	65.1 (32.2)	44.8 (24.5)	51.7 (27.4)	56.1 (29.6)	68.1 (34.2)	43.2 (22.0)
Saturated fat, g/day	24.4 (13.6)	12.7 (6.7)	22.6 (11.8)	14.0 (8.5)	18.5 (10.5)	17.5 (10.1)	23.1 (12.5)	13.9 (7.8)
Food groups, medium-size servings/day								
Whole grains	1.0 (0.8)	1.5 (0.9)	0.9 (0.7)	1.5 (0.9)	0.7 (0.6)	1.8 (0.9)	0.8 (0.6)	1.8 (0.9)
Fruits	1.2 (1.0)	2.7 (1.3)	1.6 (1.1)	2.6 (1.3)	1.2 (0.9)	2.9 (1.2)	1.1 (0.8)	3.2 (1.2)
Vegetables	1.6 (1.0)	2.9 (1.4)	1.7 (1.0)	3.1 (1.5)	1.4 (0.8)	3.3 (1.3)	1.4 (0.8)	3.4 (1.4)
Dairy	1.7 (1.3)	1.9 (1.4)	1.9 (1.4)	1.8 (1.3)	1.6 (1.2)	2.1 (1.4)	1.4 (1.1)	2.4 (1.5)
Meat								
Red meat	0.9 (0.7)	0.4 (0.4)	0.9 (0.6)	0.3 (0.4)	0.7 (0.5)	0.5 (0.5)	0.9 (0.6)	0.3 (0.3)
Processed meat	0.4 (0.4)	0.1 (0.2)	0.4 (0.4)	0.1 (0.2)	0.3 (0.3)	0.2 (0.3)	0.4 (0.4)	0.1 (0.1)

Abbreviations: AHEI, Alternative Healthy Eating Index 2010; aMED, Alternative Mediterranean Diet; DASH, Dietary Approaches to Stop Hypertension; HEI-2010, Healthy Eating Index 2010.

[a] Food values were estimated from responses to the Women's Health Initiative baseline food frequency questionnaire.

[b] Quintile of diet quality index score; scores in higher quintiles indicate better diet quality.

[c] Only 78,247 participants had measurements for alcohol.

Table 3. Risk of Colorectal Cancer by Quintile of Diet Quality Index Score, Women's Health Initiative Observational Study, 1993–2012

Diet Quality Index and Quintile[a]	Range of Participant Scores	Model 1[b]					Model 2[b]				
		No. of Cases	No. of Person-Years	HR	95% CI	*P* Value[d]	No. of Cases	No. of Person-Years	HR	95% CI	*P* Value[d]
HEI-2010											
1	15.65–46.09	212	185,209	1.00	Referent		209	179,317	1.00	Referent	
2	46.09–51.67	194	190,843	0.85	0.70, 1.04	0.112	189	184,619	0.88	0.72, 1.08	0.219
3	51.67–56.15	182	193,547	0.77	0.63, 0.94	0.011	175	187,683	0.81	0.66, 0.99	0.040
4	56.15–61.51	177	196,139	0.72	0.59, 0.87	0.001	172	190,388	0.77	0.63, 0.95	0.014
5	61.51–94.43	172	195,062	0.67	0.55, 0.82	<0.001	166	189,193	0.73	0.59, 0.90	0.003
LRT *P* value[e]					<0.001					0.032	
AHEI											
1	12.67–36.75	204	184,243	1.00	Referent		201	178,218	1.00	Referent	
2	36.75–42.62	179	188,607	0.84	0.69, 1.03	0.090	171	182,873	0.84	0.68, 1.03	0.096
3	42.62–48.01	196	192,395	0.89	0.73, 1.08	0.244	192	186,541	0.93	0.76, 1.14	0.485
4	48.01–54.60	179	196,146	0.80	0.66, 0.98	0.031	174	190,411	0.85	0.69, 1.05	0.132
5	54.60–91.61	179	199,409	0.79	0.65, 0.97	0.022	173	193,157	0.86	0.70, 1.07	0.177
LRT *P* value[e]					0.140					0.427	
aMED											
1	0–2	206	187,638	1.00	Referent		204	181,419	1.00	Referent	
2	3	188	174,225	0.99	0.81, 1.20	0.906	184	169,033	1.00	0.82, 1.23	0.962
3	4	172	193,244	0.81	0.66, 0.99	0.043	163	186,947	0.82	0.66, 1.01	0.057
4	5	158	177,315	0.81	0.66, 1.00	0.047	154	171,839	0.86	0.69, 1.06	0.158
5	6–9	213	228,378	0.85	0.70, 1.02	0.087	206	221,962	0.91	0.74, 1.11	0.358
LRT *P* value[e]					0.085					0.217	
DASH											
1	8–20	200	162,837	1.00	Referent		195	157,171	1.00	Referent	
2	21–23	181	177,983	0.80	0.66, 0.98	0.033	177	172,408	0.84	0.68, 1.03	0.092
3	24–26	201	226,357	0.69	0.56, 0.84	<0.001	193	219,409	0.72	0.59, 0.89	0.002
4	27–29	189	211,817	0.68	0.55, 0.83	<0.001	183	205,710	0.74	0.60, 0.91	0.004
5	30–39	166	181,805	0.68	0.55, 0.84	<0.001	163	176,501	0.78	0.62, 0.97	0.026
LRT *P* value[e]					<0.001					0.021	

Abbreviations: AHEI, Alternative Healthy Eating Index 2010; aMED, Alternative Mediterranean Diet; CI, confidence interval; DASH, Dietary Approaches to Stop Hypertension; HEI-2010, Healthy Eating Index 2010; HR, hazard ratio; LRT, likelihood-ratio test; MET, metabolic equivalent of task.

[a] Quintiles of diet quality index scores; scores in higher quintiles indicate better diet quality.

[b] Model 1 adjusted for age (years; as a time-dependent covariate) and race/ethnicity (African-American/black, non-Hispanic white, or other) ($n = 77{,}679$).

[c] Model 2 adjusted for age (years; as time-dependent covariate), race/ethnicity (African-American/black, non-Hispanic white, or other), physical activity (MET-hours per week), educational level (high school graduate or less, some college, college graduate or more), smoking status (never, former, or current), and hormone replacement therapy (never, former, or current) ($n = 75{,}219$).

[d] *P* value was calculated using Cox proportional hazards models.

[e] Likelihood-ratio test *P* value comparing the models with and without the addition of diet quality index scores.

Comparing diet quality index scores and their associations with CRC

Based on likelihood-ratio tests, the addition of HEI-2010 ($P = 0.03$) and DASH ($P = 0.02$) significantly improved model fit, but the addition of AHEI and aMED did not (Table 3). These findings indicate that HEI-2010 and DASH improve the models' ability to predict CRC risk beyond the prediction provided by model 2 covariates alone, while the addition of AHEI and aMED did not. Akaike information criterion and Bayesian information criterion measures indicated that the inclusion of DASH > HEI-2010 > aMED > AHEI led to the best model fit across both models (data not shown).

Component analysis of the association of diet quality index scores with CRC

When all components of each diet quality index were added to model 2 in lieu of diet quality scores, no single component of the HEI-2010, aMED, or DASH diet quality index score was significantly associated with CRC after adjustment for the other components in that score (data not shown). The AHEI alcohol component was a significant predictor (HR = 0.98, 95% CI: 0.96, 1.00; $P = 0.03$) after adjustment for all model 2 covariates and all other AHEI components.

The addition of alcohol, BMI, and energy to model 2

Energy was not consistently controlled for in AHEI, aMED, and DASH calculations, and alcohol was not a component of DASH and HEI-2010. To test for the robustness of the observed associations, we added potential confounders (alcohol, BMI, energy) and mediators (BMI) to the fully adjusted model to ensure that observations remained consistent despite the risk of overadjustment. The addition of BMI and dietary energy to model 2 shifted the hazard ratio estimates only slightly across each diet quality index quintile (Web Table 1). However, the significance of associations was attenuated in quintile 3 of HEI-2010 (from $P = 0.04$ to $P = 0.05$) and quintile 5 of DASH (from $P = 0.03$ to $P = 0.05$) with the addition of BMI to the model. Neither the addition of energy nor the addition of alcohol altered the significance (above or below $P = 0.05$) of any associations between diet quality index and CRC (data not shown).

Association of diet quality index scores with site-specific colon and rectal cancers

Scores in quintile 5 for HEI-2010 and DASH, but not aMED or AHEI, were significantly associated with reduced colon cancer risk (Table 4). Although point estimates suggested a protective association, no quintile-5 diet quality scores were significantly associated with rectal cancer. Again, a linear, protective association was observed between quintiles of the HEI-2010 diet quality score and risk of colon cancer (compared with quintile 1: HR = 0.86 (95% CI: 0.69, 1.07), $P = 0.18$ for quintile 2; HR = 0.81 (95% CI: 0.64, 1.01), $P = 0.06$ for quintile 3; HR = 0.78 (95% CI: 0.62, 0.98), $P = 0.03$ for quintile 4; and HR = 0.72 (95% CI: 0.57, 0.91), $P = 0.01$ for quintile 5). Similarly, a threshold, protective association beginning at quintile 3 was observed between quintiles of the DASH diet quality scores and risk of colon cancer (compared with quintile 1: HR = 0.82 (95% CI: 0.65, 1.02), $P = 0.08$ for quintile 2; 0.69 (95% CI: 0.55, 0.87), $P < 0.01$ for quintile 3; 0.75 (95% CI: 0.59, 0.94), $P = 0.01$ for quintile 4; and 0.77 (95% CI: 0.60, 0.98), $P = 0.04$ for quintile 5).

Stratification of the relationship between diet quality index scores and CRC by baseline characteristics

Participants' baseline characteristics were tested as effect modifiers of the relationship between diet quality index scores and CRC incidence (Web Table 2). Initially, age was a significant, multiplicative effect modifier of HEI-2010 and AHEI index quintiles ($P_{\text{interaction}} = 0.03$ for both; Web Table 2). However, after false discovery rate adjustment, no baseline characteristics (age, race/ethnicity, family history, and history of CRC screening) remained statistically significant effect modifiers of the relationship between any diet quality index scores and CRC (data not shown). Thus, these findings do not support evidence of effect modification by the variables in this data set.

Table 4. Relative Risk of Colorectal Cancer by Cancer Site for Participants in the Top Quintile of 4 Diet Quality Index Scores ($n = 83{,}702$), Women's Health Initiative Observational Study, 1993–2012

Diet Quality Index and Quintile[a]	No. of Cases	No. of Person-Years	HR[b]	95% CI[b]	*P* Value[b]
		Colon Cancer			
HEI-2010					
1	173	179,550	1.00	Referent	
5	139	189,333	0.72	0.57, 0.91	0.005
AHEI					
1	166	178,434	1.00	Referent	
5	142	193,331	0.84	0.66, 1.06	0.133
aMED					
1	171	181,596	1.00	Referent	
5	176	222,111	0.91	0.73, 1.13	0.387
DASH					
1	162	157,338	1.00	Referent	
5	139	176,640	0.77	0.60, 0.98	0.035
		Rectal Cancer			
HEI-2010					
1	21	180,250	1.00	Referent	
5	25	189,893	1.28	0.70, 2.34	0.414
AHEI					
1	23	179,049	1.00	Referent	
5	25	193,905	1.22	0.67, 2.20	0.516
aMED					
1	21	182,268	1.00	Referent	
5	26	222,887	1.21	0.67, 2.19	0.532
DASH					
1	20	157,994	1.00	Referent	
5	23	177,224	1.24	0.65, 2.35	0.508

Abbreviations: AHEI, Alternative Healthy Eating Index 2010; aMED, Alternative Mediterranean Diet; CI, confidence interval; DASH, Dietary Approaches to Stop Hypertension; HEI-2010, Healthy Eating Index 2010; HR, hazard ratio; MET, metabolic equivalent of task.

[a] Quintile of diet quality index score; scores in higher quintiles indicate better diet quality.

[b] Hazard ratio, 95% confidence interval, and *P* value from Cox regression analysis; results were adjusted for age (years; as a time-dependent covariate), race/ethnicity (African-American/black, non-Hispanic white, or other), physical activity (MET-hours per week), educational level (high school graduate or less, some college, college graduate or more), smoking status (never, former, or current), and hormone replacement therapy (never, former, or current).

DISCUSSION

In this cohort of postmenopausal US women, closer adherence to the DASH diet and the HEI-2010 dietary recommendations was associated with a reduced risk of

CRC. Higher quintiles of the HEI-2010 were associated with a lower risk of CRC, while quintiles 3–5 of the DASH diet index were observed to be associated with a similar, approximately 22%–28% lower risks compared with quintile 1. When comparing diet quality scores across all diets, the DASH diet quality score consistently improved model fit to a greater extent than other diet scores.

Our findings are supported by those of Miller et al. (14) and Reedy et al. (11), who found significant associations between lower risk of CRC and the Fung method of calculating the DASH diet quality index score (9) and HEI-2005, respectively, in the NIH-AARP study of older Americans. HEI-2010 is an update to HEI-2005, based on the 2010 Dietary Guidelines for Americans, with updates to some dietary component definitions (6). Further, Reedy et al. (11) found a CRC association only with HEI-2005 and not with the original Alternative Healthy Eating Index or Mediterranean Diet Score among women, although the DASH score was not evaluated. This supports our null findings for these 2 diet scores. Unlike AHEI-2010 and aMED, neither the DASH index nor the HEI-2010 includes an alcohol component, but the addition of alcohol to our fully adjusted models did not affect our findings. Similarly, adjustment for BMI and energy did not have a meaningful impact on the hazard ratios, suggesting that alcohol, BMI, and energy alone were not more important predictors of CRC risk above the predictive power provided by diet quality scores and model 2 covariates. Further, component analysis suggested that it is the sum of these components, rather than any single component, that is associated with CRC risk. By testing these associations in a new, well-defined cohort and using all 4 major diet pattern index scores, our current findings are supported by and substantially add to the existing evidence of associations between CRC and dietary pattern index scores.

These diet quality index scores have been associated with other diseases in this WHI cohort (38–42). Of particular relevance is the recent finding of significant protective associations between HEI-2010, aMED, and DASH and all cancer deaths in the WHI (38) and the confirmation of these findings in other cohorts as part of the Dietary Patterns Methods Project (4). While we did not find a significant association with CRC death in this study, we did observe significant protective associations with CRC incidence for HEI-2010 and DASH. Even conducting our CRC-death outcome analysis using the same covariates as those used by George et al. (38) did not result in any significant associations. This difference could be explained by a lack of power and no adjustment for CRC treatment information (which was not collected).

The WHI Observational Study is a study of a large, multiethnic/multiracial cohort with well-adjudicated CRC endpoints (22–24) that allowed for close examination of the relationship between 4 major diet quality index scores and CRC. Tests for different associations between diet quality and CRC among whites, blacks, and other racial/ethnic groups did not suggest racial/ethnic effect modification. However, we lacked statistical power for further analysis by many different race/ethnicity categories and for conducting analyses of rectal cancer. Further, dietary exposure was based on food frequency questionnaires with known bias and measurement error (43). Higher diet quality scores were observed among participants with better health indicators (increased physical activity, lower BMI, lower smoking, etc.), which raises the possibility of residual confounding. Nonetheless, our results are consistent with previous findings obtained using older editions of diet quality indices (11, 14), and because we used all 4 common diet quality scores in the same cohort, our findings add to the existing literature on diet quality indices and CRC.

In conclusion, in a cohort of postmenopausal US women, we found that higher HEI-2010 diet quality index scores were associated with lower risk of CRC and, similarly, higher DASH diet quality index scores were associated with an approximately 22%–28% lower risk of CRC. No associations were observed between any diet quality score and CRC-specific mortality. Our findings add to the evidence base for future recommendations on diet quality and CRC, such as the next edition of the continuous updates on diet and CRC risk published by the American Institute for Cancer Research and the World Cancer Research fund (2, 44).

ACKNOWLEDGMENTS

Author affiliations: Cancer Prevention Fellowship Program, National Cancer Institute, Rockville, Maryland (Ashley J. Vargas); Department of Biostatistics, Harvard T.H. Chan School of Public Health, Harvard University, Boston, Massachusetts (Ashley J. Vargas); Cancer Prevention Program, Fred Hutchinson Cancer Research Center, Seattle, Washington (Marian L. Neuhouser); Office of Disease Prevention, Office of the Director, National Institutes of Health, Rockville, Maryland (Stephanie M. George); Canyon Ranch Center for Prevention and Health Promotion, Mel and Enid Zuckerman College of Public Health, University of Arizona, Tucson, Arizona (Cynthia A. Thomson); Department of Occupational Medicine, Epidemiology, and Prevention, Hofstra Northwell School of Medicine, Hempstead, New York (Gloria Y. F. Ho); Department of Epidemiology and Population Health, Albert Einstein College of Medicine, New York, New York (Thomas E. Rohan); Department of Oncology, School of Medicine, Wayne State University, Detroit, Michigan (Ikuko Kato); Department of Pathology, School of Medicine, Wayne State University, Detroit, Michigan (Ikuko Kato); Department of Biochemistry and Molecular Medicine, School of Medicine, University of California, Davis, Davis, California (Rami Nassir); Department of Preventive Medicine, Feinberg School of Medicine, Northwestern University, Chicago, Illinois (Lifang Hou); and Division of Preventive Medicine, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts (JoAnn E. Manson).

The Women's Health Initiative (WHI) is funded by the National Heart, Lung, and Blood Institute through contracts HHSN268201100046C, HHSN268201100001C, HHSN268201100002C, HHSN268201100003C, HHSN268201100004C, and HHSN271201100004C. Additional support was provided by the National Cancer Institute Cancer Prevention Fellowship Program.

A short list of WHI investigators—*Program Office* (National Heart, Lung, and Blood Institute, Bethesda, Maryland): Jacques Rossouw, Shari Ludlam, Dale Burwen, Joan McGowan, Leslie Ford, and Nancy Geller; *Clinical Coordinating Center* (Fred Hutchinson Cancer Research Center, Seattle, Washington): Garnet Anderson, Ross Prentice, Andrea LaCroix, and Charles Kooperberg; *investigators and academic centers*: Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts—JoAnn E. Manson; MedStar Health Research Institute/Howard University, Washington, DC—Barbara V. Howard; Stanford Prevention Research Center, Stanford, California—Marcia L. Stefanick; Ohio State University, Columbus, Ohio—Rebecca Jackson; University of Arizona, Tucson/Phoenix, Arizona—Cynthia A. Thomson; University at Buffalo, Buffalo, New York—Jean Wactawski-Wende; University of Florida, Gainesville/Jacksonville, Florida—Marian Limacher; University of Iowa, Iowa City/Davenport, Iowa—Robert Wallace; University of Pittsburgh, Pittsburgh, Pennsylvania—Lewis Kuller; Wake Forest University School of Medicine, Winston-Salem, North Carolina—Sally Shumaker; and Women's Health Initiative Memory Study, Wake Forest University School of Medicine, Winston-Salem, North Carolina—Sally Shumaker. For a list of all the investigators who have contributed to WHI, please visit the WHI website (https://www.whi.org/researchers/Documents%20%20Write%20a%20Paper/WHI%20Investigator%20Long%20List.pdf).

Conflict of interest: none declared.

REFERENCES

1. Howlader N, Noone AM, Krapcho M, et al, eds. *SEER Cancer Statistics Review, 1975–2010*. Bethesda, MD: National Cancer Institute; 2013. http://seer.cancer.gov/csr/1975_2010/. (Based on November 2012 SEER data submission). Accessed July 1, 2015.
2. World Cancer Research Fund/American Institute for Cancer Research. *Food, Nutrition, Physical Activity, and the Prevention of Cancer: A Global Perspective*. 2nd ed. Washington, DC: American Institute for Cancer Research; 2007.
3. Sempos CT, Liu K, Ernst ND. Food and nutrient exposures: what to consider when evaluating epidemiologic evidence. *Am J Clin Nutr*. 1999;69(6):1330S–1338S.
4. Liese AD, Krebs-Smith SM, Subar AF, et al. The Dietary Patterns Methods Project: synthesis of findings across cohorts and relevance to dietary guidance. *J Nutr*. 2015;145(3):393–402.
5. Hu FB. Dietary pattern analysis: a new direction in nutritional epidemiology. *Curr Opin Lipidol*. 2002;13(1):3–9.
6. Guenther PM, Casavale KO, Reedy J, et al. Update of the Healthy Eating Index: HEI-2010. *J Acad Nutr Diet*. 2013;113(4):569–580.
7. Chiuve SE, Fung TT, Rimm EB, et al. Alternative dietary indices both strongly predict risk of chronic disease. *J Nutr*. 2012;142(6):1009–1018.
8. Fung TT, Rexrode KM, Mantzoros CS, et al. Mediterranean diet and incidence of and mortality from coronary heart disease and stroke in women. *Circulation*. 2009;119(8):1093–1100.
9. Fung TT, Chiuve SE, McCullough ML, et al. Adherence to a DASH-style diet and risk of coronary heart disease and stroke in women. *Arch Intern Med*. 2008;168(7):713–720.
10. Dixon LB, Balder HF, Virtanen MJ, et al. Dietary patterns associated with colon and rectal cancer: results from the Dietary Patterns and Cancer (DIETSCAN) Project. *Am J Clin Nutr*. 2004;80(4):1003–1011.
11. 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(1):38–48.
12. Zamora-Ros R, Shivappa N, Steck SE, et al. Dietary inflammatory index and inflammatory gene interactions in relation to colorectal cancer risk in the Bellvitge colorectal cancer case-control study. *Genes Nutr*. 2015;10(1):447.
13. Shivappa N, Prizment AE, Blair CK, et al. Dietary inflammatory index and risk of colorectal cancer in the Iowa Women's Health Study. *Cancer Epidemiol Biomarkers Prev*. 2014;23(11):2383–2392.
14. Miller PE, Cross AJ, Subar AF, et al. Comparison of 4 established DASH diet indexes: examining associations of index scores and colorectal cancer. *Am J Clin Nutr*. 2013;98(3):794–803.
15. Miller PE, Lazarus P, Lesko SM, et al. Diet index-based and empirically derived dietary patterns are associated with colorectal cancer risk. *J Nutr*. 2010;140(7):1267–1273.
16. Tabung FK, Steck SE, Ma Y, et al. The association between dietary inflammatory index and risk of colorectal cancer among postmenopausal women: results from the Women's Health Initiative. *Cancer Causes Control*. 2015;26(3):399–408.
17. Guenther PM, Reedy J, Krebs-Smith SM. Development of the Healthy Eating Index-2005. *J Am Diet Assoc*. 2008;108(11):1896–1901.
18. Kant AK, Schatzkin A, Graubard BI, et al. A prospective study of diet quality and mortality in women. *JAMA*. 2000;283(16):2109–2115.
19. Appel LJ, Moore TJ, Obarzanek E, et al. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. *N Engl J Med*. 1997;336(16):1117–1124.
20. 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(1):3–10.
21. Mellen PB, Gao SK, Vitolins MZ, et al. Deteriorating dietary habits among adults with hypertension: DASH dietary accordance, NHANES 1988–1994 and 1999–2004. *Arch Intern Med*. 2008;168(3):308–314.
22. Women's Health Initiative Study Group. Design of the Women's Health Initiative clinical trial and observational study. *Control Clin Trials*. 1998;19(1):61–109.
23. Langer RD, White E, Lewis CE, et al. The Women's Health Initiative Observational Study: baseline characteristics of participants and reliability of baseline measures. *Ann Epidemiol*. 2003;13(9 suppl):S107–S121.
24. Hays J, Hunt JR, Hubbell FA, et al. The Women's Health Initiative recruitment methods and results. *Ann Epidemiol*. 2003;13(9 suppl):S18–S77.
25. Patterson RE, Kristal AR, Tinker LF, et al. Measurement characteristics of the Women's Health Initiative food frequency questionnaire. *Ann Epidemiol*. 1999;9(3):178–187.
26. Block G, Hartman AM, Dresser CM, et al. A data-based approach to diet questionnaire design and testing. *Am J Epidemiol*. 1986;124(3):453–469.
27. Schakel SF, Sievert YA, Buzzard IM. Sources of data for developing and maintaining a nutrient database. *J Am Diet Assoc*. 1988;88(10):1268–1271.
28. Bowman S, Friday J, Moshfegh A. *MyPyramid Equivalents Database, 2.0 for USDA Survey Foods, 2003–2004*. Beltsville, MD: US Department of Agriculture;

2008. http://www.ars.usda.gov/SP2UserFiles/Place/80400530/pdf/mped/mped2_doc.pdf. Accessed October 16, 2015.
29. George SM, Irwin ML, Smith AW, et al. Postdiagnosis diet quality, the combination of diet quality and recreational physical activity, and prognosis after early-stage breast cancer. *Cancer Causes Control*. 2011;22(4):589–598.
30. Women's Health Initiative. *Healthy Eating Index-2005 (HEI-2005) and My Pyramid Equivalents Database 2.0 (MPED 2.0) (Beta 11/12)*. Bethesda, MD: National Heart, Lung, and Blood Institute; 2012. https://www.whi.org/researchers/data/Documents/WHI Healthy Eating Index (HEI) and MPEDs 2 0 for WHI website (112012).pdf. Accessed January 1, 2015.
31. Curb JD, McTiernan A, Heckbert SR, et al. Outcomes ascertainment and adjudication methods in the Women's Health Initiative. *Ann Epidemiol*. 2003;13(9 suppl):S122–S128.
32. Simon MS, Thomson CA, Pettijohn E, et al. Racial differences in colorectal cancer incidence and mortality in the Women's Health Initiative. *Cancer Epidemiol Biomarkers Prev*. 2011;20(7):1368–1378.
33. Huxley RR, Ansary-Moghaddam A, Clifton P, et al. The impact of dietary and lifestyle risk factors on risk of colorectal cancer: a quantitative overview of the epidemiological evidence. *Int J Cancer*. 2009;125(1):171–180.
34. Doubeni CA, Laiyemo AO, Major JM, et al. Socioeconomic status and the risk of colorectal cancer: an analysis of more than a half million adults in the National Institutes of Health-AARP Diet and Health Study. *Cancer*. 2012;118(14):3636–3644.
35. Paskett ED, Reeves KW, Rohan TE, et al. Association between cigarette smoking and colorectal cancer in the Women's Health Initiative. *J Natl Cancer Inst*. 2007;99(22):1729–1735.
36. Botteri E, Iodice S, Bagnardi V, et al. Smoking and colorectal cancer: a meta-analysis. *JAMA*. 2008;300(23):2765–2778.
37. Ritenbaugh C, Stanford JL, Wu L, et al. Conjugated equine estrogens and colorectal cancer incidence and survival: the Women's Health Initiative randomized clinical trial. *Cancer Epidemiol Biomarkers Prev*. 2008;17(10):2609–2618.
38. George SM, Ballard-Barbash R, Shikany JM, et al. Better postdiagnosis diet quality is associated with reduced risk of death among postmenopausal women with invasive breast cancer in the Women's Health Initiative. *Cancer Epidemiol Biomarkers Prev*. 2014;23(4):575–583.
39. George SM, Ballard-Barbash R, Manson JE, et al. Comparing indices of diet quality with chronic disease mortality risk in postmenopausal women in the Women's Health Initiative Observational Study: evidence to inform national dietary guidance. *Am J Epidemiol*. 2014;180(6):616–625.
40. Levitan EB, Lewis CE, Tinker LF, et al. Mediterranean and DASH diet scores and mortality in women with heart failure: the Women's Health Initiative. *Circ Heart Fail*. 2013;6(6):1116–1123.
41. Mares JA, Voland RP, Sondel SA, et al. Healthy lifestyles related to subsequent prevalence of age-related macular degeneration. *Arch Ophthalmol*. 2011;129(4):470–480.
42. Belin RJ, Greenland P, Allison M, et al. Diet quality and the risk of cardiovascular disease: the Women's Health Initiative (WHI). *Am J Clin Nutr*. 2011;94(1):49–57.
43. Neuhouser ML, Tinker L, Shaw PA, et al. Use of recovery biomarkers to calibrate nutrient consumption self-reports in the Women's Health Initiative. *Am J Epidemiol*. 2008;167(10):1247–1259.
44. World Cancer Research Fund/American Institute for Cancer Research. *Colorectal Cancer 2011 Report*. Washington, DC: American Institute for Cancer Research; 2011. http://www.aicr.org/continuous-update-project/reports/Colorectal-Cancer-2011-Report.pdf. Accessed July 1, 2015.