Diet quality and the risk of cardiovascular disease: the Women's Health Initiative (WHI)[1–3]

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ABSTRACT

Background: The association between diet quality and risk of incident cardiovascular disease (CVD) or heart failure (HF) in postmenopausal women is uncertain.

Objective: This study aimed to determine whether a conventional index [Alternate Healthy Eating Index (AHEI)] or a novel index [Women's Health Initiative (WHI) Dietary Modification Index (DMI)] of diet quality was associated with the risk of incident CVD or HF in the WHI Observational Study (WHI-OS).

Design: The WHI-OS is an observational cohort study of 93,676 women aged 50–79 y of diverse ethnicity and backgrounds followed for an average of 10.0 y for CVD events. The individual components of the AHEI and DMI were determined from the baseline WHI food-frequency questionnaire. Incident CVD was a composite of nonfatal myocardial infarction, coronary heart disease death, stroke, coronary revascularization, and incident HF. The association between AHEI or DMI and incident CVD or incident HF was determined by using Cox models adjusted for traditional CVD and HF risk factors.

Results: Women with a DMI in the highest quintile had hazard ratios (HRs) of 0.88 (95% CI: 0.80, 0.95) and 0.91 (95% CI: 0.78, 1.06) for incident CVD and HF, respectively. Women with an AHEI in the highest quintile had HRs of 0.77 (95% CI: 0.70, 0.84) and 0.70 (95% CI: 0.59, 0.82) for incident CVD and HF, respectively.

Conclusion: Overall, adherence to current nutrient guidelines (as indexed by the DMI) are associated with lower total CVD risk, and additional dietary factors (as indexed by the AHEI) were associated with a lower risk of CVD and HF. *Am J Clin Nutr* 2011; 94:49–57.

INTRODUCTION

Previous studies have shown that lower intakes of saturated and *trans* fatty acids and higher intakes of unsaturated fatty acids, dietary fiber, and vegetable protein can reduce the risk of some types of cardiovascular disease (CVD), particularly coronary heart disease (CHD) (1–5). The results from the Women's Health Initiative (WHI) Dietary Modification (DM) Trial, a randomized controlled trial of a low-fat (20% of energy) dietary pattern with increased intakes of vegetables, fruit, and grains on CHD and stroke in postmenopausal women suggested that greater reductions in saturated and *trans* fatty acids and increases in vegetables and fruit lowered the risk of CHD, but, overall, the trial was not conclusive (2). Assessing the cardiovascular results of the WHI-DM Trial was complex because the trial was designed to test the effect of a diet low in total fat on breast cancer, without specifying types of fat or other dietary components known to be associated with heart disease risk. In addition, less is known about dietary risk factors related to a broader definition of CVD that, in addition to CHD and stroke, includes heart failure (HF), which was not evaluated in the WHI-DM Trial. Importantly, whereas HF prevalence is greater in men than in women under the age of 70 y, the prevalence is greater in women after the age of 70 y (1).

To explore the effect of diet on CVD risk among postmenopausal women, we evaluated the risk of CVD by comparing 2 dietary indexes: a WHI-DM index (DMI) that was generated based on the findings from the WHI-DM Trial plus goals from the American Heart Association (AHA) guidelines and the Alternate Healthy Eating Index (AHEI)—a diet quality index developed by McCullough et al (6, 7). The AHEI includes select components of the HEI, but also provides a scoring mechanism by which to quantitate diet quality to provide dietary guidance and recommendations (6, 7).

To our knowledge, no previous studies have examined different measures of CVD risk-reducing diets and HF outcomes in postmenopausal women. The main objective of this study was to examine the association between the risk of CHD and HF outcomes in the WHI-OS and a diet low in total, saturated, and *trans* fats (DMI); rich in polyunsaturated fatty acids; high in white meat; low in red meat; and modest in alcohol consumption (AHEI).

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SUBJECTS AND METHODS

Study sample

The WHI-OS consists of a national sample of postmenopausal women (ages 50–79 y at baseline) in overall good health who expressed interest in the WHI clinical trials and were either ineligible or unwilling to be randomly assigned in the clinical trials or who received direct invitation to the WHI-OS (8). The procedures followed were in accordance with the ethical standards of participating institutions/regional committees on human experimentation, and appropriate approval was obtained to conduct these studies on human subjects. The WHI is listed in the Clinical Trials Registry at www.clinicaltrials.gov (NCT00000611), including a description of the OS. A core analytic data set was compiled from the initial 93,676 OS participants after the following exclusions were applied: 3817 because of missing data needed to compute the AHEI and DMI values and an additional 5536 because of missing covariate data. In the CVD models, an additional 4571 participants with previous CVD were excluded, which left 79,752 CVD-free participants at baseline. In HF models, an additional 1140 participants with previous HF were excluded, which left 83,183 HF-free participants at baseline.

Construction of the DMI and AHEI

Dietary data used to generate the DMI and AHEI were derived from the WHI food-frequency questionnaire (WHI-FFQ) administered at the baseline examination for all WHI participants (9). The score for the DMI was based on the following criteria: *1*) percentage of total energy intake from total fat, 2) servings of vegetables and fruit, *3*) servings of grain, *4*) percentage of energy intake from saturated fat, *5*) percentage of energy intake from *trans* fat, and *6*) total dietary cholesterol intake (2). Scoring criteria for intake of total fat, fruit and vegetable, and grains were derived from the WHI-DM trial. Criteria for saturated fat, *trans* fat, and cholesterol intake were derived from AHA goals. For each dietary variable, calculation of the distribution based on quintiles within the cohort was performed, and each participant was assigned a DMI score of 1 to 5 based on the quintile of intake, with quintile 5 serving as the most favorable (healthy) quintile. The cutoffs for the most favorable quintile (quintile 5) for each dietary variable were as follows: <20% of total energy intake derived from total fat, <7% of total energy intake derived from saturated fat, <1% of energy derived from *trans* fat, <200 mg cholesterol, >5 servings of fruit and vegetables daily, and >6 serving of grains daily. For each participant, the quintile value for each dietary factor was summed, and higher scores reflected better adherence to the DMI. The median DMI score was reported (interquintile ranges). The components of the DMI along with criteria for minimum and maximum scores are summarized in **Table 1**.

The AHEI is a composite numerical measure of dietary quality and is an alternative to the HEI, which was developed by the US Department of Agriculture (USDA) to assess adherence to the 1995 Dietary Guidelines and the 1992 Food Guide Pyramid (6, 7). The AHEI scoring method considered the following: *1*) vegetables (servings/d), *2*) fruit (servings/d), *3*) nuts and soy protein (servings/d), *4*) ratio of white to red meat (white meat is defined as poultry and fish; red meat is defined as beef, pork, lamb, and processed meats), *5*) cereal fiber (g/d), *6*) *trans* fat (% of energy), *7*) ratio of polyunsaturated to saturated fat, *8*) duration of multivitamin use (y), and *9*) alcohol intake (servings/d). The components of the AHEI along with criteria for minimum and maximum scores are summarized in **Table 2** (6, 7). The AHEI consists of a total of 9 components, 8 of which are continuously distributed variables based on a 10-point scale (0 = least healthy; 10 = most healthy). Multivitamin use was scored as follows: 2.5 = nonuse and 7.5 = use. Multivitamin use was obtained from WHI data collection of current supplement intake (either multivitamins alone or along with minerals). All components were summed to obtain a total AHEI score ranging from 2.5 (least healthy) to 87.5 (most healthy). The AHEI is reported as medians (interquintile ranges).

TABLE 1
Dietary Modification Index components and criteria for minimum and maximum scoring

Component	Criteria for[1] Minimum score (1)	Maximum score (5)
Fat (% of energy)	≥36.99	<20.00
Saturated fat (% of energy)	≥12.65	<7.00
trans Fat (% of energy)	≥2.71	<1.00
Cholesterol (mg/d)	≥352.30	<200.00
Fruit and vegetables (servings/d)	≥5.00	<2.22
Grains (servings/d)	≥6.00	<2.53

[1] The numbers 1 and 5 represent the minimum and maximum Dietary Modification Index score for each dietary variable evaluated in the index.

Ascertainment of cardiovascular disease outcomes

Two outcomes were assessed: *1*) a composite CVD measure consisting of nonfatal MI, CHD death, coronary artery bypass graft (CABG)/percutaneous transluminal coronary angioplasty (PTCA), stroke, and HF, and *2*) HF alone. CVD outcomes were adjudicated and defined as described in detail previously (10). Adjudicated (hospitalized) HF was based on the presence of at least one of the following criteria: *1*) diagnosis by a physician

TABLE 2
Alternate Healthy Eating Index components and criteria for minimum and maximum scoring

Component	Criteria for[1] Minimum score (0)	Maximum score (1)
Fruit (servings/d)	0	4
Vegetables (servings/d)	0	5
Nuts and soy protein (servings/d)	0	1
White:red meat	0	4
Fiber (g/d)	0	15
trans Fat (% of energy)	≥4	≤0.5
Polyunsaturated:saturated fat	≤0.1	≥1
Duration of multivitamin use (y)	<5	>5
Alcohol (servings/d)	0 or >2.5	0.5–1.5

[1] The numbers 0 and 1 represent the minimum and maximum Alternate Healthy Eating Index score for each dietary variable evaluated in the index.

TABLE 3
Baseline characteristics of the Women's Health Initiative (WHI) Observational Study cohort according to Dietary Modification Index (DMI) quintiles[1]

	Quintiles					
	1: <14.0 (*n* = 16,246)	2: 14.0–16.9 (*n* = 15,228)	3: 17.0–20.9 (*n* = 21,983)	4: 21.0–23.9 (*n* = 16,271)	5: ≥ 24.0 (*n* = 20,279)	*P* for trend[2]
Median DMI score[3]	12.0 (10.0, 13.0)	15.0 (14.0, 16.0)	19.0 (18.0, 20.0)	22.0 (21.0, 23.0)	26.0 (25.0, 27.0)	
Age (y)[4]	63.0 (57.0, 69.0)	64.0 (58.0, 70.0)	64.0 (58.0, 70.0)	64.0 (58.0, 69.0)	63.0 (57.0, 69.0)	0.042
African American race [*n* (%)]	1913 (11.8)	1305 (8.6)	1593 (7.2)	987 (6.1)	973 (4.8)	<0.001
Diabetes [*n* (%)]	982 (6.0)	770 (5.1)	841 (3.8)	537 (3.3)	503 (2.5)	<0.001
Coronary artery disease [*n* (%)]	556 (3.4)	477 (3.1)	721 (3.3)	520 (3.2)	736 (3.6)	0.160
BMI (kg/m^2)[4]	28.0 (24.4, 32.6)	27.0 (23.7, 31.1)	26.1 (23.3, 29.9)	25.6 (23.0, 29.1)	24.8 (22.4, 28.0)	<0.001
HDL cholesterol (mg/dL)[5]	58.0 (47.0, 72.0)	61.0 (51.0, 76.0)	60.0 (52.0, 77.0)	62.0 (51.0, 71.5)	62.0 (52.0, 73.0)	0.116
LDL cholesterol (mg/dL)[5]	124.0 (104.0, 148.0)	123.0 (104.0, 147.0)	123.0 (98.0, 147.0)	122.0 (101.5, 148.0)	124.0 (103.0, 146.0)	0.515
Triglycerides (mg/dL)[5]	135.0 (100.0, 108.0)	130.0 (93.0, 186.0)	133.0 (99.0, 187.0)	124.5 (95.5, 177.0)	120.0 (95.0, 158.0)	0.013
Systolic blood pressure (mm Hg)[4]	127.0 (116.0, 139.0)	126.5 (115.0, 139.0)	125.0 (114.0, 138.0)	125.0 (113.0, 138.0)	123.5 (112.0, 136.0)	<0.001
Smoking status [*n* (%)][6]						<0.001
Never	7824 (48.2)	7692 (50.5)	11105 (50.5)	8243 (50.7)	10155 (50.1)	
Past	6160 (37.9)	6166 (40.5)	9432 (42.9)	7180 (44.1)	9314 (45.9)	
Current	2029 (12.5)	1144 (7.5)	1143 (5.2)	616 (3.8)	530 (2.6)	
Physical activity (METs/wk)[4]	4.5 (0.0, 12.0)	7.0 (1.8, 16.0)	9.8 (3.5, 19.0)	12.3 (5.0, 22.4)	16.1 (7.5, 27.0)	<0.001
Education [*n* (%)][7]						<0.001
≤ High school diploma/GED	5213 (32.1)	3750 (24.6)	4405 (20.0)	2667 (16.4)	2642 (13.0)	
Some school after high school	6434 (39.6)	5945 (39.0)	8085 (36.8)	5574 (34.3)	6494 (32.0)	
College graduate	4468 (27.5)	5408 (35.5)	9311 (42.4)	7913 (48.6)	10,977 (54.1)	
Energy intake (kcal/d)[4]	1560.7 (1145.6, 2052.6)	1533.1 (1153.6, 2010.7)	1459.4 (1117.9, 1875.8)	1430.9 (1124.1, 1789.2)	1464.5 (1188.7, 1778.3)	<0.001
Fat intake (% of energy)[4]	40.8 (37.8, 44.3)	35.3 (32.5, 38.4)	30 (27.6, 32.8)	26.0 (23.5, 28.3)	20.6 (17.5, 23.7)	<0.001
Saturated fat intake (% of energy)	13.9 (12.6, 15.5)	11.8 (10.7, 13.2)	9.9 (8.9, 11.0)	8.3 (7.4, 9.3)	6.4 (5.3, 7.4)	<0.001
Polyunsaturated fat intake (% of energy)[4]	7.8 (6.6, 9.2)	7.0 (5.9, 8.4)	6.2 (5.2, 7.3)	5.5 (4.6, 6.5)	4.7 (3.8, 5.6)	<0.001
Monounsaturated fat intake (% of energy)[4]	15.6 (14.2, 17.1)	13.4 (12.0.2, 14.8)	11.3 (10.2, 12.6)	9.6 (8.5, 10.7)	7.5 (6.2, 8.8)	<0.001
trans Fat intake (% of energy)[4]	2.9 (2.3, 3.7)	2.4 (1.9, 3.1)	1.9 (1.5, 2.4)	1.5 (1.2, 1.9)	1.1 (0.8, 1.4)	<0.001
Cholesterol intake (% of energy)[4]	162.0 (133.1, 202.4)	134.9 (111.7, 164.4)	118.9 (97.9, 114.9)	105.3 (85.4, 128.4)	85.2 (66.5, 106.1)	<0.001
Glycemic load, available carbohydrates[4]	78.8 (57.3, 106.4)	87.1 (65.5, 115.4)	89.9 (68.6, 116.7)	93.7 (73.5, 118.1)	104.0 (83.8, 127.9)	<0.001
Glycemic index, available carbohydrates[4]	53.5 (51.0, 55.9)	52.9 (50.5, 55.3)	52.2 (49.9, 54.6)	51.5 (49.2, 53.8)	51.0 (48.8, 53.2)	<0.001
Fruit and vegetable intake (servings/d)[4]	2.3 (1.7, 3.1)	3.3 (2.4, 4.5)	4.0 (2.9, 5.3)	4.7 (3.6, 6.1)	5.9 (4.7, 7.3)	<0.001
Nuts and soy protein (servings/d)[4]	0.08 (0.03, 0.25)	0.08 (0.03, 0.28)	0.08 (0.03, 0.25)	0.08 (0.02, 0.25)	0.08 (0.02, 0.28)	<0.001
White:red meat[4]	0.58 (0.37, 0.96)	0.76 (0.48, 1.28)	1.04 (0.63, 1.83)	1.4 (0.8, 2.6)	2.21 (1.18, 4.96)	<0.001
Cereal fiber (g/d)[4]	11.0 (8.2, 14.7)	13.5 (10.2, 17.9)	15.1 (11.4, 19.6)	17.0 (13.3, 21.2)	20.5 (16.6, 25.1)	<0.001
Whole grain (g/d)[4]	3.3 (2.3, 4.8)	3.8 (2.7, 5.4)	3.9 (2.8, 5.5)	4.1 (2.9, 5.7)	4.8 (3.5, 6.5)	<0.001
Alcohol, current drinkers [*n* (%)]	10,443 (64.3)	10,423 (68.4)	15,806 (71.9)	11,810 (72.6)	14,711 (72.5)	<0.001
Alcohol (servings/d)[4]	0.12 (0.03, 0.51)	0.15 (0.06, 0.65)	0.20 (0.06, 0.75)	0.20 (0.06, 0.75)	0.20 (0.06, 0.75)	<0.001
Multivitamin use for >5 y [*n* (%)]	2860 (17.6)	3096 (20.3)	5085 (23.1)	4178 (25.7)	5604 (27.6)	<0.001

[1] Quintile 1 represents the least healthy quintile, whereas quintile 5 represents the healthiest quintile. GED, General Education Development; METs, metabolic equivalents.
[2] Values derived from a linear (continuous variables) or logistic (categorical variable) regression model with the variable of interest as a function of DMI quintiles.
[3] Values are medians; interquartile ranges in parentheses.
[4] Values are means; 95% CIs in parentheses.
[5] Data available only from blood subsample (*n* = 1014).
[6] Testing done on dichotomous variable of current smoking vs never/past smoking.
[7] Testing done on dichotomous variable of college graduate vs nongraduate.

TABLE 4
Baseline characteristics of the Women's Health Initiative (WHI) Observational Study cohort according to Alternate Healthy Eating Index (AHEI) quintiles[1]

	Quintiles					
	1: <34.5 (*n* = 16,975)	2: 34.5–42.4 (*n* = 17,152)	3: 42.5–49.4 (*n* = 18,032)	4: 49.5–57.4 (*n* = 19,200)	5: ≥57.5 (*n* = 18,498)	*P* for trend[2]
Median AHEI score[3]	28.5 (24.5, 31.5)	38.5 (36.5, 40.5)	45.5 (43.5, 47.5)	52.5 (50.5, 54.5)	62.5 (59.5, 66.5)	<0.001
Age (y)[4]	63.0 (57.0, 69.0)	64.0 (57.0, 69.0)	64.0 (58.0, 69.0)	64.0 (58.0, 69.0)	64.0 (58.0, 70.0)	<0.001
African American race [*n* (%)]	2197 (12.9)	1461 (8.5)	1230 (6.8)	1086 (5.7)	778 (4.2)	<0.001
Diabetes [*n* (%)]	991 (5.8)	851 (5.0)	744 (4.1)	655 (3.4)	382 (2.1)	<0.001
Coronary artery disease [*n* (%)]	658 (3.9)	587 (3.4)	597 (3.3)	588 (3.1)	573 (3.1)	<0.001
BMI (kg/m^2)[4]	27.8 (24.3, 32.2)	26.8 (23.8, 31.1)	26.3 (23.4, 30.2)	25.6 (23.0, 29.1)	24.6 (22.3, 27.7)	<0.001
HDL cholesterol (mg/dL)[5]	57.0 (48.0, 71.0)	60.5 (50.0, 72.0)	59.0 (50.0, 72.0)	62.0 (52.0, 76.0)	66.0 (56.0, 77.0)	<0.001
LDL cholesterol (mg/dL)[5]	126.0 (103.0, 151.0)	123.0 (102.0, 147.0)	126.5 (103.0, 144.0)	121.0 (96.0, 143.0)	120.0 (101.5, 148.0)	0.279
Triglycerides (mg/dL)[5]	132.0 (95.0, 187.5)	133.0 (97.0, 182.0)	129.5 (99.0, 188.0)	131.0 (97.0, 181.0)	120.0 (94.0, 150.0)	0.004
Systolic blood pressure (mm Hg)[4]	127.0 (116.0, 139.0)	126.0 (115.0, 139.0)	125.0 (114.0, 138.0)	125.0 (113.0, 137.0)	123.0 (112.0, 136.0)	<0.001
Smoking status [*n* (%)][6]						<0.001
Never	8644 (50.9)	8895 (51.9)	9165 (50.8)	9595 (50.0)	8705 (47.1)	
Past	6140 (36.2)	6736 (39.3)	7672 (42.5)	8644 (45.0)	9049 (48.9)	
Current	1975 (11.6)	1269 (7.4)	975 (5.4)	748 (3.9)	492 (2.7)	
Physical activity (METs/wk)[4]	3.8 (0.0, 11.7)	7.5 (1.9, 16.0)	9.8 (3.5, 19.0)	12.5 (5.0, 22.5)	16.7 (8.3, 27.3)	<0.001
Education [*n* (%)][7]						<0.001
≤ High school diploma/GED	6010 (35.4)	4359 (25.4)	3562 (19.8)	2822 (14.5)	1881 (10.2)	
Some school after high school	6739 (39.7)	6679 (38.9)	6813 (37.8)	6624 (34.5)	5629 (30.4)	
College graduate	4087 (24.1)	5973 (34.8)	7526 (41.7)	9605 (50.0)	10,830 (58.5)	
Energy intake (kcal/d)[4]	1240.0 (940.1, 1637.3)	1434.8 (1099.0, 1865.0)	1518.7 (1182.0, 1935.7)	1561.5 (1242.1, 1944.0)	1580.6 (1291.8, 1940.4)	<0.001
Fat intake (% of energy)[4]	36.6 (30.9, 41.5)	32.7 (27.4, 38.4)	29.8 (25.1, 35.4)	27.3 (22.8, 32.2)	24.1 (19.7, 28.7)	<0.001
Saturated fat intake (% of energy)[4]	12.5 (10.5, 14.6)	11.0 (9.1, 13.0)	9.9 (8.2, 11.8)	8.8 (7.2, 10.6)	7.2 (5.8, 8.9)	<0.001
Polyunsaturated fat intake (% of energy)[4]	6.6 (5.4, 8.1)	6.4 (5.1, 7.9)	6.1 (4.9, 7.5)	5.8 (4.7, 7.2)	5.6 (4.5, 6.9)	<0.001
Monounsaturated fat intake (% of energy)[4]	13.9 (11.6, 16.0)	12.4 (10.2, 14.7)	11.2 (9.2, 13.5)	10.2 (8.3, 12.3)	9.0 (7.1, 10.9)	<0.001
trans Fat intake (% of energy)[4]	2.6 (2.0, 3.4)	2.2 (1.7, 2.9)	1.9 (1.5, 2.6)	1.6 (1.2, 2.1)	1.2 (0.9, 1.6)	<0.001
Cholesterol intake (% of energy)[4]	140.4 (112.2, 180.2)	127.0 (101.4, 160.4)	118.4 (94.6, 149.1)	109.9 (86.2, 138.5)	95.7 (72.7, 122.9)	<0.001
Glycemic load, available carbohydrates[4]	71.6 (54.0, 95.5)	85.9 (64.9, 113.0)	93.5 (72.7, 119.9)	99.1 (78.7, 124.2)	104.5 (83.6, 129.1)	<0.001
Glycemic index, available carbohydrates[4]	54.1 (51.4, 56.7)	53.1 (50.6, 55.4)	52.2 (50.0, 54.4)	51.5 (49.3, 53.6)	50.6 (48.5, 52.6)	<0.001
Fruit and vegetable intake (servings/d)[4]	2.1 (1.5, 2.7)	3.1 (2.4, 4.0)	4.1 (3.1, 5.1)	5.1 (4.0, 6.3)	6.3 (5.2, 7.7)	<0.001
Nuts and soy protein (servings/d)[4]	0.03 (0.00, 0.08)	0.07 (0.02, 0.14)	0.08 (0.03, 0.21)	0.11 (0.03, 0.28)	0.21 (0.08, 0.49)	<0.001
White:red meat[4]	0.55 (0.35, 0.90)	0.78 (0.49, 1.34)	1.01 (0.63, 1.78)	1.36 (0.85, 2.52)	2.39 (1.36, 5.08)	<0.001
Cereal fiber (g/d)[4]	9.6 (7.4, 12.0)	13.1 (10.4, 16.7)	15.6 (12.5, 19.7)	18.1 (14.8, 22.3)	21.3 (17.4, 26.0)	<0.001
Whole grain (g/d)[4]	3.1 (2.1, 4.4)	3.8 (2.7, 5.4)	4.2 (3.0, 5.7)	4.4 (3.2, 6.0)	4.6 (3.4, 6.3)	<0.001
Alcohol, current drinkers [*n* (%)]	9139 (53.8)	11,169 (65.1)	12,706 (70.5)	14,641 (76.3)	15,538 (84.0)	<0.001
Alcohol (servings/d)[4]	0.06 (0.0.00, 0.26)	0.12 (0.03, 0.50)	0.15 (0.06, 0.73)	0.2 (0.06, 0.78)	0.39 (0.12, 0.81)	<0.001
Multivitamin use for >5 y [*n* (%)]	1644 (9.7)	2778 (16.2)	3843 (21.3)	5127 (26.7)	7406 (40.0)	<0.001

[1] Quintile 1 represents the least healthy quintile, whereas quintile 5 represents the healthiest quintile. GED, General Education Development; METs, metabolic equivalents.
[2] Values derived from a linear (continuous variables) or logistic (categorical variable) regression model with the variable of interest as a function of AHEI quintiles.
[3] Values are medians; interquartile ranges in parentheses.
[4] Values are means; 95% CIs in parentheses.
[5] Data available only from blood subsample (*n* = 1014).
[6] Testing done on dichotomous variable of current smoking vs never/past smoking.
[7] Testing done on dichotomous variable of college graduate vs nongraduate.

and receiving medical treatment of HF on this admission (eg, diuretic, digitalis, vasodilator, and/or angiotensin-converting enzyme inhibitor); *2*) HF diagnosed by a physician and receiving medical treatment on admission plus current medical records documenting a history of an imaging procedure showing impaired systolic or diastolic left ventricular function; *3*) pulmonary edema/congestion by chest X-ray on admission; or *4*) on admission, dilated ventricle or poor left (or right-side) ventricular function (eg, wall motion abnormalities) by echocardiography, radionuclide ventriculogram/multigated acquisition, or other contrast ventriculography or evidence of left ventricular diastolic dysfunction (10).

Statistical analyses

Potential confounders of the association between AHEI and DMI categories and incident CVD are summarized in **Tables 3** and **4**. AHEI and DMI variables were categorized into quintiles. The association between AHEI and DMI scores and risk of incident clinical composite CVD was determined by using 2 Cox proportional hazards models with 95% CIs: age and race-adjusted (model 1) and multivariate-adjusted (model 2). Model 2 included model 1 and also adjusted for education, physical activity, total energy intake, and traditional CVD risk factors [smoking status, body mass index, self-report of diabetes medication use (oral medications or insulin), hypertensive medication use, and hypercholesterolemia medication use]. The association between AHEI and DMI scores and risk of incident HF in 2 Cox models was examined as described above. Model 2 for incident HF analyses controlled for the aforementioned traditional CVD risk factors and also for traditional HF risk factors (coronary artery disease status (defined as CABG/PTCA, MI at baseline, or stroke at baseline). We also examined independent associations between individual components of the DMI and AHEI and risk of CVD or HF. For these analyses, each component was divided into 2 parts, with the break point being at the level where a participant would score ≥80% of the points for that component (4 out of 5 or 8 out of 10). The only exception to this was the multivitamin component of the AHEI, which either gave a participant 7.5 or 0 points for multivitamin use. Multivitamin use was dichotomized into use or no use. Of the 30 component comparisons, we would expect 1–2 of them to be significant at the 0.05 level by chance alone. Tests of linear trend across increasing strata of AHEI or DMI categories were conducted by treating the categories as continuous variables and defining the median value of a particular stratum as its value. All analyses were person-time based in which women contributed follow-up time until an adjudicated CVD outcome, death, loss-to follow up, or end of the follow-up period. Incidence rates were calculated as the number of incident CVD and HF events divided by the total person time of observation (risk). Differences between categories were examined by using the log-rank test for trend with an α level = 0.05 defined as statistically significant. All analyses were performed in SAS for Windows version 9.1 (SAS Institute, Cary, NC).

RESULTS

Baseline characteristics

Women with higher DMI and AHEI scores were less likely to be African American, less likely to smoke or have diabetes or CAD, had a lower BMI, were better educated, and were more physically active (Tables 3 and 4). During a mean follow up of 10.0 y, there were a total of 6006 CVD events and 1836 HF events.

DMI and incident CVD and HF

The incidence of composite CVD in women in the highest DMI quintile was 68.3/10,000 person-years and was 102.9/

TABLE 5
Multivariate-adjusted hazard ratios of incident cardiovascular disease (CVD) and heart failure (HF) based on Dietary Modification Index (DMI) score quintiles[1]

	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	*P* for trend
DMI score, CVD	<14.0	14.0–16.9	17.0–20.9	21.0–23.9	≥24.0	
No. of participants	14,164	13,389	19,561	14,543	18,094	
Person-years	120,863	117,493	176,147	132,375	167,733	
No. of CVD events	1244	1164	1459	993	1146	
Model 1[2]	1.0	0.92 (0.85, 1.00)	0.79 (0.73, 0.85)	0.73 (0.67, 0.79)	0.68 (0.63, 0.74)	<0.001
Model 2[3]	1.0	1.00 (0.92, 1.08)	0.90 (0.84, 0.98)	0.88 (0.80, 0.96)	0.88 (0.80, 0.95)	<0.001
DMI score, HF	<14.0	14.0–16.9	17.0–20.9	21.0–23.9	≥24.0	
No. of participants	14,846	13,975	20,360	15,121	18,880	
Person-years	129,133	125,142	186,628	140,155	177,759	
No. of HF events	419	370	440	274	333	
Model 1[2]	1.0	0.88 (0.76, 1.01)	0.72 (0.63, 0.83)	0.61 (0.53, 0.72)	0.61 (0.53, 0.71)	<0.001
Model 2[4]	1.0	1.02 (0.88, 1.17)	0.91 (0.80, 1.05)	0.85 (0.72, 0.99)	0.91 (0.78, 1.06)	0.045

[1] Quintile 1 represents the least healthy quintile, whereas quintile 5 represents the healthiest quintile. Associations between DMI and CVD or HF were determined by using Cox proportional hazard modeling; 95% CIs in parentheses. Models 1 and 2 were limited to participants with no missing covariate data, including both the DMI and AHEI indexes. Participants were also required to be free of the outcome of interest at baseline. Total number of participants: 79,751 for CVD and 83,182 for HF.

[2] Adjusted for age and race.

[3] CVD analysis: adjusted for model 1 plus education [≤ high school/GED (General Education Development), some college, or college graduate], physical activity, log(daily energy intake), BMI, smoking (never, past, or current), diabetes medications (self-report of taking pills or receiving insulin shots), taking pills for hypertension ever, and ever taking pills for cholesterol.

[4] HF analysis: adjusted for model 2 plus baseline coronary artery bypass graft, percutaneous transluminal coronary angioplasty, stroke, and myocardial infarction.

10,000 person-years in women in the lowest DMI quintile. The incidence of HF in women in the highest DMI quintile was 18.7 per 10,000 person-years compared with 32.4 per 10,000 person-years in women in the lowest DMI quintile. In model 1 (adjusted for age and race-ethnicity), women in the highest quintile of DMI score (DMI score $\geq$ 24) had a hazard ratio (HR) of 0.68 (95% CI: 0.63, 0.74) for incident CVD and 0.61 (95% CI: 0.53, 0.71) for incident HF (**Table 5**). The HR was 0.88 (95% CI: 0.80, 0.95) for incident CVD and 0.91 for incident HF (95% CI: 0.78, 1.06) in model 2. In individual DMI component analyses, energy from total fat, *trans* fat, cholesterol, and fruit and vegetable intakes were each associated with lower CVD risk (**Table 6**). In contrast, only cholesterol was associated with lower HF risk (Table 6).

TABLE 6
Multivariate-adjusted hazard ratios (HRs) of incident cardiovascular disease (CVD) and heart failure (HF) based on Dietary Modification Index (DMI) construct components[1]

	n	Events	HR (95% CI)	*P* value
DMI score, CVD				
Energy from fat				
>26.15%	52,886	4263	1.00 (reference)	
≤26.15%	26,866	1743	0.91 (0.86, 0.97)	0.002
Energy from saturated fat				
>8.78%	48,751	3893	1.00 (reference)	
≤8.78%	31,001	2113	0.96 (0.91, 1.01)	0.137
Energy from *trans* fat				
>1.49%	52,837	4315	1.00 (reference)	
≤1.49%	26,915	1691	0.90 (0.85, 0.95)	<0.001
Cholesterol				
>232.14 mg	23,570	1959	1.00 (reference)	
≤232.14 mg	56,182	4048	0.89 (0.83, 0.95)	<0.001
Fruit and vegetables				
<4.01 servings	38,805	3008	1.00 (reference)	
≥4.01 servings	40,947	2998	0.92 (0.87, 0.97)	0.003
Grains				
>4.52 servings	46,761	3632	1.00 (reference)	
≤4.52 servings	32,991	2374	1.02 (0.95, 1.08)	0.649
DMI score, HF				
Energy from fat				
>26.15%	55,116	1323	1.00 (reference)	
≤26.15%	28,067	513	0.97 (0.87, 1.07)	0.508
Energy from saturated fat				
>8.78%	50,757	1219	1.00 (reference)	
≤8.78%	32,426	617	0.99 (0.89, 1.10)	0.820
Energy from *trans* fat				
>1.49%	55,158	1350	1.00 (reference)	
≤1.49%	28,025	486	0.92 (0.82, 1.02)	0.120
Cholesterol				
>232.14 mg	24,561	662	1.00 (reference)	
≤232.14 mg	58,622	1174	0.82 (0.73, 0.92)	<0.001
Fruit and vegetables				
<4.01 servings	40,572	914	1.00 (reference)	
≥4.01 servings	42,611	922	0.99 (0.90, 1.09)	0.820
Grains				
>4.52 servings	48,892	1124	1.00 (reference)	
≤4.52 servings	34,291	712	0.96 (0.85, 1.07)	0.449

[1] The above models were adjusted for age, race, education [≤ high school/GED (General Education Development), some college, or college graduate], physical activity, log(daily energy intake), BMI, smoking (never, past, or current), diabetes medications (self-report of taking pills or receiving insulin shots), taking pills for hypertension ever, and ever taking pills for cholesterol.

AHEI and incident CVD and HF

The incidence of CVD in women in the highest AHEI quintile was 65.2/10,000 person-years and was 102.0/10,000 person-years in women in the lowest AHEI quintile. The incidence of HF in women in the highest AHEI quintile was 17.1/10,000 person-years and was 34.0/10,000 person-years in women in the lowest AHEI quintile. In model 1 (adjusted for age and race-ethnicity), women in the highest quintile of AHEI score (AHEI score $\geq$57.5) had an HR of 0.60 (95% CI: 0.55, 0.65) for incident CVD and of 0.48 (95% CI: 0.42, 0.56) for incident HF (**Table 7**). The HR was 0.77 (95% CI: 0.70, 0.84) for incident CVD and 0.70 (95% CI: 0.59, 0.82) for incident HF in model 2. In individual AHEI component analyses, fruit, white:red meat, *trans* fat, multivitamin use, and alcohol consumption were each associated with a lower CVD risk (**Table 8**). Only fiber and alcohol consumption were associated with lower HF risk (Table 8).

DISCUSSION

In multivariate-adjusted models, higher scores of both the AHEI and DMI, generated from dietary data collected in participants randomly assigned to the DMI, were associated with lower risks of incident CVD (generally) and incident HF (specifically) in women enrolled in the WHI-OS. Adherence to a heart-healthy diet represents one aspect of a lifestyle approach to prevent CVD and HF. This study examined 2 indexes of dietary quality: 1 novel method that expanded on the WHI-DM trial to include saturated and *trans* fat intakes and 1 existing method, the AHEI, that further incorporates other dietary factors reportedly associated with reduced CVD risk (including unsaturated fatty acids, nut and soy protein intakes, white:red meat, alcohol intake, and the ratio of polyunsaturated to saturated fats) and the risk of incident CVD, generally, and HF, specifically. This study offers unique comparisons not previously possible in other studies. By generating a diet index expanding on the low-fat dietary pattern tested in the WHI-DM, it is possible to further examine its relation to CVD and HF in a large population of postmenopausal women not engaged in the intervention but assessed by using the same baseline FFQ. These results further document the strong relation between diet quality and risk of incident HF in a population of postmenopausal women who are at increased risk of CVD.

Other studies have reported benefits of specific food groups, as part of an overall healthy dietary pattern, that are associated with a reduced risk of CVD. Both replacing red meat with chicken and fish and increasing whole grain, nut, and fruit and vegetable intakes reduced the risk of CVD in several studies (3, 11–13). Previously, researchers reported that a "prudent" dietary pattern (with higher intakes of fruit, vegetables, legumes, whole grains, poultry, and fish) lowers CVD risk, whereas a "Western" dietary pattern (with higher intakes of red and processed meats, sweets and desserts, potatoes, French fries, and refined grains) increases the risk of CVD in men and women (14, 15). The "prudent" diet also lowers the risk of diabetes mellitus and stroke (16, 17). Similar findings have been documented in clinical trials. The Lyon (Mediterranean) diet is high in α-linolenic acid and has been shown to be associated with a 70% decreased CVD

TABLE 7
Multivariate-adjusted hazard ratios of incident cardiovascular disease (CVD) and heart failure (HF) based on Alternate Healthy Eating Index (AHEI) score quintile[1]

	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	*P* for trend
AHEI score, CVD	<34.5	34.5–42.4	42.5–49.4	49.5–57.4	≥57.5	
No. of participants	14,699	15,068	16,057	17,267	16,660	
Person-years	126,150	133,224	143,991	157,472	153,775	
No. of CVD events	1287	1250	1274	1193	1002	
Model 1[2]	1.0	0.88 (0.82, 0.95)	0.82 (0.76, 0.89)	0.70 (0.64, 0.75)	0.60 (0.55, 0.65)	<0.001
Model 2[3]	1.0	0.94 (0.86, 1.01)	0.91 (0.84, 0.99)	0.82 (0.75, 0.89)	0.77 (0.70, 0.84)	<0.001
AHEI score, HF	<34.5	34.5–42.4	42.5–49.4	49.5–57.4	≥57.5	
No. of participants	15,493	15,761	16,731	17,907	17,290	
Person-years	135,376	142,080	153,060	166,242	162,058	
No. of HF events	460	399	368	332	277	
Model 1[2]	1.0	0.80 (0.70, 0.91)	0.68 (0.59, 0.78)	0.56 (0.49, 0.65)	0.48 (0.42, 0.56)	<0.001
Model 2[4]	1.0	0.86 (0.75, 0.99)	0.79 (0.69, 0.91)	0.72 (0.62, 0.84)	0.70 (0.59, 0.82)	<0.001

[1] Quintile 1 represents the least healthy quintile, whereas quintile 5 represents the healthiest quintile. Associations between AHEI and CVD or HF were determined by using Cox proportional hazard modeling; 95% CIs in parentheses. Models 1 and 2 were limited to participants with no missing covariate data, including both the Dietary Modification Index (DMI) and AHEI. Participants were also required to be free of the outcome of interest at baseline. Total number of participants: 79,751 for CVD and 83,182 for HF.

[2] Adjusted for age and race.

[3] CVD analysis: adjusted for model 1 plus education [≤ high school/GED (General Education Development), some college, or college graduate], physical activity, log(daily energy intake), BMI, smoking (never, past, or current), diabetes medications (self-report of taking pills or receiving insulin shots), taking pills for hypertension ever, and ever taking pills for cholesterol.

[4] HF analysis: adjusted for model 2 plus baseline coronary artery bypass graft, percutaneous transluminal coronary angioplasty, stroke, and myocardial infarction.

mortality (18, 19). Similarly, the DASH diet, which is rich in fruit, vegetables, and low-fat dairy products and low in saturated and total fat, lowers blood pressure and the risk of incident hypertension (20). Until now, few studies (11–15) have examined the effect of dietary quality in predicting CVD and even less is known regarding diet and the risk of HF in postmenopausal women.

The WHI-DM randomized controlled trial was designed to test the hypothesis that a low-fat dietary pattern (20% of total energy from fat) with increased intakes of vegetables, fruit, and grains reduces the risk of breast cancer, colorectal cancers, and, secondarily, CHD in postmenopausal women between the ages of 50 and 79 y (2). Results conveyed important messages regarding the need for greater specificity in dietary interventions, including qualitative changes in fatty acids, when targeting prevention of CVD. No significant differences in CHD or stroke were reported between the WHI-DM control and intervention groups; however, in subgroup analyses, trends toward greater CHD risk reduction were observed in participants with lower self-reported intakes of saturated fat or *trans* fat or a greater number of servings of vegetables and fruit despite the WHI-DM Trial not being designed uniquely to address heart disease risk (2).

The current study measured whether a diet index that expanded beyond the predominant total fat goals of the WHI-DM trial and beyond CHD risk and stroke reduced the risk of CVD and further assessed whether a diet with lower intakes of saturated fat, *trans* fat, and dietary cholesterol and higher intakes of fruit and vegetables and grains is associated with incident CVD and HF. In this study, participants in the highest quintile of the DMI score had a modest, yet significant, 12% reduction in risk of incident CVD. Although the risk of incident HF was not significantly lowered in women in the highest DMI quintile, the trend across quintiles suggests that higher DMI scores are associated with a lower HF risk.

Because other components of the diet also contribute to CVD risk (3, 4), we further incorporated the AHEI to measure dietary components not assessed in the DMI score. This included nut and soy protein intake, ratio of white to red meat, alcohol intake, and the ratio of polyunsaturated to saturated fats (6, 7). The stronger relations obtained with this index indicate that components in the AHEI not included in the DMI are important predictors of CVD and HF risk. Scores in the highest quintile of the AHEI were associated with a 23% lower risk of incident CVD and a 30% lower risk of incident HF. These findings confirm previous observations by McCullough et al reporting that the highest quintile of AHEI was linked with a 28% lower risk of CVD in the Nurses' Health Study (6, 7). These results also extend previous AHEI analyses as we report that a higher AHEI score was associated with a significantly lower risk of incident HF. Diet may potentially lower the risk of incident HF by lowering systolic blood pressure as well as lowering the risk of interim MI and/or hypertension. Taken together, these data suggest that diet quality, or nutrient density, as well as dietary total and saturated fat are important risk predictors for incident HF.

These findings are not without limitations. The FFQ provides an estimated intake of foods that are grouped together specifically for the WHI and may not lend themselves to nutrient quantification within all of the food groupings used in the DMI and AHEI. Also, the FFQ is not effective at assessing nutrient density and individual energy intake. Dietary self-report may be systematically biased toward the underreporting of energy, particularly by overweight and obese women (21). We cannot discount inaccurate adjudication of HF as a potential source of error. The subgroup analyses using serum LDL cholesterol, HDL cholesterol, and triglycerides only considered 1% of the WHI-OS cohort; this small sample size in this subgroup may have reduced our ability to detect a statistically significant attenuation of the diet-HF

TABLE 8
Multivariate-adjusted hazard ratios (HRs) of incident cardiovascular disease (CVD) and heart failure (HF) based on Alternate Healthy Eating Index (AHEI) construct components[1]

	n	Events	HR (95% CI)	*P* value
AHEI score, CVD				
Fruit				
<2.57 servings	56,182	4312	1.00 (reference)	
≥2.57 servings	23,570	1694	0.91 (0.85, 0.96)	<0.001
Vegetables				
<3.01 servings	59,251	4501	1.00 (reference)	
≥3.01 servings	20,501	1505	0.96 (0.91, 1.02)	0.227
Soy/nuts				
<0.28 servings	60,156	4529	1.00 (reference)	
≥0.28 servings	19,596	1477	1.00 (0.94, 1.06)	0.961
White:red meat				
<1.71	54,029	4346	1.00 (reference)	
≥1.71	25,723	1660	0.92 (0.87, 0.98)	0.005
Fiber				
<13.14 g	27,862	2198	1.00 (reference)	
≥13.14 g	51,890	3808	0.94 (0.89, 1.00)	0.067
Energy from *trans* fat				
>1.25 %	62,395	4966	1.00 (reference)	
≤1.25 %	17,357	1040	0.88 (0.82, 0.95)	<0.001
Polyunsaturated:saturated fat				
<0.77	57,526	4337	1.00 (reference)	
≥0.77	22,226	1669	1.00 (0.95, 1.06)	0.950
Multivitamin use				
No	61,011	4636	1.00 (reference)	
Yes	18,741	1370	0.94 (0.88, 1.00)	0.040
Alcohol				
<0.23/>1.59 servings	58,402	4676	1.00 (reference)	
0.23–1.59 servings	21,350	1330	0.86 (0.80, 0.91)	<0.001
AHEI score, HF				
Fruit				
<2.57 servings	58,582	1299	1.00 (reference)	
≥2.57 servings	24,601	537	0.97 (0.88, 1.08)	0.604
Vegetables				
<3.01 servings	61,897	1373	1.00 (reference)	
≥3.01 servings	21,286	463	1.01 (0.91, 1.13)	0.809
Soy/nuts				
<0.28 servings	62,810	1412	1.00 (reference)	
≥0.28 servings	20,373	424	0.90 (0.80, 1.01)	0.065
White:red meat				
<1.71	56,358	1367	1.00 (reference)	
≥1.71	26,825	469	0.90 (0.81, 1.00)	0.051
Fiber				
<13.14 g	29,187	704	1.00 (reference)	
≥13.14 g	53,996	1132	0.88 (0.79, 0.99)	0.026
Energy from *trans* fat				
>1.25 %	65,082	1536	1.00 (reference)	
≤1.25 %	18,101	300	0.92 (0.81, 1.05)	0.206
Polyunsaturated:saturated fat				
<0.77	59,848	1340	1.00 (reference)	
≥0.77	23,335	496	0.97 (0.87, 1.08)	0.538
Multivitamin use				
No	63,734	1445	1.00 (reference)	
Yes	19,449	391	0.90 (0.80, 1.01)	0.068
Alcohol				
<0.23/>1.59 servings	61,167	1490	1.00 (reference)	
0.23–1.59 servings	22,016	346	0.81 (0.72, 0.92)	<0.001

[1] The above models were adjusted for age, race, education [≤ high school/GED (General Education Development), some college, or college graduate], physical activity, log(daily energy intake), BMI, smoking (never, past, or current), diabetes medications (self-report of taking pills or receiving insulin shots), taking pills for hypertension ever, and ever taking pills for cholesterol.

association. Finally, whereas high DMI and AHEI scores were associated with a lower risk of incident CVD and HF, it is possible that higher diet quality scores are merely surrogate markers of an overall healthy lifestyle. In the future, randomized clinical trials probing diet and risk of incident CVD or HF are needed to unequivocally clarify the link between diet and CVD in diverse populations.

This study had several strengths, including the large sample size and ethnic diversity of the WHI-OS, which provided a representative sample for the analysis of food and nutrient exposures and risk of CVD and HF in an understudied subgroup. Second, the prospective design of our study reduced the likelihood of recall bias compared with case-control studies. Also, the focused and attentive follow-up and both peripheral and central adjudication of CVD events reduced the chances of outcome misclassification. Including 2 different indexes to study the association between diet quality and incident CVD and HF in postmenopausal women provided additional strengths not previously reported in this subgroup. To our knowledge, no previous study of the comparison between dietary patterns and nutrient density and risk of incident HF in postmenopausal women has been reported. This study was the first to apply 2 different indexes of diet quality and to document findings predictive of HF, particularly with the AHEI. Future studies are needed to further elucidate specific dietary factors and patterns that are associated with incident HF in diverse populations. Overall, this study reported that adherence to current nutrient guidelines, as indexed by the DMI, are associated with lower total CVD risk and that additional dietary factors (eg, ratio of white to red meat, multivitamin intake, and modest alcohol consumption), as indexed by the AHEI, are further associated with a lower risk of CVD and HF.

The authors' responsibilities were as follows—RJB: designed the research study (project conception, developed the overall research and analytic plan, and was primarily responsible for study oversight), wrote the manuscript, and had primary responsibility for the final content; PG: helped design the research study and wrote the manuscript; MA: wrote the manuscript; LM: helped write the manuscript; JMS: helped write the manuscript; LT: helped design the research study, helped develop the WHI FFQ, and helped write the manuscript; JL: analyzed the data and helped write the manuscript; BVH: helped write the manuscript; DL-J: helped design the study and write the manuscript; and LVH: helped design the research study, helped develop the WHI food-frequency questionnaire, guided development of the DMI, and helped write the manuscript. None of the authors had a conflict of interest to report related to this manuscript.

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