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## Dietary Patterns and Fractures in Postmenopausal Women: Results From the Women's Health Initiative

Bernhard Haring  
*University of Wurzburg*

*Et al.*

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## Original Investigation

# Dietary Patterns and Fractures in Postmenopausal Women

## Results From the Women's Health Initiative

Bernhard Haring, MD, MPH; Carolyn J. Crandall, MD, MS; Chunyuan Wu, MS; Erin S. LeBlanc, MD, MPH; James M. Shikany, DrPH; Laura Carbone, MD; Tonya Orchard, PhD, RD; Fridtjof Thomas, PhD; Jean Wactawaski-Wende, PhD; Wenjun Li, PhD; Jane A. Cauley, DrPH; Sylvia Wassertheil-Smoller, PhD

**IMPORTANCE** Considerable efforts have been undertaken to relate single nutrients to bone health. To this point, results are inconsistent. Suboptimal single nutrient intake does not occur in isolation but rather reflects a poor diet quality.

**OBJECTIVE** To assess the association between adherence to a diet quality index constructed on the basis of dietary recommendations or existing healthy dietary patterns and fractures in postmenopausal women.

**DESIGN, SETTING, AND PARTICIPANTS** Post hoc analysis was conducted of longitudinal data from 40 clinical centers throughout the United States included in the Women's Health Initiative (WHI) observational study. Participants in the prospective cohort included 93 676 women who were eligible for the WHI if they were aged 50 to 79 years. Recruitment was conducted from October 1, 1993, to December 31, 1998, with the study ending August 29, 2014. The WHI food frequency questionnaire was used to derive nutrient and food intake at baseline. Diet quality and adherence were assessed by scores on the alternate Mediterranean Diet (aMED), a 9-category measure of adherence to a Mediterranean dietary pattern; the Healthy Eating Index 2010 (HEI-2010), a 100-point measure of 12 food components; the 11-item Alternate Healthy Eating Index 2010 (AHEI-2010); or the 8-component Dietary Approaches to Stop Hypertension (DASH) diet score.

**MAIN OUTCOMES AND MEASURES** Outcome measures included incident total and hip fractures. Hazard ratios (HRs) by quintiles of dietary index scores were estimated using Cox proportional hazards regression analyses.

**RESULTS** Of the 93 676 participants, 90 014 were included in the analysis (mean [SD] age, 63.6 [7.4] years). During a median follow-up time of 15.9 years, there were 2121 cases of hip fractures and 28 718 cases of total fractures. Women scoring in the highest quintile (Q5) of the aMED index had a lower risk for hip fractures (HR, 0.80; 95% CI, 0.66-0.97), with an absolute risk reduction of 0.29% and a number needed to treat of 342 (95% CI, 249-502). No association between the aMED score and total fractures was observed (Q5 HR, 1.01; 95% CI, 0.95-1.07). Higher HEI-2010 or DASH scores tended to be inversely related to hip fracture risk, but the results were nonsignificant (Q5 HR, 0.87; 95% CI, 0.75-1.02; and Q5 HR, 0.89; 95% CI, 0.75-1.06, respectively). The AHEI-2010 score was associated with neither hip nor total fractures.

**CONCLUSIONS AND RELEVANCE** Higher adherence to a Mediterranean diet is associated with a lower risk for hip fractures. These results support that a healthy dietary pattern may play a role in maintaining bone health in postmenopausal women.

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**Author Affiliations:** Author affiliations are listed at the end of this article.

**Corresponding Author:** Bernhard Haring, MD, MPH, Department of Internal Medicine I, Comprehensive Heart Failure Center, University of Würzburg, Würzburg, Bavaria 97080, Germany (Haring\_b@ukw.de).

Osteoporotic fractures constitute a major burden for health care systems in aging societies. Although considerable research<sup>1-6</sup> has examined whether intake of nutrients involved in bone metabolism, such as protein, calcium, or unsaturated fat, can prevent fracture events, the findings are not consistent. However, suboptimal single nutrient intake does not occur in isolation but rather reflects a poor-quality diet.<sup>7</sup>

Several descriptive epidemiologic studies<sup>8-10</sup> have shown that the incidence of osteoporosis and osteoporosis-related fractures varies across nations, with a tendency of lower rates in Mediterranean compared with northern European countries. These differences have been attributed to life-style factors, including specific dietary patterns. The traditional Mediterranean-style diet emphasizes the consumption of dietary components, such as plant foods, fish, nuts, and monounsaturated fat, which have been shown<sup>11,12</sup> to impart beneficial effects on bone health. Adherence to a Mediterranean diet was previously operationalized by a dietary scoring system and modified to be applied to non-Mediterranean populations.<sup>13</sup> This Mediterranean diet score has been associated with a decreased hip fracture risk, particularly among men,<sup>14</sup> but overall evidence is inconclusive.<sup>15</sup> Moreover, data are sparse as to whether other dietary scoring systems that characterize a high-quality diet preserve bone health.<sup>16</sup> Comprehensive analyses investigating the association between various commonly recommended dietary quality indexes and fracture risk in the United States are warranted.

The primary aim of this study was to examine the association between adherence to a diet quality index constructed on the basis of dietary recommendations or existing healthy dietary patterns and bone outcomes (hip or total fractures) in a large population of postmenopausal women. Specifically, diet quality was assessed using the alternate Mediterranean Diet (aMED) score,<sup>13,17</sup> the Healthy Eating Index 2010 (HEI-2010),<sup>18</sup> the Alternate Healthy Eating Index 2010 (AHEI-2010),<sup>19,20</sup> or the Dietary Approaches to Stop Hypertension (DASH) score.<sup>21</sup> As a secondary aim, the associations between diet quality, bone mineral density (BMD), and lean body mass measurements were examined. Given prior epidemiologic data<sup>14,16</sup> and the composition of the aMED index, we hypothesized that high aMED scoring would be associated with a lower fracture risk.

## Methods

### Study Population

The study population consisted of 93 676 women enrolled in the Women's Health Initiative observational study (WHI-OS) (clinicaltrials.gov, NCT00000611).<sup>22-25</sup> The WHI-OS<sup>24</sup> examined the indicators and natural history of important causes of morbidity and mortality in postmenopausal women. Women were recruited from October 1, 1993, to December 31, 1998, at 40 clinical centers in the United States and were eligible for the WHI-OS if they were aged 50 to 79 years, were generally healthy, and were postmenopausal at the time of enrollment. Institutional review boards at participating institutions ap-

### Key Points

**Question** Does diet quality affect bone health in postmenopausal women?

**Findings** In the Women's Health Initiative observational study, of 90 014 postmenopausal women, higher diet quality based on a Mediterranean diet that emphasizes the consumption of fruits, vegetables, fish, nuts, legumes, whole grains, and intake of monounsaturated fat, as well as avoidance of red and processed meats, was found to be associated with a lower risk for hip fractures.

**Meaning** A healthy dietary pattern may play a role in maintaining bone health in postmenopausal women.

proved all protocols, and all participants provided written informed consent.

For the present analysis, data from women with extreme energy intake (ie, <600 kcal/d or >5000 kcal/d) were excluded because these reported intakes were judged to be implausible (n = 3662).<sup>26</sup> Our final study population included 90 014 women who were monitored through August 29, 2014, with a median follow-up time of 15.9 years (Figure).

### Food Frequency Questionnaires

Nutrient and food intake was derived from self-report through WHI food frequency questionnaires (WHI-FFQs) at baseline.<sup>26</sup> The WHI-FFQ is based on the Block FFQ.<sup>26,27</sup> The main differences between the measures are the addition of questions to make the WHI-FFQ more sensitive to fat intake (including low-fat food preparation methods and reduced-fat foods) and fruit and vegetable consumption.<sup>26</sup> The WHI-FFQ nutrient database was derived from the University of Minnesota Nutrition Coordinating Center food and nutrient database.<sup>28</sup> The WHI-FFQ has demonstrated good validity as a measurement of dietary intake compared with 24-hour dietary recalls and food records.<sup>26</sup> The WHI-FFQ has also been validated against biomarkers of nutrients important to bone health, including protein and polyunsaturated fatty acids.<sup>29,30</sup>

### Assessment of Dietary Patterns

Based on nutrient and food items intake, dietary indexes (aMED, HEI-2010, AHEI-2010, and DASH) were used to assess the extent of adherence to various dietary patterns.<sup>13,18,19,31-33</sup> Food items were transformed into standardized quantities with the help of the MyPyramid Equivalents Database.<sup>32,34</sup>

The aMED score was designed to assess adherence to a Mediterranean dietary pattern. Total aMED scoring ranges from 0 (nonadherence) to 9 (perfect adherence). It includes the following food items<sup>13,17,32,33</sup>: (1) fruits, (2) vegetables, (3) nuts, (4) legumes, (5) whole grains, (6) fish, (7) ratio of monounsaturated to saturated fat, (8) red and processed meats, and (9) alcohol. Participants whose intake was above the median for fruits, vegetables, nuts, legumes, whole grains, fish, or ratio of monounsaturated to saturated fat received 1 point for each category. Consumption of red and processed meat below the median was awarded 1 point, and alcohol intake between 5 and 15 g/d was awarded 1 point; otherwise, women received 0 points.

The HEI-2010 aligns with the US Dietary Guidelines for Americans of 2010, and scores range from 0 (nonadherence) to 100 (perfect adherence) points.<sup>18,32</sup> The HEI-2010 consists of 12 components as previously outlined: 6 components—total vegetables, total fruit, whole fruit, seafood proteins, plant proteins, and total protein foods—are worth 0 to 5 points each; 5 components—whole grains, low-fat dairy, fatty acids ratio ([polyunsaturated fatty acids plus monounsaturated fatty acids] to saturated fatty acids), refined grains, and sodium—are worth 0 to 10 points each; and 1 component—empty calories (energy from solid fats, added sugars, and any alcohol in excess of 13 g per 1000 kcal)—are worth 0 to 20 points. All food components except for the fatty acids ratio are scored on a density basis (per 1000 kcal or as a percentage of energy). Three components (sodium, refined grains, and empty calories) are reverse scored (ie, higher intakes receive lower scores).<sup>18</sup>

The AHEI-2010 was designed as an alternative to the HEI-2010, and scoring can range from 0 (nonadherence) to 110 (perfect adherence).<sup>19,20,31,32</sup> The AHEI-2010 includes 11 items, and each component intake is evaluated from 0 (worst) to 10 (best). The AHEI-2010 emphasizes vegetables, fruits, whole grains, nuts, legumes, vegetable proteins, long-chain  $\omega$ -3 polyunsaturated fatty acids, polyunsaturated fatty acids (excluding long-chain  $\omega$ -3 polyunsaturated fatty acids), moderate alcohol intake, and lower intakes of sugar-sweetened beverages and fruit juice, red and processed meats, and sodium as well as avoidance of *trans*-fat.

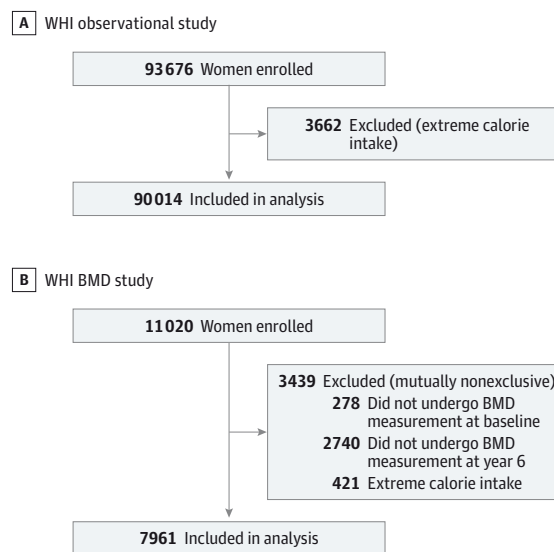
The DASH diet score considers intake of (1) fruits, (2) vegetables, (3) nuts and legumes, (4) low-fat dairy, (5) whole grains, (6) sodium, (7) sweetened beverages, and (8) red and processed meats.<sup>21,32,33</sup> The score is based on quintile rankings within the population. For fruits, vegetables, nuts and legumes, low-fat dairy, and whole grains, participants in the highest quintile receive a score of 5, those in the second-highest quintile receive a score of 4, and so on. For sodium, sweetened beverages, and red and processed meats, scoring is reversed (ie, women in the highest quintile receive a minimum score of 1, whereas participants in the lowest quintile receive a maximum score of 5). The score for each component is summed, and the overall score ranges from 8 (no adherence) to 40 (perfect adherence).

### Outcome Ascertainment

Primary outcome measures included incident hip and total fractures. In the WHI-OS, all fracture outcomes were self-reported except hip fractures, which were assigned a diagnosis by local trained physician adjudicators and centrally confirmed by a second medical record review.<sup>35,36</sup> Toe, finger, sternum, and clavicle fractures as total fracture events were excluded since these fractures are less likely related to osteoporosis.<sup>37,38</sup>

Bone mineral density at the femoral neck (hip) and total body as well as lean body mass were measured at baseline and after 6 years in a subset of WHI participants (WHI-BMD cohort [n = 11 020]) at 3 of the 40 clinical centers of the WHI (Pittsburgh, Pennsylvania; Birmingham, Alabama; and Phoenix and Tucson, Arizona) with dual-energy x-ray absorptiometry (Ho-

Figure. Study Inclusion Criteria



A, Women's Health Initiative (WHI) observational study; B, WHI bone mineral density (BMD) study.

logic QDR densitometer; Hologic Inc).<sup>39,40</sup> Of the 11 020 participants in the WHI-BMD cohort, 278 women did not undergo BMD measurements at baseline, whereas 2740 were not measured at the 6-year follow-up visit. A total of 421 women were excluded owing to extreme energy intake. The final sample size for the BMD analysis was 7961 participants (Figure). Exclusion criteria were not mutually exclusive.

### Covariate Assessment

Information on age, race/ethnicity, educational level, family income, personal history of fracture, history of falls, self-rated health, and smoking status was obtained by self-report questionnaires at baseline.<sup>22,24</sup> Physical function was assessed by a 36-item Short-Form Health Survey.<sup>41,42</sup> Current medication use was assessed by clinic interviewers.<sup>22,24</sup> History of cardiovascular disease was coded as positive if the participant reported a history of myocardial infarction, angina pectoris, atrial fibrillation, heart failure, peripheral vascular disease, coronary bypass surgery, angioplasty, or carotid endarterectomy. Women were classified as having diabetes mellitus on the basis of self-report of diabetes or self-report of diabetes treatment. For each participant, the number of self-reported chronic medical conditions (ie, stroke, any cancer, history of cardiovascular disease, arthritis, hypertension, diabetes, and emphysema) and the number of psychoactive medications (ie, anxiolytics, hypnotics, antidepressants, antipsychotics, and antiepileptic agents) was calculated.

### Statistical Analysis

To assess the associations of aMED, HEI-2010, AHEI-2010, and DASH with incident fractures, quintiles of each exposure variable of interest were formed based on the distribution of non-cases in the WHI-OS cohort. Hazard ratios (HRs) for the risk of hip and total fractures by quintiles of dietary pattern scores

Table 1. Baseline Characteristics by Lowest and Highest Quintiles (Qs) of Dietary Pattern Scoring in the WHI Health Observational Study

Characteristic	Dietary Pattern, No. (%) <sup>a</sup>							
	aMED		HEI-2010		AHEI-2010		DASH	
	Q1	Q5	Q1	Q5	Q1	Q5	Q1	Q5
Participants <sup>b</sup>	6545 (7.3)	20 819 (23.1)	17 584 (19.5)	18 409 (20.5)	16 517 (18.3)	21 047 (23.4)	13 365 (14.8)	20 499 (22.8)
Age, y								
50-59	2230 (34.1)	6381 (30.7)	6758 (38.4)	4534 (24.6)	5820 (35.2)	6391 (30.4)	5243 (39.2)	5693 (27.8)
60-69	2819 (43.1)	9355 (44.9)	7483 (42.6)	8319 (45.2)	7074 (42.8)	9411 (44.7)	5638 (42.2)	9105 (44.4)
70-79	1496 (22.9)	5083 (24.4)	3343 (19.0)	5556 (30.2)	3623 (21.9)	5245 (24.9)	2484 (18.6)	5701 (27.8)
Race/ethnicity								
White	5431 (83.0)	18 140 (87.1)	13 996 (79.6)	15 877 (86.3)	12 947 (78.4)	18 693 (88.8)	9793 (73.3)	18 255 (89.1)
African American	584 (8.9)	1145 (5.5)	1866 (10.6)	1242 (6.8)	2041 (12.4)	901 (4.3)	2019 (15.1)	886 (4.3)
Hispanic	307 (4.7)	410 (2.0)	1046 (6.0)	352 (1.9)	937 (5.7)	370 (1.8)	950 (7.1)	387 (1.9)
Other	223 (3.4)	1124 (5.4)	676 (3.8)	938 (5.1)	592 (3.6)	1083 (5.2)	603 (4.5)	971 (4.7)
BMI ≥30	2161 (33.4)	3752 (18.3)	5995 (34.5)	3178 (17.5)	6107 (37.4)	2971 (14.3)	5037 (38.2)	3232 (16.0)
Smoking, never	3199 (49.6)	10 492 (51.1)	7683 (4.4)	10 214 (56.2)	8670 (53.2)	9590 (46.2)	6203 (47.1)	10 835 (53.5)
Physical activity, ≥19 METs	922 (14.2)	7689 (37.3)	2889 (16.6)	6500 (35.7)	2120 (13.0)	8525 (40.9)	1825 (13.8)	7963 (39.3)
Self-reported health, excellent	807 (12.4)	4671 (22.6)	2443 (14.0)	3840 (21.0)	1771 (10.8)	5399 (25.8)	1504 (11.3)	4866 (23.9)
Diabetes mellitus, treated	280 (4.3)	647 (3.1)	652 (3.7)	759 (4.1)	889 (5.4)	526 (2.5)	659 (4.9)	707 (3.4)
Menopausal hormone therapy use, never	2969 (45.4)	7782 (37.4)	7855 (44.7)	7214 (39.2)	7548 (45.7)	7670 (36.5)	6262 (46.9)	7706 (37.6)
No. of psychoactive medications, <1 <sup>c</sup>	5571 (85.1)	18 582 (89.3)	15 016 (85.4)	16 405 (89.1)	13 937 (84.4)	18 885 (89.7)	11 485 (85.9)	18 201 (88.8)
No. of chronic medical conditions, <1 <sup>d</sup>	2731 (41.7)	10 162 (48.8)	7578 (43.1)	8397 (45.6)	6305 (38.2)	10 841 (51.5)	5248 (39.3)	10 184 (49.7)
History of fracture at age ≥55 y	824 (16.2)	2951 (17.7)	2096 (16.0)	2779 (18.2)	2038 (16.0)	3043 (18.2)	1510 (15.1)	2999 (18.0)
Physical function, SF-36 score >90	1868 (29.2)	9219 (45.0)	5459 (31.7)	7690 (42.6)	4406 (27.3)	10 046 (48.5)	3775 (28.9)	9108 (45.2)
Bisphosphonate use	127 (1.9)	592 (2.8)	303 (1.7)	619 (3.4)	284 (1.7)	665 (3.2)	216 (1.6)	656 (3.2)
Calcitonin use	22 (0.3)	91 (0.4)	56 (0.3)	87 (0.5)	50 (0.3)	91 (0.4)	34 (0.3)	97 (0.5)
Selective estrogen receptor modulator use	0	8 (0.04)	4 (0.02)	7 (0.04)	5 (0.03)	12 (0.06)	5 (0.04)	10 (0.05)
Alcohol intake, mean (SD), g/d	5 (12)	6 (10)	9 (17)	3 (6)	4 (12)	7 (9)	6 (13)	5 (9)
Total energy intake, mean (SD), kcal	1332 (507)	1804 (598)	1782 (742)	1428 (469)	1574 (628)	1567 (538)	1657 (653)	1590 (530)

Abbreviations: AHEI-2010, Alternate Healthy Eating Index 2010<sup>19,20</sup>; aMED, alternate Mediterranean Diet<sup>13,17</sup>; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); DASH, Dietary Approaches to Stop Hypertension<sup>21</sup>; HEI-2010, Healthy Eating Index 2010<sup>18</sup>; METs, metabolic equivalent of tasks; SF-36, 36-item Short-Form Health Survey<sup>41,42</sup>; WHI, Women's Health Initiative.

<sup>a</sup> Q1 represents the least healthy quintile; Q5, the healthiest quintile.

<sup>b</sup> Not all data were available on some characteristics.

<sup>c</sup> Medications included anxiolytics, hypnotics, antidepressants, antipsychotics, and antiepileptic agents.

<sup>d</sup> Conditions included treated diabetes mellitus, stroke, any cancer, history of cardiovascular disease, arthritis, hypertension, and emphysema.

were obtained using covariate-adjusted Cox proportional hazards regression models. Incident time to event was defined as the time from enrollment to the first occurrence of an incident hip fracture and a fracture at any anatomic site. Follow-up was censored at the date of the outcome event, end of follow-up, or date of death, whichever came first. Potential confounding was addressed by adjusting for linear age, race/ethnicity, body mass index, smoking, physical activity, self-reported health, treated diabetes mellitus, history of fracture when younger than 55, physical function score, number of chronic medical conditions, number of psychoactive medications, use of menopausal hormone therapy, and use of bisphosphonates, calcitonin, or selective-estrogen receptor modulators at baseline. The proportional hazards regression assumption was found to be valid for all analyses. With use of data from the WHI-BMD cohort, general linear regression mod-

els were applied to examine the associations of dietary scoring indexes with BMD and lean body mass at baseline and year 6 with multivariable adjustment as described above.

Statistical analyses were performed using SAS, version 9.3 (SAS Institute Inc). A 2-sided *t* test value of *P* < .05 was considered statistically significant.

## Results

Baseline characteristics of the study participants and BMD measurements by lowest and highest quintiles of the various dietary scores are reported in Table 1 and Table 2. Women scoring in the highest quintile were more likely to be older and white, to have a high physical function score, and to have less than 1 chronic medical condition; they were also more likely to be

Table 2. Baseline BMD and Body Composition Measurements by Lowest and Highest Quintiles (Qs) of Dietary Pattern Scoring in the WHI BMD Study

Characteristic	Dietary Pattern <sup>a</sup>							
	aMED		HEI-2010		AHEI-2010		DASH	
	Q1	Q5	Q1	Q5	Q1	Q5	Q1	Q5
Participants, No. (%)	1534 (19.3)	1840 (23.1)	1565 (19.7)	1653 (20.8)	1473 (18.5)	1747 (21.9)	1199 (15.1)	1801 (22.6)
BMD of the total hip, corrected, mean (SE), g/cm <sup>2b</sup>	0.85 (0)	0.86 (0)	0.85 (0)	0.87 (0)	0.85 (0)	0.86 (0)	0.85 (0)	0.86 (0)
Hip T score, No. (%)								
Normal BMD, T score $\geq -1.0$	909 (59.3)	1015 (55.2)	957 (61.2)	887 (53.7)	916 (62.2)	901 (51.6)	786 (65.6)	923 (51.2)
Low BMD, $-2.5 \leq T \text{ score} < -1.0$	567 (37.0)	739 (40.2)	552 (35.3)	665 (40.2)	510 (34.6)	750 (42.9)	381 (31.8)	770 (42.8)
Osteoporosis, T score $\leq -2.5$	58 (3.8)	86 (4.7)	56 (3.6)	101 (6.1)	47 (3.2)	96 (5.5)	32 (2.7)	108 (6.0)
Whole-body BMD, corrected, mean (SE), g/cm <sup>2b</sup>	1.01 (0)	1.03 (0)	1.01 (0)	1.03 (0)	1.00 (0)	1.03 (0)	1.01 (0)	1.03 (0)
Lean mass, mean (SE), kg	37.36 (0.10)	38.24 (0.09)	37.48 (0.10)	38.06 (0.10)	37.32 (0.11)	38.33 (0.10)	37.61 (0.12)	38.22 (0.10)
Lean mass, mean (SE), %	54.68 (0.12)	55.67 (0.11)	54.73 (0.12)	55.53 (0.12)	54.57 (0.13)	55.94 (0.12)	54.74 (0.14)	55.80 (0.12)

Abbreviations: AHEI-2010, Alternate Healthy Eating Index 2010<sup>19</sup>; aMED, alternate Mediterranean Diet<sup>13,17</sup>; BMD, bone mineral density; DASH, Dietary Approaches to Stop Hypertension<sup>21</sup>; HEI-2010, Healthy Eating Index 2010<sup>18</sup>; WHI, Women's Health Initiative.

<sup>a</sup> Q1 represents the least healthy quintile; Q5, the healthiest quintile.

<sup>b</sup> Adjusted for age, race/ethnicity, body mass index, and WHI clinical trial assignment.

physically active and to have a lower body mass index. Women in the highest quintile were additionally less likely to have never used menopausal hormone therapy and slightly more likely to have used bisphosphonates. Total body and hip BMD values were slightly higher in women in the highest quintiles.

During a median follow-up period of 15.9 years, WHI-OS documented 2121 cases of hip fractures and 28 718 cases of self-reported total fractures. The multivariate-adjusted HRs for incident hip fractures or total fractures by quintiles of dietary pattern scores are presented in Table 3. After controlling for confounding variables, women scoring in the highest quintile (Q5), reported as HR (95% CI), of aMED were at a lower risk for hip fractures (0.80 [0.66-0.97]), with an absolute risk reduction of 0.29% and a number needed to treat of 342 (95% CI, 249-502). No association between aMED and total fractures was observed (Q5 HR, 1.01 [0.95-1.07]). Higher HEI-2010 or DASH scoring tended to be inversely related to hip fracture risk (Q5 HR, 0.87 [0.75-1.02] and 0.89 [0.75-1.06], respectively), but the results were nonsignificant. No association between HEI-2010, DASH, and total fracture risk (Q5 HR, 0.98 [0.93-1.02] and 0.98 [0.94-1.03]), respectively, was found. Scores within the highest quintile of AHEI-2010 were not significantly associated with hip or total fractures (Q5 HR, 0.94 [0.80-1.09] and 1.01 [0.96-1.05], respectively). To account for the propensity to fall, the fall history was further included in our statistical modeling (eTable 1 in the Supplement); the main results did not change.

The BMD and lean body mass measurements at baseline and year 6 by quintiles of dietary pattern scoring are presented in eTable 2 and eTable 3, respectively, in the Supplement. No clinically significant differences in BMD loss and no clinically significant changes of lean body mass over time were found.

## Discussion

The primary aim of this study was to investigate the association between adherence to a diet quality index and fracture

risk in a large sample of postmenopausal women. Women who were highly adherent to a Mediterranean dietary pattern (aMED) that emphasizes the consumption of fruits, vegetables, fish, nuts, legumes, and whole grains; intake of mono-unsaturated fat; and avoidance of red and processed meats were found to have a lower risk for hip fracture, but the absolute risk reduction was small.

At this time, epidemiologic evidence<sup>8-10</sup> suggests that fracture rates vary geographically. Lifestyle differences, including diet quality, may be part of an explanation for regional and local discrepancies. Previous research<sup>16</sup> on diet quality scores based on case-control data in a Chinese population suggests that avoiding a low-quality diet is associated with a lower risk of hip fractures in elderly individuals and that the aMED score appears to be the best scoring system for consumers because of its simplicity. The aMED, HEI-2010, AHEI-2010, and DASH dietary measures have many similarities since all dietary patterns include vegetables, fruits, vegetable protein, and whole grains, but there are also distinctive differences.<sup>13,18,19,21</sup> Whereas the AHEI-2010 emphasizes low intake of red and processed meats and high intake of polyunsaturated fatty acids, the aMED promotes intake of monounsaturated fat, largely from olive oil, and fish intake. Similarly, the HEI-2010 includes an increased emphasis on seafood and plant proteins.<sup>18</sup> Both plant proteins and unsaturated fatty acids have been shown<sup>4,6</sup> to be beneficial for bone health. However, aMED does not limit sodium intake as do the HEI-2010, AHEI-2010, or, specifically, the DASH diet. Data from randomized clinical trials<sup>43</sup> suggest that adherence to the DASH diet lowers bone turnover and imparts beneficial effects on bone health.

Our data support an association between the extent of adherence to a healthy diet characterized by adherence to a Mediterranean diet and lower fracture risk. However, given the apparent risk reductions across various dietary patterns, a specific dietary index may not be associated with lower risk; rather, high diet quality reflected by various dietary indexes and their common components may achieve a lower risk. The lack of an

Table 3. HRs for Hip or Total Fractures by Quintiles (Qs) of Dietary Pattern Scores in the WHI Observational Study

Dietary Pattern, Q <sup>a</sup>	Score	Hip Fracture				Total Fracture		
		No. of Individuals	No. of Cases	Mean Follow-up, y	HR (95% CI) <sup>b</sup>	No. of Cases	Mean Follow-up, y	HR (95% CI) <sup>b</sup>
<b>aMED</b>								
Q1	<2	6545	177	12.35	1 [Reference]	1960	10.61	1 [Reference]
Q2	2-4	27 984	680	12.78	0.84 (0.70-1.01)	8694	10.91	1.01 (0.96-1.07)
Q3	4-5	18 050	396	13.15	0.77 (0.63-0.94)	5714	11.25	0.99 (0.93-1.05)
Q4	5-6	16 616	366	13.39	0.76 (0.62-0.92)	5336	11.43	0.98 (0.92-1.04)
Q5	>6	20 819	502	13.78	0.80 (0.66-0.97)	7014	11.65	1.01 (0.95-1.07)
<b>HEI-2010</b>								
Q1	<53	17 584	405	12.64	1 [Reference]	5328	10.82	1 [Reference]
Q2	53-60	17 871	406	13.06	0.93 (0.80-1.08)	5617	11.14	0.98 (0.94-1.02)
Q3	60-66	18 083	419	13.28	0.84 (0.72-0.99)	5826	11.32	0.97 (0.93-1.01)
Q4	66-72	18 067	392	13.40	0.79 (0.67-0.92)	5796	11.44	0.95 (0.91-0.99)
Q5	>72	18 409	499	13.43	0.87 (0.75-1.02)	6151	11.39	0.98 (0.93-1.02)
<b>AHEI-2010</b>								
Q1	<47	16 517	381	12.25	1 [Reference]	4862	10.51	1 [Reference]
Q2	47-53	15 997	392	12.79	0.99 (0.85-1.16)	4975	10.95	0.98 (0.94-1.03)
Q3	53-59	18 892	440	13.11	0.94 (0.80-1.09)	5936	11.23	0.97 (0.93-1.01)
Q4	59-65	17 561	399	13.60	0.92 (0.78-1.08)	5733	11.56	0.99 (0.95-1.04)
Q5	>65	21 047	509	13.86	0.94 (0.80-1.09)	7212	11.70	1.01 (0.96-1.05)
<b>DASH</b>								
Q1	<20	13 365	277	12.26	1 [Reference]	3834	10.53	1 [Reference]
Q2	20-23	18 704	456	12.84	1.02 (0.86-1.20)	5814	10.98	0.97 (0.92-1.01)
Q3	23-25	15 441	350	13.24	0.85 (0.71-1.02)	4933	11.29	0.95 (0.91-1.00)
Q4	25-28	22 005	504	13.46	0.85 (0.72-1.00)	7098	11.48	0.94 (0.89-0.98)
Q5	>28	20 499	534	13.69	0.89 (0.75-1.06)	7039	11.57	0.98 (0.94-1.03)

Abbreviations: AHEI-2010, Alternate Healthy Eating Index 2010<sup>19</sup>; aMED, alternate Mediterranean Diet<sup>13,17</sup>; DASH, Dietary Approaches to Stop Hypertension<sup>21</sup>; HEI-2010, Healthy Eating Index 2010<sup>18</sup>; HR, hazard ratio; WHI, Women's Health Initiative.

<sup>a</sup> Q1 represents the least healthy quintile; Q5, the healthiest quintile.

<sup>b</sup> Adjusted for age, race/ethnicity, body mass index, smoking status, physical activity, self-reported health, diabetes mellitus status, history of fracture at 55 years or older, physical function score, number of chronic medical conditions, number of psychoactive medications, and use of hormone therapy, bisphosphonates, calcitonin, and selective estrogen receptor modulators.

association with total fractures may be explained by the wide heterogeneity of fracture types in our analyses. However, because the propensity to fall is a major risk factor for fractures in the senior population, additional analyses accounting for fall history were undertaken—the main results did not change. Finally, since diet may also relate to muscle mass and BMD and thereby prevent fractures, we further investigated whether higher diet quality was associated with greater lean body mass or less loss of BMD. No clinically significant changes over time were observed.

Strengths of our analysis include a large, well-characterized study cohort with long-term follow-up and adjudicated hip fracture outcome events. Conversely, there are several limitations. First, because our study included only postmenopausal women in overall good health, external validity may be limited and residual confounding may explain parts of the findings since risk reduction was small. Our data showed marked differences in fracture risk across quintiles of multiple indicators of fractures; these differences may suggest the possibility

of other confounding factors. Second, assessment of dietary patterns was based on indexes that operationalize various food items derived from FFQs at baseline. Exposure variability is therefore limited. Moreover, assessment of certain nutrients, such as sodium or potassium, with FFQs is problematic.<sup>44,45</sup> Finally, outcome events on fractures other than the hip were self-reported, and misclassification bias may be present. However, previous data from WHI<sup>36</sup> show that agreements between self-reports for single-site fractures and medical records were generally high; thus, this bias can be considered as low.

## Conclusions

High diet quality characterized by adherence to a Mediterranean diet is associated with a lower risk for hip fractures. These results support the notion that following a healthy dietary pattern may play a role in the maintenance of bone health in postmenopausal women.

### ARTICLE INFORMATION

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Author Affiliations: Department of Internal Medicine I, Comprehensive Heart Failure Center, University of Würzburg, Würzburg, Bavaria,

Germany (Haring); Department of Medicine, David Geffen School of Medicine, UCLA (University of California at Los Angeles) (Crandall); Women's Health Initiative, Fred Hutchinson Cancer Center, Seattle, Washington (Wu); Kaiser Permanente Center for Health Research Northwest, Portland, Oregon (LeBlanc); Division of Preventive Medicine, School of Medicine, University of Alabama at Birmingham (Shikany); Department of Medicine, Medical College of Georgia at Georgia Regents University, Augusta (Carbone); Human Nutrition Program, Department of Human Sciences, The Ohio State University, Columbus (Orchard); Division of Biostatistics and Epidemiology, Department of Preventive Medicine, College of Medicine, University of Tennessee Health Science Center, Memphis (Thomas); Department of Epidemiology and Environmental Health, State University of New York at Buffalo (Wactawaski-Wende); Division of Preventive and Behavioral Medicine, Department of Medicine, University of Massachusetts Medical School, Worcester (Li); Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, Pennsylvania (Cauley); Department of Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, New York (Wassertheil-Smoller).

**Author Contributions:** Dr Haring and Ms Wu had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** Haring, Carbone, Wactawaski-Wende.

**Acquisition, analysis, or interpretation of data:** Haring, Crandall, Wu, LeBlanc, Shikany, Orchard, Thomas, Wactawaski-Wende, Li, Cauley, Wassertheil-Smoller

**Drafting of the manuscript:** Haring.

**Critical revision of the manuscript for important intellectual content:** All authors.

**Statistical analysis:** Haring, Wu, Thomas, Li.

**Obtained funding:** Wactawaski-Wende, Cauley, Wassertheil-Smoller.

**Administrative, technical, or material support:** Carbone, Wactawaski-Wende, Cauley, Wassertheil-Smoller.

**Study supervision:** Haring, Wassertheil-Smoller.

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**Data Sharing Statement:** Women's Health Initiative Study data are available via the BioLINCC website of the NHLBI at <https://biolincc.nhlbi.nih.gov/home/>.

**Additional Information:** A full listing of WHI investigators can be found at <https://www.whi.org/researchers/SitePages/WHI%20Investigators.aspx>. The following is a WHI short list of investigators. **Program Office:** Jacques Rossouw, Shari Ludlam, Dale Burwen, Joan McGowan, Leslie Ford, and Nancy Geller (NHLBI). **Clinical Coordinating Center:** Garnet Anderson, Ross Prentice, Andrea LaCroix, and Charles Kooperberg (Fred Hutchinson Cancer Research Center). **Investigators and Academic Centers:** JoAnn E. Manson (Brigham and Women's Hospital, Harvard Medical School); Barbara V. Howard (MedStar Health Research Institute/Howard University); Marcia L. Stefanick (Stanford Prevention Research Center); Rebecca Jackson (The Ohio State University); Cynthia A. Thomson (University of Arizona); Jean Wactawaski-Wende (University at Buffalo); Marian Limacher (University of Florida); Robert Wallace (University of Iowa); Lewis Kuller (University of Pittsburgh); Sally Shumaker (Wake Forest University School of Medicine). **Women's Health Initiative Memory Study:** Sally Shumaker (Wake Forest University School of Medicine).

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## Invited Commentary

## Mediterranean Diet and Fracture Risk

Walter C. Willett, MD, DrPH

**In this issue** of *JAMA Internal Medicine*, Haring et al<sup>1</sup> provide what appears to be the first detailed examination of a Mediterranean diet index and 3 other dietary quality indexes in association with the risk of hip and total fractures. They report that the 4 commonly used indexes predict a lower risk of hip fractures.

These a priori dietary indexes are one form of dietary pattern analyses, with the other being empirical dietary patterns based on statistical methods that take into account correlations among consumption of different foods. The use of dietary patterns in epidemiologic studies and intervention trials to complement studies of specific nutrients and foods has increased because effects of diet are likely to be strongest and clearest when contributions from multiple aspects of diet are combined. In addition, because isolating the effect of a specific nutrient or food from other highly correlated components of diet can be difficult, we can sometimes have greater confidence that an association with an overall dietary pattern is causal than we can for associations with specific components of that diet. One of the early uses of an a priori dietary index was the Healthy Eating Index (HEI), which was created by the US Department of Agriculture to describe adherence to the 1995 US Dietary Guidelines.



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Because of concerns that the focus of the 1995 guidelines—reduction of total fat and a broad increase in carbohydrates—was not supported by good evidence, we used the HEI to score the diets of participants in the Nurses' Health Study and Health Professionals Follow-up Study using dietary data that had been collected every 4 years since 1986. After adjusting for smoking, physical activity, and other health-related behaviors, HEI scores were not associated with a composite outcome of cardiovascular disease, cancer, and total mortality. Thus, we created the Alternative Healthy Eating Index, which accounted for type of fat, form of carbohydrate, and source of protein; when applied to the same dietary data, this score strongly predicted a lower risk of this composite of major chronic disease outcomes in both men and women.<sup>2</sup> Since that time, the US Dietary Guidelines and corresponding modifications of the HEI have moved closer to the diet described by the Alternative Healthy Eating Index, and both dietary indexes predict better health outcomes.<sup>3</sup> More recently, the Alternative Healthy Eating Index has been used to track US trends in diet quality since 2000, documenting a steady improvement that would account for major health benefits.<sup>4</sup> The Mediterranean Diet Index was developed to describe adherence to the traditional diet of Greece; this score and a modification for countries in which olive oil is not traditional (the alternative Mediterranean Diet