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No association between dietary patterns and risk for cognitive decline in older women with nine-year follow-up: data from the Women's Health Initiative Memory Study

Bernhard Haring, MD, MPH¹, Chunyuan Wu, MS², Yasmin Mossavar-Rahmani, PhD³, Linda Snetselaar, PhD⁴, Robert Brunner, PhD⁵, Robert B. Wallace, MD, MSc⁴, Marian L. Neuhouwer, PhD⁶, and Sylvia Wassertheil-Smoller, PhD³

¹Department of Internal Medicine I, Comprehensive Heart Failure Center, University of Würzburg, Würzburg, Bavaria, Germany

²Women's Health Initiative, Fred Hutchinson Cancer Research Center, Seattle, Washington, USA

³Department of Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, New York, USA

⁴Department of Epidemiology, University of Iowa College of Public Health, Iowa City, Iowa, USA

⁵Department of Nutrition, University of Nevada School of Medicine, Reno, Nevada, USA

⁶Public Health Sciences Division, Fred Hutchinson Cancer Research Center, Seattle, Washington, USA

Abstract

Background—Data on the association between dietary patterns and age-related cognitive decline are inconsistent.

Objective—To determine whether dietary patterns assessed by the alternate Mediterranean diet score (aMED), the Healthy Eating Index (HEI) 2010, the Alternate Healthy Eating Index (AHEI) 2010 or the Dietary Approach to Stop Hypertension (DASH) diet score are associated with cognitive decline in older women. To examine if dietary patterns modify the risk for cognitive decline in hypertensive women.

Design—Prospective, longitudinal cohort study. Food frequency questionnaires (FFQs) were used to derive dietary patterns at baseline. Hypertension was defined as self-report of current drug therapy for hypertension or clinic measurement of SBP ≥140mmHg or DBP ≥90mmHg.

Corresponding Author: Bernhard Haring, MD MPH, Department of Internal Medicine I / Cardiology, Comprehensive Heart Failure Center, University of Würzburg, Oberdürrbacherstrasse 6, Würzburg 97080, Germany, Tel: 0049 176 5959 1627, Fax: 0049 931 201 639001, ; Email: Haring_B@ukw.de

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Conflict of Interest Disclosure

The authors report no conflicts of interest.

Participants/setting—Postmenopausal women (N=6,425) aged 65 to 79 years who participated in the Women's Health Initiative Memory Study (WHIMS) and were cognitively intact at baseline.

Main Outcome Measures—Cognitive decline was defined as cases of mild cognitive impairment (MCI) or probable dementia (PD). Cases were identified through rigorous screening and expert adjudication.

Statistical Analyses performed—Cox proportional hazards models with multivariable adjustment were used to estimate the relative risk for developing MCI or PD.

Results—During a median follow-up of 9.11 years, we documented 499 cases of MCI and 390 of PD. In multivariable analyses we did not detect any statistically significant relationships across quintiles of aMED, HEI-2010, DASH and AHEI-2010 scores and MCI or PD (p_{trend} =0.30, 0.44, 0.23 and 0.45). In hypertensive women we found no significant association between dietary patterns and cognitive decline (p_{trend} =0.19, 0.08, 0.07 and 0.60).

Conclusions—Dietary patterns characterized by the aMED, HEI-2010, AHEI-2010 or DASH dietary score were not associated with cognitive decline in older women. Adherence to a healthy dietary pattern did not modify the risk for cognitive decline in hypertensive women.

Keywords

Diet; Hypertension; Mild Cognitive Impairment; Dementia; Cognitive Decline

Introduction

Cognitive decline is an increasing health problem.¹ Diet may play a role for preserving cognitive health.^{2–4} A healthy dietary pattern is known to modulate vascular risk factors such as hypertension and to exhibit neuroprotective properties. Adherence to a healthy dietary pattern may thus provide benefits for brain functioning and may be protective against dementia.⁵ To this point, investigations of various dietary approaches are gaining increasing attention and dietary patterns emerge as a potential target for reducing the burden of cognitive decline.⁶

Previous findings suggest that adherence to a Mediterranean-style diet, which emphasizes the consumption of plant foods, fish, nuts, legumes and high intake of monounsaturated fat with olive oil as the principal source⁷, may be able to slow cognitive decline^{4, 8} and lower the risk for mild cognitive impairment and dementia^{9, 10} in individuals aged 65 or older. However, results have been inconsistent and no definitive recommendation can be made at this point.^{11–14} Remaining questions include whether solely a Mediterranean dietary pattern or also other generally healthy dietary approaches may be protective against cognitive decline and if a healthy dietary pattern modifies the risk for cognitive decline in those already suffering from vascular risk factors. The effects of following a healthy diet reflected in the Healthy Eating Index (HEI) 2010¹⁵, the Alternate Healthy Eating Index (AHEI) 2010^{16, 19} or the Dietary Approach to Stop Hypertension (DASH) score^{8, 17} in relation to cognitive health have not been thoroughly investigated and comprehensive analyses are sparse.^{8, 17–19}

The Mediterranean diet assessed by the alternate Mediterranean dietary score (aMED)^{20,32} and dietary patterns reflected by the HEI-2010, AHEI-2010 or DASH diet score have many similarities, as all emphasize vegetables, fruits and whole grains, but there are also distinctive differences. For example, the aMED emphasizes intake of monounsaturated fatty acids, fish, nuts, whole grains and legumes but does not limit sodium consumption as do the HEI-2010, AHEI-2010 or the DASH diets, which attempt to counter the relationship between excess sodium consumption and hypertension.

The purpose of this study was to compare healthy dietary patterns assessed by the aMED, HEI-2010, AHEI-2010 and DASH diet score on the risk of cognitive decline in postmenopausal women aged 65 to 79 years. Second, we examined if adherence to a healthy dietary pattern modified the risk for decreased cognitive performance in hypertensive women. We hypothesized that a healthy dietary pattern would be associated with a decreased risk for cognitive decline. Furthermore, we anticipated that a healthy dietary pattern would be related to a decreased risk for cognitive decline in women with hypertension.

Methods

Study Population

The study population consisted of postmenopausal women enrolled in the Women's Health Initiative Memory Study (WHIMS) study. Details of the study design and the initial screening process have been published previously.^{21–25} WHIMS aimed to examine the effect of postmenopausal hormone treatment on cognitive function and was designed as an ancillary study to the Women's Health Initiative Hormone Trials (i.e. WHI Estrogen + Progestin trial and WHI Conjugated Equine Estrogen trial).^{21–23, 25, 26} Between May 1996 and December 1999 women aged 65 or older who were free of dementia were recruited at 40 US clinical centers.^{21, 23, 25} The WHI trial of Estrogen+Progestin ended intervention in July 2002^{21, 23} due to an adverse risk to benefit ratio. The WHI Conjugated Equine Estrogen alone intervention ended in February 2004.^{22, 25, 26} WHIMS participants continued annual post-trial cognitive assessment through the WHIMS Extension Study until July 2008 and then through the 'Women's Health Initiative Memory Study-Epidemiology of Cognitive Health Outcomes' (WHIMS-ECHO) to present. Institutional review boards at participating institutions approved all protocols and all participants provided written informed consent

The total study population consisted of 7,479 postmenopausal women. For this analysis, we excluded women with incomplete dietary information or with extreme calorie intake (i.e. <600 kcal or > 5000 kcal per day) because these reported intakes were judged to be implausible (n = 276).²⁷ Furthermore, women with missing baseline data (n=67), mild cognitive impairment at baseline (n=8), and missing follow-up data (n= 240), or covariate data (n=463) were excluded from analysis. Our final study population was 6,425 women, who were followed-up through December 31, 2012 with a median follow-up of 9.11 years.

Assessment of Dietary Patterns

Dietary intake was derived from a self-administered Women's Health Initiative food frequency questionnaire (WHI-FFQ) at baseline.^{27–29} The WHI-FFQ is based on a modified

Block FFQ that estimated mean daily nutrient intake during the previous 3-month period.^{27, 28} It includes 122 composite and single-food line items asking about frequency of consumption and portion size, 19 adjustment questions related to the type of fat intake, and 4 summary questions about the usual intakes of fruits and vegetables and fats added in cooking or at the table.^{27, 28} Dietary patterns were subsequently assessed with the following dietary scoring systems: 1) aMED, 2) HEI-2010, 3) AHEI-2010 and 4) DASH. We used the MyPyramid Equivalents Database to translate the various consumed food items into standardized quantities of dietary components of interest as previously described.^{30, 31}

For calculating aMED the following items were considered^{20, 32}: 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 one 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. The total aMED score ranged from 0 (non-adherence) to 9 (perfect adherence).

The HEI was developed by the United States Department of Agriculture's Center for Nutrition Policy and Promotion.³³ It was most recently updated in 2010 through a joint collaboration between the center and the National Cancer Institute to measure conformance to the US Dietary Guidelines for Americans.¹⁵ The HEI-2010 contains 12 components: Six components—total vegetables, total fruit, whole fruit, seafood and plant proteins, and total protein foods—are assigned 0–5 points; Five components—whole grains, dairy, fatty acids ratio [(polyunsaturated fatty acids + monounsaturated fatty acids):saturated fatty acids], refined grains, and sodium—are assigned 0–10 points; and one component—"empty calories" (energy from solid fats, added sugars, and any alcohol in excess of 13 g/1000 kcal)—is assigned 0–20 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). The HEI-2010 scores range from 0 to 100 points (perfect conformance).

The AHEI-2010 was designed as an alternative to the HEI-2010 and focuses on food and nutrients predictive of chronic disease risk.¹⁶ The AHEI-2010 includes 11 items and each component scores from 0 (worst) to 10 (best). It emphasizes vegetables, fruits, whole grains, nuts, legumes, vegetable proteins, long-chain omega-3 polyunsaturated fatty acids (n-3 PUFA), PUFA (excluding long-chain n-3 PUFA), moderate alcohol intake, avoidance of trans-fat and lower intakes of sugar-sweetened beverages (including fruit juice), red and processed meats and sodium. Total AHEI-2010 score can range from 0 (non-adherence) to 110 (perfect adherence).

For calculating the DASH diet score, we ranked participants on 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.³⁴ For fruits, vegetables, nuts and legumes, low-fat dairy and whole grains, participants in the highest quintile received a score of 5, those in the second highest quintile received a score of 4, and so on. For sodium, sweetened beverages, red and processed meats, scoring was reversed, i.e. women in the highest quintile received a minimum score of 1 whereas participants in the lowest quintile received a

maximum score of 5. The score for each component was summed and the overall score ranged from 8 (no adherence) to 40 (perfect adherence).

Ascertainment of Cognitive Decline

Cognitive decline was defined as cases of ‘mild cognitive impairment (MCI) or probable dementia (PD)’. The diagnosis and definition of MCI or PD was made following a detailed ‘4 phase protocol’ as outlined by the WHIMS trial and the WHIMS extension study until 2008.^{21, 26, 35}

In phase 1, all participants were screened annually with modified mini-mental state examinations (3MSE) which ranged from 0 to 100 with higher results reflecting better cognitive functioning.³⁶ If a participant scored at or below the cut point (80 for women with 8 or fewer years of formal education and 88 for those with 9 or more years of formal education), she progressed to further in-person cognitive testing and clinical assessment (phase 2).

In phase 2, certified technicians administered a modified Consortium to Establish a Registry for Alzheimer's Disease (CERAD) battery of neuropsychological tests.³⁷ Specifically, the battery contained tests measuring verbal fluency (animal category)³⁸, naming (15-item Boston Naming Test), verbal learning and memory (10-item, 3-trial word list memory task with delayed recall, and recognition tasks), constructional praxis (4 line drawings are copied and later recalled)³⁹, and executive function (Trail-Making Test, parts A and B)⁴⁰. Certified technicians also administered standardized interviews to assess behavioral symptoms, such as generalized anxiety, major depression, and alcohol abuse⁴¹, and the 15-item Geriatric Depression Scale⁴². Finally, both the participant and her designated informant were administered separately a standardized set of 36 items (yes/no) that assessed observed cognitive and behavioral deficits (memory, language, orientation, personality/behavior, basic and instrumental activities of daily living, social and intellectual activities, and judgment and problem solving).³⁵

After completing phase 2, participants were evaluated by a local physician (ie, geriatrician, neurologist, or geriatric psychiatrist) who was identified by the local WHIMS clinical center and approved by the WHIMS CCC as having the experience required for diagnosing dementia (phase 3). Using a standardized protocol provided by the WHIMS CCC, all available data were reviewed and the physicians performed a clinical neuropsychiatric evaluation. The physician then classified the WHIMS participant as having no dementia, MCI, or probable dementia, based on the ‘*Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)*’ criteria.

Women suspected of having PD underwent phase 4, including a noncontrast computed tomography brain scan and laboratory blood tests to rule out possible reversible causes of cognitive decline. If dementia was still suspected, the physician was required to provide the most probable etiology based on DSM-IV criteria.

In July 2008, the ‘Women’s Health Initiative Memory Study-Epidemiology of Cognitive Health Outcomes’ (WHIMS-ECHO) succeeded the WHIMS extension study. Instead of in-

clinic visits and face-to-face evaluation as in WHIMS, cognitive assessment in WHIMS-ECHO was conducted by an annual centralized, validated cognitive telephone interview for tracking changes in cognitive status.⁴³ The interview was comprised of a neuropsychological battery including a global cognitive screener (modified Telephone Interview for Cognitive Status, known as the TICSm) and additional neuropsychological tests. If a woman scored below 31 on the TICSm, the Dementia Questionnaire (DQ) was administered to a friend or family member previously identified (proxy). The DQ is a standardized, validated instrument used to reliably classify dementia when used with cognitive performance measures. A central panel of experts in the diagnosis of mild cognitive impairment syndrome and dementia reviewed the results along with the cognitive scoring history and classified participants as follows: 1) no dementia (no cognitive impairment), 2) MCI, 3) PD, 4) unable to classify -cognitive impairment, 5) unable to classify - functional impairment, and 6) unable to classify - no cognitive impairment and no dementia.

WHIMS Clinical Coordinating Center (CCC) and WHIMS-ECHO Coordinating Center (CoC) specialists reviewed and adjudicated all clinical and test data.

Covariates

Socio-demographic variables were determined by interview or self-report using standardized questionnaires at baseline.²⁹ Height was measured using a stadiometer; weight was measured with participants wearing light clothing. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. The presence of ApoE E4 allele was determined by DNA genotyping in a subset of study participants. Recreational physical activity was assessed with metabolic equivalent tasks (in hours per week) using a questionnaire on leisure activities.⁴⁴ Blood pressure was measured by certified staff using standardized procedures.²⁹ The average of two baseline readings was used for analyses. Hypertension was defined as a self-report of current drug therapy for hypertension or clinic measurement of SBP ≥ 140 mmHg or DBP ≥ 90 mmHg. Diabetes was defined as self-report of physician diagnosis or self-report of taking diabetes medication at baseline. Data on depression were based on self-report of depressive symptoms. Cardiovascular disease was coded positive if a history of myocardial infarction, angina pectoris, atrial fibrillation, heart failure, peripheral vascular disease, coronary bypass surgery, angioplasty, carotid endarterectomy or stroke was reported.

Statistical Analysis

To assess the associations of aMED, HEI-2010, AHEI-2010 and DASH with incident MCI or PD, we formed quintiles of each exposure variable of interest based on the distribution of non-cases in the cohort. Incidence rates (per 1000 person-years) of MCI or PD were calculated in each specific intake quintile. Thereafter, we calculated corresponding rate ratios by dividing the rate among women in each specific intake quintile by the rate among women in the lowest quintile of intake (reference). Cox proportional hazards models and 95% confidence intervals (95% CI) were used to estimate the relative risk for developing MCI or PD with increasing quintiles. Multivariate adjusting for confounding variables was applied by including age, race/ethnicity, education level, WHI Hormone Trial Randomization assignment (HTR arm), baseline 3MSE level as well as smoking status,

physical activity, diabetes status, hypertension status, BMI, family income, depression, history of CVD and total energy intake. Tests of linear trend across increasing quintiles were performed. To examine the interaction of aMED, HEI-2010, AHEI-2010 or DASH with baseline hypertension on the risk of MCI or PD we used Cox proportional hazards regression analyses again with multivariable adjusting for confounding variables. Finally, we performed supplementary analyses in a subset of white women for whom genetic data were available by including the presence of the ApoE E4 allele into our multivariate modelling. A two-sided p-value of 0.05 was considered statistically significant. All analyses were conducted using SAS statistical software (version 9.3; release date: July 2011; SAS Institute Inc, Cary, North Carolina).

Results

Baseline characteristics of the study participants by dietary pattern are shown in Table 1. Women scoring in the highest quintile of aMED, HEI-2010, AHEI-2010 or DASH were more likely to have higher educational attainment, but less likely to be Hispanic; they were also more likely to be physically active, have a lower BMI level and lower levels of depression.

During a median follow-up of 9.11 years, we documented 499 cases of MCI and 390 of PD. The multivariate adjusted HRs for incident MCI or PD associated with aMED, HEI-2010, AHEI-2010 or DASH are presented in Table 2. After controlling for potential confounders, no association between aMED, DASH, HEI-2010 or AHEI-2010 and the composite outcome MCI or PD across dietary quintiles was found ($p_{\text{trend}} = 0.30, 0.45, 0.44$ and 0.23). In detailed analyses, we found a significant inverse association between DASH and risk for MCI ($\text{HR}_{\text{Q5}} = 0.72$, 95% CI, 0.52, 1.02; $p_{\text{trend}} = 0.04$), but not for PD ($\text{HR}_{\text{Q5}} = 1.28$, 95% CI, 0.86, 1.91, $p_{\text{trend}} = 0.11$). Across quintiles of AHEI-2010 and aMED, women tended to be associated with a lower risk for MCI ($\text{HR}_{\text{Q5}} = 0.75$, 95% CI, 0.54, 1.03 and $\text{HR}_{\text{Q5}} = 0.82$, 95% CI, 0.59, 1.14), however, these trends were not significant ($p_{\text{trend}} = 0.10$ and 0.08). Adherence to dietary patterns as characterized by the HEI-2010 ($\text{HR}_{\text{Q5}} = 1.60$, 95% CI, 1.10, 2.33; $p_{\text{trend}} = 0.02$) but not by the aMED or AHEI-2010 ($\text{HR}_{\text{Q5}} = 1.13$, 95% CI, 0.79, 1.63; $p_{\text{trend}} = 0.46$ or $\text{HR}_{\text{Q5}} = 1.01$, 95% CI, 0.71, 1.46; $p_{\text{trend}} = 0.71$) significantly increased the risk for incident PD.

Interactions of our dietary patterns of interest on the risk for MCI or PD were examined in women with hypertension at baseline (Table 3). We did not detect any significant association between risk for MCI or PD across quintiles of aMED, HEI-2010, AHEI-2010 and DASH ($p_{\text{trend}} = 0.19, 0.08, 0.07$ and 0.60) in hypertensive women.

As genetic connections have been reported to play a significant role in the development of cognitive decline, we performed supplementary analyses in a subset of white women for whom genetic data were available by additionally adjusting our analyses for the presence of ApoE E4 allele (Supplementary Table 1).^{45, 46} We found that high adherence to a Mediterranean dietary pattern or to the AHEI-2010 was associated with a lower risk for incident MCI ($\text{HR}_{\text{Q5}} = 0.67$, 95% CI, 0.45, 1.00; $p_{\text{trend}} = 0.01$ or $\text{HR}_{\text{Q5}} = 0.64$, 95% CI, 0.44, 0.93; $p_{\text{trend}} = 0.03$). However, similar to our previous results (Table 2) we observed no

relationship between adhering to a dietary pattern assessed by aMED, HEI-2010, AHEI-2010 or DASH scoring and risk for 'MCI or PD'.

Discussion

In this large cohort of postmenopausal women aged 65 to 79 years with long-term follow-up and standardized assessment of cognitive functioning, we found no association between adhering to a dietary pattern assessed by aMED, HEI-2010, AHEI-2010 or DASH scoring and cognitive decline.

So far, the largest analyses examining the relationship between dietary pattern and cognitive status stem from the Nurses' Health Study.^{13, 19} There, long-time aMED adherence was related to only moderately better cognition but not cognitive changes in women aged 70 years.¹³ Interestingly, in the same study it was further reported that later life effects and well-being as a consequence of adhering to dietary patterns characterized by the HEI-2005, aMED or AHEI-2010 in mid-life may not necessarily extend to less cognitive decline in elderly individuals.¹⁹ Other observational studies also did not report any association between aMED and incidence of MCI or dementia.^{11, 12} On the other hand, adherence to a DASH dietary pattern or the HEI-2005 was associated with slower rates of cognitive decline and higher levels of cognitive functioning in older individuals^{8, 17, 18}, but cognitive assessment was limited. Our findings do not support an association between adherence to healthy dietary pattern and cognitive decline at older age, which is in contrast to the hypothesized biological effects of a healthy dietary pattern. Although our detailed results showed that maintaining a DASH dietary pattern tended to be associated with lower risk for MCI whereas the HEI-2010 was found to be related to PD, interpretation warrants caution as these singular findings are likely spurious and potentially driven by reverse causality.

Among potential mechanisms that relate dietary patterns to cognitive dysfunction the modification of vascular risk factors may be a key approach to reduce cognitive decline.⁵ Accordingly, we proceeded to examine the association between diet and cognitive decline in hypertensive women as so to our knowledge there is currently no information on the effect of diet on cognitive health in this subgroup of women particularly at risk for cognitive dysfunction. Again, however, we did not observe a relationship between a healthy dietary pattern and cognitive decline.

Inconsistent results on the relationship between adherence to dietary patterns characterized by the HEI-2010, AHEI-2010, aMED, DASH and risk for cognitive decline may be explained by several factors. Although, there is good evidence for the benefits of a healthy dietary pattern for cardiovascular health, the effect size is dependent on the duration of maintaining a healthy lifestyle and the absence of chronic diseases. Our study of older postmenopausal women may not have been able to capture this relationship, as our follow-up period may have been too short. Moreover, as adherence to a healthier dietary pattern is also a marker of healthier lifestyle, the true association between a healthy dietary pattern and cognitive decline may have been obscured by residual confounding. Other reasons derive from education and family income status specific to the study population. Two previous large studies that reported a relationship aMED and cognitive decline were conducted in

lower income US populations.^{9, 10} Our study population along with data from the Nurses' Health Study¹³ consisted of relatively well educated, middle to high income white women which could have reduced the association between dietary pattern and cognitive decline. Last, inconsistent results on the effect of a Mediterranean-style diet may be attributed to dietary differences between populations in US based studies and those in Mediterranean countries.⁴ Nonetheless, even in a Greek population, which appears to be highly adherent to a typical Mediterranean diet, no association between aMED and cognitive impairment was found.⁴⁷ Given these factors and the complex and delicate task to establish valid associations from observational studies, further randomized controlled clinical trials are warranted to elucidate the relationship between various dietary patterns and cognitive decline.

Our study is not without limitations. Assessment of our dietary patterns is based on indices that operationalize various (food) items and derive their information from FFQs. Although this statement has been supported by several other previous investigations using dietary indices,^{9, 18, 19} it has been an inherent methodological limitation. Furthermore, exposure variability of our study population was limited as dietary intakes were only assessed at baseline. Changing dietary habits may not have been covered adequately by our FFQs although great changes in an elderly population are unlikely to occur.^{48, 49} There may also be measurement error related to subtle beginnings of undetected memory decline, not strong enough to be considered MCI. This memory decline may have been manifested as misreporting of foods that can further attenuate the relationship between diet and cognition.

On the other hand, foods that are socially desirable to report such as fruits and vegetables may have been over-reported as evidenced by over-reporting of potassium when compared to a biomarker.⁵⁰ Furthermore, as our study only included generally healthy older women, primarily white, external validity is limited and the findings may underestimate the true association in the general population as well as may not be applicable to other ethnic groups. Finally, although the follow-up rate in our study was high (approximately 97%) we cannot exclude some bias due to loss-of follow up and missing covariate data but this influence is most likely small.

In conclusion, no significant relationship between a dietary pattern characterized by aMED, HEI-2010, AHEI-2010 or DASH and cognitive decline was found. Adherence to a healthy dietary pattern did not modify the risk for cognitive decline in hypertensive women. These results should not be viewed as discouraging to make appropriate dietary modifications following current guidelines and recommendations for the preservation of health.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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WHI Short List of 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: Clinical Coordinating Center: (Fred Hutchinson Cancer Research Center, Seattle, WA) Garnet Anderson, Ross Prentice, Andrea LaCroix, and Charles Kooperberg

Investigators and Academic Centers: (Brigham and Women's Hospital, Harvard Medical School, Boston, MA) JoAnn E. Manson; (MedStar Health Research Institute/Howard University, Washington, DC) Barbara V. Howard; (Stanford Prevention Research Center, Stanford, CA) Marcia L. Stefanick; (The Ohio State University, Columbus, OH) Rebecca Jackson; (University of Arizona, Tucson/Phoenix, AZ) Cynthia A. Thomson; (University at Buffalo, Buffalo, NY) Jean Wactawski-Wende; (University of Florida, Gainesville/Jacksonville, FL) Marian Limacher; (University of Iowa, Iowa City/Davenport, IA) Robert Wallace; (University of Pittsburgh, Pittsburgh, PA) Lewis Kuller; (Wake Forest University School of Medicine, Winston-Salem, NC) Sally Shumaker Women's Health Initiative Memory Study; (Wake Forest University School of Medicine, Winston-Salem, NC) Sally Shumaker

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Baseline characteristics of participants in the Women's Health Initiative Memory Study (n=6'425) by lowest and highest quintile of dietary pattern scoring

Table 1

Characteristic	Dietary pattern									
	aMED ^a		HEI-2010 ^b		AHEI-2010 ^c		DASH ^d			
	Quintile 1 ^e (score: <3) N = 1271	Quintile 5 ^f (score: >6) N = 1486	Quintile 1 (score: <51) N = 1267	Quintile 5 (score: >71) N = 1314	Quintile 1 (score: <47) N = 1236	Quintile 5 (score: >64) N = 1410	Quintile 1 (score: <20) N = 927	Quintile 5 (score: >28) N = 1413		
Age	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)		
	65–69 y	631 (50)	643 (43)	689 (54)	518 (39)	635 (51)	483 (52)	573 (41)		
	70–74 y	437 (34)	546 (37)	394 (31)	525 (40)	412 (33)	303 (33)	530 (38)		
Race/Ethnicity	75–79 y	203 (16)	297 (20)	184 (15)	271 (21)	189 (15)	141 (15)	310 (22)		
	White	1128 (89)	1314 (88)	1110 (88)	1155 (88)	1062 (86)	766 (83)	1307 (93)		
	African American	76 (6)	95 (6)	73 (6)	86 (7)	95 (8)	92 (10)	52 (4)		
Education	Hispanic	33 (3)	13 (1)	43 (3)	17 (1)	42 (3)	36 (4)	10 (1)		
	Other	34 (3)	64 (4)	41 (3)	56 (4)	37 (3)	33 (4)	44 (3)		
	> High-school diploma/GED	793 (62)	1195 (80)	804 (63)	1023 (78)	708 (57)	558 (60)	1149 (81)		
Family income per year	< 35,000 US\$	772 (65)	684 (49)	754 (63)	637 (52)	826 (71)	555 (64)	657 (49)		
BMI (kg/m ²)	>30	493 (39)	410 (28)	521 (41)	354 (27)	515 (42)	406 (44)	344 (24)		
Smoking	Never	655 (52)	783 (53)	604 (48)	781 (59)	697 (56)	447 (48)	783 (55)		
Hypertension		609 (48)	693 (47)	597 (47)	616 (47)	638 (52)	479 (52)	638 (45)		
Physical Activity in Metabolic Equivalents (METs)	19 MET-hours per week	142 (11)	435 (29)	149 (12)	358 (27)	114 (9)	104 (11)	416 (29)		
Diabetes		68 (5)	76 (5)	55 (4)	104 (8)	77 (6)	56 (6)	97 (7)		
Depression		21 (2)	16 (1)	30 (2)	13 (1)	26 (2)	20 (2)	10 (1)		
History of cardiovascular disease		192 (15)	198 (13)	176 (14)	188 (14)	201 (16)	145 (16)	193 (14)		

Characteristic	Dietary pattern							
	aMED ^a		HEI-2010 ^b		AHEI-2010 ^c		DASH ^d	
	Quintile 1 ^e (score: <3) N = 1271	Quintile 5 ^f (score: >6) N = 1486	Quintile 1 (score: <51) N = 1267	Quintile 5 (score: >71) N = 1314	Quintile 1 (score: <47) N = 1236	Quintile 5 (score: >64) N = 1410	Quintile 1 (score: <20) N = 927	Quintile 5 (score: >28) N = 1413
Hormone Replacement	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
3 MSE score	632 (50)	720 (48)	638 (50)	646(49)	605 (49)	690 (49)	479 (52)	692 (49)
Total Energy Intake (kcal/day)	94.93 (4.51)	95.84 (3.87)	94.99 (4.38)	95.56 (4.12)	94.71 (4.53)	95.85 (3.88)	94.63 (4.63)	96.16 (3.62)
	1354 (536)	1857 (628)	1803 (757)	1434 (492)	1588 (628)	1605 (565)	1674 (627)	1624 (563)

^a aMED, alternate Mediterranean Diet

^b HEI-2010, Healthy Eating Index–2010

^c AHEI-2010, Alternative Healthy Eating Index–2010

^d DASH, Dietary Approaches to Stop Hypertension

^e Quintile 1 represents the least healthy quintile

^f Quintile 5 represents the healthiest quintile

Table 2

Hazard Ratios (95% CI) for incident cognitive decline ('Mild Cognitive Impairment or Probable Dementia') by quintiles of dietary pattern scoring

Quintiles of Dietary Pattern	No of Individuals	Mild Cognitive Impairment (MCI)		Probable Dementia (PD)		MCI or PD	
		No of cases	Hazard Ratio (95% CI) ^a	No of cases	Hazard Ratio (95% CI) ^a	No of cases	Hazard Ratio (95% CI) ^a
aMED ^b							
Q1 ^c	1271	100	1.00 (Reference)	68	1.00 (Reference)	144	1.00 (Reference)
Q2	1224	113	1.26 (0.94, 1.68)	60	0.97 (0.67, 1.40)	153	1.13 (0.89, 1.44)
Q3	1292	106	1.08 (0.80, 1.46)	99	1.47 (1.05, 2.06)	165	1.13 (0.89, 1.44)
Q4	1152	83	0.98 (0.70, 1.35)	67	1.07 (0.73, 1.56)	127	0.97 (0.75, 1.27)
Q5 ^d	1486	90	0.82 (0.59, 1.14)	90	1.13 (0.79, 1.63)	155	0.93 (0.72, 1.20)
p-trend			0.08		0.46		0.30
HEI-2010 ^e							
Q1	1267	96	1.00 (Reference)	56	1.00 (Reference)	131	1.00 (Reference)
Q2	1286	103	1.00 (0.75, 1.35)	75	1.42 (0.97, 2.06)	149	1.12 (0.87, 1.44)
Q3	1271	82	0.82 (0.60, 1.13)	76	1.41 (0.97, 2.05)	135	1.00 (0.78, 1.30)
Q4	1287	96	0.94 (0.69, 1.27)	83	1.58 (1.09, 2.30)	152	1.12 (0.87, 1.45)
Q5	1314	115	0.90 (0.66, 1.22)	94	1.60 (1.10, 2.33)	177	1.12 (0.87, 1.44)
p-trend			0.43		0.02		0.44
AHEI-2010 ^f							
Q1	1236	107	1.00 (Reference)	67	1.00 (Reference)	150	1.00 (Reference)
Q2	1275	110	0.97 (0.73, 1.29)	76	1.05 (0.74, 1.48)	158	0.97 (0.76, 1.23)
Q3	1204	92	0.98 (0.72, 1.33)	73	1.22 (0.86, 1.75)	137	1.02 (0.80, 1.31)
Q4	1300	99	0.96 (0.71, 1.29)	87	1.28 (0.91, 1.81)	156	1.03 (0.81, 1.32)
Q5	1410	84	0.75 (0.54, 1.03)	81	1.01 (0.71, 1.46)	143	0.82 (0.64, 1.07)
p-trend			0.10		0.71		0.23
DASH ^g							
Q1	927	82	1.00 (Reference)	43	1.00 (Reference)	109	1.00 (Reference)

Quintiles of Dietary Pattern	No of Individuals	Mild Cognitive Impairment (MCI)		Probable Dementia (PD)		MCI or PD	
		No of cases	Hazard Ratio (95% CI) ^a	No of cases	Hazard Ratio (95% CI) ^a	No of cases	Hazard Ratio (95% CI) ^a
Q2	1381	117	0.94 (0.69, 1.28)	80	1.12 (0.75, 1.66)	174	1.03 (0.80, 1.34)
Q3	1156	91	0.98 (0.81, 1.36)	67	1.17 (0.77, 1.76)	124	0.94 (0.71, 1.24)
Q4	1548	109	0.82 (0.60, 1.12)	103	1.40 (0.96, 2.05)	177	0.97 (0.75, 1.25)
Q5	1413	93	0.72 (0.52, 1.02)	91	1.28 (0.86, 1.91)	160	0.93 (0.81, 1.22)
p-trend			0.04		0.11		0.45

^a adjusted for age, race, education level, WHI Hormone Trial Randomization assignment (HTR arm), baseline 3MSE level, smoking status, physical activity, diabetes status, hypertension status, BMI, family income, depression, history of CVD and total energy intake

^b aMED, alternate Mediterranean Diet

^c Quintile 1 represents the least healthy quintile

^d Quintile 5 represents the healthiest quintile

^e HEI-2010, Healthy Eating Index–2010

^f AHEI-2010, Alternative Healthy Eating Index–2010

^g DASH, Dietary Approaches to Stop Hypertension

Table 3

Association [Hazard Ratio (95% CI)] of hypertension and cognitive decline (‘Mild Cognitive Impairment or Probable Dementia’) by quintiles of dietary pattern scoring

Quintiles of Dietary Pattern	Mild Cognitive Impairment (MCI)			Probable Dementia (PD)			MCI or PD		
	Normotensive (N = 3275) No of Cases	Hypertensive (N = 3150) No of Cases	Hazard Ratio (95% CI) ^a	Normotensive (N = 3275) No of Cases	Hypertensive (N = 3150) No of Cases	Hazard Ratio (95% CI) ^a	Normotensive (N = 3275) No of Cases	Hypertensive (N = 3150) No of Cases	Hazard Ratio (95% CI) ^a
aMED^b									
Q1 ^c	47	53	1.14 (0.74, 1.76)	37	31	0.95 (0.56, 1.59)	72	72	1.09 (0.77, 1.55)
Q2	44	69	1.53 (1.03, 2.26)	24	36	1.45 (0.86, 2.45)	60	93	1.56 (1.11, 2.18)
Q3	45	61	1.17 (0.78, 1.76)	44	55	1.30 (0.85, 1.97)	72	93	1.21 (0.88, 1.68)
Q4	39	44	0.87 (0.55, 1.37)	35	32	0.91 (0.55, 1.51)	63	64	0.87 (0.60, 1.25)
Q5 ^d	39	51	1.16 (0.74, 1.80)	46	44	0.93 (0.60, 1.44)	75	80	1.01 (0.72, 1.41)
<i>p</i> -interaction			0.49			0.54			0.19
HEI-2010^e									
Q1	38	58	1.78 (1.15, 2.75)	23	33	1.79 (0.99, 3.21)	53	78	1.80 (1.24, 2.62)
Q2	47	56	0.97 (0.64, 1.47)	40	35	0.80 (0.49, 1.29)	73	76	0.88 (0.63, 1.24)
Q3	32	50	1.26 (0.79, 2.01)	34	42	1.02 (0.63, 1.64)	59	76	1.05 (0.74, 1.50)
Q4	45	51	0.96 (0.63, 1.47)	41	42	1.16 (0.74, 1.80)	71	81	1.11 (0.80, 1.55)
Q5	52	63	1.12 (0.75, 1.66)	48	46	1.08 (0.71, 1.64)	86	91	1.11 (0.81, 1.51)
<i>p</i> interaction			0.26			0.34			0.08
AHEI-2010^f									
Q1	38	69	1.68 (1.10, 2.55)	24	43	1.89 (1.11, 3.22)	54	96	1.75 (1.23, 2.50)
Q2	48	62	1.12 (0.74, 1.67)	37	39	1.03 (0.64, 1.67)	74	84	1.05 (0.76, 1.47)
Q3	46	46	0.81 (0.52, 1.25)	36	37	0.95 (0.59, 1.55)	67	70	0.91 (0.64, 1.29)
Q4	43	56	1.14 (0.75, 1.73)	45	42	0.92 (0.60, 1.43)	77	79	0.96 (0.69, 1.34)
Q5	39	45	1.22 (0.78, 1.92)	44	37	1.00 (0.63, 1.58)	70	73	1.18 (0.84, 1.67)
<i>p</i> interaction			0.22			0.26			0.07

Quintiles of Dietary Pattern	Mild Cognitive Impairment (MCI)			Probable Dementia (PD)			MCI or PD		
	Normotensive (N = 3275) No of Cases	Hypertensive (N = 3150) No of Cases	Hazard Ratio (95% CI) ^a	Normotensive (N = 3275) No of Cases	Hypertensive (N = 3150) No of Cases	Hazard Ratio (95% CI) ^a	Normotensive (N = 3275) No of Cases	Hypertensive (N = 3150) No of Cases	Hazard Ratio (95% CI) ^a
DASH ^g									
Q1	31	51	1.53 (0.94, 2.49)	16	27	1.94 (1.00, 3.76)	43	66	1.52 (1.01, 2.31)
Q2	51	66	1.06 (0.72, 1.56)	34	46	1.20 (0.74, 1.93)	75	99	1.15 (0.84, 1.58)
Q3	37	54	1.22 (0.79, 1.89)	31	36	1.04 (0.62, 1.74)	55	69	1.11 (0.77, 1.62)
Q4	55	54	1.02 (0.69, 1.50)	57	46	0.92 (0.62, 1.37)	92	85	0.99 (0.73, 1.34)
Q5	40	53	1.20 (0.77, 1.80)	48	43	1.02 (0.66, 1.58)	77	83	1.12 (0.80, 1.56)
<i>p</i> <i>interaction</i>			0.74			0.43			0.60

^a adjusted for age, race, education level, WHI Hormone Trial Randomization assignment (HTR arm), baseline 3MSE level, smoking status, physical activity, diabetes status, BMI, family income, depression, history of CVD and total energy intake

^b aMED, alternate Mediterranean Diet

^c Quintile 1 represents the least healthy quintile

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^e HEI-2010, Healthy Eating Index–2010

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