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### Publication Date

2024-05-01

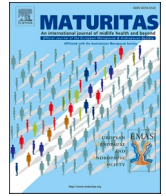
### DOI

10.1016/j.maturitas.2024.108030

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Peer reviewed



## Original article

## Associations of empirically derived dietary patterns and cognitive performance in older men: Results of the Osteoporotic Fractures in Men (MrOS) study

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## ARTICLE INFO

## Keywords:

Dietary pattern  
Older men  
Dementia  
Cognition  
Factor analysis

## ABSTRACT

**Objective:** The aim of this study was to examine associations between empirically derived dietary pattern scores and cognition, as well as risk of cognitive decline, over an average of 4.6 ( $\pm$  0.3) years in older men.

**Materials and methods:** This analysis was conducted as part of the Osteoporotic Fractures in Men (MrOS) prospective cohort study. Diet was assessed at Visit 1 (3/2000–4/2002) by food frequency questionnaire, and dietary patterns (Western and Prudent) were derived by factor analysis. The analytic cohort comprised 4231 community-dwelling American men who were aged 65 years or more. Cognitive function was assessed with the Modified Mini-Mental State exam (3MS) and the Trails B test at Visit 1 and at Visit 2 (3/2005–5/2006). Associations between dietary pattern score and cognition and risk of cognitive decline were estimated using mixed effects regression models. Model 1 was adjusted for age, clinic site and total energy intake (TEI). Model 2 was further adjusted for calcium and vitamin D supplement use, body mass index (BMI), physical activity, smoking, diabetes and hypertension (Western diet group) and education, calcium and vitamin D supplement use, depression, BMI, physical activity, smoking and stroke (Prudent diet group).

**Results:** Adherence to the Western dietary pattern was associated with higher 3MS scores and shorter Trails B test time at Visit 1 in Model 2. Adherence to the Prudent dietary pattern was associated with higher 3MS scores in Model 1 but not Model 2. There were no independent associations between dietary pattern scores and risk of cognitive decline 4.6 ( $\pm$  0.3) years later at Visit 2.

**Conclusion:** The results do not support a robust protective effect of the Prudent dietary pattern on cognition in the MrOS cohort. Associations between the Western dietary pattern and better cognitive scores should be interpreted

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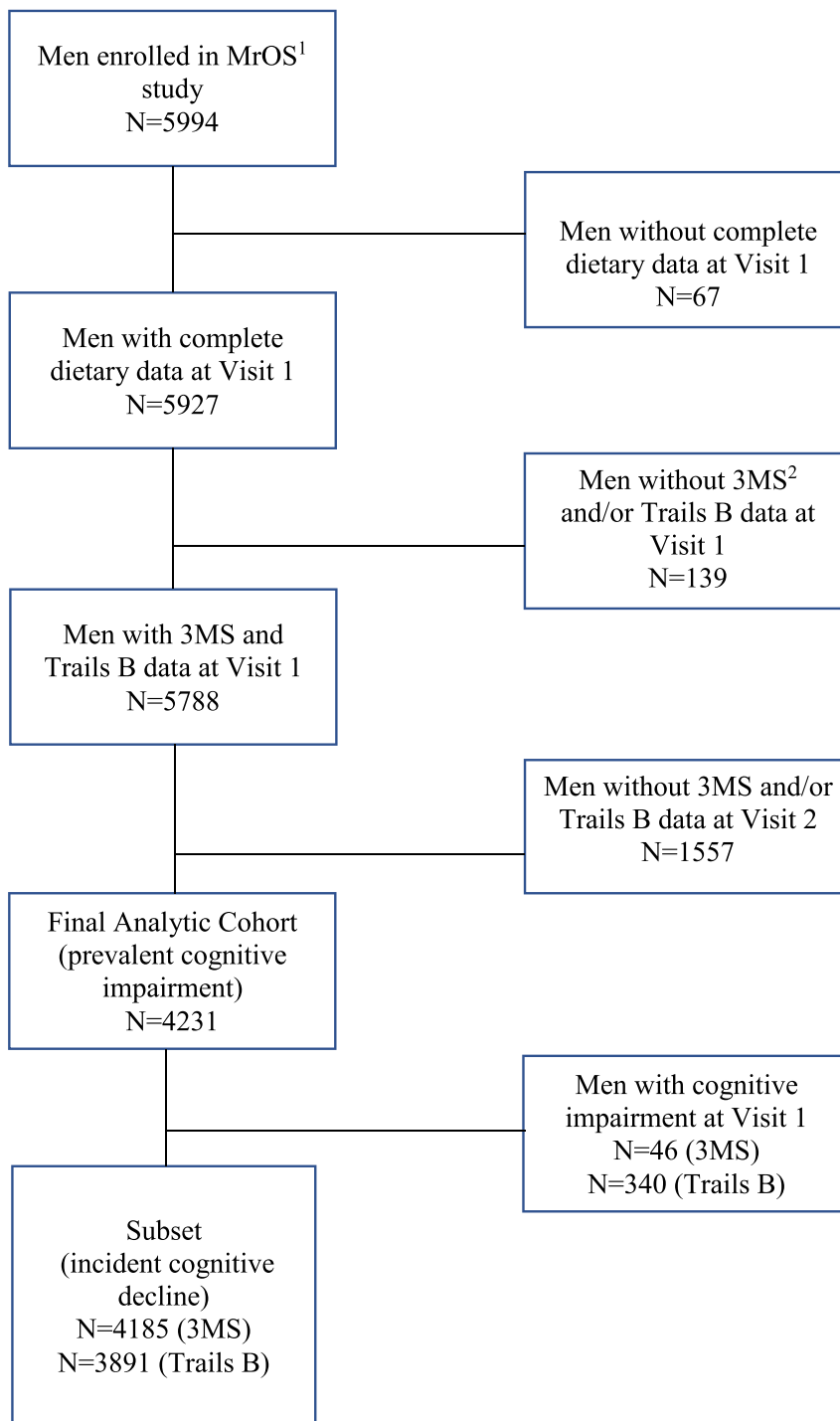
<https://doi.org/10.1016/j.maturitas.2024.108030>

Received 18 November 2023; Received in revised form 3 May 2024; Accepted 25 May 2024

Available online 31 May 2024

0378-5122/Published by Elsevier B.V.

with caution. Further research is needed to understand the complex interactions between dietary patterns and cognition in older men.



**Fig. 1.** Progression of participants through MrOS studies. Reasons for not including participants are given on the right. MrOS Visit 1 (March 2000–April 2002) MrOS Visit 2 (March 2005–May 2006); mean follow up time: 4.6 (± 0.3) years [1]MrOS, Osteoporotic Fractures in Men [2]3MS, Modified Mini-Mental State exam.

## 1. Introduction

As a leading cause of disability and dependency, dementia affects an estimated 50 million people worldwide, and 82 million are predicted to develop this devastating condition by 2030 [1]. Although the strongest risk factors for dementia are advanced age and genetics [2], lifestyle factors such as diet also impact the cognitive trajectory [1,3,4]. Diet may affect cognitive function directly and indirectly in a complex and multifactorial manner, such as through chronic diseases, oxidative stress, inflammation, neurotransmitter synthesis, cell signaling, cellular energy metabolism and cardiovascular mechanisms [5–7].

Dietary patterns may be more predictive of disease risk than individual nutrients since dietary patterns capture cumulative effects of the overall diet [3,8]. There are different approaches to assessing dietary patterns, including *a priori* (hypothesis driven) and *a posteriori* (exploratory) methods [9]. Extensive *a priori* work has focused on the Mediterranean dietary pattern, which has been shown to mitigate cognitive decline in many (but not all) studies [1]. However, there is still a need for additional research to elucidate the relationships between dietary patterns and cognitive decline [5,10,11].

*A posteriori* approaches use exploratory statistical methods to summarize the whole dietary intake into representative profiles [12]. One exploratory technique is factor analysis, which identifies dietary patterns by aggregating highly correlated food items [13]. Factor analysis allows for exploration of underlying patterns that explain variation in eating habits and accounts for complex correlations within the food matrix [14]. Compared with studies using *a priori* approaches, relatively few studies have examined dietary patterns and cognitive decline using *a posteriori* techniques [14]. Moreover, there is a paucity of longitudinal studies examining empirically derived dietary patterns and cognitive decline [12].

Derivation of dietary patterns by factor analysis has been employed in the Osteoporotic Fractures in Men (MrOS) cohort of American men, 65 years and older. Two main dietary patterns (Western and Prudent) were derived at Visit 1 (baseline), and 9.5 % of diet variability (5.3 % and 4.2 % respectively) was represented by these two patterns. The Western dietary pattern was characterized by high intakes of hamburger, fries, processed meats, gravy, cheese, ice cream, pastries, mayonnaise and white bread. The Prudent dietary pattern was characterized by high intakes of carrots, broccoli, spinach, green beans, green salad, cabbage, baked beans, tomatoes, non-fried fish and vegetable soup (Supplement 1) [15]. Similar dietary patterns have been derived in other studies and were associated with cognitive outcomes [16–18]. For example, high adherence to a Prudent dietary pattern was associated with attenuated cognitive decline based on the Modified Mini-Mental State exam (3MS) score, and high adherence to a Western dietary pattern was associated with greater cognitive decline over 6 years in a cohort of Swedish adults at least 60 years old at baseline [19].

The first aim of the present study was to examine associations of the empirically derived dietary pattern scores and cognition as assessed by 3MS score and Trails B test time in the MrOS cohort of older men. The second aim was to examine associations of the dietary pattern scores and risk of cognitive decline over an average of 4.6 ( $\pm$  0.3) years.

The hypothesis was that high adherence to the Western dietary pattern would be associated with lower cognition and greater risk of cognitive decline, whereas high adherence to the Prudent dietary pattern would be associated with higher cognition and reduced risk of cognitive decline.

## 2. Methods

### 2.1. Study population

MrOS is a prospective cohort study examining relationships between fracture risk and bone health, lifestyle and other health outcomes in older men (<https://mrosonline.ucsf.edu>) [20]. At the baseline MrOS

visit (Visit 1; 3/2000–4/2002), 5994 community-dwelling men 65 years and older were enrolled at six clinical centers (Birmingham, AL; Minneapolis, MN; Palo Alto, CA; Monongahela Valley near Pittsburgh, PA; Portland, OR; and San Diego, CA). Inclusion criteria for participation included being able to walk without assistance of another person, the ability to provide self-reported data, residing near the study site, not having a bilateral hip replacement, and not having a medical condition that would lead to imminent death [20–23]. All men provided written informed consent, and the study was approved by the Institutional Review Board at each study site, in accordance with the Helsinki Declaration. Surviving MrOS participants were invited to attend the second MrOS visit (Visit 2; 3/2005–5/2006) [15].

The present study included participants who had complete dietary data at Visit 1, as well as complete cognitive data at Visit 1 and Visit 2. A total of 4231 men were included in the final analyses (Fig. 1).

### 2.2. Exposure information

As part of Visit 1, men provided data about their dietary intake during the previous year by completing the Block 98.2 food frequency questionnaire (FFQ), which was a reduced length version of the Block 98 FFQ that was modified for the MrOS study. The Block 98.2 FFQ was based on analyses of NHANES III data and focused on foods most commonly consumed by men with similar demographic characteristics. It was also designed to capture selected nutrients that may influence the risk of osteoporosis and prostate cancer. There were 69 questions about individual food items, 14 questions related to supplement use and 13 questions regarding food preparation and low-fat foods [15,23,24]. Although the modified FFQ did not undergo validation, it is similar to reduced-length questionnaires by the Block group which have been validated [25]. For each food or beverage item, men selected from nine response categories for frequency and four response categories for portion sizes. Men could also utilize a graphical representation to estimate portion size [26]. The Block Dietary Data Systems (NutritionQuest, Berkeley, CA, USA) was used to analyze the FFQs; details have been previously published [23].

Details of the derivation of dietary patterns for MrOS Visit 1 have also been previously published [15]. Briefly, food groups were constructed using dietary data from the FFQs, and the PROC FACTOR procedure in SAS was used to derive dietary patterns. The number of dietary factors was determined based on eigenvalues on a scree plot, as well as robustness and interpretability. An eigenvalue cut point of 3 was used, and varimax rotation of the data was performed to obtain uncorrelated factors with improved interpretability. Factor loadings for each food group were calculated across the dietary patterns, and factor scores for each participant were calculated for the dietary patterns. Factor scores represent variation that is common across many variables/foods. Factor loadings indicate direction and strength of association between the original foods and a factor score. For example, a high score on factor X for a particular participant indicates that the participant consumes larger-than-average quantities of the foods with high loadings for factor X. The term “adherence” was used to describe how closely the usual intake of each participant aligned with each dietary pattern. The dietary patterns were divided into quartiles, with quartile 1 representing low adherence, and quartile 4 representing high adherence to each dietary pattern [15].

### 2.3. Outcome ascertainment

Trained staff administered cognitive tests at each clinic visit. The 3MS test measures global cognitive function on scale of 0 to 100. The 3MS test is based on the Mini Mental Status Exam (MMSE) with additional items related to long-term memory, delayed recall, abstract thinking and category fluency. Higher 3MS scores indicate better cognitive functioning, and a decrease in 3MS score suggests cognitive decline [21,27]. Cognitive function was also measured using the Trails B

**Table 1**

Baseline characteristics of MrOS participants across quartiles of Western dietary pattern score, mean  $\pm$  SD or n (%) (n = 4231 men).

Characteristic	Q1: low (N = 1057)	Q2: (N = 1058)	Q3: (N = 1058)	Q4: high (N = 1058)	p- value
Age (years)	73.2 $\pm$ 5.5	73 $\pm$ 5.4	72.6 $\pm$ 5.2	72 $\pm$ 5.1	<0.0001*
African American	30 (2.8)	32 (3)	27 (2.6)	35 (3.3)	0.770
<High school education	39 (3.7)	41 (3.9)	48 (4.5)	61 (5.8)	0.087
Married	870 (82.3)	901 (85.2)	896 (84.7)	893 (84.4)	0.287
Calcium supplement use	428 (42)	371 (36.3)	340 (33.3)	317 (31)	<0.0001*
Vitamin D supplement use	177 (17.4)	125 (12.3)	103 (10.1)	95 (9.3)	<0.0001*
GDS score $\geq$ 6	31 (4.4)	42 (6.1)	33 (4.9)	47 (7.1)	0.114
BMI (kg/m <sup>2</sup> )	26.3 $\pm$ 3.5	27.2 $\pm$ 3.7	27.6 $\pm$ 3.6	28.6 $\pm$ 4	<0.0001*
PASE score	147.9 $\pm$ 67.8	153.3 $\pm$ 65	153 $\pm$ 67	156.8 $\pm$ 68.8	0.024*
Current smoker	11 (1)	20 (1.9)	31 (2.9)	62 (5.9)	<0.0001*
Drinks per day >2	104 (9.9)	133 (12.6)	137 (13)	125 (11.8)	0.119
Total energy intake (kcal)	1171 $\pm$ 412.9	1380.2 $\pm$ 372.3	1642.1 $\pm$ 359.2	2291.7 $\pm$ 651.9	<0.0001*
Stroke	53 (5)	44 (4.2)	41 (3.9)	53 (5)	0.470
Diabetes	68 (6.4)	90 (8.5)	108 (10.2)	114 (10.8)	0.002*
Hypertension	391 (37)	416 (39.3)	442 (41.8)	466 (44.1)	0.007*

P-values for categorical data are from chi-square tests for homogeneity. P-values for continuous data are from an analysis of variance for normally distributed data and the Kruskal-Wallis test for skewed data.

BMI (Body Mass Index), GDS (Geriatric Depression Scale), MrOS (Osteoporotic Fractures in Men), PASE (Physical Activity Scale for the Elderly).

\*  $p < 0.05$ .

test. Shorter completion time of this test indicates better cognitive functioning, and an increase in completion time suggests cognitive decline [21,28]. In this study, prevalent cognitive impairment was defined as a 3MS score <80 and/or Trails B test time >1.5 standard deviations above the mean. Men who had cognitive impairment at Visit 1 ( $n = 46$  as assessed by 3MS and  $n = 340$  as assessed by Trails B test time) were excluded from the longitudinal analyses for incident cognitive decline (Fig. 1). For men without cognitive impairment at Visit 1, incident cognitive decline was defined as a 3MS score <80 by Visit 2 or decline of at least one standard deviation change in 3MS score by Visit 2. Incident cognitive decline was also defined as a Trails B test time one standard deviation or more above the sample mean change in completion time for participants without prevalent cognitive impairment at Visit 1 [29].

#### 2.4. Other measures

At Visit 1, participants completed a comprehensive questionnaire which included demographic information, medical history and lifestyle habits. Physical activity was measured with the Physical Activity Scale for the Elderly (PASE) [30]. Depression score was assessed using the Geriatric Depression Scale (GDS) [31]. Dietary supplement use (calcium and vitamin D) in the past 30 days was assessed with a computerized medication coding directory [32]. Height was measured using a wall-mounted stadiometer, and body weight was measured using balance beam or digital scales. Body mass index (BMI) was calculated using the formula weight (kg)/height (m<sup>2</sup>). Total energy intake (TEI) was estimated from FFQ data.

**Table 2**

Baseline characteristics of MrOS participants across quartiles of Prudent dietary pattern score, mean  $\pm$  SD or n (%) (n = 4231 men).

Characteristic	Q1: Low (N = 1057)	Q2: (N = 1058)	Q3: (N = 1058)	Q4: High (N = 1058)	p- value
Age (years)	72.4 $\pm$ 5.2	72.9 $\pm$ 5.4	72.8 $\pm$ 5.5	72.7 $\pm$ 5.3	0.199
African American	36 (3.4)	34 (3.2)	27 (2.6)	27 (2.6)	0.531
<High school education	62 (5.9)	38 (3.6)	49 (4.6)	40 (3.8)	0.046*
Married	867 (82)	901 (85.2)	910 (86)	882 (83.4)	0.055
Calcium supplement use	300 (29.6)	345 (33.6)	392 (38.6)	419 (40.7)	<0.0001*
Vitamin D supplement use	94 (9.3)	119 (11.6)	130 (12.9)	157 (15.3)	0.001*
GDS score $\geq$ 6	49 (7.3)	26 (3.8)	37 (5.4)	41 (5.8)	0.048*
BMI (kg/m <sup>2</sup> )	28 $\pm$ 3.8	27.4 $\pm$ 3.4	27.4 $\pm$ 3.9	26.9 $\pm$ 3.9	<0.0001*
PASE score	151.4 $\pm$ 66.4	149.8 $\pm$ 64.9	150.1 $\pm$ 66.4	159.6 $\pm$ 70.7	0.002*
Current smoker	56 (5.3)	30 (2.8)	17 (1.6)	21 (2)	<0.0001*
Drinks per day >2	141 (13.4)	125 (11.8)	127 (12)	106 (10)	0.129
Total energy intake (kcal)	1364.6 $\pm$ 549.9	1485 $\pm$ 537.7	1651 $\pm$ 549.8	1984.6 $\pm$ 680.6	<0.0001*
Stroke	64 (6.1)	50 (4.7)	38 (3.6)	39 (3.7)	0.021*
Diabetes	76 (7.2)	97 (9.2)	96 (9.1)	111 (10.5)	0.067
Hypertension	418 (39.6)	439 (41.5)	431 (40.7)	427 (40.4)	0.834

P-values for categorical data are from chi-square tests for homogeneity. P-values for continuous data are from an analysis of variance for normally distributed data and the Kruskal-Wallis test for skewed data.

BMI (Body Mass Index), GDS (Geriatric Depression Scale), MrOS (Osteoporotic Fractures in Men), PASE (Physical Activity Scale for the Elderly).

\*  $p < 0.05$ .

#### 2.5. Statistical analysis

Missing data were removed during the derivation of the analytic cohort (Fig. 1); therefore, all 4231 men had complete dietary and outcome data. Outcomes were transformed for normality (squared for 3MS score and natural log for Trails B time) and were back transformed for presentation. Baseline participant characteristics were examined across quartiles of dietary pattern score using chi-square tests for categorical variables, and ANOVA for normally distributed continuous variables or Kruskal-Wallis tests for skewed continuous variables. These results guided the selection of covariates. Covariates were chosen based on the characteristics that differed significantly across quartiles of each dietary pattern at  $p < 0.05$  (Tables 1 and 2).

To account for between-subject variation and within-subject correlations between repeated cognitive measurements, random effects regression models (PROC MIXED procedure in SAS version 9.4, SAS Institute, Cary, NC, USA) were used to model changes in cognition over time for each participant. The random effects terms included the intercept (baseline cognitive level) and slope (age/time). The restricted maximum likelihood method was used to estimate model coefficients. Time was modeled as age at the time of each cognitive assessment (calculated using date of birth) and centered on mean age at each visit.

Mixed models were run to associate 3MS score and Trails B time with age/time, exposures and their interaction. Significant interactions indicate a potential impact of the exposure on cognitive changes. Dietary pattern scores were expressed in quartiles, with quartile 1 serving as the reference. For each analysis, Model 1 was adjusted for age, clinic site and TEI. For the Western dietary pattern, Model 2 was further adjusted for calcium supplement use, vitamin D supplement use, BMI, PASE, current smoking, diabetes mellitus and hypertension. For the Prudent dietary pattern, Model 2 was further adjusted for education, calcium

**Table 3**

Associations of dietary pattern scores and cognition assessed by a) 3MS and b) Trails B test time in older men, (n = 4231).

a)	Model 1 <sup>1</sup>			Model 2 <sup>2</sup>		
	Beta-coefficient <sup>3</sup>	95 % CI	P-value	Beta-coefficient	95 % CI	P-value
Western dietary pattern						
Q1	Referent			Referent		
Q2	0.35	0, 0.71	0.05*	0.43	0.07, 0.77	0.02*
Q3	0.31	-0.07, 0.69	0.11	0.52	0.15, 0.89	0.006**
Q4	0.19	-0.29, 0.65	0.44	0.57	0.1, 1.03	0.02*
Prudent dietary pattern						
Q1	Referent			Referent		
Q2	0.80	0.44, 1.14	<0.001***	0.71	0.28, 1.12	0.001***
Q3	0.42	0.06, 0.78	0.02*	0.31	-0.13, 0.73	0.17
Q4	0.49	0.11, 0.87	0.01**	0.08	-0.39, 0.54	0.73
b)						
b)	Model 1 <sup>1</sup>			Model 2 <sup>2</sup>		
	Beta-coefficient <sup>3</sup>	95 % CI	P-value	Beta-coefficient	95 % CI	P-value
Western dietary pattern						
Q1	Referent			Referent		
Q2	-3.23	-5.93, -0.21	0.04*	-3.1	-5.15, -0.52	0.02*
Q3	-3	-5.87, 0.22	0.07	-3.5	-5.67, -0.82	0.01*
Q4	-3.3	-6.87, 0.77	0.11	-4.9	-7.47, -1.52	0.006**
Prudent dietary pattern						
Q1	Referent			Referent		
Q2	-4.48	-7.11, -1.55	0.004**	-3.02	-5.47, 0.2	0.06
Q3	0.1	-2.89, 3.42	0.95	1.90	-1.29, 6	0.27
Q4	0.05	-3.11, 3.58	0.98	2.26	-1.15, 6.64	0.21

<sup>1</sup> Adjusted for age, clinic site and total energy intake (TEI).<sup>2</sup> Model 1 plus calcium supplement use, vitamin D supplement use, BMI, PASE, current smoker, DM, HTN for Western dietary pattern. Model 1 plus education, calcium supplement use, vitamin D supplement use, GDS, BMI, PASE, current smoker, stroke for Prudent dietary pattern.<sup>3</sup> Estimated effect of the dietary pattern scores at the average age after centering on the mean age at each visit.

\* p&lt;0.05.

\*\* p&lt;0.01.

\*\*\* p&lt;0.001.

supplement use, vitamin D supplement use, GDS, BMI, PASE, current smoking and stroke.

For the analyses of dietary pattern scores and cognition, beta-coefficients represent the estimated effects of the dietary pattern scores at the average age after centering on the mean age at each visit. For the analyses of dietary pattern scores and cognitive decline, beta-coefficients of the interaction terms represent the estimated effects of the dietary pattern scores on the slope relating age and cognition. Statistical significance levels reported were two-sided. The SAS code and full model outputs are presented in Supplements 2, 3 and 4.

### 3. Results

#### 3.1. Baseline characteristics

The cohort was comprised of 4231 men, with an average age of 72.7 ( $\pm 5.3$ ) years and a mean BMI of 27.4 ( $\pm 3.8$ ) kg/m<sup>2</sup> at Visit 1. The majority (97.1 %) of men identified as White, and 84.1 % were married. Mean follow-up time was 4.6 ( $\pm 0.3$ ) years.

Baseline characteristics of the cohort by quartile of dietary pattern are presented in Tables 1 and 2. Compared with men with low adherence to the Western dietary pattern, men with high adherence were younger, had higher BMI, consumed more energy, and were more likely to smoke, have diabetes and hypertension compared with men with low adherence. Moreover, they were less likely to take calcium and vitamin D supplements. Men with high adherence to the Prudent dietary pattern were better educated, had lower BMI, and were less likely to smoke or have a history of depression or stroke compared with men with low adherence. They were more likely to take calcium and vitamin D

supplements. Men with high adherence to the Prudent dietary pattern also consumed more energy compared with men with low adherence. Men with high adherence to either dietary pattern were more active compared with men with low adherence.

#### 3.2. Cognition

At Visit 1, 46 men (1.1 %) met the definition of cognitive impairment based on 3MS score, while 340 (8 %) were considered cognitively impaired based on Trails B test time (data not shown). Compared with those in quartile 1 of the Western dietary pattern (lowest adherence), men in quartile 2 were more likely to have a higher 3MS score (positive beta-coefficient) and shorter Trails B test time (negative beta-coefficient), in Model 1. Associations between quartiles 3 and 4 of the Western dietary pattern and cognition were non-significant in Model 1 for 3MS score and Trails B test time (Table 3). However, in Model 2, associations between all three quartiles of the Western dietary pattern and cognition were significant for both 3MS score and Trails B test time.

Compared with men in quartile 1, men who were more adherent to the Prudent dietary pattern (quartiles 2, 3 and 4) were more likely to have higher 3MS scores in Model 1. These associations retained significance for quartile 2 (but not quartiles 3 and 4) in Model 2. Compared with men in quartile 1 of the Prudent dietary pattern, men in quartile 2 were more likely to have shorter Trails B test times in Model 1 (but not Model 2). Associations between quartiles 3 and 4 of the Prudent dietary pattern and Trails B test time were non-significant in both models (Table 3).

**Table 4**

Associations of dietary pattern scores and risk of cognition decline over 4.6 ( $\pm$  0.3) years assessed by a) 3MS ( $n = 4185$ ) and b) Trails B test time in older men, ( $n = 3891$ ).

a)	Model 1 <sup>1</sup>			Model 2 <sup>2</sup>		
	Beta-coefficient <sup>3</sup>	95 % CI	P-value	Beta-coefficient	95 % CI	P-value
Western dietary pattern						
Q1	Referent			Referent		
Q2	-0.09	-0.16, -0.02	0.01**	-0.09	-0.16, -0.02	0.01*
Q3	-0.06	0.01, -0.13	0.11	-0.05	0.15, -0.12	0.13
Q4	0	-0.07, 0.07	0.99	-0.01	-0.08, 0.05	0.68
Prudent dietary pattern						
Q1	Referent			Referent		
Q2	-0.02	-0.09, 0.05	0.66	0.02	-0.07, 0.10	0.67
Q3	-0.05	-0.12, 0.02	0.18	0	-0.09, 0.08	0.94
Q4	-0.04	-0.11, 0.03	0.26	-0.03	-0.12, 0.05	0.42
b)						
b)	Model 1 <sup>1</sup>			Model 2 <sup>2</sup>		
	Beta-coefficient <sup>3</sup>	95 % CI	P-value	Beta-coefficient	95 % CI	P-value
Western dietary pattern						
Q1	Referent			Referent		
Q2	0.45	-0.11, 1.05	0.12	0.43	-0.05, 1.08	0.08
Q3	0.14	-0.41, 0.74	0.64	0.08	-0.38, 0.63	0.75
Q4	0.23	-0.33, 0.85	0.43	0.3	-0.19, 0.88	0.25
Prudent dietary pattern						
Q1	Referent			Referent		
Q2	-0.16	-0.72, 0.44	0.59	-0.26	-0.78, 0.41	0.46
Q3	0.21	-0.36, 0.82	0.48	0.09	-0.47, 0.8	0.77
Q4	0.31	-0.26, 0.94	0.3	0.28	-0.31, 1.01	0.39

<sup>1</sup> Adjusted for age, clinic site and total energy intake (TEI).

<sup>2</sup> Model 1 plus calcium supplement use, vitamin D supplement use, BMI, PASE, current smoker, DM, HTN for Western dietary pattern. Model 1 plus education, calcium supplement use, vitamin D supplement use, GDS, BMI, PASE, current smoker, stroke for Prudent dietary pattern.

<sup>3</sup> Beta-coefficient of interaction terms (estimated effects of dietary pattern scores on the slope relating age and cognition).

\*  $p \leq 0.05$ .

\*\*  $p \leq 0.01$ .

### 3.3. Risk of cognitive decline

Among the 4185 men without cognitive impairment (by 3MS score) at Visit 1, 3MS scores declined by an average of 1.7 ( $\pm$  4.7) points, and 559 men (13.4 %) had developed cognitive impairment based on 3MS score by Visit 2. Additionally, among the 3891 men without cognitive impairment (by Trails B test time) at Visit 1, Trails B test time increased by an average of 1.3 ( $\pm$  44.3) seconds, and 438 men (11.3 %) were considered cognitively impaired based on Trails B test time by Visit 2 (data not shown).

Compared with those in quartile 1 of the Western dietary pattern, men in quartile 2 had increased risk of cognitive decline, as defined by lower 3MS score (negative beta-coefficient) in Model 1 and Model 2 (Table 4). Associations between quartiles 3 and 4 of the Western dietary

pattern and risk of cognitive decline by 3MS score were non-significant in both models. Associations between the Western dietary pattern and risk of cognitive decline by Trails B test time were non-significant in both models. There were no significant associations between Prudent dietary pattern score and risk of cognitive decline whether assessed by 3MS score or Trails B test time (Table 4).

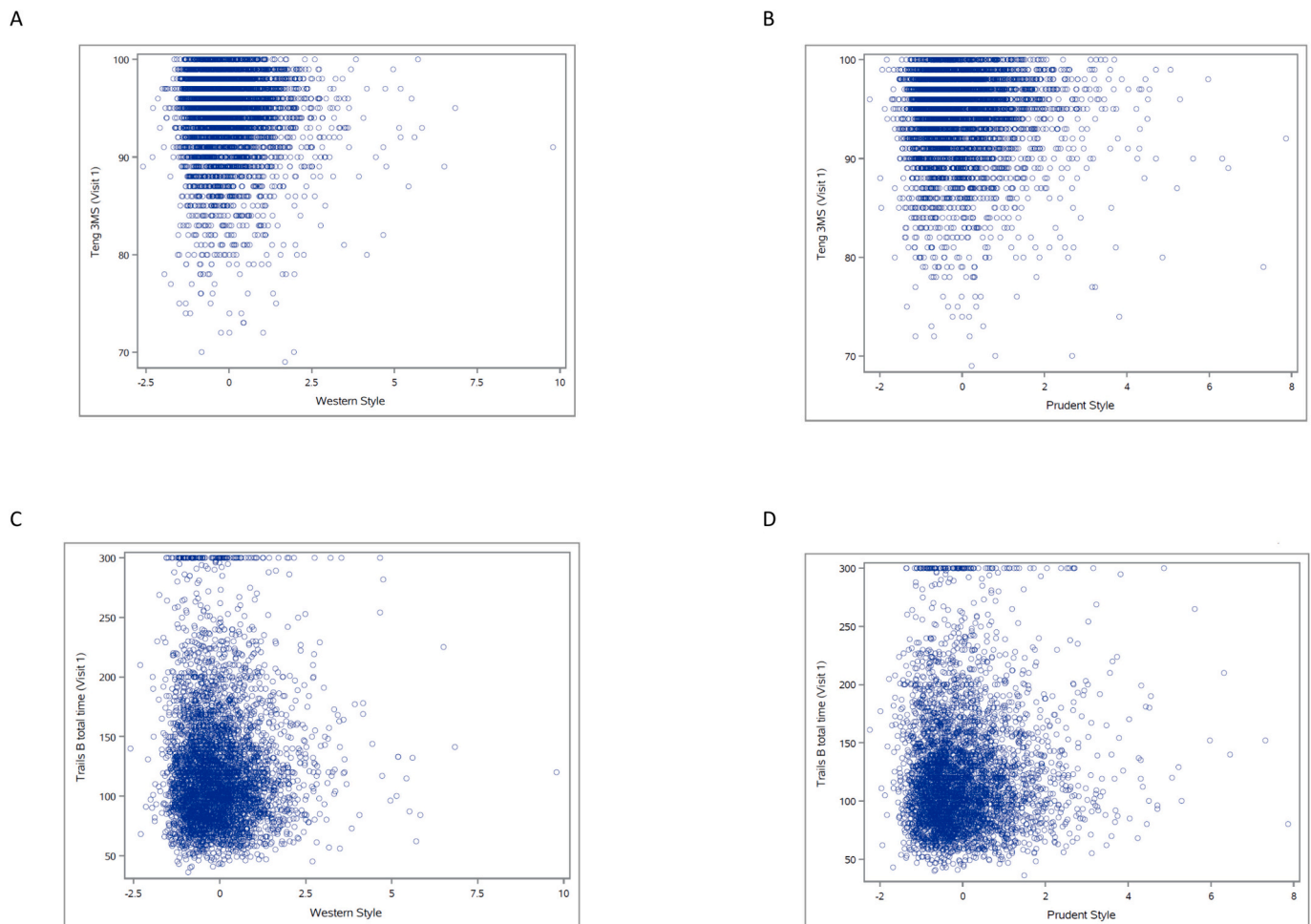
Scatterplots of dietary pattern scores and cognitive measures at both visits are presented in Figs. 2 and 3.

## 4. Discussion

Given the ubiquitous and devastating nature of dementia among older adults worldwide, relationships between modifiable lifestyle factors and cognition in aging merit investigation. The present study addresses a knowledge gap by examining associations between empirically derived dietary patterns and cognition and risk of cognitive decline in the MrOS cohort of American men 65 years and older. Overall, results do not support the hypothesis that adherence to a Prudent dietary pattern would protect against cognitive impairment and risk of cognitive decline. Contrary to the hypothesis, in Model 2, greater adherence to a Western dietary pattern was associated with better cognition but was not associated with risk of cognitive decline. It is important to note that in the present study, risk of cognitive decline is inferred from the beta-coefficient of interaction terms rather than modeled directly.

Results of the present study contribute to a mixed body of literature regarding dietary patterns and cognitive outcomes in older adults. Concordant with the present study, in the NuAge cohort of French-Canadian adults, dietary patterns were not associated with cognitive scores at baseline or over 2.9 years [12]. In a population of Japanese men and women at least 85 years old, neither a “traditional Japanese” dietary pattern (high in vegetables, seaweed, legumes and fish) nor a “noodles and confectioneries” dietary pattern (high in noodles, confectioneries and non-alcoholic beverages) was associated with cognitive function as assessed with the MMSE in a cross-sectional study [33]. Similarly, null findings between dietary patterns and MMSE scores were also reported in a slightly younger cohort (60 years and older) of Japanese adults [34]. Among adults 65–74 years old in New Zealand, there were no associations between dietary patterns (“Mediterranean,” “Western,” “Prudent”) and six domains of cognitive function [35].

Other previous studies [17,18,36] have reported significant findings between empirically-derived dietary patterns and cognition. Differing results between the present study and these previous reports could be related to heterogeneity in study population, age at baseline, length of follow-up, and variation in the derived dietary patterns and cognitive outcomes. In comparison to co-ed studies of French [17] and Quebecer participants [18], the present MrOS cohort included only American males. The majority of MrOS participants were White and thus also distinct from the REasons for Geographic and Racial Differences in Stroke (REGARDS) cohort, another American study in which 42 % of participants were Black [18]. Like others [18,36], the MrOS study utilized a FFQ to assess dietary intake, although 24 h diet records were used in the French study [17]. In all studies, “healthy” and “unhealthy” dietary patterns were identified, but the specific factor loadings of these dietary patterns varied between studies. For example, in the cohort ( $n = 3054$ ) of middle aged French adults, the healthy dietary pattern was high in fruit, whole grains, fresh dairy, vegetables, breakfast cereal, tea, vegetable fat, nuts and fish and was associated with better global cognitive function and verbal memory over a 13 year period [17]. In the Quebecer study ( $n = 1099$ ), the healthy dietary pattern was rich in vegetables, fruit, fish, poultry, and low fat dairy and was associated with higher 3MS score at baseline for participants with greater socioeconomic position (SEP) and less cognitive decline over 3 years for participants with low SEP [18]. In this study, SEP was assessed with multiple variables, including household income, educational attainment and occupational prestige. (In the MrOS study, education is typically used as a proxy for SEP since other socioeconomic data are missing or poorly



**Fig. 2.** Scatterplot of dietary pattern scores and cognitive measures at Visit 1.  
 A) Western dietary pattern score and Modified Mini-Mental State Exam (3MS) score  
 B) Prudent dietary pattern score and 3MS score  
 C) Western dietary pattern score and Trails B test time (seconds)  
 D) Prudent dietary pattern score and Trails B test time (seconds).

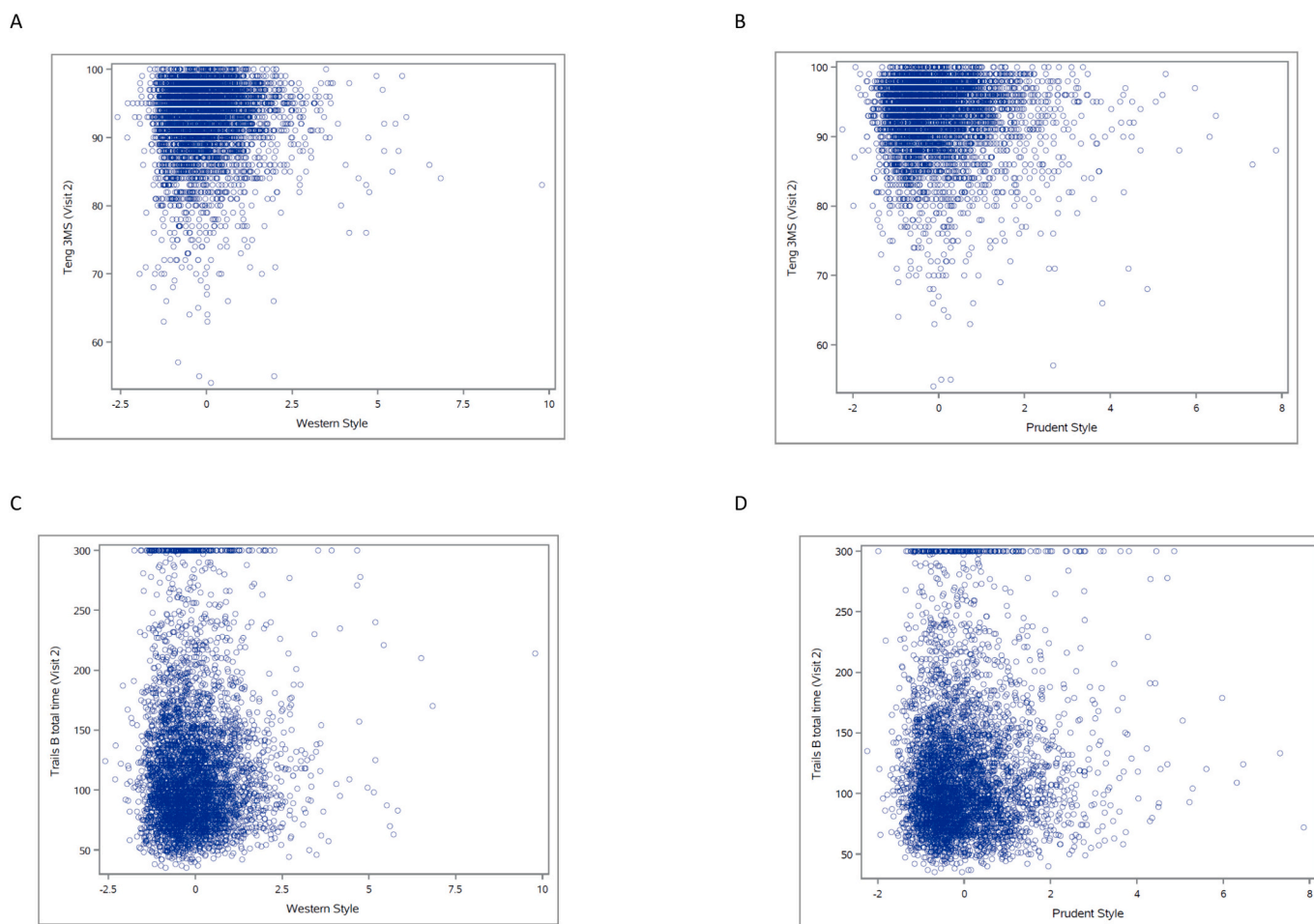
reported). Assessment of cognition has varied widely across studies, including assessment with 3MS [18], as well as the Six Item Screener (SIS), domain-specific assessments (Word List Learning [WLL] and Word List Delayed Recall [WLDL]) [36], and neuropsychological tests of verbal fluency, the RI-48 cured recall test, trail making tests and forward and backward digit spin [17].

The seemingly protective effect of the Western dietary pattern in the present study should be interpreted with caution and may have been related to covariate selection. Few previous studies have reported comparable findings, although in the REGARDS study, the highest quintile of the “convenience” dietary pattern (high in mixed dishes with meat, pizza, Chinese food and Mexican dishes) was associated with significantly higher performance on WLL [36]. Confirming associations between diet and cognitive health is challenging since, unlike single lifestyle factors such as smoking, diet is multidimensional and includes both healthy and unhealthy elements [6]. The clinical relevance of the present study may be limited, but the findings here, in the context of prior research, indicate a complex relationship between diet and cognition. Future observational studies could utilize techniques such as network analysis to model the interconnected relationships among foods consumed by participants with and without dementia [37]. Such non-intuitive (non-linear) data may serve to complement results from other approaches. Additionally, web-based FFQs with branching logic may better capture dietary intake, particularly in diverse populations,

and biomarkers of nutritional metabolism, as well as study of the microbiota, may enable the establishment of nutrient-specific neuroprotective thresholds [6].

Strengths of this study included a large sample size, enrollment from the community, validated outcome measures and adjustment for multiple potentially confounding variables. Though MrOS has been ongoing for over twenty years, use of data from Visits 1 and 2 in the present study was appropriate since men were younger and less likely to have cognitive impairment at baseline compared to later visits. Limitations of this study include a population that was predominantly White, which limits generalizability to other populations. The MrOS study did not include measurement of apolipoprotein E (APOE) gene, which is related to risk of Alzheimer's disease [38]. The brief FFQ used in this study was approximately two thirds the length of a standard FFQ and may have underestimated energy intake [15]. Additionally, factor analysis requires researchers to make subjective decisions when handling the data and is more difficult to reproduce in different populations compared with *a priori* methods [39,40]. Lastly, dietary patterns were assessed at Visit 1 but not Visit 2, and it is unknown whether participants adhered to the Prudent or Western dietary patterns during the time between these visits. Long-term adherence to either dietary pattern could be associated with cognitive measures at Visit 2, but unfortunately the study design precludes this assessment.





**Fig. 3.** Scatterplot of dietary pattern scores and cognitive measures at Visit 2  
 A) Western dietary pattern score and Modified Mini-Mental State Exam (3MS) score  
 B) Prudent dietary pattern score and 3MS score  
 C) Western dietary pattern score and Trails B test time (seconds)  
 D) Prudent dietary pattern score and Trails B test time (seconds).

## 5. Conclusion

In the MrOS cohort of men 65 and older, the Prudent dietary pattern was not associated with cognition in the fully adjusted model. Surprisingly, a Western dietary pattern was associated with better cognitive scores in the fully adjusted model, but this result should be interpreted with caution. There were no independent associations between the empirically derived dietary pattern scores and risk of cognitive decline 4.6 ( $\pm$  0.3) years later. Further research is needed to better understand the complex interactions between dietary patterns and cognition in older men.

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.maturitas.2024.108030>.

## Contributors

Tara S. Rogers-Soeder participated in the study concept and design, data analysis and interpretation, and drafting and editing of the manuscript.

Sheena Patel participated in data analysis and interpretation, drafting and editing the manuscript and critical review.

James M. Shikany participated in the study concept and design, data collection, data analysis and interpretation and critical review.

Lisa Langsetmo participated in the study concept and design, data analysis and interpretation and critical review.

Suzanne E. Judd participated in the study concept and design, data analysis and interpretation and critical review.

Kristine E. Ensrud participated by providing critical review.

Erin LeBlanc participated in data analysis and interpretation and critical review.

Jane A Cauley participated by providing critical review.

Susan Redline participated by providing critical review.

Howard A. Fink participated in data analysis and interpretation and critical review.

Nancy E. Lane participated in the study concept and design, data analysis and interpretation, drafting of the manuscript and critical review.

All authors saw and approved the final version and no other person made a substantial contribution to the paper.

## Funding

The Osteoporotic Fractures in Men (MrOS) Study is supported by National Institutes of Health (NIH) funding. The following institutes provide support: the National Institute on Aging (NIA), the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the National Center for Advancing Translational Sciences (NCATS), and NIH Roadmap for Medical Research under the following grant numbers: U01 AG027810, U01 AG042124, U01 AG042139, U01 AG042140, U01 AG042143, U01 AG042145, U01 AG042168, U01 AR066160, R01

AG066671, and UL1 TR002369.

## Ethical approval

All participants in the Osteoporotic Fractures in Men (MrOS) study provided written informed consent. The study was approved by the Institutional Review Board at each study site, in accordance with the Helsinki Declaration.

## Provenance and peer review

This article was not commissioned and was externally peer reviewed.

## Data sharing and collaboration

There are no linked research data sets for this paper. Data will be made available on request.

## Declaration of competing interest

The authors declare that they have no competing interest.

## Acknowledgements

The authors thank the participants, staff and investigators of the Osteoporotic Fractures in Men (MrOS) study.

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