

# The Mediterranean, Dietary Approaches to Stop Hypertension (DASH), and Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) Diets Are Associated with Less Cognitive Decline and a Lower Risk of Alzheimer's Disease—A Review

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## ABSTRACT

As there is currently no cure for dementia, there is an urgent need for preventive strategies. The current review provides an overview of the existing evidence examining the associations of the Mediterranean, Dietary Approaches to Stop Hypertension (DASH), and Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) diets and their dietary components with cognitive decline, dementia, and Alzheimer's disease (AD). A systematic search was conducted within Ovid Medline for studies published up to 27 March 2019 and reference lists from existing reviews and select articles were examined to supplement the electronic search results. In total, 56 articles were included. Higher adherence to the Mediterranean diet was associated with better cognitive scores in 9 of 12 cross-sectional studies, 17 of 25 longitudinal studies, and 1 of 3 trials. Higher adherence to the DASH diet was associated with better cognitive function in 1 cross-sectional study, 2 of 5 longitudinal studies, and 1 trial. Higher adherence to the MIND diet was associated with better cognitive scores in 1 cross-sectional study and 2 of 3 longitudinal studies. Evidence on the association of these dietary patterns with dementia in general was limited. However, higher adherence to the Mediterranean diet was associated with a lower risk of AD in 1 case-control study and 6 of 8 longitudinal studies. Moreover, higher adherence to the DASH or MIND diets was associated with a lower AD risk in 1 longitudinal study. With respect to the components of these dietary patterns, olive oil may be associated with less cognitive decline. In conclusion, current scientific evidence suggests that higher adherence to the Mediterranean, DASH, or MIND diets is associated with less cognitive decline and a lower risk of AD, where the strongest associations are observed for the MIND diet. *Adv Nutr* 2019;10:1040–1065.

**Keywords:** Mediterranean, DASH, MIND, dietary patterns, dietary components, nutrition, cognition, cognitive decline, dementia, Alzheimer's disease

## Introduction

In 2015 ~47 million people worldwide were diagnosed with dementia, which is the seventh leading cause of death worldwide (1). Due to the global aging population, the number of people living with dementia is expected to

increase to 75 million by 2030 (2). With estimated global costs of dementia of 818 billion US\$ in 2015, representing 1.09% of the global gross domestic product, dementia has a huge impact on societal healthcare costs (2, 3).

As there is currently no cure for dementia, preventative measures are of major importance to reduce the expected rise in dementia cases (2). To date, many studies have examined the role of nutrients and foods in the prevention of cognitive decline, dementia, and Alzheimer's disease (AD) (4–6). Over recent decades, research has shifted towards studying dietary patterns to take into account interactions between nutrients or foods and possible synergic effects of nutrients (7, 8). Three dietary patterns that have been frequently studied in relation to cognitive decline, dementia, or AD are the Mediterranean diet (9), the Dietary Approaches to Stop

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Supplemental Table 1 is available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at

<https://academic.oup.com/advances/>

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Abbreviations used: AD, Alzheimer's disease; CVD, cardiovascular disease; DASH, Dietary Approaches to Stop Hypertension; MCI, mild cognitive impairment; MIND, Mediterranean-DASH Intervention for Neurodegenerative Delay; MMSE, Mini-Mental State Examination; PREDIMED, Prevención con dieta Mediterránea; WHICAP, Washington Heights-Inwood Columbia Aging Project; 24hr, 24-h recall.

Hypertension (DASH) diet (10), and the Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) diet (11).

The Mediterranean diet is a dietary pattern that is consumed in countries surrounding the Mediterranean Sea, for example in Greece (9). Meta-analyses indicate that higher adherence to the Mediterranean diet is associated with better global cognition and episodic memory (12), a lower risk of cognitive impairment (13, 14), and a lower risk of neurodegenerative diseases (13, 15). The Mediterranean diet is characterized by a high consumption of fruits, vegetables, and olive oil, with a moderate consumption of alcohol (16, 17). Similar to the Mediterranean diet, the DASH diet also specifies a high consumption of plant-based foods and additionally limits the intake of SFAs, total fat, cholesterol, and sodium (10). The DASH dietary pattern has been developed to prevent and treat hypertension and has been shown to improve cardiovascular disease (CVD) risk factors, including systolic and diastolic blood pressure and total cholesterol (10, 18). The MIND dietary pattern has been developed to protect the brain and prevent against dementia (11). This dietary pattern is a combination of the Mediterranean diet and the DASH diet and is based on dietary components that have been shown to be neuroprotective. The MIND diet emphasizes natural plant-based foods and limited intakes of animal foods and foods high in saturated fat. Uniquely, the MIND diet also specifies the consumption of berries and green leafy vegetables (11).

So far, 10 reviews have discussed the current evidence on the association of the Mediterranean, DASH, and MIND diets with cognitive decline, dementia, or AD (19–28). However, 5 of these reviews only included a brief summary of the available evidence (19, 21–24). Of the 4 extensive reviews on the topic, 1 review only included studies of the past 5 y (27), 2 reviews only included observational studies (20, 25), and 2 also discussed intervention studies (26, 28). However, 1 of the reviews that also discussed intervention studies only included studies until 2015 (26) and the other only included cohort and intervention studies (28).

Therefore, the aim of the current review is to summarize, evaluate, and compare all existing observational and trial evidence published up to 27 March 2019 for the Mediterranean, DASH, and MIND diets and their dietary components in relation to cognitive decline, dementia, and AD in middle-aged and older adults aged  $\geq 40$  y.

## Methods

### Literature search and study design

For this review, the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines were followed. A systematic search was conducted within Ovid Medline for all studies published in English up to 27 March 2019. Search terms included terms related to cognition, dementia, AD, Mediterranean diet, DASH diet, and MIND diet (**Supplemental Table 1**). Commentaries, letters, editorials, news, and newspaper articles were not screened. A predefined protocol

was not available. The systematic search in Ovid Medline resulted in 163 articles (Supplemental Table 1). Reference lists from existing reviews and select articles were examined to identify studies that were not retrieved by the systematic search in Ovid Medline. This resulted in 6 additional studies. First, titles and abstracts were screened, resulting in 73 potentially relevant articles. Studies were included if: 1) they were performed in adults aged  $\geq 40$  y, 2) they measured exposure to  $\geq 1$  of the 3 dietary patterns of interest (Mediterranean diet, DASH diet, or MIND diet) or to dietary components as part of these 3 dietary patterns, and 3) the outcome measure was related to cognition, cognitive decline, dementia, or AD. The eligibility criteria of participants aged  $\geq 40$  y was selected, because cognitive decline has been shown to be already present in middle age (29). After full-text screening, 56 of the 73 articles were included in this review (**Figure 1**). For the dietary components of the 3 dietary patterns, evidence is restricted to articles identified using the search strategy for the Mediterranean, DASH, and MIND diets in relation to cognitive decline, dementia, and AD. Study selection and data extraction was performed by 1 researcher and checked by a second researcher.

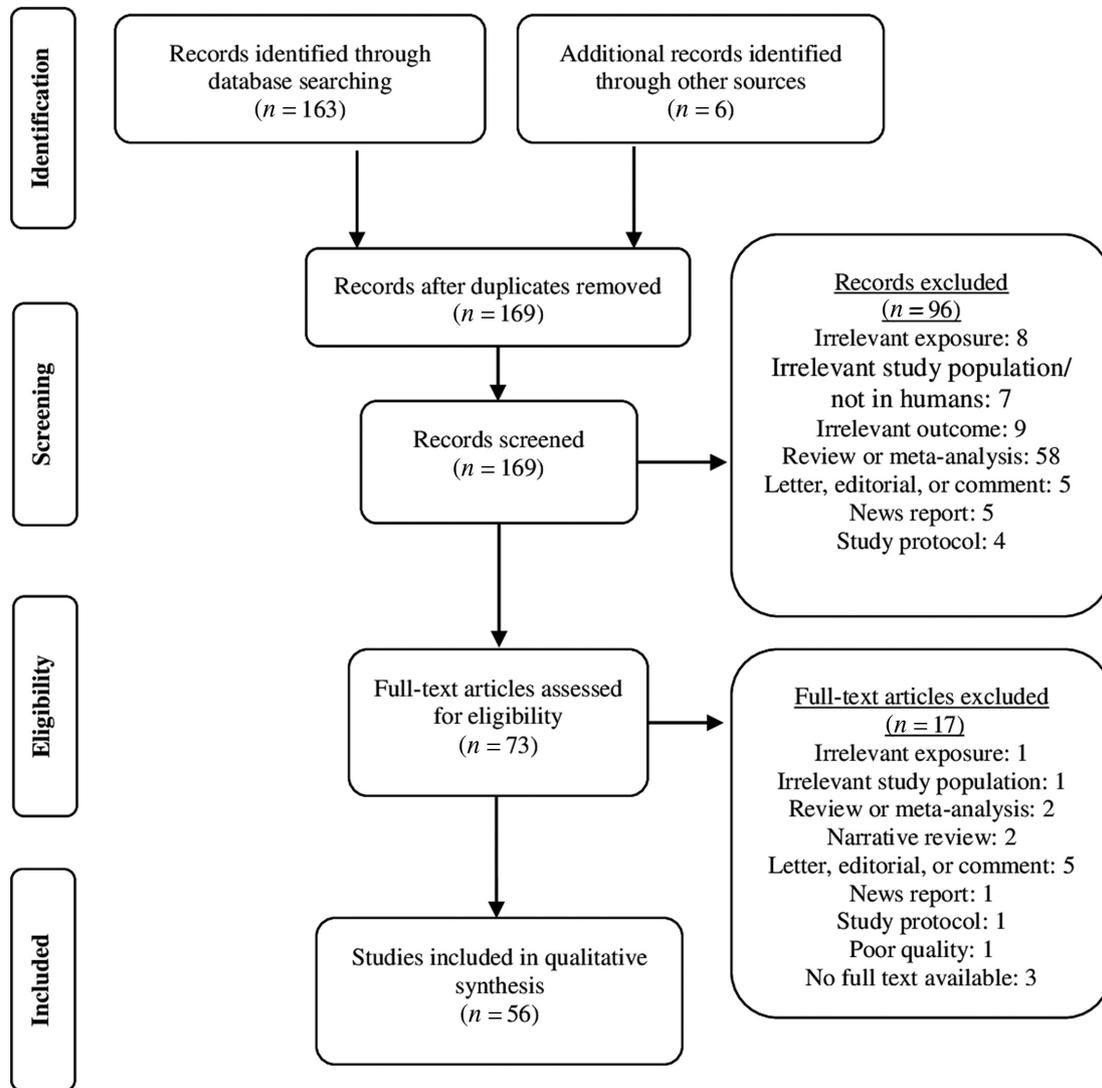
### Quality assessment

The quality of the included studies was assessed according to the following criteria: 1) number of study participants, 2) in the case of prospective studies, duration of follow-up and loss to follow-up, 3) exposure measurement, 4) outcome measurement, and 5) adjustment for potential confounders.

### Dietary pattern scores

The Mediterranean, DASH, and MIND diets all have a plant-based origin with moderate to high amounts of fish, but they differ in types and amounts of dietary components. A detailed list of components per diet can be found in **Table 1**. The assessment of these diets is described below.

Adherence to the Mediterranean diet can be assessed by 2 different scores, namely the original Mediterranean diet score by Trichopoulou et al. (9) and the alternate Mediterranean diet score by Panagiotakos et al. (30). The original score of Trichopoulou et al. ranges from 0 (minimal adherence to the Mediterranean diet) to 9 (maximal adherence) and is based on sex-specific median intake of the study population on 9 components (9). For fish, cereals, fruits + nuts, vegetables, legumes, and MUFA to SFA ratio (MUFA:SFA ratio), a value of 1 is assigned to people who have intake above the median, whereas a value of 0 is assigned to people with intake below the median. For meat and dairy, a value of 1 is assigned to people with intake below the median, whereas a value of 0 is assigned to people with intake above the median. Regarding alcohol, a value of 1 is assigned to people consuming a moderate amount. The alternate score by Panagiotakos et al. ranges from 0 (minimal adherence to the Mediterranean diet) to 55 (maximal adherence) and is based on the consumption of 11 components (30). For each dietary component, a value ranging from 0 to 5 is assigned



**FIGURE 1** Flow diagram of the identified and screened studies on the Mediterranean, DASH, and MIND diets and their dietary components in relation to cognitive decline, dementia, or AD.

to people based on predefined cut-offs of intake. For olive oil, fish, nonrefined cereals, fruits, vegetables, legumes, and potatoes a value of 5 is assigned to people with high intake, whereas for meat and meat products, poultry, and full-fat dairy products a score of 5 is assigned to people without consumption. For alcohol, a value of 5 is assigned to people consuming a moderate amount, whereas a value of 0 is assigned to people with either no intake or very high intake.

Adherence to the DASH dietary pattern can also be assessed by 2 different scores, namely the score by Folsom et al. (31) and the score by Fung et al. (32). The score by Folsom et al. is based on predefined cut-offs of intake of 11 components and ranges from 0 (minimal adherence to the DASH diet) to 11 (maximal adherence). For each dietary component a value of 0, 0.5, or 1 is assigned based on

intake (31). For total grains, whole grains, fruits, vegetables, dairy foods, and nuts + seeds + dry beans a value of 1 is assigned to people with high intake. For sodium, sweets, percentage kcal from fat, percentage kcal from SFAs, and meats + poultry + fish a value of 1 is assigned to people with low intake. The score by Fung et al. is based on 8 dietary components and for each component a score of 1 to 5 is assigned based on quintile of intake (32). For whole grains, fruits, vegetables, nuts and legumes, and low-fat dairy products a score of 5 is assigned to people with the highest quintile of intake, whereas for sodium, red and processed meats, and sweetened beverages a score of 5 is assigned to people with the lowest quintile of intake. Thus, this score ranges from 8 (minimal adherence to the DASH diet) to 40 (maximal adherence).

**TABLE 1** Overview of the dietary components included in the Mediterranean, DASH, and MIND diets

	Mediterranean diet (16, 17)	DASH diet (10)	MIND diet (11)
High amounts	Olive oil	—	Olive oil
	Fish	—	Fish
	Breads and other forms of cereals	Grains	Whole grains
	Fruits	Fruits	Berries
	Vegetables	Vegetables	Green leafy vegetables
	—	—	Other vegetables
	Legumes	Legumes	—
	Nuts	Nuts	Nuts
	Beans	—	Beans
	Seeds	Seeds	—
	—	Low-fat dairy products	—
Moderate amounts	—	—	Poultry
	Dairy products	—	—
	Poultry	Poultry	—
	Alcohol	—	Alcohol/wine
Restricted amounts	—	Fish	—
	Red meat	Red meat	Red meat and products
	Processed meat	—	—
	Sweets	Sweets	Pastries and sweets
	—	Saturated fat	—
	—	Total fat	—
	—	Cholesterol	—
	—	Sodium	—
	—	—	Cheese
—	—	Butter/margarine	
—	—	Fast fried foods	

The MIND diet score by Morris et al. is based on 15 dietary components and ranges from 0 (minimal adherence to the MIND diet) to 15 (maximal adherence) (11). A value of 0, 0.5, or 1 assigned to people for intake of each dietary component based on predefined cut-offs. For olive oil, fish, whole grains, berries, green leafy vegetables, other vegetables, nuts, beans, and poultry a value of 1 is assigned to people with high intake. For butter + margarine, cheese, red meat and products, fast fried foods, and pastries and sweets a value of 1 is assigned to people with low intake. For wine, a value of 1 is assigned to people with moderate intake.

## Results

In total, 50 observational studies and 4 randomized controlled trials were included. Key characteristics and findings of these studies, categorized by dietary pattern and study design (observational or trial) are shown in **Tables 2–6**. Considerable variations among studies were observed in the country, numbers, age and sex of participants, dietary assessment methods, and dietary components used to measure adherence score to the diets. Of the observational studies and trials, 16 studies were conducted in Mediterranean countries including Spain (33–38), Greece (39–42), Italy (43–45), and France (46–48), and 26 studies were performed in the United States (11, 49–73). The other studies were conducted in Australia (74–78), Sweden (79–81), China (82, 83), Poland

(84), Puerto Rico (85), Scotland (86), and Israel (51). Sample sizes ranged from 79 (33) to 27,842 (64) participants. The vast majority of the observational studies and trials were performed in participants aged  $\geq 60$  y ( $n = 38$ ), 6 studies only included women (52, 66, 67, 70, 72, 73), and 2 studies only included men (64, 80). Most studies assessed dietary intake with an FFQ; 9 studies used either repeated 24-h dietary recalls (33, 46, 51, 83), repeated food diaries (80, 81), a diet adherence screener (35), or a combination of these dietary assessment methods (47, 50). Evidence per dietary pattern and study design is discussed below.

## Mediterranean diet

### Cross-sectional studies.

The Mediterranean diet in relation to cognitive function, dementia, or AD was investigated in 12 cross-sectional studies and 1 case-control study (Table 2) (33, 39, 40, 49–51, 57, 61, 74, 82, 84–86). In 3 of these studies the Mediterranean diet was associated with better cognitive functioning, including Spanish ( $n = 79$ ) (33), American ( $n = 5907$ ) (57), and a combination of Israeli ( $n = 1786$ ) and American ( $n = 2791$ ) (51) participants. In addition, in 4 studies, including middle-aged and older Greek ( $n = 1864$ ) (39), Polish ( $n = 87$ ) (84), Scottish ( $n = 878$ ) (86), and Puerto Rican ( $n = 1269$ ) (85) participants, the Mediterranean diet was associated with better cognitive function in specific

**TABLE 2** Characteristics of the included observational human studies on the Mediterranean diet in relation to cognitive decline, dementia, and AD<sup>1</sup>

Authors, year, study name	Study design	Population	Follow-up (y)	Exposure	Outcome	Results	Covariates
Mosconi et al. (2018) (49), US	Cross-sectional	n = 116 (88% men) age: 50 y clinically and cognitively normal participants aged 30–60 y who were enrolled in observational brain imaging studies	—	FFQ, MeDi score	Memory (immediate and delayed recall), executive function (WAIS), and language (WAIS vocabulary) and MRI-based cortical thickness and MRI-based cortical thickness	Continuous MeDi score was significantly positively associated with MRI-based cortical thickness of the posterior cingulate cortex (standardized $\beta$ : 0.023; $P = 0.004$ ). MeDi score was not significantly associated with memory, executive function, or language	Age, sex, and APOE genotype
Anastasiou et al. (2017) (39), Greece-HELAD	Cross-sectional	n = 1864 (41% men) age: 73.0 y elderly >64 y from 2 cities in Greece, random selection from municipality records	—	SFFQ, A-MeDi score, dietary components	Cognitive status (dementia (DSM-IV, NINCDS/ADRDA criteria)) and cognitive performance (memory [GWT, CFT], language [BNT, CIMS, categories: objects and the letter A], executive functioning [TMT, verbal fluency, ASR, GST, MP, months forwards and backwards], and visuospatial perception [BLO, CDT, CFT, TMT])	Participants with a diagnosis of dementia had a significantly lower A-MeDi score compared to participants without dementia ( $P < 0.001$ ). Continuous A-MeDi score and A-MeDi score quartile were significantly associated with lower risk of dementia (OR: 0.920; 95% CI: 0.870, 0.974; $P = 0.004$ ; OR <sub>quartile</sub> : 0.440; 95% CI: 0.208, 0.969; $P$ -trend = 0.019). A-MeDi score was significantly associated with composite z-score ( $\beta$ : 0.010; $P = 0.007$ ), memory ( $\beta$ : 0.012; $P = 0.001$ ), language ( $\beta$ : 0.011; $P = 0.007$ ), and executive functioning ( $\beta$ : 0.008; $P = 0.049$ ), but not with visuospatial perception ( $P = 0.0659$ )	Age, sex, education, number of clinical comorbidities, and energy intake
Bumenthal et al. (2017) (50), US	Cross-sectional	n = 160 (33% men) age: 65.4 y sedentary adults aged $\leq 55$ y with cognitive impairment and CVD risk factors	—	FFQ and 4-d food diary, A-MeDi and A-DASH score	Verbal memory (HVLT-R, ANT), visual memory (CFT), and executive function/processing speed (ST, DST, COWA, TMT, DSST, Ruff 2&7 Test)	Higher MeDi score was not associated with verbal memory ( $P = 0.167$ ), nor with executive function/processing speed ( $P = 0.901$ ) nor with visual memory ( $P = 0.978$ )	Age, education, sex, ethnicity, total caloric intake, family history of dementia, and chronic use of anti-inflammatory medications
Hernández-Gallot & Gorri (2017) (33), Spain, Garnucha Old Age Health Study	Cross-sectional	n = 79 (48% men) age: 81.0 y noninstitutionalized Spanish elderly	—	3 24-h diet recalls and a face-to-face interview, 14-item MEDAS	Global cognition (MMSE)	Higher tertile of MEDAS score was significantly associated with better cognitive status ( $P = 0.034$ )	—
McEvoy, Guyer, Langa & Yaffe (2017) (57), US Health and Retirement Study	Cross-sectional	n = 5907 (40% men) age: 67.8 y community dwelling adults from the age of 50 y	—	163-item SFFQ, A-MeDi score, MIND diet score	Cognitive performance (global cognition score based on immediate and delayed recall, backward counting, and serial seven subtraction)	Higher A-MeDi score tertile was significantly associated with better cognitive performance ( $P$ -trend < 0.001). Higher tertile of A-MeDi score was significantly associated with lower risk of poor cognitive performance (OR <sub>T3vsT1</sub> : 0.65; 95% CI: 0.52, 0.81; $P < 0.001$ )	Sex, age, race, low education attainment, current smoking, obesity, total wealth, hypertension, diabetes mellitus, physical inactivity, depression, and total energy intake
Bajarska, Worniewicz, Suwalka & Jeszka (2014) (84), Poland	Cross-sectional	n = 87 (35% men) age: 70.0 y elderly >60 y from rural areas of Wielkopolska from a community with high risk of metabolic syndrome	—	FFQ, A-MeDi score (high vs. low), dietary components	MCI, global cognition (MMSE), attention (TMT), visual memory (PRM), executive function (ST, SOC, SWM, SSP)	High A-MeDi score was significantly associated with lower prevalence of MCI ( $P < 0.001$ ) and higher global cognition ( $\beta$ : 0.25; $P = 0.001$ ), but not with attention, visual memory, or executive function	Gender, age, education level, smoking status, family status, leisure time physical activity, and existence of metabolic syndrome
Zheida et al. (2014) (51), US and Israel National Health and Nutrition Examination Survey (NHANES) (US) and Israeli National Health and Nutrition Survey of Older Adults (MABAT ZAHAV) (Israel)	Cross-sectional	n <sub>NHANES</sub> = 2791 (50% men) age <sub>NHANES</sub> = 71.2 y n <sub>MABAT</sub> = 1786 (47% men) age <sub>MABAT</sub> = 74.9 y community dwelling population, elderly	—	24-h dietary recalls, MeDi score	Cognitive function (NHANES: cognitive function questionnaire score, MABAT ZAHAV: MMSE)	Higher MeDi score tertile was associated with better cognitive function in both the NHANES ( $P$ -trend < 0.001) and the MABAT ZAHAV ( $P$ -trend = 0.008) survey	—
Chan, Chan & Woo (2013) (82), China	Cross-sectional	n = 3670 (52% men) age >65 y Chinese elderly men and women	—	280-item FFQ, MeDi score	Cognitive function (CSH-D)	No significant association between MeDi score and cognitive function in both men (OR <sub>T3vsT1</sub> : 0.89; 95% CI: 0.56, 1.4; $P$ -trend = 0.882) and women (OR <sub>T3vsT1</sub> : 1.02; 95% CI: 0.75, 1.41; $P$ -trend = 0.952)	Age, BMI, PASE, energy intake, education level, Hong Kong community ladder, smoking status, alcohol use, number of ADLs, GDS category, and self-reported history of diabetes, hypertension, and CVD/stroke

(Continued)

**TABLE 2** (Continued)

Authors, year, study name	Study design	Population	Follow-up (y)	Exposure	Outcome	Results	Covariates
Corley, Starr, McNeill & Deary (2013) (86), Scotland LBC 1936	Cross-sectional	n = 878 (±50% men) age: 69.5 y independently living men and women of 70 y	—	168-item FFQ Mediterranean diet (22 items)	Cognitive function (IQ(MHT), general cognition (WMS-III LNS, MR, BD, DS; DST backward, SS), processing speed (SS, DS, SCRT, IT), memory LM and VPA immediate and delayed recalls, SSP forwards and backwards, LNS, DST backward, and verbal ability (NART, WTAR))	Mediterranean diet score was only positively associated with verbal ability measured with NART and measured with WTAR ( $\eta^2_{p, NART}$ : 0.006; $P = 0.024$ ; $\eta^2_{p, WTAR}$ : 0.013; $P = 0.001$ ), but not associated anymore with IQ ( $P = 0.767$ ), general cognition ( $P = 0.960$ ), processing speed ( $P = 0.205$ ), or memory ( $P = 0.870$ )	Sex, age, occupational social class, IQ at age of 11 y
Crichton, Bryan, Hodgson & Murphy (2013) (74), Australia	Cross-sectional	n = 1183 (36% men) age: 50.6 y participants from 40 to 65 y from Southern Australia	—	215-item FFQ, MeDI score, dietary components	Self-reported cognitive function (CFQ) on mistakes in tasks on perception, memory, and motor function	MeDI score was not significantly associated with self-reported cognitive function ( $P$ -trend = 0.30).	—
Katsiardanis et al. (2013) (40), Greece The Velesimo Study	Cross-sectional	n = 557 (53% men) age > 65 y elderly men and women from Velesimo	—	157-item EPIC-Greek SFFQ, A-MeDI score	Cognitive impairment (MMSE)	Continuous A-MeDI score was significantly associated with less cognitive impairment in men (OR: 0.88; 95% CI: 0.80, 0.98; $P = 0.02$ ), but more cognitive impairment in women (OR: 1.11; 95% CI: 1.00, 1.22; $P = 0.04$ )	Age, GDS, education, social activity, smoking, metabolic syndrome
Ye et al. (2013) (85), Puerto Rico BPRHS	Cross-sectional	n = 1269 age: 57.3 y adults from 45 to 75 y from Puerto Rico	—	SFFQ, MeDI score	Global cognition (MMSE), memory, executive function, attention, and cognitive impairment (MMSE)	Higher quintile of MeDI score was significantly associated with global cognition ( $\beta$ : 0.14; $P$ -trend = 0.012), but not with executive function ( $P$ -trend = 0.52), memory ( $P$ -trend = 0.39) or attention ( $P$ -trend = 0.067). Both continuous MeDI score and highest quintile of MeDI score were significantly associated with lower risk of cognitive impairment (OR: 0.87; 95% CI: 0.80, 0.94; $P < 0.001$ ; OR <sub>5th,ci</sub> : 0.51; 95% CI: 0.33, 0.79; $P$ -trend < 0.001)	Age, sex, educational attainment, household income below threshold, acculturation score, smoking status, physical activity score, supplement use, taking > 5 types of medication within the last 12 mo, BMI, hypertension, diabetes, total cholesterol, high-density lipoprotein cholesterol, and triglycerides
Scarmeas, Stern, Mayeux & Luchsinger (2006) (61), US WHICAP	Case-control	n = 1984 (32% men) age: 76.3 y elderly from 2 WHICAP cohorts	—	61-item SFFQ, MeDI score	AD (DSMIII, NINCDS-ADRDA criteria)	Both higher continuous MeDI score and higher tertile of MeDI score were significantly associated with a lower risk of AD (OR: 0.76; 95% CI: 0.67, 0.87; $P < 0.001$ ; OR <sub>3rd,ci</sub> : 0.31; 95% CI: 0.16, 0.58; $P$ -trend < 0.001). These values hardly changed after adjustment for vascular variables	Cohort, age, sex, ethnicity, education, APOE genotype, caloric intake, smoking, comorbidity index, BMI, history of stroke, diabetes mellitus, hypertension, heart disease, total cholesterol, high-density lipoprotein, triglycerides, and low-density lipoprotein
Hosking, Eramudugolla, Cherbuin, & Anstey (2019) (75), Australia, the Personality and Total Health (PATH) through Life Study	Longitudinal	n = 1220 (50% men) age: 60–64 y older Australian adults	12	CSIRO-FFQ, MeDI, A-MeDI, and MIND scores, dietary components	Cognitive impairment: MCI/dementia (Winblad criteria, NINCDS-ADRDA criteria)	Higher tertile of MeDI score was not significantly associated with cognitive impairment (OR <sub>3rd,ci</sub> : 1.30; 95% CI: 0.79, 2.15; $P$ -trend = 0.29). Higher tertile of A-MeDI score was also not significantly associated with cognitive impairment (OR <sub>3rd,ci</sub> : 0.77; 95% CI: 0.43, 1.39; $P$ -trend = 0.40)	Energy intake, age, sex, APOE $\epsilon 4$ allele, education, mental activity, physical activity, smoking status, depression, BMI, hypertension, heart disease, and stroke
Bhushan et al. (2018) (64), US HPFS	Longitudinal	n = 27,842 (100% men) age: 51 y male health professionals from the US	±6	FFQ, MeDI score, dietary components	Subjective cognitive function	Higher quintile of MeDI score was associated with a lower risk of both poor subjective cognitive function (OR <sub>5th,ci</sub> : 0.64; 95% CI: 0.55, 0.75; $P$ -trend < 0.001) and moderate subjective cognitive function (OR <sub>5th,ci</sub> : 0.76; 95% CI: 0.70, 0.83; $P$ -trend < 0.001) compared with good subjective cognitive function	Age, smoking history, diabetes, hypercholesterolemia, physical activity level, and BMI

(Continued)

**TABLE 2 (Continued)**

Authors, year, study name	Study design	Population	Follow-up (y)	Exposure	Outcome	Results	Covariates
Shakerain et al. (2018) (79), Sweden SNA-C-K	Longitudinal	n = 2223 (39% men) age: 69.5 y community residents from Kungsholmen ≥60y	6	98-item SFFQ, A-MeDi, A-DASH and MIND scores, dietary components	Global cognition (MMSE)	Higher A-MeDi score was significantly associated with less cognitive decline ( $\beta$ : 0.006; 95% CI: 0.002, 0.009; $P = 0.002$ ; $P_{\text{trend}}$ : 0.099; 95% CI: 0.036, 0.163; $P = 0.002$ ). A-MeDi score was not significantly associated with a lower risk of MMSE score $\leq 24$ ( $P = 0.204$ ; $P_{\text{testT1}} = 0.263$ )	Total caloric intake, age, sex, education, civil status, physical activity, smoking, BMI, vitamin/mineral supplement intake, vascular disorders, diabetes, cancer, depression, APOE $\epsilon 4$ , and dietary components other than those included in each dietary index
Tanaka et al. (2018) (43), Italy Invecchiare in Chianti (InCHIANTI)	Longitudinal	n = 832 age: 75.4 y (44% men) Older adults from the Chianti region in Italy	10.1	FFQ, MeDi score, dietary components	Global cognition (MMSE)	Continuous MeDi score was significantly associated with a lower risk of cognitive decline of 5 units in MMSE (HR: 0.89; 95% CI: 0.81, 0.97; $P = 0.007$ ). Higher tertile of MeDi score was also significantly associated with a lower risk of cognitive decline of 5 units in MMSE (HR <sub>T3vsT1</sub> : 0.62; 95% CI: 0.43, 0.91; $P = 0.015$ )	Age, sex, study site, chronic diseases, years of education, total energy intake, physical activity, BMI, APOE $\epsilon 4$ allele, CRP, and IL-6
Haring et al. (2016) (52), US WHIMS	Longitudinal	n = 6425 (0% men) age: 65–79y postmenopausal elderly women	9.11	Women's Health Initiative (WHI)-FFQ, MeDi score, and DASH score	MCI (MMSE and battery of neuropsychological tests (animal category, BNT, word list memory task, copying and recalling 4 line drawings, TMT))	A-MeDi score quartile was not significantly associated with reduced risk of MCI ( $P$ -trend = 0.08). In a subset of white women with further adjustment for APOE $\epsilon 4$ allele quartile of A-MeDi score was significantly associated with a lower risk of MCI (HR <sub>Q3vsQ1</sub> : 0.67; 95% CI: 0.45, 1.00; $P$ -trend = 0.01)	Age, race, education level, WHI hormone trial randomization assignment, baseline SMS level, smoking status, physical activity, diabetes, hypertension, BMI, family income, depression, history of CVD, and total energy intake
Galbete et al. (2015) (34), Spain Sun-Project	Longitudinal	n = 823 (71% men) age: 61.9y Spanish university graduates > 55 y	6–8	136-item SFFQ, MeDi score, dietary components	Cognitive function (TICS)	Lower tertile of MeDi score was significantly associated with faster cognitive decline (mean difference <sub>T1+T2vsT3</sub> : -0.56; 95% CI: -0.99, -0.13; $P = 0.011$ ; mean difference <sub>T1vsT3</sub> : -0.43; 95% CI: -0.92, 0.05; $P = 0.08$ ; mean difference <sub>T2vsT3</sub> : -0.62; 95% CI: -1.07, -0.18; $P = 0.006$ )	Age, sex, APOE genotype, follow-up time, total energy intake, BMI, smoking status, physical activity, diabetes, hypertension, hypercholesterolemia, history of CVD, and years of university education
Koyama et al. (2015) (65), US Health, Aging and Body Composition study	Longitudinal	n = 2326 (49% men) age: 70–79y African-American and white elderly	7.9	108-item block FFQ via interviews, A-MeDi score (race-specific)	Global cognition (BMS score)	Among African American, but not among whites, A-MeDi score was significantly associated with less cognitive decline (mean difference <sub>AFRICAN-AMERICANS</sub> : 0.22; 95% CI: 0.05, 0.39; $P = 0.01$ ; $P_{\text{testTRES}}$ = 0.14)	Age, sex, education, BMI, current smoking, physical activity, depression, diabetes, total energy intake, and socio-economic status
Morris et al. (2015) (53), US Rush MAF	Longitudinal	n = 923 (2.24% men) age: 58–96 y people living in retirement communities or senior public housing units in Chicago	4.5	144-item SFFQ, A-MeDi, A-DASH, and MIND scores	AD (based on NINCDS-ADRDA criteria)	Highest tertile of A-MeDi adherence was significantly associated with lower risk of AD (HR <sub>T3vsT1</sub> : 0.46; 95% CI: 0.27, 0.79; $P$ -trend = 0.006)	Age, sex, education, APOE $\epsilon 4$ , participation in cognitively stimulating activities, physical activity, total energy intake, and cardiovascular conditions
Olsson et al. (2015) (80), Sweden ULSAM	Longitudinal	n = 1038 (100% men) men from the municipality of Uppsala	12	7-d food diary, adapted MeDi score	AD (based on NINCDS-ADRDA and DSM-IV criteria), dementia, and cognitive impairment (MMSE)	Continuous MeDi score was not associated with a lower risk of AD, dementia, or cognitive impairment. Higher tertile of MeDi score was also not associated with AD ( $P$ -trend = 0.95); dementia ( $P$ -trend = 0.70); or cognitive impairment ( $P$ -trend = 0.41). In participants with energy intake according to the Goldberg cut-off, highest tertile of MeDi score was significantly associated with a lower risk of cognitive impairment (OR <sub>T3vsT1</sub> : 0.32; 95% CI: 0.11, 0.89)	Energy, education, APOE $\epsilon 4$ allele, living alone, smoking, and physical activity

(Continued)

**TABLE 2** (Continued)

Authors, year, study name	Study design	Population	Follow-up (y)	Exposure	Outcome	Results	Covariates
Qin et al. (2015) (83), China, China Health and Nutrition Survey	Longitudinal	n = 1650 (±50% men) age ≥ 55 y Chinese community dwellers	5.3	3-d 24-h recall, adapted MeDi score, dietary components	Decline in global cognition, composite z-scores and verbal memory (modified TICS)	Higher MeDi score was, only in participants ≥ 65 y, significantly associated with slower rate of decline in global cognitive scores ( $\beta$ : -0.10; 95% CI: 0.01, 0.18), composite z-scores ( $\beta$ : -0.014; 95% CI: 0.001, 0.027), and verbal memory scores ( $\beta$ : 0.016; 95% CI: 0.001, 0.030). Higher tertile of MeDi score was significantly associated with less decline of global cognitive scores ( $\beta$ : $\beta_{\text{TICS-TT}}$ : -0.28; 95% CI: 0.02, 0.54), z-scores ( $\beta$ : $\beta_{\text{TICS-TT}}$ : -0.042; 95% CI: -0.002, 0.081) and verbal memory scores ( $\beta$ : $\beta_{\text{TICS-TT}}$ : -0.047; 95% CI: 0.003, 0.091) only in participants ≥ 65 y	Age, gender, education, region, urbanization index, annual household income per capita, total energy intake, physical activity, current smoking, time since baseline, BMI, hypertension, and time interactions with each covariate
Trichopoulos et al. (2015) (41), Greece EPIC-Greece	Longitudinal	n = 401 (36% men) age >65 y elderly EPIC participants from Athens or the Attica area	6.6	150-item SFFQ, MeDi score, dietary components	Global cognition (MMSE)	MeDi score tertile was significantly associated with less mild cognitive decline (OR <sub>TICS-TT</sub> : 0.46; 95% CI: 0.25, 0.87; P-trend = 0.012), substantial cognitive decline (OR <sub>TICS-TT</sub> : 0.34; 95% CI: 0.13, 0.89; P-trend = 0.025). Results were even more striking in participants ≥ 75 y	Sex, age, years of education, BMI, physical activity, smoking status, diabetes, hypertension, cohabiting, and total energy intake
Tangney et al. (2014) (54), US MAP	Longitudinal	n = 826 (26% men) age: 81.5 y elderly living in Chicago retirement communities and subsidized housing, normal cognitive function	4.1	144-item SFFQ, A-MeDi score, A-DASH score	Global cognition (composite score of 19 tests), episodic memory (logical memory, word list recall), world list recognition, EBS), semantic memory (verbal fluency from CERAD, BNT, 12-item reading test), working memory (DST forward and backward, DO), perceptual speed (SDMT, Number Comparison (NC), Stroop Neuropsychological Screening (NS)), and visuospatial ability (JLO, SPM)	A-MeDi score was significantly associated with slower rate of change of global cognition ( $\beta$ : 0.002; P = 0.01), episodic memory ( $\beta$ : 0.003; P = 0.02), and semantic memory ( $\beta$ : 0.003; P = 0.02). A-MeDi score tertile was associated with slower rate of change of global cognition ( $\beta$ : 0.034; P = 0.003), episodic memory ( $\beta_{\text{TICS-TT}}$ : -0.040; P = 0.007), semantic memory ( $\beta_{\text{TICS-TT}}$ : -0.033; P = 0.01), and working memory ( $\beta_{\text{TICS-TT}}$ : -0.033; P = 0.01)	Total energy intake, age, sex, education, and cognitive activities
Gallucci et al. (2013) (44), Italy Treviso Longeva (TRELONG) study	Longitudinal	n = 309 (40% men) age: 79.1 y long-lived elderly from Northern Italy	7	FFQ, Mediterranean diet yes/no (based on cereal, fish, vegetables, and fruit intake)	Global cognition (MMSE)	Adherence to Mediterranean diet (yes vs. no) was not significantly associated with less cognitive decline ( $\beta$ : -0.205; P = 0.758)	—
Kesse-Guyot et al. (2013) (46), France Stroop Neuropsychological Screening (SUMI-MAX)	Longitudinal	n = 3083 (54% men) middle-aged	13	12 24-h recalls, MeDi score, MSDPS	Cognitive performance (episodic memory [RI-48 cued recall test], lexical-semantic memory [verbal fluency tasks], short-term memory [DST forward and backward], working memory [Forward Digit Span task (FDS), Backward Digit Span task (BDS)], mental flexibility [TMT])	Higher tertile of MeDi score was only associated with working memory span (P-trend = 0.003) but not with global cognition (P-trend = 0.27), episodic memory (P-trend = 0.50), short-term memory (P-trend = 0.97), mental flexibility (P-trend = 0.77), or semantic memory (P-trend <sub>semantic</sub> = 0.51; P-trend <sub>phonemic</sub> = 0.37). Higher tertile of MSDPS was significantly associated with semantic fluency on the phonemic fluency task (P-trend = 0.048), but not with semantic fluency on semantic fluency task (P-trend = 0.06), global cognition (P-trend = 0.12), episodic memory (P-trend = 0.94), short-term memory (P-trend = 0.67), working memory (P-trend = 0.49), or mental flexibility (P-trend = 0.55)	Age, sex, education, follow-up time, supplementation group during the trial phase, number of 24-h dietary records, total energy intake, BMI, occupational status, smoking status, physical activity, memory difficulties at baseline, depressive symptoms concomitant with the cognitive function assessment, and history of diabetes, hypertension, or CVD
Samieri, Okereke, Devore & Grodstein (2013) (66), US Nurses' Health Study	Longitudinal	n = 116,058 (0% men) mean age: 74.3 y women from the Nurses' Health Study ≥ 70 y	9	116-item SFFQ, adapted MeDi score, dietary components	Global cognition (TICS and composite score of TICS, EBMT, CF, DST backward), and verbal memory (immediate and delayed recalls of the EBMT and TICS)	Long-term higher quintile of MeDi score was significantly associated with better performance on TICS (mean difference <sub>Q5vsQ1</sub> : 0.06; 95% CI: 0.01, 0.11; P-trend = 0.004), global cognition (mean difference <sub>Q5vsQ1</sub> : -0.05; 95% CI: 0.01, 0.08; P-trend = 0.002) and verbal memory (mean difference <sub>Q5vsQ1</sub> : -0.06; 95% CI: 0.03, 0.10; P-trend < 0.0001) at older age. Quintile of average MeDi score was not significantly associated with change in TICS score (P-trend = 0.31), global cognition (P-trend = 0.84), or verbal memory (P-trend = 0.70)	Age, education, long-term physical activity and total energy intake, BMI, smoking, multivitamin use, and history of depression, diabetes, hypertension, hypercholesterolemia, or myocardial infarction

(Continued)

**TABLE 2 (Continued)**

Authors, year, study name	Study design	Population	Follow-up (y)	Exposure	Outcome	Results	Covariates
Samieri et al. (2013) (67), US Women's Health Study	Longitudinal	n = 6174 (0% men) age: 72 y subset of participants from the Women's Health study aged $\geq 65$ y	4	13-item SFFQ, adapted MeDi-score, dietary components	Global cognition (TICS, EBMT, CF) and verbal memory (EBMT, delayed recall of TICS 10-word list)	MeDi score quintile was not significantly associated with better average global cognition (P-trend = 0.63) or verbal memory (P-trend = 0.44), nor with change in global cognition (P-trend = 0.26) and verbal memory (P-trend = 0.40)	Treatment arm, age at initial cognitive testing, Caucasian race, high education, high income, energy intake, physical activity, BMI, smoking, diabetes, hypertension, hypercholesterolemia, hormone use, and depression
Tirova et al. (2013) (81), Sweden A follow-up of PIVUS	Longitudinal	n = 194 (52% men) age: 70.1 y subset of PIVUS participants, cognitive assessment at 75 y	5	7-d food diary, adapted MeDi-score, dietary components	Global cognition (7MS), brain volume (3D T1-weighted MRI-scan)	After adjustment continuous MeDi score was not significantly associated with global cognitive function (P = 0.13). Continuous MeDi score was not associated with gray (P = 0.19) or white (P = 0.97) matter volume or total brain volume (P = 0.32)	Gender, energy intake, education, self-reported physical activity, low-density lipoprotein, systolic blood pressure, and HOMA-IR
Tsingoulis et al. (2013) (68), United States Reasons for Geographic and Racial Differences in Stroke US REGARDS	Longitudinal	n = 17,478 (43% men) age: 64.4 y oversampling African-American subjects and from the Stroke Belt region, $\geq 45$ y	4.0	98-item block FFQ, MeDi score	Cognitive impairment Six-item-Screener (SIS)	High MeDi adherence was significantly associated with lower risk of ICI (OR: 0.87; 95% CI: 0.76, 1.00; P = 0.0460) compared with low MeDi adherence. There was no interaction between race (P = 0.2928) or Stroke Belt region (P = 0.9978) and the association of MeDi adherence with risk of ICI. Higher tertile of MeDi score was also significantly associated with lower risk of ICI (P-trend = 0.0436)	Age, sex, race, region (Stroke Belt vs. other region), educational level, income, number of packs smoked per year, weekly exercise, diabetes mellitus, hypercholesterolemia, atrial fibrillation, history of heart disease, BMI, waist circumference, systolic and diastolic blood pressure, ACE-inhibitors/angiotensin receptor blockers, $\beta$ blockers, other antihypertensive medication, depressive symptoms, and self-reported health status
Wengreen et al. (2013) (69), US Cache County Study on Memory, Health, and Aging	Longitudinal	n = 3580 ( $\pm$ 43% men) age $\geq 65$ y mainly non-Hispanic white	10.6	142-item FFQ, MeDi score, DASH score	Global cognition (3MS)	Higher quintile of MeDi score was associated with better average cognition during follow-up (mean difference <sub>observed</sub> : 0.94; P-trend = 0.0022) but was not significantly associated with rate of change of cognitive function	Age, sex, education, BMI, frequency of moderate physical activity, multivitamin and mineral supplement use, history of drinking and smoking, and history of diabetes, heart attack, or stroke
Cherbuin & Anstey (2012) (76), Australia PATH through Life Study	Longitudinal	n = 1528 ( $\pm$ 49% men) age: 60–64 y elderly random selection of residents of Canberra	4	215-item FFQ, MeDi score, dietary components	MCI, cognitive decline, cognitive disorder (CDR), any-MCD (based on MMSE, CVLT, SDMT, PP, SRT)	Continuous MeDi score was not significantly associated with risk of MCI (OR: 1.41; 95% CI: 0.95, 2.10; P = 0.087). CDR 0.5 (OR: 1.18; 95% CI: 0.88, 1.57; P = 0.266), or any-MCD (OR: 1.20; 95% CI: 0.98, 1.47; P = 0.079)	Age, sex, education, APOE $\epsilon 4$ genotype, BMI, physical activity, stroke, diabetes, hypertension, and total energy intake
Gadener, et al. (2012) (77), Australian Imaging, Biomarkers and Lifestyle Study of Aging	Longitudinal	n = 970 (42% men) age = 71.72 y HC, MCI, and AD Australian subjects $\geq 60$ y	1.5	74-item SFFQ (AD participants had assistance or validation), MeDi score	Global cognition (MMSE), episodic verbal memory (CVLT II), logical memory (WMS), and verbal executive function (D-KEFS)	Higher MeDi score was significantly associated with less change in global cognition (r: 0.098; P = 0.014), but not with change in episodic verbal memory (P = 0.472), logical memory (P = 0.779), or verbal executive function (P = 0.294)	—

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TABLE 2 (Continued)

Authors, year, study name	Study design	Population	Follow-up (y)	Exposure	Outcome	Results	Covariates
Vercautere, Grodstein, Berr & Kang (2012) (70), US, WACS	Longitudinal	n = 2504 (0% men) age ≥ 65 y female health professionals with CVD or ≥ 3 coronary risk factors	5.4	116-item SFFQ, MeDi score	Global composite score, global cognition (TICS), verbal memory (TICS 10-word list, EBMT) and category fluency	MeDi score tertile was not associated with change in global composite score (P-trend = 0.88), global cognition (P-trend = 0.53), verbal memory (P-trend = 0.97), or category fluency (P-trend = 0.64)	Age, education, total energy intake, marital status, physical activity, use of multivitamin supplements, smoking status, BMI, postmenopausal hormone therapy use, aspirin use exceeding 10 d in the previous month, nonsteroidal anti-inflammatory drug use exceeding 10 d in the previous month, history of depression, cardiovascular profile at baseline, diabetes, hypertension, hyperlipidaemia, and randomization assignment for vitamin E, vitamin C, β-carotene, and folate participation in cognitive activities, total energy intake, and the interaction between time and each dietary quality score
Tangney et al. (2011) (71), US Chicago Health and Aging Project	Longitudinal	n = 3790 (38% men) age: 75.4 y older residents, African Americans and whites	7.6	139-item FFO, A-MeDi score	Global cognition (immediate and delayed recall of the EBMT, MMSE, and SDMT)	Continuous A-MeDi score was significantly associated with reduced decline in global cognitive function (β: 0.0014; P = 0.0004). The continuous A-MeDi score (only wine and no other types of alcohol were taken into account) was also significantly reduced decline in global cognitive function (β: 0.0014; P = 0.0009)	Age, sex, race, education, hsCRP, fasting insulin, and adiponectin concentrations
Gu, Luchsinger, Stern & Scarmeas (2010) (55), US WHICAP II	Longitudinal	n = 1219 (33% men) age: 76.7 y elderly from northern Manhattan	3.8	61-item SFFQ, MeDi score	AD (DSM-III), NINCDS-ADRDA, criteria)	Higher continuous MeDi score was associated with lower risk of AD (HR: 0.87; 95% CI: 0.78, 0.97; P = 0.01). Higher tertile of MeDi score was borderline significantly associated with a lower risk of AD (HR <sub>T3vsT1</sub> : 0.68; 95% CI: 0.42, 1.08; P-trend = 0.06)	Age, gender, education, race, hsCRP, fasting insulin, and adiponectin concentrations
Roberts et al. (2010) (56), US	Longitudinal	n = 1233 (52% men) age: 70–89 y random selection of elderly residents of Olmsted County	2.2	128-item block FFO, MeDi score, dietary components	MCI (CDR, neurological evaluation [STMS, HS, LMII, YRII, AVLT, TMT, DSST, BNT, CF PC, BD])	Higher MeDi score tertile was not significantly associated with reduced risk of MCI during follow-up (HR <sub>T3vsT1</sub> : 0.75; 95% CI: 0.46, 1.21; P = 0.24)	Age, sex, education, marital status, total energy intake, practice of physical exercise, taking 5 medications or more, Center for Epidemiological Studies-Depression Scale score, APOE genotype, BMI, hypertension, hypercholesterolemia, diabetes, tobacco use, stroke, and their interaction with time
Féart, et al. (2009) (47), France, Three-City cohort	Longitudinal	n = 1410 (± 37% men) age: 75.9 y noninstitutionalized elderly community dwellers from Bordeaux	4.1	FFQ, 24-h recall, MeDi score	Global cognition (MMSE), semantic verbal fluency (ST), visual memory (BVRT), and verbal memory (FCST), and dementia and AD (examination by neurologist and DSM-IV)	Higher MeDi score was only significantly associated with less change in global cognition (β: -0.006; 95% CI: -0.01, -0.0003; P = 0.04), but not with change in semantic verbal fluency (P = 0.32), visual memory (P = 0.90) or verbal memory (P = 0.08). Highest MeDi tertile was not significantly associated with less change in performance on any cognitive test compared with lowest MeDi tertile (P <sub>MMSE</sub> = 0.06; P <sub>ST</sub> = 0.49; P <sub>BVRT</sub> = 0.50; P <sub>FCST</sub> = 0.06). However, in individuals who did not develop dementia during follow-up MeDi score and MeDi tertile were significantly associated with less decline in global cognition (β: -0.006; 95% CI: -0.011, -0.007; P = 0.03; β <sub>T3vsT1</sub> : -0.03; 95% CI: -0.05, -0.001; P = 0.04) and verbal memory (β: 0.05; 95% CI: 0.005, 0.010; P = 0.03; β <sub>T3vsT1</sub> : 0.21; 95% CI: 0.008, 0.41; P = 0.04). MeDi score and MeDi tertile were not significantly associated with risk of incident dementia (P = 0.43; P <sub>T3vsT1</sub> AD (P = 0.96; P <sub>T3vsT1</sub> = 0.71)	Age, sex, education, marital status, total energy intake, practice of physical exercise, taking 5 medications or more, Center for Epidemiological Studies-Depression Scale score, APOE genotype, BMI, hypertension, hypercholesterolemia, diabetes, tobacco use, stroke, and their interaction with time

(Continued)

**TABLE 2** (Continued)

Authors, year, study name	Study design	Population	Follow-up (y)	Exposure	Outcome	Results	Covariates
Scarmeas et al. (2009) (59), US WHICAP	Longitudinal	n = 1875 (32% men) age: 76.9 y 2 cohorts: elderly without dementia, northern Manhattan	Normal cognitive subjects: 45 ; MCI subjects: 43	61-item SFFQ, MeDI score	MCI, MCI with memory impairment, MCI without memory impairment, AD (DSM-III, NINCDS-ADRDA criteria)	Higher MeDI score was significantly associated with a lower risk of MCI (HR: 0.92; 95% CI: 0.85, 0.99; P = 0.04). Higher MeDI score tertile was most significantly associated with a lower risk of MCI (HR: 0.72; 95% CI: 0.52, 1.00; P-trend = 0.05), not significantly associated with a lower risk of MCI with memory impairment (P = 0.18), nor with a lower risk of MCI without memory impairment (P = 0.13). Higher MeDI score tertile in MCI was significantly associated with a lower risk of AD (HR: 0.52; 95% CI: 0.30, 0.91; P-trend = 0.02), but continuous MeDI score was not (P = 0.09). Higher MeDI score tertile was significantly associated with a lower risk of AD in participants with MCI without memory impairment (HR-trend: 0.50; 95% CI: 0.35, 0.79; P = 0.003), but not in participants with MCI with memory impairment (P = 0.45)	Cohort, age, sex, ethnicity, education, APOE genotype, caloric intake, BMI, and time between the first cleary assessment and the first cognitive assessment
Scarmeas et al. (2009) (60), US WHICAP	Longitudinal	n = 1880 (31% men) age: 77.2 y 2 cohorts, elderly without dementia, northern Manhattan	5.4	61-item SFFQ, MeDI score	AD (DSMIII, NINCDS-ADRDA criteria)	Higher tertile of MeDI score was independent from physical activity, significantly associated with reduced risk of AD (HR <sub>T3vsT1</sub> : 0.60; 95% CI: 0.42, 0.87; HR <sub>trend</sub> : 0.79; 95% CI: 0.66, 0.94; P = 0.008)	Cohort, age, sex, ethnicity, education, APOE ε4 allele, caloric intake, BMI, smoking, depression, leisure activities, comorbidity index, baseline clinical dementia rating score, and time between first dietary and first physical activity assessment
Psaltopoulou et al. (2008) (42), Greece EPIC-Greece	Longitudinal	n = 732 (35% men) age ≥ 60 y men and women ≥ 60 y from Attica	8.0	150-item FFQ, MeDI score, dietary components	Global cognition (MMSE)	Continuous MeDI score was not significantly associated with global cognition after follow-up (P = 0.485)	Gender, age, marital status, years of education, height, BMI, physical activity, smoking, alcohol intake, hypertension, diabetes, geriatric depression score, and energy intake
Scarmeas, Luchsinger, Mayeux & Stern (2007) (63), US prospective study of aging and dementia	Longitudinal	n = 192 (22% men) age: 82.9 y community-based participants with AD from New York > 65 y	4.4	61-item SFFQ, MeDI score	Mortality in AD	Continuous MeDI score was significantly associated with reduced risk of mortality (HR: 0.76; 95% CI: 0.65, 0.89; P = 0.001). MeDI score tertile was also significantly associated with reduced risk of mortality (HR <sub>T3vsT1</sub> : 0.27; 95% CI: 0.10, 0.69; P-trend = 0.003)	Period of recruitment, age, gender, ethnicity, education, APOE genotype, caloric intake, smoking, and BMI
Scarmeas, Stern, Tang, Mayeux & Luchsinger (2006) (62), US WHICAP	Longitudinal	n = 2258 (32% men) age: 77.2 y 2 cohorts, elderly without dementia, northern Manhattan	4.0	61-item SFFQ, MeDI score	AD (DSMIII, NINCDS-ADRDA criteria)	Higher continuous MeDI score and tertile of MeDI score were significantly associated with lower risk of AD (HR: 0.91; 95% CI: 0.83, 0.98; P = 0.015; HR <sub>T3vsT1</sub> : 0.60; 95% CI: 0.42, 0.87; P-trend = 0.007)	Cohort, age, sex, ethnicity, education, APOE genotype, caloric intake, smoking, comorbidity index, and BMI

AD, Alzheimer's disease; ADL, activities of daily living; A-MeDI, alternate Mediterranean diet; ANT, animal naming test; any-MCD, any mild cognitive disorder; ASB, anomalous sentence repetition; AVLT, auditory verbal learning test; BD, block design; BDS, backward digit span task; BULO, Benton's Judgement of Line Orientation; BNT, Boston Naming Test; BPRHS, Boston Puerto Rican Health Study; BVRT, Benton Visual Retention Test; CDR, clinical dementia rating; CDT, clock-drawing test; CF, category fluency; CF, complex figure test; CFQ, cognitive failures questionnaire; CIMS, complex ideational material subset; COVA, controlled oral word association test; CSI-D, community screening instrument for dementia; CSIRO, Commonwealth Scientific and Industrial Research Organisation; CVD, cardiovascular disease; CVLT, California Verbal Learning Test; DASH, Dietary Approaches to Stop Hypertension; D-KEFS, Delis-Kaplan Executive Function System Verbal Fluency; DO, digit ordering; DS, digit symbol; DST, digit span test; DSM, diagnostic and statistical manual of mental disorders; DSST, digit symbol substitution test; EBMT, East Boston Memory Test; EBS, East Boston Story; EPIC-Europe Prospective Investigation into Cancer and Nutrition; FCSRT, Free and Cued Selective Reminding Test; FDS, Forward Digit Span task; GDS, geriatric depression scale; GST, graphical sequence test; GWL, Greek Verbal Learning Test; HC, healthy control; HELIAD, Hellenic Longitudinal Investigation Of Ageing And Diet; HFFS, Health Professionals Follow-up Study; HS, Hachinski Scale; HWLFR, Hopkins Verbal Learning Test-Revised; ICI, incident cognitive impairment; INCHIANTI, Invecchiare in Chianti; IST, Isaacs Set Test; IT, inspection time; JLO, judgment of line orientation; LBC 1936, Lothian Birth Cohort 1936; LM, logical memory; LNS, letter-number sequencing; MABAT ZANAV, Israeli National Health and Nutrition Survey of Older Adults; MAP, Memory and Aging Project; MCI, mild cognitive impairment; MEDAS, Mediterranean Diet Adherence Screener; MeDI, Mediterranean Diet-MHT; Moray House Test; MIND, Mediterranean-DASH Intervention for Neurodegenerative Delay; MMSE, Mini-Mental State Examination; MP, motor programming; MR, matrix reasoning; MSPDS, Mediterranean-Style Dietary Pattern Score; NART, National Adult Reading Test; NC, number comparison; NHANES, National Health and Nutrition Examination Survey; NINCDS-ADRDA, National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association; PASE, physical activity scale for the elderly; PATH, Personality and Total Health; PC, picture completion; PWUS, Prospective Investigation of the Vasculature in Uppsala Seniors; PP, Purdue Pegboard; PRM, pattern recognition memory test; REGARDS, Reasons for Geographic and Racial Differences in Stroke; SCRT, simple and choice reaction time; SDMT, symbol digit modality test; SFFQ, semi-quantitative FFQ; SIS, six-item screener; SNAC-K = Swedish National study on Aging and Care in Kungholmen; SNS, Stroop Neuropsychological Screening; SOC, Stockings of Cambridge test; SPW, standard progressive matrices; SRT, simple reaction time; SS, symbol search; SSP, spatial span test; ST, Stroop Test; STMS, short test of mental status; SLMVIMAX, Supplementation With Vitamins And Mineral Antioxidants; SVM, spatial working memory test; TICS, Telephone Interview For Cognitive Status; TMT, trail making test; ULSAM, Uppsala Longitudinal Study of Adult Men; VPA, verbal paired associates; VR, visual reproduction; WACS, Women's Antioxidant Cardiovascular Study; WAIS, Wechsler Adult Intelligence Scale; WHI, Women's Health Initiative; WHICAP, Washington Heights-Inwood Columbia Aging Project; WHIMMS, Women's Health Initiative Memory Study; WMS, Wechsler Memory Scale; WTA, Wechsler Test of Adult Reading; 3MS, modified mini-mental state; 7MS, 7-minute screen.

domains, including global cognition, memory, language, executive functioning, and verbal ability. Furthermore, in a study of elderly Greek participants ( $n = 557$ ) each 1-unit increase in Mediterranean diet score was associated with a lower risk of cognitive impairment in men (OR: 0.88; 95% CI: 0.80, 0.98;  $P = 0.02$ ), but an increased risk of cognitive impairment in women (OR: 1.11; 95% CI: 1.00, 1.22;  $P = 0.04$ ) (40). Moreover, a study in US middle-aged participants ( $n = 116$ ) observed an association between higher adherence to the Mediterranean diet and larger cortical thickness of the posterior cingulate cortex ( $\beta$ : 0.023;  $P = 0.004$ ), whereas no association with cognitive function was observed (49). Adherence to the Mediterranean diet and cognitive function were not associated in the remaining 3 studies among Chinese ( $n = 3670$ ) (82), Australian ( $n = 1183$ ) (74), and US ( $n = 160$ ) (50) participants.

With respect to dementia, 1 Greek cross-sectional study ( $n = 1864$ ) investigated the association between the Mediterranean diet and dementia and showed an 8% lower risk of dementia (OR: 0.92; 95% CI: 0.87, 0.97;  $P = 0.004$ ) for a 1-unit increase in Mediterranean diet score and a 56% lower dementia risk in the highest quartile of Mediterranean diet adherence (OR<sub>Q4vs.Q1</sub>: 0.440; 95% CI: 0.208, 0.969;  $P$ -trend = 0.019) (39). In a case-control study ( $n = 1984$ ), each 1-unit increase in Mediterranean diet score was associated with a 24% lower risk of AD (OR: 0.76; 95% CI: 0.67, 0.87;  $P < 0.001$ ); additionally, the highest tertile of Mediterranean diet adherence was associated with a 69% lower risk of AD (OR<sub>T3vs.T1</sub>: 0.31; 95% CI: 0.16, 0.58;  $P$ -trend < 0.001) (61).

### Longitudinal studies.

In total, 31 longitudinal studies investigated the Mediterranean diet in relation to cognitive decline, dementia, or AD (Table 2) (34, 41–44, 46, 47, 52–56, 59, 60, 62–71, 75–77, 79–81, 83). Higher adherence to the Mediterranean diet was associated with less cognitive decline after 4 to 26 y of follow-up in 7 of 23 longitudinal studies in American ( $n = 3790 \leq 27,842$ ) (64, 68, 71), Swedish ( $n = 2223$ ) (79), Spanish ( $n = 823$ ) (34), Italian ( $n = 832$ ) (43), and Greek ( $n = 401$ ) (41) participants. In 6 studies including American ( $n = 826 \leq 16,058$ ) (54, 66, 69), Australian ( $n = 970$ ) (77), and French adults ( $n = 1410$  and 3038) (46, 47), the Mediterranean diet was associated with less cognitive decline in specific cognitive domains after 1.5 to 13 y of follow-up. Participants from the Washington Heights-Inwood Columbia Aging Project (WHICAP) ( $n = 1880$ ) showed an 8% lower risk of mild cognitive impairment (MCI) for each 1-unit increase in Mediterranean diet score (HR: 0.92; 95% CI: 0.85, 0.99;  $P = 0.04$ ) after 4.5 y of follow-up (59). However, this association was not significant when studied by Mediterranean diet adherence in tertile (HR<sub>T3vs.T1</sub>: 0.72; 95% CI: 0.52, 1.00;  $P$ -trend = 0.05). Additionally, higher adherence to the Mediterranean diet was associated with less cognitive decline in African-American older adults (mean difference: 0.22; 95% CI: 0.05, 0.39;  $P = 0.01$ ), but not in white American older adults ( $n = 2326$ ) (65). Furthermore, stratified analysis suggested a beneficial

association in Chinese participants ( $n = 1650$ ) aged  $\geq 65$  y, but not in younger participants (83). Moreover, in Swedish older men ( $n = 1038$ ) higher adherence to the Mediterranean diet was associated with a lower risk of cognitive impairment (OR<sub>T3vs.T1</sub>: 0.32; 95% CI: 0.11, 0.89) after 12 y of follow-up in a subpopulation of participants with energy intake according to the Goldberg cut-off only (80). In the other 8 studies including American ( $n = 1233 \leq 6425$ ) (52, 56, 67, 70), Italian ( $n = 309$ ) (44), Greek ( $n = 732$ ) (42), Australian ( $n = 1528$ ) (76), and Swedish participants ( $n = 194$ ) (81) the Mediterranean diet was not associated with cognitive decline after 2.2 y to  $\leq 10.6$  y of follow-up. The Mediterranean diet was not associated with total brain volume, gray matter volume, or white matter volume after 5 y of follow-up among Swedish older adults ( $n = 194$ ) (81).

With respect to dementia, Mediterranean diet adherence was not associated with dementia among French ( $n = 1410$ ) (47), Swedish ( $n = 1038$ ) (80), and Australian ( $n = 1220$ ) (75) older adults after 4.1 y to  $\leq 12$  y of follow-up. In 3 studies, 2 studies in participants from the WHICAP ( $n = 1880$  and  $n = 1984$ ) (60, 61) and 1 study in participants from the Memory and Aging Project (MAP) ( $n = 923$ ) (53), a significantly lower risk of AD was shown with higher adherence to the Mediterranean diet after 3.8 y to  $\leq 5.4$  y of follow-up. In these studies a 40 to 54% lower risk of AD was shown for the highest tertile of Mediterranean diet adherence and a 9% lower risk of AD was found for each 1-unit increase in Mediterranean diet score. The WHICAP also demonstrated a lower AD risk in people with MCI for the highest tertile of adherence (HR<sub>T3vs.T1</sub>: 0.52; 95% CI: 0.30, 0.91;  $P$ -trend = 0.02) after 4.3 y of follow-up ( $n = 1875$ ), but not when the Mediterranean diet score was analyzed per unit increase (59). Furthermore, in the WHICAP II ( $n = 1219$ ) each 1-unit increase in Mediterranean diet score was associated with a 13% lower risk of AD (HR: 0.87; 95% CI: 0.78, 0.97;  $P = 0.01$ ) after 3.8 y of follow-up (55). A borderline nonsignificant association was observed for the highest tertile of Mediterranean diet adherence (HR<sub>T3vs.T1</sub>: 0.68; 95% CI: 0.42, 1.08;  $P$ -trend = 0.06). Higher adherence to the Mediterranean diet was not associated with AD after 4.1 and 12 y of follow-up among French ( $n = 1410$ ) (47) and Swedish ( $n = 1038$ ) (80) older adults. Finally, each 1-unit increase in Mediterranean diet score was associated with a 24% lower risk of mortality from AD (HR: 0.76; 95% CI: 0.65, 0.89;  $P = 0.001$ ) among American older adults ( $n = 192$ ), where the upper Mediterranean diet adherence tertile was associated with a 73% lower AD risk (HR<sub>T3vs.T1</sub>: 0.27; 95% CI: 0.10, 0.69;  $P$ -trend = 0.003) after 4.4 y of follow-up (63).

### Trial evidence.

The effect of the Mediterranean diet on cognitive decline was reported in 5 articles, representing 3 randomized controlled trials (Table 3) (35–37, 78, 87). After a 6-mo intervention in Australian healthy elderly participants ( $n = 137$ ) no significant difference between the Mediterranean diet group and the control group was observed for the cognitive domains executive function, memory, processing speed,

**TABLE 3** Characteristics of the included randomized controlled trials on the Mediterranean and DASH diets in relation to cognitive decline, dementia, and AD<sup>1</sup>

Authors, year, study name	Population (sample size, mean age, kind of people)	Follow-up (y)	Exposure	Outcome	Results
MeDi diet Knight et al. (2016) (78), Australia Medley	n = 137 (47% men) age: 72.1 healthy men and women > 65 y	0.5	MeDi, control diet (habitual diet)	Cognitive performance executive function (ST, ILF, ELF, TOL), memory (RAVLT, DST forward and backward, LNS), processing speed (SS and coding core subtests WAIS IV), and visual-spatial memory (BVRT)	MeDi did not significantly change global cognition ( $P = 0.19$ ), executive function ( $P = 0.33$ ), memory ( $P = 0.50$ ), processing speed ( $P = 0.15$ ), or visual-spatial memory ( $P = 0.48$ ), compared with the control diet
Valls-Pedret et al. (2015) (35), Spain The Prevention con dieta Mediterranea (PREDIMED)	n = 334 (± 49% men) age: 66.9 y cognitively healthy men and women at high vascular risk $\geq 55$ y	4.1	14d-item screener, MeDi with EVOO (1 L/wk), MeDi with mixed nuts (30 g/d), low-fat control	Global cognition (MMSE, RAVLT, ASF, DS substest, VPA, CTT) divided into memory, frontal and global, MCI	Both RAVLT scores (total learning and delayed recall) significantly improved for all 3 dietary patterns. CTT part 1 significantly improved for MeDi with EVOO (mean change: $-5.77$ ; 95% CI: $-11.25$ , $-0.28$ ) and CTT part 2 significantly worsened for MeDi with nuts (mean change: $24.23$ ; 95% CI: $1.36$ , $47.10$ ) and control diet (mean change: $37.56$ ; 95% CI: $18.14$ , $56.97$ ). Compared with the control, the MeDi with EVOO caused significantly more improvement in total learning RAVLT score ( $P = 0.04$ ) and less decline in color trail test part 2 ( $P = 0.045$ ). Frontal cognition significantly improved for MeDi with EVOO (mean change: $0.23$ ; 95% CI: $0.03$ , $0.43$ ). Compared with the control group, MeDi with EVOO significantly improved in global cognition ( $P = 0.005$ ) and frontal cognition ( $P = 0.003$ ) and MeDi with nuts significantly improved memory ( $P = 0.04$ ). The rate of MCI did not significantly differ between the 3 groups ( $P = 0.28$ )
Martínez-Lapiscina et al. (2013) (37), Spain PREDIMED-NAVARRA	n = 268 (45% men) age: 74.1 y community dwelling participants at high vascular risk $\geq 55$ y	6.5	137-item FFQ, questionnaire, MeDi with EVOO, MeDi with mixed nuts, low-fat control	Global cognition (MMSE, CDT), cognitive episodic memory (VPA), verbal memory (RAVLT), visual memory (ROCF), language-Boston Naming Test (BNT), ASF, FAS), executive function (attention + immediate memory + working memory [DST, TMT], abstract reasoning [similarities] test)	MeDi with EVOO significantly increased global cognition measured with MMSE, immediate memory, immediate and delayed visual memory, and phonemic fluency compared with control and significantly increased immediate and delayed visual memory and episodic memory compared with MeDi with nuts. MeDi with nuts did not significantly differ from control in cognitive performance. Compared with control, MeDi with EVOO was significantly associated with lower risk of MCI (OR: $0.341$ ; 95% CI: $0.120$ , $0.969$ , $P = 0.044$ ), whereas MeDi with nuts was not ( $P = 0.226$ )
Martínez-Lapiscina et al. (2013) (36), Spain PREDIMED-NAVARRA	n = 522 (45% men) age: 74.6 y participants at high vascular risk $\geq 55$ y	6.5	MeDi with EVOO, MeDi with mixed nuts, low-fat control	Global cognition (MMSE, CDT)	MeDi with EVOO and was significantly associated with better global cognitive performance compared with the low-fat control diet (mean difference <sub>MMSE</sub> : $-0.62$ ; 95% CI: $0.18$ , $1.05$ ; $P = 0.005$ ; mean difference <sub>CDT</sub> : $0.51$ ; 95% CI: $0.20$ , $0.82$ ; $P = 0.001$ ). MeDi with nuts was also significantly associated with better global cognitive performance (mean difference <sub>MMSE</sub> : $-0.57$ ; 95% CI: $0.11$ , $1.03$ , $P = 0.015$ ; mean difference <sub>CDT</sub> : $0.33$ ; 95% CI: $0.003$ , $0.67$ ; $P = 0.048$ )
Wardle et al. (2000) (87), UK	n = 155 (55% men) age: 53 y participants with elevated cholesterol concentrations	0.2	MeDi (high fruit, vegetables, and fish, low-fat, MUFA), low-fat diet, waiting-list control diet	Cognitive function (motor speed [tapping speed], memory [verbal immediate free recall], choice reaction time, and attention [sustained attention task])	MeDi and low-fat diet decreased attention compared with control memory, or choice reaction time compared with the control diet ( $P < 0.001$ ). MeDi was not significantly associated with motor speed, memory, or choice reaction time compared with the control diet
DASH diet Smith et al. (2010) (58), US Exercise and Nutrition Interventions for Cardiovascular Health (ENCORE)	n = 124 (36% men) age: 52.3 overweight participants with high blood pressure	0.3	DASH diet, DASH + weight management, control	Executive function memory-learning (TMT, Stroop interference, DS, VFT, VPA, WAT) and psychomotor speed (Ruff 2&7, DSST)	DASH diet alone did not significantly improve EFML compared with the control ( $P = 0.214$ ), but did significantly improve psychomotor speed (Cohen's D: $0.440$ ; $P = 0.036$ ). DASH diet with weight management significantly improved both EFML (Cohen's D: $0.562$ ; $P = 0.008$ ) and psychomotor speed (Cohen's D: $0.480$ ; $P = 0.023$ ) compared with the control

<sup>1</sup> ASF, animals semantic fluency; BNT, Boston Naming Test; BVRT, Benton Visual Retention Test; CDT, clock-drawing test; CTT, color trail test; DASH, Dietary Approaches to Stop Hypertension; DS, digit span; DST, digit span test; DSST, digit symbol substitution test; ELF, excluded letter fluency; ENCORE, Exercise and Nutrition Interventions for Cardiovascular Health; EVOO, extra-virgin olive oil; ILF, initial letter fluency; LNS, letter-number sequencing; MCI, mild cognitive disorder; MeDi, Mediterranean Diet; Med-Ly, Mediterranean diet for cognitive function and cardiovascular health in the elderly; MMSE, Mini-Mental State Examination; PREDIMED, Prevención con Dieta Mediterránea; RAVLT, Rey Auditory Verbal Learning Test; ROCF, Rey-Osterrieth Complex Figure; SS, symbol search; ST, Stroop Test; TMT, trail making test; TOL, Tower of London; VFT, verbal fluency test; VPA, verbal paired associates; WAIS, Wechsler adult intelligence scale; WAT, word association test.

or visual-spatial memory (78). The Prevención con dieta Mediterránea (PREDIMED) trial investigated the effect of the Mediterranean diet supplemented with extra-virgin olive oil or mixed nuts on cognitive decline and compared this with a low-fat control diet in Spanish adults at high vascular risk, which resulted in 3 articles based on 3 different population samples (35–37). Higher Mediterranean diet adherence with extra-virgin olive oil during 6.5 y was related to better cognitive performance ( $n = 522$ ) (36) and a lower risk of MCI ( $n = 268$ ) (37). Higher adherence to the Mediterranean diet with extra-virgin olive oil was also related to improved global cognition and frontal cognition, but had no effect on memory and MCI after 4.1 y of intervention ( $n = 334$ ) (35). Evidence on the effect of the Mediterranean diet with nuts on cognition was mixed (35–37). Higher adherence to the Mediterranean diet with nuts did not affect the risk of MCI (35, 36). In 1 of the PREDIMED populations ( $n = 522$ ) the Mediterranean diet with nuts improved global cognition (mean difference for Mini-Mental State Examination [MMSE]: 0.57; 95% CI: 0.11, 1.03,  $P = 0.015$ ; mean difference for the clock-drawing test [CDT]: 0.33; 95% CI: 0.003, 0.67;  $P = 0.048$ ) (36), whereas another PREDIMED population ( $n = 268$ ) did not show an effect of the Mediterranean diet with nuts (37). In addition, another PREDIMED sample ( $n = 334$ ) suggested that the Mediterranean diet with nuts particularly improved memory, but not frontal and global cognition (35). The third trial investigated the effect of the Mediterranean diet and a low-fat diet on cognitive performance compared with the waiting-list control diet in 155 participants from the UK with elevated cholesterol concentrations and showed an adverse effect of both the Mediterranean diet and the low-fat diet on attention after 12 wk of intervention (87). No effect of the Mediterranean diet on motor speed, memory, and choice reaction time was found compared with the control diet.

## DASH diet

### Observational evidence.

The DASH diet in relation to cognitive decline, dementia, or AD was examined in 1 cross-sectional study (50) and 6 longitudinal studies (Table 4) (52–54, 69, 72, 79). Each 1-unit increase in DASH diet score was cross-sectionally associated with better verbal memory ( $\beta$ : 0.18;  $P = 0.018$ ), but not with visual memory nor executive function or processing speed in US participants ( $n = 160$ ) (50). Longitudinally, the highest quintile of DASH diet adherence was associated with a 28% lower risk of MCI (HR: 0.72; 95% CI: 0.52, 1.02;  $P$ -trend = 0.04) in US participants ( $n = 6425$ ) after 9.11 y of follow-up (52). In addition, each 1-unit increase in DASH diet score was associated with less change in global cognition ( $\beta$ : 0.007;  $P = 0.03$ ), episodic memory ( $\beta$ : 0.008;  $P = 0.04$ ), and semantic memory ( $\beta$ : 0.009;  $P = 0.02$ ) in US participants after 4.1 y of follow-up ( $n = 826$ ) (54). Furthermore, adherence to the DASH diet was associated with better average cognition in US older adults ( $n = 3580$ ) (mean difference<sub>Q5vs.Q1</sub>: 0.97;  $P$ -trend = 0.0001), but not with cognitive decline after 10.6 y of follow-up (69). In 2 other studies including US ( $n = 16,144$ ) (72) and Swedish

( $n = 2223$ ) (79) participants no association was found after 4.1 y and  $\leq 10.6$  y of follow-up.

In the only longitudinal study on AD in US participants ( $n = 923$ ) a 39% lower risk was shown for highest DASH diet adherence (HR<sub>T3vs.T1</sub>: 0.61; 95% CI: 0.38, 0.97;  $P$ -trend = 0.07), whereas in this study somewhat stronger inverse associations were shown for the Mediterranean and MIND diets (53).

### Trial evidence.

A randomized controlled trial investigated the effect of the DASH diet on cognition in US adults over 4 mo ( $n = 124$ ) (Table 3) (58). Psychomotor function significantly improved among participants assigned to the DASH diet alone (Cohen's D: 0.440;  $P = 0.036$ ) and among those assigned to the DASH diet with additional weight management (Cohen's D: 0.480;  $P = 0.023$ ), where the control group consumed their usual diet. However, whereas the DASH diet with additional weight management significantly improved executive function, memory, and learning (Cohen's D: 0.562;  $P = 0.008$ ), no such effect was observed for the DASH diet alone.

## MIND diet

### Observational evidence.

In 1 cross-sectional (57) and 5 longitudinal (11, 53, 73, 75, 79) studies the MIND diet was investigated in relation to cognitive decline, dementia, or AD (Table 5). Higher adherence to the MIND diet was cross-sectionally associated with better cognitive performance (global cognition score  $15.6 \pm 0.09$  and  $14.9 \pm 0.10$  in the highest and lowest tertile of MIND diet score, respectively;  $P$ -trend < 0.001) and a 35% lower risk of poor cognitive performance (OR<sub>T3vs.T1</sub>: 0.70; 95% CI: 0.56, 0.86;  $P = 0.001$ ) among US adults ( $n = 5907$ ) (57). Longitudinally, the association of the MIND diet with cognitive decline was investigated in 3 studies in Swedish older adults ( $n = 2223$ ) (79) and US adults ( $n = 960$  and  $n = 16,058$ ) (11, 73). Higher adherence to the MIND diet was associated with less cognitive decline in Swedish older adults ( $n = 2223$ ) after 6 y of follow-up (79). In addition, in 1 study including US adults ( $n = 960$ ), higher MIND diet adherence was significantly associated with less cognitive decline after 4.7 y of follow-up in all 5 measured cognitive domains, including episodic memory ( $\beta$ : 0.0090;  $P = 0.001$ ), semantic memory ( $\beta$ : 0.0113;  $P < 0.0001$ ), visuospatial ability ( $\beta$ : 0.0077;  $P = 0.002$ ), perceptual speed ( $\beta$ : 0.0097;  $P < 0.0001$ ), and working memory ( $\beta$ : 0.0060;  $P = 0.01$ ) (11). Higher MIND diet score was also associated with less global cognitive decline ( $\beta$ : 0.0106;  $P < 0.0001$ ;  $\beta$ <sub>T3vs.T1</sub>: 0.0366;  $P = 0.01$ ) with a stronger inverse association for the MIND diet compared with the Mediterranean ( $P$  for MIND compared with MeDi = 0.02) and DASH diet ( $P$  for MIND compared with DASH = 0.02) (11). No association between the MIND diet and cognitive decline was observed in US older nurses after 12.9 y of follow-up ( $n = 16,058$ ) (73).

A longitudinal study in Australian older adults ( $n = 1220$ ) showed a 53% lower risk of cognitive impairment, which

**TABLE 4** Characteristics of the included observational human studies on the DASH diet in relation to cognitive decline, dementia, and AD<sup>1</sup>

Authors, year, study name	Study design	Population	Follow-up (y)	Exposure	Outcome	Results	Covariates
Blumenthal et al. (2017) (50), US	Cross-sectional	n = 160 (83% men) age: 65.4 sedentary adults aged ≥55 y with cognitive impairment and CVD risk factors	—	FFQ and 4-d food diary, A-MeDi and A-DASH score	Verbal memory (HVLT-R, ANT), visual memory (CFT), and executive function/processing speed (ST, DST, COWA, TMT, DSST, Ruff 2&7 Test)	Higher adherence to the DASH diet was associated with better verbal memory ( $\beta$ : 0.18; $P = 0.018$ ), but not with executive function/processing speed ( $P = 0.569$ ) or visual memory ( $P = 0.248$ )	Age, education, sex, ethnicity, total caloric intake, family history of dementia, and chronic use of anti-inflammatory medications
Shakersain et al. (2018) (79), Sweden SNAC-K	Longitudinal	n = 2223 (39% men) age: 69.5 y community residents from Kungsholmen ≥60 y	6	98-item SFFQ, A-MeDi, A-DASH and MIND scores, dietary components	Global cognition (MMSE)	DASH score was not associated with cognitive decline ( $P = 0.568$ ; $P_{\text{3x,1}} = 0.472$ ), nor with risk of MMSE score $\leq 24$ ( $P = 0.970$ ; $P_{\text{3x,1}} = 0.746$ )	Total caloric intake, age, sex, education, civil status, physical activity, smoking, BMI, vitamin/mineral supplement intake, vascular disorders, diabetes, cancer, depression, APOE $\epsilon 4$ , and dietary components other than those included in each dietary index
Berendsen et al. (2017) (72), US Nurses Health Study	Longitudinal	n = 16,144 (0% men) age: 74.3 y women ≥70 y	4.1	116-item SFFQ, DASH	Global cognition (TICS and composite score of TICS, EBMT, CF, and DST backward) and verbal memory (immediate and delayed recalls of EBMT and TICS 10-word list)	Higher long-term adherence to the DASH diet was associated with better average global cognition ( $P$ -trend = 0.009), verbal memory ( $P$ -trend = 0.002), and TICS ( $P$ -trend = 0.03), but was not significantly associated with change in global cognition ( $P$ -trend = 0.51), verbal memory ( $P$ -trend = 0.68), or TICS score ( $P$ -trend = 0.98) during follow-up	Age, education, physical activity, caloric intake, alcohol intake, smoking status, multivitamin use, BMI, and history of hypercholesterolemia, myocardial infarction, and diabetes mellitus
Haring et al. (2016) (52), US WHIMS	Longitudinal	n = 6425 (0% men) age: 65–79 y postmenopausal women	9.11	FFQ, A-MeDi score and DASH score	MCI (MMSE and battery of neuropsychological tests [animal category, BNT, word list memory task, copying and recalling 4 line drawings, TMT])	Quintile of DASH score was significantly associated with lower risk of MCI (HR <sub>3x,0.1</sub> : 0.72; 95% CI: 0.52, 1.02; $P$ -trend = 0.04)	Age, race, education level, WHI hormone trial randomization assignment, baseline 3MS level, smoking status, physical activity, diabetes, hypertension, BMI, family income, depression, history of CVD, and total energy intake
Morris et al. (2015) (53), US Rush MAP	Longitudinal	n = 923 ( $\pm 24\%$ men) age: 58–98 y people living in retirement communities or senior public housing units	4.5	144-item SFFQ, A-MeDi, A-DASH, and MIND scores	AD (based on NINCDS-ADRDA criteria)	For the DASH diet only the highest tertile of adherence was significantly associated with lower risk of AD (HR <sub>3x,0.1</sub> : 0.61; 95% CI: 0.38, 0.97; $P$ -trend = 0.07)	Age, sex, education, Apolipoprotein E ( $\epsilon 4$ ), participation in cognitively stimulating activities, physical activity, total energy intake, and cardiovascular conditions
Tangney et al. (2014) (54), US MAP	Longitudinal	n = 826 (26% men) age: 81.5 y elderly living in Chicago retirement communities and subsidized housing, normal cognitive function	4.1	144-item SFFQ, A-MeDi score, A-DASH score	Global cognition (composite score of 19 tests), episodic memory (logical memory, word list recall, word list recognition, EBS), semantic memory (verbal fluency from CERAD, BNT, 12-item reading test), working memory (DST forward and backward, DO), perceptual speed (SDMT, NC SNS), and visuospatial ability (JLO, SPM)	Continuous DASH score was significantly associated with slower rate of decline in global cognition ( $\beta$ : 0.007; $P = 0.03$ ), episodic memory ( $\beta$ : 0.008; $P = 0.04$ ), and semantic memory ( $\beta$ : 0.009; $P = 0.02$ ). Tertile of DASH score was only significantly associated with a slower rate of change in global cognition ( $\beta_{\text{3x,1}}$ : 0.022; $P = 0.04$ ). DASH and MeDi scores were almost as predictive for rate of change of global cognition (standardized $\beta$ : 2.33 and 2.0, respectively)	Total energy intake, age, sex, education, and cognitive activities
Wengreen et al. (2013) (69), US Cache County Study on Memory, Health and Aging	Longitudinal	n = 3580 ( $\pm 43\%$ men) age: ≥65 y mainly non-Hispanic white	10.6	142-item FFO, MeDi score, DASH score	Global cognition (GMS)	Higher quintile of DASH score was associated with better average cognition during follow-up (mean difference <sub>3x,0.1</sub> : 0.97; $P$ -trend = 0.0001), but was not significantly associated with rate of change of cognitive function	Age, sex, education, BMI, frequency of moderate physical activity, multivitamin and mineral supplement use, history of drinking and smoking and history of diabetes, heart attack, or stroke

<sup>1</sup>AD, Alzheimer's disease; A-MeDi, alternate Mediterranean diet; ANT, animal naming test; APOE  $\epsilon 4$ , apolipoprotein E; BNT, Boston Naming Test; CERAD, Consortium to Establish a Registry for Alzheimer's Disease; CF, category fluency; CFT, complex figure test; COWA, controlled oral word association test; CVD, cardiovascular disease; DASH, Dietary Approaches to Stop Hypertension; DO, digit ordering; DSST, digit symbol substitution test; DST, digit span test; EBMT, East Boston Memory Test; EBS, East Boston Story; HVLT-R, Hopkins Verbal Learning Test-Revised; JLO, judgement of line orientation; MAP, Memory And Aging Project; MCI, mild cognitive impairment; MIND, Mediterranean-DASH Intervention for Neurodegenerative Delay; MMSE, Mini-Mental State Examination; NC, number comparison; NINCDS-ADROA, National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association; SDMT, Symbol Digit Modalities Test; SFFQ, semi-quantitative FFO; SNAC-K, Swedish National Study on Aging and Care in Kungsholmen; SNS, Stroop, Neuropsychological Screening; SPM, standard progressive matrices; ST, Stroop Test; TICS, Telephone Interview for Cognitive Status; TMT, trail making test; WHI, Women's Health Initiative; WHIMS, Women's Health Initiative Memory Study; 3MS, modified mini-mental state.

**TABLE 5** Characteristics of the included observational human studies on the MIND diet in relation to cognitive decline, dementia, and AD<sup>1</sup>

Authors, year, study name	Study design	Population	Follow-up (y)	Exposure	Outcome	Results	Covariates
McEvoy, Guyer, Langa & Yaffe (2017) (57), US Health and Retirement Study	Cross-sectional	n = 5907 (40% men) age: 67.8 y community dwelling adults from the age of 50 y	—	163-item SFFQ, A-MeDi score, MIND diet score	Cognitive performance (global cognition score based on immediate and delayed recall, backward counting and serial seven subtraction)	Higher MIND score tertile was significantly associated with better cognitive performance (P-trend < 0.001). Higher tertile of MIND score was significantly associated with lower risk of poor cognitive performance (OR <sub>T3xT1</sub> : 0.70; 95% CI: 0.56, 0.86; P = 0.001)	Sex, age, race, low education attainment, current smoking, obesity, total wealth, hypertension, diabetes mellitus, physical inactivity, depression, and total energy intake
Hosking, Eramudugolla, Cherbuin, & Anstey (2019) (75), Australia PATH Through Life Study	Longitudinal	n = 1220 (50% men) age: 60–64 y older Australian adults	12	CSIRO-FFQ, MeDi, A-MeDi, and MIND scores, dietary components	Cognitive impairment: MCI/dementia (Winbald criteria, NINCDS-ADRDA criteria)	Higher tertile of MIND score was significantly associated with a lower risk of cognitive impairment (OR <sub>T3xT1</sub> : 0.47; 95% CI: 0.24, 0.91; P-trend = 0.026)	Energy intake, age, sex, APOE ε4 allele, education, mental activity, physical activity, smoking status, depression, diabetes, BMI, hypertension, heart disease, and stroke
Berendsen et al. (2018) (73), US Nurses' Health Study	Longitudinal	n = 16,058 (0% men) age: 74.3 y older women	12.9	116-item FFQ, MIND score	Global cognition (TICS and composite score of TICS, EBMT, CF, and DST backward) and verbal memory (immediate and delayed recalls of EBMT and TICS 10-word list)	Higher adherence to MIND diet was not significantly associated with less decline in global cognition (P-trend = 0.95), verbal memory (P-trend = 0.98), or TICS score (P-trend = 0.73) during follow-up	Age, education, physical activity, caloric intake, alcohol intake, smoking status, multivitamin use, BMI, depression, and history of hypertension, hypercholesterolemia, myocardial infarction, and diabetes mellitus
Shakersain et al. (2018) (79), Sweden SNAC-K	Longitudinal	n = 2223 (39% men) age: 69.5 y community residents from Kungsholmen ≥60 y	6	98-item SFFQ, A-MeDi, A-DASH, and MIND components	Global cognition (MMSE)	Higher MIND score was significantly associated with less cognitive decline (β: 0.006; 95% CI: 0.003, 0.009; P < 0.001; β <sub>T3xT1</sub> : 0.126; 95% CI: 0.064, 0.188; P < 0.001) and with lower risk of MMSE score ≤24 (HR: 0.965; 95% CI: 0.941, 0.989; P = 0.005; HR <sub>T3xT1</sub> : 0.468; 95% CI: 0.261, 0.840; P = 0.011)	Total caloric intake, age, sex, education, civil status, physical activity, smoking, BMI, vitamin/mineral supplement intake, vascular disorders, diabetes, cancer, depression APOE ε4, and dietary components other than those included in each dietary index
Morris et al. (2015) (53), US Rush MAP	Longitudinal	n = 923 (± 24% men) age: 58–98 y people living in retirement communities or senior public housing units in Chicago	4.5	144-item SFFQ, A-MeDi, A-DASH, and MIND scores	AD (based on NINCDS-ADRDA criteria)	Both middle and high tertile of MIND diet score were significantly associated with lower risk of AD (HR <sub>T3xT1</sub> : 0.65; 95% CI: 0.44, 0.98; HR <sub>T3xT1</sub> : 0.47, 95% CI: 0.29, 0.76; P-trend = 0.002)	Age, sex, education, APOE ε4, participation in cognitively stimulating activities, physical activity, total energy intake, and cardiovascular conditions
Morris et al. (2015) (11), US Rush MAP	Longitudinal	n = 960 (25% men) age: 81.4 y elderly living in retirement communities or senior public housing units in Chicago	4.7	144-item SFFQ, MIND diet score	Global cognition, episodic memory, semantic memory, visuospatial ability, perceptual speed and working memory	MIND diet score was significantly associated with slower decline in global cognition (β: 0.0106; P < 0.0001), episodic memory (β: 0.0090; P = 0.001), semantic memory (β: 0.0113; P < 0.0001), visuospatial ability (β: 0.0077; P = 0.002), perceptual speed (β: 0.0097; P < 0.0001), and working memory (β = 0.0060; P = 0.01). Higher tertile of MIND diet score was significantly associated with slower decline of global cognitive score (β <sub>T3xT1</sub> : 0.0366; P = 0.01). MIND diet score was more protective against cognitive decline than the DASH score or MeDi score according to the standardized β coefficients (β <sub>MIND</sub> : -4.39, β <sub>MeDi</sub> : -2.46, β <sub>DASH</sub> : 2.60; P <sub>MIND vs MeDi</sub> = 0.02; P <sub>MIND vs DASH</sub> = 0.03)	Age, sex, education, participation in cognitive activities, smoking history, physical activity hours per week, total energy intake, (APOE ε4 allele, time, history of stroke, myocardial infarction, diabetes, hypertension, and interaction terms between each covariate and time)

<sup>1</sup> AD, Alzheimer's disease; A-MeDi, alternate Mediterranean diet; CF, category fluency; CSIRO, Commonwealth Scientific and Industrial Research Organisation; DASH, Dietary Approaches to Stop Hypertension; DST, digit span test; EBMT, East Boston Memory Test; MAP, Memory and Aging Project; MIND, Mediterranean-DASH Intervention for Neurodegenerative Delay; MMSE, Mini-Mental State Examination; NINCDS-ADRDA, National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association; PATH, Personality and Total Health; SFFQ, semi-quantitative FFQ; SNAC-K, Swedish National Study on Aging and Care in Kungsholmen; TICS, Telephone Interview For Cognitive Status.

included both MCI and dementia, for highest MIND diet adherence ( $OR_{T3vs.T1}$ : 0.47; 95% CI: 0.24, 0.91;  $P$ -trend = 0.026) (75). In the only longitudinal study that investigated AD, a 53% lower risk was found for highest MIND diet adherence ( $HR_{T3vs.T1}$ : 0.47; 95% CI: 0.29, 0.76) in US adults ( $n = 923$ ) after 4.5 y of follow-up (53). In addition, a 35% lower AD risk was shown for moderate MIND diet adherence ( $HR_{T3vs.T1}$ : 0.65; 95% CI: 0.44, 0.98), whereas for moderate adherence to the Mediterranean and DASH diets no significant association with AD was shown.

Evidence for the association of the dietary components of the Mediterranean, DASH, and MIND diets with cognitive decline, dementia, and AD is discussed below and presented in Table 6.

## Dietary components

### *Fish and $\omega$ -3.*

Fish consumption was cross-sectionally associated with a lower risk of dementia (39) and better attention (84), but not with global cognition (38, 39, 74, 84), visual memory (84), executive function (84), episodic verbal memory (38), working memory (38), or a lower risk of MCI (56, 84). In 2 (64, 79) of 12 (34, 41–43, 64, 66, 69, 75, 76, 79, 81, 83) longitudinal studies, fish consumption was associated with better subjective cognitive function and less cognitive decline; 1 study showed an increased risk of MCI, mild cognitive disorder, and cognitive decline (76). Another longitudinal study demonstrated an association between fish consumption and less cognitive decline for participants aged  $\geq 65$  y (83).

### *Plant-based foods.*

In 1 cross-sectional study the consumption of plant foods in general was examined, showing no association with self-reported cognitive function (74). In 2 (56, 84) of 4 (38, 39, 56, 84) cross-sectional studies an association between vegetable consumption and better cognitive function was shown; vegetable consumption was associated with better visual memory (84) and a lower risk of MCI (56). Longitudinally, vegetable consumption was associated with better subjective cognitive function and less cognitive decline in 3 (41, 64, 66) of 12 studies (34, 41, 43, 64, 66, 67, 69, 75, 76, 79, 81, 83); 1 study showed a higher risk of MCI, but not of mild cognitive disorder or cognitive decline (76). Green leafy vegetables specifically were not associated with a lower risk of cognitive impairment in a longitudinal study (75). Olive oil consumption was associated with better cognitive function or less cognitive decline for at least some cognitive domains in 2 (38, 84) of 3 (38, 39, 84) cross-sectional studies and 2 (34, 48) of 3 (34, 42, 48) longitudinal studies. Results on vegetable oil and seed oils are mixed, showing inverse (79) as well as adverse associations (42). Nut consumption, specifically walnut consumption, was cross-sectionally associated with better cognitive function (38). Longitudinally, nut consumption in general was associated with better cognitive function and a lower risk of cognitive impairment in 3 (64, 69, 75) of 9 (34, 41, 43, 64, 66, 67, 69,

75, 83) studies. Legume intake, examined in 4 cross-sectional (38, 39, 56, 84) and 12 longitudinal (34, 41, 43, 64, 66, 67, 69, 75, 76, 79, 81, 83) studies, was associated with better cognitive function in only 1 longitudinal study (69). Fruit consumption was not associated with cognitive function in cross-sectional studies (38, 39, 56, 84). In 1 (64) of 11 (34, 41, 43, 64, 66, 67, 69, 76, 79, 81, 83) longitudinal studies, fruit consumption was associated with better subjective cognitive function, but in another longitudinal study fruit consumption was associated with a higher risk of MCI. Consumption of berries specifically was not associated with cognitive impairment in a longitudinal study (75). No association between potatoes and cognitive function was observed in 2 cross-sectional studies (39, 84) and 1 longitudinal study (81). Urinary polyphenol excretion, a biomarker of dietary polyphenol intake, was associated with better immediate episodic verbal memory in a cross-sectional study, but results for delayed episodic verbal memory were mixed (38).

### *Meat.*

Meat consumption in general was associated with worse cognitive function on at least some domains in 1 (38) of 2 (38, 84) cross-sectional studies and 1 (81) of 7 (34, 41, 43, 69, 75, 76, 81) longitudinal studies. Red meat consumption specifically was associated with worse executive function in 1 (84) of 3 (39, 74, 84) cross-sectional studies, but longitudinal studies investigating red and processed meat did not show an association with cognitive decline (64, 66, 67, 69, 79, 83). The consumption of poultry was not associated with cognitive function in 3 cross-sectional studies (39, 74, 84), but was associated with less cognitive decline in 1 (79) of 2 (75, 79) longitudinal studies.

### *Grains and cereals.*

Grain and cereal consumption together was not associated with risk of MCI in a cross-sectional study (56). Cereal consumption was associated with worse cognitive function on at least some cognitive domains in 1 (38) of 2 (38, 74) cross-sectional and 1 (76) of 6 (34, 41, 43, 64, 76, 81) longitudinal studies, whereas the consumption of nonrefined cereals specifically was associated with better cognitive function in 1 (39) of 2 (39, 84) cross-sectional studies. Grain consumption, specifically refined grains, was associated with more cognitive decline in 1 (79) of 3 (69, 75, 79) longitudinal studies, but whole grain consumption was associated with better average performance on at least some cognitive domains in 2 (67, 69) of 4 (66, 67, 69, 83) longitudinal studies.

### *Saturated and unsaturated fatty acids.*

MUFA:SFA ratio was cross-sectionally associated with an increased risk of nonamnesic MCI (56), whereas an association with less cognitive decline was shown in 3 (34, 66, 67) of 9 (34, 41, 43, 45, 64, 66, 67, 69, 76) longitudinal studies. Results for consumption of MUFA or PUFA were mixed, with 1 longitudinal study showing a beneficial association with cognitive decline (45) and other longitudinal studies showing adverse associations (42, 76). A higher

**TABLE 6** Characteristics of the included observational human studies on the dietary components of the Mediterranean, DASH, and MIND diets in relation to cognitive decline, dementia, and AD<sup>1</sup>

Authors, year, study name	Study design	Population	Follow-up (y)	Exposure	Outcome	Results	Covariates
Anastasiou et al. (2017) (39), Greece HELIAD	Cross-sectional	n = 1864 (41% men) age: 73.0 y elderly >64 y from 2 cities in Greece, random selection from municipality records	—	SFFQ, A-MeDi score, dietary components	Cognitive status (dementia [DSM-IV, NINCDS/ADRDA criteria]), cognitive performance (memory [GVL, CFT]), language (BNT, CIMS, categories: objects and the letter A), executive functioning [TMT, verbal fluency, ASR, GST, MP, months forwards and backwards], and visuospatial perception [JLO, CDT, CFT, TMT])	Fish consumption was significantly associated with lower risk of dementia (OR: 0.31; 95% CI: 0.147, 0.658, $P = 0.002$ ) and consumption of nonrefined cereals was significantly associated with cognitive performance ( $\beta$ : 0.059, $P = 0.004$ ). No significant associations for potatoes, fruits, vegetables, legumes, olive oil, red meats, poultry, full-fat dairy, and alcohol with cognitive status or performance	Age, sex, education, number of clinical comorbidities, and energy intake
Bajerska, Woźniwicz, Suwaliska & Jeszka (2014) (84), Poland	Cross-sectional	n = 87 (35% men) age: 70.0 y elderly >60 y from rural areas of Wielkopolska from a community with high risk of metabolic syndrome	—	FFQ, A-MeDi score (high vs. low), dietary components	MCI, global cognition (MMSE), attention (TMT), visual memory (PRM), executive function (ST, SOC, SWM, SSP)	Consumption of fish, vegetables, and olive or rapeseed oil was positively associated with attention ( $\beta$ : -1.97; $P = 0.05$ ), visual memory ( $\beta$ : 0.09; $P = 0.01$ ), and executive function, ( $\beta_{\text{STROOP}}$ : -0.33; $P = 0.05$ ; $\beta_{\text{SSP}}$ : -0.06; $P = 0.05$ ), respectively. Consumption of full-fat dairy products was negatively associated with executive function ( $\beta_{\text{SWM}}$ : 0.02; $P = 0.05$ ). Consumption of red meat and meat products was negatively associated with executive function ( $\beta_{\text{SOC}}$ : -0.02, $P = 0.01$ ) and global cognition ( $\beta$ : -0.02; $P = 0.01$ ). No significant associations for unrefined cereals, fruit, legumes, potatoes, poultry, and alcohol with global cognition, attention, visual memory, or executive function	Gender, age, education level, smoking status, family status, leisure time physical activity, and existence of metabolic syndrome
Crichton, Bryan, Hodgson & Murphy (2013) (74), Australia	Cross-sectional	n = 1183 (36% men) age: 50.6 y adults from 40 to 65 y from Australia	—	215-item FFO, adapted MeDi score, dietary components	Self-reported cognitive function (CFQ) on mistakes in tasks on perception, memory, and motor function	Intake of plant food, fish, red meat, cereals, dairy, and poultry was not significantly associated with CFQ	Age, gender, education, BMI, exercise, smoking, and total energy intake
Valls-Pedret et al. (2012) (38), Spain, PREDIMED	Cross-sectional	n = 447 (48% men) age: 66.9 y community dwelling people $\geq 55$ y at high risk of CVD	—	137-item FFO, intake of many dietary components	Global cognition (MMSE), immediate and delayed episodic verbal memory (RAVLT) and immediate and working memory (DST)	Wine intake significantly associated with better global cognition ( $\beta$ : 0.252, $P = 0.044$ ). Total olive oil intake significantly associated with better immediate episodic verbal memory ( $\beta$ : 0.755, $P = 0.014$ ), whereas cereal intake was significantly associated with worse immediate episodic verbal memory ( $\beta$ : -0.431; $P = 0.032$ ). Intake of virgin olive oil, total olive oil, and coffee were significantly associated with better delayed episodic verbal memory ( $\beta_{\text{DST}}$ : 0.136, $P = 0.037$ ; $\beta_{\text{DST}}$ : 0.001; $\beta_{\text{coffee}}$ : 0.294, $P = 0.016$ ), whereas meat and cereal intake were significantly associated with worse delayed episodic verbal memory ( $\beta_{\text{meat}}$ : -0.845, $P = 0.020$ ; $\beta_{\text{cereal}}$ : -0.235, $P = 0.001$ ). Walnut intake was significantly associated with better working memory ( $\beta$ : 1.191, $P = 0.039$ ). Total urinary polyphenol excretion was significantly associated with better immediate episodic verbal memory ( $\beta$ : 1.208, $P = 0.015$ ), but not with delayed episodic verbal memory ( $\beta$ : 0.357, $P = 0.053$ ). Higher quintile of polyphenol excretion was significantly associated with immediate and delayed episodic verbal memory ( $P$ -trend = 0.018 and $P$ -trend = 0.003, respectively). No significant associations for vegetables, legumes, fruits, total nuts, fish, dairy products, and total alcohol	Gender, age, education, BMI, smoking, APOE $\epsilon 4$ allele, energy expenditure in physical activity, diabetes, hypertension, and hyperlipidaemia

(Continued)

**TABLE 6** (Continued)

Authors, year, study name	Study design	Population	Follow-up (y)	Exposure	Outcome	Results	Covariates
Roberts et al. (2010) (56), US	Cross-sectional	n = 1233 (52% men) age: 70–89 y random selection of residents of Olmsted County	—	128-item block FFQ, MeDi score, dietary components	MCI (CDR and neurological evaluation [STMS, HS, LMII, VRIL, AVL1, TMT, DSST, BNT, CF PC, BD]), a-MCI or na-MCI	Vegetable intake was significantly associated with lower risk of MCI (OR <sub>3y5.T1</sub> : 0.66; 95% CI: 0.44, 0.99; P = 0.05; P-trend = 0.02). (MUFA + PUFA):SFA ratio was significantly associated with lower risk of MCI (OR <sub>3y5.T1</sub> : 0.52; 95% CI: 0.33, 0.81; P = 0.004; P-trend = 0.007). When split into a-MCI and na-MCI only (MUFA + PUFA):SFA ratio was significantly associated with lower risk of a-MCI (OR <sub>3y5.T1</sub> : 0.49; 95% CI: 0.30, 0.80; P = 0.004; P-trend = 0.01) after adjustment and MUFA:SFA ratio was significantly associated with increased risk of na-MCI (OR <sub>3y5.T1</sub> : 1.70; 95% CI: 0.71, 4.08; P = 0.23; P-trend = 0.04). No significant association for legumes, fruits, dairy, grains and cereals, meat, fish, and alcohol with risk of MCI, a-MCI, or na-MCI	Age, years of education, total caloric intake, sex, stroke, APOE ε4 allele status, coronary artery disease, and depressive symptoms
Hosking, Eramudugolla, Cherbuin, & Anseiy (2019) (75), Australia PATH Through Life Study	Longitudinal	n = 1220 (50% men) age: 60–64 y older Australian adults	12	CSIRO-FFQ, MeDi, A-MeDi, and MIND scores, dietary components	Cognitive impairment: MCI/dementia (Winbald criteria, NINCDS-ADDA criteria)	Nut consumption was significantly associated with a lower risk of MCI/dementia (OR: 0.42; 95% CI: 0.21, 0.85; P = 0.016). No significant association for processed and fast fried food, sweets and pastries, green leafy vegetables, other vegetables, berries, fish, cheese, grains, beans, poultry, meat, or wine	Energy intake, age, sex, APOE ε4 allele, education, mental activity, physical activity, smoking status, depression, diabetes, BMI, hypertension, heart disease, and stroke
Bhushan et al. (2018) (79), HPPS	Longitudinal	n = 27842 (100% men) age: 51 y male health professionals from the US	±26	FFQ, MeDi score, dietary components	Subjective cognitive function	Higher quintile of intake of vegetables (β: -0.033; P < 0.001), fruits and nuts (β: -0.016; P = 0.005), or fish (β: -0.024; P < 0.001) was significantly associated with better subjective cognitive function. No significant association for legumes, cereals, red meat and meat products, MUFA:SFA ratio, milk and dairy products, or alcohol	Age, smoking history, diabetes, hypertension, depression, hypercholesterolemia, physical activity level, and BMI
Shakersain et al. (2018) (79), Sweden SNAc-K	Longitudinal	n = 2223 (39% men) age: 69.5 y community residents from Kungsholmen ≥60 y	6	98-item SFFQ, A-MeDi, A-DASH, and MIND scores, dietary components	Global cognition (MMSE)	Intake of poultry, fish, vegetable oil, wine (red and white), tea, and water was significantly associated with slower cognitive decline, whereas intake of grains (refined grains), dairy products (high-fat dairy products), milk (high-fat milk), butter (margarine), sugar and fruit juice was significantly associated with faster cognitive decline during follow-up. No significant association for vegetables, fruits, legumes, red and processed meat, ice cream, beer, spirits, and carbonated drinks	Total caloric intake, age, sex, education, civil status, physical activity, smoking, BMI, vitamin/mineral supplement intake, vascular disorders, diabetes, cancer, depression APOE ε4, and dietary components other than main exposure in each model
Tanaka et al. (2018) (43), Italy InCHIANTI	Longitudinal	n = 832 age: 75.4 y (44% men) older adults from the Chianti region in Italy	10.1	FFQ, MeDi score, dietary components	Global cognition (MMSE)	No significant associations for intake of vegetables, legumes, fish, fruits and nuts, cereal, MUFA:SFA ratio, dairy, meat or alcohol with cognitive decline	Age, sex, study site, chronic diseases, years of education, total energy intake, physical activity, BMI, APOE ε4 allele, C-reactive protein (CRP), and IL-6
Galbete et al. (2015) (34), Spain Sun Project	Longitudinal	n = 823 (71% men) age: 61.9 y Spanish university graduates <55 y	6–8	136-item SFFQ, MeDi score, dietary components	Cognitive function (TICS)	Intake of olive oil and MUFA:SFA ratio above median was significantly associated with less cognitive decline than intake below median (mean difference <sub>CO</sub> : -0.37; 95% CI: -0.68, -0.06; P = 0.020, mean difference <sub>MUFA:SFA</sub> : -0.53; 95% CI: -0.84, -0.22; P = 0.001). No significant association for fruits and nuts, vegetables, cereals, legumes, fish, meat and meat products, dairy, and alcohol with cognitive decline	Age, sex, APOE genotype, TICS score at final cognitive evaluation, follow-up time between baseline and second cognitive evaluation, total energy intake, BMI, smoking status, physical activity, diabetes, hypertension, hypercholesterolemia, history of CVD, years of university education, and all other items in the MeDi score

(Continued)

**TABLE 6** (Continued)

Authors, year, study name	Study design	Population	Follow-up (y)	Exposure	Outcome	Results	Covariates
Qin et al. (2015) (83), China Health and Nutrition Survey	Longitudinal	n = 1650 (± 50% men) age ≥ 55 y elder Chinese community dwellers	5.3	3-d 24-h recall, adapted MeDi score, dietary components	Global cognition, composite z-scores and verbal memory (modified TICS)	Fish consumption was, only in participants ≥ 65 y, associated with slower cognitive decline (mean difference: 0.34; 95% CI: 0.11, 0.56) and animal-source cooking fat was associated with faster cognitive decline (mean difference: -0.31; 95% CI: -0.55, -0.07) compared with no consumption. No significant association for vegetables, legumes and nuts, fruits, fiber-rich grains, dairy products, alcohol, and red meat and processed meat with cognitive decline Vegetable consumption was significantly associated with less substantial cognitive decline (OR: 0.39; 95% CI: 0.22, 0.69; P = 0.001), but not with mild cognitive decline (P = 0.244). No significant association for legumes, fruits and nuts, dairy products, cereals, meat, fish, alcohol, and MUFA:SFA with mild, or substantial cognitive decline	Age, gender, education, region, urbanization index, annual household income per capita, total energy intake, physical activity, current smoking, time since baseline, BMI, hypertension, and time interactions with each covariate
Trichopoulos et al. (2015) (41), Greece EPIC-Greece	Longitudinal	n = 401 (36% men) age > 65 y elderly EPIC participants from Athens or the Attica area	6.6	150-item SFFQ, MeDi score, dietary components	Global cognition (MMSE)		Sex, age, years of education, BMI, physical activity, smoking status, diabetes, hypertension, cohabiting, and total energy intake
Samieri, Okereke, Devore & Grodstein (2013) (66), US Nurses' Health Study	Longitudinal	n = 16,058 (0% men) mean age: 74.3 y women from the Nurses' Health Study ≥ 70 y	6	116-item SFFQ, adapted MeDi score, dietary components	Global cognition (TICS and composite score of TICS, EBMT, CF, DST backward), and verbal memory (immediate and delayed recalls of the EBMT and TICS)	Vegetable intake was significantly associated with less decline in global cognition (mean difference <sub>Q5vsQ1</sub> : -0.011; 95% CI: 0.001, 0.020; P-trend = 0.04). MUFA:SFA ratio was significantly associated with less decline in global cognition (mean difference <sub>Q5vsQ1</sub> : 0.013; 95% CI: 0.005, 0.021; P-trend < 0.001) and verbal memory (mean difference <sub>Q5vsQ1</sub> : -0.014; 95% CI: 0.004, 0.024; P-trend = 0.001). No significant association for legumes, fruits, whole grains, nuts, fish, red and processed meat, and alcohol with change in global cognition or verbal memory Higher quintile of MUFA:SFA ratio was associated with slower decline of global cognition (mean difference <sub>Q5vsQ1</sub> : 0.07; 95% CI: 0.01, 0.12; P-trend = 0.03) and verbal memory (mean difference <sub>Q5vsQ1</sub> : -0.07; 95% CI: 0.01, 0.14; P-trend = 0.05). However, higher quintile of MUFA:SFA ratio was associated with worse average global cognition (mean difference <sub>Q5vsQ1</sub> : -0.11, -0.02; P-trend = 0.002). Higher quintile of whole grain intake was significantly associated with better average global cognition (mean difference <sub>Q5vsQ1</sub> : 0.07; 95% CI: 0.02, 0.12; P-trend = 0.02). No significant association for fruits, vegetables, legumes, nuts, red and processed meats, and alcohol with decline in global cognition or verbal memory, nor with average global cognition or verbal memory	Age, education, long-term physical activity and energy intake, BMI, smoking, multivitamin use and history of depression, diabetes, hypertension, hypercholesterolemia, or myocardial infarction
Samieri et al. (2013) (67), US Women's Health Study	Longitudinal	n = 6174 (0% men) age: 72 y subset of participants from the Women's Health study aged ≥ 65 y	4	131-item SFFQ, adapted MeDi score, dietary components	Global cognition (TICS, EBMT, CF) and verbal memory (EBMT, delayed recall of TICS 10-word list)		Treatment arm, age at initial cognitive testing, Caucasian race, high education, high income, energy intake, physical activity, BMI, hypercholesterolemia, hormone use, and depression
Tirova et al. (2013) (81), Sweden A follow-up of PIVUS	Longitudinal	n = 194 (52% men) age: 70.1 y subset of PIVUS participants with cognitive assessment at the age of 75 y	5	7-d food diary, adapted MeDi score, dietary components	Global cognition (7MS), brain volume (BD TI-weighted MRI-scan)	Consumption of meat and meat products was significantly associated with worse global cognitive function (β: -0.26; P < 0.001) and smaller total brain volume (β: -0.16; P = 0.04). No association for alcohol, milk and milk products, PUFA:SFA, vegetables and legumes, fruits, cereals and potatoes, and fish with global cognition, total brain volume, or volume of gray or white matter	Gender, energy intake, education, self-reported physical activity, low-density cholesterol, BMI, systolic blood pressure, and HOMA-IR
Wengren et al. (2013) (69), US Cache County Study on Memory, Health and Aging	Longitudinal	n = 3580 (± 43% men) age ≥ 65 y mainly non-Hispanic white	10.6	142-item FFQ, MeDi score, DASH score, dietary components	Global cognition (3MS)	Significant better average cognitive function during follow-up for higher quintile of intake of whole grain (mean difference <sub>Q5vsQ1</sub> : 1.19; P-trend = 0.005-4), nuts and legumes (mean difference <sub>Q5vsQ1</sub> : 1.22; P-trend < 0.0001), and legumes only (mean difference <sub>Q5vsQ1</sub> : 1.16; P-trend < 0.0001). No significant association for intake of fruit, vegetables, red and processed meat, meat and meat products, low-fat dairy, sweetened beverages, sodium, all grains, fish, full-fat dairy, and MUFA:SFA ratio	Age, sex, education, BMI, frequency of moderate physical activity, multivitamin and mineral supplement use, history of drinking and smoking, and history of diabetes, heart attack, or stroke

(Continued)

TABLE 6 (Continued)

Authors, year, study name	Study design	Population	Follow-up (y)	Exposure	Outcome	Results	Covariates
Cherbuin & Anstey (2012) (76), Australia PATH Through Life Study	Longitudinal	n = 1528 (±49% men) age: 60–64 y random selection of residents of Canberra	4	215-item FFQ, MeDI score, dietary components	MCI, cognitive decline, cognitive disorder (CDR), any-MCD (based on MMSE, CVLT, SDMT, PP, and SRT)	Fish intake was associated with higher risk of MCI (OR: 1.02; 95% CI: 1.00, 1.04; P = 0.048), CDR 0.5 (OR: 1.02; 95% CI: 1.00, 1.04; P = 0.027), and any-MCD (OR: 1.02; 95% CI: 1.00, 1.03; P = 0.012). MUFA intake was significantly associated with risk of MCI (OR: 5.60; 95% CI: 1.66, 18.76; P = 0.005) and CDR 0.5 (OR: 3.10; 95% CI: 1.07, 9.02; P = 0.037). Dairy consumption was significantly associated with risk of MCI (OR: 1.01; 95% CI: 1.00, 1.01; P = 0.030) and any-MCD (OR: 1.01; 95% CI: 1.00, 1.01; P = 0.027). Fruit intake and vegetable intake were associated with risk of MCI (OR: 1.01; 95% CI: 1.00, 1.01; P = 0.022 and OR: 1.01; 95% CI: 1.00, 1.02; P = 0.020, respectively). Cereal intake was significantly associated with higher risk of any-MCD (OR: 1.01; 95% CI: 1.00, 1.01; P = 0.027). No significant association for intake of SFA, meat, legumes, MUFA:SFA ratio, or alcohol	Age, sex, education, APOE ε4 genotype, BMI, physical activity, stroke, diabetes, hypertension, and total energy intake
Berr et al. (2009) (48), France Three-city study	Longitudinal	n = 6947 (40% men) age >65 y noninstitutionalized elderly from Bordeaux, Montpellier, and Dijon	±4	FFQ, olive oil intake (none, moderate, intensive)	Global cognition (MMSE, BVRT, IST)	Intensive use of olive oil but not moderate use of olive oil, was significantly associated with reduced risk of decline in visual memory (OR <sub>T3+T1</sub> : 0.83; 95% CI: 0.69, 0.99; P = 0.04). Intensive use of olive oil was not associated with decline in verbal fluency after adjustment (P = 0.10) or with global cognition (P = 0.58). Results remained similar when data from participants with incident dementia during follow-up was removed	Age, sex, centre, education, income, baseline cognitive score, depressive symptoms, APOE ε4 allele, CVD, hypertension, diabetes, hypercholesterolemia, BMI, smoking status, and dietary intake of fruits/vegetables; ω-3 oil, fish, coffee, and alcohol
Psaloupoulou et al. (2008) (42), Greece EPIC-Greece	Longitudinal	n = 732 (35% men) age ≥60 y men and women ≥60 y from Attica	8.0	150-item FFQ, MeDI score, dietary components	Global cognition (MMSE)	PUFA intake and seed oil intake were significantly associated with worse global cognition ( $\beta_{PUFA}$ : -0.040; 95% CI: -0.088, -0.013; P = 0.004; $\beta_{SEED}$ : -0.034; 95% CI: -0.056, -0.012; P = 0.002). No significant association for SFA, MUFA, olive oil, and fish and seafood with global cognition after follow-up	Gender, age, marital status, years of education, height, BMI, physical activity, smoking, alcohol intake, hypertension, diabetes, geriatric depression score, and energy intake
Solfrizzi et al. (2006) (45), Italy, Italian Longitudinal Study on Aging	Longitudinal	n = 278 (55% men) age: 73.01 y older, nondemented, free-living subjects	8.5	77-item SFFQ, protein, carbohydrate, SFA, fiber, energy, fatty acids	Global cognition (MMSE)	High MUFA ( $\beta$ : -0.001; 95% CI: -0.002, -0.0009; P < 0.05), high PUFA ( $\beta$ : -0.006; 95% CI: -0.012, -0.0004; P < 0.05), and higher energy ( $\beta$ : -0.00001, P < 0.05) intake were significantly associated with lower decline in global cognitive function. No significant association for carbohydrates, fibers, SFA, UFASFA, and MUFA:SFA with decline in global cognition	Sex, age, education, Charlson comorbidity index, BMI, MMSE baseline score, total energy intake,

1a-MCI, amnesic mild cognitive impairment; A-MeDI, alternate Mediterranean diet; any-MCD, any mild cognitive disorder; ASR, anomalous sentence repetition; AVLT, auditory verbal learning test; APOE ε4, apolipoprotein E; BD, block design; BNT, Boston Naming Test; BVRT, Benton Visual Retention Test; CDR, clinical dementia rating; CDT, clock-drawing test; CF, category fluency; CFI, complex figure test; CIMs, complex ideational material subtest; CRP, C-reactive protein; CVD, cardiovascular disease; CVLT, California Verbal Learning Test; DASH, Dietary Approaches to Stop Hypertension; DSM, diagnostic and statistical manual of mental disorders; DSST, digit symbol substitution test; DST, digit span test; EBMT, East Boston Memory Test; EPIC, European Prospective Investigation into Cancer and Nutrition; GST, graphical sequence test; GVLIT, Greek Verbal Learning Test; HELIAD, Hellenic Longitudinal Investigation of Ageing and Diet; HS, Hadhinski Scale; InCHIANTI, Invecchiare in Chianti; IST, Isaacs Set Test; JLO, judgement of line orientation; LM, logical memory; MCI, mild cognitive impairment; MIND, Mediterranean-DASH Intervention for Neurodegenerative Delay; MMSE, Mini-Mental State Examination; MP, motor programming; na-MCI, nonamnesic mild cognitive impairment; PATH, Personality and Total Health; PC, picture completion; PIVUS, Prospective Investigation of the Vasculature in Uppsala Seniors; PP, Purdue Pegboard; PREDIMED, Prevención con Dieta Mediterránea; PRM, pattern recognition memory test; RAWLT, Rey Auditory Verbal Learning; SDMT, symbol-digit modalities test; SFFQ, semi-quantitative FFQ; SNACK, Swedish National Study on Aging and Care in Kungsholmen; SOC, Stockings of Cambridge Test; SRT, simple reaction time; SSP, spatial span test; ST, Stroop Test; STMS, short test of mental status; SWM, spatial working memory test; TICS, Telephone Interview for Cognitive Status; TMT, trail making test; VR, visual reproduction; 3MS, modified mini-mental state; 7MS, 7-minute screen

(MUFA + PUFA):SFA ratio was associated with a lower risk of MCI, and specifically amnesic MCI, in a cross-sectional study (56). No associations for SFA intake (42, 45, 76), PUFA:SFA ratio (81), or unsaturated fatty acid to SFA ratio (45) with cognitive decline were found.

### **Dairy.**

Dairy consumption was associated with worse cognitive function on at least some cognitive domains in 1 (84) of 5 (38, 39, 56, 74, 84) cross-sectional studies and 1 (79) of 8 (34, 41, 43, 64, 69, 76, 79, 83) longitudinal studies. In addition, dairy consumption was associated with a higher risk of MCI and mild neurocognitive disorder in a longitudinal study (76). No association between cheese consumption and cognitive impairment was observed in a longitudinal study (75). Consumption of milk, specifically high-fat milk, was associated with more cognitive decline in 1 (79) of 3 longitudinal (64, 79, 81) studies. In the same study margarine consumption was shown to be associated with more cognitive decline, but no association between consumption of ice cream and cognitive decline was observed (79).

### **Alcohol.**

Alcohol consumption was not associated with cognitive function in 4 cross-sectional (38, 39, 56, 84) and 9 longitudinal (34, 41, 43, 64, 66, 67, 76, 81, 83) studies. Wine consumption specifically was associated with better global cognition and less cognitive decline in 1 cross-sectional study (38) and 1 (45) of 2 (45, 75) longitudinal studies. The consumption of spirits or beers was not associated with cognitive decline in a longitudinal study (79).

### **Other dietary components.**

The consumption of sugar or fruit juice was associated with more cognitive decline in a longitudinal study (79), but intake of carbohydrates or sweetened beverages in general was not associated with cognitive decline in 2 other longitudinal studies (45, 69). No association between the consumption of fiber (45), sodium (69), processed and fast fried food (75), sweets and pastries (75), or animal-source cooking fat (83) and cognitive decline or cognitive impairment was shown longitudinally.

## **Discussion**

The evidence summarized in this review suggests that higher adherence to the Mediterranean, DASH, or MIND diets is associated with less cognitive decline and a lower risk of AD, which is mainly based on observational evidence. The number of studies examining the impact of the studied diets on dementia risk are scarce and too inconclusive to draw any conclusions. When comparing the potential impact of the different diets in respect to cognitive decline and AD, data suggest stronger inverse associations for the MIND diet compared with the Mediterranean and DASH diets (11, 53, 75). Moreover, inverse associations tend to be stronger for the Mediterranean diet with AD than the DASH diet (53). Compared with previous studies in this research field, the

current review particularly included more studies on the recently developed MIND diet.

Due to methodological differences between the included studies, i.e. study design and study population, dietary assessment methodology, and outcome measurement, the overall results should be interpreted with care.

With respect to the study design and study population, the majority of the included studies were observational studies (50/56 studies), which are known to be prone to reverse causation, potential confounding, and over adjustment (88–90). To illustrate the case of reverse causation, it is likely that participants living with dementia or cognitive decline included in a cross-sectional study report less foods than they actually consumed (88, 91). In addition, the possibility of residual confounding has to be considered, as many observational studies did not adjust for one or more potential confounders, such as *APOE*  $\epsilon$ 4 allele, sex, ethnicity, socioeconomic status, education, CVD risk factors, depression, comorbidities or medication, smoking, energy intake, BMI or obesity, physical activity, cognitive or social activity, or the use of nutritional supplements. On the other hand, the inclusion of potential intermediates may have led to over adjustment and as such to attenuation of existing true associations. Namely, the Mediterranean diet has been associated with hypertension (92), which, in turn, is associated with cerebrovascular health (93). As such, hypertension may be an intermediate pathway explaining the potential effect of the diet on cognitive decline, warranting careful modeling. Cohort-specific characteristics, e.g. age of assessment, education, sex, race, vascular risk, follow-up duration, loss to follow-up, or community dwelling compared with diagnosed with dementia, may also be responsible for differences in outcomes. For instance, in several studies, a beneficial association of the Mediterranean diet with cognitive decline was only shown for part of the study population, namely participants aged  $\geq 65$  y (83), African-American participants (65), or men (40), which limits the external validity. The 4 trials on the effect of the Mediterranean and DASH diets on cognition, dementia, or AD that were included in this review also had several limitations, including lack of baseline outcome measurements, small sample size, and relatively short duration of intervention, so no firm conclusion could be drawn from these trials.

With respect to the dietary assessment methodology, most observational studies used an FFQ and some studies used a food diary or 24-h recall (24hR). FFQs and 24hRs are known to be prone to recall bias related to memory deficits, especially in studies with elderly, cognitively impaired participants, or low-educated participants (94). Compared with 24hRs, FFQs are more limited with respect to the variety of foods assessed but often more likely to reflect the usual intake. As food diaries are usually completed during a day, they are more likely to affect eating behavior than FFQs and recalls. Besides these differences between the methods, they are all prone to measurement error related to socially desirable answers and errors in food composition tables. Differences in exposure quantification also arose from the scoring system

applied to calculate adherence to the Mediterranean, DASH, or MIND diets. Most studies examining the impact of the Mediterranean diet used the original score as described by Trichopoulos et al. (9) or the alternate Mediterranean diet score as described by Panagiotakos et al. (30). The original Mediterranean diet score is based on the median intake of the population, does not consider extremes in intake, and includes MUFA:SFA ratio instead of olive oil intake (9). As such, the statistical power may be limited in studies in non-Mediterranean countries. The score by Panagiotakos et al. uses predefined cut-offs for intake, divides intake into quintiles, and includes intake of olive oil specifically (30). DASH diet adherence was calculated by using the score by Fung et al. (32), or the score by Folsom et al. (31). Compared with the score of Folsom et al. (31), the score of Fung et al. (32) is based on relatively few dietary components. In addition, the score of Fung et al. (32) is based on intake of the study population. Finally, irrespective of the diet under study, not all studies were able to 1) capture all dietary components when constructing the dietary pattern score and 2) distinguish between dietary components in the same way (e.g. total cereal intake compared with unrefined cereals). The differences in effect sizes between the diets may for instance be explained by the absence of olive oil in the DASH diet, as olive oil was associated with better cognitive function and less cognitive decline (34, 38, 48, 84). Besides nutrition, the Mediterranean diet pyramid also includes other cultural and lifestyle factors including conviviality, culinary activities, physical activity, and adequate rest (17). Of these, physical activity and social network, which is related to conviviality, have been associated with a lower risk of cognitive decline and dementia (95). In addition, daytime napping, which is related to adequate rest, has been shown to improve alertness and performance (96).

With respect to the outcome measure, several studies only used a global screening tool, such as the MMSE, Telephone Interview for Cognitive Status (TICS), Modified Mini-Mental State Examination (3MS), or seven-minute screen (7MS), whereas other studies applied multiple cognitive tests. A global screening tool may be less sensitive to detect possible associations due to a potential ceiling effect (97), so studies using global screening tools may be more likely to present null-associations. Nevertheless, overall, the results of studies using a global screening tool were rather similar to the results of studies using multiple cognitive tests. In addition, 4 longitudinal studies did not assess cognitive status at baseline, which may have led to residual confounding due to interindividual differences in cognitive function or brain volume. Conversely, including baseline outcome measurements may also lead to an overestimation of the effects due to the possibility of a learning effect with an even larger effect with an increasing number of repetitions.

Investigating the role of nutrients, foods, and dietary patterns in relation to dementia is important as there is no cure for dementia yet. A focus on whole dietary patterns is useful as the effect of a combination of nutrients may be larger than the effect of single nutrients and because

possible interactions between nutrients are incorporated. Many observational studies have already examined the Mediterranean diet in relation to cognitive decline, dementia, or AD, but more observational studies on the DASH and MIND diets are recommended. In addition, the number of intervention studies investigating either the Mediterranean, DASH, or MIND diet is very limited, so more intervention studies on each of these dietary patterns are needed. In the United States, an intervention study on the effect of the MIND diet on cognitive decline, dementia, AD, and vascular dementia is ongoing (98). Furthermore, both observational and intervention studies examining the association of the Mediterranean, DASH, or MIND diets with brain structure are recommended, because these studies may provide insights into the exact mechanisms via which the 3 dietary patterns may protect against cognitive decline, dementia, and AD. For example, adherence to the Mediterranean diet has been associated with less decline in the cerebral metabolic rate of glucose and less increase in Pittsburgh compound B in AD-affected regions (99). Moreover, future trials could examine all 3 dietary patterns simultaneously, because this would provide interesting insights into whether the Mediterranean, DASH, or MIND diet is most protective against cognitive decline, dementia, and AD. However, it may be easier for people to change the intake of one nutrient or food than to change their whole diet. Therefore, despite the shift of research from single nutrients and foods towards whole dietary patterns, research on specific nutrients or foods is still useful. An interesting field of study is to investigate the role of olive oil in cognitive decline, dementia, and AD via both observational and intervention studies as this may be one of the most important components driving the association of the Mediterranean and MIND diets with less cognitive decline. Last of all, future research should, if possible, take into account the methodological issues described above.

## Conclusions

The results of this review suggest that higher adherence to the Mediterranean, DASH, or MIND diets is associated with less cognitive decline and a lower risk of AD, as demonstrated by 10 out of 14 cross-sectional studies, 1 case-control study, 21 out of 33 longitudinal studies, and 4 out of 6 articles on intervention studies. Evidence for an association with dementia was inconsistent. Observational studies indicate that the MIND diet may be more protective against cognitive decline and AD than the Mediterranean and DASH diets (11, 53, 75), but more evidence on the MIND diet is required to draw a firm conclusion. Furthermore, the Mediterranean diet seems more protective against AD than the DASH diet (53). Based on the studies included in the current review, in which dietary components were assessed as part of 1 of the 3 dietary patterns, olive oil consumption seems to be an important component underlying these associations (34, 38, 48, 84).

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