Mediterranean-based Diets and their Association with Cognitive Functioning in Dutch Community-Dwelling Older Adults

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1 Abbreviations

BMI: Body Mass Index

DEXA: Dual Energy X-ray Absorptiometry

MEDI-LITE score: Mediterranean Literature score

MIND: Mediterranean-DASH Intervention for Neurodegenerative Delay

MMSE: Mini-Mental State Examination

NTB: Neuropsychological Test Battery

NU-AGE: Nutrients and Ageing

SD: Standard Deviation

2 Abstract

Background: Lifestyle has become an important focus of brain health, due to its potential to delay cognitive decline. Previously, nutritional patterns such as the Mediterranean diet and the MIND diet have been associated with a reduced risk of cognitive impairment. However, there are still conflicting results regarding the effect sizes of these diets, warranting further research. Therefore, the aim of the current project was to analyze the association between adherence to the Mediterranean diet, measured by the MEDI-LITE score (Mediterranean Literature score), and cognitive function in the NU-AGE Wageningen cohort.

Methods: Food records and cognitive scores were obtained from the NU-AGE Wageningen cohort, which was a one-year randomized dietary intervention study in healthy older adults (65-79 years). The MEDI-LITE score (ranging from 0-18) was calculated from seven-day food records and was analyzed as total score, as well as in separate food categories. Four cognitive domains were created from composite Z-scores of individual neuropsychological test battery scores. Linear regression was used to model the relationship between MEDI-LITE scores and cognitive scores, and p-values were adjusted for multiple testing.

Results: In total, 248 out of 252 participants had complete data available at baseline. The MEDI-LITE total score was negatively associated with episodic memory [β -0.05 (99% CI -0.11, -0.01), p=0.022], but this trend did not remain significant after adjustment. In the separate food categories, non-significant negative trends were observed between fish and executive functioning [β -0.29 (99% CI -0.62, -0.03), p=0.026] and episodic memory [β -0.23 (99% CI -0.52, -0.06), p=0.021]. Cereal intake showed a non-significant negative trend with episodic memory [β -0.33 (99% CI -0.73, -0.07), p=0.033].

Discussion & Conclusion: We did not find a significant association between adherence to the Mediterranean diet and cognition scores in the NU-AGE Wageningen cohort. Although some other studies have reported similar non-significant associations between the Mediterranean diet and cognition, there is ample evidence that this diet improves cognitive function and delays cognitive impairment. The non-significant findings in this report could have been the result of selection bias, reverse causation, the unvalidated analysis of separate food categories of the MEDI-LITE score or the lack of distinction between types of foods (e.g. refined or non-refined cereals). Future randomized trials with generalized scores and guidelines are necessary to confirm the association between the Mediterranean diet and cognitive functioning in older adults.

3 Layman's Summary

This report describes the Mediterranean diet and its effect on brain health in older adults. The Mediterranean diet encourages to eat olive oil, fish, cereals, fruits, vegetables, legumes, and nuts. Additionally, it advises limited amounts of dairy, poultry, alcohol, and red meat. Past research has shown that the Mediterranean diet has many health benefits, including improved memory and a lower chance of developing diseases such as dementia. However, not all studies have found these positive effects, which is why additional research is important.

The goal of this project was to investigate if better adherence to the Mediterranean diet improves cognition in older adults. For this purpose, we used a dataset of a previous study, called the NU-AGE study. In this study, older adults (65-79 years) kept records of their food intake for seven days and their cognitive functioning was measured with different tests, for example presenting the participants with 15 words and seeing how many words they remembered. After these measurements, the participants were trained to eat healthier for 1 year, after which all measurements were taken again. For this project, only the data before the training were used in participants that were included in the Wageningen cohort.

For the food data, we calculated a special score (MEDI-LITE score) to quantify how well participants adhered to the Mediterranean diet. This MEDI-LITE score consisted of nine separate food categories, and for each of these categories, participants could score 0 (lowest score), 1 or 2 (highest score). These food scores were added together to form the MEDI-LITE total score, where a high MEDI-LITE total score implied that the participant followed the Mediterranean diet well.

With the data of the cognitive tests, we created four cognitive domains: global cognition, episodic memory, executive functioning, and perceptual speed. *Global cognition* includes orientation, short-term memory, and spatial insight, for example drawing a clock, whereas *episodic memory* is the explicit memory of personal experiences. *Executive functioning* is the ability to plan and manage different tasks at the same time, whereas *perceptual speed* represents the ability to quickly see differences and similarities between items. We then analyzed whether participants with high MEDI-LITE scores had higher scores in these four cognitive domains.

In the analyses, we did not find a significant association between higher MEDI-LITE scores and higher cognitive scores. This might have been caused by inclusion of too healthy participants, who had very little potential to improve their lifestyle. Another reason could be that the MEDI-LITE score includes multiple food types per food category. For example, the food category cereals contains both refined and non-refined cereals. These types can have very different effects on the brain and overall health, but they were combined in calculating the MEDI-LITE score. Therefore, it would have been better to look at the effect of individual food types within the food categories. In contrast to our results, other studies have found positive effects of the Mediterranean diet on cognition, which shows that we need more research to draw definitive conclusions.

4 Introduction

Dementia, the worst state of cognitive impairment, is an important cause of disability in older adults, with age as one of the most prominent non-modifiable risk factors. There are several subtypes of dementia, of which Alzheimer's disease is the most common (1). The multifactorial etiology of dementia is complex and diverse, varying from neuroinflammation, oxidative stress, genetic predisposition, comorbidity, and poor lifestyle. Lifestyle is an important focus of current research, as it is a modifiable risk factor for dementia. Specifically, a healthy diet might have the potential to slow down or prevent cognitive decline in older adults.

In recent years, researchers have become increasingly interested in the relation between cognition and dietary patterns, especially the Mediterranean diet, the Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) diet, and the Nutrients and Ageing (NU-AGE) diet. These diets promote high intake of fruits, vegetables, legumes, nuts, whole grains, and fish, and limit processed meat and alcohol consumption (2–5). The well-known Mediterranean diet has many beneficial health effects, and according to meta-analyses also stimulates working memory, processing speed and reasoning (3,6–9). The MIND diet and the NU-AGE diet have been developed more recently. The MIND diet was designed to stimulate brain health, and has been linked to a reduced the risk of AD and all-cause mortality (4,10,11). The NU-AGE diet is similar to the Mediterranean diet, but it specifically targets the nutritional needs of older adults and has shown promising results regarding cognitive decline and inflammation (5,12–14).

Despite the evidence of a beneficial role of the aforementioned diets on cognition, study designs and reported effect sizes differ greatly between studies, warranting further research into the association between nutrition on cognitive decline (3). For this purpose, the NU-AGE study was set up in older adults, to investigate the effect of adherence to the NU-AGE diet on age-related organ decline and cognition in a one-year multi-centered dietary intervention trial (5). Analyses of the NU-AGE cohort showed that higher adherence to the NU-AGE diet, by means of dietary counseling, resulted in improved global cognition and episodic memory (13). However, it has not yet been studied if there is an association between adherence to Mediterranean dietary patterns and cognition in the NU-AGE Wageningen cohort (n=248). Therefore, the aim of the current project is to analyze the relation between adherence to the Mediterranean Diet, measured by the literature-based MEDI-LITE score, and cognitive functioning in the NU-AGE Wageningen cohort (15,16).

In summary, this research project will help unravel the relationship between diet and cognitive decline, by analyzing the association between adherence to the Mediterranean diet and cognition.

5 Materials and Methods of the NU-AGE Wageningen cohort

5.1 Subject inclusion

The NU-AGE study was carried out in 1,250 apparently healthy, independently living European participants aged 65–80 years across the following five European centers: Norwich Medical School in the United Kingdom, Warsaw University of Life Sciences-SGGW in Poland, CHU Clermont-Ferrand in France, University of Bologna in Italy, and Wageningen University & Research (WUR) in the Netherlands (5). The design was a parallel, one-year randomized controlled trial with an intervention arm and a control arm. In each of the five centers, approximately 250 subjects were included. The study was approved by the accredited medical research ethics committees from each center.

The inclusion criteria were: 1) 65-79 years, 2) Free of disease compromising 2-year survival, 3) Free and independently living, 4) Competent to make own decisions. The following exclusion criteria were used: 1) Presence of diseases such as cancer or dementia, or a history of severe heart disease, 2) Presence of organ failure or need for special diet due to food intolerances, 3) Presence of Diabetes mellitus type 1 or type 2 with insulin therapy, 4) Chronic use of corticosteroid medication or recent use of antibiotics, 5) Change in habitual medication use, 6) BMI<18.5 kg/m^2 or >10% weight loss within 6 months, 7) Presence of frailty (17).

Screening took place from April 2012 until November 2013. Eligibility was assessed using questionnaires and informed consent was signed by all participants, prior to inclusion. After stratification, candidates were randomized 1:1 to either the control or intervention arm. During the baseline- and follow-up visits, collection of blood, urine and feces took place. Additionally, anthropometric measurements, questionnaires, DEXA-scans, physical performance, and cognitive tests were taken.

5.2 Control and Intervention groups

In total, 252 participants were recruited at Wageningen University & Research. The control arm only received information regarding general Dutch dietary guidelines. The intervention group received individualized dietary counseling from dieticians based on the NU-AGE diet, as well as vitamin-D supplements and free foods fitting the NU-AGE diet. The dieticians used motivational techniques and worked with personal goals to stimulate adherence to the NU-AGE diet. The participants received nine individual sessions, equivalent to six to seven hours of counseling over the one-year intervention. The participants filled in food diaries for seven consecutive days at baseline and after a year, following training how to keep complete food diaries. In order to measure adherence to the NU-AGE diet, NU-AGE food based dietary guidelines were used as a scoring system.

The primary outcome defined in the NU-AGE study was inflammatory status, measured as C-reactive protein plasma levels and other inflammatory blood markers. The secondary outcomes were measures of organ function and general status, such as hormone function, cardiovascular health, cognition, and mental health (5).

For the current project, the primary outcome was the relation between MEDI-LITE scores and NTB (Neuropsychological Test Battery) scores, a measure of cognitive function. This relation was analyzed cross-sectionally, using only baseline data. For these analyses, the seven-day food record data and NTB scores of the Wageningen cohort (n=252) have been kindly made available.

5.3 Dietary adherence score

Adherence to the Mediterranean diet in the NU-AGE population was measured using the literature-based MEDI-LITE score (**Table 1**), developed and validated by Sofi and colleagues (15,16). The MEDI-LITE score was calculated from the subscores of nine individual dietary categories (score 0-2), and the total score ranged from 0-18. For the category olive oil, 'occasional use' was defined as 4.5 grams/day or less, 'frequent use' was defined between 4.5 and 7 grams/day, and 'regular use' was defined as more than 7 grams/day (18). Beverages with alcohol percentages under 1.2% were excluded from the alcohol group. For dairy products, milk products and cheese were combined.

Table 1. Literature-based MEDI-LITE score

FRUIT *1 portion: 150 g*	<1 portion/d 0	1–1·5 portions/d 1	>2 portions/d 2
VEGETABLES *1 portion: 100 g*	<1 portion/d 0	1–2·5 portions/d 1	>2·5 portions/d 2
LEGUMES *1 portion: 70 g*	<1 portion/week 0	1–2 portions/week 1	>2 portions/week 2
CEREALS *1 portion: 130 g*	<1 portion/d 0	1–1·5 portions/d 1	>1·5 portions/d 2
FISH *1 portion: 100 g*	<1 portion/week 0	1–2·5 portions/week 1	>2·5 portions/week 2
MEAT AND MEAT PRODUCTS *1 portion: 80 g*	<1 portion/d 2	1–1·5 portions/d 1	>1·5 portions/d 0
DAIRY PRODUCTS *1 portion: 180 g*	<1 portion/d 2	1–1·5 portions/d 1	>1·5 portions/d 0
ALCOHOL *1 Alcohol Unit (AU) = 12 g*	<1 AU/d 1	1–2 AU/d 2	>2 AU/d 0
OLIVE OIL	Occasional use 0	Frequent use 1	Regular use 2

Derived from Sofi and colleagues (15)*. The MEDI-LITE total score ranges from 0-18.*

Analyses were conducted with the MEDI-LITE score expressed as a total score, as tertiles and separately for all individual food categories**.** The tertiles were formed after MEDI-LITE scores were calculated, in order to establish groups of approximately equal size**.** Scores from 2-5 were defined as the lowest score (n=78), scores of 6-7 were defined as the middle score (n=91), and scores of 8-14 were defined as the highest score (n=79).

5.4 Cognitive scoring

For the assessment of cognitive function of the NU-AGE research population, a comprehensive NTB was used, which was carried out at baseline and at follow-up after a year. The NTB consisted of the Mini-Mental State Examination (MMSE) (19), Verbal Fluency Category (20), Boston Naming Test (21), Constructional Praxis (22), Word List Memory (23) , Babcock story (24), Trail Making Test (25), Number Cancellation (26) and Pattern Comparison (27). As previously described, the scores of the neuropsychological subtests were combined to create cognitive domains (13). A description of the neuropsychological tests and the resulting cognitive domains can be found in Supplemental Table 9.1**.** The following four cognitive domains were used in the analyses after normality assessment: Global Cognition, Episodic memory, Executive Functioning and Perceptual Speed (Supplemental Table 9.2).

5.5 Statistical analysis

For all statistical analyses and figures, R version 4.0.1 was used (28). Prior to the current project, NU-AGE data had already been collected and organized into pre-determined food categories (intake in grams/day) and NTB scores. As to determine the associations between adherence to the Mediterranean Diet and cognition scores, the baseline data of the control and intervention groups were combined. The individual NTB scores were converted into Z scores, and these were averaged to form four cognitive domains. To model the relationship between the MEDI-LITE score and cognitive functioning, linear regression was applied. The MEDI-LITE score was used as the independent variable and the combined Z-scores of the cognitive domains as dependent variables. In addition, separate regression analyses were conducted between the individual food groups of the MEDI-LITE score and the composite Z-scores of the cognitive domains. The models were adjusted for age, gender, education, and BMI, all of which were included as covariates. Due to multiple testing, p values<0.01 were considered significant, to reduce the likelihood of type I errors.

6 Results of the NU-AGE Wageningen cohort

6.1 Baseline characteristics

Out of the 252 inclusions, 248 participants had availability of all data. The baseline characteristics are shown in **Table 2**. Mean age was 70.9 years (SD=4.06) and 55.2% of the participants were women. Furthermore, the population had a mean MMSE score of 27.7 at baseline (SD=1.78). Additionally, half of the population (49.2%) smoked.

Table 2. Baseline characteristics of the NU-AGE Wageningen cohort

Characteristics at baseline (n=248)	
Age (years)	70.9 (4.06)
Female Gender, N (%)	137 (55.2%)
Body mass index (kg/m^2)	26.0 (3.64)
Education (schoolyears)	12.3 (3.65)
MEDI-LITE Score	6.58 (2.07)
MMSE score	27.7 (1.78)
High blood pressure, N (%)	81 (32.7%)
High cholesterol, N (%)	61 (24.6%)
Diabetes, N (%)	9 (3.6%)
Current smoker, N (%)	122 (49.2%)

Data are presented as mean (standard deviation) unless reported otherwise. All characteristics were self-reported, without further information on medical conditions such as high blood pressure or diabetes. Abbreviations: MMSE = Mini-Mental State Examination; N (%) = Number in percentages.

An overview of the reached MEDI-LITE total scores, ranging from 0-18, can be found in Supplemental Tables 9.3 and 9.4. MEDI-LITE total scores of 5 (17.7%), 6 (19.4%), 7 (17.3%) and 8 (14.9%) were most frequently achieved by the participants.

Achieved MEDI-LITE score in the separate food categories, ranging from scores 0-2, can be found in Supplemental Table 9.5**.** Meat was the food category with highest adherence among the participants (59.3% score 2), meaning that more than half of the participants consumed meat less than once a day. Participants had poorest adherence to the food guidelines for legumes (87.9% score 0), olive oil (84.7% score 0) and alcohol (78.2% score 0). Given that low alcohol adherence (score 0) means more than 2 units of alcohol intake per day, a large part of the cohort thus did not remain abstinent to alcohol.

6.2 MEDI-LITE total score and cognition

The results of the analyses between adherence to the MEDI-LITE score and cognition at baseline are shown in **Table 3**. The adjusted models using covariates had higher validity than the crude models**,** indicated by higher R^2 values in the adjusted models. No significant relationship ($p<0.01$) was found between the MEDI-LITE score and cognitive domains in both adjusted and crude models (**Table 3** and Supplemental Table 9.7). However, a marginally significant negative trend, suggesting an inverse relationship, was observed between the MEDI-LITE score and episodic memory, both expressed as a total score [β -0.05 (99% CI -0.11, -0.01), p=0.022] and as a tertile [β -0.25 (99% CI -0.55, -0.05), p=0.029, *high score*]. This trend did not remain significant after correction for multiple testing.

Table 3. Association between MEDI-LITE total score and cognitive outcomes at baseline.

	Global cognition		**Episodic memory**		**Executive functioning**		**Perceptual speed**	
Predictors	*Estimates*	*p*	*Estimates*	*p*	*Estimates*	*p*	*Estimates*	*p*
MEDI-LITE middle score	-0.08 (-0.30 – 0.15)	0.367	-0.13 (-0.41 – 0.16)	0.243	-0.11 (-0.42 – 0.21)	0.377	-0.16 (-0.48 – 0.16)	0.189
MEDI-LITE high score	-0.16 (-0.40 – 0.07)	0.073	-0.25 (-0.55 – 0.05)	0.029	-0.16 (-0.48 – 0.17)	0.209	0.04 (-0.29 – 0.37)	0.752
MEDI-LITE total score	-0.03 (-0.07 – 0.02)	0.120	-0.05 (-0.11 – 0.01)	0.022	-0.03 (-0.09 – 0.03)	0.231	0.01 (-0.05 – 0.08)	0.607
R^2 middle and high score / R^2 total score	0.146 / 0.147		0.108 / 0.113		0.029 / 0.032		0.134 / 0.127	

The baseline data of 248 participants were used. MEDI-LITE score was analyzed as total score and divided into tertiles (low score 2-5, middle score 6-7 and high score 8-14), with the lowest score as reference. Data are reported as β coefficients with 99% confidence intervals. R^2 values were reported for the tertiles as well as the total score. p<0.01 was considered significant.

6.3 MEDI-LITE score in separate food categories and cognition

The effect of adherence to the different food components based upon the MEDI-LITE score and cognitive outcomes is illustrated in **Figure 1** by means of simplified forest tree plots. The adjusted and crude models for the association between MEDI-LITE subcategories and cognition can be found in Supplemental Tables 9.6 and 9.8, respectively. Although not significant following correction for multiple testing, fish intake was negatively associated with episodic memory [β -0.23 (99% CI -0.52, -0.06), p=0.021**,** *middle score*] and executive functioning [β -0.29 (99% CI -0.62, -0.03), p=0.026**,** *high score*]. Cereal consumption showed a negative trend with executive functioning [β -0.33 (99% CI -0.73, -0.07), p=0.033, *high score*]. Overall, the domains global cognition and episodic memory showed somewhat similar patterns for most food categories, whereas perceptual speed and executive functioning behaved differently.

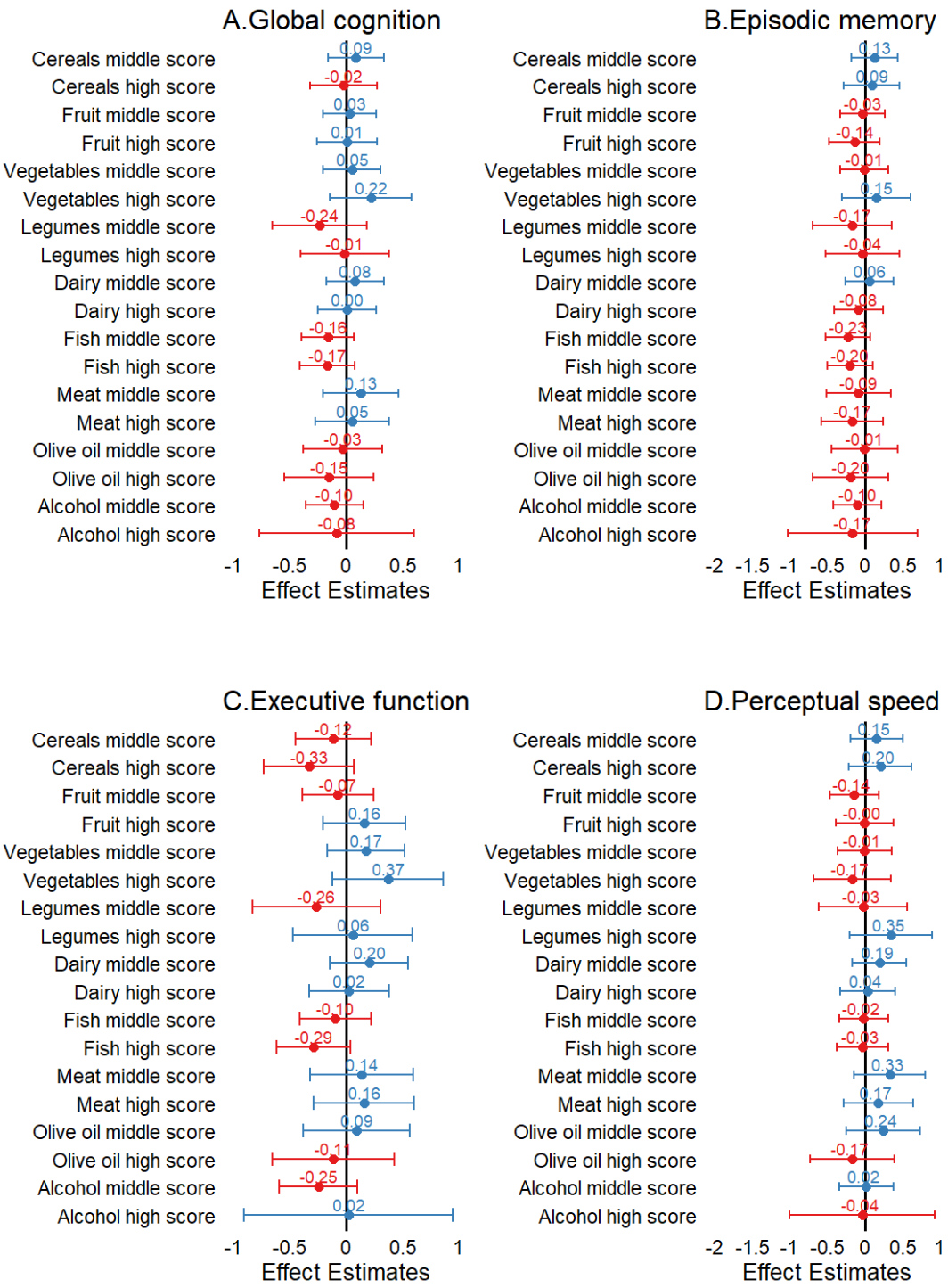

*Figure 1. Association between MEDI-LITE score separated in food categories and cognitive outcomes at baseline, illustrated for Global Cognition (**A**), Episodic Memory (**B**), Executive Function (**C**), and Perceptual Speed (**D**). MEDI-LITE score was analyzed for each food category, where the lowest score was 0 (taken as reference), the middle score was 1 and the highest score was 2. Data are reported as β coefficients with 99% confidence intervals. p<0.01 was considered significant.*

7 Discussion of the NU-AGE Wageningen cohort

7.1 Discussion of study results

The aim of the NU-AGE project was to investigate whether high adherence to the Mediterranean diet, reflected by high MEDI-LITE scores (15), was related to higher cognitive scores in the NU-AGE Wageningen cohort. The main finding of this study was that the MEDI-LITE scores and cognitive Z-scores were not significantly correlated in the NU-AGE population, illustrated by effect estimates and R^2 values that were low and non-significant. In addition, we observed an inverse association between the MEDI-LITE score and episodic memory, though not significant after correction, which even contradicts our initial hypothesis. Although previous research has shown links between adherence to the Mediterranean diet and better global cognition, as well as less cognitive impairment (6,29–31), non-significant associations have also been reported in several cohorts (32–34). The varied results regarding the effect of the Mediterranean diet may stem from differences in food recording practices, scoring systems, subcategorization of foods and cultural context between studies (30,34).

In the separate analyses of the different food categories, non-significant negative associations were found between adherence to fish guidelines and episodic memory, as well as executive functioning. In contrast to these observations, high fish intake has previously been related to a lower risk of dementia (35) and slower cognitive decline in several cohorts (36–39). This neuroprotective effect is most likely due to the high levels of omega-3 fatty acids in fish. However, some cross-sectional studies have reported a lack of association between fish intake and episodic memory or executive functioning (40,41). Notably, Cherbuin and colleagues found a correlation between high fish intake and increased development of cognitive impairment, which resembles the (non-significant) inverse relationship between fish intake and cognitive function described in the current report to certain degree. As explained by these authors, the observed negative effect of fish on cognition could possibly be explained by the influence of accompanying factors, such as the type of fish (e.g. fatty versus lean fish) that was consumed, the method of preparation that was used, and other foods that were combined with it (34).

Furthermore, though not significant, higher adherence to cereal guidelines was linked to lower executive functioning scores. Previously, cereal intake has been negatively associated with cognition, specifically intake of refined cereals (34,40,42). On the other hand, whole grains have been shown to improve cognitive function and reduce the risk of developing neurodegenerative diseases, likely due to their high content of beneficial compounds such as fibers and phenols (33,43–46). These results highlight the importance of individually assessing subtypes of food categories such as cereals, rather than analyzing these as a whole food group. As the MEDI-LITE score only included general food groups and did not account for the varying effects of food subtypes, the inverse relationships found in the NU-AGE population should be interpreted with caution.

Another theory that might explain the observed (non-significant) negative associations between certain food groups and cognition is reverse causation (3). To illustrate, some of the older adults that were included might have already had subjective cognitive complaints, which could have either led to inaccurate food records or to an excessive focus on nutrition as an effort to delay further cognitive impairment. Consequently, the Mediterranean diet adherence scores would be disproportionate to the cognition scores at baseline in these participants, but this apparent inverse relationship would only apply to this particular sample and not the general population.

7.2 Strengths and limitations

The NU-AGE project had several strengths, such as the large sample size, the randomized design, and the relatively homogenous population of healthy older adults. In addition, cognitive domains were formed as described previously, taking composite NTB scores rather than individual NTB scores, which made the results more reliable. Another strength of the NU-AGE project was the adjustment of the linear regression models with several covariates, as well as the correction for multiple testing.

The NU-AGE project also had some limitations. Firstly, selection bias might have occurred by including mostly healthy older adults and excluding older adults with comorbidities. This is reflected in the characteristics of the NU-AGE Wageningen participants, who were already very healthy at baseline (MEDI-LITE score 6.58/18), highly educated (12.3 schoolyears), with high MMSE scores (27.7/30). Therefore, the health- and educational status of the NU-AGE Wageningen cohort might not be representative of the general population of Dutch older adults in this age category**.** Secondly, the MEDI-LITE score (15,16) is only one of many scores that can be used to quantify adherence to a Mediterranean dietary pattern, making it difficult to directly compare the results to studies using other scores. Thirdly, the MEDI-LITE score was not validated for separately analysing the individual food categories within the total score, which might explain the unexpected negative associations between certain food categories and cognition. A fourth limitation is the cross-sectional design, which did not allow for assessment of the long-term effects of adherence to the Mediterranean diet on cognitive decline. Lastly, some food category guidelines were poorly adhered to by a great majority of participants, such as legumes, olive oil and alcohol (Supplemental Table 9.5). Consequently, the large group of participants scoring low in these food categories might have outbalanced the much smaller group of participants scoring high in these categories, causing higher variability and skewed results.

7.3 Conclusions and future directions

In conclusion, higher adherence to the Mediterranean diet, measured by the MEDI-LITE score, was not significantly associated with better cognitive performance in healthy older adults. The separate food categories fish and cereals showed non-significant negative associations with episodic memory and executive functioning. Although no association was observed in the current report, multiple studies have underlined the beneficial effects of the Mediterranean diet on cognition. Therefore, more randomized studies with comparable study designs and generalized nutritional scores are needed to draw definitive conclusions about the relation between adherence to Mediterranean patterns and cognitive decline. Additionally, validation of the use of separate MEDI-LITE food categories in the analyses would be relevant to give more insight into the individual effect of the separate food categories on the total MEDI-LITE score.

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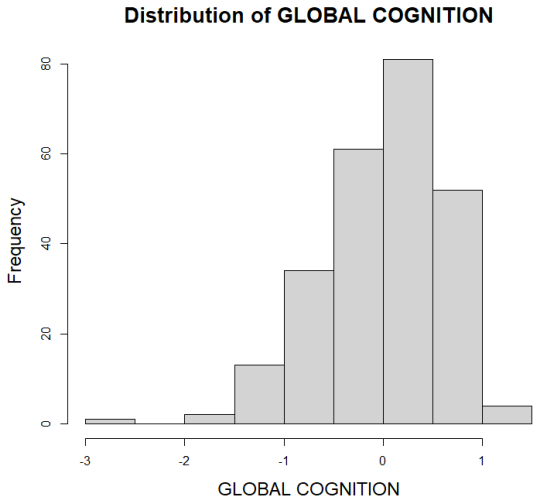
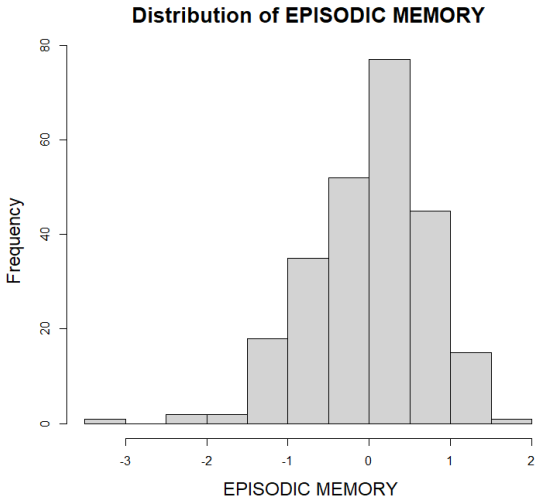
9 Supplemental data

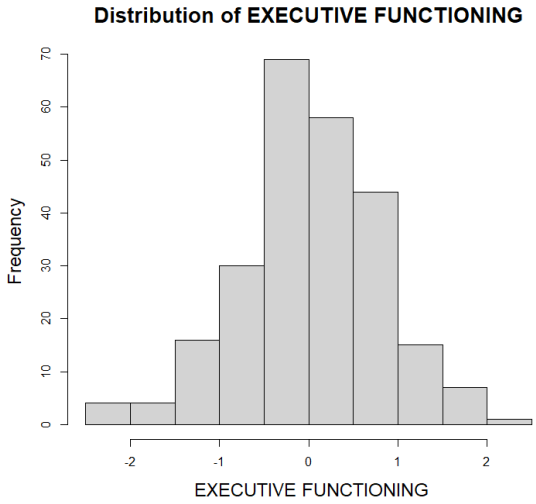
9.1 Description of NTB subtests in cognitive domains

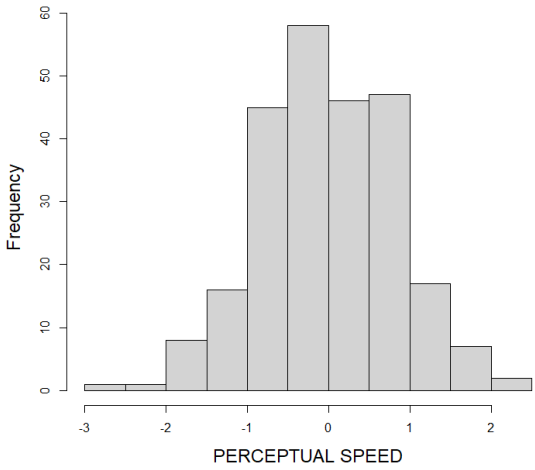
Domain	Test	Description
Global cognition	MMSE	Global screening tool, including orientation, repeating and remembering words, visual tasks
	Verbal fluency category	Name as many items as possible in a certain category in 60 seconds
	Boston Naming Test	Name fifteen objects presented as line drawings
	World-list memory immediate recall	Read list of ten words
	World-list memory delayed recall	Remember the list of ten words
	World-list memory recognition	Identify the ten words in a list also containing other words
	Constructional Praxis test immediate recall	Draw four geometric figures
	Constructional Praxis test delayed recall	Remember drawn figures
	Babcock Story immediate recall	Repeat short story
	Babcock Story delayed recall	Remember short story
	Pattern Comparison Test	Compare a list of two figures in 30 seconds
	Number Cancellation test	Cross off a certain number as fast as possible in 30 seconds
	Trail Making Test A	Connect numbers from 1-15 in ascending order
	Trail Making Test B	Connect numbers from 1-13 and letters A-L (1A-2B etc)
Episodic memory	Word-list memory (immediate + delayed + recognition)	Remember list of ten words and identify in another list
	Babcock story (immediate + delayed)	Repeat and remember short story
Executive function	Verbal fluency category	Name as many items as possible in a certain category in 60 seconds
	Trail Making Test B/A	Divide score Trail Making Test B by Trail Making Test A
Perceptual speed	Pattern Comparison Test	Compare a list of two figures in 30 seconds
	Number Cancellation test	Cross off a certain number as fast as possible in 30 seconds

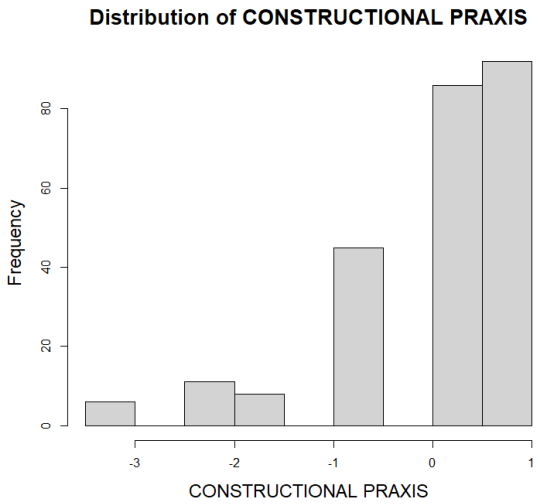
9.2 Histograms of cognitive domains

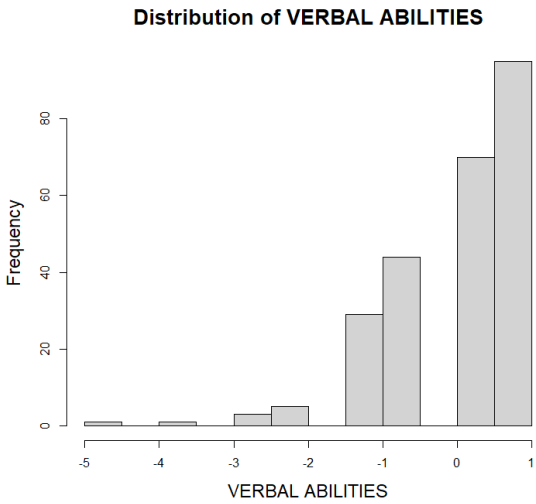










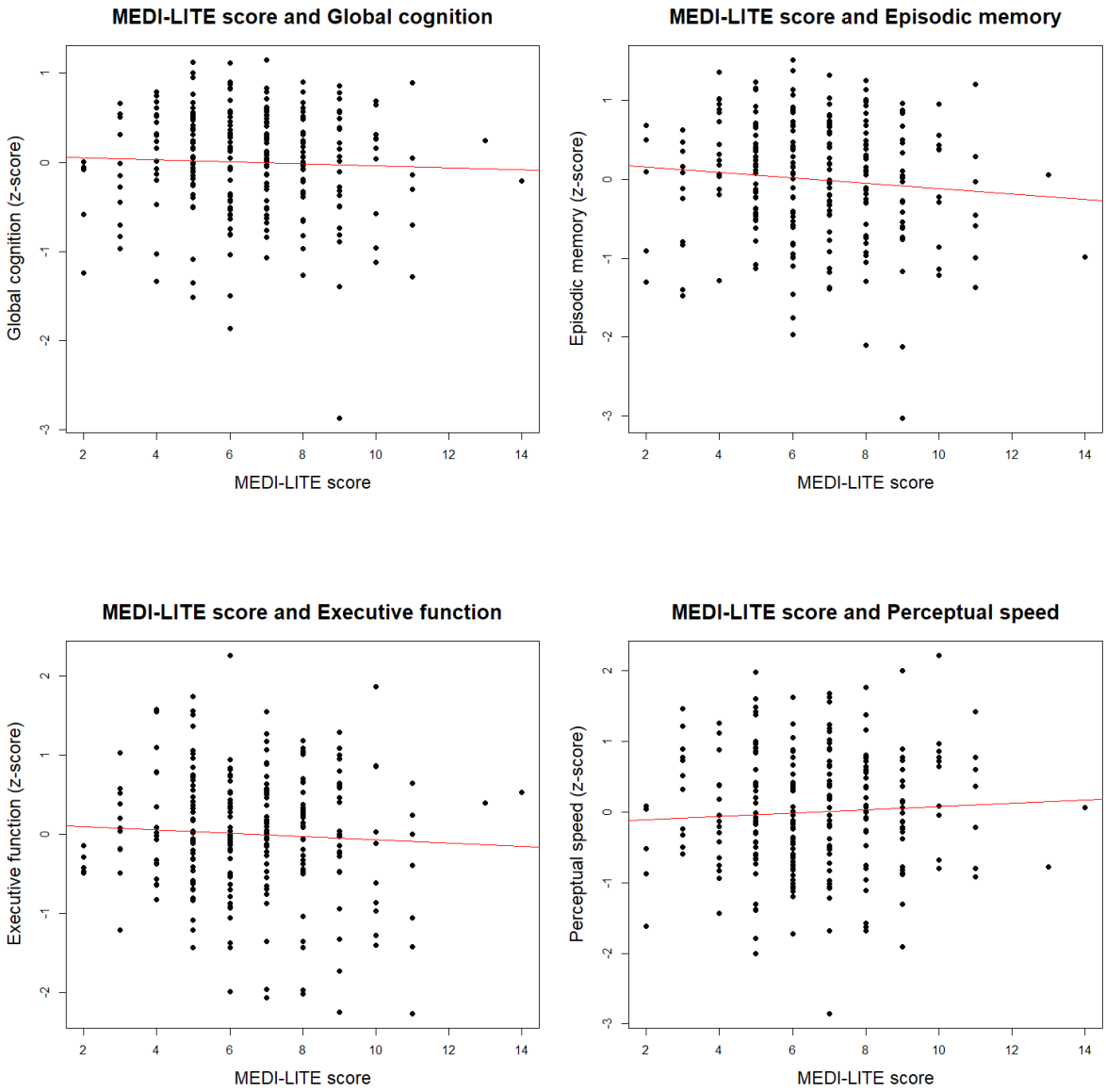


9.3 Distribution of MEDI-LITE total score

MEDI-LITE total score	Number of participants with MEDI-LITE score	% of total
1	0	0%
2	5	2.0%
3	11	4.4%
4	18	7.3%
5	44	17.7%
6	48	19.4%
7	43	17.3%
8	37	14.9%
9	23	9.3%
10	10	4.0%
11	7	2.8%
12	0	0%
13	1	0.4%
14	1	0.4%
15	0	0%
16	0	0%
17	0	0%
18	0	0%
Total	**248**	**100%**

Distribution of MEDI-LITE total scores were achieved by NU-AGE Wageningen participants. MEDI-LITE scores ranged from 0-18. Data are presented as counts (%).

9.4 Scatterplots of MEDI-LITE total score in cognitive domains



Scatterplots of the MEDI-LITE total score in the four cognitive domains (presented as z-scores).

9.5 Distribution of MEDI-LITE score per food category

MEDI-LITE food category	Number of participants with score 0 (%)	Number of participants with score 1 (%)	Number of participants with score 2 (%)
Cereals	60 (24.2%)	118 (47.6%)	70 (28.2%)
Fruit	78 (31.5%)	104 (41.9%)	66 (26.6%)
Vegetables	48 (19.4%)	166 (66.9%)	34 (13.7%)
Legumes	218 (87.9%)	14 (5.6%)	16 (6.5%)
Dairy	149 (60.1%)	49 (19.8%)	50 (20.2%)
Fish	94 (37.9%)	78 (31.5%)	76 (30.6%)
Meat	30 (12.1%)	71 (28.6%)	147 (59.3%)
Olive oil	210 (84.7%)	22 (8.9%)	16 (6.5%)
Alcohol	194 (78.2%)	49 (19.8%)	4 (2.0%)

Distribution of MEDI-LITE scores achieved by NU-AGE Wageningen participants per food category. For each food category in the MEDI-LITE score, the lowest score was 0 and the highest was 2. For the categories dairy and meat, the lower the intake, the higher the adherence score. For the alcohol category, moderate intake received the highest score, whereas high intake (>2 units per day) received the lowest adherence score. Data are presented as counts (%).

9.6 Adjusted model MEDI-LITE score in separate food categories and cognition

	Global cognition		**Episodic memory**		**Executive functioning**		**Perceptual speed**	
Predictors	*Estimates*	*p*	*Estimates*	*p*	*Estimates*	*p*	*Estimates*	*p*
Cereals middle score	0.09 (-0.16 – 0.33)	0.372	0.13 (-0.19 – 0.44)	0.294	-0.12 (-0.45 – 0.22)	0.371	0.15 (-0.20 – 0.50)	0.255
Cereals high score	-0.02 (-0.32 – 0.27)	0.830	0.09 (-0.28 – 0.46)	0.531	-0.33 (-0.73 – 0.07)	0.033	0.20 (-0.21 – 0.62)	0.207
Fruit middle score	0.03 (-0.21 – 0.26)	0.750	-0.03 (-0.32 – 0.27)	0.793	-0.07 (-0.39 – 0.24)	0.549	-0.14 (-0.47 – 0.19)	0.266
Fruit high score	0.01 (-0.26 – 0.28)	0.943	-0.14 (-0.48 – 0.20)	0.292	0.16 (-0.21 – 0.52)	0.263	-0.00 (-0.38 – 0.37)	0.975
Vegetables middle score	0.05 (-0.20 – 0.30)	0.610	-0.01 (-0.34 – 0.31)	0.908	0.17 (-0.17 – 0.52)	0.190	-0.01 (-0.37 – 0.35)	0.965
Vegetables high score	0.22 (-0.14 – 0.58)	0.118	0.15 (-0.31 – 0.61)	0.392	0.37 (-0.12 – 0.86)	0.051	-0.17 (-0.68 – 0.34)	0.388
Legumes middle score	-0.24 (-0.66 – 0.18)	0.144	-0.17 (-0.70 – 0.36)	0.407	-0.26 (-0.83 – 0.30)	0.229	-0.03 (-0.62 – 0.57)	0.909
Legumes high score	-0.01 (-0.40 – 0.38)	0.932	-0.04 (-0.53 – 0.46)	0.849	0.06 (-0.47 – 0.59)	0.774	0.35 (-0.21 – 0.90)	0.106
Dairy middle score	0.08 (-0.18 – 0.33)	0.429	0.06 (-0.26 – 0.38)	0.629	0.20 (-0.14 – 0.55)	0.130	0.19 (-0.17 – 0.55)	0.167
Dairy high score	0.00 (-0.26 – 0.26)	0.964	-0.08 (-0.41 – 0.24)	0.503	0.02 (-0.33 – 0.38)	0.855	0.04 (-0.33 – 0.40)	0.791
Fish middle score	-0.16 (-0.40 – 0.07)	0.070	-0.23 (-0.52 – 0.06)	0.044	-0.10 (-0.41 – 0.22)	0.420	-0.02 (-0.35 – 0.31)	0.891
Fish high score	-0.17 (-0.41 – 0.07)	0.071	-0.20 (-0.50 – 0.10)	0.089	-0.29 (-0.62 – 0.03)	0.021	-0.03 (-0.37 – 0.31)	0.816
Meat middle score	0.13 (-0.21 – 0.47)	0.319	-0.09 (-0.51 – 0.34)	0.602	0.14 (-0.32 – 0.59)	0.438	0.33 (-0.15 – 0.80)	0.075
Meat high score	0.05 (-0.28 – 0.38)	0.684	-0.17 (-0.58 – 0.25)	0.295	0.16 (-0.29 – 0.60)	0.356	0.17 (-0.29 – 0.64)	0.330
Olive oil middle score	-0.03 (-0.38 – 0.32)	0.819	-0.01 (-0.45 – 0.43)	0.965	0.09 (-0.38 – 0.57)	0.616	0.24 (-0.25 – 0.73)	0.207
Olive oil high score	-0.15 (-0.55 – 0.25)	0.323	-0.20 (-0.70 – 0.31)	0.311	-0.11 (-0.65 – 0.43)	0.585	-0.17 (-0.73 – 0.39)	0.439
Alcohol middle score	-0.10 (-0.36 – 0.15)	0.289	-0.10 (-0.42 – 0.22)	0.399	-0.25 (-0.59 – 0.10)	0.063	0.02 (-0.34 – 0.38)	0.899
Alcohol high score	-0.08 (-0.77 – 0.60)	0.751	-0.17 (-1.03 – 0.69)	0.614	0.02 (-0.91 – 0.95)	0.957	-0.04 (-1.00 – 0.93)	0.923
R^2	0.131		0.086		0.055		0.121	

The baseline data of 248 participants were used. The individual food components of the MEDI-LITE score *were scored as low (score 0), middle (score 1) and high (score 2). The low score was used as a reference in the linear regression. Data are reported as β coefficients with 99% confidence intervals. Age, gender, education, and BMI were used as covariates in the model (individual estimates not shown). p<0.01 was considered significant.*

9.7 Crude model MEDI-LITE total score and cognition

	Global cognition		**Episodic memory**		**Executive functioning**		**Perceptual speed**	
Predictors	*Estimates*	*p*	*Estimates*	*p*	*Estimates*	*p*	*Estimates*	*p*
MEDI-LITE middle score	-0.02 (-0.26 – 0.22)	0.827	-0.06 (-0.36 – 0.23)	0.587	-0.08 (-0.39 – 0.24)	0.524	-0.10 (-0.44 – 0.24)	0.436
MEDI-LITE high score	-0.09 (-0.34 – 0.16)	0.338	-0.18 (-0.49 – 0.13)	0.129	-0.13 (-0.45 – 0.20)	0.313	0.08 (-0.27 – 0.43)	0.548
MEDI-LITE total score	-0.01 (-0.06 – 0.04)	0.554	-0.03 (-0.09 – 0.03)	0.138	-0.02 (-0.08 – 0.04)	0.386	0.02 (-0.04 – 0.09)	0.370
R^2 middle and high score / R^2 total score	-0.004 / -0.003		0.002 / 0.005		-0.004 / -0.001		0.000 / -0.001	

The baseline data of 248 participants were used. MEDI-LITE score was analyzed as total score and divided into tertiles (low score 2-5, middle score 6-7 and high score 8-14), with the lowest tertile as the reference. Data are reported as β coefficients with 99% confidence intervals. R^2 values were reported for the tertiles as well as the total score. p<0.01 was considered significant.

9.8 Crude model MEDI-LITE score in separate food categories and cognition

	Global cognition		**Episodic memory**		**Executive functioning**		**Perceptual speed**	
Predictors	*Estimates*	*p*	*Estimates*	*p*	*Estimates*	*p*	*Estimates*	*p*
Cereals middle score	0.06 (-0.20 – 0.32)	0.553	0.08 (-0.24 – 0.40)	0.517	-0.12 (-0.45 – 0.22)	0.358	0.10 (-0.26 – 0.47)	0.469
Cereals high score	-0.03 (-0.32 – 0.27)	0.805	0.04 (-0.32 – 0.40)	0.781	-0.28 (-0.65 – 0.10)	0.056	0.18 (-0.23 – 0.59)	0.261
Fruit middle score	0.00 (-0.25 – 0.26)	0.962	-0.04 (-0.35 – 0.27)	0.713	-0.11 (-0.43 – 0.21)	0.361	-0.18 (-0.53 – 0.17)	0.180
Fruit high score	0.02 (-0.26 – 0.30)	0.862	-0.11 (-0.46 – 0.24)	0.400	0.13 (-0.23 – 0.49)	0.350	-0.01 (-0.40 – 0.39)	0.957
Vegetables middle score	0.05 (-0.22 – 0.32)	0.623	0.02 (-0.31 – 0.34)	0.904	0.12 (-0.22 – 0.46)	0.344	-0.02 (-0.39 – 0.35)	0.898
Vegetables high score	0.29 (-0.10 – 0.67)	0.054	0.24 (-0.23 – 0.71)	0.186	0.35 (-0.14 – 0.84)	0.063	-0.14 (-0.67 – 0.40)	0.504
Legumes middle score	-0.09 (-0.54 – 0.36)	0.605	-0.00 (-0.56 – 0.55)	0.997	-0.19 (-0.76 – 0.39)	0.400	0.16 (-0.47 – 0.78)	0.520
Legumes high score	-0.04 (-0.46 – 0.38)	0.805	-0.06 (-0.58 – 0.45)	0.747	0.01 (-0.53 – 0.55)	0.956	0.27 (-0.31 – 0.86)	0.228
Dairy middle score	0.03 (-0.24 – 0.31)	0.766	0.01 (-0.33 – 0.35)	0.963	0.17 (-0.19 – 0.52)	0.223	0.12 (-0.27 – 0.50)	0.433
Dairy high score	-0.01 (-0.29 – 0.27)	0.900	-0.09 (-0.44 – 0.25)	0.480	0.00 (-0.36 – 0.36)	0.994	0.02 (-0.38 – 0.41)	0.918
Fish middle score	-0.14 (-0.39 – 0.11)	0.139	-0.20 (-0.51 – 0.11)	0.091	-0.09 (-0.40 – 0.23)	0.486	0.01 (-0.34 – 0.36)	0.918
Fish high score	-0.15 (-0.41 – 0.11)	0.138	-0.17 (-0.49 – 0.15)	0.159	-0.27 (-0.60 – 0.06)	0.036	0.02 (-0.34 – 0.38)	0.889
Meat middle score	0.19 (-0.17 – 0.55)	0.169	-0.01 (-0.45 – 0.43)	0.933	0.13 (-0.33 – 0.58)	0.466	0.36 (-0.14 – 0.85)	0.065
Meat high score	0.14 (-0.19 – 0.48)	0.273	-0.05 (-0.47 – 0.37)	0.759	0.14 (-0.29 – 0.57)	0.395	0.23 (-0.24 – 0.70)	0.209
Olive oil middle score	0.04 (-0.34 – 0.42)	0.784	0.07 (-0.40 – 0.53)	0.715	0.12 (-0.36 – 0.60)	0.512	0.30 (-0.22 – 0.83)	0.133
Olive oil high score	-0.09 (-0.51 – 0.33)	0.576	-0.16 (-0.68 – 0.37)	0.438	-0.06 (-0.60 – 0.47)	0.758	-0.13 (-0.72 – 0.46)	0.574
Alcohol middle score	-0.15 (-0.42 – 0.12)	0.148	-0.14 (-0.47 – 0.19)	0.277	-0.29 (-0.63 – 0.06)	0.032	-0.03 (-0.40 – 0.35)	0.863
Alcohol high score	-0.22 (-0.96 – 0.51)	0.430	-0.34 (-1.25 – 0.57)	0.335	-0.04 (-0.98 – 0.90)	0.909	-0.21 (-1.23 – 0.82)	0.603
R^2	-0.022		-0.029		0.017		-0.012	

The baseline data of 248 participants were used. The individual food components of the MEDI-LITE score *were scored as low (score 0), middle (score 1) and high (score 2). The low score was used as a reference in the linear regression. Data are reported as β coefficients with 99% confidence intervals. p<0.01 was considered significant.*