The Mediterranean diet is associated with better cardiometabolic health for women in mid-life but not men

Nutrition, Metabolism & Cardiovascular Diseases (xxxx) xxx, xxx

Available online at www.sciencedirect.com

Nutrition, Metabolism & Cardiovascular Diseases

journal homepage: www.elsevier.com/locate/nmcd

The Mediterranean diet is associated with better cardiometabolic health for women in mid-life but not men: A PREVENT dementia cohort cross-sectional analysis

Sarah Gregory [a,*], Georgios Ntailianis [a], Oliver Shannon [b], Emma Stevenson [b], Craig Ritchie [a,c], Katie Wells [a], Graciela Muniz-Terrera [a,d]

[a] Edinburgh Dementia Prevention, Centre for Clinical Brain Sciences, University of Edinburgh, Edinburgh, EH4 2XU, UK
[b] Human Nutrition & Exercise Research Centre, Population Health Sciences Institute, Faculty of Medical Sciences, Newcastle University, Newcastle Upon Tyne, NE4 5PL, UK
[c] Scottish Brain Sciences, Edinburgh, UK
[d] Ohio University Heritage College of Osteopathic Medicine, Ohio University, Ohio, USA

Received 2 May 2023; received in revised form 12 July 2023; accepted 17 July 2023
Handling Editor: A. Siani
Available online ■ ■ ■

KEYWORDS
Diet;
Mediterranean;
Risk factor;
Cardiometabolic;
Cohort

Abstract *Background and aims:* The Mediterranean diet (MedDiet) has been associated with better cardiovascular health in a number of studies. This study aimed to explore cross-sectional associations between MedDiet adherence in the PREVENT Dementia (PREVENT) programme, stratified by sex.

Methods and results: Three MedDiet scores were calculated (MEDAS, MEDAS continuous and Pyramid) alongside a Western diet score. We used linear regression and linear mixed effects models to test for associations between the MEDAS score and cardiovascular health. Propensity scores were calculated to strengthen causality inferences from the data, and used as covariates along with total energy intake and Western diet scores. Exploratory analysis repeated the linear regression models for each individual food component. This study included 533 participants, with a mean age 51.25 (±5.40) years, and a majority of women (60.0%). Women had higher MedDiet scores across all three scoring methods, had a lower Western diet score and consumed fewer total calories. Higher MedDiet scores were associated with lower blood pressure, body mass index (BMI) and lower cardiovascular risk scores. When stratified by sex, women had significant positive associations between MedDiet scores and lower blood pressure, BMI and glycemia, whereas men only had a significant association with lower BMI.

Conclusion: There were significant associations between higher MedDiet scores and a number of cardiovascular health outcome measures. These associations were seen more consistently for women compared to men, which may have implications for the development of personalised nutritional recommendations to improve cardiovascular health.

1. Introduction

Diet is a commonly considered intervention for the management of risk for cardiovascular health. Of particular interest is the Mediterranean diet (MedDiet), an eating

* Corresponding author. Edinburgh Dementia Prevention, Outpatient Department 2, Western General Hospital, Edinburgh, EH4 3XU, UK.
E-mail address: Sarah.Gregory@ed.ac.uk (S. Gregory).

https://doi.org/10.1016/j.numecd.2023.07.020

pattern rich in fruit, nuts, vegetables, olive oil and legumes [1]. Adherence to the MedDiet has consistently been associated with beneficial effects in preventing cardiovascular disease, leading to calls for more high-quality prospective cohort studies as well as randomised control trials [2].

There is an emerging evidence base exploring the sex-specific effects of diet on cardiovascular outcomes. A four-week trial of an isoenergic MedDiet found that although both men and women saw a significant benefit in plasma lipid profiles, only men had significant improvements in insulin homeostasis. Importantly this study only included pre-menopausal women aged between 25 and 50 years of age [3]. This study also found that the MedDiet led to a more favourable low-density lipoprotein (LDL) subclass distribution [4] in men, significantly lower adiponectin concentration in men [5] and that while there was no overall difference between men and women in the effect of the diet on inflammation, individual patterns of changes were seen for men but not women [6]. A longer study in Canada found that while there were greater improvements in dietary intakes in men, which were associated with greater cardiovascular benefits when results were adjusted for baseline metabolic profiles there is no longer a significant difference [7]. When considering older adults, adherence to a MedDiet over a one-year period was associated with a reduction in systolic blood pressure (SBP), pulse pressure and urinary sodium concentrations in men but not women participants [8]. Interestingly in a subset of participants who underwent assessments of arterial stiffness, a positive effect of MedDiet adherence was seen in women but not men participants. Overall there remains a lack of studies specifically investigating sex-stratified differences in analyses of the MedDiet and its component foods [9]. Research on a similar dietary pattern (the Healthy Eating Index (HEI), found differences in which individual components were associated with cardiovascular disease risk for men and women, with lower vegetable intake in men and lower fruit intake in women [10].

A short-term controlled MedDiet intervention resulted in a lowering of the Framingham Risk Score (FRS: a 10-year risk of coronary heart disease [11]) in a Canadian population, with no differences between men and women [12]. No trials to date have reported on associations between the MedDiet and the QRisk3 score, a cardiovascular risk score more commonly used in the UK [13].

The aim of this cross-sectional analysis was to investigate associations between the MedDiet and cardiovascular risk factors (blood pressure, body mass index (BMI), waist-to-hip ratio (WHR), fasting blood glycemia, triglycerides and cholesterol (total, HDL and LDL)). Secondary analysis investigated differences between men and women with the previously described outcome measures. We hypothesised that the MedDiet would be associated with more favourable cardiovascular risk factor outcomes. We further hypothesised that we would see a larger effect for men rather than women.

2. Methods

2.1. PREVENT dementia programme

We used the baseline dataset from the PREVENT dementia programme (PREVENT). The protocol for this is well described elsewhere [14]. The baseline dataset includes 700 participants recruited at five centres across the UK and Ireland: London, Edinburgh, Cambridge, Oxford and Dublin. Participants were aged 40–59 years at baseline, free of dementia, and approximately half had at least one parent with dementia.

2.2. Ethics and consent

The PREVENT study was approved by the London-Camberwell St Giles National Health Service Research Ethics Committee (REC reference 12/LO/1023). All participants provided written informed consent prior to any protocol procedures other than the overnight fast prior to the visit, participants were free of dementia at baseline and required to have the capacity to consent at the time of study entry.

2.3. Data

We used the PREVENT baseline dataset for this analysis, following approval of a data access request (https://preventdementia.co.uk/for-researchers/). The dataset includes data from all participants who consented to join the study and completed a baseline visit.

2.4. Calculation of Mediterranean diet scores

Participants completed the Scottish Collaborative Group Food Frequency Questionnaire (SCG-FFQ). The SCG-FFQ is a validated self-report questionnaire in which participants report their consumption of 175 different foods and drinks over the last two to three months [15]. For this study consumption (grams (g)/day) of foods contributing to three MedDiet scores (the Mediterranean Diet Adherence Screener (MEDAS) score, the MEDAS continuous and the Pyramid score) were calculated using previously published scoring methods. Full details of scoring methodologies are available in the supplementary materials (Supplementary Table S1). Briefly, the MEDAS score was calculated using a binary scoring method, whereby participants were allocated 0 or 1 points for each of 14 food groups depending on whether they met consumption criteria [16]. The MEDAS continuous was developed by Shannon et al. (2019) with points allocated for the same consumption criteria as MEDAS but on a continuous scale from 0 to 1, as opposed to binary allocations [17]. Similarly, the Pyramid score is also coded on a continuous scale of 0–1 with a total possible score of 15 points [18]. Total energy intake (kcal/day) was derived from the dataset and included in the analysis. Participants with extreme energy intakes (<600 kcal, >6000 kcal were excluded from the analysis).

Please cite this article as: Gregory S et al., The Mediterranean diet is associated with better cardiometabolic health for women in mid-life but not men: A PREVENT dementia cohort cross-sectional analysis, Nutrition, Metabolism & Cardiovascular Diseases, https://doi.org/10.1016/j.numecd.2023.07.020

2.5. Calculation of western diet score

We created a Western diet score for each participant to act as a covariate in models, following findings from the Chicago Health and Aging Project that a high consumption of Western diet components attenuated the benefits of the MedDiet on cognitive outcome measures [19]. The Western diet score was calculated using a principal component analysis across 36 food groups (see Supplementary Table S2), retaining items with a factor loading of >0.20. Factor 1 reflected a Western diet score and factor 2 reflected a healthy diet pattern, with factor 1 including food items such as red meats, French fries, refined grains and snacks. The score was then calculated by summing the relevant food group and weighting according to the factor loading, with a higher score indicating a greater consumption of Western diet foods [19].

2.6. Cardiovascular outcome variables

SBP, DBP and heart rate were calculated as a mean of triplicate blood pressure measurements taken in the supine or seated position. Height and weight measurements were used to calculate BMI scores. Finally, hip and waist circumferences were used to calculate a waist-to-hip ratio. Data on fasted glycemia, triglycerides, high-density and low-density lipoprotein (HDL, LDL) values from the blood tests were included. A Framingham Risk Score (FRS) and a QRisk3 score were calculated for each participant. The FRS was calculated in R using the package 'CVrisk' [20] with the QRisk3 score calculated using the 'QRISK3' R package [21]. Details of variables contributing to each score are provided in Supplementary Table S3.

2.7. Calculating propensity scores

A propensity score is the probability that an individual would have been allocated in a particular treatment group (in this case the MedDiet) as a function of observed baseline characteristics (as would be dealt with through a randomisation process in a gold standard clinical trial) [22]. The following variables were included in the generation of the propensity score: age, sex, years of education, parental history of dementia, *APOEε4* carrier status, BMI, socio-economic status (SES) (based on occupational Office of National Statistics coding, categorised as high, moderate and low SES) and physical activity (self-reported based on frequency of engaging in low, moderate and vigorous activity). Propensity scores were adjusted in analyses were a contributing component was also included in the outcome (e.g. BMI removed from propensity score where BMI was the outcome of interest).

2.8. Statistical analysis

All statistical analyses were completed using R (Version 4.1.0). Descriptive statistics were calculated for all participants. For the main analysis, we excluded participants with missing data in the exposure, outcome and covariate variables of interest from the analysis. To test for any bias due to missing values we conducted sensitivity analyses including manually imputed data. For each outcome, we followed the same analytical steps. First, we tested the cohort as a whole and fitted univariate and fully adjusted linear regression models to test for associations between MEDAS and the cardiovascular outcomes. We then included *APOEε4* in the linear regression models as a main effect and also in an interaction term with the MEDAS score for each outcome. The partially adjusted model included the following variables: kcal/day, propensity score. In the fully adjusted model, the Western diet score was also added as a covariate. Our pre-planned stratified analysis split the dataset into men and women and re-ran the same model. We then repeated the analysis with the MEDAS continuous and then the Pyramid scores. To adjust for multiple comparisons that could emerge from running three concurrent analyses for each of the outcomes (MEDAS, MEDAS continuous, Pyramid), we corrected results using the Benjamini-Hochberg False Discovery Rate (FDR) procedure to adjust for multiple comparisons. An exploratory analysis further looked at each food component individually with the cardiovascular outcomes, to identify any individual items that were associated with cardiovascular health.

2.9. Role of the funding source

There was no involvement of the funders in the study design, collection, analysis or interpretation of the data, in the writing of the report, or in the decision to submit the paper for publication.

3. Results

3.1. Descriptive statistics

A total of 533 participants were included in this analysis after those with missing data were excluded (n = 175) and a further two participants were excluded for reporting implausible energy intakes (>6000 kcal/day). Participants had a mean age of 51.25 (±5.40) years, the majority were women (n = 320, 60.0%), had a family history of dementia (n = 279, 52.3%), were highly educated (16.71 ± 3.31 years) and a minority were *APOEε4* carriers (n = 206, 38.6%) (see Table 1). The majority of participants were Caucasian (n = 513, 96.2%). Participants had a mean MEDAS score of 5.42 (±1.73), MEDAS Continuous score of 7.27 (±1.59) and a Pyramid score of 8.10 (±1.54). The dietary scores had moderate to high correlations with each other (see Supplementary Table S4 for correlations).

Women had significantly higher MedDiet scores compared to men across all three scoring methodologies, had lower Western diet scores, consumed fewer calories, were younger and had more years of education (see Table 1). Women also had significantly lower blood pressure, BMI and waist-to-hip ratio. In the subset of participants with clinical blood results available (n = 512), women had significantly lower triglycerides, significantly higher HDL

Please cite this article as: Gregory S et al., The Mediterranean diet is associated with better cardiometabolic health for women in midlife but not men: A PREVENT dementia cohort cross-sectional analysis, Nutrition, Metabolism & Cardiovascular Diseases, https://doi.org/10.1016/j.numecd.2023.07.020

Table 1 Descriptive statistics for participants included in the analysis (n = 541), with sex-stratification and indication of any significant differences between men and women participants.

Variable	Mean (SD)/N (%)	Women *n=320*	Men *n=213*	p value
Age (years)	51.15 (5.40)	50.85 (5.28)	51.84 (5.53)	0.04
Education (years)	16.71 (3.31)	16.96 (3.54)	16.34 (2.88)	0.03
Sex (Women)	320 (60%)			
APOEε4 Carriers	206 (38.6)	126 (39.4)	80 (37.6)	0.74
Family history of dementia	279 (52.3)	172 (53.8)	107 (50.2)	0.48
Ethnicity (Caucasian)	513 (96.2)	307 (95.9)	206 (96.7)	0.20
MEDAS	5.42 (1.73)	5.59 (1.77)	5.16 (1.63)	0.004
MEDAS Continuous	7.27 (1.59)	7.44 (1.59)	7.02 (1.56)	0.003
PYRAMID	8.10 (1.55)	8.34 (1.59)	7.73 (1.40)	<0.001
Western Diet Score	4.90 (2.61)	4.58 (2.61)	5.39 (2.55)	<0.001
Calories (kcal)	2035.07 (753.13)	1939.67 (731.32)	2178.38 (764.34)	<0.001
Mean Systolic Blood Pressure (mmHg)	125.04 (15.53)	120.37 (14.65)	132.05 (14.15)	<0.001
Mean Diastolic Blood Pressure (mmHg)	76.43 (9.64)	73.77 (9.04)	80.43 (9.13)	<0.001
BMI (kg/m^2)	27.35 (5.28)	26.96 (5.99)	27.95 (3.93)	0.03
Hip Waist Ratio	0.88 (0.12)	0.84 (0.10)	0.94 (0.12)	<0.001
Glycemia[a]	5.04 (1.13)	4.96 (1.15)	5.15 (1.09)	0.06
Triglycerides[a]	1.13 (0.58)	0.97 (0.44)	1.36 (0.68)	<0.001
HDL cholesterol[a]	1.66 (0.55)	1.81 (0.52)	1.44 (0.51)	<0.001
LDL cholesterol[a]	3.33 (0.84)	3.31 (0.85)	3.35 (0.84)	0.56
FRS[b]	8.60 (6.36)	5.90 (3.15)	13.85 (6.35)	<0.001
QRISK3[c]	4.77 (4.03)	3.12 (2.37)	7.20 (4.68)	<0.001

[a] Analysis of clinical blood samples in a smaller group due to missing data, n = 512; women n = 303, men n = 209.
[b] FRS n = 531, women n = 318, men n = 213.
[c] QRISK3 n = 517, women n = 308, men n = 209. FRS: Framingham Risk Score; HDL: high density lipoprotein; kcal: kilo-calories; kg: kilograms; LDL: low density lipoprotein; m: metres; mmHg: millimetres of mercury; N: number: SD: standard deviation.

cholesterol and significantly lower FRS and QRISK3 scores with no differences between fasted glycemia or LDL cholesterol (see Table 1).

3.2. Mediterranean diet, cardiovascular health and cardiovascular risk scores

Higher adherence to the MedDiet was associated with lower SBP, DBP, BMI, FRS and QRISK3 scores with all MedDiet scoring methodologies in unadjusted, partially and fully adjusted models. The largest effect sizes on blood pressure were seen with the Pyramid score, where a 1-point increase in the Pyramid score was associated with a 1.85mmHg decrease in SBP and a 1.23mmHg decrease in DBP (SBP, fully adjusted β: -1.85, SE: 0.44, p < 0.001; DBP, fully adjusted β: -1.23, SE: 0.28, p < 0.001). Effect sizes were similar across all three scoring methodologies for BMI, with each point increase in MedDiet score resulting in an approximately 0.5 point decrease in BMI score (MEDAS, fully adjusted β: -0.53, SE: 0.15, p: 0.0007; MEDAS continuous, fully adjusted β: -0.68, SE: 0.17, p < 0.001; Pyramid β: -0.58, SE: 0.16, p: 0.0002) (see Table 2). The largest effects on the FRS and QRISK3 were also seen with the Pyramid score (FRS, fully adjusted β: -1.07, SE: 0.18, p < 0.001; QRISK3 β: -0.45, SE: 0.12, p: 0.0002) (see Table 2). Higher adherence to the MedDiet as measured by the Pyramid score was associated with lower waist-to-hip ratio in the fully adjusted model (β: -0.01, SE: 0.003, p: 0.003). A higher MEDAS continuous score was also associated with a lower waist-to-hip ratio in the fully adjusted model however this was no longer significant after FDR correction.

Higher Pyramid scores were associated with lower fasted glycemia levels (β: -0.09, SE: 0.04, p: 0.01). There were no other associations between any of the MedDiet scores and any of the other blood test results in fully adjusted models. There were no significant interactions between MEDAS scores and *APOEε4* for any of the outcome measures.

3.3. Sex stratified analysis

In women, higher adherence to the MedDiet was associated with lower SBP, DBP and BMI, with the largest association noted for the MEDAS continuous score (SBP, fully adjusted β: -1.62, SE: 0.49, p: 0.001; DBP, fully adjusted β: -1.12, SE: 0.31, p: 0.0003; BMI, fully adjusted β: -0.76, SE: 0.20, p: 0.0002). Men also had an inverse association between MedDiet and BMI across all three scores, although the effect sizes were smaller than for women. Women also had lower fasted glycemia levels with higher MedDiet adherence. Other than BMI, there were no associations seen between any of the dietary scores and the remaining cardiovascular measures for men. There was a significant association between higher MedDiet adherence and lower FRS scores for women but not men, and no significant associations between MedDiet adherence and QRISK3 scores when the dataset was stratified by sex (see Table 3 and Fig. 1).

3.4. Sensitivity analysis

A sensitivity analysis was conducted including participants who had missing data on their diet scores, with any

Please cite this article as: Gregory S et al., The Mediterranean diet is associated with better cardiometabolic health for women in mid-life but not men: A PREVENT dementia cohort cross-sectional analysis, Nutrition, Metabolism & Cardiovascular Diseases, https://doi.org/10.1016/j.numecd.2023.07.020

Table 2 Associations between dietary scores and cardiovascular risk factors. 1: unadjusted. Model 2: adjusted for propensity score and total kilo-calories (kcal). Model 3: adjusted for propensity score, total kcal and Western diet score.

Dietary score	Model 1	Model 2	Model 3
Systolic Blood Pressure			
MEDAS	β: -1.94, SE: 0.38, p < 0.001	β: -1.12, SE: 0.39, p: 0.004	β: -1.16, SE: 4.44, p: 0.009
MEDAS Continuous	β: -2.48, SE: 0.41, p < 0.001	β: -1.59, SE: 0.42, p: 0.0002	β: -1.75, SE: 0.48, p: 0.0003
Pyramid	β: -2.65, SE: 0.42, p < 0.001	β: -1.84, SE: 0.42, p < 0.001	β: -1.85, SE: 0.44, p < 0.001
Diastolic Blood Pressure			
MEDAS	β: -1.27, SE: 0.24, p < 0.001	β: -0.79, SE: 0.24, p: 0.001	β: -1.00, SE: 0.27, p: 0.0003
MEDAS Continuous	β: -1.50, SE: 0.25, p < 0.001	β: -0.97, SE: 0.26, p: 0.0002	β: -1.23, SE: 0.30, p < 0.001
Pyramid	β: -1.62, SE: 0.26, p < 0.001	β: -1.13, SE: 0.26, p < 0.001	β: -1.23, SE: 0.28, p < 0.001
BMI			
MEDAS	β: -0.66, SE: 0.13, p < 0.001	β: -0.62, SE: 0.13, p < 0.001	β: -0.53, SE: 0.15, p: 0.0007
MEDAS Continuous	β: -0.79, SE: 0.14, p < 0.001	β: -0.75, SE: 0.14, p < 0.001	β: -0.68, SE: 0.17, p < 0.001
Pyramid	β: -0.74, SE: 0.14, p < 0.001	β: -0.67, SE: 0.15, p < 0.001	β: -0.58, SE: 0.16, p: 0.0002
Hip Waist Ratio			
MEDAS	β: -0.008, SE: 0.003, p: 0.01	β: -0.002, SE: 0.003, p: 0.58	β: -0.005, SE: 0.003, p: 0.10
MEDAS Continuous	β: -0.01, SE: 0.003, p: 0.002	β: -0.003, SE: 0.003, p: 0.34	β: -0.008, SE: 0.004, p: 0.04[a]
Pyramid	β: -0.01, SE: 0.003, p < 0.001	β: -0.007, SE: 0.003, p: 0.02	β: -0.01, SE: 0.003, p: 0.003
Glycemia			
MEDAS	β: -0.08, SE: 0.03, p: 0.005	β: -0.04, SE: 0.03, p: 0.11	β: -0.02, SE: 0.03, p: 0.57
MEDAS Continuous	β: -0.11, SE: 0.03, p: 0.0005	β: -0.07, SE: 0.03, p: 0.03[a]	β: -0.05, SE: 0.04, p: 0.20
Pyramid	β: -0.14, SE: 0.03, p < 0.001	β: -0.10, SE: 0.03, p: 0.002	β: -0.09, SE: 0.04, p: 0.01
Triglyceride			
MEDAS	β: -0.04, SE: 0.01, p: 0.02	β: -0.004, SE: 0.01, p: 0.80	β: -0.009, SE: 0.02, p: 0.59
MEDAS Continuous	β: -0.04, SE: 0.02, p: 0.01	β: -0.0004, SE: 0.02, p: 0.98	β: -0.005, SE: 0.02, p: 0.79
Pyramid	β: -0.04, SE: 0.02, p: 0.02	β: -0.0008, SE: 0.02, p: 0.96	β: -0.002, SE: 0.02, p: 0.93
HDL Cholesterol			
MEDAS	β: 0.05, SE: 0.01, p: 0.0003	β: 0.03, SE: 0.01, p: 0.06	β: 0.03, SE: 0.02, p: 0.06
MEDAS Continuous	β: 0.05, SE: 0.02, p: 0.0004	β: 0.02, SE: 0.02; p: 0.15	β: 0.02, SE: 0.02, p: 0.17
Pyramid	β: 0.05, SE: 0.02, p: 0.0007	β: 0.02, SE: 0.02, p: 0.21	β: 0.02, SE: 0.02, p: 0.25
LDL Cholesterol			
MEDAS	β: 0.007, SE: 0.02, p: 0.74	β: 0.02, SE: 0.02, p: 0.38	β: 0.02, SE: 0.03, p: 0.47
MEDAS Continuous	β: 0.009, SE: 0.02, p: 0.69	β: 0.03, SE: 0.02, p: 0.29	β: 0.03, SE: 0.03, p: 0.35
Pyramid	β: -0.01, SE: 0.02, p: 0.69	β: 0.006, SE: 0.03, p: 0.82	β: 0.002, SE: 0.03, p: 0.94
FRS			
MEDAS	β: -0.64, SE: 0.16, p < 0.001	β: -0.72, SE: 0.16, p < 0.001	β: -0.71, SE: 0.19, p: 0.0002
MEDAS Continuous	β: -0.81, SE: 0.17, p < 0.001	β: -0.90, SE: 0.71, p < 0.001	β: -0.92, SE: 0.20, p < 0.001
Pyramid	β: -1.04, SE: 0.17, p < 0.001	β: -1.09, SE: 0.17, p < 0.001	β: -1.07, SE: 0.18, p < 0.001
QRisk3			
MEDAS	β: -0.28, SE: 0.10, p: 0.006	β: -0.33, SE: 0.10, p: 0.002	β: -0.33, SE: 0.12, p: 0.007
MEDAS Continuous	β: -0.35, SE: 0.11, p: 0.002	β: -0.40, SE: 0.11, p: 0.0005	β: -0.41, SE: 0.13, p: 0.002
Pyramid	β: -0.42, SE: 0.11, p: 0.0002	β: -0.46, SE: 0.11, p < 0.001	β: -0.45, SE: 0.12, p: 0.0002

[a] Not significant after FDR correction. BMI: Body Mss Index; FRS: Framingham Risk Score; HDL: high density lipoprotein; kcal: kilo-calories; LDL: low density lipoprotein.

missing data re-coded as zero consumption. There were small shifts in the effect sizes, standard errors and significance values, however there was no change which results were significant and non-significant, suggesting there is no bias in the results introduced through excluding those without full dietary data (see Supplementary Table S5).

3.5. Exploratory analysis

Olive oil consumption, consuming less than one carbonated or sweet drink portion a day and eating at least three portions of nuts per week was associated with lower blood pressure and lower BMI. Eating two or more portions of vegetables per day was associated with a higher BMI, whilst eating three or more portions of fruit per day was associated with a lower BMI. Consumption of olive oil was associated with lower glycemia concentrations while drinking at least seven portions of wine per week and at least three portions of legumes each week was associated with higher HDL concentrations. Consumption of olive oil and nuts were associated with lower FRS scores, with both of these components in addition to dairy consumption associated with lower QRISK3 scores. See Table 4 for full details.

When the dataset was split by sex, we again saw a more consistent association between food groups and cardiovascular outcomes in women compared to men (see Supplementary Table S6). Olive oil consumption was associated with blood pressure, BMI, glycemia, FRS and QRISK3 scores in women, but only with the FRS score in men. In both men and women consumption of less than one portion of carbonated or sweet drinks per week and at least three portions of nuts per week was associated with lower BMI.

Please cite this article as: Gregory S et al., The Mediterranean diet is associated with better cardiometabolic health for women in mid-life but not men: A PREVENT dementia cohort cross-sectional analysis, Nutrition, Metabolism & Cardiovascular Diseases, https://doi.org/10.1016/j.numecd.2023.07.020

Table 3 Sex stratified analysis of associations between dietary scores and cardiovascular risk factors. Model 1: unadjusted. Model 2: adjusted for propensity score and total kilo-calories (kcal). Model 3: adjusted for propensity score, total kcal and Western diet score.

Dietary score	Women			Men		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
Systolic Blood Pressure						
MEDAS	β: -1.92, SE: 0.45, p < 0.001	β: -1.20, SE: 0.45, p: 0.008	β: -1.45, SE: 0.52, p: 0.006	β: -0.90, SE: 0.59, p: 0.13	β: -0.45, SE: 0.63, p: 0.47	β: -0.16, SE: 0.70, p: 0.82
MEDAS-C	β: -2.55, SE: 0.50, p < 0.001	β: -1.70, SE: 0.50, p: 0.0007	β: -2.14, SE: 0.58, p: 0.0003	β: -1.24, SE: 0.62, p: 0.05	β: -0.78, SE: 0.67, p: 0.24	β: -0.55, SE: 0.74, p: 0.46
Pyramid	β: -2.14, SE: 0.50. p < 0.001	β: -1.35, SE: 0.49, p: 0.007	β: -1.45, SE: 0.53, p: 0.007	β: -1.78, SE: 0.69, p: 0.01[a]	β: -1.37, SE: 0.70, p: 0.05	β: -1.26, SE: 0.72, p: 0.08
Diastolic Blood Pressure						
MEDAS	β: -1.29, SE: 0.28, p < 0.001	β: -0.90, SE: 0.28, p: 0.001	β: -1.29, SE: 0.32, p < 0.001	β: -0.61, SE: 0.38, p: 0.11	β: -0.26, SE: 0.40, p: 0.52	β: -1.93, SE: 0.45, p: 0.67
MEDAS-C	β: -1.67, SE: 0.30, p < 0.001	β: -1.20, SE: 0.31, p: 0.0001	β: -1.73, SE: 0.36, p < 0.001	β: -0.59, SE: 0.40, p: 0.14	β: -0.18, SE: 0.43, p: 0.68	β: -0.08, SE: 0.47, p: 0.86
Pyramid	β: -1.41, SE: 0.31, p < 0.001	β: -0.97, SE: 0.31, p: 0.002	β: -1.18, SE: 0.33, p: 0.0004	β: -0.97, SE: 0.44, p: 0.03[a]	β: -0.63, SE: 0.45, p: 0.17	β: -0.60, SE: 0.46, p: 0.20
BMI						
MEDAS	β: -0.75, SE: 0.19, p < 0.001	β: -0.65, SE: 0.18, p: 0.0005	β: -0.51, SE: 0.22, p: 0.02[a]	β: -0.43, SE: 0.16, p: 0.008[a]	β: -0.39, SE: 0.17, p: 0.02[a]	β: -0.45, SE: 0.19, p: 0.02[a]
MEDAS-C	β: -0.95, SE: 0.20, p < 0.001	β: -0.80, SE: 0.21, p: 0.0001	β: -0.68, SE: 0.24, p: 0.006	β: -0.48, SE: 0.17, p: 0.005[a]	β: -0.44, SE: 0.18, p: 0.02[a]	β: -0.50, SE: 0.20, p: 0.01[a]
Pyramid	β: -0.79, SE: 0.21, p: 0.0002	β: -0.65, SE: 0.21, p: 0.002	β: -0.51, SE: 0.22, p: 0.02	β: -0.54, SE: 0.19, p: 0.005[a]	β: -0.48, SE: 0.19, p: 0.01[a]	β: -0.49, SE: 0.19, p: 0.01[a]
Hip:Waist Ratio						
MEDAS	β: -0.0009, SE: 0.003, p: 0.78	β: -0.002, SE: 0.003, p: 0.48	β: -0.001, SE: 0.003, p: 0.48	β: -0.01, SE: 0.005, p: 0.05	β: -0.003, SE: 0.005, p: 0.49	β: -0.006, SE: 0.005, p: 0.30
MEDAS-C	β: -0.002, SE: 0.003, p: 0.63	β: -0.003, SE: 0.004, p: 0.47	β: -0.001, SE: 0.004, p: 0.72	β: -0.01, SE: 0.005, p: 0.02[a]	β: -0.005, SE: 0.005, p: 0.29	β: -0.008, SE: 0.006, p: 0.16
Pyramid	β: -0.003, SE: 0.003, p: 0.40	β: -0.0003, SE: 0.003, p: 0.93	β: -0.003, SE: 0.004, p: 0.49	β: -0.02, SE: 0.006, p: 0.005[a]	β: -0.01, SE: 0.006, p: 0.07	β: -0.01, SE: 0.006, p: 0.06
Glycemia						
MEDAS	β: -0.11, SE: 0.04, p: 0.005	β: -0.08, SE: 0.04, p: 0.03[a]	β: -0.08, SE: 0.04, p: 0.07	β: -0.02, SE: 0.05, p: 0.65	β: 0.02, SE: 0.05, p: 0.65	β: 0.09, SE: 0.05, p: 0.10
MEDAS-C	β: -0.13, SE: 0.04, p: 0.002	β: -0.11, SE: 0.04, p: 0.01	β: -0.11, SE: 0.05, p: 0.03[a]	β: -0.06, SE: 0.05, p: 0.23	β: -0.01, SE: 0.05, p: 0.79	β: 0.04, SE: 0.06, p: 0.46
Pyramid	β: -0.14, SE: 0.04, p: 0.001	β: -0.11, SE: 0.04, p: 0.008	β: -0.11, SE: 0.05, p: 0.02	β: -0.12, SE: 0.05, p: 0.03[a]	β: -0.09, SE: 0.06, p: 0.12	β: -0.07, SE: 0.06, p: 0.24
Triglycerides						
MEDAS	β: -0.03, SE: 0.01, p: 0.03[a]	β: -0.01, SE: 0.01, p: 0.40	β: -0.02, SE: 0.02, p: 0.15	β: -0.004, SE: 0.03, p: 0.90	β: 0.01, SE: 0.03, p: 0.67	β: -0.02, SE: 0.03, p: 0.51
MEDAS-C	β: -0.04, SE: 0.02, p: 0.007	β: -0.02, SE: 0.02, p: 0.27	β: -0.03, SE: 0.02, p: 0.08	β: 0.005, SE: 0.03, p: 0.87	β: 0.03, SE: 0.03, p: 0.41	β: 0.04, SE: 0.04, p: 0.28
Pyramid	β: -0.03, SE: 0.02, p: 0.04[a]	β: -0.01, SE: 0.02, p: 0.52	β: -0.02, SE: 0.02, p: 0.32	β: 0.01, SE: 0.03, p: 0.66	β: 0.04, SE: 0.03, p: 0.28	β: 0.04, SE: 0.03, p: 0.28
HDL Cholesterol						
MEDAS	β: 0.03, SE: 0.02, p: 0.05	β: 0.02, SE: 0.02, p: 0.23	β: 0.02, SE: 0.02, p: 0.38	β: 0.04, SE: 0.02, p: 0.04[a]	β: 0.03, SE: 0.02, p: 0.15	β: 0.04, SE: 0.03, p: 0.14
MEDAS-C	β: 0.04, SE: 0.02, p: 0.05	β: 0.02, SE: 0.02, p: 0.37	β: 0.01, SE: 0.02, p: 0.59	β: 0.04, SE: 0.02, p: 0.08	β: 0.03, SE: 0.02, p: 0.27	β: 0.03, SE: 0.03, p: 0.29
Pyramid	β: 0.03, SE: 0.02, p: 0.12	β: 0.01, SE: 0.02, p: 0.46	β: 0.009, SE: 0.02, p: 0.65	β: 0.03, SE: 0.03, p: 0.22	β: 0.02, SE: 0.03, p: 0.55	β: 0.01, SE: 0.03, p: 0.58
LDL Cholesterol						
MEDAS	β: 0.003, SE: 0.03, p: 0.91	β: 0.02, SE: 0.02, p: 0.23	β: 0.02, SE: 0.02, p: 0.38	β: 0.02, SE: 0.04, p: 0.59	β: 0.02, SE: 0.04, p: 0.67	β: 0.01, SE: 0.04, p: 0.80
MEDAS-C	β: -0.006, SE: 0.03, p: 0.85	β: 0.02, SE: 0.03, p: 0.63	β: 0.01, SE: 0.04, p: 0.75	β: 0.04, SE: 0.04, p: 0.32	β: 0.04, SE: 0.04, p: 0.35	β: 0.04, SE: 0.04, p: 0.41
Pyramid	β: -0.03, SE: 0.03, p: 0.59	β: 0.001, SE: 0.03, p: 0.97	β: -0.004, SE: 0.03, p: 0.90	β: 0.01, SE: 0.04, p: 0.81	β: 0.01, SE: 0.04, p: 0.80	β: 0.007, SE: 0.04, p: 0.87
FRS						
MEDAS	β: -0.29, SE: 0.10, p: 0.003	β: -0.28, SE: 0.10, p: 0.006	β: -0.23, SE: 0.12, p: 0.05	β: -0.39, SE: 0.27, p: 0.15	β: -0.42, SE: 0.28, p: 0.14	β: -0.38, SE: 0.31, p: 0.23
MEDAS-C	β: -0.40, SE: 0.11, p:0.0003	β:-0.40, SE: 0.11, p: 0.0005	β: -0.37, SE: 0.13, p:0.005	β: -0.54, SE: 0.28, p: 0.05	β: -0.60, SE: 0.29, p: 0.04	β: -0.59, SE: 0.33, p: 0.08
Pyramid	β: -0.38, SE: 0.11, p:0.0006	β: -0.37, SE: 0.11, p: 0.001	β: -0.33, SE: 0.12, p:0.007	β: -0.77, SE: 0.31, p: 0.01	β: -0.77, SE: 0.32, p: 0.02	β: -0.74, SE: 0.32, p: 0.02
QRISK3						

Please cite this article as: Gregory S et al., The Mediterranean diet is associated with better cardiometabolic health for women in mid-life but not men: A PREVENT dementia cohort cross-sectional analysis, Nutrition, Metabolism & Cardiovascular Diseases, https://doi.org/10.1016/j.numecd.2023.07.020

Table 3 (*continued*)

Dietary score	Women			Men		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
MEDAS	β: -0.13, SE: 0.08, p: 0.10	β: -0.12, SE: 0.08, p: 0.14	β: -0.09, SE: 0.09, p: 0.33	β: -0.13, SE: 0.20, p: 0.52	β: 0.19, SE: 0.21, p: 0.36	β: -0.18, SE: 0.24, p: 0.45
MEDAS-C	β: -0.17, SE: 0.08, p: 0.04	β: -0.16, SE: 0.09, p: 0.07	β: -0.14, SE: 0.10, p: 0.16	β: 0.19, SE: 0.21, p: 0.37	β: -0.27, SE: 0.22, p: 0.23	β: -0.27, SE: 0.25, p: 0.27
Pyramid	β: -0.14, SE: 0.08, p: 0.09	β: 0.13, SE: 0.09, p: 0.13	β: -0.11, SE: 0.10, p: 0.26	β: -0.24, SE: 0.23, p: 0.30	β: -0.27, SE: 0.24, p: 0.25	β: -0.26, SE: 0.24, p: 0.29

[a] Not significant after FDR correction. BMI: Body Mss Index; FRS: Framingham Risk Score; HDL: high density lipoprotein; kcal: kilo-calories; LDL: low density lipoprotein; MEDAS-C: MEDAS Continuous.

4. Discussion

This analysis found that higher adherence to the MedDiet was associated with better cardiovascular health, as measured by the cardiovascular disease surrogate biomarkers of blood pressure, BMI, fasted glycemia concentrations. Additional adherence to the MedDiet was inversely associated with estimated cardiovascular disease risk (measured with the FRS and QRISK3 scores). The effects were consistent for women, with only BMI and diet significantly associated in men. None of the associations were explained by an interaction with *APOEε4*, which was included due to its role in cholesterol metabolism [23].

The findings in the cohort as a whole are consistent with the existing literature base, with a MedDiet associated with better cardiovascular health in a number of studies [2]. Interestingly, in our analysis not all cardiovascular outcomes selected for analyses were significantly associated with MedDiet adherence, most notably cholesterol (both HDL and LDL). Previous studies have seen this association, with an intervention trial in overweight and obese participants resulting in a significant reduction in both total plasma cholesterol and HDL cholesterol after four weeks of MedDiet adherence [24]. In this intervention, the participants allocated to a MedDiet for the trial period significantly increased their index scores from a mean score comparable to our participants (approximately 5–6) to a score of approximately 8. It may be that this higher level of adherence is needed to have an impact on cholesterol levels.

This is one of the first studies to demonstrate a benefit of the MedDiet on cardiovascular risk scores (the FRS and QRISK3), with a stronger effect seen for women compared to men on the FRS. A higher adherence to the MedDiet was associated with lower 10-year cardiovascular disease risk as quantified by these scores. This important finding suggests that in addition to demonstrating potential benefits of the dietary pattern on multiple cardiovascular

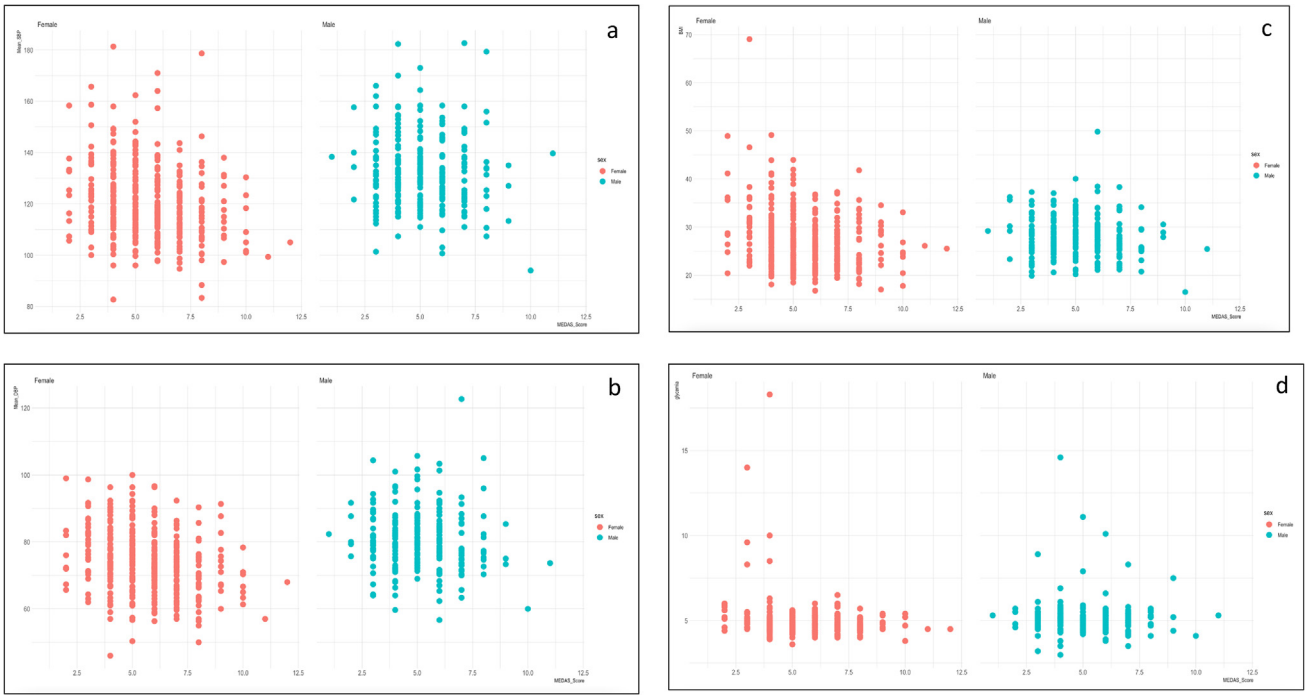

Fig. 1 Scatterplots showing the association between MEDAS Scores (x axis) and cardiovascular variables (y axis) split by female and male: (a) systolic blood pressure (SBP); (b) diastolic blood pressure (DBP); (c) body mass index (BMI); (d) fasted glucose.

Please cite this article as: Gregory S et al., The Mediterranean diet is associated with better cardiometabolic health for women in midlife but not men: A PREVENT dementia cohort cross-sectional analysis, Nutrition, Metabolism & Cardiovascular Diseases, https://doi.org/10.1016/j.numecd.2023.07.020

Table 4 Individual food components of the MEDAS score associations with cardiovascular outcome measures. Fully adjusted model presented (adjusted for propensity score and total kilocalories).

Dietary score	Systolic Blood Pressure	Diastolic Blood Pressure	BMI	Hip Waist Ratio	FRS
Olive Oil	β: -2.85, SE: 1.36, p: 0.04	β: -1.81, SE: 0.85, p: 0.03	β: -1.24, SE: 0.48, p: 0.01	β: -0.02, SE: 0.01, p: 0.08	β: -2.19, SE: 0.58, p: 0.0002
Vegetables	β: -1.69, SE: 1.41, p: 0.23	β: -1.07, SE: 0.88, p: 0.22	β: 1.04, SE: 0.50, p: 0.04	β: 0.006, SE: 0.01, p: 0.57	β: -0.38, SE: 0.61, p: 0.54
Fruit	β: -0.53, SE: 1.31, p: 0.69	β: -0.68, SE: 0.82, p: 0.41	β: -1.06, SE: 0.46, p: 0.02	β: 0.003, SE: 0.01, p: 0.80	β: -0.99, SE: 0.56, p: 0.08
Red Meat	β:-0.74, SE: 2.23, p: 0.74	β: -1.71, SE: 1.39, p: 0.22	β: -0.62, SE: 0.79, p: 0.44	β: -0.007, SE: 0.02, p: 0.69	β: 0.02, SE: 0.96, p: 0.99
Dairy	β: 0.45, SE: 2.38, p: 0.85	β: -0.72, SE: 1.48, p: 0.63	β: -0.39, SE: 0.85, p: 0.64	β: -0.02, SE: 0.02, p: 0.15	β: -0.36, SE: 1.03, p: 0.73
Carbonated/ sweet drinks	β: -3.15, SE: 1.59, p: 0.048	β: -2.16, SE: 0.99, p: 0.03	β: -2.86, SE: 0.55, $p < 0.001$	β: 0.01, SE: 0.01, p: 0.23	β: -0.97, SE: 0.69, p: 0.16
Wine	β: 0.72, SE: 1.57, p: 0.65	β: 1.65, SE: 0.98, p: 0.09	β: 0.05, SE: 0.56, p: 0.93	β: 0.003, SE: 0.01, p: 0.77	β: 0.05, SE: 0.68, p: 0.94
Pulses	β: -0.51, SE: 3.65, p: 0.16	β: -2.97, SE: 2.27, p: 0.19	β: 1.28, SE: 1.30, p: 0.32	β: -0.01, SE: 0.03, p: 0.60	β: -1.60, SE: 1.58, p: 0.31
Fish/Seafood	β: -2.26, SE: 1.38, p: 0.10	β: -1.30, SE: 0.86, p: 0.13	β: -0.42, SE: 0.49, p: 0.39	β: -0.004, SE: 0.01, p: 0.68	β: -1.00, SE: 0.60, p: 0.10
Pastries	β: 0.01, SE: 1.57, p: 0.99	β: 0.18, SE: 0.98, p: 0.86	β: -0.30, SE: 0.56, p: 0.59	β: 0.004, SE: 0.01, p: 0.75	β: -0.19, SE: 0.68, p: 0.78
Nuts	β: -4.20, SE: 1.62, p: 0.01	β: -2.53, SE: 1.01, p: 0.01	β: -2.01, SE: 0.57, p: 0.0004	β: 0.004, SE: 0.01, p: 0.72	β: -1.69, SE: 0.69, p: 0.01
White meat	β: -3.26, SE: 1.83, p: 0.08	β: -2.11, SE: 1.14, p: 0.06	β: -0.56, SE: 0.65, p: 0.39	β: 0.02, SE: 0.01, p: 0.15	β: -1.45, SE: 0.79, p: 0.07
Sofrito	β: -0.74, SE: 1.37, p: 0.59	β: -0.55, SE: 0.85, p: 0.52	β: -0.18, SE: 0.49, p: 0.72	β: -0.003, SE: 0.01, p: 0.76	β: -0.78, SE: 0.59, p: 0.19
	Glycemia	**Triglyceride**	**HDL Cholesterol**	**LDL Cholesterol**	**QRisk3**
Olive Oil	β: -0.25, SE: 0.11, p: 0.02	β: 0.09, SE: 0.05, p: 0.07	β: 0.03, SE: 0.05, p: 0.58	β: 0.08, SE: 0.08, p: 0.31	β: -0.93, SE: 0.38, p: 0.01
Vegetables	β: -0.12, SE: 0.11, p: 0.26	β: 0.01, SE: 0.05, p: 0.77	β: -0.008, SE: 0.05, p: 0.88	β: 0.13, SE: 0.08, p: 0.12	β: -0.06, SE: 0.39, p: 0.87
Fruit	β: -0.14, SE: 0.10, p: 0.18	β: 0.06, SE: 0.05, p: 0.22	β: -0.02, SE: 0.05, p: 0.71	β: 0.04, SE: 0.08, p: 0.64	β: -0.28, SE: 0.36, p: 0.44
Red Meat	β: 0.05, SE: 0.17, p: 0.78	β: -0.05, SE: 0.08, p: 0.55	β: 0.05, SE: 0.08, p: 0.50	β: -0.13, SE: 0.13. p: 0.34	β: -0.17, SE: 0.62, p: 0.78
Dairy	β: -0.56, SE: 0.19, p: 0.76	β: 0.02, SE: 0.09, p: 0.82	β: -0.06, SE: 0.09, p: 0.45	β: -0.20, SE: 0.14, p: 0.17	β: -1.49, SE: 0.66, p: 0.03
Carbonated/ sweet drinks	β: -0.06, SE: 0.13, p: 0.64	β: -0.03, SE: 0.06, p: 0.57	β: 0.008, SE: 0.06, p: 0.89	β: 0.03, SE: 0.10, p: 0.77	β: -0.26, SE: 0.44, p: 0.56
Wine	β: 0.003, SE: 0.12, p: 0.98	β: -0.03, SE: 0.06, p: 0.58	β: 0.14, SE: 0.05, p: 0.01	β: 0.11, SE: 0.09, p: 0.25	β: -0.29, SE: 0.44, p: 0.51
Pulses	β: 0.20, SE: 0.29, p: 0.48	β: -0.06, SE: 0.14, p: 0.65	β: 0.43, SE: 0.13, p: 0.001	β: 0.23, SE: 0.22, p: 0.29	β: -1.17, SE: 1.00, p: 0.24
Fish/Seafood	β: -0.02, SE: 0.11, p: 0.83	β: -0.07, SE: 0.05, p: 0.17	β: 0.07, SE: 0.05, p: 0.14	β: -0.07, SE: 0.08, p: 0.38	β: -0.58, SE: 0.38, p: 0.13
Pastries	β: 0.07, SE: 0.12, p: 0.57	β: 0.06, SE: 0.06, p: 0.28	β: 0.02, SE: 0.06, p: 0.77	β: -0.10, SE: 0.09, p: 0.28	β: -0.21, SE: 0.44, p: 0.63
Nuts	β: -0.02, SE: 0.12, p: 0.88	β: -0.02, SE: 0.60, p: 0.76	β: -0.006, SE: 0.06, p: 0.91	β: -0.03, SE: 0.09, p: 0.79	β: -0.96, SE: 0.44, p: 0.03
White meat	β: -0.20, SE: 0.14, p: 0.15	β: -0.68, SE: 0.07, p: 0.32	β: 0.10, SE: 0.06, p: 0.10	β: 0.12, SE: 0.11, p: 0.25	β: -0.34, SE: 0.51, p: 0.50
Sofrito	β: -0.07, SE: 0.11, p: 0.52	β: -0.04, SE: 0.05, p: 0.47	β: -0.02, SE: 0.05, p: 0.72	β: 0.07, SE: 0.08, p: 0.37	β: -0.32, SE: 0.38, p: 0.41

measures, the MedDiet may also confer long term cardiovascular benefits.

The analysis did not support the hypothesis that there would be a stronger association between higher MedDiet scores and better cardiovascular health in men compared to women. Although not the MedDiet, a similar dietary pattern, the HEIwas studied in healthy men and women, with the study finding that men with a high risk of cardiovascular disease had lower greens and beans intake while women with the same high cardiovascular disease risk had lower fruit, seafood, fatty acid and saturated fats intake with higher dairy intake [10]. This study suggests that although the overall scores were associated with cardiovascular risk for both sexes, the individual

Please cite this article as: Gregory S et al., The Mediterranean diet is associated with better cardiometabolic health for women in mid-life but not men: A PREVENT dementia cohort cross-sectional analysis, Nutrition, Metabolism & Cardiovascular Diseases, https://doi.org/10.1016/j.numecd.2023.07.020

components conferring benefit or risk differed between men and women. One notable difference between previous studies and the PREVENT dataset is the focus on premenopausal women [3–6], whereas our study included women who were pre-, peri- and post-menopausal. It should also be noted that the women included in this study had significantly higher MedDiet scores compared to men. This is a common finding across research studies, with women more likely to adopt MedDiet eating patterns compared to men [7]. The higher scores achieved by women may explain the associations seen with cardiovascular disease, with a theoretical threshold for cardiovascular benefit reached by women and not men.

Higher olive oil, nuts, and fruit consumption and lower consumption of carbonated or sweet drinks were all associated with better cardiovascular outcome measurements, with higher vegetable consumption associated with higher BMI. The cardiovascular health benefits of olive oil and nuts are widely reported in the literature base [25,26], however it is important to note that in this study we only saw an effect for women and not men. Fruit consumption has also been widely associated with cardiovascular health, although the evidence generally also supports vegetable consumption and this anomaly in our dataset is not possible to explain [27]. It is possible that those with higher BMIs had actually adopted healthier eating habits (i.e. an increase in vegetable consumption) to modify their weight, although it is impossible to confirm this in the context of a cross-sectional analysis. Previous research has found that women in an Australian cohort who were overweight or obese actually consumed the highest amounts of vegetables compared to those in normal or underweight categories, a finding that was not replicated in obese or overweight men [28]. The authors of that paper suggest that it may be general excessive consumption of food groups, including vegetables, that may drive this association. When the data is split by sex, it is notable that no associations with vegetable consumption are seen either for BMI or any other outcome measure, and this may be a spurious finding and should be interpreted with caution.

Using propensity scores in this analysis allows us to draw more confidence in potential causative relationships between the exposure of the MedDiet and the cardiovascular outcome measures. This approach is a strength of this analysis. Similarly, the sensitivity analysis with manual imputation of missing data with no effect of the significance of the findings is a strength of this analysis. The analysis should be replicated when follow-up data collected is complete to understand both longitudinal associations, and further explore potential causal associations in this dataset. The study does have some noted limitations. The dietary data was collected from self-report questionnaires. Whilst the questionnaire has been validated in a number of settings [15], self-report of such data is known to be potentially fallible to bias through social desirability [29] and underreporting of energy intake [30]. A further limitation to note is the lack of diversity of participants in the PREVENT cohort, with nearly all participants reporting their ethnicity as Caucasian (96.2%), and with an average of more than 16 years of education. This does not accurately reflect the UK and Irish populations, with a lack of ethnic diversity and a higher than average reported years of education.

5. Conclusion

In conclusion, our data support the notion that the consumption of a MedDiet may be beneficial for cardiovascular health, including in non-Mediterranean settings such as the UK. They also highlight potential sex-based differences in associations between MedDiet adherence and cardiovascular health, which may have implications for the development of personalised nutritional recommendations. Future research should investigate longitudinal sex-stratified associations between MedDiet adherence and cardiovascular health outcomes, as well as investigate individual food components for different associations by sex. Investigations of other dietary patterns, such as the Eatwell Guide which is relevant to the UK population, should also be considered.

Author contributions

SG: Conceptualization, Methodology, Formal Analysis, Writing- Original Draft, Writing- Reviewing and Editing; KW: Data preparation, Writing- Reviewing and Editing; GN: Data preparation, Writing-Reviewing and Editing; CWR: Supervision, Writing- Reviewing and Editing; OS: Writing- Reviewing and Editing; ES: Writing- Reviewing and Editing; GMT: Methodology, Supervision, Writing-Reviewing and Editing.

Funding

PREVENT is funded by the Alzheimer's Society (grant numbers 178, 264 and 329), Alzheimer's Association (grant number TriBEKa-17-519,007) and philanthropic donations. The analytical work was funded by the MRC (MRC UK Nutrition Research Partnership (NRP) Collaboration Award (MR/T001852/1). Prof. Muniz-Terrera acknowledges the support of the Osteopathic Heritage Foundation through funding for the Osteopathic Heritage Foundation Ralph S. Licklider, D.O., Research Endowment in the Heritage College of Osteopathic Medicine. The funders had no involvement in the protocol design, data collection, analysis or manuscript preparation. For the purpose of open access, the author has applied a creative commons attribution (CC BY) licence to any author-accepted manuscript version arising.

Please cite this article as: Gregory S et al., The Mediterranean diet is associated with better cardiometabolic health for women in midlife but not men: A PREVENT dementia cohort cross-sectional analysis, Nutrition, Metabolism & Cardiovascular Diseases, https://doi.org/10.1016/j.numecd.2023.07.020

Funders

PREVENT: Alzheimer's Society, Alzheimer's Association and philanthropic donations. Data analysis: MRC.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest. SG is funded by the MRC UK Nutrition Research Partnership (NRP) Collaboration Award (MR/T001852/1). GN and KW are funded by the PREVENT study funders (Alzheimer's Society (grant numbers 178, 264 and 329), Alzheimer's Association (grant number TriBEKa-17-519,007) and philanthropic donations). CWR is the CEO and founder of Scottish Brain Sciences and has previously received consulting fees from Biogen, Eisai, MSD, Actinogen, Roche and Eli Lilly, as well as receiving speaker fees from Roche and Eisai. CWR sits on an NIHR data safety monitoring board and is on an advisory board for Roche Diagnostics. CWR is an unpaid chair of the Brain Health Clinic Consortium (sponsored by Biogen). SG, OS, ES and GMT have no conflicts of interest to disclose. OS, ES and GMT have no declarations of interest.

Acknowledgements

We would like to acknowledge the sites involved with the project, West London NHS Trust, NHS Lothian, Cambridgeshire and Peterborough NHS Foundation Trust, Oxford Heath NHS Foundation Trust and Trinity College. Special thanks also to the PREVENT participants, the participant panel, members of the Scientific Advisory Committee, and funders for their support of the PREVENT dementia programme.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.numecd.2023.07.020.

References

[1] Trichopoulou A, et al. Mediterranean diet and cognitive decline over time in an elderly Mediterranean population. Eur J Nutr 2015;54(8):1311–21.
[2] Salas-Salvadó J, et al. Mediterranean diet and cardiovascular disease prevention: what do we know? Prog Cardiovasc Dis 2018;61(1):62–7.
[3] Bédard A, et al. Sex differences in the impact of the Mediterranean diet on cardiovascular risk profile. Br J Nutr 2012;108(8):1428–34.
[4] Bédard A, et al. Sex differences in the impact of the Mediterranean diet on LDL particle size distribution and oxidation. Nutrients 2015;7(5):3705–23.
[5] Bédard A, et al. Effects of the traditional Mediterranean diet on adiponectin and leptin concentrations in men and premenopausal women: do sex differences exist? Eur J Clin Nutr 2014;68(5):561–6.
[6] Bédard A, et al. Sex differences in the impact of the Mediterranean diet on systemic inflammation. Nutr J 2015;14:46.
[7] Leblanc V, et al. Differences between men and women in dietary intakes and metabolic profile in response to a 12-week nutritional intervention promoting the Mediterranean diet. J Nutr Sci 2015;4:e13.
[8] Jennings A, et al. Mediterranean-style diet improves systolic blood pressure and arterial stiffness in older adults. Hypertension 2019;73(3):578–86.
[9] Franconi F, Campesi I, Romani A. Is extra virgin olive oil an ally for women's and men's cardiovascular health? Cardiovasc Ther 2020;2020:6719301.
[10] Artegoitia VM, et al. Healthy eating index patterns in adults by sex and age predict cardiometabolic risk factors in a cross-sectional study. BMC Nutr 2021;7(1):30.
[11] Lloyd-Jones DM, et al. Framingham risk score and prediction of lifetime risk for coronary heart disease. Am J Cardiol 2004;94(1):20–4.
[12] Bédard A, et al. Impact of the traditional Mediterranean diet on the Framingham risk score and the metabolic syndrome according to sex. Metab Syndr Relat Disord 2014;12(2):95–101.
[13] NICE. CVD risk assessment and management. 2020. Available from: https://cks.nice.org.uk/topics/cvd-risk-assessment-management/.
[14] Ritchie CW, Wells K, Ritchie K. The PREVENT research programme–a novel research programme to identify and manage midlife risk for dementia: the conceptual framework. Int Rev Psychiatr 2013;25(6):748–54.
[15] Hollis JL, et al. Assessing the relative validity of the Scottish Collaborative Group FFQ for measuring dietary intake in adults. Publ Health Nutr 2017;20(3):449–55.
[16] Estruch R, et al. Primary prevention of cardiovascular disease with a Mediterranean diet supplemented with extra-virgin olive oil or nuts. N Engl J Med 2018;378(25):e34.
[17] Shannon OM, et al. Mediterranean diet adherence and cognitive function in older UK adults: the European Prospective Investigation into Cancer and Nutrition-Norfolk (EPIC-Norfolk) Study. Am J Clin Nutr 2019;110(4):938–48.
[18] Tong TY, et al. Prospective association of the Mediterranean diet with cardiovascular disease incidence and mortality and its population impact in a non-Mediterranean population: the EPIC-Norfolk study. BMC Med 2016;14(1):135.
[19] Agarwal P, et al. Unhealthy foods may attenuate the beneficial relation of a Mediterranean diet to cognitive decline. Alzheimers Dement 2021;17(7):1157–65.
[20] Castro V. Package 'CVrisk'. 2022. Available from, https://github.com/vcastro/CVrisk.
[21] Li Y, et al. Package 'QRISK3'. 2022. Available from: https://cran.r-project.org/web/packages/QRISK3/QRISK3.pdf.
[22] Beal SJ, Kupzyk KA. An introduction to propensity scores: what, when, and how. J Early Adolesc 2013;34(1):66–92.
[23] de Chaves EP, Narayanaswami V. Apolipoprotein E and cholesterol in aging and disease in the brain. Future Lipidol 2008;3(5):505–30.
[24] Meslier V, et al. Mediterranean diet intervention in overweight and obese subjects lowers plasma cholesterol and causes changes in the gut microbiome and metabolome independently of energy intake. Gut 2020;69(7):1258.
[25] Massaro M, et al. Effects of olive oil on blood pressure: epidemiological, clinical, and mechanistic evidence. Nutrients 2020;12(6).
[26] Bitok E, Sabaté J. Nuts and cardiovascular disease. Prog Cardiovasc Dis 2018;61(1):33–7.
[27] Liu S, et al. Fruit and vegetable intake and risk of cardiovascular disease: the Women's Health Study. Am J Clin Nutr 2000;72(4):922–8.
[28] Charlton K, et al. Fruit and vegetable intake and body mass index in a large sample of middle-aged Australian men and women. Nutrients 2014;6:2305–19. https://doi.org/10.3390/nu6062305.
[29] Hebert JR, et al. Social desirability bias in dietary self-report may compromise the validity of dietary intake measures. Int J Epidemiol 1995;24(2):389–98.
[30] Ravelli MN, Schoeller DA. Traditional self-reported dietary instruments are prone to inaccuracies and new approaches are needed. Front Nutr 2020;7:90. 90.