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Adherence to Mediterranean diet reduces the risk of metabolic syndrome: A 6-year prospective study

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Abstract *Background and aims:* Benefits of Mediterranean diet on MetS risk have been suggested, but overall prospective evidence in the general population is limited. For the first time, the prospective association of adherence to Mediterranean diet with the 6-y risk of MetS and its components was evaluated in a large cohort in Europe.
Methods and results: Subjects included were participants from the Supplémentation en Vitamines et Minéraux AntioXydants (SU.VI.MAX) study. Adherence to Mediterranean diet was assessed using traditional Mediterranean diet score (MDS), an updated Mediterranean score (MED) and Mediterranean style-dietary pattern score (MSDPS) calculated from at least three 24-h records. In 3232 subjects, the association between Mediterranean diet scores and 6-y risk of MetS was evaluated. The association between Mediterranean scores and MetS components was also estimated. A lower risk of MetS was observed with increasing MED score (*P*-trend = 0.001) and MDS (*P*-trend = 0.03) in multivariate models. The adjusted odds ratios (95% Confidence Interval) for MetS risk were 0.47 (0.32–0.69) and 0.50 (0.32–0.77) in subjects in the highest versus lowest tertile of MED score and MDS, respectively. The MED score was inversely associated with waist circumference, systolic blood pressure and triglycerides, and directly associated with HDL-cholesterol. The MDS was negatively associated with waist circumference and triglycerides, and MSDPS was positively associated with HDL-cholesterol.
Conclusions: All Mediterranean diet scores were associated in a potentially beneficial direction with components of MetS or MetS incidence. Our findings support that individuals should be

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encouraged to follow a Mediterranean dietary pattern for reduction of MetS risk. Trial Registration: clinicaltrials.gov Identifier: NCT00272428.

Introduction

Lifestyle and diet play an important role in the development of type 2 diabetes and cardiovascular diseases (CVD) that are the leading cause of death in western countries [1]. In the present context, particular attention should be paid to the metabolic syndrome (MetS), a common multicomponent condition characterized by abdominal obesity, hyperglycaemia/insulin resistance, hypertriglyceridaemia, low HDL-cholesterol, and elevated blood pressure [2]. Individuals with MetS present an increased risk of type 2 diabetes mellitus, CVD and atherosclerosis [3]. The prevalence of MetS is increasing dramatically worldwide, particularly in industrialized countries, following the increasing prevalence of obesity [4].

Reducing the prevalence of MetS and its components through dietary measures is promising because of its potential to lower the risk of type 2 diabetes and CVD. Few randomized controlled trials (RCT) have focused on the primary or secondary prevention of MetS via dietary means [5–8]. Given the complexity and costs involved with RCTs, prospective studies involving large national samples evaluating the association of a Mediterranean diet with MetS risk could offer important insights for prevention of MetS.

The adherence to a traditional Mediterranean dietary pattern including high consumption of plant foods and olive oil, low intake of saturated fat and sugar, and low/moderate consumption of wine has been associated with a lower risk of CVD and mortality in many epidemiological studies [9,10]. Nevertheless, present knowledge on the potential of Mediterranean diet to reduce the risk of MetS is based primarily on cross-sectional studies [6,11,12] and only two prospective studies in the general population [13,14]. Most of the published studies have examined adherence to the Mediterranean diet based on the Mediterranean Diet Score (MDS) which was initially established for the Greek population [15,16] while other scores have also been developed recently [14,17,18]. Thus, our aim was to assess the prospective association of adherence to a Mediterranean diet pattern with the 6-year risk of MetS in a large sample of French adults using three different Mediterranean diet-based scores and employing the most recent consensual definition of MetS [2]. In addition, as a secondary objective the associations of Mediterranean diet-based scores with individual components of MetS were also evaluated.

Methods

Study population

The SU.VI.MAX study (1994–2002) was initially designed as a randomized, placebo-controlled trial which included a total of 13,017 individuals for a planned follow-up of 8 years to test the potential efficacy of daily supplementation with antioxidant vitamins and minerals at nutritional doses (vitamin C, vitamin E, beta-carotene, selenium, and zinc) on the incidence of cancers, ischemic heart diseases and overall mortality [19]. Subjects provided written informed consent and the study was conducted according to guidelines laid down in the Declaration of Helsinki and was approved by the Ethics Committee for Studies with Human Subjects at the Paris-CochinHospital and the "Commission Nationale de l'Informatique et des Libertés".

Of the 13,017 adults initially included in the SU.VI.MAX cohort, 1281 participants with diabetes at baseline or who developed CVD during follow-up were excluded. Subjects with missing data on dietary variables ($n = 4257$) or covariates ($n = 245$) as well as those who underreported intake ($n = 63$) were excluded as well.

The current analyses were performed among the 3232 subjects free of MetS who had at least 3 dietary records available at baseline, as well as data on all relevant variables necessary to define MetS at 6-y follow-up. For the secondary objective, MetS components could be evaluated among 4888 subjects who had data available at baseline and for the given MetS components at 6-y follow-up. Specific samples were thus identified for each MetS component assuring that information on that MetS trait was available at baseline and at 6-y follow-up, independently of MetS status at baseline.

Data collection

During follow-up, all participants underwent a yearly visit, alternating blood sampling and clinical examination every other year. Information on health, diet and various lifestyle indicators were also collected. Participants were asked to provide a 24 h dietary record every two months. As previously detailed [20], subjects who had >2/3 of their records that reported <800 kcal/d in men and <500 kcal/d in women were excluded to account for underreporting. To facilitate response in coding food portions, participants were provided an instruction manual with detailed options and photographs of portions. Nutrient intakes were calculated using a food composition table [20]. Individual means of food and nutrient intake were calculated from at least three 24 h dietary records during the first two years of follow-up.

We computed three different scores to determine adherence to a Mediterranean dietary pattern. The Mediterranean diet score (MDS) was computed as previously described [16]. Briefly, medians of food group intake were calculated. For positive components (vegetables without potatoes, grains, fruits, fish, nuts, legumes, monounsaturated to saturated fatty acids ratio), 1 point was allocated if consumption was equal or above the gender-specific median value. For negative components (dairy products, meat), 1 point was allocated if consumption was below the gender-specific median value. For alcohol consumption, one point was allocated in case of ethanol consumption between 5 and 25 g/day for women and

10–50 g/day for men. The MDS could have a maximum value of 9 points. We also computed a revised Mediterranean score (MED score) adapted from our previous report [17] and intended to better reflect current dietary habits. The MED score was similar to the MDS in terms of scoring procedure according to the sex-specific median and of food-based components definitions except that the "grain" component was split into a potentially positive component, i.e. whole grain, and a potentially negative component, i.e. refined grains including refined pasta, rice, bread, breakfast cereals and pastries. In addition, a sweetened beverages (including soda and fruit juice with added sugar) component was considered. The fat component was based on olive oil use. The MED score ranged between 0 and 11 points.

The Mediterranean Style-Dietary Pattern Score (MSDPS) has recently been developed in the USA [18]. The MSDPS score estimates the degree of adherence to the recommended intakes of 13 food groups included in the Mediterranean diet pyramid [21] for a maximum score of 100 points, after standardization. Each component was scored from 0 to 10 except olive oil according to the level of adherence. Proportionally lower scores were allocated when a subject did not comply with the recommendation. Exclusive olive oil use yielded 10 points while no use yielded 0 points. Use of olive oil as well as other added fat yielded 5 points.

Finally, as the Mediterranean Pyramid did not account for consumption of certain foods (e.g. refined cereal), the score was weighted by a factor ranging from 0 to 1 reflecting the proportion of energy intake provided by the food included in the Mediterranean diet pyramid. For example, if a subject consumed 60% of energy from foods included on the Mediterranean diet pyramid, the calculated weighting factor was 0.6.

Gender, date of birth, education, smoking status and physical activity information was collected using a self-administrated questionnaire at baseline. Antidiabetic (oral agents or insulin), antihypertensive and lipid-lowering medications were self-reported via a questionnaire at baseline and at the end of follow-up. Anthropometric measurements, systolic blood pressure (SBP) and diastolic blood pressure (DBP) were performed at baseline and 6-y later. Weight was measured to the nearest 0.5 kg using an electronic scale (Seca, Hamburg Germany), with participants wearing indoor clothes and without shoes. Height was measured to the nearest 0.5 cm with a wall-mounted stadiometer. Blood pressure measurements were recorded during a clinical visit by a trained investigator using a standard mercury sphygmomanometer. Measurements were taken after a 10 min rest. Waist circumference was measured as the circumference midway between the lower ribs and iliac crests, with participants in a standing position and wearing underwear. Waist was measured to the nearest 0.5 cm using a tape measure.

Blood samples were collected after a 12-h fast; all biochemical measurements were centralized at a single laboratory. Fasting blood glucose and serum triglycerides (at all visits), baseline serum total cholesterol (Advia 1650, Bayer Diagnostic), baseline serum apolipoprotein B (nephelemetric assay, BNA Behring) and serum HDL-cholesterol at follow-up (Advia 1650, Bayer Diagnostic) were measured. HDL-cholesterol was not measured at baseline and thus, Planella's equation and the Friedewald formula were used to calculate HDL-cholesterol from total cholesterol and apolipoprotein B [22,23].

MetS status was defined using the recent interim consensus statement [2] as having at least three of the following criteria: abdominal obesity (waist circumference $\geq$94 cm for men and $\geq$80 cm for women), high blood pressure (SBP/DBP $\geq$130/85 mm Hg or antihypertensive medication), hypertriglyceridemia ($\geq$1.7 mmol/L or fibrate medication), low HDL-cholesterolemia ($<$1.03 mmol/L for men or $<$1.29 mmol/L for women) and hyperglycemia (glycemia $\geq$5.6 mmol/L or antidiabetic medication).

Statistical analyses

Baseline characteristics of the study sample were compared according to tertiles of MED score. Values are presented as means (SD) or percents for categorial variables. Reported *P*-values referred to the non-parametric Kruskal–Wallis test or trend chi-square test as appropriate. We used logistic regression to study the relationship between Mediterranean scores (tertiles) and MetS incidence among participants free of MetS at baseline (i.e. meeting less than three MetS criteria). The linear trends were estimated through the *P*-value corresponding to the Mediterranean scores treated as an ordinal variable corresponding to tertile.

A first logistic regression model was adjusted for baseline age (years) and gender (male versus female). A second logistic regression model was further adjusted for baseline total daily energy intake from diet (kcal/d), number of 24-h dietary records, baseline smoking status (never, former, current), baseline physical activity (irregular, $<$1 h/day, $\geq$1 h/day), education level (primary school, secondary school, high school or equivalent) and treatment allocation group (placebo or intervention) although we have previously reported that the intervention was not associated with risk of MetS [24]. Finally, a supplementary model was also adjusted for baseline BMI (kg/m^2) and change in BMI (kg/m^2).

Linear regression models were also run to estimate the predictive value of various Mediterranean scores on metabolic components (waist, triglycerides, HDL-cholesterol, fasting glucose, SPB, DBP) among a sub-sample with available data and who were not taking any related medications. All these components were log-transformed to improve normality, thus, geometric means (95% confidence intervals) across tertiles of Mediterranean scores are reported. The linear trend was estimated through the linear contrast test. Interactions between Mediterranean scores and energy intake were tested and were found not significant ($P > 0.05$). Post-hoc analyses were performed using the Tukey method to adjust for multiple comparisons. Statistical tests were 2-sided, with a type I error set at $<$0.05. All analyses were performed using SAS software (Release 9.1, SAS institute Inc., Cary, NC, USA).

Results

Baseline characteristics of the participants are presented across the tertiles of MED score (Table 1). Compared to

Table 1 Baseline characteristics across tertiles of MED score, SU.VI.MAX study.[a]

	Tertile 1	Tertile 2	Tertile 3	P^b
MED score cut-off	0−≤4	>4−<7	≥7−11	
N	938	1351	943	
MED score (max = 11)[c], mean (SD)	3.4a (0.8)	5.5b (0.5)	7.6c (0.9)	*<0.0001*
MSDPS (max = 100)[c], mean (SD)	19.1a (4.9)	21.6b (5.2)	24.7b (5.4)	*<0.0001*
MDS (max = 9)[c], mean (SD)	3.3a (1.2)	4.5b (1.3)	5.8c (1.2)	*<0.0001*
Age, mean (SD)[c], y	48.5a (6.4)	49.7b (6.3)	50.9c (5.8)	*<0.0001*
Male (%)	67	66	62	*0.03*
Intervention group (%)	51	51	52	*0.60*
Education (%)				*<0.0001*
Primary	23	20	16	
Secondary	39	38	37	
High	38	42	47	
Physical activity				*0.07*
Irregular	24	23	21	
<1 h/day	32	31	32	
≥1 h/day	44	46	47	
Smoking status (%)				*0.01*
Non-smoker	53	51	54	
Former smoker	32	37	37	
Smoker	16	12	8	
Energy intake[c,d], mean (SD), kcal/d	2033a (561)	1954b (559)	1929b (501)	*<0.0001*
Number of 24-h dietary records, mean (SD)	9.6a (3.4)	9.9a (3.2)	10.4b (2.9)	*<0.0001*
% Protein[c], mean (SD)	17.3a (2.6)	17.7b (2.8)	17.8b (2.6)	*<0.0001*
% Carbohydrate[c], mean (SD)	42.8a (5.7)	42.2b (6.2)	41.9b (5.9)	*0.002*
% Fat[c], mean (SD)	39.9a (4.8)	40.1a (5.3)	40.3a (5.2)	*0.35*
Alcohol[c], mean (SD), g/d	16.0a (20.1)	15.7a (17.5)	15.9a (15.4)	*0.0001*
Saturated fatty acids[c], mean (SD), g/d	39.1a (12.4)	36.2b (12.1)	33.9c (10.7)	*<0.0001*
Monounsaturated fatty acids[c], mean (SD), g/d	33.1a (10.3)	32.6a (10.4)	33.1a (9.8)	*0.34*
Polyunsaturated fatty acids[c], mean (SD), g/d	12.3a (4.4)	13.0b (4.7)	13.9c (4.6)	*<0.0001*
Beta-carotene[c], mean (SD), mg/d	3393a (2081)	4046b (2700)	4772c (2657)	*<0.0001*
Vitamin C[c], mean (SD), mg/d	85.9a (40.0)	95.1b (44.3)	105.9c (46.7)	*<0.0001*
Cholesterol[c], mean (SD), mg/d	403.9a (139.7)	389.9b (135.1)	364.0c (123.0)	*<0.0001*
Vitamin E[c], mean (SD), mg/d	11.1a (4.1)	12.3b (4.6)	13.8c (4.8)	*<0.0001*
Sodium[c], mean (SD), mg/d	3425a (1205)	3381a (1209)	3358a (1095)	*0.55*
Fiber[c], mean (SD), g/d	17.2a (5.7)	18.9b (6.4)	21.8c (7.3)	*<0.0001*

[a] Values are means ± SD or % as appropriate, $n = 3238$.
[b] *P*-values are based on non-parametric Kruskal−Wallis test or trend chi-squared test.
[c] Means annotated with the same letter are not different ($P < 0.05$).
[d] Excluding energy from alcohol.

those with lower MED score (1st tertile), participants with higher MED score (3rd tertile) were less often men, older, better educated, more active, non-smokers and had lower total energy intake. A higher MED score was associated with higher energy intake from protein and lower energy from carbohydrates. In addition, the MED score was negatively associated with intake of saturated fatty acids (SFA) and cholesterol but positively correlated with intake of poly-unsaturated fatty acids (PUFA), beta-carotene, vitamin C, vitamin E and fiber.

Among the 3232 subjects free of MetS at baseline, 214 developed MetS during the 6-y follow-up. After adjustment for age and gender, a significantly lower risk of MetS was observed with increasing MED score (*P*-trend < 0.0001), MDS (*P*-trend = 0.0001) and MSDPS (*P*-trend = 0.05) (Table 2). In the fully-adjusted model, subjects in the highest tertile of adherence to a Mediterranean diet, compared with those in the lowest tertile, showed markedly reduced ORs for MetS with MED score (OR = 0.47, 95% CI = 0.32−0.69, *P*-trend < 0.0001) and MDS (OR = 0.50, 95% CI = 0.32−0.77, *P*-trend = 0.002). Association with MSDPS was borderline significant (OR = 0.74, 95% CI = 0.52−1.06, *P*-trend = 0.10).

In an additional model accounting for baseline and 6-y change in BMI (Fig. 1), a lower risk of MetS was observed across tertiles of MED score (*P*-trend = 0.001), MDS (*P*-trend = 0.03) and MSDPS (*P*-trend = 0.06).

After adjustment for covariates and baseline value corresponding to MetS component considered, a higher MED score was associated with lower waist, SBP and triglycerides as well as higher HDL-cholesterol at the end of 6-y follow-up (Table 3). Higher MDS was significantly associated with lower waist and triglycerides after 6-y. MSDPS was positively associated with HDL-cholesterol after 6-y only.

Table 2 Mediterranean diet scores (in tertiles) related to 6-year incidence of MetS. SU.VI.MAX study.[a]

	T1	T2	T3	P[b]
MED score	0–4	5–6	≥7–11	
N cases	86	81	47	
Model 1[c]	1 (ref)	0.59 (0.43–0.81)	0.46 (0.32–0.66)	*<0.0001*
Model 2[d]	1 (ref)	0.59 (0.43–0.82)	0.47 (0.32–0.69)	*<0.0001*
MDS	0–3	4–5	≥6–9	
N cases	71	108	35	
Model 1[c]	1 (ref)	0.82 (0.60–1.12)	0.44 (0.29–0.67)	*0.0001*
Model 2[d]	1 (ref)	0.88 (0.64–1.21)	0.50 (0.32–0.77)	*0.002*
MSDPS	0–≤19.20	>19.2–≤24	>24–100	
N cases	80	73	61	
Model 1[c]	1 (ref)	0.91 (0.65–1.26)	0.70 (0.50–1.00)	*0.05*
Model 2[d]	1 (ref)	0.95 (0.68–1.33)	0.74 (0.52–1.06)	*0.10*

[a] Values are odds ratio (95% confidence interval) estimated through multivariate logistic regression.
[b] P is based on the model with Mediterranean diet score as an ordinal variable corresponding to tertile.
[c] Model 1 is adjusted for age and gender.
[d] Model 2: Model 1 + supplementation group, energy intake, education level, tobacco smoking status and physical activity.

Further adjustment for baseline BMI and change in BMI during follow-up did not drastically modify the findings (data not shown) except that the association between MDS and triglycerides was no longer significant.

Discussion

In this large prospective study carried out among French adults, we investigated the association of Mediterranean diet pattern with MetS incidence and MetS components over a fairly long period of follow-up i.e. 6 years. Better adherence to Mediterranean diet was associated with a significantly lower 6-y incidence of MetS for the traditional MDS and the MED score. Pertaining to MetS components, the MED score was predictive of most of the components, i.e. waist, triglycerides, HDL-cholesterol and SBP, while MDS and MSDPS were associated with fewer MetS components, i.e. waist and triglycerides, and HDL-cholesterol, respectively. In this study population, adherence to the Mediterranean diet was low even considering scores utilizing median values as cutoffs, i.e. MED score and MDS, illustrating that complying with a cluster of Mediterranean diet components may be challenging.

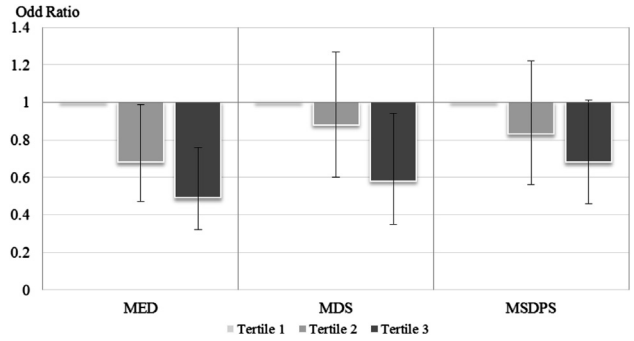

Figure 1 Mediterranean diet scores (in tertiles) related to 6-year incidence of MetS. SU.VI.MAX study Abbreviations: Mediterranean score (MED); Mediterranean diet score (MDS); Mediterranean style-dietary pattern score (MSDPS). Odds ratio are adjusted for age, gender, supplementation group, energy intake, education level, tobacco smoking status, physical activity, baseline and 6-y change in BMI.

The major strengths of the present study include its large middle-aged population and prospective design, enabling estimation of the predictive value of Mediterranean diet, using three different *a priori* indexes, for the risk of MetS and its components. In addition, the more recent and consensual MetS definition was used [2].

Some limitations of the study should be considered. Caution is needed when generalizing the present findings because of voluntary inclusion of participants providing dietary data and information required for MetS status identification during the 6-y follow-up. Indeed, such participants may have been particularly compliant and/or health-conscious, leading to homogeneity in the studied population. In addition, *a priori* indices display some inherent limitations, including arbitrary selection of components (nutrient, food groups and their constituents), the definition of cut-off values and scoring method [25]. The strength of such indices has been demonstrated with significant associations with various outcomes, in various types of subjects and countries [9]. Finally, as diet was assessed during the first two years of follow-up, we cannot rule out the possibility of change in adherence to the Mediterranean diet over time.

In the present study, the strength of the association between MetS and Mediterranean dietary pattern was dependent on the score used to evaluate adherence to a Mediterranean diet. The association between MED score and MetS risk was stronger than that observed with the traditional MDS suggesting a critical role of refined grains and sweetened beverages in driving this association. The widely used MDS [15,16] showed a negative association with MetS incidence; however, only waist circumference and blood triglycerides were negatively associated with the MDS. The only previous prospective study using the MDS involved young university graduates followed for 6 years; it showed a significantly reduced risk of MetS by following a Mediterranean dietary pattern as well as a significant negative association of MDS with waist circumference [13].

Table 3 Association between MetS components at the end of follow-up and tertiles of different Mediterranean scores[a,b].

	T1	T2	T3	P^c
MED score				
Fasting glucose (mmol/L)[d,e]	5.04a (5.01—5.07)	5.03a (5.00—5.05)	5.02a (4.99—5.05)	*0.25*
Waist circumference (cm)[d,f]	84.28a (83.68—84.89)	83.79ab (83.26—84.32)	83.23b (82.61—83.85)	*0.03*
Diastolic blood pressure (mm Hg)[d,g]	81.00a (80.41—81.60)	81.04a (80.51—81.57)	80.33a (79.72—80.94)	*0.10*
Systolic blood pressure (mm Hg)[d,h]	128.95a (128.07—129.83)	128.50a (127.72—129.28)	127.06b (126.16—127.96)	*0.001*
Triglycerides (mmol/L)[d,i]	1.01a (0.99—1.04)	1.00a (0.98—1.02)	0.95b (0.92—0.97)	*0.0001*
HDL-cholesterol (mmol/L)[d,j]	1.50a (1.48—1.52)	1.51ab (1.49—1.53)	1.53b (1.51—1.56)	*0.02*
MDS				
Fasting glucose (mmol/L)[d,e]	5.05a (5.02—5.08)	5.03a (5.00—5.05)	5.02a (4.99—5.05)	*0.37*
Waist circumference (cm)[d,f]	84.21a (83.58—84.85)	84.05a (83.55—84.55)	82.80b (82.16—83.45)	*0.0002*
Diastolic blood pressure (mm Hg)[d,g]	81.09a (80.47—81.72)	80.74a (80.25—81.24)	80.70a (80.06—81.35)	*0.33*
Systolic blood pressure (mm Hg)[d,h]	128.76a (127.84—129.69)	128.23a (127.49—128.97)	127.67a (126.72—128.63)	*0.09*
Triglycerides (mmol/L)[d,i]	1.00a (0.97—1.03)	1.00a (0.98—1.02)	0.95b (0.93—0.98)	*0.001*
HDL-cholesterol (mmol/L)[d,j]	1.50a (1.48—1.52)	1.51a (1.49—1.53)	1.52a (1.50—1.54)	*0.20*
MSDPS				
Fasting glucose (mmol/L)[d,e]	5.03a (5.00—5.06)	5.02a (5.00—5.05)	5.04a (5.01—5.07)	*0.54*
Waist circumference (cm)[d,f]	83.58a (83.01—84.16)	84.02a (83.44—84.61)	83.79a (83.21—84.38)	*0.59*
Diastolic blood pressure (mm Hg)[d,g]	81.12a (80.55—81.69)	80.80a (80.23—81.38)	80.56a (79.98—81.14)	*0.15*
Systolic blood pressure (mm Hg)[d,h]	128.67a (127.83—129.52)	128.39a (127.54—129.24)	127.66a (126.80—128.52)	*0.08*
Triglycerides (mmol/L)[d,i]	1.00a (0.98—1.03)	0.99a (0.97—1.02)	0.98a (0.95—1.00)	*0.11*
HDL-cholesterol (mmol/L)[d,j]	1.50a (1.48—1.52)	1.50a (1.48—1.52)	1.53b (1.51—1.56)	*0.01*

[a] Values are adjusted geometric means (95% confidence interval).
[b] Values are adjusted for age and gender, supplementation group, energy intake, education level, tobacco smoking status, physical activity and baseline value.
[c] P is based on the model with Mediterranean diet score as an ordinal variable corresponding to tertile.
[d] Means annotated with the same letter are not different ($P < 0.05$), Tukey post-hoc test.
[e] $N = 3880$.
[f] $N = 3924$.
[g] $N = 3276$.
[h] $N = 3276$.
[i] $N = 3880$.
[j] $N = 3999$.

A significantly lower OR for MetS was also observed in participants with a higher Mediterranean diet score in a cross-sectional study of subjects at high risk of CVD [11].

Another recent small-scale cross-sectional study showed that high adherence to Mediterranean diet was associated with a reduction in MetS odds ratio [12] but other authors did not find such an association [6]. Finally, we found a marginal association between MSDPS and MetS incidence. This is in line with the previous finding observed in the prospective Framingham offspring study [14]. However, compared to the findings of these authors, we did not find associations between the MSDPS and key MetS components, except for HDL-cholesterol, suggesting that the MSDPS score may not be directly transportable to other populations outside the US (e.g. the French population).

It is widely recognized that the Mediterranean diet may play a salient role in weight control [17,26—28]. To address how change in adiposity over time may mediate the relationship between Mediterranean diet and MetS, in regression models we further adjusted for baseline BMI and change in BMI during the follow-up. Our findings suggest that the association between Mediterranean diet and the risk of MetS was only partly driven by the impact on weight.

Mediterranean diet can play an important protective role against development of MetS through several pathways beyond obesity and abdominal adiposity. Indeed, RCT in subjects with MetS [7,29] or traits of MetS [8,30] have shown a beneficial effect of a Mediterranean-type diet on various parameters (blood triglycerides, LDL-cholesterol, insulin resistance, hypertension and inflammation status).

In conclusion, this large prospective study provides important evidence that a better adherence to traditional Mediterranean diet, may noticeably help in reducing MetS incidence, an effect mediated by its beneficial association with several MetS components namely waist circumference, hypertension, triglycerides and HDL-cholesterol. Our findings support the general concept that a Mediterranean dietary pattern, especially by limiting refined grains and sweetened beverages, could be useful for prevention of CVD and type 2 diabetes. These promising findings with both the traditional MDS and the updated MED score and reduced MetS risk merit to be confirmed in other populations including those from other non-Mediterranean countries.

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