



# Comparison of the Mediterranean diet and the Dietary Approach Stop Hypertension in reducing the risk of 10-year fatal and non-fatal CVD events in healthy adults: the ATTICA Study (2002–2012)

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## Abstract

**Objective:** To compare the Mediterranean and Dietary Approaches to Stop Hypertension (DASH) diets in deterring 10-year CVD.

**Design:** Prospective cohort ( $n$  2020) with a 10-year follow-up period for the occurrence of combined (fatal or non-fatal) CVD incidence (International Classification of Diseases (ICD)-10). Baseline adherence to the Mediterranean and DASH diets was assessed via a semi-quantitative FFQ according to the MedDietScore and DASH scores, respectively.

**Setting:** Attica, Greece.

**Participants:** Two thousand twenty individuals (mean age at baseline 45.2 (SD 14.0) years).

**Results:** One-third of individuals in the lowest quartile of Mediterranean diet consumption, as compared with 3.1 % of those in the highest quartile, developed 10-year CVD ( $P < 0.0001$ ). In contrast, individuals in the lowest and highest DASH diet quartiles exhibited similar 10-year CVD rates ( $n$  (%) of 10-year CVD in DASH diet quartiles 1 *v.* 4: 79 (14.7 %) *v.* 75 (15.3 %);  $P = 0.842$ ). Following adjustment for demographic, lifestyle and clinical confounding factors, those in the highest Mediterranean diet quartile had a 4-fold reduced 10-year CVD risk (adjusted hazard ratio (HR) 4.52, 95 % CI 1.76, 11.63). However, individuals with highest DASH diet quartile scores did not differ from their lowest quartile counterparts in developing such events (adjusted HR 1.05, 95 % CI 0.69, 1.60).

**Conclusions** High adherence to the Mediterranean diet, and not to the DASH diet, was associated with a lower risk of 10-year fatal and non-fatal CVD. Therefore, public health interventions aimed at enhancing adherence to the Mediterranean diet, rather than the DASH diet, may most effectively deter long-term CVD outcomes particularly in Mediterranean populations.

**Keywords**  
Mediterranean diet  
Dietary Approaches to Stop  
Hypertension diet  
CVD

CVD constitute one of the prevailing causes of morbidity and mortality in developed countries<sup>(1,2)</sup>. Several non-modifiable and modifiable demographic, lifestyle and clinical factors (including obesity (especially abdominal obesity), dyslipidaemia, the metabolic syndrome and/or type 2 diabetes mellitus)<sup>(3,4)</sup> alike are implicated in the onset, further progression and, ultimately, attributable mortality of CVD<sup>(5)</sup>. Although not constituting the initial triggers in all cases, both the aforementioned non-modifiable

and modifiable factors are hypothesised to be implicated via a complex interplay in disease onset and propagation through the positive feedback mechanisms of the dysregulated renin–angiotensin–aldosterone system, leading to the activation of an inflammatory cascade and lipid dysregulation<sup>(6)</sup>. Of ever-mounting public health interest, though, are modifiable lifestyle factors, such as dietary patterns, which may be altered via related interventions so as to deter CVD onset and adverse outcomes, including

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attributable morbidity and mortality rates<sup>(1,2,7)</sup>. To this effect, the Mediterranean and/or the Dietary Approaches to Stop Hypertension (DASH) dietary patterns are most often recommended for CVD prevention and deterrence of its associated health outcomes. However, limited evidence<sup>(8)</sup> and lack of international consensus often lead to conflicting public health nutrition recommendations regarding the most appropriate dietary pattern for CVD prevention, particularly in settings where the Mediterranean diet is either readily available or adopted due to target populations' socio-cultural characteristics.

Both the Mediterranean and DASH diets are rich in fruits and vegetables, cereals, pulses and nuts, entailing dietary intakes characterised by a low glycaemic load and rich antioxidant content<sup>(9,10)</sup>. The Mediterranean diet has a higher fat content as compared with the DASH diet which has a low fat content, ideally around 27%. On the one hand, the Mediterranean diet<sup>(11)</sup> is associated with numerous health benefits, including CVD prevention<sup>(12)</sup> and diminished all-cause mortality<sup>(10,13)</sup>, particularly in Mediterranean populations where it is readily adopted for socio-cultural purposes. To this effect, it appears that particular constituents of the Mediterranean diet, such as olive oil which is rich in oleic acid and polyphenols, along with physical activity<sup>(14,15)</sup>, moderate energetic intake<sup>(16)</sup> and optimal body weight<sup>(17)</sup>, deter biological pathways implicated in CVD onset and progression, such as vascular degeneration<sup>(18,19)</sup>. The antioxidant, anti-inflammatory and antithrombotic properties of the Mediterranean diet are primarily attributed to its richness in foods of plant origin, olive oil and wine. On the other hand, the DASH diet, which was originally conceived for non-Mediterranean Western populations, is primarily composed of lean meats, low-fat dairy products and whole grains, as well as plentiful fruits and vegetables<sup>(20,21)</sup>, moderate energetic intake<sup>(16)</sup> and optimal body weight<sup>(17)</sup>, deters biological pathways implicated in CVD onset and progression, such as vascular degeneration<sup>(18,19)</sup>. As of such, it entails a dietary intake low in saturated fats and cholesterol, albeit rich in fibre and micronutrients, such as Ca, Mg and K, which are essential for preserving normal blood pressure levels and, consequently, CVD prevention. Similarly to the Mediterranean diet, recent meta-analytic findings reveal that high adherence to the DASH diet, combined with reduced Na intake, is associated with diminished CVD incidence and attributable mortality rates<sup>(7)</sup>. However, the above findings are limited to Western populations where the Mediterranean diet does not prevail. To date, a comparison of the efficacies of the above dietary patterns in preventing CVD events has not been conducted, particularly in populations where either of the above diets may be readily adopted and/or proposed for public<sup>(19)</sup>. It is anticipated that such findings would provide essential insights for developing optimal public health interventions for preventing CVD<sup>(22)</sup>.

Therefore, the aim of the current study was to compare the efficacy of the Mediterranean and DASH diets in deterring 10-year fatal and non-fatal CVD events in a Mediterranean adult population.

## Materials and methods

### Setting

A population-based cohort study, with 10-year follow-up period. The study was implemented in Athens metropolitan area, the capital province of Greece, in the Attica region, which includes 78 % urban municipalities.

### Design

The ATTICA Study design and population recruitment procedures have been previously detailed<sup>(23)</sup>. A random multi-stage sampling was implemented based on the age and gender distribution of the population, in accordance with the 2001 National Census Survey. One participant per household was enrolled, while institutionalised individuals were excluded from participation. Of the initially invited 4056 individuals, 3042 agreed to participate (75 % participation rate); 1514 of the participants were male (aged  $46 \pm 13$  years; range 18–87 years) and 1528 were female (aged  $45 \pm 13$  years; range 18–89 years). The study sample did not differ from the general population with respect to the distribution of age and gender. All participants were interviewed by trained personnel (including cardiologists, nutritionists and nurse practitioners) who used standard questionnaires.

### Baseline socio-demographic and lifestyle measurements

The information about participants' characteristics was based on face-to-face interviews; collected information included demographic characteristics (e.g. age, gender and highest attained educational level), dietary and lifestyle habits (including smoking status and habitual/leisure time physical activity), as well as medical examination. In particular, based on the years of education completed and income, participants were categorised into the following educational categories: (i) low (i.e. <12 years education), (ii) moderate (i.e. including 13–16 years education) and (iii) high (i.e. >16 years education).

Dietary habits were assessed based on a validated semi-quantitative FFQ, the European Prospective Investigation into Cancer (EPIC) FFQ that was kindly provided by the Unit of Nutrition Epidemiology of Athens University Medical School<sup>(24)</sup>, according to which participants reported average weekly or daily intakes of 156 food items and drinks during the past year, as well as a Mediterranean diet questionnaire<sup>(25)</sup>. Subsequently, the approximate monthly and/or weekly frequency of food item consumption was calculated. Composite scores were employed to describe the overall dietary patterns

and to evaluate the level of adherence to the Mediterranean dietary pattern or the DASH pattern. Specifically, of the Mediterranean foods recorded, a diet score (i.e. MedDietScore<sup>®</sup>) was calculated (range 0–55) to depict adherence to dietary patterns most proximal to those of the Mediterranean diet<sup>(11,25)</sup>. Based on the derived MedDietScore, the following quartiles were constructed: (i) first quartile: MedDietScore <25), (ii) second quartile: 25.0–26.9, (iii) third quartile: 27.0–27.9 and (iv) fourth quartile: 28.0–55.0. The median MedDietScore was 26.5 (SEM 0.1). Subsequently, low adherence to the Mediterranean diet was deemed as MedDietScore  $\leq$ 27.0, while scores greater were considered as high adherence to the Mediterranean diet. Moreover, of the food and drinks recorded in the questionnaire, those most proximately associated with the DASH dietary pattern were grouped and adjusted to the scoring used in the Nurses' Health Study cohort<sup>(26)</sup>. A DASH-style score was then developed for the participants ( $n$  699 with available nutrition information through the FFQ and the rest through the Mediterranean diet questionnaire) assessing the consumption of nine food groups, including fruits, vegetables, nuts, legumes, low-fat dairies, all cereals, red and processed meats, sugary drinks and sweets<sup>(27)</sup>. The consumption of each food group was classified into quintiles, allocating a value from 1 to 5, so that a higher value reflected the consumption proposed by the DASH dietary pattern<sup>(26)</sup>. Therefore, the total DASH diet scores ranged from 9 to 45, with higher scores reflecting greater adherence to the DASH-style dietary pattern. Subsequently, based on the DASH diet scores in the current analysis, the following quartiles of consumption were constructed: (i) first quartile: DASH diet score <24, (ii) second quartile: 24.0–26.9, (iii) third quartile: 27.0–30.9 and (iv) fourth quartile: 31.0–45.0. The median DASH score was 27.0 (SEM 0.1). Low adherence to the DASH diet was deemed as scores  $\leq$ 27.0, while those higher were indicative of high adherence.

As regards smoking habits, at baseline, 'current smokers' included those who smoked at least one cigarette per day, 'never smokers' included those who have never smoked and 'former smokers' included those who had ceased smoking  $\geq$ 1 year prior to evaluation. For the assessment of physical activity status, the International Physical Activity Questionnaire<sup>(28)</sup> was used as an index of weekly energy expenditure. Physical activity was defined as >1 d/week leisure-time activity, of specific intensity and duration, during the past year. Alternatively, subjects were identified as physically inactive.

#### **Baseline anthropometric and clinical measurements' assessment**

Weight (in kg) and standing height (in m<sup>2</sup>) were used to calculate BMI; those with BMI >29.9 kg/m<sup>2</sup> were defined as obese. Waist and hip circumferences (in cm) were used to calculate waist-to-hip ratio, based on standard procedures.

At the end of the physical examination, following >30 min at rest and while in a sitting position, subjects' arterial blood pressure was measured blindly three times by a trained cardiologist on participants' right arm which was relaxed and well supported by a table, at 45° from the trunk (ELKA aneroid manometric sphygmomanometer; Von Schlieben Co.). Systolic and diastolic blood pressure levels were determined by the first perception of sound (of tapping quality) and phase V (fully muffed repetitive sounds), respectively. Individuals with systolic blood pressure  $\geq$  140 mmHg or diastolic blood pressure > 90 mmHg, or under antihypertensive medication, were classified as hypertensive. Furthermore, following 12 h of fasting, morning blood samples were collected from participants' antecubital vein and blood lipid examinations (including serum total cholesterol) were measured using the chromatographic enzymic method in a RA-1000 Technicon automatic analyzer (Dade Behring). Hypercholesterolaemia was defined as >220 mg/dl (or 5.70 mmol/l) total cholesterol levels or the use of hypolipidaemic medication. Blood glucose levels (in mg/dl) were measured with a Beckman Glucose Analyzer (Beckman Instruments). Fasting blood sugar levels >125 mg/dl, or the use of antidiabetic medication, were indicative of diabetes mellitus. The metabolic syndrome was defined by the National Cholesterol Education Program Adult Treatment Panel III (revised) definition<sup>(29)</sup>.

#### **Follow-up assessment, 2002–2012**

Follow-up assessments were conducted 10 years following initial recruitment, that is, 2012–2013. Of the initially enrolled 3042 participants at baseline, 10-year follow-up was achieved in 2583 participants (85 % participation rate; of those lost to follow-up, 224 could not be traced due to missing or erroneous contact information and 235 denied to participate). A complete CVD assessment was achieved in 2020 participants. The follow-up examination included the retrieval of detailed information from participants' medical records. When lacking accurate records, participants were evaluated by face-to-face interview by trained study investigators. The re-examination included (i) vital status (death from any cause or due to CVD) or (ii) development of CHD (including myocardial infarction, angina pectoris, other identified forms of ischemia – WHO-ICD coding 410–414.9, 427.2, 427.6 – heart failure of different types and chronic arrhythmias – WHO-ICD coding 400.0–404.9, 427.0–427.5, 427.9) or development of stroke (WHO-ICD coding 430–438).

Some differences in the baseline characteristics were observed between those who participated to follow-up and those who did not participate regarding the distribution of age ( $46 \pm 14$  *v.*  $41 \pm 11$  years,  $P < 0.001$ ), history of hypertension (31 *v.* 24 %,  $P = 0.001$ ), diabetes (8 *v.* 3 %,  $P < 0.001$ ), hypercholesterolaemia (41 *v.* 33 %,  $P = 0.004$ )



and smoking status (55 *v.* 61%,  $P < 0.001$ ), whereas no differences were reported regarding the distribution of gender ( $P = 0.613$ ), obesity status ( $P = 0.208$ ) and eating habits ( $P = 0.560$ ).

### Statistical analysis

Categorical variables are presented as absolute and relative frequencies ( $n$ , %). Continuous variables are presented as mean (M)  $\pm$  standard deviation; the normality of their distributions was assessed with P–P plots. The baseline characteristics between CVD-free and CVD event groups were compared overall and stratified according to gender. The frequencies of categorical variables were compared with Pearson's  $\chi^2$  test. The Student's  $t$  test and Mann–Whitney  $U$  test were used to compare normally and non-normally distributed continuous variables between groups, respectively. Ordinal variables were compared between groups with the likelihood-ratio test. The probability of time to CVD fatal or non-fatal events was depicted with Kaplan–Meier curves. CVD survival rates, according to baseline quartiles of dietary consumption for the MedDietScore and DASH diet scores, were compared between groups with the Log-rank test. Cox proportional hazard models were used to explore the effects of baseline quartiles of MedDietScore and DASH diet scores on 10-year fatal and non-fatal CVD events. Unadjusted and adjusted hazard ratios (HR) and the corresponding 95% CI were calculated separately for MedDietScore and DASH diet quartile scores (independent factors) in relation to 10-year incidence of CVD (outcome)<sup>(30)</sup>. Multivariable models included adjustment for potential confounding factors, that is, age, gender, physical activity status, weight category, smoking, history of hypertension, hypercholesterolaemia, diabetes and the metabolic syndrome. The proportionality assumption for the Cox models was assessed graphically. The level of significance was set to  $P < 0.05$ . STATA 15 software was used for all analyses (M Psarros and Associates/StataCorp LLC).

## Results

### Baseline Mediterranean diet and DASH diet scores in relation to 10-year incidence of fatal and non-fatal CVD

Among the study sample ( $n$  2020, 49.8% ( $n$  1006) males) with an overall mean age at a baseline of 45.2 (SD 14.0) years (Table 1), the 10-year combined (fatal or non-fatal) CVD incidence rate was 15.7% ( $n$  317 cases).

As shown in Table 2, as compared with their CVD-event free counterparts, at baseline, individuals who subsequently developed 10-year CVD events were of older mean age, more often male, of lower educational status, and with lower mean MedDietScore. However, it is of note that they did not differ with respect to mean baseline DASH diet

scores. In addition, they more often presented at baseline with several well-established CVD risk factors, including abnormal waist-to-hip ratio, hypertension and hypercholesterolaemia, as well as diabetes and the metabolic syndrome.

Comparisons of the proportion of study participants who developed 10-year CVD events according to their adherence to the Mediterranean and DASH diets at baseline are illustrated in Fig. 1. As shown in Table 3, among individuals in the lowest quartile of Mediterranean diet score, one-third ( $n$  168) developed 10-year fatal or non-fatal CVD events. In contrast, among those adhering to the highest quartile of Mediterranean diet consumption (namely MedDietScore ranging between 28.0 and 55.0), only 3.1% ( $n$  15) subsequently developed 10-year CVD events. As of such, it is inferred that individuals with highest adherence to the Mediterranean diet had a 15-fold lower risk than their lowest adherence counterparts to manifest 10-year CVD events (Table 4; unadjusted HR 15.75, 95% CI 9.12, 27.20). Similar trends were observed in both genders, albeit documented most prominently among women ( $n$  of 10-year CVD events in MedDietScore quartiles 1 *v.* 4: 53 (36%) *v.* 11 (2.5%);  $P < 0.0001$ ) rather than men ( $n$  of 10-year CVD events in MedDietScore quartiles 1 *v.* 4: 115 (32.2%) *v.* 4 (9.3%);  $P < 0.0001$ ). On the other hand, when assessed according to the DASH diet, individuals in the lowest and highest quartiles of consumption exhibited similar rates of manifesting 10-year CVD ( $n$  of 10-year CVD events in DASH diet quartiles 1 *v.* 4: 79 (14.7%) *v.* 75 (15.3%);  $P = 0.842$ ). Furthermore, the occurrence of 10-year CVD did not significantly differ among those with lowest, as opposed to highest, quartile DASH scores in either men ( $n$  of 10-year CVD events in DASH diet quartiles 1 *v.* 4: 54 (20.0%) *v.* 51 (22.2%);  $P = 0.599$ ) or women ( $n$  of 10-year CVD events in DASH Diet quartiles 1 *v.* 4: 25 (9.4%) *v.* 24 (9.3%);  $P = 0.086$ ).

### Time to fatal and non-fatal CVD events according to baseline Mediterranean diet and Dietary Approaches to Stop Hypertension diet scores

Figure 2 presents the Kaplan–Meier curve for differences in the probability and time to developing combined (fatal or non-fatal) CVD events, according to baseline quartile consumption levels of the MedDietScore and DASH diet scores. As illustrated, individuals within the highest quartile of the MedDietScore were significantly less likely than their lowest quartile counterparts to subsequently develop CVD events (Log-rank test  $P < 0.001$ ). In contrast, when assessed according to baseline DASH diet scores, no significant associations were detected between the corresponding lowest and highest quartiles of consumption in relation to 10-year CVD (Log-rank test  $P = 0.788$ ).

**Table 1** Baseline characteristics of ATTICA study participants (*n* 2020), according to the level of adherence to the Mediterranean and Dietary Approaches to Stop Hypertension (DASH) diets\*

	Overall		Low adherence to the Mediterranean diet ( $\leq 27.0$ )		High adherence to the Mediterranean diet ( $> 27.0$ )		<i>P</i>	Low adherence to the DASH diet ( $\leq 27.0$ )		High adherence to the DASH diet ( $> 27.0$ )		<i>P</i>
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%		<i>n</i>	%	<i>n</i>	%	
Age (years)							<0.0001 <sup>a</sup>					<0.008 <sup>a</sup>
Mean		45.2		51.0		36.2			44.3		46.0	
SD		14.0		12.6		10.7			14.6		13.2	
Gender (men)	1006	49.8	854	69.8	152	19.1	<0.0001 <sup>b</sup>	500	51.8	506	48.0	<0.084 <sup>b</sup>
Educational status							<0.0001 <sup>c</sup>					0.793 <sup>c</sup>
Low	1237	62.4	807	67.0	430	55.4		595	62.7	642	62.2	
Moderate	714	36.0	383	31.8	331	42.7		338	35.6	376	36.4	
High	30	1.5	15	1.2	15	1.9		16	1.7	14	1.4	
Average daily energetic intake (kJ)							0.379 <sup>d</sup>					0.985 <sup>d</sup>
Mean		9949		10 058		9799			9949		9954	
SD		3975		3975		3983			4125		3845	
Physically active	825	40.8	493	40.3	332	41.7	0.548 <sup>b</sup>	375	38.9	450	42.7	0.954 <sup>b</sup>
BMI (kg/m <sup>2</sup> )							<0.0001 <sup>a</sup>					<0.051 <sup>a</sup>
Mean		26.3		28.4		23.0			26.1		26.5	
SD		4.5		4.1		2.7			4.4		4.6	
Weight category							<0.0001 <sup>c</sup>					0.116 <sup>c</sup>
Normal/underweight	842	41.7	231	18.9	611	77.0		423	44.0	419	39.7	
Overweight	811	40.2	637	52.1	174	21.9		378	39.3	433	41.9	
Obese	364	18.0	355	29.0	9	1.1		161	16.7	203	19.2	
Abnormal waist-to-hip ratio	777	40.5	867	70.9	217	27.3	<0.0001 <sup>b</sup>	505	52.5	579	54.9	0.283 <sup>b</sup>
Current smokers	857	42.6	528	43.3	329	41.4	0.414 <sup>b</sup>	409	42.5	448	42.6	0.975 <sup>b</sup>
Systolic blood pressure (mmHg)							<0.0001 <sup>d</sup>					0.913 <sup>d</sup>
Mean		123.0		129.5		113.0			123.0		123.0	
SD		18.4		17.7		14.4			18.2		18.5	
Diastolic blood pressure (mmHg)							0.038 <sup>d</sup>					0.166 <sup>d</sup>
Mean		79.0		82.7		73.3			78.6		79.4	
SD		11.6		11.0		10.1			11.2		11.9	
Blood glucose (mg/dl)							<0.0001 <sup>d</sup>					0.857 <sup>d</sup>
Mean		93.3		97.2		87.2			93.2		93.4	
SD		24.1		27.2		16.8			24.2		24.1	
Hypercholesterolaemia	860	42.6	649	53.1	211	26.6	<0.0001 <sup>b</sup>	391	40.6	469	44.5	0.084 <sup>b</sup>
Hypertension	598	31.5	516	44.6	82	11.1	<0.0001 <sup>b</sup>	273	29.9	325	33.0	0.147 <sup>b</sup>
Diabetes	145	7.2	134	11.0	11	1.4	<0.0001 <sup>b</sup>	71	7.4	74	7.0	0.765 <sup>b</sup>
Metabolic syndrome	399	19.8	365	29.8	34	4.3	<0.0001 <sup>b</sup>	178	18.4	221	20.9	0.158 <sup>b</sup>

\*Continuous variables are presented as mean  $\pm$  SD and categorical variables as absolute and relative frequencies (*n* and %).

*P*-values referring to differences between CVD events and CVD-free events during the 10-year follow-up, derived using the following: <sup>a</sup>Student's *t* test for normally distributed continuous variables, <sup>b</sup> $\chi^2$  test for categorical variables, <sup>c</sup>Likelihood-ratio test for ordinal categorical variables and <sup>d</sup>Mann-Whitney test for non-normally distributed continuous variables.

**Table 2** Baseline characteristics among ATTICA study participants (*n* 2020) in relation to the 10-year fatal or non-fatal incidence of CVD\*

	CVD-free events ( <i>n</i> 1703)		CVD events ( <i>n</i> 317)		<i>P</i>
	<i>n</i>	%	<i>n</i>	%	
Age (years)					<0.0001 <sup>a</sup>
Mean		42.8		57.8	
SD		12.8		13.2	
Gender (men)	808	47.4	198	62.5	<0.0001 <sup>b</sup>
Educational status					<0.0001 <sup>c</sup>
Low	1003	59.9	234	76.2	
Moderate	645	38.5	69	22.5	
High	26	1.6	4	1.3	
Average daily energetic intake (kJ)					0.451 <sup>d</sup>
Mean		9912		10 238	
SD		3866		4724	
MedDietScore (0–55)					<0.0001 <sup>d</sup>
Mean		26.4		22.8	
SD		6.3		6.5	
DASH score (0–45)					0.197 <sup>d</sup>
Mean		27.1		27.5	
SD		5.1		5.2	
Physically active	696	40.9	129	40.7	0.954 <sup>b</sup>
BMI (kg/m <sup>2</sup> )					<0.0001 <sup>a</sup>
Mean		26.0		27.9	
SD		4.4		4.5	
Weight category					<0.0001 <sup>c</sup>
Normal/underweight	762	44.8	80	25.2	
Overweight	660	38.8	151	47.6	
Obese	278	16.4	86	27.1	
Abnormal waist-to-hip ratio	611	37.6	166	56.8	<0.0001 <sup>b</sup>
Current smokers	740	43.6	117	37.1	0.035 <sup>b</sup>
Systolic blood pressure (mmHg)					<0.0001 <sup>d</sup>
Mean		121.3		132.6	
SD		17.6		19.6	
Diastolic blood pressure (mmHg)					<0.0001 <sup>d</sup>
Mean		78.4		82.3	
SD		11.4		11.8	
Blood glucose (mg/dl)					<0.0001 <sup>d</sup>
Mean		91.4		103.5	
SD		21.7		33.0	
Hypercholesterolaemia	679	39.9	181	57.1	<0.0001 <sup>b</sup>
Hypertension	448	28.0	150	50.7	<0.0001 <sup>b</sup>
Diabetes	77	4.5	68	21.5	<0.0001 <sup>b</sup>
Metabolic syndrome	283	16.6	116	36.6	<0.0001 <sup>b</sup>

DASH, Dietary Approaches to Stop Hypertension.

\*Continuous variables are presented as mean (M) ± SD and categorical variables as absolute and relative frequencies (*n* and %).*P*-values referring to differences between CVD events and CVD-free events during the 10-year follow-up, derived using the following: <sup>a</sup>Student's *t* test for normally distributed continuous variables, <sup>b</sup>χ<sup>2</sup> test for categorical variables, <sup>c</sup>Likelihood-Ratio test for ordinal categorical variables and <sup>d</sup>Mann–Whitney test for non-normally distributed continuous variables.

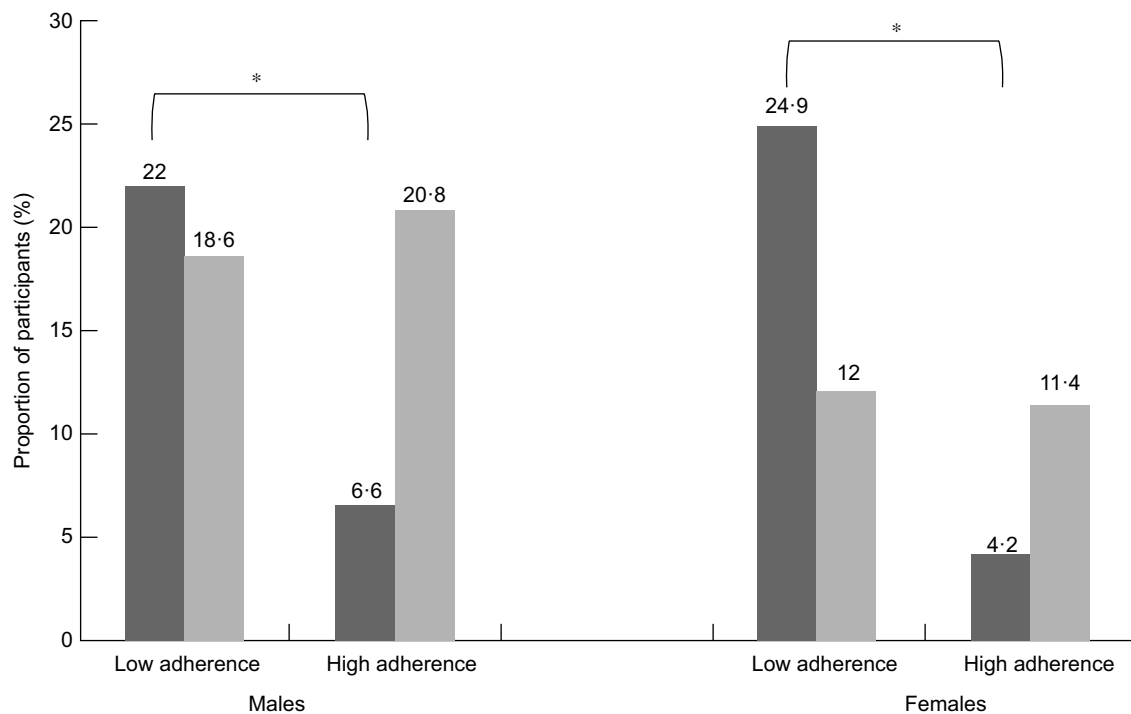
### **Risk of 10-year fatal and non-fatal CVD events according to the Mediterranean diet and Dietary Approaches to Stop Hypertension diet scores**

As shown in Table 4, following the adjustment for several known confounding factors (including age, gender, physical activity, weight category, smoking, hypertension, hypercholesterolaemia, diabetes and the metabolic syndrome), as compared with individuals within the lowest quartile of MedDietScore consumption, those within the highest quartile of consumption had a 4-fold risk to not develop 10-year fatal or non-fatal CVD events (adjusted HR 4.52, 95 % CI 1.76, 11.63). It is of interest that although it was initially observed that persons within the third quartile of the MedDietScore consumption revealed an approximately 2-fold age- and gender-adjusted differential risk for developing 10-year

CVD events, this association was not sustained following comprehensive adjustment for all of the aforementioned demographic, lifestyle and clinical confounding factors (adjusted HR 1.92, 95 % CI 0.92, 3.98). Finally, it is noteworthy that when assessed according to baseline DASH diet score, individuals with highest quartile scores did not significantly differ from their lowest quartile counterparts in developing 10-year combined fatal and non-fatal CVD events (adjusted HR 1.05, 95 % CI 0.69, 1.60).

### **Discussion**

With an ever-ageing population in developed countries, the elucidation of the most effective dietary pattern for preventing CVD is an emerging public health priority for



**Fig. 1** Comparisons of the proportion of ATTICA study participants ( $n$  2020) who developed 10-year CVD events according to their adherence to the Mediterranean and Dietary Approaches to Stop Hypertension (DASH) diets at baseline. At baseline, low (namely quartiles 1 and 2) and high (quartiles 3 and 4) adherence to the Mediterranean and DASH diets were assessed separately. According to the baseline level of adherence, the proportion of individuals with 10-year CVD events is depicted. As shown, both males and females with higher baseline adherence to the Mediterranean diet were significantly less likely to develop 10-year CVD events ( $P < 0.0001$ ). Such an association was not sustained when evaluated according to baseline adherence to the DASH diet among either males ( $P = 0.599$ ) or females ( $P = 0.086$ ). \* $P < 0.0001$ . ■, Mediterranean diet; ■, DASH diet

securing both citizens' quality of life and concomitantly minimising healthcare-associated costs<sup>(31)</sup>. Such evidence is anticipated to best inform optimal and effective public health strategies<sup>(32)</sup> for deterring CVD and, ultimately, diminishing attributable hospitalisation costs. The current study compared the efficacy of the Mediterranean and DASH dietary patterns in deterring 10-year fatal and non-fatal CVD events in a Mediterranean adult population. The main study findings revealed that one-third of individuals at the lowest quartile of Mediterranean diet consumption at baseline (as compared with 3 % of those at the highest quartile) developed 10-year fatal or non-fatal CVD events. Furthermore, with regard to time to CVD events, individuals within the highest quartile of the MedDietScore were significantly less likely than their lowest quartile counterparts to subsequently develop CVD events. In contrast, when assessed according to the DASH diet, individuals in the lowest and highest quartiles of consumption exhibited similar rates of manifesting 10-year CVD. Moreover, no significant associations were detected between the corresponding lowest and highest quartiles of DASH consumption in relation to time to occurrence of CVD events. Following the adjustment for several known confounding factors, those within the highest quartile of consumption were in excess of 4-fold more likely to not develop 10-year fatal

or non-fatal CVD events. When assessed according to baseline DASH diet score, individuals with highest quartile scores did not significantly differ from their lowest quartile counterparts in developing 10-year combined fatal and non-fatal CVD events. Hence, in the Mediterranean population examined, high adherence to the Mediterranean diet, and not the DASH diet, was associated with a reduction in the frequency and time to occurrence of 10-year fatal and non-fatal CVD. Therefore, the study findings support that in similar populations and settings, public health interventions aimed at enhancing adherence to the Mediterranean diet, rather than the DASH diet, may most effectively deter long-term CVD outcomes.

There exists mounting evidence regarding the cardio-protective effects of adhering to the Mediterranean diet in populations residing both within its indigenous region and beyond<sup>(33–35)</sup>. Similarly, the DASH diet was originally developed and further adopted for deterring CVD, particularly in Western (i.e. non-Mediterranean) populations<sup>(7)</sup>. In the present investigation regarding the comparison of the adoption of these diets in a Mediterranean population in relation to long-term (namely 10-year) fatal and non-fatal CVD outcomes, high adherence to the Mediterranean diet apparently deterred adverse health outcomes. In contrast, adoption of the DASH diet did not apparently protect participants from the manifestation of long-term CVD.

**Table 3** Baseline characteristics of dietary intake based on the Mediterranean and Dietary Approaches to Stop Hypertension (DASH) diets (expressed in quartiles of diet scores) among ATTICA study participants in relation to the 10-year fatal or non-fatal incidence of CVD, according to gender\*

	CVD-free events		CVD events		P
	n	%	n	%	
Overall (n 2020)					
Mediterranean diet score					<0.0001
First quartile (scores <25.0)	337	19.8	168	53.0	
Second quartile (scores 25–26.9)	606	35.6	112	35.3	
Third quartile (scores 27.0–27.9)	286	16.8	22	6.9	
Fourth quartile (scores 28.0–55.0)	474	27.8	15	4.7	
DASH score					0.842
First quartile (scores <23.9)	457	26.8	79	24.9	
Second quartile (scores 24.0–26.9)	359	21.1	70	22.1	
Third quartile (scores 27.0–30.9)	471	27.7	93	29.3	
Fourth quartile (scores 31.0–45.0)	416	24.4	75	23.7	
Males (n 1006)					
Mediterranean diet score					<0.0001
First quartile (scores <25.0)	242	30.0	115	58.1	
Second quartile (scores 25–26.9)	424	52.5	73	36.9	
Third quartile (scores 27.0–27.9)	103	12.7	6	3.0	
Fourth quartile (scores 28.0–55.0)	39	4.8	4	2.0	
DASH score					0.599
First quartile (scores <23.9)	216	26.7	54	27.3	
Second quartile (scores 24.0–26.9)	191	23.6	39	19.7	
Third quartile (scores 27.0–30.9)	220	27.2	54	27.3	
Fourth quartile (scores 31.0–45.0)	181	22.4	51	25.8	
Females (n 1014)					
Mediterranean diet score					<0.0001
First quartile (scores <25.0)	95	10.6	53	44.5	
Second quartile (scores 25–26.9)	182	20.3	39	32.8	
Third quartile (scores 27.0–27.9)	183	20.4	16	13.4	
Fourth quartile (scores 28.0–55.0)	435	48.6	11	9.2	
DASH score					0.086
First quartile (scores <23.9)	241	26.9	25	21.0	
Second quartile (scores 24.0–26.9)	168	18.8	31	26.1	
Third quartile (scores 27.0–30.9)	251	28.0	39	32.8	
Fourth quartile (scores 31.0–45.0)	235	26.3	24	20.2	

Categorical variables are expressed as absolute and relative frequencies (n and %).

\*P-values refer to differences between CVD events and CVD-free events during the 10-year follow-up, derived using the likelihood-ratio test.

**Table 4** Unadjusted and adjusted hazard ratios (HR, 95% CI) of Mediterranean and Dietary Approaches to Stop Hypertension (DASH) diet quartile scores in relation to 10-year incidence of fatal and non-fatal CVD events (outcome) among ATTICA study participants\*

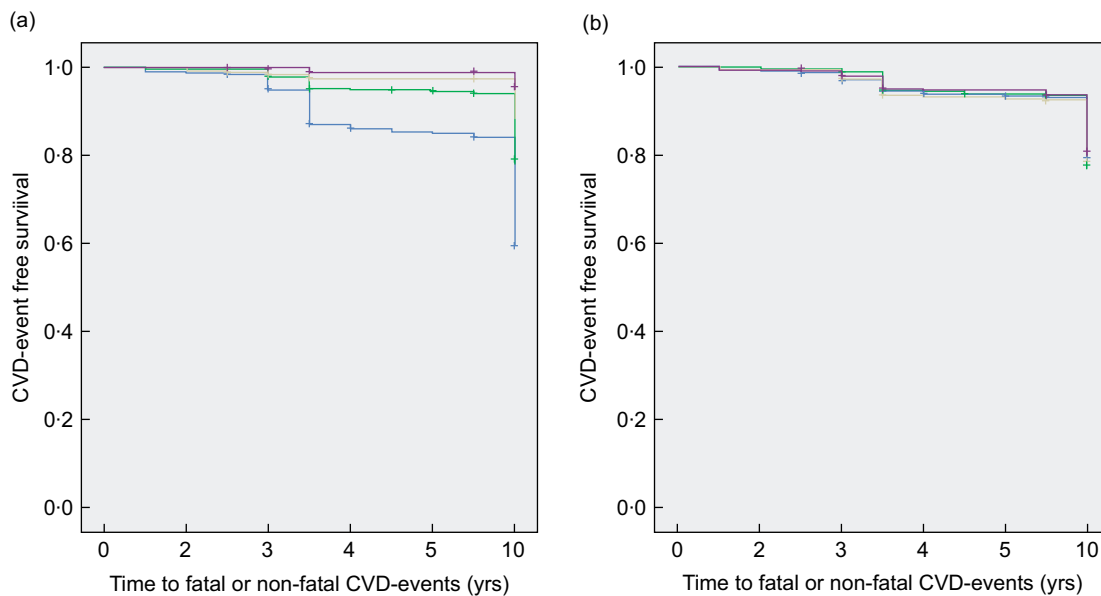
	Unadjusted		Age-adjusted		Age- and gender-adjusted		Fully adjusted	
	HR	95% CI	HR	95% CI	HR	95% CI	HR†	95% CI
Mediterranean diet score								
First quartile (scores <25.0)		1.00		1.00		1.00		1.00
Second quartile (scores 25–26.9)	2.70	2.05, 3.55	1.57	1.08, 2.02	1.48	1.08, 2.02	1.44	0.98, 2.11
Third quartile (scores 27.0–27.9)	6.48	4.04, 10.38	2.61	1.55, 4.41	2.06	1.14, 3.72	1.92	0.92, 3.98
Fourth quartile (scores 28.0–55.0)	15.75	9.12, 27.20	3.85	2.04, 7.26	2.91	1.44, 5.85	4.52	1.76, 11.63
DASH score								
First quartile (scores <23.9)		1.00		1.00		1.00		1.00
Second quartile (scores 24.0–26.9)	0.89	0.63, 1.26	0.87	0.59, 1.28	0.87	0.59, 1.29	0.88	0.59, 1.33
Third quartile (scores 27.0–30.9)	0.88	0.63, 1.21	0.93	0.65, 1.34	0.91	0.64, 1.31	1.02	0.69, 1.50
Fourth quartile (scores 31.0–45.0)	0.96	0.68, 1.35	0.98	0.67, 1.42	0.97	0.66, 1.42	1.05	0.69, 1.60

HR, hazard ratios.

\*All comparisons are conducted in relation to the corresponding first quartile score.

†Adjusted HR and 95% CI: adjusted HR for age, gender, physical activity, educational status, weight category, smoking status, hypertension, hypercholesterolaemia, diabetes and the metabolic syndrome at baseline.





**Fig. 2** (colour online) Kaplan–Meier curves for depicting the probability and time to occurrence of combined (fatal or non-fatal) CVD events according to the Mediterranean diet and Dietary Approaches to Stop Hypertension (DASH) diet scores at baseline in the ATTICA study population ( $n$  2020). Individuals with higher baseline Mediterranean diet quartile scores were significantly less likely to develop 10-year CVD events ((a) Log-rank test  $P < 0.0001$ ;  $\square$ , quartile 1 (scores  $<25.0$ );  $\square$ , quartile 2 (scores  $25.0$ – $26.9$ );  $\square$ , quartile 3 (scores  $27.0$ – $27.9$ );  $\square$ , quartile 4 (scores  $28.0$ – $55.0$ )). This observed association was not sustained when evaluated according to baseline DASH diet quartile scores ((b) Log-rank test  $P = 0.788$ ;  $\square$ , quartile 1 (scores  $<24.0$ );  $\square$ , quartile 2 (scores  $24.0$ – $26.9$ );  $\square$ , quartile 3 (scores  $27.0$ – $30.9$ );  $\square$ , quartile 4 (scores  $31.0$ – $45.0$ ))

The DASH diet, as originally conceived for non-Mediterranean Western populations, is primarily composed of lean meats, low-fat dairy products and whole grains, including an abundance of fruits and vegetables<sup>(20,21)</sup>. It entails a dietary intake low in total fat (around 27% of daily energy intake), saturated fats and cholesterol, nevertheless rich in fibre and micronutrients (namely Ca, Mg and K), which is pivotal for maintaining and/or achieving normotension, particularly in individuals with high blood pressure<sup>(36)</sup>, and preventing hypertension<sup>(37)</sup>. It has been shown that adherence to the DASH diet ultimately deters CVD, since such dietary practices are associated with diminished CVD incidence and attributable mortality rates<sup>(7)</sup>. Recent meta-analytic findings arising from prospective international cohort studies<sup>(38)</sup> show that high adherence to the DASH diet, as evident by comparing individuals of the highest *v.* lowest intake categories, results in a 20% reduction in CVD occurrence<sup>(7)</sup>, as well as mortality<sup>(38)</sup>. In addition, findings arising from the Atherosclerosis Risk in Communities Study in the USA entailing an extensive 25-year follow-up period reveal that, as compared with their counterparts with the lowest quintiles of dietary intakes, adults aged 45–64 years with the highest quintiles of either the alternative Mediterranean diet or DASH diet had significantly lower risks, of comparable magnitudes, of incident CVD and attributable mortality<sup>(39)</sup>. However, the above findings are limited to Western populations where the Mediterranean diet does not prevail, and as of such the alternative Mediterranean diet is adopted and evaluated instead.

The current study confirms previous reports demonstrating that adherence to the DASH diet is not associated with diminished rates of CVD incidence<sup>(4)</sup> and/or mortality<sup>(4,40)</sup>. These findings have been primarily confirmed not only in Mediterranean populations but also in Western populations which are not indigenous to the Mediterranean region. Specifically, in postmenopausal women aged 55–69 years, adherence to the DASH diet was not associated with mortality attributable to CVD, including specifically CHD or stroke<sup>(41)</sup>. In addition, findings arising from the Women's Health Initiative displayed that the Mediterranean diet, as opposed to the DASH diet, was solely associated with the occurrence of sudden cardiac death in postmenopausal women<sup>(42)</sup>. Furthermore, among older adults participating in the Cardiovascular Health Study and evaluated over 21.5 years, adherence to the DASH diet was not associated with the occurrence of heart failure<sup>(43)</sup>. As of such, there is mounting evidence both within and beyond Mediterranean populations that the adoption of the DASH diet may deter hypertension, albeit without conferring protection from long-term adverse CVD outcomes and mortality rates<sup>(44)</sup>.

Several plausible hypotheses exist for explicating why adoption of the Mediterranean diet, as opposed to the DASH diet, may incur enhanced protection from long-term adverse CVD outcomes.

First, due to its inherent nature and design, it is upheld that the DASH diet is most likely to have greatest blood pressure lowering effects among individuals with hypertension<sup>(45)</sup> and/or other adverse metabolic profiles



associated with CVD<sup>(27)</sup>, posing them at baseline at greater risk for developing CVD outcomes and hence biasing study findings towards the null hypothesis. Second, as also entailed in the current study, the methods employed for assessing Na intake often lack accuracy since Na intake, which is a crucial component of the DASH dietary pattern, is often not well characterised by an FFQ<sup>(27,42)</sup>. Since the reduction in Na intake induces blood pressure lowering effects particularly among hypertensive individuals<sup>(46)</sup>, study findings may be further biased in favour of the null hypothesis. Nevertheless, withstanding the aforementioned considerations regarding the assessment of Na intake, adherence to the DASH diet has been shown to be associated with CVD outcomes, including coronary artery disease<sup>(47)</sup>, stroke<sup>(48,49)</sup>, and overall with a wide array of non-Mediterranean populations. Even so, it is upheld that beyond nutrient intake, the Mediterranean diet confers additional widespread attributes for preventing CVD. Particularly in Mediterranean settings, this dietary pattern is associated with the daily adoption of a constellation of lifestyle practices, such as moderate body weight, physical activity and active social networks which enhance psychosocial and cognitive function, including social interaction, participation in leisure activities and physical activities and sleep quality<sup>(50,51)</sup>. A concomitant lack of adherence to the Mediterranean diet and physical activity leads to overweight/obesity and ultimately CVD. Overweight and obesity<sup>(52)</sup>, as well as waist circumference and central obesity<sup>(53)</sup>, have been previously documented as risk factors for CVD as they increase adipokine- and leptin-mediated adrenergic tone and trigger dysregulation of the renin–angiotensin–aldosterone system<sup>(6)</sup>. Central obesity and non-adherence to the Mediterranean diet are associated with a chronic inflammation<sup>(54)</sup> and CVD-related inflammatory markers<sup>(55)</sup>, respectively. While the exact underlying beneficial mechanisms by which social networks additionally drive this interplay remain to be elucidated<sup>(56,57)</sup>, given the aforementioned positive impacts of the above constellation of lifestyle factors on CVD health<sup>(58)</sup>, the above cumulatively emphasise the importance of adopting a comprehensive lifestyle, rather than solely a dietary pattern, which may comprehensively prevent the onset and further progression of CVD.

Collectively, the current study findings reveal that targeted primary and secondary prevention strategies for deterring CVD are hence most likely favoured through the recommended adoption of the Mediterranean diet, rather than DASH diet, particularly in Mediterranean populations. Such streamlined strategies would likely benefit most if a global approach, encompassing both dietary and lifestyle modifications as entailed in the Mediterranean diet, was adopted. Ultimately, particularly in Mediterranean populations, such preemptive interventions may diminish the disease burden and associated healthcare costs attributable to CVD.

### **Strengths and limitations**

The study strengths include the prospective cohort study design employed among a representative randomly selected, population-based sample residing in the most densely populated urban district of Greece, wherein high background prevalence rates of CVD have been documented<sup>(59,60)</sup>. The duration of follow-up extended 10 years, allowing for sufficient evaluation of the outcomes of interest, while simultaneously deterring a misclassification bias secondary to disease latency. Even so, the study limitations include that the study shares all the limitations associated with observational investigations encompassing single baseline measurements. Specifically, while adherence to the Mediterranean diet (MedDietScore) and DASH diets was measured, either changes in dietary patterns over time and/or complete dietary analysis for nutrient components was not evaluated within the context of the current investigation. Even so, due to the extended follow-up period entailed, it is upheld that dietary patterns more accurately predict CVD risk as they provide a more comprehensive understanding of how dietary factors cumulatively affect the risk of disease. Finally, initiation of pharmaceutical treatment was not evaluated within the context of the current analysis, as could potentially mediate CVD outcomes. However, since fatal and non-fatal CVD events were assessed as a combined outcome, this limitation was overcome. Moreover, it is upheld that such treatment effects would only bias towards the null hypothesis, and as of such our findings are an underestimation of true effect sizes.

### **Conclusions**

Since particularly Mediterranean populations may benefit most from adhering to the Mediterranean, rather than DASH, diet for preventing 10-year fatal and non-fatal CVD, the implementation of corresponding streamlined public health nutritional interventions may deter both CVD and related adverse health outcomes. Further investigations are necessary to provide insights regarding the potential added value of implementing such an approach in other non-Mediterranean populations.

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