Full research paper

European Journal of Preventive Cardiology

ESC European Society of Cardiology

European Journal of Preventive Cardiology
2019, Vol. 26(18) 1957–1967

DOI: 10.1177/2047487319866023
journals.sagepub.com/home/cpr
SAGE

Prevalence of hyperlipidaemia in adults and its relation to the Mediterranean diet: the Hellenic National Nutrition and Health Survey (HNNHS)

Emmanuella Magriplis[1], Demosthenes Panagiotakos[2], Anastasia-Vasiliki Mitsopoulou[1], Dimitra Karageorgou[1], Ioanna Bakogianni[1], Ioannis Dimakopoulos[1], Renata Micha[1], George Michas[1], Michail Chourdakis[3], George P Chrousos[4], Eleftheria Roma[4] and Antonis Zampelas[1]

Abstract

Objectives: A long-term abnormal blood lipid profile increases the risk of cardiovascular disease (CVD). A probable protective role may be played by the Mediterranean diet. The aim of this study was to assess prevalence of dyslipidaemia, assess blood lipid status and treatment and examine the association between blood lipids, dyslipidaemia and Mediterranean diet.

Methods: Data were from the Hellenic National Nutrition and Health Survey (HNNHS). Data from 3775 adults (40.8% males) were obtained by trained personnel and disease status was categorized according to the International Classification of Diseases codes (10th version). Blood lipid measurements were obtained from a subsample ($N = 1080$, mean age 40.1 years; 37.8% male). The Mediterranean diet score (MedDiet score) was calculated from 24-h recalls. The relationships between higher MedDiet score (>23), lipid levels and status were examined using linearized multiple linear and logistic regressions, respectively.

Results: In total, 20.7% of the population was dyslipidaemic, with 59.0% (no sex differences) receiving treatment, and 46.6% of the treated having a normal lipid profile. Lipid status awareness was 35.5% (64.5% unaware). Males aged 19–39 had higher total cholesterol, low-density lipoprotein cholesterol and triglycerides, and lower high-density lipoprotein cholesterol levels than females (in mg/dl; p for all <0.05); these were significantly higher in overweight and obese individuals in all age groups, except high-density lipoprotein cholesterol (p for all <0.001). Higher MedDiet score was associated with significantly lower low-density lipoprotein cholesterol in the pooled sample (−6.39 mg/dl; 95% confidence interval (CI): −12.60, 0.17), in all males (−10.61 mg/dl; 95% CI: −19.89, −1.34) and in overweight and obese males (−15.6 mg/dl; 95% CI: −29.25, −1.94).

Conclusion: This study underlines the abnormal lipid profile in the young, mostly male, population who are highly unaware and under-treated.

Keywords

Hyperlipidaemia, Mediterranean diet, risk factors

Received 27 March 2019; accepted 6 July 2019

Introduction

Based on evidence, the cumulative effectal blood lipid profile and continued dyslipidaemia increases the risk of cardiovascular disease (CVD).[1,2] Screening across all age groups has been, therefore, recommended by the American Heart Association and the European

[1]Department of Food Science and Human Nutrition, Agricultural University of Athens, Greece
[2]Department of Nutrition and Dietetics, School of Health Science and Education Harokopio University, Athens, Greece
[3]Laboratory of Hygiene, Social & Preventive Medicine and Medical Statistics, Department of Medicine, Faculty of Health Sciences, Aristotle University of Thessaloniki, Greece
[4]First Department of Pediatrics, Medical School, National and Kapodistrian University of Athens, Greece

Corresponding author:
Antonis Zampelas, Principal Investigator, Department of Food Science and Human Nutrition, Agricultural University of Athens, Iera Odos 75, Athens 11855, Greece.
Email: azampelas@aua.gr

Society of Cardiology as a preventative tool for decreasing primary and early CVD onset.[3,4] The new guidelines include lipid biomarkers, among others, in their list with other established CVD risk factors (i.e. smoking, high blood pressure, high blood sugar, etc.), to help health care professionals determine individualized risk and treatment provision.[4] Screening is also required in order to increase population awareness of their blood lipid status. According to latest reports, awareness in Greece was low (about 40%),[5] with reported ranges in other countries from 45.5 in Brazil[6] to over 70% in Iran.[7] In the past years population awareness of blood lipid status has increased in the USA, with the specific parameter being necessary in order to promote primary prevention.

Studies have shown that the blood lipid profile, including total and low-density lipoprotein (LDL) cholesterol, high triglycerides and low high-density lipoprotein (HDL) cholesterol, contributes to CVD risk,[8,9] in addition to other lifestyle factors. Specific lifestyle factors are highly associated with the lipid profile, including smoking,[10] diet, physical inactivity and body weight status.[11] In Greece, a high blood lipid profile was reported from a subnational study,[5] with an increase observed since the 1980s. In Crete, 45 years after the Seven Countries Study, farmers had 16% higher total cholesterol levels, associated with an increase in red meat consumption, and a decrease in Mediterranean diet adherence.[12]

In relation to dyslipidaemia, the Mediterranean diet has been associated with positive health outcomes[13–16] and has been widely investigated as protective against cardiovascular disease since the first findings reported by Ancel Keys in the Seven Countries Study.[17,18] Panagiotakos et al. reported that MedDiet can be used complementarily to lipid therapy to further ameliorate lipid levels,[5] for secondary prevention of dyslipidaemia. The secondary prevention of the Mediterranean diet, compared with a low-fat diet, has also been shown in newly diagnosed type 2 diabetics, via the prevention of the progression of subclinical atherosclerosis.[19]

Current information from national representative population-based nutrition and health studies is lacking in the Hellenic population for all age groups on the prevalence of dyslipidaemia, blood lipid distribution and population awareness, as well as proportion of the dyslipidaemic individuals on treatment. The population's adherence to the Mediterranean diet, from detailed quantifiable data, such as 24-h recalls, is also missing.

The aim of this study was primarily to assess the prevalence of dyslipidaemia in the Greek population, in total and in the three main subareas, using medical history reports, from a nationally representative sample. The secondary aim was to assess blood lipid distribution, awareness, treatment and lipid control in a subsample of the population. The association between blood lipids and dyslipidaemia with the Mediterranean diet was also examined.

Methods

Study population

The Hellenic National and Nutrition Health Survey (HNNHS) is a population-based survey, carried out in all regions of Greece, following a multistage stratified sampling design, based on age, sex and area of residence, as provided by the National Statistical Service (2011 Census). The study was carried out from September 2013 to May 2015 and surveyed non-institutionalized civilians of all ages living in Greece. A total of 4574 subjects (42.5% male) participated, of whom 3775 adults (40.8% male) enrolled in this study. Details of sampling and design can be found elsewhere.[20]

All individuals enrolled in the study were interviewed by trained personnel and blood sample determinations were performed in a subsample of these ($n = 1080$; 28.6% of the adult population; mean age 40.1 years (15.2); 37.8% male; no significant differences found with primary sample in age and sex). The number of participants enrolled provided adequate power (92%) for an effect size of 20% at $a = 0.05\%$ level. Institutionalized individuals, pregnant and lactating women and adults unable to provide informed consent due to any cause (mental impairment, psychiatric condition, drug abuse, vision or hearing loss) unless a first degree relative was able to assist were excluded. All work was carried out upon obtaining individual consent and approval by the Ethics Committee of the Department of Food Science and Human Nutrition of the Agricultural University of Athens and by the Hellenic Data Protection Authority.

Parameters investigated

An interview based questionnaire was used to obtain information on sociodemographics, anthropometric characteristics, medication intake and lifestyle status (such as smoking habits and level of physical activity). Hyperlipidaemia was evaluated through medical history in the total sample, by experienced clinicians according to the International Classification of Diseases – 10th version. Individuals were categorized with hyperlipidaemia, following a Computer Assisted Personalized Interview (CAPI), in order to estimate the prevalence of high cholesterol or triglycerides in the population. Individuals were categorized as hyperlipidaemic if they had high cholesterol or high triglycerides or were on lipid lowering medication, or if they had been diagnosed at least once in the past by a clinician as having high cholesterol or high triglycerides, as is common in epidemiological studies. Information on hyperlipidaemia was provided from 3663 adults (97% of sample; 39.9% male). Blood lipids were measured and anthropometry was performed in subjects who provided consent.

Blood lipid measurement and dyslipidaemia categorization. Each individual visited one of the five mobile units where medical evaluation and anthropometry were completed. All blood samples were collected in the morning, upon having fasted for at least 10 h, between 08:00 h and 10:00 h, All biochemical examinations were carried out using enzymatic methods in Cobas Integra 400 analyser. HDL cholesterol was determined after precipitation of the apolipoprotein B containing lipoproteins with dextran-magnesium-chloride. LDL cholesterol was calculated using the Friedwald formula: [(total cholesterol) – (HDL-cholesterol) – 1/5 (triglycerides)].

Individuals whose blood was analysed for lipids were categorized with hyperlipidaemia if they had high fasting serum cholesterol (>200 mg/dl) or high triglycerides (>150 mg/dl) or were on treatment. Hyperlipidaemia from blood measurements was estimated in order to have a comparable measure for hyperlipidaemia derived from CAPI, as well as to assess population awareness. Dyslipidaemia was used to account for the whole lipid profile (total, LDL and HDL cholesterol and triglycerides) for more complete analysis, based on blood sample determinations. Dyslipidaemia among individuals measured was diagnosed if individuals were on lipid lowering medications or had any or a combination of the following: high cholesterol (>200 mg/dl), high triglycerides (>150 mg/dl), high LDL cholesterol (>110 mg/dl), low HDL cholesterol (<40 mg/dl).

Parameters associated with dyslipidaemia were also evaluated, including population status awareness, dyslipidaemics receiving treatment and the proportion of those treated that were controlled. These parameters were examined since they are of great public health interest for primary or secondary prevention and definitions used are in accordance with previous studies. More specifically 'awareness' was defined as the proportion of adults with measured high fasted blood lipids (cholesterol or triglycerides) that actually knew their hypercholesterolaemic or hypertriglyceridaemic state (had reported correctly); 'treated' meant the individuals with dyslipidaemia who received lipid lowering medications; 'controlled' meant the individuals on treatment who had lipid profiles within normal ranges (as measured by HNNHS).

Sociodemographic and lifestyle. Specifics on age, sex and educational level were acquired by highly trained health professionals. Educational level was classified into three groups: group I had elementary schooling or lower; group II had up to high-school education or technical college; and group III had a college or higher degree of education.

Smoking habits and physical activity level were also reported. Individuals were classified as smokers or non-smokers. Physical activity was evaluated using the International Physical Activity Questionnaire (IPAQ) adapted for adults and elderly. Physical activity was defined as light, moderate or high, according to the IPAQ, as per calculation guidelines.[21] Individuals scoring below the light activity level were categorized as sedentary. Weight (kg) and height (m) were measured, from which body mass index (BMI) was derived (weight/height^2 (kg/m^2)).

Mediterranean diet adherence assessment. Adherence to the Mediterranean diet was assessed using the MedDiet score derived and validated by Panagiotakos et al. (2006).[15] Two 24-h recalls were used, one during the first interview and the second via telephone after 8–20 days on a different non-consecutive day, using specific and validated food atlases for food quantification. Details on the process have been published.[22] Food groups from the 24-h recall were derived as per the MedDiet score. Specifically, this pattern consists of daily consumption of fruits and vegetables, olive oil, non-refined cereals–carbohydrates (bread, pasta, rice, cereals, etc.) and dairy products in moderation, and a weekly intake of fish and pulses/legumes, poultry, olives and nuts. Red meat and by-products are consumed on a monthly basis and alcohol in moderation. Specific scores were applied based on mean intake per day of each of these foods, determined by the two recalls, for each individual. The MedDiet score ranges from 0 to 55 (higher score levels indicate greater adherence to the Mediterranean diet and low scores suggest a 'Western-type' dietary pattern) with Panagiotakos et al.[15] reporting that an 11 unit increase in diet score was associated with a 37% odds reduction in acute coronary events. The MedDiet score achieved by individuals in the HNNHS study was, therefore, divided into 0–11, 12–22, 23–34, 35–44 and 45–55. Limited numbers of individuals scored either very low or very high, therefore, the final MedDiet categories were 0–22, 23–34 and 35–55 (seen in Table 1) in order to achieve power in the analyses conducted.

Statistical analyses

To account for the survey's complex design and in order to better reflect known strata in the population,

Table 1. Baseline characteristics of the HNNHS study's adult participants by sex.

	Total $N = 3775$	Males $n = 1541$	Females $n = 2234$	p-value for sex
Age, years, mean (SD)	43.6 (18.7)	43.1 (18.4)	44.0 (18.8)	<**0.001**
Weight, kg, mean (SD)	73.2 (15.5)	82.8 (13.6)	66.7 (13.2)	<**0.001**
MedDiet score	28.7 (6.5)	28.1 (6.6)	29.0 (6.3)	<**0.001**
MedDiet score, status, *n* (%)				**0.004**
0–22	616 (17.1)	286 (19.5)	330 (15.5)	
23–34	2219 (61.7)	896 (61.0)	1323 (62.2)	
35–55	761 (21.2)	288 (19.6)	473 (22.3)	
Weight status, *n* (%)				
Healthy weight	1906 (52.3)	625 (41.8)	1281 (59.7)	<**0.001**
Overweight	1159 (31.8)	623 (41.6)	536 (25.0)	
Obese	577 (15.8)	248 (16.6)	329 (15.3)	
Educational status, level, *n* (%)				<**0.001**
Low	468 (12.4)	153 (9.9)	315 (14.1)	
Medium	1377 (36.6)	626 (40.7)	751 (33.7)	
High	1921 (51.0)	758 (49.3)	1163 (52.2)	
Smoking status, *n* (%)				<**0.001**
Non-smoker	2510 (66.5)	959 (62.2)	1551 (69.4)	
Smoker, daily or occasional	1265 (33.5)	582 (37.8)	683 (30.6)	
Physical activity status, *n* (%)				<**0.001**
Sedentary	286 (7.8)	136 (9.0)	150 (6.9)	
Light	515 (14.0)	233 (15.4)	282 (13.0)	
Moderate	1415 (38.5)	527 (34.8)	888 (41.0)	
Active	1463 (39.8)	617 (40.8)	846 (39.1)	
Coronary heart disease, % (SE)[a]	2.3 (0.3)	3.7 (0.6)	0.9 (0.1)	<0.001
Diabetes mellitus, % (SE)[a]	5.2 (0.4)	5.2 (0.6)	5.0 (0.6)	0.892

Significant at $p<0.05$.
[a]Weighted proportions by population, age and sex distribution.

a weighted average of the population (total population/sampled population) was obtained, accounting for the Primary Sample Unit (= household).

Normally distributed continuous variables are presented as mean ±SD and skewed (triglycerides) as median and range (25th to 75th percentiles). Categorical variables are shown as absolute numbers and frequencies (%) and data were compared using chi-square test. Analyses were stratified by sex, and dyslipidaemia and blood lipid distribution by age group, to account for and examine population differences. Student *t*-test was used to compare sex differences for normally distributed data, Mann–Whitney for skewed and one-way analysis of variance (ANOVA) for age-group differences upon log transforming skewed data. ANOVA was followed by Tukey's test to examine and report actual significant group differences.

The weighted (by age, sex and area) prevalence of dyslipidaemia was reported with respective linearized standard errors (SEs), to account for the complexity of the study's design (svy: command for survey design in Stata). Linear estimator combinations were used to examine the differences by age group and/or sex and/or area.

Extended Mantel–Haenszel statistics were performed by sex to examine linear trends between in mean blood lipid distribution and proportion of dyslipidaemia, by age group (p for trend).

Multiple linear and logistic regression, for survey data, was used to examine the association between continuous blood lipid measured and the odds of having high cholesterol or high triglycerides, with higher Mediterranean diet adherence, respectively. The models were adjusted for age, sex, weight status, education, physical activity level and smoking status. All analyses were also adjusted for two baseline health conditions, including diabetes and coronary heart disease. Differences for scores of 35–55 compared with 23–34 and lipid levels or status did not differ, therefore >23 was selected as the cut-off to simplify the model. Beta coefficient and odds ratios (ORs) with corresponding

95% confidence intervals (CIs) and linearized SE were derived. All p-value estimates were based on two-sided tests. The STATA 14.0 (StataCorp., Texas Ltd.) statistical package was used for the analysis.

Results

Excluding diabetes prevalence, all baseline variables of the study population significantly differed by sex (listed in Table 1). All further analyses were therefore stratified by sex.

Prevalence of hyperlipidaemia and treatment

In total, 20.7% of the whole population (weighted by age, sex and area) was hyperlipidaemic (no sex differences), with 59.0% (no sex differences) of the hyperlipidaemic population receiving treatment (79.1% of the hyperlipidaemic population over 60 years old; statistically significant difference by sex groups $p < 0.05$; Table 2). From the treated population only 46.6% had normal blood lipid levels and, hence, were categorized as being controlled. Almost two-thirds of the population (64.5% in total; 82.3% in the 19–39 year, 59% in the 40–59 year and 42.2% in the 60+ year age group; data not shown) were unaware (had incorrectly reported) of their lipid status as per lipid measurements, upon accounting for medication intake as well.

Blood lipid distribution

In the subsample which had blood samples analysed, total mean lipid levels by age group, stratified by sex, are shown in Table 3. Males aged 19–39 years had higher mean total cholesterol, triglyceride and LDL cholesterol levels compared with females of the same age group. HDL cholesterol was overall lower in males than in females in all age groups (p for all <0.05; Table 3). In males, the increase in mean levels (total cholesterol, LDL cholesterol and triglycerides) from age group 19–39 to 40–59 years, was followed by a significant decrease after 60 years of age. This was depicted in the prevalence of hypercholesterolaemia as well, since a significant decrease was found (30.9% for individuals 60+ years compared with 61.3% of those 40–59 years), primarily due to medical treatment, highly observed in adults 60+ years. In total 38.6% of the blood analysed population were hypercholesterolaemic and 13.9% were hypertriglyceridaemic. Hyperlipidaemia (blood analysis – adults with high cholesterol or high triglycerides) was 21.8% in the total population in comparison with CAPI results (20.7%), although these are not directly comparable. Dyslipidaemia in the blood samples was 50.1% irrespective of treatment (including individuals with normal lipid levels when on lipid lowering treatment) and increased in a linear trend by age group in both males and females ($p < 0.001$).

Weight status and lipid profile

Mean lipid levels by weight status, as per BMI category, by sex, are shown in Figure 1. In both males and females mean total cholesterol, LDL cholesterol and triglycerides were significantly higher in overweight and obese individuals (BMI $> 25\,kg/m^2$) than in those of a healthy weight (BMI $18–25\,kg/m^2$). Mean HDL cholesterol levels were significantly lower among

Table 2. Prevalence of adults diagnosed with hyperlipidaemia and percentage of those treated, based on medical history, in total and by age group and sex.

	Age group			
	Total $N = 3663$	19–39 $n = 1868$	40–59 $n = 962$	60+ $n = 833$
Hyperlipidaemia, % (SE)	20.7 (0.01)	5.6 (0.01)^{a,b}	27.4 (0.02)^{a,c}	41.9 (0.02)^{b,c}
Total treated population, % (SE)	59 (0.02)	14.4 (0.04)^{a,b}	45.9 (0.03)^{a,c}	79.1 (0.03)^{b,c}

	Males $N = 1462$			Females $N = 2201$		
	19–39 $n = 777$	40–59 $n = 344$	60+ $n = 341$	19–39 $n = 1091$	40–59 $n = 618$	60+ $n = 492$
Hyperlipidaemia, % (SE)	7.2 (0.01)^{a}	27.4 (0.03)^{b}	38.1 (0.03)^{c}	4.2 (0.01)^{a}	27.5 (0.02)^{b}	43.7 (0.02)^{c}
Total treated population, % (SE)	18.3 (0.06)	47.1 (0.06)^{b}	80.5 (0.04)^{c}	8.2 (0.1)^{b}	44.9 (0.04)^{b}	77.9 (0.03)^{c}

SE indicates linearized standard error. ^{a,b,c}Denote statistically significant differences in hyperlipidaemia prevalence (weighted proportions by age and sex distribution) by age-group in total population and between sex (of same age group). Same superscript indicates significant difference. Significance at $a = 0.05$ level, two-tailed Student t-test.

Table 3. Percentage distribution of dyslipidaemia in blood sampled in a subgroup of the adult Greek population by sex and age group.

	Total	Age group				Age group			
	$N=1094$	19–39 $n=252$	40–59 $n=106$	60+ $n=55$		19–39 $n=372$	40–59 $n=213$	60+ $n=95$	
	Males				*p*-value[aa]	Females			*p*-value[aa]
Total cholesterol, mean (SD)	192 (41.4)	186.7 (43.6)[a]	213.7 (40.5)[a,b]	187.3 (37.1)[b]	<0.001	174.8 (31.5)[a,c]	212.3 (39.5)[a]	214.1 (39.7)[c]	<0.001
Triglycerides, median (range)	83 (61, 119)	89[a,c] (68, 129.5)	118[a] (86, 166)	111[c] (85, 152)	<0.001[bb]	62 (51, 82)[a,b,c]	88 (68, 114)[a,b]	101 (82, 139)[b,c]	<0.001[bb]
HDL cholesterol, mean (SE)	57.8 (15.2)	50.2 (12.3)	48.9 (12.5)	47.5 (13.5)	0.287	63.7 (14.3)	61.6 (14.1)	62.1 (15.9)	0.210
LDL cholesterol, mean (SE)	115.1 (36.6)	113.5 (35.0)[a]	136.5 (35.2)[a,b]	112.2 (32.8)[b]	<0.001	96.5 (28.3)[a,c]	131.6 (36.1)[a]	129.3 (37.5)[c]	<0.001
Hypercholesterolaemia, %	38.6	31.4[a]	61.3[a,b]	30.9[b]	0.04	18.8[a,c]	62.0[a]	61.1[c]	<0.001[cc]
Hypertriglyceridaemia, %	13.9	18.7[a]	31.1[a]	25.5	0.05	3.8[a,c]	12.7[a]	16.8[c]	<0.001[cc]
Dyslipidaemia[dd], %	50.1	50.8[a,c]	74.5[a]	70.9[c]	<0.001[cc]	24.5[a,c]	66.2[a]	72.6[c]	<0.001[cc]

Hypercholesterolaemia when serum cholesterol >200 mg/dl. Hypertriglyceridaemia when serum triglycerides > 150 mg/dl.
[a,b,c]denote statistical differences by age-group. Same superscript indicates significant difference.
[aa]Statistical difference between age groups for each sex, at $p<0.05$, using one way analysis of variance and Tukey test.
[bb]One way analysis following log transformation.
[cc]Significant *p* for trend, following extended Mantel–Haenszel statistics.
[dd]Dyslipidaemia defined as having high cholesterol or triglycerides (and combination of these) or high low-density lipoprotein or low high-density lipoprotein or when on lipid lowering medication.

overweight and obese individuals of both sexes than among healthy weight subjects (p for all, <0.01).

MedDiet score and lipid profile

Total LDL cholesterol was significantly lower in the total sample, in all males and in overweight and obese males, when sub-analysis was carried out, for those achieving a MedDiet score > 23 (Table 4 and Figure 2). In detail, in a fully adjusted model (educational level, physical activity, body weight status, age, total energy consumption and smoking status), LDL cholesterol levels significantly decreased in the total sample ($p=0.044$) and in males ($p=0.018$) with greater adherence, to MedDiet score > 23, but not in female individuals (Table 4). LDL cholesterol decreased by 6.39 mg/dl (95% CI: –12.60, –0.17) in the total sample and 10.61 mg/dl (95% CI: –19.88, –1.34) in males, for those achieving a MedDiet score > 23. The predictive margins for LDL cholesterol (mean and 95% CI) by MedDiet score category can be seen in Figure 2 for the total sample and for males. A significant decrease in mean LDL cholesterol was found only among overweight and obese males, with LDL cholesterol decreasing by 15.6 mg/dl with high Mediterranean diet adherence (b-coefficient −15.6; 95% CI: −29.25, −1.94). When the same analysis (for all blood lipids) was performed using minimal adjustment (including body weight status and age alone), the b-coefficient for total LDL cholesterol in males was −11.9 mg/dl, SE: 4.73; $p=0.012$. An interaction (p for sex#MedDiet score interaction = 0.042), hence possible effect modification was found only for fasted LDL cholesterol levels, decreasing to –12.43 (4.7) (95% CI: –21.52, –3.28) for adults achieving > 23 MedDiet score (from 6.39; 95% CI: –12.60, –0.17). No substantial changes were found in the total sample nor in any other lipid variables.

The effect of higher Mediterranean diet adherence (score >23) on the odds of hypercholesterolaemia was significant in males only, in a fully adjusted model, with males achieving a score >23, being 46% less likely to have high total cholesterol levels (ranging from 6% to 69%) compared with those scoring lower than 23 (OR: 0.56; 95% CI: 0.31, 0.94). No significant association was found between MedDiet score and hypertriglyceridaemia.

Discussion

Results from the HNNHS, a representative national survey, resulted in a hyperlipidaemia prevalence of 21–22%, both from medical examination interview and from measured blood lipid levels. As a representative study, if the results are extrapolated to the Hellenic

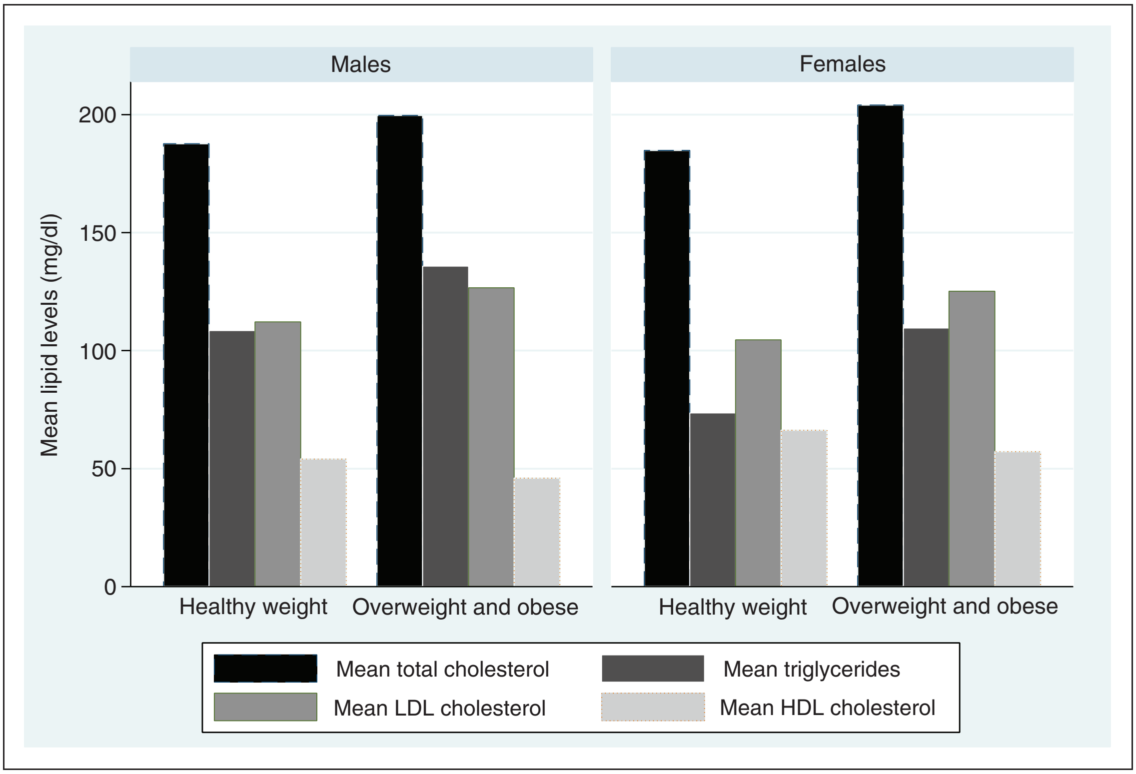

Figure 1. Mean blood lipid levels in mg/dl for healthy and overweight adults, by sex. Pairwise mean comparison, Tukey's test for each blood lipid by sex; p for all <0.01. Bar charts weighted by age and sex.
LDL: low-density lipoprotein; HDL: high-density lipoprotein

Table 4. Multiple linear regression and logistic regression evaluating the odds of blood determined hypercholesterolaemia or hypertriglyceridaemia by MedDiet score[a] category, by sex, in a fully adjusted model.

	Total sample		Males		Females	
	b-coefficient[b]	95% CI	b-coefficient[b]	95% CI	b-coefficient[b]	95% CI
Total cholesterol						
Score > 23	−3.2	−9.29, 2.81	−6.62	−16.18, 2.96	1.40	−5.83, 8.64
LDL cholesterol						
Score > 23	**−6.39**	**−12.60, −0.17**	**−10.61**	**−19.878, −1.339**	0.79	−6.72, 8.30
HDL cholesterol						
Score > 23	1.17	−1.13, 3.48	1.27	−1.78, 4.34	0.38	−3.04, 3,79
Triglycerides[c]						
Score > 23	−0.05	−0.13, 0.03	−0.06	−0.19, 0.07	−0.03	−0.12, 0.06
Logistic regression						
	Odds ratio[d]			95% CI	Odds ratio[d]	95% CI
Hypercholesterolaemia						
Score > 23	0.72	0.49–1.06	**0.54**	**0.31, 0.94**	0.89	0.34, 2.31
Hypertriglyceridaemia						
Score > 23	0.98	0.57–1.69	1.10	0.57, 2.13	0.76	0.28, 2.06

Model fully adjusted for educational level, physical activity, weight status, age, total energy consumption and smoking status.
[a]MedDiet score >23 (range 0–55) compared with very low score 0–22.
[b]Linearized multiple regression analysis.
[c]Log transformed prior to regression analysis.
[d]Linearized multiple logistic regression analysis.
CI: confidence interval; LDL: low-density lipoprotein; HDL: high-density lipoprotein.

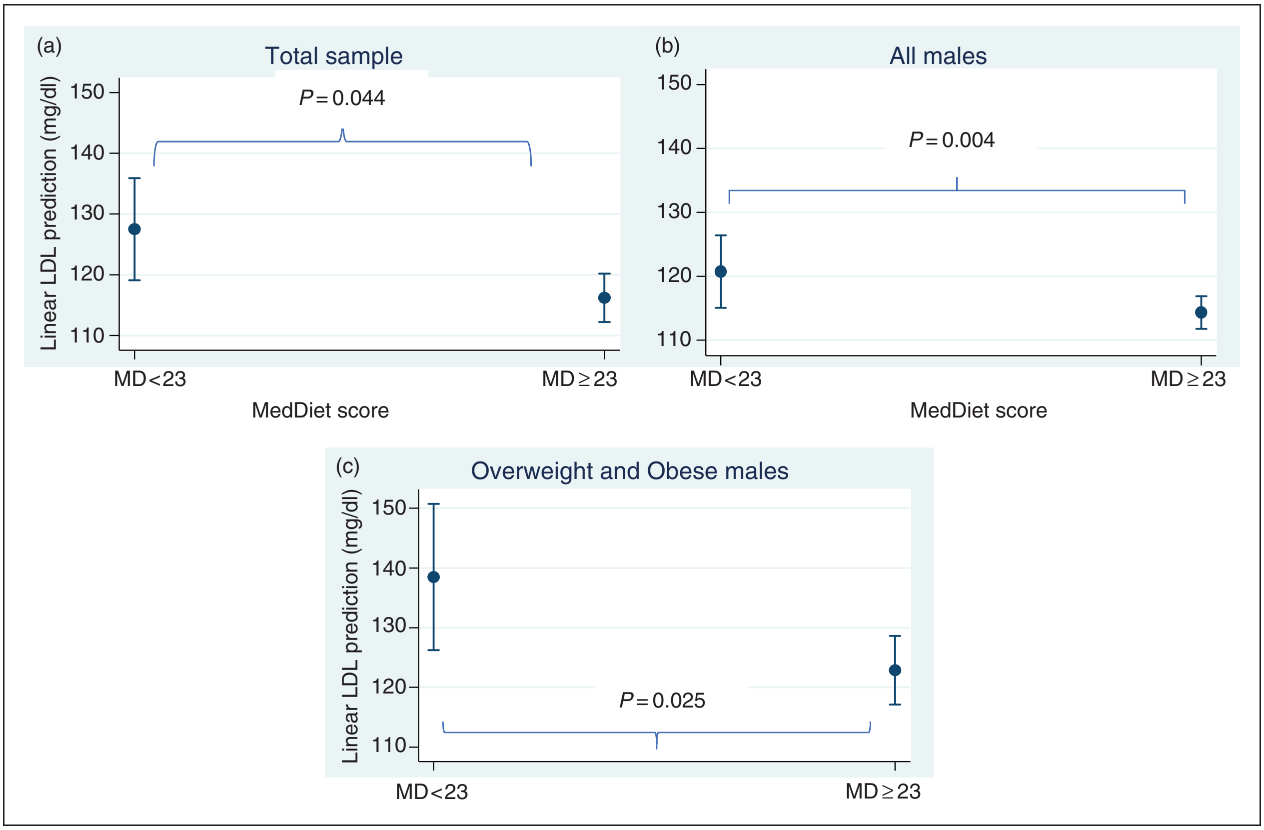

Figure 2. LDL cholesterol margin plots for total sample, all males and overweight-obese males, by MedDiet score category (low *vs.* high). Margins plot following linearized multiple regression analysis ((a) fully adjusted model for age, educational level, IPAQ score, energy intake, smoking status, body mass index category and sex; (b) whole model excluding sex; (c) whole model excluding BMI category and sex); for overweight and obese individuals using fully adjusted model in (c)).
LDL: low-density lipoprotein; MD: MedDiet; IPAQ: International Physical Activity Questionnaire

adult population, about two million Greek adults are at risk of having hyperlipidaemia and, hence, at high risk for CVD. Dyslipidaemia, which includes either high cholesterol or triglycerides, or low HDL, or high LDL, affected half of the population measured. Higher Mediterranean diet adherence was significantly associated with lower LDL cholesterol in the total population with clinically significant lower values observed in all males and those overweight and obese, but not in females. Also, males, but again not females, with a higher MedDiet score had 45% lower odds of having high cholesterol, underlining the need for more studies that evaluate physiological sex differences or potential effect modification, as found in this study.

In agreement with this study's findings, gender and age-related differences were recently reported by Lifelines, a large cross-sectional population-based Dutch study.[23] The authors reported a steep increase in LDL cholesterol in men from 20 to 49 years of age, while in women the levels increased after their 35th year. Sex differences were readily apparent in young adults and older individuals, with males having higher mean lipid levels when young but lower than females after 60 years of age, although fewer females over 60 were overweight and obese and MedDiet scores did not significantly differ (data not shown). The latter has been reported by other researchers, showing that a higher percentage of women over 50 years old had higher cholesterol levels than men,[24,25] a finding reported in Greece as well.[5] This finding can potentially be explained by the lower proportion of females treated in the younger age groups than males.

Compared with previously reported results, more males had high triglycerides and approximately 39% of the population had high cholesterol levels compared with approximately 42% reported by the ATTICA study in 2004.5 Although the results are not directly comparable, it can be concluded that over the past decade (2004 to 2014, when the information was gathered) the lipid profile of the Hellenic population is relatively steady, although it has increased compared with results reported in the 1980s and compared with those from the Seven Countries Study. This can be explained by the increased prevalence of overweight and obesity found in this study and the low adherence to the Mediterranean diet by the majority of the population.

The effects of the economic crisis that started in Greece in 2008 cannot be estimated in this study.

The public health problem of dyslipidaemia and CVD risk in the Greek adult population is underlined by the fact that almost two-thirds of the population found to have abnormal lipid levels were unaware of their lipid status, especially young adults, results similar to other national health studies.[6,26,27] Furthermore, only a small percentage of young adults were treated, despite increases reported in the USA,[11] while only one-quarter of the population with known abnormal lipid levels was under control (less than half (46.6%) of those treated). These results agree with a subnational study conducted in Attica, Greece, 14 years ago,[5] strengthening the need for population-based public health programmes underlying the risks of dyslipidaemia and emphasizing lifestyle and dietary modifications. A recent study evaluating the factors associated with poor LDL cholesterol control reported significantly higher odds of higher LDL cholesterol among those undertreated due to statin side effects and low adherence to statin intake, and increased odds for high LDL cholesterol when individuals consumed fish less than three times per week.[28] The effect of diet on LDL cholesterol was also demonstrated by a longitudinal child oriented dietary intervention, where the intervention resulted to a decrease in fat intake not only in children but also in their parents, with a subsequent LDL cholesterol decrease in mothers only.[29]

The influence of MedDiet score on LDL cholesterol was stratified by body weight status. This was done to account for the high prevalence of overweight and obese individuals in the HNNHS, and the significantly higher lipid profile found among overweight and obese individuals. The mean LDL cholesterol decrease with higher MedDiet score observed was statistically significant and in most cases clinically significant, reaching up to 29.3 mg/dl decreases in overweight and obese males. No differences were found in women in comparison with other studies,[13] although the latter used nutritional counselling on the Mediterranean diet prior to dietary data collection. Also, sex may act as an effect modifier on MedDiet and LDL cholesterol levels, since the interaction term was significant and resulted to a further decrease in LDL cholesterol levels with higher MedDiet score. The potential mechanism needs further investigation. Furthermore, based on a recent study reporting Mediterranean food and inflammation associations in adolescence,[30] sex observed differences may be explained by the higher mean LDL cholesterol found in young males, hence the longer period that males were at risk, compared with females. It can also be due to the hormonal changes that occur in women, especially oestrogen level decreases, after the age of 45. In support of these studies' findings, Lopez-Garcia et al.[31] reported an inverse association between higher Mediterranean diet adherence and all-cause mortality in males and females; however, CVD mortality was significantly lower only in males, with pooled results being non-significant. It should also be underlined that most of the data available include males. The Seven Countries Study[17,32,33] enrolled and reported the potential protective effect of the Mediterranean diet on middle aged men. Other studies,[16,32–34] including clinical ones,[35] have reported the beneficial effects of the Mediterranean diet in the total sample. More studies are, therefore, required to understand the potential sex differences, accounting for the complex hormonal changes that occur during menopause.

This study has some limitations that must be considered. It cannot establish causation nor temporal relations, due to its cross-sectional nature. Only one-third of the population consented to provide a blood sample; sampling bias, however, was low, since a-posteriori tests showed that the samples did not vary by sex and age. Generalizability of the sample measured can also be questioned, although the results between measurements and diagnosis from medical history were statistically similar. Also, LDL cholesterol was calculated and not measured, although errors result when triglycerides are very high, which was not the case in our population, granted that only 0.4% of the population had triglyceride levels over 400 md/dl.

The study overall, as nationally representative, is highly informative for the Hellenic and European population, and although it verifies the high prevalence of dyslipidaemia in older adults, it also underlines the abnormal lipid profile in the young, mostly male, population. Also, the high percentage of unawareness and under-treatment, especially in the two younger age groups, is a public health problem. The potential protective role of the Mediterranean diet on LDL cholesterol and the sex differences observed need to be further examined with cohort studies. The information gathered on the lipid profile and the prevalence of dyslipidaemia can be used to derive health policies that will create awareness and reinforce acceptable treatment approaches.

Author contribution

Conceptualization, EM and DP; methodology, EM, AVM and DP; software, EM and DK; validation, DP and AA; formal analysis, EM, investigation, ID, AZ, GM, ID and RM; writing – original draft preparation, E.; writing – review and editing, ER, MC, GC ER; supervision, AZ.

Acknowledgements

Renata Micha and Dimitra Kerageorgou: present address: Friedman School of Nutrition Science and Policy, Tufts

University, Boston, USA; George Michas: present address: Department of Cardiology, 'Elpis' General Hospital of Athens, Greece. Special thanks to all the fieldworkers. Contributors: Evangelia Fappa, Eleni-Maria Theodoraki, Eirini Trichia, Theodora-Eirini Sialvera, Aggeliki Varytimiadi, Eleni Spyreli, Antonis Koutelidakis, George Karlis, Stauroula Zacharia, Anna Papageorgiou, Triantafyllia Ntouroupi, Sophia-Maria Tsaniklidou, Kostantina Argyri (all Department of Food Science and Human Nutrition, Agricultural University of Athens, Greece, except Antonis Koutelidakis: Department of Food Science and Nutrition, University of Aegean, Mytilini, Greece). Advisory Committee: Georgios Dedoussis (Department of Nutrition and Dietetics, School of Health Science and Education Harokopio University, Athens, Greece), George Dimitriadis (2nd Department of Internal Medicine, Research Institute and Diabetes Centre, National and Kapodistrian University of Athens, 'Attikon' University Hospital, Haidari, Greece), Yannis Manios (Department of Nutrition and Dietetics, School of Health Science and Education Harokopio University, Athens, Greece), George P Chrousos, Eleftheria Roma (both First Department of Pediatrics, Medical School, National and Kapodistrian University of Athens, Greece).

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: the study was co-funded by Greece (Ministry of Health) and the European Union (European Social Fund) under the Operational Program 'Human Resources Development 2007–2013'.

References

1. Nejat A, Mirbolouk M, Mohebi R, et al. Changes in lipid measures and incident coronary heart disease: Tehran Lipid & Glucose Study. *Clin Biochem* 2014; 47: 1239–1244.
2. Nomikos T, Panagiotakos D, Georgousopoulou E, et al. Hierarchical modelling of blood lipids' profile and 10-year (2002-2012) all cause mortality and incidence of cardiovascular disease: The ATTICA study. *Lipids Health Dis* 2015; 14: 108.
3. Piepoli MF, Hoes AW, Agewall S, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice. *Eur J Prev Cardiol* 2016; 23: NP1–NP96.
4. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the management of blood cholesterol: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2019; 73(24): e285–e350. DOI: 10.1016/j.jacc.2018.11.003.
5. Panagiotakos DB, Pitsavos C, Chrysohoou C, et al. Status and management of blood lipids in Greek adults and their relation to socio-demographic, lifestyle and dietary factors: The ATTICA Study. Blood lipids distribution in Greece. *Atherosclerosis* 2004; 173: 353–361.
6. Lotufo PA, Santos RD, Figueiredo RM, et al. Prevalence, awareness, treatment, and control of high low-density lipoprotein cholesterol in Brazil: Baseline of the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil). *J Clin Lipidol* 2016; 10: 568–576.
7. Aryan Z, Mahmoudi N, Sheidaei A, et al. The prevalence, awareness, and treatment of lipid abnormalities in Iranian adult: Surveillance of risk factors of noncommunicable diseases in Iran 2016. *J Clin Lipidol* 2018; 12(6): 1471–1481. DOI: 10.1016/j.jacl.2018.08.001.
8. Fruchart JC, Sacks F, Hermans MP, et al. The Residual Risk Reduction Initiative: A call to action to reduce residual vascular risk in patients with dyslipidemia. *Am J Cardiol* 2008; 102(10 Suppl.): 1k–34k.
9. Gordon DJ, Probstfield JL, Garrison RJ, et al. High-density lipoprotein cholesterol and cardiovascular disease. Four prospective American studies. *Circulation* 1989; 79: 8–15.
10. Wong ND, Zhao Y, Quek RGW, et al. Residual atherosclerotic cardiovascular disease risk in statin-treated adults: The Multi-Ethnic Study of Atherosclerosis. *J Clin Lipidol* 2017; 11: 1223–1233.
11. Saydah S, Bullard KM, Cheng Y, et al. Trends in cardiovascular disease risk factors by obesity level in adults in the United States, NHANES 1999–2010. *Obesity (Silver Spring)* 2014; 22: 1888–1895.
12. Vardavas CI, Linardakis MK, Hatzis CM, et al. Cardiovascular disease risk factors and dietary habits of farmers from Crete 45 years after the first description of the Mediterranean diet. *Eur J Cardiovasc Prev Rehabil* 2010; 17: 440–446.
13. Bihuniak JD, Ramos A, Huedo-Medina T, et al. Adherence to a Mediterranean-style diet and its influence on cardiovascular risk factors in postmenopausal women. *J Acad Nutr Diet* 2016; 116: 1767–1775.
14. Menotti A, Alberti-Fidanza A and Fidanza F. The association of the Mediterranean Adequacy Index with fatal coronary events in an Italian middle-aged male population followed for 40 years. *Nutr Metab Cardiovasc Dis* 2012; 22: 369–375.
15. Panagiotakos DB, Pitsavos C and Stefanadis C. Dietary patterns: A Mediterranean diet score and its relation to clinical and biological markers of cardiovascular disease risk. *Nutr Metab Cardiovasc Dis* 2006; 16: 559–568.
16. Hoevenaar-Blom MP, Nooyens AC, Kromhout D, et al. Mediterranean style diet and 12-year incidence of cardiovascular diseases: The EPIC-NL cohort study. *PloS One* 2012; 7: e45458.
17. Menotti A and Puddu PE. How the Seven Countries Study contributed to the definition and development of the Mediterranean diet concept: A 50-year journey. *Nutr Metab Cardiovasc Dis* 2015; 25: 245–252.
18. Keys A, Menotti A, Karvonen MJ, et al. The diet and 15-year death rate in the seven countries study. *Am J Epidemiol* 1986; 124: 903–915.

19. Maiorino MI, Bellastella G, Petrizzo M, et al. Effect of a Mediterranean diet on endothelial progenitor cells and carotid intima-media thickness in type 2 diabetes: Follow-up of a randomized trial. *Eur J Prev Cardiol* 2017; 24(4): 399–408. DOI: 10.1177/2047487316676133.
20. Magriplis E, Dimakopoulos I, Karageorgou D, et al. Aims, design and preliminary findings of the Hellenic National Nutrition and Health Survey (HNNHS). *BMC Med Res Methodol* 2019; 19: 37.
21. Hagströmer M1, Oja P, Sjöström M. IPA Questionnaire. *Guidelines for data processing and analysis of the International Physical Activity Questionnaire (IPAQ). Public Health Nutr* 2006; 9(6): 755–762.
22. Magriplis E, Dimakopoulos I, Karageorgou D, et al. Aims, design and preliminary findings of the Hellenic National Nutrition and Health Survey (HNNHS). *BMC Med Res Methodol* 2019; 19(1): 37. DOI: 10.1186/s12874-018-0655-y.
23. Balder JW, de Vries JK, Nolte IM, et al. Lipid and lipoprotein reference values from 133,450 Dutch Lifelines participants: Age- and gender-specific baseline lipid values and percentiles. *J Clin Lipidol* 2017; 11: 1055–1064.e1056.
24. Ginsberg HN. Lipoprotein metabolism and its relationship to atherosclerosis. *Med Clin N AM* 1994; 78: 1–20.
25. Wilson PW, Abbott RD and Castelli WP. High density lipoprotein cholesterol and mortality. The Framingham Heart Study. *Arteriosclerosis* 1988; 8: 737–741.
26. Supiyev A, Nurgozhin T, Zhumadilov Z, et al. Prevalence, awareness, treatment and control of dyslipidemia in older persons in urban and rural population in the Astana region, Kazakhstan. *BMC Public Health* 2017; 17: 651.
27. McDonald M, Hertz RP, Unger AN, et al. Prevalence, awareness, and management of hypertension, dyslipidemia, and diabetes among United States adults aged 65 and older. *J Gerontol A Biol Sci Med Sci* 2009; 64: 256–263.
28. Munkhaugen J, Sverre E, Otterstad JE, et al. Medical and psychosocial factors and unfavourable low-density lipoprotein cholesterol control in coronary patients. *Eur J Prev Cardiol* 2017; 24: 981–989.
29. Jaakkola JM, Pahkala K, Rönnemaa T, et al. Longitudinal child-oriented dietary intervention: Association with parental diet and cardio-metabolic risk factors. The Special Turku Coronary Risk Factor Intervention Project. *Eur J Prev Cardiol* 2017; 24: 1779–1787.
30. Arouca A, Michels N, Moreno LA, et al. Associations between a Mediterranean diet pattern and inflammatory biomarkers in European adolescents. *Eur J Nutr* 2018; 57: 1747–1760.
31. Lopez-Garcia E, Rodriguez-Artalejo F, Li TY, et al. The Mediterranean-style dietary pattern and mortality among men and women with cardiovascular disease. *Am J Clin Nutr* 2014; 99: 172–180.
32. Stewart RAH, Wallentin L, Benatar J, et al. Dietary patterns and the risk of major adverse cardiovascular events in a global study of high-risk patients with stable coronary heart disease. *Eur Heart J* 2016; 37: 1993–2001.
33. Tyrovolas S and Panagiotakos DB. The role of Mediterranean type of diet on the development of cancer and cardiovascular disease, in the elderly: A systematic review. *Maturitas* 2010; 65: 122–130.
34. Kastorini CM, Panagiotakos DB, Chrysohoou C, et al. Metabolic syndrome, adherence to the Mediterranean diet and 10-year cardiovascular disease incidence: The ATTICA study. *Atherosclerosis* 2016; 246: 87–93.
35. Hernaez A, Castaner O, Elosua R, et al. Mediterranean diet improves high-density lipoprotein function in high-cardiovascular-risk individuals: A randomized controlled trial. *Circulation* 2017; 135: 633–643.