

Original article

Greater Adherence to a Mediterranean Dietary Pattern Is Associated With Improved Plasma Lipid Profile: the Aragon Health Workers Study Cohort



José L. Peñalvo,^{a,*} Belén Oliva,^a Mercedes Sotos-Prieto,^{a,b} Irina Uzhova,^a Belén Moreno-Franco,^c Montserrat León-Latre,^c and José María Ordovás^{a,d}

^aÁrea de Epidemiología y Genética de Poblaciones, Fundación Centro Nacional de Investigaciones Cardiovasculares (CNIC), Madrid, Spain

^bDepartment of Nutrition, Harvard School of Public Health, Boston, Massachusetts, United States

^cUnidad de Prevención Cardiovascular, Instituto Aragonés de Ciencias de la Salud (I+CS), Zaragoza, Spain

^dNutrition and Genomics Laboratory, Jean Mayer US Department of Agriculture Human Nutrition Research Center on Aging at Tufts University, Boston, Massachusetts, United States

Article history:

Received 4 July 2014

Accepted 9 September 2014

Available online 16 January 2015

Keywords:

Mediterranean diet

Dietary pattern

Factor analysis

Diet score

Plasma lipids

ABSTRACT

Introduction and objectives: There is wide recognition of the importance of healthy eating in cardiovascular health promotion. The purpose of this study was to identify the main dietary patterns among a Spanish population, and to determine their relationship with plasma lipid profiles.

Methods: A cross-sectional analysis was conducted of data from 1290 participants of the Aragon Workers Health Study cohort. Standardized protocols were used to collect clinical and biochemistry data. Diet was assessed through a food frequency questionnaire, quantifying habitual intake over the past 12 months. The main dietary patterns were identified by factor analysis. The association between adherence to dietary patterns and plasma lipid levels was assessed by linear and logistic regression.

Results: Two dietary patterns were identified: a Mediterranean dietary pattern, high in vegetables, fruits, fish, white meat, nuts, and olive oil, and a Western dietary pattern, high in red meat, fast food, dairy, and cereals. Compared with the participants in the lowest quintile of adherence to the Western dietary pattern, those in the highest quintile had 4.6 mg/dL lower high-density lipoprotein cholesterol levels ($P < .001$), 8 mg/dL lower apolipoprotein A1 levels ($P = .005$) and a greater risk of having decreased high-density lipoprotein cholesterol (odds ratio = 3.19; 95% confidence interval, 1.36–7.5; P -trend = .03). Participants adhering to the Mediterranean dietary pattern had 3.3 mg/dL higher high-density lipoprotein cholesterol levels ($P < .001$), and a ratio of triglycerides to high-density lipoprotein cholesterol that was 0.43 times lower ($P = .043$).

Conclusions: Adherence to the Mediterranean dietary pattern is associated with improved lipid profile compared with a Western dietary pattern, which was associated with a lower odds of optimal high-density lipoprotein cholesterol levels in this population.

© 2014 Sociedad Española de Cardiología. Published by Elsevier España, S.L.U. All rights reserved.

La mayor adherencia a un patrón de dieta mediterránea se asocia a una mejora del perfil lipídico plasmático: la cohorte del Aragon Health Workers Study

RESUMEN

Introducción y objetivos: Hay un amplio reconocimiento de la importancia de una dieta saludable para la promoción de la salud cardiovascular. El objetivo de este estudio es identificar los principales patrones alimentarios en la población española y determinar su relación con los perfiles lipídicos plasmáticos.

Métodos: Se llevó a cabo un análisis transversal de los datos obtenidos en 1.290 participantes de la cohorte del Aragon Workers Health Study. Se utilizaron protocolos estandarizados para la obtención de datos clínicos y bioquímicos. Se evaluó la dieta a través de un cuestionario de frecuencia de alimentación, cuantificando el consumo habitual durante los 12 meses previos. Se identificaron los principales patrones de dieta mediante un análisis factorial. Se evaluó la asociación entre la adherencia a los patrones de dieta y las concentraciones plasmáticas de lípidos mediante regresión lineal y logística.

Resultados: Se identificaron dos patrones de dieta: un patrón de dieta mediterránea, rica en verduras, frutas, pescado, carnes blancas, frutos secos y aceite de oliva, y un patrón de dieta occidental, rico en carnes rojas, comida rápida, productos lácteos y cereales. En comparación con los participantes que se

Palabras clave:

Dieta mediterránea

Patrón de dieta

Análisis factorial

Puntuación de dieta

Lípidos plasmáticos

SEE RELATED ARTICLE:

<http://dx.doi.org/10.1016/j.rec.2014.11.021>, Rev Esp Cardiol. 2015;68:279–81.

* Corresponding author: Área de Epidemiología y Genética de Poblaciones, Centro Nacional de Investigaciones Cardiovasculares (CNIC), Melchor Fernández Almagro 3, 28029 Madrid, Spain.

E-mail address: jlpenalvo@cnic.es (J.L. Peñalvo).

<http://dx.doi.org/10.1016/j.rec.2014.09.019>

1885-5857/© 2014 Sociedad Española de Cardiología. Published by Elsevier España, S.L.U. All rights reserved.

encontraban en el quintil más bajo de adherencia al patrón de dieta occidental, los que se encontraban en el quintil más alto presentaron cifras de colesterol unido a lipoproteínas de alta densidad 4,6 mg/dl menores ($p < 0,001$) y de apolipoproteína A1, 8 mg/dl menores ($p = 0,005$) y mayor riesgo de mostrar una disminución del colesterol unido a lipoproteínas de alta densidad (*odds ratio* = 3,19; intervalo de confianza del 95%, 1,36–7,5; p de tendencia = 0,03). Los participantes con adherencia al patrón de dieta mediterránea presentaron cifras de colesterol unido a lipoproteínas de alta densidad 3,3 mg/dl mayores ($p < 0,001$) y un cociente de triglicéridos/colesterol unido a lipoproteínas de alta densidad 0,43 veces inferior ($p = 0,043$).

Conclusiones: La adherencia al patrón de dieta mediterránea se asocia a una mejora del perfil lipídico en comparación con lo que se observa con un patrón de dieta occidental, que se asoció a menor probabilidad de que los valores de colesterol unido a lipoproteínas de alta densidad fueran óptimos en esta población.
© 2014 Sociedad Española de Cardiología. Publicado por Elsevier España, S.L.U. Todos los derechos reservados.

Abbreviations

ApoA1: apolipoprotein A1
HDL-C: high density lipoproteins cholesterol
MDP: Mediterranean dietary pattern
TG: triglycerides
WDP: Western dietary pattern

INTRODUCTION

Cardiovascular disease is well recognized as a major public health problem.¹ Given the direct influence of unhealthy dietary habits on its development and progression,² prevention through promoting a healthy way of eating at all population levels is a public health priority.³

The diet-disease relationship can be addressed from different perspectives, from the single nutrient approach to assessment of overall diet quality.⁴ This latter approach accounts for the likely interactions between dietary components and other lifestyle-related habits and may be better suited to identify behavioral determinants of cardiovascular disease rather than explore nutrient-induced etiological mechanisms. Evidence on how the overall diet quality impacts health is also more easily translated to broader audiences and policymakers, helping to underpin effective public health strategies. In this regard, the traditional Mediterranean dietary pattern (MDP), high in plant-based dietary sources, white meat, fish, and olive oil, and low in red meat and processed food, is well known for its cardioprotective effect^{5,6} and is recommended worldwide. Moreover, the traditional MDP has also been proposed as a plausible explanation of the Mediterranean paradox, ie, a high prevalence of cardiovascular disease risk factors along with a low incidence of cardiac events,⁷ and as a priority for primary and secondary cardiovascular disease prevention.⁸

Although the Mediterranean region has recently experienced a transition toward a more westernized dietary pattern and diet varies significantly between the countries of this area, depending on the agricultural and cultural settings, evidence shows that the MDP is associated with improved plasma lipid profile, including increased high-density lipoprotein cholesterol (HDL-C) concentration and decreased levels of low-density lipoproteins, triglycerides (TG), and total cholesterol.^{9–11} Furthermore, the effect of the MDP on apolipoprotein A1 (ApoA1) concentration has also been studied.^{12,13} Some studies have reported an increase of ApoA1 concentrations with Mediterranean diet¹⁴ and reductions in ApoA1 catabolic rate.¹⁵

In view of these findings, our aim was to identify the current major dietary patterns prevalent in a population of Spanish workers, the Aragon Workers Health Study cohort, and to

investigate their association with plasma lipid profile as an intermediate indicator of future cardiovascular outcomes.

METHODS

Study Population

Details of the study design and methodology used have previously been published.¹⁶ In brief, the Aragon Workers Health Study is a prospective cohort aimed at investigating the determinants of the development and progression of subclinical atherosclerosis in a middle-aged population. The study population consisted of a random sample of 5690 employees of the General Motors Spain automobile-assembly plant located in Zaragoza (Spain) who were free of cardiovascular disease at baseline.¹⁶ Each year, a random one-third of the study participants aged 40 to 55 years are selected for subclinical atherosclerosis imaging, clinical and physical examination, and diet, behavior, and lifestyle assessment. The present cross-sectional study was carried out in a subsample of 1593 participants with complete dietary data at baseline. Of these, 104 participants with extreme values for total energy intake (< 800 or > 4200 Kcal, and < 500 or > 3500 for men and women, respectively),¹⁷ and 199 participants with missing data were excluded. The final sample available for analysis consisted of 1290 participants. The study was approved by the central Institutional Review Board of Aragón CEICA (*Comité Ético de Investigación de Aragón*), and all study participants provided written informed consent.¹⁶

Dietary Assessment

Habitual food intakes over the past 12 months were collected through a validated 136-item food-frequency questionnaire, administered by trained dietician.^{18,19} The frequency of consumption varied from “never or almost never” to “more than 6 times per day”. Individuals' total energy and nutrient intakes were derived through a standardized nutrient database (ENDB).²⁰ Using this data, factor analysis was used to determine the main dietary patterns prevalent in our population. Furthermore, to validate the results of factor analysis, previously reported diet quality indices (AHEI [Alternate Healthy Eating Index],²¹ aMED [alternate MD Index],²² MEDAS [MD Adherence Screener],²³ and the recently developed MEDLIFE [MEDiterranean LIFestyle Index]²⁴) were computed. The details of the indices' development and scoring systems are described elsewhere.^{21–24}

Blood and Urine Collection

At baseline, participants provided a clinical history, including the occurrence of any clinical events and hospitalizations over the

past year, indicating the presence of a personal or family history of early cardiovascular disease, current medication use, and, if diagnosed, hypertension, diabetes, or dyslipidemia. Seated resting blood pressure was measured by using an OMRON M10-IT (OMRON Healthcare Co Ltd; Japan) automatic oscillometric sphygmomanometer. Three measurements were taken and the average of the measurements was used for the analysis. Blood and urine samples were collected at baseline and were processed and stored for further analysis and biobanking. Fasting serum glucose, TG, total cholesterol, and HDL-C concentrations were measured by spectrophotometry (Chemical Analyzer ILAB 650, Instrumentation Laboratory). Low-density lipoprotein cholesterol was calculated using the Friedewald formula. Levels of HDL-C of ≥ 40 mg/dL and ≥ 50 mg/dL for men and women, respectively, were considered optimal.²⁵ Serum ApoA1, B100, and lipoprotein (a) were measured by kinetic nephelometry (Immunochemistry Analyzer IMAGE 800, Beckman Coulter), and fasting serum insulin by immunoenzymatic chemiluminescence (Access Immunoassay System, Beckman Coulter). Whole blood glycated hemoglobin was measured by reverse-phase cationic exchange chromatography and quantification by double wave-length colorimetry quantification (Analyzer ADAMS A1c HA-810, Arkray Factory). The HOMA (Homeostatic Model Assessment) index was used to assess insulin resistance using glucose and insulin data.²⁶

Physical Activity Assessment

Leisure time physical activity was assessed using the Spanish-validated version²⁷ of the Nurses' Health Study and Health Professionals' Follow-up study physical activity questionnaires.^{28,29} Participants were asked about the average weekly time spent on 17 different types of physical activity, which was multiplied by its typical energy expenditure, expressed in metabolic equivalent transfer units,³⁰ and summed over all activities, to estimate the total level of physical activity spent per week.

Assessment of Other Variables

Anthropometric measurements of body weight, height, and waist circumference were performed at baseline following standardized procedures.³¹ Data were also collected on baseline sociodemographics, education, smoking history, and employment.

Statistical Analysis

The main dietary patterns were determined by factor analysis by deriving factor loading for predefined food groups using Varimax rotation option. Combinations of eigen values, the scree plot, and interpretability were used to determine the number of factors retained. Each factor had an eigen value > 0.3 . Factor scores were computed for each participant for each dietary pattern by summing intakes of food groups weighted by their factor loadings. Based on the score, participants were then divided into quintiles of adherence into the specific dietary pattern. To describe baseline characteristics, categorical variables are presented as count and percentage, and continuous variables as mean (standard deviation). The *P*-trend was tested using the factor adherence as a continuous term in the regression model. The consistency of the factor analysis-derived patterns was tested by comparing factor loadings with *a priori*-defined scores, namely the AHEI, the aMED, the MEDAS, and the recently developed MEDLIFE by studying the strength of the association across quintiles of factor score. Linear regression analyses were conducted between plasma lipid

concentrations and dietary pattern scores after controlling for the following possible confounders: age, sex, education level, dietary energy, physical activity level, plasma lipid-lowering medication, and body mass index. The odds ratio for decreased HDL-C concentration was assessed through logistic regression (adjusted for the same possible confounders as in linear regression) analysis across quintiles of dietary patterns (the first quintile was set as a reference). STATA 12.0 (StataCorp LP; College Station, Texas, United States) was used for all statistical analyses.

RESULTS

Food Consumption Pattern

Food items from the food frequency questionnaire were classified into 17 main food groups (Table 1 supplementary material). Based on the factor loading of the food groups, 2 main dietary patterns were identified (Table 1). The first dietary pattern was characterized by higher intakes of vegetables, fresh fruits, nuts, fish, olive oil and, to a lesser extent, regular consumption of nonfat dairy products and white meat and was named the "Mediterranean dietary pattern" (MDP). The second dietary pattern was characterized by higher intakes of cereals, red meat, full-fat dairy products, fast food, desserts and sweets, and, to a lesser extent, by regular consumption of vegetable oils, soda, coffee, tea and wine/beer and was named the "Western dietary pattern" (WDP). The food group of legume pulses contributed to both patterns and was not considered determinant. These 2 patterns accounted for 22% of the variance of total food intake.

Dietary Patterns and Their Agreement With Diet Quality Indices

The analysis of the association between the 2 dietary patterns identified in our population and previously reported dietary indices capturing a healthy diet/lifestyle and the Mediterranean diet is shown in Table 2. All indices were positively associated with the MDP, indicating that those participants with higher adherence to the MDP also scored highly in distinct *a priori* indices. In contrast, all indices were inversely associated with the WDP,

Table 1
Factor Loading Matrix for Dietary Patterns

Food groups	MDP	WDP
Vegetables	0.6671	0.0350
Fresh fruit	0.4862	-0.1168
Cereals	-0.0164	0.4117
Pulses	0.2180	0.3945
Nuts	0.4339	0.0228
Fish	0.5816	0.0845
White meat	0.3527	-0.0454
Red meat	0.1107	0.6221
Dairy	-0.0613	0.4469
Nonfat dairy	0.2292	-0.4307
Fast food	-0.0110	0.5378
Sweets	-0.0327	0.5482
Olive oil	0.4568	0.0078
Vegetable oils	-0.3630	0.2840
Coffee and tea	0.0567	0.2742
Soda	-0.0517	0.2927
Wine	0.0210	0.1812

MDP, Mediterranean dietary pattern; WDP, Western dietary pattern.

suggesting that this pattern is indeed associated with lower quality diets. This association between *a priori* and *a posteriori*-derived dietary patterns provides additional reliability to the results.

Sociodemographic Characteristics and Cardiovascular Risk Factors

Baseline characteristics according to quintiles of the 2 major dietary patterns (MDP and WDP) among the 1290 participants are shown in Table 3. As energy intake was not considered during factor analysis, adherence to both factors increased with energy intake due to the wider variety of foods consumed by those with higher caloric intake. On average, those participants in the highest quintile of adherence to the MDP were slightly older ($P = .01$), were either less likely to currently smoke ($P < .001$) or were more likely to be a former smokers ($P < .001$), were more physically active ($P < .001$), and had higher energy intake ($P < .001$) compared with those in the lowest quintile. Adherence to none of the patterns was associated with cardiovascular risk factors or biochemistry indicators, either across the quintiles of distribution (P -trend $> .05$) or when we compared the samples in extreme quintiles ($P > .05$). In contrast, participants with the highest adherence to the WDP were slightly younger men, belonged to families of 3 or more members, and had a lower education level ($P < .05$). No differences were found for cardiovascular risk factors except for a lower percentage of medication use ($P < .05$ for all medication) and a higher prevalence of smoking ($P < .001$) among those adhering more closely to the WDP.

Dietary Pattern Adherence and Plasma Lipids

Plasma lipid concentrations across quintiles of adherence to the MDP and WDP are shown in Table 4. Fully adjusted linear regression models were used for comparison. On average, participants adhering more closely to the MDP had higher HDL-C (quintile 1 = 51.5 mg/dL; quintile 5 = 54.8 mg/dL; $P < .001$) and a lower TG/HDL-C ratio (quintile 1 = 3.38; quintile 5 = 2.95; $P = .043$). In contrast, participants who scored high on the WDP had significantly ($P < .001$) lower HDL-C (quintile 1 = 54.5 mg/dL; quintile 5 = 49.9 mg/dL), and serum ApoA1 (quintile 1 = 147 mg/dL; quintile 5 = 139 mg/dL; $P = .005$). Figure shows the risk of having HDL-C lower than 40 mg/dL for men and lower than 50 mg/dL for women across quintiles of adherence to the WDP and MDP. The risk of having lower HDL-C increased with greater adherence to the WDP (quintile 5 vs quintile 1, odds ratio = 3.19; 95%

confidence interval, 1.36–7.50; P -trend = .03). Regarding the MDP, the trend across quintiles was not significant (quintile 5 vs quintile 1, odds ratio = 0.603; 95% confidence interval, 0.329–1.100; P -trend = .203).

DISCUSSION

In this study, we investigated the relationship between overall diet quality expressed by adherence to *a posteriori*-derived dietary patterns and plasma lipid profile as an intermediate indicator of cardiovascular risk. Previous studies have suggested that adherence to a healthy diet is linked to improved health-related behaviors.³² Analysis of the dietary patterns of a Dutch population revealed that individuals who followed a pattern high in dairy products, meat, and processed food were more likely to be less educated, less physically active, and heavy smokers.³³ In contrast, those with a higher intake of vegetables and vegetable oils, pasta, rice, fish, white meat, and wine were likely to have a higher education level and to be more physically active.³³

There is scientific evidence that choosing a healthier dietary pattern depends on socioeconomic status.³⁴ This is true in Spain, where a recent study among university graduates found that the Mediterranean diet, to some extent, was expensive.³⁵ In our study, individuals with a lower education and income might face economic barriers to the MDP, and are thus prone to the WDP or a similar high-fat pattern, giving preference to a less expensive and less healthy diet, whereas a more highly educated population with a higher income might be more able to afford certain healthier food items, which on average are considered expensive. Additionally, more highly educated participants might have better nutrition knowledge and greater awareness of the effects of exposure to a low-quality diet on risk of disease progression; therefore they would develop the healthier dietary pattern. As for lifestyle habits, in our study only physical activity was positively associated with increased adherence to the MDP and smoking with a lower or higher adherence to MDP or WDP, respectively. Current smokers tended to be less health-conscious and to have a lower degree of self-awareness of their health-related behaviors, including diet, than those who either never smoked or gave up smoking.³⁶ Smoking causes an increased turnover of micronutrients,³⁷ thus putting smokers who follow the WDP at greater risk of chronic disease compared with nonsmokers, not only due to the unhealthy dietary intake characterized by the WDP, but also due to malnutrition.³⁸

Table 2
Association Between *a Posteriori*-defined Dietary Patterns and *a Priori*-defined Dietary Indices

	Quintiles of adherence to the pattern					<i>P</i> -trend
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	
MDP						
MEDLIFE	9.31 (2.32)	10.40 (2.00)	11.10 (2.32)	12.10 (2.17)	13.30 (2.28)	<.001
MEDAS	4.95 (1.44)	6.01 (1.30)	6.57 (1.36)	7.10 (1.35)	7.94 (1.56)	<.001
AHEI	42.4 (7.25)	46.1 (6.67)	49.6 (6.61)	51.8 (7.10)	58.2 (7.51)	<.001
aMED	2.61 (1.37)	3.34 (1.47)	3.82 (1.50)	4.45 (1.44)	5.45 (1.48)	<.001
WDP						
MEDLIFE	11.6 (2.69)	11.3 (2.69)	11.3 (2.75)	11.1 (2.60)	10.9 (2.29)	.001
MEDAS	6.94 (1.78)	6.64 (1.71)	6.54 (1.69)	6.35 (1.72)	6.09 (1.63)	<.001
AHEI	50.2 (9.40)	50.1 (8.93)	50.1 (8.89)	49.4 (8.70)	48.3 (8.05)	.002
aMED	4.56 (1.56)	4.18 (1.81)	4.07 (1.61)	3.59 (1.80)	3.29 (1.65)	<.001

AHEI, Alternate Healthy Eating Index; aMED, alternate MD Index; MEDAS, MD Adherence Screener; MEDLIFE, MEDiterranean LIFestyle Index; MDP, Mediterranean dietary pattern; WDP, Western dietary pattern.
The results are expressed as mean (standard deviation).

Table 3
Baseline Characteristics by Quintiles of Adherence

	Quintiles* of adherence to MDP					P-trend	P-value (quintile 1 vs quintile 5)
	Quintile 1 [†] 258 (-3.08 to 0.84)	Quintile 2 258 (-0.84 to -0.28)	Quintile 3 258 (-0.28 to 0.23)	Quintile 4 258 (0.23-0.79)	Quintile 5 258 (0.80-3.84)		
Demographics							
Age, mean (SD), y	50.8 (3.80)	51.1 (3.66)	51.7 (3.6)	51.4 (3.61)	51.5 (3.45)	.010	.021
Number of family members, mean (SD)	3.20 (1.06)	3.23 (1.03)	3.21 (0.89)	3.16 (0.93)	3.19 (0.96)	.669	.862
Number of children, mean (SD)	1.50 (0.82)	1.49 (0.734)	1.52 (0.755)	1.51 (0.74)	1.53 (0.72)	.392	.648
Gender (female)	7 (2.71)	16 (6.20)	12 (4.65)	18 (6.98)	11 (4.3)	.392	.337
CVD history	2 (0.78)	2 (0.79)	0 (0)	1 (0.41)	3 (1.2)	.427	.637
Education level							
≤ high school	240 (93.0)	246 (95.3)	244 (94.5)	238 (92.6)	245 (95)	.952	.354
> high school	18 (6.98)	12 (4.65)	14 (5.43)	19 (7.39)	13 (5.04)		
CVD risk factors							
Medication: Dyslipemia	36 (14.2)	38 (15.1)	31 (12.4)	35 (14.5)	35 (14.1)	.979	.970
Medication: Diabetes	11 (4.40)	10 (3.98)	8 (3.19)	7 (2.89)	11 (4.5)	.327	.977
Medication: Hypertension	60 (23.6)	54 (21.4)	47 (18.8)	51 (21)	56 (22.5)	.556	.763
Body mass index, mean (SD), kg/m ²	27.8 (3.56)	27.7 (3.62)	27.7 (3.74)	28.1 (3.67)	28.0 (3.33)	.370	.575
Waist circumference, mean (SD), cm	98.0 (9.70)	97.9 (9.47)	96.9 (10.5)	97.8 (10)	97.7 (8.9)	.628	.687
Systolic blood pressure, mean (SD), mmHg	125.0 (14.0)	126.0 (14.7)	125.1 (13.5)	125.9 (14.9)	126 (14.6)	.864	.379
Diastolic blood pressure, mean (SD), mmHg	83.5 (9.2)	83.7 (9.5)	82.8 (9.2)	84.3 (10.1)	83.4 (9.80)	.790	.664
Smoking status							
Smoker	103 (40.1)	74 (29.0)	85 (33.2)	90 (35.9)	53 (20.9)	<.001	<.001
Nonsmoker	82 (31.9)	90 (35.3)	92 (35.9)	81 (32.3)	86 (33.9)	.913	.639
Former smoker	72 (28.0)	91 (35.7)	79 (30.9)	80 (31.9)	115 (45.3)	<.001	<.001
Lifestyle							
Energy intake, mean (SD), kcal	2540 (673)	2697 (655)	2797 (573)	2875 (622)	3069 (578)	.000	<.001
Physical activity, mean (SD), METs-h/week	30.5 (18.3)	33.3 (19.6)	31.7 (18.2)	34.6 (20.3)	38.2 (22.4)	<.001	<.001
Sleep, mean (SD), h, business d	6.36 (0.92)	6.25 (0.92)	6.17 (0.89)	6.25 (1.07)	6.27 (1.03)	.619	.302
Biochemistry							
Glucose, mean (SD), mg/dL	98.7 (15.8)	101.0 (21.7)	98.6 (18.3)	98.7 (17.3)	99.9 (18.2)	.904	.458
Insulin, mean (SD), uU/mL	8.71 (7.01)	7.68 (5.80)	7.28 (4.9)	8.14 (5.6)	7.75 (5.02)	.230	.087
Glycated hemoglobin, mean (SD), %	5.56 (0.47)	5.56 (0.60)	5.54 (0.5)	5.55 (0.5)	5.57 (0.56)	.836	.890
Insuline resistance, mean (SD), HOMA	2.18 (2.00)	1.95 (1.70)	1.82 (1.4)	2.07 (1.7)	1.96 (1.49)	.342	.178
C-reactive protein, mean (SD), mg/dL	0.320 (0.73)	0.262 (0.20)	0.322 (0.4)	0.273 (0.3)	0.24 (0.29)	.081	.105
	Quintiles* of adherence to WDP					P-trend	P-value (quintile 1 vs quintile 5)
	Quintile 1 258 (-3.09 to -0.85)	Quintile 2 258 (-0.84 to -0.25)	Quintile 3 258 (-0.25 to 0.25)	Quintile 4 258 (0.25-0.83)	Quintile 5 258 (0.84-4.41)		
Demographics							
Age, mean (SD), y	51.6 (3.60)	51.3 (3.85)	51.7 (3.44)	51.0 (3.57)	50.8 (3.69)	.003	.012
Number of family members, mean (SD)	3.00 (0.98)	3.20 (0.97)	3.17 (0.99)	3.29 (0.97)	3.33 (0.92)	<.001	<.001
Number of children, mean (SD)	1.38 (0.76)	1.53 (0.74)	1.51 (0.79)	1.55 (0.76)	1.59 (0.69)	<.001	.001
Sex (female)	30 (11.60)	17 (6.59)	14 (5.43)	2 (0.77)	1 (0.39)	<.001	<.001
CVD history	4 (1.61)	0 (0.00)	1 (0.40)	2 (0.81)	1 (0.39)	.310	.168
Education level							
≤ high school	236 (91.5)	237 (92.2)	245 (94.9)	244 (94.5)	251 (97.3)	.002	.004
> high school	22 (8.50)	20 (7.78)	13 (5.04)	14 (5.43)	7 (2.70)		
CVD risk factors							
Medication: dyslipemia	50 (20.40)	31 (12.50)	42 (16.90)	31 (12.60)	21 (8.24)	<.001	<.001
Medication: diabetes	17 (7.00)	8 (3.24)	8 (3.21)	8 (3.25)	6 (2.36)	.026	.014
Medication: hypertension	71 (28.9)	49 (19.7)	67 (26.7)	47 (19.0)	34 (13.3)	<.001	<.001
Body mass index, mean (SD), kg/m ²	28.1 (3.71)	27.8 (3.69)	27.8 (3.60)	27.9 (3.64)	27.5 (3.27)	.123	.054
Waist circumference, mean (SD), cm	97.6 (10.80)	97.3 (10.40)	97.9 (9.36)	97.8 (9.52)	97.7 (8.50)	.637	.983
Systolic blood pressure, mean (SD), mmHg	126 (14.9)	125 (14.2)	125 (14.6)	126.8 (14.1)	125 (14.0)	.626	.742
Diastolic blood pressure, mean (SD), mmHg	83.4 (9.80)	82.8 (9.30)	83.8 (9.90)	84.3 (9.80)	83.5 (8.96)	.281	.874
Smoking status							
Smoker	54 (20.9)	77 (30.2)	73 (29.1)	83 (32.9)	118 (45.9)	<.001	<.001

Table 3 (Continued)

Baseline Characteristics by Quintiles of Adherence

	Quintiles* of adherence to WDP					P-trend	P-value (quintile 1 vs quintile 5)
	Quintile 1 258 (-3.09 to -0.85)	Quintile 2 258 (-0.84 to -0.25)	Quintile 3 258 (-0.25 to 0.25)	Quintile 4 258 (0.25-0.83)	Quintile 5 258 (0.84-4.41)		
Nonsmoker	107 (41.5)	86 (33.7)	82 (32.7)	93 (36.9)	63 (24.5)	<.001	<.001
Former smoker	97 (37.60)	92 (36.19)	96 (38.20)	76 (30.20)	76 (29.60)	.014	.054
Lifestyle							
Energy intake, mean (SD), kcal	2093 (455)	2518 (413)	2769 (448)	3085 (410)	3514 (408)	<.001	<.001
Physical activity, mean (SD), METs-h/week	31.4 (19.3)	35.2 (20.9)	33.6 (20.7)	34.7 (20.5)	33.3 (18.2)	.194	.266
Sleep, mean (SD), h, business d	6.25 (0.91)	6.21 (1.01)	6.31 (0.92)	6.26 (1.10)	6.27 (0.91)	.808	.847
Biochemistry							
Glucose, mean (SD), mg/dL	99.9 (18.0)	98.5 (14.5)	99.8 (17.1)	99.2 (19.9)	99.1 (21.3)	.915	.657
Insulin, mean (SD), uU/mL	7.49 (6.03)	7.6 (4.48)	7.88 (5.90)	8.32 (6.28)	7.87 (5.90)	.919	.902
Glycated hemoglobin, mean (SD), %	5.56 (0.57)	5.53 (0.46)	5.56 (0.52)	5.56 (0.59)	5.55 (0.55)	.721	.828
Insuline resistance, mean (SD), HOMA	2.00 (1.75)	1.89 (1.26)	2.00 (1.70)	2.13 (1.89)	1.98 (1.77)	.863	.909
C-reactive protein, mean (SD), mg/dL	0.290 (0.39)	0.337 (0.35)	0.272 (0.35)	0.276 (0.31)	0.250 (0.21)	.131	.235

CVD, cardiovascular disease; HOMA, Homeostatic Model Assessment; MDP, Mediterranean dietary pattern; WDP, Western dietary pattern.
Data are expressed as No. (%) or median (standard deviation).

* Quintiles are described by No. (minimum-maximum).

The results of our study on HDL-C are in agreement with both observational studies and clinical trials.^{9,10,39} Overall, a higher intake of refined and processed food, which characterizes the WDP, is associated with a lower HDL-C level, while closer adherence to the MDP will more likely result in increased HDL-C. One plausible underlying mechanism explaining the association between the WDP and lower HDL-C could be greater consumption of refined carbohydrates among those who follow the WDP. Refined carbohydrates tend to increase visceral adiposity, decrease insulin sensitivity, and stimulate hepatic *de novo* lipogenesis, which result in reduced HDL-C levels.⁴⁰ In contrast, the favorable effect of the MDP on HDL-C could be due to higher consumption of olive oil among the MDP population. Olive oil has been related to higher levels of trienoic prostaglandins, resulting in amelioration of plasma lipid profile, such as an increase in serum HDL-C.⁴¹

Some observational studies have shown an independent beneficial effect of physical activity on lipid profile.⁴² The role played by physical activity in altering the association between diet and lipid profile was to some extent observed in our study. Controlling for physical activity in the model slightly weakened the association between the MDP and TG/HDL-C ratio, and ApoA1 among those who followed the MDP, indicating that physical activity could indeed be partly associated with improvement of some components of the lipid profile.

Some authors have claimed that the effect of adherence to the healthy MDP on lipid profile is due to its favorable effect on obesity.⁴³ Although greater compliance with the MDP was seen to be associated with a lower obesity risk, adjustment for body mass index as a proxy of obesity, according to our results, only slightly altered the association between diet and lipid profile, indicating

Table 4

Plasma Lipids by Quintiles of Adherence to Main Dietary Patterns

	TG, mg/dL	Cholesterol, mg/dL	HDL-C, mg/dL	LDL-C, mg	TG/HDL-C ratio	ApoA1, mg/dL	ApoB, mg/dL	Lipoprotein (a), mg/dL
MDP								
Quintile 1	156 (145-168)	222 (218-227)	51.5 (50.1-52.9)	141 (137-144)	3.38 (3.07-3.69)	143 (141-146)	105 (102-108)	30.8 (26-35.5)
Quintile 2	157 (146-168)	221 (217-225)	52.5 (51.1-53.8)	137 (134-141)	3.33 (3.03-3.63)	146 (143-148)	104 (101-107)	34.6 (29.8-39.4)
Quintile 3	146 (135-157)	221 (217-225)	52.2 (50.9-53.6)	141 (137-144)	3.13 (2.82-3.43)	143 (140-145)	104 (101-107)	35.4 (29.8-39.1)
Quintile 4	152 (141-163)	228 (223-232)	54.5 (53.1-55.9)	144 (140-148)	3.09 (2.78-3.40)	147 (145-150)	108 (105-111)	35.8 (31-40.7)
Quintile 5	145 (134-157)	226 (222-231)	54.8 (53.4-56.2)	143 (139-147)	2.95 (2.64-3.27)	147 (144-149)	107 (104-110)	33.3 (28.4-38.2)
P-trend	.139	.066	<.001	.081	.043	.069	.276	.384
WDP								
Quintile 1	152 (138-166)	224 (218-229)	54.5 (52.7-56.2)	141 (136-146)	3.09 (2.71-3.47)	147 (144-150)	104 (101-108)	32.6 (26.6-38.7)
Quintile 2	146 (134-158)	226 (221-230)	55.0 (53.6-56.4)	142 (138-146)	2.96 (2.64-3.27)	149 (146-151)	106 (103-109)	33.3 (28.4-38.2)
Quintile 3	151 (140-162)	226 (222-230)	53.4 (52.0-54.8)	143 (139-147)	3.15 (2.85-3.46)	146 (144-148)	107 (104-110)	36.6 (31.8-41.5)
Quintile 4	153 (141-164)	224 (219-228)	52.7 (51.3-54.2)	141 (137-145)	3.21 (2.89-3.53)	144 (141-146)	106 (103-109)	31.1 (26.2-36)
Quintile 5	155 (142-169)	219 (214-225)	49.9 (48.2-51.6)	139 (134-144)	3.47 (3.09-3.85)	139 (136-142)	105 (102-109)	35.1 (29-41.2)
P-trend	.419	.189	<.001	.414	.101	.005	.963	.992

Apo, apolipoprotein; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MDP, Mediterranean dietary pattern; TG, triglycerides; WDP, Western dietary pattern.

Adjusted means (95% confidence interval) for age, sex, education level, energy intake, physical activity level, plasma lipid-lowering medication, and body mass index.

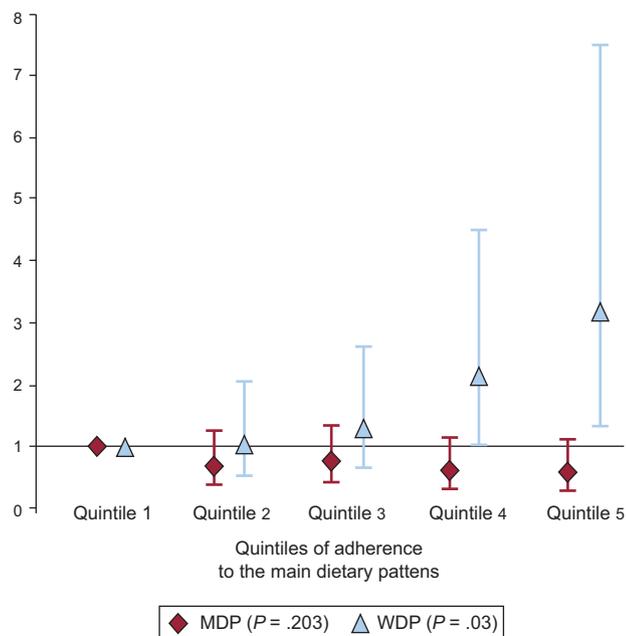


Figure. Odds ratio and 95% confidence interval for low high-density lipoprotein cholesterol levels across quintiles of adherence to the main dietary patterns. MDP, Mediterranean dietary pattern; WDP, Western dietary pattern.

that the improvements in plasma lipids observed were more likely to be due to adherence to the dietary pattern rather than to a change in body mass index.

Although not directly observed in our study, diet influences serum TG level, which has been reported in several studies.⁴⁴ In our study, we observed an inverse association between the MDP and the TG/HDL-C ratio, known as a surrogate index directly related to coronary heart risk, especially myocardial infarction.⁴⁵ Omega-3 polyunsaturated fatty acids, which are abundant in the MDP, are known to reduce TG synthesis, which will result in a lower TG/HDL-C ratio,⁴⁶ therefore adherence to the MDP, even with nonincreasing HDL-C concentration, will likely result in a lower risk for the development of coronary heart disease.

Even though a direct association between adherence to the MDP and ApoA1 was observed in our study, as well as in several other studies,^{11,14,47} the evidence regarding this relationship is still inconsistent. Taking into account the importance of apolipoproteins in cardiovascular disease prediction,⁴⁸ future studies are required to confirm our results.

Over the years, epidemiological studies have demonstrated an inverse association between HDL-C levels and cardiovascular risk,⁴⁹ such as in the Framingham Heart Study, where an increase of 5 mg/dL in HDL-C concentrations was associated with a 21% lower cardiovascular risk.⁵⁰ However, some recent studies have challenged this evidence, showing that increases in HDL-C are not necessary related to a lower risk of myocardial infarction and that its protective effect still needs to be further investigated.⁵¹

A posteriori-derived dietary patterns could only partially explain the variance in total food intake in this population, and therefore the influence of other minor dietary patterns attenuating the observed associations cannot be ruled out. In addition, the results of studies based on factor analyses largely depend on subjective decisions taken by the researchers regarding the grouping of food items into food categories. In our study, consumption of food items such as legume pulses, cereals, and wine was associated with a high-fat, high-carbohydrate diet (WDP). These items were originally considered as essential parts of

the traditional MDP, and could indicate an ongoing dietary transition from the traditional MDP to the current Mediterranean-based pattern followed in Spain. It is known that the same dietary pattern significantly differs between distinct populations, suggesting, for instance, that the MDP studied in 2 different countries might also differ.⁵²

Strengths and Limitations

An advantage of our study is the validation of an *a posteriori*-defined dietary pattern through comparison with *a priori* defined indices of diet quality. Based on our results, it can be concluded that factor analysis-defined dietary patterns are valid tools to assess the relationship between overall diet quality and biomarkers of diseases. In relation to the associations found, and due to the cross-sectional design of our study, a causal relationship cannot be established. In addition, this sample may not be representative of the general population, because these participants were mostly men and active workers and therefore healthy or at least without disabling diseases. As in most diet-related studies, reporting biases due to social desirability of overreporting healthier food items and underreporting less favorable foods also cannot be ruled out.

CONCLUSIONS

Higher adherence to the MDP was associated with improved plasma lipid profile while adherence to a WDP decreased the odds of optimal HDL-C levels in this cohort of Spanish workers.

ACKNOWLEDGMENTS

We thank the participants and the personal of the Aragon Health Workers Study cohort for their collaboration.

FUNDING

This study was financially supported by the FIS (*Fondo de Investigaciones Sanitarias*) of the ISCIII (*Instituto de Salud Carlos III*) of Spain, project PI11/00403.

CONFLICTS OF INTEREST

None declared.

SUPPLEMENTARY MATERIAL



Supplementary material associated with this article can be found in the online version available at [doi:10.1016/j.rec.2014.09.019](https://doi.org/10.1016/j.rec.2014.09.019).

REFERENCES

- Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;380:2095–128.
- Lopez-Garcia E, Rodriguez-Artalejo F, Li TY, Fung TT, Li S, Willett WC, et al. The Mediterranean-style dietary pattern and mortality among men and women with cardiovascular disease. *Am J Clin Nutr*. 2014;99:172–80.
- Lichtenstein AH, Appel LJ, Brands M, Carnethon M, Daniels S, Franch HA, et al. Diet and lifestyle recommendations revision 2006: a scientific statement from the American Heart Association Nutrition Committee. *Circulation*. 2006;114:82–96.

4. Berciano S, Ordovás JM. Nutrición y salud cardiovascular. *Rev Esp Cardiol*. 2014;67:738–47.
5. Estruch R, Ros E, Salas-Salvadó J, Covas MI, Corella D, Arós F, et al.; PREDIMED Study Investigators. Primary prevention of cardiovascular disease with a Mediterranean diet. *N Engl J Med*. 2013;368:1279–90.
6. Estruch R, Martínez-González MA, Corella D, Salas-Salvadó J, Ruiz-Gutiérrez V, Covas MI, et al.; PREDIMED Study Investigators. Effects of a Mediterranean-style diet on cardiovascular risk factors: a randomized trial. *Ann Intern Med*. 2006;145:1–11.
7. Soriguer F, García-Escobar E, Morcillo S, García-Fuentes E, Rodríguez de Fonseca F, Oliveira G, et al. Mediterranean diet and the Spanish paradox. A hypothesis. *Med Hypotheses*. 2013;80:150–5.
8. Arós F, Estruch R. Dieta mediterránea y prevención de la enfermedad cardiovascular. *Rev Esp Cardiol*. 2013;66:771–4.
9. Kastorini CM, Milionis HJ, Esposito K, Giugliano D, Goudevenos JA, Panagiotakos DB. The effect of Mediterranean diet on metabolic syndrome and its components: a meta-analysis of 50 studies and 534,906 individuals. *J Am Coll Cardiol*. 2011;57:1299–313.
10. Grosso G, Mistretta A, Frigiola A, Gruttadauria S, Biondi A, Basile F, et al. Mediterranean diet and cardiovascular risk factors: a systematic review. *Crit Rev Food Sci Nutr*. 2014;54:593–610.
11. Sotos-Prieto M, Luben R, Khaw KT, Wareham NJ, Forouhi NG. The association between Mediterranean Diet Score and glucokinase regulatory protein gene variation on the markers of cardiometabolic risk: an analysis in the European Prospective Investigation into Cancer (EPIC)-Norfolk study. *Br J Nutr*. 2014;112:1–10.
12. Vincent-Baudry S, Defoort C, Gerber M, Bernard MC, Verger P, Helal O, et al. The Medi-RIVAGE study: reduction of cardiovascular disease risk factors after a 3-mo intervention with a Mediterranean-type diet or a low-fat diet. *Am J Clin Nutr*. 2005;82:964–71.
13. Bradbury KE, Crowe FL, Appleby PN, Schmidt JA, Travis RC, Key TJ. Serum concentrations of cholesterol, apolipoprotein A-I and apolipoprotein B in a total of 1694 meat-eaters, fish-eaters, vegetarians and vegans. *Eur J Clin Nutr*. 2014;68:178–83.
14. Solá R, Fitó M, Estruch R, Salas-Salvadó J, Corella D, De La Torre R, et al. Effect of a traditional Mediterranean diet on apolipoproteins B, A-I, and their ratio: a randomized, controlled trial. *Atherosclerosis*. 2011;218:174–80.
15. Richard C, Couture P, Desroches S, Lichtenstein AH, Lamarche B. Effect of an isoenergetic traditional Mediterranean diet on apolipoprotein A-I kinetic in men with metabolic syndrome. *Nutr J*. 2013;12:76.
16. Casasnovas JA, Alcaide V, Civeira F, Guallar E, Ibañez B, Borreguero JJ, et al. Aragon workers' health study—design and cohort description. *BMC Cardiovasc Disord*. 2012;12:45.
17. Willett WC. *Nutritional epidemiology*. 2nd ed. New York: Oxford University Press; 1998.
18. De la Fuente-Arrillaga C, Ruiz ZV, Bes-Rastrollo M, Sampson L, Martínez-González MA. Reproducibility of an FFQ validated in Spain. *Public Health Nutr*. 2010;13:1364–72.
19. Martín-Moreno JM, Boyle P, Gorgojo L, Maisonneuve P, Fernández-Rodríguez JC, Salvini S, et al. Development and validation of a food frequency questionnaire in Spain. *Int J Epidemiol*. 1993;22:512–9.
20. Slimani N, Deharveng G, Unwin I, Southgate DA, Vignat J, Skeie G, et al. The EPIC nutrient database project (ENDB): a first attempt to standardize nutrient databases across the 10 European countries participating in the EPIC study. *Eur J Clin Nutr*. 2007;61:1037–56.
21. McCullough ML, Feskanich D, Stampfer MJ, Giovannucci EL, Rimm EB, Hu FB, et al. Diet quality and major chronic disease risk in men and women: moving toward improved dietary guidance. *Am J Clin Nutr*. 2002;76:1261–71.
22. Fung TT, Rexrode KM, Mantzoros CS, Manson JE, Willett WC, Hu FB. Mediterranean diet and incidence of and mortality from coronary heart disease and stroke in women. *Circulation*. 2009;119:1093–100.
23. Schröder H, Fitó M, Estruch R, Martínez-González MA, Corella D, Salas-Salvadó J, et al. A short screener is valid for assessing Mediterranean diet adherence among older Spanish men and women. *J Nutr*. 2011;141:1140–5.
24. Sotos-Prieto M, M-FB, Ordovás JM, León M, Casasnovas JA, Peñalvo JL. Design and development of an instrument to measure overall lifestyle habits for epidemiological research: the Mediterranean Lifestyle (MEDLIFE) index. *Public Health Nutr*. 2014;15:1–9.
25. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation*. 2002;106:3143–421.
26. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia*. 1985;28:412–9.
27. Martínez-González MA, López-Fontana C, Varo JJ, Sánchez-Villegas A, Martínez JA. Validation of the Spanish version of the physical activity questionnaire used in the Nurses' Health Study and the Health Professionals' Follow-up Study. *Public Health Nutr*. 2005;8:920–7.
28. Chasan-Taber S, Rimm EB, Stampfer MJ, Spiegelman D, Colditz GA, Giovannucci E, et al. Reproducibility and validity of a self-administered physical activity questionnaire for male health professionals. *Epidemiology*. 1996;7:81–6.
29. Wolf AM, Hunter DJ, Colditz GA, Manson JE, Stampfer MJ, Corsano KA, et al. Reproducibility and validity of a self-administered physical activity questionnaire. *Int J Epidemiol*. 1994;23:991–9.
30. Ainsworth BE, Haskell WL, Herrmann SD, Meckes N, Bassett Jr DR, Tudor-Locke C, et al. 2011 Compendium of Physical Activities: a second update of codes and MET values. *Med Sci Sports Exerc*. 2011;43:1575–81.
31. Gordon CCCW, Roche AF. Stature, recumbent length, and weight. In: Lohman TGR, Martorell R, editors. *Anthropometric Standardization Reference Manual*. Champaign: Human Kinetics; 1988. p. 3–8.
32. Randall E, Marshall JR, Graham S, Brasure J. High-risk health behaviors associated with various dietary patterns. *Nutr Cancer*. 1991;16:135–51.
33. Van Dam RM, Grievink L, Ocke MC, Feskens EJ. Patterns of food consumption and risk factors for cardiovascular disease in the general Dutch population. *Am J Clin Nutr*. 2003;77:1156–63.
34. Groth MV, Fagt S, Brøndsted L. Social determinants of dietary habits in Denmark. *Eur J Clin Nutr*. 2001;55:959–66.
35. Lopez CN, Martínez-González MA, Sánchez-Villegas A, Alonso A, Pimenta AM, Bes-Rastrollo M. Costs of Mediterranean and western dietary patterns in a Spanish cohort and their relationship with prospective weight change. *J Epidemiol Community Health*. 2009;63:920–7.
36. Cade JE, Margetts BM. Relationship between diet and smoking—is the diet of smokers different? *J Epidemiol Community Health*. 1991;45:270–2.
37. Northrop-Clewes C, Thurnham DI. Monitoring micronutrients in cigarette smokers. *Clin Chim Acta*. 2007;377:14–38.
38. Shils MS, Ross AC, Caballero B, Cousins RJ. *Modern Nutrition in Health and Disease*. 10th ed. Baltimore: Lippincott: Williams & Wilkins; 2005.
39. Damasceno NR, Sala-Vila A, Cofan M, Pérez-Heras AM, Fitó M, Ruiz-Gutiérrez V, et al. Mediterranean diet supplemented with nuts reduces waist circumference and shifts lipoprotein subfractions to a less atherogenic pattern in subjects at high cardiovascular risk. *Atherosclerosis*. 2013;230:347–53.
40. Stanhope KL, Schwarz JM, Keim NL, Griffen SC, Bremer AA, Graham JL, et al. Consuming fructose-sweetened, not glucose-sweetened, beverages increases visceral adiposity and lipids and decreases insulin sensitivity in overweight/obese humans. *J Clin Invest*. 2009;119:1322–34.
41. Alarcón de la Lastra C, Barranco MD, Motilva V, Herrerías JM. Mediterranean diet and health: biological importance of olive oil. *Curr Pharm Des*. 2001;7:933–50.
42. Monda KL, Ballantyne CM, North KE. Longitudinal impact of physical activity on lipid profiles in middle-aged adults: the Atherosclerosis Risk in Communities Study. *J Lipid Res*. 2009;50:1685–91.
43. Dow CA, Thomson CA, Flatt SW, Sherwood NE, Pakiz B, Rock CL. Predictors of improvement in cardiometabolic risk factors with weight loss in women. *J Am Heart Assoc*. 2013;2:e000152. <http://dx.doi.org/10.1161/JAHA.113.000152>.
44. Villegas R, Salim A, Collins MM, Flynn A, Perry IJ. Dietary patterns in middle-aged Irish men and women defined by cluster analysis. *Public Health Nutr*. 2004;7:1017–24.
45. Jeppesen J, Hein HO, Suadicani P, Gyntelberg F. Triglyceride concentration and ischemic heart disease: an eight-year follow-up in the Copenhagen Male Study. *Circulation*. 1998;97:1029–36.
46. Harris WS, Bulchandani D. Why do omega-3 fatty acids lower serum triglycerides? *Curr Opin Lipidol*. 2006;17:387–93.
47. Fung TT, Rimm EB, Spiegelman D, Rifai N, Tofler GH, Willett WC, et al. Association between dietary patterns and plasma biomarkers of obesity and cardiovascular disease risk. *Am J Clin Nutr*. 2001;73:61–7.
48. Di Angelantonio E, Sarwar N, Perry P, Kaptoge S, Ray KK, Thompson A, et al. Major lipids, apolipoproteins, and risk of vascular disease. *JAMA*. 2009;302:1993–2000.
49. Jacobs Jr DR, Mebane IL, Bangdiwala SI, Criqui MH, Tyroler HA. High density lipoprotein cholesterol as a predictor of cardiovascular disease mortality in men and women: the follow-up study of the Lipid Research Clinics Prevalence Study. *Am J Epidemiol*. 1990;131:32–47.
50. Grover SA, Kaouache M, Joseph L, Barter P, Davignon J. Evaluating the incremental benefits of raising high-density lipoprotein cholesterol levels during lipid therapy after adjustment for the reductions in other blood lipid levels. *Arch Intern Med*. 2009;169:1775–80.
51. Voight BF, Peloso GM, Orho-Melander M, Frikke-Schmidt R, Barbalic M, Jensen MK, et al. Plasma HDL cholesterol and risk of myocardial infarction: a mendelian randomisation study. *Lancet*. 2012;380:572–80.
52. Slimani N, Fahey M, Welch AA, Wirfält E, Stripp C, Bergström E, et al. Diversity of dietary patterns observed in the European Prospective Investigation into Cancer and Nutrition (EPIC) project. *Public Health Nutr*. 2002;5:1311–28.