Original Research

Comparison of the Dietary Antioxidant Profiles of 21 *a priori* Defined Mediterranean Diet Indexes

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ABSTRACT

Background The Mediterranean Diet (MD) is a dietary pattern that features a high quotient of antioxidant-rich foods. Differences in the level of dietary antioxidants intake reflected by different MD indexes has received little research attention.

Objective The purpose of this study was to compare the dietary antioxidant profile of 21 *a priori* defined indexes of adherence to the MD.

Design A cross-sectional study.

Participants/setting A total of 14,756 participants belonging to two Spanish European Prospective Investigation into Cancer and Nutrition cohorts, aged 32 to 69 years, recruited between 1992 and 1996, were included.

Main outcome measure Participants provided information on diet through a validated diet history questionnaire. Antioxidants (vitamin C, beta carotene and a-tocopherol), total antioxidant capacity, total polyphenols, flavonoids, and polyphenol antioxidant content score were estimated using different food composition databases. Twenty-one MD indexes were operationalized.

Statistical analysis Spearman correlation coefficients between the indexes were calculated and hierarchical clustering was applied to identify cluster groups. Weighted kappa statistic was estimated to value the scoring agreements between indexes. Antioxidant profiles between the MD indexes were compared based on geometric mean intakes. The relationship between each MD index with the components of the antioxidant profile was evaluated using linear multivariable regression analysis.

Results Correlation patterns between the MD indexes showed that about half of the indexes were moderately-to-weakly correlated with each other (rho$<$0.5). The main cluster groups derived denoted the high-, moderate-, and low-correlated MD indexes. Three MD indexes (MD pattern-2002, Prevention with MD, and Alternate MD index) presented the highest mean intakes of antioxidant vitamins, total antioxidant capacity, total polyphenols, flavonoids, and polyphenol antioxidant content score. These and other indexes (mainly those belonging to the MD Scale group) captured higher intake levels of dietary antioxidants overall.

Conclusions The level of dietary antioxidant intake that is captured through the different MD indexes differed due to the variation in their construction. Study results also suggest that some MD indexes reflect a higher antioxidant profile.

THE MEDITERRANEAN DIET (MD) IS A WIDELY recognized, mainly plant-based food dietary pattern (eg, fruits and vegetables, olive oil, nuts, legumes, and unprocessed cereals)[1] that provides a relatively high amount of antioxidant nutrients and hundreds of nonnutritive constituents with important biological activities.[2] These naturally occurring antioxidants have a well-established chronic disease risk-lowering effect due to their exceptional antioxidative and anti-inflammatory effects.[3,4] Defining the ideal MD pattern has become challenging and, as a result, since the first MD index emerged in 1995,[5] a number of MD indexes have been published to adapt the universally known

MD to existing regional variations in the MD concept.[6] Several other MD indexes have also been developed to bet- ter reflect progress made in our knowledge of what is termed an MD pattern.[6] All these MD indexes tend to resemble the MD pattern but they differ considerably by virtue of the components and scoring schemes.[7] Indeed, as has been shown in a cross-comparison study of 10 MD indexes, all included indexes were valid to measure adherence to the MD, but a low correlation was found between most of them.[8] Owing to these differing MD definitions, it is plausible to assume that their health effect benefits are not equal in magnitude. For instance, the antioxidant potential of a

existing MD indexes is, on the whole, far from being well established. It is also not certain whether the oxidative and inflammatory-reducing effects of the MD on the basis of the dietary supply of antioxidants is alike among the MD indexes.

Rather than considering the isolated effect of individual nutrient antioxidants, it has been argued that dietary total antioxidant capacity (TAC) represents an available measure of the nonenzymatic antioxidant global network.[9] TAC has been therefore proposed as a tool for investigating the synergistic effects of dietary antioxidants.[9-11] Another measure accounting for the global polyphenol intake is the polyphenol antioxidant content (PAC) score.[12] The antioxidants (vitamins C and E, phenolic compounds, and carotenoids), traditionally known as dietary antioxidants, also reflect the antioxidant potential of the diet.[10]

A previous study evaluated four published MD indexes with regard to dietary TAC intake,[13] namely the MD Score-2001,[14] the Alternate Mediterranean Diet Index (aMED),[15] the Modified MD (MMD-2005),[16] and the Mediterranean Diet Quality Index (MDQI).[17] That study reported a positive and statistically significant relationship between dietary TAC and adherence to these MD indexes but specific nutrient antioxidants were not considered. With regard to polyphenols, a study by Pounis and colleagues[12] explored how the MD is related to the intake of flavonoids, lignans, and the PAC score, finding a positive trend of association as well. A higher antioxidant status of vitamin A, vitamin C, and vitamin E has been also related to a higher adherence to the MD.[18] No further studies have been published on this topic.

Because interest in the development and use of MD indexes continues to grow, due in part to the dietary pattern's potential for the prevention of oxidative/inflammatory-related diseases, it becomes vital to examine their antioxidant potential. Differences with respect to this antioxidant potential could be explained by dissimilarities between the indexes. Therefore, the aim of this study was to comparatively evaluate the dietary antioxidant profile of 21 indexes of adherence to the MD that have been previously identified in the literature,[7] and to further analyze the correlations among them.

MATERIALS AND METHODS

A cross-sectional study was conducted within the European Prospective Investigation into Cancer and Nutrition (EPIC) study.

Study Population

EPIC is a large cohort study that was designed to identify the many risk factors leading to the development of cancer and other chronic diseases. EPIC-Spain is the Spanish arm of the European cohort. Participants belonging to two Spanish cohorts (EPIC-Granada and EPIC-Gipuzkoa), recruited between 1992 and 1996, were included in this study (16,296 adults aged between 32 and 69 years). Details of the design and methodology of the study have been described elsewhere.[19,20] Approval for the study was obtained from the ethical review boards of the International Agency for Research on Cancer and specifically for EPIC-Spain from the Medical Ethical Committee of Bellvitge Hospital (Barcelona, Spain). All participants provided written informed consent.

RESEARCH SNAPSHOT

Research Question: Do *a priori* defined Mediterranean diet (MD) indexes equally reflect dietary intake of antioxidants?

Key Findings: In this cross-sectional study conducted among 14,756 participants belonging to two Spanish European Prospective Investigation into Cancer and Nutrition cohorts, weak-to-moderate correlation strengths among 21 MD indexes were observed. The levels of antioxidants intake varied largely among the MD indexes as a result of these differences. Some of the MD indexes showed a higher antioxidant profile in terms of intakes of antioxidant vitamins, total antioxidant capacity, and flavonoids, supporting their epidemiologic application to evaluate dietedisease relationships.

Three hundred twenty-five individuals with extreme values of energy intake, below the first percentile (836 kcal/ day) and above the 99th percentile (4,119 kcal/day) of the distribution of energy intake, respectively, were excluded. In addition, 1,215 participants with prevalent diseases (eg, cancer) at baseline were excluded, leaving 14,756 healthy participants available for analyses.

DIETARY AND LIFESTYLE FACTORS ASSESSMENT

The participants of the EPIC-Granada and EPIC-Guipuzkoa cohorts provided information about their dietary intake through a validated diet history questionnaire.[21] The ques- tionnaire was administered through face-to-face interviews to ask participants about the frequency of consumption of more than 600 food items in the previous year, also consid- ering the influence of seasonal food availability as well as other particular dietary issues, such as added fats and con- sumption of alcoholic beverages.[21] Intake of nutrients along with total energy intake were derived from the EPIC Nutrient Database-EPIC food composition data tables.[22]

Apart from diet, participants were also asked to provide information about their lifestyle habit, including smoking status (never, former, and current smoker, along with smoking habit-related variables such as intensity and duration of smoking). In addition, height and weight measurements were taken using standard protocols.[23] Body mass index was calculated as weight in kilograms divided by the square of height in meters. Information on occupational and leisure activities, collected through a validated physical activity questionnaire, was used to define physical activity levels as inactive, moderately inactive, moderately active, and active (in metabolic equivalent units).[24]

Antioxidant Profile

Information on intake of antioxidant vitamins (vitamin C, beta carotene, and a-tocopherol) were derived from the EPIC nutrient database,[22] and that of dietary TAC from published TAC values of 210 food items,[25,26] distinguishing by three TAC methods: total radical-trapping antioxidant parameter (TRAP), ferric reducing-antioxidant power (FRAP), and trolox equivalent antioxidant capacity (TEAC). Oxygen radical absorbance capacity (ORAC) was calculated using the US Department of Agriculture database.[27] Coffee may be a strong

Table 1. Characteristics of the study populations of European Prospective into Cancer and Nutrition-Granada and European Prospective into Cancer and Nutrition-Gipuzkoa at baseline (N¼14,756; 1992-1996)

Characteristic	Men (n[5,517)	Women (n[9,239)	*P* value[a]	Granada (n[6,625)	Gipuzkoa (n[8,131)	*P* value[a]
	←————————*n* (%)————————!			←————————*n* (%)————————!		
Lifetime nonsmoker	1,671 (30.3)	6,831 (73.9)	<0.001	4,422 (66.7)	4,080 (50.2)	<0.001
Physically inactive[b]	1,132 (20.5)	4,604 (49.8)	<0.001	3,486 (52.6)	2,250 (27.7)	<0.001
Men				1,526 (23.3)	3,991 (49.1)	<0.001
	)*mean standard deviation*◢			)*mean standard deviation*◢		
Age (y)	51.2 7.3	48.8 8.5	<0.001	49.8 8.6	49.6 7.7	>0.05
Body mass index	28.2 3.4	28.2 4.8	>0.05	29.1 4.6	27.5 3.9	<0.001
MD[c] index[d] (score range)						
MD Scale-1995 (0-8)	4.01 1.50	3.96 1.52	>0.05	3.92 1.52	4.03 1.49	<0.001
MD Scale-2003 (0-9)	5.06 1.60	3.87 1.61	<0.001	4.06 1.71	4.52 1.68	<0.001
MD Scale-2013 (0-10)	4.92 1.59	3.90 1.62	<0.001	4.11 1.74	4.43 1.62	<0.001
Modified MD-2005 (0-9)	5.20 1.54	3.80 1.58	<0.001	3.96 1.68	4.61 1.67	<0.001
MD Pattern-2002 (8-40)	29.1 4.7	24.6 4.5	<0.001	25.0 4.9	27.3 5.0	<0.001
MD Pattern-2003 (0-18)	10.8 2.0	10.8 1.8	>0.05	11.1 1.7	10.7 1.9	<0.001
MD Pattern-2006 (10-30)	20.2 2.7	18.6 2.6	<0.001	19.2 2.8	19.2 2.7	>0.05
MSDPS[e] (0-120)	69.7 14.0	70.1 12.2	>0.05	70.9 11.5	69.2 13.9	<0.001
MDQI[f] (14-0)	6.45 2.12	6.44 2.13	>0.05	6.11 2.01	6.71 2.18	<0.001
ITAMED[g] (0-11)	4.52 1.74	4.06 1.70	<0.001	4.09 1.69	4.35 1.76	<0.001
Alternate MD Index (0-9)	3.25 1.40	2.94 1.39	<0.001	3.05 1.41	3.06 1.40	>0.05
Relative MD Scale (0-18)	9.78 2.70	7.89 2.63	<0.001	8.20 2.77	8.91 2.80	<0.001
MD Score-2001 (0-8)	3.16 1.44	2.85 1.41	<0.001	3.11 1.43	2.85 1.43	<0.001
MD Score-2004 (9-27)	19.7 2.5	17.7 2.5	<0.001	18.0 2.8	18.8 2.6	<0.001
MD Score-2005 (0-55)	33.5 4.3	32.9 4.4	<0.001	33.7 4.0	32.7 4.6	<0.001
MD Score-2007 (0-55)	33.3 4.7	33.9 4.0	<0.001	34.4 3.7	33.1 4.6	<0.001
Cardioprotective MD Scale (0-9)	5.10 1.51	5.59 1.49	<0.001	5.74 1.39	5.14 1.56	<0.001
PREDIMED[h] (0-14)	8.78 1.47	7.85 1.17	<0.001	8.06 1.26	8.32 1.43	<0.001
L-based[i] (0-18)	9.95 2.01	9.82 2.21	<0.001	10.1 2.2	9.68 2.09	<0.001
MEDLIFE[j] (0-18)	9.83 1.83	9.00 1.74	<0.001	9.13 1.74	9.46 1.86	<0.001
MDSS (0-24)	11.7 2.9	11.1 3.1	<0.001	11.2 3.1	11.4 3.0	<0.001
Dietary factors[d]						
Vitamin C (mg/d)	147 77	144 73	<0.05	145 69	145 79	>0.05
a-Tocopherol (mg/d)	16.1 7.7	11.8 5.7	<0.001	10.9 5.1	15.4 7.4	<0.001
Beta carotene (mg/d)	2,570 1,523	2,454 1,508	<0.001	2,374 1,454	2,598 1,556	<0.001
TRAP[k] (mmol trolox equivalents/d)	5,588 3,629	2,952 1,667	<0.001	3,023 1,909	4,682 3,293	<0.001
FRAP[l] (mmol iron/d)	15,348 7,903	9,245 4,459	<0.001	9,580 4,925	13,113 7,444	<0.001
TEAC-ABTS[m] (mmol trolox equivalents/d)	5,384 2,979	3,276 1,667	<0.001	3,396 1,818	4,609 2,777	<0.001
ORAC[n] (mmol trolox equivalents/d)	15,808 6,996	12,557 5,753	<0.001	12,159 5,166	15,088 7,050	<0.001
TP[o] (mg/d)	1,921 816	1,602 704	<0.001	1,596 672	1,823 817	<0.001

Flavonoids (mg/d)	484	297	311	206	<0.001	322	209	420 285	<0.001

(*continued on next page*)

Table 1. Characteristics of the study populations of European Prospective into Cancer and Nutrition-Granada and European Prospective into Cancer and Nutrition-Gipuzkoa at baseline (N¼14,756; 1992-1996) (*continued*)

Characteristic	Men (n[5,517)	Women (n[9,239)	*P* value[a]	Granada (n[6,625)	Gipuzkoa (n[8,131)	*P* value[a]
	←*mean standard deviation*!			←*mean standard deviation*!		
PAC[p] score (e28 to 28)	6.77 11.70	—3.62 11.10	<0.001	—2.66 11.70	2.65 12.50	<0.001
Energy intake (kcal/d)	2,521 601	1,779 491	<0.001	1,820 565	2,248 640	<0.001
Alcohol (g/d)	27.4 26.5	4.05 8.48	<0.001	5.09 11.90	19.0 24.2	<0.001
Vegetables (g/d)	255 149	235 129	<0.001	240 136	245 138	<0.05
Fruits and nuts (g/d)	339 251	319 221	<0.001	314 196	337 259	<0.001

[a]Statistical differences by sex and center were evaluated using Student *t* test or Wilcoxon tests for continuous variables, and C^2 test for categorical variables. Information was complete for all variables, except for smoking status (n¼7 missing).
[b]Physical inactivity was categorized as defined by the European Prospective into Cancer and Nutrition physical activity index.[24]
[c]MD¼Mediterranen Diet.
[d]Indexes and dietary intakes were not adjusted for energy intake.
[e]MSDPS¼Mediterranean-Style Dietary Pattern Score.
[f]Scored inversely.
[g]ITAMED¼Italian Mediterranean Index.
[h]PREDIMED¼Prevention with MD.
[i]L-based¼literature-based adherence score to the MD.
[j]MEDLIFE¼Mediterranean Lifestyle Index.
[k]TRAP¼total radical-trapping antioxidant parameter.
[l]FRAP¼ferric-reducing antioxidant power.
[m]TEAC-ABTS¼Trolox equivalent antioxidant capacity.
[n]ORAC¼oxygen radical antioxidant capacity.
[o]TP¼total polyphenols.
[p]PAC¼polyphenol antioxidant content score.

confounder of the TAC in vivo potential due to its high content in melanoidins; that is, products produced during the coffee roasting process. They are the main contributors to the in vitro antioxidant capacity of coffee and they are generally considered poorly absorbable and bioavailable compounds.[28,29] Dietary TAC of coffee was therefore subtracted from the total dietary TAC intake.

Total polyphenols (TP), dietary flavonoids and lignans were calculated using databases on polyphenol contents in food,[30-32] and Phenol Explorer (Phenol-Explorer: An online comprehensive database on polyphenol contents in foods, Unité de Nutrition Humaine, Clermont-Ferrand, France). Details on the quantification of the dietary intake of these compounds in the EPIC study population can be found elsewhere.[33,34] Adherence to the PAC score was calculated as described by Pounis and colleagues.[12]

Computation of Indexes of Adherence to the MD

Twenty-one MD indexes previously identified in the literature[7] were operationalized to evaluate the adherence to each MD index in the study population. These indexes were: the MD Scale (MDS) in different versions: MDS-1995,[5] MDS-2003,[35] and MDS-2013[36]; the MMD-2005[16]; the Mediterranean Dietary Pattern (MDP) in different versions: MDP-2002,[37] MDP-2003,[38] and MDP-2006[39]; the Mediterranean-Style Dietary Pattern Score (MSDPS)[40]; the MDQI[17]; Italian Mediterranean Index (ITAMED)[41]; the aMED[15]; the Relative MD Score (rMED)[42]; the MD Score in different versions: MD Score-2001,[14] MD Score-2004,[43] MD Score-2005,[44] and MD Score-2007[45]; the Cardioprotective

MD Score (Cardio)[46]; the Mediterranean food pattern of the PREDIMED study (PREDIMED)[47]; the literature-based adher- ence score to the MD[48]; the Mediterranean Lifestyle index (MEDLIFE),[49] of which only the dietary components of the index were considered (ie, the social habits components were removed); and the Mediterranean Diet Serving Score (MDSS).[50] Operationalization of all the indexes was done following the definition provided in the original study. For instance, in the case of the rMED score, each component was calculated considering tertiles of intakes (except for olive oil and alcohol consumption), whereas for the aMED score, sex-specific medians of intake were considered. Points were assigned depending upon the cutoffs considered and the MD components presumed to fit the MD definition provided in the score.

Food groups, foods, and nutrient intakes were considered to compute every index. Overall, vegetables, fruits, legumes, nuts, cereals, fish, olive oil, and moderate alcohol consumption were considered as positive components, whereas meat and processed meat and dairy products were considered as negative components. Intake of food groups and foods was considered in grams per day. For those indexes considering the frequency of consumption in servings on a daily, weekly, or monthly basis, the intake by serving size was multiplied as established in the index. Because the indexes differed in the scales used to assess adherence to the MD, they were equalized into low, medium, and high adherence to the MD categories by tertiles based on the distribution of adherence among the study population (Tertile 1¼low, Tertile 2¼medium, and Tertile 3¼high). Some but not all indexes considered energy-adjusted foods or nutrients in the index

scoring, which was not taken into consideration to allow a standardized comparison of the indexes. Thus, all indexes were operationalized as energy-unadjusted indexes.

Statistical Analysis

To describe baseline characteristics by sex and center, means standard deviation were used for continuous variables and frequencies for categorical variables. Differences across these groups were evaluated by using Student *t* test (or Wilcoxon test where appropriate) and C^2 test, respectively.

The relationship between the indexes was explored using Spearman correlation coefficients (skewness and Shapiro-Wilk test indicated nonnormal distributions of the index scale). Spearman correlation coefficients were further used to create a hierarchical clustering of the MD indexes (tree height¼41.5) based on the dissimiliarty index [1-Abs (correlation)], as distance metric.[51] This hierarchical clustering process consists of grouping the most similar pairs of samples on the basis of their lowest dissimilarity. The strength of agreement between the indexes and weights for agreements were estimated via Cohen's kappa.[52] For the latter, linear weights of the differences in categories (tertiles) were used. Thus, not only the strength of the relationship but also the degree of agreement classification between the MD indexes was evaluated.

The dietary antioxidant profile was calculated as mean intake of the aforementioned antioxidants across the tertiles of adherence to the MD indexes. Geometric mean intakes adjusted for age, sex, center, and total energy intake were estimated by linear regression models. Intakes of dietary antioxidants were previously adjusted for energy intake through the residual method,[53] and log-transformed to approximate a normal distribution. Differences in mean intakes of antioxidant vitamins, TAC, TP, flavonoids, and the PAC score between the MD indexes (considering the highest tertile of adherence to the MD index for comparison purposes) were assessed with the Kruskal-Wallis test. The same procedures were used for analyses by intake of food groups. All analyses were conducted for both sexes combined and separately for men and women in stratified analyses.

Linear regression analysis was used to evaluate the association between each MD adherence index on the continuum (independent variable) with the intake of every dietary antioxidant (dependent variable) in crude and multivariate models adjusted for age, sex, center, energy intake, smoking, body mass index, and physical activity (key variables influencing dietary intake). Standardized beta coefficients were calculated per standard deviation of each score. The R^2 statistic; that is, the coefficient of determination, was extracted from every regression model as a measure of the proportion of the variance that is explained by the independent variable. Differencs by sex were evaluated in stratified analyses to test whether effect measures differ between men and women. The goodness of fit was evaluated by examining the normality of the residuals, as well as the homocedasticity and colinearity between the observed and predicted values.

P values were based on two-sided tests and significance was considered at the 5% level. Furthermore, to control the

rate of false positives, all *P* values were adjusted for multiple comparisons as proposed by Benjamini and Hochberg.[54] All data analyses were performed using Stata statistical software package version 12.0[55] and R version 3.3.2.[56]

RESULTS

Table 1 shows the characteristics of the study population by the MD indexes, their components, and nutrients/ antioxidants. Most women never smoked and half were physically inactive, their daily intake of food and nutrients was lower, and they adhered less to the MD indexes (lower mean adherence) than men. By center, participants of the Gipuzkoa cohort were more frequently smokers, leaner, and physically active. They also showed a higher energy intake, a higher intake of foods and nutrients (except vitamin C), and in general a higher adherence to the MD (in 12 MD indexes). Table 2 shows correlation coefficients between the MD indexes and cluster groups. The strongest correlations (rho≥0.7) were observed between 20 pairs of MD indexes. This supposed 10% of all the correlations analyzed (n¼210). Several other correlation coefficients ranged between 0.5 and 0.7 (35% of the correlations), or were below 0.5 (55% of the correlations).

The main clusters groups rendered included the high- (MMD-2005, MDS-2003, and MDS-2013), the moderate- (MDP-2002, MDP-2006, and rMED; MD Score-2005, MD-Score 2007, and Cardio), and the low-correlated MD in- dexes (MDSPS and MDP-2003), which made up an entirely independent cluster (data not shown). As shown by the Cohen kappa statistics (Table 3), agreement between the in- dexes in tertiles classification was on average relatively high (60% to 80% of participants were classified in the same or adjacent tertiles). Overall, agreement were lowest (agreement <70%) between the MDS indexes and MDP-2003; MDQI, MSDPS, and MD Score-2005; and Cardio. A high proportion of this agreement was due to chance (55% to 65%), with the MSDPS index showing the highest degree in agreement by chance (59% to 65%).

Table 4 shows age, sex, center, and energy-adjusted mean intakes of the antioxidants evaluated in the third tertile of adherence of each index; intakes in the lowest tertile are shown in Table 5 (available at www.jandonline.org). The Figure represents this data for MD indexes with the highest and lowest antioxidant profile and for selected dietary antioxidants. Overall, in the third tertile of adherence there were three MD indexes (MDP-2002, PREDIMED, and aMED) presenting the highest mean intakes of antioxidants vitamins (vitamin C: >115 mg/day, a-tocopherol: >7.0 mg/day, and b carotene: >2,400 mg/day), TAC (TRAP: >1,900 mmol trolox equivalents [TE]/day, FRAP: >6,100 mmol iron/day, TEAC-ABTS: >2,100 mmol TE/day, and ORAC: >7,900 mmol TE/day), TP (>1,090 mg/day), flavonoids (>170 mg/day), and the highest PAC score (>2.75). The Cardio index also ranked among the highest levels of dietary TAC, TP, flavonoids, and vitamin C; the MSDPS index regarding dietary TAC (TRAP, FRAP, and TEAC-ABTS), flavonoids and the PAC score, and the ITAMED index for ORAC, TP, flavonoids, vitamin C, and PAC score. In contrast, values of these antioxidants were notably lower for the MEDLIFE and MDSS indexes.

By intake of foods that are part of the definition of the MD dietary pattern (Table 6, available at www.jandonline.org), it

Table 2. Spearman correlation coefficients between indexes of adherence to the Mediterranean Diet (MD) in two European Prospective into Cancer and Nutrition-Spain cohorts (n¼14,756; 1992-1996)[a]

MD index[b]	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)	(16)	(17)	(18)	(19)	(20)	(21)
(1)	1.00																				
(2)	0.73																				
(3)	0.63	0.82																			
(4)	0.64	0.92	0.80																		
(5)	0.55	0.71	0.62	0.75																	
(6)	0.32	0.33	0.18	0.26	0.41																
(7)	0.52	0.65	0.66	0.69	0.76	0.31															
(8)	0.23	0.23	0.14	0.20	0.27	0.31	0.31														
(9)	e0.50	e0.56	e0.45	e0.40	e0.49	e0.47	e0.48	e0.38													
(10)	0.37	0.46	0.44	0.45	0.58	0.29	0.55	0.29	e0.43												
(11)	0.49	0.66	0.70	0.65	0.61	0.36	0.63	0.23	e0.49	0.53											
(12)	0.62	0.80	0.64	0.82	0.77	0.39	0.78	0.31	e0.56	0.56	0.62										
(13)	0.58	0.57	0.53	0.48	0.45	0.21	0.51	0.15	e0.56	0.45	0.45	0.50									
(14)	0.49	0.64	0.68	0.70	0.74	0.31	0.80	0.15	e0.34	0.53	0.66	0.71	0.44								
(15)	0.40	0.43	0.33	0.40	0.44	0.36	0.46	0.22	e0.48	0.22	0.44	0.49	0.37	0.37							
(16)	0.51	0.54	0.42	0.49	0.54	0.51	0.59	0.41	e0.66	0.49	0.62	0.66	0.52	0.43	0.72						
(17)	0.39	0.43	0.38	0.38	0.44	0.45	0.50	0.35	e0.59	0.43	0.62	0.47	0.46	0.38	0.53	0.76					
(18)	0.44	0.61	0.52	0.62	0.70	0.31	0.61	0.33	e0.47	0.53	0.54	0.67	0.36	0.55	0.36	0.48	0.35				
(19)	0.59	0.65	0.60	0.60	0.50	0.35	0.58	0.29	e0.63	0.40	0.52	0.62	0.63	0.46	0.57	0.70	0.68	0.42			
(20)	0.49	0.63	0.59	0.61	0.57	0.32	0.56	0.33	e0.49	0.49	0.51	0.65	0.43	0.52	0.29	0.47	0.31	0.52	0.49		
(21)	0.38	0.45	0.37	0.47	0.41	0.23	0.50	0.20	e0.31	0.33	0.40	0.54	0.21	0.42	0.32	0.46	0.39	0.43	0.47	0.37	1.00

[a]Correlation coefficients derived from Spearman correlation. All correlation coefficients were statistically significant ($P<0.01$). Correlations ≥0.7 are in boldface type.

[b]These indexes were: (1) the MD Scale-1995[5]; (2) MD Scale-2003[35]; (3) MDS-2013[36]; (4) the Modified MD-2005[16]; (5) the Mediterranean Dietary Pattern-2002[37]; (6) Mediterranean Dietary Pattern-2003[38]; (7) Mediterranean Dietary Pattern-2006[39]; (8) Mediterranean-Style Dietary Pattern Score[40]; (9) the MD Quality Index[17]; (10) Italian Mediterranean Index[41]; (11) the Alternate MD Index[15]; (12) the Relative MD Score[42]; (13) MD Score-2001[14]; (14) MD Score-2004[43]; (15) MD Score-2005[44]; (16) MD Score-2007[45]; (17) the Cardioprotective MD Score[46]; (18) the Mediterranean food pattern of the PREDIMED Study[47]; (19) the literature-based adherence score to the MD[48]; (20) the Mediterranean Lifestyle Index[49] of which only the dietary components of the index were considered (ie, the social habits components were removed); and (21) Mediterranean Diet Serving Score.[50]

Table 3. Agreement (Agr) and expected agreement (Exp Agr) of the index tertiles scoring between Mediterranean Diet (MD) Scale-1995, MD Scale-2003, MD Scale-2013, and modified MD-2005 and all other MD indexes in two European Prospective into Cancer and Nutrition-Spain cohorts (n¼414,756; 1992-1996)

	MD Scale-1995			MD Scale-2003			MD Scale-2013			Modified MD-2005		
MD index	% Agre % Exp Agr	k[a]	*P* value[b]	% Agre % Exp Agr	k[a]	*P* value[b]	% Agre % Exp Agr	k[a]	*P* value[b]	% Agre % Exp Agr	k[a]	*P* value[b]
MD Scale-1995				78.50-57.75	0.49	<0.001	77.77-60.68	0.43	<0.001	77.86-60.21	0.44	<0.001
MD Scale-2003	78.50-57.70	0.49	<0.001				80.42-55.55	0.56	<0.001	85.13-55.20	0.67	<0.001
MD Scale-2013	77.77-60.68	0.43	<0.001	80.42-55.55	0.56	<0.001				83.87-59.08	0.61	<0.001
Modified MD-2005	77.86-60.21	0.44	<0.001	85.13-55.20	0.67	<0.001	83.87-59.08	0.61	<0.001			
MD Pattern-2002	73.70-58.83	0.36	<0.001	76.73-54.88	0.48	<0.001	75.57-57.62	0.42	<0.001	80.95-57.32	0.55	<0.001
MD Pattern-2003	69.52-61.72	0.20	<0.001	66.39-57.38	0.21	<0.001	63.90-59.57	0.11	<0.001	65.56-59.14	0.16	<0.001
MD Pattern-2006	71.47-57.19	0.33	<0.001	74.34-54.07	0.44	<0.001	76.14-56.16	0.46	<0.001	77.48-55.91	0.49	<0.001
MSDPS[c]	69.80-65.13	0.13	<0.001	64.21-58.88	0.13	<0.001	65.81-62.75	0.08	<0.001	66.81-62.22	0.12	<0.001
MD Quality Index[d]	47.02-58.44	e0.27	>0.05	39.05-54.05	e0.33	>0.05	46.45-57.65	e0.26	>0.05	47.13-57.40	e0.24	>0.05
ITAMED[e]	69.97-60.62	0.24	<0.001	69.27-56.01	0.30	<0.001	70.85-59.09	0.29	<0.001	71.03-58.72	0.30	<0.001
Alternate MD Index	75.09-63.40	0.32	<0.001	75.42-57.94	0.42	<0.001	79.78-61.25	0.48	<0.001	78.11-60.77	0.44	<0.001
Relative MD Score	76.70-59.90	0.42	<0.001	80.73-55.39	0.57	<0.001	77.21-58.59	0.45	<0.001	84.49-58.26	0.63	<0.001
MD Score-2001	77.88-63.41	0.40	<0.001	73.32-58.27	0.36	<0.001	74.53-61.07	0.35	<0.001	72.54-60.58	0.30	<0.001
MD Score-2004	73.44-60.70	0.32	<0.001	74.91-56.16	0.43	<0.001	78.91-59.09	0.48	<0.001	79.38-58.72	0.50	<0.001
MD Score-2005	68.68-57.96	0.26	<0.001	67.71-54.56	0.29	<0.001	66.00-56.78	0.21	<0.001	68.22-56.51	0.27	<0.001
MD Score-2007	73.35-59.78	0.34	<0.001	70.95-55.41	0.35	<0.001	69.73-58.44	0.27	<0.001	71.96-58.11	0.33	<0.001
Cardioprotective MD Score	68.82-58.52	0.25	<0.001	68.17-56.08	0.28	<0.001	66.78-56.53	0.24	<0.001	66.67-56.18	0.24	<0.001
PREDIMED[f]	70.70-59.88	0.27	<0.001	76.62-58.74	0.43	<0.001	69.88-56.55	0.31	<0.001	72.95-56.07	0.38	<0.001
L-based[g]	76.31-60.20	0.40	<0.001	75.50-56.39	0.44	<0.001	75.07-58.35	0.40	<0.001	74.57-57.97	0.40	<0.001
MEDLIFE[h]	73.16-60.34	0.32	<0.001	74.00-55.42	0.42	<0.001	75.71-59.11	0.41	<0.001	76.80-58.77	0.44	<0.001
MD Serving Score	69.79-59.62	0.25	<0.001	69.24-56.02	0.30	<0.001	68.04-57.88	0.24	<0.001	71.01-57.52	0.32	<0.001

[a]Cohen's kappa was calculated based on the observed vs the expected agreement considering agreement between the same or adjacent tertiles (weighted kappa). % Agreement ≥0.8 is in boldface type.
[b]*P* value for Cohen's kappa.
[c]MSDPS¼Mediterranean-Style Dietary Pattern Score.
[d]Scored inversely.

[e]ITAMED¼Italian Mediterranean Index.
[f]PREDIMED¼Prevention with MD.
[g]L-based¼literature-based adherence score to the MD.
[h]MEDLIFE¼Mediterranean Lifestyle Index.

Table 4. Adjusted mean daily intakes standard error (SE) of dietary antioxidants in the highest tertile of adherence to the Mediterranean Diet (MD) indexes in the two European Prospective into Cancer and Nutrition-Spain cohorts (1992-1996)[a]

MD index	Sample size in highest tertile[b]	Vitamin C (mg/d)	a-Tocopherol (mg/d)	Beta Carotene (mg/d)	TRAP[c] (mmol trolox equivalents/d)	FRAP[d] (mmol iron/d)	TEAC-ABTS[e] (mmol trolox equivalents/d)	ORAC[f] (mmol trolox equivalents/d)	TP[g] (mg/d)	Flavonoids (mg/d)	PAC Score[h]
		←——————————————————————————————mean SE——————————————————————————————!									
MD Scale-1995	2,404	105 8	6.01 0.34	2,039 178	1,691 137	5,569 361	1,903 137	7,426 441	1,015 60	138 14	2.64 0.43
MD Scale-2003	3,762	93.5 6.0	5.93 0.26	1,910 138	1,664 106	5,384 274	1,843 104	6,411 315	885 43	133 10	2.13 0.28
MD Scale-2013	3,606	113 7	6.92 0.32	2,123 155	1,538 102	5,167 272	1,764 102	7,098 346	998 48	127 10	2.00 0.27
Modified MD-2005	3,814	95.4 6.2	6.28 0.30	1,874 138	1,489 98	5,037 264	1,701 99	6,307 316	882 44	116 9	2.30 0.29
MD Pattern-2002	4,143	155 9	7.12 0.33	2,560 180	2,065 129	6,394 320	2,202 122	9,282 420	1,299 58	191 13	3.09 0.34
MD Pattern-2003	2,714	82.6 5.8	5.68 0.26	1,684 145	1,588 113	4,811 285	1,645 107	5,551 322	766 44	119 10	2.70 0.45
MD Pattern-2006	4,703	113 6	6.33 0.26	2,070 134	1,411 86	4,943 239	1,653 89	7,347 310	1,022 43	122 8	2.15 0.26
MSDPS[i]	1,620	118 12	5.42 0.38	1,740 203	2,012 194	5,940 477	2,121 182	7,672 570	1,061 79	212 20	3.26 0.62
MD Quality Index	5,011	95.2 5.2	6.01 0.23	2,024 129	1,734 99	5,439 255	1,844 94	6,316 266	869 36	129 9	2.63 0.33
ITAMED[j]	3,428	118 8	6.31 0.31	1,836 142	1,781 122	5,536 323	1,908 120	8,013 402	1,082 53	183 14	3.55 0.46
Alternate MD Index	2,247	117 8	7.18 0.40	2,501 214	1,969 150	6,108 389	2,108 144	7,981 456	1,093 62	170 15	2.75 0.44
Relative MD Score	3,781	104 7	6.21 0.27	1,979 139	1,764 110	5,664 285	1,945 108	7,111 342	980 47	146 11	2.53 0.31
MD Score-2001	2,113	115 9	6.21 0.35	2,134 203	1,741 146	5,364 365	1,846 137	7,671 441	1,052 58	149 15	2.62 0.47
MD Score-2004	3,355	100 7	6.49 0.33	1,852 138	1,380 94	4,817 263	1,621 98	6,924 345	960 47	115 9	2.03 0.28
MD Score-2005	4,394	94.2 5.5	5.97 0.25	1,685 113	1,627 100	5,190 260	1,799 99	5,998 274	838 38	129 9	1.94 0.26
MD Score-2007	3,793	114 6	6.53 0.25	2,285 154	1,901 109	5,915 286	2,037 106	7,554 325	1,042 44	161 11	2.20 0.30
Cardioprotective MD Score	3,696	123 6	6.25 0.24	2,094 138	2,071 117	6,085 300	2,156 113	8,170 345	1,109 45	204 13	2.65 0.39
PREDIMED[k]	2,415	141 12	7.45 0.39	2,400 231	2,056 167	6,390 417	2,177 154	8,078 514	1,138 72	173 16	3.48 0.47
L-based[l]	3,330	108 6	5.86 0.26	2,066 143	1,874 125	5,847 319	2,026 122	7,041 316	982 43	142 11	2.12 0.32
MEDLIFE[m]	3,709	81.6 5.7	6.06 0.29	1,670 125	1,448 96	4,716 252	1,571 92	5,656 310	773 42	104 9	2.45 0.32
MD Serving Score	3,566	99.7 6.4	5.80 0.28	1,773 141	1,415 97	4,658 262	1,569 95	6,938 336	962 46	124 9	1.70 0.24
Minimume maximum[n]		82-155	5.42-7.45	1,670-2,560	1,380-2,071	4,658-6,394	1,569-2,202	5,551-9,282	766-1,299	104-212	1.70-3.55

[a]Geometric means were derived from generalized linear models adjusted for age continuous, sex, center, and energy intake continuous. Intakes ranking among the five highest are shown in boldface type.
[b]Reference values in lowest tertile of adherence: MD scale-1995 ≤3; MD scale-2003 ≤4; MD scale-2013 ≤3; Modified MD-2005 ≤3; MD Pattern-2002 ≤24; MD Pattern-2003 ≤12; MD Pattern-2006 ≤18; MSDPS ≤69; MD quality index ≥ 8; ITAMED ≤3; alternate MD index ≤2; relative MD score ≤7; MD score-2001 ≤2; MD score-2004 ≤17; MD score-2005 ≤32; MD score-2007 ≥32; Cardioprotective MD score ≥5; PREDIMED ≤7; L-based ≤9; MEDLIFE ≤8, and MD serving score ≤10.
[c]TRAP¼total radical-trapping antioxidant parameter.
[d]FRAP¼ferric-reducing antioxidant power.
[e]TEAC-ABTS¼Trolox equivalent antioxidant capacity.
[f]ORAC¼oxygen radical antioxidant capacity.
[g]TP¼total polyphenols.
[h]PAC¼polyphenol antioxidant content. Range¼e28 to 28.
[i]MSDPS¼Mediterranean-style dietary pattern score.
[j]ITAMED¼Italian Mediterranean Index.
[k]PREDIMED¼Prevention with MD.

[l]L-based¼literature-based adherence score to MD.
[m]MEDLIFE¼Mediterranean Lifestyle Index.
[n]Differences between extreme values of mean intakes maximum and minimum were all statistically significant at $P<0.001$.

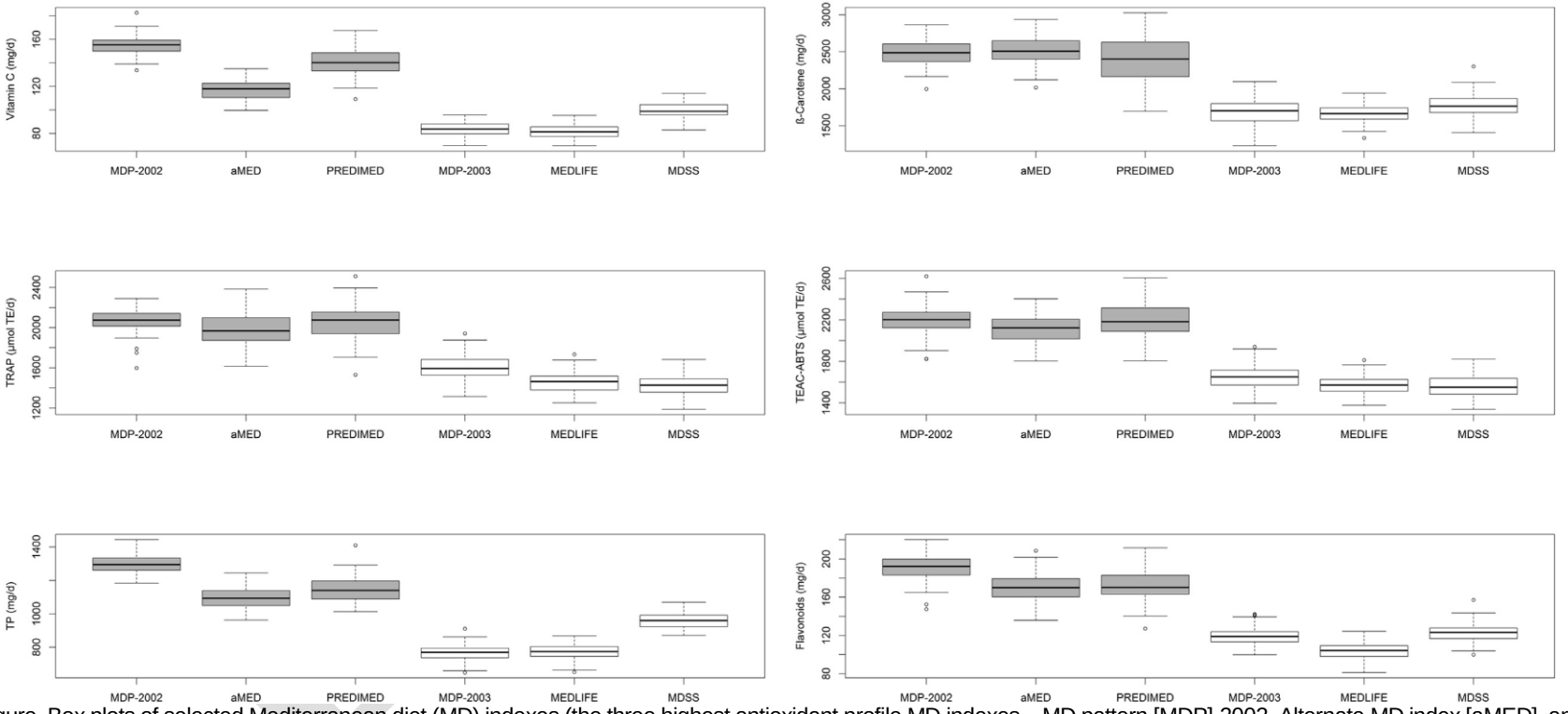

Figure. Box plots of selected Mediterranean diet (MD) indexes (the three highest antioxidant profile MD indexes—MD pattern [MDP]-2002, Alternate MD index [aMED], and Prevention with MD [PREDIMED]—on the left and with grey fills, and the lowest antioxidant profile MD indexes—MDP-2003, Mediterranean Lifestyle Index [MEDLIFE], and MS serving score [MDSS]—on the right and not filled) showing adjusted mean intakes (and corresponding standard error above and below the mean) of dietary antioxidants (vitamin C, beta carotene, and total antioxidant capacity, including total radical-trapping antioxidant parameter [TRAP], trolox equivalent antioxidant capacity [TEAC-ABTS], total polyphenols [TP], and flavonoids). Adjusted mean intakes (geometric means) were adjusted for age, sex, center, and total energy intake, and derived from linear regression models after log transformation to approximate a normal distribution. The bottom and top of the boxes are the first and third quartiles, and the band inside the box is the (normalized) mean value. Outliers are plotted as individual points.

was also observed that MD indexes capturing the highest antioxidant intakes were those showing the highest intake of fruits (MDP-2002, ITAMED, and Cardio: >230 g/day) and vegetables (MDS-1995, MDP-2002, and PREDIMED: >320 g/day), as well as olive oil (>23 mL/day for MDP-2002) and wine (>50 mL/day for PREDIMED); the lowest intakes of these food groups were observed for the MEDLIFE (fruits: 122 g/day) and MDP-2003 (vegetables: 233 g/day) indexes. Intakes of non-MD constituents (meat and meat products) were also highest for the MDP-2002 and PREDIMED indexes. The same MD indexes were, in general, found to be related to a higher mean intake of dietary antioxidants (Tables 7 and 8, available at www.jandonline.org) and food groups in both men and women (data not shown). Differences between extreme values of mean intakes of nutrients and food groups across MD indexes were all statistically significant ($P<0.001$).

Table 9 shows multivariate adjusted regression coefficients on the relationship between the MD indexes and the dietary antioxidants. All MD indexes were positively related with dietary TAC, in terms of TRAP, FRAP, TEAC-ABTS, and ORAC ($P<0.01$). Overall, every 1-standard deviation increment in the adherence of the MD indexes was related to statistically significant increments in intakes of dietary TAC. The indexes producing the highest increments in dietary TAC intake were PREDIMED (TRAP: 0.24 mmol TE/day, FRAP: 0.28 mmol iron/day, TEAC-ABTS: 0.27 mmol TE/day, ORAC: 0.40 mmol TE/day); MDS-1995 (TRAP: 0.22 mmol TE/day, FRAP: 0.26 mmol iron/day, TEAC-ABTS: 0.24 mmol TE/day, and ORAC: 0.34 mmol TE/day); MDS-2003 (TRAP: 0.16 mmol TE/day, FRAP: 0.21 mmol iron/d, TEAC-ABTS: 0.20 mmol TE/day, and ORAC: 0.39 mmol TE/day); and MDP-2002 (TRAP: 0.29 mmol TE/day, FRAP: 0.33 mmol iron/d, TEAC-ABTS: 0.33 mmol TE/day, and ORAC: 0.59 mmol TE/day). Estimates were comparable to those derived from age, sex, center, and energy-adjusted only models (data not shown). The proportion of variance explained by the indexes ranged between 20% and 60% at the maximum among all dietary TAC methods. All MD indexes were also positively ($P<0.001$) related with the other antioxidants, except a-tocopherol for some MD indexes (PREDIMED and MDQI). Three MD indexes, namely MDP-2002, PREDIMED, and aMED, captured overall higher intake levels of dietary antioxidants. Spearman correlation analyses between dietary antioxidants and MD indexes showed that roughly the same MD indexes exhibited the highest correlation coefficients (Table 10, available at www.jandonline.org). The proportion of variance varied largely depending on the MD index and antioxidant evaluated (eg, from 37% to 58% for the PAC score to 7% to 23% for beta carotene). Differences by sex were not apparent (data not shown).

DISCUSSION

In this large study population from to two Spanish EPIC cohorts, adherence to the MD was assessed through 21 indexes, whereby adherence was considered as a latent attribute of the MD dietary pattern. Higher intakes of dietary antioxidant vitamins, TAC, TP, flavonoids, and PAC score were evidenced in the upper level of adherence to the MD indexes compared with the low adherence level. Moreover, irrespective of the MD index, adherence to the MD was related to higher intakes of nutrient antioxidants, although to varying degrees. All of the included MD indexes reflect the traditional MD pattern,[57]

but a few of them, specifically MDP-2002,[37] PREDIMED,[47] and aMED,[15] showed the highest intakes of dietary antioxidants. Although the MD indexes were positively correlated with each other, the strength of the correlation was mostly moderately weak. Different cluster groups were evidenced and differences across MD indexes in the degree of agreement in classification into low, medium, and high adherence groups were also noted.

The MD is a well-known healthy dietary pattern that is associated with a reduced risk of developing inflammatory-related diseases such as cancer.[57,58] *A priori* defined indexes of adherence to the MD have been the subject of considerable amounts of research and study in recent years. As a consequence, a multitude of MD indexes have been developed to improve the indexes' potential for disease risk reduction by accommodating the new evidences gained on healthy MD-like components, to adapt the data of the various studies, and also to encompass all of the existing MD style habits around the Mediterranean basin.[1,7,59] Despite all MD indexes reflecting the traditional MD pattern, their differing scoring schemes may result in significant differences in estimating the intake of food groups and nutrients.[7] This has been shown in the current study with regard to the intake of dietary antioxidants. Dietary antioxidants provided by the MD (eg, phenolic compounds, carotenoids, and vitamin C from fruits and vegetables) are the cornerstones of the anti-inflammatory and antioxidative effects; that is, health-related properties, exerted by this dietary pattern.[59,60] Although these indexes have been validated in several other studies with regard to their potential in reducing disease occurrence (eg, cancer, cardiovascular diseases, diabetes, and neurodegenerative diseases),[40,43,44,48,61] overall and cause-specific mortality,[16,48] as well as associated determinants (ie, obesity),[45] little attention has been paid to evaluating them concurrently with regard to their antioxidant profile. The few studies available on this subject include the study by Davis and colleagues[59] on a quantitative assessment of food groups and nutrients of 15 MD indexes, and the study by Puchau and colleagues[13] on dietary TAC intake according to four MD indexes (n¼153 participants). In the first study,[59] a literature review comparing data reported in studies conducted among different populations, antioxidant mean intakes were reported to vary between two to five times between the MD indexes (eg, flavonoids from 79 to 345 mg/day). In the second study,[13] varying mean adherence levels of the MD Score-2001,[14] the aMED,[15] the MMD-2005,[16] and the MDQI[17] across quintiles of dietary TAC (FRAP) values were also shown. In addition, a weaker correlation was observed between TAC and MDQI.[13] The current study, conducted within a single study population, has also shown that intake of antioxidants varies largely among the MD indexes (eg, flavonoids from 104 to 212 mg/day). Findings of this study also suggest that there is considerable variation in TAC values depending on the MD index, with MDQI[17] being among the indexes showing the lowest mean TAC values. No other study has compared dietary intakes of flavonoids, TP, and vitamins by MD index concurrently in the same study population. However, other antioxidant compounds such as selenium, long-chain n-3 polyunsaturated fatty acids, or plant sterols were not considered in the current study due to lack of data on these nutrients. Overall, three MD indexes (MDP-2002,[37] PREDIMED,[47] and aMED[15]) reflected a higher intake of dietary antioxidant in terms of vitamins (C, a-tocopherol, and beta carotene), TAC

Table 9. Linear regression analyses on the relationship between dietary antioxidants (total antioxidant capacity, antioxidant vitamins, total polyphenols [TP], flavonoids, and polyphenol antioxidant content [PAC] score) and the Mediterranean Diet (MD) indexes in the two European Prospective into Cancer and Nutrition-Spain cohorts (n¼14,756; 1992-1996)[a]

	Total Radical-Trapping Antioxidant Parameter (mmol trolox equivalents/d)			Ferric-Reducing Antioxidant Power (mmol iron/d)			Trolox Equivalent Antioxidant Capacity (mmol trolox equivalents/d)			Oxygen Radical Antioxidant Capacity (mmol trolox equivalents/d)		
MD index	b	95% CI	R^2	b	95% CI	R^2	b	95% CI	R^2	b	95% CI	R^2
MD Scale-1995	.22	(.21 to .24)	0.37	.26	(.25 to .27)	0.43	.24	(.23 to .25)	0.38	.34	(.33 to .35)	0.33
MD Scale-2003	.16	(.15 to .18)	0.34	.21	(.20 to .23)	0.40	.20	(.18 to .21)	0.36	.39	(.37 to .40)	0.35
MD Scale-2013	.14	(.13 to .16)	0.34	.22	(.20 to .23)	0.40	.20	(.19 to .21)	0.36	.40	(.38 to .41)	0.35
Modified MD-2005	.14	(.13 to .16)	0.33	.19	(.18 to .20)	0.39	.18	(.17 to .20)	0.35	.39	(.37 to .40)	0.33
MD Pattern-2002	.29	(.27 to .30)	0.37	.33	(.32 to .35)	0.44	.33	(.31 to .34)	0.39	.59	(.57 to .60)	0.44
MD Pattern-2003	.05	(.04 to .07)	0.32	.09	(.07 to .10)	0.37	.08	(.07 to .09)	0.33	.24	(.22 to .25)	0.27
MD Pattern-2006	.02	(.01 to .03)	0.32	.11	(.09 to .12)	0.37	.09	(.08 to .11)	0.33	.45	(.44 to .47)	0.37
MSDPS[b]	.15	(.14 to .17)	0.34	.16	(.15 to .17)	0.39	.17	(.16 to .18)	0.35	.24	(.23 to .25)	0.27
MD Quality Index[c]	e.16	(e.18; e.15)	0.35	e.21	(e.23 to e.20)	0.41	e.20	(e.21 to e.19)	0.36	e.39	(e.38 to e.41)	0.40
ITAMED[d]	.09	(.08 to .11)	0.33	.13	(.12 to .14)	0.38	.14	(.13 to .16)	0.34	.46	(.45 to .47)	0.42
Alternate MD Index	.11	(.10 to .12)	0.33	.18	(.16 to .19)	0.39	.17	(.16 to .19)	0.35	.40	(.39 to .42)	0.37
Relative MD Score	.13	(.11 to .14)	0.33	.18	(.17 to .19)	0.39	.17	(.16 to .19)	0.35	.41	(.40 to .43)	0.36
MD Score-2001	.08	(.07 to .09)	0.33	.13	(.12 to .15)	0.38	.12	(.11 to .13)	0.34	.42	(.41 to .43)	0.39
MD Score-2004	.03	(.02 to .05)	0.32	.12	(.10 to .13)	0.37	.11	(.09 to .12)	0.33	.44	(.42 to .45)	0.35
MD Score-2005	.10	(.08 to .11)	0.33	.14	(.12 to .15)	0.38	.13	(.12 to .14)	0.34	.22	(.21 to .23)	0.26
MD Score-2007	.03	(.02 to .05)	0.32	.11	(.09 to .12)	0.37	.11	(.09 to .12)	0.34	.45	(.43 to .46)	0.41
Cardioprotective MD Score	.03	(.02 to .05)	0.32	.10	(.09 to .11)	0.37	.11	(.09 to .12)	0.34	.47	(.46 to .48)	0.42
PREDIMED[e]	.24	(.22 to .25)	0.37	.28	(.27 to .29)	0.43	.27	(.26 to .29)	0.39	.40	(.39 to .42)	0.35
L-based[f]	.10	(.08 to .11)	0.33	.15	(.14 to .16)	0.39	.14	(.13 to .16)	0.34	.41	(.39 to .42)	0.38
MEDLIFE[g]	.15	(.14 to .16)	0.34	.19	(.17 to .20)	0.40	.18	(.17 to .19)	0.35	.32	(.30 to .33)	0.31
MD Serving Score	.04	(.02 to .05)	0.32	.07	(.06 to .08)	0.37	.07	(.06 to .08)	0.33	.18	(.17 to .20)	0.25

	Vitamin C (mg/d)			a-Tocopherol (mg/d)			Beta Carotene (mg/d)			TP (mg/d)			Flavonoids (mg/d)			PAC Score		
	b	95% CI	R^2	b	95% CI	R^2	b	95% CI	R^2	b	95% CI	R^2	b	95% CI	R^2	b	95% CI	R^2
MD Scale-1995	.31	(.29 to .32)	0.15	.08	(.07 to .10)	0.34	.21	(.20 to .23)	0.10	.35	(.33 to .36)	0.30	.22	(.21 to .24)	0.26	.37	(.36 to .39)	0.46
MD Scale-2003	.36	(.35 to .38)	0.18	.11	(.10 to .13)	0.34	.27	(.26 to .29)	0.12	.40	(.39 to .42)	0.32	.20	(.19 to .22)	0.25	.38	(.37 to .39)	0.45

MD Scale-2013	.35	(.33 to .36)	0.16	.30	(.29 to .31)	0.41	.26	(.24 to .28)	0.11	.41	(.39 to .42)	0.33	.19	(.18 to .21)	0.25	.34	(.33 to .35)	0.43

(*continued on next page*)

Table 9. Linear regression analyses on the relationship between dietary antioxidants (total antioxidant capacity, antioxidant vitamins, total polyphenols [TP], flavonoids, and polyphenol antioxidant content [PAC] score) and the Mediterranean Diet (MD) indexes in the two European Prospective into Cancer and Nutrition-Spain cohorts (n¼14,756; 1992-1996)[a] (*continued*)

	Vitamin C (mg/d)			a-Tocopherol (mg/d)			Beta Carotene (mg/d)			TP (mg/d)			Flavonoids (mg/d)			PAC Score		
	b	95% CI	R^2	b	95% CI	R^2	b	95% CI	R^2	b	95% CI	R^2	b	95% CI	R^2	b	95% CI	R^2
Modified MD-2005	.38	(.37 to .40)	0.17	.10	(.09 to .12)	0.34	.31	(.29 to .33)	0.13	.41	(.39 to .42)	0.30	.19	(.18 to .21)	0.24	.39	(.37 to .40)	0.43
MD Pattern-2002	.65	(.63 to .66)	0.33	.08	(.07 to .10)	0.34	.52	(.50 to .53)	0.23	.62	(.61 to .64)	0.44	.36	(.35 to .38)	0.30	.62	(.61 to .63)	0.58
MD Pattern-2003	.26	(.25 to .28)	0.13	e.10	(e.11 to e.09)	0.34	.27	(.25 to .28)	0.12	.25	(.24 to .27)	0.25	.11	(.10 to .13)	0.23	.24	(.23 to .25)	0.38
MD Pattern-2006	.44	(.42 to .45)	0.20	.08	(.06 to .09)	0.34	.36	(.34 to .37)	0.15	.47	(.46 to .49)	0.35	.13	(.12 to .15)	0.23	.33	(.32 to .35)	0.40
MSDPS	.21	(.20 to .23)	0.11	e.11	(e.12 to e.10)	0.35	.10	(.08 to .11)	0.07	.25	(.24 to .26)	0.25	.19	(.17 to .20)	0.25	.28	(.27 to .30)	0.40
MD Quality Index[c]	e.40	(e.42 to e.39)	0.21	.01	(.01 to .02)	0.33	e.27	(e.29 to e.26)	0.13	e.46	(e.46 to e.45)	0.39	e.23	(e.25 to e.22)	0.27	e.36	(e.37 to e.34)	0.45
ITAMED	.43	(.42 to .45)	0.24	.08	(.07 to .10)	0.34	.29	(.27 to .31)	0.14	.47	(.46 to .48)	0.40	.26	(.25 to .28)	0.28	.34	(.33 to .36)	0.44
Alternate MD Index	.40	(.39 to .42)	0.22	.21	(.20 to .22)	0.38	.34	(.32 to .35)	0.17	.42	(.41 to .44)	0.36	.20	(.25 to .28)	0.25	.36	(.35 to .37)	0.45
rMED	.41	(.39 to .42)	0.20	.04	(.03 to .06)	0.33	.32	(.30 to .34)	0.14	.43	(.42 to .45)	0.34	.19	(.17 to .21)	0.24	.39	(.38 to .41)	0.45
MD Score-2001	.36	(.34 to .37)	0.18	.09	(.07 to .10)	0.34	.27	(.25 to .29)	0.13	.43	(.42 to .44)	0.36	.18	(.16 to .19)	0.24	.28	(.27 to .29)	0.40
MD Score-2004	.41	(.39 to .43)	0.18	.21	(.19 to .22)	0.36	.31	(.29 to .33)	0.12	.45	(.44 to .47)	0.33	.15	(.13 to .17)	0.23	.33	(.31 to .34)	0.40
MD Score-2005	.23	(.21 to .24)	0.11	e.06	(e.07 to e.04)	0.34	.17	(.15 to .18)	0.08	.24	(.22 to .25)	0.24	.11	(.10 to .12)	0.23	.25	(.23 to .26)	0.38
MD Score-2007	.46	(.44 to .47)	0.26	.02	(.01 to .04)	0.33	.35	(.34 to .37)	0.17	.47	(.46 to .48)	0.40	.17	(.16 to .19)	0.24	.34	(.33 to .35)	0.44
Cardioprotective MD Score	.49	(.48 to .50)	0.28	.05	(.04 to .06)	0.34	.34	(.33 to .36)	0.16	.50	(.49 to .51)	0.41	.21	(.20 to .23)	0.26	.35	(.33 to .36)	0.44
PREDIMED	.39	(.38 to .41)	0.19	.01	(.01 to .03)	0.33	.31	(.29 to .33)	0.13	.41	(.40 to .43)	0.32	.27	(.26 to .29)	0.27	.45	(.44 to .46)	0.49
L-based	.39	(.38 to .41)	0.21	.04	(.03 to .06)	0.33	.27	(.26 to .29)	0.13	.43	(.41 to .44)	0.36	.19	(.18 to .21)	0.25	.32	(.30 to .33)	0.42
MEDLIFE	.28	(.27 to .30)	0.14	.06	(.04 to .07)	0.34	.25	(.23 to .27)	0.11	.32	(.32 to .34)	0.29	.16	(.15 to .17)	0.24	.31	(.29 to .32)	0.41
MD Serving Score	.22	(.21 to .24)	0.11	e.03	(e.04 to e.01)	0.33	.13	(.12 to .15)	0.07	.20	(.18 to .22)	0.22	.08	(.07 to .10)	0.22	.22	(.21 to .24)	0.37

[a]*P* values were statistically significant, Benjamini-Hochberg correction ($P<0.001$) and MD pattern-2006 for total radical-trapping antioxidant parameter ($P<0.05$), except MD quality index and PREDIMED for a-tocopherol ($P>0.05$). Estimates were adjusted for age (continuous), sex, center, energy intake (continuous), body mass index (continuous), smoking status (never, current, former, missing for 7 observations), and physical activity (inactive, moderately inactive, moderately active, active). The five highest antioxidant intake increments are shown in boldface type.

[b]MSDPS¼Mediterranean-Style Dietary Pattern Score.

[c]Scored inversely; that is, a higher score relates to a lower adherence to the MD.

[d]ITAMED¼Italian Mediterranean Index.

[e]PREDIMED¼Prevention with MD.

[f]L-based¼literature-based adherence score to the MD.

[g]MEDLIFE¼Mediterranean Lifestyle Index.

(TRAP, FRAP, TEAC-ABTS, and ORAC), TP, and flavonoids (including PAC score[12]) when comparing mean intakes in the highest tertile of adherence. On the contrary, the MEDLIFE[49] and MDSS[50] indexes showed the poorest antioxidant profile. Furthermore, increasing levels of adherence to the MD indexes (comparison between Tertile 1 and Tertile 3), were generally related to higher intake levels of the antioxidants (Table 4 and Table 5 [available at www.jandonline.org]), specially the three top MD indexes aforementioned. These indexes have also shown a relationship with antioxidants in other studies: aMED[15] with dietary and serum beta carotene[62] and PREDIMED[47] and MD Score-2005[44] with dietary and plasma TAC,[63,64] among others. Evidence from other studies also supports the beneficial effects of an MD for reducing risk of cancer, cardiovascular diseases, and other chronic noncommunicable diseases.[48]

As noted above, the differences in MD indexes concerning food groups components, scoring schemes in quantitative measures (grams per day or servings per day), and cutoffs (fixed amounts or population distributions) may explain the differences encountered in the levels of intakes of foods and antioxidants. A clear illustration of this effect was observed among some MD indexes (ie, MDS-1995[5] and its modifications MDS-2003[35] and MMD-2005[16]). For instance, the MDS-1995[5] considered sex-specific medians of vegetable intake, whereas the MDS-2003[35] version adopted populationwide medians, among other differences.[7,59] Indeed, as shown in the current study, mean intake of vegetables in the third tertile of adherence to the MD was lower in the MDS-2003[35] index compared with the MDS-1995[5] index. The many other differences among the MD indexes reflected by food and nutrient intakes shown here confirm that great variations exist in the food/nutrient antioxidant profile. Such differences not only influence variations in conformity to the traditional MD definition, but could also influence health outcomes differently.

Findings of this study also support that MD indexes are not highly correlated with each other. In fact, as has been reported in another study that compared the correlation and reliability of 10 MD indexes in a population sample of 336 participants,[8] about half of the correlations between the MD indexes were weak (rho <0.5). The reasons for this weak tie between the MD indexes are, again, most probably due to the wide differences in the MD indexes' scoring schemes.[7,8] This study showed that the correlation strength of the MD indexes was high among those sharing common features, either the classic MD indexes (ie, the MDS series) or the MD indexes focusing on novel MD components (ie, L-based[48] and MDSS[50]). These groups comprised distinctive cluster groups. On the other hand, despite that the degree of adherence to the MD indexes was similar on average, significant differences among them were seen with regard to ranking agreement in tertile groups, revealing, once again, that the existing MD indexes are extremely uneven.

The limitations of this study are inherent to the definition of the MD indexes themselves. At present, *a priori* defined indexes allow encompassing the dietary complexity of the whole diet. However, they are difficult to replicate in other studies due to variations in assessments of food and nutrient intakes.[65] Thus, findings of the current study may not be generalizable to other settings. Because this was a cross-sectional study, it is not possible to assess causality, nor can

any conclusion be drawn on effects exerted by the MD regarding antioxidant intake. Also, given that tertiles of adherence to the MD indexes were considered, the fact that certain MD indexes achieved a better adherence fit cannot be discarded. However, using other categories for comparison of nutrient intake among MD indexes (observed or score range divided into three) yielded the same results (data not shown). Strengths of this study include the methodical approach used to concurrently compare a group of MD indexes in the same study population, considering tertiles of adherence to the MD indexes, issues of inter-MD index concordance, and modeling the relationship between adherence to the MD indexes and the antioxidant profiles. This study considered an ample set of dietary antioxidants (vitamins, TP, and fla- vonoids) as well as global indicators accounting for the di- etary antioxidant potential (TAC and PAC score[12]). In addition to carrying out this study in a large population sample, the assessment of dietary intake by means of the diet history method and extensive food composition data sources is another added value. Nonenergy-adjusted MD indexes according to tertiles were used to base the analyses on similar comparison groups, estimating further adjusted dietary antioxidant levels.

CONCLUSIONS

This is the first study that has applied a wide range of *a priori* MD indexes to perform a comparative study of the dietary antioxidant profiles. Although the basis for all these indexes is a mostly plant-based dietary pattern, they differ regarding their operationalization and definition. This heterogeneity was manifest by the weak-to-moderate correlations among the MD indexes. Moreover, differences in intake levels of dietary antioxidants were observed according to the MD in- dex and some of the evaluated MD indexes showed a higher antioxidant profile. However, the extent to which these dif- ferences among MD indexes influence health determinants is unclear. Future research needs in the area include compara- tive evaluations of MD indexes regarding disease outcomes and nutrient intake.

References

1. Trichopoulou A, Martínez-González MA, Tong TY, et al. Definitions and potential health benefits of the Mediterranean diet: Views from experts around the world. *BMC Med*. 2014;12:112.
2. Saura-Calixto F, Goñi I. Definition of the Mediterranean diet based on bioactive compounds. *Crit Rev Food Sci Nutr*. 2009;49(2):145-152.
3. Kaulmann A, Bohn T. Carotenoids, inflammation, and oxidative stress; implications of cellular signaling pathways and relation to chronic disease prevention. *Nutr Res*. 2017;34(11):907-929.
4. Shahidi F, Ambigaipalan P. Phenolics and polyphenolics in foods, beverages and spices: Antioxidant activity and health effects. A review. *J Funct Food*. 2015;18:820-897.
5. Trichopoulou A, Kouris-Blazos A, Wahlqvist ML, et al. Diet and overall survival in elderly people. *BMJ*. 1995;311(7018):1457-1460.
6. Bach A, Serra-Majem L, Carrasco JL, et al. The use of indexes evaluating the adherence to the Mediterranean diet in epidemiological studies: A review. *Public Health Nutr*. 2006;9(1A):132-146.
7. Hernández Ruiz A, García-Villanova B, Guerra Hernández EJ, Amiano P, Azpiri M, Molina Montes E. Description of indexes based on the adherence to the Mediterranen dietary pattern: A review. *Nutr Hosp*. 2015;32(5):1872-1884.
8. Milà-Villarroel R, Bach-Faig A, Puig J, et al. Comparison and evaluation of the reliability of indexes of adherence to the Mediterranean diet. *Public Health Nutr*. 2011;14(12A):2338-2345.

9. Serafini M, Del Rio D. Understanding the association between dietary antioxidants, redox status and disease: Is the total antioxidant capacity the right tool? *Redox Rep*. 2004;9(3):145-152.
10. Perez-Jimenez J, Diaz-Rubio ME, Saura-Calixto F. Contribution of macromolecular antioxidants to dietary antioxidant capacity: A study in the Spanish Mediterranean diet. *Plant Foods Hum Nutr*. 2015;70(4):365-370.
11. Bartosz G. Non-enzymatic antioxidant capacity assays: Limitations of use in biomedicine. *Free Radic Res*. 2010;44(7):711-720.
12. Pounis G, Di Castelnuovo A, Bonaccio M, et al. Flavonoid and lignan intake in a Mediterranean population: Proposal for a holistic approach in polyphenol dietary analysis, the Moli-sani Study. *Eur J Clin Nutr*; 2015;July:1-8.
13. Puchau B, Zulet MA, De Echávarri AG, Hermsdorff HHM, Martínez JA. Dietary total antioxidant capacity: A novel indicator of diet quality in healthy young adults. *J Am Coll Nutr*. 2009;28(6):648-656.
14. Woo J, Woo KS, Leung SSF, et al. The Mediterranean score of dietary habits in Chinese populations in four different geographical areas. *Eur J Clin Nutr*. 2001;55(3):215-220.
15. Fung TT, McCullough ML, Newby PK, et al. Diet-quality scores and plasma concentrations of markers of inflammation and endothelial dysfunction. *Am J Clin Nutr*. 2005;82(1):163-173.
16. Trichopoulou A, Orfanos P, Norat T, et al. Modified Mediterranean diet and survival: EPIC-elderly prospective cohort study. *BMJ*. 2005;330(7498):991-998.
17. Scali J, Richard A, Gerber M. Diet profiles in a population sample from Mediterranean southern France. *Public Health Nutr*. 2001;4(2):173-182.
18. Azzini E, Polito A, Fumagalli A, Intorre F, Venneria E, Durazzo A, et al. Mediterranean diet effect: An Italian picture. *Nutr J*. 2011;10(1):125.
19. Riboli E, Hunt K, Slimani N, Ferrari P, Norat T, Fahey M, et al. European Prospective Investigation into Cancer and Nutrition (EPIC): Study populations and data collection. *Public Health Nutr*. 2003;5(6B):1113-1124.
20. González CA, Navarro C, Martínez C, et al. El estudio prospectivo Europeo sobre cáncer y nutrición (EPIC). *Rev Esp Salud Publica*. 2004;78(2):167-176.
21. Markers B. Relative validity and reproducibility of a diet history questionnaire in Spain. III. Biochemical markers. EPIC Group of Spain. European Prospective Investigation into Cancer and Nutrition. *Int J Epidemiol*. 1997;26(suppl 1):S110-S117.
22. Slimani N, Deharveng G, Unwin I, 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(9):1037-1056.
23. Haftenberger M, Lahmann PH, Panico S, et al. Overweight, obesity and fat distribution in 50- to 64-year-old participants in the European Prospective Investigation into Cancer and Nutrition (EPIC). *Public Health Nutr*. 2002;5(6B):1147-1162.
24. Wareham NJ, Jakes RW, Rennie KL, et al. Validity and repeatability of a simple index derived from the short physical activity questionnaire used in the European prospective investigation into cancer and nutrition (EPIC) study. *Public Health Nutr*. 2003;6(4):407-413.
25. Pellegrini N, Serafini M, Colombi B, et al. Total antioxidant capacity of plant foods, beverages and oils consumed in Italy assessed by three different in vitro assays. *J Nutr*. 2003;133(9):2812-2819.
26. Pellegrini N, Serafini M, Salvatore S, Del Rio D, Bianchi M, Brighenti F. Total antioxidant capacity of spices, dried fruits, nuts, pulses, cereals and sweets consumed in Italy assessed by three different in vitro assays. *Mol Nutr Food Res*. 2006;50(11):1030-1038.
27. Haytowitz D, Bhagwat S. USDA Database for the Oxygen Radical Absorbance Capacity (ORAC) of selected foods, Release 2. http://www.ars.usda.gov/ba/bhnrc/ndl. Published May 2010. Accessed September 20, 2015.
28. Delgado-Andrade C, Morales FJ. Unraveling the contribution of melanoidins to the antioxidant activity of coffee brews. *J Agric Food Chem*. 2005;53(5):1403-1407.
29. Morales FJ, Somoza V, Fogliano V. Physiological relevance of dietary melanoidins. *Amino Acids*. 2012;42(4):1097-1109.
30. Human B. USDA Database for the flavonoid content of selected foods. Release 2:1-131. http://www.ars.usda.gov//Data/Flavonoid_.pdf. Accessed September 20, 2015.

31. Bhagwat S, Haytowitz DB, Holden JM. USDA Database for the Isoflavone Content of selected foods. http://www.ars.usda.gov/SP2UserFiles/Place/12354500/Data/isoflav/Isoflav_R2.pdf. Accessed September 20, 2015.
32. USDA Database for the poanthocyanidin content of selected foods. https://www.ars.usda.gov/ARSUserFiles/80400525/Data/PA/PA.pdf. Accessed September 20, 2015.
33. Zamora-Ros R, Jimenez C, Cleries R, et al. Dietary flavonoid and lignan intake and mortality in a Spanish cohort. *Epidemiology*. 2013;24(5):726-733.
34. Zamora-Ros R, Knaze V, Luján-Barroso L, et al. Estimated dietary intakes of flavonols, flavanones and flavones in the European Prospective Investigation into Cancer and Nutrition (EPIC) 24 hour dietary recall cohort. *Br J Nutr*. 2011;106(12):1915-1925.
35. Trichopoulou A, Costacou T, Bamia C, Trichopoulos D. Adherence to a Mediterranean diet and survival in a Greek population. *N Engl J Med*. 2003;348(6):2599-2608.
36. Asghari G, Mirmiran P, Hosseni-Esfahani F, Nazeri P, Mehran M, Azizi F. Dietary quality among tehranian adults in relation to lipid profile: Findings from the tehran lipid and glucose study. *J Health Popul Nutr*. 2013;31(1):37-48.
37. Martínez-González MA, Fernández-Jarne E, Serrano-Martínez M, Marti A, Martinez JA, Martín-Moreno JM. Mediterranean diet and reduction in the risk of a first acute myocardial infarction: An operational healthy dietary score. *Eur J Nutr*. 2002;41(4):153-160.
38. Ciccarone E, Di Castelnuovo A, Salcuni M, et al. A high-score Mediterranean dietary pattern is associated with a reduced risk of peripheral arterial disease in Italian patients with type 2 diabetes. *J Thromb Haemost*. 2003;1(8):1744-1752.
39. Sánchez-Villegas A, Bes-Rastrollo M, Martínez-González MA, Serra-Majem L. Adherence to a Mediterranean dietary pattern and weight gain in a follow-up study: The SUN cohort. *Int J Obes (Lond)*. 2006;30(2):350-358.
40. Rumawas ME, Dwyer JT, McKeown NM, Meigs JB, Rogers G, Jacques PF. The development of the Mediterranean-style dietary pattern score and its application to the American diet in the Framingham Offspring Cohort. *J Nutr*. 2009;139(6):1150-1156.
41. Agnoli C, Krogh V, Grioni S, et al. A priorie‐defined dietary patterns are associated with reduced risk of stroke in a large Italian cohort. *J Nutr*. 2011;141(8):1552-1558.
42. Buckland G, González CA, Agudo A, et al. Adherence to the Mediterranean diet and risk of coronary heart disease in the spanish EPIC cohort study. *Am J Epidemiol*. 2009;170(12):1518-1529.
43. Schroder H, Marrugat J, Vila J, MI C, Elosua R. Adherence to the traditional Mediterranean diet is inversely associated with body mass index and obesity in a Spanish population. *J Nutr*. 2004;134:3355-3361.
44. Pitsavos C, Panagiotakos DB, Tzima N, Chrysohoou C, Economou M. Adherence to the Mediterranean diet is associated with total antioxidant capacity in healthy adults: The ATTICA study. *Am J Clin Nutr*. 2005;82(3):694-699.
45. Panagiotakos DB, Pitsavos C, Arvaniti F, Stefanadis C. Adherence to the Mediterranean food pattern predicts the prevalence of hypertension, hypercholesterolemia, diabetes and obesity, among healthy adults; the accuracy of the MedDietScore. *Prev Med*. 2007;44(4):335-340.
46. Martínez-González MA, Fernández-Jarne E, Serrano-Martínez M, Wright M, Gomez-Gracia E. Development of a short dietary intake questionnaire for the quantitative estimation of adherence to a cardioprotective Mediterranean diet. *Eur J Clin Nutr*. 2004;58(11):1550-1552.
47. Schroder H, Fito M, Estruch R, et al. A short screener is valid for assessing Mediterranean diet adherence among older spanish men and women. *J Nutr*. 2011;141(6):1140-1145.
48. Sofi F, Macchi C, Abbate R, Gensini GF, Casini A. Mediterranean diet and health status: an updated meta-analysis and a proposal for a literature-based adherence score. *Public Health Nutr*. 2013;17(12):2769-2782.
49. Sotos-Prieto M, Moreno-Franco B, 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;18(2):1-9.
50. Monteagudo C, Mariscal-Arcas M, Rivas A, Lorenzo-Tovar ML, Tur JA, Olea-Serrano F. Proposal of a Mediterranean diet serving score. *PLoS One*. 2015;10(6):e0128594.

51. McLachlan GJ. Cluster analysis and related techniques in medical research. *Stat Methods Med Res*. 1992;1(1):27-48.
52. Cohen J. A Coefficient of agreement for nominal scales. *Educ Psychol Meas*. 1960;20(1):37-46.
53. Willett WC, Howe GR, Kushi L. Adjustment for total energy intake in epidemiologic studies. *Am J Clin Nutr*. 1997;65(suppl):1220S-1228S.
54. Benjamini Y, Hochberg Y. Controlling the false discovery rate: A practical and powerful approach to multiple testing. *J R Stat Soc Ser B*. 1995;57(1):289-300.
55. Stata Statistical Software Release 12. Cary, NC: StataCorp; 2011.
56. R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2014.
57. Martinez-Gonzalez MA, Martin-Calvo N. Mediterranean diet and life expectancy; beyond olive oil, fruits, and vegetables. *Curr Opin Clin Nutr Metab Care*. 2016;19(6):401-407.
58. Gotsis E, Anagnostis P, Mariolis A, Vlachou A, Katsiki N, Karagiannis A. Health benefits of the Mediterranean diet: An update of research over the last 5 years. *Angiology*. 2015;66(4):304-318.
59. Davis C, Bryan J, Hodgson J, Murphy K. Definition of the mediterranean diet: A literature review. *Nutrients*. 2015;7(11):9139-9153.
60. Parkinson L, Cicerale S. The health benefiting mechanisms of virgin olive oil phenolic compounds. *Molecules*. 2016;21(12):1734.
61. Schwingshackl L, Hoffmann G. Adherence to Mediterranean diet and risk of cancer: A systematic review and meta-analysis of observational studies. *Int J Cancer*. 2014;135(8):1884-1897.
62. Witkowska A, Zujko ME, Mironczuk-Chodakowska I. The effect of a Mediterranean diet model on serum beta-carotene concentration. A preliminary assessment. *Rocz Panstw Zakl Hig*. 2013;64(2):123-127.
63. Razquin C, Martinez JA, Martinez-Gonzalez MA, Mitjavila MT, Estruch R, Marti A. A 3 years follow-up of a Mediterranean diet rich in virgin olive oil is associated with high plasma antioxidant capacity and reduced body weight gain. *Eur J Clin Nutr*. 2009;63(12):1387-1393.
64. Zamora-Ros R, Serafini M, Estruch R, Lamuela-Raventos RM, Martínez-González MA, Salas-Salvado J, et al. Mediterranean diet and non enzymatic antioxidant capacity in the PREDIMED study: Evidence for a mechanism of antioxidant tuning. *Nutr Metab Cardiovasc Dis*. 2013;23(12):1167-1174.
65. Kant AK. Dietary patterns and health outcomes. *J Am Diet Assoc*. 2004;104(4):615-635.

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STATEMENT OF POTENTIAL CONFLICT OF INTEREST

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AUTHOR CONTRIBUTIONS

A. Hernández Ruiz, B. García-Villanova, and E. Molina-Montes drafted the manuscript. A. Hernández Ruiz and E. Molina-Montes performed the statistical analyses. E. Molina-Montes, E. Guerra-Hernández, P. Amiano, and B. García-Villanova conceived and designed the study. M.-J. Sánchez and M. Dorronsoro participated in the recruitment of the participants and collected the data. All authors gave conceptual advice and all reviewed and approved the final manuscript.

Table 5. Adjusted mean daily intakes ± standard error (SE) of dietary antioxidants in the lowest tertile of adherence to the Mediterranean Diet (MD) indexes in the two European Prospective into Cancer and Nutrition-Spain cohorts (1992-1996)[a]

MD index	Sample size of lowest tertile[b]	Vitamin C (mg/d)		a-Tocopherol (mg/d)		Beta Carotene (mg/d)		TRAP[c] (mmol trolox equivalents/d)		FRAP[d] (mmol iron/d)		TEAC-ABTS[e] (mmol trolox equivalents/d)		ORAC[f] (mmol trolox equivalents/d)		TP[g] (mg/d)		Flavonoids (mg/d)		PAC Score[h]	
		←								mean		SE									→
MD Scale-1995	5,591	57.9	3.6	4.60	0.21	1,093	72	1,035	65	3,417	174	1,135	65	3,904	209	529	29	77.7	6.6	1.44	0.25
MD Scale-2003	2,994	55.5	2.9	4.47	0.17	1,050	57	1,034	56	3,390	147	1,130	55	3,677	160	500	22	73.5	5.2	1.72	0.26
MD Scale-2013	4,870	52.8	3.6	4.13	0.18	1,023	73	1,111	79	3,531	200	1,165	74	3,503	207	475	28	76.0	7.4	1.66	0.35
Modified MD-2005	4,855	55.9	3.7	4.03	0.30	1,147	82	1,206	86	3,801	221	1,275	83	3,881	224	517	29	83.5	8.9	2.15	0.52
MD Pattern-2002	5,627	59.0	3.5	4.07	0.19	1,084	69	1,195	75	3,715	187	1,236	70	3,869	200	520	26	80.6	7.1	1.87	0.49
MD Pattern-2003	2,714	44.3	2.9	4.26	0.20	758	50	802	54	2,860	153	938	56	2,975	162	414	22	53.8	4.7	1.60	0.24
MD Pattern-2006	6,057	59.9	3.7	4.39	0.20	1,192	77	1,146	74	3,733	194	1,231	71	3,934	205	534	27	78.7	6.6	2.20	0.38
MSDPS[i]	4,967	63.1	4.1	5.00	0.25	1,137	82	1,163	78	3,831	205	1,278	77	3,883	213	540	29	73.2	6.4	1.55	0.25
MD Quality Index	4,534	46.9	3.2	4.10	0.22	818	61	810	60	2,796	164	924	62	2,996	173	417	24	56.7	5.3	1.11	0.21
ITAMED[j]	5,430	66.4	3.7	4.42	0.20	1,156	73	1,781	122	3,482	176	1,173	66	4,218	197	579	27	81.3	6.4	1.27	0.23
Alternate MD Index	5,328	53.2	3.4	4.10	0.19	992	68	1,050	75	3,427	190	1,136	72	3,495	188	473	25	70.4	6.5	1.60	0.28
Relative MD Score	4,786	53.5	3.5	4.22	0.21	1,045	72	1,004	71	3,305	188	1,089	69	3,600	200	482	26	68.5	6.4	1.67	0.34
MD Score-2001	5,688	43.0	2.7	4.17	0.19	899	56	911	60	3,015	159	997	59	2,968	157	402	21	58.3	5.0	1.25	0.19
MD Score-2004	5,536	61.3	4.0	4.35	0.20	1,161	81	1,380	94	4,157	235	1378	87	4,050	230	548	31	87.2	8.1	1.91	0.43
MD Score-2005	5,979	47.9	3.1	4.28	0.20	1,004	67	936	60	3,142	161	1,022	59	3,238	178	441	24	58.2	5.0	1.92	0.29
MD Score-2007	5,443	44.0	2.8	4.10	0.21	827	55	828	59	2,869	159	936	58	2,941	155	402	21	52.6	4.7	1.50	0.25
Cardioprotective MD Score	4,245	50.2	2.7	4.41	0.19	1,029	60	883	53	3,068	143	1,010	53	3,268	146	451	20	55.9	4.2	1.58	0.21

(*continued on next page*)

Table 5. Adjusted mean daily intakes ± standard error (SE) of dietary antioxidants in the lowest tertile of adherence to the Mediterranean Diet (MD) indexes in the two European Prospective into Cancer and Nutrition-Spain cohorts (1992-1996)[a] (*continued*)

MD index	Sample size of lowest tertile[b]	Vitamin C (mg/d)		a-Tocopherol (mg/d)		Beta Carotene (mg/d)		TRAP[c] (mmol trolox equivalents/d)		FRAP[d] (mmol iron/d)		TEAC-ABTS[e] (mmol trolox equivalents/d)		ORAC[f] (mmol trolox equivalents/d)		TP[g] (mg/d)		Flavonoids (mg/d)		PAC Score[h]	
		←								*mean*		*SE*									→
PREDIMED[k]	5,154	64.6	3.0	4.49	0.16	1,241	62	1,176	58	3,857	151	1,291	57	4,182	166	573	22	83.9	5.3	1.87	0.26
L-based[l]	6,218	52.8	3.1	4.39	0.20	1,077	69	952	61	3,229	164	1,072	61	3,437	172	472	23	66.6	5.4	1.44	0.22
MEDLIFE[m]	4,989	55.7	3.6	4.25	0.20	1,019	69	1,033	70	3,476	187	1,143	69	3,713	206	502	28	75.1	6.7	1.49	0.29
MD Serving Score	6,269	55.3	3.4	4.61	0.20	1,120	70	1,122	72	3,587	184	1,177	67	3,457	182	480	25	72.5	6.0	1.99	0.30
Minimume maximum[n]		43.0-66.4		4.03-5.00		758-1,241		802-1,781		2,796-4,157		924-1,378		2,941-4,218		402-579		52.6-87.2		1.11-2.15	

[a]Geometric means were derived from generalized linear models adjusted for age continuous, sex, center, and energy intake continuous. Intakes ranking among the five highest are shown in boldface type.

[b]Reference values in lowest tertile of adherence: MD scale-1995 ≤3; MD scale-2003 ≤4; MD scale-2013 ≤3; Modified MD-2005 ≤3; Modified DP-2002 ≤24; Modified DP-2003 ≤12; Modified DP-2006 ≤18; MSDPS ≤69; MD quality index ≥ 8; ITAMED ≤3; alternate MD index ≤2; relative MD score ≤7; MD score-2001 ≤2; MD score-2004 ≤17; MD score-2005 ≤32; MD score-2007 ≥32; Cardioprotective MD score ≥5; PREDIMED ≤7; L-based ≤9; MEDLIFE ≤8, and MD serving score ≤10.

[c]TRAP¼total radical-trapping antioxidant parameter.

[d]FRAP¼ferric-reducing antioxidant power.

[e]TEAC-ABTS¼Trolox equivalent antioxidant capacity.

[f]ORAC¼oxygen radical antioxidant capacity.

[g]TP¼total polyphenols.

[h]PAC¼polyphenol antioxidant content score. Range¼e28 to 28.

[i]MSDPS¼Mediterranean-style dietary pattern score.

[j]ITAMED¼Italian Mediterranean Index.

[k]PREDIMED¼Prevention with MD.

[l]L-based¼literature-based adherence score to MD.

[m]MEDLIFE¼Mediterranean Lifestyle Index.

[n]Differences between extreme values of mean intakes maximum and minimum were all statistically significant at $P<0.001$.

Table 6. Adjusted mean daily intakes standard error (SE) of selected food groups[a] (g/d) in the highest tertile of adherence to the Mediterranean Diet (MD) indexes in the two European Prospective into Cancer and Nutrition-Spain cohorts (1992-1996)[b]

MD index	Sample size of highest tertile[c]	Vegetables		Fruits		Legumes		Nuts		Cereals		Fish		Olive oil		Wine		Meat and meat Products		Dairy Products		Fats (Animal Origin)	
		←———										mean		SE									——!
MD Scale-1995	2,404	334	27	166	20	32.7	3.2	3.98	1.19	93.1	6.0	31.3	4.0	14.3	1.6	14.8	4.7	49.7	4.5	51.8	9.6	1.28	0.25
MD Scale-2003	3,762	275	20	145	14	25.2	2.0	4.48	1.09	89.8	4.9	49.3	4.2	15.3	1.3	27.9	5.6	56.0	4.1	64.0	9.0	1.69	0.23
MD Scale-2013	3,606	308	22	184	18	26.8	2.3	4.61	0.94	90.0	5.2	49.4	4.2	14.7	1.7	13.9	3.4	55.7	4.3	64.2	9.0	1.83	0.27
Modified MD-2005	3,814	300	22	143	15	28.2	2.2	4.96	1.22	105	5	54.6	4.5	20.5	2.0	32.3	6.4	56.2	4.1	68.4	9.7	1.95	0.29
MD Pattern-2002	4,143	437	28	261	24	24.7	2.3	4.90	1.15	78.6	4.7	61.0	4.9	23.6	1.9	21.1	4.3	58.4	4.5	79.6	10.6	1.93	0.25
MD Pattern-2003	2,714	233	18	129	14	17.3	1.8	3.88	0.94	61.5	4.2	36.7	3.4	12.2	0.9	18.1	4.8	57.2	5.4	71.5	10.2	1.47	0.20
MD Pattern-2006	4,703	312	20	172	15	32.3	2.4	3.26	0.59	95.1	4.5	53.2	4.1	20.5	1.5	9.83	2.47	57.5	3.8	103	11.6	1.95	0.26
MSDPS[d]	1,620	245	31	219	33	31.3	3.6	1.40	0.56	66.9	6.0	37.4	5.9	14.2	1.5	38.8	14.6	52.9	5.9	199	23.4	1.63	0.36
MD Quality Index	5,011	318	19	141	12	18.8	1.5	4.46	0.98	66.7	3.2	54.1	3.8	14.2	0.8	17.7	4.4	54.0	3.6	59.3	6.2	1.60	0.19
ITAMED[e]	3,428	283	24	238	22	21.2	2.2	5.26	1.46	60.4	4.4	39.7	4.3	16.8	1.7	15.4	3.9	46.7	4.1	82.4	11.5	1.42	0.19
Alternate MD Index	2,247	323	26	179	18	26.5	2.8	4.71	1.09	77.3	5.8	48.5	5.2	14.3	1.7	24.1	7.1	46.6	4.8	93.7	14.8	1.59	0.29
Relative MD Score	3,781	316	22	158	15	30.7	2.4	4.12	0.99	97.9	5.2	48.9	4.0	19.2	1.4	31.6	6.5	53.8	3.9	64.5	8.0	1.83	0.27
MD Score-2001	2,113	327	32	213	22	22.1	2.5	3.06	1.05	68.0	5.2	42.7	5.6	13.7	1.5	9.24	4.00	50.0	5.4	43.3	8.8	1.86	0.33
MD Score-2004	3,355	276	21	147	16	30.9	2.6	3.72	0.72	112	6	55.2	4.8	19.1	2.2	10.2	2.3	59.3	5.0	82.5	12.5	2.17	0.33
MD Score-2005	4,394	242	16	133	12	25.3	1.7	3.98	0.91	84.4	4.0	41.9	3.4	14.2	1.0	13.2	3.3	60.4	4.5	49.4	7.1	2.07	0.29
MD Score-2007	3,793	323	21	176	15	24.2	1.9	3.91	0.97	70.4	4.0	48.1	4.1	14.7	0.9	18.5	5.3	47.1	3.7	77.1	8.5	1.57	0.23
Cardioprotective MD Score	3,696	282	17	241	15	20.9	1.5	4.47	1.07	49.9	3.6	42.9	4.1	13.6	0.9	22.4	7.3	53.4	4.0	79.2	8.5	1.53	0.23
PREDIMED[f]	2,415	426	42	190	26	31.5	3.8	7.78	2.16	72.5	5.6	69.3	6.6	18.5	1.9	50.7	11.5	64.2	5.5	66.5	10.5	1.52	0.25
L-based[g]	3,330	299	20	182	15	23.2	1.8	2.86	0.75	89.1	4.7	41.8	3.6	14.9	1.2	15.2	5.4	49.1	4.0	49.8	7.4	2.08	0.32
MEDLIFE[h]	3,709	272	21	122	14	24.7	2.1	4.41	1.10	90.0	5.0	44.4	3.8	16.7	1.6	24.0	5.2	55.4	4.3	71.1	9.0	1.79	0.25
MD Serving Score	3,566	263	22	183	16	29.3	2.5	3.06	0.79	119	5	43.4	3.8	17.9	1.2	15.2	4.1	73.7	5.1	65.6	8.0	1.58	0.24
Minimumemaximum[i]		233-437		122-261		17.3-32.7		1.40-7.78		50-119		31.3-69.3		12.2-23.6		9.2-50.7		46.6-73.7		43-199		1.28-2.17	

[a]Food groups include those presumed to fit (vegetables, fruits, legumes, nuts, cereals, fish, olive oil, and wine) or not fit (dairy products, meat and meat products, and animal fats) the definition of the traditional MD pattern.
[b]Geometric means were derived from generalized linear models adjusted for age continuous, sex, center, and energy intake continuous. Intakes ranking among the five highest are shown in boldface type.
[c]Reference values in highest tertile of adherence: MD scale-1995 ≥6; MD scale-2003 ≥6; MD scale-2013 ≥6; modified MD-2005 ≥6; MD Pattern 2002 ≥30; MD Pattern 2003 ≥13; MD Pattern 2006 ≥21; MSDPS ≥90; MD quality index ≤5; ITAMED ≥6; alternate MD index ≥5; relative MD score ≥11; MD score-2001 ≥5; MD score-2004 ≥21; MD score-2005 ≥36; MD score-2007 ≥37; Cardioprotective MD score ≥6; PREDIMED ≥10; L-based ≥12; MEDLIFE ≥ 11 and MDSS ≥ 14.
[d]MSDPS¼Mediterranean-style dietary pattern score.

[e]ITAMED¼Italian Mediterranean Index.
[f]PREDIMED¼Prevention with MD.
[g]L-based¼literature-based adherence score to the MD.
[h]MEDLIFE¼Mediterranean Lifestyle Index.
[i]Differences between extreme values of mean intakes maximum and minimum were all statistically significant at $P<0.001$.

Table 7. Adjusted mean daily intakes standard error (SE) of dietary antioxidants in the highest tertile of adherence to the Mediterranean Diet (MD) indexes by men in the two European Prospective into Cancer and Nutrition-Spain cohorts (1992-1996)[a]

MD index	Sample size of highest tertile[b]	Vitamin C (mg/d)		a-Tocopherol (mg/d)		Beta Carotene (mg/d)		TRAP[c] (mmol trolox equivalents/d)		FRAP[d] (mmol iron/d)		TEAC-ABTS[e] (mmol trolox equivalents/d)		ORAC[f] (mmol trolox equivalents/d)		TP[g] (mg/d)		Flavonoids (mg/d)		PAC[h] Score	
		←mean		SE→																	
MD Scale-1995	904	152	19	6.40	0.63	2,802	403	1,577	236	5,451	618	1,842	236	9,658	938	1,362	130	152	23	3.03	0.65
MD Scale-2003	2,257	98.3	8.6	5.56	0.34	1,866	181	1,416	128	4,831	341	1,640	130	6,648	440	923	60	127	12	2.16	0.33
MD Scale-2013	2,049	123	11	6.72	0.43	2,138	214	1,197	115	4,371	322	1,486	121	7,600	508	1,069	70	119	12	2.07	0.34
Modified MD-2005	2,439	106	9	5.82	0.35	1,816	171	1,331	118	4,614	318	1,569	120	6,723	432	946	60	121	12	2.37	0.35
MD Pattern-2002	2,704	148	11	6.57	0.40	2,263	205	1,532	127	5,125	332	1,741	125	8,959	521	1,254	71	159	13	2.53	0.34
MD Pattern-2003	1,134	93.4	10.3	5.97	9.46	1,726	235	1,424	162	4,496	413	1,519	155	6,007	533	850	73	114	14	2.08	0.45
MD Pattern-2006	2,521	113	9	5.67	0.33	1,714	158	1,020	90	3,927	264	1,285	96	7,470	440	1,042	60	106	10	1,98	0.30
MSDPS[i]	729	142	24	4.83	0.54	1,728	310	1,462	238	4,802	644	1,682	245	8,615	960	1,211	139	190	27	2.67	0.68
MD Quality Index	1,854	116	11	6.35	0.40	1,964	202	1,393	139	4,860	384	1,653	146	7,555	502	1,070	71	134	15	2.40	0.42
ITAMED[j]	1,588	126	13	5.75	0.45	1,609	188	1,274	146	4,359	403	1,474	150	8,211	603	1,132	83	151	18	2.92	0.51
Alternate MD Index	988	114	12	6.30	0.52	2,170	278	1,492	176	4,878	465	1,664	175	7,863	673	1,089	92	139	19	2.19	0.47
Relative MD Score	2,257	104	9	5.92	0.35	1,796	167	1,505	129	5,051	342	1,722	130	7,224	458	992	63	139	13	2.62	0.39
MD Score-2001	977	118	14	6.27	0.57	2,024	295	1,466	203	4,872	529	1,638	199	8,271	716	1,137	94	138	20	2.51	0.61
MD Score-2004	2,105	102	9	6.25	0.42	1,560	150	1,099	99	4,054	288	1,348	106	6,928	430	961	59	98.4	10.0	1.76	0.29
MD Score-2005	1,848	106	10	6.01	0.42	1,740	183	1,294	129	4,441	345	1,537	132	6,315	448	912	64	118	12	1.95	0.34
MD Score-2007	1,398	107	10	6.27	0.42	1,906	221	1,557	161	5,099	428	1,755	161	7,371	524	1,025	71	148	17	2.23	0.45
Cardioprotective MD Score	993	136	14	6.60	0.53	1,912	244	1,844	217	5,765	570	2,042	220	9,262	723	1,269	97	201	25	2.27	0.58
PREDIMED[k]	1,663	148	15	7.49	0.50	2,350	279	1,801	185	5,898	469	2,018	176	8,228	635	1,168	90	162	17	3.12	0.49
L-based[l]	1,249	107	10	5.63	0.42	2,004	230	1,388	168	4,787	453	1,629	171	7,444	553	1,042	75	134	16	1.92	0.40

(*continued on next page*)

Table 7. Adjusted mean daily intakes standard error (SE) of dietary antioxidants in the highest tertile of adherence to the Mediterranean Diet (MD) indexes by men in the two European Prospective into Cancer and Nutrition-Spain cohorts (1992-1996)[a] (*continued*)

MD index	Sample size of highest tertile[b]	Vitamin C (mg/d)	a-Tocopherol (mg/d)	Beta Carotene (mg/d)	TRAP[c] (mmol trolox equivalents/d)	FRAP[d] (mmol iron/d)	TEAC-ABTS[e] (mmol trolox equivalents/d)	ORAC[f] (mmol trolox equivalents/d)	TP[g] (mg/d)	Flavonoids (mg/d)	PAC[h] Score
		←——————————————————————————————mean SE——————————————————————————————→									
MEDLIFE[m]	1,960	87.3 8.7	5.83 0.40	1,539 165	1,102 107	3,933 299	1,290 109	5,750 437	809 60	93.9 10.1	2.10 0.33
MD Serving Score	1,514	103 11	5.47 0.42	1,751 217	907 101	3,342 296	1,106 107	6,222 501	908 72	93.5 10.7	1.10 0.22
Minimumemaximum[n]		87-152	4.83-7.49	1,539-2,802	907-1,844	3,342-5,898	1,106-2,042	5,750-9,658	809-1,362	93.5-201	1.10-3.12

[a]Geometric means were derived from generalized linear models adjusted for age continuous, sex, center and energy intake continuous. Intakes ranking among the five highest are shown in boldface type.
[b]Reference values in highest tertile of adherence: MD scale-1995 ≥6; MD scale-2003 ≥6; MD scale-2013 ≥6; modified MD-2005 ≥6; modified DP-2002 ≥30; modified DP-2003 ≥3; modified DP-2006 ≥21; MSDPS ≥90; MD quality index ≤5; ITAMED ≥ 6; alternate MD index ≥5; relative MD score ≥11; MD score-2001 ≥5; MD score-2004 ≥21; MD score-2005 ≥36; MD score-2007 ≥37; Cardioprotective MD score ≥6; PREDIMED ≥10; L-based ≥12; MEDLIFE ≥11, and MD serving score ≥14.
[c]TRAP¼total radical-trapping antioxidant parameter.
[d]FRAP¼ferric-reducing antioxidant power.
[e]TEAC-ABTS¼Trolox equivalent antioxidant capacity.
[f]ORAC¼oxygen radical antioxidant capacity.
[g]TP¼total polyphenols.
[h]PAC¼polyphenol antioxidant content score.
[i]MSDPS¼Mediterranean-style dietary pattern score.
[j]ITAMED¼Italian Mediterranean Index.
[k]PREDIMED¼Prevention with MD.
[l]L-based¼literature-based adherence score to the MD.
[m]MEDLIFE¼Mediterranean Lifestyle Index.
[n]Differences between extreme values of mean intakes maximum and minimum were all statistically significant at $P<0.001$.

Table 8. Adjusted mean daily intakes (SE) of dietary antioxidants in the highest tertile of adherence to the Mediterranean Diet (MD) indexes by women in the two European Prospective into Cancer and Nutrition-Spain cohorts (1992-1996)[a]

MD Index	Sample size of highest tertile[b]	Vitamin C (mg/d)		a-Tocopherol (mg/d)		Beta Carotene (mg/d)		TRAP[c] (mmol trolox equivalents/d)		FRAP[d] (mmol iron/d)		TEAC-ABTS[e] (mmol trolox equivalents/d)		ORAC[f] (mmol trolox equivalents/d)		TP[g] (mg/d)		Flavonoids (mg/d)		PAC score[h]	
		←mean	SE→																		
MD Scale-1995	1,500	102	8	5.99	0.34	1,932	175	1,261	98	4,475	290	1,551	111	6,179	389	871	54	104	11	1.61	0.33
MD Scale-2003	1,505	107	9	6.46	0.37	2,228	208	1,701	126	5,542	349	1,941	132	6,493	418	917	59	130	13	1.74	0.36
MD Scale-2013	1,557	119	10	7.28	0.43	2,344	217	1,724	130	5,677	369	1,973	138	6,834	423	979	60	126	13	1.64	0.35
Modified MD-2005	1,375	97.5	9.2	7.09	0.50	2,165	230	1,485	122	5,212	362	1,770	135	6,017	431	856	61	101	12	1.88	0.41
MD Pattern-2002	1,439	200	17	8.12	0.51	3,761	368	2,734	217	8,049	547	2,855	215	10,440	664	1,494	94	231	22	3.63	0.64
MD Pattern-2003	1,580	85.3	6.6	5.29	0.28	1,779	172	1,393	110	4,403	297	1,527	111	5,222	347	729	48	109	11	3.12	0.70
MD Pattern-2006	2,182	129	9	7.18	0.35	2,824	222	1,736	123	5,828	348	2,026	134	7,451	401	1,053	57	133	12	2.10	0.37
MSDPS[i]	891	122	14	5.87	0.47	2,048	277	2,019	205	5,987	515	2,187	197	7,473	678	1,040	92	203	24	3.11	0.78
MD Quality Index	2,874	96.6	5.7	5.83	0.24	2,203	153	1,605	95	5,075	257	1,743	95	5,883	277	812	38	116	9	2.38	0.37
ITAMED[j]	1,840	130	10	6.72	0.38	2,295	206	1,973	143	6,033	395	2,155	148	8,015	479	1,096	64	199	18	3.40	0.55
Alternate MD Index	1,259	129	11	7.69	0.52	3,018	300	2,167	185	6,747	503	2,385	184	8,091	541	1,115	74	186	19	3.04	0.62
Relative MD Score	1,524	124	10	6.59	0.37	2,618	245	1,826	140	5,916	389	2,077	149	7,288	481	1,041	67	144	5	2.08	0.40
MD Score-2001	1,136	124	11	6.12	0.38	2,386	252	1,826	160	5,530	411	1,974	156	7,034	466	992	63	145	17	2.34	0.56
MD Score-2004	1,250	111	11	6.87	0.47	2,615	270	1,827	159	6,150	461	2,134	177	7,009	520	996	74	139	17	2.34	0.53
MD Score-2005	2,546	95.7	6.2	5.96	0.27	1,803	133	1,454	97	4,806	269	1,689	102	5,797	301	811	42	116	10	1.58	0.29
MD Score-2007	2,395	130	8	6.63	0.27	2,706	193	1,848	109	5,882	300	2,057	112	7,574	355	1,063	49	155	12	1.98	0.31
Cardioprotective MD Score	2,703	123	7	5.97	0.24	2,181	144	1,914	109	5,723	288	2,056	109	7,440	329	1,023	44	184	13	2.54	0.42
PREDIMED[k]	752	159	19	7.65	0.56	3,093	449	2,157	251	6,602	668	2,256	241	8,548	874	1,220	121	180	30	3.73	0.87
L-based[l]	2,081	117	8	5.96	0.28	2,197	164	1,781	118	5,604	320	1,990	124	6,702	329	948	46	130	12	1.78	0.34

(*continued on next page*)

Table 8. Adjusted mean daily intakes (SE) of dietary antioxidants in the highest tertile of adherence to the Mediterranean Diet (MD) indexes by women in the two European Prospective into Cancer and Nutrition-Spain cohorts (1992-1996)[a] (*continued*)

MD Index	Sample size of highest tertile[b]	Vitamin C (mg/d)	a-Tocopherol (mg/d)	Beta Carotene (mg/d)	TRAP[c] (mmol trolox equivalents/d)	FRAP[d] (mmol iron/d)	TEAC-ABTS[e] (mmol trolox equivalents/d)	ORAC[f] (mmol trolox equivalents/d)	TP[g] (mg/d)	Flavonoids (mg/d)	PAC score[h]
		←———— *mean*					*SE* ————!				
MEDLIFE[m]	1,749	89.5 7.8	6.36 0.36	2,095 189	1,557 121	5,012 330	1,714 122	5,748 401	786 55	101 11	2.54 0.50
MD Serving Score	2,052	112 8	6.08 0.34	1,995 185	1,565 116	5,092 324	1,757 120	7,630 404	1,049 54	133 12	1.99 0.36
Minimumemaximum[n]		85-200	5.29-8.12	1,779-3,761	1,261-2,734	4,403-8,049	1,527-2,855	5,222-10,440	786-1,494	101-231	1.58-3.73

[a]Geometric means were derived from generalized linear models adjusted for age continuous, sex, center and energy intake continuous. Intakes ranking among the five highest are shown in boldface type.
[b]Reference values in highest tertile of adherence: MD scale-1995 ≥6; MD scale-2003 ≥6; MD scale-2013 ≥6; modified MD-2005 ≥6; modified DP-2002 ≥30; modified DP-2003 ≥3; modified DP-2006 ≥21; MSDPS ≥90; MD quality index ≤5; ITAMED ≥ 6; alternate MD index ≥5; relative MD score ≥11; MD score-2001 ≥5; MD score-2004 ≥21; MD score-2005 ≥36; MD score-2007 ≥37; Cardioprotective MD score ≥6; PREDIMED ≥10; L-based ≥12; MEDLIFE ≥11, and MD serving score ≥14.
[c]TRAP¼total radical-trapping antioxidant parameter.
[d]FRAP¼ferric-reducing antioxidant power.
[e]TEAC-ABTS¼Trolox equivalent antioxidant capacity.
[f]ORAC¼oxygen radical antioxidant capacity.
[g]TP¼total polyphenols.
[h]PAC¼polyphenol antioxidant content.
[i]MSDPS¼Mediterranean-style dietary pattern score.
[j]ITAMED¼Italian Mediterranean Index.
[k]PREDIMED¼Prevention with MD.
[l]L-based¼literature-based adherence score to the MD.
[m]MEDLIFE¼Mediterranean Lifestyle Index.
[n]Differences between extreme values of mean intakes maximum and minimum were all statistically significant at $P<0.001$.

Table 10. Spearman correlation coefficients between indexes of adherence to the Mediterranean Diet (MD) and dietary antioxidants in two European Prospective into Cancer and Nutrition-Spain cohorts (n¼14,756; 1992-1996)[a]

MD index	Vitamin C	a-Tocopherol	Beta Carotene	TRAP[b]	FRAP[c]	TEAC-ABTS[d]	ORAC[e]	TP[f]	Flavonoids	PAC Score[g]
	←——————————————————————————Spearman correlation coefficient——————————————————————————!									
MD Scale-1995	0.37	0.23	0.30	0.36	0.39	0.37	0.44	0.44	0.33	0.43
MD Scale-2003	0.39	0.34	0.33	0.47	0.49	0.46	0.52	0.51	0.41	0.52
MD Scale-2013	0.39	0.51	0.33	0.42	0.48	0.45	0.54	0.53	0.40	0.50
Modified MD-2005	0.39	0.43	0.37	0.52	0.55	0.52	0.55	0.53	0.45	0.57
MD Pattern-2002	0.55	0.46	0.50	0.65	0.67	0.64	0.69	0.69	0.58	0.74
MD Pattern-2003	0.27	e0.12	0.26	0.14	0.12	0.12	0.20	0.22	0.13	0.18
MD Pattern-2006	0.46	0.38	0.41	0.37	0.44	0.41	0.58	0.58	0.37	0.50
MSDPS[h]	0.24	e0.09	0.12	0.18	0.18	0.20	0.26	0.27	0.25	0.28
MD Quality Index[i]	e0.41	0.01	e0.28	e0.22	e0.24	e0.23	e0.42	e0.45	e0.26	e0.30
ITAMED[j]	0.46	0.22	0.33	0.31	0.31	0.32	0.55	0.55	0.40	0.44
Alternate MD Index	0.48	0.35	0.42	0.34	0.37	0.37	0.52	0.53	0.35	0.45
Relative MD Score	0.44	0.34	0.40	0.49	0.52	0.49	0.56	0.56	0.43	0.56
MD Score-2001	0.39	0.13	0.29	0.20	0.23	0.22	0.46	0.47	0.26	0.31
MD Score-2004	0.41	0.50	0.37	0.44	0.50	0.47	0.57	0.56	0.41	0.53
MD Score-2005	0.28	0.03	0.22	0.20	0.24	0.23	0.27	0.29	0.19	0.28
MD Score-2007	0.51	0.06	0.40	0.19	0.21	0.22	0.45	0.49	0.24	0.32
Cardioprotective MD Score	0.53	0.03	0.38	0.10	0.12	0.14	0.46	0.49	0.24	0.26
PREDIMED[k]	0.41	0.29	0.33	0.52	0.54	0.53	0.53	0.52	0.49	0.61
L-based[l]	0.47	0.12	0.34	0.22	0.26	0.26	0.48	0.51	0.29	0.34
MEDLIFE[m]	0.39	0.24	0.29	0.37	0.39	0.37	0.41	0.41	0.31	0.42
MD Serving Score	0.33	0.16	0.21	0.24	0.27	0.26	0.36	0.36	0.26	0.32

[a]Correlation coefficients derived from Spearman correlation. All correlation coefficients were positive statistically significant ($P<0.001$), except for a-tocopherol (in MD pattern-2003 and MSDPS). Correlations ≥0.5 are shown in boldface type.
[b]TRAP¼total radical-trapping antioxidant parameter.
[c]FRAP¼ferric-reducing antioxidant power.
[d]TEAC-ABTS¼Trolox equivalent antioxidant capacity.
[e]ORAC¼oxygen radical antioxidant capacity.
[f]TP¼total polyphenols.
[g]PAC¼polyphenol antioxidant content.
[h]MSDPS¼Mediterranean-Style Dietary Pattern Score.

[i]Scored inversely.
[j]ITAMED¼Italian Mediterranean Index.
[k]PREDIMED¼Prevention with MD.
[l]L-based¼literature-based adherence score to the MD.
[m]MEDLIFE¼Mediterranean Lifestyle Index.