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Adherence to the Mediterranean Diet Is Associated with Lower Abdominal Adiposity in European Men and Women[1–3]

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Abstract

Given the lack of consistent evidence of the relationship between Mediterranean dietary patterns and body fat, we assessed the cross-sectional association between adherence to a modified Mediterranean diet, BMI, and waist

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[3] Supplemental Tables 1–3 are available with the online posting of this paper at jn.nutrition.org.

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circumference (WC). A total of 497,308 individuals (70.7% women) aged 25–70 y from 10 European countries participated in this study. Diet was assessed at baseline using detailed validated country-specific questionnaires, and anthropometrical measurements were collected using standardized procedures. The association between the degree of adherence to the modified-Mediterranean Diet Score (mMDS) (including high consumption of vegetables, legumes, fruits and nuts, cereals, fish and seafood, and unsaturated:saturated fatty acids ratio; moderate alcohol intake; and low consumption of meat and meat products and dairy products) and BMI (kg·m^{-2}) or WC (cm) was modeled through mixed-effects linear regression, controlling for potential confounders. Overall, the mMDS was not significantly associated with BMI. Higher adherence to the Mediterranean diet was significantly associated with lower WC, for a given BMI, in both men (−0.09; 95% CI −0.14 to −0.04) and women (−0.06; 95% CI −0.10 to −0.01). The association was stronger in men (−0.20; 95% CI −0.23 to −0.17) and women (−0.17; 95% CI −0.21 to −0.13) from Northern European countries. Despite the observed heterogeneity among regions, results of this study suggest that adherence to a modified Mediterranean diet, high in foods of vegetable origin and unsaturated fatty acids, is associated with lower abdominal adiposity measured by WC in European men and women. J. Nutr. 139: 1728–1737, 2009.

Introduction

Obesity is one of the greatest public health challenges of the 21st century. Its prevalence has tripled in many European countries since the 1980s and the numbers of those affected continue to rise at an alarming rate. Almost 400 million adults from European countries are estimated to be overweight and ~130 million to be obese. If the prevalence continues to increase at the same rate as in the 1990s, ~150 million adults in Europe may be obese by 2010 (1). Mediterranean countries in Southern Europe have a higher prevalence of obesity than countries in Northern Europe (2,3). For illustration, the WHO estimates that the prevalence of obesity in Greek adults (aged >30 y) is >30%, whereas in Denmark it is <13% (1,2). Lifestyle changes are the major determinants of the rapid rise in the prevalence of obesity worldwide, with genetic factors likely to modify the individual susceptibility to these lifestyle changes. The etiology of obesity is multifactorial; however, the root physiological cause is energy imbalance as a consequence of low physical activity (PA)[36] and/or high energy intake (EI) (3–5).

The traditional Mediterranean diet has been described as the dietary pattern found in the olive-growing areas of the Mediterranean region in the late 1950s and early 1960s, when the consequences of World War II had been overcome but before fast-food culture had reached the area. It is characterized by a high intake of vegetables, legumes, fruits and nuts, cereals (mainly unrefined), a high intake of olive oil but a low intake of saturated lipids, a moderately high intake of fish, a low-to-moderate intake of dairy products (mostly in the form of yogurt and cheese), a low intake of meat and poultry, and a regular but moderate intake of alcohol, primarily in the form of wine and generally during meals (6). The Mediterranean diet has been associated with better health and greater longevity (6–15). It has been suggested that this dietary pattern may also be protective against the development of obesity through its high-fiber content and low energy density (4,16–18). However, others have speculated that the high-fat content (particularly from olive oil) of the Mediterranean diet may promote excess EI and weight gain and hence may explain the high prevalence of overweight and obesity in Mediterranean countries (19). Epidemiological evidence of an association between adherence to a Mediterranean-type diet and overweight/obesity is limited and conflicting and there are important methodological differences and limitations in previous studies that make it difficult to compare results (10,11,16,18,20–26).

Our objective in this study was to assess in a large population from Europe, including Mediterranean, Central, and Northern European countries with diverse dietary patterns, the cross-sectional association between the maintenance of a dietary pattern in conformity with the Mediterranean diet and measurements of general obesity (BMI) and abdominal fat as assessed by waist circumference (WC). The present study was designed to overcome some of the methodological limitations reported in previous studies by including a large sample size, standardized methods of dietary and anthropometrical assessment, and appropriate control for confounders and effect modifiers of the association between diet and obesity.

Methods

Study design. This was a cross-sectional study conducted in participants of the European Prospective Investigation into Cancer and Nutrition–Physical Activity, Nutrition, Alcohol, Cessation of Smoking, Eating Out of Home and Obesity (EPIC-PANACEA) project.

Study population. EPIC is a multi-center, prospective cohort study investigating the role of metabolic, dietary, lifestyle, and environmental factors in the development of cancer and other chronic diseases. Briefly, between 1992 and 2000, 519,931 apparently healthy volunteers aged between 25 and 70 y were recruited in 23 centers from 10 European countries (Denmark, France, Germany, Greece, Italy, The Netherlands, Norway, Spain, Sweden, and the United Kingdom). In France, Norway, Utrecht (The Netherlands), and Naples (Italy), only women were included. The selection of the study population in each center was largely influenced by practical considerations and therefore the sample is not intended to be representative of each region. Approval for this study was obtained from the ethical review boards of the International Agency for Research on Cancer and from all local institutions where participants had been recruited for the EPIC study. Details of the recruitment and study design have been published elsewhere (27–29).

Participants with no dietary data available (n = 6611), those in the lowest and highest 1% of the cohort distribution of the ratio of reported total EI:energy requirement (n = 10,209) (30), those with no information on lifestyle variables (n = 64), those with missing BMI (n = 4719), and pregnant women (n = 623) were excluded from the present analyses. In addition, 18 participants with height < 130 cm, 321 participants with BMI <16 kg·m^{-2}, 16 participants with a WC >160 cm, and 42 participants with both a WC <60 cm and a BMI >25 kg·m^{-2} were not considered for the present study. Thus, 497,308 individuals (145,578 men and 351,730 women) were included in the present study.

[36] Abbreviations used: BMR, basal metabolic rate; EI, energy intake; EPIC-PANACEA, European Prospective Investigation into Cancer and Nutrition–Physical Activity, Nutrition, Alcohol, Cessation of Smoking, Eating Out of Home and Obesity; mMDS, modified-Mediterranean diet score; PA, physical activity; WC, waist circumference.

TABLE 1 Selected characteristics of the EPIC-PANACEA participants by sex and country[1]

Gender and country	*n*	Age	BMI	WC	High educational level[2]	High PA level[3]	Current smokers
Men		*y*	$kg \cdot m^{-2}$	*cm*	*%*	*%*	*%*
Greece	10,566	53.1 ± 12.8	27.8 ± 3.8	98.2 ± 10.4	29.7	39.5	39.1
Italy	14,247	50.3 ± 7.6	26.4 ± 3.4	92.6 ± 9.3	42.9	50.5	30.5
Spain	15,192	50.8 ± 7.2	28.4 ± 3.4	99.4 ± 9.0	23.4	48.4	40.2
UK Healthy	10,636	46.7 ± 15.1	24.4 ± 3.4	88.1 ± 7.7	67.4	47.5	16.7
UK General	13,146	59.1 ± 9.3	26.2 ± 3.3	93.6 ± 9.7	26.8	37.1	12.6
Germany	22,265	52.6 ± 7.6	27.0 ± 3.6	95.5 ± 10.1	47.7	48.9	24.4
The Netherlands	10,041	43.3 ± 11.1	25.5 ± 3.5	90.5 ± 10.8	47.7	67.8	38.5
Denmark	26,558	56.6 ± 4.4	26.6 ± 3.6	96.0 ± 9.9	36.0	59.6	37.4
Sweden	22,927	52.2 ± 11.1	25.6 ± 3.4	93.7 ± 10.1	41.3	39.2	22.7
Total	145,578	52.4 ± 10.2	26.5 ± 3.6	94.7 ± 10.2	42.4	49.5	29.2
Women							
Greece	15,207	53.5 ± 12.4	28.6 ± 5.2	87.7 ± 12.7	30.0	20.3	16.9
Italy	31,265	50.7 ± 8.1	25.7 ± 4.3	80.0 ± 10.5	36.5	24.2	26.1
Spain	25,189	48.4 ± 8.4	28.2 ± 47	87.4 ± 11.2	15.9	16.2	18.7
France	71,874	52.9 ± 6.7	22.9 ± 3.2	n.a.[4]	88.5	40.7	8.7
UK Healthy	36,452	43.9 ± 14.3	23.5 ± 3.7	72.8 ± 8.0	59.0	43.0	10.0
UK General	18,872	57.1 ± 9.3	25.7 ± 4.4	79.6 ± 10.9	21.2	29.1	11.8
Germany	29,447	49.4 ± 9.0	25.7 ± 4.7	81.0 ± 11.6	34.5	44.4	18.4
The Netherlands	28,881	51.3 ± 11.4	25.2 ± 4.2	80.8 ± 10.7	49.0	65.0	27.6
Denmark	29,191	56.8 ± 4.4	25.6 ± 4.4	82.1 ± 11.2	22.1	57.2	31.5
Sweden	29,573	52.5 ± 10.6	24.8 ± 4.2	77.9 ± 10.4	39.6	38.4	25.0
Norway	35,779	48.2 ± 4.3	24.4 ± 3.8	n.a.[4]	41.3	n.a.	31.3
TOTAL	351,730	51.1 ± 12.4	24.9 ± 4.4	80.5 ± 11.5	49.2	39.4	19.5

[1] Values are mean ± SD.
[2] High educational level means secondary school or university degree level.
[3] High PA level means moderately active to active PA.
[4] n.a., Not Available (no measurements of WC were taken in France and Norway; no measurements of PA were taken in Norway).

Anthropometric assessment. Anthropometric measurements were taken in most EPIC centers using similar, standardized procedures, with the exception of the "health-conscious" group based in Oxford (UK), in which anthropometric values were predicted (n = 47,088), and France (n = 71,874) and Norway (n = 35,779), where self-reported anthropometric values were used (31). For the UK health-conscious group (a heterogeneous group of ovo-lacto vegetarians, pure vegans, fish but not meat eaters, and meat eaters), linear regression models were used to predict sex- and age-specific anthropometric values from participants with both measured and self-reported body measures, as previously described (27,32,33). In Norway, only self-reported values of weight and height were obtained. In French centers, weight and height were measured in 31% of all women, whereas self-reports were available for all women. Given that, for most of the French sample, the time interval between the date of the questionnaire (when self-reported anthropometric values were obtained) and the date of anthropometric measurements was very long (mean difference 3.8 y), only self-reported anthropometric values were considered in the present study. Also, due to the long time interval, prediction equations from self-reports could not be determined.

In participating centers where actual anthropometric measurements were taken, weight and height were measured to the nearest 0.1 kg, and —depending on study center—to the nearest 0.1, 0.5, or 1.0 cm, respectively, with participants wearing no shoes. BMI was calculated as $kg \cdot m^{-2}$. WC was measured either at the narrowest torso circumference (France; Italy; Utrecht, The Netherlands; Denmark) or at the midpoint between the lower ribs and iliac crest (Bilthoven, The Netherlands; Potsdam, Germany; Malmö, Sweden; Oxford general population, UK). In Spain, Greece, Heidelberg (Germany), and Cambridge (UK), a combination of methods was used, although most participants were measured at the narrowest torso circumference (31). For this study, body weight and WC were corrected to reduce heterogeneity due to protocol differences in clothing worn during measurement. Briefly, for participants who were normally dressed and without shoes, 1.5 kg for weight and 2.0 cm for WC were subtracted from the original measurement, whereas for participants in light clothing and without shoes, 1 kg for weight was subtracted (31).

Self-reported, instead of measured, anthropometric values were also used in an additional 0.3% of the sample (n = 1419) for weight and height and in an additional 0.2% of the sample (n = 990) for WC.

Data on WC were missing for 136,640 individuals (27.5% of the sample). Most of these missing observations were from France, Norway, and Umea (Sweden), where information on WC was not obtained; these individuals were excluded from the analyses on WC.

Dietary assessment and modified-Mediterranean Diet Score. Usual dietary intakes were measured using country-specific validated questionnaires. Most centers adopted a self-administered FFQ of 88–266 food items. In Greece, all centers in Spain, and in Ragusa (Italy), the questionnaire was administered at personal interviews. In Malmo (Sweden) and the UK, a questionnaire method combined with a food record over 7 or 14 d was used (27,29,34,35). Nutrient intakes were calculated using food composition tables specific to the country (36). Validation studies were conducted during the EPIC pilot phase to test the reproducibility and validity of the dietary assessment methods used in different EPIC countries. The reference method used in these validation studies was 12 monthly 24-h recalls covering 1 calendar year. Most centers also used plasma concentrations of vitamin C, vitamin E, and β-carotene and 24-h urinary excretion of nitrogen as reference methods (34,37).

For each participant, daily intakes (g) of vegetables, legumes, fruits and nuts, cereals, fish and seafood, dairy products, meat and meat products (including red meat, poultry, processed meat, game, and offals), alcohol, SFA, monounsaturated fatty acids, PUFA, and fiber were estimated. Also, total daily EI as well as percentage of energy provided

TABLE 2 Selected characteristics of the EPIC-PANACEA participants by sex and levels of mMDS category[1]

	Men				Women			
mMDS Category (score range):	Low (0–3)	Medium (4–5)	High (6–9)	P^1	Low (0–3)	Medium (4–5)	High (6–9)	P^1
n	47,965	52,059	45,554		113,329	143,753	94,648	
Age,[2] *y*	52.1 ± 10.7	52.3 ± 10.2	52.9 ± 9.7	<0.0001	51.2 ± 10.0	51.0 ± 9.7	51.0 ± 9.6	<0.0001
BMI,[2] *kg·m*$^{-2}$	26.6 ± 3.7	26.5 ± 3.6	26.4 ± 3.6	<0.0001	25.1 ± 4.5	25.0 ± 4.4	24.7 ± 4.2	<0.0001
WC,[2] *cm*	95.1 ± 10.5	94.7 ± 10.2	94.3 ± 10.0	<0.0001	81.2 ± 11.7	80.7 ± 11.5	79.6 ± 11.2	<0.0001
EI,[2] *kJ/d*	10,174 ± 2688	10,581 ± 2792	10,955 ± 2701	<0.0001	7292 ± 2092	7757 ± 2202	8197 ± 2131	<0.0001
Energy density,[2,3] *kJ/g*	5.7 ± 1.2	5.6 ± 1.1	5.4 ± 1.0	<0.0001	5.6 ± 1.1	5.4 ± 1.0	5.2 ± 0.9	<0.0001
Proteins,[2] *% total energy*	16 ± 3	16 ± 3	15 ± 3	<0.0001	17 ± 3	17 ± 3	16 ± 3	<0.0001
Carbohydrates,[2] *% total energy*	42 ± 8	43 ± 7	44 ± 7	<0.0001	44 ± 7	45 ± 7	46 ± 7	<0.0001
Fat,[2] *% total energy*	37 ± 7	36 ± 6	35 ± 6	<0.0001	37 ± 6	36 ± 6	35 ± 6	<0.0001
Alcohol,[2] *% total energy*	6 ± 8	6 ± 6	6 ± 5	<0.0001	3 ± 5	3 ± 4	3 ± 3	<0.0001
Fiber,[2] *g/d*	20 ± 7	24 ± 9	29 ± 10	<0.0001	19 ± 6	23 ± 7	27 ± 8	<0.0001
Vegetables,[2] *g/d*	143 ± 116	187 ± 145	243 ± 168	<0.0001	163 ± 108	218 ± 140	279 ± 156	<0.0001
Legumes,[2] *g/d*	13 ± 24	16 ± 28	19 ± 31	<0.0001	10 ± 16	14 ± 20	19 ± 25	<0.0001
Fruits and nuts,[2] *g/d*	164 ± 169	221 ± 203	283 ± 227	<0.0001	195 ± 159	256 ± 190	322 ± 202	<0.0001
Cereals and products,[2] *g/d*	217 ± 114	254 ± 125	293 ± 131	<0.0001	172 ± 86	202 ± 97	235 ± 104	<0.0001
Fish and seafood,[2] *g/d*	25 ± 25	35 ± 33	47 ± 39	<0.0001	25 ± 24	38 ± 35	51 ± 44	<0.0001
Dairy products,[2] *g/d*	413 ± 289	337 ± 267	274 ± 230	<0.0001	379 ± 230	320 ± 218	271 ± 199	<0.0001
Meat & products,[2] *g/d*	129 ± 68	126 ± 70	121 ± 71	<0.0001	93 ± 50	89 ± 52	80 ± 52	<0.0001
Alcohol,[2] *g/d*	20 ± 28	21 ± 24	22 ± 19	<0.0001	7 ± 13	8 ± 12	9 ± 10	<0.0001
Fatty acids ratio,[4]	1.4 ± 0.4	I1.5 ± 0.5	1.7 ± 0.6	<0.0001	1.3 ± 0.4	1.5 ± 0.5	1.7 ± 0.5	<0.0001
High educational level,[5] %	36.0	39.3	43.6	<0.0001	43.2	47.2	50.9	<0.0001
High PA level,[6] %	45.9	49.4	52.8	<0.0001	35.3	39.2	44.4	<0.0001
Current smokers, *%*	34.3	29.6	24.4	<0.0001	22.2	19.5	16.8	<0.0001
Plausible EI,[7] %	61.2	64.9	70.0	<0.0001	62.6	66.0	71.7	<0.0001

[1] Values are means ± SD or %.
[2] The level of significance (*P*-value) of the observed differences among group means was tested using 1-way ANOVA; differences in percentages among groups were tested using chi-squared test.
[3] Energy density was calculated as daily EI (kJ) from foods (excluding all nonalcoholic beverages) divided by the total weight of food consumed (g).
[4] Sum of monounsaturated fatty acids and PUFA to SFA.
[5] High educational level means secondary school or university degree level.
[6] High PA level means moderately active to active PA.
[7] Percentage of individuals with plausible EI according to their estimated BMR (method of Goldberg) (39).

by macronutrients (total proteins, carbohydrates, and lipids) and alcohol were considered for the present study. Energy density was calculated for each participant as daily EI (kJ) from foods only (excluding all nonalcoholic beverages) divided by the total weight of food consumed (g).

A variant of the Mediterranean Diet score constructed by Trichopoulou et al. (6,13) with potentially wide applicability in non-Mediterranean countries was used in the present study. This variant differs from the original score, because it includes both monounsaturated fatty acids and PUFA in its definition (instead of monounsaturated fatty acids only) (12,14). The modified-Mediterranean Diet Score (mMDS) included 9 nutritional components characteristic of the Mediterranean dietary pattern: some with a presumably beneficial effect on health (vegetables, legumes, fruits and nuts, cereals, fish and seafood, ratio of the sum of monounsaturated and polyunsaturated:saturated lipids, and moderate alcohol consumption) and others with a presumably detrimental effect (meat and meat products and dairy products). Values of 0 or 1 were assigned to each component (except for alcohol intake, as indicated below) using the sex- and center-specific medians among participants as cutoff values (sex- and center-specific medians shown in Supplemental Tables 1 and 2). Specifically, persons with a below-median consumption of components with a presumably beneficial effect were assigned a value of 0, whereas persons with consumption equal to or above the median were given a value of 1. In contrast, persons with a below-median consumption of components with a presumably detrimental effect were assigned a value of 1, whereas persons whose consumption of these components was equal to or above the corresponding median were given a value of 0. For alcohol, a value of 1 was given to men whose consumption of alcohol was from 10 to <50 g/d and a value of 0 otherwise, whereas for women, the corresponding cutoffs were 5 and 25 g/d. Thus, an mMDS, as both monounsaturated fatty acids and PUFA were included in the numerator of the lipid ratio, was constructed to apply across Europe. This score could take a value from 0 (minimal adherence to the Mediterranean diet) to 9 (maximal adherence to the Mediterranean diet) and was further categorized as low (0–3 points), medium (4–5 points), and high (6–9 points) adherence to the modified Mediterranean diet.

Assessment of other covariates. Standard questionnaires were used to collect information on the participants' sociodemographic characteristics and lifestyle variables (27). These variables were controlled for in the present study, because they may be related both to dietary habits and body fatness. Information on smoking status (never smoker, former smoker, and current smoker), educational level (according to the maximum achieved school level: primary school, technical school, secondary school, and university degree), PA according to a validated PA index (classified in 4 categories: inactive, moderately inactive, moderately active, and active, derived from the cross-tabulation of PA at work categorized as no or sedentary job, standing job, manual job, or heavy manual job; and the nonworking activities of cycling and sport categorized as no leisure PA, ≤0.5 h/d, >0.5 to ≤1 h/d, or >1 h/d) (38), and menopausal status in women (premenopausal, perimenopausal, and postmenopausal) were included as covariates in the present study.

Statistical analyses. Data were analyzed separately for men and women. Descriptive analysis relied on cross-tabulations, showing percentages within groups for categorical variables as well as group

TABLE 3 Association between the mMDS and BMI in EPIC-PANACEA participants

	Men				Women			
mMDS	β[1]	95% CI	*P*	*P* for heterogeneity[2]	β[1]	95% CI	*P*	*P* for heterogeneity[2]
Model 1	−0.01	(−0.05 to 0.04)	0.731		−0.03	(−0.07 to 0.01)	0.108	
Model 2	0.01	(−0.03 to 0.05)	0.788		−0.01	(−0.04 to 0.02)	0.531	
Model 3	0.03	(−0.01 to 0.08)	0.127		0.04	(0.01 to 0.08)	0.011	
Subgroup analyses								
No illness[3]	−0.00	(−0.04 to 0.04)	0.863		−0.02	(−0.05 to 0.01)	0.174	
Plausible EI[4]	0.01	(−0.03 to 0.04)	0.752		−0.01	(−0.03 to 0.02)	0.697	
Measured anthropometry[5]	0.01	(−0.03 to 0.05)	0.780		−0.01	(−0.04 to 0.03)	0.654	
Stratified analyses								
By age group								
<60 y old	−0.00	(−0.04 to 0.04)	0.949	0.002	−0.01	(−0.04 to 0.02)	0.425	0.354
≥60 y old	0.01	(−0.05 to 0.06)	0.837		−0.01	(−0.06 to 0.03)	0.569	
By BMI category								
<18.5 kg·m^{-2}	0.01	(−0.02 to 0.04)	0.503	<0.0001	0.01	(−0.00 to 0.02)	0.116	0.005
18.5 – <25 kg·m^{-2}	0.03	(0.01 to 0.04)	< 0.0001		0.01	(0.00 to 0.02)	0.005	
25 – <30 kg·m^{-2}	−0.01	(−0.02 to 0.00)	0.182		−0.01	(−0.01 to 0.00)	0.216	
≥30 kg·m^{-2}	−0.02	(−0.04 to 0.00)	0.109		−0.01	(−0.04 to 0.01)	0.262	
By region[6]								
Southern Europe	0.04	(−0.00 to 0.08)	0.051	0.023	0.01	(−0.04 to 0.05)	0.799	0.434
Central Europe	−0.03	(−0.11 to 0.04)	0.419		−0.03	(−0.08 to 0.02)	0.255	
Northern Europe	−0.05	(−0.12 to 0.02)	0.137		−0.02	(−0.06 to 0.02)	0.368	
By PA[7]								
Low PA	0.02	(−0.03 to 0.07)	0.488	0.044	−0.02	(−0.05 to 0.02)	0.361	0.138
High PA	−0.02	(−0.05 to 0.02)	0.347		−0.00	(−0.04 to 0.04)	0.884	
By region and PA								
Southern Europe								
Low PA	0.08	(0.03 to 0.12)	0.002	<0.0001	−0.00	(−0.05 to 0.05)	0.978	0.899
High PA	−0.00	(−0.04 to 0.04)	0.917		0.02	(−0.04 to 0.08)	0.487	
Central Europe								
Low PA	−0.04	(−0.13 to 0.05)	0.343	0.493	−0.04	(−0.09 to 0.02)	0.190	0.088
High PA	−0.03	(−0.09 to 0.04)	0.400		−0.02	(−0.07 to 0.03)	0.408	
Northern Europe								
Low PA	−0.08	(−0.14 to −0.03)	0.003	0.611	−0.06	(−0.12 to 0.01)	0.085	0.774
High PA	−0.08	(−0.16 to −0.01)	0.034		−0.04	(−0.07 to 0.01)	0.024	

[1] Increase or decrease in BMI per 1-unit increase in the mMDS; multilevel mixed-effects linear regression models. Model 1: Crude model; Model 2: fully adjusted model (controlling for all potential confounders: age, educational level, PA level, smoking status, height, EI, misreporting of EI, and menopausal status in women); Model 3: fully adjusted model without control for EI; models used in stratified analyses and subgroup analyses correspond to MODEL 2 (fully adjusted model).

[2] Test of heterogeneity among groups in the stratified analyses.

[3] Analysis excluding participants with heart disease, stroke, diabetes mellitus, and/or cancer.

[4] Analysis excluding over-reporters and under-reporters of EI (method of Goldberg) (39); in this model, misreporting of EI was not added as a confounder factor.

[5] Analyses excluding participants with self-reported anthropometry.

[6] Countries by region: Southern Europe (Greece, Italy, and Spain), Central Europe (France, UK, Germany, The Netherlands), Northern Europe (Denmark, Sweden, and Norway).

[7] Low level of PA means inactive or moderately inactive; high PA means moderately active or active.

means and SD for the continuous ones. The level of significance of the observed differences among group means was tested using 1-way ANOVA; differences in percentages among groups were tested using the chi-square test. Descriptive data on BMI, WC, and other covariates by country and mMDS categories were presented.

The explanatory variable in models used in the present study was adherence to a modified Mediterranean diet as measured by the mMDS; outcome variables were general obesity measured by BMI and abdominal fat mass measured by WC. The overall association between mMDS and BMI or WC was modeled using multilevel mixed-effects linear regression with random effect on both intercept and slope, taking into account the clustering of the data within countries (level 3) and within centers (level 2; individuals are the first level in the analyses).

We fit crude (univariate) and multivariate-adjusted models controlling for the following potential confounders (as fixed effects): age (in years, continuous), educational level (categorical), PA level (categorical), smoking status (categorical), height (in cm, continuous), and menopausal status (in women only; categorical). There were participants with missing values for PA level (13.7%) and educational level (1.2%). We treated participants with missing data as a separate category for these 2 variables.

To take into account possible misreporting of EI, the ratio of reported EI:predicted basal metabolic rate (EI:BMR) was calculated and participants were classified as under-reporters (EI:BMR <1.14), plausible reporters (EI:BMR = 1.14–2.1), or over-reporters (EI:BMR >2.1) of EI based on the cutoff points proposed by Goldberg (39). Misreporting of EI (categorical variable: under-reporter, plausible reporter, over-reporter) was included in the model as a confounder factor.

To account for the influence of BMI on WC, analyses on WC were conducted with and without adjustment for BMI (in kg·m^{-2}, continu-

TABLE 4 Association between the mMDS and WC in EPIC-PANACEA participants

mMDS	Men				Women			
	β[1]	95% CI	P	P for heterogeneity[2]	β[1]	95% CI	P	P for heterogeneity[2]
Model 1	−0.18	(−0.33 to −0.03)	0.018		−0.24	(−0.37 to −0.10)	<0.0001	
Model 2	−0.09	(−0.14 to −0.04)	<0.0001		−0.06	(−0.10 to −0.01)	0.010	
Model 3	−0.09	(−0.14 to −0.04)	<0.0001		−0.05	(−0.10 to −0.01)	0.018	
Model 4	−0.08	(−0.21 to 0.05)	0.209		−0.08	(−0.18 to 0.01)	0.081	
Subgroup analyses								
No illness[3]	−0.09	(−0.14 to −0.04)	0.001		−0.06	(−0.11 to −0.02)	0.010	
Plausible EI[4]	−0.09	(−0.14 to −0.05)	<0.0001		−0.05	(−0.09 to −0.01)	0.019	
Measured anthropometry[5]	−0.09	(−0.14 to −0.04)	<0.0001		−0.06	(−0.10 to −0.01)	0.010	
Stratified analyses								
By age group								
<60 y old	−0.09	(−0.14 to −0.04)	<0.0001	0.838	−0.06	(−0.10 to −0.01)	0.021	<0.0001
≥60 y old	−0.09	(−0.16 to −0.02)	0.010		−0.03	(−0.09 to 0.04)	0.384	
By BMI category								
<18.5 kg·m^{-2}	0.18	(−0.10 to 0.45)	0.213	<0.0001	−0.03	(−0.11 to 0.06)	0.505	<0.0001
18.5 – <25 kg·m^{-2}	−0.08	(−0.13 to −0.03)	0.002		−0.07	(−0.10 to −0.04)	<0.0001	
25 – <30 kg·m^{-2}	−0.09	(−0.14 to −0.04)	<0.0001		−0.07	(−0.11 to −0.02)	0.003	
≥30 kg·m^{-2}	−0.17	(−0.25 to −0.09)	<0.0001		−0.08	(−0.15 to 0.00)	0.054	
By region[6]								
Southern Europe	−0.06	(−0.11 to −0.02)	0.009	0.009	−0.01	(−0.06 to 0.03)	0.613	<0.0001
Central Europe	−0.06	(−0.16 to 0.05)	0.272		−0.08	(−0.15 to −0.02)	0.013	
Northern Europe	−0.20	(−0.23 to −0.17)	<0.0001		−0.17	(−0.21 to −0.13)	<0.0001	
By PA[7]								
Low PA	−0.11	(−0.16 to −0.06)	<0.0001	0.298	−0.06	(−0.11 to −0.01)	0.015	0.546
High PA	−0.08	(−0.13 to −0.03)	<0.0001		−0.06	(−0.11 to −0.01)	0.020	
By region and PA								
Southern Europe								
Low PA	−0.07	(−0.13 to −0.02)	0.004	0.506	−0.02	(−0.07 to 0.04)	0.553	0.354
High PA	−0.05	(−0.10 to 0.00)	0.057		0.01	(−0.06 to 0.08)	0.739	
Central Europe								
Low PA	−0.07	(−0.17 to 0.03)	0.179	0.449	−0.10	(−0.19 to −0.01)	0.026	0.298
High PA	−0.05	(−0.13 to 0.03)	0.248		−0.07	(−0.13 to −0.01)	0.021	
Northern Europe								
Low PA	−0.21	(−0.26 to −0.17)	<0.0001	0.591	−0.16	(−0.22 to −0.11)	<0.0001	0.268
High PA	−0.20	(-0.24 to −0.17)	<0.0001		−0.19	(−0.24 to −0.15)	<0.0001	

[1] Increase or decrease in WC per 1-unit increase in the mMDS; multilevel mixed-effects linear regression models. Model 1: Crude model; model 2: fully adjusted model (controlling for all potential confounders: age, educational level, PA level, smoking status, height, EI, misreporting of EI, menopausal status in women, and BMI); model 3: fully adjusted model without control for EI; model 4: fully adjusted model without control for BMI; models used in stratified analyses and subgroup analyses correspond to model 2 (fully adjusted model).
[2] Test of heterogeneity among groups in the stratified analyses.
[3] Analysis excluding participants with heart disease, stroke, diabetes mellitus, and/or cancer.
[4] Analysis excluding over-reporters and under-reporters of EI (method of Goldberg) (39); in this model, misreporting of EI was not added as a confounder factor.
[5] Analyses excluding participants with self-reported anthropometry.
[6] Countries by region: Southern Europe (Greece, Italy, and Spain), Central Europe (France, UK, Germany, The Netherlands), Northern Europe (Denmark, Sweden, and Norway).
[7] Low level of PA means inactive or moderately inactive; high PA means moderately active or active.

ous). Also, given that closer adherence to the Mediterranean diet has been linked to a high EI (25), models were conducted with and without adjusting for total EI (kJ/d, continuous).

Sensitivity analyses were performed excluding participants with any chronic disease at baseline (heart disease, stroke, diabetes mellitus, and/or cancer), excluding misreporters of energy (according to the Goldberg classification) (39) and those with self-reported anthropometric values.

Models were also run after stratification for the following variables: age group (<60 y and ≥60 y), European region (Southern Europe, Central Europe, and Northern Europe), BMI category (underweight BMI, <18.5 kg·m^{-2}, normal weight BMI, 18.5 to <25 kg·m^{-2}, overweight BMI, 25 to <30 kg·m^{-2}, and obese BMI, ≥30 kg·m^{-2}), and PA (grouped as low level of PA, inactive or moderately inactive, and high level of PA, moderately active or active). Tests of heterogeneity among different strata were obtained by adding interaction terms between mMDS and the above-mentioned variables.

The extent of heterogeneity between the country-specific estimates of association was tested by adding an interaction term between mMDS and the variable denoting country in the model.

Country-specific associations between mMDS and BMI or WC were estimated using general linear models (in countries with 1 center only) or multilevel mixed-effects linear regression models (in countries with several centers). The specification of the mixed models was dictated by the interaction between mMDS and the variable denoting center; hence, in countries in which the interaction was significant (P-value < 0.05), linear mixed models with random effects on both intercept and slope

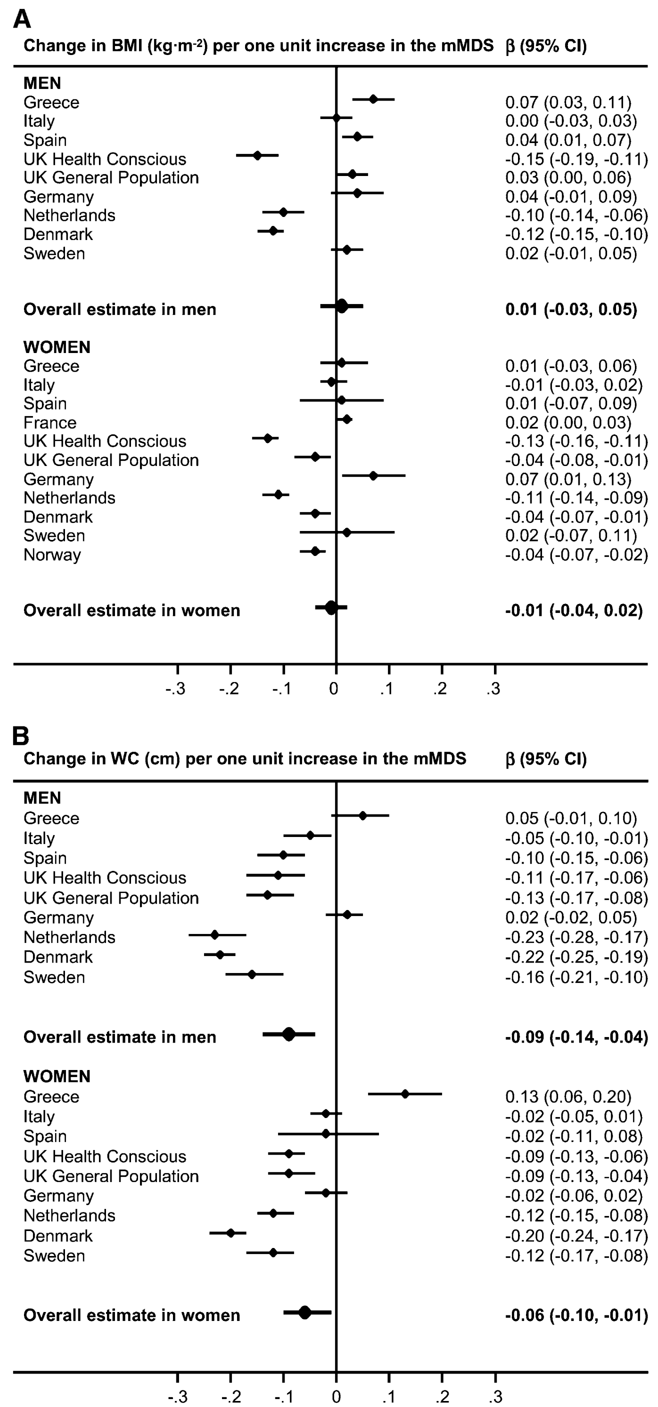

FIGURE 1 Country- and sex-specific associations between the mMDS and BMI (*A*) or WC (*B*) in EPIC-PANACEA participants. Effect estimate (β) and 95% CI of the mMDS on BMI, derived by multilevel mixed-effects linear regression and controlled for potential confounders: age, educational level, PA level, smoking status, height, EI, misreporting of EI, and menopausal status in women only and BMI for WC only.

were used. When there was no evidence of heterogeneity among centers (P-value for the interaction ≥ 0.05), the association was modeled through mixed-effects linear regression with random effect on intercept only.

The association between the mMDS and waist:hip ratio, adjusting for BMI and the above-indicated confounders, was also estimated. The observed association was very similar to that obtained in models including WC as the outcome variable; therefore, these results are not shown in the present study. In addition, models were analyzed using a different version of the mMDS constructed using the sex-specific EPIC-wide medians of calibrated dietary data. Overall, results obtained using this version of the mMDS were similar in magnitude and direction and therefore these are not shown in the present study.

A P-value < 0.05 was regarded as significant. All statistical analyses were performed with the STATA statistical package 9.0.

Results

Among the countries participating in this study, Greece and Spain had the highest mean BMI (~28 kg·m^{-2} in both men and women) and WC (>98 cm in men and 87 cm in women). The lowest BMI and WC were in men and women from the UK health conscious group and in women from France (**Table 1**).

BMI and WC were significantly lower in participants in the highest category of the mMDS compared with those in the lowest category (**Table 2**). Total EI, as well as the percentage of plausible reporters of EI, significantly increased with increasing mMDS category. Higher mMDS was inversely related to energy density in both men and women. Men and women within the highest category of the mMDS had a greater intake of carbohydrates (expressed as percentage of energy) and fiber (g/d) and a lower intake of proteins and fat (expressed as percentages of energy) compared with those within the lowest category of the mMDS. Alcohol consumption expressed either in g/d or in percentage of total energy was higher in those with higher mMDS compared with those with lower mMDS. Percentages of men and women with high educational levels and high PA levels were higher and the percentage of smokers was lower in those with high mMDS compared with low mMDS.

The mMDS was not associated with BMI in either crude (**Table 3**, model 1) or multi-adjusted (model 2) models. When EI was excluded from the model (model 3), there was an overall positive association in women. There was evidence of heterogeneity in the association of mMDS with BMI among age groups, European regions, categories of BMI in men and women, and levels of PA in men. In stratified analyses by European region and level of PA, we observed a positive and significant association between mMDS and BMI in men from Southern Europe with low levels of PA; however, mMDS was unrelated to BMI in Southern European men with a high level of PA.

The mMDS was inversely and significantly associated with WC in both crude and fully adjusted analyses (**Table 4**, models 1 and 2); hence, for a given BMI, men and women had a lower WC when they scored 1 point higher in their mMDS. There was no change in the magnitude of the association between mMDS and WC after excluding EI (model 3) in either men or women. When BMI was not controlled for in the models assessing the relationship between mMDS and WC (model 4), the direction of the associations in both sexes was similar, although not significant (P = 0.209 in men and P = 0.081 in women). The inverse association between mMDS and WC was stronger in men and women from Northern European countries and in obese individuals; however, in additional analyses, we observed that the stronger inverse association between mMDS and WC among the obese was significant only in Central and Northern European countries. In Southern Europe, the inverse association between mMDS and WC was stronger among normal-weight individuals and weaker among the overweight and obese (Supplemental Table 3).

There was evidence of heterogeneity among the countries in the association between mMDS and BMI in both men and women (**Fig. 1***A*) (P-value for heterogeneity < 0.0001); in men and women from the UK health conscious group, women from the UK general population, men and women from The Netherlands and Denmark, and in women from Norway, significant inverse associations between mMDS and BMI were observed. The association observed for all other countries was null or positive. On the other hand, there was a significant inverse association between mMDS and WC in men from most countries included in this European study, except for Greece and Germany (Fig. 1*B*) (*P*-value for heterogeneity among countries < 0.0001). In women, significant inverse associations between mMDS and WC were observed in UK (both general and health conscious populations), The Netherlands, Denmark, and Sweden; in women from Greece, a significant positive association was observed (*P*-value for heterogeneity among countries < 0.0001).

To investigate heterogeneity of effects across countries, we tested in post-hoc analyses the relationship of country-specific variables (percentage of individuals with high educational level, high PA level, and current smokers) with country-specific estimates of the association between mMDS and BMI or WC, using univariate and multivariate meta-regression modeling (Supplemental Table 4). We observed that countries in which the percentage of physically active individuals was higher tended to have stronger inverse associations between the mMDS and BMI (results from univariate meta-regression: $P = 0.023$ in men and 0.081 in women) or WC ($P = 0.078$ in men and 0.037 in women). The association persisted in multivariate meta-regression models.

Discussion

Adherence to a variant of the Mediterranean diet, which is high in vegetables, legumes, fruits and nuts, cereals, fish and seafood, and unsaturated fatty acids (in relation to saturated fat), together with moderate alcohol consumption and low intake of meat and meat products and dairy products, was not significantly associated with BMI in this cross-sectional study. However, an inverse and significant association between mMDS and WC was observed after adjustment for BMI in European men and women. These results suggest that Mediterranean dietary patterns of consumption may be related to body fat distribution. Nevertheless, these overall estimates should be interpreted with caution, given the observed heterogeneity among countries in the associations between mMDS and BMI or WC.

The advantages of this study include its large sample size of almost 500,000 individuals, the use of data of participants from 10 European countries with diverse dietary habits, and the use of validated questionnaires. We used a priori defined dietary score to study dietary patterns; this makes it possible to capture the extremes of the exposure of interest and preempts nutritional confounding (40). Also, sensitivity analyses were performed excluding participants with self-reported anthropometric data and those with a history of diabetes, cancer, heart disease, or stroke. The main limitation of the study is its cross-sectional design, thus limiting inference on the time sequence of the association between Mediterranean diet and adiposity. In addition, selection bias, recall bias, and residual confounding might be present. Finally, although our dietary assessment methods are validated, they do contain measurement errors.

It has been argued that diets with high lipid content, such as the Mediterranean diet, may induce excess EI and hence weight gain (19,41,42). However, other studies showed no conclusive evidence that any specific macronutrient composition of the diet affects body weight, as long as energy balance is maintained (43–45). In this and other studies (8,25), the Mediterranean diet score was associated with higher EI. Nevertheless, it may be possible that this association is methodologically driven given that, first, the fat intake of those with better adherence to the Mediterranean diet was not higher than those with lower mMDS, and second, EI was not corrected for when constructing the score. However, if we consider Mediterranean diet score to be inherently positively associated with EI, then control for EI might not be a biologically optimal procedure (25). When EI was not controlled for, women with a high mMDS also had a high BMI score. There were no major changes in the results of the association between mMDS and WC after excluding EI from the models. The lower energy density and higher fiber content of the Mediterranean diet may explain its inverse association with central adiposity (17).

The results concerning Greece in this investigation differ slightly from those previously reported (25). It should be noted that the 2 studies differ in the following: inclusion and exclusion criteria; subtraction in the present analysis of 1 kg from the measured body weight to account for light clothing of the Greek participants during weight measurement; calculation of the lipid ratio in the Greek study as monounsaturated to saturated, as contrasted to mono plus polyunsaturated to saturated used in this analysis; utilization in this study of confounders that were applicable to all participating centers; and the control for misreporting of EI in the present study.

Other cross-sectional studies assessing the effect of a priori-defined Mediterranean diet on measurements of obesity have been conducted (10,21,22,24,26). Three of 5 studies found that higher adherence to the Mediterranean diet was associated with lower prevalence of overweight or obesity or with lower BMI (10,21,24). In 2 of these studies, the association between Mediterranean diet and waist:hip ratio was also estimated (21,22) and in one of them, a significant inverse association was observed (21). Results from cohort and intervention studies are more consistent with a possible role of the Mediterranean diet in preventing overweight/obesity (11,16,20,23,46). We observed heterogeneity among European regions in the association between adherence to the Mediterranean diet and measurements of body fatness. Reasons for such heterogeneity are difficult to elucidate. The presence of reverse causality bias due to the high prevalence of obesity in Southern Europe may be one plausible explanation. It is possible that obese individuals have adopted a particular diet composition (i.e. a healthier diet) as a consequence of their obesity and/or its health complications. This would involve an attenuation of the real association between the mMDS and measurements of adiposity in Southern Europe, as observed in this study. In addition, post hoc meta-regression analyses showed that differences in the percentage of physically active individuals among countries may also explain part of the heterogeneity. In countries where the percentage of physically active people was low, such as Mediterranean countries in Southern Europe, mMDS was unrelated or positively associated with measures of body fatness. Furthermore, an effect modification of the association between mMDS and BMI was observed in Mediterranean men; hence, the mMDS was associated with high BMI only in Mediterranean men with low levels of PA, whereas mMDS was unrelated to BMI in men with high levels of PA. This observation would support the theory that the problem of obesity in Greece and other Mediterranean countries is likely to be related to limited PA in conjunction with excessive positive energy balance brought about by the westernization of their diet (4,25,47–49). On the other hand, promotion of the Mediterranean diet as a model of healthy eating in non-Mediterranean countries may have led to changes in dietary patterns in certain sectors of the population and may cluster with other healthy lifestyles such as PA and maintenance of a healthy weight (49). In conclusion, we observed that adherence to a Mediterranean diet, modified to apply across Europe, which is rich in foods of vegetable origin and unsaturated fatty acids, was associated with lower WC in European men and women with diverse dietary patterns after controlling for BMI, total EI, and other potential confounders. The inverse association between mMDS and WC generally was stronger in men and women from Northern European regions who were overweight or obese. Therefore, although appropriate energy balance is a crucial determinant of body mass, results from this study suggest that specific compositions of the diet (i.e. food patterns in conformity with the Mediterranean diet) may be linked to fat distribution. Nevertheless, given the limitations of this cross-sectional study, future prospective studies are needed to confirm these results.

Literature Cited

1. WHO Regional Office for Europe. Obesity in Europe [cited 2008 24 Jun]. Available from: http://www.euro.who.int/obesity.
2. WHO Health topics: Obesity [cited 2008 25 Jun]. Available from: http://www.who.int/topics/obesity/en/.
3. de Ferranti S, Mozaffarian D. The perfect storm: obesity, adipocyte dysfunction, and metabolic consequences. Clin Chem. 2008;54:945–55.
4. Trichopoulos D. In defense of the Mediterranean diet. Eur J Clin Nutr. 2002;56:928–9, author reply 30–1.
5. Tur JA, Serra-Majem L, Romaguera D, Pons A. Profile of overweight and obese people in a Mediterranean region. Obes Res. 2005;13:527–36.
6. Trichopoulou A, Costacou T, Bamia C, Trichopoulos D. Adherence to a Mediterranean diet and survival in a Greek population. N Engl J Med. 2003;348:2599–608.
7. Benetou V, Trichopoulou A, Orfanos P, Naska A, Lagiou P, Boffetta P, Trichopoulos D. Conformity to traditional Mediterranean diet and cancer incidence: the Greek EPIC cohort. Br J Cancer. 2008;99:191–5.
8. Martinez-Gonzalez MA, de la Fuente-Arrillaga C, Nunez-Cordoba JM, Basterra-Gortari FJ, Beunza JJ, Vazquez Z, Benito S, Tortosa A, Bes-Rastrollo M. Adherence to Mediterranean diet and risk of developing diabetes: prospective cohort study. BMJ. 2008;336:1348–51.
9. Mitrou PN, Kipnis V, Thiebaut AC, Reedy J, Subar AF, Wirfalt E, Flood A, Mouw T, Hollenbeck AR, et al. Mediterranean dietary pattern and prediction of all-cause mortality in a US population: results from the NIH-AARP Diet and Health Study. Arch Intern Med. 2007;167:2461–8.
10. Panagiotakos DB, Polystipioti A, Papairakleous N, Polychronopoulos E. Long-term adoption of a Mediterranean diet is associated with a better health status in elderly people; a cross-sectional survey in Cyprus. Asia Pac J Clin Nutr. 2007;16:331–7.
11. Tortosa A, Bes-Rastrollo M, Sanchez-Villegas A, Basterra-Gortari FJ, Nunez-Cordoba JM, Martinez-Gonzalez MA. Mediterranean diet inversely associated with the incidence of metabolic syndrome: the SUN prospective cohort. Diabetes Care. 2007;30:2957–9.
12. Trichopoulou A, Bamia C, Norat T, Overvad K, Schmidt EB, Tjonneland A, Halkjaer J, Clavel-Chapelon F, Vercambre MN, et al. Modified Mediterranean diet and survival after myocardial infarction: the EPIC-Elderly study. Eur J Epidemiol. 2007;22:871–81.
13. Trichopoulou A, Kouris-Blazos A, Wahlqvist ML, Gnardellis C, Lagiou P, Polychronopoulos E, Vassilakou T, Lipworth L, Trichopoulos D. Diet and overall survival in elderly people. BMJ. 1995;311:1457–60.
14. Trichopoulou A, Orfanos P, Norat T, Bueno-de-Mesquita B, Ocke MC, Peeters PH, van der Schouw YT, Boeing H, Hoffmann K, et al. Modified Mediterranean diet and survival: EPIC-elderly prospective cohort study. BMJ. 2005;330:991.
15. Sofi F, Cesari F, Abbate R, Gensini GF, Casini A. Adherence to Mediterranean diet and health status: meta-analysis. BMJ. 2008;337:a1344.
16. Buckland G, Bach A, Serra-Majem L. Obesity and the Mediterranean diet: a systematic review of observational and intervention studies. Obes Rev. 2008;11:1372–78.
17. Schroder H. Protective mechanisms of the Mediterranean diet in obesity and type 2 diabetes. J Nutr Biochem. 2007;18:149–60.
18. WHO. The challenge of obesity in the WHO European region and the strategies for response. Copenhagen (Denmark): The Regional Office for Europe of the WHO; 2007.
19. Ferro-Luzzi A, James WP, Kafatos A. The high-fat Greek diet: a recipe for all? Eur J Clin Nutr. 2002;56:796–809.
20. Mendez MA, Popkin BM, Jakszyn P, Berenguer A, Tormo MJ, Sanchez MJ, Quiros JR, Pera G, Navarro C, et al. Adherence to a Mediterranean diet is associated with reduced 3-year incidence of obesity. J Nutr. 2006;136:2934–8.
21. Panagiotakos DB, Chrysohoou C, Pitsavos C, Stefanadis C. Association between the prevalence of obesity and adherence to the Mediterranean diet: the ATTICA study. Nutrition. 2006;22:449–56.
22. Rossi M, Negri E, Bosetti C, Dal Maso L, Talamini R, Giacosa A, Montella M, Franceschi S, La Vecchia C. Mediterranean diet in relation to body mass index and waist-to-hip ratio. Public Health Nutr. 2008;11:214–7.
23. Sanchez-Villegas A, Bes-Rastrollo M, Martinez-Gonzalez 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;30:350–8.
24. Schroder H, Marrugat J, Vila J, Covas MI, Elosua R. Adherence to the traditional mediterranean diet is inversely associated with body mass index and obesity in a Spanish population. J Nutr. 2004;134:3355–61.
25. Trichopoulou A, Naska A, Orfanos P, Trichopoulos D. Mediterranean diet in relation to body mass index and waist-to-hip ratio: the Greek European Prospective Investigation into Cancer and Nutrition Study. Am J Clin Nutr. 2005;82:935–40.
26. Fung TT, McCullough ML, Newby PK, Manson JE, Meigs JB, Rifai N, Willett WC, Hu FB. Diet-quality scores and plasma concentrations of markers of inflammation and endothelial dysfunction. Am J Clin Nutr. 2005;82:163–73.
27. Riboli E, Hunt KJ, Slimani N, Ferrari P, Norat T, Fahey M, Charrondiere UR, Hemon B, Casagrande C, et al. European Prospective Investigation into Cancer and Nutrition (EPIC): study populations and data collection. Public Health Nutr. 2002;5:1113–24.
28. Riboli E, Kaaks R. The EPIC Project: rationale and study design. European Prospective Investigation into Cancer and Nutrition. Int J Epidemiol. 1997;26 Suppl 1:S6–14.
29. Bingham S, Riboli E. Diet and cancer: the European Prospective Investigation into Cancer and Nutrition. Nat Rev Cancer. 2004;4:206–15.
30. Ferrari P, Slimani N, Ciampi A, Trichopoulou A, Naska A, Lauria C, Veglia F, Bueno-de-Mesquita HB, Ocke MC, et al. Evaluation of under- and overreporting of energy intake in the 24-hour diet recalls in the European Prospective Investigation into Cancer and Nutrition (EPIC). Public Health Nutr. 2002;5:1329–45.
31. Haftenberger M, Lahmann PH, Panico S, Gonzalez CA, Seidell JC, Boeing H, Giurdanella MC, Krogh V, Bueno-de-Mesquita HB, 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;5:1147–62.
32. Spencer EA, Appleby PN, Davey GK, Key TJ. Validity of self-reported height and weight in 4808 EPIC-Oxford participants. Public Health Nutr. 2002;5:561–5.
33. Spencer EA, Roddam AW, Key TJ. Accuracy of self-reported waist and hip measurements in 4492 EPIC-Oxford participants. Public Health Nutr. 2004;7:723–7.
34. Kaaks R, Riboli E. Validation and calibration of dietary intake measurements in the EPIC project: methodological considerations. European Prospective Investigation into Cancer and Nutrition. Int J Epidemiol. 1997;26 Suppl 1:S15–25.
35. Slimani N, Kaaks R, Ferrari P, Casagrande C, Clavel-Chapelon F, Lotze G, Kroke A, Trichopoulos D, Trichopoulou A, et al. European Prospective Investigation into Cancer and Nutrition (EPIC) calibration study: rationale, design and population characteristics. Public Health Nutr. 2002;5:1125–45.
36. Deharveng G, Charrondiere UR, Slimani N, Southgate DA, Riboli E. Comparison of nutrients in the food composition tables available in the nine European countries participating in EPIC. European Prospective Investigation into Cancer and Nutrition. Eur J Clin Nutr. 1999;53:60–79.
37. Kaaks R, Slimani N, Riboli E. Pilot phase studies on the accuracy of dietary intake measurements in the EPIC project: overall evaluation of results. European Prospective Investigation into Cancer and Nutrition. Int J Epidemiol. 1997;26 Suppl 1:S26–36.

38. Wareham NJ, Jakes RW, Rennie KL, Schuit J, Mitchell J, Hennings S, Day NE. 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;6:407–13.
39. Goldberg GR, Black AE, Jebb SA, Cole TJ, Murgatroyd PR, Coward WA, Prentice AM. Critical evaluation of energy intake data using fundamental principles of energy physiology: 1. Derivation of cut-off limits to identify under-recording. Eur J Clin Nutr. 1991;45:569–81.
40. Trichopoulos D, Lagiou P. Mediterranean diet and cardiovascular epidemiology. Eur J Epidemiol. 2004;19:7–8.
41. Astrup A, Grunwald GK, Melanson EL, Saris WH, Hill JO. The role of low-fat diets in body weight control: a meta-analysis of ad libitum dietary intervention studies. Int J Obes Relat Metab Disord. 2000;24:1545–52.
42. Astrup A, Ryan L, Grunwald GK, Storgaard M, Saris W, Melanson E, Hill JO. The role of dietary fat in body fatness: evidence from a preliminary meta-analysis of ad libitum low-fat dietary intervention studies. Br J Nutr. 2000;83 Suppl 1:S25–32.
43. Sacks FM, Bray GA, Carey VJ, Smith SR, Ryan DH, Anton SD, McManus K, Champagne CM, Bishop LM, et al. Comparison of weight-loss diets with different compositions of fat, protein, and carbohydrates. N Engl J Med. 2009;360:859–73.
44. Willett WC. Dietary fat and obesity: an unconvincing relation. Am J Clin Nutr. 1998;68:1149–50.
45. Willett WC. Is dietary fat a major determinant of body fat? Am J Clin Nutr. 1998;67:S556–62.
46. Shai I, Schwarzfuchs D, Henkin Y, Shahar DR, Witkow S, Greenberg I, Golan R, Fraser D, Bolotin A, et al. Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet. N Engl J Med. 2008;359:229–41.
47. Garcia-Closas R, Berenguer A, Gonzalez CA. Changes in food supply in Mediterranean countries from 1961 to 2001. Public Health Nutr. 2006;9:53–60.
48. Serra-Majem L, Ribas L, Lloveras G, Salleras L. Changing patterns of fat consumption in Spain. Eur J Clin Nutr. 1993;47 Suppl 1:S13–20.
49. Willett WC. The Mediterranean diet: science and practice. Public Health Nutr. 2006;9:105–10.