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Adherence to the Mediterranean diet in metabolically healthy and unhealthy overweight and obese European adolescents; the HELENA study

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AUTHOR CONTRIBUTION

IL conceived the hypothesis, LA drafted the manuscript and performed the statistical analysis; IH, FBO, JRR, SDH, YM, AM, CJ, KW, GB, MK, AK, CB, RPC, FG, MGG, LAM and IL contributed to the interpretation and discussion of the results. All authors contributed to the interpretation and discussion of the results, and critically revised the drafted manuscript and made the final approval of the version to be submitted.

ABSTRACT

Purpose: To examine the adherence to the Mediterranean dietary pattern (MDP) in metabolically healthy overweight or obese (MHO) and metabolically unhealthy obese (MUO) European adolescents.

Methods: In this cross-sectional study 137 overweight/obese adolescents aged 12-17 years old from the HELENA study were included. Height, weight, waist circumference and skinfolds thicknesses were measured and body mass index (BMI) and body fat percent were calculated. Systolic and diastolic blood pressure, glucose, HDL-cholesterol, triglycerides and cardiorespiratory fitness (20-m shuttle run test) were measured. MHO and MUO phenotypes were categorized following the Jolliffe and Janssen criteria. Two non-consecutive 24-h recalls were used for dietary intake assessment and the adherence to the MDP was calculated using the Mediterranean dietary pattern score (MDP score) (range 0-9).

Results: A total of 45 (22 girls) adolescents (32.8%) were categorized as MHO. The adherence to the MDP was significantly higher in MHO than in MUO adolescents regardless of age, sex, body fat percentage, energy intake and center (MDP score: 4.6±1.6 *vs*. 3.9±1.5, p=0.036), but this difference became non-significant after further adjustment for cardiorespiratory fitness. Participants who had a low adherence to the MDP (MDP score ≤4) had a higher likelihood of having MUO phenotype regardless of sex, age, energy intake, center and body fat percentage (OR 2.2; 95% CI, 1.01-4.81, p=0.048).

Conclusions: Adherence to the MDP might be beneficial to maintain metabolic health in overweight/obese adolescents, yet cardiorespiratory fitness seems to play a key role on the metabolic phenotype.

Keywords: Metabolic health, obesity, Mediterranean diet, adolescents, cardiorespiratory fitness

Abbreviations

MHO, metabolically healthy overweight or obesity

MUO, metabolically unhealthy overweight/obese

MDP, Mediterranean dietary pattern

MDP score, Mediterranean dietary pattern score

BMI, body mass index

HDL, high density lipoprotein

LDL, low density lipoprotein

TG, triglycerides

HELENA-DIAT, HELENA-Dietary Assessment Tool

INTRODUCTION

Childhood and adolescence obesity prevalence has increased over the last few decades [1]. This chronic disease is associated with cardiometabolic risk factors such as insulin resistance, dyslipidemia and hypertension [2]. However, several studies reported the existence of metabolically healthy phenotypes, referred to as metabolically healthy overweight or obesity (MHO), in whom no obesity associated comorbidities are found, whereas obesity associated with metabolic abnormalities is known as metabolically unhealthy overweight or obesity (MUO)[3].

Although there is no a standard definition of MHO, which in turn leads to vary the rates of MHO, the prevalence of the healthy phenotype seems to be close to 30% of population with obesity and it is also negatively associated with obesity degree [4,5,6].

Diet and physical activity are lifestyle determinants of health closely related to obesity and its complications [5]. Nowadays, nutrition research focuses more on examining the impact of dietary patterns such as the Mediterranean diet (MDP) on health outcomes, instead of exploring the effect of nutrients or individual food groups on health status. Thereby, dietary patterns offer a more holistic description of dietary habits considering also the possible interactions among nutrients and foods [6]. The MDP shows the typical dietary pattern followed by people from Creta, Greece and Southern Italy in the 1960s [7]. This Mediterranean region was the area with the highest life expectancy and with the lowest incidence of coronary heart disease in the world. Adherence to the MDP has been associated with a reduction in cardiovascular and all-cause mortality and type 2 diabetes incidence [8,9]. MDP is characterized by high intakes of vegetables, fruits, nuts, cereals, legumes and olive oil as the principal source of fat, moderate to-high- intake of fish, moderate consumption of dairy products and wine (during meals) and low consumptions of meat and poultry [7]. Several studies reported that adherence to the MDP improves health status in youths [9]. Accordingly, we hypothesized that MHO adolescents might have a higher adherence to this dietary pattern than their MUO peers. The current study aimed to examine the association between the adherence to MDP and metabolic health status in overweight and obese European adolescents from the Healthy Lifestyle in Europe by Nutrition in Adolescence (HELENA) study.

MATERIAL AND METHODS

Study design

The HELENA study is a multicenter cross-sectional study which was designed to evaluate the nutritional status and lifestyle in adolescents (12.5-17.5 years) from 10 European cities between 2006 and 2007 [10]. Among the total sample of 3,528 participants, blood samples were randomly selected and collected in a subsample of 1,069 adolescents [10]. A detailed description of the HELENA study procedures and methodology has been published elsewhere [11,12] . All adolescents participating in the study and their parents or legal guardians had to sign an informed written consent so that they could be enrolled in the study. The study protocol was approved by the corresponding local Human Research Review Committees of the centers involved, which were the following ones: Athens in Greece, Dortmund in Germany, Gent in Belgium, Lille in France, Roma in Italy, Stockholm in Sweden, Vienna in Austria and Zaragoza in Spain. For the target of the current study, a total of 137 (14.8±1.3 years, 48.9 % girls) overweight or obese adolescents from whom dietary and biomarkers data were available were included (**Fig. 1**).

Anthropometry and cardiometabolic risk factors

Anthropometric assessment was performed to categorize weight status, as well as to examine body composition. Weight (SECA 861, Hamburg, Germany) and height (SECA 225, Hamburg, Germany) were measured with a high-precision scale to the nearest 0.05 kg and with a telescopic height measuring instrument to the nearest 0.1cm, respectively [11]. BMI was determined as body weight divided by height squared (kg/m^2) and overweight and obesity status were categorized according to the World Obesity Federation criteria [12]. A non-elastic tape (SECA 200) to the nearest 0.1 cm was used for waist circumference measurement. In addition, tricipital and subscapular skinfold thicknesses were measured (Holtain) and body fat percentage was computed using the Slaughter equation [13]. Blood pressure (systolic and diastolic) was measured twice with a 10 minutes time period between, using a clinical automated digital blood pressure device (OMRON) and the lowest value was recorded. Glucose, triglycerides and HDL-cholesterol, were obtained from blood samples collected after 10-h overnight fast by following an established blood collection and analysis protocol [14]. Cardiorespiratory fitness was determined using the 20-m shuttle run test as described elsewhere [15]. Briefly, adolescents had to run between two lines 20m apart following an audio signal from a recorded CD. The audio signal started with an 8.5km/h speed increasing by 0.5km/h per minute. When the participants did not reach the end line along with the audio signal on two consecutive times or when the adolescent stopped because of exhaustion the test was finished. Thereby, aerobic fitness was examined calculating the maximal oxygen consumption (ml/kg/min) using the equation suggested by Leger et al [16].

MHO and MUO classification criteria

Several criteria have been proposed for metabolic health classification in pediatric populations. Nevertheless, in the current study, in order to establish the criteria for classifying metabolic status we followed the definition of MHO proposed by Ortega et al, which are a detailed criteria based on a comprehensive review of the literature summarized into 7 scientific arguments (for more information, see tables 2 and 3 of the review) [17]. The criteria for the classification of overweight/obese individuals as MHO or MUO of this review is in accordance with previous large collaborative studies and international organizations agreements, and it is also appropriate for using with youths [17]. This definition recommends the use of the *criterium* proposed by Jolliffe and

Janssen [18] for adolescent population, since they classify metabolically healthy and unhealthy status based on specific sex and age cut-off points. Using these criteria, adolescents were considered as MHO if they met zero of the criteria; whereas adolescents were considered as MUO if they presented one or more of the following cardiometabolic risk factors: high systolic and/or diastolic blood pressure, high blood glucose level, high triglycerides (TG) levels and low values of HDL-cholesterol. In accordance with previous studies, waist circumference was not included in the definition of metabolic health, considering that it is above the established thresholds in the majority of individuals with overweight or obesity[18,20].

Dietary intake assessment

Two non-consecutive computerized 24-h recalls were used to assess dietary intake in a time span of two weeks. These 24-h recalls were collected using the HELENA-Dietary Assessment Tool (HELENA-DIAT) 24-h dietary recall software, a nutrition assessment tool which is organized in six meal occasions (breakfast, mid-morning snack, midday meal, afternoon snack, evening meal and evening snack) referring to the day before the interview. This 24-h recalls were self-reported, but the adolescents were helped by trained dieticians [20].

Adherence to the MDP was determined as the sum of the score assigned to nine food groups and nutrients, including seven positive and two negative dietary components. The current scale was based on the MDP scale of Trichopoulou et al [7]. Dietary intake of vegetables, fruits and nuts, cereals roots, pulses, fish, dairy products and unsaturated to saturated fat ratio were scored positively, scoring 1 point when the intakes were above the sex-specific median (50^{th} percentile) and scoring 0 when the intakes were below the sex-specific median (see **Supplemental Table 1** to find information about food intake and adherence to the MDP in the whole HELENA sample including non-overweight adolescents). The intake of dairy products was considered as a positive dietary component because in adolescence dairy products are recommended due to growth and development processes. The intakes of fruits, nuts and olives were included in the fruit and nuts variable; bread, cereals, flour, rice cereals, pasta and potatoes were considered as cereal roots; and dairy products included milk, yoghurt and cheese. In contrast, meat and processed meat and alcohol consumption were scored inversely. The value of 0 was given to a meat intake above the sex-specific median and a value of 1 when the intake was below the median. Alcohol intake was considered as an unhealthy product in adolescents and therefore a value of 1 was given if there was no consumption, while a value of 0 if there was any alcohol intake. Likewise, the range of the Mediterranean diet score (MDP score) ranged from 0 (minimal adherence) to 9 points (maximal adherence). Thereafter, the adherence to the MDP was classified into two groups, low (≤4 points) and high (>5 points) adherence to the MDP.

Statistical analysis

Independent *t* tests were used to identify differences between MHO and MUO groups in continuous variables, while to examine differences in categorical variables chi-square tests were used. Age and tanner stage were categorized to classify younger (age below median) from older adolescents (age equal or above median) and adolescents with lower puberty stage (below or equal puberty stage III) from those participants with high sexual maturation (equal or above IV). (Variables with a non-normal distribution (glucose, triglycerides, HDL-cholesterol, systolic and diastolic blood pressure, cardiorespiratory fitness and MDP score) were logarithmically transformed. As the adherence to the MDP should be higher in the Southern (Athens, Rome and Zaragoza) than in Central-Northern

(Dortmund, Ghent, Lille, Stockholm and Vienna) European countries, this categorical variable thereafter called center (Central-Northern *vs*. Southern country) was used as covariate in the analyses. As there were no statistically significant differences in the prevalence of MHO and MUO phenotypes according to the maternal educational level, the socioeconomic status of the parents was not included as a confounder in the analyses. Differences in adherence to the MDP between MHO and MUO groups were analyzed using univariate linear models with sex, age, energy intake and center (model 1); sex, age, energy intake, center and body fat percentage (model 2) and sex, age, energy intake, center, body fat percentage and cardiorespiratory fitness (model 3) as covariates. Binary logistic regression models were developed to analyze the relationship between adherence to the MDP (low *vs.* high MDP score score) and metabolic phenotypes (MHO *vs*. MUO) adjusted for sex, age, energy intake and center (model 1); sex, age, energy intake, center and body fat percentage (model 2) and finally using sex, age, energy intake, center and cardiorespiratory fitness (model 3) as covariates. Sensitivity analyses were carried out with continuous odds ratio to analyze the relationship between the adherence to the MDP and metabolic phenotypes. Statistical analyses were carried out with the statistical software SPSS version 20.0 (SPSS Inc, Chicago) with a level of significance of α=0.05.

RESULTS

Anthropometric and biological characteristics in MHO and MUO adolescents are shown in **Table 1.** Weight, BMI, maternal educational level and the percentage of participants with obesity were significantly higher in MUO compared to MHO groups ($p<0.05$, Table 1). In contrast, sex, age, pubertal status, height, waist circumference, body fat percentage and maternal educational level did not differ between the two metabolic phenotypes. Overall, as expected due to the definition of the metabolic phenotype, MHO adolescents had a healthier cardiovascular profile, i.e., lower values of TG, systolic and diastolic blood pressure and higher levels of HDL ($p<0.001$, Table 1). There were no significant differences ($p=0.915$) in the distribution of MHO and MUO adolescents across the Center-North and South of Europe (**Supplemental Table 2**).

Table 2 shows dietary intake in MHO and MUO adolescents. Higher fish intake (%33.3) was observed in MHO than in MUO adolescents ($p<0.05$, Table 2). In contrast, intake of vegetables, fruits and nuts, cereal roots, pulses, unsaturated to saturated fatty acids ratio, dairy products, meat and alcohol were similar in MHO and MUO (Table 2). The adherence to the MDP in MHO and MUO adolescents is shown in **Fig. 2**. It was observed that the MDP score was significantly higher in MHO than in MUO adolescents regardless of age, sex, energy intake and center (4.5±1.7 *vs*. 3.9±1.6, in MHO and MUO respectively, $p=0.044$, Model 1, **Fig. 2**). This difference was strengthened when body fat percentage was entered into the model (4.6±1.6 *vs*. 3.9±1.5, $p=0.036$, Model 2, **Fig. 2**), but it was diminished and became statistically non-significant after further adjustment for cardiorespiratory fitness (4.3±1.6 *vs*. 3.9±1.6, $p=0.323$, Model 3, **Fig. 2**). Odds ratios (OR) for having obesity-associated risk factors according to the adherence to the MDP categories (low *vs*. high) are shown in **Fig. 3**. It was observed that adolescents with low adherence to the MDP (MDP score ≤4) had higher likelihood of having MUO phenotype regardless of sex, age, energy intake, center and body fat percent (OR 2.2; 95%CI, 1.01-4.81, p=0.048, Model 2, **Fig. 3**). However, when the analyses were further adjusted with cardiorespiratory fitness the results were attenuated and became non-significant (OR 1.8; 95%CI, 0.74-4.46, p=0.051, Model 3, **Fig. 3**). After sensitivity analyses with continuous OR, it was observed that the odds ratio between the adherence to the MDP and MUO metabolic phenotype was below one (OR 0.8; 95% CI, 0.58-0.97, sex, age, energy intake, center and body fat percentage adjusted p=0.032), which means that higher adherence to the MDP is associated with lower likelihood of being MUO.

DISCUSSION

The main finding of the current study is that overweight or obese adolescents with a healthier metabolic profile (i.e., MHO) present higher adherence to the MDP (≈7%) compared to adolescents who have already developed cardiometabolic risk factors, and as a consequence, have a worse metabolic profile. Thus, a higher score of the MDP scale was observed among MHO than in their MUO peers, which could be due to higher fish intake observed among MHO participants. Indeed, having a low adherence to the MDP increased by twice the likelihood of having obesity-associated risk factors, and as consequence, having MUO phenotype.

As expected, the majority of the cardiometabolic risk factors were higher in MUO than in MHO adolescents. It was observed that approximately 33% of males and females did not show cardiometabolic risk factors associated to excess adiposity. These findings are in line with previous studies which reported that around a third part of teenagers with obesity could be classified as MHO [21]. In any case, the prevalence of each group studied certainly depends on the metabolic syndrome status criteria used to classify individuals into MHO and MUO [17]. Moreover, the metabolic profile seems to worsen when increasing adiposity and/or duration of obesity [22]. A recent study observed that the MHO phenotype decreased with age in both genders [22]. Thus, MHO rates ranged between 4.2% and 68% in childhood and adolescence, whereas MHO prevalence in adulthood across Europe was 7-28% and 2-19% for women and men, respectively [22,3]. In our study, on the contrary, the metabolic status did not differ across pubertal development stages or with age.

The effect of the diet quality or dietary patterns on metabolic phenotypes has already been studied. For instance, researches of the National Health and Nutrition Examination Survey examined the Healthy Eating Index in adolescents and adults with obesity and showed that the diet quality was higher among MHO compared with MUO, which stands for having a better compliance to the American Dietary Guidelines [5,23]. These findings concur with the results of the current study suggesting that the adherence to the MDP could be a protective factor to develop the MUO phenotype. In contrast, other authors did not find any significant difference in macro/micronutritional composition among middle-aged obese adults with MHO and MUO phenotypes and neither healthy obesity was associated with increased diet quality [24,25].

The benefits of adherence to the MDP on metabolic risk have been extensively studied. A higher adherence to the MDP has been related to lower BMI, glucose level and a better lipid profile in children and adolescents [26]. Similarly, Zhong et al. observed that adherence to MDP was associated with better glycemic control and lipid profile among adolescents with type 1 diabetes who were less than twenty years-old at diagnosis [27]. In this last study, adherence to the MDP was assessed using the KIDMED questionnaire, and precisely, an increase of two-points out of twelve in the KIDMED score (≈%17 higher adherence) was associated with 4 mg/dL lower total cholesterol and 3.4 mg/dL lower LDL-cholesterol [27]. In another study with hypercholesterolemic children, after 12-month of nutritional intervention based on MDP, an approximately 10% decrease of total and LDL-cholesterol levels was observed [28]. Although several studies have examined the influence of the adherence to the MDP on cardiovascular health in children and adolescents [26,28], as far as we are aware, there is no previous study examining the adherence to the MDP on MHO and MUO phenotypes in youths which hampers comparisons among studies.

The present study demonstrated that adolescents with a healthy metabolic profile showed to have a higher fish intake compared to those with metabolic abnormalities. The effect of fish intake in metabolic status has previously been studied by different authors.

Likewise, Kim et al. observed that high fish intake was associated with lower TG and blood pressure and higher HDL cholesterol levels [6,29]. Thus, individuals who were in the highest third of fish intake had 65% lower risk of having metabolic syndrome comparing with those in the lowest third. The possible preventive role of fish consumption in the development of the metabolic syndrome in adults was examined in a systematic review, and the authors concluded that fish consumption may improve metabolic health [31]. Dietary fatty acid composition is also likely to be involved in the protective role of metabolic syndrome [7,31]. Previous studies proposed that polyunsaturated fatty acids in fish could be the possible connectors between dietary intake and health benefits [29,32]. This observation is in accordance with the higher fish consumption (≈33%) observed in our sample of MHO compared to MUO adolescents. In contrast, other studies did not observe any significant association between dietary fish intake and metabolic status [34] or showed that this preventive role of fish might be gender-related [35]. Unexpectedly, in a previous study of Danish adolescents, fish intake was associated with a poorer metabolic profile [36].

We observed that the difference in the adherence to MDP between MHO and MUO groups became non-significant after further adjustment for cardiorespiratory fitness. However, this finding should be interpreted carefully due to the missing values for cardiorespiratory fitness in the sample that could affect this observation. Cardiorespiratory fitness is an important health marker [37] which has been associated with a healthier cardiovascular status and a lower risk of metabolic factors already in children [38]. In line with our results, other studies reported that metabolic health is influenced by cardiorespiratory fitness in adolescents [39]. In this way, in a recent review Ortega et al. examined the role of fitness in MHO and suggested that higher cardiorespiratory fitness level may be a key characteristic of MHO phenotype [40]. To the opposite, other authors did not find any association between fitness and MHO phenotype in youth; nonetheless, lower levels of fatness and the lack of hepatic steatosis were strongly associated with MHO phenotype in these adolescents [41].

Strengths and limitations

This study has several limitations. First and foremost, the sample size is low due to the inclusion criteria considered in the current study (overweight/obesity status, blood samples and dietary intake data available). Nevertheless, adolescents were randomly chosen to collect blood samples in order to avoid selection bias in the HELENA study [10]. Second, the cross-sectional design of the study should be also considered as a limitation since it does not help to determine causality and directionality of the relationships. We cannot absolutely exclude that dietary data could reflect any medical or dietary advice received prior to recruitment. However, its probability is low because one of the inclusion criteria in the HELENA study was that all study participants should be at least apparently healthy. Although can indeed being dietary assessment challenging among adolescents, the 24-h dietary recall methods that was used in the HELENA study has been evaluated and has shown good validity and accuracy in adolescents [42].

In conclusion, findings of the current study suggest that MHO adolescents have a higher adherence to the MDP compared to MUO adolescents which might be mainly due to a higher fish intake, supporting the possible preventive role of the MDP and its components in the metabolic syndrome development. Moreover, cardiorespiratory fitness might also play a key role in the healthy metabolic phenotype. Hence, nutritional and lifestyle education programs focused on children and adolescents which include physical activity are needed to achieve healthy dietary habits, as well as to increase cardiorespiratory fitness, with the aim of improving metabolic health and preventing obesity-related comorbidities in later life.

CONFLICTS OF INTEREST

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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FIGURE LEGENDS

Fig. 1 Flow diagram of study participants.

Fig. 2 Adherence to the Mediterranean diet in metabolically healthy overweight/obese (MHO, n=45) and metabolically unhealthy overweight/obese (MUO, n=92) adolescents. Bars are values of adjusted means and error bars are standard error of means. Model 1 was adjusted for sex, age, energy intake and center; Model 2: was additionally adjusted with body fat percentage (MHO/MUO n=43/88); Model 3: was further adjusted with cardiorespiratory fitness (MHO/MUO n=30/77).

Fig. 3 Odds ratios (boxes) and 95% confidence intervals (error bars represent values) after adjusting for sex, age, energy intake and center (Model 1), additionally adjusted for body fat percentage (Model 2) and adjusted for sex, age, energy intake, center and cardiorespiratory fitness (Model 3).

Table 1. Anthropometric and biological characteristics in metabolically healthy overweight or obese (MHO) and metabolically unhealthy overweight or obese (MUO) adolescents participating in the HELENA Study.

	MHO n=45	**MUO n=92**	**p**
	Mean (SD)	Mean (SD)	
Age (years)	14.7 (1.3)	14.7 (1.4)	0.812
Sex (males/females)	23/22	47/45	0.998
High puberty stage (N, %)	29 (64.4)	63 (68.5)	0.637
Older adolescents (N, %)	20 (44.4)	50 (54.3)	0.276
Weight (kg)	70.5 (12.2)	77.2 (14.7)	**0.004**
Height (cm)	164.8 (10.4)	167.4 (9)	0.071
Waist circumference (cm)	81.8 (7.7)	84.3(8.4)	0.083
Body mass index (kg/m^2)	25.9 (0.5)	27.4 (0.3)	**0.012**
Obese (N, %)	6 (13.3)	31 (33.7)	**0.012**
Body fat (%)	32.4 (9.4)	35.5 (8.8)	0.065
High maternal educational level (N, %)	9 (20)	17 (18.5)	0.534
Glucose (mmol/L)	4.9 (0.3)	5.1 (0.5)	0.056
Triglycerides (mmol/L)	0.7 (0.3)	1.1 (0.6)	**<0.001**
HDL cholesterol (mmol/L)	1.4 (0.2)	1.2 (0.2)	**<0.001**
Systolic blood pressure (mmHg)	113.5 (8.0)	127.5 (15.6)	**<0.001**
Diastolic blood pressure (mmHg)	61.5 (9.1)	70.1 (8.2)	**<0.001**
Cardiorespiratory fitness (ml/kg/min)	39.9 (10.8)	36.7 (8.2)	0.148

SD: Standard deviation; HDL: High-density lipoprotein; High puberty stage equal or above IV Tanner stage; Older adolescents: age equal or above median). Student´s *t* test was used to compare mean differences between MHO and MUO groups in continuous variables, while chi-square test was used to examine mean differences in categorical variables. Although analyses were carried out with logarithmically transformed values, non-transformed data are shown in the table in order to make an easier interpretation.

Table 2. Dietary intake in metabolically healthy overweight or obese (MHO) and metabolically unhealthy overweight or obese (MUO) adolescents.

	Overweight participants		
	MHO (n=45)	**MUO (n=92)**	**p**
	Mean (SD)	Mean (SD)	
Vegetables (g/day)	102 (79)	92 (57)	0.436
Fruits and nuts (g/day)	113 (88)	118 (77)	0.766
Cereal roots (g/day)	320 (122)	295 (110)	0.235
Pulses (g/day)	5 (14)	9 (28)	0.255
Fish (g/day)	24 (24)	16 (16)	**0.040**
FU/FS ratio (day)	0.93 (0.19)	0.93 (0.16)	0.923
Dairy products (g/day)	262 (305)	184 (164)	0.113
Meat (g/day)	140 (75)	147 (73)	0.612
Alcohol (g/day)	0.4 (0.7)	0.6 (1.2)	0.316
Mediterranean diet score (0-9)	4.5 (1.7)	3.9 (1.6)	**0.044**
High adherence (N, %)	25 (55.6)	34 (37)	**0.039**

SD: Standard deviation; FU/FS ratio: unsaturated to saturated fatty acids ratio. Although analyses were carried out with logarithmically transformed values, non-transformed data are shown in the table in order to make an easier interpretation.

Supplemental Table 1. Sex-specific median intakes in the whole sample of adolescents participating in the HELENA study whose dietary data were available.

	Males (n=1077)	**Female (n=1253)**
	Median (range)	Median (range)
Vegetables (g/day)	78 (5,410)	82 (7, 538)
Fruits and nuts (g/day)	99 (8,671)	113 (5, 629)
Cereal roots (g/day)	320 (109, 719)	257 (74, 626)
Pulses (g/day)	2 (0, 319)	1 (0, 304)
Fish (g/day)	12 (0, 126)	13 (0,111)
FU/FS ratio (day)	0.87 (0.53, 1.71)	0.88 (0.55, 2.01)
Dairy products (g/day)	207 (16, 2398)	153 (7, 1296)
Meat (g/day)	157 (11, 630)	123 (13, 458)
Alcohol (g/day)	0.5 (0, 54.4)	0.3 (0, 30.4)
Mediterranean diet score (0-9)	4 (0, 8)	4 (0, 8)
High adherence (N, %)	451 (41,9%)	564 (45%)

FU/FS ratio: unsaturated to saturated fatty acids ratio.

Supplemental table 2. Distribution of metabolically healthy overweight or obese (MHO) and metabolically unhealthy overweight or obese (MUO) adolescents and the adherence to the Mediterranean dietary pattern of participants across Center-North and South European regions.

	Metabolic phenotype			**Mediterranean diet score**	
	MHO (n)	**MUO (n)**	***P****	**Mean ± SD**	***P****
Regions					
Center-North Europe	**25**	**52**	**0.915**	**3.9 ± 1.5**	**0.060**
Dortmund	5	23		3.7 ± 1.5	
Ghent	3	5		4 ± 1.3	
Lille	6	6		3.5 ± 1.5	
Stockholm	8	6		4.7 ± 1.5	
Vienna	3	12		3.6 ± 1.4	
South Europe	**20**	**40**		**4.5 ± 1.7**	
Athens	6	20		3.5 ± 1.6	
Rome	11	16		5.1 ± 1.3	
Zaragoza	3	4		6.1 ± 0.7	

SD: Standard deviation. *P values show the difference across Center-North *vs* South Europe gradient.

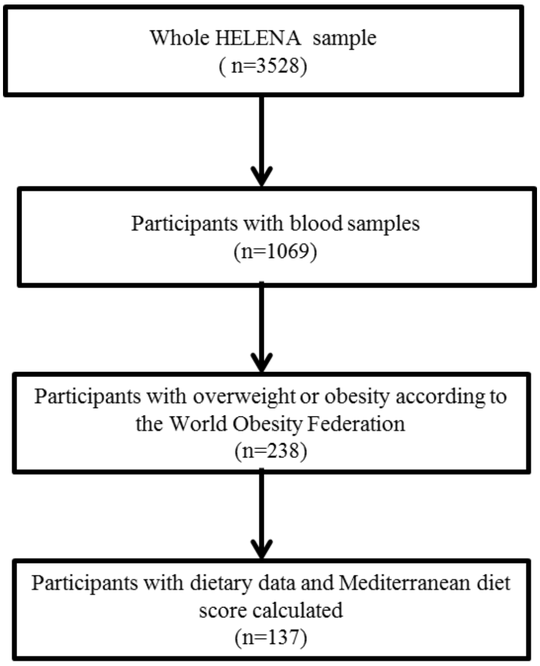
Whole HELENA sample
(n=3528)
Participants with blood samples
(n=1069)
Participants with overweight or obesity according to the World Obesity Federation
(n=238)
Participants with dietary data and Mediterranean diet score calculated
(n=137)

Fig. 1

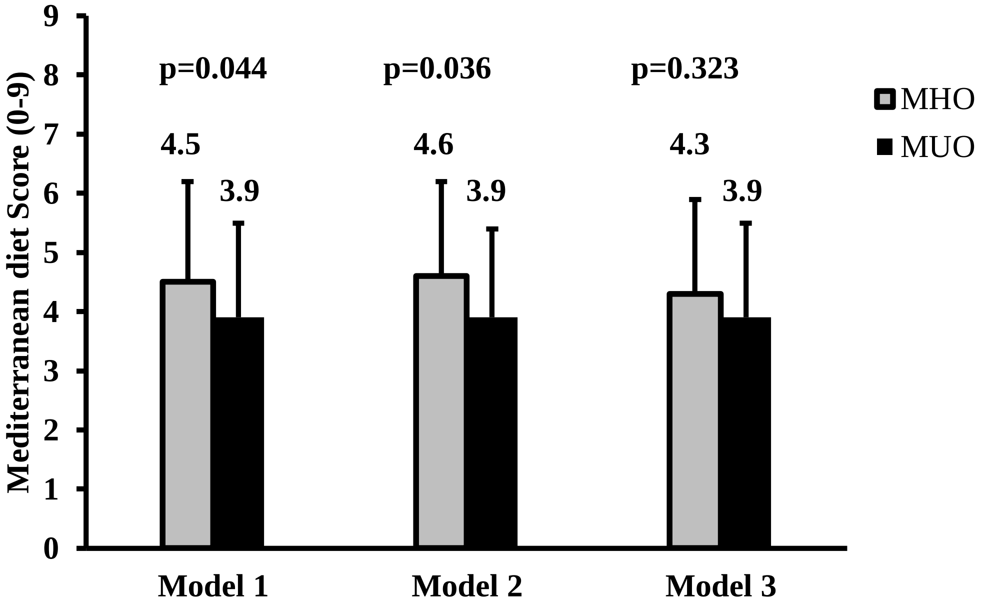
Mediterranean diet Score (0-9)
p=0.044
p=0.036
p=0.323
4.5
3.9
4.6
3.9
4.3
3.9
MHO
MUO
Model 1
Model 2
Model 3
0
1
2
3
4
5
6
7
8
9

Fig. 2

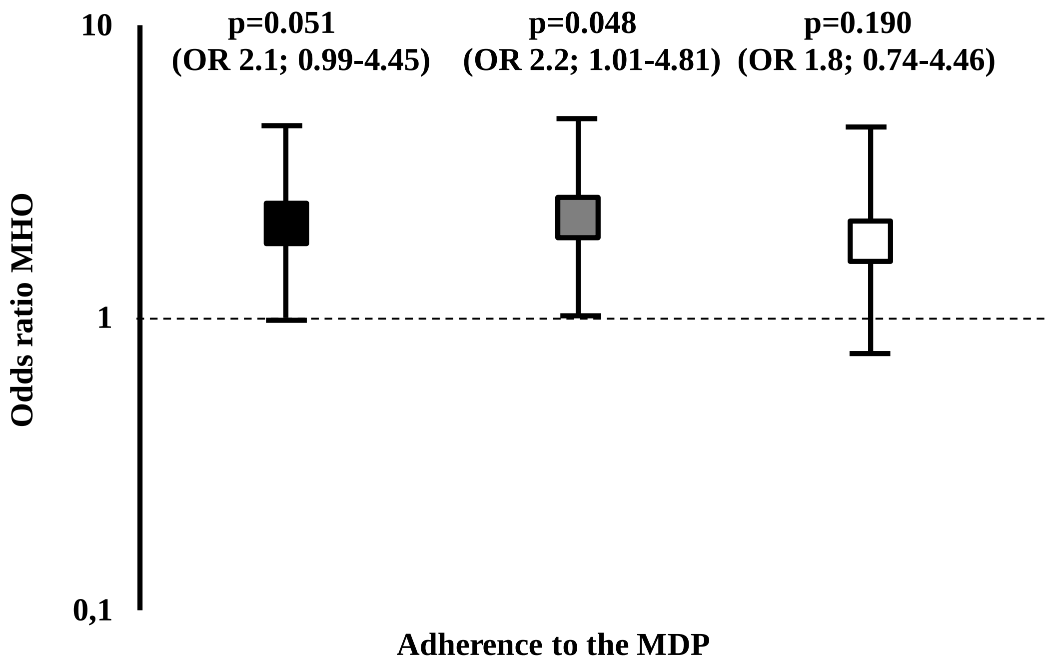
10
1
0,1
Odds ratio MHO
p=0.051
(OR 2.1; 0.99-4.45)
p=0.048
(OR 2.2; 1.01-4.81)
p=0.190
(OR 1.8; 0.74-4.46)
Adherence to the MDP

Fig. 3