

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

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56

#### 57 **AUTHOR CONTRIBUTION**

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

63

64 **ABSTRACT**

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

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

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

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

87

88 **Keywords:** Metabolic health, obesity, Mediterranean diet, adolescents, cardiorespiratory  
89 fitness  
90  
91 **Abbreviations**  
92 MHO, metabolically healthy overweight or obesity  
93 MUO, metabolically unhealthy overweight/obese  
94 MDP, Mediterranean dietary pattern  
95 MDP score, Mediterranean dietary pattern score  
96 BMI, body mass index  
97 HDL, high density lipoprotein  
98 LDL, low density lipoprotein  
99 TG, triglycerides  
100 HELENA-DIAT, HELENA-Dietary Assessment Tool  
101

## 102 INTRODUCTION

103 Childhood and adolescence obesity prevalence has increased over the last few decades  
104 [1]. This chronic disease is associated with cardiometabolic risk factors such as insulin  
105 resistance, dyslipidemia and hypertension [2]. However, several studies reported the  
106 existence of metabolically healthy phenotypes, referred to as metabolically healthy  
107 overweight or obesity (MHO), in whom no obesity associated comorbidities are found,  
108 whereas obesity associated with metabolic abnormalities is known as metabolically  
109 unhealthy overweight or obesity (MUO)[3].

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

113 Diet and physical activity are lifestyle determinants of health closely related to  
114 obesity and its complications [5]. Nowadays, nutrition research focuses more on  
115 examining the impact of dietary patterns such as the Mediterranean diet (MDP) on health  
116 outcomes, instead of exploring the effect of nutrients or individual food groups on health  
117 status. Thereby, dietary patterns offer a more holistic description of dietary habits  
118 considering also the possible interactions among nutrients and foods [6]. The MDP shows  
119 the typical dietary pattern followed by people from Creta, Greece and Southern Italy in  
120 the 1960s [7]. This Mediterranean region was the area with the highest life expectancy  
121 and with the lowest incidence of coronary heart disease in the world. Adherence to the  
122 MDP has been associated with a reduction in cardiovascular and all-cause mortality and  
123 type 2 diabetes incidence [8,9]. MDP is characterized by high intakes of vegetables, fruits,  
124 nuts, cereals, legumes and olive oil as the principal source of fat, moderate to-high- intake  
125 of fish, moderate consumption of dairy products and wine (during meals) and low  
126 consumptions of meat and poultry [7]. Several studies reported that adherence to the MDP

127 improves health status in youths [9]. Accordingly, we hypothesized that MHO  
128 adolescents might have a higher adherence to this dietary pattern than their MUO peers.  
129 The current study aimed to examine the association between the adherence to MDP and  
130 metabolic health status in overweight and obese European adolescents from the Healthy  
131 Lifestyle in Europe by Nutrition in Adolescence (HELENA) study.  
132

## 133 MATERIAL AND METHODS

### 134 Study design

135 The HELENA study is a multicenter cross-sectional study which was designed to evaluate  
136 the nutritional status and lifestyle in adolescents (12.5-17.5 years) from 10 European  
137 cities between 2006 and 2007 [10]. Among the total sample of 3,528 participants, blood  
138 samples were randomly selected and collected in a subsample of 1,069 adolescents [10].  
139 A detailed description of the HELENA study procedures and methodology has been  
140 published elsewhere [11,12] . All adolescents participating in the study and their parents  
141 or legal guardians had to sign an informed written consent so that they could be enrolled  
142 in the study. The study protocol was approved by the corresponding local Human  
143 Research Review Committees of the centers involved, which were the following ones:  
144 Athens in Greece, Dortmund in Germany, Gent in Belgium, Lille in France, Roma in  
145 Italy, Stockholm in Sweden, Vienna in Austria and Zaragoza in Spain. For the target of  
146 the current study, a total of 137 (14.8±1.3 years, 48.9 % girls) overweight or obese  
147 adolescents from whom dietary and biomarkers data were available were included (**Fig.**  
148 **1**).

149

### 150 Anthropometry and cardiometabolic risk factors

151 Anthropometric assessment was performed to categorize weight status, as well as to  
152 examine body composition. Weight (SECA 861, Hamburg, Germany) and height (SECA  
153 225, Hamburg, Germany) were measured with a high-precision scale to the nearest 0.05  
154 kg and with a telescopic height measuring instrument to the nearest 0.1cm, respectively  
155 [11]. BMI was determined as body weight divided by height squared ( $\text{kg/m}^2$ ) and  
156 overweight and obesity status were categorized according to the World Obesity  
157 Federation criteria [12]. A non-elastic tape (SECA 200) to the nearest 0.1 cm was used



158 for waist circumference measurement. In addition, tricipital and subscapular skinfold  
159 thicknesses were measured (Holtain) and body fat percentage was computed using the  
160 Slaughter equation [13]. Blood pressure (systolic and diastolic) was measured twice with  
161 a 10 minutes time period between, using a clinical automated digital blood pressure  
162 device (OMRON) and the lowest value was recorded. Glucose, triglycerides and HDL-  
163 cholesterol, were obtained from blood samples collected after 10-h overnight fast by  
164 following an established blood collection and analysis protocol [14]. Cardiorespiratory  
165 fitness was determined using the 20-m shuttle run test as described elsewhere [15].  
166 Briefly, adolescents had to run between two lines 20m apart following an audio signal  
167 from a recorded CD. The audio signal started with an 8.5km/h speed increasing by  
168 0.5km/h per minute. When the participants did not reach the end line along with the audio  
169 signal on two consecutive times or when the adolescent stopped because of exhaustion  
170 the test was finished. Thereby, aerobic fitness was examined calculating the maximal  
171 oxygen consumption (ml/kg/min) using the equation suggested by Leger et al [16].

172

### 173 **MHO and MUO classification criteria**

174 Several criteria have been proposed for metabolic health classification in pediatric  
175 populations. Nevertheless, in the current study, in order to establish the criteria for  
176 classifying metabolic status we followed the definition of MHO proposed by Ortega et  
177 al, which are a detailed criteria based on a comprehensive review of the literature  
178 summarized into 7 scientific arguments (for more information, see tables 2 and 3 of the  
179 review) [17]. The criteria for the classification of overweight/obese individuals as MHO  
180 or MUO of this review is in accordance with previous large collaborative studies and  
181 international organizations agreements, and it is also appropriate for using with youths  
182 [17]. This definition recommends the use of the *criterium* proposed by Jolliffe and

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

192

### 193 **Dietary intake assessment**

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

201 Adherence to the MDP was determined as the sum of the score assigned to nine  
202 food groups and nutrients, including seven positive and two negative dietary components.  
203 The current scale was based on the MDP scale of Trichopoulou et al [7]. Dietary intake  
204 of vegetables, fruits and nuts, cereals roots, pulses, fish, dairy products and unsaturated  
205 to saturated fat ratio were scored positively, scoring 1 point when the intakes were above  
206 the sex-specific median (50<sup>th</sup> percentile) and scoring 0 when the intakes were below the  
207 sex-specific median (see **Supplemental Table 1** to find information about food intake

208 and adherence to the MDP in the whole HELENA sample including non-overweight  
209 adolescents). The intake of dairy products was considered as a positive dietary component  
210 because in adolescence dairy products are recommended due to growth and development  
211 processes. The intakes of fruits, nuts and olives were included in the fruit and nuts  
212 variable; bread, cereals, flour, rice cereals, pasta and potatoes were considered as cereal  
213 roots; and dairy products included milk, yoghurt and cheese. In contrast, meat and  
214 processed meat and alcohol consumption were scored inversely. The value of 0 was given  
215 to a meat intake above the sex-specific median and a value of 1 when the intake was  
216 below the median. Alcohol intake was considered as an unhealthy product in adolescents  
217 and therefore a value of 1 was given if there was no consumption, while a value of 0 if  
218 there was any alcohol intake. Likewise, the range of the Mediterranean diet score (MDP  
219 score) ranged from 0 (minimal adherence) to 9 points (maximal adherence). Thereafter,  
220 the adherence to the MDP was classified into two groups, low ( $\leq 4$  points) and high ( $> 5$   
221 points) adherence to the MDP.

222

### 223 **Statistical analysis**

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

233 (Dortmund, Ghent, Lille, Stockholm and Vienna) European countries, this categorical  
234 variable thereafter called center (Central-Northern *vs.* Southern country) was used as  
235 covariate in the analyses. As there were no statistically significant differences in the  
236 prevalence of MHO and MUO phenotypes according to the maternal educational level,  
237 the socioeconomic status of the parents was not included as a confounder in the analyses.  
238 Differences in adherence to the MDP between MHO and MUO groups were analyzed  
239 using univariate linear models with sex, age, energy intake and center (model 1); sex, age,  
240 energy intake, center and body fat percentage (model 2) and sex, age, energy intake,  
241 center, body fat percentage and cardiorespiratory fitness (model 3) as covariates. Binary  
242 logistic regression models were developed to analyze the relationship between adherence  
243 to the MDP (low *vs.* high MDP score score) and metabolic phenotypes (MHO *vs.* MUO)  
244 adjusted for sex, age, energy intake and center (model 1); sex, age, energy intake, center  
245 and body fat percentage (model 2) and finally using sex, age, energy intake, center and  
246 cardiorespiratory fitness (model 3) as covariates. Sensitivity analyses were carried out  
247 with continuous odds ratio to analyze the relationship between the adherence to the MDP  
248 and metabolic phenotypes. Statistical analyses were carried out with the statistical  
249 software SPSS version 20.0 (SPSS Inc, Chicago) with a level of significance of  $\alpha=0.05$ .  
250

## 251 RESULTS

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

262 **Table 2** shows dietary intake in MHO and MUO adolescents. Higher fish intake  
263 (%33.3) was observed in MHO than in MUO adolescents ( $p < 0.05$ , Table 2). In contrast,  
264 intake of vegetables, fruits and nuts, cereal roots, pulses, unsaturated to saturated fatty  
265 acids ratio, dairy products, meat and alcohol were similar in MHO and MUO (Table 2).  
266 The adherence to the MDP in MHO and MUO adolescents is shown in **Fig. 2**. It was  
267 observed that the MDP score was significantly higher in MHO than in MUO adolescents  
268 regardless of age, sex, energy intake and center ( $4.5 \pm 1.7$  vs.  $3.9 \pm 1.6$ , in MHO and MUO  
269 respectively,  $p = 0.044$ , Model 1, **Fig. 2**). This difference was strengthened when body fat  
270 percentage was entered into the model ( $4.6 \pm 1.6$  vs.  $3.9 \pm 1.5$ ,  $p = 0.036$ , Model 2, **Fig. 2**),  
271 but it was diminished and became statistically non-significant after further adjustment for  
272 cardiorespiratory fitness ( $4.3 \pm 1.6$  vs.  $3.9 \pm 1.6$ ,  $p = 0.323$ , Model 3, **Fig. 2**). Odds ratios  
273 (OR) for having obesity-associated risk factors according to the adherence to the MDP  
274 categories (low vs. high) are shown in **Fig. 3**. It was observed that adolescents with low  
275 adherence to the MDP (MDP score  $\leq 4$ ) had higher likelihood of having MUO phenotype

276 regardless of sex, age, energy intake, center and body fat percent (OR 2.2; 95%CI, 1.01-  
277 4.81, p=0.048, Model 2, **Fig. 3**). However, when the analyses were further adjusted with  
278 cardiorespiratory fitness the results were attenuated and became non-significant (OR 1.8;  
279 95%CI, 0.74-4.46, p=0.051, Model 3, **Fig. 3**). After sensitivity analyses with continuous  
280 OR, it was observed that the odds ratio between the adherence to the MDP and MUO  
281 metabolic phenotype was below one (OR 0.8; 95% CI, 0.58-0.97, sex, age, energy intake,  
282 center and body fat percentage adjusted p=0.032), which means that higher adherence to  
283 the MDP is associated with lower likelihood of being MUO.

284

## 285 **DISCUSSION**

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

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

307 The effect of the diet quality or dietary patterns on metabolic phenotypes has  
308 already been studied. For instance, researches of the National Health and Nutrition  
309 Examination Survey examined the Healthy Eating Index in adolescents and adults with

310 obesity and showed that the diet quality was higher among MHO compared with MUO,  
311 which stands for having a better compliance to the American Dietary Guidelines [5,23].  
312 These findings concur with the results of the current study suggesting that the adherence  
313 to the MDP could be a protective factor to develop the MUO phenotype. In contrast, other  
314 authors did not find any significant difference in macro/micronutritional composition  
315 among middle-aged obese adults with MHO and MUO phenotypes and neither healthy  
316 obesity was associated with increased diet quality [24,25].

317         The benefits of adherence to the MDP on metabolic risk have been extensively  
318 studied. A higher adherence to the MDP has been related to lower BMI, glucose level and  
319 a better lipid profile in children and adolescents [26]. Similarly, Zhong et al. observed  
320 that adherence to MDP was associated with better glycemic control and lipid profile  
321 among adolescents with type 1 diabetes who were less than twenty years-old at diagnosis  
322 [27]. In this last study, adherence to the MDP was assessed using the KIDMED  
323 questionnaire, and precisely, an increase of two-points out of twelve in the KIDMED  
324 score ( $\approx 17\%$  higher adherence) was associated with 4 mg/dL lower total cholesterol and  
325 3.4 mg/dL lower LDL-cholesterol [27]. In another study with hypercholesterolemic  
326 children, after 12-month of nutritional intervention based on MDP, an approximately 10%  
327 decrease of total and LDL-cholesterol levels was observed [28]. Although several studies  
328 have examined the influence of the adherence to the MDP on cardiovascular health in  
329 children and adolescents [26,28], as far as we are aware, there is no previous study  
330 examining the adherence to the MDP on MHO and MUO phenotypes in youths which  
331 hampers comparisons among studies.

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



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

350 We observed that the difference in the adherence to MDP between MHO and  
351 MUO groups became non-significant after further adjustment for cardiorespiratory  
352 fitness. However, this finding should be interpreted carefully due to the missing values  
353 for cardiorespiratory fitness in the sample that could affect this observation.  
354 Cardiorespiratory fitness is an important health marker [37] which has been associated  
355 with a healthier cardiovascular status and a lower risk of metabolic factors already in  
356 children [38]. In line with our results, other studies reported that metabolic health is  
357 influenced by cardiorespiratory fitness in adolescents [39]. In this way, in a recent review  
358 Ortega et al. examined the role of fitness in MHO and suggested that higher  
359 cardiorespiratory fitness level may be a key characteristic of MHO phenotype [40]. To

360 the opposite, other authors did not find any association between fitness and MHO  
361 phenotype in youth; nonetheless, lower levels of fatness and the lack of hepatic steatosis  
362 were strongly associated with MHO phenotype in these adolescents [41].

### 363 **Strengths and limitations**

364 This study has several limitations. First and foremost, the sample size is low due  
365 to the inclusion criteria considered in the current study (overweight/obesity status, blood  
366 samples and dietary intake data available). Nevertheless, adolescents were randomly  
367 chosen to collect blood samples in order to avoid selection bias in the HELENA study  
368 [10]. Second, the cross-sectional design of the study should be also considered as a  
369 limitation since it does not help to determine causality and directionality of the  
370 relationships. We cannot absolutely exclude that dietary data could reflect any medical or  
371 dietary advice received prior to recruitment. However, its probability is low because one  
372 of the inclusion criteria in the HELENA study was that all study participants should be at  
373 least apparently healthy. Although can indeed being dietary assessment challenging  
374 among adolescents, the 24-h dietary recall methods that was used in the HELENA study  
375 has been evaluated and has shown good validity and accuracy in adolescents [42].

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

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387

388 **CONFLICTS OF INTEREST**

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

390 interest.

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516 **FIGURE LEGENDS**

517 **Fig. 1** Flow diagram of study participants.

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

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

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**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.

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

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

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.

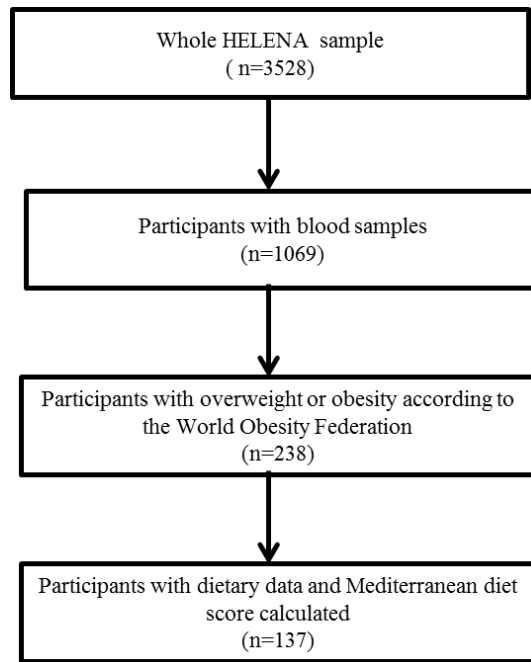
	<b>Males (n=1077)</b>	<b>Female (n=1253)</b>
	Median (range)	Median (range)
<b>Vegetables (g/day)</b>	78 (5,410)	82 (7, 538)
<b>Fruits and nuts (g/day)</b>	99 (8,671)	113 (5, 629)
<b>Cereal roots (g/day)</b>	320 (109, 719)	257 (74, 626)
<b>Pulses (g/day)</b>	2 (0, 319)	1 (0, 304)
<b>Fish (g/day)</b>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

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

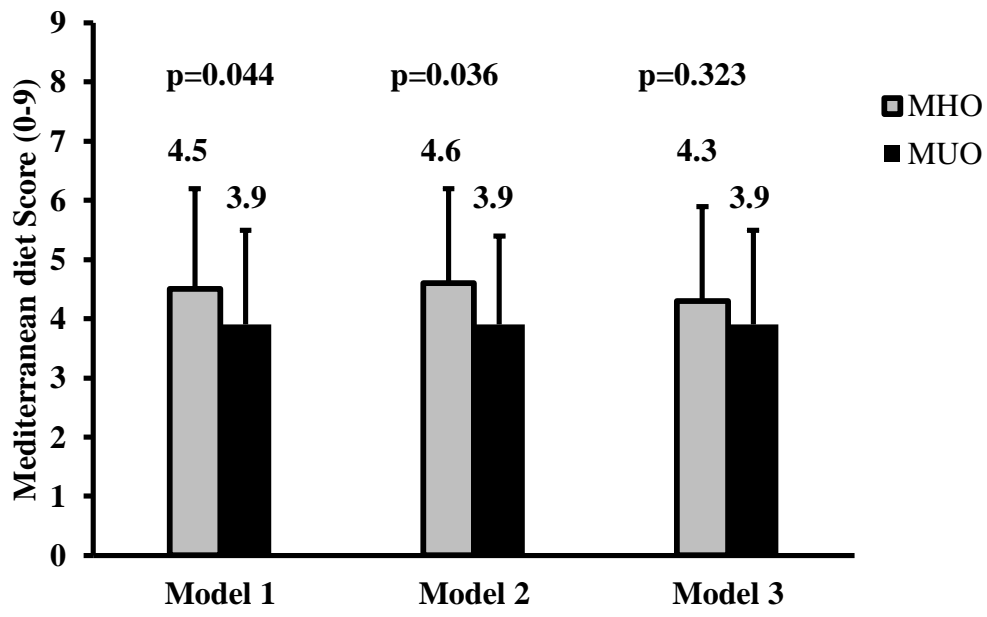
**Supplemental table 2.** Distribution of metabolically healthy overweight or obese (MHO) and metabolically unhealthy overweight or obese (MUO) adolescents and the adherence to the Mediterranean dietary pattern of participants across Center-North and South European regions.

	Metabolic phenotype		<i>P</i> *	Mediterranean diet score	
	MHO (n)	MUO (n)		Mean ± SD	<i>P</i> *
<b>Regions</b>					
<b><i>Center-North Europe</i></b>	<b>25</b>	<b>52</b>	<b>0.915</b>	<b>3.9 ± 1.5</b>	<b>0.060</b>
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	
<b><i>South Europe</i></b>	<b>20</b>	<b>40</b>		<b>4.5 ± 1.7</b>	
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.



**Fig. 1**



**Fig. 2**

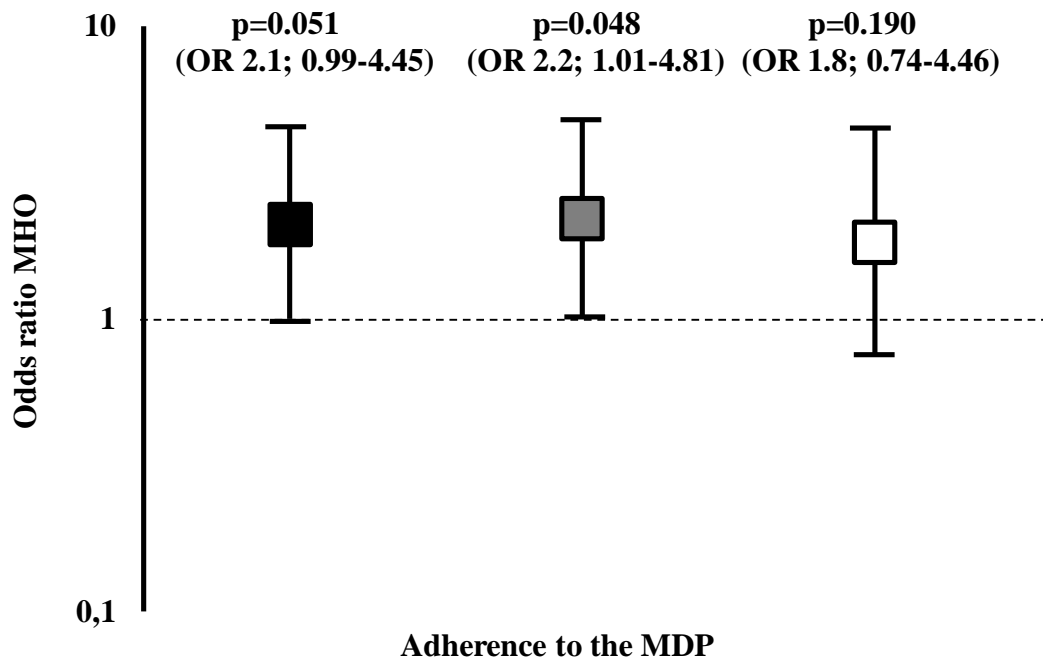


Fig. 3