

# Adherence to a Mediterranean diet is associated with a better health-related quality of life: a possible role of high dietary antioxidant content

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## ABSTRACT

**Objectives:** Mediterranean diet (MD) is associated with a reduced risk of major chronic disease. Health-related quality of life (HRQL) is a valid predictor of mortality. The aim of this study is to investigate the association between MD and HRQL and to examine the possible role of dietary antioxidants, fibre content and/or fatty acid components.

**Design:** Cross-sectional study on a sample of Italian participants enrolled in the Moli-sani Project, a population-based cohort study. Food intake was recorded by the Italian European prospective investigation into cancer and nutrition study food frequency questionnaire. Adherence to MD was appraised by a Greek Mediterranean diet score (MDS), an Italian Mediterranean diet index (IMI) and by principal component analysis (PCA). HRQL was assessed by the 36-Item Short Form Health Survey.

**Setting:** Molise region, Italy.

**Participants:** 16 937 participants of 24 325 Italian citizens (age $\geq$ 35).

**Main outcomes:** Dietary patterns and HRQL.

**Results:** *Mental* health was associated consistently and positively with MDS, IMI and an 'Olive oil and vegetable' pattern (PCA1), but negatively with an 'Eggs and sweets' pattern (PCA3). *Physical* health was associated positively with MDS and PCA1, but negatively with a 'Meat and pasta' pattern. Subjects with the highest MD adherence had 42% (MDS), 34% (IMI) or 59% (PCA1) statistically significant multivariable odds of being in the uppermost level of mental health, as compared with subjects in the lowest category. The associations disappeared after further adjustment for either total food antioxidant content or dietary fibre, while they were not modified by the inclusion of either monounsaturated or polyunsaturated fatty acids. Individuals in the highest PCA1 or PCA3 had significantly higher odds of being in the top level of physical health.

**Conclusions:** Adherence to an MD pattern is associated with better HRQL. The association is stronger with mental health than with physical health. Dietary total antioxidant and fibre content independently explain this relationship.

## ARTICLE SUMMARY

### Article focus

- Investigating the association between adherence to the Mediterranean diet and health-related quality of life.
- Examining the possible role of dietary antioxidants, fibre intake and/or fatty acid components in explaining the association.

### Key messages

- Mental health is positively associated with a Mediterranean diet and inversely linked to 'Eggs and sweets' dietary pattern.
- The association is mainly accounted for not only by the total antioxidant content but also by the fibre dietary content.
- Fatty acid compounds do not explain the association between the Mediterranean diet and health-related quality of life.

### Strengths and limitations of this study

- This study is apparently the first to provide a likely account of dietary antioxidants for the direct association between the Mediterranean diet and health-related quality of life.
- For the first time, this topic was addressed by using simultaneously two a priori Mediterranean scores and the *a posteriori* dietary patterns obtained by principal component analysis.
- The present study was cross-sectional and shares all the limitations of this study type; in particular, the inference of possible causality is unwarranted.

## INTRODUCTION

Mediterranean diet (MD) is a healthy eating pattern associated with reduced risk for cardiovascular and neurodegenerative diseases and some types of cancer.<sup>1-3</sup> This dietary pattern is characterised by the wide consumption of plant foods, cereals, legumes, fish and olive oil as the main source of fat

and moderate red wine consumption. The biological mechanisms for chronic disease prevention associated with an MD pattern are high amounts of antioxidants, polyphenols and other compounds such as monounsaturated and polyunsaturated fatty acids.<sup>4-7</sup>

Health-related quality of life (HRQL) refers to an individual's subjective evaluation of his own health and well-being<sup>8</sup> and has rapidly become an important issue in modern times since Western societies are facing a process of increasing population ageing. Self-perceived health status is closely associated with cardiovascular disease (CVD) and all-cause mortality and many studies have found that self-health ratings are important predictors of mortality for persons with cardiovascular disease,<sup>9-10</sup> middle-aged subjects<sup>11</sup> and young adults.<sup>12</sup> So far, few studies have investigated the relationship between MD and self-rated health in a general population.

Recent evidence suggests a positive correlation between adherence to MD and HRQL,<sup>13-14</sup> not only in adults but also in adolescents.<sup>15</sup> Further evidence has recently supported the relationship between MD and depression showing a potential protective role of MD against the onset of depressive symptoms.<sup>16-17</sup>

One of the most accredited hypotheses is that MD is positively associated with better overall health status and reduced risk of major chronic diseases because of its high content of different beneficial compounds, such as antioxidants, largely present in leafy vegetables, fruits, olive oil and red wine, monounsaturated (olive oil) or polyunsaturated fatty acids (mainly from fish and nuts<sup>5</sup>), dietary fibre<sup>18-19</sup> or low glycaemic index.<sup>20</sup>

Our study aimed to test the association of MD and other dietary patterns with mental and physical health to examine the possible role played by total food antioxidant content (FAC), dietary fibre and monounsaturated or polyunsaturated fatty acids.

## SUBJECTS AND METHODS

### Study population

The study population consisted of participants in the Moli-sani Project, a population-based cohort study which randomly recruited 24 325 citizens of Molise, a region placed between central and southern Italy. Between March 2005 and April 2010, men and women aged  $\geq 35$  years were randomly recruited from subjects included in the city-hall registries of Molise.<sup>21</sup> Exclusion criteria were pregnancy, disturbances in understanding/willing processes, ongoing poly traumas or coma and refusal to sign the informed consent form.

After exclusion of subjects reporting a personal history of cardiovascular disease (angina, myocardial infarction, heart failure, revascularisation procedures and stroke; 5.7%), cancer (3.1%) or of those for whom there was no information available on health-related quality of life (21.7%) or dietary habits (3.9%), 16 937 subjects were finally included in the analysis presented.

Comparison between the sample considered in the present study ( $n=16\,937$ ) and excluded participants ( $n=7388$ ) showed a substantial homogeneity for sex ( $p=0.23$ ). The sample included was younger ( $53\pm 10.8$  vs  $62\pm 12.1$ ;  $p<0.0001$ ) and had higher social status ( $p<0.0001$ ), income ( $p<0.0001$ ) or education ( $p<0.0001$ ). Potential selection biases could emerge since the 36-Item Short Form Health Survey (SF-36) questionnaire was self-administered and the topic not easily understandable by the elderly or people with a lower educational level or social status. In addition, we excluded subjects with CVD or cancer, which are medical conditions related to ageing and somehow to social status.

### Dietary information

The validated Italian European prospective investigation into cancer and nutrition study food frequency questionnaire was used to evaluate food intake.<sup>22-23</sup> The questionnaire, computerised with tailor-made software, allowed participants to be interviewed in an interactive way, by including illustrations of sample dishes of definite size or by reference to standard portion size. To simplify interpretation of data and to minimise within-person variations in intakes of individual foods, 188 food items were classified into 45 predefined food groups on the basis of similar nutrient characteristics or culinary usage (see online supplementary appendix 2).

Moderate alcohol intake was defined as regularly drinking no more than one drink a day by women, and no more than two drinks a day for men.

Food consumption patterns were generated by using Principal Components Analysis (PCA) conducted on the correlation matrix of 45 food groups.<sup>24</sup> Three main factors emerged, in agreement with previous findings in the same population.<sup>24</sup> The pattern identified as 'Olive Oil and Vegetables' was characterised by high positive loadings for olive oil, vegetables, legumes, soups, fruits and fish. The pattern named 'Meat and pasta' was characterised by high positive loadings for pasta, cooked tomatoes, red meat, animal fats and alcoholic beverages, and negative loadings of breakfast cereals and yogurt. The 'Eggs and Sweets' pattern was characterised by high positive loadings for eggs, margarines, processed meat and sugar and sweets.

We evaluated the adherence to MD by using the MD score (MDS) elaborated by Trichopoulou *et al.*<sup>25</sup> Scoring was based on the intake of the following nine items: vegetables, legumes, fruit and nuts, dairy products, cereals, meat and meat products, fish, alcohol, and the ratio of monounsaturated:saturated fat. For most items, consumption above the study median received 1 point; all other intakes received 0 point. For dairy products, meat and meat products, consumption below the median received 1 point. Medians are gender specific. For ethanol, men who consumed 10-50 g/day and women who consumed 5-25 g/day received 1 point; otherwise, the score was 0. The possible scores ranged between 0 and 9, the latter reflecting the maximal adherence.

We also used a newly proposed Italian Mediterranean diet index (IMI) whose score is based on the intake of 11 items: high intake of six typical Mediterranean foods (pasta; typical Mediterranean vegetables such as raw tomatoes, leafy vegetables, onion and garlic, salad, and fruiting vegetables; fruit; legumes; olive oil and fish); low intake of four non-Mediterranean foods (soft drinks, butter, red meat and potatoes) and alcohol consumption. If consumption of typical Mediterranean foods was in the third tertile of the distribution, the person received 1 point; all other intakes received 0 point. If consumption of non-Mediterranean foods was in the first tertile of the distribution, the person received 1 point. Ethanol received 1 point for intake up to 12 g/day; abstainers and persons who consumed >12 g/day received 0 points. Possible scores ranged from 0 to 11.<sup>26</sup> Such an Italian index was conceived to better capture healthy eating including foods more typically consumed in Italy.

The total FAC score was used to measure the antioxidant content from the diet. Its construction was already described in a previous study conducted within the Moli-sani cohort.<sup>27</sup> Briefly, the content in the antioxidant vitamins and phytochemicals of each food group was derived by using the food composition tables from the Istituto Nazionale di Ricerca per gli Alimenti e la Nutrizione and the US Department of Agriculture (USDA). Healthy foods, according to an MD pattern, were categorised into either high or low antioxidant content. The total FAC score was constructed for a comparative evaluation of the consumption of these two groups. Coffee, chocolate and wine were not included in the analysis, despite their high antioxidant content, as their healthiness is reportedly limited to only moderate consumption. As the main antioxidant components of a healthy diet, the following items were considered: selenium, vitamins C, A and E, tocopherol- $\beta$ , tocopherol- $\gamma$  and tocopherol- $\delta$ , carotene- $\beta$  and carotene- $\alpha$ , lycopene, lutein and all types of flavonoids.

Monounsaturated, saturated or polyunsaturated fatty acids and fibre intake from diet was expressed as g/day.

### Data collection

Body mass index (BMI) was calculated as kg/m<sup>2</sup>. Waist circumferences was measured according to the National Institute of Health, Heart, Lung and Blood guidelines.<sup>28</sup> Blood pressure was measured by an automatic device (OMRON-HEM-705CP) three times on the non-dominant arm, with the patient lying down for about 5 min. Hypertension was defined as systolic BP $\geq$ 140 mm Hg and/or diastolic BP $\geq$ 90 mm Hg or by the use of pharmacological treatment.<sup>29</sup> Diabetes was defined if the glucose level was  $\geq$ 126 mg/dL or by the use of pharmacological treatment. Hypercholesterolaemia status was defined if the total cholesterol level was  $\geq$ 240 mg/dL or by the use of antihyperlipidemic treatment.

Physical activity was assessed by a structured questionnaire (24 questions on working and leisure time and sport participation) and expressed as daily energy expenditure in metabolic equivalent task-hours (MET/

day). Serum lipids and glucose were assayed by enzymatic reaction methods using an automatic analyser (ILab 350, Instrumentation Laboratory (IL), Milan, Italy). Low-density lipoprotein cholesterol was calculated according to Friedewald.

### Health-related quality of life and socioeconomic variables

Health-related quality of life was assessed by using the validated Italian version of the self-administered SF-36.<sup>30</sup> SF-36 is a general health scale that is widely used and thoroughly validated<sup>31</sup> and has been translated into a number of languages, including Italian.

The questionnaire contains 36 items measuring eight multi-item parameters of health status covering the following domains: physical functioning, role limitations because of physical health problems, bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional problems and mental health. The first four domains deal with physical aspects and generate the physical component score, while the next four reflect psychological features and generate the mental component score.

For each domain, z-scores are calculated, summed and the sum transformed to a scale from 0 (the worst possible condition) to 100 (the best possible condition).<sup>32</sup>

In our study, the two scores expressed as continuous variables were then ranked into quartiles to allow specific statistical analyses.

Income categories were considered as low ( $\leq$ 10 000 euros/year), low-medium ( $>10\ 000\leq$ 20 000 euros/year), medium-high ( $>20\ 000\leq$ 40 000 euros/year) and high ( $>40\ 000$  euros/year).

Socioeconomic status (SES) was expressed as a score based on five variables: dwelling ownership and ratio between the number of rooms and the number of living-in family members (rooms per person), currently and at childhood, and the availability of hot water at home at childhood. The five components were dichotomised according to the median value, and a score of one was attributed to the category supposed to be a marker of higher social status in comparison with the opposite category: thus, we assigned a score of 1 to people living in a house with living-in family members/room density  $>0.6$ , dwelling ownership or with availability of hot water and a score of 0 to people with living-in family members/room density  $\leq 0.6$ , no dwelling ownership or with unavailability of hot water. The total SES score did not include either income or education.

Education level was divided into two categories:  $\leq 8$  years of studies (0 point) and  $>8$  years of studies (1 point).

### STATISTICS

Values for continuous variables are means $\pm$ standard deviation (SD). Analysis of variance for continuous or categorical variables was applied to test the associations in table 1. Multivariable linear regression analysis was

used for testing the association between mental and physical health scores (considered as continuous dependent variables) with adherence to MDS or dietary patterns (considered as continuous independent variables); linear regression coefficients were multiplied by SD of the independent variable. In this way, regression coefficients represent the variation in mental or physical scores for a 1 SD change in independent variables, thus allowing comparability of the strength of the association among MDS, IMI or dietary patterns with mental and physical health.

By using multivariable logistic regression analysis, odds ratios (ORs) with a corresponding 95% confidence intervals (CI) were calculated to quantify the association of mental and physical health scores with adherence to dietary patterns. Four categories of adherence to MD were considered, ranging from low (0–2 points for MDS and IMI) to high (>6 points for MDS and  $\geq 5$  points for IMI) adherence. Dietary patterns from PCA were ranked into quartiles. For logistic regression analysis, the first quartiles of mental ( $n=4234$ ) or physical health were opposed to the fourth quartile ( $n=4234$ ). Participants with intermediate values (second and third quartiles) were excluded from this analysis to focus on the two extreme categories of self-reported health.

For linear and logistic regression analysis, potential confounders included as covariates in the models were age, sex, BMI, total energy intake, total physical activity, education, income, total socioeconomic status, smoking, diabetes, hypertension and hypercholesterolaemia. A specific category was created either for income or SES in order to account for missing values in the multivariable analyses.

Further adjustments for FAC, dietary fibre and fatty acids components were considered for testing their role in explaining the association among mental and physical health and MD markers.

The data analysis was generated using SAS/STAT software, V.9.1.3 of the SAS System for Windows 2009. SAS Institute Inc and SAS are registered trademarks of SAS Institute Inc, Cary, North Carolina, USA.

## RESULTS

Table 1 shows the characteristics of the whole population according to the quartiles of mental and physical component scores. People in the uppermost quartile of self-reported *mental* health were 62.5% men and showed higher levels of leisure-time physical activity and a higher prevalence of high and medium-high income. Subjects in the highest quartile of *physical* health were younger, had lower BMI, as well as higher education, income and socioeconomic status. In addition, they had a lower prevalence of obesity, hypertension, diabetes and hypercholesterolaemia.

In table 2, the association between dietary scores and mental and physical health (considered as continuous variables) is reported.

Self-reported mental health was positively associated with greater adherence to MD in the fully adjusted model ( $\beta=0.33$ ; 0.36; 0.50 for MDS, IMI and olive oil and vegetables pattern, respectively) but inversely related to unhealthy dietary patterns ( $\beta=-0.33$  for the eggs and sweets dietary pattern). The same positive association with MD was found for self-reported physical health, although the  $\beta$ -coefficients were lower than those observed for mental health ( $\beta=0.15$ ; 0.08; 0.15 for MDS, IMI and olive oil and vegetables pattern). Conversely, physical health was negatively associated with the meat and pasta dietary pattern ( $\beta=-0.11$ ).

Multivariable logistic regression analysis showed that the odds of being in the uppermost level of mental health clearly increased according to the categories of adherence to the Mediterranean-like eating patterns (table 3). People in the highest category of adherence had either 42% (MDS) or 34% (IMI) or 59% (olive oil and vegetables pattern) statistically significant higher probabilities to be in the uppermost category of mental health than those in the lowest group of MD adherence (table 3).

Logistic regression analysis showed different results regarding physical health (table 4). Higher MD adherence was not associated with increased odds of being in the highest physical health category. Modest results were found only for the olive oil and vegetable pattern for which ORs of 22% for the highest category of adherence were detected ( $p$  value=0.01). However, physical health was inversely correlated with adherence to the meat and pasta pattern, (table 4) but positively correlated with the eggs and sweets pattern; in the latter case, people in the low-medium or highest quartile had 24% more chances to be in the top category of the physical component score (table 4).

MDS was positively associated with all four domains of mental health ( $\beta=0.49$  and standard error (SE) $\pm 0.06$ ;  $\beta=0.25$  and SE $\pm 0.06$ ;  $\beta=0.16$  and SE $\pm 0.06$ ;  $\beta=0.38$  and SE $\pm 0.07$ ; for vitality, social functioning, role limitation and mental health, respectively,  $p<0.05$  for all) and with three out of four domains of physical health ( $\beta=0.34$  and SE $\pm 0.06$ ;  $\beta=0.18$  and SE $\pm 0.06$ ;  $\beta=0.16$  and SE $\pm 0.05$ ; for physical functioning, role limitation due to physical functioning and general health, respectively,  $p<0.05$  for all), whereas no association was found for bodily pain ( $\beta=-0.01$  and SE $\pm 0.03$ ;  $p=0.73$ ).

All the associations described above remained unchanged after further exclusion of subjects with diabetes ( $n=1240$ ;  $p<0.003$  for all).

### Dietary antioxidant, fibre intake and fatty acids content

In this study, we also tested the possible accounting of key dietary components of MD for the association between dietary scores and mental or physical health.

The FAC score was positively associated with MDS ( $\beta=0.27$ , SE $\pm 0.01$ ;  $P$  for trend $<0.0001$ ;  $\beta=0.36$ , SE $\pm 0.01$ ;  $P$  for trend $<0.0001$ ;  $\beta=0.20$ , SE $\pm 0.003$ ;  $P$  for trend $<0.0001$  for MDS, IMI and olive oil and vegetables pattern,

**Table 1** Characteristics of the population according to mental and physical component scores quartiles

	All (n=16937)	Mental component score quartiles				p Value	Physical component score quartiles				p Value
		First (1.8–40.8) (n=4234)	Second (40.8–48.2) (n=4234)	Third (48.2–54.3) (n=4235)	Fourth (54.3–77.9) (n=4234)		First (12.2–44.6) (n=4234)	Second (44.6–48.6) (n=4234)	Third (48.6–51.3) (n=4235)	Fourth (51.3–68.6) (n=4234)	
Age (years; means ±SD)	53.0 (10.8)	53.8 (11.1)	53.2 (10.9)	52.6 (10.4)	52.4 (10.5)	<0.0001*	57.8 (11.8)	53.2 (10.2)	51.3 (9.8)	49.6 (9.3)	<0.0001*
Sex (males, %)	48.4	31.3	45.4	54.2	62.5	<0.0001	41.0	49.1	53.6	49.7	<0.0001
Body mass index (kg/m <sup>2</sup> )	27.7 (4.6)	27.6 (4.9)	27.7 (4.6)	27.7 (4.6)	27.9 (4.5)	0.05*	29.2 (5.2)	27.9 (4.5)	27.2 (4.2)	26.4 (4.1)	<0.0001*
Leisure time physical activity (MET-h/day; means ±SD)	2.11 (1.82)	1.74 (1.44)	1.92 (1.67)	2.23 (1.90)	2.39 (2.01)	<0.0001*	1.65 (1.45)	2.00 (1.82)	2.24 (1.93)	2.22 (1.79)	0.0001*
Working physical activity (MET-h/day; means ±SD)	14.3 (11.9)	13.4 (11.4)	14.6 (12.7)	14.3 (12.0)	14.9 (11.6)	0.52*	17.4 (14.9)	15.0 (12.3)	13.5 (11.0)	12.9 (10.2)	<0.0001*
Educational level (%) (≥8 years)	55.3	54.5	53.5	57.2	55.8	0.05	32.7	54.2	63.8	70.4	<0.0001
Income (%)**						0.04					<0.0001
Low	3.9	5.3	3.7	3.4	3.3		7.2	3.3	2.5	2.8	
Low-medium	24.9	23.4	25.2	24.6	26.4		28.3	25.9	22.5	22.9	
Medium-high	18.4	15.8	17.8	19.5	20.4		12.5	19.1	21.1	20.9	
High	11.1	9.23	10.7	12.1	12.5		5.5	10.7	13.3	14.9	
Socioeconomic status**						0.21					<0.0001
Low	29.8%	30.3%	30.5%	28.9%	29.5%		37.0%	32.1%	26.3%	24.7%	
Medium	29.9%	31.4%	29.5%	29.4%	29.2%		32.2%	30.4%	29.5%	27.3%	
High	36.5%	34.1%	36.1%	38.4%	37.4%		26.5%	34.6%	40.4%	44.5%	
Daily energy intake (Kcal/ day; means ±SD)	2149 (628)	2105 (625)	2149 (621)	2160 (622)	2183 (641)	<0.0001*	2066 (645)	2168 (629)	2189 (630)	2174 (603)	0.0005*
Current smokers (%)	24.8	26.3	25.5	23.7	23.7	<0.0001	21.1	25.6	25.1	27.3	0.001
Obesity (%)	27.0	26.2	27.3	26.5	27.8	0.09	38.2	28.8	22.8	18.0	<0.0001
Diabetes (%)	7.3	6.9	7.3	6.9	8.2	0.07	11.3	8.0	5.8	4.2	<0.0001
Hypertension (%)	50.6	49.6	51.2	50.6	50.9	0.04	61.3	52.1	48.0	40.9	<0.0001
Hypercholesterolaemia (%)	27.8	28.5	27.4	27.6	27.7	0.08	30.5	29.9	27.3	23.5	<0.0001

\*p for trend. p Values are adjusted for sex and age.

\*\*Numbers do not add up to 100% due to missing values.

**Table 2** Multivariate regression coefficients (95% CI) for the association of Mediterranean diet scores or other dietary patterns with mental and physical component scores and further adjustment for food antioxidant content (FAC) or dietary fibre

	$\beta^*$		95% CI		p Value**		$\beta^*$		95% CI		p Value**		B*		95% CI		p Value**		
Mental component score																			
Mediterranean diet	0.33		0.18 to 0.49		<0.0001		0.08		-0.09 to 0.25		0.35		0.13		-0.04 to 0.29		0.13		0.13
Italian Mediterranean index	0.36		0.20 to 0.51		<0.0001		0.03		-0.14 to 0.22		0.67		0.15		-0.01 to 0.32		0.15		0.07
Olive oil and vegetables pattern	0.50		0.34 to 0.65		<0.0001		0.19		-0.003 to 0.38		0.05		0.32		0.15 to 0.50		0.32		0.0004
Meat and pasta pattern	0.07		-0.10 to 0.24		0.44		0.05		-0.12 to 0.21		0.59		0.14		-0.03 to 0.31		0.14		0.11
Eggs and sweets pattern	-0.33		-0.52 to -0.14		0.001		-0.18		-0.39 to 0.01		0.06		-0.16		-0.36 to 0.04		-0.16		0.11
Physical component score																			
Mediterranean diet	0.15		0.06 to 0.24		0.001		0.13		0.03 to 0.21		0.01		0.16		0.07 to 0.26		0.16		0.001
Italian Mediterranean index	0.08		-0.003 to 0.16		0.06		0.06		-0.04 to 0.15		0.26		0.08		-0.01 to 0.17		0.08		0.09
Olive oil and vegetables pattern	0.15		0.06 to 0.24		0.001		0.15		0.04 to 0.26		0.01		0.17		0.06 to 0.27		0.17		0.0010
Meat and pasta pattern	-0.11		-0.20 to -0.02		0.02		-0.12		-0.22 to -0.03		0.01		-0.11		-0.20 to -0.01		-0.11		0.03
Eggs and sweets pattern	-0.02		-0.13 to 0.08		0.71		0.004		-0.11 to 0.12		0.94		-0.01		-0.12 to 0.10		-0.01		0.90

\*Regression coefficients represent the variation in mental or physical component scores for a one standard deviation change in MDS, IMI or dietary patterns.

\*\*p for trend values obtained from fully adjusted model for age, sex, BMI, total energy intake, total physical activity, education, income, total socioeconomic status, smoking, diabetes, hypertension, hypercholesterolemia.

respectively) but inversely associated with the eggs and sweets pattern ( $\beta=-0.04$ ,  $SE\pm 0.04$ ; P for trend<0.0001), while no significant relationship was observed with the meat and pasta pattern ( $\beta=0.005$ ,  $SE\pm 0.003$ ; P for trend=0.16). The FAC score was significantly related to mental health ( $\beta=0.25$ ,  $SE\pm 0.04$ ; P for trend<0.0001) but not to physical health ( $\beta=0.002$ ,  $SE\pm 0.02$ ; P for trend=0.92).

The inclusion of the FAC score in the multivariable models abolished the association between MD and mental health (table 2). Similar results were obtained when the FAC score was included in the logistic regression analysis model (table 3).

Monounsaturated fatty acids were positively associated with mental health ( $\beta=0.04$ ,  $SE\pm 0.01$ ; P for trend=0.0004) but not with physical health ( $\beta=0.01$ ,  $SE\pm 0.01$ ; P for trend=0.06).

Polyunsaturated fatty acids were positively associated with MDS ( $\beta=0.10$ ,  $SE\pm 0.01$ ; p for trend<0.0001;  $\beta=0.20$ ,  $SE\pm 0.01$ ; p for trend<0.0001;  $\beta=0.22$ ,  $SE\pm 0.004$ ; p for trend<0.0001 for MDS, IMI and olive oil and vegetables pattern, respectively) and the eggs and sweets pattern ( $\beta=0.19$ ,  $SE\pm 0.003$ ; p for trend<0.0001) but inversely linked to the meat and pasta pattern ( $\beta=-0.07$ ,  $SE\pm 0.004$ ; p for trend<0.0001). No relationship was found between polyunsaturated fatty acids and mental ( $\beta=0.03$ ,  $SE\pm 0.05$ ; P for trend=0.52) or physical health ( $\beta=-0.05$ ,  $SE\pm 0.03$ ; P for trend=0.08).

Saturated fatty acids were positively associated with physical health ( $\beta=0.02$ ,  $SE\pm 0.01$ ; P for trend=0.006) but not with mental health ( $\beta=-0.01$ ,  $SE\pm 0.01$ ; P for trend=0.21).

The inclusion of dietary monounsaturated or saturated fatty acids in the multivariable model did not modify the association between MD and mental (p<0.0001) or physical health (p<0.05 for all; for the IMI adjusted for monounsaturated fatty acids p value=0.17) (see online supplementary table). Similarly, no changes were recorded after including dietary polyunsaturated fatty acids in the multivariate models (p<0.05 for both mental and physical health) (see online supplementary table).

Dietary fibre consumption was positively associated with MDS ( $\beta=0.15$ ,  $SE\pm 0.002$ ), IMI ( $\beta=0.16$ ,  $SE\pm 0.002$ ) and the olive oil and vegetable pattern ( $\beta=0.08$ ,  $SE\pm 0.001$ ; p values<0.0001 for all) but inversely associated with the meat and pasta ( $\beta=-0.02$ ,  $SE\pm 0.001$ ; p<0.0001) and the eggs and sweets patterns ( $\beta=-0.04$ ,  $SE\pm 0.001$ ; p<0.0001). Fibre content was also positively associated with either mental health or less consistently with the physical component score ( $\beta=0.11$ ,  $SE\pm 0.01$ , p<0.0001;  $\beta=0.02$ ,  $SE\pm 0.01$ , p=0.01 respectively).

Once the fibre content from the diet was included in the fully adjusted model, the association between the Mediterranean-like eating patterns and mental health was clearly reduced for both MDS ( $\beta=0.33$ , p<0.0001 decreased to  $\beta=0.13$ , p=0.13) and IMI ( $\beta=0.36$ , p<0.0001 decreased to  $\beta=0.15$ , p=0.07), suggesting indeed a role of dietary fibres for the explanation of the observed association between either MDS or IMI and better mental

**Table 3** ORs of being in the uppermost level of mental component score according to Mediterranean diet adherence or other dietary patterns

	Mental component score			Mental component score			Mental component score		
	OR	(95%CI)	P for trend	OR Further adjusted for FAC	(95%CI)	P for trend	OR Further adjusted for Fibres	(95%CI)	P for trend
<b>Medscore</b>									
Low (0–2)	-1-	(Referent)	0.001	-1-	(Referent)	0.81	-1-	(Referent)	0.45
Low-medium (3–4)	1.18	(1.02 to 1.37)		1.10	(0.95 to 1.28)		1.11	(0.96 to 1.29)	
Medium-high (5–6)	1.20	(1.04 to 1.40)		1.03	(0.88 to 1.21)		1.06	(0.91 to 1.25)	
High (7–9)	1.42	(1.17 to 1.73)		1.11	(0.90 to 1.37)		1.16	(0.93 to 1.44)	
<b>Italian Mediterranean index</b>									
Low (0–2)	-1-	(Referent)	<0.0001	-1-	(Referent)	0.14	-1-	(Referent)	0.006
Low-medium (3)	1.13	(1.00 to 1.28)		1.06	(0.94 to 1.20)		1.09	(0.97 to 1.24)	
Medium-high (4)	1.26	(1.11 to 1.43)		1.12	(0.97 to 1.29)		1.18	(1.03 to 1.35)	
High (≥5)	1.34	(1.18 to 1.52)		1.10	(0.94 to 1.27)		1.19	(1.03 to 1.37)	
<b>Olive oil and vegetables pattern</b>									
Low	-1-	(Referent)	<0.0001	-1-	(Referent)	0.002	-1-	(Referent)	<0.0001
Low-medium	1.24	(1.09 to 1.41)		1.17	(1.02 to 1.34)		1.20	(1.05 to 1.37)	
Medium-high	1.32	(1.16 to 1.51)		1.19	(1.02 to 1.39)		1.26	(1.10 to 1.44)	
High	1.59	(1.39 to 1.83)		1.33	(1.12 to 1.58)		1.45	(1.25 to 1.68)	
<b>Meat and pasta pattern</b>									
Low	-1-	(Referent)	0.50	-1-	(Referent)	0.60	-1-	(Referent)	0.20
Low-medium	0.99	(0.87 to 1.13)		1.01	(0.89 to 1.15)		1.02	(0.89 to 1.16)	
Medium-high	1.07	(0.94 to 1.22)		1.07	(0.94 to 1.22)		1.11	(0.97 to 1.26)	
High	1.03	(0.89 to 1.19)		1.02	(0.88 to 1.17)		1.07	(0.93 to 1.24)	
<b>Eggs and sweets pattern</b>									
Low	-1-	(Referent)	0.15	-1-	(Referent)	0.69	-1-	(Referent)	0.96
Low-medium	0.86	(0.75 to 0.98)		0.88	(0.77 to 1.01)		0.89	(0.78 to 1.02)	
Medium-high	0.93	(0.81 to 1.07)		0.97	(0.85 to 1.12)		0.99	(0.86 to 1.14)	
High	0.86	(0.73 to 1.01)		0.94	(0.80 to 1.10)		0.96	(0.82 to 1.13)	

ORs are from multivariable logistic regression analyses adjusted for age, sex, body mass index, total energy intake, total physical activity, education, income, total socioeconomic status, smoking, diabetes, hypertension, hypercholesterolaemia.

**Table 4** ORs of being in the uppermost level of Physical component score according to Mediterranean diet adherence or other dietary patterns

	Physical component score			Physical component score			Physical component score		
	OR	(95% CI)	P for trend	OR	(95% CI)	P for trend	OR	(95% CI)	P for trend
				Further adjusted for FAC			Further adjusted for Fibres		
<b>Medscore</b>									
Low (0–2)	-1-	(Referent)	0.11	-1-	(Referent)	0.22	-1-	(Referent)	0.04
Low-medium (3–4)	1.03	(0.87 to 1.20)		1.00	(0.85 to 1.18)		1.05	(0.89 to 1.23)	
Medium-high (5–6)	1.08	(0.92 to 1.27)		1.05	(0.88 to 1.25)		1.13	(0.95 to 1.34)	
High (7–9)	1.16	(0.94 to 1.44)		1.13	(0.90 to 1.43)		1.24	(0.98 to 1.57)	
<b>Italian mediterranean index</b>									
Low (0–2)	-1-	(Referent)	0.40	-1-	(Referent)	0.54	-1-	(Referent)	0.24
Low-medium (3)	1.02	(0.89 to 1.17)		1.00	(0.87 to 1.15)		1.03	(0.90 to 1.18)	
Medium-high (4)	1.05	(0.91 to 1.21)		1.03	(0.89 to 1.20)		1.07	(0.92 to 1.24)	
High (≥5)	1.05	(0.92 to 1.21)		1.05	(0.89 to 1.23)		1.09	(0.93 to 1.27)	
<b>Olive oil and vegetables pattern</b>									
Low	-1-	(Referent)	0.01	-1-	(Referent)	0.01	-1-		0.002
Low-medium	1.13	(0.98 to 1.30)		1.12	(0.97 to 1.30)		1.15	(0.99 to 1.32)	
Medium-high	1.18	(1.02 to 1.36)		1.18	(1.00 to 1.39)		1.21	(1.05 to 1.40)	
High	1.22	(1.05 to 1.41)		1.28	(1.06 to 1.54)		1.28	(1.09 to 1.51)	
<b>Meat and pasta pattern</b>									
Low	-1-	(Referent)	0.02	-1-	(Referent)	0.01	-1-		0.015
Low-medium	0.96	(0.84 to 1.11)		0.96	(0.83 to 1.11)		0.96	(0.83 to 1.11)	
Medium-high	0.83	(0.71 to 0.96)		0.82	(0.71 to 0.95)		0.82	(0.71 to 0.96)	
High	0.86	(0.73 to 1.01)		0.85	(0.72 to 1.00)		0.86	(0.73 to 1.01)	
<b>Eggs and sweets pattern</b>									
Low	-1-	(Referent)	0.05	-1-	(Referent)	0.03	-1-		0.05
Low-medium	1.24	(1.08 to 1.44)		1.25	(1.08 to 1.44)		1.25	(1.08 to 1.44)	
Medium-high	1.14	(0.98 to 1.32)		1.14	(0.98 to 1.33)		1.14	(0.98 to 1.33)	
High	1.24	(1.05 to 1.47)		1.26	(1.06 to 1.50)		1.24	(1.04 to 1.49)	

ORs are from multivariable logistic regression analyses adjusted for age, sex, body mass index, total energy intake, total physical activity, education, income, total socioeconomic status, smoking, diabetes, hypertension, hypercholesterolaemia.



health (table 2). No significant changes were detected regarding the physical component score after adjustment for dietary fibre (table 2). The logistic regression analysis provided similar results (tables 3 and 4).

We performed further analysis by gender (data not shown) but failed to find any statistically significant sex-related difference in the association of mental or physical scores with MDS or other dietary patterns as measured by specific terms of interaction (all  $p > 0.05$ ).

## DISCUSSION

In this large sample of a general adult population from the Moli-sani study, health-related quality of life was associated with high adherence to Mediterranean-like eating patterns and inversely related to unhealthy dietary habits. Our data agree with previous findings within Mediterranean cohorts,<sup>13 14</sup> although in our study the relationship with MD was more consistent for mental health than for physical health.

Adherence to an MD pattern has been positively associated with reduced risk for a wide range of chronic diseases, including neurodegenerative disorders<sup>1</sup> and cognitive decline,<sup>33 34</sup> which are closely linked to self-perceived mental health.<sup>35 36</sup> The beneficial effects of MD have been ascribed to its essential components. Antioxidants and polyphenols, largely present in Mediterranean foods, such as plant foods, fruits, olive oil and red wine, have anti-inflammatory properties and have been proven to exert a positive role against cardiovascular diseases and cancer.<sup>5 37</sup> Also, monounsaturated fatty acids intake, whose major source is represented by olive oil, was found to be associated with a reduced prevalence of risk factors for major chronic disease,<sup>38 39</sup> while a higher consumption of dietary fibre has beneficial effects on CVD risk reduction and is linked to a lower risk of fatal ischaemic heart disease.<sup>18 19</sup> In the wake of this evidence, we sought to examine whether the positive relationship between higher adherence to MD patterns and highest HRQL could be accounted for by the total antioxidant content from diet or by other compounds such as monounsaturated or polyunsaturated fatty acids or dietary fibre.

Higher intake of dietary antioxidants accounted for the positive association between MD adherence and higher mental status. In contrast, the levels of dietary antioxidants were not associated with physical health and thus failed to explain the observed relationship between higher adherence to MD and better self-reported physical status. Dietary fibre too was positively linked to improved mental health and apparently contributed to the explanation of the positive association with MD, however in a less consistent way as compared to the antioxidant intake. As observed with the antioxidant content, dietary fibre did not account for the association between physical health and higher adherence to MD.

Conversely, neither monounsaturated nor polyunsaturated fatty acids from the diet modified the association

between MD and better quality of life. However, data on polyunsaturated fatty acids should be taken with precaution since we could not distinguish the two major classes of polyunsaturated fatty acids (omega-3 or omega-6), which have opposing biological activities.

Previous studies have investigated the role of the basic components of MD on quality of life finding direct associations between some of its components and HRQL, such as fish consumption with mental health<sup>40</sup> or with self-reported physical health.<sup>41</sup> Inverse associations were also found between fruit and vegetables consumption and incidence of depressive symptoms.<sup>42</sup> Yet this kind of approach fails to consider diet as a whole, most likely ending up with underestimating the interactions among several foods and nutrients.<sup>43</sup> In addition to using a more traditional tool to evaluate adherence to healthy habits by using two a priori scores, our study approached overall diet as a combination of healthy and less healthy foods with an a posteriori approach which is able to catch the real dietary habits of people and accounts for correlations between score components.

Although previous studies had provided interesting data on the direct association between MD and better HRQL,<sup>14</sup> so far they have not approached the issue of possible mediators that are able to explain the observed beneficial effects of MD on self-reported health status.

Positive associations between antioxidants intake and cognitive function have been largely documented<sup>44 45</sup> and were mainly ascribed to the preventing and retarding activity of antioxidants on the uncontrolled production of free radicals that might yield beneficial effects on the frontal/subcortical brain systems, with likely enhancement of cognitive functions.<sup>34</sup> Oxidative stress has been implicated in the pathophysiology of many neuropsychiatric disorders<sup>46</sup> such as schizophrenia, bipolar disorder<sup>47</sup> and major depression.<sup>48</sup>

Recent epidemiological studies have confirmed a correlation between diet and depression, pointing out the importance of a diet rich in antioxidants and other essential compounds typical of MD in reducing the risk of depression, which may explain the positive effects in improving mental health.<sup>49</sup>

Regarding physical health, there are several biological and physiological mechanisms that could explain the beneficial effects of an MD pattern, such as reduced vascular inflammation and coagulation markers or improved endothelial function,<sup>50 51</sup> all factors that are likely to be related to a better physical health status. However, in our study, neither the antioxidant content of diet nor the dietary fibre intake affected the association between Mediterranean scores and physical health. Improved physical health was also associated with higher adherence to the eggs and sweets pattern, characterised by high positive loadings of eggs, margarines, processed meat and sugar and sweets. Despite being rich in less healthy foods, this pattern has a high content of polyunsaturated fatty acids that could explain the positive relationship with improved physical health, as

suggested by previous studies.<sup>40</sup> However, the inclusion of polyunsaturated fatty acids in the model did not change this association. In the absence of any valid food compound that is able to explain the association between physical health and the eggs and sweets pattern, we cannot exclude a possible reverse-causality effect. Indeed, this eating pattern is mainly adopted by young people who are more confident about their physical health and thus could be more likely to disregard healthy dietary patterns. Although the data were age adjusted, a possible residual confounding due to age and other unmeasured age-related conditions cannot be excluded.

### Strengths of this study

This work represents one of the few studies investigating the relationship between dietary patterns and health-related quality of life in a Mediterranean country. An additional strength is the large sample used for testing the association. In addition, it is apparently the first study to provide a likely account of antioxidants from the diet for the direct association between MD and HRQL to address this topic by using simultaneously two a priori Mediterranean scores and the a posteriori dietary patterns obtained by principal component analysis.

### Limitations of this study

The present study was cross-sectional and shares all the limitations of this study type; in particular, inference of possible causality is unwarranted since it is not possible to determine whether the diet promotes well-being or whether those who 'feel better' choose to eat a healthy diet. However, in order to account for this reverse causality bias, we excluded from the analysis subjects with previous cancer, cardiovascular disease or diabetes as these conditions may have led to changes in their diet. We measured the overall intake of antioxidants by using a score based on estimates of micronutrient intake from the food frequency questionnaire. We recognise that this approach is challenging and that our indirect antioxidant intake assessment could have lower accuracy than direct measurements, which conversely are more difficult to perform in a very large sample size population.

Caution is needed in extending the results presented here to larger contexts since the data were collected in a region located between central and southern Italy, Mediterranean by tradition and culture.<sup>17</sup> Yet, the main characteristics of our sample are comparable to those of the Italian Cardiovascular Epidemiological Observatory,<sup>52</sup> a large survey including random samples of the general population all over Italy; therefore, our sample could be considered to be representative at least of the Italian population.

### CONCLUSIONS

Our data indicate a positive association between adherence to the Mediterranean diet and self-reported

mental and physical health status. The association is more obvious for mental than for physical health.

This large cross-sectional study has offered interesting indications on this issue by highlighting a major role played by dietary antioxidants in explaining the relationship between MD and HRQL. This is important in order to advance the hypothesis on the cause–effect relationship between MD and HRQL and to plan new strategies for the prevention of mental health decline in the general population.

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## **Appendix 1**

### **Moli-sani project Investigators**

**Steering Committee:** Licia Iacoviello , Chairperson, Maria Benedetta Donati and Giovanni de Gaetano (Campobasso,Italy), Simona Giampaoli (Roma, Italy)

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May 2008) (Campobasso, Italy).

## Appendix 2 Food grouping used in the dietary pattern analyses

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<b>Foods or food groups</b>	<b>Food items</b>
Potatoes	Potatoes
Cooked vegetables	Leafy vegetables, root vegetables, cabbages, onion, carrots, mushrooms, egg plants, artichokes, sweet peppers, spinach, pumpkins, canned vegetables in oil, pickled vegetables
Raw vegetables	Raw leafy vegetables, raw tomatoes
Tomatoes (cooked)	Tomato sauces, tomatoes
Legumes	Beans, lentils, peas, chick peas
Fruit	Apples, pears, kiwi, bananas, grapes, peaches, apricots, oranges, tangerines, plums, strawberries, melon, khaki, figs, cherries
Nuts and dried fruit	Peanuts, almonds, hazelnuts, walnuts, dried figs, dried dates, prune
Olives	Olives
Milk	Milk
Yogurt	Yogurt
Fresh cheese	Mozzarella, ricotta cheese, taleggio cheese, gorgonzola cheese, melted cheese slices, other soft cream cheese
Seasoned cheese	Fontina cheese, emmenthal, gruyere, parmesan, caciocavallo cheese, other seasoned cheese
Pasta and other grains	Pasta, yellow maize meal
Rice	Rice
Bread	White bread, bread with oil and other bread
Crisp bread, rusks	Breads sticks, crisp bread
Breakfast cereals	Breakfast cereals
Salty biscuits	Crackers
Red meat	Beef, pork, lamb, horse, game, veal, other meats
White meat	Chicken, turkey, rabbit

Processed meat	Sausages, ham, bologna sausage, dried beef, salami
Offals	Liver, offals
Canned fish	Canned tuna fish and other fish
Crustaceans, molluscs	Crustaceans, molluscs
Fish	Other fish
Egg	Eggs
Vegetables oils	Seed oils (except olive oils)
Olive oil	Olive oil
Butter	Butter
Margarines	Margarines
Animal fats	Visible fat from meat, poultry skin, fat from ham
Sugar & sweets	Sugar, honey, cakes, ice cream, confections, pastry, pudding
Fruit juices	Orange juice, grapefruit juices, other fruit juices
Soft drinks	Soft drinks
Coffee	Coffee
Tea	Tea
Other sauces	Dressing sauces for pasta other than tomato sauce
Mayonnaises	Mayonnaises
Soups	Vegetable soups
Bouillon	Meat and stock-cube broth
Snacks	Vegetable quiche
Pizza	Pizza
Wine	Red wine, rosé wine, white wine
Spirits	Alcoholic beverages other than wine or beer
Beer	Beer

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**Supplementary material. Multivariate regression coefficients (95% CI) for the association of Mediterranean diet scores or other dietary patterns with mental and physical component score further adjusted for fatty acids**

	$\beta^*$	95% CI	P value**	$\beta^*$	95% CI	P value**	$\beta^*$	95% CI	P value**
	Further adjusted for MUFAs			Further adjusted for PUFAs			Further adjusted for SFAs		
<b>Mental Component Score</b>									
<b>Mediterranean Diet</b>	0.31	0.16 to 0.46	<.0001	0.34	0.18 to 0.49	<.0001	0.34	0.18 to 0.51	<.0001
<b>Italian Mediterranean Index</b>	0.32	0.17 to 0.48	<.0001	0.37	0.22 to 0.53	<.0001	0.36	0.20 to 0.51	<.0001
<b>Olive oil and vegetables pattern</b>	0.61	0.40 to 0.82	<.0001	0.58	0.40 to 0.74	<.0001	0.50	0.34 to 0.65	<.0001
<b>Pasta and Meat pattern</b>	0.06	-0.10 to 0.23	0.47	0.07	-0.10 to 0.24	0.42	0.04	-0.14 to 0.21	0.64
<b>Eggs and sweets pattern</b>	-0.44	-0.64 to -0.24	<.0001	-0.42	-0.63 to -0.21	0.0001	-0.35	-0.57 to -0.13	0.001
<b>Physical Component Score</b>									
<b>Mediterranean Diet</b>	0.13	0.05 to 0.21	0.001	0.15	0.06 to 0.23	0.0005	0.20	0.10 to 0.28	0.0005
<b>Italian Mediterranean Index</b>	0.07	-0.02 to 0.15	0.17	0.08	0.002 to 0.17	0.04	0.08	0.003 to 0.17	0.04
<b>Olive oil and vegetables pattern</b>	0.15	0.04 to 0.27	0.01	0.18	0.10 to 0.28	0.0002	0.15	0.05 to 0.23	0.001
<b>Pasta and Meat pattern</b>	-0.11	-0.26 to -0.02	0.02	-0.12	-0.21 to -0.02	0.02	-0.10	-0.20 to -0.001	0.04
<b>Eggs and sweets pattern</b>	-0.06	-0.17 to 0.06	0.33	-0.01	-0.13 to 0.11	0.83	-0.10	-0.20 to 0.05	0.23

\*Regression coefficients represent the variation in mental or physical component scores for a one standard deviation change in Medscore, IMI or dietary patterns.

\*\* p for trend values obtained from fully adjusted model for age, sex, BMI, total energy intake, total physical activity, education, income, total socioeconomic status, smoking, diabetes, hypertension, hypercholesterolemia.