Determinants, trends and health outcomes associated with the Mediterranean diet in the population of Dalmatia, Croatia

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Mentor:

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Contents

1. ABBREVIATIONS

aOR	Adjusted odds-ratio
BMI	Body mass index
CI	Confidence interval
CHD	Coronary heart disease
CVD	Cardiovascular disease
CVI	Cerebrovascular insult
FFQ	Food frequency questionnaire
HbA_1c	Glycated hemoglobin
HC	Hip circumference
HDL	High-density lipoprotein
IQR	Interquartile range
JIS	Joint Interim Statement
LDL	Low-density lipoprotein
MD	Mediterranean diet
MDSS	Mediterranean Diet Serving Score
OR	Odds-ratio
P	P-value
SES	Socio-economic status
WC	Waist circumference
WHR	Waist-to-hip ratio
WHtR	Waist-to-height ratio

2. OVERVIEW OF DOCTORAL THESIS RESEARCH

This thesis is based on three scientific publications:

1. Kolčić I*, **Relja A***, Gelemanović A, Miljković A, Boban K, Hayward C, et al. Mediterranean diet in the southern Croatia - does it still exist? Croatian medical journal. 2016;57(5):415-24. *(*The first two authors contributed equally.)*

2. **Pribisalić A**, Popović R, Salvatore FP, Vatavuk M, Mašanović M, Hayward C, et al. The Role of Socioeconomic Status in Adherence to the Mediterranean Diet and Body Mass Index Change: A Follow-Up Study in the General Population of Southern Croatia. Nutrients. 2021;13(11):3802.

3. **Relja A**, Miljković A, Gelemanović A, Bošković M, Hayward C, Polašek O, et al. Nut Consumption and Cardiovascular Risk Factors: A Cross-Sectional Study in a Mediterranean Population. Nutrients. 2017;9(12).

2.1 INTRODUCTION

2.1.1 Background

One of the foremost global public health challenges is an epidemic of non-communicable diseases, primarily due to prevalent unhealthy lifestyles. An unhealthy diet was attributed to a major portion of this risk, with 11 million attributable deaths in 2017 (1). The leading global dietary risk factors for death and disability were high sodium intake and the low intake of whole grains and fruits (1). Those highly preventable risk factors could be addressed by adopting scientifically proven healthy diets at the population level. One of the well-described healthy eating models, in particular, is the Mediterranean diet (MD). It is one of the most commonly investigated nutritional patterns, with a large body of evidence showing that adherence to MD can sustain and preserve human health. Numerous health benefits of MD have been recorded (2), including reduced all-cause mortality (3-5), primary prevention of cardiovascular disease (6, 7), reduced cancer incidence and mortality (4, 8), and reduced risk for development of type 2 diabetes, obesity and metabolic syndrome (9-12). The benefits of MD also include safeguarding mental health (13-15) and overall better health-related quality of life (16, 17).

The most prominent characteristics of the MD are the use of olive oil as the primary fat source, an abundance of vegetables, fruits, nuts, and whole grains daily, with moderate red wine and legumes consumption, while animal products are more of a relish, and the priority is given to fish and white meat over the red and processed type of meat (18). Many definitions and various scoring systems are being used to assess the dietary pattern and compliance to the Mediterranean diet (19), which is a consequence of the availability and types of locally produced foods, lifestyle and tradition (20). A new scoring system was proposed to assess the individual compliance to the Mediterranean diet - Mediterranean Diet Serving Score (MDSS), which was claimed to be an accessible, valid, and accurate instrument to assess Mediterranean diet adherence based on the consumption of foods and food groups per meal, day, and week (21). Its advantage is that it includes as many as 14 groups of foods, adding 1, 2, or 3 points to the total score, based on the frequency of consumption and the relative importance of the particular foods, without assigning negative points (21).

Interestingly, although the definition of MD places nuts upfront and requires their daily intake (22), such intense consumption is not common even among populations of the Mediterranean region (23-25). A growing body of evidence suggests that nuts are protective against cardiovascular diseases, cancer, diabetes, metabolic syndrome, and hypertension (26-

33), with daily nut consumption reported to decrease the all-cause mortality risk (34-37). Furthermore, cardiovascular risk factors, namely body weight (38), blood pressure (39, 40), blood lipids (41), glucose (42), and uric acid (43), were also inversely associated with nut intake, suggesting their positive systemic role. Even though nuts contain high amounts of fat, their consumption has repeatedly been shown not to be associated with weight gain (44-46) but with moderate weight loss or weight stability (38).

Furthermore, it was consistently shown that people who are more adherent to the MD had more favourable anthropometric indicators (47). For example, a large cohort study with 12 years of follow-up showed that people with high adherence to the MD had a lower risk of becoming overweight/obese, experienced a lesser 5-year change in waist circumference, and had a lower 5-year weight change in case of normal weight at baseline (47). Additionally, MD was more effective in long-term weight loss (over two years of follow-up) in patients with metabolic syndrome than a prudent control diet (48). Hence, MD could be considered a good model for keeping the weight stable across life and a primary tool for individualized sustainable weight loss (49). In this context, the MD and the overall Mediterranean lifestyle could lend themselves "as the most appropriate regime for disease prevention, a sort of complete lifestyle plan for the pursuit of healthcare sustainability" (50).

While the MD is traditionally practised in the countries of the Mediterranean basin, the global nutrition transition has resulted in deviation from the traditional plant-based diets towards a higher intake of animal-source food, added sugar, and vegetable oils (51). Unfortunately, an overall declining trend in adherence to the MD has been previously demonstrated in many Mediterranean countries (52-54), especially in younger generations (55-60). A rapid spread of highly processed foods, coupled with a sedentary lifestyle, is believed to be the driving force behind the pandemic of chronic diseases like obesity, diabetes, and cardiovascular diseases. The process of Westernization during the period from 1961 to 2001 was especially pronounced in the European countries of the Mediterranean basin (61), where the discrepancies between Mediterranean countries and regions have started to emerge more consistently (62).

Besides the greater convenience of a diet relying on processed foods and ready-to-eat fast food to save time and effort, these foods are also readily available in our modern urbanized environments. They are appetizing, tasty and frequently cheaper than whole foods. Indeed, the monetary associated with the MD is one of the downsides. Some studies have shown that greater adherence to the MD was associated with a higher dietary cost (63-65), especially compared to a Western dietary pattern (66), so it is not surprising to find that the lowest-income households had the lowest adherence to the MD, poorer health (50) and the highest obesity prevalence (67). However, it was shown that a higher educational status could mitigate poorer diet in lower-income countries (68), demonstrating a complex interplay between different socio-economic determinants and dietary habits. Additionally, it may be challenging to disentangle how socio-economic status (SES) contributes to various health outcomes, as SES can be defined by using several characteristics. SES characteristics include objective indicators, such as attained level of education, profession, employment/unemployment status, income, and the subjective perception of one's wealth compared to others within the same community. Despite this complexity, the impact of socio-economic status on dietary patterns is undeniably important, making it a priority in terms of the need for effective public health interventions and broader political, economic, and societal interventions against inequalities.

In general, based on geographical location and cultural heritage, the population of the Adriatic region of Croatia is considered adherent to the MD and the Mediterranean lifestyle (69). Also, Croatia was one of the countries that participated in the inscription of MD on the UNESCO's Representative List of the Intangible Cultural Heritage of Humanity (70). However, the MD and its particular composition and the role of different socio-economic characteristics in the MD pattern and BMI change in the population of Dalmatia in Southern Croatia have been marginally investigated. Despite potential health benefits, investigation of the determinants of nut consumption in the general population is also very scarce in the literature (36, 71), leaving a substantial gap in knowledge. Nevertheless, Croatia is heavily encumbered with non-communicable diseases (72), ranking high among the leading countries in Europe regarding the prevalence of overweight and obesity, with as much as 58% of the adult population being affected (73). This undesirable trend is present even in young children, with as many as 35.9% of 7-9-year-olds who are overweight or obese (74). Therefore, a particular need to investigate the determinants of Mediterranean diet adherence and its association with the health-related outcomes, as well as the contribution of several socio-economic factors in the pattern of MD in the population of Dalmatia in Southern Croatia. The results will provide a comparable source for any further international comparisons.

2.1.2 Research aims and hypothesis

Research aims are:

1) to assess the compliance with the Mediterranean dietary pattern and its constituting components,
2) to estimate the temporal trend in adherence to the MD and the contribution of several socio-economic factors in the changing pattern of both the MD and BMI in a follow-up study in the population of Dalmatia in southern Croatia, and
3) to investigate the association between nut consumption and the MD with various cardiovascular risk factors (central obesity indices, dyslipidemia, elevated fibrinogen, hypertension, diabetes, elevated glycated haemoglobin (HbA_1c), metabolic syndrome, and gout).

Research hypotheses are:

1) Women and the elderly are more adherent to the MD.
2) Higher socioeconomic status is associated with higher adherence to the MD.
3) The temporal trend in MD adherence is negative in the population of Dalmatia in southern Croatia.
4) Higher adherence to the MD and nut intake are associated with better health-related outcomes, namely lower indices of central obesity, and lower prevalence of dyslipidemia, elevated fibrinogen, hypertension, diabetes, elevated glycated haemoglobin (HbA_1c), metabolic syndrome, and gout.

2.2 MATERIALS AND METHODS

All three papers have included the same target population and very similar methodology and procedures, which justifies their compilation. Furthermore, the studies are investigating different, but sequential and coherent research questions, enabling their adequacy for being compiled in this proposed thesis.

2.2.1 Study participants

All three published studies were performed within the "10,001 Dalmatians" study (75, 76). The main objective of the "10,001 Dalmatians" study was to explore genetic and environmental risk factors by creating a biobank in the isolated populations of the Adriatic islands. The study was initiated in 1999 and had been investigating the health of isolated island communities ever since (77).

Chronologically, the initial field study was performed between 2003 and 2004 on the Island of Vis (n = 1,029). An additional 969 subjects were enrolled from the Island of Korčula in 2007 (the Town of Korčula and surrounding settlements), followed by 1,012 subjects from the City of Split in 2008–2009. Finally, 857 subjects were included in 2013 from the villages of Smokvica and Čara, situated in the central part of the Island of Korčula, and 1,121 subjects were included from 2014 to 2015 from the towns of Blato (n=985) and Vela Luka (n=136) on the western part of the Island of Korčula.

The field-based follow-up data collection was performed in 2011 for the subjects from the Island of Vis (n = 482, response rate 46.8%, mean follow-up of 7.5 years), in 2013 for the subjects from the Town of Korčula who were initially included in 2007 (n= 366; 37.8%; mean follow-up of 5.3 years), and in 2012–2013 for the subjects from the City of Split (n = 512; 50.6%, mean follow-up of 4.4 years). The main reason for the different follow-up times between study sites is the use of an open cohort sampling approach; this inevitably led to a different amount of time that each participant could be followed for. Subjects from Smokvica, Čara, Blato, and Vela Luka (n = 1,978) were not included in the follow-up due to their initial inclusion in 2013–2015, after which no additional data collections were done within the "10,001 Dalmatians" study.

The participants were recruited with a population-based convenient sampling approach, based on generalized invitations targeting subjects of age (≥18 years), without any other restrictions or exclusion criteria. The "10,001 Dalmatians" study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Ethics Committee of the University of Split School of Medicine (protocol code 2181-198-03-04/10-

11-0008). All respondents were informed of the study aims and goals, benefits, and risks, and were asked to sign an informed consent before entering the study.

Two out of the three published studies were cross-sectional (papers *"Mediterranean diet in the southern Croatia – does it still exist?"*, and *"Nut Consumption and Cardiovascular Risk Factors: A Cross-Sectional Study in a Mediterranean Population"*), while the remaining was a follow-up study *(paper "The Role of Socioeconomic Status in Adherence to the Mediterranean Diet and Body Mass Index Change: A Follow-Up Study in the General Population of Southern Croatia"*).

The descriptive cross-sectional study from the paper *"Mediterranean diet in the southern Croatia – does it still exist?"* aimed to portray the contemporary dietary patterns and included only participants recruited after 2010 during either their follow-up or upon their first enrolment. The participants originated from the Island of Vis (n=401; recruited in 2011), the Island of Korčula (n=1980; recruited in 2012-2014), and the City of Split (n=512; recruited in 2012-2013).

The cross-sectional study from the paper *"Nut Consumption and Cardiovascular Risk Factors: A Cross-Sectional Study in a Mediterranean Population"* included participants from the "10,001 Dalmatians" study upon their first enrollment: subjects from the Island of Vis (n = 1,027, sampled during 2003–2004 period), Island of Korčula (n = 2,581, sampled during 2007 and 2012–2015 period) and the City of Split (n = 1,012, sampled in 2008–2009 period).

The follow-up study from the paper "*The Role of Socioeconomic Status in Adherence to the Mediterranean Diet and Body Mass Index Change: A Follow-Up Study in the General Population of Southern Croatia*" included all the participants from the "10,001 Dalmatians" study upon their first enrollment, and also upon their follow-up. Therefore, the total number of participants was N=4,988 for the initial and N=1,342 for the follow-up study.

2.2.2 Data collection and measurements

Each participant from the "10,001 Dalmatians" was offered an array of clinical measurements, which included blood and urine testing, followed by blood pressure and anthropometric measurements, electrocardiography, arterial stiffness, spirometry, heel bone density (dual-energy X-ray absorptiometry, DEXA), ophthalmological examination and other clinically relevant examinations. Using standard operating procedures, trained nurses and medical doctors collected anthropometric and clinical measurements. After providing the fasting blood and urine sample, participants filled out an extensive self-administered questionnaire that included demographic characteristics, detailed socioeconomic status, dietary habits, smoking habits, alcohol consumption, physical activity, medical history, and important cardiovascular disease risk factors. Older adults and those with disabilities were offered assistance during surveying by a team of nine trained surveyors. Medical records or subjects' responses were used to extract relevant medical history information, including previous diagnoses and the use of medications. The list included hypertension, type 2 diabetes, coronary heart disease (CHD), cerebrovascular insult (CVI), cancer, bipolar disorder, hyperlipidemia, and gout.

Urine samples were immediately pre-processed at the study site, while the fasting blood samples were shipped frozen to specialized and accredited laboratories that used the same standard methods for determining concentrations of selected biochemical parameters.

2.2.3 Blood pressure and anthropometry

Blood pressure was measured twice by a manual mercury sphygmomanometer (calibrated weekly), at least five minutes apart, in a sitting position, after at least 10 min of rest. An average value of two measurements was taken for the analysis. Subjects were considered to have hypertension if they (a) reported a previous diagnosis of hypertension or (b) reported the use of anti-hypertensive medication or (c) had a mean systolic blood pressure ≥140 mmHg or mean diastolic pressure ≥90 mmHg (78). Anthropometric measurements were performed using standard procedures, including body height, body weight, waist circumference (WC), and hip circumference (HC). Body mass index (BMI) was calculated using measured height and weight, and subjects were divided into three categories, representing subjects with normal body weight (from 18.5 to 24.9 kg/m^2), overweight (25.0 to 29.9 kg/m^2), and obese subjects (≥30.00 kg/m^2). Besides body mass index (BMI), other measures such as waist-to-hip ratio (WHR) and waist-to-height ratio (WHtR) were calculated to represent relative measures of central obesity. The cut-off value for elevated WC was ≥94 cm for men and ≥80 cm for women (79); for elevated WHR it was ≥0.85 for women and ≥0.90 for men (79), and for WHtR it was ≥0.50 for both sexes (80).

2.2.4 Biochemistry

Biochemical parameters included total cholesterol, low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), triglycerides, glucose, HbA_1c, uric acid, and fibrinogen. Fasting blood samples were collected from the antecubital vein into EDTA and serum tubes and pre-processed immediately in remote study sites. They were shipped frozen (-80°C) to two specialized and accredited laboratories (HRN EN ISO 15189) in Zagreb (samples collected from Vis Island and Split were analyzed in "Labor Centar" and samples from Korčula Island were analyzed in "Breyer Laboratory"). Both laboratories used the same standard methods for determining concentrations of glucose, HbA_1c, uric acid, blood lipids, and fibrinogen (measured using the Clauss method).

Subjects whose fasting glucose level exceeded 7.0 mmol/l or those who reported a previous diagnosis of diabetes type 2 were considered to be diabetic (81). Metabolic syndrome was defined using the Joint Interim Statement (JIS) definition and the cut-off value used for elevated waist circumference was ≥80 cm for women and ≥94 cm for men (82). Subjects who had elevated uric acid (≥404 µmol/l for men and ≥338 µmol/l for women (83) or had a record in medical history were considered positive for gout. The cut-off level for elevated cholesterol was ≥5.0 mmol/l, for LDL cholesterol, it was ≥3.0 mmol/l, and for triglycerides, the cut-off was ≥1.7 mmol/l (82). HDL values of ≤1.03 mmol/l for men and ≤1.29 mmol/l for women were considered as reduced HDL concentrations (82). Information on taking medications for dyslipidemia was also taken into account. The concentration of fibrinogen was considered to be lowered if ≤1.5 g/l, normal if between 1.51-4.0 g/l, or elevated if the concentration was ≥4.0 g/l (84).

2.2.5 Lifestyle characteristics

The lifestyle characteristics were assessed with smoking status, alcohol intake, and physical activity. Smoking status was assigned as current smoker, ex-smoker (stopped more than one year ago), and never-smoker.

Alcohol intake was measured in units per week to combine all the types of alcohol a subject could have consumed during the week (beer, wine, and hard liquor). In cases of consumption of ≥28 units/week for men and ≥21 units/week for women, a subject was classified as an excessive drinker (85), or a moderate drinker in cases of consuming less (1–27 units/week for men and 1–20 units/week for women), while those who did not consume any alcohol were considered non-drinkers.

The level of physical activity was assessed from the survey; light activity was assigned when the subject reported sitting or light physical activity during both work and leisure time. A moderate level of physical activity was assigned if a subject declared a moderate level of physical exertion in at least one part of the day. In contrast, intensive activity was assigned to all subjects who reported hard labour or other intense physical activity during either part of the day.

2.2.6 Socioeconomic characteristics

Socioeconomic status was assessed using three determinants: education, subjective material status, and objective material status.

Education level was measured as years of formal schooling and later classified as corresponding to the Croatian educational system. The groups were constructed according to the number of completed years of schooling, which corresponded to primary education (≤8 years of schooling), secondary (high school level with 9–12 years of schooling), and higher education (≥13 years of schooling). For the follow-up study, the socio-economic status was only assessed during the initial data collection when only 17 subjects reported being students and therefore were automatically included in the higher education group.

Subjective material status was assessed based on the participant's perception of her/his material status in comparison to other people in their community. Possible responses to this question were 'much worse than the average', 'somewhat worse than the average', 'the same as others', 'better than the average', 'much better than the average'. These responses were grouped into three categories for easier interpretation: worse than average (responses 'much worse than average' and 'somewhat worse than average'), average ('the same as others'), and better than average (including answers 'better than average' and 'much better than average').

The assessment of objective material status was based on 16 validated questions forming the composite index (86) indicating the wealth of the subject. The questions referred to the material items or goods in the subject's possession, including heating system, wooden floors, video/DVD recorder, telephone, computer, two TVs, freezer, dishwasher, water supply system, flushing toilet, bathroom, library with more than 100 books, paintings or other art objects, a car, vacation house or second apartment, boat. The responses were summed and classified into four quartile categories according to the distribution in the study population (first quartile with values ≤8, second 9–10, third 11–12, and fourth quartile with values 13–16).

Additional variable indicating the recession period (before/after) was included in the follow-up study to take into account the financial crisis of 2007–2008 and many economic and social changes that had happened in Croatia during such a long study period of observation (from 2003–2015). Therefore, the variable denoted the recession period as having started in target population after 2008 (including subsequent years).

2.2.7 Diet composition and Mediterranean diet assessment

The assessment of the diet composition was based on a food frequency questionnaire (FFQ), based on which the Mediterranean Diet Serving Score (MDSS) was calculated. The

FFQ consisted of 55 questions on commonly consumed foods, with six possible responses (every day, 2–3 times a week, once a week, once a month, rarely, and never), investigating the frequency of consumption of different foods. Mediterranean diet adherence was assessed using the MDSS, which incorporates 14 specific food groups representing the modern MD pyramid: fruit, vegetables, cereals, potatoes, olive oil, nuts, dairy products, legumes, eggs, fish, white meat, red meat, sweets, and fermented beverages—namely wine (21). According to the proposed MDSS approach (21), we created 14 categories of foods that comprised the Mediterranean diet: fruit (including two questions; fresh and dried fruit), vegetables (5 questions; leafy, rooted, cruciferous, tomatoes, canned, and pickled vegetables), cereals (5 questions; white bread, wholegrain bread, rice, pasta, muesli), potatoes, olive oil, nuts, dairy products (5 questions; milk, yoghurt, sour cream, hard cheese, cottage cheese), legumes, eggs, fish (4 questions; blue fish, white fish, mollusks, octopus), white meat (2 questions; chicken, turkey), red meat (6 questions; beef, calf, pork, lamb, sausages, pancetta), sweets (7 questions; cakes, chocolate, cookies, bonbons, jam, sweetened fruit juice, fizzy drinks), fermented beverages (4 questions; red and white wine, red and white bevanda).

MDSS requires a daily intake of vegetables, fruit, olive oil, and cereals (intake of each group is awarded three points for two or more servings a day). Daily intake is encouraged for nuts and dairy products (each group is awarded two points for one or more servings a day) and for wine (one or two glasses per day, awarded with one point) (21). The remaining food groups are awarded one point. Namely, red meat and sweets should be among the less frequently eaten foods (two or fewer servings per week), while potatoes, legumes, eggs, fish, and white meat should be consumed weekly. In this way, the foods that are more beneficial for health and should be consumed several times a day bring greater weight to the final score, while the foods like red meat, eggs, potatoes, and sweets that should be kept at a low frequency of consumption bring lesser weight to the final score. More detailed rules for assigning points for food group intake are listed in Table 1**.** The maximum possible MDSS was 24 points with no negative points. Additionally, the cut-off of ≥14 points was considered good compliance with the MD (21). This questionnaire was also validated for use in the Croatian population in the short form (87). Some subjects were excluded from the analyses due to missing values in the FFQ or the inability to calculate the MDSS at baseline.

Table 1. *The required MDSS food components' intakes and points*

	ADVISED CONSUMPTION	POINTS AWARDED
VEGETABLES	*≥ 2 portions / main meal*	3
FRUIT	*1-2 portions / main meal*	3
CEREALS	*1-2 portions / main meal*	3
OLIVE OIL	*1 portion / main meal*	3
DAIRY PRODUCTS	*2 portions / day*	2
NUTS	*1-2 portions / day*	2
WINE	*1-2 glasses / day*	1
FISH	*≥ 2 portions / week*	1
LEGUMES	*≥ 2 portions / week*	1
EGGS	*2-4 portions / week*	1
POTATO	*≤ 3 portions / week*	1
SWEETS	*≤ 2 portions / week*	1
RED MEAT	*< 2 portions / week*	1
WHITE MEAT	*2 portions / week*	1
	TOTAL SCORE	**24**

Nut consumption frequency was assessed using one question, and all types of nuts were included (tree nuts and peanuts). Subjects were classified into four categories: daily nut consumers (reported nut intake “every day”), weekly consumers (reported “2–3 times a week” nut intake), monthly (reported “once a week” or “once a month”) and those who consume nuts infrequently or never (reported “rarely” or “never”).

2.2.8 Statistical Analysis

All categorical variables were described using absolute numbers and percentages, and numerical variables were described with medians and interquartile ranges (IQR), due to frequent non-normal distribution assessed using the Kolmogorov-Smirnov test. Differences between groups for categorical variables were examined with χ^2, and for numerical variables with Kruskal–Wallis. Additionally, the differences between included subgroups were analyzed with Mann–Whitney U for pairwise comparison of numerical variables and χ^2 for categorical variables. Spearman rank test was used to test correlations between variables. The multivariate analyses included ordinal, logistic, and linear regression, all controlled for known confounding factors. Adjusted odds ratios (OR) and 95% confidence intervals (CI) were provided for multivariate ordinal and logistic regression models, while betas and 95% CI were provided for multivariate linear regression. As each study included different variables of interest, more details on regression models and specific analyses are listed separately below. Nevertheless, the significance level was set at $P<0.05$ (two-sided), and all statistical analyses were performed using IBM SPSS Statistics v19 (IBM, Armonk, NY, USA).

2.2.8.1 Study "Mediterranean diet in southern Croatia - does it still exist?"

Multivariate logistic regression analysis was used to investigate the characteristics associated with compliance to the MD, using the upper quartile of 14 points as a cut-off (MDSS≥14 points). Therefore, the dependent binary variable corresponds to a proposed MDSS cut-off for a good compliance with the MD (21). The model included six covariates: age (3 age group categories: 18.0–34.9 years, 35.0–64.9 years, and ≥65.0 years), sex, place of residence (Vis, Korčula, Split), years of schooling, smoking status, and level of physical activity. All covariates were categorical variables to provide a better understanding of the results. In all instances, we provided OR and 95% CI.

2.2.8.2 Study "The Role of Socioeconomic Status in Adherence to the Mediterranean Diet and Body Mass Index Change: A Follow-Up Study in the General Population of Southern Croatia. "

Univariate and multivariate logistic regression analyses (enter method) were used to assess the association between three SES characteristics (education level, subjective material status, objective material status) and overall adherence to the MD (MDSS ≥ 14 points) at baseline. Additionally, multivariate logistic regression analysis was used to assess adherence predictors for each of the 14 MD food groups within the MD scoring system. All multivariate models also included age (3 age group categories: 18.0–34.9 years, 35.0–64.9 years, and ≥65.0 years), sex, place of residence (Vis, Korčula, Split), number of previously diagnosed chronic diseases, smoking status, level of physical activity, and BMI as confounding factors. There were only 53 subjects in the baseline sample with a BMI less than 18.5 kg/m2, and we have excluded them from the regression analysis due to the small sample size of the group. Additionally, to control for the potential confounding effects of 2007–2008, we included a variable denoting the data collection period as either before or after the recession period in all of the regression models. All of the included covariates were entered as categorical variables to easier interpret the results. OR and 95% CI were provided for both univariate and multivariate logistic regression models. Correlations between the three variables describing socioeconomic status were tested using the Spearman rank test, before using them together in logistic regression models; none of the Spearman's rho values were higher than 0.401.

Linear regression models were used to assess the association between absolute change in MDSS and BMI across the follow-up period with different subjects' characteristics. The main predictor variables were again the three SES characteristics (education level, subjective material status, and objective material status), and the models also included important confounding variables: age, follow-up time, sex, place of residence, number of previously diagnosed chronic diseases, smoking status, level of physical activity, BMI at baseline, and MDSS at baseline. Additionally, the model with BMI change during the follow-up as an outcome variable also included the MDSS absolute change during the follow-up as a covariate.

The change in the prevalence of the adherence to the MD and each of the MD food groups between baseline (t_0) and the follow-up period (t_1) was assessed by calculating the percent change, using the following formula:

$$\text{MD adherence }(\%)_{\text{change}} = \frac{\text{MD adherence}(\%)_{t_1} - \text{MD adherence}(\%)_{t_0}}{\text{MD adherence}(\%)_{t_0}} * 100.$$

Additionally, the absolute change in MDSS and BMI between baseline (t_0) and the follow-up period (t_1) was calculated using the following formulas:

$$\text{MDSS}_{\text{change}} = \text{MDSS}_{t_1} - \text{MDSS}_{t_0},$$
$$\text{BMI}_{\text{change}} = \text{BMI}_{t_1} - \text{BMI}_{t_0}.$$

The Wilcoxon signed-rank test and McNemar test were used to compare the differences between paired data for repeated measurements (baseline vs. follow-up).

2.2.8.3 Study "Nut Consumption and Cardiovascular Risk Factors: A Cross-Sectional Study in a Mediterranean Population."

The 405 subjects who reported a previous diagnosis of either coronary heart disease or cerebrovascular insult were excluded from all the multivariate analyses of the association of nut consumption with different cardiovascular risk factors to test the hypothesis only in subjects at risk of cardiovascular disease.

The multivariate analysis included ordinal regression and logistic regression. Ordinal regression analysis was used to identify the characteristics associated with the ordinal dependent variables: BMI and fibrinogen (each variable was analysed in a separate model). Covariates in these three models included sex, age (3 age group categories: 18.0–34.9 years, 35.0–64.9 years, and ≥65.0 years), place of residence (Vis, Korčula, Split), education attainment (years of schooling), quartiles of material status, smoking status, alcohol intake, overall adherence to the MD (MDSS ≥14 points), nut consumption, level of physical activity, WHtR (only in fibrinogen models), and four chronic diseases (hypertension, diabetes, metabolic syndrome, and gout). In each model, the highest value of the ordinal dependent variable was used as a referent point (BMI ≥30 kg/m^2; fibrinogen ≥4.0 g/L). Beta values were transformed into OR using the exponential value of beta, with 95% CI (exponential values of beta's lower and upper bounds).

A logistic regression analysis was used to identify the characteristics associated with the binary outcome variables: waist circumference, WHR, WHtR as binary outcomes (normal or ref. elevated), hypertension, diabetes, elevated HbA_1c, metabolic syndrome, gout, elevated triglycerides, elevated cholesterol, elevated LDL cholesterol, and decreased HDL cholesterol. All the logistic regression models were controlled for known confounding factors: sex, age, cohort effect (place of residence), years of schooling, quartiles of material status, smoking status, alcohol intake, overall adherence to the MD, nut consumption, level of physical activity, WHtR and four chronic diseases (hypertension, diabetes, metabolic syndrome, and gout), except in models where these were dependent variables. Metabolic syndrome was omitted as a covariate in the regression models for elevated triglycerides, cholesterol, LDL cholesterol, HDL cholesterol and fibrinogen due to its failure to meet the model diagnostic criteria (Hosmer–Lemeshow test). On the other hand, models with chronic diseases or central obesity indices as outcome variables did include metabolic syndrome as a covariate, except in the model where metabolic syndrome was a dependent variable. Using this approach, all the models built for the analysis had a good fit (Hosmer and Lemeshow test P-values were > 0.05).

2.3 RESULTS

2.3.1 Paper "Mediterranean diet in the southern Croatia - does it still exist?"

After the exclusions of participants due to missing values needed for the calculation of MDSS, the analysis included N=2,768 subjects from three study sites; 385 originated from the island of Vis, 1,874 from the island of Korčula, and 509 from the City of Split (Table 2).

Table 2. *Adherence to the Mediterranean diet (14 food components and the overall adherence expressed as MDSS≥14 points), according to the place of residence in a total sample of 2,768 subjects.*

	Place of residence			
	Island of Korčula n=1,874	**Island of Vis** n=385	**City of Split** n=509	**P-values**
Sex; n (%)				
men	685 (36.6)	153 (39.7)	201 (39.5)	0.301 (0.238[KV];0.224[KS]; 0.939[VS])
women	1189 (63.4)	232 (60.3)	308 (60.5)	
Years of age; median (IQR)	55.0 (40.7-65.3)	63.5 (54.1 – 73.1)	58.0 (47.0-66.0)	<0.001 (<0.001[KV];<0.001[KS];<0.001[VS])
Education (years of schooling); median (IQR)	12 (9-12)	11 (6-12)	12 (12-16)	<0.001 (<0.001[KV];<0.001[KS];<0.001[VS])
Smoking status; n (%)				
current smokers	522 (29.7)	99 (25.7)	84 (20.0)	
ex-smokers	369 (21.0)	49 (12.7)	132 (31.4)	<0.001 (<0.001[KV];<0.001[KS];<0.001[VS])
never-smokers	983 (52.4)	237 (61.6)	293 (57.6)	
Physical activity; n (%)				
light	341 (18.2)	148 (38.4)	136 (26.7)	
moderate	1210 (64.6)	200 (51.9)	356 (69.9)	<0.001 (<0.001[KV];<0.011[KS];<0.003[VS])
intensive	174 (9.3)	21 (5.5)	8 (1.6)	
MDSS; median (IQR)	10 (8-13)	12 (9-14)	11 (8-15)	<0.001 (<0.001[KV]; <0.001[KS]; 0.401[VS])
MDSS≥14 points; n (%)	352 (18.8)	123 (31.9)	160 (34.4)	<0.001 (<0.001[KV]; <0.001[KS]; 0.885[VS])
MDSS components adherence; n (%)				
fruit	937 (50.0)	228 (59.2)	320 (62.9)	<0.001 (<0.001[KV]; <0.001 [KS]; 0.268 [VS])
vegetables	521 (27.8)	127 (33.0)	216 (42.4)	<0.001 (0.041[KV]; <0.001 [KS]; 0.004 [VS])
cereals	1625 (86.7)	365 (94.8)	405 (79.6)	<0.001 (<0.001[KV]; <0.001[KS];<0.001[VS])
potatoes	1229 (65.6)	334 (86.8)	462 (90.8)	<0.001 (<0.001[KV]; <0.001[KS]; 0.066 [VS])
olive oil	1283 (68.5)	296 (76.9)	328 (64.4)	<0.001 (0.001[KV]; 0.085 [KS]; <0.001 [VS])
nuts	86 (4.6)	10 (2.6)	57 (11.2)	<0.001 (0.078[KV]; <0.001[KS]; <0.001[VS])
dairy products	339 (18.1)	84 (21.8)	106 (20.8)	0.132 (0.088[KV]; 0.160 [KS]; 0.742[VS])
legumes	412 (22.2)	78 (20.3)	122 (24.0)	0.406 (0.454[KV]; 0.341[KS]; 0.196[VS])
eggs	462 (24.7)	80 (20.8)	134 (26.3)	0.148 (0.105[KV]; 0.440[KS]; 0.058[VS])
fish	1161 (62.0)	252 (65.5)	286 (56.2)	0.013 (0.196[KV]; 0.018[KS]; 0.006[VS])
white meat	758 (40.4)	136 (35.3)	185 (36.3)	0.069 (0.067[KV]; 0.093[KS]; 0.778[VS])
red meat	548 (29.2)	127 (33.0)	201 (39.5)	<0.001 (0.144[KV]; <0.001[KS]; 0.050[VS])
sweets	597 (31.9)	105 (27.3)	164 (32.2)	0.185 (0.077[KV]; 0.876[KS]; 0.122[VS])
wine	315 (16.8)	125 (32.5)	136 (26.7)	<0.001 (<0.001[KV]; <0.001[KS]; 0.064[VS])

MDSS- Mediterranean Diet Serving Score. [KV] Pairwise comparison P-value: Korčula vs. Vis. [KS] Pairwise comparison P-value: Korčula vs. Split. [VS]Pairwise comparison P-value: Vis vs. Split.

The study revealed rather unsatisfactory adherence to the MD in Southern Croatia. In total, 22.9% of participants reported a dietary pattern adherent to the MD pyramid according to the MD scoring system criteria, with an MDSS median of 11 of the maximal 24 points (IQR 8-13). The median MDSS was as low as 10 among participants from the Island of Korčula, 11 among those from Split, and 12 among subjects from the Island of Vis, although participants from the island of Vis did not statistically differ from those from Split (Table 2).

There was a wide range of variability in the compliances with the 14 MDSS food components, as stated in Table 2. The required high intake of vegetables (≥2 servings/main meal) was poorly met in this study: only 28% of participants from Korčula adhered to the daily vegetable consumption requirement, 33% from Vis, and 42% from Split. Fruit consumption showed overall better results, ranging from 50% in Korčula to 63% in Split. The required intake of cereals as recommended by the MD scoring system (1-2 portions / main meal) was met by most of the participants stratified by the place of residence (ranging from 80% in Split to 95% in Vis). Olive oil intake was commonly reported (64-77%). Satisfactory fish consumption was generally present in more than 56% of the participants (stratified by place of residence), with the highest proportion recorded among participants from Vis (66%). The worst result for a particular component was recorded for nuts intake, whereas as little as 3% of subjects from Vis reported eating nuts every day, and the situation was not much better among the participants from Korčula (5%), and Split (11%). The participants from Korčula had lower compliance for potato intake (66%) compared to participants from Vis and Split (87% and 91%, respectively). MDSS recommendations for dairy products, legumes, eggs, and wine consumption were met by 17-26% of the participants, while those for meat and sweets were met by 29-40% (stratified by place of residence). The prevalence of compliance to the guidelines for sweets, white meat, eggs, legumes, and dairy products did not differ across the three subgroups according to the place of residence (Table 2).

Better compliance with the overall Mediterranean diet, as well as with the majority of the MDSS components, was recorded among the oldest participants. Breakdown into three groups according to the subject's age revealed substantial differences in favour of higher MDSS in the elderly group (all P <0.001, Table 3). Overall, only 12% of subjects from the youngest group were identified as adherent to MD, while the corresponding figure in the eldest age groups was 34%. Significant differences in compliance across three age groups were identified for all MDSS food components except white meat, dairy products, nuts, and cereals (Table 3).

Table 3. *Adherence to the Mediterranean diet (14 food components and the overall adherence expressed as MDSS≥14 points), according to the age group in a total sample of 2,768 subjects.*

	Age groups			P-values
	18.0 – 34.9 n=372	**35.0 – 64.9** n=1,617	**≥65.0 years** n=779	
Sex; n(%)				
men	149 (40.1)	571 (35.3)	319 (40.9)	0.016 (0.086*;0.772†; 0.007‡)
woman	223 (59.9)	1046 (64.6)	460 (59.1)	
Education (years of schooling); median (IQR)	12.0 (11.0-15.0)	12.0 (11.0-13.0)	11.0 (6.0-12.0)	<0.001 (<0.001*;<0.001†;<0.001‡)
Smoking status; n (%)				
current smokers	163 (45.4)	478 (32.4)	64 (9.2)	<0.001 (<0.001*;<0.001†;<0.001‡)
ex-smokers and never-smokers	209 (54.6)	1139 (67.6)	715 (90.8)	
Physical activity; n (%)				
light	85 (23.3)	284 (18.7)	256 (36.1)	
moderate	252 (69.0)	1102 (72.5)	412 (58.0)	<0.001 (<0.001*;<0.001†;<0.001‡)
intensive	28 (7.7)	133 (8.8)	42 (5.9)	
MDSS; median (IQR)	9.0 (7.0 – 11.0)	11.0 (8.0-13.0)	12.0 (9.0-14.0)	<0.001 (<0.001*; <0.001†; <0.001‡)
MDSS≥14 points; n (%)	46 (12.4)	324 (20.0)	265 (34.0)	<0.001 (0.001*; <0.001†; <0.001‡)
MDSS components adherence; n (%)				
fruit	132 (35.5)	863 (53.4)	490 (62.9)	<0.001 (<0.001*; <0.001†; <0.001‡)
vegetables	95 (25.5)	471 (29.1)	298 (38.3)	<0.001 (0.166*; <0.001†; <0.001‡)
cereals	316 (84.9)	1403 (86.8)	676 (86.8)	0.632 (0.356*; 0.400†; 0.993‡)
potatoes	314 (84.4)	1195 (73.9)	516 (66.2)	<0.001 (<0.001*; <0.001†; <0.001‡)
olive oil	193 (51.9)	1082 (66.9)	632 (81.1)	<0.001 (<0.001*; <0.001†; <0.001‡)
nuts	19 (5.1)	88 (5.4)	46 (5.9)	0.835 (0.796*; 0.584†; 0.644‡)
dairy products	78 (21.0)	308 (19.0)	143 (18.4)	0.571 (0.398*; 0.293†; 0.685‡)
legumes	80 (21.5)	320 (19.8)	212 (27.2)	<0.001 (0.473*; 0.037†; <0.001‡)
eggs	115 (30.9)	416 (25.7)	145 (18.6)	<0.001 (0.041*; <0.001†; <0.001‡)
fish	185 (49.7)	978 (60.5)	536 (68.8)	<0.001 (<0.001*; <0.001†; <0.001‡)
white meat	150 (40.3)	618 (38.2)	311 (39.9)	0.617 (0.452*; 0.897†; 0.423‡)
red meat	93 (25.0)	493 (30.5)	290 (37.2)	<0.001 (0.037*; <0.001†; 0.001‡)
sweets	74 (19.9)	493 (30.5)	299 (38.4)	<0.001 (<0.001*; <0.001†; <0.001‡)
wine	45 (12.1)	327 (20.2)	204 (26.2)	<0.001 (<0.001*; <0.001†; 0.001‡)

MDSS: Mediterranean Diet Serving Score.
** Pairwise comparison P-value: 18.0-34.9 years vs. 35.0–64.9 years.*
† Pairwise comparison P-value: 18.0-35 years vs. ≥65 years.
‡ Pairwise comparison P-value: 34.9-64.9 years vs. ≥65 years.

Furthermore, the breakdown by sex and age suggested somewhat better indices in women and older age groups, with only one significant result: good compliance to the MD differed according to age groups only in women (*P* =0.024) (Figure 1).

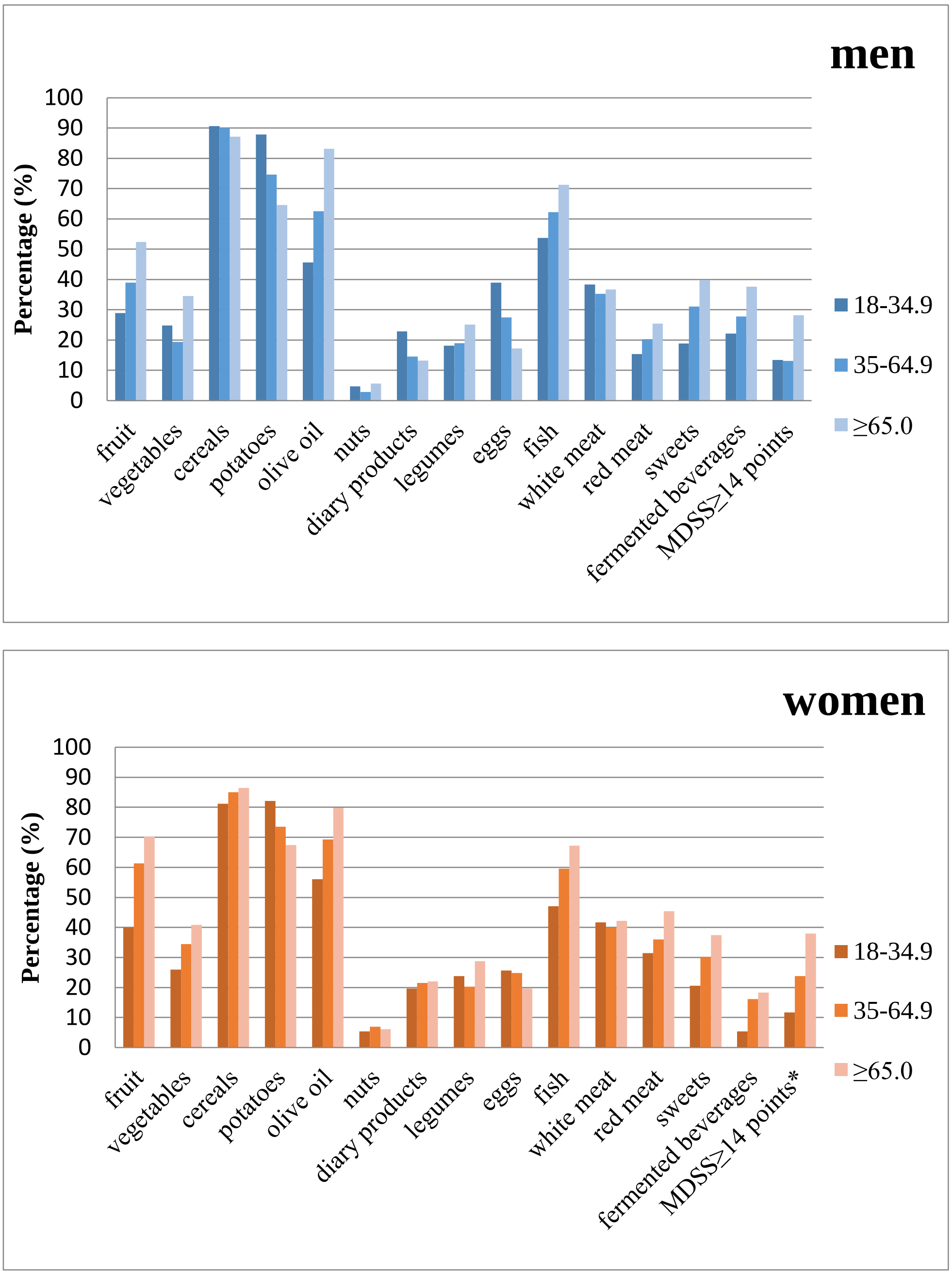

Figure 1. *Adherence to the MD (14 food components and the overall adherence expressed as MDSS≥14 points), according to the sex and age group in a total sample of 2,768 subjects (significant differences at the level of P<0.05 between age groups are denoted with an asterisk; χ2 test).*

Logistic regression analysis revealed several variables to be strongly associated with adherence to the Mediterranean diet (MDSS ≥14 points). For instance, men had 48% lesser odds of showing compliance to the MD compared to women (OR =0.52, 95% CI 0.42-0.65, *P* <0.001), while the youngest age group had 70% and middle age group 56% lesser odds compared to the oldest participants (OR =0.30, 95% CI 0.20-0.45, *P* <0.001 and OR=0.44, 95% CI 0.35-0.56, *P* <0.001 respectively) (Table 4). Both the participants from Vis and those from Split showed greater odds for good adherence to the Mediterranean diet (OR =1.99, 95% CI 1.50-2.64, *P* <0.001 and OR =1.67, 95% CI 1.28-2.19, *P* <0.001, respectively) (Table 4). Physical activity, lower education, and smoking were marginal predictors or lacked significance (Table 4). The regression model yielded good data fit (Hosmer and Lemeshow P =0.225, Nagelke R^2 =0.101).

***Table 4**. Characteristics associated with adherence to the Mediterranean diet (MDSS≥14 points) using the multivariate logistic regression analysis (N=2,768).*

	MDSS≥14 points
	Adjusted odds ratio (95% confidence interval); *P*
Sex (referent (ref.): women)	
men	0.52 (0.42 – 0.65); <0.001
Age (years, ref: ≥65.0)	
35.0– 64.9	0.44 (0.35-0.56); <0.001
18.0–34.9	0.30 (0.20-0.45); <0.001
Place of residence (ref: Korčula)	
Split	1.67 (1.28-2.19); <0.001
Vis	1.99 (1.50-2.64); <0.001
Education (years of completed education*, ref: ≥13)	
<8	0.57 (0.39-0.83); 0.003
8-10	0.70 (0.49-0.99); 0.045
11-12	0.61 (0.48-0.79); <0.001
Smoking status (ref: non-smokers)	
smokers	0.77 (0.60-0.99); 0.045
Physical activity (ref: intensive)	
light	0.61 (0.40-0.93); 0.021
moderate	0.71 (0.48-1.04); 0.080

Adjusted odds ratios, 95% confidence intervals and P-values were calculated using a multivariate logistic regression model simultaneously adjusted for all the covariates listed in this table (enter method).
**Categorized into four categories according to years of completed education: less than completed primary school (<8), completed primary school and/or a few years of high school (8-10), completed high school (11-12), and more than high school (≥13).*

2.3.2 Paper "The Role of Socioeconomic Status in Adherence to the Mediterranean Diet and Body Mass Index Change: A Follow-Up Study in the General Population of Southern Croatia."

After the exclusions of participants due to missing values needed for the calculation of MDSS, the analysis included N=4,671 subjects upon their initial enrolment and N=1,342 subjects for the follow-up analysis. Therefore, the analysis of initially enrolled participants included n=1,012 subjects from the Island of Vis (sampled during 2003–2004 period), n=2,651 subjects from the Island of Korčula (sampled during 2007 and 2012–2015 period), and n=1,008 subjects from the City of Split (sampled in 2008–2009 period). The follow-up analysis included participants with field-based follow-up data; subjects from the Island of Vis followed up in 2011 (n=482, response rate 46.8%, mean follow-up of 7.5 years), subjects from the Town of Korčula who were initially included in 2007 and followed-up in 2013 (n=366; 37.8%; mean follow-up of 5.3 years), and subjects from the City of Split followed-up in 2012–2013 (n=494; 48.8%, mean follow-up of 4.4 years).

A wide range of adherence to MDSS components was present (from as low as 2.7% for nuts in subjects from Vis, and up to 97.4% adherence for cereals in the same group), with a rather low prevalence of adherence to the MD in the entire sample (28.5%). The lowest prevalence was recorded for subjects from the Island of Korčula (26.8%), followed by those from the City of Split (30.4%), and the Island of Vis (31.1%), although participants from the Island of Vis did not statistically differ from those from the City of Split. The median MDSS was the lowest in subjects from the Island of Korčula (11 out of 24 points; IQR 6), and it was slightly higher in both subjects from the City of Split and the Island of Vis (median 12; IQR 5) (Table 5).

Less than half of all of the subjects were compliant with the daily requirement for vegetable intake (lowest on Korčula; 37.0%), while it was a little better for intake of fruit (lowest on Korčula; 52.8%), and olive oil (lowest on Vis; 57.9%). Only 22.3% of subjects from the Island of Korčula, 25.3% from the Island of Vis and 26.8% from the City of Split adhered to the daily dairy products consumption requirement, which was similar for wine (17.3%-20.2%). Consistently, the best adherence was recorded for cereals and the lowest for nuts (Table 5).

Table 5. *Adherence to the Mediterranean diet (14 food components and the overall adherence expressed as MDSS≥14 points), according to the place of residence in a total sample of 4,671 subjects.*

	Place of residence			
	Island of Vis n = 1,012	**Island of Korčula** n = 2,651	**City of Split** n = 1,008	**P-values**
Sex; n (%)				
men	423 (41.8)	967 (36.5)	391 (38.8)	0.011 (0.003^{VK}, 0.168^{VS}, 0.196^{KS})
women	589 (58.2)	1684 (63.5)	617 (61.2)	
Years of age; median (IQR)	56.00 (24.00)	55.00 (23.25)	52.00 (21.00)	<0.001 (<0.001^{VK},<0.001^{VS},<0.001^{KS})
Education (years of schooling); median (IQR)	11.00 (4.00)	12.00 (3.00)	12.00 (4.00)	<0.001 (<0.001^{VK}, <0.001^{VS}, <0.001^{KS})
Subjective material status; median (IQR)	3.00 (0.00)	3.00 (1.00)	3.00 (1.00)	<0.001 (<0.001^{VK}, <0.001^{VS}, <0.001^{KS})
Objective material status; median (IQR)	10.00 (5.00)	10.00 (3.00)	12.00 (3.00)	<0.001 (<0.001^{VK}, <0.001^{VS}, <0.001^{KS})
Body mass index (kg/m^2); median (IQR)	27.08 (6.05)	24.59 (5.94)	26.60 (5.63)	<0.001 (<0.001^{VK}, 0.024^{VS}, <0.001^{KS})
Chronic diseases*; n(%)				
none	542 (53.6)	1565 (59.0)	677 (67.2)	
1	289 (28.6)	677 (25.5)	248 (24.6)	<0.001 (0.011^{VK}, <0.001^{VS}, <0.001^{KS})
≥2	181 (17.9)	409 (15.4)	83 (8.2)	
Smoking status; n (%)				
current smokers	288 (28.5)	741 (28.0)	266 (26.5)	
ex-smokers	303 (30.0)	584 (22.2)	275 (27.4)	<0.001 (0.001^{VK}, 0.105^{VS}, 0.005^{KS})
never-smokers	419 (41.5)	1306 (49.6)	464 (46.2)	
Physical activity; n (%)				
light	264 (26.2)	537 (20.5)	358 (35.6)	
moderate	580 (57.5)	1815 (69.2)	610 (60.7)	<0.001 (<0.001^{VK}, <0.001^{VS}, <0.001^{KS})
intensive	164 (16.3)	271 (10.3)	37 (3.7)	
MDSS; median (IQR)	12.00 (5.00)	11.00 (6.00)	12.00 (5.00)	<0.001 (<0.001^{VK}, 0.554^{VS}, 0.001^{KS})
MDSS≥14 points; n (%)	315 (31.1)	711 (26.8)	306 (30.4)	0.012 (0.009^{VK}, 0.708^{VS}, 0.033^{KS})
MDSS components adherence; n (%)				
fruit	596 (58.9)	1399 (52.8)	636 (63.1)	<0.001 (0.001^{VK}, 0.053^{VS}, <0.001^{KS})
vegetables	439 (43.4)	980 (37.0)	418 (41.5)	0.001 (<0.001^{VK}, 0.385^{VS}, 0.012^{KS})
cereals	986 (97.4)	2367 (89.3)	929 (92.2)	<0.001 (<0.001^{VK}, <0.001^{VS}, 0.009^{KS})
olive oil	586 (57.9)	1835 (69.2)	643 (63.8)	<0.001 (<0.001^{VK}, 0.007^{VS}, 0.002^{KS})
nuts	27 (2.7)	117 (4.4)	71 (7.0)	<0.001 (0.015^{VK}, <0.001^{VS}, 0.001^{KS})
dairy products	256 (25.3)	592 (22.3)	270 (26.8)	0.010 (0.057^{VK}, 0.446^{VS}, 0.005^{KS})
potatoes	686 (67.8)	1774 (66.9)	823 (81.6)	<0.001 (0.617^{VK}, <0.001^{VS}, <0.001^{KS})
legumes	326 (32.2)	714 (26.9)	252 (25.0)	0.001 (0.002^{VK}, <0.001^{VS}, 0.236^{KS})
eggs	297 (29.3)	662 (25.0)	246 (24.4)	0.013 (0.007^{VK}, 0.012^{VS}, 0.723^{KS})
fish	838 (82.8)	1769 (66.7)	692 (68.7)	<0.001 (<0.001^{VK}, <0.001^{VS}, 0.269^{KS})
white meat	499 (49.3)	1077 (40.6)	381 (37.8)	<0.001 (<0.001^{VK}, <0.001^{VS}, 0.118^{KS})
red meat	261 (25.8)	700 (26.4)	248 (24.6)	0.537 (0.705^{VK}, 0.539^{VS}, 0.266^{KS})
sweets	181 (17.9)	808 (30.5)	168 (16.7)	<0.001 (<0.001^{VK}, 0.469^{VS}, <0.001^{KS})
wine	204 (20.2)	459 (17.3)	177 (17.6)	0.124 (0.046^{VK}, 0.136^{VS}, 0.861^{KS})

**chronic diseases included any or more than one of the following diagnoses: hypertension, diabetes, CHD, CVI, cancer, bipolar disorder, hyperlipidemia and gout. MDSS: Mediterranean Diet Serving Score. ^{VK} Pairwise comparison P-value: Vis vs. Korčula. ^{VS} Pairwise comparison P-value: Vis vs. Split. ^{KS} Pairwise comparison P-value: Korčula vs. Split.*

Logistic regression analysis revealed several characteristics that were strongly associated with adherence to the MD in the entire sample (Table 6).

Table 6. *Characteristics associated with adherence to the Mediterranean diet (MDSS≥14 points) in the total sample (N=4,671), as determined by the logistic regression analysis.*

		MDSS≥14 points Adjusted odds ratio (95% confidence interval); *P*
Sex (ref. men)		
	woman	1.85 (1.58, 2.17); <0.001
Age years (ref: 18.0-34.9)		
	35.0-64.9	1.99 (1.54, 2.57); <0.001
	≥65.0	3.81 (2.83, 5.12); <0.001
Place of residence (ref: Split)		
	Vis	1.04 (0.84, 1.29); 0.696
	Korčula	1.63 (1.31, 2.02); <0.001
Education (years of schooling, ref: elementary 0-8)		
	high school (9-12)	0.93 (0.77, 1.14); 0.492
	higher (≥13)	1.19 (0.95, 1.5); 0.130
Subjective material status (ref: worse than average)		
	average	1.14 (0.91, 1.44); 0.258
	better than average	1.16 (0.89, 1.51); 0.267
Objective material status (ref: 1st quartile)		
	2nd quartile	1.38 (1.12, 1.70); 0.002
	3rd quartile	1.29 (1.04, 1.61); 0.020
	4th quartile	1.93 (1.53, 2.43); <0.001
Chronic diseases* (ref: ≥2)		
	1	0.93 (0.75, 1.17); 0.546
	none	0.93 (0.75, 1.16); 0.507
Smoking status (ref: current smokers)		
	ex-smokers	1.40 (1.14, 1.71); 0.001
	never-smokers	1.36 (1.13, 1.63); 0.001
Physical activity (ref: light)		
	moderate	1.44 (1.21, 1.70); <0.001
	intensive	1.50 (1.15, 1.97); 0.003
Body mass index category (ref: 18.0-24.9)		
	25.0-29.9 kg/m²	0.98 (0.83, 1.16); 0.834
	≥30.0 kg/m²	0.84 (0.68, 1.05); 0.123
The economic crisis of 2007-2008 (ref: before)		
	after	0.31 (0.25, 0.38); <0.001

Adjusted odds ratios, 95% confidence intervals and P-values were calculated using a multivariate logistic regression model simultaneously adjusted for all the covariates listed in this table (enter method).
**chronic diseases included any or more than one of the following diagnoses: hypertension, diabetes, CHD, CVI, cancer, bipolar disorder, hyperlipidemia and gout;*

Women presented higher odds of adherence compared to men (OR =1.85, 95% CI 1.58-2.17, *P* <0.001), while the oldest age group had 3.81 fold higher odds of adherence compared to the youngest subjects (95% CI 2.83-5.12, *P* <0.001) (Table 6). In the fully adjusted model, subjects from the Island of Korčula presented higher odds of adherence compared to the subjects from the City of Split (OR =1.63, 95% CI 1.31-2.02, *P* <0.001). Education level and subjective material status were not associated with adherence to the MD in the adjusted model, unlike objective material status. The wealthiest subjects, according to the objective material status (those in the fourth quartile of distribution) were almost twice as likely to be adherent to the MD, compared to subjects in the lowest quartile (OR =1.93, 95% CI 1.53-2.43, *P* <0.001). Subjects in the second and third quartile of objective material status also had greater odds of adhering to the MD. Subjects who never smoked and ex-smokers presented with higher odds of adherence to the MD, compared to current smokers (OR =1.36, 95% CI 1.13-1.63, *P* =0.001; OR =1.40, 95% CI 1.14-1.71, *P* =0.001, respectively). Subjects with higher levels of physical activity were also more likely to adhere to the MD. BMI and diagnosis of chronic diseases were not associated with adherence to the MD. The study period was statistically significantly associated with adherence to the MD, in a way that MD adherence was less likely in the period after the recession (OR =0.31, 95% CI 0.25-0.38, *P* <0.001) (Table 6). The fully adjusted regression model yielded a good data fit (Hosmer and Lemeshow P =0.304; Nagelkerke R^2 =0.100).

Determinants of adherence to MD food components are shown in Table 7. Women were more likely to adhere to the recommended intake of fruit, vegetables, olive oil, nuts, diary, and red meat, but they were less likely to adhere to eggs and wine intake MD recommendations compared to men (women most commonly abstained from alcohol intake).

Older subjects had higher odds of meeting the recommendations for fruit, vegetables, cereals, olive oil, nuts, fish, red meat, sweets, and wine intake, but lower odds for adherence to potatoes and eggs than the youngest group of subjects (Table 7).

The highest level of education was associated with lesser adherence to the MD guidelines for intake of cereals, olive oil, legumes, fish, and white meat, in contrast to higher adherence to appropriate intake of dairy products, potatoes and red meat compared to the subjects with the lowest level of education (Table 7).

Subjective material status was less associated with MD food components intake, unlike the objective material status that was presented as the most prominent socioeconomic indicator for the overall adherence to the MD and several food groups. Compared to subjects in the lowest quartile of objective material status, subjects belonging to higher quartiles presented with an increasing trend of compliance with fruit, vegetables, olive oil, and fish intake recommendations, but also with the decreasing compliance for the intake of red meat and sweets (Table 7).

Obese subjects (BMI 30≥kg/m2) were 34% more likely to adhere to recommendations for sweets, but also 30% less likely to adhere to recommendations for cereals intake, and 42% less adherent for nuts (Table 7).

The study period after the recession was associated with 68% decreased odds for adherence to vegetable intake recommendations, 55% decreased odds for cereals adherence, 50% for fruit, 49% for fish, 47% for legumes, 36% for dairy products, 31% for potatoes, and 29% decreased odds for adherence to olive oil intake. On the other hand, we recorded 39% increased odds for adherence to red meat, and 23% increased adherence to sweets intake recommendations after the recession (Table 7).

Table 7. *Characteristics associated with compliance to the 14 MDSS food components, as determined by the multivariate logistic regression analysis (N = 4,671).*

	Fruit aOR (95% CI); *P*	**Vegetables** aOR (95% CI); *P*	**Cereals** aOR (95% CI); *P*	**Olive oil** aOR (95% CI); *P*	**Nuts** aOR (95% CI); *P*	**Dairy** aOR (95% CI); *P*	**Potatoes** aOR (95% CI); *P*	**Legumes** aOR (95% CI); *P*	**Eggs** aOR (95% CI); *P*	**Fish** aOR (95% CI); *P*	**White meat** aOR (95% CI); *P*	**Red meat** aOR (95% CI); *P*	**Sweets** aOR (95% CI); *P*	**Wine** aOR (95% CI); *P*
Sex (ref. man)														
woman	2.42 (2.10, 2.78);<0.001	1.91 (1.55, 2.06);<0.001	0.82 (0.64, 1.05);0.110	1.22 (1.06, 1.40);0.007	1.97 (1.40, 2.78);<0.001	1.59 (1.35, 1.86);<0.001	0.97 (0.83, 1.12);0.652	1.13 (0.98, 1.31);0.102	0.82 (0.71, 0.95);0.009	1.08 (0.93, 1.26);0.286	1.04 (0.91, 1.19);0.520	1.96 (1.67, 2.30);<0.001	1.00 (0.85, 1.17);0.981	0.39 (0.33, 0.46);<0.001
Age (years, ref: 18.0-34.9)														
35.0-64.9	1.61 (1.32, 1.96);<0.001	1.56 (1.27, 1.93);<0.001	1.44 (1.06, 1.96);0.020	1.43 (1.18, 1.73);<0.001	1.35 (0.82, 2.20); 0.235	0.98 (0.78, 1.21); 0.823	0.58 (0.46, 0.73);<0.001	1.01 (0.82, 1.26);0.901	0.84 (0.69, 1.03); 0.091	1.32 (1.08, 1.61); 0.006	1.01 (0.84, 1.22);0.923	1.23 (0.98, 1.56); 0.075	1.90 (1.45, 2.49);<0.001	1.69 (1.29, 2.22);<0.001
≥65.0	2.83 (2.21, 3.62);<0.001	2.33 (1.81, 3.00);<0.001	1.40 (0.94, 2.09);0.101	2.40 (1.87, 3.07);<0.001	1.92 (1.09, 3.40); 0.024	1.24 (0.95, 1.63); 0.117	0.75 (0.59, 0.95);0.018	1.29 (0.99, 1.67);0.055	0.63 (0.48, 0.81);<0.001	2.01 (1.55, 2.60);<0.001	0.90 (0.71, 1.14);0.370	1.58 (1.20, 2.09); 0.001	2.42 (1.78, 3.29);<0.001	2.41 (1.76, 3.31);<0.001
Place of residence (ref: Split)														
Vis	0.84 (0.68, 1.02); 0.083	1.08 (0.89, 1.32); 0.419	2.76 (1.72, 4.41);<0.001	0.70 (0.58, 0.86); 0.001	0.46 (0.28, 0.75); 0.002	1.13 (0.91, 1.41); 0.254	0.64 (0.51, 0.80);<0.001	1.22 (0.99, 1.51); 0.068	1.40 (1.13, 1.74); 0.002	2.16 (1.72, 2.71);<0.001	1.40 (1.16, 1.70);0.001	1.03 (0.82, 1.29); 0.804	0.83 (0.64, 1.07); 0.144	1.27 (0.99, 1.63); 0.057
Korčula	0.98 (0.79, 1.22); 0.849	1.63 (1.33, 2.00);<0.001	1.10 (0.74, 1.64); 0.629	1.53 (1.22, 1.91);<0.001	0.67 (0.43, 1.04); 0.072	1.14 (0.91, 1.43); 0.258	0.58 (0.48, 0.70);<0.001	1.54 (1.24, 1.92);<0.001	0.98 (0.78, 1.24); 0.880	1.44 (1.14, 1.81); 0.002	1.08 (0.88, 1.32);0.457	0.89 (0.70, 1.12); 0.319	1.82 (1.42, 2.34);<0.001	1.08 (0.83, 1.40); 0.561
Education (ref: 0-8)														
high school (9-12)	1.17 (0.98, 1.41); 0.085	1.06 (0.89, 1.27); 0.521	0.74 (0.53, 1.04); 0.081	0.66 (0.54, 0.79);<0.001	1.07 (0.69, 1.66); 0.760	1.07 (0.87, 1.31); 0.535	1.43 (1.19, 1.71);<0.001	0.72 (0.60, 0.87); 0.001	1.04 (0.86, 1.27); 0.675	0.77 (0.63, 0.94); 0.011	0.76 (0.64, 0.90);0.002	1.14 (0.94, 1.40); 0.188	1.05 (0.86, 1.28); 0.653	1.12 (0.89, 1.41); 0.324
higher (13+)	1.20 (0.97, 1.49); 0.092	1.16 (0.94, 1.44); 0.171	0.60 (0.41, 0.88); 0.010	0.69 (0.55, 0.86); 0.001	1.61 (1.00, 2.59); 0.051	1.32 (1.04, 1.67); 0.022	2.41 (1.92, 3.03);<0.001	0.80 (0.64, 0.99); 0.045	0.92 (0.73, 1.16); 0.487	0.78 (0.62, 0.99); 0.040	0.73 (0.59, 0.89);0.002	1.89 (1.50, 2.38);<0.001	1.01 (0.79, 1.28); 0.943	1.25 (0.96, 1.62); 0.101
Subjective material status (ref: worse than average)														
average	1.23 (1.00, 1.51); 0.050	1.01 (0.83, 1.25); 0.894	0.88 (0.60, 1.28); 0.500	1.17 (0.95, 1.43); 0.135	1.22 (0.71, 2.10); 0.470	1.09 (0.86, 1.38); 0.461	1.05 (0.85, 1.30); 0.633	1.04 (0.84, 1.30); 0.690	0.74 (0.59, 0.91); 0.005	1.07 (0.86, 1.34); 0.517	1.02 (0.84, 1.25);0.812	0.81 (0.66, 1.01); 0.059	0.89 (0.72, 1.12); 0.324	1.19 (0.91, 1.56); 0.209
better than average	1.20 (0.95, 1.52); 0.126	1.02 (0.81, 1.29); 0.853	0.82 (0.54, 1.25); 0.364	1.27 (1.01, 1.61); 0.045	1.75 (0.98, 3.12); 0.058	1.10 (0.84, 1.43); 0.499	1.22 (0.96, 1.56); 0.106	1.02 (0.80, 1.31); 0.861	0.76 (0.59, 0.97); 0.029	1.12 (0.87, 1.44); 0.369	0.98 (0.78, 1.22);0.845	0.68 (0.53, 0.87); 0.002	0.90 (0.69, 1.16); 0.402	1.12 (0.83, 1.52); 0.459
Objective material status (ref: 1st quartile)														
2nd quartile	1.24 (1.03, 1.50); 0.025	1.20 (0.99, 1.45); 0.057	1.39 (1.00, 1.91); 0.048	1.35 (1.12, 1.63); 0.002	1.21 (0.78, 1.87); 0.387	1.11 (0.89, 1.37); 0.349	0.87 (0.71, 1.06); 0.158	1.18 (0.97, 1.43); 0.103	1.08 (0.88, 1.33); 0.445	1.43 (1.17, 1.74);<0.001	1.00 (0.84, 1.20);0.967	0.73 (0.60, 0.89); 0.002	0.75 (0.62, 0.92); 0.007	0.99 (0.78, 1.26); 0.938
3rd quartile	1.28 (1.06, 1.56); 0.011	1.36 (1.12, 1.65); 0.002	1.31 (0.95, 1.81); 0.102	1.49 (1.23, 1.81);<0.001	0.74 (0.46, 1.19); 0.216	1.11 (0.89, 1.37); 0.349	0.73 (0.60, 0.89); 0.002	1.15 (0.94, 1.40); 0.187	1.14 (0.92, 1.4); 0.232	1.72 (1.41, 2.11);<0.001	0.92 (0.77, 1.10);0.367	0.65 (0.53, 0.80);<0.001	0.63 (0.51, 0.78);<0.001	1.04 (0.81, 1.32); 0.778
4th quartile	1.57 (1.27, 1.94);<0.001	1.66 (1.34, 2.05);<0.001	1.30 (0.92, 1.84); 0.140	2.27 (1.83, 2.83);<0.001	1.35 (0.86, 2.14); 0.195	1.32 (1.05, 1.67); 0.019	0.80 (0.64, 1.00); 0.050	1.04 (0.83, 1.30); 0.737	1.18 (0.94, 1.48); 0.160	2.23 (1.78, 2.79);<0.001	0.93 (0.76, 1.13);0.460	0.62 (0.50, 0.78);<0.001	0.70 (0.55, 0.88); 0.003	1.29 (1.00, 1.67); 0.054

	Fruit aOR (95% CI); *P*	**Vegetables** aOR (95% CI); *P*	**Cereals** aOR (95% CI); *P*	**Olive oil** aOR (95% CI); *P*	**Nuts** aOR (95% CI); *P*	**Dairy** aOR (95% CI); *P*	**Potatoes** aOR (95% CI); *P*	**Legumes** aOR (95% CI); *P*	**Eggs** aOR (95% CI); *P*	**Fish** aOR (95% CI); *P*	**White meat** aOR (95% CI); *P*	**Red meat** aOR (95% CI); *P*	**Sweets** aOR (95% CI); *P*	**Wine** aOR (95% CI); *P*
Chronic diseases* (ref: ≥2)														
1	0.92 (0.74, 1.14); 0.465	0.94 (0.76, 1.15); 0.529	1.50 (1.04, 2.17); 0.030	0.99 (0.79, 1.24); 0.923	1.25 (0.77, 2.05); 0.370	0.94 (0.74, 1.20); 0.622	0.94 (0.76, 1.17); 0.573	1.05 (0.84, 1.31); 0.681	1.06 (0.84, 1.35); 0.619	1.10 (0.87, 1.38); 0.436	1.00 (0.81, 1.22);0.964	0.97 (0.78, 1.21); 0.782	0.70 (0.56, 0.86); 0.001	1.21 (0.94, 1.58); 0.144
none	0.86 (0.70, 1.06); 0.156	0.91 (0.74, 1.11); 0.341	1.33 (0.94, 1.90); 0.111	0.88 (0.71, 1.09); 0.241	1.13 (0.69, 1.85); 0.614	1.13 (0.90, 1.43); 0.303	1.10 (0.89, 1.36); 0.380	1.09 (0.87, 1.35); 0.462	1.24 (0.98, 1.57); 0.073	1.06 (0.84, 1.33); 0.641	0.96 (0.79, 1.17);0.700	0.73 (0.59, 0.92); 0.006	0.53 (0.43, 0.66);<0.001	1.29 (1.00, 1.66); 0.052
Smoking status (ref: current smokers)														
ex-smokers	1.87 (1.56, 2.24);<0.001	1.04 (0.87, 1.25); 0.650	1.12 (0.82, 1.54); 0.475	1.26 (1.05, 1.51); 0.014	1.52 (0.98, 2.37); 0.062	1.02 (0.83, 1.25); 0.878	1.09 (0.89, 1.32); 0.402	1.01 (0.83, 1.22); 0.943	0.85 (0.70, 1.03); 0.096	1.29 (1.06, 1.58); 0.010	0.94 (0.79, 1.12);0.519	1.22 (0.99, 1.50); 0.060	1.05 (0.86, 1.29); 0.635	1.18 (0.94, 1.47); 0.145
never-smokers	2.03 (1.73, 2.37);<0.001	1.01 (0.86, 1.18); 0.940	1.22 (0.94, 1.60); 0.137	1.12 (0.96, 1.31); 0.154	1.58 (1.07, 2.32); 0.021	1.09 (0.92, 1.30); 0.326	0.93 (0.78, 1.10); 0.378	0.98 (0.83, 1.16); 0.826	1.02 (0.86, 1.21); 0.803	1.05 (0.89, 1.23); 0.598	0.92 (0.79, 1.07);0.293	1.22 (1.02, 1.46); 0.026	0.84 (0.70, 1.01); 0.064	1.05 (0.86, 1.29); 0.636
Physical activity (ref: light)														
moderate	1.24 (1.07, 1.45); 0.005	1.43 (1.22, 1.67);<0.001	0.83 (0.63, 1.08); 0.169	1.29 (1.11, 1.50); 0.001	1.12 (0.79, 1.57); 0.524	0.98 (0.83, 1.16); 0.840	0.88 (0.75, 1.04); 0.140	1.50 (1.26, 1.77);<0.001	1.13 (0.96, 1.34); 0.152	1.33 (1.14, 1.56);<0.001	0.94 (0.81, 1.09);0.395	0.99 (0.84, 1.16); 0.873	1.17 (0.98, 1.39); 0.085	0.93 (0.77, 1.13); 0.471
intensive	1.24 (0.97, 1.59); 0.081	1.75 (1.37, 2.23);<0.001	1.38 (0.83, 2.30); 0.220	1.48 (1.15, 1.90); 0.002	1.06 (0.58, 1.96); 0.842	0.84 (0.63, 1.12); 0.228	0.58 (0.45, 0.74);<0.001	1.61 (1.25, 2.08);<0.001	1.08 (0.83, 1.40); 0.570	1.87 (1.42, 2.48);<0.001	1.08 (0.86, 1.36);0.521	0.70 (0.52, 0.93); 0.014	1.04 (0.79, 1.38); 0.775	0.72 (0.53, 0.98); 0.036
Body mass index category (ref:18.0-24.9)														
25.0-29.9	0.99 (0.85, 1.15); 0.850	0.99 (0.85, 1.15); 0.891	0.82 (0.63, 1.07); 0.147	0.94 (0.81, 1.10); 0.465	0.92 (0.66, 1.28); 0.629	0.92 (0.78, 1.09); 0.350	1.16 (0.99, 1.36); 0.076	1.03 (0.88, 1.21); 0.717	1.00 (0.85, 1.18); 0.990	1.09 (0.93, 1.28); 0.291	1.07 (0.93, 1.24);0.339	1.04 (0.88, 1.23); 0.630	1.19 (1.00, 1.41); 0.049	0.89 (0.74, 1.07); 0.214
≥30.0	0.97 (0.80, 1.18); 0.780	0.97 (0.80, 1.18); 0.748	0.70 (0.51, 0.98); 0.037	0.85 (0.70, 1.04); 0.108	0.58 (0.36, 0.93); 0.025	0.99 (0.80, 1.23); 0.961	1.21 (0.98, 1.48); 0.070	1.17 (0.95, 1.43); 0.139	0.89 (0.72, 1.10); 0.264	0.97 (0.79, 1.19); 0.767	0.91 (0.76, 1.10);0.328	0.84 (0.67, 1.04); 0.102	1.34 (1.08, 1.66); 0.009	0.80 (0.63, 1.02); 0.071
The economic crisis of 2007-2008 (ref: before)														
after	0.50 (0.41, 0.60);<0.001	0.32 (0.27, 0.39);<0.001	0.45 (0.32, 0.63);<0.001	0.71 (0.58, 0.86); 0.001	1.04 (0.68, 1.57); 0.864	0.64 (0.52, 0.78);<0.001	0.69 (0.57, 0.83);<0.001	0.53 (0.44, 0.64);<0.001	1.10 (0.89, 1.35); 0.371	0.51 (0.42, 0.63);<0.001	0.93 (0.77, 1.11);0.397	1.39 (1.13, 1.71); 0.002	1.23 (1.01, 1.50); 0.043	0.97 (0.77, 1.22); 0.796

aOR—Adjusted odds ratios; 95% CI—95% confidence intervals; calculated using multivariate logistic regression model simultaneously adjusted for all the covariates listed in this table.
MDSS: Mediterranean Diet Serving Score.
** chronic diseases included any or more than one of the following diagnoses: hypertension, diabetes, CHD, CVI, cancer, bipolar disorder, hyperlipidemia and gout;*

The overall change in adherence to the MD of subjects included in the follow-up was insignificant, with a borderline insignificant decrease in the adherence to the MD (by 8.5%; from 36.6% of adherent subjects at study baseline to 33.5% in the follow-up; *P* =0.056) (Table 8). Furthermore, the highest overall increase in adherence was recorded for nuts (127.5%), and sweets (112.6%) (denoting reduced intake), followed by red meat (56.4%) (also denoting reduced intake), and wine (50.0%). On the other hand, the most significant decrease in adherence was recorded for vegetables (−35.1%), followed by fish (−23.4%), white meat (−11.6%), cereals (−10.9%), and dairy products (−9.6%). At the same time, the average BMI had increased by 6,5%, from 25.76 kg/m^2 at the baseline of the study to 27.44 kg/m^2 at the follow-up period (P<0.001) (Table 8).

Table 8. *Adherence to the Mediterranean Diet (14 food components and the overall adherence expressed as MDSS≥14 points) at baseline and at the follow-up (N=1,342; 366 subjects from Korčula, 494 from Split, and 482 subjects from Vis).*

	Baseline n=1,342	**Follow up** n= 1,342	**Percent change (%)**	***P***
Sex; n (%)				
men	503 (37.5)			
women	839 (62.5)			
Years of age; median (IQR)	55.00 (18.00)	62.01 (16.96)		
Body mass index (kg/m^2); median (IQR)	25.76 (5.74)	27.44 (5.06)	6.5	<0.001
MDSS ≥14 points; n (%)	491 (36.6)	449 (33.5)	−8.5	0.056
MDSS components adherence; n (%)				
fruit	868 (64.7)	848 (63.2)	−2.3	0.341
vegetables	643 (47.9)	417 (31.1)	−35.1	<0.001
cereals	1277 (95.2)	1138 (84.8)	−10.9	<0.001
potatoes	985 (73.4)	1183 (88.2)	20.2	<0.001
olive oil	893 (66.5)	927 (69.1)	3.9	0.112
nuts	68 (5.1)	156 (11.6)	127.5	<0.001
dairy products	356 (26.5)	309 (23.0)	−9.6	0.030
legumes	400 (29.8)	457 (34.1)	14.4	0.011
eggs	339 (25.3)	405 (30.2)	19.4	0.002
fish	1036 (77.2)	793 (59.1)	−23.4	<0.001
white meat	556 (41.4)	487 (36.3)	−11.6	0.005
red meat	347 (25.9)	544 (40.5)	56.4	<0.001
sweets	276 (20.6)	588 (43.8)	112.6	<0.001
wine	268 (20.0)	403 (30.0)	50.0	<0.001

MDSS: Mediterranean Diet Serving Score.

Table 9. *Characteristics associated with the absolute change in the Mediterranean Diet Serving Score and the BMI across the follow-up period, as determined by the linear regression model (sample size is 1,342 subjects; all independent variables were included in the model simultaneously).*

	MDSS change during follow-up Beta (95% CI); *P*	**BMI change during follow-up** Beta (95% CI); *P*
Sex (ref. men)		
women	0.41 (0.00, 0.83); 0.049	0.33 (0.06, 0.60); 0.016
Age at baseline (years)	0.05 (0.03, 0.06); <0.001	0.01 (−0.02, 0.00); 0.192
Follow up time (years)	0.03 (−0.09, 0.16); 0.571	0.07 (−0.15, 0.01); 0.099
Place of residence (ref: Split)		
Vis	0.28 (−0.75, 1.32); 0.590	0.86 (0.18, 1.54); 0.013
Korčula	0.00 (−0.81, 0.81); 0.992	3.68 (3.15, 4.21); <0.001
Education (ref: 0-8)		
high school (9-12)	−0.11 (−0.67, 0.46); 0.708	−0.05 (−0.42, 0.32); 0.799
higher (13+)	0.71 (0.07, 1.36); 0.031	0.06 (−0.36, 0.48); 0.769
Subjective material status (ref: worse than average)		
average	0.05 (−0.59, 0.69); 0.872	0.15 (−0.26, 0.57); 0.468
better than average	−0.01 (−0.72, 0.71); 0.982	0.11 (−0.36, 0.57); 0.655
Objective material status (ref: 1st quartile)		
2nd quartile	−0.14 (−0.71, 0.43); 0.637	0.07 (−0.30, 0.44); 0.724
3rd quartile	0.02 (0.56, 0.59); 0.955	0.06 (−0.31, 0.44); 0.733
4th quartile	−0.06 (−0.68, 0.56); 0.859	0.02 (−0.38, 0.42); 0.921
Chronic diseases* (ref: ≥2)		
1	−0.23 (−0.91, 0.44); 0.497	0.24 (−0.19, 0.68); 0.276
none	−0.02 (−0.68, 0.64); 0.946	0.26 (−0.17, 0.69); 0.240
Smoking (ref: current smokers)		
ex-smokers	−0.20 (−0.74, 0.34); 0.468	−0.07 (−0.42, 0.28); 0.707
never-smokers	0.12 (−0.38, 0.62); 0.632	0.02 (−0.31, 0.34); 0.909
Physical activity (ref: light)		
moderate	0.72 (0.27, 1.16); 0.002	−0.02 (−0.31, 0.27); 0.887
intensive	0.69 (−0.02, 1.40); 0.057	0.23 (0.24, 0.70); 0.331
BMI at baseline (kg/m^2)	−0.03 (−0.09, 0.02); 0.188	−0.11 (−0.14, −0.07); <0.001
MDSS at baseline	−0.64 (−0.70, −0.58); <0.001	−0.07 (−0.12, −0.03); 0.001
MDSS change during follow-up		−0.04 (−0.07, 0.00); 0.041

**chronic diseases included any or more than one of the following diagnoses: hypertension, diabetes, CHD, CVI, cancer, bipolar disorder, hyperlipidemia and gout. MDSS: Mediterranean Diet Serving Score. BMI: body mass index.*

Linear regression analysis revealed several variables significantly associated with the MDSS change during the follow-up period (Table 9). MDSS change was positively associated with female gender (β =0.41; 95% CI 0.00 – 0.83; *P* =0.049), age (β =0.05; 95% CI 0.03 – 0.06); *P* <0.001), highest level of education (β=0.71; 95% CI 0.07 – 1.36; *P* =0.031), and with moderate physical activity (β =0.72; 95% CI 0.27 – 1.16; *P* =0.002). MDSS at baseline displayed a negative association with the MDSS change (β =−0.64; 95% CI −0.70 – −0.58; *P*

<0.001), while BMI at baseline, smoking, chronic diseases, place of residence, objective and subjective material status were not associated with the absolute change in the MDSS (Table 9). The regression model yielded good data fit (Durbin Watson = 1.994; Adjusted R^2 = 0.280).

BMI change during the follow-up period was significantly associated with female gender, place of residence, BMI at baseline, MDSS at baseline and MDSS absolute change (Table 4). Women demonstrated positive association with BMI change compared to men (β =0.33; 95% CI 0.06 – 0.60; *P* =0.016), as well as the subjects from the Island of Vis and Korčula compared to subjects from the City of Split (β =0.86; 95% CI 0.18 – 1.54; *P* =0.013, and β =3.68; 95% CI 3.15 – 4.21; *P* <0.001, respectively). BMI at baseline, MDSS at baseline, and MDSS change during the follow-up were all significantly negatively associated with the BMI change (β=−0.11; 95% CI −0.14 – −0.07; *P* <0.001, β=−0.07; 95% CI −0.12 – −0.03; *P* =0.001, β=−0.04; 95% CI −0.07 – 0.00; *P* =0.041, respectively), while none of the socioeconomic characteristics were associated with absolute BMI change (Table 9). The regression model yielded good data fit (Durbin Watson =1.972; Adjusted R^2 =0.354).

2.3.3 Paper "Nut Consumption and Cardiovascular Risk Factors: A Cross-Sectional Study in a Mediterranean Population."

After excluding participants due to missing values for at least one of the important characteristics needed in the analysis (anthropometric measurements, biochemistry, medical history, or nut consumption), a total of N= 4,416 subjects were included in the analysis. Therefore, the analysis included subjects from three Dalmatian settlements: the Island of Vis (n= 992), the Island of Korčula (n= 2,435), and the City of Split (n= 989) (Table 10).

Additionally, 405 subjects reported a previous diagnosis of either coronary heart disease or cerebrovascular insult and were excluded from all the multivariate analyses of the association of nut consumption with different cardiovascular risk factors, to test the hypothesis only in subjects at risk of cardiovascular disease.

Daily nut consumption was reported in only 212 subjects (4.8%): 7.1% of subjects from Split, 4.7% in subjects from Korčula, while only 2.7% of subjects from the Island of Vis consumed nuts daily. Overall, adherence to the Mediterranean diet was reported in 1,274 subjects (28.8%), ranging from 27.4% for subjects from the Island of Korčula to 30.8% for the participants from the Island of Vis (Table 10).

Overweight, obesity and some chronic diseases were highly prevalent, with as many as 405 subjects (9.2%) who reported having CVD in their medical history, and some of them reported having both CHD and CVI (Table 10).

A high prevalence of metabolic syndrome was observed (as high as 60.9% in Vis), followed by hypertension (ranging from 23.9% in Split to 30.8% in Korčula), while obesity was also most common in Vis (26.2%) (Table 10).

Table 10. *Demographic characteristics, the prevalence of chronic diseases, lifestyle characteristics, compliance to the Mediterranean diet (MDSS ≥ 14), and nut consumption frequency according to the place of residence in a total sample of N=4,416 subjects.*

	Place of residence			
	Island of Vis *n* = 992	**Island of Korčula** *n* = 2,435	**City of Split** *n* = 989	**P-values**
Sex; *n* (%)				
men	414 (41.7)	907 (37.2)	382 (38.6)	0.050 (0.014[VK], 0.158[VS], 0.451[KS])
women	578 (58.3)	1528 (62.8)	607 (61.4)	
Age years; median (IQR)	56.0 (23.0)	55.0 (23.0)	52.0 (21.0)	<0.001 (<0.001[VK],<0.001[VS],<0.001[KS])
Education (years of schooling); median (IQR)	11.0 (4.0)	12.0 (3.0)	12.0 (4.0)	<0.001 (<0.001[VK],<0.001[VS],<0.001[KS])
Material status; median (IQR)	10.0 (5.0)	10.0 (3.0)	12.0 (3.0)	<0.001 (<0.001[VK],<0.001[VS],<0.001[KS])
BMI (kg/m^2); *n* (%)				
<25.0	301 (30.3)	1287 (52.9)	345 (34.9)	<0.001(<0.001[VK], 0.027[VS],<0.001[KS])
25.0–29.9	431 (43.4)	830 (34.1)	429 (43.4)	
≥30.0	260 (26.2)	318 (13.1)	215 (21.7)	
CVD; *n* (%)	139 (14.0)	214 (8.79)	52 (5.3)	<0.001 (<0.001[VK],<0.001[VS],<0.001[KS])
CHD; *n* (%)	117 (11.8)	184 (7.6)	40 (4.0)	<0.001 (<0.001[VK],<0.001[VS],<0.001[KS])
CVI; *n* (%)	30 (3.0)	50 (2.1)	15 (1.5)	0.061 (0.088[VK], 0.024[VS], 0.297[KS])
Diabetes; *n* (%)	65 (6.6)	174 (7.1)	42 (4.2)	0.007 (0.536 [VK], 0.023 [VS], 0.002 [KS])
Hypertension; *n* (%)	294 (29.6)	750 (30.8)	236 (23.9)	<0.001 (0.502[VK], 0.004[VS], <0.001[KS])
Metabolic syndrome; *n* (%)	604 (60.9)	1048 (45.3)	353 (35.7)	<0.001 (<0.001[VK],<0.001[VS],<0.001[KS])
Gout; *n* (%)	63 (6.4)	157 (6.5)	28 (2.8)	<0.001 (0.912[VK], <0.001[VS], <0.001[KS])
Smoking; *n* (%)				
current smoker	283 (28.5)	662 (27.2)	262 (26.5)	<0.001 (<0.001[VK], 0.072[VS], 0.015[KS])
ex-smoker	300 (30.2)	551 (22.6)	269 (27.2)	
never-smoker	409 (41.2)	1222 (50.2)	458 (46.3)	
Alcohol intake; *n* (%)				
excessive	150 (15.1)	484 (19.9)	130 (13.1)	<0.001 (<0.001[VK],0.255[VS],<0.001[KS])
moderate	435 (43.9)	1137 (46.7)	466 (47.1)	
none	407 (41.0)	814 (33.4)	393 (39.7)	
Physical activity; *n* (%)				<0.001 (<0.001[VK],<0.001[VS],<0.001[KS])
light	257 (25.9)	481 (19.8)	351 (35.5)	
moderate	574 (57.9)	1698 (69.7)	603 (61.0)	
intensive	161 (16.2)	256 (10.5)	35 (3.5)	
MDSS ≥ 14 points; *n* (%)	306 (30.8)	668 (27.4)	300 (30.3)	0.068 (0.045[VK], 0.804[VS], 0.088[KS])
Nut consumption; *n* (%)				
infrequently or never	785 (79.1)	1162 (47.7)	494 (49.9)	<0.001 (<0.001[VK],<0.001[VS],<0.001[KS])
monthly	132 (13.3)	880 (36.1)	264 (26.7)	
weekly	48 (4.8)	278 (11.4)	161 (16.3)	
daily	27 (2.7)	115 (4.7)	70 (7.1)	

BMI: body mass index. CVD: cardiovascular disease. CHD: coronary heart disease. CVI: cerebrovascular insult. MDSS: Mediterranean Diet Serving Score.
[VK] Pairwise comparison P-value: Vis vs. Korčula.
[VS] Pairwise comparison P-value: Vis vs. Split.
[KS] Pairwise comparison P-value: Korčula vs. Split.

Among investigated biochemical parameters, nut consumption was associated with HDL cholesterol, fibrinogen, total cholesterol, and LDL cholesterol, while adherence to the Mediterranean diet was associated only with fibrinogen levels (Table 11).

Subjects who consumed nuts monthly had lower odds for a decreased level of HDL cholesterol compared to non-consumers (OR =0.75, 95% CI 0.62–0.92; *P* =0.005), while subjects who consumed nuts weekly and daily also had the same result, but the difference did not reach statistical significance in pairwise comparisons, even though the overall P-value indicated a significant result (*P* =0.026, Table 11).

On the other hand, only subjects who consumed nuts weekly had increased odds for the concomitant presence of increased total cholesterol and LDL cholesterol, but without overall significance (OR =1.35, 95% CI 1.02–1.79; *P* =0.037 and OR = 1.46, 95% CI 1.11–1.94; *P* =0.008, respectively; Table 11).

Subjects who consumed nuts had lower odds of having an elevated fibrinogen level (OR =0.66, 95% CI 0.56–0.79; *P* <0.001 in monthly consumers, OR =0.65, 95% CI 0.52–0.83; *P*<0.001 in weekly consumers), while for daily consumers the result was just above the significance threshold limit, Table 11).

Interestingly, only one significant result for the association between biochemical parameters with the adherence to the Mediterranean diet was obtained: participants who did not adhere to the Mediterranean diet had lower odds for the elevated fibrinogen (OR= 0.78, 95% CI 0.66–0.91; *P* =0.002; Table 11).

There was no significant association between nut intake and adherence to the Mediterranean diet with triglycerides, so the corresponding regression data are not presented here.

Table 11. *Characteristics associated with cholesterol, LDL, HDL, and fibrinogen as determined by the multivariate logistic regression analyses (sample size is 4,011 subjects without previous cardiovascular disease CVD diagnosis; all independent variables included in the model are listed in the table).*

	Cholesterol (≥5 mmol/L) aOR (95% CI); *P*	**LDL (≥3 mmol/L)** aOR (95% CI); *P*	**HDL (≤1.03 mmol/L♂, ≤1.29 mmol/L♀)** aOR (95% CI); *P*	**Fibrinogen (ref: ≥4.0 g/L)** aOR (95% CI); *P*
Sex (ref: women)				
men	0.86 (0.71–1.04); 0.128	0.92 (0.76–1.11); 0.364	0.78 (0.63–0.96); 0.020	0.75 (0.63–0.89); 0.001
Age (years, ref: 18.0–34.9)				
35.0–64.9	4.56 (3.67–5.66); <0.001	3.67 (2.96–4.55); <0.001	0.54 (0.42–0.70); <0.001	1.46 (1.16–1.84); 0.001
≥65.0	4.88 (3.59–6.64); <0.001	4.40 (3.26–5.94); <0.001	0.45 (0.32–0.63); <0.001	1.86 (1.39–2.48); <0.001
Place of residence (ref: Split)				
Vis	0.97 (0.75–1.26); 0.837	0.71 (0.55–0.91); 0.007	0.10 (0.07–0.14); <0.001	0.51 (0.41–0.63); <0.001
Korčula	0.91 (0.74–1.12); 0.369	0.89 (0.72–1.09); 0.265	0.44 (0.36–0.54); <0.001	0.31 (0.26–0.37); <0.001
Education (years of schooling, ref: ≥13)				
0–8	1.00 (0.76–1.32); 0.995	0.89 (0.68–1.16); 0.395	1.00 (0.74–1.34); 0.989	1.25 (0.98–1.58); 0.069
9–12	1.09 (0.89–1.33); 0.388	1.12 (0.92–1.36); 0.259	1.08 (0.87–1.33); 0.482	1.25 (1.05–1.50); 0.014
Material status (ref: 4th quartile)				
1st quartile	1.17 (0.90–1.52); 0.244	1.07 (0.83–1.37); 0.625	0.85 (0.64–1.12); 0.246	0.80 (0.64–1.00); 0.054
2nd quartile	0.98 (0.77–1.24); 0.842	0.98 (0.77–1.23); 0.843	1.02 (0.80–1.31); 0.873	0.73 (0.60–0.90); 0.003
3rd quartile	1.06 (0.84–1.33); 0.649	1.08 (0.86–1.36); 0.506	1.29 (1.02–1.63); 0.034	0.80 (0.65–0.97); 0.025
Smoking (ref: never-smoker)				
current- smoker	1.13 (0.93–1.38); 0.215	1.15 (0.95–1.40); 0.158	1.63 (1.32–2.00); <0.001	1.11 (0.93–1.32); 0.244
ex-smoker	1.15 (0.93–1.43); 0.203	1.07 (0.87–1.32); 0.505	1.07 (0.85–1.34); 0.562	1.03 (0.86–1.23); 0.746
Alcohol intake (ref: none)				
excessive	1.38 (1.05–1.82); 0.022	1.05 (0.81–1.37); 0.703	0.49 (0.37–0.65); <0.001	0.58 (0.46–0.74); <0.001
moderate	1.10 (0.91–1.32); 0.344	0.98 (0.82–1.18); 0.832	0.63 (0.52–0.76); <0.001	0.82 (0.70–0.96); 0.015
MDSS ≥14 points (ref: yes)				
no	0.94 (0.77–1.15); 0.543	1.01 (0.84–1.23); 0.881	1.18 (0.96–1.45); 0.112	0.78 (0.66–0.91); 0.002

	Cholesterol (≥5 mmol/L) aOR (95% CI); *P*	**LDL (≥3 mmol/L)** aOR (95% CI); *P*	**HDL (≤1.03 mmol/L♂, ≤1.29 mmol/L♀)** aOR (95% CI); *P*	**Fibrinogen (ref: ≥4.0 g/L)** aOR (95% CI); *P*
Nut consumption (ref: infrequently or never)				
daily	1.26 (0.83–1.92); 0.281	1.11 (0.75–1.65); 0.599	0.74 (0.48–1.13); 0.160	0.71 (0.51–1.01); 0.051
weekly	1.35 (1.02–1.79); 0.037	1.46 (1.11–1.94); 0.008	0.81 (0.62–1.07); 0.141	0.65 (0.52–0.83); <0.001
monthly	1.05 (0.86–1.27); 0.648	1.03 (0.85–1.24); 0.789	0.75 (0.62–0.92); 0.005	0.66 (0.56–0.79); <0.001
Physical activity (ref: intensive)				
light	0.89 (0.65–1.23); 0.487	1.01 (0.75–1.36); 0.954	1.02 (0.73–1.42); 0.914	1.05 (0.80–1.37); 0.713
moderate	0.94 (0.71–1.25); 0.678	1.09 (0.84–1.42); 0.514	0.81 (0.60–1.10); 0.178	0.91 (0.72–1.15); 0.437
WHtR ≥0.5 (ref: yes)				
no	0.53 (0.43–0.65); <0.001	0.47 (0.38–0.57); <0.001	0.41 (0.32–0.52); <0.001	0.74 (0.61–0.90); 0.002
Hypertension* (ref: yes)				
no	0.90 (0.72–1.11); 0.304	0.91 (0.74–1.11); 0.357	0.80 (0.66–0.99); 0.036	0.89 (0.75–1.05); 0.161
Diabetes[#] (ref: yes)				
no	1.48 (1.11–1.98); 0.007	1.54 (1.17–2.03); 0.002	0.56 (0.42–0.74); <0.001	0.86 (0.67–1.10); 0.221
Gout[$] (ref: yes)				
no	0.80 (0.63–1.03); 0.083	1.04 (0.83–1.30); 0.740	0.63 (0.50–0.80); <0.001	1.01 (0.83–1.23); 0.895

*MDSS—Mediterranean Diet Serving Score. WHtR—waist-to-height ratio. ♂: males. ♀: woman. *: systolic ≥ 140 mmHg or diastolic ≥ 90 mmHg or treated for hypertension. #: ≥7 mmol/L or treated for diabetes type 2. $: uric acid ≥404 µmol/L ♂, ≥338 µmol/L ♀ or gout.*
Multivariate logistic regression models were built separately for cholesterol, LDL, and HDL. A multivariate ordinal regression model was used for the analysis of the characteristics associated with elevated fibrinogen.
Adjusted odds ratios (aOR), 95% confidence intervals (CI), and P-values were calculated using multivariate regression models; each of the seven models presented here was simultaneously adjusted for all covariates listed in this table.

Nut consumption frequency was associated with an elevated waist-to-height ratio (WHtR, overall *P* =0.036) and waist-to-hip ratio (WHR, overall *P* =0.033), while no association was recorded for BMI in subjects without a previous CVD diagnosis (Table 12).

Subjects who reported weekly nut consumption had lower odds for elevated WHtR, compared to those who never consumed nuts (OR =0.72, 95% CI 0.54–0.96; *P* =0.026), similarly for subjects who consumed nuts monthly (OR =0.78, 95% CI 0.63–0.97; *P* =0.022), whereas the daily nut consumers exhibited no difference compared to the non-consumers (OR = 0.70; 95% CI 0.45–1.08; *P* =0.104; Table 12).

A similar finding was for elevated WHR, where subjects who consumed nuts weekly and monthly had 23% lower odds for being centrally obese (OR =0.77, 95% CI 0.60–0.99; *P* =0.045 and OR =0.77, 95% CI 0.64–0.93; *P* =0.007, respectively), while daily consumers had a non-significant result (OR =0.87; 95% CI 0.60–1.28; *P* =0.485; Table 12).

When clinical outcomes (diabetes, elevated HbA_1c, metabolic syndrome) were investigated for the association between nut intake and presence of chronic diseases, a significant result was recorded only for monthly consumers who had 20% lower odds for having metabolic syndrome compared to the never-consumers (OR =0.80, 95% CI 0.66–0.96; *P* =0.016; Table 12).

Interestingly, participants who did not adhere to the Mediterranean diet had higher odds for obesity (OR =1.23, 95% CI 1.06–1.42: *P* =0.007), and lower odds for the concomitant presence of both diabetes and elevated HbA1c (OR =0.66, 95% CI 0.51–0.86; *P* =0.002; OR =0.57, 95% CI 0.43–0.75; *P* <0.001, respectively; Table 12), which indicates that subjects with diabetes had better adherence to this preventative nutritional pattern.

There was no significant association between nut intake nor the adherence to the Mediterranean diet with waist circumference, hypertension, and gout, so the corresponding regression data are not presented here.

Table 12. *Characteristics associated with Waist-to-Height Ratio, Waist-to-Hip Ratio, Body Mass Index, diabetes, elevated Hb1c, and metabolic syndrome as determined by the multivariate logistic regression analyses (sample size is 4,011 subjects without previous cardiovascular disease CVD diagnosis; all independent variables included in the model are listed in the table).*

	Waist-to-Height Ratio (≥0.5) aOR (95% CI); *P*	**Waist-to-Hip Ratio (≥0.90 ♂, ≥0.85 ♀)** aOR (95% CI); *P*	**Body Mass Index (Referent ≥ 30)** aOR (95% CI); *P*	**Diabetes (≥7 mmol/L or Treated for Diabetes Type 2)** aOR (95% CI); *P*	**Elevated HbA1c (≥6.5 mmol/L or Treated for Diabetes Type 2)** aOR (95% CI); *P*	**Metabolic Syndrome** aOR (95% CI); *P*
Sex (ref: women)						
men	1.97 (1.57–2.46); <0.001	2.55 (2.08–3.12); <0.001	2.34 (2.01–2.73); <0.001	2.32 (1.74–3.09); <0.001	1.77 (1.29–2.42); <0.001	0.71 (0.59–0.86); <0.001
Age (years, ref: 18.0–34.9)						
35.0–64.9	3.64 (2.91–4.55); <0.001	4.12 (3.28–5.17); <0.001	2.06 (1.68–2.54); <0.001	2.71 (1.28–5.73); 0.009	2.46 (1.04–5.79); 0.040	2.24 (1.66–3.02); <0.001
≥65.0	7.95(5.34–11.85);<0.001	6.70 (4.84–9.29); <0.001	1.55 (1.20–2.00); 0.001	3.69 (1.69–8.03); 0.001	3.43 (1.42–8.31); 0.006	3.16 (2.24–4.47); <0.001
Place of residence (ref: Split)						
Vis	0.87 (0.65–1.15); 0.326	1.18 (0.92–1.53); 0.195	0.80 (0.66–0.98); 0.029	0.97 (0.65–1.44); 0.876	0.96 (0.61–1.50); 0.844	2.19 (1.71–2.80); <0.001
Korčula	1.41 (1.14–1.76); 0.002	1.35 (1.11–1.64); 0.003	0.38 (0.32–0.45); <0.001	1.25 (0.88–1.77); 0.206	1.64 (1.11–2.43); 0.013	1.09 (0.89–1.34); 0.392
Education (years of schooling, ref: ≥13)						
0–8	2.36 (1.67–3.34); <0.001	2.42 (1.81–3.24); <0.001	1.23 (1.00–1.52); 0.055	1.52 (1.03–2.24); 0.035	1.51 (0.99–2.3); 0.056	1.44 (1.11–1.86); 0.006
9–12	1.30 (1.06–1.60); 0.013	1.21 (1.00–1.46); 0.054	1.16 (0.99–1.36); 0.068	1.17 (0.84–1.65); 0.352	1.11 (0.76–1.61); 0.599	0.98 (0.81–1.20); 0.866
Material status (ref: 4th quartile)						
1st quartile	0.65 (0.49–0.87); 0.003	0.99 (0.76–1.27); 0.908	0.86 (0.70–1.06); 0.154	1.31 (0.88–1.94); 0.178	1.67 (1.07–2.60); 0.025	0.96 (0.75–1.24); 0.770
2nd quartile	0.94 (0.72–1.22); 0.639	1.17 (0.92–1.47); 0.200	0.88 (0.73–1.07); 0.197	1.37 (0.94–2.00); 0.100	1.63 (1.06–2.52); 0.027	0.94 (0.74–1.18); 0.573
3rd quartile	0.84 (0.65–1.07); 0.157	1.09 (0.87–1.36); 0.444	0.94 (0.78–1.13); 0.498	1.33 (0.91–1.92); 0.137	1.75 (1.15–2.68); 0.010	0.97 (0.78–1.21); 0.780
Smoking (ref: never-smoker)						
current-smoker	0.81 (0.66–1.00); 0.046	1.04 (0.86–1.26); 0.657	0.81 (0.69–0.95); 0.011	0.88 (0.63–1.21); 0.418	0.86 (0.60–1.22); 0.398	1.04 (0.86–1.27); 0.664
ex-smoker	1.36 (1.06–1.74); 0.015	1.22 (0.99–1.51); 0.064	1.13 (0.97–1.33); 0.127	0.93 (0.70–1.25); 0.647	0.97 (0.70–1.33); 0.832	1.03 (0.85–1.26); 0.747
Alcohol intake (ref: none)						
excessive	0.93 (0.68–1.27); 0.663	1.46 (1.10–1.93); 0.008	0.83 (0.68–1.02); 0.083	0.81 (0.56–1.18); 0.274	0.69 (0.46–1.04); 0.076	1.14 (0.88–1.47); 0.312
moderate	0.88 (0.72–1.08); 0.212	1.14 (0.95–1.37); 0.147	0.72 (0.62–0.84); <0.001	0.71 (0.54–0.94); 0.019	0.60 (0.44–0.82); 0.001	0.88 (0.73–1.06); 0.170

	Waist-to-Height Ratio (≥0.5) aOR (95% CI); *P*	**Waist-to-Hip Ratio (≥0.90 ♂, ≥0.85 ♀)** aOR (95% CI); *P*	**Body Mass Index (Referent ≥ 30)** aOR (95% CI); *P*	**Diabetes (≥7 mmol/L or Treated for Diabetes Type 2)** aOR (95% CI); *P*	**Elevated HbA₁c (≥6.5 mmol/L or Treated for Diabetes Type 2)** aOR (95% CI); *P*	**Metabolic Syndrome** aOR (95% CI); *P*
MDSS ≥14 points (ref: yes)						
no	0.94 (0.75–1.16); 0.547	1.18 (0.97–1.42); 0.090	1.23 (1.06–1.42); 0.007	0.66 (0.51–0.86); 0.002	0.57 (0.43–0.75); <0.001	0.99 (0.83–1.19); 0.932
Nut consumption (ref: infrequently or never)						
daily	0.70 (0.45–1.08); 0.104	0.87 (0.60–1.28); 0.485	0.85 (0.62–1.16); 0.315	0.58 (0.31–1.08); 0.088	0.67 (0.35–1.26); 0.210	0.83 (0.57–1.21); 0.338
weekly	0.72 (0.54–0.96); 0.026	0.77 (0.60–0.99); 0.045	0.92 (0.75–1.14); 0.470	0.77 (0.50–1.18); 0.233	0.85 (0.54–1.34); 0.475	0.88 (0.68–1.14); 0.339
monthly	0.78 (0.63–0.97); 0.022	0.77 (0.64–0.93); 0.007	1.02 (0.88–1.19); 0.774	0.84 (0.63–1.12); 0.247	0.80 (0.58–1.09); 0.155	0.80 (0.66–0.96); 0.016
Physical activity (ref: intensive)						
light	1.07 (0.74–1.55); 0.702	1.03 (0.74–1.42); 0.875	1.17 (0.92–1.49); 0.197	1.66 (1.08–2.55); 0.021	2.15 (1.31–3.52); 0.002	0.98 (0.73–1.32); 0.909
moderate	1.12 (0.81–1.55); 0.505	1.02 (0.77–1.37); 0.872	1.01 (0.82–1.25); 0.891	1.34 (0.91–1.97); 0.135	1.64 (1.04–2.57); 0.032	0.80 (0.62–1.04); 0.093
WHtR ≥0.5 (ref: yes)						
no	/	/	/	1.00 (0.6–1.66); 0.986	0.57 (0.30–1.08); 0.083	0.14 (0.10–0.18); <0.001
Hypertension* (ref: yes)						
no	0.56 (0.42–0.74); <0.001	0.68 (0.54–0.84); <0.001	0.66 (0.57–0.77); <0.001	0.56 (0.43–0.72); <0.001	0.58 (0.44–0.77); <0.001	0.33 (0.28–0.40); <0.001
Diabetes# (ref: yes)						
no	0.94 (0.56–1.58); 0.815	0.52 (0.34–0.80); 0.003	0.76 (0.61–0.94); 0.013	/	/	0.19 (0.14–0.27); <0.001
Metabolic syndrome (ref: yes)						
no	0.14 (0.11–0.18); <0.001	0.35 (0.29–0.42); <0.001	0.35 (0.30–0.40); <0.001	0.18 (0.13–0.26); <0.001	0.25 (0.18–0.36); <0.001	/
Gout$ (ref: yes)						
no	0.38 (0.26–0.55); <0.001	0.45 (0.34–0.60); <0.001	0.59 (0.50–0.71); <0.001	0.90 (0.69–1.18); 0.453	0.86 (0.64–1.15); 0.306	0.61 (0.49–0.75); <0.001

*MDSS—Mediterranean Diet Serving Score. WHtR—waist-to-height ratio. ♂: males. ♀: woman. *: systolic ≥ 140 mmHg or diastolic ≥ 90 mmHg or treated for hypertension. #: ≥7 mmol/L or treated for diabetes type 2. $: uric acid ≥404 µmol/L ♂, ≥338 µmol/L ♀ or gout.*
Multivariate logistic regression models were built separately for waist-to-height ratio, waist-to-hip ratio, diabetes, elevated HbA_{1c}, and metabolic syndrome. Multivariate ordinal regression model was used for the analysis of the characteristics associated with Body Mass Index (BMI).
Adjusted odds ratios (aOR), 95% confidence intervals (CI) and P-values were calculated using multivariate regression models; each of the seven models presented here was simultaneously adjusted for all covariates listed in this table.

2.4 DISCUSSION

The results of this study revealed a rather unsatisfactory situation in Southern Croatia in terms of Mediterranean diet consumption, with a rather low prevalence of adherence to the MD in the entire sample (28.5%), especially among younger individuals (14.0%). Subjects included in the follow-up had higher adherence to the MD at baseline (36.6%), with a borderline insignificant decline at the end of the follow-up period (33.5%). On the other hand, BMI had increased on average by 6.5% in subjects available for follow-up.

Mediterranean diet

The MD prevalence was within the expected range compared to the results from other Mediterranean countries and Croatia. For example, findings from the literature vary anywhere between 14% of adherent people in Northern Italy (88) to 45% in the Balearic Islands (89). Earlier studies from Croatian islands also revealed a worrisome pattern of dietary habits, with a predominant change towards higher consumption of meat, pasta, and cakes (90). The study of the population from the coastal region of the Adriatic Sea yielded even more devastating results; only 2.4% of the general population in urban areas and 3.4% in rural areas practised MD defined as “daily intake of fruits and vegetables, brown bread and whole grains, using olive oil as the main source of fat, consumption of fish and moderate wine drinking with meals” (91). Methodological differences and particularly the definition of the Mediterranean diet adherence between these studies and this study prevent further in-depth comparisons (19), but the majority of the studies do report a rather low percentage of people whose dietary pattern resembles the Mediterranean diet, especially in youngest generations (52, 92-94).

Better compliance with the overall Mediterranean diet and the majority of the MDSS components was recorded among the oldest group of subjects, especially women, which is in line with many previous studies (21, 95, 96). The worst result for a particular component was recorded for nuts consumption, where as little as 3% of people from Island Vis reported eating nuts every day, and the situation was not much better in the subjects from the Island of Korčula (4%) and Split (7%). This is particularly misfortunate because a recent field trial showed that daily consumption of mixed nuts (30 grams/day) reduced the incidence of major cardiovascular events by 28% in people at high cardiovascular risk, but with no cardiovascular disease and after a median follow-up of 4.8 years (97), while an observational study showed a 47% reduction in all-cause mortality and 36% reduction in cancer deaths in people who ate nuts ≥8 times/month, compared to those who never ate nuts during a median follow-up of 4.3 years (98).

Furthermore, these results are mainly in line with previous studies, which showed that female gender and non-smokers (99-101), older adults (99, 102, 103), and more physically active people displayed higher adherence to the MD pattern, while higher body mass index was generally associated with lower adherence to MD (100-102, 104). These results partially replicated such associations, as subjects with higher levels of physical activity had up to 50% greater probability to be adherent to the MD in comparison to the ones with light activity, while BMI was not significantly associated with adherence to the MD in overall sample. This is in contrast to some previous findings (105-107), but in line with some of the studies (108, 109). These differences between previous results are probably due to the employed study design (cross-sectional vs longitudinal, observational vs experimental design), and characteristics of included subjects (primarily age and health status), leaving the association between adherence to the MD and BMI a topic for further investigation and open discussion.

Unfortunately, many Mediterranean societies are moving away from their traditional dietary pattern, while some countries in Northern Europe and around the world are adopting a Mediterranean-like dietary pattern (52). For example, previous studies have indicated a persistent moderate-to-weak adherence to the MD across several southern European countries, including Spain, Portugal, Italy, Greece, and Cyprus (110). Some variations can be expected, probably due to the applied methodological framework and different instruments used to assess MD adherence (111). For example, one study from Spain showed a poor level of adherence to the MD in the general population and specific areas of Spain (112), while another one showed moderate adherence (113).

Nevertheless, deflection from traditional MD diet and lifestyle represents a lost opportunity, not only from the perspective of achieving less-than-ideal individual and population health, but also from the perspective of environmental protection, possible degradation of sociocultural food values, and loss of positive local economic returns (114). This deflection from the traditional dietary, as well as other lifestyle factors, might as well be the driving force behind the observed high burden of overweight and hypertension (115), hyperlipidemia (116), type 2 diabetes (117) and metabolic syndrome (118) in the populations of the Mediterranean region of Croatia. Unfortunately, the final result of this detrimental situation is also observed in the concurrent mortality patterns (119).

Mediterranean diet and socioeconomic status

Previous studies have demonstrated that individual and contextual socio-economic factors are strong determinants of dietary habits and that poorer socio-economic groups are less likely to follow a healthy lifestyle (120). On the other hand, social position in terms of education, occupational class, and income level represents a good predictor of healthy eating behaviour (121, 122). In general, highly educated people have higher incomes and a healthier consumption pattern (123) and tend to follow MD recommendations (122). Higher educational status was also associated with better nutritional intakes in lower GDP countries, while lower-income countries and lower education groups had poorer diets, particularly in terms of micronutrient intake (124). That could be explained by the fact that greater adherence to the Mediterranean diet was associated with higher dietary costs, which might represent a barrier to healthy eating (63). For instance, in a study including a representative national sample of 3,534 children and young people from Spain, researchers have found that high adherence to the MD was more expensive than low adherence by 0.71 Euros per day (125).

The current economic and social European context- the increasing crisis, lack of jobs, various challenges due to the COVID-19 pandemic and consequent fall in income associated with cost inflation, could make people inclined to save money in all possible ways. In this context, the most exposed are the disadvantaged groups because they prefer buying food at low prices that are often of low quality (126). Foods of lower nutritional value and lower-quality diets generally cost less per calorie and tend to be selected by groups of lower socioeconomic status (127). On the other hand, people with low socio-economic status do not obtain the same health outcomes as those with high socio-economic status, even if both groups follow the same eating pattern (128). Concretely, high adherence to the MD was associated with cardiovascular protection in higher but not in lower socioeconomic groups from Italy, with similar results observed for both education level and household income groups (128).

In some European countries, it was demonstrated that socio-economic status could modulate adherence to the MD (107, 129). For example, in a study carried out in the adult population from the Balearic Islands, people with higher educational and socio-economic levels showed higher rates of adherence to the Mediterranean pattern (89). On the other hand, adherence to the MD in the South of Italy was found to be at low levels due to poor knowledge of MD and its' beneficial effects (130). Whereas the social status in France was important for healthy eating only through an interaction between the level of education and the area of residence (120). This study revealed a similar association between education and MD, where less educated people had a reduced likelihood of being adherent to the MD. But, when we included more subjects and added additional socio-economic indicators in the analysis (subjective and objective material status), we did not corroborate such a finding. Hence, we have identified only a significant association between the overall adherence to the MD and objective material status. Subjects reporting the highest objective material status (fourth quartile) demonstrated a 93% higher probability of adhering to MD than those belonging to the first quartile of objective material status, with similar findings for subjects within second and third quartile groups (38% and 29%, respectively). This was in line with previous results, where higher household income was positively associated with greater adherence to the MD (67, 131).

Mediterranean diet food components and socioeconomic status

Interestingly, subjects with higher educational attainment had a greater probability of appropriate adherence to dairy products, potatoes, and red meat intake recommendations, but they exhibited lesser adherence to cereals, olive oil, legumes, fish, and white meat intake recommendations. This represents a considerable departure from the traditional MD pattern. For example, Biesbroek et al. revealed that people with low education consumed more potatoes, whereas highly educated people consumed more olive oil and fish (132). Another study showed that highly educated people in Italy also consumed white meat slightly less than in the past (88), while Bonaccio et al. had a similar conclusion for the consumption of white meat, but again opposite when it comes to people with high educational status and consumption of olive oil and fish (128). Similarly, higher educational status was shown to be positively associated with fish intake (133). Other MD food components were equally consumed by all educational groups, as previously shown in another study by Bonaccio et al. (67).

As already mentioned, we failed to find any association between subjective material status and adherence to the MD, whereas objective material status presented as the most prominent socio-economic indicator for overall adherence to the MD and several food groups. For example, subjects in the higher quartiles of material status had higher adherence to fruit, vegetables, olive oil, and fish intake recommendations and lower adherence to red meat and sweets intake. Interestingly, olive oil and fish intake had an opposing contribution of educational level and material status to their adherence, such that lower education and higher material status were both associated with their greater adherence. This could be explained by the fact that older, less educated people from Dalmatia, especially from remote islands, still tend to produce their own olive oil, and they catch fish on their own, which could be behind their higher intake of these foods (statement based on personal communication with subjects included in the study).

Temporal trends of the Mediterranean diet

The effect of the economic crisis of 2007-2008 on the adherence to the MD was a topic of several previous studies. For instance, it was found that adherence to the MD was lower in subjects from Italy reporting a negative impact of the crisis on their diet (134). Additionally, the prevalence of adherence to MD among southern Italian citizens enrolled within the Moli-sani study was 31.3% during the 2005-2006 period, which dramatically fell during 2007-2010 (18.3%), most strongly affecting elderly, less affluent people, and urban areas dwellers (135). These results also revealed decreased odds for adherence to the MD and different food groups, i.e. adherence odds for vegetables, cereals, fruit, fish, legumes, dairy products, potatoes, and olive oil. On the other hand, the odds of adherence to red meat and sweets recommendations increased after the recession.

Similar findings were demonstrated in Portugal, where a significant decrease in fish, fruit and vegetables consumption was recorded from 2005/2006 to 2014 (56). A cross-sectional study from Greece showed that parents who reported that financial crisis affected their food spending also reported lower consumption of fruits, carbohydrate foods, and legumes, and increased intake of nutrient-poor/energy-dense foods, while their children reduced weekly consumption of vegetables and increased weekly consumption of nutrient-poor/energy-dense foods (136). These and other recent evidence show a possible involvement of the economic crisis, and material resources as strong determinants of the adherence to the MD in the period after the recession started (137), given that a direct positive association between the cost of the diet and adherence to the MD has been established (64). However, it is hard to distinguish the contribution of recession due to economic crisis from the impact of the steady process of westernization of traditional dietary habits, including MD. For instance, FAO noted that "the Mediterranean region is passing through a 'nutritional transition' in which problems of undernutrition coexist with overweight, obesity and food-related chronic diseases"(138). For example, an ecological study of the changes in food patterns in Europe over the last 40 years revealed that the greatest changes have occurred in Mediterranean Europe (139). For instance, an increase of 20% in total energy availability was noted, alongside with 48% increase in energy availability from lipids, and a 20% decrease from carbohydrates, with a significant fall in the energy supplied by cereals (30%) and wine (55%), while the contribution of milk and dairy products increased by 78% and 24%, respectively (139). For example, it was estimated that the Spanish diet shifted away from the traditional MD, now containing three times more meat, dairy and sugar products and a third fewer fruits, vegetables, and cereals (140).

Similar deviations were detected in the fraction of the sample available for the follow-up. For example, vegetable adherence was reduced by 35%, followed by a reduction in fish adherence by 23%, white meat by 12%, cereals by 11%, dairy products by 10%, while fruit adherence was reduced by only 2%. However, there were a few positive trends, such as an increase in adherence to nuts (128%), sweets (113%; denoting reduced intake), red meat (56%; also denoting reduced intake), and wine (50%). Overall, the adherence to the MD remained stable, probably a consequence of differences in specific MD food constituents.

As already mentioned, a continuous increase in red and processed meat has been observed over the last couple of decades, while fruit, cereals, and vegetable consumption has decreased in different countries (51, 141, 142). These findings align with these trends, except for red meat intake, for which compliance was improved. Interestingly, an improvement over time was also recorded for sweets adherence in this study, which was in contrast to the findings from Portugal, where sweets/desserts consumption was significantly higher in 2014 compared to 2005/2006 (56). However, a similar decreased trend for sweets intake was observed in Northern Italy (88), and Norway, Sweden, and Finland (143). A study conducted among adults in Lebanon showed a decrease in the consumption of bread, fruits, fresh fruit juices, milk and eggs, whereas the consumption of added fats and oils, poultry, cereals and cereal-based products, chips and salty crackers, sweetened milk and hot beverages increased over time (144). These findings indicate slightly different, yet similar patterns of change in different populations.

The important next step in any effort to improve dietary habits in the communities is identifying factors associated with such changes, to implement targeted interventions. We have conducted such an analysis, which pointed to several characteristics associated with the change in adherence to the MD over time. Female gender, age at baseline, the highest level of education, and moderate physical activity were positively associated with MDSS change during follow-up in a multivariate model. On the other hand, the MDSS score at baseline was negatively associated with the MDSS change during the follow-up, indicating that people with the higher baseline adherence to the MD tended to recede over time, while those with lower adherence strived toward increasing adherence to the MD. These findings highlight a continuous change in the dietary patterns in the population, requiring constant monitoring of the trends and identification of the drivers of such change.

Mediterranean diet and health-related outcomes

The traditional Mediterranean diet was shown beneficial in preventing weight gain and abdominal obesity (47). On the other hand, a lower educational level was often associated with a higher prevalence of overweight and obesity (67, 145), the same as economic affluence on a country level, reflecting a potential adverse outcome concomitant with economic growth (146). While the relationship between socioeconomic status and health outcomes was frequently emphasized for the Mediterranean area (145), the synergy between those two determinants was not substantially investigated in the population of Southern Croatia. These results indicate that the average BMI had increased from 25.76 kg/m^2 at baseline to 27.44 kg/m^2 during the follow-up period. This is consistent with the trend of increasing rates of obesity across 147 countries (146). BMI change during follow-up was positively associated with the female gender, and negatively with initial BMI, initial adherence to the MD, and change in adherence to the MD, as found in the regression analysis. This means that people with lower BMI at the beginning of the study tended to experience a rise in BMI, while those who started with higher values managed to diminish it over time. An encouraging finding is that individuals with higher-level/scores of MD adherence experienced lower BMI change or even a decrease.

Furthermore, the importance of nut intake as one of the key food components of the MD, as well the associations of health-related outcomes with the adherence to the MD were further investigated within the study. Nut consumption in this study was associated with reduced odds for decreased HDL cholesterol and reduced odds for increased fibrinogen, while total cholesterol and LDL cholesterol did not reach the significance level (when overall P value was observed) and triglycerides did not exhibit any association with nut intake within this study. Previous studies have also shown various results concerning the impact of nut consumption on blood lipid levels. Some have found beneficial effects, while others did not record any difference in blood lipids between nut consumers and non-consumers (41, 46, 147-149). A possible explanation for these findings is in the different definitions used for nut consumption (type, frequency, and amount of nuts consumed), different time frames of follow-up, and different confounding factors taken into account. For instance, in a Cochrane review and meta-analysis with 3 trials included, substantial heterogeneity was found between the trials for the effect of nut consumption on total cholesterol and triglyceride levels, while for HDL cholesterol and LDL cholesterol no effect of nut consumption has been identified (46).

Subjects in this study who consumed nuts weekly and monthly had lower odds of having an elevated fibrinogen level, which is considered an inflammatory marker. This is a confirmation of the previous finding of lower levels of fibrinogen (and other inflammatory markers) in people who consumed nuts and seeds more frequently (150). Regarding this, the finding of a recent study in the urban population of Catania, Italy, was particularly interesting because it demonstrated that the main dietary sources of total polyphenols were nuts (151). It is, therefore plausible that the cardiovascular disease risk reduction effect of nut intake is, at least in part, due to these compounds, which are well known to counteract the burden of oxidative stress and thus limit the effects of cellular ageing (152).

Nut intake effects on glucose and insulin levels and diabetes risk have also been previously investigated. The majority of studies have shown the beneficial impact of nut consumption. For example, a meta-analysis of 12 randomized controlled dietary trials including individuals with diabetes has shown that daily nut consumption (a median dose of 56 g/d during ≥3 weeks) lowered HbA_1c by 0.07% (95% CI:-0.10, -0.03%; P=0.0003) and fasting glucose by 0.15 mmol/L (95% CI: -0.27, -0.02 mmol/L; P=0.03), compared to the control diets (42). Another meta-analysis including 25 observational studies and 2 clinical trials found that nut consumption has been associated with a reduction in diabetes risk by 13% (based on 6 studies and 13,308 events; RR: 0.87, 95% CI 0.81-0.94) (153). Furthermore, the PREDIMED study showed that people who consumed a Mediterranean diet enriched with daily nut intake (30 g/ day; 15 g of walnuts, 7.5 g of hazelnuts, and 7.5 g of almonds) had an 18% reduction in risk for incident diabetes (hazard ratio of 0.82, 95% CI 0.61-1.10) compared to the control group which received advice on a low-fat diet (33). This cross-sectional study failed to confirm these results. On the contrary, subjects who did not comply with a Mediterranean diet had lower odds for the presence of diabetes and elevated HbA_1c (OR=0.66, 95% CI 0.51-0.86 and OR=0.57, 95% CI 0.43-0.75, respectively). Since this is a cross-sectional study, this result is easily explained by the adoption of a healthy dietary pattern in those who were diagnosed with diabetes type 2, as a tertiary prevention measure.

Interestingly, the study revealed the association between nut consumption and indices of central obesity (defined by the waist-to-height and waist-to-hip ratios), while at the same time, there was no association with direct measures, namely waist circumference or BMI. Indeed, relative measures are better for detecting cardiometabolic risk factors and adverse health outcomes (80), indirectly suggesting that nuts could be contributing to the favourable cardiovascular profile. A large population-based cohort study, with over 370,000 people, reported that those who consumed nuts >1 time/week exhibited a slightly reduced weight gain (-0.10 kg; 95% CI -0.15, -0.04) over five years of follow-up (compared to non-consumers), and a 5% lower risk of becoming overweight or obese, compared to non-consumers (38). A potential explanation for these findings could be found in the high satiety effect of nuts, such as almonds, whose consumption has been shown to have the same satiety impact as baked foods with the equivalent energy and macronutrient content (154). A similar result was obtained in another experimental study in subjects at increased risk of type 2 diabetes, where almond consumption, especially eaten as a snack, lowered serum glucose responses post-prandially and reduced hunger and desire to eat (155). Another study confirmed that the metabolizable energy value of walnuts was as much as 21% smaller than predicted, possibly explaining why nut intake should not be considered a risk factor for excessive weight gain (156), especially if consumed moderately (about 30g per day). These findings are especially important given the trends in obesity worldwide since nut consumption could be used in metabolism and appetite control.

Habitual nut intake as a preventive measure could protect against cardiovascular disease complications and death, especially in people with lower adherence to the Mediterranean diet (41, 157) and diabetes (148). We found no such association between nut intake and the presence of the diagnosis of hypertension, diabetes or gout, but we did find some indication of the association between monthly nut intake and lower odds for metabolic syndrome presence (OR=0.80, 95% CI 0.66-0.96). A recent meta-analysis of randomized controlled trials also identified a beneficial effect of tree nuts on metabolic syndrome criteria through modest decreases in triglycerides and fasting blood glucose (158).

Systematic education about the potential health benefits of nut intake, with a special emphasis on the absence of obesity risk, for both health professionals and lay population, is needed. Good quality studies and evidence-based dietary guidelines should be put forward in health education and promotion to clarify the doubts and correct erroneous assumptions about nut intake. Indeed, an international group of authors recently published the lifestyle recommendations for the prevention and management of metabolic syndrome and these have included the consumption of nuts, alongside legumes, cereals (whole grains), fruits, vegetables, fish, and low-fat dairy products (31).

Final considerations

Overall, the importance of a healthy lifestyle and dietary habits came to the forefront of attention due to the COVID-19 pandemic. For example, preliminary findings from the ecological study showed that adherence to the Mediterranean diet was negatively associated with both COVID-19 cases and related deaths in Spain and other 23 OECD countries, which authors contributed to the anti-inflammatory properties of the Mediterranean diet (159). On the other hand, an unhealthy lifestyle, associated metabolic disturbances, and concomitant chronic diseases were shown to increase the risk for adverse outcomes after SARS-CoV-2 infection (160). Therefore, the insights from these studies should be used to inform the necessary and targeted public health interventions to increase the MD uptake to ensure beneficial outcomes at the individual and the population level. This is relevant from the perspective of population health and delivery of adequate health care, as well as from the perspective of economic, social, and cultural development and preservation of cultural heritage for generations to come. In addition, adherence to the Mediterranean diet has a much more favourable environmental footprint (44), which is of utmost importance in small and fragile habitats, such as the remote islands.

2.5 SCIENTIFIC CONTRIBUTION AND LIMITATIONS OF THESIS RESEARCH

The Mediterranean diet and its constitutional components in the population of Dalmatia have been marginally investigated, where a similar analysis of the association of nut intake with many health outcomes is seldom seen in the literature. This is the first study that has examined both the characteristics associated with habitual nut consumption frequency and the association between nut intake and cardiovascular health-related risks in Croatia and beyond, adding new insights into the existing knowledge of factors associated with nut intake and its impact on human health. Furthermore, the relationship between socioeconomic status and health outcomes was frequently emphasized for the Mediterranean area, but the synergy between those two determinants was not substantially investigated in the population of Southern Croatia or other Mediterranean countries.

Limitations of this study include the use of the convenient sampling approach and possible recall bias. Other types of bias, like volunteer bias due to the convenience sampling approach, and confounding by indication, could also have affected the results and conclusions. Another important limitation of this study that needs to be mentioned here is the use of the cross-sectional design, which cannot establish a causal relationship between the cause and the effect. However, the use of the additional follow-up confirmed the initial findings and time trends.

Another limitation is the broad sampling period of subjects included in this study, which extended from 2003 to 2015. Each study site was sampled in different periods, which were never over-lapping. So this issue was mitigated by using the multivariate approach in the analysis, and the place of residence was one of the predictors included in the models. To further control for the effect of the study period in the logistic regression analysis, we included the actual follow-up time as one of the predictor variables and the variable "economic crisis of 2007-2008". We also managed to obtain a smaller than ideal sample size and lesser response rate in the follow-up study (28.7%) due to the older age of the subjects and their inability to participate in the follow-up examination.

The question on nut consumption included all nuts, not distinguishing between different types of nuts or the amount of consumed nuts, which disabled us from the further detailed characterization of specific nut consumption. A low frequency of 5% of daily nut consumers could have affected the statistical power for detecting the association between nut intake and investigated risk factors. This could explain the results obtained in the regression models, without any statistically significant result of the association between daily nut intake and the outcomes compared to non-consumers, unlike for weekly and monthly nut intake groups.

Advantages of the study include a relatively large overall sample size, inclusion of many potential predictors and confounding factors, and sampling from the general population of inhabitants from the Mediterranean region of Croatia. A comparable tool to assess MD was applied, thus providing a reliable source of information for wider-scale international comparisons and monitoring of nutritional trends and transitions.

Another good aspect of this study is the analysis of the association of nut intake and MD with many health outcomes, which is seldom seen in the literature. Still, there is much to be investigated, since there are many discrepancies in results from different studies, especially in the effect of nut intake on intermediate-risk factors like blood lipid levels and also on clinical endpoints (cardiovascular diseases, diabetes, cancer, etc.). To elucidate the actual mechanisms and unbiased effects of nut intake on various health outcomes, a larger size and well-controlled experimental study (for many confounding factors) and of longer duration are needed. Nevertheless, there is a sufficient amount of evidence pointing to various health benefits of habitual nut intake, which should be included in the recommendations for prevention and management of overweight and obesity, as well as common cardiovascular risk factors.

Overall, determinants, trends, and health outcomes associated with the Mediterranean diet were so far only marginally investigated in the population of Dalmatia in Croatia, and we are filling this gap.

2.6 SUMMARY

One of the foremost public health challenges today and on the global level are non-communicable disease, arising mostly due to an unhealthy lifestyle. Especially high burden represents an unhealthy diet. The Mediterranean diet is one of the most commonly investigated nutritional pattern with a large body of evidence showing that adherence to it can sustain and preserve human health, with numerous health benefits already being recorded. The most prominent characteristics of the MD are the use of olive oil as the primary fat source, an abundance of vegetables, fruits, nuts, and whole grains daily, moderate red wine and legumes consumption, while animal products are more of a relish, and the priority is given to fish and white meat over red and processed meat.

The research aims of this thesis are to assess the compliance with the Mediterranean dietary pattern and its constituting components, to estimate the temporal trend in adherence to the Mediterranean diet and the contribution of several socio-economic factors in the changing pattern of both the Mediterranean diet and body mass index in a follow-up study, and to investigate the association between nut consumption and various cardiovascular risk factors in the population of Dalmatia in Southern Croatia.

The results of this study revealed a rather unsatisfactory situation in Southern Croatia in terms of Mediterranean diet consumption. A wide range of adherence to MDSS components was present (from as low as 4.6% for nuts, and up to 91.7% adherence for cereals), with a rather low prevalence of adherence to the Mediterranean diet in the entire sample (28.5%), especially among younger individuals (14.0%). Better compliance with the overall Mediterranean diet, as well as for the majority of the MDSS components was recorded among the oldest group of subjects, especially women. We failed to find any association between subjective material status and adherence to the Mediterranean diet, whereas objective material status presented as the most prominent socio-economic indicator for the overall adherence to the Mediterranean diet, but also several food groups.

Subjects included in the follow-up had higher adherence to the Mediterranean diet at baseline (36.6%), with a borderline insignificant decline at the end of the follow-up period (33.5%). The multivariate model revealed that female gender, older age at baseline, the highest level of education, and a moderate level of physical activity were positively associated, while the MDSS at baseline was negatively associated with the MDSS change during the follow-up. On the other hand, BMI had increased on average by 6.5% in subjects available for follow-up. BMI change during follow-up was positively associated with the female gender, and negatively with initial BMI, initial adherence to the MD, and change in adherence to the MD, as found in the regression analysis.

Nut consumption in this study was associated with reduced odds for decreased HDL cholesterol and reduced odds for increased fibrinogen, while total cholesterol and LDL cholesterol did not reach the significance level (when overall P value was observed) and triglycerides did not exhibit any association with nut intake within this study. The study also revealed the association between nut consumption and indices of central obesity (defined by the waist-to-height and waist-to-hip ratios), while at the same time there was no association with direct measures, namely waist circumference or BMI. We found no such association between nut intake and the presence of the diagnosis of hypertension, diabetes or gout, but we did find some indication of the association between monthly nut intake and lower odds for metabolic syndrome presence. Interestingly, we found that subjects who did not comply with a Mediterranean diet had lower odds for the presence of diabetes and elevated HbA_1c, but higher odds for obesity.

Overall, the importance of a healthy lifestyle and healthy dietary habits came to the frontline of attention due to the COVID-19 pandemic. The insights from these studies should be used to inform the necessary and targeted public health interventions aimed at increasing the MD uptake to ensure beneficial outcomes at the individual and the population level. This is relevant from the perspective of population health and delivery of adequate health care, as well as from the perspective of economic, social, and cultural development, and preservation of cultural heritage for generations to come.

2.7 SUMMARY IN CROATIAN (SAŽETAK)

Jedan od najvećih javnozdravstvenih izazova danas na globalnoj razini su nezarazne bolesti, koje uglavnom nastaju zbog nezdravog načina života. Posebno veliko opterećenje predstavlja nezdrava prehrana. Mediteranska prehrana jedan je od najčešće istraživanih prehrambenih obrazaca s velikim brojem dokaza koji pokazuju da njezino pridržavanje može održati i očuvati ljudsko zdravlje, uz brojne zabilježene zdravstvene prednosti. Najistaknutije karakteristike mediteranske prehrane su korištenje maslinovog ulja kao primarnog izvora masti, svakodnevno obilje povrća, voća, orašastih plodova i cjelovitih žitarica, umjerena konzumacija crnog vina i mahunarki, dok su životinjski proizvodi više užitak a u odnosu na crveno i prerađeno meso prednost ima riba i bijelo meso.

Ciljevi istraživanja ovog doktorskog rada su procijeniti usklađenost s mediteranskim načinom prehrane i njegovim sastavnim komponentama, procijeniti vremenski trend pridržavanja mediteranske prehrane i doprinos nekoliko socio-ekonomskih čimbenika u promjeni obrasca mediteranske prehrane i indeksa tjelesne mase u ponovljenoj studiji, kao i istražiti povezanost između konzumacije orašastih plodova i različitih kardiovaskularnih čimbenika rizika u populaciji Dalmacije u južnoj Hrvatskoj.

Rezultati ovog istraživanja pokazali su prilično nezadovoljavajuću situaciju u južnoj Hrvatskoj u pogledu pridržavanja mediteranskoj prehrani. Prisutan je širok raspon pridržavanja pojedinim komponentama MDSS-a (od čak 4,6% za orašaste plodove, do 91,7% pridržavanja za žitarice), s prilično niskom prevalencijom pridržavanja mediteranskoj prehrani u cijelom uzorku (28,5%), osobito među mlađim osobama (14,0%). Bolja usklađenost s cjelokupnom mediteranskom prehranom, kao i za većinu komponenti MDSS-a zabilježena je kod najstarije skupine ispitanika, posebice žena. Nismo uspjeli pronaći povezanost između subjektivnog materijalnog statusa i pridržavanja mediteranske prehrane, dok je objektivni materijalni status predstavljen kao najistaknutiji socio-ekonomski pokazatelj za cjelokupno pridržavanje mediteranske prehrane, ali i nekoliko skupina namirnica.

Ispitanici uključeni u praćenje imali su veću privrženost mediteranskoj prehrani na početku (36,6%), s graničnim neznatnim padom na kraju razdoblja praćenja (33,5%). Multivarijatni model je otkrio da su ženski spol, starija dob na početku, najviša razina obrazovanja i umjerena razina tjelesne aktivnosti bili pozitivno povezani, dok je MDSS na početku bio negativno povezan s promjenom MDSS-a tijekom praćenja. S druge strane, indeks tjelesne mase se u prosjeku povećao za 6,5% kod ispitanika dostupnih za praćenje. Promjena BMI tijekom praćenja bila je pozitivno povezana sa ženskim spolom, a negativno s početnim

BMI-om, početnim pridržavanjem mediteranskoj prehrani i promjenom pridržavanja mediteranskoj prehrani, kao što je pronađeno u regresijskoj analizi.

Konzumacija orašastih plodova u ovoj studiji bila je povezana sa smanjenim izgledima za smanjenje HDL kolesterola i smanjenim izgledima za povećanje fibrinogena, dok ukupni kolesterol i LDL kolesterol nisu dosegli razinu značajnosti (kada je promatrana ukupna P vrijednost), a trigliceridi nisu pokazali nikakvu povezanost s unosom orašastih plodova unutar ove studije. Studija je također otkrila povezanost između konzumacije orašastih plodova i indeksa središnje pretilosti (definiranih omjerima struka prema visini, te struka i boka), dok u isto vrijeme nije bilo povezanosti s izravnim mjerama, odnosno opsegom struka ili indeksom tjelesne mase. Nismo pronašli takvu povezanost između unosa orašastih plodova i prisutnosti dijagnoze hipertenzije, dijabetesa ili gihta, ali smo pronašli neke naznake povezanosti između mjesečnog unosa orašastih plodova i nižih izgleda za prisutnost metaboličkog sindroma. Zanimljiv je rezultat da ispitanici koji se nisu pridržavali mediteranske prehrane imaju manje šanse za prisutnost dijabetesa i povišen HbA1c, ali veće šanse za pretilost.

Općenito, važnost zdravog načina života i zdravih prehrambenih navika došla je u prvi plan pozornosti zbog pandemije COVID-19. Uvidi iz ovih studija trebali bi se koristiti za informiranje o potrebnim i ciljanim javno-zdravstvenim intervencijama usmjerenim na povećanje prihvaćanja mediteranske prehrane kako bi se osigurali korisni ishodi na razini pojedinca i populacije. To je relevantno iz perspektive zdravlja stanovništva i pružanja adekvatne zdravstvene skrbi, kao i iz perspektive gospodarskog, društvenog i kulturnog razvoja, te očuvanja kulturne baštine za generacije koje dolaze.

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3. RESUME

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SCIENTIFIC PAPERS

1. Lojić Kapetanović A, Lukezić M, Pribisalić A, Poljak D, Polašek O. Modeling the COVID-19 epidemic in Croatia: a comparison of three analytic approaches. Croat Med J. 2022;63(3):295-8. Epub 2022/06/21.

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4. COPY OF PUBLICATIONS

1. Kolčić I*, **Relja A***, Gelemanović A, Miljković A, Boban K, Hayward C, et al. Mediterranean diet in the southern Croatia - does it still exist? Croatian medical journal. 2016;57(5):41524. *(*The first two authors contributed equally.)*

2. **Pribisalić A**, Popović R, Salvatore FP, Vatavuk M, Mašanović M, Hayward C, et al. The Role of Socioeconomic Status in Adherence to the Mediterranean Diet and Body Mass Index Change: A Follow-Up Study in the General Population of Southern Croatia. Nutrients. 2021;13(11):3802.

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Mediterranean diet in the southern Croatia – does it still exist?

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Aim To assess the adherence to the Mediterranean diet in the population of Dalmatia in southern Croatia.

Methods A cross-sectional study was performed within the 10 001 Dalmatians cohort, encompassing 2768 participants from Korčula and Vis islands and the City of Split, who were recruited during 2011-2014. Using the data obtained from food frequency questionnaire we calculated the Mediterranean Diet Serving Score (MDSS). Multivariate logistic regression was used to identify the characteristics associated with the adherence to the Mediterranean diet, with age, sex, place of residence, education attainment, smoking, and physical activity as covariates.

Results The median MDSS score was 11 out of maximum 24 points (interquartile range 8-13), with the highest score recorded on the island of Vis. Participants reported a dietary pattern that had high compliance with the Mediterranean diet guidelines for consumption of cereals (87% met the criteria), potatoes (73%), olive oil (69%), and fish (61%), moderate for consumption of fruit (54%) and vegetables (31%), and low for consumption of nuts (6%). Overall, only 23% of the participants were classified as being adherent to the Mediterranean diet, with a particularly low percentage among younger participants (12%) compared to the older ones (34%). Men were less likely to show good adherence (odds ratio 0.52, 95% confidence interval 0.42-0.65).

Conclusion This study revealed rather poor compliance with the current recommendations on the Mediterranean diet composition in the population of Dalmatia. Public health intervention is especially needed in younger age groups and in men, who show the greatest departure from traditional Mediterranean diet and lifestyle.

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Mediterranean diet is one of the most commonly investigated nutritional patterns, marked by numerous beneficial health effects. It is traditionally practiced in countries of the Mediterranean basin, especially Greece, Italy, and Spain (1). Described benefits included cardiovascular diseases prevention (2), reversion of the metabolic syndrome (3), prevention of the invasive breast cancer (4), prostate (5), and colorectal cancer (6), prevention of the age-related cognitive decline (7), and even a protective role in asthma among children (8,9). Additionally, in Swedish population a 2-year survival increase was observed among people with higher compliance with the Mediterranean diet (10). Mediterranean diet was also shown to reduce the risk of cardiovascular and all-cause mortality both in people diagnosed with diabetes type 2 (11) and in healthy population (12). However, a Cochrane systematic review that included randomized controlled trials published until 2012 found only a modest effect of the Mediterranean diet or its components on the cardiovascular risk factors reduction (13), possibly due to methodological differences and design limitations of the published studies. More recently, results from the PREDIMED study, a large randomized controlled field trial in individuals at high risk of cardiovascular disease became available (14), confirming the beneficial effects of the Mediterranean diet on cardiometabolic health (15) and its role in the primary prevention of cardiovascular diseases (16).

The dietary pattern and compliance with the Mediterranean diet has so far been assessed using many definitions and various scoring systems (17). This is a consequence of several factors, including the availability and types of locally produced foods, lifestyle, and tradition (18). The most prominent characteristics of the Mediterranean diet are the use of olive oil (preferably virgin oil) as the primary fat source, abundant consumption of vegetables, fruits, nuts, and whole grains daily, with moderate red wine and legumes consumption. Animal products are more of a relish, and the priority is given to fish and white meat over red and processed meat (19). Recently, a new scoring system has been proposed to assess the individual compliance with the Mediterranean diet – Mediterranean Diet Serving Score (MDSS), claimed to be easy, valid, and accurate instrument to assess the Mediterranean diet adherence based on the consumption of foods and food groups per meal, day, and week (20). Its advantage is that it includes as many as 14 groups of foods, adding 1, 2, or 3 points to the total score based on the consumption frequency and the relative importance of the particular foods, without assigning negative points (20).

Nutritional transition, marked with the rapid spread of highly processed foods rich in sugar and saturated fats and fast food, as opposed to the home cooking (21), coupled with the sedentary lifestyle, is believed to be the driving force behind the pandemic of chronic diseases like obesity, diabetes, and cardiovascular diseases. Unfortunately, these trends have also spread to the Mediterranean countries, resulting in a switch from the traditional diet toward western diets (22).

Mediterranean diet and its particular composition in the Dalmatian population has previously been marginally investigated, using various study approaches and scoring (23,24). The aim of this study was to assess the compliance with the Mediterranean dietary pattern and its constituting components in the population of the island of Korčula, island of Vis, and the City of Split, Croatia. This is the first study that uses a systematic and validated approach to estimate the prevalence and factors associated with the adherence to the Mediterranean diet in a large population-based sample, and thus provide a reliable source of information for international comparisons and monitoring of nutritional trends and transition.

MATERIALS AND METHODS

This cross-sectional study was performed within the "10,001 Dalmatians" cohort study (25,26). "10,001 Dalmatians" study was initiated in 1999, and has been investigating the health of isolated island communities ever since (27). This descriptive cross-sectional study included only participants recruited after 2010 during either their follow-up or upon their first enrolment, in order to portrait the contemporary dietary patterns. The participants originated from the island of Vis (N = 401; recruited in 2011), the island of Korčula (N = 1980; recruited in 2012-2014), and the City of Split (N = 512; recruited in 2012-2013). The participants were recruited in the study following general practitioner's advice, newspaper and radio announcements, or distribution of posters and leaflets. In order to participate, the participants had to be of age (18 or more years) and had to sign the informed consent prior to the enrolment. The study protocol was approved by the ethical board of the Medical School, University of Split (approval number 2181-198-03-04/10-11-0008).

Every participant provided a blood and urine sample following an overnight fast and gave the medical history, after which they filled in an extensive self-administered questionnaire, consisting of questions on dietary habits, smoking, alcohol consumption, physical activity, and socioeconomic status. Additionally, anthropometric and clinically relevant measurements were performed by trained medical doctors and nurses using standard operating procedures.

Mediterranean diet assessment

A food frequency questionnaire was used to assess the dietary pattern. It consisted of 55 questions, with 6 available answers regarding the frequency of consumption (every day, 2-3 times a week, once a week, once a month, rarely, never). These questions were about olive oil and other fat consumption, milk and dairy products, various groups of vegetables, fruit, nuts, legumes, various meats, fish, and sea foods, eggs, sweets, potatoes, rice, pasta, and bread. Additionally, there were 4 questions about wine (red and white) and *bevanda* (mixture of red or white wine and water) consumption expressed in liters per week. According to the proposed MDSS approach (20), we created 14 categories of foods that comprised Mediterranean diet: fruit (including 2 questions; fresh and dried fruit), vegetables (5 questions; leafy, rooted, cruciferous, tomatoes, canned, and pickled vegetables), cereals (5 questions; white bread, wholegrain bread, rice, pasta, muesli), potatoes, olive oil, nuts, dairy products (5 questions; milk, yoghurt, sour cream, hard cheese, cottage cheese), legumes, eggs, fish (4 questions; blue fish, white fish, mollusks, octopus), white meat (2 questions; chicken, turkey), red meat (6 questions; beef, calf, pork, lamb, sausages, pancetta), sweets (7 questions; cakes, chocolate, cookies, bonbons, jam, sweetened fruit juice, fizzy drinks), fermented beverages (4 questions; red and white wine, red and white *bevanda*). If the participants reported daily consumption of olive oil, fruit, vegetables, and cereals, they were awarded 3 points, for daily consumption of nuts and dairy products they were awarded 2 points, and for the consumption of the remaining 8 categories they were awarded 1 point. These included potatoes (if consumed ≤3 servings/week), legumes (≥2 servings/week), eggs (2-4 servings/week), fish (≥2 servings/week), white meat (2 servings/week), red meat (<2 servings/week), sweets (≤2 servings/week), and fermented beverages (1 glass/d of wine or *bevanda* for women, 2 glasses/d for men; beer was not included) (20). In case these guidelines were exceeded for meat, eggs, potatoes, sweets, and wine or not reached for other categories, the participant would get 0 points. In this way, the foods that are more beneficial for health and should be consumed several times a day bring greater weight to the final score, while the foods like red meat, eggs, potatoes, and sweets that should be kept at low frequency of consumption bring lesser weight to the final score. The MDSS is based on the new Mediterranean diet pyramid, which places vegetables at the base of the pyramid, alongside with the cereals, olive oil, and fruit (28). Since our questionnaire allowed the highest frequency of consumption to be once a day, we combined 5 different types of vegetables (leafy, rooted, cruciferous, tomatoes, canned, and pickled vegetables) and thus awarded 3 points only to those participants who reported daily consumption of at least 2 types of vegetables or to those who consumed at least one type of vegetables every day plus the combination of other types, which added up to a consumption frequency of ≥7 days a week. The maximum possible MDSS score was 24 points, and the cut-off of ≥13.5 points was considered as good compliance (20). We excluded 125 participants from the analysis due to missing values needed for MDSS items calculation.

Lifestyle and socioeconomic characteristics

Besides diet, we assessed other lifestyle indicators, such as smoking and physical activity. According to the smoking status, we divided participants into smokers (those who reported current smoking or ceased smoking less than a year ago) and non-smokers. Physical activity was assessed during the working part of the day and during the leisure time, with four responses: intensive, moderate, light, and sitting. The number of completed years of schooling (educational attainment) was used in the estimation of the socioeconomic status.

Statistical analysis

Categorical variables are shown as numbers and percentages, and numerical variables are shown as median and interquartile ranges (IQR), due to non-normal distribution assessed using Kolmogorov-Smirnov test. X^2 test was used to investigate the differences between groups for categorical variables, and Kruskal-Wallis test was used for numerical variables. Mann-Whitney U test was used as a *post-hoc* test for numerical variables and X^2 test for categorical variables. Correlation between MDSS score and age and education expressed as years of schooling was performed using Spearman rank test. Finally, multivariate logistic regression analysis was used to investigate the characteristics associated with greater compliance with the Mediterranean diet, using the upper quartile of 14 points as a cut-off, which also corresponds to a proposed MDSS cut-off for good compliance with the Mediterranean diet (20). The model included six covariates: age, sex, place of residence, years of schooling, smoking, and physical activity. Age and years of schooling were classified into categories in order to provide better understanding of the results. Age was classified into three categories (18-34.9 years, 35-64.9, and ≥65 years), while years of schooling were divided in four categories (<8 years, 8-10, 11-12, and ≥13 years). In all instances we provided odds ratios (OR) and 95% confidence intervals (CI). Significance level was set at $P<0.05$. Statistical software used was IBM SPSS Statistics v19 (IBM, Armonk, NY, USA).

RESULTS

The analysis included 2768 participants from three study sites (Table 1). The overall median MDSS score was 11 out of 24 points (IQR 8-13). The highest median MDSS score of 12 points was recorded on Vis (IQR 9-14), followed by 11 points in Split (IQR 8-15) and 10 points on Korčula (IQR 8-13). There was a significant difference between participants from Korčula and Vis as well as between Korčula and Split (both $P<0.001$), while participants from Vis did

TABLE 1. **Participants' demographic characteristics and prevalence of compliance with 14 Mediterranean Diet Serving Score (MDSS) components and overall good Mediterranean diet adherence (MDSS≥14 points) according to the place of residence**

	Korčula island N = 1874	Vis island N = 385	Split N = 509	Overall *P* (post-hoc test *P* values)
Sex; n (%)				
men	685 (36.6)	153 (39.7)	201 (39.5)	0.301 (0.238*;0.224†; 0.939‡)
women	1189 (63.4)	232 (60.3)	308 (60.5)	
Age (years); median (interquartile range, IQR)	55.0 (40.7-65.3)	63.5 (54.1-73.1)	58.0 (47.0-66.0)	<0.001(<0.001*; <0.001†; <0.001‡)
Years of schooling; median (IQR)	12 (9-12)	11 (6-12)	12 (12-16)	<0.001 (<0.001*; <0.001†; <0.001‡)
Smoking; n (%)				
current smokers	522 (27.9)	99 (25.7)	84 (16.5)	<0.001 (0.001*; <0.001†; <0.001‡)
ex-smokers	369 (19.7)	49 (12.7)	132 (25.9)	
never-smokers	983 (52.4)	237 (61.6)	293 (57.6)	
Physical activity; n (%)				
light	341 (18.2)	148 (38.4)	136 (26.7)	<0.001 (<0.001*; <0.001†; <0.001‡)
moderate	1210 (64.6)	200 (51.9)	356 (69.9)	
intensive	174 (9.3)	21 (5.5)	8 (1.6)	
Body mass index (kg/m²); median (IQR)	26.8 (24.0-29.7)	28.0 (25.6-30.9)	27.2 (24.6-30.0)	<0.001 (<0.001*;0.011†; 0.003‡)
MDSS; median (IQR)	10 (8-13)	12 (9-14)	11 (8-15)	<0.001 (<0.001*; <0.001†; 0.401‡)
MDSS in 18-34.9 age group; median (IQR)	9.0 (7.0-11.0)	11.5 (6.8-13.3)	10.0 (8.0-14.0)	0.006 (0.242*;0.002†; 0.969‡)
MDSS in 35-64.9 age group; median (IQR)	10.0 (8.0-13.0)	11.0 (9.0-13.0)	11.0 (8.0-14.0)	<0.001 (0.012*; <0.001†; 0.397‡)
MDSS in ≥65.0 age group; median (IQR)	11.0 (9.0-14.0)	13.0 (10.0-15.0)	13.0 (10.0-15.0)	<0.001 (<0.001*;0.035†; 0.377‡)
MDSS components; n (%)				
fruit	937 (50.0)	228 (59.2)	320 (62.9)	<0.001 (0.001*; <0.001†; 0.268‡)
vegetables	521 (27.8)	127 (33.0)	216 (42.4)	<0.001 (0.041*; <0.001†; 0.004‡)
cereals	1625 (86.7)	365 (94.8)	405 (79.6)	<0.001 (<0.001*; <0.001†; <0.001‡)
potatoes	1229 (65.6)	334 (86.8)	462 (90.8)	<0.001 (<0.001*; <0.001†; 0.066‡)
olive oil	1283 (68.5)	296 (76.9)	328 (64.4)	<0.001 (0.001*; 0.085†; <0.001‡)
nuts	86 (4.6)	10 (2.6)	57 (11.2)	<0.001 (0.078*; <0.001†; <0.001‡)
dairy products	339 (18.1)	84 (21.8)	106 (20.8)	0.132 (0.088*; 0.160†; 0.742‡)
legumes	412 (22.2)	78 (20.3)	122 (24.0)	0.406 (0.454*; 0.341†; 0.196‡)
eggs	462 (24.7)	80 (20.8)	134 (26.3)	0.148 (0.105*; 0.440†; 0.058‡)
fish	1161 (62.0)	252 (65.5)	286 (56.2)	0.013 (0.196*; 0.018†; 0.006‡)
white meat	758 (40.4)	136 (35.3)	185 (36.3)	0.069 (0.067*; 0.093†; 0.778‡)
red meat	548 (29.2)	127 (33.0)	201 (39.5)	<0.001 (0.144*; <0.001†; 0.050‡)
sweets	597 (31.9)	105 (27.3)	164 (32.2)	0.185 (0.077*; 0.876†; 0.122‡)
wine	315 (16.8)	125 (32.5)	136 (26.7)	<0.001 (<0.001*; <0.001†; 0.064‡)
MDSS≥14 points; n (%)	352 (18.8)	123 (31.9)	160 (34.4)	<0.001 (<0.001*; <0.001†; 0.885‡)

*Post-hoc test *P* values: Korčula vs Vis.
†Post-hoc test *P* values: Korčula vs Split.
‡Post-hoc test *P* values: Vis vs Split.

TABLE 2. Participants' demographic characteristics and prevalence of compliance with 14 Mediterranean Diet Serving Score (MDSS) components and overall good Mediterranean diet adherence (MDSS≥14 points), according to the age group

	Age groups			
	18-34.9 years (N = 372)	35-64.9 years (N = 1617)	65 and more (N = 779)	Overall *P* (post-hoc test *P* values)
Sex; n (%)				
men	149 (40.1)	571 (35.3)	319 (40.9)	0.016 (0.086*;0.772†; 0.007‡)
women	223 (59.9)	1046 (64.7)	460 (59.1)	
Years of schooling; median (interquartile range, IQR)	12.0 (11.0-15.0)	12.0 (11.0-13.0)	11.0 (6.0-12.0)	<0.001 (<0.001*; <0.001†; <0.001‡)
Smoking; n (%)				
current smokers	163 (45.4)	478 (32.4)	64 (9.2)	<0.001 (<0.001*; <0.001†; <0.001‡)
never-smokers and ex-smokers	209 (54.6)	1139 (67.6)	715 (90.8)	
Physical activity; n (%)				
light	85 (23.3)	284 (18.7)	256 (36.1)	<0.001 (0.130*; <0.001†; <0.001‡)
moderate	252 (69.0)	1102 (72.5)	412 (58.0)	
intensive	28 (7.7)	133 (8.8)	42 (5.9)	
MDSS; median (IQR)	9.0 (7.0-11.0)	11.0 (8.0-13.0)	12.0 (9.0-14.0)	<0.001 (<0.001*; <0.001†; <0.001‡)
MDSS components; n (%)				
fruit consumption	132 (35.5)	863 (53.4)	490 (62.9)	<0.001 (<0.001*; <0.001†; <0.001‡)
vegetables	95 (25.5)	471 (29.1)	298 (38.3)	<0.001 (0.166*; <0.001†; <0.001‡)
cereals	316 (84.9)	1403 (86.8)	676 (86.8)	0.632 (0.356*; 0.400†; 0.993‡)
potatoes	314 (84.4)	1195 (73.9)	516 (66.2)	<0.001 (<0.001*; <0.001†; <0.001‡)
olive oil	193 (51.9)	1082 (66.9)	632 (81.1)	<0.001 (<0.001*; <0.001†; <0.001‡)
nuts	19 (5.1)	88 (5.4)	46 (5.9)	0.835 (0.796*; 0.584†; 0.644‡)
dairy products	78 (21.0)	308 (19.0)	143 (18.4)	0.571 (0.398*; 0.293†; 0.685‡)
legumes	80 (21.5)	320 (19.8)	212 (27.2)	<0.001 (0.473*; 0.037†; <0.001‡)
eggs	115 (30.9)	416 (25.7)	145 (18.6)	<0.001(0.041*; <0.001†; <0.001‡)
fish	185 (49.7)	978 (60.5)	536 (68.8)	<0.001 (<0.001*; <0.001†; <0.001‡)
white meat	150 (40.3)	618 (38.2)	311 (39.9)	0.617 (0.452*; 0.897†; 0.423‡)
red meat	93 (25.0)	493 (30.5)	290 (37.2)	<0.001 (0.037*; <0.001†; 0.001‡)
sweets	74 (19.9)	493 (30.5)	299 (38.4)	<0.001 (<0.001*; <0.001†; <0.001‡)
wine	45 (12.1)	327 (20.2)	204 (26.2)	<0.001 (<0.001*; <0.001†; 0.001‡)
MDSS≥14 points; n (%)	46 (12.4)	324 (20.0)	265 (34.0)	<0.001 (0.001*; <0.001†; <0.001‡)

*Post-hoc test *P* values: 18-34.9 years vs 35–64.9 years.
†Post-hoc test *P* values: 18-35 years vs ≥65 years.
‡Post-hoc test *P* values: 34.9-64.9 years vs ≥65 years.

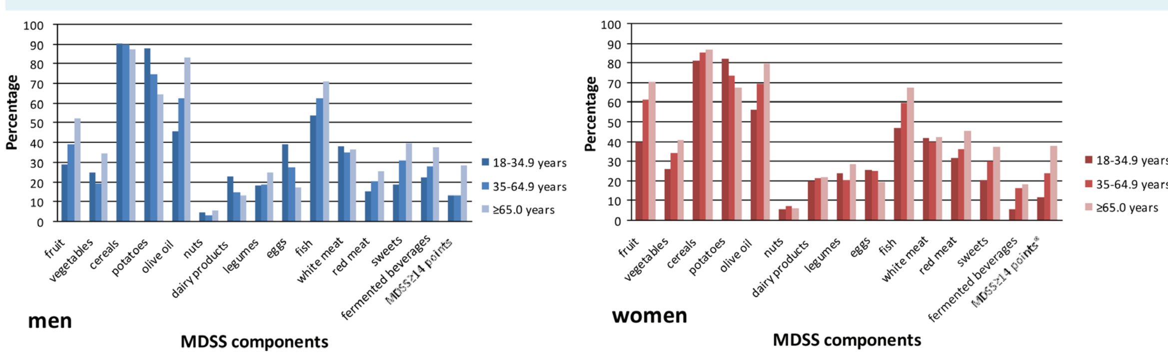

FIGURE 1. Prevalence of compliance with 14 Mediterranean Diet Serving Score (MDSS) components and overall good Mediterranean diet adherence (MDSS≥14 points), according to sex and age groups (significant differences at the level of $P < 0.05$ between age groups are denoted with asterisk; χ^2 test).

not differ from those from Split (Table 1). This difference was observed across all three age groups, with the exception for the youngest age group, where participants from Korčula did not differ from participants from Vis (Table 1). There was a wide range of variability in the compliance with the MDSS components, from only 3% of participants meeting the requirements for nuts consumption on Vis, to as much as 95% for cereals (Table 1). Overall, low percentages of participants met some of the MDSS components criteria; only 28% of participants from Korčula adhered to the daily vegetable consumption requirement, 33% from Vis, and 42% from Split. MDSS recommendations for dairy products, legumes, eggs, and wine consumption were met by 17%-26% of the participants, while those for meat and sweets were met by 29%-40% of the participants (Table 1). In total, 635 (22.9%) participants reported a dietary pattern adherent to the Mediterranean diet pattern according to the MDSS criteria. Participants from Vis displayed less difference from participants from Split than from participants from Korčula regarding the adherence to the MDSS components (Table 1). The prevalence of compliance to the guidelines for sweets, white meat, eggs, legumes, and dairy products did not exhibit difference across three subgroups according to the place of residence (Table 1).

Breakdown by sex and age suggested somewhat better indices in women and older age group, with only one significant result: good compliance to the Mediterranean diet differed according to age groups only in women ($P = 0.024$) (Figure 1).

Breakdown into three groups according to the participant's age revealed higher MDSS scores in the elderly group, with a significant difference between all three age groups (all $P < 0.001$) (Table 2). Correlation between age and MDSS score was also significant in the whole sample ($\rho = 0.256$, $P < 0.001$; data not shown), as well as in the subgroups according to the place of residence ($\rho = 0.243$, $P < 0.001$ in Korčula; $\rho = 0.276$, $P < 0.001$ in Vis; $\rho = 0.189$, $P < 0.001$ in Split). Education (years of schooling) was not correlated with the MDSS score ($\rho = -0.006$, $P = 0.736$ in the whole sample; $\rho = -0.045$, $P = 0.057$ in Korčula; $\rho = -0.045$, $P = 0.387$ in Vis; $\rho = 0.113$, $P = 0.011$ in Split).

TABLE 3. **Characteristics associated with good adherence to the Mediterranean diet (MDSS≥14 points) using the multivariate logistic regression analysis***

	Unadjusted odds ratio (95% confidence interval); *P*	Adjusted odds ratio (95% confidence interval); *P*
Sex		
women (Ref.)	1.00	1.00
men	0.62 (0.51-0.75); <0.001	0.52 (0.42-0.65); <0.001
Age		
65 and more (Ref.)	1.00	1.00
35-65	0.49 (0.40-0.59); <0.001	0.44 (0.35-0.56); <0.001
18-35	0.27 (0.19-0.39); <0.001	0.30 (0.20-0.45); <0.001
Place of residence		
Korčula	1.00	1.00
Split	1.98 (1.59-2.47); <0.001	1.67 (1.28-2.19); <0.001
Vis	2.03 (1.59-2.59); <0.001	1.99 (1.50-2.64); <0.001
Years of schooling		
13 or more	1.00	1.00
under 8	1.04 (0.77-1.40); 0.788	0.57 (0.39-0.83); 0.003
8-10	0.80 (0.59-1.08); 0.140	0.70 (0.49-0.99); 0.045
11-12	0.56 (0.45-0.69); <0.001	0.61 (0.48-0.79); <0.001
Smoking		
non-smokers and ex-smokers	1.00	1.00
smokers	0.61 (0.49-0.77); <0.001	0.77 (0.60-0.99); 0.045
Physical activity		
intensive	1.00	1.00
light	1.17 (0.80-1.70); 0.420	0.61 (0.40-0.93); 0.021
moderate	0.98 (0.69-1.40); 0.934	0.71 (0.48-1.04); 0.080

*MDSS – Mediterranean Diet Serving Score.

Only 12% of participants from the youngest group met the MDSS cut-off criterion, while the corresponding figure in the oldest age group was 34% (Table 2). White meat, dairy products, nuts, and cereals were the only MDSS components that did not exhibit difference in compliance across three age groups (Table 2).

Logistic regression analysis revealed several variables to be strongly associated with the good adherence to the Mediterranean diet (MDSS≥14 points). For instance, men had lesser odds of showing good compliance compared to women (OR 0.52, 95% CI 0.42-0.65, $P<0.001$), while the youngest age group had 70% lesser odds compared to the oldest participants (OR 0.30, 95% CI 0.20-0.45, $P<0.001$) (Table 3). Both the participants from Vis and those from Split showed greater odds for good adherence to the Mediterranean diet (OR 1.99, 95% CI 1.50-2.64, $P<0.001$ and OR 1.67, 95% CI 1.28-2.19, $P<0.001$, respectively) (Table 3). Physical activity, lower education, and smoking were marginal predictors or lacked significance (Table 3). The regression model yielded good data fit (Hosmer and Lemeshow $P=0.225$, Nagelke $R^2=0.101$).

DISCUSSION

This study revealed rather unsatisfactory Mediterranean diet consumption in southern Croatia. The median MDSS score was as low as 10 out of maximum 24 points among participants from Korčula, 11 among those from Split, and 12 among those from Vis. A similar study performed in Spain reported an average MDSS score among women of 12.5 ± 2.7 (20). The percentage of participants who adhered to the Mediterranean diet in our study was comparable to or lower than figures obtained in other Mediterranean countries, eg, 32% in Greece (29) and 18% in Italy (30). However, it is not possible to make any in-depth comparisons between these studies and our results due to methodological differences and the differences in the definition of the Mediterranean diet adherence (17). However, the majority of the studies do report a rather low percentage of people whose dietary pattern resembles the Mediterranean diet, especially in the youngest generations (30-33).

The required high intake of vegetables (≥2 servings/main meal) was poorly met in this study, especially among participants from Korčula (28%), younger people (26%), and men (as low as 19% in the middle age group). Although rather low, these percentages surpass those from Spain, where only 11% of women met the same criterion (20). This suggests that this is a very restrictive criterion, although it is one of the most important ones according to the recent scientific evidence on the health benefits of the plant-based diet compared to the meat-based diets (34,35).

Fruit consumption showed overall better results, with the lowest consumption among the youngest men (29%) and the highest among the oldest women (70%). Olive oil intake was commonly reported, but slightly less commonly than in Spain (20). Satisfactory fish consumption was generally present in more than 50% of the participants, with the highest proportion recorded among elderly men (71%) and the lowest among youngest women (47%).

The worst result for a particular component was recorded for nuts consumption, where as little as 3% of people from Vis reported eating nuts every day, and the situation was not much better among the participants from Korčula (5%) and Split (11%). This is particularly unfortunate because a recent field trial showed that daily consumption of mixed nuts (30 g/d) reduced the incidence of major cardiovascular events by 28% in people at high cardiovascular risk, but with no cardiovascular disease and after a median follow-up of 4.8 years (16). Also, an observational study showed a 47% reduction in all-cause mortality and 36% reduction in cancer deaths in people who ate nuts ≥8 times/month, compared to those who never ate nuts during a median follow-up of 4.3 years (36). Additionally, consumption of nuts was also shown to be protective against cognitive decline in elderly people (37), or even to improve cognitive function (7).

A better compliance with the overall Mediterranean diet, as well as with the majority of the MDSS components, was recorded among the oldest participants, especially women, even though without reaching statistical significance, which is in line with many previous studies (20,38,39). Participants from Vis had the highest prevalence of compliance to MDSS components and overall the highest prevalence of Mediterranean diet adherence (MDSS≥14 points). After stratification according to age groups, participants from Korčula showed the poorest compliance, while participants from Vis and Split showed a similar dietary pattern.

Earlier studies from Croatian islands also revealed a worrisome pattern of dietary habits, with a predominant shift toward higher consumption of meat, pasta, and cakes (23). A study from the coastal region of Adriatic Sea yielded even more devastating results; only 2.4% of the general population in urban areas and 3.4% in rural areas ate Mediterranean diet defined as "daily intake of fruits and vegetables, brown bread and whole grains, using olive oil as the main source of fat, consumption of fish and moderate wine drinking with meals" (40). This departure from the traditional diet, as well as other lifestyle factors, such as high prevalence of smoking in both island populations and overall lower levels of physical activity, as demonstrated in this study, might as well be responsible for the observed high burden of overweight and hypertension (41), hyperlipidemia (24), type 2 diabetes (42), and metabolic syndrome (43) in the Mediterranean region of Croatia. This detrimental situation is also reflected in the concurrent mortality patterns (unpublished data, Rehberg J et al, 2016).

Limitations of this study include the use of the convenient sampling approach, possible recall bias, and a slightly different food frequency questionnaire from the one used in the study that proposed the MDSS score (20). A number of other possible confounders were omitted, but we applied a validated and simple tool to assess the compliance with the Mediterranean diet, which enables wider-scale international comparisons. One of the confounding factors not taken into account is the morbidity pattern, especially age-related diseases, which could have affected dietary habits as well as the adherence to the Mediterranean diet. Given the high prevalence of chronic diseases in the investigated population (41-43), it would be expected that people, especially elderly persons, would show greater adherence to the healthy Mediterranean diet as a form of both preventive measure and treatment, but in the oldest group we demonstrated the prevalence of good Mediterranean diet adherence of only 34%.

This study suggests a diminishing adherence to the traditional Mediterranean diet and lifestyle, especially in the younger generations, which needs to be considered as a public health priority and reversed not only for the population health benefits, but also as a part of the cultural heritage safe-keeping. In addition, adherence to the Mediterranean diet has much more favorable environmental footprint (44), which is of utmost importance in small and fragile habitats, such as the remote islands.

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Ethnical approval received from the ethics board of the Medical School, University of Split (approval number 2181-198-03-04/10-11-0008).

Declaration of authorship IK conceived the study idea; IK, IR, CH, and OP designed the study plan; IK, AR, AG, AM, KB, and OP collected the data; IK, AR, and OP performed the analysis; IK and AR drafted the initial version of the text; all authors participated in discussions on the intellectual content and approved the final version for publication. All authors are held accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Competing interests OP is a statistical editor in the *Croatian Medical Journal*. To ensure that any possible conflict of interest relevant to the journal has been addressed, this article was reviewed according to best practice guidelines of international editorial organizations. All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

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nutrients

MDPI

Article

The Role of Socioeconomic Status in Adherence to the Mediterranean Diet and Body Mass Index Change: A Follow-Up Study in the General Population of Southern Croatia

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Abstract: The Mediterranean diet (MD) is one of the most healthful dietary patterns, beneficial for humans and the environment. However, the MD has recently exhibited a declining trend, especially in younger and less affluent people. This study investigated the association between socioeconomic indicators and adherence to the MD in 4671 adult subjects from Dalmatia, Croatia (age range 18–98 years; 61.9% were women). Additionally, in the follow-up we examined the change in adherence to the MD and in BMI (subsample, N = 1342; 62.5% were women; mean follow-up time of 5.8 years). The adherence to the MD was based on the Mediterranean Diet Serving Score (range 0–24 points, cut-off value $\geq$ 14 points), with a prevalence in the overall sample of 28.5%. Higher odds of adherence to the MD were recorded in women, older subjects, and those with higher level of objective material status, while it was less likely in the period after economic crisis of 2007–2008. Additionally, we detected no change in adherence to the MD in the follow-up subsample (−8.5%, p = 0.056), but there was an increase in BMI (+6.5%, p < 0.001). We recorded an increase in adherence for nuts (+127.5%), sweets (+112.6%), red meat (+56.4%), and wine (+50.0%), unlike the reduction in adherence for vegetables (−35.1%), fish (−23.4%), white meat (−11.6%), cereals (−10.9%), and dairy products (−9.6%). Similar results were obtained across all quartiles of objective material status. Over time, the absolute change in the MD score was positively associated with female gender, age, higher education, and moderate physical activity, but it was negatively associated with adherence to the MD at baseline. BMI change was positively associated with female gender, and negatively with initial BMI, initial adherence to the MD, and MD change. Our findings point towards a less than ideal adherence to the MD in the general population of southern Croatia, and identify important characteristics associated with adherence change over time, informing necessary interventions aimed at increasing MD uptake.

Keywords: Mediterranean diet; adherence; BMI; socioeconomic status

1. Introduction

Unhealthy lifestyle and unhealthy diet in particular are among the foremost public health challenges, with as many as 11 million deaths globally being attributable to suboptimal diet in 2017 [1]. The leading global dietary risk factors for death and disability were high sodium intake, low intake of whole grains, and low intake of fruits [1]. These are highly preventable risk factors that could be addressed by adopting scientifically proven healthy diets at the population level.

One model of healthy eating that is particularly well described in the literature is the Mediterranean diet (MD), which is especially healthful compared to a more westernized dietary pattern [2]. MD is characterized by a high intake of plant-based foods, such as daily intake of vegetables, fruit, whole grains, olive oil, nuts and seeds, and weekly intake of dairy, fish and legumes, alongside frugal use of meat, eggs and sweets [3]. There is a large body of evidence showing that adherence to the MD can preserve human health, with the extra bonus of ensuring environmental sustainability [4,5]. The health benefits of MD are numerous [6,7]. The most important positive effects include reduced all-cause mortality [6,8,9], primary prevention of cardiovascular disease [10], lower cancer incidence and mortality [6,11], reduced risk for development of type II diabetes [12–14], obesity and metabolic syndrome [13]. Benefits of MD also include safeguarding of mental health, such as better cognitive performance with higher adherence to the MD [15], reduced risk of depression and cognitive impairment [16], lesser mental distress [17], and overall better health-related quality of life [18,19]. Moreover, MD was even shown to be an efficient treatment strategy for major depressive episodes [20].

Regardless of these and other health benefits of MD and other traditional diets, global nutrition transition caused by modernization and increased incomes has resulted in deviation from traditional plant-based diets towards higher intake of animal-source food, added sugar and vegetable oils [21]. An analysis of the supply of the most important food components of the traditional MD in several Mediterranean countries has revealed that these countries have experienced a process of Westernization during the period from 1961 to 2001, which was especially pronounced in the European countries of the Mediterranean basin [22].

Major constitutional components of the MD, such as fruit, vegetables, olive oil and fish are still present within the dietary pattern, but the discrepancies between Mediterranean countries and regions have started to emerge more consistently [23]. For example, MD decline was observed in Malta, unlike Sardinia, which was accredited to "modernity and improved living conditions, enhanced commercial availability and increased diversity of food preparation" [24]. However, an overall declining trend in adherence to the MD has been previously demonstrated in many Mediterranean countries [25–27], especially in younger generations [28–33]. On the other hand, some countries have experienced an increase in adherence to the MD among adolescents, such as Israel, where increased consumption of fruits, vegetables, cereals, dairy products, and decreased negative eating behaviors were recorded in 2016 compared to 2003 [34].

Besides the greater convenience of a diet relying on processed foods and ready-to-eat fast food, saving time and effort, these foods are also readily available in our modern urbanized environments. They are appetizing and tasty, and they may be cheaper than whole foods. Indeed, the question of a monetary cost behind the Mediterranean dietary pattern has been previously investigated. Some of these previous studies have shown that greater adherence to the MD was associated with a higher dietary cost [35–37], especially if it is compared to a Western dietary pattern [38]. Therefore, it is not surprising to consistently find that the lowest-income households had the lowest adherence to the MD and the highest obesity prevalence [39]. However, it was shown that a higher educational status could exhibit a mitigating effect on poorer diet in lower income countries [40]. These findings demonstrate a complex interplay between different socio-economic determinants and dietary habits.

Furthermore, since we can define socio-economic status (SES) by using several characteristics, it may be challenging to disentangle the main SES contributor to various health outcomes. SES characteristics include objective indicators, such as attained level of education, profession, employment/unemployment status, income, and the subjective perception of one's wealth compared to other people within the same community. Despite this complexity, the impact of SES on dietary pattern is undeniably important. This effect was summarized nicely in a recent paper stating that people "who are better off consume healthier diets than those less well-to-do" [41]. Unfortunately, a clear link between low SES, poor health and obesity was also recognized [41], making it a double priority in terms of the need for effective public health interventions and more broader political, economic and societal interventions against inequalities. In this context, the MD and the overall Mediterranean lifestyle could lend itself "as the most appropriate regime for disease prevention, a sort of complete lifestyle plan for the pursuit of healthcare sustainability" [41]. Indeed, it was consistently shown that people more adherent to the MD had more favorable anthropometric indicators. For example, a large cohort study with a mean of 12 years of follow-up showed that people with high adherence to the MD had a lower risk of becoming overweight/obese, experienced lesser 5-year change in waist circumference, and had lower 5-year weight change in the case of normal weight at baseline [42]. Additionally, MD was found to be more effective in long-term weight loss (over two years of follow-up) in patients with metabolic syndrome than a prudent control diet [43]. It was also found that in older Mediterranean individuals with excess weight, those subjects who desired higher weight loss actually had lower adherence to the MD and higher prevalence of obesity [44]. Hence, MD could serve as a good model for both keeping weight stable across life, and for sustainable weight loss [45].

There is a paucity of studies investigating the trend in adherence to the MD in Croatia. In general, based on geographical location and cultural heritage, the population of the Adriatic region of Croatia is adherent to the MD and the Mediterranean lifestyle [46]. Additionally, Croatia was one of the countries that supported in the inclusion of MD on the UNESCO's Representative List of the Intangible Cultural Heritage of Humanity [47]. However, the role of different socio-economic characteristics in the MD pattern and BMI change in Croatia has been only marginally investigated. It was previously shown that a lower education level was associated with lower adherence to the MD in the population of southern Croatia, while the overall prevalence of adherence to the MD was also rather low [31]. On the other hand, Croatia is heavily encumbered with non-communicable diseases [48], and ranks high among the leading countries in Europe regarding the prevalence of overweight and obesity, with 58% of the adult population being affected [49]. This undesirable trend is present even in young children, with as many as 35.9% of 7–9 year-olds being overweight or obese [50]. Therefore, our aim was to estimate the temporal trend in adherence to the MD and the contribution of several socio-economic factors in the changing pattern of the MD and BMI in a follow-up study including a large sample from Dalmatia, Croatia.

2. Materials and Methods

2.1. Study Participants

This study included 4988 subjects, between 18 and 98 years old, from several settlements in Dalmatia, Croatia, upon their initial enrolment within the "10,001 Dalmatians" study [51], while the follow-up data were available for 1342 subjects. The main objective of the "10,001 Dalmatians" study was to explore genetic and environmental risk factors by creating a biobank in the isolated populations of the Adriatic islands.

Chronologically, the initial field study was performed during 2003 and 2004 on the Island of Vis (N = 1029). An additional 969 subjects were enrolled from the Island of Korčula in 2007 (the Town of Korčula and surrounding settlements), followed by 1012 subjects from the City of Split in 2008–2009. Finally, 857 subjects were included in 2013 from the villages of Smokvica and Čara, situated in the central part of the Island of Korčula, and 1121 subjects were included during 2014–2015 from the towns of Blato and Vela Luka on the western part of the Island of Korčula.

The initial population-based convenient sampling approach employed personal invitations by general practitioners, postal invitations, local media and support from other local stakeholders, namely local governments and priests. Only subjects older than 18 were eligible to participate in the study, without any other restrictions or exclusion criteria.

After being formally informed of the study objectives, subjects signed the informed consent before the enrolment.

The field-based follow-up data collection was performed in 2011 for the subjects from the Island of Vis (N = 482, response rate 46.8%, mean follow-up of 7.5 years). In 2013 we collected follow-up data for the subjects from the Town of Korčula who were initially included in 2007 (N = 366; 37.8%; mean follow-up of 5.3 years), and in 2012–2013 for the subjects from the City of Split (N = 494; 48.8%, mean follow-up of 4.4 years). The main reason for the different follow-up times between study sites is the use of an open cohort sampling approach; this inevitably led to a different amount of time that each participant could be followed for. Subjects from Smokvica, Čara, Blato and Vela Luka (N = 1978) were not included in the follow-up due to their initial inclusion in 2013–2015, after which no additional data collections were done within the "10,001 Dalmatians" study.

The study was approved by the Ethical Committee of the University of Split School of Medicine.

2.2. Data Collection and Measurements

Trained nurses and medical doctors performed anthropometric measurements and collected clinically relevant information using the standard operating procedures at the newly established study site in each location. Individual medical histories were taken, together with an extensive self-administered questionnaire (including demographic characteristics, detailed socioeconomic status, dietary habits, smoking habits, alcohol consumption, and physical activity). Elderly people and those with any disabilities were offered assistance during surveying by a team of nine trained surveyors.

Medical records or subjects' responses were used to extract relevant medical history information, including previous diagnoses and the usage of medications for hypertension, diabetes, coronary heart disease (CHD), cerebrovascular insult (CVI), cancer, bipolar disorder, hyperlipidemia and gout.

2.3. Socioeconomic Status

Socioeconomic status was assessed during the initial data collection using three determinants: education, subjective material status, and objective material status. Education was categorized into three groups in order to correspond to the Croatian educational system [52]. The three groups were constructed according to the number of completed years of schooling, which corresponded to primary education ($\leq$8 years of schooling), secondary (high school level with 9–12 years of schooling), and higher education ($\geq$13 years). Only 17 subjects reported being students during the initial data collection, and they were automatically included in the higher education group of education.

Subjective material status was assessed based on the participant's perception of her/his material status in comparison to other people in their community. Possible responses on this question were 'much worse than the average', 'somewhat worse than the average', 'the same as others', 'better than the average', 'much better than the average'. These responses were grouped into three categories for easier interpretation: worse than average (responses 'much worse than average' and 'somewhat worse than average'), average ('the same as others'), and better than average (including answers 'better than average' and 'much better than average').

Assessment of objective material status was obtained based on the possession of 16 material items or goods, including heating system, wooden floors, video/DVD recorder, telephone, computer, two TVs, freezer, dishwasher, water supply system, flushing toilet, bathroom, library with more than 100 books, paintings or other art, a car, vacation house or second apartment, and boat, as in our previous study [53]. The sum of those items in the subject's possession indicated the wealth of the subject. Based on the distribution of these wealth scores, quartiles of objective material status were formed: the first quartile with values $\leq$ 8, second quartile with 9–10, third quartile with 11–12, and fourth quartile with values 13–16, as in our previous study [52].

Formal income was not taken into account due to the long period of observation included in this study (from 2003–2015), during which many economic and social changes happened in Croatia, including the financial crisis of 2007–2008. In order to take this into account in our analysis, we have introduced the variable for the recession period (before/after), denoting it as having started in our target population after 2008 (and including subsequent years).

2.4. Mediterranean Diet Assessment

Assessment of the Mediterranean dietary pattern was based on the food frequency questionnaire (FFQ), which was adjusted for application in the population of Dalmatia. There were 55 questions on commonly consumed foods, with 6 possible responses (every day, 2–3 times a week, once a week, once a month, rarely, and never), investigating the frequency of consumption of olive oil and other fats, milk and dairy products, vegetables, fruits, nuts, legumes, various meats, fish and sea foods, eggs, sweets, potatoes, rice, pasta, and bread [31,52]. Mediterranean diet adherence was assessed using the Mediterranean Diet Serving Score (MDSS), which incorporates 14 typical food groups representing the modern MD pyramid: fruit, vegetables, cereals, potatoes, olive oil, nuts, dairy products, legumes, eggs, fish, white meat, red meat, sweets, and fermented beverages—namely wine [54]. MDSS and adherence to the MD were calculated as described previously [31,52], and subjects were classified as adherent to the MD in case they had reached ≥14 points (the range was 0–24 points, with no negative points). MDSS requires a daily intake of vegetables, fruit, olive oil, and cereals (intake of each group is awarded with three points for two or more servings a day). Daily intake is encouraged for nuts and dairy products (each group is awarded with two points for one or more servings a day), and for wine (one or two glasses per day, awarded with one point) [54]. The remaining food groups are awarded with one point. Namely, red meat and sweets should be among the less frequently eaten foods (two or less servings per week), while potatoes, legumes, eggs, fish, and white meat should be consumed weekly. This questionnaire was also validated for use in the Croatian population in the short form [55].

We have excluded 317 subjects from the analysis due to missing values in the FFQ and the inability to calculate the MDSS at baseline.

2.5. Lifestyle Characteristics

Besides diet and socioeconomic factors, we assessed other lifestyle indicators, such as smoking and physical activity. According to smoking status, we divided subjects into current smokers, ex-smokers (those who reported they ceased smoking more than a year ago), and those who had never smoked. Assessment of physical activity included activity during both the working part of the day and the leisure part of the day. Those subjects who reported hard intensity labour or other high-intensity activity during either part of the day were considered as intensively physically active. Subjects who reported moderate intensity of physical activity in either part of the day were considered moderately active, while all others reporting either sitting or light physical activity in both parts of the day were considered as having light physical activity.

Additionally, body mass index (BMI) was calculated using measured height and weight. BMI was divided into three categories, representing subjects with normal body weight (from 18.5 to 24.9 kg/m^2), overweight (25.0 to 29.9 kg/m^2), and obese subjects (≥30.00 kg/m^2).

2.6. Statistical Analysis

All categorical variables were described using absolute numbers and percentages. All numerical variables were described using median and interquartile range (IQR), due to non-normal distribution, which was tested using the Kolmogorov–Smirnov test. The χ^2 test was used to examine the differences between groups for categorical variables and Kruskal–Wallis for numerical variables. We additionally investigated the differences between included subgroups; Mann–Whitney U test was used for pairwise comparison of numerical variables and χ^2 for categorical variables.

Univariate and multivariate logistic regression analysis (enter method) were used to assess the association between three SES characteristics (education level, subjective material status, objective material status) and overall adherence to the MD (MDSS $\geq$ 14 points) at baseline. Additionally, multivariate logistic regression analysis was used for assessing predictors for adherence for each of the 14 MD food groups within the MDSS scoring system. All multivariate models included age, sex, place of residence, number of chronic diseases diagnosed previously, smoking, physical activity, and BMI as confounding factors. There were only 53 subjects in the baseline sample with BMI less than 18.5 kg/m^2, and we have excluded them from the regression analysis due to the small sample size of the group. Additionally, in order to control for the potential confounding effects of the recession of 2007–2008, we included a variable denoting the time period of data collection as being either before or after the recession period in all of the regression models. All of the included covariates were entered as categorical variables to enable easier interpretation of the results. Odds ratios (OR) and 95% confidence intervals (CI) were provided for both univariate and multivariate logistic regression models. Correlations between the three variables describing socioeconomic status were tested using the Spearman rank test, before using them together in logistic regression models; none of the Spearman's rho values were higher than 0.401.

Linear regression models were used to assess the association between absolute change in MDSS and BMI across the follow-up period with different subjects' characteristics. The main predictor variables were again the three SES characteristics (education level, subjective material status, and objective material status), and the models also included important confounding variables: age, follow-up time, sex, place of residence, number of chronic diseases diagnosed previously, smoking, physical activity, BMI at baseline, and MDSS at baseline. Additionally, the model with BMI change during the follow-up as an outcome variable also included the MDSS absolute change during the follow-up as a covariate.

The change in the prevalence of the adherence to the MD and each of the MDSS food groups between baseline (t_0) and the follow-up time period (t_1) was assessed by calculating the percent change, using the following formula:

$$MD\ adherence\ (\%)_{change} = \frac{\text{MD adherence}(\%)_{t_1} - \text{MD adherence}(\%)_{t_0}}{\text{MD adherence}(\%)_{t_0}} * 100, \quad (1)$$

Additionally, the absolute change in MDSS score and BMI between baseline (t_0) and the follow-up time period (t_1) was calculated using the following formulas:

$$MDSS_{change} = \text{MDSS}_{t_1} - \text{MDSS}_{t_0} \quad (2)$$

$$BMI_{change} = \text{BMI}_{t_1} - \text{BMI}_{t_0} \quad (3)$$

The Wilcoxon signed-rank test and McNemar test were used to compare the differences between paired data for repeated measurements (baseline vs. follow-up).

The significance level was set at $p < 0.05$. All statistical analyses were carried out using IBM SPSS Statistics v21 (IBM, Armonk, NY, USA).

3. Results

The analysis included 4671 subjects in total (Table 1). Subjects from the Island of Vis were on average older, less educated, and had the highest average BMI (median of 27.08; IQR 6.05). The median MD adherence score (MDSS) was the lowest in subjects from the Island of Korcula (11 out of 24 points; IQR 6), and it was slightly higher in both subjects from the City of Split and the Island of Vis (median 12; IQR 5). Significant differences in median MDSS score were also recorded between settlements and according to age groups (Table 1). A wide range of adherence to MDSS components was present, ranging from as low as 2.7% for nuts in subjects from Vis, and up to 97.4% adherence for cereals in the same group (Table 1).

Table 1. Demographic characteristics and adherence to the MD (14 food components and overall adherence expressed as MDSS ≥ 14 points), according to the place of residence in a total sample of 4671 subjects.

	Island of Vis N = 1012	Island of Korčula N = 2651	City of Split N = 1008	Overall *p* (Pairwise Comparison *p* Values)
Sex; *n* (%)				
Men	423 (41.8)	967 (36.5)	391 (38.8)	0.011 (0.003 V-K, 0.168 V-S, 0.196 K-S)
Women	589 (58.2)	1684 (63.5)	617 (61.2)	
Age (years); median (IQR)	56.00 (24.00)	55.00 (23.25)	52.00 (21.00)	<0.001 (<0.001 V-K, <0.001 V-S, <0.001 K-S)
Education (years of schooling); median (IQR)	11.00 (4.00)	12.00 (3.00)	12.00 (4.00)	<0.001 (<0.001 V-K, <0.001 V-S, <0.001 K-S)
Subjective material status; median (IQR)	3.00 (0.00)	3.00 (1.00)	3.00 (1.00)	<0.001 (<0.001 V-K, <0.001 V-S, <0.001 K-S)
Objective material status; median (IQR)	10.00 (5.00)	10.00 (3.00)	12.00 (3.00)	<0.001 (<0.001 V-K, <0.001 V-S, <0.001 K-S)
Body mass index (kg/m^2); median (IQR)	27.08 (6.05)	24.59 (5.94)	26.60 (5.63)	<0.001 (<0.001 V-K, 0.024 V-S, <0.001 K-S)
Chronic diseases *; *n* (%)				
None	542 (53.6)	1565 (59.0)	677 (67.2)	<0.001 (0.011 V-K, <0.001 V-S, <0.001 K-S)
1	289 (28.6)	677 (25.5)	248 (24.6)	
≥2	181 (17.9)	409 (15.4)	83 (8.2)	
Smoking (pack years); median (IQR)	0.00 (10.00)	0.00 (3.00)	0.00 (3.00)	0.004 (0.002 V-K, 0.007 V-S, 0.804 K-S)
Smoking; *n* (%)				
current smokers	288 (28.5)	741 (28.0)	266 (26.5)	<0.001 (0.001 V-K, 0.105 V-S, 0.005 K-S)
ex-smokers	303 (30.0)	584 (22.2)	275 (27.4)	
never-smokers	419 (41.5)	1306 (49.6)	464 (46.2)	
Physical activity; *n* (%)				
light	264 (26.2)	537 (20.5)	358 (35.6)	<0.001 (<0.001 V-K, <0.001 V-S, <0.001 K-S)
moderate	580 (57.5)	1815 (69.2)	610 (60.7)	
intensive	164 (16.3)	271 (10.3)	37 (3.7)	
MDSS; median (IQR)	12.00 (5.00)	11.00 (6.00)	12.00 (5.00)	<0.001 (<0.001 V-K, 0.554 V-S, 0.001 K-S)
MDSS according to age group; median (IQR)				
18.0–34.9	10.00 (5.00)	9.00 (5.00)	10.00 (5.00)	0.009 (0.004 V-K, 0.225 V-S, 0.068 K-S)
35.0–64.9	12.00 (5.00)	11.00 (6.00)	12.00 (5.00)	0.001 (0.004 V-K, 0.982 V-S, 0.003 K-S)
≥65.0	12.00 (5.00)	12.00 (6.00)	13.00 (5.00)	<0.001 (0.009 V-K, <0.001 V-S, <0.001 K-S)

Table 1. *Cont.*

	Island of Vis N = 1012	Island of Korčula N = 2651	City of Split N = 1008	Overall p (Pairwise Comparison p Values)
MDSS components adherence; n (%)				
fruit	596 (58.9)	1399 (52.8)	636 (63.1)	<0.001 (0.001 $^{V\text{-}K}$, 0.053 $^{V\text{-}S}$, <0.001 $^{K\text{-}S}$)
vegetables	439 (43.4)	980 (37.0)	418 (41.5)	0.001 (<0.001 $^{V\text{-}K}$, 0.385 $^{V\text{-}S}$, 0.012 $^{K\text{-}S}$)
cereals	986 (97.4)	2367 (89.3)	929 (92.2)	<0.001 (<0.001 $^{V\text{-}K}$, <0.001 $^{V\text{-}S}$, 0.009 $^{K\text{-}S}$)
olive oil	586 (57.9)	1835 (69.2)	643 (63.8)	<0.001 (<0.001 $^{V\text{-}K}$, 0.007 $^{V\text{-}S}$, 0.002 $^{K\text{-}S}$)
nuts	27 (2.7)	117 (4.4)	71 (7.0)	<0.001 (0.015 $^{V\text{-}K}$, <0.001 $^{V\text{-}S}$, 0.001 $^{K\text{-}S}$)
dairy products	256 (25.3)	592 (22.3)	270 (26.8)	0.010 (0.057 $^{V\text{-}K}$, 0.446 $^{V\text{-}S}$, 0.005 $^{K\text{-}S}$)
potatoes	686 (67.8)	1774 (66.9)	823 (81.6)	<0.001 (0.617 $^{V\text{-}K}$, <0.001 $^{V\text{-}S}$, <0.001 $^{K\text{-}S}$)
legumes	326 (32.2)	714 (26.9)	252 (25.0)	0.001 (0.002 $^{V\text{-}K}$, <0.001 $^{V\text{-}S}$, 0.236 $^{K\text{-}S}$)
eggs	297 (29.3)	662 (25.0)	246 (24.4)	0.013 (0.007 $^{V\text{-}K}$, 0.012 $^{V\text{-}S}$, 0.723 $^{K\text{-}S}$)
fish	838 (82.8)	1769 (66.7)	692 (68.7)	<0.001 (<0.001 $^{V\text{-}K}$, <0.001 $^{V\text{-}S}$, 0.269 $^{K\text{-}S}$)
white meat	499 (49.3)	1077 (40.6)	381 (37.8)	<0.001 (<0.001 $^{V\text{-}K}$, <0.001 $^{V\text{-}S}$, 0.118 $^{K\text{-}S}$)
red meat	261 (25.8)	700 (26.4)	248 (24.6)	0.537 (0.705 $^{V\text{-}K}$, 0.539 $^{V\text{-}S}$, 0.266 $^{K\text{-}S}$)
sweets	181 (17.9)	808 (30.5)	168 (16.7)	<0.001 (<0.001 $^{V\text{-}K}$, 0.469 $^{V\text{-}S}$, <0.001 $^{K\text{-}S}$)
wine	204 (20.2)	459 (17.3)	177 (17.6)	0.124 (0.046 $^{V\text{-}K}$, 0.136 $^{V\text{-}S}$, 0.861 $^{K\text{-}S}$)
Adherence to the MD (MDSS $\geq$ 14 points); n (%)	315 (31.1)	711 (26.8)	306 (30.4)	0.012 (0.009 $^{V\text{-}K}$, 0.708 $^{V\text{-}S}$, 0.033 $^{K\text{-}S}$)
Adherence to the MD according to age group (MDSS $\geq$ 14 points); n (%)				0.012 (0.026 $^{V\text{-}K}$, 0.745 $^{V\text{-}S}$, 0.070 $^{K\text{-}S}$)
18.0–34.9 years	22 (20.0)	49 (12.3)	26 (14.8)	
35.0–64.9 years	158 (29.3)	393 (25.4)	203 (30.5)	
$\geq$65.0 years	135 (37.2)	269 (38.4)	77 (46.1)	

IQR—interquartile range; MDSS—Mediterranean Diet Serving Score; MD—Mediterranean diet; p values for categorical variables were obtained with the chi-squared test, and for numerical variables with the Kruskal–Wallis test. Pairwise comparison p values for categorical variables were obtained with the chi-squared test, and for numerical variables with Mann–Whitney U test. * chronic diseases included any or more than one of the following diagnoses: hypertension, diabetes, CHD, CVI, cancer, bipolar disorder, hyperlipidemia and gout. $^{V\text{-}K}$ Pairwise comparison p value: Island of Vis vs. Island of Korčula. $^{V\text{-}S}$ Pairwise comparison p value: Island of Vis vs. City of Split. $^{K\text{-}S}$ Pairwise comparison p value: Island of Korčula vs. City of Split.

Less than half of all of the subjects were compliant with the daily requirement for vegetable intake (lowest on Korčula; 37.0%), while it was a little better for intake of fruit (lowest on Korčula; 52.8%), and olive oil (lowest on Vis; 57.9%). Only 22.3% of subjects from the Island of Korčula, 25.3% from the Island of Vis and 26.8% from the City of Split adhered to the daily dairy products consumption requirement, which was similar for wine (17.3–20.2%). Consistently, the best adherence was recorded for cereals, and the lowest for nuts (Table 1). A total of 1332 subjects (28.5%) were considered as being adherent to the MD pattern in the overall sample. The lowest prevalence was recorded for subjects from the Island of Korčula (26.8%), followed by those from the City of Split (30.4%), and the Island of Vis (31.1%). There was a significant difference in the prevalence of adherence to the MD according to age groups and place of residence, and a significant result was obtained for the comparison between subjects from Vis and Korčula (p = 0.026; Table 1).

Logistic regression analysis revealed several characteristics that were strongly associated with adherence to the MD throughout the entire sample (Table 2). Women presented higher odds of adherence compared to men (OR = 1.85, 95% CI 1.58–2.17, p < 0.001), while the oldest age group had 3.81-fold higher odds of adherence compared to the youngest subjects (95% CI 2.83–5.12, p < 0.001; Table 2). In the fully adjusted model, subjects from the Island of Korčula presented with higher odds of adherence compared to the subjects from the City of Split (OR = 1.63, 95% CI 1.31–2.102, p < 0.001). Education level and subjective material status were not associated with adherence to the MD in the adjusted model, unlike objective material status. The wealthiest subjects according to the objective material status (those in the fourth quartile of distribution) were almost twice as likely to be adherent to the MD, compared to subjects in the lowest quartile (OR = 1.93, 95% CI 1.53–2.43, p < 0.001). Subjects in the second and third quartile of objective material status also had greater odds of being adherent to the MD (Table 2).

Table 2. Characteristics associated with adherence to the MD (MDSS ≥ 14 points) in the total sample (N = 4671), as determined by the logistic regression analysis.

	Unadjusted Odds Ratio (95% Confidence Interval); *p*	**Adjusted Odds Ratio (95% Confidence Interval); *p***
Sex		
Male; Ref.	1.00	1.00
Female	1.60 (1.39, 1.83); <0.001	1.85 (1.58, 2.17); <0.001
Age group		
18–34.9; Ref.	1.00	1.00
35–64.9	2.29 (1.82, 2.88); <0.001	1.99 (1.54, 2.57); <0.001
≥65.0	3.89 (3.05, 4.97); <0.001	3.81 (2.83, 5.12); <0.001
Place of residence		
City of Split; Ref.	1.00	1.00
Island of Vis	1.04 (0.86, 1.25); 0.708	1.04 (0.84, 1.29); 0.696
Island of Korčula	0.84 (0.72, 0.99); 0.033	1.63 (1.31, 2.02); <0.001
Education (Years of schooling)		
elementary (0–8); Ref.	1.00	1.00
high school (9–12)	0.69 (0.78, 0.80); <0.001	0.93 (0.77, 1.14); 0.492
higher (13+)	0.94 (0.79, 1.12); 0.494	1.19 (0.95, 1.5); 0.130
Subjective material status		
worse than average; Ref.	1.00	1.00
average	1.13 (0.92, 1.39); 0.250	1.14 (0.91, 1.44); 0.258
better than average	1.28 (1.03, 1.61); 0.028	1.16 (0.89, 1.51); 0.267

Table 2. *Cont.*

	Unadjusted Odds Ratio (95% Confidence Interval); *p*	Adjusted Odds Ratio (95% Confidence Interval); *p*
Objective material status		
1st quartile; Ref.	1.00	1.00
2nd quartile	1.12 (0.94, 1.35); 0.216	1.38 (1.12, 1.70); 0.002
3rd quartile	0.98 (0.82, 1.17); 0.791	1.29 (1.04, 1.61); 0.020
4th quartile	1.52 (1.27, 1.83); <0.001	1.93 (1.53, 2.43); <0.001
Chronic diseases *		
≥2; Ref.	1.00	1.00
1	0.85 (0.69, 1.04); 0.107	0.93 (0.75, 1.17); 0.546
none	0.69 (0.57, 0.82); <0.001	0.93 (0.75, 1.16); 0.507
Smoking		
current smokers; Ref.	1.00	1.00
ex-smokers	1.70 (1.41, 2.03); <0.001	1.40 (1.14, 1.71); 0.001
never-smokers	1.75 (1.49, 2.06); <0.001	1.36 (1.13, 1.63); 0.001
Physical activity		
light; Ref.	1.00	1.00
moderate	1.24 (1.07, 1.45); 0.005	1.44 (1.21, 1.70); <0.001
intensive	1.16 (0.91, 1.48); 0.222	1.50 (1.15, 1.97); 0.003
Body mass index category #		
18.0–24.9 (kg/m^2); Ref.	1.00	1.00
25.0–29.9 (kg/m^2)	0.92 (0.79, 1.05); 0.218	0.98 (0.83, 1.16); 0.834
≥30.0 (kg/m^2)	0.79 (0.66, 0.95); 0.013	0.84 (0.68, 1.05); 0.123
The economic crisis of 2007–2008		
before; Ref.	1.00	1.00
after	0.40 (0.35, 0.46); <0.001	0.31 (0.25, 0.38); <0.001

Adjusted odds ratios, 95% confidence intervals and *p* values were calculated using a multivariate logistic regression model simultaneously adjusted for all the covariates listed in this table (enter method). * chronic diseases included any or more than one of the following diagnoses: hypertension, diabetes, CHD, CVI, cancer, bipolar disorder, hyperlipidemia and gout; # 53 subjects with BMI < 18.5 kg/m^2 were excluded from the analysis due to small sample size of the group and negative impact on the model performance.

Subjects who never smoked and ex-smokers presented with higher odds of adherence to the MD, compared to current smokers (OR = 1.36, 95% CI 1.13–1.63, $p = 0.001$; OR = 1.40, 95% CI 1.14–1.71, $p = 0.001$, respectively). Subjects with higher levels of physical activity were also more likely to be adherent to the MD (Table 2). BMI and diagnosis of chronic diseases were not associated with adherence to the MD. The study period was statistically significantly associated with adherence to the MD, in a way that MD adherence was less likely in the period after the recession (OR = 0.31, 95% CI 0.25–0.38, $p < 0.001$; Table 2).

The fully adjusted regression model yielded a good data fit (Hosmer and Lemeshow $p = 0.304$; Nagelkerke R2 = 0.100).

Determinants of adherence to MD food components are shown in Supplemental Table S1. Women were more likely to be adherent to the recommended intake of fruit, vegetables, olive oil, nuts, diary, and red meat, but they were less likely to be adherent to the eggs and wine intake MD recommendations compared to men (women most commonly abstained from alcohol intake). Older subjects had higher odds for meeting the recommendations for fruit, vegetables, cereals, olive oil, nuts, fish, red meat, sweets, and wine intake, but lower odds for potatoes and eggs adherence compared to the youngest group of subjects. The highest level of education was associated with lesser adherence to the MD guidelines for intake of cereals, olive oil, legumes, fish, and white meat, in contrast to a higher adherence to appropriate intake of dairy products, potatoes and red meat compared to subjects with the lowest level of education (Supplemental Table S1). Subjective material status was less associated with MD food components intake, unlike the objective material status.

Compared to subjects in the lowest quartile of objective material status, subjects belonging to higher quartiles presented with an increasing trend of compliance with fruit, vegetables, olive oil, and fish intake recommendations, but also with a decreasing compliance for the intake of red meat and sweets (Supplemental Table S1).

Obese subjects (BMI 30 $\geq$ kg/m^2) were 34% more likely to adhere to recommendations for sweets, but also 30% less likely to adhere to recommendations for cereals intake, and 42% less adherent for nuts.

The study period after the recession was associated with 68% decreased odds for adherence to vegetables intake recommendations, 55% decreased odds for cereals adherence, 50% for fruit, 49% for fish, 47% for legumes, 36% for dairy products, 31% for potatoes, and 29% decreased odds for adherence to olive oil intake. On the other hand, we recorded 39% increased odds for adherence to red meat and 23% increased adherence to sweets intake recommendation after recession (Supplemental Table S1).

In order to assess the change in Mediterranean diet compliance over time, 1342 subjects were included in the follow-up study. A breakdown by four quartiles of the objective material status demonstrated significant changes in adherence for several MD food groups across the follow-up period (Figure 1). A distinct pattern of change was recorded, with the most prominent and significant decrease in adherence to the recommended intake of vegetables, followed by a decrease in fish and cereals recommended intake across all quartiles of objective material status (Figure 1). On the other hand, a significant increase in adherence for nuts was reported across all quartiles of material status (corresponding to increased intake), followed by an increase in sweets, potatoes and red meat (decreased intake), wine, legumes, and eggs adherence (increased intake). The exception was adherence to wine, legumes, and eggs recommendations in subjects within the lowest quartile of the objective material status, where these results were not significant. Based on such diverse results in individual MDSS food groups, the overall change in adherence to the MD was insignificant in all of the quartiles of objective material status (Figure 1). A similar result was obtained in the total group of subjects included in the follow-up, with a borderline insignificant decrease in adherence to the MD (by 8.5%; from 36.6% of adherent subjects at study baseline, to 33.5% in the follow-up; p = 0.056; Table 3). Furthermore, the highest overall increase in adherence was recorded for nuts (127.5%), and sweets (112.6%), followed by red meat (56.4%), and wine (50.0%). On the other hand, the most significant decrease in adherence was recorded for vegetables (−35.1%), followed by fish (−23.4%), white meat (−11.6%), cereals (−10.9%), and dairy products (−9.6%). At the same time, the average BMI had increased from 25.76 kg/m^2 at baseline of the study to 27.44 kg/m^2 at the follow-up time period (p < 0.001).

Linear regression analysis revealed several variables that were significantly associated with the MDSS change during the follow-up period (Table 4). MDSS change was positively associated with female gender (β = 0.41; 95% CI 0.00–0.83; p = 0.049), age (β = 0.05; 95% CI 0.03–0.06); p < 0.001), highest level of education (β = 0.71; 95% CI 0.07–1.36; p = 0.031), and with moderate physical activity (β = 0.72; 95% CI 0.27–1.16; p = 0.002). MDSS at baseline displayed a negative association with the MDSS change (β = −0.64; 95% CI −0.70–−0.58; p < 0.001), while BMI at baseline, smoking, chronic diseases, place of residence, objective and subjective material status were not associated with the absolute change in the Mediterranean Diet Serving Score. The regression model yielded a good data fit (Durbin–Watson = 1.994; Adjusted R2 = 0.280).

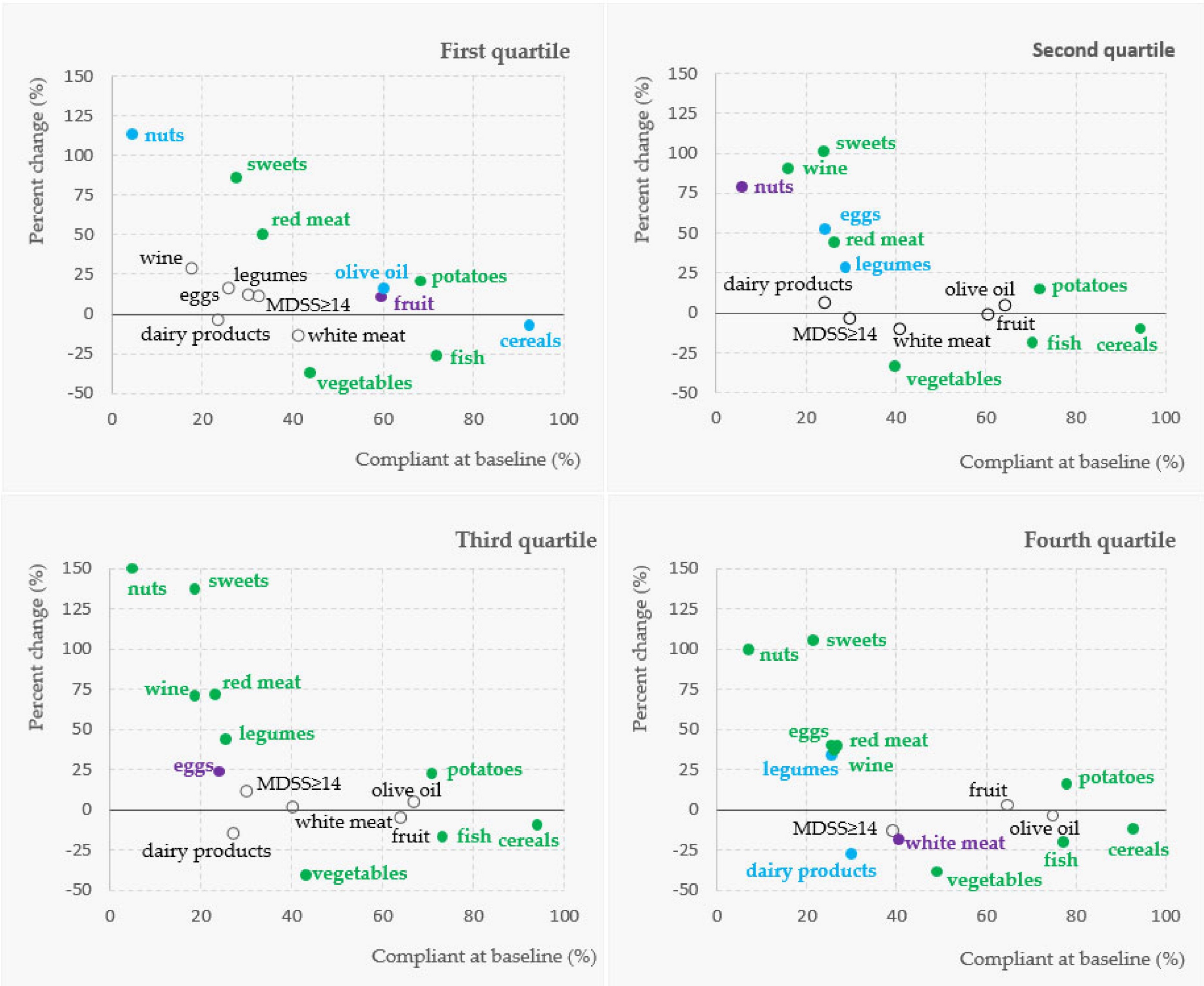

Figure 1. Change in adherence to the MD food components and the overall MD (MDSS $\geq$ 14 points), expressed as a percentage change from baseline to the follow-up, according to the objective material status category. Significant results at the level of $p < 0.05$ are denoted with the full circle (green < 0.001, blue < 0.01, purple < 0.05, McNemar test).

Table 3. Adherence to 14 MD food groups and the overall MD (MDSS $\geq$ 14 points) at baseline and at the follow-up (N = 1342; 366 subjects from Korčula, 494 from Split, and 482 subjects from Vis).

		Baseline N = 1342	**Follow Up N = 1342**	**Percent Change (%)**	***p***
Sex; *n* (%)					
	men	503 (37.5)	-	-	-
	women	839 (62.5)			
Age (years); median (IQR)		55.00 (18.00)	62.01 (16.96)	-	-
Age group; *n* (%)					
	18.0–34.99	127 (9.5)	58 (4.3)	-	-
	35.0–64.99	926 (69.0)	724 (53.9)		
	65+	289 (21.5)	560 (41.7)		
Body mass index (kg/m^2); median (IQR)		25.76 (5.74)	27.44 (5.06)	6.5	<0.001
Adherence to the MD (MDSS $\geq$ 14 points); *n* (%)		491 (36.6)	449 (33.5)	−8.5	0.056

Table 3. *Cont.*

	Baseline N = 1342	Follow Up N = 1342	Percent Change (%)	*p*
MDSS components adherence; *n* (%)				
fruit	868 (64.7)	848 (63.2)	−2.3	0.341
vegetables	643 (47.9)	417 (31.1)	−35.1	<0.001
cereals	1277 (95.2)	1138 (84.8)	−10.9	<0.001
potatoes	985 (73.4)	1183 (88.2)	20.2	<0.001
olive oil	893 (66.5)	927 (69.1)	3.9	0.112
nuts	68 (5.1)	156 (11.6)	127.5	<0.001
dairy products	356 (26.5)	309 (23.0)	−9.6	0.030
legumes	400 (29.8)	457 (34.1)	14.4	0.011
eggs	339 (25.3)	405 (30.2)	19.4	0.002
fish	1036 (77.2)	793 (59.1)	−23.4	<0.001
white meat	556 (41.4)	487 (36.3)	−11.6	0.005
red meat	347 (25.9)	544 (40.5)	56.4	<0.001
sweets	276 (20.6)	588 (43.8)	112.6	<0.001
wine	268 (20.0)	403 (30.0)	50.0	<0.001

MDSS—Mediterranean Diet Serving Score. MD—Mediterranean Diet. *p* values for categorical variables were obtained using McNemar test and for numerical using Wilcoxon Signed-Ranks Test.

Table 4. Characteristics associated with the absolute change in the Mediterranean Diet Serving Score (MDSS) and the BMI across the follow-up period, as determined by the linear regression model (sample size is 1342 subjects; all independent variables were included in the model simultaneously).

	MDSS Change during Follow-Up Beta (95% Confidence Interval); *p*	BMI Change during Follow-Up Beta (95% Confidence Interval); *p*
Sex		
Male; Ref.	1.00	1.00
Female	0.41 (0.00, 0.83); 0.049	0.33 (0.06, 0.60); 0.016
Age at baseline (years)	0.05 (0.03, 0.06); <0.001	−0.01 (−0.02, 0.00); 0.192
Follow up time (years)	0.03 (−0.09, 0.16); 0.571	−0.07 (−0.15, 0.01); 0.099
Place of residence		
City of Split; Ref.	1.00	1.00
Island of Vis	0.28 (−0.75, 1.32); 0.590	0.86 (0.18, 1.54); 0.013
Island of Korčula	0.00 (−0.81, 0.81); 0.992	3.68 (3.15, 4.21); <0.001
Education (years of schooling)		
elementary (0–8); Ref.	1.00	1.00
high school (9–12)	−0.11 (−0.67, 0.46); 0.708	−0.05 (−0.42, 0.32); 0.799
higher (13+)	0.71 (0.07, 1.36); 0.031	0.06 (−0.36, 0.48); 0.769
Subjective material status		
worse than average; Ref.	1.00	1.00
average	0.05 (−0.59, 0.69); 0.872	0.15 (−0.26, 0.57); 0.468
better than average	−0.01 (−0.72, 0.71); 0.982	0.11 (−0.36, 0.57); 0.655
Objective material status		
1st quartile; Ref.	1.00	1.00
2nd quartile	−0.14 (−0.71, 0.43); −0.637	0.07 (−0.30, 0.44); 0.724
3rd quartile	0.02 (−0.56, 0.59); 0.955	0.06 (−0.31, 0.44); 0.733
4th quartile	−0.06 (−0.68, 0.56); 0.859	0.02 (−0.38, 0.42); 0.921

Table 4. *Cont.*

	MDSS Change during Follow-Up Beta (95% Confidence Interval); *p*	BMI Change during Follow-Up Beta (95% Confidence Interval); *p*
Chronic diseases *		
≥2; Ref.	1.00	1.00
1	−0.23 (−0.91, 0.44); 0.497	0.24 (−0.19, 0.68); 0.276
none	−0.02 (−0.68, 0.64); 0.946	0.26 (−0.17, 0.69); 0.240
Smoking		
current smokers; Ref.	1.00	1.00
ex-smokers	−0.20 (−0.74, 0.34); 0.468	−0.07 (−0.42, 0.28); 0.707
never-smokers	0.12 (−0.38, 0.62); 0.632	0.02 (−0.31, 0.34); 0.909
Physical activity		
light; Ref.	1.00	1.00
moderate	0.72 (0.27, 1.16); 0.002	−0.02 (−0.31, 0.27); 0.887
intensive	0.69 (−0.02, 1.40); 0.057	0.23 (−0.24, 0.70); 0.331
BMI at baseline (kg/m^2)	−0.03 (−0.09, 0.02); 0.188	−0.11 (−0.14, −0.07); <0.001
MDSS at baseline	−0.64 (−0.70, −0.58); <0.001	−0.07 (−0.12, −0.03); 0.001
MDSS change during follow-up	-	−0.04 (−0.07, 0.00); 0.041

* Chronic diseases included any or more than one of the following diagnoses: hypertension, diabetes, CHD, CVI, cancer, bipolar disorder, hyperlipidemia and gout. MDSS—Mediterranean Diet Serving Score.

BMI change during the follow-up period was significantly associated with female gender, place of residence, BMI at baseline, MDSS at baseline and MDSS absolute change (Table 4). Women experienced higher odds for BMI increase compared to men (β = 0.33; 95% CI 0.06–0.60; p = 0.016), the same as subjects from the Island of Vis and Korčula compared to subjects from the City of Split (β = 0.86; 95% CI 0.18–1.54; p = 0.013, and β = 3.68; 95% CI 3.15–4.21; $p < 0.001$, respectively). BMI at baseline, MDSS at baseline, and MDSS change during the follow-up were all significantly negatively associated with the BMI change (β = −0.11; 95% CI −0.14–−0.07; $p < 0.001$, β = −0.07; 95% CI −0.12–−0.03; p = 0.001, β = −0.04; 95% CI −0.07–0.00; p = 0.041, respectively), while none of the socio-economic characteristics were associated with absolute BMI change. The regression model yielded good data fit (Durbin–Watson = 1.972; Adjusted R2 = 0.354).

4. Discussion

Our results demonstrated a rather low prevalence of adherence to the MD over the entire sample (28.5%), especially among younger individuals (14.0%). Subjects included in the follow-up had a higher adherence to the MD at baseline (36.6%), with a borderline insignificant decline at the end of the follow-up period (33.5%). On the other hand, BMI had increased on average by 6.5% in subjects available for follow-up.

Our result for MD prevalence was within the expected range, compared to the results from other Mediterranean countries and from Croatia. For example, findings from the literature vary anywhere between 14% of adherent people in Northern Italy [56] to 45% in Balearic Islands [57]. Our current study identified a slightly higher prevalence of adherence to the MD compared to our previous results, when we identified 23% of subjects as adherent to the MD [31]. This difference is due to a smaller sample and different period included in the previous study [31].

Unfortunately, many Mediterranean societies are moving away from their traditional dietary pattern, while some countries in Northern Europe and around the world are adopting a Mediterranean-like dietary pattern [25]. For example, previous studies have indicated a persistent moderate-to-weak adherence to the MD across several southern European countries, including Spain, Portugal, Italy, Greece, and Cyprus [58]. Some variations can be expected, probably due to the applied methodological framework and different instruments used for assessing adherence to the MD [55]. For example, one study from Spain showed a poor level of adherence to the MD in the general population and specific areas of Spain [59], while another one showed moderate adherence [60]. Nevertheless, deflection from a traditional MD diet and lifestyle represents a lost opportunity, not only from the perspective of achieving less-than-ideal individual and population health, but also from the perspective of environmental protection, possible degradation of sociocultural food values, and loss of positive local economic returns [61]. Additionally, a higher prevalence of adherence to the MD in the population can also serve as a safeguard from consumption of ultra-processed foods [62]. This was shown even in very young children from Spain, whose adherence to the traditional MD was inversely associated with energy intake from ultra-processed foods [63].

Previous studies have demonstrated that individual and contextual socio-economic factors are strong determinants of dietary habits and that poorer socio-economic groups are less likely to follow a healthy lifestyle [64]. On the other hand, social position in terms of education, occupational class, and income level represents a good predictor for healthy eating behavior [65,66]. People with a higher educational status have been shown to have a healthier consumption pattern [67]. Higher educational status was also associated with better nutritional intakes in lower GDP countries, while lower-income countries and lower education groups had poorer diets, particularly in terms of micronutrients intake [40].

The current economic and social European context—the increasing crisis, lack of jobs, various challenges due to the COVID-19 pandemic and consequent fall in income associated with cost inflation—could make people inclined to save money in all possible ways. In this context, the most exposed are the disadvantaged groups because they prefer buying food at low prices that are often of low quality [68]. Foods of lower nutritional value and lower-quality diets generally cost less per calorie and tend to be selected by groups of lower socioeconomic status [69]. On the other hand, people with low socio-economic status do not obtain the same health outcomes as those with high socio-economic status, even if both groups follow the same eating pattern [70]. Concretely, high adherence to the MD was associated with cardiovascular protection in higher but not in lower socio-economic groups from Italy, with a similar result observed for both education level and household income groups [70].

In some European countries, it was demonstrated that socio-economic status could modulate adherence to the MD [71,72]. For example, in a study carried out in the adult population from the Balearic Islands, people with a higher educational and socio-economic level showed higher rates of adherence to the Mediterranean pattern [57]. On the other hand, adherence to the MD in the South of Italy was found to be at low levels due to poor knowledge on MD concerning its beneficial effects [73], whereas social status in France was important for healthy eating only through an interaction between level of education and area of residence [64]. A similar association between education and MD was observed in our previous study from Croatia, where less educated people had a reduced likelihood of being adherent to the MD [31]. On the other hand, our current study did not corroborate such a finding, probably due to the inclusion of additional socio-economic indicators in the analysis (subjective and objective material status). Hence, we have identified only a significant association between overall adherence to the MD and objective material status. Subjects reporting the highest objective material status (fourth quartile) demonstrated a 93% higher probability of adhering to the MD than those belonging to the first quartile of objective material status, with similar findings for subjects within the second and third quartile groups (38% and 29%, respectively). This was in line with previous results, where higher household income was positively associated with greater adherence to the MD [39,74].

Interestingly, subjects with a higher educational attainment had a greater probability for appropriate adherence to dairy products, potatoes, and red meat intake recommendations, but they exhibited lesser adherence to cereals, olive oil, legumes, fish, and white meat intake recommendations. This represents a considerable departure from the traditional MD pattern. For example, Biesbroek et al. revealed that people with low education consumed more potatoes, whereas highly educated people consumed more olive oil and fish [75]. Another study showed that highly educated people in Italy also consumed white meat slightly less than in the past [56], while Bonaccio et al. had a similar conclusion for the consumption of white meat, which was again opposite when it came to people with high educational status and consumption of olive oil and fish [70]. Similarly, higher educational status was shown to be positively associated with fish intake [76]. Other MD food components were equally consumed by all educational groups in our sample, as previously shown in another study by Bonaccio et al. [39].

In general, highly educated people have a higher income, and they tend to follow MD recommendations [66]. This could be explained by the fact that greater adherence to the Mediterranean diet was associated with higher dietary cost, which might represent a barrier to healthy eating [35]. For instance, in a study including a representative national sample of 3534 children and young people from Spain, researchers have found that high adherence to the MD was more expensive than low adherence by 0.71 Euros per day [37].

Interestingly, we failed to find any association between subjective material status and adherence to the MD, whereas objective material status presented as the most prominent socio-economic indicator for overall adherence to the MD and for several food groups. For example, subjects in the higher quartiles of material status had higher adherence to fruit, vegetables, olive oil, and fish intake recommendations, but also lower adherence to red meat and sweets intake. Interestingly, olive oil and fish intake had an opposing contribution of educational level and material status to their adherence, such that lower education and higher material status were both associated with greater adherence. This could be explained by the fact that older, less educated people from Dalmatia, especially from remote islands, still tend to produce their own olive oil, and they catch fish on their own, which could be behind their higher intake of these foods (statement based on personal communication with subjects included in the study).

Our results are largely in line with previous studies, which showed that female gender and non-smokers [77–79], older adults [77,80,81], and more physically active people displayed higher adherence to the MD pattern, while higher body mass index was generally associated with lower adherence to the MD [78–80,82]. Our results partially replicated such associations, as subjects with higher levels of physical activity had up to a 50% greater probability of being adherent to the MD in comparison to the ones with light activity, while BMI was not significantly associated with adherence to the MD in our overall sample. This is in contrast to some previous findings [72,83,84], but in line with some studies [85,86]. These differences between previous results are probably due to the employed study design (cross-sectional vs. longitudinal, observational vs. experimental design), and characteristics of included subjects (primarily age and health status), leaving the association between adherence to the MD and BMI a topic for further investigation and open discussion.

The effect of the economic crisis of 2007–2008 on the adherence to the MD was a topic of several previous studies. For instance, it was found that adherence to the MD was lower in subjects from Italy reporting a negative impact of the crisis on their diet [87]. Additionally, the prevalence of adherence to MD among southern Italian citizens enrolled within the Moli-sani study was 31.3% during the 2005–2006 period, which dramatically fell during 2007–2010 (18.3%), most strongly affecting elderly, less affluent people, and urban areas dwellers [88]. Our results also revealed decreased odds for adherence to different food groups, i.e., adherence odds for vegetables, cereals, fruit, fish, legumes, dairy products, potatoes, and olive oil. On the other hand, odds of adherence to red meat and sweets recommendations increased after the recession.

Similar findings were demonstrated in Portugal, where a significant decrease in consumption of fish, fruit and vegetables was recorded from 2005/2006 to 2014 [29]. A cross-sectional study from Greece showed that parents who reported that the financial crisis affected their food spending also reported lower consumption of fruits, carbohydrate foods, and legumes, and increased intake of nutrient-poor/energy-dense foods, while their children had reduced weekly consumption of vegetables and increased weekly consumption of nutrient-poor/energy-dense foods [89]. These and other recent evidence show a possible involvement of the economic crisis, and material resources as strong determinants of adherence to the MD in the period after the recession started [90], given that a direct positive association between the cost of the diet and adherence to the MD has been established [36]. However, it is hard to distinguish the contribution of recession due to the economic crisis from the impact of the steady process of westernization of traditional dietary habits, including MD. For instance, it was noted by FAO that "the Mediterranean region is passing through a 'nutritional transition' in which problems of undernutrition coexist with overweight, obesity and food related chronic diseases" [91]. For example, an ecological study of the changes in food patterns in Europe over the last 40 years revealed that the greatest changes have occurred in Mediterranean Europe [92]. For instance, an increase of 20% in total energy availability was noted, alongside with a 48% increase in energy availability from lipids, and 20% decrease from carbohydrates, with a significant fall in the energy supplied by cereals (30%) and wine (55%), while the contribution of milk and dairy products increased by 78% and 24%, respectively [92]. For example, it was estimated that the Spanish diet shifted away from the traditional MD, now containing three times more meat, dairy and sugar products, and a third fewer fruits, vegetables, and cereals [93]. In our sample available for follow-up, we have detected similar deviations. For example, to our great dismay, vegetables adherence was reduced by 35%, followed by a reduction in fish adherence by 23%, white meat by 12%, cereals by 11%, and dairy products by 10%, while fruit adherence was reduced by only 2%. However, we did record a few positive trends, such as an increase in adherence for nuts (128%), sweets (113%; denoting reduced intake), red meat (56%; also denoting reduced intake), and wine (50%). Overall, the adherence to the MD remained stable, which was probably a consequence of differences in specific MD food constituents.

As already mentioned, a continuous increase in red and processed meat has been observed over the last couple of decades, while fruit, cereals, and vegetable consumption has decreased in different countries [21,94,95]. Our findings are in line with these trends, except for red meat intake, for which compliance was improved. To our satisfaction, an improvement over time was also recorded for sweets adherence in our study, which was in contrast to the findings from Portugal, where sweets/desserts consumption was significantly higher in 2014 compared to 2005/2006 [29]. However, a similar decreased trend for sweets intake were observed in Northern Italy [56], and Norway, Sweden, and Finland [96]. A study conducted among adults in Lebanon showed a decrease in the consumption of bread, fruits, fresh fruit juices, milk and eggs, whereas the consumption of added fats and oils, poultry, cereals and cereal-based products, chips and salty crackers, sweetened milk and hot beverages increased over time [97]. These findings indicate slightly different, yet similar patterns of change in different populations. The important next step in any effort to improve dietary habits in communities is the identification of factors associated with such changes, in order to be able to implement targeted interventions. We have conducted such an analysis, which pointed to several characteristics associated with the change in adherence to the MD over time. Female gender, older age at baseline, the highest level of education, and a moderate level of physical activity were positively associated with MDSS change during follow-up in a multivariate model. On the other hand, the MDSS score at baseline was negatively associated with the MDSS change during the follow-up, indicating that people with a higher baseline adherence to the MD tended to recede over time, while those with lower adherence strived toward increasing adherence to the MD. These findings highlight a continuous change of dietary patterns in the population, requiring constant monitoring of trends and identification of the drivers of such change. This is relevant from the perspective of population health and delivery of adequate health care, as well as from the perspective of economic, social and cultural development.

The importance of a healthy lifestyle and healthy dietary habits came to the frontline of attention due to the COVID-19 pandemic. For example, preliminary findings from the ecological study showed that Mediterranean diet adherence was negatively associated with both COVID-19 cases and related deaths in Spain and 23 other OECD countries, which the authors attributed to the anti-inflammatory properties of the Mediterranean diet [98]. On the other hand, an unhealthy lifestyle and associated metabolic disturbances and concomitant chronic diseases were shown to increase the risk for adverse outcomes after SARS-CoV-2 infection [99].

The traditional Mediterranean diet was shown to be beneficial in the prevention of weight gain and abdominal obesity [42]. On the other hand, a lower educational level was often found to be associated with a higher prevalence of overweight and obesity [39,100]—the same as economic affluence at a country level, reflecting a potential adverse outcome concomitant with economic growth [101]. While the relationship between socio-economic status and health outcomes was frequently emphasized for the Mediterranean area [100], the synergy between those two determinants was not substantially investigated in the population of Southern Croatia. Our results indicate that the average BMI had increased from 25.76 kg/m^2 at baseline to 27.44 kg/m^2 during the follow-up period. This is consistent with the trend of increasing rates of obesity across 147 countries [101]. BMI change during follow-up was positively associated with female gender, and negatively with initial BMI, initial adherence to the MD, and with change in adherence to the MD, as found in the regression analysis. This means that people with a lower BMI at the beginning of the study tended to experience a rise in BMI, while those who started with higher values managed to diminish it over time. An encouraging finding is that individuals with a higher-level/score in MD adherence experienced lower BMI change or even its decrease.

An important limitation of our study that needs to be mentioned here is the use of the cross-sectional design for estimating the association between socio-economic status and adherence to the MD, which limits the inference on causality. However, we did employ an additional follow-up study design in order to confirm the initial findings and observe time trends, as well as to investigate the association between initial socio-economic status and change in adherence to the MD, and BMI change in our sample. Another limitation is the broad sampling period of subjects included in our study, which stretched from 2003 to 2015. In order to control for the effect of the study period in the logistic regression analysis, we included the actual follow-up time as one of the predictor variables, as well as the variable "economic crisis of 2007–2008". We also managed to obtain a smaller than ideal sample size and lesser response rate in the follow-up study (28.7%), due to the older age of subjects and their inability to participate in the follow-up examination. Advantages of the study include a relatively large overall sample size, inclusion of many potential predictors, and sampling from the general population of inhabitants from the Mediterranean region of Croatia. Determinants of Mediterranean diet adherence were so far only marginally investigated in the population of Dalmatia in Croatia, and we are filling this gap.

In conclusion, this is the first study from Croatia to examine the changes in adherence to the MD over time. Additionally, we have identified several important characteristics associated with greater adherence to the MD and with its change over time. These insights should be used to inform the necessary and targeted interventions aimed at increasing MD uptake in order to ensure beneficial outcomes. These include, but are not limited to, the promotion and advancement of individual and population health, ensuring environmental sustainability, and positive impacts on local economies and tourism, as well as the very important outcome of the preservation of cultural heritage for generations to come.

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/nu13113802/s1, Table S1: Characteristics associated with adherence to the main food groups within the Mediterranean diet serving score (MDSS), as determined by the multivariate logistic regression analysis (N = 4671).

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curation, all authors; writing—original draft preparation, A.P., R.P., F.P.S., M.V., M.M. and I.K.; writing—review and editing, all authors.; visualization, A.P., M.V. and I.K.; supervision, O.P. and I.K.; funding acquisition, I.K., O.P. and C.H. All authors have read and agreed to the published version of the manuscript.

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Informed Consent Statement: Informed written consent was obtained from all subjects involved in the study.

Data Availability Statement: The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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nutrients

MDPI

Supplementary Table S1. Characteristics associated with adherence to the main food groups within the Mediterranean diet serving score (MDSS), as determined by the multivariate logistic regression analysis (N = 4,671)

	Fruit aOR (95% CI); *P*	**Vegetables** aOR (95% CI); *P*	**Cereals** aOR (95% CI); *P*	**Olive oil** aOR (95% CI); *P*	**Nuts** aOR (95% CI); *P*	**Dairy** aOR (95% CI); *P*	**Potatoes** aOR (95% CI); *P*	**Legumes** aOR (95% CI); *P*	**Eggs** aOR (95% CI); *P*	**Fish** aOR (95% CI); *P*	**White meat** aOR (95% CI); *P*	**Red meat** aOR (95% CI); *P*	**Sweets** aOR (95% CI); *P*	**Wine** aOR (95% CI); *P*
Sex														
Male; Ref.	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Female	2.42 (2.10, 2.78); <0.001	1.91 (1.55, 2.06); <0.001	0.82 (0.64, 1.05); 0.110	1.22 (1.06, 1.40); 0.007	1.97 (1.40, 2.78); <0.001	1.59 (1.35, 1.86); <0.001	0.97 (0.83, 1.12); 0.652	1.13 (0.98, 1.31); 0.102	0.82 (0.71, 0.95); 0.009	1.08 (0.93, 1.26); 0.286	1.04 (0.91, 1.19); 0.520	1.96 (1.67, 2.30); <0.001	1.00 (0.85, 1.17); 0.981	0.39 (0.33, 0.46); <0.001
Age group (years)														
18-34 Ref.	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
35-64.9	1.61 (1.32, 1.96); <0.001	1.56 (1.27, 1.93); <0.001	1.44 (1.06, 1.96); 0.020	1.43 (1.18, 1.73); <0.001	1.35 (0.82, 2.20); 0.235	0.98 (0.78, 1.21); 0.823	0.58 (0.46, 0.73); <0.001	1.01 (0.82, 1.26); 0.901	0.84 (0.69, 1.03); 0.091	1.32 (1.08, 1.61); 0.006	1.01 (0.84, 1.22); 0.923	1.23 (0.98, 1.56); 0.075	1.90 (1.45, 2.49); <0.001	1.69 (1.29, 2.22); <0.001
≥65.0	2.83 (2.21, 3.62); <0.001	2.33 (1.81, 3.00); <0.001	1.40 (0.94, 2.09); 0.101	2.40 (1.87, 3.07); <0.001	1.92 (1.09, 3.40); 0.024	1.24 (0.95, 1.63); 0.117	0.75 (0.59, 0.95); 0.018	1.29 (0.99, 1.67); 0.055	0.63 (0.48, 0.81); <0.001	2.01 (1.55, 2.60); <0.001	0.90 (0.71, 1.14); 0.370	1.58 (1.20, 2.09); 0.001	2.42 (1.78, 3.29); <0.001	2.41 (1.76, 3.31); <0.001
Place of residence														
City of Split; Ref.	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Island of Vis	0.84 (0.68, 1.02); 0.083	1.08 (0.89, 1.32); 0.419	2.76 (1.72, 4.41); <0.001	0.70 (0.58, 0.86); 0.001	0.46 (0.28, 0.75); 0.002	1.13 (0.91, 1.41); 0.254	0.64 (0.51, 0.80); <0.001	1.22 (0.99, 1.51); 0.068	1.40 (1.13, 1.74); 0.002	2.16 (1.72, 2.71); <0.001	1.40 (1.16, 1.70); 0.001	1.03 (0.82, 1.29); 0.804	0.83 (0.64, 1.07); 0.144	1.27 (0.99, 1.63); 0.057

Island of Korčula	0.98 (0.79, 1.22); 0.849	1.63 (1.33, 2.00); <0.001	1.10 (0.74, 1.64); 0.629	1.53 (1.22, 1.91); <0.001	0.67 (0.43, 1.04); 0.072	1.14 (0.91, 1.43); 0.258	0.58 (0.48, 0.70); <0.001	1.54 (1.24, 1.92); <0.001	0.98 (0.78, 1.24); 0.880	1.44 (1.14, 1.81); 0.002	1.08 (0.88, 1.32); 0.457	0.89 (0.70, 1.12); 0.319	1.82 (1.42, 2.34); <0.001	1.08 (0.83, 1.40); 0.561
Education (years of schooling)														
elementary (0-8); Ref.	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
high school (9- 12)	1.17 (0.98, 1.41); 0.085	1.06 (0.89, 1.27); 0.521	0.74 (0.53, 1.04); 0.081	0.66 (0.54, 0.79); <0.001	1.07 (0.69, 1.66); 0.760	1.07 (0.87, 1.31); 0.535	1.43 (1.19, 1.71); <0.001	0.72 (0.60, 0.87); 0.001	1.04 (0.86, 1.27); 0.675	0.77 (0.63, 0.94); 0.011	0.76 (0.64, 0.90); 0.002	1.14 (0.94, 1.40); 0.188	1.05 (0.86, 1.28); 0.653	1.12 (0.89, 1.41); 0.324
higher (13+)	1.20 (0.97, 1.49); 0.092	1.16 (0.94, 1.44); 0.171	0.60 (0.41, 0.88); 0.010	0.69 (0.55, 0.86); 0.001	1.61 (1.00, 2.59); 0.051	1.32 (1.04, 1.67); 0.022	2.41 (1.92, 3.03); <0.001	0.80 (0.64, 0.99); 0.045	0.92 (0.73, 1.16); 0.487	0.78 (0.62, 0.99); 0.040	0.73 (0.59, 0.89); 0.002	1.89 (1.50, 2.38); <0.001	1.01 (0.79, 1.28); 0.943	1.25 (0.96, 1.62); 0.101
Subjective material status														
worse than average; Ref.	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
average	1.23 (1.00, 1.51); 0.050	1.01 (0.83, 1.25); 0.894	0.88 (0.60, 1.28); 0.500	1.17 (0.95, 1.43); 0.135	1.22 (0.71, 2.10); 0.470	1.09 (0.86, 1.38); 0.461	1.05 (0.85, 1.30); 0.633	1.04 (0.84, 1.30); 0.690	0.74 (0.59, 0.91); 0.005	1.07 (0.86, 1.34); 0.517	1.02 (0.84, 1.25); 0.812	0.81 (0.66, 1.01); 0.059	0.89 (0.72, 1.12); 0.324	1.19 (0.91, 1.56); 0.209
better than average	1.20 (0.95, 1.52); 0.126	1.02 (0.81, 1.29); 0.853	0.82 (0.54, 1.25); 0.364	1.27 (1.01, 1.61); 0.045	1.75 (0.98, 3.12); 0.058	1.10 (0.84, 1.43); 0.499	1.22 (0.96, 1.56); 0.106	1.02 (0.80, 1.31); 0.861	0.76 (0.59, 0.97); 0.029	1.12 (0.87, 1.44); 0.369	0.98 (0.78, 1.22); 0.845	0.68 (0.53, 0.87); 0.002	0.90 (0.69, 1.16); 0.402	1.12 (0.83, 1.52); 0.459

Objective material status														
1st quartile; Ref.	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
2nd quartile	1.24 (1.03, 1.50); 0.025	1.20 (0.99, 1.45); 0.057	1.39 (1.00, 1.91); 0.048	1.35 (1.12, 1.63); 0.002	1.21 (0.78, 1.87); 0.387	1.11 (0.89, 1.37); 0.349	0.87 (0.71, 1.06); 0.158	1.18 (0.97, 1.43); 0.103	1.08 (0.88, 1.33); 0.445	1.43 (1.17, 1.74); <0.001	1.00 (0.84, 1.20); 0.967	0.73 (0.60, 0.89); 0.002	0.75 (0.62, 0.92); 0.007	0.99 (0.78, 1.26); 0.938
3rd quartile	1.28 (1.06, 1.56); 0.011	1.36 (1.12, 1.65); 0.002	1.31 (0.95, 1.81); 0.102	1.49 (1.23, 1.81); <0.001	0.74 (0.46, 1.19); 0.216	1.11 (0.89, 1.37); 0.349	0.73 (0.60, 0.89); 0.002	1.15 (0.94, 1.40); 0.187	1.14 (0.92, 1.4); 0.232	1.72 (1.41, 2.11); <0.001	0.92 (0.77, 1.10); 0.367	0.65 (0.53, 0.80); <0.001	0.63 (0.51, 0.78); <0.001	1.04 (0.81, 1.32); 0.778
4th quartile	1.57 (1.27, 1.94); <0.001	1.66 (1.34, 2.05); <0.001	1.30 (0.92, 1.84); 0.140	2.27 (1.83, 2.83); <0.001	1.35 (0.86, 2.14); 0.195	1.32 (1.05, 1.67); 0.019	0.80 (0.64, 1.00); 0.050	1.04 (0.83, 1.30); 0.737	1.18 (0.94, 1.48); 0.160	2.23 (1.78, 2.79); <0.001	0.93 (0.76, 1.13); 0.460	0.62 (0.50, 0.78); <0.001	0.70 (0.55, 0.88); 0.003	1.29 (1.00, 1.67); 0.054
Chronic diseases*														
≥2; Ref.	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
1	0.92 (0.74, 1.14); 0.465	0.94 (0.76, 1.15); 0.529	1.50 (1.04, 2.17); 0.030	0.99 (0.79, 1.24); 0.923	1.25 (0.77, 2.05); 0.370	0.94 (0.74, 1.20); 0.622	0.94 (0.76, 1.17); 0.573	1.05 (0.84, 1.31); 0.681	1.06 (0.84, 1.35); 0.619	1.10 (0.87, 1.38); 0.436	1.00 (0.81, 1.22); 0.964	0.97 (0.78, 1.21); 0.782	0.70 (0.56, 0.86); 0.001	1.21 (0.94, 1.58); 0.144
none	0.86 (0.70, 1.06); 0.156	0.91 (0.74, 1.11); 0.341	1.33 (0.94, 1.90); 0.111	0.88 (0.71, 1.09); 0.241	1.13 (0.69, 1.85); 0.614	1.13 (0.90, 1.43); 0.303	1.10 (0.89, 1.36); 0.380	1.09 (0.87, 1.35); 0.462	1.24 (0.98, 1.57); 0.073	1.06 (0.84, 1.33); 0.641	0.96 (0.79, 1.17); 0.700	0.73 (0.59, 0.92); 0.006	0.53 (0.43, 0.66); <0.001	1.29 (1.00, 1.66); 0.052
Smoking														
current smokers; Ref.	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
ex, smokers	1.87 (1.56, 2.24); <0.001	1.04 (0.87, 1.25); 0.650	1.12 (0.82, 1.54); 0.475	1.26 (1.05, 1.51); 0.014	1.52 (0.98, 2.37); 0.062	1.02 (0.83, 1.25); 0.878	1.09 (0.89, 1.32); 0.402	1.01 (0.83, 1.22); 0.943	0.85 (0.70, 1.03); 0.096	1.29 (1.06, 1.58); 0.010	0.94 (0.79, 1.12); 0.519	1.22 (0.99, 1.50); 0.060	1.05 (0.86, 1.29); 0.635	1.18 (0.94, 1.47); 0.145
never, smokers	2.03 (1.73, 2.37); <0.001	1.01 (0.86, 1.18); 0.940	1.22 (0.94, 1.60); 0.137	1.12 (0.96, 1.31); 0.154	1.58 (1.07, 2.32); 0.021	1.09 (0.92, 1.30); 0.326	0.93 (0.78, 1.10); 0.378	0.98 (0.83, 1.16); 0.826	1.02 (0.86, 1.21); 0.803	1.05 (0.89, 1.23); 0.598	0.92 (0.79, 1.07); 0.293	1.22 (1.02, 1.46); 0.026	0.84 (0.70, 1.01); 0.064	1.05 (0.86, 1.29); 0.636

Physical activity														
light; Ref.	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
moderate	1.24 (1.07, 1.45); 0.005	1.43 (1.22, 1.67); <0.001	0.83 (0.63, 1.08); 0.169	1.29 (1.11, 1.50); 0.001	1.12 (0.79, 1.57); 0.524	0.98 (0.83, 1.16); 0.840	0.88 (0.75, 1.04); 0.140	1.50 (1.26, 1.77); <0.001	1.13 (0.96, 1.34); 0.152	1.33 (1.14, 1.56); <0.001	0.94 (0.81, 1.09); 0.395	0.99 (0.84, 1.16); 0.873	1.17 (0.98, 1.39); 0.085	0.93 (0.77, 1.13); 0.471
intensive	1.24 (0.97, 1.59); 0.081	1.75 (1.37, 2.23); <0.001	1.38 (0.83, 2.30); 0.220	1.48 (1.15, 1.90); 0.002	1.06 (0.58, 1.96); 0.842	0.84 (0.63, 1.12); 0.228	0.58 (0.45, 0.74); <0.001	1.61 (1.25, 2.08); <0.001	1.08 (0.83, 1.40); 0.570	1.87 (1.42, 2.48); <0.001	1.08 (0.86, 1.36); 0.521	0.70 (0.52, 0.93); 0.014	1.04 (0.79, 1.38); 0.775	0.72 (0.53, 0.98); 0.036
Body mass index category #														
18.0-24.9; Ref.	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
25.0-29.9	0.99 (0.85, 1.15); 0.850	0.99 (0.85, 1.15); 0.891	0.82 (0.63, 1.07); 0.147	0.94 (0.81, 1.10); 0.465	0.92 (0.66, 1.28); 0.629	0.92 (0.78, 1.09); 0.350	1.16 (0.99, 1.36); 0.076	1.03 (0.88, 1.21); 0.717	1.00 (0.85, 1.18); 0.990	1.09 (0.93, 1.28); 0.291	1.07 (0.93, 1.24); 0.339	1.04 (0.88, 1.23); 0.630	1.19 (1.00, 1.41); 0.049	0.89 (0.74, 1.07); 0.214
≥30.0	0.97 (0.80, 1.18); 0.780	0.97 (0.80, 1.18); 0.748	0.70 (0.51, 0.98); 0.037	0.85 (0.70, 1.04); 0.108	0.58 (0.36, 0.93); 0.025	0.99 (0.80, 1.23); 0.961	1.21 (0.98, 1.48); 0.070	1.17 (0.95, 1.43); 0.139	0.89 (0.72, 1.10); 0.264	0.97 (0.79, 1.19); 0.767	0.91 (0.76, 1.10); 0.328	0.84 (0.67, 1.04); 0.102	1.34 (1.08, 1.66); 0.009	0.80 (0.63, 1.02); 0.071
The economic crisis of 2007–2008														
before; Ref.	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
after	0.50 (0.41, 0.60); <0.001	0.32 (0.27, 0.39); <0.001	0.45 (0.32, 0.63); <0.001	0.71 (0.58, 0.86); 0.001	1.04 (0.68, 1.57); 0.864	0.64 (0.52, 0.78); <0.001	0.69 (0.57, 0.83); <0.001	0.53 (0.44, 0.64); <0.001	1.10 (0.89, 1.35); 0.371	0.51 (0.42, 0.63); <0.001	0.93 (0.77, 1.11); 0.397	1.39 (1.13, 1.71); 0.002	1.23 (1.01, 1.50); 0.043	0.97 (0.77, 1.22); 0.796

Aor—Adjusted odds ratios; 95% CI—95% confidence intervals; calculated using multivariate logistic regression model simultaneously adjusted for all the covariates listed in this table. * chronic diseases included any or more than one of the following diagnoses: hypertension, diabetes, CHD, CVI, cancer, bipolar disorder, hyperlipidemia and gout; # 53 subjects with BMI < 18.5 kg/m^2 were excluded from the analysis due to small sample size of the group and negative impact on the model performance.

nutrients

MDPI

Article

Nut Consumption and Cardiovascular Risk Factors: A Cross-Sectional Study in a Mediterranean Population

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Abstract: Nuts are often considered beneficial for health, yet few studies have examined determinants of their intake and the associations between nut consumption and various cardiovascular disease risk factors. The aim of this study was to identify factors associated with nut intake in a Mediterranean population, in Croatia, and to investigate the association of nut intake and various cardiovascular risk factors. Methods: Subjects from the Island of Vis, Island of Korčula and the City of Split were included in this cross-sectional study (n = 4416 in total; 4011 without known cardiovascular disease). Survey responses, medical records and clinically relevant measurements were utilized. Multivariate ordinal and logistic regression models were used in the analysis, adjusting for known confounding factors. Results: As low as 5% of all subjects reported daily, and 11% reported weekly, nut consumption. The characteristics associated with more frequent nut intake were female gender (Odds ratio (OR) = 1.39; 95% confidence interval (CI) 1.19–1.62), highest level of education (1.42; 1.15–1.76) and material status (1.58; 1.29–1.93), smoking abstinence (1.21; 1.04–1.42 in never-smokers and 1.22; 1.02–1.46 in ex-smokers), Mediterranean diet adherence (1.87; 1.62–2.15), and absence of central obesity (1.29; 1.09–1.53), absence of diabetes (1.30; 1.02–1.66) and metabolic syndrome (1.17; 1.01–1.36). Subjects who consumed nuts had more favorable waist-to-height (overall p = 0.036) and waist-to-hip ratios (0.033), lesser odds of elevated fibrinogen (p < 0.001 in both weekly and monthly nut consumers) and reduced high-density lipoprotein (HDL) cholesterol (p = 0.026), compared to non-consumers. Conclusions: It appears that frequent nut consumption is an integral part of a healthy lifestyle and better socioeconomic status. A beneficial association of nut intake with cardiovascular risk factors was confirmed in this study.

Keywords: nuts; food intake; obesity; hypertension; diabetes; dyslipidemia; metabolic syndrome

1. Introduction

Nuts have been identified as one of the most nutrient dense foods, rich in monounsaturated and polyunsaturated fatty acids, protein, fiber, vitamins and minerals [1]. They have also been found to contain an abundance of many other important phytochemicals, including phenolic acids, phytosterols and flavonoids, proanthocyanidins and stilbenes, phytates, sphingolipids, alkylphenols and lignans, which have antioxidative, anti-inflammatory, anti-proliferative, antiviral, chemopreventive and hypocholesterolaemic effects [2]. A small but growing body of evidence suggests that nuts are protective against cardiovascular diseases, cancer, diabetes, metabolic syndrome and hypertension [3–6]. Daily nut consumption decreased the all-cause mortality risk by 20% in large cohort studies from the United States of America (USA) [7], and a combined cohort study performed both in the USA and China [8]. This finding was also confirmed in other recent meta-analyses [9,10]. Furthermore, specific mortalities due to diabetes, respiratory diseases and infectious diseases were inversely associated with nut consumption in a meta-analysis, which included 20 cohort studies [3]. Cardiovascular risk factors, namely body weight [11], blood pressure [12,13], blood lipids [14], glucose (in diabetics) [15] and uric acid [16] were also inversely associated with nut intake. Even though nuts contain very high amounts of fat, their consumption has repeatedly been shown not to be associated with weight gain [11,17–19], but instead with moderate weight loss or weight stability, as reported in a large prospective study, involving 373,000 participants from 10 European countries [11]. Despite these findings, there is still a common belief that nut intake is associated with weight gain risk, even among health care professionals [20].

The definition of a Mediterranean diet places nuts up front and demands their intake on a daily basis, together with vegetables, fruit, olive oil and cereals [21]. Unfortunately, such intense consumption is not common, even among populations of the Mediterranean region [22–24]. A recent study performed in the population of Dalmatia, in the coastal region of Croatia, revealed a disappointingly low prevalence of daily nut consumption, ranging from 3% on the Island of Vis to 11% in the City of Split [25].

Previously published experimental studies on nut effects were small in size and of very short durations. Hence, limited input was available for a 2015 Cochrane review, with only five randomized control trials [17]. New results from the PREDIMED interventional study from Spain have recently become available [26,27]. This study yielded some promising and confirming results, especially for the beneficial effect of the Mediterranean diet enriched with nuts for the prevention of cardiovascular disease (CVD) events, such as myocardial infarction, stroke or CVD death [28]. However, the participants of this study allocated to the nut consuming group also received nutritional education on Mediterranean diet adherence, making it hard to disassociate the positive effects of nuts from the overall healthy eating pattern [18].

Despite potential health benefits, investigation into the determinants of nut consumption in the general population is very scarce in the literature [10,29], leaving a substantial gap in knowledge. Therefore, the aim of this study was to determine the factors associated with nut consumption, as well as to investigate the association between nut consumption and various cardiovascular risk factors, namely central obesity indices, dyslipidemia, elevated fibrinogen, hypertension, diabetes, elevated glycated haemoglobin (HbA1c), metabolic syndrome and gout, in a population-based sample in Dalmatia, Croatia.

2. Materials and Methods

2.1. Study Participants and Methods

This cross-sectional study initially included 4984 subjects from the "10,001 Dalmatians" project [30]. Subjects from three Dalmatian settlements were included: the Island of Vis (*n* = 1027, sampled during 2003–2004 period), Island of Korčula (*n* = 2581, sampled during 2007 and 2012–2015 period) and the City of Split, which is the second largest city in Croatia (*n* = 1012; sampled in 2008–2009 period). A population-based sampling approach was based on generalized invitations to all island inhabitants, targeting subjects who were of age (18 or more years). The sampling scheme employed direct postal invitations, radio appearances and support from the local stakeholders (general practitioners (GPs) and local governments), yielding almost systematic responses. All respondents were informed on the study aims and goals, benefits and risks, and were asked to sign an informed consent before entering the study. The study was approved by the Ethical Board of the University of Split School of Medicine (approval number 2181-198-03-04/10-11-0008).

2.2. Clinical Measurements

Each subject was offered an array of clinical measurements, which included blood and urine testing, followed by blood pressure and anthropometric measurements, electrocardiography, arterial stiffness, spirometry, heel bone density (dual-energy X-ray absorptiometry, DEXA), ophthalmological examination and other clinically relevant examinations. Subjects were also asked to fill in an extensive self-administered questionnaire, which included questions on important cardiovascular disease risk factors: demographic characteristics, medical history, socioeconomic status, smoking, alcohol consumption, physical activity, and dietary habits. Elderly people and those with disabilities were offered assistance during surveying, by a team of nine trained surveyors.

Medical records or subjects' responses were used to extract relevant medical history information, including previous diagnoses and the use of medications. The list included hypertension, type 2 diabetes, coronary heart disease (CHD), cerebrovascular insult (CVI), cancer, bipolar disorder, hyperlipidemia and gout.

2.2.1. Blood Pressure and Anthropometric Indices

Blood pressure was measured twice by manual mercury sphygmomanometer (calibrated weekly), at least five minutes apart, in a sitting position, after at least 10 min of rest. An average value of two measurements was taken for the analysis. Subjects were considered to have hypertension if they (a) reported a previous diagnosis of hypertension or (b) reported the use of anti-hypertensive medication or (c) had a mean systolic blood pressure ≥140 mmHg or mean diastolic pressure ≥90 mmHg [31]. Anthropometric measurements were performed using standard procedures [32], including body height, body weight, waist circumference (WC) and hip circumference (HC). Besides body mass index (BMI), we also calculated waist-to-hip ratio (WHR) and waist-to-height ratio (WHtR) as relative measures of central obesity. The cut-off value for elevated WC was ≥94 cm for men and ≥80 cm for women [32]; for elevated WHR it was ≥0.85 for women and ≥0.90 for men [32], and for WHtR it was ≥0.50 for both sexes [33].

2.2.2. Biochemistry

Biochemical parameters included total cholesterol, low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), triglycerides, glucose, HbA_1c, uric acid and fibrinogen. Fasting blood samples were collected from the antecubital vein into EDTA and serum tubes and pre-processed immediately in remote study sites. They were shipped frozen (−80 °C) to 2 specialized and accredited laboratories (HRN EN ISO 15189) in Zagreb (samples collected from Vis Island and Split were analyzed in "Labor Centar" and samples from Korčula Island were analyzed in "Breyer Laboratory"). Both laboratories used the same standard methods for determining concentrations of glucose, HbA_1c, uric acid, blood lipids and fibrinogen (measured using the Clauss method).

Subjects whose fasting glucose level exceeded 7.0 mmol/L or those who reported a previous diagnosis of type 2 diabetes were considered to be diabetic [34]. Metabolic syndrome was defined using the Joint Interim Statement (JIS) definition and the cut off values used for elevated waist circumference were ≥80 cm for women and ≥94 cm for men [35]. Subjects who had elevated uric acid (≥404 μmol/L for men and ≥338 μmol/L for women [36]) or had a record in medical history were considered positive for gout. The cut-off level for elevated cholesterol was ≥5.0 mmol/L, for LDL cholesterol it was ≥3.0 mmol/L, and for triglycerides the cut-off was ≥1.7 mmol/L [35]. HDL values of ≤1.03 mmol/L for men and ≤1.29 mmol/L for women were considered reduced HDL concentrations [35]. Information on taking medications for dyslipidemia was also taken into account. The concentration of fibrinogen was considered to be lowered if it was ≤1.5 g/L, normal if it was between 1.51–4.0 g/L or elevated if the concentration was ≥4.0 g/L [37].

2.3. Socioeconomic and Lifestyle Characteristics Associated with Cardiovascular Disease Risk

Socioeconomic status was assessed according to education level and material status. Education level was measured as years of formal schooling, and later classified into three categories (corresponding to the primary, secondary and higher education system in Croatia) as follows: lower education level (with ≤8 years of finished school), intermediate (9–12 years), and higher education (≥13 years of schooling). An assessment of material status was based on 16 validated questions forming the composite index [38], consisting of a list of items in the subject's possession (heating system, wooden floors, video/DVD recorder, telephone, computer, two TVs, freezer, dishwasher, water supply system, flushing toilet, bathroom, library with more than 100 books, paintings or other art objects, a car, vacation house or second apartment, boat). The responses were summed and classified into four quartile categories, according to the distribution in the study population (first quartile with values ≤8, second 9–10, third 11–12, and fourth quartile with values 13–16).

Lifestyle characteristics, such as smoking, alcohol intake, and physical activity were also recorded. Smoking status was assigned as current smoker, ex-smoker (stopped more than 1 year ago) and never-smoker. Alcohol intake was measured in units per week, in order to combine all the types of alcohol a subject could have consumed during the week (beer, wine and hard liquor). In cases of consumption of ≥28 units/week for men and ≥21 units/week for women, a subject was classified as an excessive drinker [39], or a moderate drinker in cases of consuming less (1–27 units/week for men and 1–20 units/week for women), while those who did not consume any alcohol were considered non-drinkers. The level of physical activity was assessed from the survey; light activity was assigned when subject reported sitting or light physical activity during both work and leisure time. A moderate level of physical activity was assigned if a subject declared a moderate level of physical exertion in at least one part of the day, while intensive activity was assigned to all subjects who reported hard labor or other intense types of physical activity during either part of the day.

2.4. Assessment of Dietary Pattern and Nut Intake

Assessment of the diet composition was based on a 55 question survey, specifically adjusted for the population of Dalmatia [25]. Each question had six possible responses regarding the usual frequency of consumption (every day, 2–3 times a week, once a week, once a month, rarely and never). The questionnaire captured the information on olive oil and other fat intake, dairy, vegetables, fruit, nuts, potatoes, cereals (rice, pasta, bread), legumes, eggs, white and red meats, fish and sea foods, sweets, and wine (for details see [25]). Adherence to the Mediterranean diet was assessed according to the recently proposed Mediterranean Diet Serving Score (MDSS), which demands daily intake of vegetables, fruit, olive oil cereals, nuts, dairy products and wine, while other groups of food should be consumed weekly [40]. The MDSS score has a maximum of 24 points, and those foods which are considered beneficial for health and should be consumed daily contribute 3 points, while foods like red meat and sweets contribute 1 point if consumed in ≤2 servings per week [25]. Finally, we also classified all subjects on the basis of their Mediterranean diet compliance, by MDSS score—the upper quartile limit was set at 14 points (out of maximum 24), indicating good adherence to Mediterranean diet [40].

Nut consumption frequency was assessed using one question, and all types of nuts were included (tree nuts and peanuts). Subjects were classified into four categories: daily nut consumers (reported nut intake "every day"), weekly consumers (reported "2–3 times a week" nut intake), monthly (reported "once a week" or "once a month") and those who consume nuts infrequently or never (reported "rarely" or "never").

2.5. Statistical Analysis

Due to missing values for at least one of the important characteristics needed in the analysis (anthropometric measurements, biochemistry, medical history or nut consumption), we excluded

35 subjects from the Island of Vis, 146 subjects from the Island of Korčula, and 23 subjects from the City of Split. Secondly, we removed 405 subjects, since they reported a previous diagnosis of either coronary heart disease or cerebrovascular insult. These subjects were included only in the bivariate analyses, and excluded from all the multivariate analyses of the association of nut consumption with different cardiovascular risk factors, in order to test the hypothesis only in subjects at risk of cardiovascular disease. Additionally, a sub-analysis was performed, including only elderly subjects (>65 years of age, n = 897), who were at an increased risk for cardiovascular diseases.

All categorical variables were described using absolute numbers and percentages, and numerical variables were described with medians and interquartile ranges (IQR), due to frequent non-normal distribution. Differences between groups for categorical variables were examined with chi-squared tests, and for numerical variables with Kruskal–Wallis tests. Post-hoc analyses were performed using the Mann–Whitney U test for numerical variables and chi-squared tests for categorical variables.

The multivariate analysis included ordinal regression and logistic regression. Ordinal regression analysis was used to identify the characteristics associated with the ordinal dependent variables: nut consumption, BMI and fibrinogen (each variable was analysed in a separate model). Covariates in these three models included sex, age (3 age group categories: 18–34.9 years, 35.0–64.9 years, and $\geq$65.0 years, as in our previous study [25]), place of residence (Vis, Korčula, Split), education attainment, quartiles of material status, smoking, alcohol intake, Mediterranean diet adherence (MDSS $\geq$14 points), nut consumption (only in BMI and fibrinogen models), physical activity, WHtR, and four chronic diseases (hypertension, diabetes, metabolic syndrome, and gout). In all 3 models the highest value of the ordinal dependent variable was used as a referent point (daily nut consumption; BMI $\geq$30 kg/m^2; fibrinogen $\geq$4.0 g/L). Beta values were transformed into odds ratios using the exponential value of beta, with 95% confidence interval (exponential values of beta's lower and upper bounds).

A logistic regression analysis was used to identify the characteristics associated with the binary outcome variables: BMI, waist circumference, WHR, WHtR as binary outcomes (normal or elevated), hypertension, diabetes, elevated HbA_1c, metabolic syndrome, gout, elevated triglycerides, elevated cholesterol, elevated LDL cholesterol, and decreased HDL cholesterol. All the logistic regression models were controlled for known confounding factors: sex, age, cohort effect (place of residence), years of schooling, quartiles of material status, smoking, alcohol intake, MDSS compliance, nut consumption, physical activity, WHtR and four chronic diseases (hypertension, diabetes, metabolic syndrome and gout), except in models where these were dependent variables. Metabolic syndrome was omitted as a covariate in the regression models for elevated triglycerides, cholesterol, LDL cholesterol, HDL cholesterol and fibrinogen, due to its failure to meet the model diagnostic criteria (Hosmer–Lemeshow test). On the other hand, models with chronic diseases as outcome variables did not include metabolic syndrome as a covariate. Using this approach, all the models built for the analysis had a good fit (Hosmer and Lemeshow test p-values were > 0.05). Significance level was set at $p < 0.05$ (two-sided). All statistical analyses were performed using IBM SPSS Statistics v19 (IBM, Armonk, NY, USA).

3. Results

This cross-sectional study included 4416 subjects from three populations, two from eastern Adriatic islands and one mainland population on the coastline. Almost all of the characteristics differed between the sub-samples according to the place of residence, except the gender composition, Mediterranean diet serving score (MDSS), and CVI in the medical history (Table 1). Overweight, obesity and some of the chronic diseases were highly prevalent, with as many as 405 subjects (9.2%) who reported having CVD in their medical history, and some of them reported having both CHD and CVI (Table 1). Daily nut consumption was reported in 7.1% of subjects from Split, 4.7% in subjects from Korčula, while only 2.7% of subjects from the Island of Vis consumed nuts daily (Table 1).

A high prevalence of metabolic syndrome was observed (as high as 60.9% in Vis), followed by hypertension (ranged from 23.9% in Split to 30.8% in Korčula), while obesity was also most common in Vis (26.2%) (Table 1).

Table 1. Demographic characteristics, prevalence of chronic diseases, lifestyle characteristics, Mediterranean diet compliance (MDSS ≥ 14) and nut consumption frequency according to the place of residence.

	Island of Vis *n* **= 992**	**Island of Korčula** *n* **= 2435**	**City of Split** *n* **= 989**	**Overall** *p* **(Post-Hoc Test** *p***-Values)**
Sex; *n* (%)				
Men	414 (41.7)	907 (37.2)	382 (38.6)	0.050 (0.014 ^{VK}, 0.158 ^{VS}, 0.451 ^{KS})
Women	578 (58.3)	1528 (62.8)	607 (61.4)	
Age (years); median (interquartile range (IQR))	56.00 (23.0)	55.0 (23.0)	52.0 (21.0)	<0.001 (<0.001 ^{VK}, <0.001 ^{VS}, <0.001 ^{KS})
Education (years of schooling); median (IQR)	11.0 (4.0)	12.0 (3.0)	12.0 (4.0)	<0.001 (<0.001 ^{VK}, <0.001 ^{VS}, <0.001 ^{KS})
Material status; median (IQR)	10.0 (5.0)	10.0 (3.0)	12.0 (3.0)	<0.001 (<0.001 ^{VK}, <0.001 ^{VS}, <0.001 ^{KS})
BMI (kg/m^2); *n* (%)				
<25.0 (normal)	301 (30.3)	1287 (52.9)	345 (34.9)	<0.001 (<0.001 ^{VK}, 0.027 ^{VS}, <0.001 ^{KS})
25.0–29.9 (overweight)	431 (43.4)	830 (34.1)	429 (43.4)	
≥30.0 (obese)	260 (26.2)	318 (13.1)	215 (21.7)	
CVD; *n* (%)	139 (14.0)	214 (8.79)	52 (5.3)	<0.001 (<0.001 ^{VK}, <0.001 ^{VS}, <0.001 ^{KS})
CHD; *n* (%)	117 (11.8)	184 (7.6)	40 (4.0)	<0.001 (<0.001 ^{VK}, <0.001 ^{VS}, <0.001 ^{VS})
CVI; *n* (%)	30 (3.0)	50 (2.1)	15 (1.5)	0.061 (0.088 ^{VK}, 0.024 ^{VS}, 0.297 ^{VS})
Diabetes (history); *n* (%)	65 (6.6)	174 (7.1)	42 (4.2)	0.007 (0.536 ^{VK}, 0.023 ^{VS}, 0.002 ^{KS})
Hypertension (history); *n* (%)	294 (29.6)	750 (30.8)	236 (23.9)	<0.001 (0.502 ^{VK}, 0.004 ^{VS}, <0.001 ^{KS})
Metabolic syndrome; *n* (%)	604 (60.9)	1048 (45.3)	353 (35.7)	<0.001 (<0.001 ^{VK}, <0.001 ^{VS}, <0.001 ^{VS})
Gout (history); *n* (%)	63 (6.4)	157 (6.5)	28 (2.8)	<0.001 (0.912 ^{VK}, <0.001 ^{VS}, <0.001 ^{KS})
Smoking; *n* (%)				
current smoker	283 (28.5)	662 (27.2)	262 (26.5)	<0.001 (<0.001 ^{VK}, 0.072 ^{VS}, 0.015 ^{KS})
ex-smoker	300 (30.2)	551 (22.6)	269 (27.2)	
never-smoker	409 (41.2)	1222 (50.2)	458 (46.3)	
Alcohol intake; *n* (%)				
excessive	150 (15.1)	484 (19.9)	130 (13.1)	<0.001 (<0.001 ^{VK}, 0.255 ^{VS}, <0.001 ^{KS})
moderate	435 (43.9)	1137 (46.7)	466 (47.1)	
none	407 (41.0)	814 (33.4)	393 (39.7)	
Physical activity; *n* (%)				
light	257 (25.9)	481 (19.8)	351 (35.5)	<0.001 (<0.001 ^{VK}, <0.001 ^{VS}, <0.001 ^{KS})
moderate	574 (57.9)	1698 (69.7)	603 (61.0)	
intensive	161 (16.2)	256 (10.5)	35 (3.5)	
MDSS ≥ 14 points; *n* (%)	306 (30.8)	668 (27.4)	300 (30.3)	0.068 (0.045 ^{VK}, 0.804 ^{VS}, 0.088 ^{KS})
Nut consumption; *n* (%)				
infrequently or never	785 (79.1)	1162 (47.7)	494 (49.9)	<0.001 (<0.001 ^{VK}, <0.001 ^{VS}, <0.001 ^{KS})
monthly	132 (13.3)	880 (36.1)	264 (26.7)	
weekly	48 (4.8)	278 (11.4)	161 (16.3)	
daily	27 (2.7)	115 (4.7)	70 (7.1)	

BMI: body mass index. CVD: cardiovascular disease. CHD: coronary heart disease. CVI: cerebrovascular insult. MDSS: Mediterranean Diet Serving Score. *p*-values for categorical variables were obtained with chi-squared tests, and for numerical variables with the Kruskal–Wallis test. Post-hoc test *p*-values for categorical variables were obtained with chi-squared tests, and for numerical variables with the Mann–Whitney U test. ^{VK} Post-hoc test *p*-Value: Vis vs. Korčula. ^{VS} Post-hoc test *p*-Value: Vis vs. Split. ^{KS} Post-hoc test *p*-Value: Korčula vs. Split.

A bivariate analysis of the entire sample (*n* = 4416) revealed that nut consumption frequency was associated with all of the investigated characteristics, except with HDL cholesterol (Table S1). Daily consumption was more common in women (75.5% vs. 24.5% in men), subjects who never smoked (54.7% vs. 19.3% in current smokers), and those compliant with the Mediterranean diet (69.3% vs. 30.7% in non-compliant), suggesting a pattern of a healthier lifestyle (Table S1). Subjects who never consumed nuts had a higher prevalence of obesity (BMI ≥ 30 kg/m^2 in 19.9% non-consumers vs. 12.7% in daily consumers) and a higher prevalence of central obesity (elevated WHR in 74.6% vs. 64.9% in daily consumers, p = 0.002; elevated WHtR in 81.7% non-consumers vs. 75.4% in daily consumers, p = 0.024; Table S1). A similar pattern was also present in subjects who consumed nuts weekly and monthly (Table S1). There was no difference in the bivariate analysis for the prevalence of elevated cholesterol levels or LDL and HDL cholesterol levels, between daily consumers of nuts and non-consumers, while triglycerides were more frequently elevated in non-consumers (29.3% vs. 19.3% in daily consumers, $p = 0.002$; Table S1). Daily consumers and non-consumers had a similar prevalence of hypertension, diabetes, and gout, while metabolic syndrome was more frequent in non-consumers (52.3% vs. 42.6%, $p = 0.008$, Table S1).

When the confounding variables were taken into account in the multivariate ordinal regression model and only those subjects without a previous CVD diagnosis were included ($N = 4011$), several characteristics remained independently associated with nut consumption (Table 2). Higher odds for more frequent nut consumption were recorded in women (odds ratio (OR) = 1.39; 95% confidence interval (CI) 1.19–1.62; $p < 0.001$), subjects with the highest educational attainment (OR = 1.42; 95% CI 1.15–1.76; $p = 0.001$, compared to lowest), highest quartile of material status (OR = 1.58; 95% CI 1.29–1.93; $p < 0.001$, compared to lowest), non-smoking status compared to current smokers (OR = 1.21, 95% CI 1.04–1.42; $p = 0.015$ in never-smokers and OR = 1.22, 95% CI 1.02–1.46; $p = 0.034$ in ex-smokers), and compliance with the Mediterranean diet (OR = 1.87; 95% CI 1.62–2.15; $p < 0.001$) (Table 2). A similar finding was also recorded in subjects who were exposed to less intensive physical activity (OR = 1.34; 95% CI 1.04–1.73; $p = 0.023$ for light and OR = 1.30; 95% CI 1.04–1.63; $p = 0.022$ for moderate physical activity, compared to intensive), subjects who were not centrally obese (OR = 1.29; 95% CI 1.09–1.53; $p = 0.003$) and those who did not have diabetes (OR = 1.30; 95% CI 1.02–1.66; $p = 0.031$), or metabolic syndrome (OR = 1.17; 95% 1.01–1.36; $p = 0.042$) (Table 2).

Table 2. Characteristics associated with nut consumption, as determined by the ordinal regression model (sample size is 4011 subjects without a previous diagnosis of cardiovascular diseases; all independent variables included in the model are listed in the table).

	Daily Nut Consumption **Adjusted Odds Ratio (95% Confidence Interval); *p*-Value**
Sex (referent (ref): male)	
Female	1.39 (1.19–1.62); <0.001
Age (years, ref: 18–34.9)	
≥65.0	0.98 (0.76–1.23); 0.897
35–64.9	1.03 (0.85–1.25); 0.767
Place of residence (ref: Split)	
Island of Vis	0.34 (0.28–0.42); <0.001
Island of Korčula	1.12 (0.96–1.31); 0.140
Education (years of schooling, ref: 0–8)	
≥13	1.42 (1.15–1.76); 0.001
9–12	1.15 (0.95–1.39); 0.143
Material status (ref: 1st quartile)	
4th quartile	1.58 (1.29–1.93); <0.001
3rd quartile	1.17 (0.97–1.42); 0.103
2nd quartile	1.17 (0.97–1.42); 0.096
Smoking (ref: current smoker)	
never-smoker	1.21 (1.04–1.42); 0.015
ex-smoker	1.22 (1.02–1.46); 0.034
Alcohol intake (ref: none)	
excessive	1.18 (0.96–1.45); 0.123
moderate	1.15 (0.99–1.33); 0.059
MDSS compliance (ref: no)	
yes	1.87 (1.62–2.15); <0.001
Physical activity (ref: intensive)	
light	1.34 (1.04–1.73); 0.023
moderate	1.30 (1.04–1.63); 0.022
WHtR (≥0.5, ref: yes)	
no	1.29 (1.09–1.53); 0.003
Hypertension (systolic ≥140 mmHg or diastolic ≥90 mmHg or treated for hypertension, ref: yes)	
no	0.96 (0.82–1.13); 0.633

Table 2. *Cont.*

	Daily Nut Consumption Adjusted Odds Ratio (95% Confidence Interval); *p*-Value
Diabetes (≥7 mmol/L or treated for diabetes type 2, ref: yes)	
no	1.30 (1.02–1.66); 0.031
Metabolic syndrome (ref: yes)	
no	1.17 (1.01–1.36); 0.042
Gout (uric acid ≥404 μmol/L ♂, ≥338 μmol/L ♀ or treated for gout, ref: yes)	
no	1.04 (0.87–1.25); 0.647

MDSS: Mediterranean Diet Serving Score. WHtR: waist to height ratio. ♂: males. ♀: woman. The responses for material status were summed and classified into four quartile categories, according to the distribution in the study population (first quartile with values ≤8, second 9–10, third 11–12, and fourth quartile with values 13–16). Adjusted odds ratios, 95% confidence intervals and *p*-Values were calculated using a multivariate ordinal regression model, simultaneously adjusted for all the covariates listed in this table.

Nut consumption frequency was associated with an elevated waist-to-height ratio (WHtR, overall $p = 0.036$) and waist-to-hip ratio (WHR, overall $p = 0.033$), while no association was recorded for waist circumference or BMI in subjects without a previous CVD diagnosis (Table 3). Subjects who reported weekly nut consumption had lower odds for elevated WHtR, compared to those who never consumed nuts (OR = 0.72, 95% CI 0.54–0.96; $p = 0.026$), similarly for subjects who consumed nuts monthly (OR = 0.78, 95% CI 0.63–0.97; $p = 0.022$). Daily nut consumers exhibited no difference compared to the non-consumers (OR = 0.70; 95% CI 0.45–1.08; $p = 0.104$; Table 3). A similar finding was for elevated WHR, where subjects who consumed nuts weekly and monthly had 23% lower odds for being centrally obese (OR = 0.77, 95% CI 0.60–0.99; $p = 0.045$ and OR = 0.77, 95% CI 0.64–0.93; $p = 0.007$, respectively), while daily consumers had a non-significant result (OR = 0.87; 95% CI 0.60–1.28; $p = 0.485$; Table 3). Other characteristics associated with the presence of central obesity, in both WHtR and WHR models, included male gender, older age, living in Korčula (compared to Split), lower educational attainment, ex-smoker status compared to never-smoked (only for WHtR), excessive alcohol intake (only for WHR). Higher material status (only for WHtR), current smoking, compared to never-smokers, and absence of hypertension, diabetes (only for WHR), metabolic syndrome and gout were associated with decreased odds of being centrally obese (Table 3).

Among investigated biochemical parameters, nut consumption was associated with HDL cholesterol, fibrinogen, total cholesterol and LDL cholesterol, while triglycerides did not exhibit such an association (Table 4). Subjects who consumed nuts monthly had lower odds for a decreased level of HDL cholesterol compared to non-consumers (OR = 0.75, 95% CI 0.62–0.92; $p = 0.005$), while subjects who consumed nuts weekly and daily also had the same result, but the difference did not reach statistical significance in pair-wise comparisons, even though the overall *p*-Value indicated a significant result ($p = 0.026$, Table 4). On the other hand, only subjects who consumed nuts weekly had increased odds for the concomitant presence of increased total cholesterol and LDL cholesterol, but without overall significance (OR = 1.35, 95% CI 1.02–1.79; $p = 0.037$ and OR = 1.46, 95% CI 1.11–1.94; $p = 0.008$, respectively; Table 4). Subjects who consumed nuts had lower odds for having an elevated fibrinogen level (OR = 0.66, 95% CI 0.56–0.79; $p < 0.001$ in monthly consumers, OR = 0.65, 95% CI 0.52–0.83; $p < 0.001$ in weekly consumers), while for daily consumers the result was just above the significance threshold limit, Table 4). In a sub-analysis, including only elderly subjects (>65 years of age) who are at increased risk for cardiovascular diseases, only one statistically significant association was found: between nut intake and elevated fibrinogen level (OR = 0.58, 95% CI 0.39–0.84; $p = 0.004$ in subjects consuming nuts monthly compared to non-consumers; Table S2).

Table 3. Association of anthropometric indices with nut consumption frequency as determined by the regression models (sample size is 4011 subjects without previous cardiovascular disease diagnosis; all independent variables included in the model are listed in the table).

	Waist-to-Height Ratio (≥0.5) Adjusted Odds Ratio (95% Confidence Interval); *p*-Value	**Waist-to-Hip Ratio (≥0.90 cm ♂, ≥0.85 cm ♀) Adjusted Odds Ratio (95% Confidence Interval); *p*-Value**	**Waist Circumference (≥94 cm ♂, ≥80 cm ♀) Adjusted Odds Ratio (95% Confidence Interval); *p*-Value**	**Body Mass Index (Referent ≥ 30) Adjusted Odds Ratio (95% Confidence Interval); *p*-Value**
Sex (referent (ref): female)				
Male	1.97 (1.57–2.46); <0.001	2.55 (2.08–3.12); <0.001	0.35 (0.28–0.43); <0.001	2.34 (2.01–2.73); <0.001
Age (years, ref: 18–34.9)	Overall $p < 0.001$	Overall $p < 0.001$	Overall $p < 0.001$	-
≥65	7.95 (5.34–11.85); <0.001	6.70 (4.84–9.29); <0.001	2.85 (2.03–4.01); <0.001	1.55 (1.20–2.00); 0.001
35–64.9	3.64 (2.91–4.55); <0.001	4.12 (3.28–5.17); <0.001	2.45 (1.97–3.05); <0.001	2.06 (1.68–2.54); <0.001
Place of residence (ref: Split)				
Island of Vis	0.87 (0.65–1.15); 0.326	1.18 (0.92–1.53); 0.195	0.67 (0.51–0.89); 0.005	0.80 (0.66–0.98); 0.029
Island of Korčula	1.41 (1.14–1.76); 0.002	1.35 (1.11–1.64); 0.003	1.10 (0.88–1.36); 0.410	0.38 (0.32–0.45); <0.001
Education (years of schooling, ref: ≥13)	Overall $p < 0.001$	Overall $p < 0.001$	Overall $p < 0.001$	-
0–8	2.36 (1.67–3.34); <0.001	2.42 (1.81–3.24); <0.001	2.06 (1.49–2.86); <0.001	1.23 (1.00–1.52); 0.055
9–12	1.30 (1.06–1.60); 0.013	1.21 (1.00–1.46); 0.054	1.24 (1.01–1.52); 0.041	1.16 (0.99–1.36); 0.068
Material status (ref: 4th quartile)	Overall $p = 0.017$	Overall $p = 0.462$	Overall $p = 0.381$	-
1st quartile	0.65 (0.49–0.87); 0.003	0.99 (0.76–1.27); 0.908	0.78 (0.59–1.04); 0.089	0.86 (0.70–1.06); 0.154
2nd quartile	0.94 (0.72–1.22); 0.639	1.17 (0.92–1.47); 0.200	0.93 (0.73–1.20); 0.601	0.88 (0.73–1.07); 0.197
3rd quartile	0.84 (0.65–1.07); 0.157	1.09 (0.87–1.36); 0.444	0.93 (0.73–1.18); 0.560	0.94 (0.78–1.13); 0.498
Smoking (ref: never-smoker)	Overall $p < 0.001$	Overall $p = 0.173$	Overall $p = 0.039$	-
current smoker	0.81 (0.66–1.00); 0.046	1.04 (0.86–1.26); 0.657	1.01 (0.82–1.24); 0.952	0.81 (0.69–0.95); 0.011
ex-smoker	1.36 (1.06–1.74); 0.015	1.22 (0.99–1.51); 0.064	1.33 (1.05–1.67); 0.017	1.13 (0.97–1.33); 0.127
Alcohol intake (ref: none)	Overall $p = 0.454$	Overall $p = 0.028$	Overall $p = 0.865$	-
excessive	0.93 (0.68–1.27); 0.663	1.46 (1.10–1.93); 0.008	1.03 (0.77–1.37); 0.849	0.83 (0.68–1.02); 0.083
moderate	0.88 (0.72–1.08); 0.212	1.14 (0.95–1.37); 0.147	0.97 (0.79–1.19); 0.735	0.72 (0.62–0.84); <0.001
MDSS compliance (ref: yes)				
no	0.94 (0.75–1.16); 0.547	1.18 (0.97–1.42); 0.090	0.87 (0.70–1.08); 0.201	1.23 (1.06–1.42); 0.007
yes	1.00	1.00	1.00	1.00
Nut consumption (ref: infrequently or never)	Overall $p = 0.036$	Overall $p = 0.033$	Overall $p = 0.413$	-
daily	0.70 (0.45–1.08); 0.104	0.87 (0.60–1.28); 0.485	0.98 (0.63–1.53); 0.941	0.85 (0.62–1.16); 0.315
weekly	0.72 (0.54–0.96); 0.026	0.77 (0.60–0.99); 0.045	0.84 (0.63–1.11); 0.222	0.92 (0.75–1.14); 0.470
monthly	0.78 (0.63–0.97); 0.022	0.77 (0.64–0.93); 0.007	0.86 (0.70–1.05); 0.147	1.02 (0.88–1.19); 0.774
Physical activity (ref: intensive)	Overall $p = 0.776$	Overall $p = 0.986$	Overall $p = 0.306$	-
light	1.07 (0.74–1.55); 0.702	1.03 (0.74–1.42); 0.875	1.25 (0.88–1.77); 0.205	1.17 (0.92–1.49); 0.197
moderate	1.12 (0.81–1.55); 0.505	1.02 (0.77–1.37); 0.872	1.07 (0.79–1.46); 0.645	1.01 (0.82–1.25); 0.891

Table 3. *Cont.*

	Waist-to-Height Ratio (≥0.5) Adjusted Odds Ratio (95% Confidence Interval); *p*-Value	Waist-to-Hip Ratio (≥0.90 cm ♂, ≥0.85 cm ♀) Adjusted Odds Ratio (95% Confidence Interval); *p*-Value	Waist Circumference (≥94 cm ♂, ≥80 cm ♀) Adjusted Odds Ratio (95% Confidence Interval); *p*-Value	Body Mass Index (Referent ≥ 30) Adjusted Odds Ratio (95% Confidence Interval); *p*-Value
Hypertension (systolic ≥ 140 mmHg or diastolic ≥ 90 mmHg or treated for hypertension, ref: yes)				
No	0.56 (0.42–0.74); <0.001	0.68 (0.54–0.84); <0.001	0.70 (0.54–0.90); 0.006	0.66 (0.57–0.77); <0.001
Diabetes (≥7 mmol/L or treated for diabetes type 2, ref: yes)				
No	0.94 (0.56–1.58); 0.815	0.52 (0.34–0.80); 0.003	0.96 (0.61–1.52); 0.862	0.76 (0.61–0.94); 0.013
Metabolic syndrome (ref: yes)				
No	0.14 (0.11–0.18); <0.001	0.35 (0.29–0.42); <0.001	0.09 (0.06–0.11); <0.001	0.35 (0.30–0.40); <0.001
Gout (uric acid ≥ 404 µmol/L ♂, ≥338 µmol/L ♀ or gout, ref: yes)				
No	0.38 (0.26–0.55); <0.001	0.45 (0.34–0.60); <0.001	0.42 (0.31–0.58); <0.001	0.59 (0.50–0.71); <0.001

MDSS: Mediterranean Diet Serving Score. ♂: males. ♀: woman. Multivariate logistic regression models were built separately for waist-to-height ratio, waist-to-hip ratio and waist circumference. A multivariate ordinal regression model was used for the analysis of the characteristics associated with Body Mass Index (BMI). Adjusted odds ratios, 95% confidence intervals and *p*-Values were calculated using multivariate regression models; each of the four models was simultaneously adjusted for all covariates listed in this table.

Table 4. Characteristics associated with unfavorable biochemical parameters; lipid levels as determined by the multivariate logistic regression models and elevated fibrinogen as determined by ordinal regression model (sample size is 4011 subjects without previous cardiovascular disease diagnosis; all independent variables included in the model are listed in the table).

	Cholesterol (≥5 mmol/L) Adjusted Odds Ratio (95% Confidence Interval); *p*-Value	LDL (≥3 mmol/L) Adjusted Odds Ratio (95% Confidence Interval); *p*-Value	HDL (≤1.03 mmol/L ♂, ≤1.29 mmol/L ♀) Adjusted Odds Ratio (95% Confidence Interval); *p*-Value	Triglycerides (≥1.7 mmol/L) Adjusted Odds Ratio (95% Confidence Interval); *p*-Value	Fibrinogen (ref: ≥4.0 g/L) Adjusted Odds Ratio (95% Confidence Interval); *p*-Value
Sex (referent (ref): female)					
Male	0.86 (0.71–1.04); 0.128	0.92 (0.76–1.11); 0.364	0.78 (0.63–0.96); 0.020	1.95 (1.62–2.34); <0.001	0.75 (0.63–0.89); 0.001
Age (years, ref: 18–34.9)	Overall *p* < 0.001	Overall *p* <0.001	Overall *p* < 0.001	Overall *p* < 0.001	-
≥65	4.88 (3.59–6.64); <0.001	4.40 (3.26–5.94); <0.001	0.45 (0.32–0.63); <0.001	1.14 (0.81–1.61); 0.446	1.86 (1.39–2.48); <0.001
35–64.9	4.56 (3.67–5.66); <0.001	3.67 (2.96–4.55); <0.001	0.54 (0.42–0.70); <0.001	1.61 (1.20–2.15); 0.001	1.46 (1.16–1.84); 0.001
Place of residence (ref: Split)					
Island of Vis	0.97 (0.75–1.26); 0.837	0.71 (0.55–0.91); 0.007	0.10 (0.07–0.14); <0.001	0.68 (0.54–0.87); 0.002	0.51 (0.41–0.63); <0.001
Island of Korčula	0.91 (0.74–1.12); 0.369	0.89 (0.72–1.09); 0.265	0.44 (0.36–0.54); <0.001	0.65 (0.53–0.8); <0.001	0.31 (0.26–0.37); <0.001
Education (years of schooling, ref: ≥13)	Overall *p* = 0.595	Overall *p* = 0.117	Overall *p* = 0.703	Overall *p* = 0.392	-
0–8	1.00 (0.76–1.32); 0.995	0.89 (0.68–1.16); 0.395	1.00 (0.74–1.34); 0.989	1.19 (0.92–1.55); 0.177	1.25 (0.98–1.58); 0.069
9–12	1.09 (0.89–1.33); 0.388	1.12 (0.92–1.36); 0.259	1.08 (0.87–1.33); 0.482	1.06 (0.87–1.30); 0.539	1.25 (1.05–1.50); 0.014

Table 4. *Cont.*

	Cholesterol (≥5 mmol/L) Adjusted Odds Ratio (95% Confidence Interval); *p*-Value	LDL (≥3 mmol/L) Adjusted Odds Ratio (95% Confidence Interval); *p*-Value	HDL (≤1.03 mmol/L ♂, ≤1.29 mmol/L ♀) Adjusted Odds Ratio (95% Confidence Interval); *p*-Value	Triglycerides (≥1.7 mmol/L) Adjusted Odds Ratio (95% Confidence Interval); *p*-Value	Fibrinogen (ref: ≥4.0 g/L) Adjusted Odds Ratio (95% Confidence Interval); *p*-Value
Material status (ref: 4th quartile)	Overall $p = 0.495$	Overall $p = 0.775$	Overall $p = 0.010$	Overall $p = 0.240$	-
1st quartile	1.17 (0.90–1.52); 0.244	1.07 (0.83–1.37); 0.625	0.85 (0.64–1.12); 0.246	1.22 (0.94–1.57); 0.128	0.80 (0.64–1.00); 0.054
2nd quartile	0.98 (0.77–1.24); 0.842	0.98 (0.77–1.23); 0.843	1.02 (0.80–1.31); 0.873	1.23 (0.98–1.56); 0.078	0.73 (0.60–0.90); 0.003
3rd quartile	1.06 (0.84–1.33); 0.649	1.08 (0.86–1.36); 0.506	1.29 (1.02–1.63); 0.034	1.23 (0.98–1.54); 0.068	0.80 (0.65–0.97); 0.025
Smoking (ref: never-smoker)	Overall $p = 0.311$	Overall $p = 0.364$	Overall $p < 0.001$	Overall $p < 0.001$	-
current smoker	1.13 (0.93–1.38); 0.215	1.15 (0.95–1.40); 0.158	1.63 (1.32–2.00); <0.001	1.69 (1.39–2.06); <0.001	1.11 (0.93–1.32); 0.244
ex-smoker	1.15 (0.93–1.43); 0.203	1.07 (0.87–1.32); 0.505	1.07 (0.85–1.34); 0.562	1.30 (1.07–1.58); 0.009	1.03 (0.86–1.23); 0.746
Alcohol intake (ref: none)	Overall $p = 0.071$	Overall $p = 0.838$	Overall $p < 0.001$	Overall $p = 0.250$	-
excessive	1.38 (1.05–1.82); 0.022	1.05 (0.81–1.37); 0.703	0.49 (0.37–0.65); <0.001	1.04 (0.81–1.34); 0.744	0.58 (0.46–0.74); <0.001
moderate	1.10 (0.91–1.32); 0.344	0.98 (0.82–1.18); 0.832	0.63 (0.52–0.76); <0.001	0.89 (0.74–1.07); 0.227	0.82 (0.70–0.96); 0.015
MDSS compliance (ref: yes)					
no	0.94 (0.77–1.15); 0.543	1.01 (0.84–1.23); 0.881	1.18 (0.96–1.45); 0.112	0.93 (0.78–1.12); 0.437	0.78 (0.66–0.91); 0.002
Nut consumption (ref: infrequently or never)	Overall $p = 0.169$	Overall $p = 0.063$	Overall $p = 0.026$	Overall $p = 0.494$	-
daily	1.26 (0.83–1.92); 0.281	1.11 (0.75–1.65); 0.599	0.74 (0.48–1.13); 0.160	0.78 (0.52–1.16); 0.221	0.71 (0.51–1.01); 0.051
weekly	1.35 (1.02–1.79); 0.037	1.46 (1.11–1.94); 0.008	0.81 (0.62–1.07); 0.141	0.86 (0.65–1.13); 0.270	0.65 (0.52–0.83); <0.001
monthly	1.05 (0.86–1.27); 0.648	1.03 (0.85–1.24); 0.789	0.75 (0.62–0.92); 0.005	0.95 (0.79–1.15); 0.619	0.66 (0.56–0.79); <0.001
Physical activity (ref: intensive)	Overall $p = 0.766$	Overall $p = 0.632$	Overall $p = 0.053$	Overall $p = 0.182$	-
light	0.89 (0.65–1.23); 0.487	1.01 (0.75–1.36); 0.954	1.02 (0.73–1.42); 0.914	1.13 (0.85–1.51); 0.395	1.05 (0.80–1.37); 0.713
moderate	0.94 (0.71–1.25); 0.678	1.09 (0.84–1.42); 0.514	0.81 (0.60–1.10); 0.178	0.95 (0.74–1.22); 0.685	0.91 (0.72–1.15); 0.437
WHtR (≥0.5, ref: yes)					
no	0.53 (0.43–0.65); <0.001	0.47 (0.38–0.57); <0.001	0.41 (0.32–0.52); <0.001	0.29 (0.22–0.38); <0.001	0.74 (0.61–0.90); 0.002
Hypertension (systolic ≥ 140 mmHg or diastolic ≥ 90 mmHg or treated for hypertension, ref: yes)					
no	0.90 (0.72–1.11); 0.304	0.91 (0.74–1.11); 0.357	0.80 (0.66–0.99); 0.036	0.68 (0.57–0.81); <0.001	0.89 (0.75–1.05); 0.161
Diabetes (≥7 mmol/L or treated for diabetes type 2, ref: yes)					
no	1.48 (1.11–1.98); 0.007	1.54 (1.17–2.03); 0.002	0.56 (0.42–0.74); <0.001	0.57 (0.45–0.73); <0.001	0.86 (0.67–1.10); 0.221
Gout (uric acid ≥404 µmol/L ♂, ≥338 µmol/L ♀ or gout, ref: yes)					
no	0.80 (0.63–1.03); 0.083	1.04 (0.83–1.30); 0.740	0.63 (0.50–0.80); <0.001	0.41 (0.34–0.50); <0.001	1.01 (0.83–1.23); 0.895

MDSS—Mediterranean Diet Serving Score. WHtR—waist-to-height ratio. ♂: males. ♀: woman. Multivariate logistic regression models were built separately for cholesterol, LDL, HDL and triglycerides. Multivariate ordinal regression model was used for the analysis of the characteristics associated with elevated fibrinogen. Adjusted odds ratios, 95% confidence intervals and *p*-Values were calculated using multivariate regression models; each of the five models presented here was simultaneously adjusted for all covariates listed in this table.

Table 5. Characteristics associated with hypertension, diabetes, metabolic syndrome and gout as determined by the multivariate logistic regression analyses (sample size is 4011 subjects without previous cardiovascular disease diagnosis; all independent variables included in the model are listed in the table).

	Hypertension (Systolic ≥140 mmHg or Diastolic ≥90 mmHg or Treated for Hypertension) Adjusted Odds Ratio (95% Confidence Interval); *p*-Value	**Diabetes (≥7 mmol/L or Treated for Diabetes Type 2) Adjusted Odds Ratio (95% Confidence Interval); *p*-Value**	**Elevated HbA1c (≥6.5 mmol/L or Treated for Diabetes Type 2) Adjusted Odds Ratio (95% Confidence Interval); *p*-Value**	**Metabolic Syndrome Adjusted Odds Ratio (95% Confidence Interval); *p*-Value**	**Gout (Uric Acid ≥404 mmol/L ♂-≥338 mmol/L ♀ or Gout) Adjusted Odds Ratio (95% Confidence Interval); *p*-Value**
Sex (referent (ref): female)					
male	1.29 (1.06–1.56); 0.011	2.32 (1.74–3.09); <0.001	1.77 (1.29–2.42); <0.001	0.71 (0.59–0.86); <0.001	1.91 (1.55–2.37); <0.001
Age (years, ref: 18–34.9)	Overall p < 0.001	Overall p = 0.002	Overall p = 0.006	Overall p < 0.001	Overall p = 0.070
≥65	10.75 (6.66–17.36); <0.001	3.69 (1.69–8.03); 0.001	3.43 (1.42–8.31); 0.006	3.16 (2.24–4.47); <0.001	1.24 (0.83–1.86); 0.294
35–64.9	5.37 (3.41–8.46); <0.001	2.71 (1.28–5.73); 0.009	2.46 (1.04–5.79); 0.040	2.24 (1.66–3.02); <0.001	0.96 (0.67–1.38); 0.833
Place of residence (ref: Split)					
Island of Vis	0.62 (0.48–0.80); <0.001	0.97 (0.65–1.44); 0.876	0.96 (0.61–1.50); 0.844	2.19 (1.71–2.80); <0.001	1.44 (1.07–1.93); 0.015
Island of Korčula	0.98 (0.80–1.22); 0.888	1.25 (0.88–1.77); 0.206	1.64 (1.11–2.43); 0.013	1.09 (0.89–1.34); 0.392	1.19 (0.92–1.53); 0.186
Education (years of schooling, ref: ≥13)	Overall p = 0.001	Overall p = 0.087	Overall p = 0.089	Overall p = 0.002	Overall p = 0.006
0–8	1.44 (1.11–1.86); 0.006	1.52 (1.03–2.24); 0.035	1.51 (0.99–2.3); 0.056	1.44 (1.11–1.86); 0.006	1.62 (1.21–2.18); 0.001
9–12	0.93 (0.75–1.15); 0.494	1.17 (0.84–1.65); 0.352	1.11 (0.76–1.61); 0.599	0.98 (0.81–1.20); 0.866	1.24 (0.97–1.58); 0.086
Material status (ref: 4th quartile)	Overall p = 0.062	Overall p = 0.381	Overall p = 0.062	Overall p = 0.957	Overall p = 0.372
1st quartile	1.33 (1.03–1.71); 0.029	1.31 (0.88–1.94); 0.178	1.67 (1.07–2.60); 0.025	0.96 (0.75–1.24); 0.770	0.81 (0.61–1.08); 0.154
2nd quartile	1.25 (0.98–1.58); 0.070	1.37 (0.94–2.00); 0.100	1.63 (1.06–2.52); 0.027	0.94 (0.74–1.18); 0.573	0.79 (0.61–1.04); 0.094
3rd quartile	1.03 (0.82–1.30); 0.802	1.33 (0.91–1.92); 0.137	1.75 (1.15–2.68); 0.010	0.97 (0.78–1.21); 0.780	0.87 (0.67–1.13); 0.306
Smoking (ref: never-smoker)	Overall p = 0.001	Overall p = 0.706	Overall p = 0.698	Overall p = 0.897	Overall p < 0.001
current smoker	0.65 (0.53–0.80); <0.001	0.88 (0.63–1.21); 0.418	0.86 (0.60–1.22); 0.398	1.04 (0.86–1.27); 0.664	0.67 (0.52–0.86); 0.002
ex-smoker	0.78 (0.64–0.95); 0.014	0.93 (0.70–1.25); 0.647	0.97 (0.70–1.33); 0.832	1.03 (0.85–1.26); 0.747	1.27 (1.02–1.57); 0.031
Alcohol intake (ref: none)	Overall p = 0.969	Overall p = 0.062	Overall p = 0.005	Overall p = 0.057	Overall p = 0.005
excessive	0.99 (0.76–1.28); 0.921	0.81 (0.56–1.18); 0.274	0.69 (0.46–1.04); 0.076	1.14 (0.88–1.47); 0.312	1.60 (1.21–2.13); 0.001
moderate	1.01 (0.84–1.23); 0.882	0.71 (0.54–0.94); 0.019	0.60 (0.44–0.82); 0.001	0.88 (0.73–1.06); 0.170	1.27 (1.01–1.58); 0.038
MDSS compliance (ref: yes)					
no	1.14 (0.95–1.37); 0.152	0.66 (0.51–0.86); 0.002	0.57 (0.43–0.75); <0.001	0.99 (0.83–1.19); 0.932	1.15 (0.93–1.42); 0.194
Nut consumption (ref: infrequently or never)	Overall p = 0.248	Overall p = 0.212	Overall p = 0.355	Overall p = 0.103	Overall p = 0.435
daily	1.15 (0.79–1.68); 0.470	0.58 (0.31–1.08); 0.088	0.67 (0.35–1.26); 0.210	0.83 (0.57–1.21); 0.338	1.13 (0.73–1.76); 0.577
weekly	0.91 (0.69–1.20); 0.516	0.77 (0.50–1.18); 0.233	0.85 (0.54–1.34); 0.475	0.88 (0.68–1.14); 0.339	0.97 (0.71–1.33); 0.868
monthly	1.17 (0.97–1.41); 0.109	0.84 (0.63–1.12); 0.247	0.80 (0.58–1.09); 0.155	0.80 (0.66–0.96); 0.016	0.85 (0.68–1.06); 0.150

Table 5. *Cont.*

	Hypertension (Systolic ≥140 mmHg or Diastolic ≥90 mmHg or Treated for Hypertension) Adjusted Odds Ratio (95% Confidence Interval); *p*-Value	**Diabetes (≥7 mmol/L or Treated for Diabetes Type 2) Adjusted Odds Ratio (95% Confidence Interval); *p*-Value**	**Elevated HbA1c (≥6.5 mmol/L or Treated for Diabetes Type 2) Adjusted Odds Ratio (95% Confidence Interval); *p*-Value**	**Metabolic Syndrome Adjusted Odds Ratio (95% Confidence Interval); *p*-Value**	**Gout (Uric Acid ≥404 mmol/L ♂-≥338 mmol/L ♀ or Gout) Adjusted Odds Ratio (95% Confidence Interval); *p*-Value**
Physical activity (ref: intensive)	Overall $p = 0.518$	Overall $p = 0.063$	Overall $p = 0.009$	Overall $p = 0.046$	Overall $p = 0.275$
light	0.87 (0.65–1.17); 0.355	1.66 (1.08–2.55); 0.021	2.15 (1.31–3.52); 0.002	0.98 (0.73–1.32); 0.909	1.31 (0.94–1.82); 0.114
moderate	0.86 (0.66–1.11); 0.253	1.34 (0.91–1.97); 0.135	1.64 (1.04–2.57); 0.032	0.80 (0.62–1.04); 0.093	1.23 (0.92–1.64); 0.165
WHtR (≥0.5, ref: yes)					
no	0.52 (0.39–0.68); <0.001	1.00 (0.6–1.66); 0.986	0.57 (0.30–1.08); 0.083	0.14 (0.10–0.18); <0.001	0.39 (0.27–0.57); <0.001
Hypertension (systolic ≥140 mmHg or diastolic ≥90 mmHg or treated for hypertension, ref: yes)					
no	na	0.56 (0.43–0.72); <0.001	0.58 (0.44–0.77); <0.001	0.33 (0.28–0.40); <0.001	0.50 (0.41–0.61); <0.001
Diabetes (≥7 mmol/L or treated for diabetes type 2, ref: yes)					
no	0.57 (0.44–0.74); <0.001	na	na	0.19 (0.14–0.27); <0.001	0.91 (0.69–1.19); 0.488
Metabolic syndrome (ref: yes)					
no	0.33 (0.28–0.40); <0.001	0.18 (0.13–0.26); <0.001	0.25 (0.18–0.36); <0.001	na	0.61 (0.49–0.75); <0.001
Gout (Uric acid ≥404 µmol/L ♂, ≥338 µmol/L ♀ or gout, ref: yes)					
no	0.50 (0.41–0.61); <0.001	0.90 (0.69–1.18); 0.453	0.86 (0.64–1.15); 0.306	0.61 (0.49–0.75); <0.001	na

MDSS: Mediterranean Diet Serving Score. WHtR: waist-to-height ratio. Na: not applicable. ♂: males. ♀: woman. Multivariate logistic regression models were built separately for hypertension, diabetes, metabolic syndrome and gout. Adjusted odds ratios, 95% confidence intervals and *p*-Values were calculated using multivariate logistic regression; each of the four models was simultaneously adjusted for all covariates listed in this table, with an exception of excluding predictor variables in models where those variables were the outcome variables (marked with "na").

When clinical outcomes were investigated for the association between nut intake and presence of chronic diseases, only one result was significant: monthly consumers had 20% lower odds for having metabolic syndrome compared to the never-consumers (OR = 0.80, 95% CI 0.66–0.96; $p = 0.016$; Table 5). Interestingly, participants who did not adhere to the Mediterranean diet had lower odds for the concomitant presence of both diabetes and elevated HbA1c (OR = 0.66, 95% CI 0.51–0.86; $p = 0.002$; OR = 0.57, 95% CI 0.43–0.75; $p < 0.001$, respectively; Table 5), which indicates that subjects with diabetes had better adherence to this preventative nutritional pattern. There was no association between nut intake and hypertension or gout presence (Table 5). In a sub-analysis, including only participants older than >65 years of age, there was only one significant association with nut intake: elevated HbA1c (OR = 0.29, 95% CI 0.10–0.87; $p = 0.028$ in daily nut consumers compared to non-consumers; Table S3).

4. Discussion

The results of this study indicate that as low as 5% of all subjects reported daily, and 11% reported weekly, nut consumption. More frequent nut consumption was reported by women, people with the highest level of education and material status and those with healthier lifestyles—non-smokers, more adherent to the Mediterranean diet and in subjects who were free from central obesity, diabetes and metabolic syndrome. Subjects who reported weekly and monthly nut intake were less likely to suffer from elevated waist-to-height and waist-to-hip ratios, elevated fibrinogen and reduced HDL cholesterol, compared to non-consumers.

A low prevalence of nut consumption was previously reported in Croatia—as low as 5.5% of island inhabitants reported daily nut consumption [25]. This percent varies even across the Mediterranean region, ranging from 55% of women in Southern Spain [40], to as low as 8% in the Molise region of Italy [41]. However, these figures also seem to show a positive pattern of change across time, as seen in the case of Northern Italy, where an increase in nut consumption was recorded between 2010 and 2016 [22]. A similar increase in nut consumption in the population of Southern Croatia can be seen only within the population of the City of Split, where 7% of participants consumed nuts daily in 2008–2009 period, while in 2012–2013 period, there 11% were daily consumers [25]. The same pattern was not present in the remote island populations of Vis, possibly due to less favorable socioeconomic environment and remoteness.

A recent study in New Zealand investigated predictors of nut consumption, where the daily whole nut consumption frequency of 6.9% was similar to our findings [29]. That study identified several factors associated with daily nut consumption: older age (51–70 years OR = 5.99, 95% CI 2.84–12.66), while overweight and obese subjects had reduced odds for daily whole nut intake (0.62, 0.39–0.97 in overweight, and 0.54, 0.33–0.89 in obese subjects) [29]. Additionally, the mean amount of whole nuts eaten in grams per day was associated with sex, age, ethnicity and deprivation, an area-based measure which reflected both material and social deprivation [29]. Similar results were obtained in our study, except that we did not detect the age effect on nut consumption.

Nut consumption, in this study, was associated with reduced odds for decreased HDL cholesterol and reduced odds for increased fibrinogen, while total cholesterol and LDL cholesterol did not reach the significance level (when the overall *p*-Value was observed) and triglycerides did not exhibit any association with nut intake within this study. Previous studies have also shown various results in regard to the impact of nut consumption on blood lipid levels. Some have found beneficial effects, while others did not record any difference in blood lipids between nut consumers and non-consumers [14,17,42–44]. A possible explanation for these findings is in the different definitions used for nut consumption (type, frequency and amount of nuts consumed), different time frames of follow-up and different confounding factors taken into account. For instance, in a Cochrane review and meta-analysis with three trials included, substantial heterogeneity was found between the trials for the effect of nut consumption on total cholesterol and triglyceride levels, while for HDL cholesterol and LDL cholesterol, no effect of nut consumption has been identified [17].

Subjects in this study who consumed nuts weekly and monthly had lower odds for having an elevated fibrinogen level, which is considered an inflammatory marker. This is a confirmation of a previous finding of lower levels of fibrinogen (and other inflammatory markers) in people who consumed nuts and seeds more frequently [45]. In regard to this, the finding of a recent study in the urban population of Catania, Italy, was particularly interesting because it demonstrated that the main dietary sources of total polyphenols were nuts [46]. It is therefore plausible that the cardiovascular diseases risk reduction effect of nut intake is, at least in part, due to these compounds, which are well known to counteract the burden of oxidative stress and thus limit the effects of cellular aging [47].

The nut intake effect on glucose and insulin levels and diabetes risk has also been previously investigated. The majority of studies have shown a beneficial impact of nut consumption. For example, a meta-analysis of 12 randomized controlled dietary trials, including individuals with diabetes showed that daily nut consumption (a median dose of 56 g/day over $\geq$3 weeks) lowered HbA1c by 0.07% (95% CI: −0.10, −0.03%; $p = 0.0003$) and fasting glucose by 0.15 mmol/L (95% CI: −0.27, −0.02 mmol/L; $p = 0.03$), compared to control diets [15]. Another meta-analysis, including 25 observational studies and two clinical trials, found that nut consumption was associated with a reduction in diabetes risk by 13% (based on six studies and 13,308 events; RR: 0.87, 95% CI 0.81–0.94) [48]. Furthermore, the PREDIMED study showed that people who consumed a Mediterranean diet enriched with daily nut intake (30 g/day; 15 g of walnuts, 7.5 g of hazelnuts, and 7.5 g of almonds) had an 18% reduction in risk for the incidence of diabetes (hazard ratio of 0.82, 95% CI 0.61–1.10) compared to the control group, who received advice on a low-fat diet [28]. Our cross-sectional study failed to confirm these results. On the contrary, subjects who did not comply with a Mediterranean diet had lower odds for the presence of diabetes and elevated HbA1c (OR = 0.66, 95% CI 0.51–0.86 and OR = 0.57, 95% CI 0.43–0.75, respectively). Since this is a cross-sectional study, this result is easily explained by the adoption of a healthy dietary pattern in those who were diagnosed with type 2 diabetes, as a tertiary prevention measure. A similar result was recorded for total and LDL cholesterol, since subjects who consumed nuts weekly presented increased odds for concomitant presence of increased levels of these blood lipids. This finding could also be a consequence of a high-fat diet content, which has been shown to raise plasma cholesterol, LDL cholesterol, and HDL cholesterol [49].

More frequent nut consumption in this study was also seen in subjects who were free from diabetes, metabolic syndrome and central obesity (defined by the waist-to-height and waist-to-hip ratios). At the same time, there was no association with direct measures, namely waist circumference and BMI. Interestingly, relative measures have been shown to be better for detecting cardiometabolic risk factors and adverse health outcomes [33], indirectly suggesting that nuts could be contributing to the favorable cardiovascular profile. A large population-based cohort study, with over 370,000 people, reported that those who consumed nuts >1 time/week exhibited a slightly reduced weight gain (−0.10 kg; 95% CI −0.15, −0.04) over a 5 year of follow-up period (compared to non-consumers), and had a 5% lower risk of becoming overweight or obese, compared to non-consumers [11]. A potential explanation for these findings could be found in the high satiety effect of nuts, such as almonds, whose consumption has been shown to have the same satiety impact as baked foods with the equivalent energy and macronutrient content [50]. A similar result was obtained in another experimental study in subjects at increased risk of type 2 diabetes, where almond consumption, especially eaten as a snack, lowered serum glucose responses post-prandially and managed to reduce hunger and desire to eat [51]. Another study confirmed that the metabolizable energy value of walnuts was as much as 21% smaller than predicted, possibly explaining why nut intake should not be considered a risk factor for excessive weight gain [52], especially if consumed moderately (about 30 g per day). These findings are especially important, given the trends of obesity worldwide, since nut consumption could be used in metabolism and appetite control. Systematic education about the potential health benefits of nut intake, with a special emphasis on the absence of obesity risk, for both health professionals and lay population is needed. Good quality studies and evidence based dietary guidelines should be put forward in health education and promotion, in order to clarify doubts and correct erroneous assumptions about nut intake. Indeed, an international group of authors recently published lifestyle recommendations for the prevention and management of metabolic syndrome and these included the consumption of nuts, alongside legumes, cereals (whole grains), fruits, vegetables, fish, and low-fat dairy products [53].

Habitual nut intake, as a preventive measure, could offer protection against cardiovascular disease complications and death, especially in people with lower adherence to the Mediterranean diet [14,41] and diabetes [43]. We found no such association between nut intake and the presence of the diagnosis of hypertension, diabetes or gout, but we did find some indication of the association between monthly nut intake and lower odds for metabolic syndrome presence (OR = 0.80, 95% CI 0.66–0.96). A recent meta-analysis of randomized controlled trials also identified a beneficial effect of tree nuts on metabolic syndrome criteria, through modest decreases in triglycerides and fasting blood glucose [54].

Study Limitations and Advantages

Study limitations include cross-sectional study design, which cannot establish a causal relationship between the cause and the effect. Namely, participants who experienced a decline in their health could have started consuming nuts as a preventive measure, which could be seen in observed association between weekly nut consumption and elevated cholesterol and LDL cholesterol. Recall bias and other types of bias, like volunteer bias, due to the convenience sampling approach, and confounding by indication, could have affected the results and conclusions. The question on nut consumption included all nuts, not distinguishing between different types of nuts or the amount of consumed nuts, which disabled us from further detailed characterization of specific nut consumption. A low frequency of 5% of daily nut consumers could have affected the statistical power for detecting the association between daily nut intake and investigated risk factors. This could explain the results obtained in the regression models, without any statistically significant result for the association between daily nut intake and the outcomes compared to non-consumers, unlike for weekly and monthly nut intake groups. Additionally, this study was stretched over a 2003–2015 period, and performed as a series of cross-sectional studies, introducing the possibility for time trends in nut consumption of unknown direction to influence the results differently in the three observed populations, according to the place of residence. Each study site was sampled in different time periods, which were never over-lapping. This issue was mitigated by using the multivariate approach in the analysis, and the place of residence was one of the predictors included in the models. The future research direction that could corroborate current findings is a follow-up analysis of the nut intake frequency and the association of nut intake and health outcomes in this population. Further study should also take into account the effect of aging and the trend of nut consumption.

Interestingly, we found that a less intense physical activity level was also associated with more frequent nut consumption. This particular finding could be explained by the fact that self-reported physical activity level did not describe only leisure physical activities promoting health, like sports or gym, but an overall daily living activity, including work. The minority of subjects who reported intensive physical activity (10%) most commonly were manual workers, who usually have a lesser educational level, which in turn could be associated with decreased health awareness and reduced odds of nut consumption.

The advantage of the study is its relatively large sample size, gathered from a general population in the Mediterranean region of Croatia. Another good aspect of this study is the analysis of the association of nut intake with many health outcomes, which is seldom seen in the literature. To the best of our knowledge, this is the first study that has examined both the characteristics associated with habitual nut consumption frequency and the association between nut intake and cardiovascular health related risks in Croatia and beyond.

This study adds new insights into the existing knowledge of factors associated with nut intake and the impact of nut consumption on human health. Still, there is much to be investigated, since there are many discrepancies in results from different studies, especially con the effect of nut intake on intermediate risk factors, like blood lipid levels, and also on clinical endpoints (cardiovascular diseases, diabetes, cancer, etc.). In order to elucidate the actual mechanisms and unbiased effects of nut intake on various health outcomes, a larger size and well controlled experimental study (for many confounding factors) and of longer duration is needed. A good model could be found in the PREDIMED study, but within that study, nuts were used on top of the Mediterranean diet intervention, so it was not easy to estimate the effects of nuts themselves [28]. Nevertheless, there is a sufficient amount of evidence pointing to various health benefits of habitual nut intake, which should be included in the recommendations for prevention and management of overweight and obesity, as well as common cardiovascular risk factors.

5. Conclusions

The results of this study bring forward important findings, identifying several factors associated with more frequent habitual nut intake and beneficial associations between nut intake and several cardiovascular risk factors. Given the potential health benefits of nut consumption, these insights should be taken into account when planning for cardiovascular health interventions and their implementations, on both an individual and population level.

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Conflicts of Interest: The authors declare no conflict of interest.

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Table S1. Characteristics associated with frequency of nut consumption (entire sample; n=4,416).

	Daily nut consumption n= 212	Weekly nut consumption n= 487	Monthly nut consumption n= 1,276	Infrequent or never nut consumption n= 2,441	Overall *p* (post-hoc test p-Values)
Sex; n (%)					<0.001 (0.173^{DW}, <0.001^{DM}, <0.001^{DN} 0.001^{WM}, <0.001^{WN}, 0.054^{MN})
men	52 (24.5)	144 (29.6)	490 (38.6)	1017 (41.7)	
women	160 (75.5)	343 (70.4)	786 (61.6)	1424 (58.3)	
Age (years); median (interquartile range (IQR))	58.0 (19.75)	53.0 (21.0)	51.0 (22.0)	56.0 (23.0)	<0.001 (<0.001^{DW}, <0.001^{DM}, 0.060^{DN} 0.035^{WM}, <0.001^{WN}, <0.001^{MN})
Education (years of schooling); median (IQR)	12.0 (4.0)	12.0 (3.0)	12.0 (3.0)	12.0 (4.0)	<0.001 (0.438 ^{DW}, 0.173^{DM}, <0.001^{DN} 0.001^{WM}, <0.001^{WN}, <0.001^{MN})
Material status; median (IQR)	11.0 (4.0)	11.0 (4.0)	11.0 (4.0)	10.0 (4.0)	<0.001 (0.073^{DW}, 0.786^{DM}, <0.001^{DN}, 0.001^{WM}, <0.001^{WN}, <0.001^{MN})
Smoking; n (%)					0.008 (0.431^{DW}, 0.021^{DM}, 0.011^{DN}, 0.059^{WM}, 0.012^{WN}, 0.625^{MN})
current smokers	41 (19.3)	115 (23.6)	361 (28.3)	690 (28.3)	
ex-smokers	55 (25.9)	114 (23.4)	315 (24.7)	636 (26.1)	
never-smokers	116 (54.7)	258 (53.0)	600 (47.0)	1115 (45.7)	
Alcohol intake; n (%)					0.001 (0.098^{DW}, 0.025^{DM}, 0.403^{DN}, 0.256^{WM}, 0.012^{WN}, 0.002^{MN})
excessive	32 (15.1)	70 (14.4)	225 (17.6)	437 (17.9)	
moderate	90 (42.5)	248 (50.9)	631 (49.5)	1069 (43.8)	
none	90 (42.5)	169 (34.7)	420 (32.9)	935 (38.3)	
MDSS≥14 points; n (%)	147 (69.3)	189 (38.8)	301 (23.6)	637 (26.1)	<0.001 (<0.001^{DW}, <0.001^{DM}, <0.001^{DN}, <0.001^{WM}, <0.001^{WN}, 0.095^{MN})
Physical activity; n (%)					<0.001 (0.588^{DW}, 0.414^{DM}, 0.041^{DN}, 0.006^{WM}, <0.001^{WN}, 0.019^{MN})
light	51 (24.1)	122 (25.1)	304 (23.8)	612 (25.1)	
moderate	147 (69.3)	342 (70.2)	852 (66.8)	1532 (62.8)	
intensive	14 (6.6)	23 (4.7)	120 (9.4)	295 (12.1)	
BMI (kg/m²); n (%)					<0.001 (0.550^{DW}, 0.405^{DM}, 0.017^{DN}, 0.662^{WM}, <0.001^{WN}, <0.001^{MN})
≤25.0 (normal)	102 (48.1)	242 (49.7)	605 (47.4)	984 (40.3)	
25.0-29.9 (overweight)	83 (39.2)	172 (35.3)	464 (36.4)	971 (39.8)	
≥30.0 (obese)	27 (12.7)	73 (15.0)	207 (16.2)	486 (19.9)	
Waist circumference (≥94 cm♂, ≥80cm♀); n (%)	169 (80.1)	360 (74.2)	919 (72.5)	1909 (78.9)	<0.001 (0.096^{DW}, 0.021^{DM}, 0.695^{DN}, 0.475^{WM}, 0.022^{WN}, <0.001^{MN})
WHR (≥0.90 ♂, ≥0.85♀); n (%)	137 (64.9)	296 (61.0)	805 (63.6)	1800 (74.6)	<0.001 (0.330^{DW}, 0.718^{DM}, 0.002^{DN}, 0.313^{WM}, <0.001^{WN}, <0.001^{MN})

WHtR (≥0.5); n %	159 (75.4)	348 (71.8)	932 (73.6)	1975 (81.7)	<0.001 (0.326[DW], 0.583[DM], 0.024[DN], 0.446[WM], <0.001[WN], <0.001[MN])
Cholesterol (≥5 mmol/L); n (%)	164 (77.4)	378 (77.6)	892 (69.9)	1841 (75.4)	<0.001 (0.940[DW], 0.027[DM], 0.529[DN], 0.001[WM], 0.301[WN], <0.001[MN])
HDL (≤1.03 mmol/L♂, ≤1.29 mmol/L♀); n (%)	35 (16.5)	95 (19.5)	231 (18.1)	493 (20.2)	0.321 (0.349[DW], 0.575[DM], 0.197[DN], 0.497[WM], 0.729[WN], 0.126[MN])
LDL (≥3 mmol/L); n (%)	158 (74.5)	377 (77.4)	884 (69.3)	1795 (73.5)	0.003 (0.408[DW], 0.122[DM], 0.753[DN], 0.001[WM], 0.074[WN], 0.006[MN])
Triglycerides (≥1.7 mmol/L); n (%)	41 (19.3)	106 (21.8)	302 (23.7)	714 (29.3)	<0.001 (0.469[DW], 0.166[DM], 0.002[DN], 0.397[WM], 0.001[WN], <0.001[MN])
CHD; n (%)	13 (6.1)	25 (5.1)	59 (4.6)	244 (10.0)	<0.001 (0.592[DW], 0.346[DM], 0.068[DN], 0.658[WM], 0.001[WN], <0.001[MN])
CVI; n (%)	4 (1.9)	8 (1.6)	17 (1.3)	66 (2.7)	0.041 (0.819[DW], 0.526[DM], 0.477[DN], 0.662[WM], 0.173[WN], 0.007[MN])
Hypertension (Systolic ≥140 mmHg or Diastolic ≥90 mmHg or treated for hypertension); n (%)	73 (34.4)	141 (29.0)	391 (30.7)	896 (36.8)	<0.001 (0.148[DW], 0.279[DM], 0.496[DN], 0.471[WM], 0.001[WN], <0.001[MN])
Diabetes (≥7 mmol/L or treated for diabetes type 2); n (%)	20 (9.4)	39 (8.0)	105 (8.2)	318 (13.0)	<0.001 (0.533[DW], 0.558[DM], 0.132[DN], 0.880[WM], 0.002[WN], <0.001[MN])
HbA1c (≥6.5 mmol/L or treated for diabetes); n (%)	19 (9.0)	35 (7.2)	85 (6.7)	255 (10.4)	0.001 (0.419[DW], 0.224[DM], 0.496[DN], 0.695[WM], 0.028[WN], <0.001[MN])
Metabolic syndrome; n (%)	87 (42.6)	189 (39.5)	471 (39.0)	1258 (52.3)	<0.001 (0.449[DW], 0.327[DM], 0.008[DN], 0.845[WM], <0.001[WN], <0.001[MN])
Gout (Uric acid ≥404 µmol/L♂, ≥338 µmol/L♀ or gout); n (%)	34 (16.9)	71 (15.0)	191 (16.0)	513 (21.6)	<0.001 (0.526[DW], 0.747[DM], 0.122[DN], 0.602[WM], 0.001[WN], <0.001[MN])

MDSS - Mediterranean Diet Serving Score. BMI - body mass index. WHR – waist-to-hip ratio. WHtR – waist-to-height ratio. CHD - coronary heart disease. CVI - cerebrovascular insult. ♂: males. ♀: woman. *p*-Values for categorical variables were obtained with chi-squared test, and for numerical with Kruskal-Wallis test. Post-hoc test *p*-Values for categorical variables were obtained with chi-squared test, and for numerical with Mann-Whitney U test. [DW] Post-hoc test *p*-Value: daily vs. weekly. [DM] Post-hoc test *p*-Value: daily vs. monthly. [DN] Post-hoc test *p*-Value: daily vs. never. [WM] Post-hoc test *p*-Value: weekly vs. monthly. [WN] Post-hoc test *p*-Value: weekly vs. infrequently or never. [MN] Post-hoc test *p*-Value: monthly vs. infrequently or never.

Table S2. Characteristics associated with unfavorable biochemical parameters; lipid levels as determined by the multivariate logistic regression models and elevated fibrinogen as determined by ordinal regression model (sample size is 897 subjects without previous cardiovascular disease diagnosis and older than 65 years of age; all independent variables included in the model are listed in the table).

	Cholesterol (≥5 mmol/L) Adjusted odds ratio (95% confidence interval); *p*-Value	**LDL (≥3 mmol/L)** Adjusted odds ratio (95% confidence interval); *p*-Value	**HDL (≤1.03 mmol/L♂, ≤1.29 mmol/L♀)** Adjusted odds ratio (95% confidence interval); *p*-Value	**Triglycerides (≥1.7 mmol/L)** Adjusted odds ratio (95% confidence interval); *p*-Value	**Fibrinogen (≥4.0 g/l is referent)** Adjusted odds ratio (95% confidence interval); *p*-Value
Sex (referent (ref): female)					
male	0.67 (0.43-1.01); 0.120	0.81 (0.52-1.27); 0.360	0.35 (0.21-0.59); <0.001	1.04 (0.71-1.53); 0.845	0.96 (0.67-1.37); 0.806
Age (years) median (interquartile range (IQR))	0.96 (0.92-1.00); 0.047	0.98 (0.95-1.02); 0.324	1.00 (0.96-1.05); 0.837	0.97 (0.94-1.00); 0.086	1.01 (0.98-1.05); 0.384
Place of residence (ref: Split)					
Island of Vis	2.07 (1.05-4.10); 0.035	1.34 (0.70-2.55); 0.379	0.09 (0.04-0.18); <0.001	0.56 (0.34-0.93); 0.024	0.41 (0.26-0.67); <0.001
Island of Korčula	1.20 (0.67-2.14); 0.538	1.01 (0.58-1.78); 0.962	0.35 (0.21-0.58); <0.001	0.44 (0.28-0.70); <0.001	0.23 (0.15-0.35); <0.001
Education (years of schooling, ref: ≥13)	Overall *p* = 0.154	Overall *p* = 0.043	Overall *p* = 0.294	Overall *p* = 0.328	-
0-8	0.58 (0.31-1.10); 0.101	0.59 (0.32-1.08); 0.086	1.27 (0.66-2.46); 0.471	1.46 (0.88-2.42); 0.147	2.12 (1.30-3.44); 0.002
9-12	0.88 (0.48-1.64); 0.692	1.05 (0.59-1.89); 0.864	1.60 (0.86-2.96); 0.135	1.21 (0.74-1.98); 0.448	1.49 (0.94-2.36); 0.092
Material status (ref: 4th quartile)	Overall *p* = 0.624	Overall *p* = 0.055	Overall *p* = 0.107	Overall *p* = 0.329	-
1st quartile	1.47 (0.77-2.80); 0.243	1.54 (0.84-2.81); 0.159	1.01 (0.51-2.00); 0.976	1.31 (0.77-2.23); 0.326	0.76 (0.46-1.24); 0.267
2nd quartile	1.32 (0.69-2.53); 0.402	1.35 (0.74-2.47); 0.334	1.12 (0.56-2.21); 0.750	1.10 (0.64-1.91); 0.726	0.88 (0.54-1.45); 0.618
3rd quartile	1.12 (0.57-2.18); 0.749	1.24 (0.65-2.34); 0.512	1.88 (0.94-3.78); 0.075	1.58 (0.90-2.77); 0.114	0.95 (0.56-1.61); 0.847
Smoking (ref: never-smokers)	Overall *p* = 0.803	Overall *p* = 0.408	Overall *p* = 0.806	Overall *p* = 0.226	-
current smokers	0.94(0.47-1.87); 0.860	1.44 (0.72-2.90); 0.303	0.87 (0.43-1.78); 0.712	1.56 (0.94-2.57); 0.085	1.27 (0.78-2.05); 0.340
ex-smokers	0.85 (0.52-1.38); 0.507	0.87 (0.55-1.36); 0.535	0.85 (0.50-1.45); 0.548	1.11 (0.75-1.63); 0.609	0.86 (0.59-1.24); 0.418
Alcohol intake (ref: none)	Overall *p* = 0.196	Overall *p* = 0.504	Overall *p* = 0.182	Overall *p* = 0.320	-
excessive	1.74 (0.87-3.48); 0.114	1.23 (0.65-2.35); 0.528	0.62 (0.30-1.26); 0.183	1.13 (0.67-1.91); 0.643	0.69 (0.41-1.15); 0.153
moderate	1.01 (0.64-1.61); 0.960	0.89 (0.57-1.38); 0.609	0.68 (0.44-1.06); 0.088	0.83 (0.57-1.20); 0.323	0.92 (0.65-1.29); 0.620
MDSS compliance (ref: yes)					
no	0.86 (0.56-1.31); 0.478	0.83 (0.55-1.23); 0.345	1.30 (0.85-2.00); 0.229	0.81 (0.58-1.12); 0.204	0.83 (0.61-1.13); 0.231
Nut consumption (ref: infrequently or never)	Overall *p* = 0.350	Overall *p* = 0.470	Overall *p* = 0.142	Overall *p* = 0.303	-
daily	1.71 (0.68-4.27); 0.253	1.02 (0.48-2.20); 0.950	1.37 (0.64-2.89); 0.416	0.69 (0.34-1.40); 0.308	0.65 (0.35-1.22); 0.183
weekly	1.79 (0.84-3.65); 0.136	1.76 (0.87-3.55); 0.115	0.65 (0.33-1.29); 0.222	0.62 (0.35-1.11); 0.107	0.80 (0.48-1.32); 0.379
monthly	1.21 (0.74-1.97); 0.445	1.11 (0.70-1.76); 0.660	0.64 (0.38-1.06); 0.083	1.03 (0.70-1.52); 0.878	0.58 (0.39-0.84); 0.004
Physical activity (ref: intensive)	Overall *p* = 0.689	Overall *p* = 0.610	Overall *p* = 0.517	Overall *p* = 0.207	-
light	1.00 (0.47-2.13); 0.996	0.70 (0.34-1.43); 0.326	0.98 (0.46-2.10); 0.958	1.52 (0.84-2.73); 0.166	1.10 (0.64-1.88); 0.725
moderate	0.83 (0.42-1.64); 0.596	0.79 (0.41-1.53); 0.486	0.77 (0.38-1.56); 0.474	1.12 (0.66-1.91); 0.672	0.64 (0.40-1.04); 0.074
WHtR (≥ 0.5, ref: yes)					
no	0.47 (0.21-1.05); 0.066	0.32 (0.15-0.66); 0.002	0.33 (0.09-1.15); 0.081	0.37 (0.14-0.99); 0.049	0.96 (0.49-1.90); 0.913

Hypertension (systolic ≥140 mmHg or diastolic ≥90 mmHg or treated for hypertension, ref: yes)					
no	0.76 (0.51-1.14); 0.184	0.83 (0.57-1.22); 0.348	0.93 (0.61-1.41); 0.717	0.72 (0.52-1.00); 0.051	1.31 (0.97-1.77); 0.082
Diabetes (≥7 mmol/L or treated for diabetes type 2, ref: yes)					
no	1.89 (1.20-2.97); 0.006	1.63 (1.05-2.54); 0.030	0.56 (0.35-0.90); 0.017	0.87 (0.59-1.29); 0.493	1.01 (0.69-1.48); 0.951
Gout (uric acid ≥404 µmol/L♂, ≥338 µmol/L♀ or gout, ref: yes)					
no	1.47 (0.97-2.24); 0.073	1.22 (0.82-1.84); 0.328	0.64 (0.41-0.99); 0.045	0.43 (0.31-0.60); <0.001	0.90 (0.65-1.26); 0.541

MDSS - Mediterranean Diet Serving Score. WHtR - waist-to-height ratio. ♂: males. ♀: woman. Multivariate logistic regression models were built separately for cholesterol, LDL, HDL and triglycerides. Multivariate ordinal regression model was used for the analysis of the characteristics associated with elevated fibrinogen. Adjusted odds ratios, 95% confidence intervals and *p*-Values were calculated using multivariate regression models; each of the five models presented here was simultaneously adjusted for all the covariates listed in this table.

Table S3. Characteristics associated with hypertension, diabetes, metabolic syndrome and gout as determined by the multivariate logistic regression analyses (sample size is 897 subjects without previous cardiovascular disease diagnosis and older than 65 years of age; all independent variables included in the model are listed in the table).

	Hypertension (systolic ≥140 mmHg or diastolic ≥90 mmHg or treated for hypertension) Adjusted odds ratio (95% confidence interval); *p*-Value	**Diabetes (≥7 mmol/L or treated for diabetes type 2)** Adjusted odds ratio (95% confidence interval); *p*-Value	**Elevated HbA1c (≥6.5 mmol/L or treated for diabetes type 2)** Adjusted odds ratio (95% confidence interval); *p*-Value	**Metabolic syndrome** Adjusted odds ratio (95% confidence interval); *p*-Value	**Gout (uric acid ≥404 mmol/L♂- ≥338 mmol/L♀ or gout)** Adjusted odds ratio (95% confidence interval); *p*-Value
Sex (referent (ref): female)					
male	1.29 (0.90-1.86); 0.171	1.99 (1.24-3.19); 0.005	1.33 (0.80-2.19); 0.268	0.36 (0.24-0.53); <0.001	1.12 (0.75-1.67); 0.575
Age (years)	0.99 (0.97-1.03); 0.779	1.02 (0.98-1.06); 0.268	1.04 (1.00-1.08); 0.038	0.97 (0.94-1.00); 0.069	1.05 (1.01-1.08); 0.006
Place of residence (ref: Split)					
Island of Vis	0.59 (0.36-0.95); 0.032	0.98 (0.50-1.92); 0.949	0.97 (0.46-2.07); 0.940	2.37 (1.35-4.17); 0.003	1.75 (0.98-3.14); 0.060
Island of Korčula	1.07 (0.70-1.63); 0.771	1.38 (0.75-2.55); 0.296	1.91 (0.97-3.77); 0.061	0.84 (0.53-1.33); 0.454	1.66 (0.98-2.80); 0.061
Education (years of schooling, ref: ≥13)	Overall $p = 0.007$	Overall $p = 0.150$	Overall $p = 0.417$	Overall $p = 0.653$	Overall $p = 0.020$
0-8	1.62 (1.03-2.57); 0.038	1.93 (0.99-3.73); 0.052	1.60 (0.80-3.22); 0.186	1.20 (0.73-1.99); 0.466	1.16 (0.69-1.93); 0.579
9-12	0.93 (0.60-1.44); 0.749	1.67 (0.88-3.20); 0.119	1.41 (0.71-2.80); 0.330	1.02 (0.63-1.64); 0.948	0.66 (0.40-1.09); 0.106
Material status (ref: 4th quartile)	Overall $p = 0.497$	Overall $p = 0.031$	Overall $p = 0.092$	Overall $p = 0.444$	Overall $p = 0.581$
1st quartile	0.81 (0.50-1.32); 0.405	1.79 (0.88-3.64); 0.111	1.41 (0.68-2.93); 0.350	0.74 (0.43-1.25); 0.260	0.70 (0.41-1.17); 0.173
2nd quartile	0.88 (0.54-1.44); 0.618	1.71 (0.83-3.53); 0.147	1.23 (0.58-2.60); 0.596	1.00 (0.58-1.73); 0.992	0.74 (0.44-1.26); 0.264
3rd quartile	0.68 (0.41-1.15); 0.148	2.84 (1.37-5.87); 0.005	2.24 (1.06-4.73); 0.034	0.96 (0.54-1.71); 0.891	0.81 (0.46-1.41); 0.452
Smoking (ref: never-smokers)	Overall $p = 0.210$	Overall $p = 0.166$	Overall $p = 0.347$	Overall $p = 0.549$	Overall $p = 0.005$

current smokers	1.11 (0.69-1.79); 0.660	0.61 (0.30-1.24); 0.173	0.76 (0.36-1.62); 0.481	0.83 (0.48-1.43); 0.502	0.69 (0.38-1.24); 0.210
ex-smokers	0.75 (0.52-1.08); 0.121	1.26 (0.80-1.99); 0.324	1.32 (0.80-2.17); 0.274	0.81 (0.54-1.22); 0.315	1.69 (1.15-2.51); 0.008
Alcohol intake (ref: none)	Overall $p = 0.474$	Overall $p = 0.473$	Overall $p = 0.496$	Overall $p = 0.009$	Overall $p = 0.220$
excessive	0.73 (0.44-1.21); 0.228	0.79 (0.42-1.46); 0.448	0.76 (0.39-1.48); 0.422	1.59 (0.90-2.82); 0.109	1.06 (0.62-1.82); 0.837
moderate	0.92 (0.65-1.30); 0.639	0.76 (0.48-1.19); 0.224	0.76 (0.47-1.21); 0.248	0.76 (0.51-1.14); 0.187	1.36 (0.93-1.99); 0.115
MDSS compliance (ref: yes)					
no	1.34 (0.99-1.83); 0.062	0.59 (0.40-0.87); 0.008	0.60 (0.40-0.91); 0.015	1.14 (0.80-1.62); 0.458	1.63 (1.16-2.31); 0.005
Nut consumption (ref: infrequently or never)	Overall $p = 0.496$	Overall $p = 0.583$	Overall $p = 0.051$	Overall $p = 0.659$	Overall $p = 0.968$
daily	0.97 (0.53-1.78); 0.921	0.61 (0.26-1.43); 0.253	0.29 (0.10-0.87); 0.028	0.84 (0.43-1.64); 0.607	0.89 (0.44-1.82); 0.757
weekly	1.18 (0.72-1.96); 0.509	0.88 (0.45-1.72); 0.704	0.71 (0.34-1.47); 0.360	0.75 (0.43-1.30); 0.306	0.99 (0.57-1.72); 0.968
monthly	1.32 (0.91-1.91); 0.148	0.79 (0.49-1.28); 0.337	0.61 (0.36-1.01); 0.056	0.82 (0.55-1.23); 0.345	0.91 (0.61-1.37); 0.660
Physical activity (ref: intensive)	Overall $p = 0.770$	Overall $p = 0.291$	Overall $p = 0.336$	Overall $p = 0.484$	Overall $p = 0.112$
light	0.97 (0.56-1.70); 0.927	1.69 (0.84-3.39); 0.141	1.68 (0.79-3.56); 0.176	0.85 (0.45-1.62); 0.632	0.95 (0.52-1.73); 0.863
moderate	0.88 (0.53-1.44); 0.605	1.31 (0.69-2.46); 0.410	1.29 (0.65-2.56); 0.470	0.73 (0.41-1.30); 0.291	1.38 (0.81-2.36); 0.236
WHtR (≥ 0.5, ref: yes)					
no	0.61 (0.31-1.21); 0.158	1.26 (0.41-3.89); 0.692	0.68 (0.15-3.05); 0.611	0.17 (0.08-0.37); <0.001	0.75 (0.30-1.92); 0.554
Hypertension (systolic ≥140 mmHg or diastolic ≥90 mmHg or treated for hypertension, ref: yes)					
no	na	0.67 (0.45-1.01); 0.054	0.64 (0.42-0.99); 0.046	0.48 (0.34-0.67); <0.001	0.50 (0.36-0.71); <0.001
Diabetes (≥7 mmol/L or treated for diabetes type 2, ref: yes)					
no	0.68 (0.46-1.02); 0.064	na	na	0.21 (0.12-0.36); <0.001	0.85 (0.57-1.27); 0.436
Metabolic syndrome (ref: yes)					
no	0.47 (0.33-0.65); <0.001	0.20 (0.11-0.36); <0.001	0.22 (0.12-0.41); <0.001	na	0.56 (0.38-0.84); 0.005
Gout (uric acid ≥404 μmol/L♂-≥338 μmol/L♀ or gout); yes is referent					
no	0.50 (0.36-0.70); <0.001	0.84 (0.56-1.26); 0.399	0.92 (0.60-1.41); 0.694	0.54 (0.36-0.81); 0.003	na

MDSS - Mediterranean Diet Serving Score. WHtR – waist-to-height ratio. na – not applicable. ♂: males. ♀: woman. Multivariate logistic regression models were built separately for hypertension, diabetes, metabolic syndrome and gout. Adjusted odds ratios, 95% confidence intervals and p-Values were calculated using multivariate logistic regression; each of the four models was simultaneously adjusted for all covariates listed in this table, with an exception of excluding predictor variables in models where those variables were the outcome variables (marked with ''na'').