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ORIGINAL CONTRIBUTION

Adherence to a priori dietary indexes and baseline prevalence of cardiovascular risk factors in the PREDIMED-Plus randomised trial

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Abstract

Purpose Cardiovascular disease remains the global leading cause of death. We evaluated at baseline the association between the adherence to eight a priori high-quality dietary scores and the prevalence of individual and clustered cardiovascular risk factors (CVRF) in the PREDIMED-Plus cohort.

Methods All PREDIMED-Plus participants (6874 men and women aged 55–75 years, with overweight/obesity and metabolic syndrome) were assessed. The prevalence of 4 CVRF (hypertension, obesity, diabetes, and dyslipidaemia), using standard diagnoses criteria, were considered as outcomes. The adherence to eight a priori-defined dietary indexes was calculated. Multivariable models were fitted to estimate differences in mean values of factors and prevalence ratios for individual and clustered CVRF.

Results Highest conformity to any dietary pattern did not show inverse associations with hypertension. The modified Mediterranean Diet Score (PR = 0.95; 95% CI 0.90–0.99), Mediterranean Diet Adherence Score (MEDAS) (PR = 0.94; 95% CI 0.89–0.98), the pro-vegetarian dietary pattern (PR = 0.95; 95% CI 0.90–0.99) and the Alternate Healthy Eating Index 2010 (PR = 0.92; 95% CI 0.87–0.96) were inversely associated with prevalence of obesity. We identified significant inverse trend among participants who better adhered to the MEDAS and the Prime Diet Quality Score (PDQS) in the mean number of CVRF across categories of adherence. Better adherence to several high-quality dietary indexes was associated with better blood lipid profiles and anthropometric measures.

Conclusions Highest adherence to dietary quality indexes, especially Mediterranean-style and PDQS scores, showed marginal associations with lower prevalence of individual and clustered CVRF among elderly adults with metabolic syndrome at high risk of cardiovascular disease

Keywords Hypertension · Obesity · Type 2 diabetes · Dyslipidemias · Dietary pattern · Mediterranean diet

Introduction

Cardiovascular disease (CVD) remains the top cause of death and burden of disease, with an estimated global prevalence of 422 million cases in 2015 [1]. Several major causal risk factors for CVD have been identified, including hypertension, type 2 diabetes (T2D), dyslipidaemia, obesity and cigarette smoking [2–4], and higher burden of risk factors is associated with a rising lifetime risk for CVD [5, 6].

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According to the most important previous population-based study which assessed a representative sample of the Spanish population, the estimated prevalence of hypertension in Spain was 33.1%, the prevalence of dyslipidaemia was 50.3%, the prevalence of T2D was 6.9% and the prevalence of obesity was 23% [7, 8].

In the past years, there has been an increasing interest in studying holistic dietary approaches to disease prevention [9]. The use of hypothesis-oriented (a priori) dietary scores based on available evidence is appealing, as they capture dietary complexity, circumvent nutritional individual confounders by including them in the score, and capture possible effect modification among nutritional variables. The approach to build these patterns consists in summarizing the diet by means of a single score that results from a function of different components (foods, food groups or a combination of foods and nutrients), that are selected based on prior knowledge or scientific evidence [10, 11]. Limitations of this approach are the equal weight usually given to each component of the diet scores, thus assuming the same importance for each of them, and its inability to explain the physiological processes mediating its health effects [12].

Several investigations have documented the benefits of adhering to dietary patterns as defined by a priori diet-quality index scores. In the Mediterranean SUN cohort, greater adherence to a pro-vegetarian pattern or a DASH-style diet was associated to reduced risk of metabolic syndrome [13]. In three distinct US cohorts, better conformity to four high-quality dietary indexes showed consistent inverse associations with all-cause and CVD mortality [14–16], and individuals with higher scores, compared to those with lower ones in three out of four indexes showed a significant lower incidence of T2D in a multi-ethnic cohort [17].

However, despite the above-cited evidence, investigations focused on studying the associations of a broad range of a priori dietary indexes with cardiovascular risk in the same sample are still scarce. Therefore, within the framework of the PREDIMED-Plus trial, we cross-sectionally examined the association between adherence to eight a priori high-quality dietary scores and the baseline prevalence of individual and clustered cardiovascular risk factors (CVRF), including hypertension, T2D, obesity, and dyslipidaemia.

Materials and methods

The PREDIMED-Plus [18] is a 6-year, multicentre, parallel-group, randomised trial of combined dietary and physical activity intervention for primary CVD prevention in individuals with metabolic syndrome. The Institutional Review Boards of all participating institutions approved the study protocol, which followed the standards of the Declaration of Helsinki, including written informed consent provided by all participants. The trial was registered in 2014 at the International Standard Randomized Controlled Trial Registry (ISRCTN89898870).

Participants and recruitment

After the Institutional Review Board of all participating institutions approved the study protocol, the selection process began by identifying names of potential participants from the records of more than 200 primary care health centres. The clinical records of these persons were individually reviewed to exclude those who did not meet eligibility criteria. Eligible participants were community-dwelling men and women aged 55–75 and 60–75 years, respectively, free of CVD at baseline, who were overweight or obese [body mass index (BMI) ≥ 27 and < 40 kg/m^2] and met at least three criteria for the metabolic syndrome (fasting glucose ≥ 100 mg/dl, triglycerides ≥ 150 mg/dl, HDL-cholesterol < 40 mg/dl in men or < 50 mg/dl in women, blood pressure ≥ 130/85 mmHg, abdominal obesity in a Caucasian population ≥ 80 cm in women and ≥ 94 cm in men, or in a South American population ≥ 80 cm in women and ≥ 90 cm in men) [19]. Participants with a documented history of previous cardiovascular disease, cancer, impossibility to follow the recommended diet (due to cultural beliefs, swallowing disorders, or other reasons) or those who had any other condition that may interfere with the adherence to the study protocol were excluded. Family doctors approached them via telephone call or during clinical visits, and if participants were interested in participating, a face-to-face interview was scheduled to explain the purpose and characteristics of the study. We recruited 6874 participants from October 2013 to December 2016 in 23 Spanish centres [18].

Participants were randomly allocated in a 1:1 ratio to an intensive weight-loss intervention group, based on an energy-restricted Mediterranean diet adapted to each participant's needs to encourage their compliance, physical activity promotion and behavioural support, or a control group encouraged to adhere to an unrestricted-energy Mediterranean diet (MedDiet), without any advice to increase physical activity, and receiving conventional health care. In the present study, we excluded participants out of the predefined energy intake limits by Willett (< 500 or > 3500 kcal for women, < 800 or > 4200 kcal for men) [20] ($n = 254$).

This is a cross-sectional assessment conducted with the baseline data of the PREDIMED-Plus trial. Data from the present study were collected only at the baseline visit. This visit took place after a 4-week run-in period and immediately before subsequent randomization into the aforementioned groups. In this visit, anthropometric measurements (weight, height, waist, and hip circumferences) and blood pressure were recorded, and biological samples (blood samples, morning spot urines samples and nail samples) were collected. Participants filled a general information questionnaire to collect information on medical history, family history and use of medication, a MedDiet questionnaire, and physical activity questionnaires. In this visit, participants underwent a physical activity evaluation, the chair test, which records the number of times a participant comes from a sit position to a full standing position in 30 s, and assess functional strength which approximates to the way the body works in everyday life. Participants assigned to the intervention group also received a pedometer to self-monitor the number of steps they walk each day [18].

Dietary assessment

Usual diet during the past year was assessed with a 143-item semi-quantitative food-frequency questionnaire which was previously and repeatedly validated in Spain and assessed food habits in the past year [21–23]. Frequencies of consumption of the food items were reported on an incremental scale with 9 levels (never or almost never, 1–3 times/month, once per week, 2–4 times/week, 5–6 times/week, once per day, 2–3 times/day, 4–6 times/day, and > 6 times/day). The questionnaire included the typical portion sizes (weights) for all food items. Reported frequencies of food consumption were converted into frequencies per day, and multiplied by the weight of the typical portion size indicated to obtain the intake in g/d [22]. The FFQ was completed by participants assisted by the dietitian, at baseline, in the third screening visit, at 6 months of follow-up, and yearly thereafter [18].

We tested eight previously published dietary indexes. The Mediterranean Diet Score (MDS) included 9 components (8 food groups and a ratio of monounsaturated to saturated lipids), scored 0 or 1 point if their intake (measured in g/day) was below or above the sex-specific median [24]. The modified Mediterranean Diet Score (mMDS) and the Mediterranean-like Dietary Score (MLDS) were calculated according to the tertile distribution of food consumption, except for red wine [25]. We also computed the 14-point Mediterranean Diet Adherence Screener (MEDAS), previously used in the PREDIMED trial [26]; the Pro-vegetarian food pattern (PVG), defined as a dietary index that tries to capture a preference for plant-derived foods instead of animal origin foods [27]; the Alternate Healthy Eating Index 2010 (AHEI-2010), based on foods and nutrients associated with lower risk of chronic disease in clinical and epidemiological investigations [28]; the Carbohydrate Quality Index (CQI), which estimates the quality of dietary carbohydrates [29]; and the Prime Diet Quality Score (PDQS), based on the Prime Screen Questionnaire developed for clinical use to quickly assess diet quality [30]. Further information on the composition and calculations of these dietary indexes can be found in Online resource 1. We categorised participants according to their adherence to each of these dietary scores into rough quartiles of adherence (low, low–medium, medium–high and high adherence).

Given the current state of the art in nutritional epidemiology, that is focused on whole dietary patterns with several definitions of a high-quality dietary pattern, we included several of them (eight in total) to better appraise the effect of high-quality dietary patterns on CVRF and to be able to compare them. However, for the sake of brevity we selected two of them for the main manuscript and present the associations for the rest of them in the supplementary material.

Measurements and outcomes

A general questionnaire was used to obtain information on socio-demographic variables, smoking status, medical conditions (T2D), medication use, and family history of illness. Physical activity was measured using the validated Minnesota-REGICOR Short Physical Activity questionnaire [31]. Participants also underwent the 30-s chair stand test, a field test to assess functional strength which approximates to the way the body works in everyday life.

Anthropometric variables were measured by trained personnel according to the PREDIMED-Plus protocol. Weight and height were measured with high-quality electronic calibrated scales and a wall-mounted stadiometer, respectively. BMI was calculated by dividing the weight (kg) by height squared (m^2). Obesity was defined as a BMI ≥ 30 kg/m^2. Waist circumference was measured halfway between the last rib and the iliac crest using an anthropometric tape. All anthropometric variables were determined in duplicate, and the mean value of both measurements was used.

Blood pressure was measured in triplicate with a validated semi-automatic oscillometer (Omron HEM-705CP, the Netherlands) after 5 min of rest while the participant was in a seated position. A participant was considered hypertensive if the average of the three measurements of systolic blood pressure was ≥ 130 mmHg or ≥ 85 mmHg for diastolic blood pressure, or if the participant reported use of antihypertensive drugs.

Blood samples were collected after an overnight fast and stored at − 80 °C in a central laboratory until analysis. Biochemical analyses were performed on fasting plasma glucose, total cholesterol, HDL-cholesterol and triglyceride concentrations in local laboratories using standard enzymatic methods. T2D was diagnosed by standard methods [32]. Current diabetes was defined as previous diagnosis of diabetes self-reported at inclusion, or baseline-glycated haemoglobin (HbA1c) ≥ 6.5%, use of antidiabetic medication, or having fasting glucose > 126 mg/dl in the screening visit (three contacts during the run-in period prior to randomization where trained staff evaluated the likelihood of participants to attend the scheduled sessions and complete correctly the assessment tools. In these visits, anthropometric and biochemical measurements were recorded [18]) plus fasting glucose > 126 mg/dl at baseline visit. Dyslipidaemia was defined as having either hypercholesterolemia (total cholesterol ≥ 240 mg/dl) [33], or hypertriglyceridemia (total triglycerides ≥ 150 mg/dl), or low HDL-cholesterol (< 40 mg/dl in men or < 50 mg/dl in women).

Statistical analysis

We performed a descriptive analysis of general characteristics according to quartiles of adherence to each of the eight dietary indexes. Categorical variables were presented as percentages, and compared with the Chi squared test. We tested quantitative variables for normality using the Shapiro–Wilk test, and given that most data were not normally distributed, quantitative variables were shown as medians and interquartile range (percentiles 25–75), and differences were tested with the Kruskal–Wallis test.

We fitted logistic regression models and, given the high prevalence of CVRF, instead of presenting the odds ratios (OR), we used a correction method [34] to estimate prevalence ratios (PR) and their 95% confidence intervals (95% CI). The correction calculates the PR as the quotient between the OR and a denominator comprised by $[(1 - P_0) + (P_0 \times \mathrm{OR})]$ where P_0 is the prevalence in the reference category. As dependent variables we used each of the four binary variables (hypertension, T2D, obesity, and dyslipidaemia), or another binary variable representing the simultaneous presence of several clustered CVRF. The independent variable (adherence to each of the eight dietary indexes) was categorized in roughly quartiles (low, low–medium, medium–high, and high), and it was introduced in the models by means of three dummy variables for the three upper levels, leaving the lowest category of adherence to each index as the reference.

Potential confounders included as covariates were sex, age, smoking status (current, former or never), family history of CVD, obesity and T2D (yes/no), total energy intake (kcal/day, continuous), physical activity (METs-min/week, continuous), educational level (primary or less, secondary, or university), marital status (married, yes/no), living alone (yes/no), being retired (yes/no), previous weight-loss through dieting (yes/no), and centre (categorised in quartiles by number of participants). We conducted further analyses additionally adjusting for use of anti-hypertensive medication and lipid-lowering drugs. We used robust variance estimators to account for intra-cluster correlations in all regression models, considering as clusters the members of the same household, and adjusted for multiple testing, using the Simes' multiple testing procedure and showing the corrected *p* values [35].

Tests of linear trends across quartiles of adherence to each of the eight dietary indexes were conducted, assigning the median value of each quartile and considering them as continuous variables.

In addition, we fitted linear regression models with the adherence to the dietary indexes (measured as continuous variables) as the independent variable to estimate adjusted differences in mean levels of CVRF clinical measurements (blood pressure, fasting glucose levels, BMI, waist circumference, LDL-cholesterol, HDL-cholesterol, and triglycerides levels) for 1 standard deviation (SD) difference in the respective dietary pattern. Additional linear regression models were fitted to assess the differences for 1 SD difference of intake of food groups (in g/day) positively scored in most indexes (vegetables, fruits, cereals, legumes, nuts, fish and olive oil, intake measured as continuous variables) in mean levels of CVRF clinical measurements.

All corrected *p* values lower than 0.05 were considered statistically significant. Analyses were performed using STATA version 13.0 (StataCorp, College Station, TX, USA). We used the PREDIMED-Plus baseline database generated in December 2017.

Results

Per study protocol, most CVRF were highly prevalent: over 80% of participants were hypertensive, over 70% were obese, and over 90% had dyslipidaemia. Also, by study design nearly 30% of participants had T2D. In addition, 95.1% of participants had at least 2 CVRF, 66.6% had at least 3 CVRF, and 17.8% had all 4 clustered CVRF.

General characteristics of the study participants are shown in Table 1 and Online resources 2–4. Participants in the upper quartile of adherence to the eight dietary indexes, compared to those in the lower quartile, were more likely to be older, women (except in the MDS, where men showed greater conformity, and the mMDS and PVG, where no significant differences were found), prone to be more physically active, and more likely to report a family history of premature coronary heart disease (except in the MDS, mMDS, PVG and CQI, where no significant differences were shown). They also tended to have lower diastolic blood pressure (though the trend was reversed in the MDS and MEDAS), lower BMI (though the trend was reversed in the CQI) and triglycerides levels, and higher HDL-cholesterol levels.

Prevalence ratios for individual CVRF according to categories of adherence to the dietary indexes are presented in Table 2 (MEDAS) and in Table 3 (PDQS) and Online resources 5–10 (MDS, mMDS, MLDS, PVG, AHEI-2010, and CQI).

Participants who showed the highest adherence, compared to the lowest, did not show a significantly reduced prevalence of hypertension across any of the eight dietary indexes evaluated.

Table 1 General characteristics according to categories of adherence to the Mediterranean Diet Adherence Screener, Alternate Healthy Eating Index 2010 and the Prime Diet Quality Score in the PREDIMED-PLUS cohort [26, 28, 30]

Characteristics	Mediterranean Diet Adherence Screener (MEDAS)				Alternate Healthy Eating Index 2010 (AHEI-2010)				Prime Diet Quality Score (PDQS)			
	Low (≤ 6)	Low-medium (7)	Medium–high (8)	High (9–14)	Low (≤ 63)	Low-medium (64–69)	Medium–high (70–75)	High (76–98)	Low (≤ 19)	Low-medium (20-21)	Medium–high (22–24)	High (25–36)
n	2084	1370	1283	1883	1809	1683	1571	1557	2226	1359	1806	1229
Hypertension (%)	86.5	86.3	86.7	84.7	85.9	85.0	86.2	86.9	86.5	86.5	85.1	85.6
Diabetes (%)	28.2	31.4	27.6	29.0	27.5	30.1	27.9	30.5	28.9	31.9	28.2	26.9*
Obesity (%)	76.4	72.5	73.6	70.5*	76.0	75.0	72.4	69.6*	74.5	73.6	73.1	71.5
Dyslipidaemia (%)	92.5	90.7	90.9	90.2	91.9	90.7	90.6	91.3	91.6	91.5	90.4	91.1
Age (years) Median (IQR[a])	64 (61–68)	65 (61–69)	65 (61–69)	65 (62–69)*	64 (60–68)	65 (61–68)	66 (62–69)	66 (62–70)*	64 (61–68)	65 (61–68)	65 (62–69)	65 (62–69)*
Women (%)	43.6	47.9	50.9	51.8*	34.9	48.1	54.4	57.7*	36.5	47.2	53.7	62.5*
Body-mass index (kg/m^2) median (IQR)	32.5 (30.1–35.1)	32.1 (29.8–34.9)	32.3 (29.8–35.2)	32.3 (29.6–34.4)*	32.4 (30.1–35)	32.4 (30–35)	32.3 (29.7–35)	32.3 (29.5–34.4)*	32.3 (29.9–35)	32.2 (29.9–35)	32 (29.8–34.7)	32 (29.6–34.8)
Weight (kg) median (IQR)	87.3 (78.9–97)	85.1 (77.5–94.4)	85.9 (77.0–94.9)	85.9 (75.6–93.1)*	88.8 (80.4–98)	86.1 (77.8–95.3)	84.5 (76.5–93.5)	84.5 (74.5–91.6)*	87.7 (79.5–96.9)	85.8 (77.8–94.6)	84.3 (76.2–93.9)	84.3 (74.5–92.4)*
Waist (cm) median (IQR)	108 (102–115)	107 (101.3–114.3)	107 (101–114)	107 (100–112.3)*	108.7 (102.5–115.5)	107.3 (101.8–114.3)	106.5 (100.6–114)	106.5 (99.4–112)*	108.4 (102.3–115.5)	107 (101.8–114)	106 (100.3–113)	106 (99–112.5)*
Waist-to-height ratio Median (IQR)	66.0 (62.3–70)	65.7 (62.1–70)	65.8 (61.9–70.1)	65.8 (61.7–69.3)*	65.7 (62–69.9)	66 (62.3–70.1)	65.6 (61.8–70.1)	65.6 (61.8–69.2)*	66 (62.2–70.3)	65.7 (62.2–69.8)	65.5 (61.8–69.5)	65.5 (61.8–69.7)*
Smoking												
Current smoker (%)	14.8	12.0	11.9	10.3*	15.2	13.7	10.3	9.7*	15.8	12.1	11.0	8.4*
Former smoker (%)	43.0	43.6	43.1	43.7	48.9	43.7	40.3	39.6	45.9	44.3	42.5	38.9
Highest attained educational level												
Primary school or less	47.2	51.2	49.7	50.3*	43.1	48.8	53.7	53.0*	46.9	49.1	52.1	50.3*

Table 1 (continued)

Characteristics	Mediterranean Diet Adherence Screener (MEDAS)				Alternate Healthy Eating Index 2010 (AHEI-2010)				Prime Diet Quality Score (PDQS)			
	Low (≤ 6)	Low-medium (7)	Medium–high (8)	High (9–14)	Low (≤ 63)	Low-medium (64–69)	Medium–high (70–75)	High (76–98)	Low (≤ 19)	Low-medium (20-21)	Medium–high (22–24)	High (25–36)
Complete secondary	31.6	27.8	29.4	25.8	32.6	28.4	27.7	25.6	30.3	29.9	27.1	26.9
University	21.3	21.0	20.9	24.0	24.4	22.8	18.6	21.4	22.8	21.0	20.8	22.9
Non-European origin (%)	3.6	2.6	1.7	1.6*	3.7	2.1	2.0	1.9*	2.9	2.4	1.6	2.9*
Willingness to change diet Median (IQR)	3 (2–3)	3 (2–3)	3 (2–3)	3 (3–3)*	3 (2–3)	3 (3–3)	3 (3–3)	3 (3–3)	3 (2–3)	3 (3–3)	3 (3–3)	3 (3–3)
Married (%)	75.6	75.5	78.0	76.8	77.1	76.2	76.4	75.9	77.2	79.0	75.8	73.1*
Living alone (%)	12.0	11.2	13.2	13.0	10.8	11.9	13.2	13.7*	10.5	10.3	13.3	16.6*
Retired (%)	51.6	57.2	58.5	57.8*	53.2	55.3	56.4	58.9*	54.9	53.2	57.0	58.7*
Self-reported previous depression (%)	21.3	21.0	20.3	20.2	19.2	21.0	21.6	21.3	19.2	19.7	21.3	23.8*
Family history of premature CHD[b] (%)	14.0	17.9	17.1	18.4*	14.6	18.7	15.7	18.0*	14.2	16.2	17.9	19.9*
Family history of type 2 diabetes (%)	41.2	40.4	42.3	41.6	39.4	41.6	42.2	42.6	40.7	42.2	40.9	42.5
Family history of obesity (%)	49.2	50.1	48.2	49.4	48.7	50.0	48.2	50.0	48.6	47.8	49.8	51.2
Leisure time physical activity (METs/min-week) Median (IQR)	1682 (839–3217)	1948 (879–3357)	1979 (920–3592)	1979 (1254–3984)*	1736 (839–3337)	1904 (865–3427)	2098 (1059–3580)	2098 (1119–3742)*	1727 (839–3197)	1958 (892–3484)	2098 (1049–3657)	2098 (1229–4005)*

Table 1 (continued)

Characteristics	Mediterranean Diet Adherence Screener (MEDAS)				Alternate Healthy Eating Index 2010 (AHEI-2010)				Prime Diet Quality Score (PDQS)			
	Low (≤6)	Low-medium (7)	Medium–high (8)	High (9–14)	Low (≤63)	Low-medium (64–69)	Medium–high (70–75)	High (76–98)	Low (≤19)	Low-medium (20-21)	Medium–high (22–24)	High (25–36)
Chair test (#/30 s) Median (IQR)	13 (10–16)	13 (10–15)	13 (10–15)	13 (11–16)*	13 (11–16)	13 (11–15)	13 (10–15)	13 (11–16)*	13 (11–16)	13 (11–16)	13 (10–16)	13 (10–15)
Total energy intake (kcal/d) Median (IQR)	2355 (1994–2771)	2289 (1913–2688)	2304 (1948–2668)	2304 (1996–2719)*	2479 (2076–2900)	2294 (1912–2674)	2234 (1898–2636)	2234 (1991–2653)*	2371 (1999–2779)	2317 (1957–2737)	2318 (1983–2674)	2318 (1919–2653)*
Carbohydrate intake (%E) Median (IQR)	41.3 (36.7–46.1)	41.3 (36.5–45.9)	40.9 (36.5–45.8)	40.9 (35.4–44.3)*	41.6 (36.4–46.3)	41.3 (36.4–45.9)	41.2 (36.7–45.7)	41.2 (35.3–43.9)*	40.8 (35.8–45.5)	41.2 (36.3–46.1)	40.9 (36.4–45.6)	40.9 (36.4–45.1)
Protein intake (%E) Median (IQR)	16.0 (14.4–17.8)	16.3 (14.6–18.3)	16.6 (14.9–18.4)	16.6 (14.9–18.6)*	15.9 (14.2–17.8)	16.5 (14.7–18.4)	16.6 (14.9–18.4)	16.6 (15.0–18.5)*	15.5 (13.9–17.2)	16.3 (14.7–18.0)	16.7 (15.1–18.5)	16.7 (15.8–19.3)*
Fat intake (%E) median (IQR)	39.2 (34.7–43.6)	39.3 (34.6–43.7)	39.0 (34.4–43.7)	39.0 (35.4–44.5)*	38.0 (33.8–42.4)	39.0 (34.2–43.4)	39.4 (35.0–43.9)	39.4 (36.8–45.6)*	39.6 (34.9–44.0)	39.2 (34.5–43.7)	39.4 (34.8–43.9)	39.4 (35.0–43.8)
Previous weight-loss dieting (%)	43.3	41.8	44.8	41.7	42.6	44.9	41.4	42.2	39.2	43.0	44.0	47.6*

MET metabolic equivalent of task, *E* energy intake

*$p < 0.05$

[a]IQR: interquartile range, quartiles 25–75

[b]Family history of premature coronary heart disease assessed in screening phase with a positive answer by the participant to a question about a myocardial infarction in next of kin that was included in the general questionnaire

Table 2 Prevalence ratios for individual cardiovascular risk factors according to categories of adherence to the Mediterranean Diet Adherence Screener (MEDAS) [26]

	Low (≤ 6) $n = 2084$	Low-medium (7) $n = 1370$	Medium–high (8) $N = 1283$	High (9–14) $n = 1883$	corrected p for trend
Hypertension, %	86.5	86.3	86.7	84.7	
Sex and age adjusted	1 (ref.)	0.99 (0.96–1.02)	1.00 (0.97–1.02)	0.97 (0.94–1.00)*	0.037
Multivariate adjusted[a]	1 (ref.)	0.99 (0.96–1.02)	1.00 (0.97–1.03)	0.97 (0.94–1.00)	0.124
Diabetes, %	28.2	31.4	27.6	29.0	
Sex and age adjusted	1 (ref.)	1.11 (1.00–1.23)	0.99 (0.88–1.10)	1.03 (0.93–1.14)	0.921
Multivariate adjusted[a]	1 (ref.)	1.14 (1.02–1.26)	1.00 (0.89–1.12)	1.08 (0.98–1.20)	0.619
Obesity, %	76.4	72.5	73.6	70.5	
Sex and age adjusted	1 (ref.)	0.95 (0.91–0.99)*	0.96 (0.92–1.00)	0.92 (0.88–0.96)*	< 0.001
Multivariate adjusted[a]	1 (ref.)	0.95 (0.91–0.99)*	0.96 (0.92–1.01)	0.94 (0.89–0.98)*	0.008
Dyslipidaemia, %	92.5	90.7	90.9	90.2	
Sex and age adjusted	1 (ref.)	0.98 (0.96–1.00)	0.98 (0.96–1.00)	0.98 (0.95–1.00)*	0.023
Multivariate adjusted[a]	1 (ref.)	0.98 (0.95–1.00)	0.98 (0.96–1.01)	0.98 (0.96–1.00)	0.302

*Corrected $p < 0.05$

[a]Adjusted for sex, age (continuous), smoking (never smoked, current, former), family history of cardiovascular disease, obesity and type 2 diabetes (yes/no), energy intake (continuous), physical activity (continuous), educational level (primary, secondary and university), married (yes/no), living alone (yes/no), retired (yes/no), previously weight-loss dieting (yes/no), and node (categorised in quartiles by number of participants)

Table 3 Prevalence ratios for individual cardiovascular risk factors according to categories of adherence to the Prime Diet Quality Score [30]

	Low (≤ 19) $n = 2226$	Low-medium (20–21) $n = 1359$	Medium–high (22–24) $N = 1806$	High (25–36) $n = 1229$	corrected p for trend
Hypertension, %	86.5	86.5	85.1	85.6	
Sex and age adjusted	1 (ref.)	1.00 (0.97–1.03)	0.98 (0.95–1.00)	0.98 (0.95–1.01)	0.117
Multivariate adjusted[a]	1 (ref.)	1.00 (0.97–1.02)	0.98 (0.95–1.00)	0.98 (0.95–1.01)	0.218
Diabetes, %	28.9	31.9	28.2	26.9	
Sex and age adjusted	1 (ref.)	1.13 (1.02–1.25)*	1.01 (0.91–1.11)	0.98 (0.87–1.09)	0.625
Multivariate adjusted[a]	1 (ref.)	1.13 (1.02–1.25)	1.02 (0.92–1.13)	1.00 (0.88–1.12)	0.954
Obesity, %	74.5	73.6	73.1	71.5	
Sex and age adjusted	1 (ref.)	0.98 (0.94–1.02)	0.97 (0.94–1.01)	0.95 (0.90–0.99)*	0.018
Multivariate adjusted[a]	1 (ref.)	0.98 (0.94–1.02)	0.98 (0.93–1.01)	0.95 (0.91–1.00)	0.101
Dyslipidaemia, %	91.6	91.5	90.4	91.1	
Sex and age adjusted	1 (ref.)	1.00 (0.97–1.02)	0.99 (0.96–1.01)	0.99 (0.97–1.01)	0.300
Multivariate adjusted[a]	1 (ref.)	1.00 (0.97–1.02)	0.99 (0.96–1.01)	0.99 (0.97–1.01)	0.572

*Corrected $p < 0.05$

[a]Adjusted for sex, age (continuous), smoking (never smoked, current, former), family history of cardiovascular disease, obesity and type 2 diabetes (yes/no), energy intake (continuous), physical activity (continuous), educational level (primary, secondary and university), married (yes/no), living alone (yes/no), retired (yes/no), previously weight-loss dieting (yes/no), and node (categorised in quartiles by number of participants)

Participants classified in the upper quartile of conformity to several high-quality dietary patterns, compared to those in the lowest quartile, showed significant inverse associations with obesity prevalence, and inverse linear trends across quartiles of adherence. The PRs were 0.95 (95% CI 0.90–0.99; corrected p for trend = 0.048) for the mMDS (21–28 points vs. ≤ 16 points); 0.94 (95% CI 0.89–0.98; corrected p for trend = 0.008) for the MEDAS (9–14 points vs. ≤ 6 points), 0.95 (95% CI 0.90–0.99; corrected p for trend = 0.088) for the PVG (40–42 points vs. ≤ 36 points), and 0.92 (95% CI 0.87–0.96; corrected p for trend < 0.001) for the AHEI-2010 (76–98 points vs. ≤ 63 points). However, participants who showed the highest adherence (compared to the poorest) to the other four indexes did not show a significantly lower prevalence of obesity.

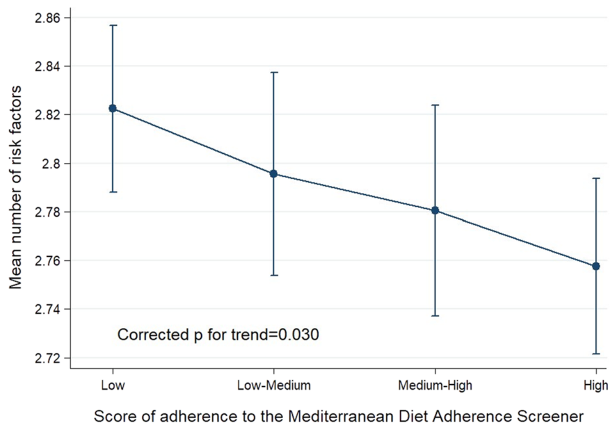

Fig. 1 Mean number of cardiovascular risk factors (hypertension, T2D, obesity and dyslipidaemia) according to quartiles of adherence to the Mediterranean Diet Adherence Screener (MEDAS)

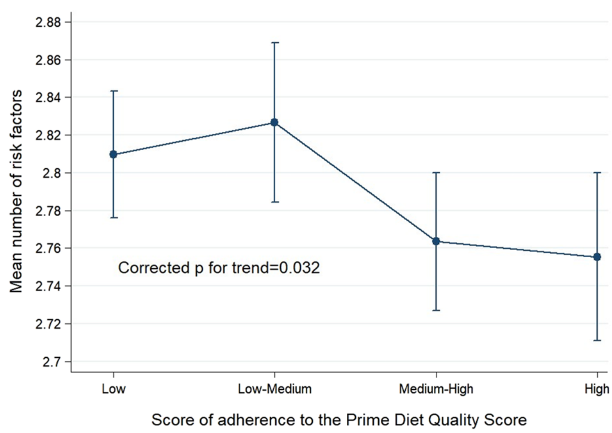

Fig. 2 Mean number of cardiovascular risk factors (hypertension, T2D, obesity and dyslipidaemia) according to quartiles of adherence to the Prime Diet Quality Score (PDQS)

No significant inverse associations were detected between closer adherence to any of the eight dietary indexes and dyslipidaemia or T2D. Nevertheless, we found a significantly increased prevalence of T2D in participants with the highest adherence to the MLDS (PR = 1.24; 95% CI 1.11–1.38; corrected p for trend = 0.001), AHEI-2010 (PR = 1.15; 95% CI 1.03–1.28; corrected p for trend = 0.079), and CQI (PR = 1.16; 95% CI 1.04–1.29; corrected p for trend = 0.020).

When we assessed the mean number of risk factors across categories of adherence to each of the eight high-quality dietary indexes, we only identified significant inverse trends among participants who better adhered to the MEDAS and the PDQS (Figs. 1, 2).

To address a possible reverse causality bias by known baseline diabetes status (participants who had received a diagnosis of diabetes, especially those recently diagnosed, may tend to show better adherence to healthy dietary patterns than non-diabetic participants), we conducted an additional analysis excluding T2D from the count of CVRF (but further adjusting for T2D). Our speculations about changes in dietary habits after a diabetes diagnosis are not in agreement with the results reported on lifestyle and diet by Chong et al. [36], but they are consistent with many other findings [37–39]. We found a reduced prevalence for having 2 or more clustered CVRF in participants who better adhered to the MEDAS (PR = 0.97; 95% CI 0.95–0.99) and those who showed a medium-to-high adherence to the mMDS (PR = 0.98; 95% CI 0.95–1.00), and PDQS (PR = 0.98; 95% CI 0.96–1.00). In addition, participants who better adhered to the MLDS (PR = 0.92; 95% CI 0.85–0.98), MEDAS (PR = 0.90; 95% CI 0.84–0.95), AHEI-2010 (PR = 0.90; 95% CI 0.84–0.96), and PDQS (PR = 0.92; 95% CI 0.86–0.99) showed a significantly lower prevalence of having three clustered CVRF (Online resource 11).

To address the role of medication on dietary habits, we conducted an analysis additionally adjusting for use of antihypertensive medication and lipid lowering drugs. Our findings did not change substantially. However, those participants who had the highest adherence, compared to the poorest, to the MLDS (PR = 0.93; 95% CI 0.86–0.98; corrected p for trend = 0.026) showed a significantly reduced prevalence of hypertension (Online resource 12).

When we fitted linear regression models adjusted for the above-mentioned potential confounders, we found that only better conformity to the CQI was significantly associated with lower mean systolic blood pressure, with $\beta = -1.063$ mmHg (-1.488 to -0.638; corrected $p < 0.001$). On the contrary, a higher average systolic blood pressure was found for each 1-point SD for better adherence to the MEDAS ($\beta = +0.523$ mmHg; 95% CI $+0.112$ to $+0.933$; corrected $p = 0.013$). Likewise, participants with a better conformity to the CQI showed a lower average diastolic blood pressure ($\beta = -0.485$ mmHg; 95% CI -0.724 to -0.246; corrected $p < 0.001$), while higher diastolic blood pressure was observed for each 1-point SD higher adherence to the MDS ($\beta = +0.426$ mmHg; 95% CI $+0.174$ to $+0.677$; corrected $p = 0.003$) and MEDAS ($\beta = +0.672$ mmHg; 95% CI $+0.432$ to $+0.911$; corrected $p < 0.001$). Moreover, participants who showed better adherence to most dietary indexes had lower average BMI, waist circumference and triglycerides levels and higher average HDL-cholesterol levels, while we did not observe significant changes in average blood glucose and LDL-cholesterol levels across any of the dietary indexes evaluated (Online resource 13).

The individual assessment of each individual food component (amounts consumed, in g/day) with SBP among those foods which were positively scored in most dietary scores, showed that vegetables and nuts exhibited the strongest inverse association among all these food items.

Specifically, for each 1-SD in the consumption of vegetables, the observed average difference in SBP was –0.702 mmHg; 95% CI − 1.124 to − 0.279; corrected $p = 0.003$, and for each 1-SD in the consumption of nuts the average difference in SBP was − 0.552 mmHg; 95% CI − 0.972 to − 0.132; corrected $p = 0.025$. Moreover, only 1-point SD difference in the intake of vegetables was associated with a significant decrease in DBP ($\beta = -0.384$ mmHg; 95% CI − 0.625 to − 0.143; corrected $p = 0.004$). A difference of 1-point SD of intake of nuts was associated with lower BMI ($\beta = -0.244$ kg/m^2; 95% CI –0.325 to − 0.164; corrected $p < 0.001$). Also, higher intake of nuts ($\beta = -0.604$ cm; 95% CI − 0.817 to − 0.391; corrected $p < 0.001$) and fruits ($\beta = -0.310$ cm; 95% CI − 0.530 to − 0.090; corrected $p = 0.013$) reduced average waist circumference. In addition, increased intakes of vegetables and fish were associated with higher average levels of HDL-cholesterol. No significant changes were observed according to differences (1-SD) in the intake of any food group and average blood glucose or triglycerides levels across any of the eight dietary indexes evaluated (Online resource 14).

Discussion

In this cross-sectional study of older participants with overweight or obesity and metabolic syndrome conducted within the framework of the PREDIMED-Plus trial, we found that participants who reported the highest adherence, compared to the poorest, to previously published high-quality dietary indexes, showed modest reductions in the prevalence of some individual or clustered CVRF.

We only found a lower hypertension prevalence in participants who had better adherence to the MLDS after adjusting for anti-hypertensive and lipid-lowering medication, although paradoxically better conformity to the MDS and the MEDAS was associated with elevated average SBP and DBP in this cross-sectional assessment. When we assessed differences in median adherence to each pattern in participants who were and were not treated with anti-hypertensive medication, significant differences were found only in the median adherence to the MLDS across groups (data not shown). Therefore, to what extent anti-hypertensive medication might explain these findings remains uncertain. Several studies have reported that closer adherence to dietary patterns characterised by the high consumption of vegetables, fruit, nuts, whole grain cereals, legumes and fish, and low consumption of meat products showed favourable effects on blood pressure [40–42], presumably due to the consumption of polyphenol-rich foods and reduced intake of detrimental foods [43, 44].

Participants with the highest levels of adherence to Mediterranean-style dietary indexes (mMDS and MEDAS), the AHEI-2010, and with moderate-to-high adherence to the PVG showed the lowest prevalence of obesity. Moreover, most of the eight a priori dietary indexes evaluated were significantly related to lower average BMI and waist circumference, in line with prior studies. In a cross-sectional assessment of the PREDIMED trial, consistent inverse associations between adherence to the MedDiet and three indexes of obesity (BMI, waist circumference and waist-to-height ratio) were found [45]. In the EPIC-Italy prospective cohort study, highest adherence to a typical Italian Mediterranean diet, compared to poorest adherence, was associated with lower average weight gain and a reduced risk of becoming overweight or obese [46]. Similarly, the Healthy Eating Index (HEI) and its modified versions showed inverse associations with BMI and waist circumference [47]. We hypothesize that an increased consumption of low energy-dense foods (and extra-virgin olive oil or nuts, despite their high energy-dense profile) [48], as well as fibre-rich foods that promote satiety and reduce energy intake [49], can account for the beneficial effects of these dietary patterns on obesity.

Despite the lack of significant associations between a higher adherence to the Mediterranean-style dietary indexes and dyslipidaemia, we observed positive associations between better conformity to the MedDiet (assessed with most Mediterranean-style scores) and higher HDL-cholesterol levels, which concur with prior evidence. In a Spanish cohort, participants who better adhered to a MedDiet pattern showed improved plasma lipid profiles in comparison to participants with poorer adherence [50]. Likewise, in the PREDIMED trial, participants allocated to the interventions group with MedDiet enriched with either nuts or extra-virgin olive oil had improved lipoprotein profiles, with a shift towards less atherogenic patterns [51, 52].

Though past investigations have consistently reported that adherence to healthy diets predicted a reduced risk for developing T2D [53–55], in our study we did not find any evidence of inverse associations between better conformity to any of the eight dietary patterns assessed and lower plasma glucose levels, probably due to reverse causality bias, given the known diabetic status by participants at baseline. Moreover, when adherence was evaluated with the MLDS, AHEI-2010 and CQI indexes we found an increased prevalence of T2D, and the dose–response shape across quartiles of adherence in MLDS and CQI indexes showed a significant positive linear trend. Given the cross-sectional study design, these results suggest the possible existence of a reverse causation bias, i.e., participants with diabetes self-aware about their health status may adopt healthier lifestyles and consequently report better adherence to high-quality dietary patterns. In addition, we cannot discard some social desirability effect that can be present to some extent in self-reported dietary intakes [56]. Thus, participants may tend to present themselves in a more favourable way, reporting higher intake of beneficially perceived food components, and lower intakes of supposedly detrimental food groups.

When excluding T2D from the considered CVRF, we found inverse associations between better conformity to high-quality dietary indexes and lower prevalence of all three remaining clustered CVRF. Our findings are in agreement with previous studies reporting that better adherence to healthy dietary patterns was associated with a lowered risk for exhibiting a clustering of CVRF or the metabolic syndrome [57–60].

Altogether, the MEDAS index showed the best performance among all evaluated dietary indexes. Participants who best adhered to the MEDAS showed the lowest prevalence of obesity. In addition, we found an inverse linear trend across quartiles of adherence in the mean number of CVRF. The beneficial synergistic combination of antioxidants, polyphenols (reducing vascular oxidative stress and inflammation), minerals, and phytochemicals [61, 62], and the high content of dietary fibre (controlling glycemic and insulin responses because of its effects on gastric emptying and macronutrient absorption from the gut [63]) and n-3 polyunsaturated and monounsaturated fatty acids (with known anti-inflammatory effects, and also by means of increasing HDL-cholesterol and reducing triglycerides levels [64]) may explain the beneficial effect of plant-based dietary patterns on metabolic syndrome and its components.

The present study shows a variety of findings across dietary indexes and outcomes. This variety could be attributed to the variability across dietary scores because they included different components, and the different cutoff points. All this might lead to a variable within-subject degree of adherence depending on the index used [65].

A major strength of this study is the use of eight previously published dietary indexes, widely used and recognized. However, our study also has limitations. First, the potential reverse causation bias is a major limitation inherent to the cross-sectional study design. Second, the study population, including older adults with the metabolic syndrome, limits the generalizability of our findings to younger or healthier populations. In addition, we did not use a specific adapted cutoff value to define obesity in this elderly population, and this issue is duly acknowledged. Other limitation was the possible seasonal variation in the dietary patterns of study participants. However, we did not expect great variations on dietary patterns, as participants completed the FFQ taking into account the whole previous year. Finally, the use of self-reported dietary information might lead to some degree of misclassification.

To conclude, our findings suggest that some of the high-quality dietary patterns evaluated might be factors potentially useful for addressing CVRF, even when they are already present. Further longitudinal studies are necessary to establish the causal relationships between better conformity to these dietary patterns and cardiovascular risk.

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Compliance with ethical standards

Conflict of interest E Ros is a consultant for the California Walnut Commission. J. Salas-Salvadó is a non-payed member of the Scientific Advisory Board of the International Nut and Dried Fruit Foundation and received research grants through his Institution of research. The other authors declare that they have no conflict of interests.

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