



Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Sex-specific dietary patterns and their association with metabolic syndrome: Insights from a cross-sectional analysis

Mónica Lavinia Popescu^a, María Rubín-García^{a,b,c,*}, Laura Álvarez-Álvarez^{a,b},
 Estefanía Toledo^{d,e}, Dolores Corella^{d,f}, Jordi Salas-Salvadó^{d,g,h}, Karla Alejandra Pérez-Vega^{d,i},
 J Alfredo Martínez^{d,j,k,l}, Ángel M. Alonso-Gómez^{d,m}, Julia Wärnberg^{d,n}, Jesús Vioque^{c,o},
 Dora Romaguera^{d,p}, José López-Miranda^{d,q}, Ramón Estruch^{d,r}, Francisco J. Tinahones^{d,s},
 José Lapetra^{d,t}, Luís Serra-Majem^{d,u}, Naomi Cano-Ibáñez^{c,v}, Josep A. Tur^{d,w}, Roi Naveiro^x,
 Xavier Pintó^{d,y}, Miguel Delgado-Rodríguez^{c,z}, María Ortiz-Ramos^{aa}, Josep Vidal^{ab,ac},
 Clotilde Vázquez^{d,ad}, Lidia Daimiel^{d,ae,af}, Emilio Ros^{d,ag}, Zenaida Vázquez-Ruiz^{d,e},
 Nancy Babio^{d,g,h}, Jose V. Sorlí^{d,f}, Olga Castañer^{c,i}, Antonio García-Ríos^{d,q},
 Sandra González-Palacios^{c,o}, María Zulet^{d,j}, Jadwiga Konieczna^{d,p}, Rosa Casas^{d,r},
 Paloma Masso-Guijarro^{v,ah}, Lucas Tojal-Sierra^{d,m}, Ana M. Gómez-Pérez^{d,s},
 Juan Carlos Cenoz-Osinaga^d, Irene Valverde^{d,g,h},
 Rebeca Fernández-Carrión^{d,f}, Helmut Schröder^{c,i},
 Antonio P. Arenas Larriva^{d,q}, Laura Torres-Collado^{c,o}, Ana García-Arellano^{e,ai},
 Antoni Palau-Galindo^{g,h,aj}, Montserrat Fitó^{d,i}, Vicente Martín-Sánchez^{a,b,c},
 Tania Fernández-Villa^{a,b,c}

^a Departamento de Ciencias Biomédicas, Área de Medicina Preventiva y Salud Pública, Universidad de León, León, Spain

^b Grupo de Investigación en Interacciones Gen-Ambiente y Salud (GIIGAS) / Instituto de Biomedicina (IBIOMED), Universidad de León, León, Spain

^c CIBER de Epidemiología y Salud Pública (CIBERESP), Instituto de Salud Carlos III, Madrid, Spain

^d Centro de Investigación Biomédica en Red Fisiopatología de La Obesidad y La Nutrición (CIBEROBN), Institute of Health Carlos III, Madrid, Spain

^e University of Navarra, Department of Preventive Medicine and Public Health, IDISNA, Pamplona, Spain

^f Department of Preventive Medicine, University of Valencia, Valencia, Spain

^g Universitat Rovira I Virgili, Departament de Bioquímica I Biotecnologia, Unitat de Nutrició, Reus, Spain

^h Institut D'Investigació Sanitària Pere Virgili (IISPV), Alimentació, Nutrició, Desenvolupament I Salut Mental (ANUT-DSM), Reus, Spain

ⁱ Unit of Cardiovascular Risk and Nutrition, Hospital Del Mar Medical Research Institute (IMIM), Barcelona, Spain

^j Department of Nutrition, Food Sciences, and Physiology, Center for Nutrition Research, University of Navarra, IdiSNA, Pamplona, Spain

^k Precision Nutrition and Cardiometabolic Health Program. IMDEA Food, CEI UAM + CSIC, Madrid, Spain

^l Departamento de Medicina y Endocrinología, Universidad de Valladolid, Valladolid, Spain

^m Bioaraba Health Research Institute, Cardiovascular, Respiratory and Metabolic Area, Osakidetza Basque Health Service, Araba University Hospital, University of the Basque Country UPV/EHU, Vitoria-Gasteiz, Spain

ⁿ Department of Nursing, University of Málaga, Institute of Biomedical Research in Malaga (IBIMA), Málaga, Spain

^o Instituto de Investigación Sanitaria y Biomédica de Alicante. Universidad Miguel Hernández (ISABIAL-UMH). Alicante, Spain

^p Research Group on Nutritional Epidemiology & Cardiovascular Physiopathology (NUTRECOR), Health Research Institute of the Balearic Islands (IdISBa), University Hospital Son Espases (HUSE), Palma de Mallorca, Spain

^q Department of Internal Medicine, Maimonides Biomedical Research Institute of Cordoba (IMIBIC), Reina Sofia University Hospital, University of Cordoba, Cordoba, Spain

^r Department of Internal Medicine, Institut D'Investigacions Biomèdiques August Pi Sunyer (IDIBAPS), Hospital Clinic, Institut de Recerca en Nutrició I Seguretat Alimentària (INSA-UB), University of Barcelona, Barcelona, Spain

^s Virgen de La Victoria Hospital, Department of Endocrinology, Instituto de Investigación Biomédica de Málaga (IBIMA), University of Málaga, Málaga, Spain

^t Department of Family Medicine, Research Unit, Distrito Sanitario Atención Primaria Sevilla, Sevilla, Spain

^u Research Institute of Biomedical and Health Sciences (IUIBS), University of Las Palmas de Gran Canaria & Centro Hospitalario Universitario Insular Materno Infantil (CHUIMI), Canarian Health Service, Las Palmas de, Gran Canaria, Spain

^v Department of Preventive Medicine and Public Health, University of Granada, Instituto de Investigación Biosanitaria Ibs.Granada, Granada, Spain

* Corresponding author. Facultad de Ciencias de la Salud, Departamento de Ciencias Biomédicas, Área de Medicina Preventiva y Salud Pública. Campus de Vegazana s/n, 24071, León, Spain.

E-mail address: mrubig@unileon.es (M. Rubín-García).

<https://doi.org/10.1016/j.dsx.2024.103123>

Received 22 December 2023; Received in revised form 17 September 2024; Accepted 19 September 2024

Available online 24 September 2024

1871-4021/© 2024 Research Trust of DiabetesIndia (DiabetesIndia) and National Diabetes Obesity and Cholesterol Foundation (N-DOC). Published by Elsevier Ltd.

This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

^w Research Group on Community Nutrition & Oxidative Stress, University of Balearic Islands, Palma de, Mallorca, Spain

^x CUNEF Universidad, Madrid, Spain

^y Lipids and Vascular Risk Unit, Internal Medicine, Hospital Universitario de Bellvitge-IDIBELL, Hospitalet de Llobregat, Barcelona, Spain

^z Division of Preventive Medicine, Faculty of Medicine, University of Jaén, Jaén, Spain

^{aa} Department of Endocrinology and Nutrition, Instituto de Investigación Sanitaria Hospital Clínico San Carlos (IdiSSC), Madrid, Spain

^{ab} CIBER Diabetes y Enfermedades Metabólicas (CIBERDEM), Instituto de Salud Carlos III (ISCIII), Madrid, Spain

^{ac} Department of Endocrinology, Institut D' Investigacions Biomèdiques August Pi Sunyer (IDIBAPS), Hospital Clinic, University of Barcelona, Barcelona, Spain

^{ad} Department of Endocrinology and Nutrition, Hospital Fundación Jiménez Díaz. Instituto de Investigaciones Biomédicas IISFJD. University Autonoma, Madrid, Spain

^{ae} Nutritional Control of the Epigenome Group. Precision Nutrition and Obesity Program. IMDEA Food, CEI UAM + CSIC, Madrid, Spain

^{af} Departamento de Ciencias Farmacéuticas y de La Salud, Faculty de Farmacia, Universidad San Pablo-CEU, CEU Universities, Boadilla Del Monte, Spain

^{ag} Lipid Clinic, Department of Endocrinology and Nutrition, Institut D' Investigacions Biomèdiques August Pi Sunyer (IDIBAPS), Hospital Clínic, Barcelona, Spain

^{ah} Instituto de Investigación Biosanitaria de Granada (IBS.GRANADA), Preventive Medicine Unit, University Hospital Virgen de Las Nieves, Granada, Spain

^{ai} Osasunbidea, Servicio Navarro de Salud, Atención Primaria, Pamplona, Spain

^{aj} ABS Reus V. Centre D'Assistència Primària Marià Fortuny. Salut Sant Joan de Reus – Baix Camp, Reus, Spain

ARTICLE INFO

Keywords:

Dietary patterns

Metabolic syndrome

Principal component analysis

Cluster analysis

Sex approach

ABSTRACT

Aims: This study aims to identify *a posteriori* dietary patterns with a sex approach and to evaluate their association with metabolic syndrome criteria.

Methods: Cross-sectional study conducted in 6821 men and women between 55 and 75 years of age. Forty-two food groups were analyzed from dietary information collected with food frequency questionnaires, using principal component analysis and cluster analysis and then information from both statistical methods was compared. Prevalences were calculated for each cluster group, based on the number and types of metabolic syndrome criteria they met.

Results: Following principal component analysis, two dietary patterns labeled “healthy” and “unhealthy” were identified in both men and women, due to the presence of foods that are considered more or less healthy. These same dietary patterns were found in cluster analysis plus an “intermediate” cluster consisting of both healthy and unhealthy foods. The presence of metabolic syndrome is related to the “healthy” dietary pattern in women and to the “unhealthy” dietary pattern in men. Comparison of the two statistical approaches showed a high level of correlation between them (weighted Kappa = 0.703 in women and weighted Kappa = 0.691 in men).

Conclusions: Adherence to both healthy and unhealthy dietary pattern appears to be related to the development of MS. The differences found by sex make it necessary to develop interventions with a sex-specific approach.

1. Introduction

Metabolic syndrome (MS) has become a public health problem, of uncertain cause and difficult management. In recent decades, its prevalence has increased, currently reaching a prevalence of about 25–30 % worldwide, with significant differences according to age, ethnicity and sex [1,2]. According to the harmonized criteria for MS proposed by Alberti et al. [3], one of its most prevalent components is central obesity, along with high blood pressure (HBP), the modifiable factor that most increases cardiovascular risk (CVR) [4]. Overall, MS is associated with the risk of developing type 2 diabetes, cardiovascular disease and total mortality [5]. Although there may be a genetic predisposition to develop it [6], its main risk factors are modifiable, so it could be prevented by improving lifestyle habits, such as increased physical activity and a healthy diet [7].

In recent decades, the study of dietary patterns (DP) has been promoted, in order to investigate the role of diet on overall health, beyond the effect of specific foods and nutrients. It seems that DPs are more determinant than isolated nutrients in defining population consumption patterns [8].

As for *a posteriori* DPs, although multiple patterns of this type have been identified, in general terms, they can be summarized in two opposing trends: a healthy pattern represented mainly by the Mediterranean diet and an unhealthy one, represented by the Western consumption pattern [9–11]. An increasing number of studies are comparing the DPs obtained with different statistical methods, since these analyses are based on methods in which decisions are made that may have some subjectivity [12]. Several studies have shown a direct relationship of those less healthy DPs with cardiovascular events and mortality [13,14].

Current studies indicate that there is a direct relationship between unhealthy eating and MS, but it remains to be determined whether there are differences in the type of diet according to sex and according to the

number of components or type of MS criteria [15–17]. It is important to take sex into account, due to the biological differences between men and women, as well as the existing differences in the diet of both sexes and this is not often done in previous research literature [18]. On the other hand, although the relationship between MS and DPs has been the subject of many scientific studies [9,10,19], it is necessary to study the effects of diet on the development of MS, as well as the type of DP followed by people already affected by MS.

Our hypothesis is that there are differences between the dietary patterns observed in men and women. It is necessary to identify these differences and make interventions according to the consumption patterns by sex. Regarding metabolic syndrome, a healthy pattern should have a positive impact on health even when pathology is already present.

Therefore, the main objective of this study was to identify *a posteriori* sex-focused DPs and to evaluate their association with MS criteria.

2. Material & methods

2.1. Study design

This is a cross-sectional analysis of data collected at baseline that identifies *a posteriori* DPs, of the participants included in the PREvención con Dieta MEDiterranea (PREDIMED)-Plus trial. This is a randomized, multicenter, parallel-group, 6-year, primary cardiovascular prevention trial that is currently in progress at 23 Spanish recruiting centers (universities, hospitals and research institutes). The recruitment period was from September 2013 to December 2016. In general, the inclusion criteria were determined by age range and the following clinical characteristics: men between 55 and 75 years and women between 60 and 75 years who had a body mass index (BMI) between 27 and 40 kg/m² and met at least three diagnostic criteria for MS as defined by the *International Diabetes Federation, the American Heart Association and the National*

Heart, Lung and Blood Institute [3] and had no previous cardiovascular event.

The trial was registered in the International Standard Randomized Controlled Trial (ISRCTN89898870). The trial protocol includes more detailed information and is available on the website: <http://predimedplus.com> and in previous publications [20,21] (Supplementary Material-Table S4).

A total of 9677 subjects were included in a run-in period to identify and select participants most likely to meet the study protocol, of which 6874 participants were eligible for the study and were included in the trial. After excluding those participants who did not submit complete nutritional information, 6821 subjects were included in the present study (Supplementary Material-Fig. S1). Data were analyzed using the available PREDIMED-Plus database, dated March 12, 2019.

2.2. Variables and data collection

Data on age, sex, educational levels, anthropometric measurements, dietary habits, and lifestyle, as well as blood samples for biochemical analyses, were collected at the baseline visit. Anthropometric assessments were measured according to the PREDIMED-Plus protocol. BMI was calculated as weight (kilograms) divided by the square of height (square meters). Biochemical analyses were performed using overnight fasting blood samples by standard enzymatic methods to determine parameters such as fasting plasma glucose, triglycerides or cholesterol. Blood pressure was measured in triplicate with a validated semi-automatic oscillometer in a seated position.

MS criteria according to the updated harmonized definition [3] are elevated waist circumference (WC) (≥ 102 cm in men; ≥ 88 cm in women), elevated triglycerides (TG) (≥ 150 mg/dL) or treatment, reduced HDL-C (< 40 mg/dL in men; < 50 mg/dL in women) or treatment, high blood pressure (HBP) (systolic ≥ 130 and/or diastolic ≥ 85 mm Hg) or treatment and elevated fasting glucose or treatment (≥ 100 mg/dL).

2.3. Dietary information

Data on dietary intake were obtained at baseline, just before randomization, by trained registered dietitians using a semiquantitative food frequency questionnaire (FFQ) with 143 items previously validated for the Spanish population [22]. This questionnaire collects information on food consumption during the previous year with nine possible responses, ranging from never or almost never to more than six times a day. Based on the frequency of consumption, the intake of each food is estimated in grams per day.

2.4. A posteriori dietary patterns

As a first step, the 143-FFQ items were classified into 42 food groups (Supplementary Material-Table S1), using factor analysis. The adequacy of the sample was previously assessed using the Kaiser-Meyer-Olkin measure and Barlett's test of sphericity. The analysis eliminated foods with null intakes or with intakes below the 25th percentile of the sample, finally performing the analysis with the 30 food groups that had the greatest influence on the overall mean intake [23].

Principal component analysis (PCA) was performed using Stata v.14 statistical package. The components were defined by the Kaiser criterion or eigenvalue > 1 . The eigenvalue of a factor is defined as the amount of total variance of the sample that can be explained by a given factor, for a better understanding, this value is extrapolated to a percentage to give the percentage of variance explained by each factor. The identified groups were orthogonally rotated with Varimax rotation to simplify the structure and improve its interpretability. Each component was constructed with the food groups which were more strongly correlated, as long as the factor loading was $\geq |0.35|$. In these cases, those food groups were considered to contribute significantly to the pattern and were used

to calculate the scores. PCA was initially performed separately for men and women, and Tucker's congruence coefficient was used to assess consistency between sexes [24].

On the other hand, a cluster analysis (CA) was performed using the statistical program R, version 3.6.1 and the *kmeans* function of the base package. Considering that the optimal number of clusters has a subjective component, different heuristic validation methods have been used. The number of clusters proposed by 25 different mathematical indices was calculated and the analysis was performed with the most prevalent value. Finally, according to these indices and the consistency supported by the scientific literature consulted, the optimal number of clusters, for both men and women, was determined as three [25]. To describe each cluster, the mean consumption of the selected food groups was calculated by sex and each cluster was defined by the most consumed food groups. Differences between the means of each cluster were tested with ANOVA tests and multiple comparisons between the three groups were performed with Bonferroni post estimation analysis.

2.5. Statistical analysis

Sex descriptive analyses were performed to define baseline characteristics, continuous variables were described by mean and standard deviation (SD) and categorical variables by n and percentage. Sex comparisons were performed with Pearson's test (χ^2) for categorical variables or with the *t*-test for continuous variables. Significance of all statistical tests was based on a bilateral contrast set at $p < 0.05$.

In order to compare the PCA with the CA, the mean and SD of each factor in each cluster group were calculated. Regressions were performed between the factors and each cluster group to check their correlation (β coefficient) and obtain the R^2 of the model, thus checking the total variance of each factor explained by each cluster group. In addition, for men and women separately, the weighted Kappa index was calculated.

After DP determination, prevalences were calculated in each cluster group, for men and women, according to the number of components and types of MS criteria they met. Differences between these groups according to sex were assessed with Pearson's test (χ^2).

3. Results

The baseline characteristics of the study participants are shown in

Table 1
Baseline characteristics of the study participants.

	Men		Women		p-value
	n (mean)	% (SD)	n (mean)	% (SD)	
Age (y)	3509 63.73	51.44 5.31	3312 66.27	48.56 4.06	< 0.001
Education level					< 0.001
primary school	1340	38.42	1923	59.24	
secondary school	1144	32.80	826	25.45	
more than secondary	1004	28.78	497	15.31	
Diabetes	1020	29.07	836	25.24	< 0.001
Fasting plasma glucose (mg/dl)	112.67	29.23	108.89	26.62	< 0.001
Waist circumference (cm)	111.01	8.79	103.97	9.25	< 0.001
Systolic blood pressure (mmHg)	141.10	16.49	137.93	17.24	< 0.001
Diastolic blood pressure (mmHg)	82.63	9.78	79.02	9.76	< 0.001
HDL-c (mg/dl)	43.80	10.30	52.70	11.66	< 0.001
Triglycerides (mg/dl)	158.38	85.71	145.28	66.67	< 0.001
BMI (kg/m^2)	32.28	3.28	32.86	3.61	< 0.001
Total energy intake (Kcal/d)	2563.90	644.75	2258.32	576.33	< 0.001

Continuous variables are described using mean and standard deviation (SD) and categorical variables using n and percentage.

Table 1. The mean age of the study participants exceeded 60 years, with women being older than men. In terms of education level, the low schooling rates of women compared to men was significant at all three academic levels. Regarding the components of MS, men presented worse metabolic control with slightly higher values of glucose levels, blood pressure, triglycerides and total energy intake. On the other hand, women had a slightly higher BMI than men.

3.1. Principal component analysis

As a result of the PCA (Supplementary Material-Table S2), two patterns were identified, labeled “healthy” and “unhealthy”. The first consisted of 9 items, including: nuts, seasonal fruits, vegetables, legumes, *sofrito* (sauce made with tomato and onion, leek, or garlic, simmered with olive oil), fish and seafood, and salads. The second or “unhealthy” pattern consisted of 10 items with the following composition: potatoes, olives, ultra-processed foods, sauces, non-distilled beverages, cottage cheese, sweets, white cereals, red meat and offal. In the sex distribution, two dietary patterns were obtained in both men and women. Among the differences found, higher factor loadings were observed for whole dairy products and milkshakes among men, as well as higher loadings for nuts and *gazpacho* (a Spanish cold soup based on tomato, cucumber, garlic, stale bread, olive oil, water and salt) among women. In the healthy pattern, women had a higher vegetable intake. As for the unhealthy pattern, women had a higher intake of cottage cheese, sweets white cereals and red meat and offal. The percentage of variance

explained is similar in men and women, the healthy pattern is able to explain 8.9 % of the total variance of the diet in both men and women, while the unhealthy one explains 7.4 % in women and 7.7 % in men.

3.2. Cluster analysis

In the CA (Supplementary Material-Table S3), three clusters were obtained, of which two are well differentiated, while the remaining one is formed by a mixed group of individuals who consume both healthy and unhealthy foods, practically to the same extent (cluster 2 or intermediate). As for the other two clusters, they are formed by individuals who adhere to a “healthy” and to an “unhealthy” one. The mean of the most consumed foods in each cluster was significantly different from the rest ($p < 0.05$), thus defining which foods belonged to each cluster.

The unhealthy cluster was composed of individuals with higher intakes (grams/day) of 17 items: whole dairy products, milkshakes, cottage cheese, red meat and offal, eggs, *sofrito*, potatoes, olives, olive oil, sweets, processed and ultra-processed foods, white cereals, sauces, non-distilled beverages, juices and soft drinks, coffee and tea. The healthy cluster consisted of individuals with higher intakes of 14 items: skimmed dairy products, vegetables (green vegetables, white vegetables and other vegetables), legumes, nuts, seafood and fish, salads, *gazpacho*, seasonal fruit and white meats (chicken and rabbit), legumes and whole grains. In the stratified analysis by sex, among men, there is a greater tendency towards whole milk products, milkshakes, red meat and offal, processed foods, olives, white cereals, juices and soft drinks and non-distilled

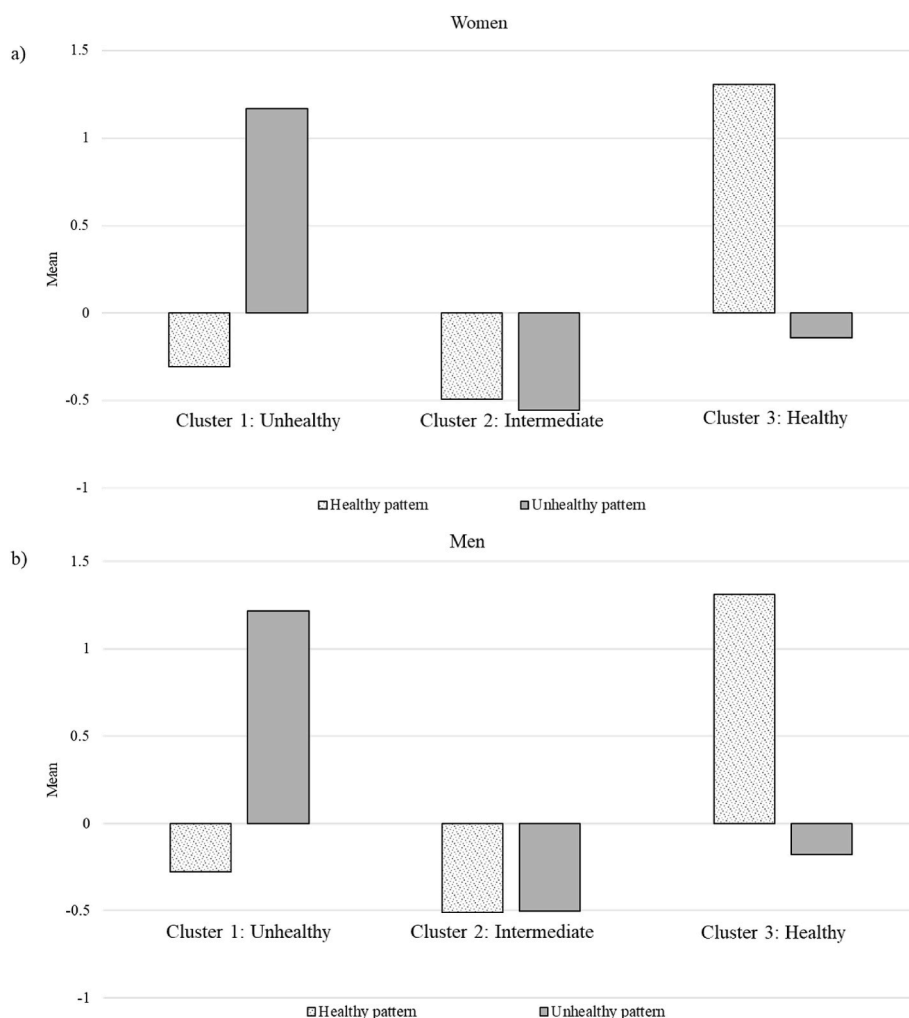


Fig. 1. Mean of each component identified in the principal component analysis in each cluster by sex.

beverages. Meanwhile, among women, there is a higher intake of skimmed dairy, green and white vegetables and whole grains. As for the intermediate pattern, there is a higher intake of wholegrain cereals among women and of dairy products (skimmed and whole), fruit (regular and seasonal), cereals (white and whole) and non-distilled beverages among men. Also in the mixed pattern, olive oil is consumed similarly by men and women.

3.3. Comparison between cluster analysis and principal component analysis

Fig. 1 shows the mean of each pattern obtained in the PCA and in each cluster by sex. As shown in Fig. 1a and Table 2, women grouped in the unhealthy cluster explain a higher percentage of variability (49 %) in the unhealthy pattern, while in the healthy cluster, the highest percentage of variability is explained by the healthy pattern (56 %). Similar data were found in men (Fig. 1b and Table 2), with a percentage of variability related to the unhealthy cluster and the unhealthy pattern of 48 %, as well as a percentage of variability associated with the healthy pattern and the healthy cluster of 57 %. The expected agreement beyond chance between the clusters and the identified patterns was 70 % (weighted Kappa of 0.703) in women and 69 % (weighted Kappa of 0.691) in men. In both cases, the intermediate cluster did not correlate with any of the identified patterns.

Table 3 shows the MS criteria met by the study participants. 14.5 % met all inclusion criteria: WC, TG, reduced HDL-c, HBP and high glycemia, while 33.3 % met only four. Most individuals (51.7 %) met only three inclusion criteria, with elevated WC, HBP and high glycemia being the most prevalent (27.2 %), followed by WC, HBP, high glycemia and TG (15.40 %). In general, individuals tended to group in the intermediate cluster.

In the distribution by sex (Table 4) and without taking into account the intermediate cluster, the tendency of men towards the unhealthy cluster was observed with a higher number of MS criteria: with 26.1 % in the healthy cluster compared to 23.3 % in the unhealthy one in those men with 5 MS components ($p = 0.269$). Contrary to men, women grouped more in the healthy cluster when they had fewer components (with 3 criteria) of MS: 27.3 % grouped in the healthy cluster versus 24.5 % in the unhealthy one ($p = 0.063$). These differences by sex, were not significant between men and women who met 5 criteria and were grouped in the healthy cluster (26.1 % vs. 23.8 %, respectively, $p = 0.399$). However, significant differences were found between men and women who met 3 criteria and were grouped in the healthy cluster (24.3 % vs. 27.3 %, respectively, $p = 0.017$).

4. Discussion

4.1. Main findings

The results of our study suggest the identification of two *a posteriori* DPs, regardless of the statistical technique used (PCA or CA), with high concordance when analyzed separately for men and women. The composition of these two patterns was similar to that observed in other studies, with some variations depending on the dietary and cultural habits of the studied population [26–28]. The healthy pattern presented

characteristics of several patterns considered healthy: Mediterranean dietary pattern (high intake of vegetables, fruits and nuts, legumes, fish, whole grains, olive oil as the main culinary fat) [29] or the Atlantic dietary pattern (typical of northern Spain and Portugal, characterized by a majority intake of fish, seafood, potatoes, legumes, cereals, fruits, dairy product and vegetables) [30]. The “unhealthy” pattern was composed of foods included in the Western pattern (meat, processed meat and poultry, refined grains, sweets, desserts, fast food, soft drinks and sweetened beverages).

4.2. Dietary patterns: principal components analysis vs cluster analysis

As for the statistical techniques used in the determination of a *posteriori* DP, PCA is the most widely used [31–33], followed by CA [32,34], with few studies comparing the two methods [10,12,24]. Our PCA identified two opposing patterns in both men and women, while in the CA three clusters were found: a healthy one, an unhealthy one and a third, intermediate, majority cluster. Although in the CA olive oil was included in the unhealthy cluster, in the PCA it was not included in any group, neither in men nor in women. This may be due to the fact that both olive oil and virgin olive oil were included in the same group in the analysis and that the use of fats remains controversial, especially when consumed with other foods such as ultra-processed fried foods [35]. As for the consumption of extra virgin olive oil, studies show that it slightly lowers LDL cholesterol levels and may reduce some CVR factors, although more solid evidence needs to be generated [36,37]. The strongest evidence has been generated in the PREDIMED trial, which showed a reduction in cardiovascular events in people who had followed a Mediterranean diet supplemented with extra virgin olive oil and nuts, compared to a diet restrictive in fat intake [38]. Other foods that do not fit any pattern were found in the PCA, such as coffee and tea, eggs or juices and soft drinks. This could be due to the fact that these foods are consumed similarly among people following both healthy and unhealthy diets. Whereas consumption of juices and soft drinks [39] has been found to have a detrimental effect due to their high amount of free sugars, moderate consumption of coffee or tea [40] is not related to an increase in MS components. As for egg consumption, recent studies [41] associate it with an increase in CVR in the context of a cholesterol-rich diet. Olives and non-distilled beverages were grouped in the total analysis in the unhealthy pattern, however, in the analysis by sex, they did not belong to any group, demonstrating the importance of the approach by sex. Olive consumption, although generally considered healthy, is associated in the Iberian Peninsula with snacking and increased salt intake [42]. As to the reproducibility of the DPs identified by the two techniques described above, a correlation was observed between healthy and unhealthy DP in both men and women, in PCA and CA. This allowed us to identify the mixed group that did not correlate with either of the other two PCA patterns. Other studies comparing both methods agree on the consistency between them [24,43].

The existence of a mixed majority cluster can be explained by the tendency of people to consume foods of all types or to have a less defined eating pattern. Other studies have described an intermediate cluster, although, unlike ours, they consist of foods with minimal intakes in the population [24] or simply include food groups that are distinct from each other [44]. Most studies tend to label all individuals in one or the

Table 2
Mean of each component identified in the principal component analysis in each cluster and variability by sex.

Cluster	Women				Men			
	Healthy pattern		Unhealthy pattern		Healthy pattern		Unhealthy pattern	
	Mean (SD)	R ²	Mean (SD)	R ²	Mean (SD)	R ²	Mean (SD)	R ²
1.Unhealthy	−0.31 (0.67)	0.033	1.17 (0.84)	0.487	−0.28 (0.69)	0.025	1.21 (0.89)	0.482
2.Intermediate	−0.49 (0.57)	0.233	−0.55 (0.56)	0.296	−0.51 (0.56)	0.265	−0.50 (0.55)	0.256
3.Healthy	1.31 (0.80)	0.558	−0.14 (0.78)	0.007	1.31 (0.76)	0.569	−0.18 (0.78)	0.010

Table 3
Percentage of total sample, men and women distributed according to the number and type of metabolic syndrome components and to the cluster.

						Total	Men			Women		
							C1	C2	C3	C1	C2	C3
5 components	WC	HBP	Glycemia	TG	HDL	14.5	3.8	7.3	3.3	3.5	7.4	3.8
	WC	HBP	Glycemia	TG		15.4	4.6	9.5	3.8	3.1	6.7	3.0
4 components	WC	HBP	Glycemia	HDL		8.5	1.5	3.6	2.0	2.9	4.8	2.4
	WC	HBP	TG	HDL		6.5	1.5	2.8	1.5	1.7	3.6	2.0
3 components	WC	Glycemia	TG	HDL		1.9	0.3	1.0	0.5	0.5	1.0	0.5
	HBP	Glycemia	TG	HDL		1.0	0.4	0.8	0.5	0.1	0.1	0.0
	WC	HBP	Glycemia			27.2	6.2	12.9	7.0	7.5	13.9	6.9
	WC	HBP	TG			9.7	2.8	5.1	1.9	2.5	4.9	2.3
	WC	HBP	HDL			5.9	1.0	2.3	1.2	2.1	3.5	1.7
	WC	Glycemia	TG			2.9	0.7	1.3	0.9	0.9	1.4	0.7
	WC	Glycemia	HDL			1.6	0.3	0.6	0.4	0.4	0.8	0.7
	WC	TG	HDL			1.5	0.2	0.5	0.3	0.7	0.7	0.7
	HBP	Glycemia	TG			1.4	0.6	1.4	0.6	0.1	0.1	0.0
	HBP	TG	HDL			0.7	0.2	0.6	0.3	0.0	0.2	0.0
	HBP	Glycemia	HDL			0.6	0.2	0.5	0.5	0.0	0.0	0.0
	Glycemia	TG	HDL			0.2	0.1	0.2	0.1	0.0	0.0	0.0

*C1 = Unhealthy cluster; C2 = Intermediate cluster; C3 = Healthy cluster; HBP indicates high blood pressure; TG indicates hypertriglyceridemia, WC indicates waist circumference.

Table 4
Sex differences according to the number of metabolic syndrome criteria.

	Men							Women						
	Total	C1		C2		C3		Total	C1		C2		C3	
		n	%	n	%	n	%		n	%	n	%	n	%
5 components	505	132	26.1	256	50.7	117	23.2	487	116	23.8	246	50.5	125	25.7
4 components	1203	293	24.4	618	51.4	292	24.3	1065	273	25.6	533	50.0	259	24.3
3 components	1780	432	24.3	891	50.1	457	25.7	1741	475	27.3	839	48.2	427	24.5

*C1 = Unhealthy cluster; C2 = Intermediate cluster; C3 = Healthy cluster.

other, depending on their similarities [9,45]. The finding of this mixed cluster may be due to the fact that people do not only consume healthy or unhealthy foods, but continuously mix all kinds of foods. According to some studies [46,47], dietary variety would not be as beneficial compared to a healthy diet in the prevention of MS. This could explain the presence of a majority mixed pattern in a population meeting the criteria for MS. Nevertheless, some dietary recommendations considered healthy, such as decreasing fat intake, need further studies to demonstrate their relationship with MS [36].

4.3. Sex approach and metabolic syndrome

In terms of the MS criteria met, approximately half of the population sample met only three criteria for MS, with WC being the most prevalent, followed by HBP and elevated glycemia. Overall, central obesity is the most prevalent component of MS [48], being, along with HBP, one of the components that most increases CVR [4]. Also WC is the most modifiable through lifestyle changes [49]. Analyses by sex allowed us to identify differences in the criteria for MS. We observed that as the number of MS criteria increased, more men tended to cluster in the unhealthy group, while more women clustered in the healthy group. This finding may be due to differences in response to non-pharmacological treatment in men and women, as well as in lifestyle habits [16], but also to a possible change in dietary habits after diagnosis (reverse causality) [50]. Regarding treatment response, some authors report differences in lifestyle modifications and weight loss between men and women, as well as a better response to non-pharmacological treatment among men [16], with the Mediterranean diet being one of the most beneficial [20,29]. The biological and biochemical differences, the distribution of central obesity, lifestyle and dietary habits, as well as the different lipid and hormonal profile make it necessary to analyze DP by sex [16,51]. There is a vast literature [10,15,

24] that analyzes, separately, DP in men and women, although research in this field still needs to be increased.

4.4. Clinical relevance

The use of different statistical methods to determine dietary patterns and the comparison of the results obtained provide consistency and greater clinical relevance. The identification of a mixed dietary pattern, consisting of individuals consuming both healthy and unhealthy foods and its association with MS criteria represents a novelty and opens up new lines of research. Furthermore, the differences found between men and women highlight the importance of considering sex analysis and developing prevention strategies in line with the findings.

4.5. Limitations

. Our population consists of elderly Spanish individuals with MS, so our results cannot be extrapolated to the general Spanish population or to other countries. Furthermore, it is a cross-sectional study with its own limitation. In addition, PREDIMED-Plus participants present metabolic disorders and some of them follow specific therapeutic diets. Another limitation is that the self-reported dietary information may have led to some misclassification and possible measurement errors, however, the FFQ was administered by trained dietitians and previously validated in the Spanish adult population showing good reproducibility and validity [22]. Another limitation related to pattern analyses is that they do not allow to specifically identify the particular dietary component within the pattern that may be responsible for the observed differences between population subgroups. That is another reason for performing analyses by sex.

4.6. Strengths

The present study has a number of strengths, such as the multicenter design, the large sample size and the detailed and high quality information collected by qualified interviewers. Another strength of our study is the determination of patterns using different statistical methods, both PCA and CA and the comparison of both. A strength that can be considered novel is the identification of a mixed pattern, consisting of people consuming both healthy and unhealthy foods. Also, this mixed pattern was determined using mathematical methods to determine the optimal number of clusters. Finally, sex-differentiated patterns are created, taking into account the differences between men and women.

5. Conclusions

The DPs identified by using two statistical techniques, PCA and CA, have had a high concordance, both in men and women. The finding of a majority intermediate pattern in the CA explains the tendency of this population to consume both healthy and unhealthy foods altogether. Adherence to both healthy and unhealthy DPs appears to be related to the development of MS, such that women who meet more criteria for MS adhere more to the healthy pattern than men. Therefore, to develop effective interventions for DPs modification, a sex-specific approach is necessary.

Funding

The PREDIMED-Plus trial was supported by the European Research Council (Advanced Research Grant 2013–2018, 340918) to Dr Martínez-González, and the official funding agency for biomedical research of the Spanish government, Instituto de Salud Carlos III, through the Fondo de Investigación para la Salud, which is cofunded by the European Regional Development Fund (5 coordinated Fondo de Investigación para la Salud projects led by Dr. Salas-Salvadó and Dr Vidal, including the following projects: PI13/00673, PI13/00492, PI13/00272, PI13/01123, PI13/00462, PI13/00233, PI13/02184, PI13/00728, PI13/01090, PI13/01056, PI14/01722, PI14/00636, PI14/00618, PI14/00696, PI14/01206, PI14/01919, PI14/00853, PI14/01374, PI14/00972, PI14/00728, PI14/01471, PI16/00473, PI16/00662, PI16/01873, PI16/01094, PI16/00501, PI16/00533, PI16/00381, PI16/00366, PI16/01522, PI16/01120, PI17/00764, PI17/01183, PI17/00855, PI17/01347, PI17/00525, PI17/01827, PI17/00532, PI17/00215, PI17/01441, PI17/00508, PI17/01732, PI17/00926, PI19/00957, PI19/00386, PI19/00309, PI19/01032, PI19/00576, PI19/00017, PI19/01226, PI19/00781, PI19/01560, PI19/01332, PI20/01802, PI20/00138, PI20/01532, PI20/00456, PI20/00339, PI20/00557, PI20/00886, PI20/01158), the Especial Action Project titled Implementación y evaluación de una intervención intensiva sobre la actividad física Cohorte PREDIMED-Plus grant to Dr Salas-Salvadó, the Recercaixa grant to Dr Salas-Salvadó (2013ACUP00194), a CICYT (Consejo Interinstitucional de Ciencia y Tecnología) grant (AGL2016–75329-R), a grant from the Generalitat Valenciana (APOSTD/2019/136 to R.B) and Generalitat de Catalunya (SGR-2019 to R.E), grants from the Consejería de Salud de la Junta de Andalucía (PI0458/2013, PS0358/2016, and PI0137/2018), grants from the Generalitat Valenciana (PROMETEO/2017/017 and PROMETEO/2021/21), a SEMERGEN (Sociedad Española de Médicos de Atención Primaria) grant, EU-COST (European Cooperation in Science and Technology) Action CA16112, a grant of support to research groups number 35/2011 from the Balearic Islands Government, grants from IDISBA (Instituto de Investigación Sanitaria Islas Baleares), funds from the European Regional Development Fund (CIBEROBN CB06/03 and CB12/03) and from the European Commission (EAT2BENI-CE_H2020_SFS2016). Juan de la Cierva-Incorporación research grant (IJC2019-042420-I/AEI/10.13039/501100011033) from Agencia Estatal de Investigación to JK. INSA-Ma María de Maeztu Unit of Excellence (grant CEX2021-001234-M funded by MICIN/AEI/

FEDER, UE). The funding sponsors had no role in the design of the study; in the collection, analyses, or interpretation of the data; in the writing of the article, or in the decision to publish the results.

Author disclosure statement

Dr Estruch reports grants from Cerveza y Salud, Spain, and Fundación Dieta Mediterránea, Spain. Additionally, personal fees for given lectures from Brewers of Europe, Belgium; Fundación Cerveza y Salud, Spain; Pernod Ricard, Mexico; Instituto Cervantes, Albuquerque, NM; Instituto Cervantes, Milan, Italy; Instituto Cervantes, Tokyo, Japan; Lilly Laboratories, Spain; and Wine and Culinary International Forum, Spain; and nonfinancial support to organize a National Congress on Nutrition. Dr Ros reports grants, personal fees, nonfinancial support and other support from the California Walnut Commission, during the conduct of the study; grants, personal fees, nonfinancial support, and other support from Alexion; grants, personal fees, and other support from Sanofi Aventis; personal fees, nonfinancial support, and other support from Ferrer International; personal fees, nonfinancial support, and other support from Danone; personal fees and nonfinancial support from Merck Sharp Dohme; personal fees and other support from Amarin, outside the submitted work. Dr Lamuela-Raventós reports personal fees from Cerveceros de España, personal fees and other support from Adventia, other support from Ecoveritas, outside the submitted work. Dr Salas-Salvadó reported receiving research support from the Instituto de Salud Carlos III, Ministerio de Educación y Ciencia, the European Commission, the US National Institutes of Health; receiving consulting fees or travel expenses from Eroski Foundation, Instituto Danone, Nestle, and Abbott Laboratories, receiving nonfinancial support from Hojiblanca, Patrimonio Comunal Olivarero, the California Walnut Commission, Almond Board of California, La Morella Nuts, Pistachio Growers, and Borges; serving on the board of and receiving grant support through his institution from the International Nut and Dried Foundation and the Eroski Foundation; and personal fees from Instituto Danone; and serving in the Board of Danone Institute International.

The remaining authors have no disclosures to report.

Acknowledge the use of AI-written text

The authors declare that no text written with AI has been used for this publication.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Miguel Angel Martinez Gonzalez reports financial support was provided by the European Research Council. Dr. Salas-Salvado and Dr. Vidal reports financial support was provided by Instituto de Salud Carlos III, through the Fondo de Investigación para la Salud, which is cofunded by the European Regional Development Fund. Dr Salas-Salvado reports financial support was provided by the Especial Action Project titled Implementación y evaluación de una intervención intensiva sobre la actividad física Cohorte PREDIMED-Plus grant. Dr Salas-Salvado reports financial support was provided by the Recercaixa grant (2013ACUP00194). PREDIMED-Plus study reports financial support was provided by Inter-institutional Council of Science and Technology. PREDIMED-Plus study reports financial support was provided by Government of Valencia. Dr. Estruch reports financial support was provided by Generalitat de Catalunya (SGR-2019). PREDIMED-Plus study reports financial support was provided by Consejería de Salud de la Junta de Andalucía. PREDIMED-Plus study reports financial support was provided by Government of Valencia. Vicente Martin Sanchez reports financial support was provided by A SEMERGEN (Sociedad Española de Médicos de Atención Primaria) grant. PREDIMED-Plus study reports financial support was provided by EU-COST (European Cooperation in

Science and Technology) Action CA16112. Research group number 35 2011 reports financial support was provided by Balearic Islands Government. PREDIMED-Plus reports financial support was provided by Grants from IDISBA (Instituto de Investigación Sanitaria Islas Baleares). PREDIMED-Plus reports financial support was provided by European Regional Development Fund. PREDIMED-Plus reports financial support was provided by The European Commission (EAT2BENICE_H2020_SFS2016). Jadwiga Konieczna reports financial support was provided by State Agency of Research. PREDIMED-Plus reports financial support was provided by INSA-Ma María de Maeztu Unit of Excellence. Dr Estruch reports a relationship with Cerveza y Salud, Spain, and Fundacion Dieta Mediterranea that includes: funding grants. Dr Estruch reports a relationship with Brewers of Europe, Fundacion Cerveza y Salud, Pernod Ricard, Instituto Cervantes, Instituto Cervantes, Instituto Cervantes Japan, Lilly Laboratories, and Wine and Culinary International Forum that includes: speaking and lecture fees. Dr Ros reports a relationship with the California Walnut Commission, Alexion, Sanofi Aventis, Ferrer International, Danone, Merck Sharp Dohme, Amarin that includes: funding grants, non-financial support, and speaking and lecture fees. Dr Lamuela-Raventos reports a relationship with Cerveceros de España, Adventia, Ecoveritas, that includes: consulting or advisory. Dr Salas Salvado reports a relationship with Instituto de Salud Carlos III, Ministerio de Educación y Ciencia, the European Commission, the US National Institutes of Health that includes: non-financial support. Dr Salas Salvado reports a relationship with from Eroski Foundation, Instituto Danone, Nestle, and Abbott Laboratories that includes: consulting or advisory and travel reimbursement. Dr Salas Salvado reports a relationship with Hojiblanca, Patrimonio Comunal Olivarero, the California Walnut Commission, Almond Board of California, La Morella Nuts, Pistachio Growers, and Borges that includes: non-financial support. Dr Salas Salvado reports a relationship with International Nut and Dried Foundation and the Eroski Foundation that includes: board membership and funding grants. Dr Salas Salvado reports a relationship with Instituto Danone and Board of Danone Institute International that includes: board membership and consulting or advisory. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

The authors especially thank the PREDIMED-Plus participants for the enthusiastic collaboration, the PREDIMED-Plus personnel for outstanding support, and the personnel of all associated primary care centers for the exceptional effort. CIBEROBN, CIBERESP, and CIBERDEM are initiatives of Instituto de Salud Carlos III (ISCIII), Madrid, Spain.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.dsx.2024.103123>.

References

- [1] Hirode G, Wong RJ. Trends in the prevalence of metabolic syndrome in the United States, 2011–2016. *JAMA, J Am Med Assoc* 2020;323:2526–8. <https://doi.org/10.1001/jama.2020.4501>.
- [2] Dang AK, Le HT, Nguyen GT, Mamun AA, Do KN, Thi Nguyen LH, et al. Prevalence of metabolic syndrome and its related factors among Vietnamese people: a systematic review and meta-analysis. *Diabetes Metab Syndr Clin Res Rev* 2022;16: 102477. <https://doi.org/10.1016/j.dsx.2022.102477>.
- [3] Alberti KGMM, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the international diabetes federation task force on epidemiology and prevention; National heart, lung, and blood institute; American heart association; World heart federation; International. *Circulation* 2009;120:1640–5. <https://doi.org/10.1161/CIRCULATIONAHA.109.192644>.
- [4] Yusuf S, Joseph P, Rangarajan S, Islam S, Mente A, Hystad P, et al. Modifiable risk factors, cardiovascular disease, and mortality in 155 722 individuals from 21 high-income, middle-income, and low-income countries (PURE): a prospective cohort study. *Lancet* 2020;395:795–808. [https://doi.org/10.1016/S0140-6736\(19\)32008-2](https://doi.org/10.1016/S0140-6736(19)32008-2).
- [5] Silveira Rossi JL, Barbalho SM, Reverete de Araujo R, Bechara MD, Sloan KP, Sloan LA. Metabolic syndrome and cardiovascular diseases: Going beyond traditional risk factors. *Diabetes Metab Res Rev* 2022;38:e3502. <https://doi.org/10.1002/dmrr.3502>.
- [6] Bovolini A, Garcia J, Andrade MA, Duarte JA. Metabolic syndrome pathophysiology and predisposing factors. *Int J Sports Med* 2021;42:199–214. <https://doi.org/10.1055/a-1263-0898>.
- [7] Castro-Barquero S, Ruiz-León AM, Sierra-Pérez M, Estruch R, Casas R. Dietary strategies for metabolic syndrome: a comprehensive review. *Nutrients* 2020;12: 1–21. <https://doi.org/10.3390/nu12102983>.
- [8] Hu FB. Dietary pattern analysis: a new direction in nutritional epidemiology. *Curr Opin Lipidol* 2002;13:3–9. <https://doi.org/10.1097/00041433-200202000-00002>.
- [9] Fabiani R, Naldini G, Chiavarini M. Dietary patterns and metabolic syndrome in adult subjects: a systematic review and meta-analysis. *Nutrients* 2019;11:2056. <https://doi.org/10.3390/nu11092056>.
- [10] Kim Y, Kim YM, Shin MH, Koh SB, Chang Kim H, Kim MK. Empirically identified dietary patterns and metabolic syndrome risk in a prospective cohort study: the Cardiovascular Disease Association Study. *Clin Nutr* 2022;41:2156–62. <https://doi.org/10.1016/j.clnu.2022.07.038>.
- [11] Zhang Y, Wei Y, Tang D, Lu J, Zhang N, Hu Y, et al. Association of major dietary patterns and different obesity phenotypes in Southwest China: the China Multi-Ethnic Cohort (CMEC) Study. *Eur J Nutr* 2023;62:465–76. <https://doi.org/10.1007/s00394-022-02997-7>.
- [12] Stricker MD, Onland-Moret NC, Boer JMA, van der Schouw YT, Verschuren WMM, May AM, et al. Dietary patterns derived from principal component- and k-means cluster analysis: long-term association with coronary heart disease and stroke. *Nutr Metabol Cardiovasc Dis* 2013;23:250–6. <https://doi.org/10.1016/j.numecd.2012.02.006>.
- [13] Becerra-Tomás N, Blanco Mejía S, Vigiulouk E, Khan T, Kendall CWC, Kahleova H, et al. Mediterranean diet, cardiovascular disease and mortality in diabetes: a systematic review and meta-analysis of prospective cohort studies and randomized clinical trials. *Crit Rev Food Sci Nutr* 2020;60:1207–27. <https://doi.org/10.1080/10408398.2019.1565281>.
- [14] Gomez-Delgado F, Katsiki N, Lopez-Miranda J, Perez-Martinez P. Dietary habits, lipoprotein metabolism and cardiovascular disease: from individual foods to dietary patterns. *Crit Rev Food Sci Nutr* 2021;61:1651–69. <https://doi.org/10.1080/10408398.2020.1764487>.
- [15] Song S, Kim S, Lee JE. Sex consideration in diet-biomarker-related indices: a systematic review. *Publ Health Nutr* 2018;21:2617–29. <https://doi.org/10.1017/S1368980018001490>.
- [16] Pucci G, Alcidi R, Tap L, Battista F, Mattace-Raso F, Schillaci G. Sex- and gender-related prevalence, cardiovascular risk and therapeutic approach in metabolic syndrome: a review of the literature. *Pharmacol Res* 2017;120:34–42. <https://doi.org/10.1016/j.phrs.2017.03.008>.
- [17] Santilli F, D'Ardes D, Guagnano MT, Davi G. Metabolic syndrome: sex-related cardiovascular risk and therapeutic approach. *Curr Med Chem* 2017;24:2602–27. <https://doi.org/10.2174/0929867324666170710121145>.
- [18] Crea F, Battipaglia I, Andreotti F. Sex differences in mechanisms, presentation and management of ischaemic heart disease. *Atherosclerosis* 2015;241:157–68. <https://doi.org/10.1016/j.atherosclerosis.2015.04.802>.
- [19] Di Daniele N. Association of dietary patterns with metabolic syndrome. *Nutrition* 2020;12(12):1–3. <https://doi.org/10.3390/nu12092840>.
- [20] Sayón-Orea C, Razquin C, Bulló M, Corella D, Fitó M, Romaguera D, et al. Effect of a nutritional and behavioral intervention on energy-reduced mediterranean diet adherence among patients with metabolic syndrome: interim analysis of the PREDIMED-plus randomized clinical trial. *JAMA, J Am Med Assoc* 2019;322: 1486–99. <https://doi.org/10.1001/jama.2019.14630>.
- [21] Martínez-González MA, Buil-Cosiales P, Corella D, Bulló M, Fitó M, Vioque J, et al. Cohort profile: design and methods of the PREDIMED-Plus randomized trial. *Int J Epidemiol* 2019;48:387–3880. <https://doi.org/10.1093/ije/dyy225>.
- [22] De La Fuente-Arillaga C, Vazquez Ruiz Z, Bes-Rastrollo M, Sampson L, Martinez-González MA. Reproducibility of an FFQ validated in Spain. *Publ Health Nutr* 2010;13:1364–72. <https://doi.org/10.1017/S1368980009993065>.
- [23] Franssen HP, May AM, Stricker MD, Boer JMA, Hennig C, Rosseel Y, et al. A posteriori dietary patterns: how many patterns to retain? *J Nutr* 2014;144: 1274–82. <https://doi.org/10.3945/jn.113.188680>.
- [24] Thorpe MG, Milte CM, Crawford D, McNaughton SA. A comparison of the dietary patterns derived by principal component analysis and cluster analysis in older Australians. *Int J Behav Nutr Phys Activ* 2016;13. <https://doi.org/10.1186/s12966-016-0353-2>.
- [25] Devlin UM, McNulty BA, Nugent AP, Gibney MJ. The use of cluster analysis to derive dietary patterns: methodological considerations, reproducibility, validity and the effect of energy mis-reporting. *Proc Nutr Soc* 2012;71:599–609. <https://doi.org/10.1017/S0029665112000729>.
- [26] Jayedi A, Soltani S, Abdolshahi A, Shab-Bidar S. Healthy and unhealthy dietary patterns and the risk of chronic disease: an umbrella review of meta-analyses of prospective cohort studies. *Br J Nutr* 2020;124:1133–44. <https://doi.org/10.1017/S0007114520002330>.
- [27] Karageorgou D, Magriplis E, Bakogianni I, Mitsopoulou AV, Dimakopoulos I, Micha R, et al. Dietary patterns and cardiovascular disease in Greek adults: the

- hellenic national nutrition and health survey (HNNHS). *Nutr Metabol Cardiovasc Dis* 2020;30:201–13. <https://doi.org/10.1016/j.numecd.2019.09.024>.
- [28] Shridhar K, Satija A, Dhillon PK, Agrawal S, Gupta R, Bowen L, et al. Association between empirically derived dietary patterns with blood lipids, fasting blood glucose and blood pressure in adults - the India migration study. *Nutr J* 2018;17: 1–12. <https://doi.org/10.1186/s12937-018-0327-0>.
- [29] Martínez-González MA, Gea A, Ruiz-Canela M. The mediterranean diet and cardiovascular health: a critical review. *Circ Res* 2019;124:779–98. <https://doi.org/10.1161/CIRCRESAHA.118.313348>.
- [30] Tejera-Perez C, Sanchez-Bao A, Bellido-Guerrero D, Casanueva FF. The Southern European Atlantic diet. *Minerva Endocrinol* 2021;46:145–60. <https://doi.org/10.23736/S2724-6507.20.03381-7>.
- [31] San-Cristobal R, Navas-Carretero S, Celis-Morales C, Brennan L, Walsh M, Lovegrove JA, et al. Analysis of dietary pattern impact on weight status for personalised nutrition through on-line advice: the food4Me Spanish cohort. *Nutrients* 2015;7:9523–37. <https://doi.org/10.3390/nu7115482>.
- [32] Zhao J, Li Z, Gao Q, Zhao H, Chen S, Huang L, et al. A review of statistical methods for dietary pattern analysis. *Nutr J* 2021;20:1–18. <https://doi.org/10.1186/s12937-021-00692-7>. 201 2021.
- [33] Edefonti V, De Vito R, Dalmartello M, Patel L, Salvatori A, Ferraroni M. Reproducibility and validity of A posteriori dietary patterns: a systematic review. *Adv Nutr* 2020;11:293–326. <https://doi.org/10.1093/advances/nmz097>.
- [34] Ocké MC. Evaluation of methodologies for assessing the overall diet: dietary quality scores and dietary pattern analysis. *Proc Nutr Soc* 2013;72:191–9. <https://doi.org/10.1017/S0029665113000013>.
- [35] Hao J, Zhou P, Qiu H. Association between ultra-processed food consumption and frailty in American elder people: evidence from a cross-sectional study. *J Nutr Health Aging* 2022;26:688–97. <https://doi.org/10.1007/s12603-022-1824-6>.
- [36] Schwingshackl L, Krause M, Schmucker C, Hoffmann G, Rucker G, Meerpohl JJ. Impact of different types of olive oil on cardiovascular risk factors: a systematic review and network meta-analysis. *Nutr Metabol Cardiovasc Dis* 2019;29:1030–9. <https://doi.org/10.1016/j.numecd.2019.07.001>.
- [37] Franconi F, Campesi I, Romani A. Is extra virgin olive oil an ally for women's and men's cardiovascular health? *Cardiovasc Ther* 2020;2020. <https://doi.org/10.1155/2020/6719301>.
- [38] Estruch R, Ros E, Salas-Salvadó J, Covas M-I, Corella D, Arós F, et al. Primary prevention of cardiovascular disease with a mediterranean diet supplemented with extra-virgin olive oil or nuts. *N Engl J Med* 2018;378:e34. <https://doi.org/10.1056/nejmoa1800389>.
- [39] Malik VS, Hu FB. Sugar-sweetened beverages and cardiometabolic health: an update of the evidence. *Nutrients* 2019;11:1840. <https://doi.org/10.3390/nu11081840>.
- [40] Chieng D, Kistler PM. Coffee and tea on cardiovascular disease (CVD) prevention. *Trends Cardiovasc Med* 2022;32:399–405. <https://doi.org/10.1016/J.TCM.2021.08.004>.
- [41] Zhao B, Gan L, Graubard BI, Männistö S, Albanes D, Huang J. Associations of dietary cholesterol, serum cholesterol, and egg consumption with overall and cause-specific mortality: systematic review and updated meta-analysis. *Circulation* 2022;145:1506–20. <https://doi.org/10.1161/CIRCULATIONAHA.121.057642>.
- [42] Rocha J, Borges N, Pinho O. Table olives and health: a review. *J Nutr Sci* 2020;9: e57. <https://doi.org/10.1017/jns.2020.50>.
- [43] Newby PK, Muller D, Tucker KL. Associations of empirically derived eating patterns with plasma lipid biomarkers: a comparison of factor and cluster analysis methods. *Am J Clin Nutr* 2004;80:759–67. <https://doi.org/10.1093/ajcn/80.3.759>.
- [44] Song P, Zhang X, Li Y, Man Q, Jia S, Zhang J, et al. MetS prevalence and its association with dietary patterns among Chinese middle-aged and elderly population: results from a national cross-sectional study. *Nutrients* 2022;14. <https://doi.org/10.3390/nu14245301>.
- [45] Basora J, Villalobos F, Pallegà-Millán M, Babio N, Goday A, Zomeño MD, et al. Deprivation index and lifestyle: baseline cross-sectional analysis of the predimed-plus catalonia study. *Nutrients* 2021;13:3408. <https://doi.org/10.3390/nu13103408>.
- [46] De Oliveira Otto MC, Padhye NS, Bertoni AG, Jacobs DR, Mozaffarian D. Everything in moderation - dietary diversity and quality, central obesity and risk of diabetes. *PLoS One* 2015;10:e0141341. <https://doi.org/10.1371/journal.pone.0141341>.
- [47] de Oliveira Otto MC, Anderson CAM, Dearborn JL, Ferranti EP, Mozaffarian D, Rao G, et al. Dietary diversity: implications for obesity prevention in adult populations: a science advisory from the American heart association. *Circulation* 2018;138:160–8. <https://doi.org/10.1161/CIR.0000000000000595>.
- [48] Engin A. The definition and prevalence of obesity and metabolic syndrome. *Adv Exp Med Biol* 2017;960:1–17. https://doi.org/10.1007/978-3-319-48382-5_1. Springer New York LLC.
- [49] Rezagholizadeh F, Djafarian K, Khosravi S, Shab-Bidar S. A posteriori healthy dietary patterns may decrease the risk of central obesity: findings from a systematic review and meta-analysis. *Nutr Res* 2017;41:1–13. <https://doi.org/10.1016/J.NUTRES.2017.01.006>.
- [50] Sattar N, Preiss D. Reverse causality in cardiovascular epidemiological research: more common than imagined? *Circulation* 2017;135:2369–72. <https://doi.org/10.1161/CIRCULATIONAHA.117.028307>.
- [51] Kang Y, Kim J. Gender difference on the association between dietary patterns and metabolic syndrome in Korean population. *Eur J Nutr* 2016;55:2321–30. <https://doi.org/10.1007/s00394-015-1127-3>.