UNIVERSIDAD DE GRANADA

Facultad de Medicina

Departamento de Medicina Preventiva y Salud Pública

Programa de Doctorado en Medicina Clínica y Salud Pública

“Déficits de Nutrientes en Pacientes con Síndrome Metabólico. Diferencias Regionales e Influencia del Nivel Socioeconómico y Cultural”

"Nutritional inadequate intake in subjects with Metabolic Syndrome. Influence of geographical area of residence, socioeconomic status and cultural level”

Tesis Doctoral

Naomi Cano Ibáñez

Granada, 2019

Editor: Universidad de Granada. Tesis Doctorales
Autor: Naomi Cano Ibáñez
ISBN: 978-84-1306-306-5
URI: http://hdl.handle.net/10481/57195

“Déficits de Nutrientes en Pacientes con Síndrome Metabólico. Diferencias Regionales e Influencia del Nivel Socioeconómico y Cultural”

Tesis Doctoral que presenta **NAOMI CANO IBÁÑEZ** para aspirar al título de Doctora con Mención Internacional

Granada, 10 de Septiembre de 2019.

Directores de la Tesis Doctoral

Dña. Aurora Bueno Cavanillas

Catedrática de Medicina Preventiva y Salud Pública

Universidad de Granada

D. Alfredo Gea Sánchez

Profesor Contratado Doctor de Medicina Preventiva y Salud Pública

Universidad de Navarra

Para la realización de esta Tesis Doctoral la doctoranda ha disfrutado de una Ayuda del Programa de Formación de Profesorado Universitario, financiada por el Ministerio de Educación, Cultura y Deporte del Gobierno de España (ref. FPU14/03630). La estancia de investigación realizada durante los meses de Septiembre a Diciembre de 2017 en la Universidad de Harvard T.H. Chan School of Public Health (Boston, Estados Unidos) fue financiada por el Programa de Movilidad Internacional de Estudiantes de Doctorado, convocado por el programa propio de movilidad de la Universidad de Granada.

La doctoranda y los directores de Tesis desean agradecer a todos los investigadores implicados en el Estudio PREDIMED-Plus la oportunidad de vincular el proyecto de Tesis al estudio Predimed-Plus y a todos los participantes incluidos en el estudio su generosidad para proporcionar la información requerida. Si ellos la elaboración de esta Tesis Doctoral no hubiese sido posible.

“He visto a pocos morir de hambre, de comer, cientos”

Benjamin Franklin

AGRADECIMIENTOS

Dicen que los sueños se hacen realidad. Yo hoy puedo constatarlo. Tras 4 duros años de siembra, la época de recolecta ha finalizado y el fruto de la constancia y el trabajo ha visto la luz.

A lo largo de este proceso han sido muchas las personas que han caminado a mi lado, guiándome, ayudándome y levantándome cuando las piedras que se encontraban en él hacían que me cayese.

En primer lugar quisiera expresar mi más sincera gratitud a mis directores de tesis. A **Doña Aurora Bueno Cavanillas**, ejemplo de constancia y trabajo en estado puro; a quien admiro por su calidad científica pero aún más por su humanidad y proximidad. No sólo mi directora de tesis, una amiga, una confidente y un paño de lágrimas cuando lo he necesitado. Mi referente y mi maestra. Gracias por haberme brindado esta maravillosa oportunidad y por confiar en mí cuando ni yo misma lo hacía. A D**on Alfredo Gea**, mi guía en la lejanía. A pesar de la distancia, tan cercano siempre. Ejemplo maravilloso de juventud y talento. De trabajo y perseverancia. De amabilidad, paciencia y predisposición infinita. Gracias por convertir mis dificultades en oportunidades.

A **Don Miguel Ángel Martínez González**, por embarcarme en el estudio PREDIMED-Plus. Por brindarme la maravillosa oportunidad de aprender en este ambicioso proyecto y por abrirme las puertas de Harvard. Al Doctor Frank Hu y a todos los integrantes del Departamento de Nutrición de Harvard T.H. Chan School of Public Health, por acogerme durante mi estancia, ayudarme a mejorar y mostrarme otras formas distintas de hacer investigación.

A todos y cada uno de los **profesores y miembros** que conforman el **Departamento de Medicina Preventiva y Salud Pública**, a los que están y a los que ya no. Más que un Departamento, una gran familia. Especialmente a **Doña Milagros Fernández Crehuet**, a quien estimo profundamente y la culpable en gran parte de que hoy esté aquí. A **Don Miguel García**, ironía y descaro personificado, por esas conversaciones certeras. A **Don Pablo Lardelli**, por ayudarme siempre que lo he necesitado. A Don **José Juan Jiménez**, ejemplo de rigurosidad y buen hacer. A **Don Miguel Espigares**, veteranía y humildad en estado puro, por sus consejos. A todos vosotros, gracias por hacerme sentir una más desde el primer día, por aconsejarme, y darme continuamente palabras de ánimo durante estos años de trabajo. A todas las jóvenes promesas de esta gran familia, **Carmen, Eladio, Virginia, Sandra, Rocío Barrios, Rocío Olmedo, Inma, Macarena, Pilar, Juan Pedro, Luis Miguel, Mario, Eva, César** y mis niñas bonitas de Farmacia; **Elena Espigares y Elena Moreno**. Por su compañerismo y el apoyo incondicional prestado. Este Departamento es afortunado por poder contar con vuestro afán de superación y el amor que ponéis en vuestro trabajo diario.

A **Blanca y Laura**, y todas aquellas que han pasado por el equipo PREDIMED-Plus Granada. Las dificultades y vicisitudes han formado parte de vuestra rutina, pero han sido superadas con el esfuerzo y la dedicación que os caracteriza.

A mis amigas, las de toda la vida. A **Vanesa, Elisa y Arancha**. Mis guerreras incansables, inconformistas y revolucionarias. Porque sé que os alegráis de mis progresos y porque aunque no nos hayamos visto demasiado últimamente, estáis ahí siempre que lo necesito.

A mi familia. A ti **papá,** que no pudiste ir al colegio, porque en aquella época era más importante llevar un trozo de pan a tu casa para poder comer que estudiar. A ti, que a pesar de que aprendiste a sumar con 4 piedras y un maestro garrotero mientras guardabas el ganado, fuiste tú quien me enseñó mejor que nadie a contar. Eres y serás para mí el mejor matemático y el mejor profesor del mundo. A mi **madre**, tú que fuiste mi primer amor y mi bastón. Mujer de los pies a la cabeza en la más amplia acepción de la palabra. Por muchas trabas que la vida te ha puesto, has resurgido y te has reinventado haciéndote más fuerte en cada obstáculo que has ido superando. Sólo le pido a la vida una cosa, y es que algún día pueda ser como tú. A vosotros dos, que habéis dedicado vuestra vida sólo a trabajar y que habéis pasado "muchas fatigas" para que vuestros hijos pudiesen tener lo que vosotros no pudisteis alcanzar, gracias infinitas. Jamás habrá tiempo ni espacio suficiente para devolveros todo lo que habéis hecho por mí. Perdonad mis errores y mi ausencia en los últimos años. No olvidéis nunca que sois el espejo donde me miro cada día y mi fuente de inspiración, os quiero más que a nada en este mundo.

A mi **hermano**, por cuidarme y protegerme sin pedir nada a cambio. Por repetirme hasta la saciedad lo orgulloso que se siente de mí. Por hacerme sentir única y especial. Hoy solo quiero que sepas que daría mi vida por ti si lo necesitases. A ti y a Maribel, gracias por darme el mayor tesoro que un hermano podría darme, mis sobrinos **Pablo y Álvaro**. A ellos, que son mis dos pequeños corazones y la motivación de cada día. A ellos, porque el amor que les tengo traspasa provincias. Porque son mi debilidad y el mejor antídoto para la tristeza y el aburrimiento.

A **Carlos**, mi compañero de vida. Por sufrir y sufrirme en este proceso. Por dejarlo todo para acompañarme a cumplir mis sueños. Por respetar todas y cada una de las decisiones que he tomado en el camino, sin trabas, sin reproches. Por sus: "Rubia tú puedes con eso y con más" que soplaban como bocanadas de aire fresco en días turbios. En definitiva, por esperarme paciente 10 años. Al fin ha llegado nuestro momento, ahora comienza una nueva vida juntos. Te quiero.

A los que ya no están, pero que confío puedan seguir viéndome allá donde quiera que se encuentren. Sé que os habría hecho realmente feliz ver a vuestra niña hoy.

A todos y cada uno de vosotros, GRACIAS. Un pedacito de esta tesis también es vuestra.

ÍNDICE

ÍNDICE

ABSTRACT/RESUMEN ... 1

1. INTRODUCCIÓN ... 7

1.1. Conceptos Generales ... 9

1.2. Importancia sanitaria de las enfermedades no transmisibles relacionadas con la nutrición ... 12

1.3. Importancia sanitaria de las enfermedades no transmisibles relacionadas con la nutrición: la situación en España ... 16

1.4.Patrones dietéticos y enfermeddes no transmisibles: a propósito de la enfermedad cardiovascular ... 17

1.5. Dieta Mediterránea: manejo de las enfermedades no transmisibles y adecuación de la ingesta nutricional ... 19

1.6. Situación alimentaria en España: ingesta alimentaria y déficits nutricionales ... 21

1.7. Factores asociados a la ingesta dietética ... 22

1.8. Envejecimiento y alimentación: la situación en España ... 24

2. JUSTIFICATION ... 27

3. HYPOTHESIS ... 31

4. OBJECTIVES/OBJETIVOS ... 35

5.METHODS ... 39

5.1. Study design, participants and data collection procedures ... 41

5.2. General dietary assessment ... 44

5.3. Mediterranean Diet assessment ... 44

5.4. Assessment of dietary quality ... 45

5.4.1. Nutritional inadequacies ... 45

5.4.2. Nutrient Density ... 46

5.4.3. Dietary Diversity ... 46

5.4.4. Assessment of non-dietary variables ... 47

5.4.5. Statistical analysis ... 48

6. RESULTADOS ... 51

6.1.Introducción de los resultados obtenidos ... 53

6.1.1. Diet quality and nutrient density in subjects with metabolic syndrome: Influence of socioeconomic status and lifestyle factors. A cross-sectional assessment in the PREDIMED-Plus study ... 55

6.1.2. Dietary intake in population with metabolic syndrome: Is the prevalence of inadequate intake influenced by geographical area? Cross-sectional analysis from PREDIMED-plus study 81

6.1.3. Dietary Diversity and Nutritional Adequacy among an Older Spanish Population with Metabolic Syndrome in the PREDIMED-Plus Study: A Cross-Sectional Analysis 115

6.1.4. Effect of changes in adherence to Mediterranean diet on nutrient density after one-year of follow-up: Results from the PREDIMED-Plus Study 147

7. DISCUSIÓN 173

7.1. Principales hallazgos 176

7.1.1. La adecuación de la ingesta nutricional y la influencia de los factores socioeconómicos, demográficos y de estilo de vida sobre la calidad dietética 176

7.1.2. Influencia del Área Geográfica en la ingesta alimentaria e inadecuación nutricional 178

7.1.3. Influencia de la diversidad dietética en la inadecuación nutricional y factores asociados a esta variable 179

7.1.4. Efecto de la intervención dirigida a incrementar la adherencia a la Dieta Mediterránea sobre la Densidad Nutricional 181

7.2. Limitaciones de la Tesis Doctoral 182

7.2.1. Extrapolación de los resultados obtenidos a la población general 182

7.2.2. Factores asociados a la ingesta dietética no incluidos en los análisis 182

7.2.3. Diseño del estudio 183

7.2.4. Fuentes de información utilizadas para estimar la ingesta alimentaria 183

7.2.5. Otros factores 184

7.3. Utilidad Práctica de los Resultados Obtenidos 184

7.4. Estrategias Futuras de Investigación 186

8. CONCLUSIONS/CONCLUSIONES 187

9. REFERENCIAS BIBLIOGRÁFICAS 191

ABSTRACT/RESUMEN

ABSTRACT

This Doctoral Thesis is devoted to the study of the nutritional intake in Spanish older adults with overweight/obesity and metabolic syndrome, both nutrition-related non-communicable diseases that have increased in the last few decades and that are the main causes of mortality and disability in older adults in Spain. Although some studies have analysed the dietary intake of the Spanish population, the study of the influence of socioeconomic, demographic and other variables related to dietary intake over the dietary quality have not been extensively studied in our country before.

Using the data obtained at the PREDIMED-Plus study, a large primary cardiovascular prevention trial conducted in Spanish healthy participants with overweight/obesity and Metabolic Syndrome, we aimed:

1. To assess the adequacy of basal dietary intake according to the European and International dietary reference intakes, as well as to investigate the influence of socioeconomic and lifestyle factors on nutrient inadequate intake and nutrient density.

2. To describe the food intake and nutrient profiles according to the geographical area of residence, and to analyse the influence of this variable over inadequate nutrient intake.

3. To estimate the relationship between dietary diversity and nutrient adequacy and identify which socioeconomic, demographic or lifestyles variables are associated with dietary diversity.

4. To assess the effect of improving Mediterranean Diet adherence on nutrient density after one year of follow-up at the PREDIMED-Plus trial.

To obtain the proper results, we used different statistical strategies (i.e. logistic regression, linear regression, etc.). After that, several facts can be concluded. Despite, the patients analysed are subjects with Metabolic Syndrome and overweight/obese, they exhibited suboptimal nutrient intake, particularly for dietary fiber, vitamins A, D, E and B_9, calcium and magnesium. Lower nutrient density and higher inadequate nutrient intake was related to sex (higher for men), poor lifestyles (lower physical activity and Mediterranean Diet adherence and smoking status). The dietary pattern of Spain slightly differ among geographical areas (inhabitants in the North area consumed lower amounts of vegetables and fish but more sugar and alcohol). Furthermore, even within the same country, geographical area was significantly associated with inadequate nutrient intake, the higher rates of inadequate nutrient intake was observed for people in the North area. On the other hand, lower levels of dietary diversity are related to men, smokers, lower levels of Mediterranean Diet adherence and not being married, being the influence of dietary diversity notorious over the inadequateness, since as dietary diversity increased, risk of inadequate nutrients intake decreased.

Finally, we have also noted that when Mediterranean Diet adherence increases the nutrient density also does. Thus, the PREDIMED-Plus dietary intervention is a feasible strategy to improve nutrient density in Spanish population at high risk of cardiovascular disease with overweight or obesity.

The knowledge generated by this Thesis may contribute to the application of different nutritional interventions aimed to reduce the nutritional deficiencies in vulnerable groups of population as older adults in order to prevent or mitigate the progression of non-communicable diseases. The nutritional approach could contribute to decrease the costs in health care derived from these diseases.

RESUMEN

El desarrollo de esta Tesis Doctoral se centra en el estudio de la ingesta nutricional en adultos españoles mayores con sobrepeso/obesidad y Síndrome Metabólico. Tanto el sobrepeso/obesidad como el Síndrome Metabólico se consideran enfermedades no transmisibles relacionadas directamente con la nutrición, cuya prevalencia se han incrementado en las últimas décadas constituyendo una de las principales causas de discapacidad y mortalidad de adultos mayores en España.

Aunque algunos estudios han analizado la ingesta dietética de la población española, el análisis de la influencia que los factores socioeconómicos, demográficos y otras variables relacionadas con la ingesta dietética ejerce sobre la calidad dietética no ha sido estudiado de forma detallada en nuestro país anteriormente.

A través de los datos obtenidos en el estudio PREDIMED-Plus, un ensayo clínico de prevención primaria de enfermedad cardiovascular realizado en España en adultos mayores sanos con sobrepeso/obesidad y Síndrome Metabólico, pretendemos:

1. Evaluar la adecuación basal de la ingesta dietética según las ingestas dietéticas de referencia Europeas e Internacionales, así como investigar la influencia que el nivel socioeconómico y los estilos de vida ejercen sobre la ingesta inadecuada de nutrientes y la densidad nutricional.

2. Describir la ingesta alimentaria y los perfiles nutricionales según el área geográfica de residencia, y analizar la influencia de esta variable sobre la ingesta inadecuada de nutrientes.

3. Analizar la asociación entre la diversidad dietética y la adecuación de nutrientes e identificar qué variables socioeconómicas, demográficas y de estilo de vida se relacionan con la diversidad dietética.

4. Evaluar el efecto que supone la mejora de la adherencia a la Dieta Mediterránea en la densidad nutricional de la dieta después un año de intervención en el estudio PREDIMED-Plus.

Para poder obtener los resultados adecuados, se utilizaron distintos análisis estadísticos (por ejemplo: regresión logística, regresión lineal, etc.), encontrándose que a pesar de que los individuos analizados son sujetos con Síndrome Metabólico y sobrepeso/obesidad, éstos exhibieron una ingesta de nutrientes por debajo de las recomendaciones, particularmente para la fibra dietética, vitaminas A, D, E, B_9, calcio y magnesio. Una menor densidad nutricional y una

mayor ingesta inadecuada de nutrientes se asociaron con el sexo (hombres), estilos de vida poco saludables (menor nivel de actividad física y adherencia a Dieta Mediterránea y ser fumador). Además, el patrón dietético en España difiere ligeramente entre áreas geográficas (los habitantes de la zona Norte, consumen menos pescado y verduras, pero más cantidad de azúcar y alcohol). Incluso dentro del mismo país, el área geográfica se asoció significativamente con una ingesta inadecuada de nutrientes, observándose también las tasas más altas de ingesta inadecuada en las personas del área Norte. Por otro lado, la diversidad dietética se asoció directamente con la ingesta inadecuada de nutrientes, así pues, cuando la diversidad dietética aumentaba, el riesgo de inadecuación nutricional disminuía; estando los niveles más bajos de diversidad dietética asociados con los hombres, los fumadores, aquellos sujetos con niveles más bajos de adherencia a la Dieta Mediterránea y aquellos individuos que no estaban casados.

Finalmente, la adherencia a la Dieta Mediterránea ejerce una impronta significativa en la densidad nutricional; así cuando la adherencia a este patrón dietético aumenta, la densidad de nutrientes también lo hace. Siendo por tanto la intervención dietética realizada en el estudio PREDIMED-Plus, una estrategia factible para mejorar la densidad de nutrientes en población adulta mayor española con alto riesgo de enfermedad cardiovascular y sobrepeso/obesidad.

El conocimiento generado por esta Tesis Doctoral puede contribuir a la aplicación de diferentes intervenciones nutricionales destinadas a reducir las deficiencias nutricionales en grupos vulnerables de la población, como lo son los adultos mayores, con objeto de prevenir o mitigar la progresión de enfermedades no transmisibles; ayudando a disminuir los costos asistenciales producidos por el auge de estas enfermedades.

1. INTRODUCCIÓN

1. INTRODUCCIÓN

1.1. Conceptos Generales

Esta Tesis Doctoral está enmarcada dentro del ensayo clínico multicéntrico PREDIMED-Plus. El presente trabajo tiene como objetivo principal estudiar la influencia que ejercen determinados factores demográficos y socioeconómicos sobre la ingesta alimentaria mediante el análisis epidemiológico de la dieta de pacientes adultos mayores con Síndrome Metabólico en España. Para comenzar pues, es necesario introducir y definir algunos conceptos relacionados con el tema de estudio que irán apareciendo a lo largo del manuscrito.

En primer lugar comenzaremos con las características que definen la inclusión de la población en el estudio y que vienen recogidas en el protocolo del ensayo clínico PREDIMED-Plus. Los participantes a incluir en el estudio debían ser sujetos adultos mayores (55-75 años hombres, 60-75 años mujeres) con sobrepeso u obesidad y Síndrome Metabólico.

Pese a que quizá pueda parecer obvio, es conveniente definir la condición de *sobrepeso y/o de obesidad*. Según la Organización Mundial de la Salud (OMS), el sobrepeso/obesidad se define como una acumulación anormal o excesiva de grasa que puede ser perjudicial para la salud. El índice de masa corporal es una herramienta sencilla y representa la forma más usual de medir esta condición en la población. Sin embargo, es importante señalar que los puntos de corte de índice de masa corporal para clasificar a los sujetos, son distintos en función de la población que se analice (Gillum & Sempos, 2005). De forma estándar se considera que un sujeto presenta sobrepeso cuando su índice de masa corporal es ≥25 kg/m^2, mientras que la obesidad se presenta cuando el individuo muestra un índice de masa corporal ≥30 kg/m^2 (De Onis & Habicht, 1996). En cualquier caso, en nuestro estudio se incluirán participantes con un índice de masa corporal comprendido entre 27-40 kg/m^2, ya que por un lado valores inferiores a 27 kg/m^2 en adultos mayores europeos raramente se han asociado a comorbilidades y puede llegar a confundirse en aquellos sujetos que presentan una complexión antropométrica atlética (Eveleth et al., 1998); y por otro lado porque un índice de masa corporal superior a 40 kg/m^2 categoriza al sujeto como obeso tipo mórbido, representando el valor mínimo para estrategias de pérdida de peso no restringidas exclusivamente al ámbito de la intervención nutricional (cirugía bariátrica) (Sauerland et al., 2005).

En cuanto al término, *Síndrome Metabólico,* la evidencia actual disponible tiende a definirlo como: “Un grupo de afecciones que aumentan el riesgo de padecer una enfermedad cardiovascular” (Alberti, Zimmet, & Shaw, 2005). Se denomina por tanto Síndrome Metabólico al conjunto de alteraciones metabólicas definido por al menos la presencia de tres de los siguientes indicadores: obesidad de distribución central, disminución de las concentraciones de lipoproteínas de alta densidad (cHDL) unido al incremento de las lipoproteínas de alta densidad (cLDL), elevación de las concentraciones de triglicéridos, aumento de la presión arterial e hiperglucemia (Alberti et al., 2009). Sin embargo, la *American Association of Clinical Endrocrinologists* excluyó la obesidad como componente del Síndrome Metabólico debido a que la consideró como un factor contribuyente de la resistencia insulínica, más que una consecuencia derivada de ésta (Grundy et al., 2005).

A pesar de ello, y teniendo en cuenta la evidencia actual que refrenda la obesidad como un factor de riesgo importante para la diabetes tipo 2 (Blüher, 2019), este componente ha sido incluido en la acepción de Síndrome Metabólico como criterio inclusivo para la población del Estudio PREDIMED-Plus.

Centrándonos ya en el ámbito nutricional, es ineludible definir el concepto de *patrón alimentario*. Éste no es más que el conjunto de alimentos que un individuo, grupo o población consume de manera ordinaria y frecuente. El patrón alimentario se halla influenciado por elementos de tipo socioeconómico y espacial, haciéndolo heterogéneo (Andreeva et al., 2016). Así pues, fenómenos como la globalización y el desarrollo económico han contribuido de manera importante en la modificación del patrón alimentario tradicional de la población (Oberlander, Disdier, & Etilé, 2017). Entendiendo estas generalidades, es factible definir el concepto de *Patrón Dietético Mediterráneo*. La Dieta Mediterránea fue descrita en profundidad en la década de 1960 por el estudioso Ancel Keys en su estudio de los 7 países (Keys et al., 1966). Como características fundamentales, podemos definir la Dieta Mediterránea como un patrón alimentario caracterizado por la frugalidad o moderación del consumo alimentario amén de una ingesta elevada de vegetales, frutas, legumbres, frutos secos, cereales integrales, pescado y aceite de oliva en detrimento del consumo de ácidos grasos saturados, cereales refinados, carnes rojas y productos procesados (Trichopoulou et al., 2014). El interés especial que despierta este patrón dietético se desprende de su relación positiva en la prevención de enfermedades crónicas tales como el cáncer, enfermedades neurodegenerativas y enfermedad cardiovascular. Efecto que se atribuye principalmente al valor nutricional de este patrón alimentario, contribuyendo al aporte adecuado de energía y nutrientes para la población (Naska & Trichopoulou, 2014).

De lo expuesto anteriormente, se desprende la idea de que en salud pública es mucho más importante el estudio los patrones dietéticos que de los alimentos en sí. Y es que, la alimentación en su conjunto, es la encargada de prevenir la enfermedad, aportando los nutrientes necesarios en las dosis adecuadas (Schulze, Hoffmann, Kroke, & Boeing, 2003). En este momento, es necesario describir qué se entiende por *ingestas recomendadas.* Las ingestas diarias recomendadas de energía y nutrientes fueron concebidas originalmente para prevenir las deficiencias nutricionales existentes durante la segunda mitad del siglo XX, época caracterizada por la desnutrición crónica global. Sin embargo el enfoque actual tiene una visión distinta, subrayando principalmente el uso de las ingestas recomendadas como forma de prevención de las enfermedades crónicas más prevalentes en sociedades desarrolladas, en las que la dieta juega un papel fundamental (Murphy & Poos, 2002).

De esta forma surge el concepto de *"Ingestas Dietéticas de Referencia" (Dietary Reference Intakes, DRIs)* propuestas por el *Institute of Medicine (IOM)* para población americana pero que son ampliamente utilizadas a nivel internacional, y que incluyen un rango de valores de referencia que se emplean para planificar y evaluar la ingesta de nutrientes en personas sanas (Health, 2018). Estos valores son evaluados periódicamente por un comité de expertos que revisan la evidencia disponible sobre los valores tanto de micronutrientes como de macronutrientes, incluyendo no sólo la tradicional perspectiva de déficit, sino también de ingesta excesiva de macronutrientes como eje fundamental en el desarrollo de enfermedades crónicas (Willet, 2013).

De forma esquemática los valores que propone la *Food and Nutrition Board del Institute of Medicine* son los siguientes:

-*Recommended daily average (RDA*): Nivel promedio de ingesta diaria de un nutriente suficiente para cumplir con los requisitos nutricionales poblacionales establecidos.

-*Adequate intake (AI)*: Valor de ingesta diaria de un nutriente que se establece cuando la evidencia es insuficiente para desarrollar el RDA, estableciéndose un nivel mínimo que garantice la adecuación nutricional.

-*Upper Limit (UL*): La cantidad máxima de un nutriente que puede ser consumido de forma segura durante un largo periodo de tiempo sin causar efectos adversos en la salud.

En Europa, estos valores dietéticos de referencia han sido postulados por la *European Food Safety Agency (EFSA*) variando ligeramente con los propuestos por la IOM. De forma notoria, la principal discrepancia entre ambos y que afecta al análisis de nuestros resultados, es que las recomendaciones americanas realizan una distinción entre los adultos mayores (categorizándolos en dos grupos: de 51-70 años y mayores de 70 años) mientras que las recomendaciones Europeas establecen como un todo a aquellos sujetos mayores de 18 años. Independientemente de la fuente de consulta, las ingestas recomendadas contemplan la variabilidad individual y han sido estimadas de forma específica para grupos homogéneos de edad, sexo y situación fisiológica del individuo.

Como se verá más adelante, esta Tesis Doctoral se centrará en analizar factores estrechamente ligados al déficit nutricional en adultos mayores con Síndrome Metabólico en España. Uno de los factores asociados a la adecuación nutricional es la *diversidad dietética*. La diversidad dietética puede resumirse en una mítica frase del ilustre Grande Covián a mediados del siglo pasado *"Coma de todo, pero poco".* Actualmente, entidades de renombre tales como la Sociedad Española de Nutrición Comunitaria (Aranceta Bartrina et al., 2016) siguen transmitiendo de forma inequívoca el mismo mensaje: *"Siga una dieta variada, moderada y equilibrada".* Sin duda alguna, estos mensajes nutricionales han calado de forma notoria y trascendente en la población aunque no siempre se utilizan en el sentido adecuado, sino que con frecuencia constituyen la excusa perfecta para incluir en la dieta alimentos no saludables.

El precepto en el que se basa la variedad dietética o diversidad dietética como un indicador indirecto de la calidad dietética, viene apoyado por el número de diferentes grupos de alimentos consumidos durante un periodo de tiempo determinado, haciendo esta variedad aumentar la probabilidad de cubrir los requerimientos nutricionales individuales (Murphy et al., 2006). Sin embargo, hasta el momento existe controversia sobre si una alta diversidad dietética se relaciona con la mejora de ciertas enfermedades crónicas o por el contrario supone un empeoramiento y agravamiento de la patología de base (Karimbeiki et al., 2018; Tian, Xu, Zhang, & Wang, 2017). No obstante, estos resultados están condicionados a un factor intrínsecamente ligado a la diversidad dietética, la ingesta calórica total consumida.

Es preciso incidir, que el término *diversidad dietética* empleado en esta Tesis doctoral albergará sólo los grupos alimentarios incluidos en las guías dietéticas de referencia para población española (Aranceta Bartrina et al., 2016) obviando los alimentos cuyo consumo no está recomendado; y que además el indicador de diversidad dietética empleado estará ajustada por la ingesta energética individual consumida por el sujeto.

Al igual que la diversidad dietética es un indicador de calidad dietética, la *densidad nutricional* es otro proxy dietético que permite la valoración cuantitativa alimentaria. La densidad nutricional puede definirse como el ratio de nutrientes presentes en una dieta en relación al contenido calórico de la misma (Nicklas, Drewnowski, & O'Neil, 2013). Así pues, dietas con una elevada densidad nutricional y escasa densidad energética han resultado ser efectivas en la prevención y tratamiento de las enfermedades crónicas, principalmente para la obesidad (Drewnowski, 2018).

Habiendo aclarado de forma escueta los principales conceptos que ocuparán el estudio de esta Tesis Doctoral, comenzamos con el análisis y estudio en profundidad de los mismos.

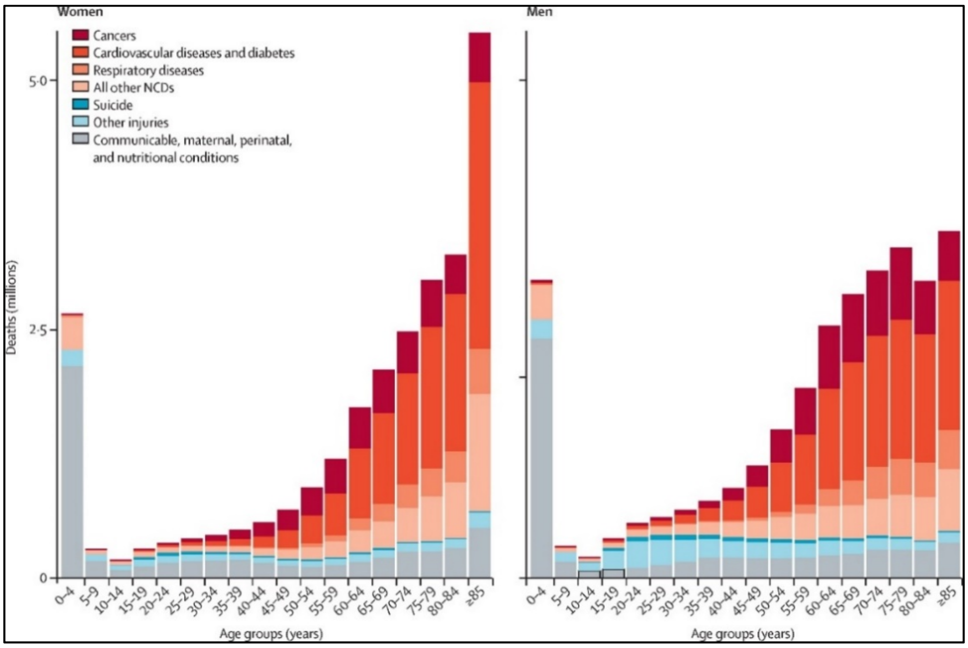
1.2. Importancia sanitaria de las enfermedades no transmisibles relacionadas con la nutrición

En las últimas décadas, la prevalencia de las enfermedades no transmisibles relacionadas con la nutrición como la obesidad, la diabetes mellitus tipo 2, el cáncer y las enfermedades cardiovasculares han aumentado a nivel global. Según el último informe sobre enfermedades no transmisibles emitido el 1 de Julio de 2018 por la OMS (Nishtar et al., 2018), se estima que más 41 millones de personas murieron durante la pasada anualidad como consecuencia de las enfermedades no transmisibles en todo el mundo, lo que equivale al 71% del total de la mortalidad registrada.

Las enfermedades no transmisibles afectan a grandes sectores de la población y son la principal causa de mortalidad prematura y discapacidad, lo que origina sociedades menos productivas a la par que se incrementan los costes asistenciales sanitarios, suponiendo una importante carga económica para el país que lo sustenta (Muka et al., 2015; Murray & Lopez, 2013).

Aunque como se ha comentado anteriormente, las enfermedades no transmisibles han sido responsables de una proporción sustancial de muertes en personas de todas las edades; es especialmente llamativa la carga de éstas en sectores de la población de edades más avanzadas. Este fenómeno puede apreciarse claramente en un estudio publicado recientemente por la revista *The Lancet* (Vos et al., 2016) *(Figura 1)* en el que se muestra la carga global de mortalidad por distintas causas de enfermedad estratificada por edad de la población.

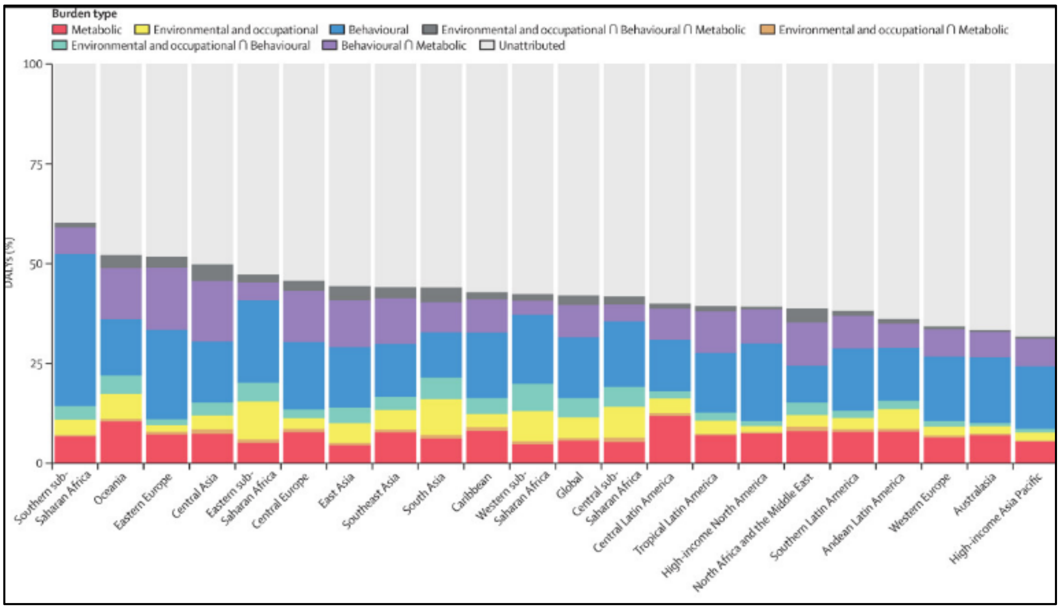
Figura 1. Número de muertes en 2016 por enfermedades no transmisibles, lesiones y enfermedades transmisibles, maternas, perinatales y nutricionales.



Fuente: (Vos et al., 2016)

Por otro lado, es importante destacar que las enfermedades no transmisibles están sufriendo una transición epidémica y una tendencia creciente a nivel mundial, convirtiéndose en un auténtico problema de salud pública. Tradicionalmente, éstas estaban principalmente restringidas a sociedades más desarrolladas y económicamente avanzadas. Sin embargo, con el cambio de siglo y la transformación económica y social que han experimentado los países en desarrollo, las cifras de afectos por estas patologías se han equiparado a las de poblaciones con mayores recursos (Beaglehole & Yach, 2003; Hu, 2011; Vos et al., 2016). Este advenimiento puede apreciarse de forma patente en la siguiente gráfica en la que se evalúan globalmente distintos grupos de riesgo sobre la carga mundial de la enfermedad y su evolución a lo largo del tiempo por países *(Figura 2)* (Forouzanfar et al., 2015). De esto puede obtenerse una conclusión manifiesta: “Los países en desarrollo deben hacer frente a una doble carga de enfermedad” (Hu, 2011); por un lado las enfermedades transmisibles circunscritas a un entorno sociodeprimido que se caracteriza por sistemas sanitarios pobres, y por otro lado a la creciente incidencia de enfermedades no transmisibles, ligadas al desarrollo de dichas sociedades.

Figura 2. Proporción global de años perdidos por discapacidad por todas las causas atribuibles a factores de riesgo conductuales, ambientales, ocupacionales y metabólicos y sus superposiciones por países para ambos sexos en 2015

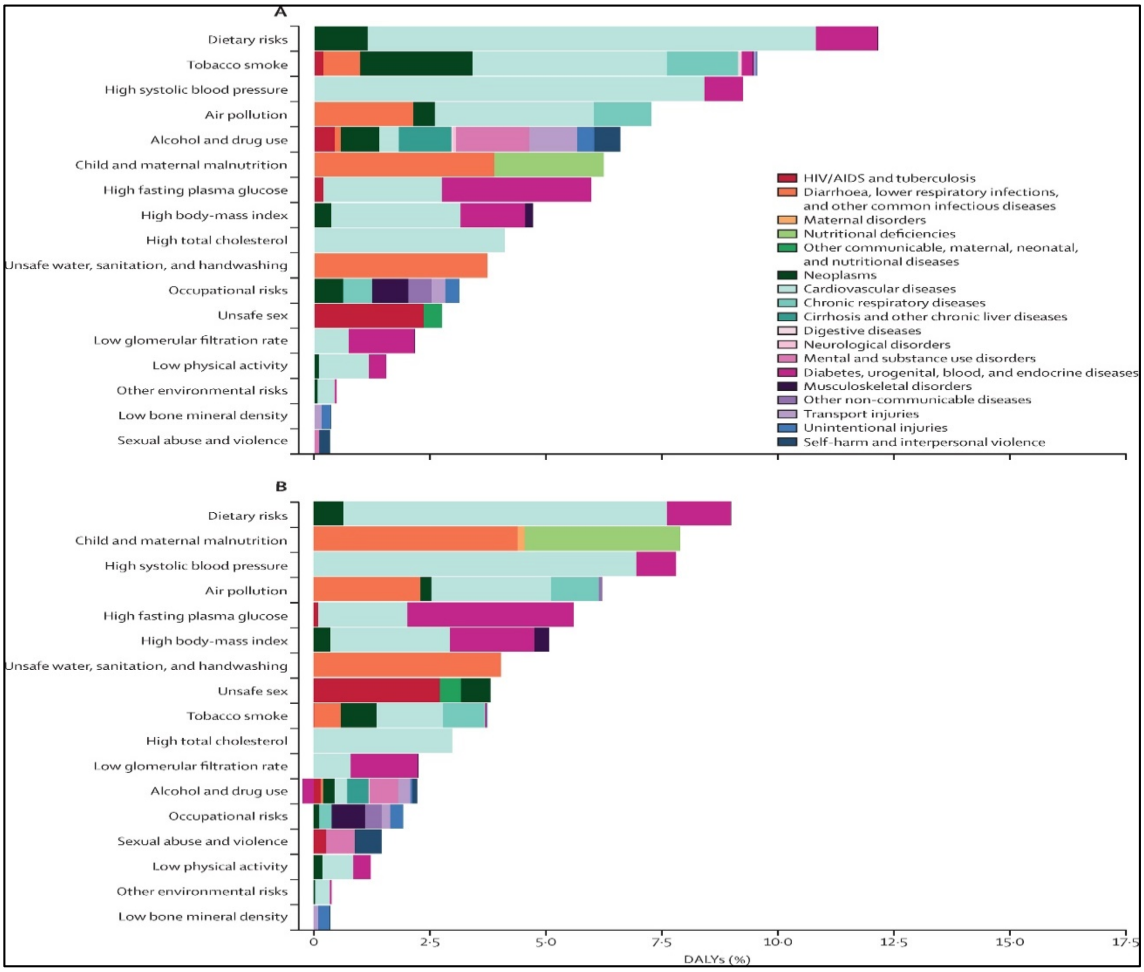


Fuente: (Forouzanfar et al., 2015).

El hecho de que las cifras de mortalidad o años de vida perdidos por discapacidad sean similares o incluso superiores en los países de bajos ingresos no es un dato que pueda ser obviado. Debemos recordar que entre los principales factores de riesgo para el desarrollo de una enfermedad no transmisible se encuentran aquellos determinantes de salud modificables propuestos por Marc Lalonde (Lalonde, 1974). Entre ellos, el estilo de vida y más concretamente la alimentación y la actividad física, destacan sobre los demás ejerciendo una impronta fundamental en la prevención y control de dichas enfermedades (Beaglehole et al., 2008).

Se estima que en 2015, el principal factor de riesgo para el desarrollo de una enfermedad no transmisible en ambos sexos fue una alimentación no saludable. Este factor de riesgo representó el 12.2% (I.C. 95%, 10.8-13.6) del total de años perdidos de vida para hombres y el 9.0% (I.C. 95%, 7.8-10.3) para mujeres a nivel mundial (*Figura 3*) (Forouzanfar et al., 2015). Teniendo en cuenta estos datos, la modificación de este factor de riesgo supondría principalmente la prevención de tres grandes grupos de enfermedades no transmisibles: cáncer, diabetes y enfermedad cardiovascular (Kimokoti & Millen, 2016; Passi, 2017).

Figura 3. Años de Vida Perdidos por Discapacidad globales atribuibles a los factores de riesgo de modificables (A) hombres y (B) mujeres en 2015



Fuente: (Forouzanfar et al., 2015)

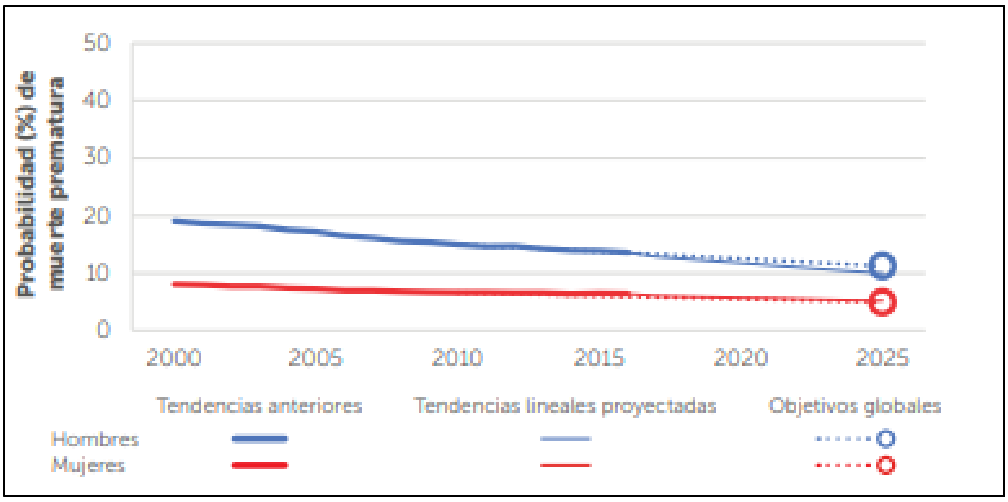
Este cambio epidemiológico en salud está particularmente ligado a la adquisición de hábitos alimentarios propios de las sociedades occidentalizadas. La modernización de las sociedades y el auge del desarrollo económico parecen ir ligados a un patrón dietético no saludable, caracterizado por el consumo de azúcares, grasas saturadas y alimentos refinados y procesados (Malik, Willett, & Hu, 2013). Sin embargo este fenómeno no sólo se circunscribe a sociedades en desarrollo, sino que ésta transición alimentaria también ha afectado a la población adulta mayor europea (Kehoe, Walton, & Flynn, 2019), y en concreto a la población española, que será tratada con más detalle a continuación.

Paradójicamente y a pesar de los esfuerzos comunitarios que estriban en el impulso de líneas estratégicas enfocadas en la promoción de estilos de vida saludables, se espera que la carga mundial de las enfermedades no transmisibles aumente aún más durante las próximas décadas (Lozano et al., 2018). Este fenómeno será el resultado del aumento de la población mundial y los cambios demográficos, derivados fundamentalmente del envejecimiento poblacional, de la urbanización, y de la escasa regulación comunitaria en materia de seguridad alimentaria. Así pues, las últimas tendencias globales, proyectan que la población de más de 60 años será el colectivo poblacional más afectado por las enfermedades no transmisibles, duplicándose estas cifras para el año 2030 si los patrones conductuales de estilos de vida actuales no son revertidos (Fullman et al., 2017).

1.3. Importancia sanitaria de las enfermedades no transmisibles relacionadas con la nutrición: la situación en España

En los últimos años está teniendo lugar en nuestro país un incremento sin precedentes a lo que se refiere a enfermedades no transmisibles. Según los datos de la OMS en el año 2018, las enfermedades no transmisibles ocasionaron el 91% de todas las muertes, siendo el 28% atribuible a las enfermedades cardiovasculares, seguido del cáncer (26%) y otras enfermedades no transmisibles (24%) (WHO, 2018b). Sin embargo, si tenemos en cuenta las tendencias pasadas y las proyecciones futuras inmediatas sobre la probabilidad de muerte prematura debido a las enfermedades no transmisibles *(figura 4)*, se puede apreciar que en ambos sexos se experimentará una ligera disminución para el año 2025. A pesar de ello, este dato positivo no es suficiente teniendo en cuenta la carga asistencial económica y la pérdida de productividad que generan estas enfermedades (Bloom, Cafiero, & Jané-Llopis, 2011).

Figura 4. Riesgo de mortalidad prematura (%) debido a enfermedades no transmisibles en España



Fuente: (WHO, 2018b)

Quizá la tendencia descrita pueda explicarse por las peculiaridades sanitarias tan notorias que presenta España en comparación con otros países de la Unión Europea con características económicas similares. Principalmente, puede destacarse la cobertura universal gratuita del Sistema Nacional de Salud que facilita la prevención secundaria y terciaria de la enfermedad, y la implementación de algunas acciones preventivas a nivel primario (Toth, 2010). Estas diferencias podrían ser las responsables en cierta forma de la reducción de la mortalidad prematura, sin embargo esta condición no sustenta una alternativa a la reducción de las enfermedades no transmisibles, sino que supone una sobrecarga asistencial y un incremento económico de la sanidad en España (Muka et al., 2015).

A este hecho además se une el progresivo envejecimiento de la población española, la idiosincrasia económica propia de las comunidades autonómicas españolas, que tienen un gasto sanitario dispar y las políticas de salud heterogéneas que obstaculizan la puesta en marcha en común de programas para la prevención de las enfermedades no transmisibles basados en la modificación de factores de riesgos inherentes a la aparición de las mismas (Martínez Cía et al., 2018). Es lógico pensar por tanto, que una apuesta conjunta, pública y centrada en la puesta en marcha de programas preventivos nacionales podría repercutir de forma directa, homogénea y positiva en la población española.

1.4. Patrones dietéticos y enfermedades no transmisibles: a propósito de la enfermedad cardiovascular

Entre los principales motivos del incremento de las enfermedades no transmisibles que afectan tanto a países desarrollados como a países en desarrollo, pueden encontrarse el empeoramiento de los estilos de vida y la alimentación (Afshin et al., 2019).

Si bien los estándares de vida han mejorado, nótese la disponibilidad y diversificación alimentaria, el acceso a los servicios sanitarios y la mejora del nivel educativo poblacional; esta globalización también circunscribe consecuencias negativas en términos de patrones de alimentación no saludables, disminución de la actividad física y empeoramiento de los estilos de vida (mayor consumo de tabaco y alcohol) (Vineis, 2017), derivados de la industrialización, la urbanización, el desarrollo económico y la globalización de los mercados.

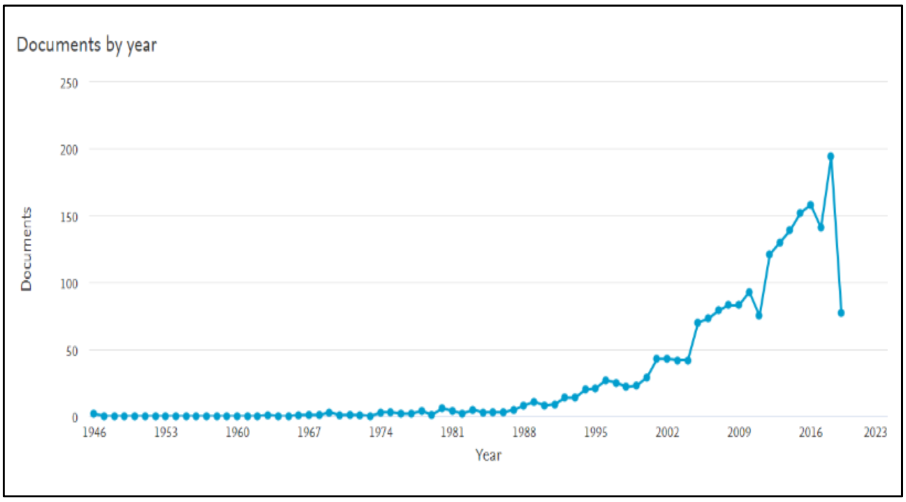
Sin embargo, lo esperanzador de esta cuestión es que los factores de riesgo mencionados anteriormente y que son causas contribuyentes en el desarrollo y progresión de las enfermedades no transmisibles, son modificables (Guilbert, 2003).

Concerniente a la alimentación, los cambios en los patrones dietéticos han ocasionado un incremento significativo de las enfermedades no transmisibles, destacando principalmente la obesidad, la diabetes mellitus, el Síndrome Metabólico, la enfermedad cardiovascular y algunos tipos de cáncer. El informe de consenso de la OMS del año 2003, *Dieta, Nutrición y Prevención de Enfermedades Crónicas* (WHO, 2003), ratifica la asociación entre nutrición y enfermedades no transmisibles, pudiendo ser ésta protectora o de riesgo en función del patrón dietético que el sujeto presente.

Refiriéndonos propiamente la ingesta alimentaria, la propia acepción de patrón dietético hace referencia a la dieta del individuo en su conjunto, empleándose un enfoque dietético holístico donde se examina el efecto de la alimentación global sobre las enfermedades no transmisibles. Conceptualmente, este enfoque representa una visión más amplia de los alimentos y nutrientes de consumo y por tanto puede ser más predictivo sobre el riesgo de sufrir una determinada enfermedad (Hu, 2002).

Debido al creciente interés de la nutrición como herramienta terapéutica de las enfermedades no transmisibles, diversos estudios epidemiológicos han analizado la asociación entre patrones dietéticos (con un acercamiento temático enfocado a la adherencia a dichos patrones) sobre la prevención, desarrollo y progresión de las enfermedades no transmisibles. Se puede constatar esta propensión simplemente introduciendo en la base de datos Scopus la ecuación de búsqueda *(dietary patterns)* AND *(chronic disease* OR non communicable disease*),* donde se observa cómo desde el año 1946 hasta la actualidad el número de trabajos publicados ha ido aumentando de forma sustancial (*figura 5*).

Figura 5. Documentos publicados sobre patrones dietéticos y ENT desde 1946 hasta 2019



Fuente: (Base de datos SCOPUS, 2019)

Las técnicas epidemiológicas nutricionales más utilizadas hasta el momento permiten evaluar la dieta mediante la composición de índices de calidad de dos formas distintas: En primer lugar mediante índices predefinidos o conocidos como *"índices a priori",* estos índices se basan en el cálculo de una puntuación de calidad general dietética basada en el cumplimiento de las guías dietéticas y las hipótesis plausibles actuales. Por otro lado, la construcción de *"índices a posteriori"* analiza la ingesta dietética en relación a la cantidad alimentaria consumida por el individuo, considerando la variabilidad total de la ingesta alimentaria, utilizando para ello técnicas basadas en el análisis de componentes principales, análisis factorial y análisis de conglomerados (Willet, 2013).

Independientemente de la técnica empleada, los grandes estudios epidemiológicos realizados tanto a nivel nacional como internacional han identificado diversos patrones dietéticos en la población, siendo mayoritarios los siguientes: patrón dietético "occidentalizado" o *westernized dietary pattern* y el patrón dietético "prudente" o *prudent dietary pattern,* para ser fieles a la concepción en la que son descritos (Tucker, 2010); y el patrón dietético "mediterráneo" o *mediterranean dietary pattern* característico de la cuenca mediterránea aunque extensible a otros países (Martínez-González, Hershey, Zazpe, & Trichopoulou, 2017) y que será tratado con más detalle con posterioridad.

El patrón dietético "prudente" se caracteriza por un elevado consumo de frutas, verduras, legumbres pescado, pollo y cereales integrales, mientras que el patrón dietético "occidentalizado" lo hace por una mayor ingesta de carnes rojas y procesadas, dulces, patatas fritas y cereales refinados. Ambos patrones dietéticos han sido ampliamente estudiados en grandes cohortes poblacionales americanas, entre ellos en el estudio *Nurses´s Health Study* y el *Health Professional´s Follow-up Study*, encontrándose una asociación protectora frente a enfermedad cardiovascular en aquellos sujetos situados en el quintil más alto de adherencia al patrón "prudente" (RR=0.70, I.C.95% 0.56-0-86). Mientras que por el contrario, se estableció una mayor asociación de riesgo en aquellos sujetos con una alta adherencia al patrón "occidentalizado" (Hu, 2002).

Lo realmente interesante es que la inmensa mayoría de la evidencia científica sobre adherencia a patrones dietéticos en relación con el desarrollo de las enfermedades no transmisibles, se centra en la enfermedad cardiovascular. Este hecho no puede ser atribuido al simple azar ya que es notorio el peso que la enfermedad cardiovascular ejerce tanto en poblaciones desarrolladas como en vías de desarrollo, siendo ésta la principal causa de muerte y discapacidad a nivel mundial (Benjamin et al., 2017). Es lógico por tanto pensar, que los esfuerzos se centren en prevenirla.

1.5. Dieta Mediterránea: manejo de las enfermedades no transmisibles y adecuación de la ingesta nutricional

La Dieta Mediterránea es uno de los patrones dietéticos que junto al patrón "prudente" mencionado anteriormente, ha ocupado el centro de atención de la investigación epidemiológica nutricional en las últimas décadas.

El patrón de Dieta Mediterránea tradicional fue definido en la década de los años 60 por el pionero Ancel Keys en el estudio de los 7 países, donde se compararon los hábitos alimentarios de diferentes países (Estados Unidos, Japón, Finlandia, Países Bajos, antigua Yugoslavia, Grecia e Italia) en relación al riesgo de desarrollar una enfermedad cardiovascular. Los resultados fueron notables, destacándose principalmente la menor tasa de mortalidad por cardiopatía coronaria en aquellos países situados en la cuenca mediterránea (Keys et al., 1966). Inicialmente, estos hallazgos se explicaron bajo el prisma de la ingesta aislada de nutrientes, en concreto de la reducción del consumo de ácidos grasos saturados; sin tener en cuenta el patrón dietético general que caracterizaba a esas poblaciones.

La acepción actual de Dieta Mediterránea ha variado ligeramente, estando este patrón determinado principalmente por la frugalidad o moderación en la ingesta alimentaria y el consumo de aceite de oliva como principal fuente de grasa dietética, junto a una alta ingesta de alimentos vegetales, frutas, cereales integrales, legumbres y frutos secos en detrimento del consumo de bebidas azucaradas, productos procesados y alimentos de origen animal, principalmente carnes rojas (Trichopoulou et al., 2014).

Estos componentes del patrón Dietético Mediterráneo podrían explicar los mecanismos potenciales que sustentan los beneficios de la Dieta Mediterránea en la reducción del riesgo de las enfermedades no transmisibles. Principalmente cabe destacar entre otros muchos nutrientes, el contenido en fibra dietética, el perfil lipídico rico en ácidos grasos monoinsaturados y polinsaturados y otros componentes como los polifenoles, que poseen propiedades antioxidantes y antinflamatorias. Esta mixtura dietética podría ser la "culpable" de modular diversos factores de riesgo ampliamente conocidos en el desarrollo y progresión de las enfermedades no transmisibles, específicamente de la enfermedad cardiovascular.

Los hallazgos científicos publicados hasta el momento han puesto de manifiesto los beneficios que posee la Dieta Mediterránea como herramienta efectiva en la prevención y remisión de la progresión de las enfermedades no transmisibles (Martínez-González et al., 2015). Y es que, aunque ha quedado patente el papel de este patrón sobre las enfermedades neurodegenerativas, enfermedades mentales como la depresión y ciertos tipos de cáncer (Carlos et al., 2018), la principal enfermedad no transmisible estudiada en relación al patrón Dietético Mediterráneo ha sido la enfermedad cardiovascular.

El papel que ejerce este patrón en los factores de riesgo de enfermedad cardiovascular ha sido ampliamente evidenciado, sugiriendo que la Dieta Mediterránea no solo se asocia de manera inversa con el riesgo de padecer una enfermedad cardiovascular (Estruch et al., 2013), sino que también tiene efectos beneficiosos sobre los factores de riesgo que actúan en el desarrollo de la misma: diabetes tipo 2, Síndrome Metabólico, hipertensión arterial, triglicéridos, cLDL y peso corporal (Salas-Salvadó, Becerra-Tomás, García-Gavilán, Bulló, & Barrubés, 2018).

Al efecto que la Dieta Mediterránea tiene en relación a los resultados positivos en salud hay que adicionarle la adecuación de la ingesta nutricional. Algunos estudios observacionales han mostrado una correlación positiva entre la adherencia a este patrón dietético y la menor prevalencia de ingesta deficitaria de vitaminas y minerales. Este hecho puede estar refrendado en la inclusión de una amplia variedad alimentaria, permitiendo por un lado cumplir con las recomendaciones nutricionales, y por otro lado lograr prevenir el desarrollo y aminorar la progresión de las enfermedades no transmisibles.

Respecto a este último punto, precisamente la ingesta deficitaria de algunos nutrientes, por ejemplo; un consumo inadecuado de vitaminas con un rol antioxidante (A, C y E) o polifenoles dietéticos se han asociado a un mayor riesgo de enfermedades neurodegenerativas (Samieri, 2018), Síndrome Metabólico (Goncalves & Amiot, 2017), enfermedad cardiovascular (Jenkins et al., 2018; Mendonça et al., 2019) y diabetes tipo 2 (Guasch-Ferré, Merino, Sun, Fitó, & Salas-Salvadó, 2017; Medina-Remón et al., 2016; Salas-Salvadó et al., 2016). Por otro lado, la ingesta adecuada de minerales como el magnesio, potasio y calcio se ha asociado a reducciones en la presión arterial, marcadores inflamatorios y oxidativos y mejoras en la sensibilidad insulínica (Salas-Salvadó et al., 2018). Y es que, el patrón Dietético Mediterráneo, incluye alimentos con una elevada densidad nutricional y un bajo aporte calórico, contribuyendo a una dieta caracterizada por una considerable cantidad de los nutrientes antes mencionados. Este hecho sustenta el precepto de que el patrón Dietético Mediterráneo es una herramienta útil en la prevención o mitigación de la progresión de las enfermedades no transmisibles, siendo parcialmente atribuible a que esta dieta aporta la cantidad adecuada de nutrientes (Peng, Berry, & Goldsmith, 2019).

En base a estos preceptos, se concibe el pionero estudio PREDIMED (*Prevención con Dieta Mediterránea)*, hasta el momento el mayor estudio clínico-nutricional llevado a cabo en nuestro país. Este estudio epidemiológico se caracterizó por el reclutamiento de más de 7000 participantes con alto riesgo de sufrir una enfermedad cardiovascular siendo aleatorizados en tres grupos de intervención: dos grupos que recibieron consejos de Dieta Mediterránea y fueron suplementados bien con aceite de oliva virgen extra, o bien con una mezcla de frutos secos, y un tercer grupo que siguió recomendaciones sobre una alimentación baja en grasa (Martinez-Gonzalez, Corella, et al., 2012).

Los resultados obtenidos mostraron que seguir un patrón de alimentación mediterráneo era efectivo para la prevención no sólo de las enfermedades cardiovasculares (Martínez-González et al., 2015), sino de otras enfermedades no transmisibles como el cáncer de mama (Toledo et al., 2015) y el Síndrome Metabólico (Salas-Salvadó et al., 2008). A partir de los resultados de PREDIMED nace el estudio PREDIMED-Plus, que pretende demostrar que la pérdida de peso mediante una intervención intensiva sobre el estilo de vida con Dieta Mediterránea hipocalórica, promoción del ejercicio físico y terapia conductual es eficaz a largo plazo para la prevención primaria de la enfermedad cardiovascular, amén de ser superior a la observada en PREDIMED (Martínez-González et al., 2018).

1.6. Situación alimentaria en España: ingesta alimentaria y déficits nutricionales

España es un país del sur de Europa, enclavado en la cuenca mediterránea, que posee una gran cultura gastronómica basada en alimentos propios del patrón Dietético Mediterráneo, siendo por tanto alimentos de elevada calidad nutricional. Paradójicamente y aunque algunos estudios sugieren que la adherencia a Dieta Mediterránea es mayor en España que otros países mediterráneos (Benhammou et al., 2016), la evolución actual de los patrones de consumo alimentario españoles reflejan el abandono progresivo de esta dieta (León-Muñoz et al., 2012); siendo reemplazada por patrones dietéticos occidentalizados.

Así pues, se viene observando desde hace décadas cómo el consumo de alimentos de elevada densidad energética pero de escaso valor nutricional, han asaltado los hogares españoles (Moreno, Sarría, & Popkin, 2002). Este fenómeno explicaría que al mismo tiempo que aumentan de forma constante las cifras de obesidad, Síndrome Metabólico, diabetes y enfermedad cardiovascular lo hagan también los déficits específicos de determinados micronutrientes (Agarwal, Reider, Brooks, & Fulgoni, 2015). Así, algunos estudios observacionales han descrito que la población española con sobrepeso y obesidad no alcanza las cantidades recomendadas de magnesio, calcio y vitaminas A, C, D, y E (Aranceta et al., 2001).

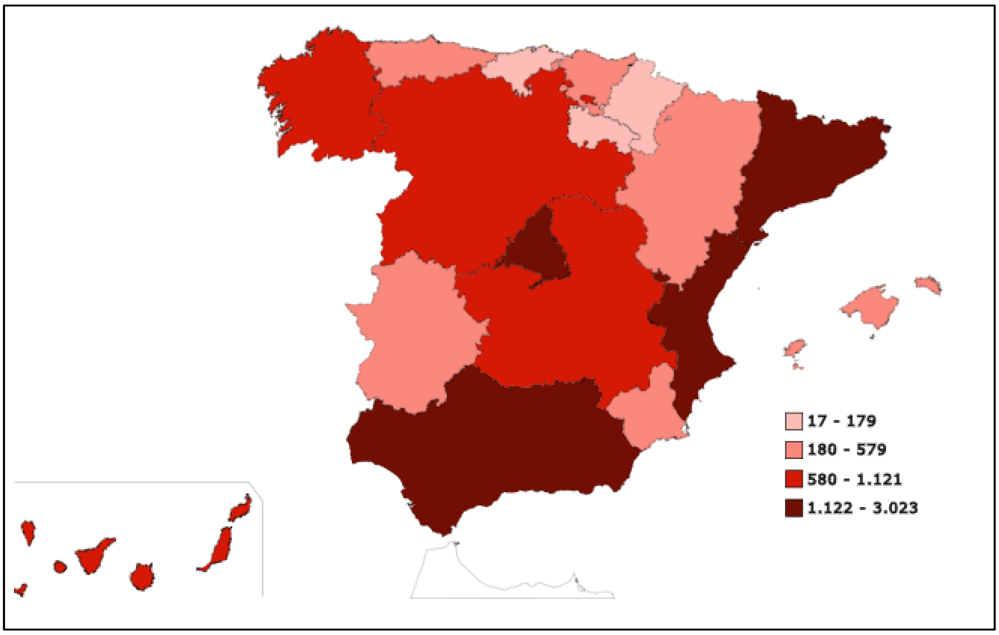
El estudio ANIBES sobre hábitos alimentarios de la población española (Ruiz et al., 2016) destaca en sus conclusiones la estabilidad del consumo medio de alimentos de la población española, matizando sin embargo, que el consumo de cereales integrales, verduras y legumbres se encuentran por debajo de las recomendaciones, en contraposición a lo encontrado para la ingesta de productos alimentarios como grasas animales, dulces y embutidos que se sitúan por encima de los niveles de consumo aconsejados. Estos mismos resultados, han sido corroborados por la *Encuesta Nacional de Ingesta Dietética Española* (ENIDE) en su última publicación del año 2017 (AESAN, 2017).

A pesar de que los datos globales de los paneles de consumo alimentario proporcionados por el *Ministerio de Agricultura, Pesca y Alimentación* (MAPAMA) señalan diferencias en el consumo absoluto de macronutrientes entre regiones españolas (MAPAMA, 2018), actualmente no se dispone de información que permita analizar en detalle las fortalezas y debilidades de la dieta actual de la población española permitiendo comparar además la calidad de la dieta entre diferentes regiones.

Y es que, algunos estudios llevados a cabo en nuestro país han sugerido que el nivel de adherencia a Dieta Mediterránea varía significativamente entre regiones (Alemán et al., 2016). Este dato resulta cuanto menos llamativo, ya que el enfoque tradicional de los estudios realizados hasta el momento se ha basado en analizar las diferencias en la ingesta dietética entre países. Independientemente de la importancia de este hecho, se ha obviado la posibilidad de que la calidad dietética varíe incluso dentro del mismo país ya que cada territorio posee unos determinados factores culturales y socioeconómicos inherentes que pueden afectar a las elecciones alimentarias y por ende a la calidad de la dieta.

Por tanto a nivel general, la mayor o menor calidad de la dieta podría explicar parcialmente, entre otras, las importantes diferencias existentes en las tasas de mortalidad por enfermedad cardiovascular, concretamente de infarto agudo de miocardio en España. En relación a la afectación de salud por este fenómeno, puede afirmarse que existe un menor gradiente norte-sur, según reflejan los datos absolutos del INE en el año 2018 (*figura 6*).

Figura 6. Defunciones por infarto agudo de miocardio en ambos sexos en población adulta española en el año 2018 por comunidades autónomas



Fuente: (INE, 2018)

1.7. Factores asociados a la ingesta dietética

Las características de la población que obran a favor o en contra de la adherencia a un determinado patrón dietético, pueden considerarse factores asociados a la ingesta dietética. Estos factores son especialmente útiles para la identificación de grupos poblacionales de alto riesgo de ingestas dietéticas inadecuadas. Su identificación permite centrar los esfuerzos intervencionales con la finalidad de mejorar su patrón dietético y estilo de vida para reducir la prevalencia de enfermedades no transmisibles relacionadas derivadas de una alimentación no saludable.

Algunos estudios epidemiológicos realizados han identificado factores asociados a los patrones dietéticos. Entre esos factores destacan los factores sociodemográficos, económicos, de estilo de vida y condición morbosa (Doyle, Borrmann, Grosser, Razum, & Spallek, 2017; Mayén et al., 2016; Zazpe et al., 2010). Sin embargo, cabe destacar que estos factores han sido estudiados como predictores de adherencia a corto o largo plazo tras la realización de una intervención dietética a la que han sido sometidos los individuos. Otro aspecto importante a considerar es la escasez de trabajos que abordan el efecto la temática sobre inadecuación nutricional en pacientes con sobrepeso/obesidad. De esta forma, la evidencia actual se centra en el estudio del exceso energético dietético consumido por esta población, más que en la ingesta deficitaria ocasionada precisamente por el contenido energético excesivo.

Por estas razones, todos los descritos a continuación, son factores asociados únicamente a la adherencia a un patrón dietético, obviando su relación con otras características que definen la calidad dietética tales como la diversidad dietética y la adecuación nutricional en base a los requerimientos nutricionales determinados para la población.

En primer lugar, la edad. La edad ha sido postulada como un determinante esencial en relación a la adherencia a un patrón dietético saludable. Según se ha descrito, los cambios dietéticos y el mantenimiento de los mismos son más favorables en poblaciones de mediana edad (45-60 años) (Hiza, Casavale, Guenther, & Davis, 2013) presentando los estratos de edades más extremas (población joven y anciana) un riesgo más elevado de adherencia a patrones menos saludables o de mayor resistencia al cambio dietético, originando dietas poco saludables y monótonas. En ambos casos, puede achacarse a la falta de conocimiento sobre el binomio alimentación-salud y/o a la falta de habilidades culinarias. En los ancianos se uniría además la pérdida de funcionalidad que podría limitar no sólo la fase temprana de la alimentación (adquisición y preparación de los alimentos) (Atkins et al., 2015; Schröder et al., 2004), sino también los problemas dentales propios de este colectivo, que limitarían las alternativas alimentarias (Westenhoefer, 2005).

El sexo es otro factor que tampoco puede ser obviado. En líneas generales, los estudios descriptivos han otorgado una notable asociación positiva entre ser mujer y la adherencia a un patrón dietético saludable (Conklin, Forouhi, Surtees, Wareham, & Monsivais, 2015). Este singular aspecto podría ser explicado por el rol tradicional que la mujer ha ocupado dentro del hogar, permitiéndole el aprendizaje de habilidades culinarias. Amén de que en este colectivo se ha observado que la preocupación por el estado de salud y la estética son mayores, haciendo por tanto que este sector poblacional esté más concienciado en la elección de alimentos más saludables y posea mayores habilidades culinarias, siendo más fácil llevar una dieta saludable (Kiefer, Rathmanner, & Kunze, 2005; Ramos, Brooks, García-Moya, Rivera, & Moreno, 2013).

Otros factores relacionados con el estilo de vida, como la práctica de actividad física, y la baja ingesta de alcohol y tabaco también se han asociado de forma positiva con la adherencia a patrones dietéticos saludables (Alkerwi et al., 2017; de Freitas et al., 2017). Aunque los individuos pudiesen llevar técnicas compensatorias para contrarrestar los efectos perniciosos del sedentarismo o consumo de alcohol y drogas con una buena alimentación (Gabhainn, Nolan, Kelleher, & Friel, 2002); es más sensato intuir en líneas generales, que individuos que se preocupan por mantener un estilo de vida saludable lo hagan de igual forma con su alimentación.

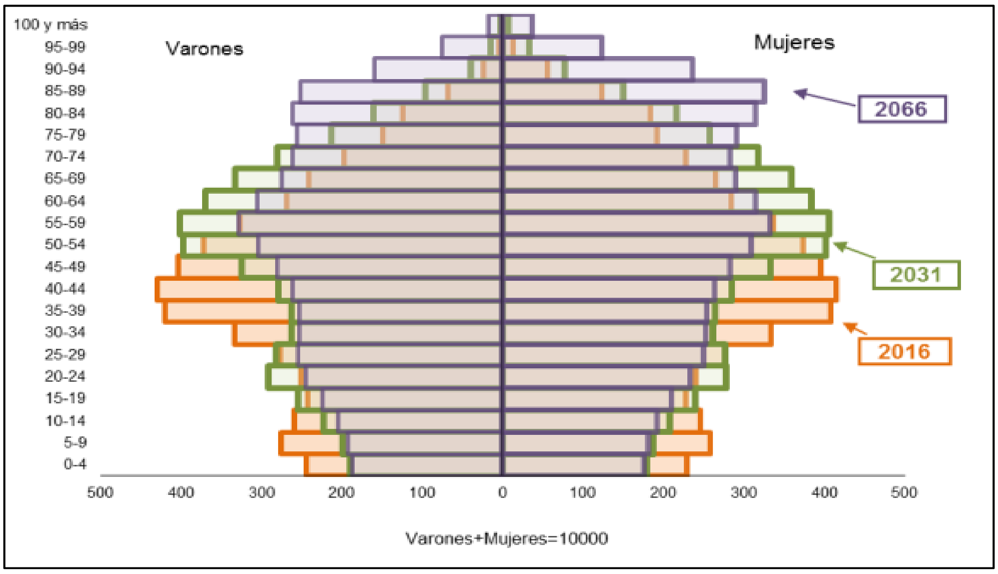
Otras condiciones referentes al individuo como el estatus socioeconómico o el nivel cultural también han sido descritas, constituyendo ambas una relación inexorable entre adherencia dietética y estatus social (Fekete & Weyers, 2016). Ambos factores van unidos entre sí en la mayoría de las ocasiones, permitiendo por un lado un mayor nivel económico la accesibilidad a alimentos de mayor coste (Fukuda et al., 2017) y por otro lado, el nivel cultural habilitando la alfabetización nutricional (Schoufour et al., 2018). Entendiéndose por alfabetización, el proceso de educación nutricional, que afecta principalmente a aquellos individuos con mayores niveles educativos y por ende serán éstos quienes sean más proclives a la adopción de hábitos dietéticos saludables.

Finalmente debemos tener en cuenta las variables relacionadas con la oferta de alimentos, en particular con la disponibilidad, accesibilidad y en ocasiones, estrategias de promoción que condicionan la elección de alimentos. Si nos referimos a los nutrientes, se deben contemplar también las diferentes estrategias para preparar y combinar los alimentos. En este sentido las tradiciones culinarias y/o gastronómicas de cada región pueden influir notablemente sobre la calidad de la dieta, en particular en un país tan rico y variado como España en cuanto a su oferta gastronómica.

1.8. Envejecimiento y alimentación: la situación en España

Aunque los datos demográficos mundiales señalan un descenso de la natalidad acompañado de un incremento del envejecimiento poblacional, los datos en España, con un índice sintético de fecundidad de 1.3, son aún más pronunciados que en otros países. Según los datos de la prospección demográfica mundial proporcionado por el observatorio de esperanza de vida de la OMS (WHO, 2018a), en el año 2040, España será el país de la Unión Europea con mayor esperanza de vida (85.8 años para las mujeres) y el cuarto de todo el mundo, siendo únicamente superado por Japón, Suiza y Singapur. Las prospecciones realizadas por el INE en el año 2016 muestran el envejecimiento progresivo que sufrirá la población española (*figura 7*). No sólo por el descenso de la natalidad, sino también por un aumento de la longevidad. Entre las principales razones de este último fenómeno, puede destacarse el papel que ha ejercido la tradicional Dieta Mediterránea en nuestro país (Bamia et al., 2007).

Figura 7. Prospecciones demográficas de la población española para ambos sexos



Fuente: (INE, 2016)

Aunque como comentábamos anteriormente, el patrón alimentario tradicional basado en la Dieta Mediterránea está experimentando una involución a nivel general; la población adulta mayor española sigue conservando en parte las costumbres culinarias tradicionales derivadas de la cultura gastronómica de nuestro país, en contraposición de lo experimentado por otros sectores de la población (Ruiz et al., 2016).

A pesar de ello, y aun conservando la herencia cultural de la Dieta Mediterránea, los adultos mayores son altamente susceptibles a inadecuaciones dietéticas (Visser et al., 2017), siendo por tanto un colectivo de alto riesgo si tenemos en cuenta el papel protector que la dieta ejerce sobre el control de las enfermedades no transmisibles.

Fundamentalmente la relación negativa entre envejecimiento y alimentación, estriba por un lado en los cambios fisiológicos y por otro lado por los cambios socioeconómicos que caracterizan a este grupo etario y que irrumpen fuertemente en la vida del sujeto (Freisling, Knaze, & Slimani, 2013). Entre ellos cabe destacar los cambios dentales, el incremento de la dependencia, la presencia de comorbilidades que precisan de un incremento del gasto farmacológico, el aumento de la soledad y la pérdida adquisitiva derivada de la interrupción de las actividades laborales entre otros (Atkins et al., 2015; Schröder et al., 2004).

Todos estos factores se asocian directamente con la ingesta dietética (Westenhoefer, 2005). El estatus económico y funcional ejerce una acción manifiesta sobre las elecciones alimentarias y la preparación de los alimentos, pudiendo dar lugar a dietas monótonas y uso de alimentos precocinados de dudoso valor nutricional (Dean, Raats, Grunert, & Lumbers, 2009). Además, la presencia de comorbilidades y tratamiento farmacológico característicos del proceso de envejecimiento, pueden afectar a la absorción nutricional, conduciendo a déficits de nutrientes que a su vez pueden agravar la patología de base o impulsar la aparición de una nueva enfermedad (Mensink et al., 2013).

El estudio *Survey in Europe on Nutrition and the Elderly* (SENECA) llevado a cabo en 8 países europeos, señaló que la población adulta mayor presentaba déficit de micronutrientes específicos, especialmente significativos para la vitamina D, K, B_9, B_{12}, calcio, magnesio y hierro entre otros (De Groot, Verheijden, De Henauw, Schroll, & Van Staveren, 2004). De forma no enigmática, este estudio encontró que en aquellos individuos cuya ingesta energética era inferior a 2000 kcal, la probabilidad de presentar ingestas inadecuadas de al menos 1 nutriente era mayor en comparación con aquellos individuos cuya ingesta energética era mayor. Sin embargo, debemos tener en cuenta que los requerimientos energéticos durante esa etapa de la vida disminuyen, y que además se produce lo que se conoce como "anorexia del anciano", que no es sino la pérdida de apetito en el mayor originando un declive de la ingesta alimentaria (Dent, Hoogendijk, & Wright, 2019).

Finalmente, debe subrayarse que una dieta hipercalórica no asegura que la ingesta de nutrientes se encuentre dentro de los valores recomendados, sino que incluso podría producir el efecto contrario (Schröder, Vila, Marrugat, & Covas, 2008). Ante esta situación, una de las posibles soluciones existentes es la adopción de patrones dietéticos alimentarios saludables que presenten una elevada densidad nutricional y aseguren una ingesta alimentaria variada a fin de reducir las ingestas nutricionales deficitarias y controlar la progresión de las enfermedades no transmisibles de forma específica en adultos mayores (Lammes, Törner, & Akner, 2009).

2. JUSTIFICATION

2. JUSTIFICATION

The facts that justify the need to carry out an investigation in Spain in the field of the analytical nutritional epidemiology in order to assess the associated factors with an inadequate dietary intake in older adult at high risk of cardiovascular disease, can be summarized in the following points:

1. **Foreseeable evolution of the health problem**. As explained in the first part of this Doctoral Thesis (introduction section), the incidence of non-communicable diseases has risen in Spain in recent years (Haro et al., 2014). Due to the ageing of the population, this problem will still be greater in next decades (Schneider & Guralnik, 1990). Among the modifiable risks factors, dietary intake plays an important role in the prevention and management of these diseases. However, the traditional healthy dietary pattern in Spain is being replaced by non-healthy dietary habits. Older adults with chronic diseases are the main vulnerable group exposed to nutritional risk (Aranceta et al., 2001). Overweight people who do not reach the adequate nutrient intake get worsening their chronic condition. Besides, nutritional inadequacy could be increased by a calorie-restricted diet. In view of the current situation, prioritize preventive actions based on nutritional approachment to improve the good health of the population and reduce health care costs that comes from nutrition-non communicable diseases may be a feasible and efficient strategy.

2. **Absence of earlier research.** Leaving aside the above considerations, is important to note that the main approachment to the study of the associated factors to the dietary intake have been postulated under the same point of view: "predictors of short, medium or long adherence to differents dietary patterns after a nutritional intervention" (Zazpe et al., 2010). However, the influence of these factors in the quality of diet is still uncertain. A deep knowledge about them could guide nutritional interventions could help to identify the most highly affected populations groups at high risk of inadequate dietary intake. Furthermore, the traditional approach to the study of dietary intake in overweight/obese population has focused on overeating, not taken into account if this population has nutritional deficiencies associated to hypercaloric intake (Hruby & Hu, 2015). The assessment of micronutrient's dietary intake could guide preventive interventions before inadequateness may have a negative impact on the wellbeing and quality of life.

3. **Availability of sources of information.** Thanks to support from the PREDIMED-Plus study, we had access to database of older adults participants recruited for the study. This database includes a vast amount of information related to dietary intake but also to socioeconomic, demographic and lifestyles variables (Martínez-González et al., 2018). Some features that make this information potentially useful for nutritional epidemiological research are:

   - The use of a standardized protocol which reduces information bias about food intake and socioeconomic, demographic and lifestyle variables, as well as health status information.
   - Wide geographical coverage that includes 23 centres of recruitment displaced all over the national territory.
   - Monitored and protocolled nutritional intervention
   - Follow-up of the population through time, with the same protocol for collecting data.

3. HYPOTHESIS

3. HYPOTHESIS

The hypothesis that underlies this research is that, in spite of the study sample is not representative of the general population, an appropriate analysis of the PREDIMED-Plus database of aged population with overweight/obesity and Metabolic Syndrome will provide useful data for nutritional intervention. The a priori hypotheses that underlie these points are as follows:

1. Despite the dietary pattern of obese or overweight population is characterized by overconsumption, there are several inadequate nutrients intake. These inadequacies are mainly influenced by socioeconomic and lifestyle factors.

2. Dietary intake and nutrient's inadequateness differ among different geographic regions within the same country.

3. Dietary diversity is related to adequate nutrient intake. A greater dietary diversity is associated with a lower number of inadequate nutrient intake.

4. Changes in dietary pattern toward greater Mediterranean Diet adherence are associated to an improvement in nutrients intake.

To test these hypotheses, the aims listed below were chosen as the focus of this Doctoral Thesis.

4. OBJECTIVES/OBJETIVOS

4. OBJECTIVES

Overall Aims

To study the influences of socioeconomic, demographic and lifestyles determinants over the quality of the diet in older adults at high risk of cardiovascular disease in Spain at baseline and after one year of follow-up of the PREDIMED-Plus study.

Specific Aims

1. To assess the adequacy of dietary intake according to the European and International DRIs, as well as to investigate the influence of socioeconomic and lifestyle factors on:

    1.1 Nutrient inadequate intake

    1.2 Nutrient density

2. To evaluate the food intake and nutrient profiles according to the geographical area of residence, besides to analyse the influence of the geographical area of residence over inadequate nutrient intake.

3. To estimate the relationship between dietary diversity and nutrient adequacy and assess the association between dietary diversity and socioeconomic, demographic or lifestyles variables.

4. To assess the effect of improving Mediterranean Diet adherence over nutrient density after one year of follow-up at the PREDIMED-Plus trial.

4. OBJETIVOS

Objetivo general

Estudiar la influencia de los determinantes socioeconómicos, demográficos y de estilo de vida en la calidad de la dieta de adultos mayores con alto riesgo de enfermedad cardiovascular en España, a nivel basal y después de un año de seguimiento en el estudio PREDIMED-Plus.

Objetivos Específicos

1. Evaluar la adecuación de la ingesta dietética de acuerdo a las ingestas dietéticas de referencia tanto Europeas como internacionales, así como investigar la influencia de los factores socioeconómicos y de estilo de vida sobre:

    1.1. Ingesta inadecuada de nutrientes

    1.2. Densidad de nutrientes

2. Conocer la ingesta de alimentos y perfil nutricional según el área geográfica de residencia de los participantes, y analizar la influencia de esta variable sobre la ingesta inadecuada de nutrientes.

3. Estimar la relación entre la diversidad dietética y la adecuación nutricional e identificar qué variables socioeconómicas, demográficas o de estilos de vida están asociadas con la diversidad dietética.

4. Evaluar el efecto de la mejora de la adherencia a la Dieta Mediterránea sobre la densidad nutricional después de un año de seguimiento en el ensayo PREDIMED-Plus.

5. METHODS

5. METHODS

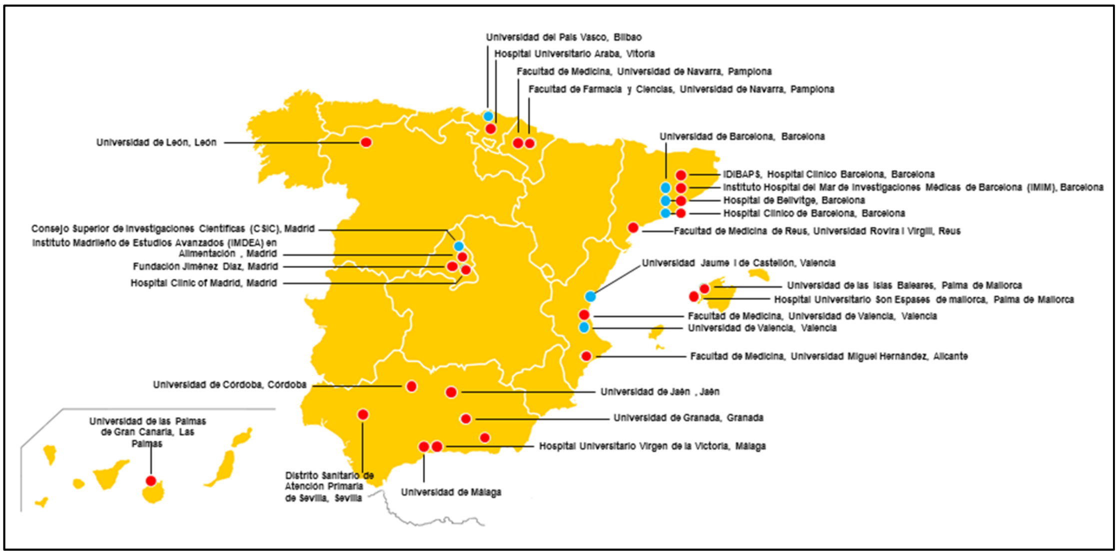
This section will describe the overall methodology used for this Doctoral Thesis; the specific methodology will be reported in more detail in each one of the published articles included as part of this dissertation.

As we have recognized before, we have done this work thanks to the support given by the PREDIMED-Plus study. For this reason, we considered that is important to describe the design of the study, the characteristics of the participants as well as the data collection procedures.

5.1. Study design, participants and data collection procedures

The PREDIMED-Plus study is a clinical trial, conceived to demonstrate the health benefits of the energy restricted Mediterranean Diet and physical activity specifically for the primary prevention of cardiovascular disease. Therefore, the PREDIMED-Plus study is a 6-year multicenter *(figure 8)* (23 nodes of recruitment displaced through the national territory), randomized and parallel group.

Figure 8. Map of Spain with the nodes of recruitment



Fuente: (Martínez-González et al., 2018)

Although the similarities in the principal outcome between PREDIMED and PREDIMED-Plus study are minimal, the intervention is completely different. After corroborate the beneficial effect of Mediterranean Dietary pattern supplemented with olive oil or nuts of the PREDIMED study, it would have been unethical not to recommend this pattern. For this reason, in the PREDIMED-Plus study there is two groups: intervention group, exposed to an intensive weight loss intervention program based on an energy-restricted traditional Mediterranean Diet, physical activity promotion and behavioural support, and the control group based on only standard Mediterranean Diet advice. It is important to note that the trial was registered in 2014 at the International Standard Randomized Controlled Trial (www.isrctn.com/ISRCTN89898870).

As we based our analysis on the participants of the PREDIMED-Plus study, is necessary to describe the inclusion criteria of the study. The participants were adults aged 55-75 for men and 60-75 for women with a body mass index ≥27 and <40 kg/m^2 who met at least three criteria for the metabolic syndrome, according to the harmonized criteria of the International Diabetes Federation and the American Heart Association and National Heart, Lung and Blood Institute (Alberti et al., 2009) and without history of cardiovascular, neurological or endocrine diseases, the inclusion/exclusion criteria are summarized as follow in tables 1 and 2. *(Table 1 and 2).*

Table 1. Inclusion criteria in the PREDIMED-Plus clinical trial

Inclusion Criteria
Men: 55-75 years old
Women: 60-75 years old
Body mass index: ≥27 and <40 kg/m^2
Met at least three criteria for metabolic syndrome: ▪ Waist circumference ≥80 cm in women and ≥94 cm in men ▪ Triglyceride level ≥ 150 mg/dL ▪ Blood glucose ≥ 100 mg/dL or use of oral antidiabetic drugs ▪ Systolic blood pressure ≥ 130 mmHg and diastolic blood pressure ≥ 85 mmHg or use of antihypertensive drugs ▪ HDL-cholesterol level < 40 mg/dL for men and <50 mg/dL for women

Table 2. Exclusion criteria in the PREDIMED-Plus clinical trial

Exclusion Criteria
Illiteracy or inability/unwillingness to give written informed consent or communicate with study staff.
Institutionalization (the participant is a permanent or long-stay resident in a care home).
Documented history of previous cardiovascular disease, including: angina; myocardial infarction; coronary revascularization procedures; stroke (ischemic or haemorrhagic, including transient ischemic attacks); symptomatic peripheral artery disease that required surgery or was diagnosed with vascular imaging techniques; ventricular arrhythmia; uncontrolled atrial fibrillation; congestive heart failure (New York Heart Association Class III or IV); hypertrophic myocardiopathy; and history of aortic aneurism >=5.5 cm in diameter or aortic aneurism surgery.
Active malignant cancer or history of malignancy within the last 5 years (except non melanoma skin cancer).
Inability to follow the recommended diet (for religious reasons, swallowing disorders, etc.) or to carry out physical activity.
A low predicted likelihood to change dietary habits according to the Prochaska and DiClemente Stages of Change Model
Inability to follow the scheduled intervention visits (lack of autonomy, inability to walk, lack of stable address, travel plans, etc.).
Inclusion in another program that provides advice on weight loss (> 5 kg) in the six months before the selection visit.
History of surgical procedures for weight loss or intention to undergo bariatric surgery in the next 12 months.
History of small or large bowel resection.
History of inflammatory bowel disease.
Obesity of known endocrine origin (except for treated hypothyroidism).
Food allergy to any component of the Mediterranean diet.
Immunodeficiency or HIV-positive status.
Cirrhosis or liver failure.
Serious psychiatric disorders: schizophrenia, bipolar disorder, eating disorders, or depression with hospitalization within the last 6 months.
Any severe co-morbidity condition with less than 24 months' life expectancy.
Alcohol abuse or addiction (or total daily alcohol intake >50 g) or drug abuse within the past 6 months.
History of major organ transplantation.
Concurrent therapy with immunosuppressive drugs or cytotoxic agents
Current treatment with systemic corticosteroids.
Current use of weight loss medication.
Concurrent participation in another randomized clinical trial.
Patients with an acute infection or inflammation (e.g. pneumonia) will be allowed to participate in the study 3 months after resolution of their condition.
Any other condition that may interfere with adherence to the study protocol.

For more information the participant's recruitment methods are described in more detail in a specific publication (Martínez-González et al., 2018).

However, is important to highlight that considering the objectives of this thesis, we have to excluded some participants (specified in each published article) due the fact that we did not have information about their dietary intake or because some participants reported values for total energy intake outside predefined limits (<800 kcal/day or >4000 kcal/day for men); (<500 kcal/day or >3500 kcal)/day for women) in accordance with specified nutritional recommendations (Willet, 2013).

On the other hand, as noted in the objectives section, the main components that this thesis incorporates are related to the quality of the diet and the possible factors that influence it. Firstly, we are going to describe in general terms how the usual dietary intake was assessed, the methods used to evaluate diet quality and, secondly we will explain what non-dietary variables were considered in the statistical analysis.

5.2. General dietary assessment

Data on dietary intake were collected at baseline by trained nutritionists in each recruitment centre. Thus, all participants were asked to complete a 143-item semi-quantitative Food Frequency Questionnaire that have been previously validated in Spanish adult population (Fernández-Ballart et al., 2010). Specifically, this questionnaire included 9 frequency options for a specified serving size (never or almost never, 1–3 times a month, once a week, 2–4 times a week, 5–6 times a week, once a day, 2–3 times per day, 4–6 times a day, and more than 6 times a day). The information about nutrients/food-groups intakes were obtained by multiplying serving sizes derived from the food frequency questionnaire by the consumption frequency reported by participant. The questionnaire was completed prior the randomization and once per year.

Therefore, energy and nutrient intakes were calculated as frequency multiplied by nutrient composition of specified portion size for each food item, using a computer program based on information available in Spanish food composition tables (Moreiras, Carbajal, Cabrera, & Cuadrado, 2013). We classified food items in 11 food groups (dairy products, meats and processed meats, fish and seafood, vegetables, fruits, cereals, potatoes, fats, nuts, precooked, sauces and beverages) in order to estimate the food groups of dietary intake.

5.3. Mediterranean Diet assessment

Baseline adherence to the energy-restricted Mediterranean Diet (er-Mediterranean Diet) was appraised by a 17 item score, a modified form of a previously validated tool (Martinez-Gonzalez, Garcia-Arellano, et al., 2012). This tool was used to evaluate compliance with the intervention and as a key element to guide the motivation interviews during the follow-up study. Compliance with each of the 17 items relating to characteristic food habits was scored with 1 point if the goal was met or 0 points otherwise. Therefore, the total er-MedDiet score range was 0-17, with 0 meaning no adherence and 17 meaning maximum adherence to MedDiet.

The study participants completed the questionnaire prior the randomization and also once yearly during the intervention follow-up. In the published articles 1 and 3, this variable was stratified in tertiles as follows, [low: (tertil 1: <7 points), moderate: (tertil 2: 8–10 points) and high adherence: (tertil 3: >11 points)], whereas in article 2 this variable was also used as continuous. Finally, in article 4 we used this variable to measure changes in er-Mediterranean Diet adherence after 1 year of follow-up. The changes in adherence to er-Mediterranean Diet, were categorised in tertiles as follows: small changes of er-Mediterranean Diet adherence (1st tertile, ≤1 points, including negative values), medium (2nd tertile, 2-4 points) or large changes of adherence (3rd tertile, ≥5 points).

5.4 . Assessment of dietary quality

5.4.1. Nutritional inadequacies

The dietary intake of a selection of nutrients including carbohydrates, total fat, monounsaturated, polyunsaturated and saturated fatty acids, protein, dietary fibre, vitamins A, B_1, B_6, B_9, B_{12}, C, D, E, calcium, phosphorus, magnesium, iron, iodine, potassium, selenium and zinc was compared with age and sex-specific requirements of these nutrients according to the DRIs for American population (IOM). The DRIs are appropriate for assessing the nutrient adequacy of groups and individuals being the general term for a set of reference values used (Willet, 2013). Intake levels above DRI imply a low likelihood of inadequate intake. To decrease potential measurement errors derived from the use of the food frequency questionnaire, we also calculated the proportion of individuals with intakes below two thirds (2/3) of the DRIs. This was the criterion used in order to estimate the risk for inadequate nutrients intake used by other authors in a Spanish cohort (Aranceta et al., 2001). Despite the DRIs are used in international epidemiological studies, and taken into account that our cohort is European, we estimated the proportion of inadequate intake according to European Food Safety Agency (EFSA) (EFSA, 2018). We would highlight that the results obtained were based only on dietary intake data, excluding supplements and/or biochemical parameters.

Depending on the nutrient´s database proportionated by the PREDIMED-Plus study we analysed differents nutrients (i.e. in articles 1 and 2 we only analysed 10 nutrients, whereas in article 3 and 4 we included 17 because the database was higher than the database available before). Thus, and according to the median data obtained of nutritional inadequacies, we considered that people presented inadequacies when they reported values of at least 3 inadequacies. The number of nutrients with inadequate intake was determined for each participant.

5.4.2. Nutrient Density

The nutrient density of a diet indicates the ratio of the nutrients present in a diet according to its caloric value (Nicklas et al., 2013). To evaluate the nutrient density of the diet, the density intake of dietary fibre, vitamins and minerals were calculated by dividing absolute nutrient intake by total energy intake according to the criteria used by other authors (Schröder et al., 2004). Thus, the nutrient density was expressed as nutrient intake per 1000 kcal and it was determined for each participant. This variable was used in articles 1 and 4. Moreover, in article 4 we included the changes in nutrient density after 1 year of follow-up as the main outcome variable. Finally, we calculated the mean percentage change for each nutrient as follows: 100*((baseline nutrient density – nutrient density at 1 year)/ baseline nutrient density).

5.4.3. Dietary Diversity

Using the 143-item validated food frequency questionnaire mentioned above, we calculated an energy-adjusted dietary diversity score. This score of diversity was calculated using the method originally described by Kant (Kant, Schatzkin, Harris, Ziegler, & Block, 1993). We included five food groups: vegetables, fruits, cereals, dairy products and protein food groups (which includes legumes, meat, fish, eggs and nuts). The election criteria of this food groups are based on the recommendations given by the Spanish guideline´s pyramid (Aranceta Bartrina et al., 2016). The vegetable group was divided into four subgroups, including: green vegetables, tomatoes, yellow vegetables and mushrooms. The cereal group included potatoes and refined or whole grain cereals (bread, pasta, rice and breakfast cereals). The fruit group included all fresh fruit products divided in three categories: citrus fruits, tropical fruits and other seasonal fruits. The dairy group included all kinds of milk, yogurt and cheese. Protein food groups included legumes (peas, beans, lentils and chickpeas), white meats (poultry and rabbit), fish (oily fish, white fish and other shellfish/seafood), eggs and nuts. These foods groups were used to define the food variety groups. Non-recommended food groups (that should be consumed as little as possible), including sugar food groups (pastries, pies, biscuits, chocolate, fruit in sugar syrup and fruit juices) and food groups with high salt and/or saturated fats (butter, margarine, unhealthy vegetable fats, red meat, processed meats, sauces, pre-cooked dishes, condiments and snacks) were not included in the analysis as they are less healthy products and their variety is not desirable (Aranceta Bartrina et al., 2016). Therefore, we only analysed diversity of recommended food groups, because the more important question was the percentage of total energy supplied by these food groups and our analyses were adjusted for total energy intake.

To be counted as a consumer for any of the food group categories reported previously, a subject should consume at least half of the recommended serving during one day (for example, if the Spanish nutritional recommendation advises a usual protein intake of three servings per week, for each protein item, participants should consume at least 1.5/7 servings/day). Within each food group, we summed up the number of items consumed. Each of the five predefined food categories received a maximum diversity score of 2 points, therefore the sum was rescaled to a 0-to-2 score by multiplying the score by 2 and dividing by the maximum score in that food group. Total dietary diversity score was the sum of the scores of the five main groups, theoretically ranging between 0 and 10 points. The score was adjusted for total energy intake, due to the general concern that high food variety might be a consequence of overconsumption of energy (Kennedy, 2004). Finally, the dietary diversity score was categorized in quartiles (Q) and the cut off points were 3.8, 4.6 and 5.4. The variety in each food group was classified into four categories (C): C1 = 0 points, C2 ≥0–≤0.5 points, C3 ≥0.5-≥1 points and C4≥1 point.

5.4.4. Assessment of non-dietary variables

Trained staff of PREDIMED-Plus study documented information using a standardized protocol by the using of a questionnaire on sociodemographic data and lifestyle behaviours (Martínez-González et al., 2018). The participant´s variables included were:

1. **Sociodemographic variables**

-Sex: male and female.
-Age: included as categorical variable (55-70 years or more than 70 years) or continuous variable.
-Educational level: primary, secondary and tertiary level. Tertiary level includes university studies.
-Marital status: married, widowed, divorced/single or "other category" which includes single participants and those who are priests or nuns who were categorized as "religious".
-Loneliness: this variable includes information about if the participants lived alone or not.
-Employment status: retired, employed, housekeeper and "other category" that includes unemployed (with/without salary), incapacity and students.

2. **Lifestyle variables**

-Smoking status: non-smoker, current smoker or never smoker.
-Alcohol intake: measure as continuous variable in grams per day (collected using the food frequency questionnaire mentioned previously).
-Physical activity: less active, moderately active and active. This classification was based on the level of physical activity of the participants using a validated Spanish version of the Minnesota questionnaire (Elosua et al., 2000; Elosua, Marrugat, Molina, Pons, & Pujol, 1994).

3. Anthropometric variables

-Weight and height: these variables were measured at each visit with participants in light clothing and without shoes or accessories, using a high quality electronic scale. Height was measured with calibrated wall-mounted stadiometer

-Waist circumference: was measured midway between the lowest rib and the iliac crest, after normal exhalation, using an anthropometric tape.

-Body mass index: this variable was calculated as the weight in kilograms divided by the height in meters squared.

In the following figure we show a summary of when data were collected per trained staff in the PREDIMED-Plus trial.

Table 3. Data about the information collected during the baseline and follow-up of the PREDIMED-Plus study

	RUN-IN PERIOD												
	S1	S2	S3	Baseline	M-6	Y-1	Y-2	Y-3	Y-4	Y-5	Y-6	Y-7	Y-8
1. ELIGIBILITY QUESTIONNAIRE	X												
2. 3-DAY FOOD REGISTER	e		c										
3. ANTHROPOMETRIC MEASUREMENTS*	X		X	X	X	X	X	X	X	X	X	X	X
4. GENERAL QUESTIONNAIRE				X									
5. 143-ITEM FFQ			X		X	X	X	X	X	X	X	X	X
6. MEDITERRANEAN DIET QUESTIONNAIRE (17/14-Items)**				X	X	X	X	X	X	X	X	X	X
7. PHYSICAL ACTIVITY QUESTIONNAIRE‡	e†		c†	X	X	X	X	X	X	X	X	X	X
8. CHAIR TEST (Physical activity evaluation)				X	X	X	X	X	X	X	X	X	X
9. ACCELEROMETERS			e	X	X	X	X	X	X	X	X	X	X
10. FOLLOW-UP QUESTIONNAIRE					X	X	X	X	X	X	X	X	X
11. ELECTROCARDIOGRAM	X				X	X	X	X	X	X	X	X	X
12. BLOOD PRESSURE MEASUREMENT	X		X	X	X	X	X	X	X	X	X	X	X
13. BLOOD SAMPLE COLLECTION				X	X	X		X		X		X	X
14. MORNING SPOT URINE COLLECTION				X	X	X		X		X		X	X
15. NAIL COLLECTION				X		X		X		X		X	X
16. COGNITIVE-NEUROPSYCHOLOGICAL TESTS≠			X				X		X		X		X
17. PSYCHOPATHOLOGICAL QUESTIONNAIRES€	e		X			X	X	X	X	X	X	X	X
18. QUALITY OF LIFE QUESTIONNAIRES≈	e		X			X		X		X		X	

S: Screening visit; FFQ: Food-frequency questionnaire; M: Month; e: Delivery ; c: Collection.
* Anthropometric measurements include: weight, height, waist circumference and hip circumference.
‡ Short version of the Minnesota leisure time physical activity questionnaire; PAR-Q, RAPA (RAPA1 and RAPA2) questionnaires; and the NHS sedentary lifestyle questionnaire
† Long version of the Minnesota leisure time physical activity questionnaire.
**Short questionnaires on adherence to the Mediterranean Diet. The control group uses the same 14-item questionnaire that was used in the PREDIMED trial (Schroeder et al., 2011). The intervention group uses the 17-item energy-restricted Mediterranean diet questionnaire (see below).
≠Mini-Mental Status Examination, clock test, phonological verbal fluency test (animals + P), the reverse series of digits test (WAIS-III), and the trail making test.
€Beck Depression Inventory (BDI-II), multidimensional scale of weight locus of control, eating disorders diagnostic criteria, and SF-36 quality of life scale.

5.4.5. Statistical analysis

For data analysis we used two differents databases generated by the PREDIMED-Plus study. For articles 1, 2 we used the database generated in June 2017, and for article 3 we used the database generated in August 2017, whereas for article 4 we used the database generated in March 2019. All analyses were cross-sectional except for the analysis performed to answer the objective 4 (article 4 with a prospective evaluation). All statistical analysis were performed using Stata (12.0, StataCorp LP, Tx. USA). Qualitative variables were described as frequencies whereas the quantitative variables were expressed as means and standard deviations. The significance level was set at 5%. Pearson´s Chi-square and Student t-test (for categorical and continuous variables, respectively) were performed. Factorial ANOVA, ANCOVA or ANOVA test were performed in order to estimate differences depending of the objective set. Linear regression models were fitted if the dependent variable was continuous, whereas we performed logistic regression models if the dependent variable was dichotomous. These models were controlled by potential confounding factors. These factors were the sociodemographic, lifestyle, anthropometric variables mentioned previously.

6. RESULTADOS

6. RESULTADOS

6.1 Introducción de los resultados obtenidos

En relación a la presentación de los resultados obtenidos en esta Tesis Doctoral y, en consecuencia, de ordenar los cuatro trabajos que de ella se han obtenido, hemos optado por emplear un orden basado en la secuencia lógica con la que estos deberían aparecer y de cómo han sido formulados los objetivos; aunque el orden cronológico de publicación no haya sido el mismo. Los resultados obtenidos han sido plasmados en cuatro artículos originales. Tres de ellos ya han sido publicados en revistas de primer cuartil. No obstante, es importante señalar, que el último de los trabajos realizados, se encuentra bajo revisión desde el 23 de Mayo de 2019 en la revista *European Journal of Nutrition*, y en consecuencia, aún no ha sido publicado. Sin embargo, de acuerdo a los objetivos planteados en esta memoria, hemos decidido incluirlo para abordar el efecto de la intervención nutricional sobre la calidad dietética en la población estudiada.

TRABAJOS REALIZADOS

Artículo 1. Cano-Ibáñez N, Gea A, Ruiz-Canela M, Corella D, Salas-Salvadó J, Schröder H, et al. Diet quality and nutrient density in subjects with metabolic syndrome: influence of socioeconomic status and lifestyle factors. A cross-sectional assessment in the PREDIMED-Plus study 2019. Clinical Nutrition. 2019; https://doi.org/10.1016/j.clnu.2019.04.032

El primer artículo titulado *"Diet quality and nutrient density in subjects with metabolic syndrome: Influence of socioeconomic status and lifestyle factors. A cross-sectional assessment in the PREDIMED-Plus study" da respuesta al objetivo específico 1 de la Tesis, evaluándose* en primer lugar la calidad dietética de estos individuos (medida como la ingesta inadecuada de nutrientes de acuerdo a las ingestas dietéticas de referencia Americanas y Europeas, y la densidad nutricional). Tras la aproximación descriptiva, se estudió la influencia que los factores socioeconómicos y de estilo de vida ejercían en ambas, mediante análisis de regresión logística y lineal ajustados por variables confusoras. *Los resultados* mostraron que a pesar de la elevada densidad energética de la dieta, la densidad nutricional era escasa. De esta primera aproximación se obtuvo que aproximadamente el 17% de la población analizada presentó déficit nutricional en al menos 4 de los 10 nutrientes incluidos en el estudio; siendo especialmente característico el déficit de vitaminas liposolubles (A, D, y E) y vitaminas del grupo B, en concreto vitaminas B_9 y B_{12}, calcio, magnesio y fibra dietética. Estos déficits fueron más acentuados en los hombres que en las mujeres. No en vano, el análisis de los factores asociados a la ingesta inadecuada y densidad nutricional mostró que una mayor densidad nutricional y una menor ingesta deficitaria, se asociaron de forma directa y estadísticamente significativa con ser mujer, tener un mayor nivel educativo y mayor adherencia a la Dieta Mediterránea; mientras que tener estilos de vida no saludables (fumar y/o ser sedentario) se asociaron de forma inversa.

6.1.1. Diet quality and nutrient density in subjects with metabolic syndrome: Influence of socioeconomic status and lifestyle factors. A cross-sectional assessment in the PREDIMED-Plus study

[Cano-Ibáñez N, Gea A, Ruiz-Canela M, Corella D, Salas-Salvadó J, Schröder H, et al. Diet quality and nutrient density in subjects with metabolic syndrome: influence of socioeconomic status and lifestyle factors. A cross-sectional assessment in the PREDIMED-Plus study 2019. Clinical Nutrition. 2019; https://doi.org/10.1016/j.clnu.2019.04.032]

Datos de la Publicación:

- Factor de impacto en JCR 2017: 5.496
- Ránking: 8/83
- Categoría: *Nutrition & Dietetics*
- Cuartil: Q1.

ARTICLE IN PRESS

Clinical Nutrition xxx (xxxx) xxx

Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

Original article

Diet quality and nutrient density in subjects with metabolic syndrome: Influence of socioeconomic status and lifestyle factors. A cross-sectional assessment in the PREDIMED-Plus study

Naomi Cano-Ibáñez [a, b, c, *], Alfredo Gea [d, e, f], Miguel Ruiz-Canela [d, e, f], Dolores Corella [f, g], Jordi Salas-Salvadó [f, h, i, j], Helmut Schröder [b, k], Eva Mª. Navarrete-Muñoz [b, l], Dora Romaguera [f, m], J. Alfredo Martínez [e, f, n, o], F. Javier Barón-López [f, p], José López-Miranda [f, q], Ramón Estruch [f, r], Blanca Riquelme-Gallego [a], Ángel Alonso-Gómez [f, s], Josep A. Tur [f, t], Francisco J. Tinahones [f, u], Lluis Serra-Majem [f, v], Vicente Martín [b, w], José Lapetra [f, x], Clotilde Vázquez [f, y], Xavier Pintó [f, z], Josep Vidal [aa, ab], Lidia Daimiel [o], José Juan Gaforio [b, ac], Pilar Matía [ad], Emilio Ros [f, aa], Rebeca Fernández-Carrión [f, g], Andrés Díaz-López [f, h, i, j], M. Dolors Zomeño [k, ae], Inmaculada Candela [b, l], Jadwiga Konieczna [f, m], Itziar Abete [e, f, n], Pilar Buil-Cosiales [d, f, af], Josep Basora [f, h, i, j], Montserrat Fitó [f, k], Miguel A. Martínez-González [d, e, f, ag], Aurora Bueno-Cavanillas [a, b, c]

[a] Department of Preventive Medicine and Public Health, University of Granada, Granada, Spain
[b] CIBER de Epidemiología y Salud Pública(CIBERESP), Instituto de Salud Carlos III (ISCIII), Madrid, Spain
[c] Instituto de Investigación Biosanitaria de Granada, IBS GRANADA, Granada, Spain
[d] Department of Preventive Medicine and Public Health, Medical School, University of Navarra, Pamplona, Spain
[e] Navarra Institute for Health Research (IdisNa), Pamplona, Spain
[f] CIBER Fisiopatología de la Obesidad y Nutrición (CIBEROBN), Instituto de Salud Carlos III (ISCIII), Madrid, Spain
[g] Department of Preventive Medicine, University of Valencia, Valencia, Spain
[h] Universitat Rovira i Virgili, Department de Bioquímica I Biotecnologia, Unitat de Nutrició, Reus, Spain
[i] Institut d'Investigació Sanitària Pere Virgili (IISPV), Reus, Spain
[j] University Hospital of Sant Joan de Reus, Nutrition Unit, Reus, Spain
[k] Unit of Cardiovascular Risk and Nutrition, Institut Hospital del Mar de Investigaciones Médicas Municipal d'Investigació Médica (IMIM), Barcelona, Spain
[l] Nutritional Epidemiology Unit, Miguel Hernández University, ISABIAL-FISABIO, Alicante, Spain
[m] Health Research Institute of the Balearic Islands (IdISBa), Palma de Mallorca, Spain
[n] Department of Nutrition, Food Sciences, and Physiology, Center for Nutrition Research, University of Navarra, Pamplona, Spain
[o] Nutritional Genomics and Epigenomics Group, IMDEA Food, CEI UAM + CSIC, Madrid, Spain
[p] Department of Public Health, University of Málaga-IBIMA, Málaga, Spain
[q] Lipids and Atherosclerosis Unit, Department of Internal Medicine, Maimonides Biomedical Research Institute of Córdoba (IMIBIC), Reina Sofía University Hospital, University of Córdoba, Córdoba, Spain
[r] Department of Internal Medicine, Institut d'Investigacions Biomèdiques August Pi I Sunyer (IDIBAPS), Hospital Clinic, University of Barcelona, Barcelona, Spain
[s] Department of Cardiology, OSI ARABA, University Hospital Araba, University of the Basque Country UPV/EHU, Vitoria-Gasteiz, Spain
[t] Research Group on Community Nutrition & Oxidative Stress, University of Balearic Islands, Palma de Mallorca, Spain
[u] Virgen de la Victoria Hospital, Department of Endocrinology, Instituto de Investigación Biomédica de Málaga (IBIMA), University of Málaga, Málaga, Spain
[v] Research Institute of Biomedical and Health Sciences, University of Las Palmas de Gran Canaria, Las Palmas de Gran Canaria, Spain
[w] Institute of Biomedicine (IBIOMED), University of León, León, Spain
[x] Department of Family Medicine, Research Unit, Distrito Sanitario Atención Primaria Sevilla, Sevilla, Spain
[y] Department of Endocrinology, Fundación Jiménez-Díaz, Madrid, Spain
[z] Lipids and Vascular Risk Unit, Internal Medicine, Hospital Universitario de Bellvitge, Hospitalet de Llobregat, Spain
[aa] Endocrinology and Nutrition Service, IDIBAPS, Hospital Clinic, Barcelona, Spain
[ab] CIBER Diabetes y Enfermedades Metabólicas (CIBERDEM), Instituto de Salud Carlos III (ISCIII), Madrid, Spain
[ac] Centro de Estudios Avanzados en Olivar y Aceites de Oliva, Universidad de Jaén, Jaén, Spain
[ad] Department of Endocrinology and Nutrition, Instituto de Investigación Sanitaria Hospital Clínico San Carlos (IdISSC), Madrid, Spain

Abbreviations: AI, adequate intake; AR, average requirements; BMI, body mass index; CHO, carbohydrates; CVD, cardiovascular disease; DRI, dietary reference intake; EFSA, European Food Safety Agency; FFQ, food frequency questionnaire; MedDiet, Mediterranean diet; MetS, metabolic syndrome; MUFAs, monounsaturated fatty acids; PUFAs, polyunsaturated fatty acids; RAPA, rapid assessment of physical activity; SFAs, saturated fatty acids.

* Corresponding author. Department of Preventive Medicine and Public Health, University of Granada, Avda. De la Investigación 11, 18016 Granada, Spain.
E-mail address: ncaiba@ugr.es (N. Cano-Ibáñez).

https://doi.org/10.1016/j.clnu.2019.04.032

Please cite this article as: Cano-Ibáñez N et al., Diet quality and nutrient density in subjects with metabolic syndrome: Influence of socioeconomic status and lifestyle factors. A cross-sectional assessment in the PREDIMED-Plus study, Clinical Nutrition, https://doi.org/10.1016/j.clnu.2019.04.032

[ae] Human Nutrition Unit, Blanquerna-Ramon Llull University, Barcelona, Spain
[af] Atención Primaria, Servicio Navarro de Salud-Osasunbidea, Pamplona, Spain
[ag] Harvard TH Chan School of Public Health, Department of Nutrition, Boston, USA

ARTICLE INFO

Article history:
Received 15 October 2018
Accepted 24 April 2019

Keywords:
Diet quality
Nutrient density
Mediterranean diet
Socioeconomic factors
Lifestyle factors
Metabolic syndrome

SUMMARY

Background: Socioeconomic disparities and lifestyle factors are likely to determine the overall quality of the diet. In addition, overeating is compatible with inadequate micronutrient intake and it can lead to adverse health outcomes.
Objective: To assess adequacy of dietary nutrient intake and to investigate the influence of socioeconomic and lifestyle factors on nutrient density in a large primary cardiovascular prevention trial conducted in healthy participants with metabolic syndrome (MetS) to assess the cardiovascular effects of an energy-restricted Mediterranean diet (PREDIMED-Plus).
Methods: Baseline cross-sectional analysis of the PREDIMED-Plus trial with 6646 Spanish participants (aged 55–75 years in men and 60–75 years in women) with overweight/obesity and MetS. Energy and nutrient intake (for 10 nutrients) were calculated using a validated 143-item Food Frequency Questionnaire (FFQ) and nutrient density was estimated dividing the absolute nutrient intake by total energy intake. The prevalence of inadequate intake was estimated according to dietary reference intakes. Multivariable linear regression models were fitted to examine associations between socioeconomic status or lifestyle factors and nutrient density.
Results: A considerable proportion of the screened participants showed a deficient intake of vitamins A, D, E, B_9, calcium, magnesium and dietary fibre. Inadequate intake of four or more of the ten nutrients considered was present in 17% of participants. A higher nutrient density was directly and significantly associated with female sex, higher educational level and a better adherence to the Mediterranean diet. Lifestyle factors such as non-smoking and avoidance of sedentary lifestyles were also independently associated with better nutrient density.
Conclusions: Patients with MetS, despite being overweight, exhibited suboptimal nutrient intake, especially among men. Low nutrient density diet can be largely explained by differences in socioeconomic and lifestyle factors. These results highlight the importance of focussing on nutritional education in vulnerable populations, taking into account nutrient requirements.

1. Introduction

Nutrition-related non-communicable diseases (NCDs) are the main causes of mortality and disability especially in older adults. Moreover, in the last few decades the global burden of disease attributed to NCDs has increased [1].

One of the main explanations for this dramatic increase is the worsening of lifestyles and diet [2]. However, both are modifiable risk factors, being promising targets for the prevention of NCDs. Regarding diet, poor dietary habits contribute to micronutrient deficiencies, increasing the risk of chronic diseases and playing an important role in the ageing process, especially in older adults who have MetS [3]. A growing accrual of evidence has confirmed that the Mediterranean Diet (MedDiet) represents an effective tool for the prevention or mitigation of the progression of CVD and other NCDs [4]. This may be partially attributable to the fact that MedDiet provides most of the nutrients in their right proportions [5].

Spain is a southern European country with a huge gastronomic culture based on foods with high nutritional quality and linked to the Mediterranean dietary pattern [6]. Notwithstanding, the incidence of overweight and obesity, cardiovascular disease (CVD), type 2 diabetes mellitus, cancer, musculoskeletal disorders and metabolic syndrome (MetS) has risen in Spain during the last 2–3 decades, as has happened worldwide [7]. Nowadays, the current dietary pattern is moving away from the traditional MedDiet pattern, leading to increased consumption of meat/meat products, ultra-processed foods, and other food items with high energy density but with poor nutritional quality [8]. For this reason, it is important to note that diet with a high nutrient density content is an informative criterion for the quality of the diet: The nutrient density of a diet indicates the ratio of the nutrients present in a diet according to its caloric value [9]. Now, with this changing dietary pattern there is an elevated percentage of aged Spanish population with overweight or obesity who do not reach the dietary recommended intakes (DRIs) for magnesium, calcium, selenium and vitamins A, B_1, B_9, C, D, and E [10,11].

While still partly keeping the traditional culinary customs of the MedDiet, older adults are highly susceptible to diet misconceptions and therefore, are one of the main groups placed at high nutritional risk [12]. In addition, increasing age is accompanied by a decrease in autonomy and economic capacity; both variables are tightly associated to sociocultural status, and can influence food variability and diet quality [13]. Furthermore, the ageing process is associated with a higher prevalence of NCDs and poly-pharmacy; both of these are associated with changes in dietary habits that can lead to nutrient deficiencies that on their part may also contribute to some NCDs, thus leading to a vicious circle. For example, deficient intakes of antioxidants and some vitamins (A, B, C and E) have been associated with increased risk of dementia [14,15], MetS and CVD [16,17]. Other health conditions such as diabetes type 2 or osteoporosis have been related to vitamin D and calcium deficiencies [18,19].

The assessment of the dietary intake of micronutrients could guide preventive interventions before inadequate dietary intakes may have a negative impact on the wellbeing and quality of life. This approach will also be efficient and may contribute to decrease the costs in health care [12].

Please cite this article as: Cano-Ibáñez N et al., Diet quality and nutrient density in subjects with metabolic syndrome: Influence of socioeconomic status and lifestyle factors. A cross-sectional assessment in the PREDIMED-Plus study, Clinical Nutrition, https://doi.org/10.1016/j.clnu.2019.04.032

The purpose of the present study was to assess adequacy of dietary intake according to DRIs and to investigate the influence of socioeconomic and lifestyle factors on nutrient density. This assessment was done in a large primary cardiovascular prevention trial conducted in healthy participants with metabolic syndrome (MetS) and designed to assess the cardiovascular effects of an energy-restricted MedDiet.

2. Materials and methods

2.1. Study design

A cross-sectional analysis on baseline data of the PREDIMED-Plus study was conducted; PREDIMED-Plus is a 6-year multicentre, randomized, parallel-group, ongoing primary prevention trial in Spain to assess the effect on CVD morbidity and mortality of an intensive weight loss intervention program based on an energy-restricted traditional Mediterranean diet, physical activity promotion and behavioural support, in comparison to usual care intervention only with energy-unrestricted MedDiet (control group). The participant recruitment methods and data collection are described in more detail in a specific publication [20] and at (http://predimedplus.com). The respective Institutional Review Board (IRB) of all centres approved the study protocol. The trial was registered in 2014 at the International Standard Randomized Controlled Trial (www.isrctn.com/ISRCTN89898870). All participants provided written informed consent.

2.2. Participants and data collection procedures

The population studied consisted of 6874 participants recruited for the PREDIMED-Plus trial. Recruitment took place from October 2013 to November 2016 with the participation of 23 centres (universities, hospitals and research institutes) in Spain. Participants were recruited from Primary Care Centres of the National Health System.

Eligible participants were adults (aged 55–75 in men; 60–75 in women) with overweight/obesity (body mass index (BMI) ≥27 and <40 kg/m^2) who met at least three of the following components of the MetS: waist circumference ≥80 cm in women and ≥94 cm in men, triglyceride level ≥ 150 mg/dL, blood glucose ≥ 100 mg/dL or use of oral antidiabetic drugs, systolic blood pressure ≥ 130 mmHg and diastolic blood pressure ≥ 85 mmHg or use of antihypertensive drugs and/or HDL-cholesterol level < 40 mg/dL for men and <50 mg/dL for women, according to the harmonized criteria of the International Diabetes Federation and the American Heart Association and National Heart, Lung and Blood Institute [21] and without other active neurological or endocrine diseases.

The present study was based on a cross-sectional analysis of baseline data from the PREDIMED-Plus study. Out of a total sample of 6874 participants recruited for the PREDIMED-Plus trial, a total of 228 participants were excluded for the current analysis (Fig. 1): 47 participants did not complete the food frequency questionnaire (FFQ) at baseline, and 181 participants reported values for total energy intake outside predefined limits (<3347 kJ/800 kcal/day or >17,573 kJ/4000 kcal/day for men); (<2510 kJ/500 kcal/day or >14,644 kJ/3500 kcal)/day for women) in accordance with specified nutritional recommendations [22]. A final sample of 6646 participants was analysed.

2.3. Dietary assessment

Data on dietary intake were collected at baseline. All participants were asked to complete a 143-item semi-quantitative FFQ previously validated in Spain [23,24]. The FFQ was administrated by trained nutritionists. The questionnaire included 9 frequency options for a specified serving size (never or almost never, 1–3 times a month, once a week, 2–4 times a week, 5–6 times a week, once a day, 2–3 times per day, 4–6 times a day, and more than 6 times a day). Nutrients/food-groups intakes were obtained by multiplying serving sizes by consumption frequency. Energy and nutrient intakes were calculated as frequency multiplied by nutrient composition of specified portion size for each food item, using a computer program based on information available in Spanish food composition tables [25,26]. We classified food items in 11 food groups (dairy products, meats and processed meats, fish and seafood, vegetables, fruits, cereals, potatoes, fats, nuts, precooked, sauces and beverages). Baseline adherence to the MedDiet was appraised by a 17 item score, which contained some modifications regarding a previously validated tool [27], and used to evaluate compliance with the intervention and as a key element to guide the motivation interviews during the follow-up study. Compliance with each of the 17 items relating to characteristic food habits was scored with 1 point if the goal was met or 0 points otherwise. Therefore, the total MedDiet score range was 0–17, with 0 meaning no adherence and 17 meaning maximum adherence to MedDiet.

2.4. Diet quality

The dietary intake of a selection of nutrients including carbohydrates (CHO), total fat, monounsaturated (MUFAs), polyunsaturated (PUFAs) and saturated fatty acids (SFAs), protein, dietary fibre, vitamin A, B_1, B_9, B_{12}, C, D, E, calcium and magnesium, was compared with age and sex-specific requirements of these nutrients according to the DRIs for American population [28]. The DRIs are appropriate for assessing the nutrient adequacy of groups and individuals [28]. DRI is the general term for a set of reference values used to plan and assess nutrient intakes for healthy people. These values vary by age and sex and include Recommended Dietary Allowances (RDA), Adequate Intake (AI) and Tolerable Upper Intake Level (UL). Intake levels above DRI imply a low likelihood of inadequate intake. To decrease potential measurement errors derived from the use of the FFQ, we also calculated the proportion of individuals with intakes below two thirds (2/3) of the DRIs. This was the criterion used in order to estimate the risk for inadequate nutrients intake [29]. Furthermore, we estimated the proportion of inadequate intake according to European Food Safety Agency (EFSA) average requirements (AR), taking as reference adequate intake (AI) when AR were not available [30]. Results were based only on dietary intake data, excluding supplements. To evaluate the nutrient density of the diet, density intake of dietary fibre, vitamins and minerals were calculated by dividing absolute nutrient intake by total energy intake. The nutrient density was expressed as nutrient intake per 1000 kcal. The number of nutrients with inadequate intake was determined for each participant. We studied

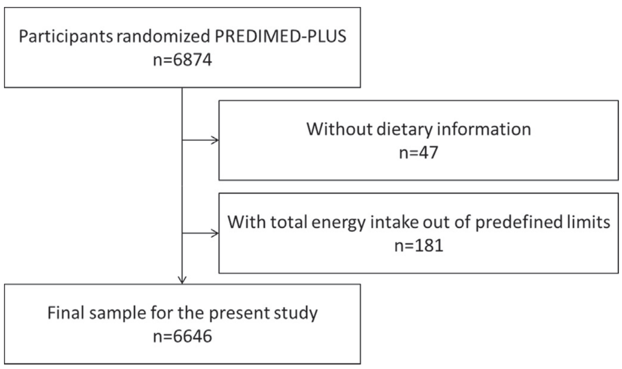


Fig. 1. Flow-chart of participants.

Please cite this article as: Cano-Ibáñez N et al., Diet quality and nutrient density in subjects with metabolic syndrome: Influence of socioeconomic status and lifestyle factors. A cross-sectional assessment in the PREDIMED-Plus study, Clinical Nutrition, https://doi.org/10.1016/j.clnu.2019.04.032

the proportion of participants who presented inadequate intake for 4 or more out of the 10 assessed nutrients (fibre, vitamin A, B_1, B_9, B_{12}, C, D, E, calcium and magnesium).

2.5. Assessment of non-dietary variables

At baseline, trained staff collected information about socioeconomic and lifestyle factors. The variables included were sex, age, education level (primary level, secondary level and tertiary level which includes university studies), civil and employment status and whether they lived alone or not. Other lifestyle variables such as smoking habits, alcohol intake (grams per day) and physical activity where recorded. Physical activity information was gathered using the Rapid Assessment of Physical Activity (RAPA), the questionnaire for sedentary behaviours of the Nurses' Health Study and the abbreviated Minnesota Physical activity questionnaire validated for Spanish population [31–34].

2.6. Statistical analysis

We used PREDIMED-Plus baseline database generated in August 2017. All analyses were cross-sectional and performed using Stata (12.0, StataCorp LP, Tx. USA). Analyses were conducted for men and women separately because differences in dietary habits were expected. Qualitative variables were described as frequencies whereas the quantitative variables were expressed as means and standard deviations (SD). The significance level was set at 5%. Pearson's Chi-square and *T* student test (for categorical and continuous variables, respectively) were used to assess differences in baseline characteristics of participants. Factorial ANOVA was used to estimate energy intake, adherence to the MedDiet and dietary intakes according to sex and age groups predefined (51–70 years and more than 70 years). We also calculated the 95% confidence interval (CI) of the proportion of inadequate intake of micronutrients (defined above as the proportion of subjects who met less than 2/3 of DRIs). Adherence to MedDiet was categorized in tertiles. The association between nutrient density (dependent variable) and socioeconomic and lifestyle factors (independent variables) was assessed by multiple linear regression adjusted for potential confounders [sex, age (55–70 years or more than 70 years), smoking habit (current smoker, former smoker, never smoker), physical activity (3 categories), educational level (primary, secondary, tertiary, insufficient data), marital status (married, widowed, divorced/separated, other), employment status (retired, employed, housekeeper, other) and MedDiet adherence [low: (tertil 1: <7 points), moderate: (tertil 2: 8–10 points) and high adherence: (tertil 3: >11 points)] BMI, CHO, MUFAs, PUFAs, SFAs [35]]. Logistic regression was used to examine associations between inadequate nutrient intake in ≥4 nutrients and socioeconomic and lifestyle factors.

3. Results

Table 1 shows the baseline characteristics of participants according to sex. Women were older than men. Excluding men from 55 to 59 years, mean age among men would be 66.07 years, with no difference with mean age in women. The main differences between men and women were in smoking habit (more men than women were current smokers (16.7%) or former smokers (60.9%)), physical activity (more men than women were classified as moderate active or active, but still more than half of men were less active), educational level (tertiary studies were more frequent among men (15.0%)), and women were living alone more often than men.

Adherence to the MedDiet, total energy intake, and nutrient densities by sex and age according to total energy intake are shown in Table 2. In both sexes, adherence to the MedDiet was higher in those individuals older than 70 years, being higher in women than in men. Total energy intake decreased with age in both sexes. The oldest women had higher nutrient densities for CHO, protein and fibre intake. Total fat and MUFAs intake was lower in those participants younger than 70 years old and in women compared with the respective counterparts. The micronutrient density intake was higher in women than in men and in the older persons compared to the younger for vitamins A, B1, C, calcium and magnesium. There was interaction by age and sex for PUFAs, vitamins A and E. In order to exclude possible sex differences attributable to age, this analysis was redone excluding men younger than 60 years (Supplementary Table 1), and the results obtained did not change. Macro/micronutrient intake by age and sex are shown in Supplementary material (Supplementary Table 2).

The proportion of participants with intake under 2/3 DRIs (two-thirds of DRIs) was estimated in order to avoid overestimation of micronutrient intake and are presented in Table 3. A low intake of dietary fibre, vitamin A, B_9, D, E, calcium and magnesium was frequent in all study groups. Comparisons by sex yielded the highest prevalence of inadequate intake of dietary fibre, vitamin A and magnesium in men compared to women. The opposite was detected for vitamin E and calcium, where men showed a lower prevalence of inadequacies. According to age, the proportion of participants with a low intake of macro and micronutrients was higher in the youngest group (55–70 years), except for dietary fibre. For comparison, Supplementary Table 3 shows the proportion of participants with an intake of nutrients below the DRIs. Supplementary Table 4 shows the same results as for Table 3 when

Table 1
Baseline characteristics of the PREDIMED-Plus study participants analysed by sex (*n* = 6646).

	Men	Women	*P* value
n	3431	3215	
Age (y), *n* (%)			
≤70 y[a]	3012 (87.8)	2661 (82.8)	<0.001
>70 y	419 (12.2)	554 (17.2)	
Mean ± SD	63.7 ± 5.3	66.3 ± 4.0	<0.001
Smoking habit, *n* (%)			
Never smoker	752 (21.9)	2158 (67.1)	<0.001
Former smoker	2088 (60.9)	795 (24.7)	
Current smoker	573 (16.7)	252 (7.8)	
Insufficient data	18 (0.5)	10 (0.3)	
Physical activity			
Less active	1906 (55.8)	2055 (64.1)	<0.001
Moderately active	713 (20.9)	536 (16.7)	
Active	799 (23.4)	613 (19.1)	
Educational level, *n* (%)			
Primary school	1312 (38.3)	1895 (59.0)	<0.001
Secondary school	1118 (32.6)	794 (24.2)	
Tertiary school	980 (28.6)	483 (15.0)	
Insufficient data	20 (0.6)	40 (1.3)	
Marital status, *n* (%)			
Married	2907 (85.2)	2165 (67.5)	<0.001
Widowed	110 (3.2)	580 (18.1)	
Divorced/separated	247 (7.2)	272 (8.5)	
Others[b]	149 (4.4)	190 (5.9)	
Living alone, *n* (%)	241 (7.1)	585 (18.2)	<0.001
Employment status, *n* (%)			
Retired	2067 (60.5)	1639 (51.2)	<0.001
Employed	1001 (29.3)	364 (11.4)	
Housekeeper	6 (0.2)	975 (30.4)	
Others[c]	345 (10.1)	226 (7.1)	

Values are presented as means ± SD for continuous variables and *n* (%) for categorical variables. Pearson's chi-square test was performed for categorical variables and *T* student test for continuous variables.
[a] This age category includes 55–70 years for males, and 60–70 years for females.
[b] Includes religious and single.
[c] Includes unemployed (with/without salary) incapacity, and students.

Please cite this article as: Cano-Ibáñez N et al., Diet quality and nutrient density in subjects with metabolic syndrome: Influence of socioeconomic status and lifestyle factors. A cross-sectional assessment in the PREDIMED-Plus study, Clinical Nutrition, https://doi.org/10.1016/j.clnu.2019.04.032

Table 2
Adherence to Mediterranean diet, total energy intake and nutrient Density by sex and age according to total energy intake.

	Men			Women		*P* value[a]	*P* value[b]	*P* value[c]
	55–59 y	60–70 y	>70 y	60–70 y	>70 y			
n	892	2120	419	2661	554			
MedDiet adherence[d]	7.8 ± 2.6	8.2 ± 2.7	8.5 ± 2.7	8.9 ± 2.6	9.0 ± 2.6	<0.001	<0.001	0.405
Total energy (kcal/d)	2539 ± 581	2508 ± 546	2433 ± 560	2212 ± 496	2161 ± 495	<0.001	0.044	0.520
CHO (g/1000 kcal)	100.3 ± 17.3	100.8 ± 16.5	102 ± 17	103 ± 17	106 ± 18	<0.001	0.009	0.201
Protein (g/1000 kcal)	40.0 ± 6.8	39.6 ± 6.6	39.8 ± 6.1	43.4 ± 6.8	43.5 ± 6.7	<0.001	0.334	0.794
Total Fat (g/1000 kcal)	43.8 ± 7.2	43.4 ± 7.0	43.2 ± 7.3	44.3 ± 7.4	43.4 ± 7.5	0.025	0.081	0.183
MUFA (g/1000 kcal)	22.4 ± 4.9	22.6 ± 5.0	22.3 ± 5.0	23.1 ± 5.3	22.6 ± 5.1	0.031	0.064	0.381
PUFA (g/1000 kcal)	6.9 ± 2.0	7.0 ± 2.0	7.1 ± 2.2	7.1 ± 2.1	7.0 ± 2.0	0.913	0.173	0.036
SFA (g/1000 kcal)	11.3 ± 2.3	10.9 ± 2.1	10.9 ± 2.2	11.0 ± 2.3	10.7 ± 2.3	0.915	0.003	0.141
Total fibre (g/1000 kcal)	9.7 ± 3.0	10.3 ± 3.2	11.0 ± 3.2	12.2 ± 3.4	12.2 ± 3.8	<0.001	<0.001	0.244
Alcohol (g/1000 kcal)	6.4 ± 6.3	6.9 ± 6.6	6.5 ± 6.1	2.0 ± 3.3	1.7 ± 3.0	<0.001	0.042	0.848
Vitamin A (μg/1000 kcal)	435 ± 258	447 ± 255	463 ± 299	513 ± 291	475 ± 242	<0.001	0.057	0.005
Vitamin B_1 (mg/1000 kcal)	0.7 ± 0.1	0.7 ± 0.1	0.7 ± 0.1	0.7 ± 0.1	0.8 ± 0.1	<0.001	0.014	0.495
Vitamin B_9 (μg/1000 kcal)	133 ± 35	141 ± 38	146 ± 37	163 ± 42	167 ± 47	<0.001	<0.001	0.477
Vitamin B_{12} (μg/1000 kcal)	4.1 ± 1.8	4.2 ± 2.1	4.2 ± 2.1	4.4 ± 1.9	4.4 ± 1.7	<0.001	0.770	0.235
Vitamin C (mg/1000 kcal)	72 ± 32	78 ± 33	82 ± 33	98 ± 38	101 ± 42	<0.001	<0.001	0.831
Vitamin D (μg/1000 kcal)	2.4 ± 1.4	2.5 ± 1.4	2.5 ± 1.5	2.8 ± 1.6	2.8 ± 1.6	<0.001	0.034	0.377
Vitamin E (mg/1000 kcal)	4.3 ± 1.3	4.3 ± 1.4	4.4 ± 1.5	4.7 ± 1.4	4.5 ± 1.2	<0.001	0.060	<0.001
Calcium (mg/1000 kcal)	406 ± 123	415 ± 118	419.1 ± 117.6	470.5 ± 131.9	485.7 ± 133.3	<0.001	0.042	0.227
Magnesium (mg/1000 kcal)	2539 ± 581	2508 ± 546	167.9 ± 32.1	183.0 ± 34.3	184.0 ± 35.2	<0.001	<0.001	0.353

Values are mean ± SD unless otherwise indicated.
Factorial ANOVA was used.
[a] *P* value for sex.
[b] *P* value for age.
[c] *P* value interaction between sex and age.
[d] MedDiet adherence: adherence to Mediterranean diet using the 17 item questionnaire adherence with scale 0–17 points.

using the EFSA dietary recommendations. Inadequate intake is higher for all nutrients except for vitamins A, B_1 and B_9, which show figures slightly low.

Table 4 shows the results from the logistic regression model fitted using inadequate intake of 4 or more out of 10 micronutrients as the dependent variable. An inadequate intake of 4 or more of the 10 assessed nutrients was observed in 16.6% of participants. This figure was almost twofold in men (21.3%) compared with women (11.7%). When we used the EFSA recommendations, 38.2% of participants had inadequate intake of 4 or more of the ten nutrients analysed (Fig. 2), with a higher rate in men (44.0%) than in women (32.0%) (Supplementary Table 5). Female sex, not being a smoker, being moderately active and the presence of a higher adherence to the MedDiet were inversely and significantly associated with inadequate intake of 4 or more micronutrients (i.e., these factors were associated with a lower probability of inadequate intake).

Finally, we fitted a multivariable linear regression model to compare nutrient density (g/1000 kcal) of 7 nutrients (fibre, vitamin A, B_9, D, E, calcium and magnesium) across categories of lifestyle and sociodemographic variables (Table 5). Female sex was significantly associated with a higher density of all assessed nutrients. The participants older than 70 years showed a higher nutritional density of fibre, but a lower density of vitamin A, D and E. Participants with lower educational level had lower density of fibre, vitamin B_9, and magnesium. And finally, a higher adherence to the MedDiet was significantly associated with higher nutrient density for all assessed nutrients except for vitamin E.

Table 3
Proportion of participants with an intake of macro and micronutrient below 2/3 DRIs by sex and age.

	DRI[b]	Men		*P* value[c]	Women		*P* value[c]
		≤70 y[a]	>70 y		≤70 y[a]	>70 y	
		% below 2/3 DRI			% below 2/3 DRI		
CHO	130 g/d	0.2	0	0.321	0.5	0.2	0.310
Protein	56–46 g/d	0.0	0.5	0.004	0.1	0	0.516
Dietary fibre	30–21 g/d	27.9	24.3	0.120	3.7	4.4	0.502
Vitamin A	900–700 μg/d	19.6	19.2	0.878	6.0	8.3	0.046
Vitamin B_1	1.2–1.1 mg/d	0.5	0.7	0.501	0.4	0.5	0.691
Vitamin B_9	400 μg/d	21.3	19.7	0.448	17.9	19.4	0.403
Vitamin B_{12}	2.4 μg/d	0.1	0.2	0.267	0	0.2	0.224
Vitamin C	90–75 mg/d	1.3	1.4	0.785	0.3	0.2	0.618
Vitamin D	15–20, 15–20 μg/d	84.2	98.1	<0.001	83.6	98.0	<0.001
Vitamin E	15 mg/d	49.0	49.8	0.773	52.0	52.0	<0.001
Calcium	1.0–1.2, 1.2–1.2 g/d	12.5	27.9	<0.001	25.7	24.8	0.677
Magnesium	420–420, 420–320 mg/d	8.3	9.6	0.350	1.3	1.5	0.721

[a] This age category includes 55–70 years for males, and 60–70 years for females.
[b] Dietary reference intake: where a single value is displayed, DRI is the same for all analysed groups. If 2 values are displayed, DRI differs between sexes and the first value is DRI for men and the second number is DRI for women. Where 4 value are displayed, DRI varies also for age groups; values are DRIs for men ≤70 y, men >70 y, women ≤70 y, and women >70 y respectively. Values are presented as %.
[c] Pearson's chi-square test was performed.

Please cite this article as: Cano-Ibáñez N et al., Diet quality and nutrient density in subjects with metabolic syndrome: Influence of socioeconomic status and lifestyle factors. A cross-sectional assessment in the PREDIMED-Plus study, Clinical Nutrition, https://doi.org/10.1016/j.clnu.2019.04.032

Table 4
Multivariable[a] logistic regression model for inadequate intake of 4 or more out 10 micronutrients according to baseline socioeconomic and lifestyle factors among men and women in the PREDIMED-Plus study participants analysed.

	≥4 inadequate intake (95% confidence interval)	Odds ratio (95% confidence interval)	*P* value
Sex			
Men	21.3 (20.0–22.6)	1 (ref)	
Women	11.7 (10.6–12.8)	0.33 (0.28–0.39)	<0.001
Age			
≤70 y[b]	16.5 (15.5–17.5)	1 (ref)	
>70 y	17.5 (15.1–19.9)	1.35 (1.12–1.62)	0.001
Smoking habitsrowhead			
Current smoker	22.4 (19.5–25.3)	1 (ref)	
Former smoker	18.6 (17.1–20.0)	0.76 (0.62–0.93)	0.008
Never smoker	13.1 (11.9–14.3)	0.68 (0.55–0.84)	<0.001
Physical activity			
Less active	17.4 (16.2–18.6)	1 (ref)	
Moderately active	14.1 (12.1–16.0)	0.79 (0.67–0.94)	0.007
Active	17.0 (15.0–19.0)	1.04 (0.89–1.23)	0.609
Educational level			
Tertiary	18.1 (16.1–20.1)	1 (ref)	
Secondary	18.2 (16.5–19.9)	0.98 (0.82–1.18)	0.861
Primary	15.1 (13.8–16.3)	0.89 (0.75–1.06)	0.186
Mediterranean diet			
Low adherence	22.4 (20.7–24.0)	1 (ref)	
Medium adherence	15.7 (14.3–17.1)	0.53 (0.46–0.61)	<0.001
High adherence	9.3 (7.9–10.8)	0.25 (0.21–0.30)	<0.001

[a] The multivariable model includes all variables presented in the table and is additionally adjusted for BMI (continuous, kg/m^2), marital status (4 categories), employment status (4 categories), living alone (yes/no), and total energy intake (continuous, kcal).
[b] This age category includes 55–70 years for males, and 60–70 years for females.

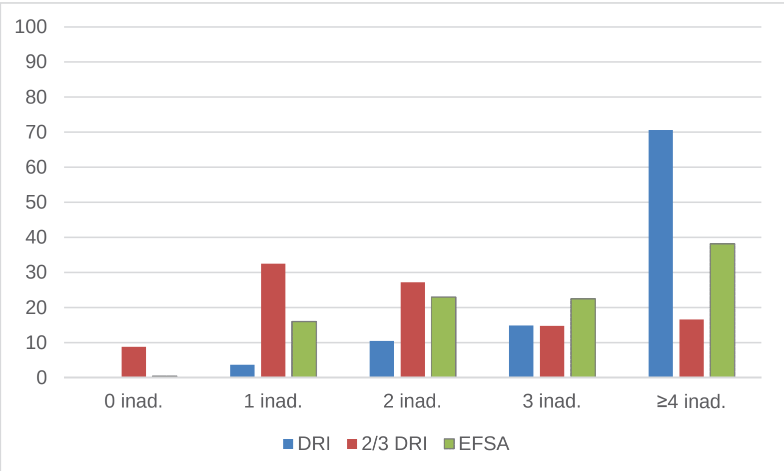


Fig. 2. Inadequate nutrient intake prevalence according to dietary recommendations (Americans DRI and EFSA AR/AI) in the PREDIMED-Plus study participants. Abbreviations: AI, adequate intake; AR, average requirements; DRI, dietary reference intake; EFSA, European Food Safety Agency.

4. Discussion

The current study analysed nutrient intake data in a large sample of adult participants (older than 55 years) with MetS in Spain. One of the main findings was that, for most of the nutrients analysed (fibre, vitamin A, B_1, B_9, B_{12}, C, D, E, calcium and magnesium), this population was exposed to dietary risks due to the inadequacies in terms of consumption of micronutrients. Regarding micronutrient density intake, our findings showed some clear differences in sociodemographic and lifestyle factors such as sex, age, adherence to MedDiet, smoking habits and physical activity for the majority of the micronutrients analysed.

The analysis of macronutrient intake in our population revealed that energy coming from total fat intake was well above the upper recommended limit (30%) by DRIs postulated by the Institute of Medicine for population with moderate physical activity [36] and European recommendations [30]. However, the most recent recommendations in the US do not set any limit for total fat intake [37]. Current dietary guidelines emphasize the need to improve the quality more than the quantity of dietary fat. In fact, the PREDIMED study showed the benefits of a relatively fat-rich MedDiet compared to a low-fat diet on major chronic diseases [38] and provided evidence of the beneficial effect of the replacement of SFAs with PUFAs or MUFAs on CVD risk [39]. In this sense, we found a fat profile with SFAs intake lower than 10% and PUFAs intake around 6%. In our study, protein intake was above recommended intake (15%) whereas CHO intake was below the updated dietary recommendations (45–65%) [30,36]. A study that evaluated the macronutrient distribution in Spanish population showed concurrent results, taking into account the distribution by sex and age of the assessed group [40].

Please cite this article as: Cano-Ibáñez N et al., Diet quality and nutrient density in subjects with metabolic syndrome: Influence of socioeconomic status and lifestyle factors. A cross-sectional assessment in the PREDIMED-Plus study, Clinical Nutrition, https://doi.org/10.1016/j.clnu.2019.04.032

Table 5
Coefficients of a multivariable linear regression model fitted to assess difference in nutrient density by several variables. The coefficients should be interpreted as differences (95% confidence interval) of mean nutrient density in g/1000 kcal.

	Total fibre	Vitamin A	Vitamin B_9	Vitamin D	Vitamin E	Calcium	Magnesium
	g/1000 kcal	µg/1000 kcal	µg/1000 kcal	µg/1000 kcal	mg/1000 kcal	mg/1000 kcal	mg/1000 kcal
Sex							
Men	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)
Women	1.3 (1.12, 1.46)	33.4 (16.71, 50.02)	15.2 (13.10, 17.32)	0.2 (0.09, 0.27)	0.3 (0.20, 0.34)	38.5 (31.16, 45.79)	12.2 (10.45, 13.87)
Age							
≤70 y[a]	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)
>70 y	0.3 (0.08, 0.48)	−21.9 (−41.09, −2.75)	1.2 (−1.22, 3.64)	−0.1 (−0.20, 0.01)	−0.08 (−0.16, −0.01)	4.0 (−4.46, 12.37)	−0.5 (−2.49, 1.45)
Smoking habits							
Current smoker	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)
Former smoker	0.4 (0.16, 0.60)	−12.8 (−34.04, 8.37)	1.9 (−0.80, 4.57)	0.1 (−0.01, 0.21)	0.04 (−0.04, 0.13)	10.4 (1.04, 19.66)	2.9 (0.73, 5.09)
Never smoker	0.5 (0.28, 0.74)	−2.9 (−25.16, 19.42)	3.5 (0.71, 6.35)	0.1 (0.01, 0.25)	0.07 (−0.02, 0.17)	19.6 (9.77, 29.34)	3.9 (1.59, 6.18)
Physical activity status							
Less active	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)
Moderately active	0.4 (0.22, 0.58)	5.7 (−11.72, 23.02)	4.1 (1.85, 6.25)	−0.1 (−0.10, 0.08)	0.08 (0.01, 0.16)	4.4 (−3.20, 12.05)	3.4 (1.61, 5.18)
Active	0.2 (−0.01, 0.34)	−16.7 (−33.53, 0.11)	2.0 (−0.17, 4.09)	−0.1 (−0.14, 0.04)	−0.04 (−0.12, 0.03)	−2.4 (−9.75, 5.02)	0.6 (−1.15, 2.31)
Educational status							
Tertiary	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)
Secondary	−0.1 (−0.29, −0.09)	0.9 (−17.79, 19.66)	−3.7 (−6.02, −1.28)	0.1 (−0.09, 0.11)	−0.07 (−0.14, 0.01)	−3.5 (−11.69, 4.76)	−2.8 (−4.71, −0.86)
Primary	−0.1 (−0.27, −0.10)	10.3 (−7.68, 28.26)	−2.9 (−5.17, −0.62)	−0.1 (−0.13, 0.06)	−0.01 (−0.09, 0.07)	−1.5 (−9.37, 6.41)	−4.7 (−6.59, −2.89)
Civil status							
Married	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)
Widowed	−0.3 (−0.53, −0.02)	14.6 (−11.84, 41.10)	−0.8 (−4.18, 2.52)	−0.1 (−0.24, 0.04)	0.1 (−0.10, 0.12)	0.4 (−11.18, 12.07)	−0.9 (−3.66, 1.78)
Divorced/separated	0.3 (0.05, 0.62)	20.3 (−7.23, 47.89)	1.7 (−1.82, 5.15)	−0.1 (−0.22, 0.08)	0.2 (0.06, 0.29)	6.0 (−6.14, 18.01)	4.1 (1.26, 6.92)
Others[b]	0.2 (0.13, 0.55)	−7.4 (−40.23, 25.39)	−0.7 (−4.82, 3.49)	−0.1 (−0.21, 0.13)	0.1 (−0.07, 0.21)	−10.2 (−24.64, 4.17)	1.2 (−2.18, 4.57)
Living alone							
Yes	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)
No	−0.2 (−0.50, 0.04)	22.7 (−3.58, 49.03)	1.1 (−2.20, 4.46)	−0.2 (−0.31, −0.03)	0.1 (−0.07, 0.15)	−3.9 (−15.43, 7.68)	−2.2 (−4.87, 0.54)
MedDiet adherence							
Low	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)
Medium	1.33 (1.17, 1.48)	35.4 (20.17, 50.60)	12.9 (11.01, 14.87)	0.38 (0.30, 0.46)	0.09 (−0.03, 0.16)	33.3 (26.58, 39.95)	15.2 (13.64, 16.77)
High	3.05 (2.86, 3.24)	66.5 (48.09, 84.83)	29.7 (27.41, 32.06)	0.75 (0.65, 0.84)	0.24 (−0.17, 0.32)	69.7 (61.67, 77.80)	33.4 (31.46, 35.23)

The multivariable model includes all variables presented above and is additionally adjusted for body mass index (continuous, kg/m^2), employment status (4 categories), carbohydrates intake (continuous), MUFA intake (continuous), PUFA intake (continuous), and SFA intake (continuous).
[a] This age category includes 55–70 years for males, and 60–70 years for females.
[b] Includes religious and single.

Among dietary factors, dietary fibre intake could play an interesting role in the treatment of overweight MetS patients [41]. In Spain, the average of dietary fibre intake of adult population has been estimated to be 17.8 g/day, and therefore does not meet adequate intake recommendations [42]. The mean intake of dietary fibre in our study was slightly over 25 g/d, the figure provided by AR [30] or 2/3 DRI [43] but still close to 1 in 4 men did not reach an adequate intake of dietary fibre.

The estimated total average energy intake in this study was higher than in other studies such as the ANIBES study [44]. However, despite the high energy intake, 16.6% of the participants in our study (21.3% of men and 11.7% of women) presented an inadequate intake of four out of the ten nutrients assessed. This figure increased (38.2%) when we took into account average Requirement/Adequate Intakes from the European Food Safety Authority [30]. Although malnutrition in developed countries is scarce, some reviews of published data indicate a high prevalence of inadequate micronutrients intake across European countries, especially in non-Mediterranean elderly population [45,46] but similar to those found in aged Spanish population [47].

High adherence to the MedDiet pattern was related, as expected, to a good adequacy of micronutrients intake [48]. This association could be explained by the fact that the diet of these overweight patients is high in energy density but poor in nutritional quality, leading to several deficits in nutrient intake. This relationship has also been noted by other authors, who have described a greater number of nutritional deficiencies in obese populations in comparison with normal-weight populations [49,50].

Recent studies have demonstrated that populations who meet the recommendations for magnesium and calcium have reduced risk of MetS [51]. In our sample, around a 9.0% of men showed an inadequate intake of magnesium. Other studies in Spain and also in some non-Mediterranean countries showed lower intake of magnesium compared to our results [52,53]. These disparities could be attributed to the use of different tools to assess dietary intake, leading to a potential underestimation of micronutrient intake. The same circumstance is found for calcium consumption: mean calcium intake was lower than recommended for an aged population, with the prevalence of inadequate calcium intake being higher in older men (27.9%) than in younger men or in women. In other studies that evaluated the intake of calcium in older adults in Europe, the mean intakes were similar to our findings [54].

We observed an elevated percentage of inadequate intakes of some fat-soluble vitamins such as vitamins A, D and E. The mean intake of vitamin A or vitamin E was higher than previously reported in the Spanish population [10]. However, as shown in Table 3

Please cite this article as: Cano-Ibáñez N et al., Diet quality and nutrient density in subjects with metabolic syndrome: Influence of socioeconomic status and lifestyle factors. A cross-sectional assessment in the PREDIMED-Plus study, Clinical Nutrition, https://doi.org/10.1016/j.clnu.2019.04.032

a considerable proportion of the subjects presented a deficient intake of vitamin A, D and E. These results are similar to those found in other studies which showed low intake of these vitamins in all or most of the elderly subjects analysed [55–58]. In addition to the traditional role played in bone health, low concentrations of plasma vitamin D have also been linked to a higher risk of developing MetS [59]. In Spain, the lack of an appropriate intake of these fat-soluble vitamins in obese population could be explained by a frequency of consumption of dairy products below the recommended by dietary guidelines [40].

MetS is characterized by a high oxidative stress. In this sense, a low intake of antioxidant nutrients could worsen the evolution of this disease [60]. Whereas some other authors have suggested a high risk of inadequate intake of vitamin C, especially in the European elderly population [46], we found that vitamin C intake was adequate in more than 90% of our participants, probably because of a high intake of fruits and vegetables in Spain compared to other European countries [61,62].

Inadequate nutrient intake could be related to a decrease in total energy intake by ageing or by a loss weight diet [63]. In order to analyse changes in nutrient intake we estimated nutrient density dividing by total energy intake [64]. We found a decrease in energy consumption with age in both sexes; however, nutrient density was higher in elderly ages, especially in women, compared to younger adults. The prevalence of nutrient deficits reported by Schröder et al. [47] was higher than the figure among our participants, but they included younger people. We also penalized our estimation considering that intake was adequate when it was above two thirds of the DRI recommendation [28].

A determinant of low nutrient density in our population was male sex. Better nutrient density and less prevalence of inadequacy of nutrients intake was observed in women compared with men. Findings from other studies suggest that a healthy food choice may be mediated by sex. In this sense women have a higher awareness and better knowledge of nutrition than men, which could be due to the traditional role that women have played as housekeepers and caregivers [65,66].

Lifestyle behaviours, in particular smoking habit (being a smoker) and physical activity (being less active) were inversely associated to nutrient density in our study. Alkerwi et al. [67] also reported an inverse association between diet quality and tobacco consumption in the Luxembourg adult population. A recent study has suggested that the dietary nutrient density, such as fibre intake, increases with energy intake but does not depend on smoking habits and physical activity [68]. However, our findings showed that both factors were significantly related to the density of dietary fibre and the other micronutrients assessed.

Evidence indicates that socioeconomic status has an effect on diet quality [69]. On the one hand, marital status has been reported as a strong predictor of a higher quality diet: being married or cohabitation has been directly associated with a major nutrient density intake [70,71]. Loneliness, especially among men, is linked to a negative state and a motivation to adopt a healthy diet. This is probably influenced by traditional gender roles and could be related to household disruption after death or divorce [72]. However, we have not found a significant association between this factor and nutrient density (shown in Table 5). We need take into account that in the PREDIMED-Plus study the most of the participants were married and not living alone.

On the other hand, a higher educational level was a significant predictor of better micronutrient density. This result is similar to the findings of other studies [73,74]. This could be mediated by a higher nutritional knowledge leading to better food choices with higher density of nutrients. The nutritional knowledge may be easily modified with a correct nutritional intervention. However, educational level is often a proxy for socioeconomic status, which may also mediate food choices.

MedDiet adherence was strongly related to nutrient density for most of the micronutrient analysed. This fact is consistent with other studies [11] and supports the promotion of the traditional MedDiet to improve adequate nutrients intake.

Our study has some limitations. First, the study sample is not representative of the general population. Due to the trial inclusion and exclusion criteria, only older adults with MetS were included. Second, it is probable that other possible determinants of dietary quality have not been evaluated in this study. Nevertheless, the most prominent socioeconomic and lifestyle factors in the literature have been analysed. Third, the cross-sectional design of the study precludes causal inference. Irrespective of the direction of association, the determinants included in the analysis have a high potential to improve the quality of the diet in the older adult population and allows us to detect groups of people more prone to nutrient deficiencies. Fourth, we used a FFQ to measure dietary intakes. Despite the FFQ used having been validated in adult Spanish population and has a good reproducibility and validity [75], it might not be the ideal tool to measure micronutrient intake [76]. For this reason, we considered that there was an inadequacy only when the intake did not reach 2/3 of the DRIs, correcting the possible bias introduced by the FFQ and assuming in any case that the inadequate micronutrient intake should be superior to the figures which we estimated. When we used AR provided by EFSA [30] we obtained very similar results. Fifth, it is important to consider the fact that NCDs, besides pharmacological treatments, produce changes in dietary habits and in nutrient metabolism, which have not been assessed. Finally, we recognise that differences in selection criteria for age in men (55–75 years old) and women (60–75 years old) could explain differences between sexes. However, excluding males 55–59 years we found the same results for sex differences. Nonetheless, this study focuses on MetS rather than on age.

Some strengths of our study are the large sample size ($n = 6646$), the use of a standardized protocol which reduces information bias about food intake and socioeconomic and lifestyles variables as well as the inclusion of community-dwelling aged population and the vast amount of baseline information collected in a large ongoing primary prevention trial.

In conclusion, despite the moderate adherence to the MedDiet of participants in the PREDIMED-Plus trial at baseline, there was a high prevalence of inadequate intake of several nutrients, particularly vitamins A, D, E, B_9 and calcium. Nutrient density intake was related to sex (higher for women). A better lifestyle (not smoking, physical activity and MedDiet adherence) was found to be associated with better nutrient density intake. Our findings highlight the importance of focussing on nutritional education in those vulnerable population, taking into account nutrient requirements.

Statement of authorship

N.C.-I., A.G., M.R.-C., D.C., J.S.-S., H.S, E.N.-M., D.R., J.A.M., F.J.B.-L., J.L.-M., R.E., B.R.-G., A.A.G., J.A.T., F.T., L.S.-M., V.M., J.L., C.V., X.P., J.V., L.D., J.J.G., P.M., E.R., R.F.-C., R.F.-C., A.D.-L., M.D.-Z., I.C., J.K., I.A., P.B.-C., J.B., M.F., M.A.M.-G., and A.B.-C., collected all the data from the PREDIMED-Plus trial. N.C.-I., A.G., and A.B.-C. designed the study; performed the analysis; and wrote the first draft of the manuscript. All authors contributed to the editing of the manuscript. All authors approved the final version of the manuscript.

Please cite this article as: Cano-Ibáñez N et al., Diet quality and nutrient density in subjects with metabolic syndrome: Influence of socioeconomic status and lifestyle factors. A cross-sectional assessment in the PREDIMED-Plus study, Clinical Nutrition, https://doi.org/10.1016/j.clnu.2019.04.032

Funding sources

The PREDIMED-Plus trial was supported by the European Research Council (Advanced Research Grant 2013–2018; 340918) grant to Miguel Ángel Martínez-González and by the official funding agency for biomedical research of the Spanish Government, ISCIII through the Fondo de Investigación para la Salud (FIS), which is co-funded by the European Regional Development Fund (four coordinated FIS projects led by Jordi Salas-Salvadó and Josep 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, 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. The Especial Action Project entitled: "Implementación y Evaluación de una intervención intensiva sobre la actividad física Cohorte PREDIMED-Plus" grant to Jordi Salas-Salvadó, the Recercaixa grant to Jordi Salas-Salvadó (2013ACUP00194), the grant from the Consejería de Salud de la Junta de Andalucía (PI0458/2013; PS0358/2016), the PROMETEO/2017/017 grant from the Generalitat Valenciana, the SEMERGEN grant, and CIBEROBN and FEDER funds (CB06/03), ISCIII. International Nut&Dried Fruit Council- FESNAD Nº201302: Miguel Ángel Martínez-González. J. K. is supported by the "FOLIUM" program within the FUTURMed project. Talent for the medicine within the future from the Fundació Institut d'Investigació Sanitària Illes Balears. This call is co-financed at 50% with charge to the Operational Program FSE 2014–2020 of the Balearic Islands. None of the funding sources took part in the design, collection, analysis or interpretation of the data, or in the decision to submit the manuscript for publication. N.C–I holds a grant from the Ministry of Education of Spain (FPU14/03630). The corresponding author had full access to all the data in the study and had final responsibility to submit for publication.

Conflicts of interest

J.S.-S. reports serving on the board of and receiving grant support through his institution from International Nut and Dried Fruit Council; receiving consulting personal fees from Danone, Font Vella Lanjarón, Nuts for Life and Eroski; and receiving grant support through his institution from Nut and Dried Fruit Foundation and Eroski. E.R., reports grants, non-financial support and other fees from California Walnut Commission and Alexion; personal fees and non-financial support from Merck, Sharp & Dohme; personal fees, non-financial support and other fees from Aegerion and Ferrer International; grants and personal fees from Sanofi Aventis; grants from Amgen and Pfizer and; personal fees from Akcea, outside of the submitted work. X.P., reports serving on the board of and receiving consulting personal fees from Sanofi Aventis, Amgen and Abbott laboratories; receiving lecture personal fees from Esteve, Lacer and Rubio laboratories. L.D. reports grants from Fundación Cerveza y Salud. J.J.G. reports receiving grants from the Diputación Provincial de Jaén and the Fundación Caja Rural de Jaén. All other authors declare no competing interests.

Acknowledgements

The principal author (N.C.-I), wish to express her gratitude to the Ministry of Education of Spain for the grant received (FPU14/3630).

The authors wish to thank Dr. Ingrid de Ruiter, PhD, for English language and editing support.

Steering committee: J. Salas-Salvadó (Coordinator), M.A. Martínez-González, M. Fitó, E. Ros, FJ. Tinahones, D. Corella and R. Estruch.

Executive Committee: J. Salas-Salvadó, M.A. Martínez-González, D. Corella, M. Fitó, J. Vioque, D. Romaguera, J.A Martínez, J. Wärnberg, J. Lopez-Miranda, R. Estruch, A. Bueno-Cavanillas, Á.M. Alonso-Gómez, J.A. Tur, FJ. Tinahones, L. Serra-Majem, V. Martin, J. Lapetra, C. Vázquez, X. Pinto, J. Vidal, L. Daimiel, M. Delgado-Rodríguez, M.A. Rubio and E. Ros.

Dietary and Lifestyle Intervention Committee: J. Salas-Salvadó (chair), M.A. Martínez-González, M. Fitó and R. Estruch; ***Dietary Intervention***: J. Salas-Salvadó (chair), N. Babio, E. Ros, A. Sánchez-Tainta; ***Physical Exercise***: M. Fitó (chair), H. Schröder, A. Marcos, D. Corella, J. Warnberg; ***Behavioural support***: R. Estruch (chair), F. Fernández-Aranda, C. Botella and J. Salas-Salvadó.

Clinical Event Ascertainment Committee: F. Arós (Chair), M. Aldamiz, A. Alonso-Gómez, L. Forga, A. García-Layana, J. Portu, J. Timiraos, A. González-Pinto, I. Zorrilla, M. Martínez-Kareaga, P. Seoane.

Chair: Dr. Fernando Arós
Cardiology: Dr. Angel Alonso-Gómez; Dr. Fernando Arós
Neurology: Dr. Juan Timiraos
Internal Medicine: Dr. Mikel Aldamiz; Dr. Joseba Portu
Endocrinology: Dr. Lluis Forga
Ophthalmology: Dr. Alfredo García-Layana
Psychiatry: Dr. Ana González Pinto; Dr. Iñaki Zorrilla
Oncology: Dr. Mireia Martínez; Dr. Patricia Seoane

Independent Data and Safety Monitoring Board: M.J. Stampfer (Harvard School of Public Health), J. Sabate (Loma Linda University), A. Astrup (Copenhagen University), F. Fernandez-Aviles (Universidad Complutense of Madrid), X. Pi-Sunyer (Columbia University).

Support groups: C. Botella, F. Fernandez-Aranda, R. Lamuela, A. Marcos, M.P. Portillo, E. Ros, G. Sáez, F. Arós, E. Gómez-Gracia

Rovira i Virgili University, Department of Biochemistry and Biotechnology, Human Nutrition Unit, University Hospital of Sant Joan de Reus, Pere Virgili Institute for Health Research, Reus, Spain: R. Pedret Llaberia, R. Gonzalez, R. Sagarra Álamo, F. París Palleja, J. Balsells, J.M. Roca, T. Basora Gallisa, J. Vizcaino, P. Llobet Alpizarte, C. Anguera Perpiñá, M. Llauradó Vernet, C. Caballero, M. Garcia Barco, M.D. Morán Martínez, J. García Rosselló, A. Del Pozo, C. Poblet Calaf, P. Arcelin Zabal, X. Floresví, M. Ciutat Benet, A. Palau Galindo, J.J. Cabré Vila, F. Dolz Andrés, M. Soler, M. Gracia Vidal, J. Vilalta J. Boj Casajuana, M. Ricard, F. Saiz, A. Isach, M. Sanchez Marin Martinez, E. Granado Font, C, Lucena Luque, C. Mestres Sola, M. Bulló, N. Babio, N. Becerra-Tomás, G. Mestres, J. Basora, G. Mena-Sánchez, L. Barrubés Piñol, M. Gil Segura, C. Papandreou, N. Rosique-Esteban, S. Chig, I. Abellán Cano, V. Ruiz García, A. Salas-Huetos, I. Paz-Graniel, L. Sánchez Niembro, P. Hernandez-Alonso, S. Canudas, L. Camacho-Barcia, J. García-Gavilán, A. Díaz-López.

Department of Preventive Medicine and Public Health, University of Navarra-Navarra Institute for Health Research (IdiSNA), Pamplona, Spain: E. Toledo, P. Buil-Cosiales, Z. Vázquez-Ruiz, C. Razquin, M. Bes-Rastrollo, A. Gea, A. Sanchez Tainta, B. SanJulian Aranguren, E. Goñi, L. Goñi, M.J. Cobo, A. Rico-Campa, F.J. Basterra Gortari, A. Garcia Arellano, J. Diez-Espino, O. Lecea-Juarez, J. Carlos Cenoz-Osinaga, I. Alvarez-Alvarez, M.C. Sayon-Orea, C.I. Fernandez-Lázaro, L. Ruiz-Estigarribia, J. Bartolome-Resano, E. Toledo, E. Lozano-Oloriz, B. Cano-Valles, S. Eguaras, E. Pascual Roquet-Jalmar, I. Galilea-Zabalza, H. Lancova, R. Ramallal, M.L. Garcia-Perez, V. Estremera-Urabayen, M.J. Ariz-Arnedo, C. Hijos-Larraz, C. Fernandez-Alfaro, B. Iñigo-Martinez, R. Villanueva Moreno, S. Martin-Almendros, L. Barandiaran-Bengoetxea, C. Fuertes-Goñi, A. Lezaun-Indurain, M.J. Guruchaga-Arcelus, O. Olmedo-Cruz, L. Escriche-Erviti, R. Ansorena-Ros, R.

Sanmatin-Zabaleta, J. Apalategi-Lasa, J. Villanueva-Telleria, M.M. Hernández-Espinosa, L. Herrera-Valdez, L. Dorronsoro-Dorronsoro, Lourdes Echeverria-Lizarraga (†), J.A. Cabeza-Beunza, P. Fernández-Urretavizcaya, P. Gascó-García, C. Royo-Jimenez, J. Moran-Pí, F. Salazar-Fernández, F.J. Chasco-Ros, F. Cortés-Ugalde, J.J. Jurio-Burgui, P. Pascual-Pascual, A.I. Rodríguez-Ezpeleta, M. Esparza-Cáceres, C. Arroyo-Azpa, M. Rodríguez-Sanz de Galdeano, T. Forcen-Alonso, M. Armendariz-Marcotegui, A. Brugos-Larumbe, A. Arillo, B. López-Aisa.

Department of Preventive Medicine, University of Valencia, University Jaume I, Conselleria de Sanitat de la Generalitat Valenciana, Valencia, Spain: J.I. González, J.V. Sorlí, O. Portolés, R. Fernández-Carrión, C. Ortega-Azorín, R. Barragán, E.M. Asensio, O. Coltell, C. Sáiz, R. Osma, E. Férriz, I. González-Monje, F. Giménez-Fernández, L. Quiles, P. Carrasco, P. Guillem-Saiz, A. Carratalá-Calvo, C. Valero-Barceló, F. Antón, C. Mir, S. Sánchez-Navarro, J. Navas, I. González-Gallego, L. Bort-Llorca, L. Pérez-Ollero, M. Giner-Valero, R. Monfort-Sáez, J. Nadal-Sayol, V. Pascual-Fuster, M. Martínez-Pérez, C. Riera, M.V. Belda, A. Medina, E. Miralles, M.J. Ramírez-Esplugues, M. Rojo-Furió, G. Mattingley, M.A. Delgado, M.A. Pages, Y. Riofrío, L. Abuomar, N. Blasco-Lafarga, R. Tosca, L. Lizán, A.M. Valcarce, M.D. Medina, R. Monfort, S. de Valcárcel, N. Tormo, O. Felipe-Román, S. Lafuente, E.I. Navío, G. Aldana, J.V. Crespo, J.L. Llosa, L. González-García, R. Raga-Marí.

Cardiovascular Risk and Nutrition Research Group, Endocrinology Service, Neurosciences Programme, Clinical Research Unit at the Hospital del Mar Medical Research Institute (IMIM), Barcelona. Medicine Departament, Universitat Autònoma de Barcelona, Barcelona, Spain: M. Fitó, O. Castañer, M.A. Muñoz, M.D. Zomeño, A. Hernaéz, L. Torres, M. Quifer, R. Llimona, G Freixer, KA. Pérez-Vega, M. Farràs, R. Elosua, J. Vila, I. Subirana, S. Pérez, A. Goday, J.J. Chillaron Jordan, J.A. Flores Lerroux, D. Benaiges Boix, G. Llauradó, M. Farré, E. Menoyo, A. Aldea-Perona, M. Pérez-Otero, D. Muñoz-Aguayo, S. Gaixas, G. Blanchart, A. Sanllorente, M. Soria, J. Valussi, A. Cuenca, L. Forcano, A. Pastor, A. Boronat, S. Tello, M. Cabañero, L. Franco, H. Schröder, R. De la Torre, C. Medrano, J. Bayó, M.T. García, V. Robledo, P. Babi, E. Canals, N. Soldevila, L. Carrés, C. Roca, M.S. Comas, G. Gasulla, X. Herraiz, A. Martínez, E. Vinyoles, J.M. Verdú, M. Masague Aguade, E. Baltasar Massip, M. López Grau, M. Mengual, V. Moldon, M. Vila Vergaz, R. Cabanes Gómez, Ciurana, M. Gili Riu, A. Palomeras Vidal, F Peñas F, A Raya, M.A. Sebastian, M. Valls, J. Guerrero, M. Marne, E. Minguella, M. Montenegro, A. Sala, M.R. Senan, N. Talens, N. Vera.

Nutritional Epidemiology Unit, Miguel Hernandez University, ISABIAL-FISABIO, Alicante, Spain: J. Vioque, M. García-de-la-Hera, E.M. Navarrete-Muñoz, S. Gonzalez-Palacios, L. Torres-Collado, L. Compañ-Gabucio, A. Oncina-Canovas, L. Notario-Barandiaran, D. Orozco-Beltran, S. Pertusa Martínez, A. Asensio, I. Candela-García, J.M. Zazo, C. Gisbert Sellés, N. Fernándis-Brufal, J. Román Maciá, C. Sánchez Botella, M. García Muñoz, C. Barceló, M.C. Altozano-Rodado, N. Iranzo García, M.C. Martínez Vergara, M.A. Sempere Pascual, S.J. Miralles Gisbert, A. González Botella, C.M. López García, R. Valls Enguix, N. Gómez Bellvert, I. López Aguilera, R. Lloret Macián, A. Pastor Morell, E. Alonso Bartolomé, J.J. Ballester Baixauli, M.T. Cano Sánchez, B.E. Ayús Rojo, E.P. Cases Pérez, C. Tercero Maciá, L.A. Mira Castejón, I.A. García García, M. Jordá Ballesta, C. Pastor Polo, E. Puig Agulló.

Hospital Son Espases (HUSE) and Institute for Health Research Illes Balears (IdISBa), Palma de Mallorca, Spain: M. Fiol, M. Moñino, A. Colom, J. Konieczna, M. Morey, R. Zamanillo, A.M. Galmés-Panadés, V. Pereira, M.A. Martín, A. Yáñez, J. Llobera, J. Ripoll, R. Prieto, F. Grases, A. Costa, C. Fernández-Palomeque, E. Fortuny, M. Noris, S. Munuera, F. Tomás, F. Fiol, A. Jover, J.M. Janer, C. Vallespir, I. Mattei, N. Feuerbach, M. del Mar Sureda, S. Vega, L. Quintana, A. Fiol, M. Amador, S. González, J. Coll, A. Moyá, T. Piqué Sistac, M.D. Sanmartín Fernández, M.C. Piña Valls, M.A. Llorente San Martín, J. Pou Bordoy.

Department of Nutrition, Food Sciences, and Physiology, Center for Nutrition Research, University of Navarra, Pamplona, Spain: I. Abete, I. Cantero, C. Cristobo, I. Ibero-Baraibar, M. Zulet, J. Ágreda-Peiró, M.D. Lezáun-Burgui, N. Goñi-Ruiz, R. Bartolomé-Resano, E. Cano-Cáceres, T. Elcarte-López, E. Echarte-Osacain, B. Pérez-Sanz, I. Blanco-Platero, A. Andueza- Azcárate, A. Gimeno-Aznar, E. Ursúa-Sesma, B. Ojeda-Bilbao, J. Martinez-Jarauta, L. Ugalde-Sarasa, B. Rípodas-Echarte, M.V. Güeto-Rubio, C. Napal-Lecumberri, MD Martínez-Mazo, E Arina-Vergara, A. Parra-Osés, F. Artal-Moneva, F. Bárcena-Amigo, F. Calle-Irastoza, J. Abad-Vicente, J.I. Armendáriz-Artola, P. Iñigo-Cibrian, J. Escribano-Jarauta, J. Ulibarri-delportillo, B. Churio-Beraza, Y. Monzón-Martínez, E. Madoz-Zubillaga, C. Arroniz.

University of Málaga and Institute of Biomedical Research in Malaga (IBIMA), Málaga, Spain: F.J. Barón-López, J.C. Fernández García, N. Pérez-Farinós, N. Moreno-Morales, M. del C. Rodríguez-Martínez, J. Pérez-López, J.C. Benavente-Marín, E. Crespo Oliva, E. Contreras Fernández, F.J. Carmona González, R. Carabaño Moral, S. Torres Moreno, M.V. Martín Ruíz, M. Alcalá Cornide, V. Fuentes Gómez.

Lipids and Atherosclerosis Unit, Department of Internal Medicine, Maimonides Biomedical Research Institute of Cordoba (IMIBIC), Reina Sofia University Hospital, University of Cordoba, Cordoba, Spain: J. López-Miranda, A. Garcia-Rios, J. Criado García, A.I. Jiménez Morales, A. Ortiz Morales, J.D. Torres Peña, F.J. Gómez Delgado, J.F. Alcalá, A. León Acuña, A.P. Arenas Larriva, F. Rodríguez Cantalejo, J. Caballero Villaraso, I. Nieto Eugenio, P. Coronado Carvajal, M.C del Campo Molina, P.J. Peña Orihuela, I. Perez Corral, G. Quintana Navarro.

Department of Internal Medicine, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Hospital Clínic, University of Barcelona, Barcelona, Spain: R. Casas, M. Domenech, C. Viñas, S. Castro-Barquero, A.M. Ruiz-León, R. Losno, L. Tarés, A. Jordán, R. Soriano, M. Camafort, C. Sierra, E. Sacanella, A. Sala-Vila, J. M. Cots, I. Sarroca, M. García, N. Bermúdez, A. Pérez, I. Duaso, A. de la Arada, R. Hernández, C. Simón, M.A. de la Poza, I. Gil, M. Vila, C. Iglesias, N. Assens, M. Amatller, LL. Rams, T. Benet, G. Fernández, J. Teruel, A. Azorin, M. Cubells, D. López, J.M. Llovet, M.L. Gómez, P. Climente, L. de Paula, J. Soto, C. Carbonell, C. Llor, X. Abat, A. Cama, M. Fortuny, C. Domingo, A. I. Liberal, T. Martínez, E. Yañez, M. J. Nieto, A. Pérez, E. Lloret, C. Carrazoni, A. M. Belles, C. Olmos, M. Ramentol, M. J. Capell, R. Casas, I. Giner, A. Muñoz, R. Martín, E. Moron, A. Bonillo, G. Sánchez, C. Calbó, J. Pous, M. Massip, Y. García, M.C. Massagué, R. Ibañez, J. Llaona, T. Vidal, N. Vizcay, E. Segura, C. Galindo, M. Moreno, M. Caubet, J. Altirriba, G. Fluxà, P. Toribio, E. Torrent, J. J. Anton, A. Viaplana, G. Vieytes, N. Duch, A. Pereira, M. A. Moreno, A. Pérez, E. Sant, J. Gené, H. Calvillo, F. Pont, M. Puig, M. Casasayas, A. Garrich, E. Senar, A. Martínez, I. Boix, E. Sequeira, V. Aragunde, S. Riera, M. Salgado, M. Fuentes, E. Martín, A. Ubieto, F. Pallarés, C. Sala, A. Abilla, S. Moreno, E. Mayor, T. Colom, A. Gaspar, A. Gómez, L. Palacios, R. Garrigosa.

Departament of Preventive Medicine and Public Health, University of Granada, Granada, Spain: N. Cano Ibáñez, L. García Molina, B. Riquelme Gallego, A. López Maldonado, E.M. Garrido, A. Baena Dominguez, F. García Jiménez, E. Thomas Carazo, A. Jesús Turnes González, F. González Jiménez, F. Padilla Ruiz, J. Machado Santiago, M.D. Martínez Bellón, A. Pueyos Sánchez, L. Arribas Mir, R. Rodríguez Tapioles, F. Dorador Atienza, L. Baena Camus, C. Osorio Martos, D. Rueda Lozano, M. López Alcázar, F. Ramos Díaz, M. Cruz Rosales Sierra, P. Alguacil Cubero, A. López Rodriguez, F. Guerrero García, J. Tormo Molina, F. Ruiz Rodríguez.

OSI ARABA, University Hospital Araba, Vitoria, Spain: I. Salaverria, A. Alonso-Gómez, M.C. Belló, L. Tojal, L. Goicolea, C. Sorto, A

Please cite this article as: Cano-Ibáñez N et al., Diet quality and nutrient density in subjects with metabolic syndrome: Influence of socioeconomic status and lifestyle factors. A cross-sectional assessment in the PREDIMED-Plus study, Clinical Nutrition, https://doi.org/10.1016/j.clnu.2019.04.032

Goikoetxea, A. Casi Casanellas, M.L. Arnal Otero, J. Ortueta Martínez De Arbulo, J. Vinagre Morgado, J. Romeo Ollora, J. Urraca, M.I. Sarriegui Carrera, F.J. Toribio, E. Magán, A. Rodríguez, S. Castro Madrid, M.T. Gómez Merino, M. Rodríguez Jiménez, M. Gutiérrez Jodra, B. López Alonso, J. Iturralde Iriso, C. Pascual Romero, A. Izquierdo De La Guerra.

Research Group on Community Nutrition & Oxidative Stress, University of Balearic Islands, Palma de Mallorca, Spain: M. Abbate, E. Angullo, E. Argelich, M.M. Bibiloni, C. Bouzas, X. Capó, S. Carreres, L. Gallardo, J.M. Gámez, B. García, C. García, A. Julibert, C. Gómez, I. Llompart, A. Martorell, C.M. Mascaró, D. Mateos, M, Monserrat, S. Montemayor, A. Pons, A. Pouso, J. Ramos, V. Ramos, T. Ripoll, T. Rodríguez, L. Sanz, A. Sureda, S. Tejada, L. Ugarriza.

Virgen de la Victoria Hospital, University of Málaga, Málaga, Spain: M.R. Bernal López, M. Macías González, J. Ruiz Nava, J.C. Fernández García, A. Muñoz Garach, A. Vilches Pérez, A. González Banderas, A.V. Alarcón-Martín, M. García Ruiz de Mier, J. Alcaide Torres, A. Vargas Candela, M. León Fernández, R. Hernández Robles, S. Santamaría Fernández, J.M. Marín.

University of Las Palmas de Gran Canaria, Las Palmas, Spain: J. Álvarez-Pérez, E.M. Díaz Benítez, F. Díaz-Collado, A. Sánchez-Villegas, J. Pérez-Cabrera, L.T. Casañas-Quintana, R.B. García-Guerra, I. Bautista-Castaño, C. Ruano-Rodríguez, F. Sarmiento de la Fe, J.A. García-Pastor, B. Macías-Gutiérrez, I. Falcón-Sanabria, C. Simón-García, A.J. Santana-Santana, J.B. Álvarez-Álvarez, B.V. Díaz-González, J.M. Castillo Anzalas, R.E. Sosa-Also, J. Medina-Ponce.

Biomedicine Institute (IBIOMED); University of León, and Primary Health Care Management of León (Sacyl), León, Spain: S. Abajo Olea, A. Adlbi Sibai, A. Aguado Arconada, L. Álvarez, E. Carriedo Ule, M. Escobar Fernández, J.I. Ferradal García, J.P. Fernández Vázquez, M. García González, C. González Donquiles, C. González Quintana, F. González Rivero, M. Lavinia Popescu, J.I. López Gil, J. López de la Iglesia, A. Marcos Delgado, C. Merino Acevedo, S. Reguero Celada, M. Rodríguez Bul, L. Vilorio-Marqués.

Department of Family Medicine, Distrito Sanitario Atención Primaria Sevilla, Sevilla, Spain: J.M. Santos-Lozano, L. Miró-Moriano, C. Domínguez-Espinaco, S. Vaquero-Díaz, F.J. García-Corte, A. Santos-Calonge, C. Toro-Cortés, N. Pelegrina-López, V. Urbano-Fernández, M. Ortega-Calvo, J. Lozano-Rodríguez, I. Rivera-Benítez, M. Caballero-Valderrama, P. Iglesias-Bonilla, P. Román-Torres, Y. Corchado-Albalat, L. Mellado-Martín.

Department of Endocrinology and Nutrition, Hospital Fundación Jimenez Díaz. Instituto de Investigaciones Biomédicas IISFJD. University Autonoma, Madrid, Spain: A.I. de Cos, S. Gutierrez, S. Artola, A. Galdon, I. Gonzalo.

Lipids and Vascular Risk Unit, Internal Medicine, University Hospital of Bellvitge- IDIBELL, Hospitalet de Llobregat, Barcelona, Spain: X. Pintó, A. Galera, M. Gimenez-Gracia, E. de la Cruz, R. Figueras, M. Poch, R. Freixedas, F. Trias, I. Sarasa, M. Fanlo-Maresma, H. Lafuente, M. Liceran, A. Rodriguez-Sanchez, C. Pallarols, E. Gómez-Sanchez, V. Esteve-Luque, J. Monedero, X. Corbella, E. Corbella.

Department of Endocrinology, IDIBAPS, Hospital Clinic, University of Barcelona, Barcelona, Spain: A. Altés, I. Vinagre, C. Mestre, J. Viaplana, M. Serra, J. Vera, T. Freitas, E. Ortega, I. Pla, R. Olbeyra.

Nutritional Genomics and Epigenomics Group, Institute IMDEA-Food, CEI UAM+CSIC, Madrid, Spain: J.M. Ordovás, V. Micó, L. Berninches, M.J. Concejo, J. Muñoz, M. Adrián, Y. de la Fuente, C. Albertos, E. Villahoz, M.L. Cornejo, C. Cuesta. Montero A., Valdés, MC.

Division of Preventive Medicine, University of Jaén, Jaén, Spain: M. Delgado-Rodríguez, J.J. Gaforio, S. Moraleda, N. Liétor, J.I. Peis, T. Ureña, M. Rueda, M.I. Ballesta.

Department of Endocrinology and Nutrition, Hospital Clínico San Carlos, Instituto de Investigación Sanitaria del Hospital Clínico San Carlos (IdISSC), Madrid, España (Spain para internacionales: C. Moreno Lopera, C. Aragoneses Isabel, M.A. Sirur Flores, M. Ceballos de Diego, T. Bescos Cáceres, Y. Peña Cereceda, M. Martínez Abad, R. Cabrera Vélez, M. González Cerrajero, M.A. Rubio Herrera, M. Torrego Ellacuría, A. Barabash Bustelo, M. Ortiz Ramos, A. Larrad Sainz.

Department of Basic and Clinical Psychology and Psychobiology, University Jaume I, Castellón de la Plana, Spain: R. Baños, A. García-Palacios.

Oxidative Pathology Unit. Department of Biochemistry and Molecular Biology, School of Medicine-INCLIVA, Service of Clinical Analyses, University Hospital Doctor Peset, Valencia, Spain. University of Valencia, Valencia Spain: G. Sáez Tormo (Sáez GT), N. Estañ-Capell, A. Iradi Casal, L. Monzó Beltrán, C. Bañuls Morant, E. Alonso Iglesias, D. Acevedo León, A. Hernando Espinilla, A. Mora Herranz, S. Alcover Sáez, J. Murado Pardo, J. Ventura Gayete, ML Santaolaria Ayora, A. Carbonell Moncho, M, Tortajada-Girbés.

Department of Preventive Medicine, University of Malaga, Malaga, Spain: J. Fernández-Crehuet Navajas, M. Gutiérrez Bedmar, A. García Rodriguez, A. Mariscal Larrubia, M. Carnero Varo, C. Muñoz Bravo.

Department of Psychiatry, University Hospital of Bellvitge, Barcelona, Spain:

F. Fernández-Aranda, S. Jiménez-Murcia, N. Mallorqui-Bagué, R. Granero, Z. Agüera, M. Lozano-Madrid.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnu.2019.04.032.

References

[1] Haro JM, Tyrovolas S, Garin N, Diaz-Torne C, Carmona L, Sanchez-Riera L, et al. The burden of disease in Spain: results from the global burden of disease study 2010. BMC Med 2014;12(1).

[2] Roberts CK, Barnard RJ. Effects of exercise and diet on chronic disease. J Appl Physiol 2005;98(1):3–30.

[3] ter Borg S, Verlaan S, Hemsworth J, Mijnarends DM, Schols JMGA, Luiking YC, et al. Micronutrient intakes and potential inadequacies of community-dwelling older adults: a systematic review. Br J Nutr 2015;113(8):1195–206.

[4] Richter CK, kulas-Ray AC, Kris-Etherton PM. Recent findings of studies on the Mediterranean diet: what are the implications for current dietary recommendations? Endocrinol Metab Clin N Am 2014;43(4):963–80.

[5] Donini LM, Serra-Majem L, Bulló M, Gil Á, Salas-Salvadó J. The Mediterranean diet: culture, health and science. Br J Nutr 2015;113(S2):S1–3.

[6] Bach-Faig A, Fuentes-Bol C, Ramos D, Carrasco JL, Roman B, Bertomeu IF, et al. The Mediterranean diet in Spain: adherence trends during the past two decades using the Mediterranean adequacy index. Publ Health Nutr 2011;14(4):622–8.

[7] Passi SJ. Prevention of non-communicable diseases by balanced nutrition: population-specific effective public health approaches in developing countries. Curr Diabetes Rev 2017;13(5):461–76.

[8] Varela-Moreiras G, Ávila JM, Cuadrado C, del Pozo S, Ruiz E, Moreiras O. Evaluation of food consumption and dietary patterns in Spain by the food consumption survey: updated information. Eur J Clin Nutr 2010;64:S37–43.

[9] Nicklas TA, Drewnowski A, O'Neil CE. The nutrient density approach to healthy eating: challenges and opportunities. Publ Health Nutr 2013;17(12):2626–36.

[10] Olza J, Aranceta-Bartrina J, González-Gross M, Ortega RM, Serra-Majem L, Varela-Moreiras G, et al. Reported dietary intake and food sources of zinc, selenium, and vitamins A, E and C in the Spanish population: findings from the ANIBES study. Nutrients 2017;9(7).

[11] Schröder H, Vila J, Marrugat J, Covas MI. Low energy density diets are associated with favorable nutrient intake profile and adequacy in free-living elderly men and women. J Nutr 2008;138(8):1476–81.

[12] Visser M, Volkert D, Corish C, Geisler C, de Groot LC, Cruz-Jentoft AJ, et al. Tackling the increasing problem of malnutrition in older persons: the malnutrition in the elderly (MaNuEL) knowledge hub. Nutr Bull 2017;42(2):178–86.

Please cite this article as: Cano-Ibáñez N et al., Diet quality and nutrient density in subjects with metabolic syndrome: Influence of socioeconomic status and lifestyle factors. A cross-sectional assessment in the PREDIMED-Plus study, Clinical Nutrition, https://doi.org/10.1016/j.clnu.2019.04.032

[13] Atkins JL, Ramsay SE, Whincup PH, Morris RW, Lennon LT, Wannamethee SG. Diet quality in older age: the influence of childhood and adult socio-economic circumstances. Br J Nutr 2015;113(9):1441–52.
[14] Basambombo LL, Carmichael PH, Côté S, Laurin D. Use of vitamin E and C supplements for the prevention of cognitive decline. Ann Pharmacother 2017;51(2):118–24.
[15] Samieri C. Epidemiology and risk factors of Alzheimer's disease: a focus on diet. Neuromethods 2018:15–42.
[16] Goncalves A, Amiot MJ. Fat-soluble micronutrients and metabolic syndrome. Curr Opin Clin Nutr Metab Care 2017;20(6):492–7.
[17] Jenkins DJA, Spence JD, Giovannucci EL, Kim YI, Josse R, Vieth R, et al. Supplemental vitamins and minerals for CVD prevention and treatment. J Am Coll Cardiol 2018;71(22):2570–84.
[18] Lanham-New SA. Role of calcium and vitamin D in the prevention (and treatment) of osteoporotic fracture. Surgery 2009;27(2):47–54.
[19] Cano A, Chedraui P, Goulis DG, Lopes P, Mishra G, Mueck A, et al. Calcium in the prevention of postmenopausal osteoporosis: EMAS clinical guide. Maturitas 2018;107:7–12.
[20] Martinez-Gonzalez M, Buil-Cosiales P, Vioque J, Romaguera D, Martínez JA, López-Miranda J, et al. Cohort profile: design and methods of the PREDIMED-Plus randomized trial. Int J Epidemiol 2018;48:387–8.
[21] 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 Atherosclerosis Society; and International Association for the study of obesity. Circulation 2009;120(16):1640–5.
[22] Willet W. Nutritional epidemiology. 3rd ed. New York: Oxford University Press; 2013.
[23] Martin-moreno JM, Boyle P, Gorgojo L, Maisonneuve P, Fernandez-rodriguez JC, Salvini S, et al. Development and validation of a food frequency questionnaire in Spain. Int J Epidemiol 1993;22(3):512–9.
[24] De La Fuente-Arrillaga C, Vzquez Ruiz Z, Bes-Rastrollo M, Sampson L, Martinez-González MA. Reproducibility of an FFQ validated in Spain. Publ Health Nutr 2010;13(9):1364–72.
[25] Mataix Verdu J. Tabla de composición de alimentos españoles. (Spanish food composition tables). Granada: Universidad de Granada; 2003.
[26] Moreiras O, Carbajal A, Cabrera L, Cuadrado C. Tablas de composición de alimentos/Guía de Prácticas. 16th ed. Madrid: Edici ones Pirámide; 2013.
[27] Martínez-González MA, Fernández-Jarne E, Serrano-Martínez M, Wright M, Gomez-Gracia E. Development of a short dietary intake questionnaire for the quantitative estimation of adherence to a cardioprotective Mediterranean diet. Eur J Clin Nutr 2004;58(11):1550–2.
[28] IOM. Nutrient recommendations: dietary reference intakes. Available from: https://ods.od.nih.gov/Health_Information/Dietary_Reference_Intakes.aspx.
[29] Aranceta J, Serra-Majem L, Pérez-Rodrigo C, Llopis J, Mataix J, Ribas L, et al. Vitamins in Spanish food patterns: the eVe study. Publ Health Nutr 2001;4(6A):1317–23.
[30] EFSA. Dietary reference values and dietary guidelines. Available from: https://www.efsa.europa.eu/en/topics/topic/dietary-reference-values.
[31] Elosua R, Garcia M, Aguilar A, Molina L, Covas MI, Marrugat J. Validation of the Minnesota leisure time physical activity questionnaire in Spanish women. Med Sci Sports Exerc 2000;32(8):1431–7.
[32] Elosua R, Marrugat J, Molina L, Pons S, Pujol E. Validation of the Minnesota leisure time physical activity questionnaire in Spanish men. Am J Epidemiol 1994;139(12):1197–209.
[33] Topolski TD, LoGerfo J, Patrick DL, Williams B, Walwick J, Patrick MB. The rapid assessment of physical activity (RAPA) among older adults. Prev Chronic Dis 2006;3(4).
[34] Martínez-González MA, López-Fontana C, Varo JJ, Sánchez-Villegas A, Martinez JA. Validation of the Spanish version of the physical activity questionnaire used in the nurses' health study and the health professionals' follow-up study. Publ Health Nutr 2005;8(7):920–7.
[35] Sanchez-Tainta A, Zazpe I, Bes-Rastrollo J, Salas-Salvado J, Bullo M, Vicente Sorli J, et al. Nutritional adequacy according to carbohydrates and fat quality. Eur J Nutr 2016;55(1):93–106.
[36] Dietary Reference Intakes. Dietary reference intakes: applications in dietary assessment. 2000.
[37] Wang DD, Hu FB. Dietary fat and risk of cardiovascular disease: recent controversies and advances. Ann Rev Nutr. p. 423-446.
[38] Salas-Salvadó J, Fernández-Ballart J, Ros E, Martínez-González MA, Fitó M, Estruch R, et al. Effect of a Mediterranean diet supplemented with nuts on metabolic syndrome status: one-year results of the PREDIMED randomized trial. Arch Intern Med 2008;168(22):2449–58.
[39] Guasch-Ferré M, Babio N, Martínez-González MA, Corella D, Ros E, Martín-Peláez S, et al. Dietary fat intake and risk of cardiovascular disease and all-cause mortality in a population at high risk of cardiovascular disease. Am J Clin Nutr 2015;102(6):1563–73.
[40] Ruiz E, Ávila JM, Valero T, del Pozo S, Rodriguez P, Aranceta-Bartrina J, et al. Macronutrient distribution and dietary sources in the Spanish population: findings from the ANIBES study. Nutrients 2016;8(3).
[41] Hosseinpour Niazi S, Mirmiran P, Sohrab G, Hosseini Esfahani F, Azizi F. Association between dietary fiber intake and metabolic syndrome: Tehran lipid and glucose study. Iran J Epidemiol 2012;7(4):19–28.
[42] De Mora BRRC, Conde LPO. Preliminary results on dietary fibre intake in Spain and health benefits associated to soluble fiber intake. Rev Española Nutr Comunitaria 2010;16(3):147–53.
[43] Murphy SP, Poos MI. Dietary reference intakes: summary of applications in dietary assessment. Publ Health Nutr 2002;5(6 A):843–9.
[44] Ruiz E, Ávila JM, Valero T, Pozo SD, Rodriguez P, Aranceta-Bartrina J, et al. Energy intake, profile, and dietary sources in the Spanish population: findings of the ANIBES study. Nutrients 2015;7(6):4739–62.
[45] Mensink GBM, Fletcher R, Gurinovic M, Huybrechts I, Lafay L, Serra-Majem L, et al. Mapping low intake of micronutrients across Europe. Br J Nutr 2013;110(4):755–73.
[46] Roman Viñas B, Ribas Barba L, Ngo J, Gurinovic M, Novakovic R, Cavelaars A, et al. Projected prevalence of inadequate nutrient intakes in Europe. Ann Nutr Metabol 2011;59(2–4):84–95.
[47] Schröder H, Marrugat J, Covas M, Elosua R, Pena A, Weinbrenner T, et al. Population dietary habits and physical activity modification with age. Eur J Clin Nutr 2004;58(2):302–11.
[48] Castro-Quezada I, Román-Viñas B, Serra-Majem L. The Mediterranean diet and nutritional adequacy: a review. Nutrients 2014;6(1):231–48.
[49] Moizé V, Deulofeu R, Torres F, De Osaba JM, Vidal J. Nutritional intake and prevalence of nutritional deficiencies prior to surgery in a Spanish morbidly obese population. Obes Surg 2011;21(9):1382–8.
[50] Frame-Peterson LA, Megill RD, Carobrese S, Schweitzer M. Nutrient deficiencies are common prior to Bariatric surgery. Nutr Clin Pract 2017;32(4):463–9.
[51] Moore-Schiltz L, Albert JM, Singer ME, Swain J, Nock NL. Dietary intake of calcium and magnesium and the metabolic syndrome in the National Health and Nutrition Examination (NHANES) 2001–2010 data. Br J Nutr 2015;114(6):924–35.
[52] Rosanoff A, Weaver CM, Rude RK. Suboptimal magnesium status in the United States: are the health consequences underestimated? Nutr Rev 2012;70(3):153–64.
[53] Olza J, Aranceta-Bartrina J, González-Gross M, Ortega RM, Serra-Majem L, Varela-Moreiras G, et al. Reported dietary intake, disparity between the reported consumption and the level needed for adequacy and food sources of calcium, phosphorus, magnesium and vitamin D in the Spanish population: findings from the ANIBES study. Nutrients 2017;9(2).
[54] Gennari C. Calcium and vitamin D nutrition and bone disease of the elderly. Publ Health Nutr 2001;4(2 B):547–59.
[55] Berner YN, Stern F, Polyak Z, Dror Y. Dietary intake analysis in institutionalized elderly: a focus on nutrient density. J Nutr Health Aging 2002;6(4):237–42.
[56] Toffanello ED, Inelmen EM, Minicuci N, Campigotto F, Sergi G, Coin A, et al. Ten-year trends in vitamin intake in free-living healthy elderly people: the risk of subclinical malnutrition. J Nutr Health Aging 2011;15(2):99–103.
[57] Manios Y, Moschonis G, Lambrinou CP, Tsoutsoulopoulou K, Binou P, Karachaliou A, et al. A systematic review of vitamin D status in southern European countries. Eur J Nutr 2017:1–36.
[58] Lips P. Worldwide status of vitamin D nutrition. J Steroid Biochem Mol Biol 2010;121(1–2):297–300.
[59] Guasch A, Bulló M, Rabassa A, Bonada A, Del Castillo D, Sabench F, et al. Plasma vitamin D and parathormone are associated with obesity and atherogenic dyslipidemia: a cross-sectional study. Cardiovasc Diabetol 2012;11.
[60] Ahn S, Jun S, Kang M, Shin S, Wie GA, Baik HW, et al. Association between intake of antioxidant vitamins and metabolic syndrome risk among Korean adults. J Nutr Health 2017;50(4):313–24.
[61] Lesser S, Pauly L, Volkert D, Stehle P. Nutritional situation of the elderly in Eastern/Baltic and Central/Western Europe – the Ageing Nutrition project. Ann Nutr Metabol 2008;52(Suppl. 1):62–71.
[62] Nicklett EJ, Kadell AR. Fruit and vegetable intake among older adults: a scoping review. Maturitas 2013;75(4):305–12.
[63] Ter Borg S, Verlaan S, Mijnarends DM, Schols JMGA, De Groot LCPGM, Luiking YC. Macronutrient intake and inadequacies of community-dwelling older adults, a systematic review. Ann Nutr Metabol 2015;66(4):242–55.
[64] Lammes E, Törner A, Akner G. Nutrient density and variation in nutrient intake with changing energy intake in multimorbid nursing home residents. J Hum Nutr Diet 2009;22(3):210–8.
[65] Kiefer I, Rathmanner T, Kunze M. Eating and dieting differences in men and women. J Men's Health Gend 2005;2(2):194–201.
[66] Hsiao PY, Mitchell DC, Coffman DL, Allman RM, Locher JL, Sawyer P, et al. Dietary patterns and diet quality among diverse older adults: the University of Alabama at Birmingham study of aging. J Nutr Health Aging 2013;17(1):19–25.
[67] Alkerwi A, Baydarlioglu B, Sauvageot N, Stranges S, Lemmens P, Shivappa N, et al. Smoking status is inversely associated with overall diet quality: findings from the ORISCAV-LUX study. Clin Nutr 2017;36(5):1275–82.
[68] García-Meseguer MJ, Delicado-Soria A, Serrano-Urrea R. Fiber patterns in young adults living in different environments (USA, Spain, and Tunisia). anthropometric and lifestyle characteristics. Nutrients 2017;9(9).
[69] Fekete C, Weyers S. Social inequalities in nutrition: evidence, causes and interventions. Bundesgesundheitsblatt – Gesundheitsforsch – Gesundheitsschutz 2016;59(2):197–205.
[70] Deierlein AL, Morland KB, Scanlin K, Wong S, Spark A. Diet quality of urban older adults age 60 to 99 years: the cardiovascular health of seniors and built environment study. J Acad Nutr Diet 2014;114(2):279–87.

Please cite this article as: Cano-Ibáñez N et al., Diet quality and nutrient density in subjects with metabolic syndrome: Influence of socioeconomic status and lifestyle factors. A cross-sectional assessment in the PREDIMED-Plus study, Clinical Nutrition, https://doi.org/10.1016/j.clnu.2019.04.032

[71] Stringhini S, Sabia S, Shipley M, Brunner E, Nabi H, Kivimaki M, et al. Association of socioeconomic position with health behaviors and mortality. J Am Med Assoc 2010;303(12):1159–66.
[72] Charlton KE. Elderly men living alone: are they at high nutritional risk? J Nutr Health Aging 1999;3(1):46–7.
[73] Shatenstein B, Gauvin L, Keller H, Richard L, Gaudreau P, Giroux F, et al. Individual and collective factors predicting change in diet quality over 3 years in a subset of older men and women from the NuAge cohort. Eur J Nutr 2016;55(4):1671–81.
[74] Livingstone KM, Olstad DL, Leech RM, Ball K, Meertens B, Potter J, et al. Socioeconomic inequities in diet quality and nutrient intakes among Australian adults: findings from a nationally representative cross-sectional study. Nutrients 2017;9(10).
[75] Fernández-Ballart JD, Piñol JL, Zazpe I, Corella D, Carrasco P, Toledo E, et al. Relative validity of a semi-quantitative food-frequency questionnaire in an elderly Mediterranean population of Spain. Br J Nutr 2010;103(12): 1808–16.
[76] Ortiz-Andrellucchi A, Sánchez-Villegas A, Doreste-Alonso J, de Vries J, de Groot L, Serra-Majem L. Dietary assessment methods for micronutrient intake in elderly people: a systematic review. Br J Nutr 2009;102(Suppl. 1): S118–49.

Please cite this article as: Cano-Ibáñez N et al., Diet quality and nutrient density in subjects with metabolic syndrome: Influence of socioeconomic status and lifestyle factors. A cross-sectional assessment in the PREDIMED-Plus study, Clinical Nutrition, https://doi.org/10.1016/j.clnu.2019.04.032

Supplementary table 1. Adherence to Mediterranean diet, total energy intake and nutrient Density by sex and age according to total energy intake

	Men		*Women*		*P value*[a]	*P value*[b]	*P value*[c]
	60-70 y	*>70 y*	*60-70 y*	*>70 y*			
n	*2120*	*419*	*2661*	*554*			
MedDiet adherence	8.2±2.7	8.5±2.7	8.9±2.6	9.0±2.6	<0.001	0.381	0.406
Total energy (Kcal/d)	2508±546	2433±560	2212±496	2161±495	<0.001	0.037	0.513
CHO (g/1000 kcal)	100.8±16.5	102±17	103±17	106±18	<0.001	0.009	0.205
Protein (g/1000 kcal)	39.6±6.6	39.8±6.1	43.4±6.8	43.5±6.7	<0.001	0.496	0.793
Total Fat (g/1000 kcal)	43.4±7.0	43.2±7.3	44.3±7.4	43.4±7.5	0.025	0.041	0.183
MUFA (g/1000 kcal)	22.6±5.0	22.3±5.0	23.1±5.3	22.6±5.1	0.032	0.030	0.383
PUFA (g/1000 kcal)	7.0±2.0	7.1±2.2	7.1±2.1	7.0±2.0	0.914	0.829	0.037
SFA (g/1000 kcal)	10.9±2.1	10.9±2.2	11.0±2.3	10.7±2.3	0.914	0.019	0.137
Total fiber (g/1000 kcal)	10.3±3.2	11.0±3.2	12.2±3.4	12.2±3.8	<0.001	<0.001	0.250
Alcohol (g/1000 kcal)	6.9±6.6	6.5±6.1	2.0±3.3	1.7±3.0	<0.001	0.069	0.842
Vitamin A (µg/1000 kcal)	447±255	463±299	513±291	475±242	<0.001	0.270	0.005
Vitamin B_1 (mg/1000 kcal)	0.7±0.1	0.7±0.1	0.7±0.1	0.8±0.1	<0.001	0.004	0.497
Vitamin B_9 (µg/1000 kcal)	141±38	146±37	163±42	167±47	<0.001	<0.001	0.485
Vitamin B_{12} (µg/1000 kcal)	4.2±2.1	4.2±2.1	4.4±1.9	4.4±1.7	<0.001	0.761	0.238
Vitamin C (mg/1000 kcal)	78±33	82±33	98±38	101±42	<0.001	0.011	0.833
Vitamin D (µg/1000 kcal)	2.5±1.4	2.5±1.5	2.8±1.6	2.8±1.6	<0.001	0.778	0.382
Vitamin E (mg/1000 kcal)	4.3±1.4	4.4±1.5	4.7±1.4	4.5±1.2	<0.001	0.061	<0.001
Calcium (mg/1000 kcal)	415±118	419.1±117.6	470.5±131.9	485.7±133.3	<0.001	0.035	0.230
Magnesium (mg/1000 kcal)	2508±546	167.9±32.1	183.0±34.3	184.0±35.2	<0.001	0.078	0.359

Values are mean ± SD unless otherwise indicated.
Factorial ANOVA was used
[a]P value for sex
[b]P value for age
[c]P value interaction between sex and age
[d]MedDiet Adherence: Adherence to Mediterranean diet using the 17 item questionnaire adherence with scale 0 to 17 points

Supplementary table 2. Macro/micronutrient intake by age and sex in the PREDIMED-PLUS study sample

	Men		*Women*		*P value*[a]	*P value*[b]	*P value*[c]
	≤70 y[d]	*>70 y*	*≤70 y*[d]	*>70 y*			
n	3012	419	2661	554			
CHO (% of kcal)	40.3±6.7	40.7±6.7	41.4±6.9	42.3±7.0	<0.001	0.005	0.241
Protein (% of kcal)	15.9±2.7	15.9±2.4	17.4±2.7	17.4±2.7	<0.001	0.667	0.994
Total fat (% of kcal)	39.2±6.3	38.9±6.6	39.9±6.7	39.1±6.7	0.040	0.022	0.259
MUFA (% of kcal)	20.3±4.5	20.1±4.5	20.8±4.8	20.3±4.6	0.021	0.031	0.311
PUFA (% of kcal)	6.3±1.8	6.4±2.0	6.4±1.9	6.3±1.8	0.787	0.704	0.022
SFA (% of kcal)	9.9±2.0	9.8±1.9	9.9±2.0	9.7±2.0	0.457	0.003	0.392
CHO (g/d)	255±75	249±79	230±67	229±69	<0.001	0.251	0.265
Protein (g/d)	99±23	96±22	95±21	93±21	<0.001	0.001	0.523
Total fat (g/d)	109±29	105±27	98±28	94±27	<0.001	<0.001	0.834
MUFA (g/d)	56±16	54±15	51±16	49±15	<0.001	<0.001	0.995
PUFA (g/d)	18±6	18±7	16±6	15±6	<0.001	0.10	0.254
SFA (g/d)	28±9	26±8	25±8	23±8	<0.001	<0.001	0.785
Total fiber (g/d)	25±9	26.5±8.8	26.7±8.9	26.8±8.6	0.003	0.014	0.035
Alcohol (g/d)	17±18	16±16	5±8	4±7	<0.001	0.045	0.639
Vitamin A (µg/d)	1097±640	1099±682	1114±647	1012±568	0.123	0.026	0.022
Vitamin B_1 (mg/d)	1.6±0.4	1.6±0.4	1.6±0.4	1.6±0.4	0.306	0.253	0.839
Vitamin B_9 (µg/d)	342±99	350±99	355±103	354±108	0.018	0.310	0.183
Vitamin B_{12} (µg/d)	10.1±4.5	9.9±4.8	9.7±4.4	9.3±4.2	0.001	0.088	0.415
Vitamin C (mg/d)	188±83	195±80	213±85	213±89	<0.001	0.211	0.348
Vitamin D (µg/d)	6.1±3.4	6.0±3.4	6.2±3.4	5.9±3.4	0.892	0.173	0.307
Vitamin E (mg/d)	10.8±4.1	10.7±4.1	10.4±3.9	9.6±3.2	<0.001	0.001	0.001
Calcium (mg/d)	1025±351	1006±331	1032±342	1036±331	0.133	0.551	0.317
Magnesium (mg/d)	407±105	405±108	402±108	393±101	0.020	0.145	0.36

Values are means ± SD unless otherwise indicated.
Factorial ANOVA was used
[a]P value for sex
[b]P value for age
[c]P value interaction between sex and age
[d]This age category includes 55-70years for males, and 60-70 years for females

Supplementary table 3. Proportion of participants with intake of macro and micronutrient below DRIs by sex and age.

		Men			*Women*		
		≤70 y[a]	>70 y		≤70 y[a]	>70 y	
	DRI[b]	% below DRI		P value[c]	% below DRI		P value[c]
CHO	130 g/d	2.7	3.4	0.463	4.9	4.5	0.720
Protein	56-46 g/d	1.8	1.9	0.805	0.5	1.1	0.136
Dietary fiber	30-21 g/d	76.9	71.6	0.019	27.6	27.4	0.901
Vitamin A	900-700 µg/d	49.2	52.2	0.264	26.8	32.8	0.004
Vitamin B_1	1.2-1.1 mg/d	13.5	16.4	0.109	7.9	9.4	0.251
Vitamin B_9	400 µg/d	76.3	70.2	0.007	71.0	72.6	0.440
Vitamin B_{12}	2.4 µg/d	0.2	0.7	0.088	0.3	0.7	0.203
Vitamin C	90-75 mg/d	7.6	7.9	0.821	1.8	2.2	0.550
Vitamin D	15-20, 15-20 µg/d	98.9	100.0	0.028	99.0	99.8	0.052
Vitamin E	15 mg/d	88.1	87.0	0.538	90.1	95.1	<0.001
Calcium	1.0-1.2, 1.2-1.2 g/d	52.7	74.3	<0.001	71.0	69.8	0.553
Magnesium	420-420, 420-320 mg/d	60.0	58.7	0.602	23.7	23.7	0.995

[a]This age category includes 55-70years for males, and 60-70 years for females
[b]Dietary Reference Intake: where a single value is displayed, DRI is the same for all analysed groups. If 2 values are displayed, DRI differs between sexes and the first value is DRI for men and the second value is DRI for women. Where 4 values are displayed, DRI varies also for age groups; values are DRIs for men ≤70 y, men >70 y, women ≤70 y, and women >70 y respectively. Values are presented as %. [c]Pearson's chi-square test was performed.

Supplementary table 4. Proportion of participants with intake of macro and micronutrient below AR according to EFSA criteria by sex.

		Men	*Women*	
	AR/AI[a]	% below AR	% below AR	*P value*[c]
CHO	45%	0	0.5	0.302
Dietary fiber	25 g/d	55.5	47.9	<0.001
Vitamin A	570-490 µg/d	16.9	7.8	<0.001
Vitamin B_1[b]	0.72-0.66 mg/d	0.4	0.2	0.201
Vitamin B_9	250 µg/d	15.9	13.9	0.024
Vitamin B_{12}	4 µg/d	2.8	3.5	0.109
Vitamin C	90-80 mg/d	7.7	2.4	<0.001
Vitamin D	15 µg/d	98.9	99.0	<0.001
Vitamin E	13-11 mg/d	78.3	66.3	<0.001
Calcium	950 mg/d	46.2	44.6	0.194
Magnesium	350-300 mg/d	32.3	16.5	<0.001

[a]AR/AI: Average requirements or adequate intake according to criteria proposed by EFSA. Where a single value is displayed, AR is the same for all analysed groups. If 2 values are displayed, AR differs between sexes and the first value is AR for men and the second number is AR for women.
[b]Vitamin B_1: Values are expressed by total energy intake (kcal/day)
[c]Pearson's chi-square test was performed.

Supplementary Table 5. Multivariable[a] logistic regression model for inadequate intake of 4 or more out 10 micronutrients according to criteria proposed by EFSA assessing baseline socioeconomic and lifestyle factors among men and women in the PREDIMED-Plus study participants analysed

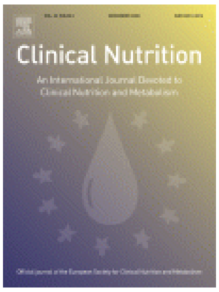
	≥4 inadequate intake (95% Confidence Interval)	*Odds Ratio (95% Confidence Interval)*	*P value*
Sex			
Men	44.0 (42.3-45.6)	1 (ref)	
Women	32.0 (30.4-33.6)	0.28 (0.23-0.32)	<0.001
Age			
≤70 y[b]	38.3 (37.0-40.0)	1 (ref)	
> 70 y	37.6 (34.5-40.7)	0.93 (0.78-1.12)	0.448
Smoking habits			
Current smoker	46.7 (43.2-50.1)	1 (ref)	
Former smoker	40.7 (38.8-42.5)	0.65 (0.53-0.80)	<0.001
Never smoker	33.2 (31.4-34.9)	0.63 (0.51-0.79)	<0.001
Physical Activity			
Less active	38.6 (37.1-40.1)	1 (ref)	
Moderately active	36.5 (33.8-39.1)	0.73 (0.62-0.85)	<0.001
Active	38.6 (36.0-41.2)	0.90 (0.77-1.05)	0.180
Educational level			
Tertiary	38.2 (35.7-40.7)	1 (ref)	
Secondary	39.9 (37.6-42.1)	1.03 (0.86-1.22)	0.779
Primary	37.2 (35.5-38.9)	1.02 (0.86-1.20)	0.844
Mediterranean Diet			
Low Adherence	46.4 (44.4-48.5)	1 (ref)	
Medium Adherence	38.2 (36.4-40.1)	0.44 (0.38-0.51)	<0.001
High Adherence	25.1 (22.9-27.3)	0.20 (0.17-0.24)	<0.001

[a]The multivariable model includes all variables presented in the table and is additionally adjusted for BMI (continuous, Kg/m^2), marital status (4 categories), employment status (4 categories), living alone (yes/no), and total energy intake (continuous, kcal)

[b]This age category includes 55-70years for males, and 60-70 years for females

Copyright Clearance Center RightsLink®

Home | Create Account | Help



Title: Diet quality and nutrient density in subjects with metabolic syndrome: Influence of socioeconomic status and lifestyle factors. A cross-sectional assessment in the PREDIMED-Plus study

Author: Naomi Cano-Ibáñez,Alfredo Gea,Miguel Ruiz-Canela,Dolores Corella,Jordi Salas-Salvadó,Helmut Schröder,Eva Ma. Navarrete-Muñoz,Dora Romaguera,J. Alfredo Martínez,F. Javier Barón-López,José López-Miranda,Ramón Estruch,Blanca Riquelme-Gallego et al.

Publication: Clinical Nutrition

Publisher: Elsevier

Date: Available online 2 May 2019

LOGIN

If you're a copyright.com user, you can login to RightsLink using your copyright.com credentials.

Already **a RightsLink user** or want to learn more?

Please note that, as the author of this Elsevier article, you retain the right to include it in a thesis or dissertation, provided it is not published commercially. Permission is not required, but please ensure that you reference the journal as the original source. For more information on this and on your other retained rights, please visit: https://www.elsevier.com/about/our-business/policies/copyright#Author-rights

BACK | CLOSE WINDOW

TRABAJOS REALIZADOS

Artículo 2. Cano-Ibáñez N, Bueno-Cavanillas A, Martínez-González MA, Corella D, Salas-Salvadó J, Zomeño MD, et al. Dietary intake in population with metabolic syndrome: Is the prevalence of inadequate intake influenced by geographical area? Cross-sectional analysis from PREDIMED-plus study. Nutrients. 2018; 10(11).

El segundo artículo, *"Dietary intake in population with Metabolic Syndrome: Is the prevalence of inadequate intake influenced by geographical area? Cross-Sectional Analysis from PREDIMED-Plus study"*, dio respuesta al objetivo específico número 2 de la presente Tesis. En esta publicación se analiza cómo difiere la ingesta alimentaria entre distintas áreas españolas, permitiendo confirmar la hipótesis de que el área geográfica, con sus características culturales y peculiaridades culinarias, ejerce una impronta influencia en la ingesta alimentaria y por ende en el perfil nutricional y la adecuación de nutrientes de acuerdo a las ingestas dietéticas recomendadas. Así pues, los hallazgos mostraron diferencias estadísticamente significativas en el consumo de diversos grupos alimentarios, siendo aquellos de mejor calidad nutricional (verduras, frutos secos, legumbres y/o pescados) consumidos en menor proporción por los individuos que residían en el Norte de España. Dado que la ingesta alimentaria y el perfil nutricional variaban significativamente en las áreas geográficas analizadas, se observó que las ingestas de fibra, vitamina A, E, calcio y magnesio fueron más bajas en estos individuos en comparación con el resto de participantes del estudio; encontrándose una prevalencia agrupada de ingesta inadecuada del 19%. El análisis de regresión logística ajustada mostró que el área geográfica de residencia ejercía una impronta significativa en la ingesta deficitaria; siendo mayor en el Área Norte en comparación con las tres áreas restantes introducidas en nuestro análisis.

6.1.2. Dietary intake in population with metabolic syndrome: Is the prevalence of inadequate intake influenced by geographical area? Cross-sectional analysis from PREDIMED-plus study

[Cano-Ibáñez N, Bueno-Cavanillas A, Martínez-González MA, Corella D, Salas-Salvadó J, Zomeño MD, et al. Dietary intake in population with metabolic syndrome: Is the prevalence of inadequate intake influenced by geographical area? Cross-sectional analysis from PREDIMED-plus study. Nutrients. 2018; 10(11)].

<u>Datos de la Publicación:</u>

- Factor de impacto en JCR 2017: 4.196
- Ránking: 18/83
- Categoría: *Nutrition & Dietetics*
- Cuartil: Q1.

nutrients

MDPI

Article

Dietary Intake in Population with Metabolic Syndrome: Is the Prevalence of Inadequate Intake Influenced by Geographical Area? Cross-Sectional Analysis from PREDIMED-Plus Study

Naomi Cano-Ibáñez [1,2,*], Aurora Bueno-Cavanillas [1,2], Miguel A. Martínez-González [3,4,5], Dolores Corella [5,6], Jordi Salas-Salvadó [5,7], M. Dolors Zomeño [8,9], Manoli García-de-la-Hera [2,10], Dora Romaguera [5,11], J. Alfredo Martínez [5,12,13], F. Javier Barón-López [5,14], Antonio García-Ríos [5,15], Ramón Estruch [5,16], Laura García-Molina [1,2], Ángel Alonso Gómez [5,17], Josep A. Tur [5,18], Francisco Tinahones [5,19], Lluis Serra-Majem [5,20], Naiara Cubelos-Fernández [21], José Lapetra [5,22], Clotilde Vázquez [5,23], Xavier Pintó [5,24], Josep Vidal [25,26], Lidia Daimiel [13], José Juan Gaforio [2,27], Pilar Matía [28], Emilio Ros [5,29], Javier Diez-Espino [3,5,30], Rebeca Fernández-Carrión [5,6], Josep Basora [5,7], Montse Fitó [5,8], Juan Manuel Zazo [2,10], Antoni Colom [5,11], Estefanía Toledo [3,5], Andrés Díaz-López [5,7], Miguel Ángel Muñoz [31], Miguel Ruiz-Canela [3,4,5] and Alfredo Gea [3,5]

1. Department of Preventive Medicine and Public Health, University of Granada, 18011 Granada, Spain; abueno@ugr.es (A.B.-C.); lgarmol@ugr.es (L.G.-M.)
2. CIBER of Epidemiology and Public Health (CIBERESP), Carlos III Institute of Health, 28029 Madrid, Spain; manoli@umh.es (M.G.-d.-l.-H.); jgaforio@ujaen.es (J.J.G.); juanmazazo@gmail.com (J.M.Z.)
3. Department of Preventive Medicine and Public Health, Medical School, University of Navarre, 31008 Pamplona, Spain; mamartinez@unav.es (M.A.M.-G.); javierdiezesp@ono.com (J.D.-E.); etoledo@unav.es (E.T.); mcanela@unav.es (M.R.-C.); ageas@unav.es (A.G.)
4. Department of Nutrition, Harvard T.H. Chan School of Public Health, Boston, MA 02115, USA
5. CIBER Physiopathology of Obesity and Nutrition (CIBEROBN), Carlos III Institute of Health, 28029 Madrid, Spain; dolores.corella@uv.es (D.C.); jordi.salas@urv.cat (J.S.-S.); doraromaguera@yahoo.es (D.R.); jalfmtz@unav.es (J.A.M.); baron@uma.es (F.J.B.-L.); angarios2004@yahoo.es (A.G.-R.); restruch@clinic.ub.es (R.E.); angelmago13@gmail.com (Á.A.G.); pep.tur@uib.es (J.A.T.); fjtinahones@hotmail.com (F.T.); lluis.serra@ulpgc.es (L.S.-M.); jlapetra@ono.com (J.L.); clotilde.vazquez@fjd.es (C.V.); xpinto@bellvitgehospital.cat (X.P.); eros@clinic.ub.es (E.R.); rebeca.fernandez@uv.es (R.F.-C.); jbasora.tarte.ics@gencat.cat (J.B.); mfito@imim.es (M.F.); antonicolom@gmail.com (A.C.); andres.diaz@urv.cat (A.D.-L.)
6. Department of Preventive Medicine, University of Valencia, 46010 Valencia, Spain
7. Human Nutrition Unit, Biochemistry and Biotechnology Department, IISPV, Universitat Rovira i Virgili, 43002 Reus, Spain
8. Unit of Cardiovascular Risk and Nutrition, Institut Hospital del mar de Investigaciones Médicas Municipal d'Investigació Médica (IMIM), 08003 Barcelona, Spain; mariadoloreszf@blanquerna.edu
9. Human Nutrition Unit, Blanquerna-Ramon Llull University, 08001 Barcelona, Spain
10. Miguel Hernández University, ISABIAL-FISABIO, 03202 Alicante, Spain
11. Health Research Institute of the Balearic Islands (IdISBa), 07120 Palma de Mallorca, Spain
12. Department of Nutrition, Food Sciences and Physiology, Center for Nutrition Research, University of Navarra, 31008 Pamplona, Spain
13. Nutritional Genomics and Epigenomics Group, IMDEA Food, CEI UAM + CSIC, 28049 Madrid, Spain; lidia.daimiel@imdea.org
14. Department of Public Health, University of Málaga-IBIMA, 29016 Málaga, Spain
15. Lipids and Atherosclerosis Unit, Department of Internal Medicine, Maimonides Biomedical Research Institute of Córdoba (IMIBIC), Reina Sofía University Hospital, University of Córdoba, 14004 Córdoba, Spain
16. Department of Internal Medicine, IDIBAPS, Hospital Clinic, University of Barcelona, 08036 Barcelona, Spain
17. Department of Cardiology, OSI ARABA, University Hospital Araba, University of the Basque Country (UPV/EHU), 48940 Vitoria-Gasteiz, Spain

[18] Research Group on Community Nutrition & Oxidative Stress, University of Balearic Islands, 07122 Palma de Mallorca, Spain
[19] Virgen de la Victoria Hospital, Department of Endocrinology, University of Málaga, 29010 Málaga, Spain
[20] Institute for Biomedical Research, University of Las Palmas de Gran Canaria, 35016 Las Palmas, Spain
[21] Institute of Biomedicine (IBIOMED), University of León, 24071 León, Spain; n.cubelos.fernandez@gmail.com
[22] Department of Family Medicine, Research Unit, Distrito Sanitario Atención Primaria, 41013 Sevilla, Spain
[23] Department of Endocrinology, Fundación Jiménez-Díaz, 28040 Madrid, Spain
[24] Lipids and Vascular Risk Unit, Internal Medicine, Hospital Universitario de Bellvitge, Hospitalet de Llobregat, 08907 Barcelona, Spain
[25] Department of Endocrinology, IDIBAPS, Hospital Clinic, University of Barcelona, 08036 Barcelona, Spain; jovidal@clinic.cat
[26] CIBER Diabetes y Enfermedades Metabólicas (CIBERDEM), Instituto de Salud Carlos III (ISCIII), 28029 Madrid, Spain
[27] Centro de Estudios Avanzados en Olivar y Aceites de Oliva, University of Jaén, 23071 Jaén, Spain
[28] Department of Endocrinology and Nutrition, Instituto de Investigación Sanitaria Hospital Clínico San Carlos (IdISSC), 28040 Madrid, Spain; pilar.matia@gmail.com
[29] Lipid Clinic, Department of Endocrinology and Nutrition, Institut d'Investigació Biomédiques August Pi Sunyer (IDIBAPS), Hospital Clinic, 08036 Barcelona, Spain
[30] Servicio Navarro de Salud, Osasunbidea, 31002 Pamplona, Spain
[31] Primary Care Division of Barcelona, Institut Català de la Salud-IDIAP Jordi Gol, 08007 Barcelona, Spain; mamunoz.bcn.ics@gencat.cat
* Correspondence: ncaiba@ugr.es; Tel.: +34-958-24-00-00

Received: 15 October 2018; Accepted: 31 October 2018; Published: 4 November 2018

Abstract: Inadequate diet influences chronic diseases such as cardiovascular disease (CVD), the leading cause of death in Spain. CVD figures vary from one geographical region to another; this could be associated with different food choices. Our aim was to analyse the influence of geographical area on nutrient intakes among the Spanish adult population with Metabolic Syndrome (MetS). We analysed cross-sectional baseline data from the PREDIMED-Plus study: 6646 Spanish adults, aged 55–75 years, with overweight/obesity and MetS in four geographical areas. A validated 143-item Food Frequency Questionnaire (FFQ) was used to assess energy and nutrient intakes. The prevalence of inadequate nutrient intake was estimated according to Dietary Reference Intakes (DRIs). Multivariable-adjusted logistic regression was used to assess the relationship between geographical area (North, Central, East and South areas) and inadequate nutrient intake. People in the North area consumed significantly lower amounts of vegetables and fish but more sugar and alcohol ($p < 0.001$) than other areas. Dietary fibre, vitamin A, E, calcium and magnesium intakes were all lower among men of North area than in the other areas ($p < 0.001$). Sex (women), non-smoker and physical activity were also associated to adequate nutrient intake. Geographical area influences nutrient intakes. Its effect on dietary quality should be taken into account when planning food policies.

Keywords: dietary intake; PREDIMED-Plus study; metabolic syndrome; place of residence; geographical area; nutrient adequacy

1. Introduction

Over the last decades, overweight and obesity have increased in most regions and countries worldwide [1]. A similar situation has been described in Spain. The prevalence of overweight has increased in the last 20 years with obesity figures now twice what they were twenty years ago and they have especially increased in the aged adult Spanish population [2]. The global burden of obesity and overweight can be explained by the increase in the consumption of diets with high energy density and low nutritional value, a consequence of the acquisition of Westernized dietary patterns [3].

A healthy dietary pattern which includes low amounts of saturated fat, salt and refined carbohydrates and promotes the consumption of high amounts of fruit, vegetables and whole grains have proved not only to reduce the risk of overweight and obesity but also to have a direct effect on chronic diseases incidence and prognosis which affect global health [4].

The traditional Mediterranean diet (MedDiet) described in the 1950s and 1960s [5], is characterized by frugality or moderation on food consumption, a high intake of vegetables, legumes, fruits and nuts, unrefined cereals, fish and olive oil and a low intake of saturated lipids, dairy products and red meat [6]. MedDiet prevents diseases that especially affect the aged population, such as neurodegenerative diseases, diabetes mellitus and some types of cancer [7–10]. Furthermore, MedDiet has also been associated with protection against some of the leading causes of morbidity and mortality worldwide, in particular cardiovascular disease (CVD) and metabolic syndrome (MetS) [11,12]. MetS is a well-described condition in the causative pathway of cardiovascular disease attributable to clustering factors that includes central obesity, insulin resistance, dyslipidaemia and hypertension [13].

Moreover, accumulated evidence suggests that the elevated overweight and obesity rates around the world are linked to MetS, coexisting with nutritional deficits in the adult population [14]. In this context, it is important to note that an increase in adherence to MedDiet is associated with better diet quality and lower prevalence of deficient intake of certain micronutrients. That is, the MedDiet has demonstrated supportive effects, not only on the protection against chronic diseases but also on the aged population's nutritional status [15].

The nutritional status of the aged population is an important public health issue; adequate dietary intake plays an important role in the healthy aging process. For a variety of reasons, that include economic, social and physiologic changes, aged adults are at risk of low dietary quality. Aging is accompanied by an increased need in several nutrients, such as vitamins and minerals, whereas the overall caloric requirements decline [16,17]. In this sense, the consumption of a high-quality diet such as MedDiet is essential to reduce malnutrition figures in older adults. Although some studies suggest that the adherence to MedDiet in Spain is greater than in other Mediterranean countries [18], recently published data on dietary patterns in Spanish adults indicated that adherence to the MedDiet has substantially declined [19].

In fact, besides age, sex or cultural level, the adherence to the MedDiet in Spain varies significantly among geographical areas. As an example, the Southern regions of Spain had the lowest score for adherence to the MedDiet in comparison with Northern regions [20,21], even though other authors have reported that place of residence has limited influence on dietary intake in the adult and senior adult population [22]. Therefore, differences in dietary intake do not only differ among Mediterranean countries but also within the same country, most likely because each area has its own gastronomic culture influenced by particular socioeconomic and cultural factors related to food choices and other determinants of dietary intake [20]: This could be responsible for the North-South cardiovascular mortality gradient in Spain [23].

To our knowledge little is known about dietary intake and inadequate nutrient intake among the older Spanish adults with MetS from different geographical areas of Spain. Our aim was to analyse the influence of geographical area on nutrient intakes among the Spanish adult population with MetS.

2. Materials and Methods

2.1. Study Design

This research represents a cross-sectional study on baseline data of the PREDIMED-Plus trial study. PREDIMED-Plus study is a 6-year Spanish multicentre ongoing randomized, parallel-group clinical trial testing the effect on CVD morbimortality of an intensive weight-loss intervention program based on an energy-restricted traditional MedDiet, physical activity promotion and behavioural support, in comparison with a usual care intervention only with energy-unrestricted Mediterranean diet (control group). The participant recruitment methods and data collection are fully described in a publication by Martinez-Gonzalez MA et al. [24] and at http://predimedplus.com/. The PREDIMED-Plus study protocol was approved according to the ethical standards of the Declaration of Helsinki by the respective Institutional Review Board (IRB) in each centre and registered at the International Standard Randomized Controlled Trial (ISRCT), with number 89898870. For more information, http://www.isrctn.com/ISRCTN89898870. Registration date: 24 July 2014. Informed consent was obtained from all individual participants included in the study.

2.2. Participants and Data Collection Procedures

The population of the study consisted of a total sample of 6874 aged adults of both genders that were selected and randomized in 23 centres of recruitment, including different universities, hospitals and Spanish research institutes, of the PREDIMED-Plus clinical trial from 14 Spanish provinces (Alicante, Barcelona, Cordoba, Granada, Jaen, Las Palmas de Gran Canaria, Leon, Madrid, Malaga, Mallorca, Navarra, Sevilla, Valencia and Vitoria), from October 2013 to November 2016. These centres recruited participants from Primary Care Health clinics belonging to the National Health System. Potential eligible participants were adult men aged between 55 and 75 years and women between 60 and 75 years with a body mass index between ≥27 and <40 kg/m^2 and meeting at least 3 criteria for MetS [13] but with no previous CVD. Participants were organized into 4 different areas (Figure 1) according to geographical area of residence (Nielsen areas) [22]. However, some regions have been grouped with contiguous geographical area, in the same way that other authors have described previously [20], due to the small sample size. North area (green-North) includes the northern areas: Leon, Navarra and the Basque Country. Central area (yellow-Central) comprises the central area of the country: Madrid. East area (blue-East) is composed of the areas located in eastern Spain: Cataluña, Valencia and Balearic Islands. Finally, South area (red-South) covers the south of Spain (Andalucía) and Canary Islands.

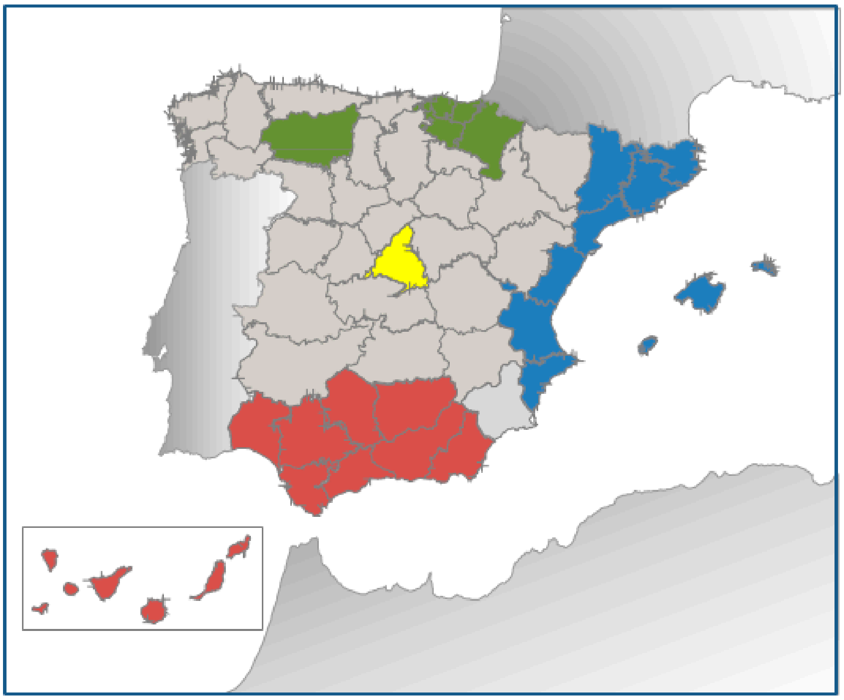


Figure 1. Map of Spain with the geographical areas analysed.

For the current analysis, 228 participants were excluded (Figure 2) because they reported values for total energy intake outside of the predefined limits (<800 kcal/day or >4000 kcal/day for men); (<500 kcal/day or >3500 kcal)/day for women). These limits were set in accordance with recommendations by Willett in Nutritional Epidemiology [25]. In addition, 47 participants were excluded because they did not complete the Food Frequency Questionnaire (FFQ). After applying these exclusion criteria, a final sample of 6646 participants was analysed.

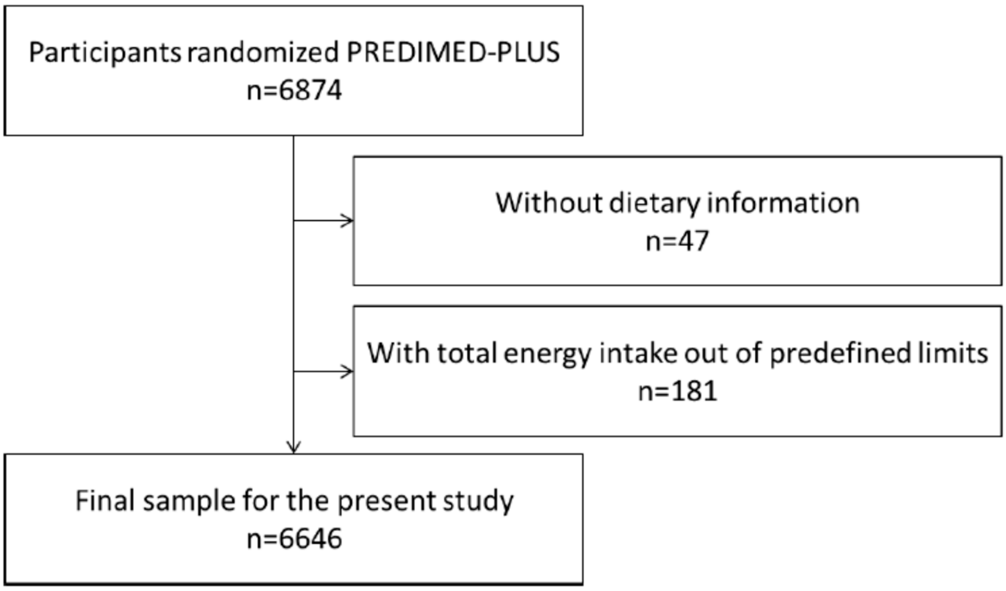


Figure 2. Flow-chart of participants.

2.3. Assessment of Dietary Intake

Trained nutritionists collected baseline food intake data in their baseline interview using the PREDIMED FFQ, which has been previously validated in Spanish subjects [26,27]. The FFQ included 143 food items, arranged into 11 food groups, taking into account the similarities of their nutrient profiles (vegetables, fruits, legumes, cereals, milk and dairy products, meat and meat products, fish and seafood, olive oil, nuts, sugars and sweets and eggs). The FFQ includes 9 possible answers for consumption frequency ranging from never/seldom to >6 servings/day. The indicated frequencies of consumption were converted to intakes per day and multiplied by the weight of the portion size indicated by the participant and expressed as grams per day [28]. Nutrient information was derived using Spanish food composition tables [29,30]. Subjects were asked about MedDiet adherence via a 17-item screening questionnaire, which contains modifications to a previously validated 14 items questionnaire [31], used to evaluate compliance with the intervention and was also a key element to guide the motivation interviews during the study follow-up. Compliance with each of the 17 items relating to characteristic food habits was scored with 1 point and 0 points for non-adherence. Therefore, the total score range was 0–17, with 0 meaning no adherence and 17 meaning maximum adherence. Adherence to MedDiet was categorised in tertiles, as low level of adherence (1st tertile, $\leq$7 points), medium (2nd tertile, 8–10 points) or high level of adherence (3rd tertile, $\geq$11 points). Dietary intake of total energy, total fat and fatty acids: monounsaturated (MUFAs), polyunsaturated (PUFAs) and saturated (SFAs), proteins and carbohydrates were estimated. Dietary fibre and alcohol intake were also measured. Inadequate nutrient intake of dietary fibre and vitamins A, D, E, B_{12}, B_6, B_9 and minerals such as calcium, magnesium and phosphorus were analysed according to the Dietary Reference Intakes (DRIs) for the American population for each participant [32]. DRIs is the general term for a set of reference values used to plan and assess nutrient intakes of healthy people. These values vary by age and sex and include the Recommended Dietary Allowance (RDA): average daily level of intake sufficient to meet the nutrient requirements of nearly all (97–98%) healthy people, Adequate Intake (AI): established when evidence is insufficient to develop an RDA and is set at a level assumed to ensure nutritional adequacy and Tolerable Upper Intake Level (UL): maximum daily intake unlikely to cause adverse health effects [33]. Intake levels above DRI imply a low likelihood of inadequate intake. To decrease possible measurement errors derived from FFQ, we estimated the proportion of individuals with intakes below two thirds (2/3) of the DRIs, correcting the possible bias introduced by the FFQ and assuming in any case that the actual inadequate intake should be higher than the figures which were estimated [34]. Furthermore, we have estimated the inadequate intake according to the European Food Safety Agency (EFSA) average requirements (AR), taking as reference AI when AR were not available [35]. We also studied the proportion of participants with inadequate intake of 3 or more out of 6 nutrients. Results were based on dietary intake data only, excluding intake of supplements.

2.4. Assessment of Non-Dietary Intake

During the baseline visit, trained staff of PREDIMED-Plus trial documented information using a baseline questionnaire on sociodemographic data and lifestyle behaviours. The variables included were sex, age (55–70 years and >70 years), geographical area (North, Central, East or South area), education level (primary level, secondary level and tertiary level that includes university studies), civil status (married, widowed, divorced/singled or others) and whether they lived alone or not. Other lifestyle variables such as smoking habits, alcohol intake (grams per day) and physical activity were taken into account. Physical activity information was gathered using the validated Spanish version of the Minnesota questionnaire [36,37].

2.5. Statistical Analysis

We used the PREDIMED-Plus baseline database generated in August 2017. Qualitative variables were analysed through their frequency distribution, whereas quantitative variables were expressed as means and standard deviations (SD). Pearson's chi-square tests and Analysis of Variance (ANOVA) (for categorical and continuous variables, respectively) were used to assess differences in baseline characteristics of participants according to geographical area. Also, ANCOVA was used to estimate dietary intakes, adherence to MedDiet and nutrient profiles according to geographical area adjusted for sex and age. The significance level was set at 5%. The main outcome of this analysis was inadequate intake of micronutrients, defined for each nutrient as a daily intake below 2/3 of DRIs and set at 95% confidence interval (CI). We also repeated the analysis defining inadequate intake according to AR/AI proposed by EFSA. Geographical area was the principal independent variable. The associations between geographical area and inadequate intakes were summarized using odds ratios and 95% CI obtained via multiple-adjusted logistic regression models. The logistic regression model was adjusted for sex, age (55–70 years and >70 years), adherence to MedDiet (low, medium and high adherence), total energy intake, smoking habits (current, former or never smoker), physical activity (less active, moderately active and active), living alone, diabetic status and educational level (primary, secondary and tertiary). A logistic regression model was used to examine the associations between the place of residence and inadequate nutrient intake (defined as deficient intake for 3 or more nutrients) adjusted for the same potential confounding factors mentioned above.

Vitamins B_6, B_{12} and phosphorus intakes were excluded from the logistic regression model, because a binary test showed these to be asymmetrically distributed and also a low proportion of subjects presented inadequate intake of these micronutrients. In addition, the intake of vitamin D was also excluded from the statistical analysis because it was deficient in a high proportion of the population (over 80%). All analysis were cross-sectional and performed using Stata (12.0, StataCorp LP, College Station, TX, USA).

3. Results

3.1. Baseline Characteristics of the Population and Food Intake

The baseline characteristics of participants and the food group intake in grams per day by geographical area are shown in Table 1. Mean patient age was 65.0 ± 4.9 years and 51.6% (n = 3431) of participants were male. When baseline characteristics were compared according to the four geographical areas included, differences were found in age, smoking habits, physical activity, cultural level and civil status. Regarding physical activity, 21.3% reported they were active, while 59.8% did not. Central area had the highest rates of active population (37.0%). The majority of the population had a primary educational level (48.3%, primary school) but, differences were evident among the 4 areas. The highest percentage of participants with only primary school (54.9%) was observed in South area.

Table 1. Baseline characteristics of the PREDIMED-Plus study participants by geographical areas (total population n = 6646).

	Total Population (n = 6646)	North Area (n = 1436)	Central Area (n = 493)	East Area (n = 2938)	South Area (n = 1779)	p Value
Sex, n (%)						
Male	3431 (51.6)	823 (57.3)	264 (53.6)	1478 (50.3)	866 (48.7)	<0.001
Female	3215 (48.4)	613 (42.7)	229 (46.5)	1460 (49.7)	913 (51.3)	
Age, n (%)						
55–70 years	5673 (85.4)	1203 (83.8)	444 (90.0)	2478 (84.3)	1548 (87.0)	<0.001
>70 years	973 (14.6)	233 (16.2)	49 (9.9)	460 (15.7)	231 (13.0)	
Mean ± SD	65.0 ± 4.9	65.2 ± 5.0	64.1 ± 4.9	65.2 ± 4.9	64.6 ± 4.8	<0.001
Smoking habits, n (%)						
Current smoker	825 (12.4)	180 (12.5)	53 (10.8)	357 (12.2)	235 (13.2)	<0.001
Former smoker	2883 (43.4)	690 (48.3)	256 (51.9)	1251 (42.6)	683 (38.4)	
Never smoker	2910 (43.8)	555 (38.7)	180 (36.5)	1325 (45.1)	850 (47.8)	
Insufficient data	28 (0.4)	8 (0.6)	4 (0.8)	5 (0.2)	11 (0.6)	
Diabetes mellitus, n (%)	1818 (27.4)	349 (24.3)	125 (25.4)	846 (28.8)	498 (28.0)	0.001
Physical Activity, n (%)						
Less active	3961 (59.8)	712 (49.8)	350 (71.4)	1720 (58.6)	1179 (66.7)	<0.001
Moderately active	1249 (18.9)	261 (18.3)	71 (14.5)	584 (19.9)	333 (18.8)	
Active	1412 (21.3)	457 (32.0)	69 (14.1)	629 (21.5)	257 (14.5)	
Education level, n (%)						
Tertiary	1463 (22.0)	305 (21.2)	181 (37.0)	654 (22.3)	323 (18.2)	<0.001
Secondary	1912 (28.8)	443 (30.9)	184 (37.6)	827 (28.2)	458 (25.7)	
Primary	3207 (48.3)	674 (46.9)	121 (24.7)	1436 (48.9)	976 (54.9)	
Insufficient data	60 (0.9)	14 (1.0)	3 (0.6)	21 (0.7)	22 (1.2)	
Civil status, n (%)						
Married	5072 (76.6)	1109 (77.9)	351 (72.1)	2240 (76.5)	1372 (77.1)	<0.001
Widowed	690 (10.4)	150 (10.5)	38 (7.8)	313 (10.7)	189 (10.2)	
Divorced/Separated	519 (7.8)	82 (5.8)	53 (10.9)	244 (8.3)	140 (7.9)	
Others [a]	339 (5.1)	83 (5.8)	45 (9.2)	133 (4.5)	78 (4.4)	
Living alone, n (%)	826 (12.5)	180 (12.6)	77 (15.7)	365 (12.4)	204 (11.5)	0.100
Diabetic, n (%)	1818 (27.4)	349 (24.3)	125 (25.4)	846 (28.8)	498 (28.0)	0.001

Values are presented as mean ± SD for continuous variables and n (%) for categorical variables. Pearson's chi-square test was performed for categorical variables and ANOVA test for continuous variables. [a] includes single and religious.

3.2. Description of Food Intake, Adherence to MedDiet and Nutrient Profiles in the Different Geographical Areas Analysed

Evaluation of food group intake, adherence to MedDiet and nutrient profiles among geographical areas of Spain adjusted for age and sex are shown in Table 2. According to the geographical area, the estimated adjusted mean intakes of fruits, sugar and sweets, olive oil, cereals and eggs were significantly higher among those participants living in North area than among those living in the other areas ($p < 0.001$). Whereas the intake of vegetables, nuts, legumes, fish and seafood were the lowest compared with the others geographical territories analysed ($p < 0.001$). The evaluation of food intake by sex and age among the geographical areas is shown in the Supplementary Materials (Table S1). In order to evaluate differences in MedDiet adherence across the geographical areas, we compared the mean score. The overall adherence score was 8.5 ± 2.7 (data not shown). According to geographical area, the East area showed the worst mean score of adherence, which was significantly lower than the mean score obtained in Central and South areas. The South area showed the lowest total energy intake, although, the contribution of healthy fats such as MUFAs and PUFAs was higher compared to the other geographical areas. Alcohol intake was higher in North area. The adherence to MedDiet and nutrients profile among areas stratified by sex and age is presented in Supplementary Table S2. Mean adherence to MedDiet increased in aged population (more than 70 years) in both sexes, being higher in women than in men. Total energy intake decreased with age in both sexes. Alcohol intake was higher in men than in women independently of age or place of residence, being the highest in the North area.

3.3. Evaluation of Inadequate Nutrient Intake According to Recommended Intakes

Table 3 shows the proportion of participants who showed nutrient intake below 2/3 of DRIs by geographical area. An inadequate intake of dietary fibre, vitamins A, B_9, E and calcium was common in all the analysed groups of participants. Comparing the inadequate intakes by sex, men showed a higher prevalence than women of inadequate intake for most of the nutrients analysed. For the majority of nutrients, the prevalence of inadequate intake increased in women in older ages but not in men, except for calcium. In accordance to geographical areas, the North area presented the highest prevalence of inadequate intake for most nutrients analysed, except for vitamin B_9 and dietary fibre, while East area presented the lowest prevalence of deficient intake for all the micronutrients analysed but differences are statistically significant only among the youngest participants and only for vitamins A, D and E. These results are similar if the EFSA recommendations are used (Table S3).

Table 2. Intake of food groups (g/day), adherence to MedDiet and nutrient profiles among geographical areas analysed (total population *n* = 6646).

	North Area		**Central Area**		**East Area**		**South Area**		
n	**(*n* = 1436)**		**(*n* = 493)**		**(*n* = 2938)**		**(*n* = 1779)**		***p* Value**
	Mean	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**	
Food group intake									
Vegetables (g/day)	291.1	284.1–298.2	327.8	315.1–340.5	335.8	330.8–34.7	331.5	325.1–337.9	<0.001
Fruits (g/day)	389.6	380.0–400.1	366.0	347.0–385.0	332.5	325.1–339.8	366.9	357.4–376.5	0.001
Legumes (g/day)	18.8	18.2–19.4	20.6	19.6–21.7	19.7	19.3–20.1	23.2	22.7–23.8	<0.001
Cereals (g/day)	173.4	169.4–177.4	150.2	143.0–157.3	142.8	140.0–145.5	143.8	140.2–147.4	<0.001
Milk/dairy products (g/day)	367.0	356.6–377.3	387.3	368.7–405.9	320.8	313.6–328.1	357.9	348.6–367.3	<0.001
Meat/meat products (g/day)	150.8	147.9–153.7	143.6	138.4–148.8	155.4	153.4–157.5	125.7	123.1–128.3	<0.001
Olive oil (g/day)	42.9	42.0–43.8	35.9	34.4–37.5	40.6	40.0–41.2	37.0	36.2–37.8	<0.001
Fish/seafood (g/day)	95.7	93.3–98.1	109.8	105.4–114.1	102.5	100.9–104.2	99.5	97.3–101.7	<0.001
Nuts (g/day)	12.9	12.–13.8	16.3	14.7–17.9	15.0	14.4–15.6	15.5	14.7–16.3	<0.001
Sugar/sweets (g/day)	32.6	31.1–34.2	29.5	26.7–32.2	25.5	24.5–26.6	23.2	21.8–24.6	<0.001
Eggs (g/day)	25.9	25.3–26.5	24.1	23.0–25.2	22.6	22.1–23.0	23.0	22.5–23.6	<0.001
Adherence to MedDiet									
MedDiet Q-P17 [a], mean	8.6	8.4–8.7	9.2	9.0–9.5	8.1	8.0–8.2	8.9	8.8–9.0	<0.001
Energy intake and nutrient profiles, mean									
Total energy intake (kcal/day)	2425.0	2397.6–2452.3	2398.8	2349.7–2447.9	2357.6	2338.5–2376.6	2301.0	2276.3–2325.7	<0.001
Total fat intake (%)	38.3	38.0–38.6	38.5	37.9–39.1	40.4	40.1–40.6	39.0	38.7–39.3	<0.001
Monounsaturated fat (%)	19.9	19.7–20.2	19.5	19.1–19.9	21.0	20.8–21.1	20.3	20.1–20.5	<0.001
Polyunsaturated fat (%)	6.1	6.0–6.2	6.3	6.1–6.5	6.4	6.3–6.4	6.5	6.4–6.6	<0.001
Saturate fat (%)	9.5	9.4–9.6	10.1	9.9–10.2	10.3	10.2–10.3	9.6	9.5–9.6	<0.001
Carbohydrate intake (%)	41.8	41.1–42.1	41.6	41.0–42.3	39.8	39.6–40.1	41.8	41.5–42.1	<0.001
Protein intake (%)	16.3	16.1–16.4	17.0	16.7–17.2	16.8	16.7–16.9	16.4	16.3–16.5	<0.001
Alcohol intake (g/day)	13.5	12.8–14.2	10.4	9.1–11.6	10.6	10.1–11.1	9.7	9.1–10.4	<0.001
Fibre intake (g/day)	25.8	25.4–26.3	26.4	25.6–27.3	25.8	25.4–26.1	26.2	25.8–26.6	0.191

Values are presented as means adjusted by age and sex. ANCOVA test was performed. [a] MedDiet Q-P17, adherence to Mediterranean diet questionnaire 17 point cut off.

Table 3. Participants with nutrient intake below 2/3 of DRIs by geographical areas, age and sex.

Nutrient	Group	DRI [a]	North Area	Central Area	East Area	South Area	p Value [1]
Dietary fibre	Male 55–70	30 g/day	28.1	28.4	27.0	29.2	0.744
	Male >70	30 g/day	19.4	27.8	24.0	29.4	0.442
	Female 60–70	21 g/day	2.3	4.6	4.1	4.0	0.310
	Female >70	21 g/day	3.7	6.9	5.6	2.2	0.383
***p* value [2]**			<0.001	<0.001	<0.001	<0.001	
Vitamin A	Male 55–70	900 µg/day	28.8	21.2	15.8	16.6	<0.001
	Male >70	900 µg/day	25.5	16.7	17.3	17.4	0.353
	Female 60–70	700 µg/day	8.6	5.8	5.6	5.2	0.078
	Female >70	700 µg/day	8.2	6.9	10.4	5.1	0.341
***p* value [2]**			<0.001	<0.001	<0.001	<0.001	
Vitamin B_9	Male 60–70	400 µg/day	19.3	18.5	22.2	22.6	0.250
	Male >70	400 µg/day	17.4	22.2	18.8	23.9	0.667
	Female 55–70	400 µg/day	15.7	17.3	17.4	20.2	0.204
	Female >70	400 µg/day	11.9	24.1	21.9	21.0	0.092
***p* value [2]**			0.128	0.819	0.020	0.649	
Vitamin D	Male 60–70	15 µg/day	89.0	75.7	83.6	83.0	<0.001
	Male >70	20 µg/day	99.0	100.0	97.6	97.8	0.786
	Female 55–70	15 µg/day	87.9	77.5	82.0	85.0	0.002
	Female >70	20 µg/day	98.5	93.1	97.2	100.0	0.061
***p* value [2]**			<0.001	0.021	<0.001	<0.001	
Vitamin E	Male 55–70	15 mg/day	63.7	52.3	43.3	43.6	<0.001
	Male >70	15 mg/day	56.1	50.0	44.7	54.4	0.214
	Female 60–70	15 mg/day	63.1	48.6	49.0	50.4	<0.001
	Female >70	15 mg/day	70.2	44.8	61.8	61.6	0.062
***p* value [2]**			0.178	0.826	<0.001	<0.001	
Calcium	Male 55–70	1000 mg/day	14.2	8.6	11.7	13.5	0.090
	Male >70	1200 mg/day	22.5	11.1	30.8	30.4	0.163
	Female 60–70	1200 mg/day	25.3	19.7	26.7	25.7	0.268
	Female >70	1200 mg/day	21.6	27.6	24.3	28.3	0.625
***p* value [2]**			<0.001	0.002	<0.001	<0.001	
Magnesium	Male 55–70	420 mg/day	10.2	8.1	7.6	7.7	0.206
	Male >70	420 mg/day	12.2	5.6	8.7	9.8	0.718
	Female 60–70	320 mg/day	1.0	1.7	1.2	1.5	0.846
	Female >70	320 mg/day	1.5	3.5	1.2	1.5	0.819
***p* value [2]**			<0.001	0.042	<0.001	<0.001	

DRI [a]: Dietary Reference Intake. Pearson's Chi-Square test was used to estimate differences among prevalence of inadequate nutrient intakes according to geographical area for each age and sex strata (*p* value [1]) and also to estimate differences among prevalence of inadequate nutrient intakes according to age and sex, for each geographical area (*p* value [2]).

3.4. Assessment of the Influence of the Geographical Area on Inadequate Nutrient Intake

We examined the possible effect of geographical area on the inadequate intake of nutrients (Table 4), with North area as the reference category. The unadjusted logistic regression model revealed that the geographical area influenced the inadequate intake for all the nutrients analysed except for dietary fibre. In this sense, not living in the North area was significantly associated with a lower likelihood of inadequate intake of vitamin A, E, calcium and magnesium ($p < 0.001$). However, for vitamin B_9, the East and the South areas had a higher probability of inadequate intake in comparison with the Northern reference area (OR = 1.19 and 1.31 respectively, $p < 0.001$). When we used the EFSA dietary recommendations, we obtained very similar results (Table S4). The influence of demographics (age, sex and place of residence) and other socioeconomic and lifestyle variables on inadequate nutrient intake according to the DRIs criteria is presented in the Supplementary Materials (Table S5). Inadequate nutrient intake was influenced by geographical area and sex. It was also inversely associated with better adherence to the MedDiet, total energy intake, not diabetic, being moderately active and being a non-smoker ($p < 0.001$). The Supplementary Table S6, shows similar associations according to EFSA criteria for all nutrients except for calcium.

Table 4. Results from the logistic regression model of micronutrient inadequate intakes according to 2/3 DRIs by geographical areas.

Nutrient		North Area	Central Area	East Area	South Area
Dietary fibre	Model 1	1 (Ref.)	1.08 (0.81−1.43)	0.92 (0.78−1.10)	0.97 (0.80−1.17)
	Model 2	1 (Ref.)	1.03 (0.72−1.46)	0.80 (0.65−0.98)	0.92 (0.73−1.15)
Vitamin A	Model 1	1 (Ref.)	0.66 (0.49−0.89)	0.51 (0.43−0.61)	0.49 (0.40−0.59)
	Model 2	1 (Ref.)	0.57 (0.41−0.80)	0.43 (0.35−0.52)	0.40 (0.32−0.50)
Vitamin B_9	Model 1	1 (Ref.)	1.09 (0.83−1.44)	1.19 (1.01−1.41)	1.31 (1.10−1.57)
	Model 2	1 (Ref.)	0.98 (0.70−1.36)	0.97 (0.80−1.17)	1.09 (0.88−1.34)
Vitamin E	Model 1	1 (Ref.)	0.58 (0.47−0.72)	0.52 (0.45−0.59)	0.54 (0.47−0.62)
	Model 2	1 (Ref.)	0.47 (0.36−0.61)	0.30 (0.26−0.35)	0.30 (0.25−0.36)
Calcium	Model 1	1 (Ref.)	0.70 (0.52−0.94)	1.07 (0.91−1.26)	1.11 (0.93−1.32)
	Model 2	1 (Ref.)	0.53 (0.38−0.76)	0.86 (0.72−1.04)	0.80 (0.65−0.98)
Magnesium	Model 1	1 (Ref.)	0.80 (0.50−1.28)	0.68 (0.52−0.89)	0.70 (0.51−0.95)
	Model 2	1 (Ref.)	0.39 (0.21−0.75)	0.35 (0.25−0.50)	0.33 (0.22−0.49)

Values are presented as OR and 95% CI for the inadequate intake of micronutrients as categorical variable according to area of residence. Model 1: This model has not been adjusted for any variable. Model 2: has been adjusted by sex, age, smoking habits, physical activity, educational status, diabetic status, living alone, total energy intake and adherence to MedDiet.

3.5. Multivariable Logistic Regression Model for Inadequate Intake of 3 or More out 6 Micronutrients According to Place of Residence

Table 5 shows the result from the logistic regression model fitted using inadequate intake of 3 or more out of 6 micronutrients as the dependent variable. In the North area, 19.0% of participants showed inadequate intake for 3 or more. Dwellers of Central, East and South areas had a lower probability of inadequate intake for 3 or more micronutrients ($p < 0.05$). When we used AR/AI provided by the EFSA, we obtained higher figures (Table S7), reaching 40.8% of participants with inadequate intake in the North area.

Table 5. Multivariable logistic regression model for inadequate intake of 3 or more out 6 micronutrients according to geographical area.

	≥3 Inadequate Intake % Prevalence (95% CI)	Adjusted Odds Ratio (95% CI)	*p* Value
Geographical area			
North area	19.0 (17.0–21.1)	1 (Ref.)	
Central area	16.3 (12.8–19.7)	0.65 (0.46–0.94)	0.021
East area	15.9 (14.6–17.2)	0.57 (0.47–0.70)	<0.001
South area	16.8 (15.0–18.5)	0.59 (0.47–0.74)	<0.001

Results are expressed as OR and 95% CI for the inadequate intake of ≥3 micronutrients as categorical variables according to geographical area. The model has been adjusted for sex, age, smoking habits, physical activity, educational status, diabetic status, living alone, total energy intake and adherence to MedDiet.

4. Discussion

Our results show significant differences between dietary intake patterns among the different geographical areas included, characterized by cultural, economic and gastronomic diversity. These differences are maintained across the different age and sex strata, coinciding with differences in the prevalence of inadequate intake of micronutrients such as vitamin A, E, B_9, Ca and Mg. The differences found in adequate nutrient intake among the geographical areas studied could be attributable to different dietary intakes that were also influenced by sex, not being smoker, not being diabetic and being active.

The traditional MedDiet pattern has been associated with a higher consumption of vegetables, fruits, fish, legumes and nuts [38]. However, the current dietary pattern in Spain is turning into a Westernized diet, including the overweight or obese adult population, with high consumption of sugar and meat products and a decline in the consumption of vegetables and fruits [39]. Although our results suggest that the main estimated food groups consumed were vegetables and fruits, meat and processed meat intake were elevated, while fish, seafood and legumes consumption seemed to be lower according to the recommended intakes. However, compared to a Spanish food consumption survey carried out in 2013, our estimate intake of fish and legumes was slightly higher (100.7 g/day/person versus 88.7 g/day/person and 22.1 g/day/person versus 13.9 g/day/person for fish and legumes, respectively). In contrast, egg intake was somewhat lower (23.5 versus 27.1) [40]. Egg consumption in our study was under the usually recommended levels [41], probably due to the general (but unfounded) concern that egg consumptions may increase blood cholesterol levels [42].

Depending on geographical areas, differences in food intake were found. The inhabitants of North area, especially men, consumed more sugars, sweets and alcohol than the other three areas. These data are also reflected in another Spanish study which reported that adult males from the North of Spain had higher intakes of these food groups than adult males from other Spanish areas [22]. Surprisingly, East area, the main area of fruit production in Spain, showed the lowest fruit consumption. The same was observed for olive oil consumption in South area, in spite of being the greatest olive oil producing region in the world. These data are also consistent with findings in another Spanish survey [20].

Food choices depend on individual's elections, conditioned by cultural influences, demographic and socio-economic factors [43]. In addition to the geographical area, age and sex were important factors in determining food intake. According to our data, a higher consumption of vegetables, fruits and fish or seafood was found in women compared with men. Other previous studies also corroborated these findings, highlighting that females consumed more fruit and vegetables than males, decreasing the risk of nutrient deficiencies [44]. In our study, oldest people (more than 70 years) tend to have a higher consumption of vegetables, fruits, legumes, nuts and fish compared to a younger adult population. Similar findings have been previously reported in a Swiss community-dwelling sample [45].

People in Mediterranean countries such as Spain, have decreased their adherence to the MedDiet pattern, which was traditionally high [46]. Our results show only a moderate MedDiet adherence in most of the areas analysed. Other studies indicated a similar adherence to MedDiet at baseline interview [47]. According to the geographical area, the lowest mean score of adherence to MedDiet was found in East area, especially in younger adult men, which barely reached a compliance score of 8 out of 17 points. This finding can be explained by the low intake of fish and fruits, a surprising outcome as the geographical location of this area is on the Mediterranean coast and has an extensive agricultural tradition. This result is similar to previous findings reported in the DIMERICA study [20]. Furthermore, the percentage of the population in the first tertile of adherence to MedDiet (low adherence) reached a maximum of 48.9% in men (55–70 years) in the East area and a minimum of 16.7% in women (>70 years) in the Central area. The data described by other authors consistently show a high adherence to MedDiet in women and the aged population [48,49]. However, this phenomenon could be attributable to a generational effect (cohort effect).

Energy and nutrient intakes in our population revealed a diet high in proteins and lipids and low in carbohydrates. In this sense, protein intake and total fat intake were above the upper recommended limits (15% and 30% of total energy intake, respectively) [50]. Other authors have shown a similar nutrient distribution in Spanish population [51]. Despite the fact that in our study total fat intake was higher than recommended for adult population, recent results from PREDIMED study have postulated that fat quality intake is a major nutritional determinant of quality of diet and cardiovascular benefits can be obtained with a relatively fat-rich diet [52]. Particularly, the adequate intake of MUFAs and PUFAs in our study, mainly due to a high consumption of olive oil, has been previously associated with a lower risk of CVD [53]. On the one hand, the intake of SFAs was not higher than 10% in most of the areas analysed, except in the East area, probably because this area recorded the highest consumption of meat and meat products compared to the other geographical territories. On the other hand, low intakes of carbohydrates and dietary fibre may be linked to low consumption of cereals, vegetables and fruits in our population study, influenced by an abandonment of traditional eating choices [54].

Nutrient availability can be compromised by unbalanced dietary patterns, especially for specific population groups whose requirements are increased because of age or diseases [55]. In elderly, the decrease of energy, as a result of lower food consumption has been described as an essential factor for inadequate nutrient intake [56]. Despite our population having a higher energy intake, the results in the present study suggest that they present several nutritional inadequate intakes (dietary fibre, vitamins A, B_9, E, calcium and magnesium). Consequently, other authors put forward that micronutrient deficiencies occur frequently in overweight or obese subjects due to poor-nutritional habits and high intake of energy-dense foods [57]. In our study, the prevalence of inadequate intake was increased in elderly women but not in men for the majority of nutrients, except for calcium. This fact can be explained by an increase of milk and dairy products consumption, due to the general concern about their effects and properties on aged women bones [58]. In accordance with place of residence, the North area presented the highest prevalence of inadequate nutrient for most of the nutrients analysed, except for vitamin B_9 and dietary fibre. This may be as consequence of their high intake of meat and meat products and cereals, as shown in Table 3, compared with the other geographical areas.

Determinants of diet quality are multilevel and include food choices influenced by demographic variables, socioeconomic and cultural factors [59]. When comparing data from this study with a recent one which suggested that place of residence has a limited influence on dietary intake [22], our study shows that geographical area was a predictive factor of nutrient adequacy, with the highest inadequate nutrient intake in inhabitants of the North area for the majority of the nutrients analysed. In the same line, the analysis of the association between place of residence and dietary intake among North American adult women showed regional disparities in dietary intake influenced by food environment and food customs [60]. Furthermore, findings from this study, suggest that lifestyle behaviours, in particular smoking status (not being a smoker) and physical activity (being more active), were associated in a significant positive way the adequacy of nutrient intakes. Other study carried out in Brazil found a similar association for adequate minerals intake [61]. Other factors, for instance sex, have been postulated as criterion for an adequate dietary intake [62]. A study that assessed the role of diet knowledge, reported that women followed a healthy diet compared with men due to higher knowledge about food choices [63]. These results are consistent with findings in our work in which women had lower risk of inadequate nutrient intake than men.

Finally, micronutrient intakes in elderly adults are related to socioeconomic and cultural level factors, so that participants with a high educational level and from a high social class had overall higher micronutrient intakes [64,65]. Nevertheless, we have not found this relationship, presumably because most of our participants had a similar socioeconomic and cultural level, so variability in these determinants was small.

Our study has some limitations and several strengths. Firstly, the methodological nature of a cross-sectional analysis, does not allow to address causality, although the possibility of reverse causality bias as an alternative, non-casual, explanation of our results is unlikely (nutrient intake cannot predict geographical area). Secondly, the present findings cannot be extrapolated to other population groups given that our study participants are aged adults with overweight/obesity and MetS and the sample is not representative of the general population. However, our sample is large enough to be representative of this specific population group. Thirdly, the exposure measurement of dietary intake could be influenced by the retrospective way to assess dietary intake. Although the FFQ used has been validated in adult Spanish population and has good reproducibility and a relatively good validity [28], this questionnaire may be subject to potential bias with under-reporting being a common error. For this reason, we have considered that there is an inadequate intake only when the intake does not reach 2/3 of the DRIs, with the aim to compensate the possible bias introduced by the FFQ and assuming in any case that the actual inadequate micronutrient intake should be superior to the estimated figures. However, the bias introduced would be non-differential, affecting uniformly the different geographical areas. Finally, it is unknown if the participants have always resided in the same geographical area, however, the internal migration fluxes in Spain have been low in the last twenty years, affecting mainly young people [66,67]. Among the strengths of the PREDIMED-Plus study we must point out the use of a standardized protocol which reduces information bias about food intake, socioeconomic and lifestyles variables and the election of a large sample highly representative of the Spanish older adults with MetS (n = 6646), as well as the inclusion of community-dwelling older population that contributes to determine the modification on nutrient intakes related to geographical disparities. Finally, to our knowledge, no study in Spain has analysed the influence of geographical area on nutrient intake in older adult population at high risk of CVD.

5. Conclusions

Despite the higher figures of overweight and obesity in older adult population at high risk of CVD, there are significant inadequate nutritional intakes. Even within the same country, geographical area was significantly associated with inadequate nutrient intake. The dietary pattern of the aged adult population leaves sufficient room from improvement in relationship with the promotion of the MedDiet adherence, as well as to ensure adequate micronutrients intake. If we want to change dietetic habits in a population we need to take into account their roots and peculiarities. Therefore, it is important to show the basal differences in nutrient intake among the different study centres. This will be useful to fully understanding the results of the PREDIMED-Plus study and in addition, if this intervention is successful to extend it to other countries.

Supplementary Materials: The following materials are available online at http://www.mdpi.com/2072-6643/10/11/1661/s1, Table S1: Intake of food groups (g/day) in both sexes divided by geographical areas and age, Table S2: MedDiet adherence, total energy intake and profile of macronutrients, fibre and alcohol intake by geographical areas (total population n = 6646) among 55–75 years population, Table S3: Participants with nutrient intake below AR/AI proposed by EFSA by geographical areas, age and sex, Table S4: Logistic regression model of micronutrients inadequate intake according to EFSA by geographical areas, Table S5: Logistic regression model of micronutrients deficiency intake according to 2/3 DRIs by areas, Table S6: Logistic regression model of micronutrients deficiency intake according to EFSA by areas, Table S7: Multivariable logistic regression model for inadequate intake of 3 or more out 6 micronutrients in accordance with criteria by EFSA according to geographical area.

Author Contributions: N.C.-I., A.B.-C., M.A.M.-G., D.C., J.S.-S., M.D.Z., M.G.-H., D.R., J.A.M., F.J.B.-L., A.G.-R., R.E., L.G.-M., A.A.G., J.A.T., F.T., L.S.-M., N.C.-F., J.L., C.V., X.P., J.V., L.D., J.J.G., P.M., E.R., J.D.-E., R.F.-C., J.B., M.F., J.M.Z., A.C., E.T., A.D.-L., M.A.M., M.R.-C., and A.G. collected all the data from the PREDIMED-Plus trial. N.C.-I., A.G. and A.B.-C. designed the study; performed the analysis; and wrote the first draft of the manuscript and all authors contributed to the editing of the manuscript. All authors approved the final version of the manuscript.

Funding: The PREDIMED-Plus trial was supported by the official funding agency for biomedical research of the Spanish government, ISCIII through the Fondo de Investigación para la Salud (FIS), which is co-funded by the European Regional Development Fund (three coordinated FIS projects led by J.S.-S and J.V., 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, 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), the Especial Action Project entitled: Implementación y evaluación de una intervención intensiva sobre la actividad física Cohorte PREDIMED-Plus grant to J.S.-S, the European Research Council (Advanced Research Grant 2013–2018; 340918) grant to M.A.M.-G., the Recercaixa grant to J.S.-S (2013ACUP00194), the grant from the Consejería de Salud de la Junta de Andalucía (PI0458/2013; PS0358/2016), the PROMETEO/2017/017 grant from the Generalitat Valenciana, the SEMERGEN grant and FEDER funds (CB06/03). None of the funding sources took part in the design, collection, analysis or interpretation of the data, or in the decision to submit the manuscript for publication. The corresponding authors had full access to all the data in the study and had final responsibility to submit for publication.

Acknowledgments: The first author would like to acknowledge support by the Ministry of Education of Spain (FPU14/03630). The authors especially thank the PREDIMED-Plus participants for their collaboration and the PREDIMED-Plus staff for their support and effort. The authors would like to thank Ingrid de Ruiter, MBChB for English language assistance.

Conflicts of Interest: J.S.-S. reports serving on the board of and receiving grant support through his institution from International Nut and Dried Fruit Council; receiving consulting personal fees from Danone, Font Vella Lanjarón, Nuts for Life and Eroski; and receiving grant support through his institution from Nut and Dried Fruit Foundation and Eroski. E.R., reports grants, non-financial support and other fees from California Walnut Commission and Alexion; personal fees and non-financial support from Merck, Sharp & Dohme; personal fees, non-financial support and other fees from Aegerion and Ferrer International; grants and personal fees from Sanofi Aventis; grants from Amgen and Pfizer and; personal fees from Akcea, outside of the submitted work. X.P., reports serving on the board of and receiving consulting personal fees from Sanofi Aventis, Amgen and Abbott laboratories; receiving lecture personal fees from Esteve, Lacer and Rubio laboratories. L.D. reports grants from Fundación Cerveza y Salud. J.J.G. reports receiving grants from the Diputación Provincial de Jaén and the Fundación Caja Rural de Jaén. All other authors declare no competing interests.

References

1. Abarca-Gómez, L.; Abdeen, Z.A.; Hamid, Z.A.; Abu-Rmeileh, N.M.; Acosta-Cazares, B.; Acuin, C.; Adams, R.J.; Aekplakorn, W.; Afsana, K.; Aguilar-Salinas, C.A.; et al. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: A pooled analysis of 2416 population-based measurement studies in 128·9 million children, adolescents, and adults. *Lancet* **2017**, *390*, 2627–2642. [CrossRef]
2. Basterra-Gortari, F.J.; Bes-Rastrollo, M.; Ruiz-Canela, M.; Gea, A.; Martinez-Gonzalez, M.Á. Prevalence of obesity and diabetes in Spanish adults 1987–2012. *Med. Clin.* **2017**, *148*, 250–256. [CrossRef] [PubMed]
3. Pérez-Rodrigo, C.; Gianzo-Citores, M.; Gil, Á.; González-Gross, M.; Ortega, R.M.; Serra-Majem, L.; Varela-Moreiras, G.; Aranceta-Bartrina, J. Lifestyle patterns and weight status in Spanish adults: The ANIBES study. *Nutrients* **2017**, *9*, 606. [CrossRef] [PubMed]
4. Kimokoti, R.W.; Millen, B.E. Nutrition for the Prevention of Chronic Diseases. *Med. Clin. N. Am.* **2016**, *100*, 1185–1198. [CrossRef] [PubMed]
5. Varela-Moreiras, G.; Ávila, J.M.; Cuadrado, C.; del Pozo, S.; Ruiz, E.; Moreiras, O. Evaluation of food consumption and dietary patterns in Spain by the Food Consumption Survey: Updated information. *Eur. J. Clin. Nutr.* **2010**, *64*, S37–S43. [CrossRef] [PubMed]
6. Trichopoulou, A.; Corella, D.; Martínez-González, M.A.; Soriguer, F.; Ordovas, J.M. The Mediterranean diet and cardiovascular epidemiology. *Nutr. Rev.* **2006**, *64* (Suppl. 101), S13–S19. [CrossRef]
7. Dinu, M.; Pagliai, G.; Casini, A.; Sofi, F. Mediterranean diet and multiple health outcomes: An umbrella review of meta-analyses of observational studies and randomised trials. *Eur. J. Clin. Nutr.* **2018**, *72*, 30–43. [CrossRef] [PubMed]
8. Knight, A.; Bryan, J.; Murphy, K. The Mediterranean diet and age-related cognitive functioning: A systematic review of study findings and neuropsychological assessment methodology. *Nutr. Neurosci.* **2017**, *20*, 449–468. [CrossRef] [PubMed]
9. Wang, Y.; Hao, Q.; Su, L.; Liu, Y.; Liu, S.; Dong, B. Adherence to the Mediterranean Diet and the Risk of Frailty in Old People: A Systematic Review and Meta-Analysis. *J. Nutr. Health Aging* **2018**, *22*, 613–618. [CrossRef] [PubMed]

10. Godos, J.; Zappalà, G.; Bernardini, S.; Giambini, I.; Bes-Rastrollo, M.; Martinez-Gonzalez, M. Adherence to the Mediterranean diet is inversely associated with metabolic syndrome occurrence: A meta-analysis of observational studies. *Int. J. Food Sci. Nutr.* **2017**, *68*, 138–148. [CrossRef] [PubMed]
11. Grosso, G.; Marventano, S.; Yang, J.; Micek, A.; Pajak, A.; Scalfi, L.; Galvano, F.; Kales, S.N. A comprehensive meta-analysis on evidence of Mediterranean diet and cardiovascular disease: Are individual components equal? *Crit. Rev. Food Sci. Nutr.* **2017**, *57*, 3218–3232. [CrossRef] [PubMed]
12. Martínez-González, M.A.; Salas-Salvadó, J.; Estruch, R.; Corella, D.; Fitó, M.; Ros, E. Benefits of the Mediterranean Diet: Insights from the PREDIMED Study. *Prog. Cardiovasc. Dis.* **2015**, *58*, 50–60. [CrossRef] [PubMed]
13. Alberti, K.G.; International Diabetes Federation Task Force on Epidemiology and Prevention; Hational Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; International Association for the Study of Obesity. 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 atherosclerosis society; And international association for the study of obesity. *Circulation* **2009**, *120*, 1640–1645. [PubMed]
14. Agarwal, S.; Reider, C.; Brooks, J.R.; Fulgoni, V.L. Comparison of Prevalence of Inadequate Nutrient Intake Based on Body Weight Status of Adults in the United States: An Analysis of NHANES 2001–2008. *J. Am. Coll. Nutr.* **2015**, *34*, 126–134. [CrossRef] [PubMed]
15. Martí, A.Z.; Ferrer Cascales, R.; Sánchez, J.A.H.; Pérez, A.L. Adherence to the mediterranean diet and its relation to nutritional status in older people. *Nutr. Hosp.* **2015**, *31*, 1667–1674.
16. Fávaro-Moreira, N.C.; Krausch-Hofmann, S.; Matthys, C.; Vereecken, C.; Vanhauwaert, E.; Declercq, A.; Bekkering, G.E.; Duyck, J. Risk factors for malnutrition in older adults: A systematic review of the literature based on longitudinal data. *Adv. Nutr.* **2016**, *7*, 507–522. [CrossRef] [PubMed]
17. Bernstein, M. Nutritional Needs of the Older Adult. *Phys. Med. Rehab. Clin. N. Am.* **2017**, *28*, 747–766. [CrossRef] [PubMed]
18. Benhammou, S.; Heras-González, L.; Ibáñez-Peinado, D.; Barceló, C.; Hamdan, M.; Rivas, A.; Mariscal-Arcas, M.; Olea-Serrano, F.; Monteagudo, C. Comparison of Mediterranean diet compliance between European and non-European populations in the Mediterranean basin. *Appetite* **2016**, *107*, 521–526. [CrossRef] [PubMed]
19. León-Munoz, L.M.; Guallar-Castillón, P.; Graciani, A.; López-García, E.; Mesas, A.E.; Aguilera, M.T.; Banegas, J.R.; Rodríguez-Artalejo, F. Adherence to the mediterranean diet pattern has declined in Spanish adults. *J. Nutr.* **2012**, *142*, 1843–1850. [CrossRef] [PubMed]
20. Abellán Alemán, J.; Zafrilla Rentero, M.P.; Montoro-García, S.; Mulero, J.; Pérez Garrido, A.; Leal, M.; Guerrero, L.; Ramos, E.; Ruilope, L.M. Adherence to the "Mediterranean diet" in Spain and its relationship with cardiovascular risk (DIMERICA study). *Nutrients* **2016**, *8*, 680. [CrossRef] [PubMed]
21. Katsarou, A.; Tyrovolas, S.; Psaltopoulou, T.; Zeimbekis, A.; Tsakountakis, N.; Bountziouka, V.; Gotsis, E.; Metallinos, G.; Polychronopoulos, E.; Lionis, C.; et al. Socio-economic status, place of residence and dietary habits among the elderly: The Mediterranean islands study. *Public Health Nutr.* **2010**, *13*, 1614–1621. [CrossRef] [PubMed]
22. Samaniego-Vaesken, M.D.; Partearroyo, T.; Ruiz, E.; Aranceta-Bartrina, J.; Gil, Á.; González-Gross, M.; Ortega, R.M.; Serra-Majem, L.; Varela-Moreiras, G. The influence of place of residence, gender and age influence on food group choices in the Spanish population: Findings from the ANIBES study. *Nutrients* **2018**, *10*, 392. [CrossRef] [PubMed]
23. Bertomeu, V.; Castillo-Castillo, J. Cardiovascular disease in Spain today. From risk factors to morbidity. *Rev. Esp. Cardiol. Supl.* **2008**, *8*, 2E–9E.
24. Martínez-González, M.Á.; Corella, D.; Salas-Salvadó, J.; Ros, E.; Covas, M.I.; Fiol, M.; Wärnberg, J.; Arós, F.; Ruíz-Gutiérrez, V.; Lamuela-Raventós, R.M.; et al. Cohort Profile: Design and methods of the PREDIMED study. *Int. J. Epidemiol.* **2018**, *41*, 377–385. [CrossRef] [PubMed]
25. Willet, W. *Nutritional Epidemiology*, 3rd ed.; Oxford University Press: New York, NY, USA, 2013.
26. Martin-moreno, J.M.; Boyle, P.; Gorgojo, L.; Maisonneuve, P.; Fernandez-rodriguez, J.C.; Salvini, S.; Willett, W.C. Development and validation of a food frequency questionnaire in Spain. *Int. J. Epidemiol.* **1993**, *22*, 512–519. [CrossRef] [PubMed]

27. De La Fuente-Arrillaga, C.; Vzquez Ruiz, Z.; Bes-Rastrollo, M.; Sampson, L.; Martinez-González, M.A. Reproducibility of an FFQ validated in Spain. *Public Health Nutr.* **2010**, *13*, 1364–1372. [CrossRef] [PubMed]
28. Fernández-Ballart, J.D.; Piñol, J.L.; Zazpe, I.; Corella, D.; Carrasco, P.; Toledo, E.; Perez-Bauer, M.; Martínez-González, M.Á.; Salas-Salvadó, J.; Martín-Moreno, J.M. Relative validity of a semi-quantitative food-frequency questionnaire in an elderly Mediterranean population of Spain. *Br. J. Nutr.* **2010**, *103*, 1808–1816. [CrossRef] [PubMed]
29. Moreiras, O.C.A.; Cabrera, L.; Cuadrado, C. *Tablas de Composición de Alimentos*; (Spanish Food Composition Tables); Pirámide: Madrid, Spain, 2003.
30. Mataix-Verdú, J.; García Diz, L.; Mañas Almendros, M.; Emilio, M.d.V.; Llopis González, J. *Tablas de Composición de Alimentos*, 4th ed.; Universidad de Granada: Granada, Spain, 2009.
31. Schröder, H.; Fitó, M.; Estruch, R.; Martínez-González, M.A.; Corella, D.; Salas-Salvadó, J.; Lamuela-Raventós, R.; Ros, E.; Salaverría, I.; Fiol, M.; et al. A Short Screener Is Valid for Assessing Mediterranean Diet Adherence among Older Spanish Men and Women. *J. Nutr.* **2011**, *141*, 1140–1145. [CrossRef] [PubMed]
32. IOM. Nutrient Recommendations: Dietary Reference Intakes. Available online: https://www.ncbi.nlm.nih.gov/books/NBK56068/table/summarytables.t2/?report=objectonly (accessed on 10 May 2018).
33. Health NIo. Nutrient Recommendations: Dietary Reference Intakes (DRI) 2018. Available online: https://ods.od.nih.gov/Health_Information/Dietary_Reference_Intakes.aspx (accessed on 10 May 2018).
34. Ortiz-Andrellucchi, A.; Sánchez-Villegas, A.; Doreste-Alonso, J.; de Vries, J.; de Groot, L.; Serra-Majem, L. Dietary assessment methods for micronutrient intake in elderly people: A systematic review. *Br. J. Nutr.* **2009**, *102* (Suppl. 1), S118–S149. [CrossRef] [PubMed]
35. EFSA. Dietary Reference Values and Dietary Guidelines. Available online: https://www.efsa.europa.eu/en/topics/topic/dietary-reference-values (accessed on 26 September 2018).
36. Elosua, R.; Marrugat, J.; Molina, L.; Pons, S.; Pujol, E. Validation of the minnesota leisure time physical activity questionnaire in Spanish men. *Am. J. Epidemiol.* **1994**, *139*, 1197–1209. [CrossRef] [PubMed]
37. Elosua, R.; Garcia, M.; Aguilar, A.; Molina, L.; Covas, M.I.; Marrugat, J. Validation of the Minnesota leisure time physical activity questionnaire in Spanish women. *Med. Sci. Sports Exerc.* **2000**, *32*, 1431–1437. [CrossRef] [PubMed]
38. Martínez-González, M.Á.; Hershey, M.S.; Zazpe, I.; Trichopoulou, A. Transferability of the Mediterranean diet to non-Mediterranean countries. What is and what is not the Mediterranean diet. *Nutrients* **2017**, *9*, 1226. [CrossRef] [PubMed]
39. Ruiz, E.; Ávila, J.M.; Valero, T.; del Pozo, S.; Rodriguez, P.; Aranceta-Bartrina, J.; Gil, Á.; González-Gross, M.; Ortega, R.M.; Serra-Majem, L.; et al. Energy intake, profile, and dietary sources in the spanish population: Findings of the ANIBES study. *Nutrients* **2015**, *7*, 4739–4762. [CrossRef] [PubMed]
40. Varela-Moreiras, G.; Ruiz, E.; Valero, T.; Ávila, J.M.; del Pozo, S. The Spanish diet: An update. *Nutr. Hosp.* **2013**, *28* (Suppl. 5), 13–20. [PubMed]
41. Aranceta, J.B.; Arija, V.V.; Maíz, E.A.; Martínez, E.D.; Ortega, R.A.; Pérez-Rodrigo, C.; Quiles, J.I.; Rodríguez, A.M.; Román, B.V.; Salvador, G.C.; et al. Dietary Guidelines for the Spanish population (SENC, diciembre 2016); the new graphic icon of healthy food. *Nutr. Hosp.* **2016**, *33*, 1–48.
42. Vazquez-Ruiz, Z.; de la Fuente-Arrillaga, C.; Bes-Rastrollo, M.; Zazpe, I.; Santiago, S.; Razquin, C.; Toledo, E.; Martinez-Gonzalez, M.Á. Egg consumption and dyslipidemia in a mediterranean cohort. *Nutr. Hosp.* **2018**, *35*, 153–161. [PubMed]
43. Beydoun, M.A.; Fanelli-Kuczmarski, M.T.; Allen, A.; Beydoun, H.A.; Popkin, B.M.; Evans, M.K.; Zonderman, A.B. Monetary value of diet is associated with dietary quality and nutrient adequacy among urban adults, differentially by sex, race and poverty status. *PLoS ONE* **2015**, *10*, e0140905. [CrossRef] [PubMed]
44. Oconnor, L.; Walton, J.; Flynn, A. Dietary energy density: Estimates, trends and dietary determinants for a nationally representative sample of the Irish population (aged 5–90 years). *Br. J. Nutr.* **2015**, *113*, 172–180. [CrossRef] [PubMed]
45. Schuh, D.S.; Pellanda, L.C.; Guessous, I.; Marques-Vidal, P. Trends and determinants of change in compliance to dietary guidelines in a Swiss community-dwelling sample. *Prev. Med.* **2018**, *111*, 198–203. [CrossRef] [PubMed]

46. Bonaccio, M.; Bes-Rastrollo, M.; de Gaetano, G.; Iacoviello, L. Challenges to the Mediterranean diet at a time of economic crisis. *Nutr. Metab. Cardiovasc. Dis.* **2016**, *26*, 1057–1063. [CrossRef] [PubMed]
47. Zazpe, I.; Sanchez-Tainta, A.; Estruch, R.; Lamuela-Raventos, R.M.; Schröder, H.; Salas-Salvado, J.; Corella, D.; Fiol, M.; Gomez-Gracia, E.; Aros, F.; et al. A Large Randomized Individual and Group Intervention Conducted by Registered Dietitians Increased Adherence to Mediterranean-Type Diets: The PREDIMED Study. *J. Am. Diet. Assoc.* **2008**, *108*, 1134–1144. [CrossRef] [PubMed]
48. Jurado, D.; Burgos-Garrido, E.; Diaz, F.J.; Martínez-Ortega, J.M.; Gurpegui, M. Adherence to the Mediterranean Dietary Pattern and Personality in Patients Attending a Primary Health Center. *J. Acad. Nutr. Diet.* **2012**, *112*, 887–891. [CrossRef] [PubMed]
49. Patino-Alonso, M.C.; Recio-Rodríguez, J.I.; Belio, J.F.; Colominas-Garrido, R.; Lema-Bartolomé, J.; Arranz, A.G.; Agudo-Conde, C.; Gomez-Marcos, M.A.; García-Ortiz, L.; EVIDENT Group. Factors associated with adherence to the mediterranean diet in the adult population. *J. Acad. Nutr. Diet.* **2014**, *114*, 583–589. [CrossRef] [PubMed]
50. Dietary Reference Intakes. *Dietary Reference Intakes: Applications in Dietary Assessment*; National Academy Press: Washington, DC, USA, 2000.
51. Ruiz, E.; Ávila, J.M.; Valero, T.; del Pozo, S.; Rodriguez, P.; Aranceta-Bartrina, J.; Gil, Á.; González-Gross, M.; Ortega, R.M.; Serra-Majem, L.; et al. Macronutrient distribution and dietary sources in the spanish population: Findings from the ANIBES study. *Nutrients* **2016**, *8*, 177. [CrossRef] [PubMed]
52. Sánchez-Tainta, A.; Zazpe, I.; Bes-Rastrollo, M.; Salas-Salvadó, J.; Bullo, M.; Sorlí, J.V.; Corella, D.; Covas, M.I.; Arós, F.; Gutierrez-Bedmar, M.; et al. Nutritional adequacy according to carbohydrates fat quality. *Eur. J. Nutr.* **2016**, *55*, 93–106. [CrossRef] [PubMed]
53. Guasch-Ferré, M.; Babio, N.; Martínez-González, M.A.; Corella, D.; Ros, E.; Martín-Peláez, S.; Estruch, R.; Arós, F.; Gómez-Gracia, E.; Fiol, M.; et al. Dietary fat intake risk of cardiovascular disease all-cause mortality in a population at high risk of cardiovascular disease. *Am. J. Clin. Nutr.* **2015**, *102*, 1563–1573. [PubMed]
54. Naska, A.; Trichopoulou, A. Back to the future: The Mediterranean diet paradigm. *Nutr. Metab. Cardiovasc. Dis.* **2014**, *24*, 216–219. [CrossRef] [PubMed]
55. Agarwal, E.; Miller, M.; Yaxley, A.; Isenring, E. Malnutrition in the elderly: A narrative review. *Maturitas* **2013**, *76*, 296–302. [CrossRef] [PubMed]
56. ter Borg, S.; Verlaan, S.; Hemsworth, J.; Mijnarends, D.M.; Schols, J.M.; Luiking, Y.C.; de Groot, L.C. Micronutrient intakes and potential inadequacies of community-dwelling older adults: A systematic review. *Br. J. Nutr.* **2015**, *113*, 1195–1206. [CrossRef] [PubMed]
57. Roussel, A.M. Micronutrient deficiencies in obesity: Metabolic and clinical consequences. *Nutr. Clin. Metab.* **2017**, *31*, 268–275. [CrossRef]
58. Hallkvist, O.M.; Johansson, J.; Nordström, A.; Nordström, P.; Hult, A. Dairy product intake and bone properties in 70-year-old men and women. *Arch. Osteoporos.* **2018**, *13*, 9. [CrossRef] [PubMed]
59. Shatenstein, B.; Gauvin, L.; Keller, H.; Richard, L.; Gaudreau, P.; Giroux, F.; Gray-Donald, K.; Jabbour, M.; Morais, J.A.; Payette, H. Baseline determinants of global diet quality in older men and women from the NuAge cohort. *J. Nutr. Health Aging* **2013**, *17*, 419–425. [CrossRef] [PubMed]
60. Newby, P.K.; Noel, S.E.; Grant, R.; Judd, S.; Shikany, J.M.; Ard, J. Race and region have independent and synergistic effects on dietary intakes in black and white women. *Nutr. J.* **2012**, *11*, 25. [CrossRef] [PubMed]
61. Sales, C.H.; Fontanelli, M.D.M.; Vieira, D.A.S.; Marchioni, D.M.; Fisberg, R.M. Inadequate dietary intake of minerals: Prevalence and association with socio-demographic and lifestyle factors. *Br. J. Nutr.* **2017**, *117*, 267–277. [CrossRef] [PubMed]
62. de Souza Fernandes, D.P.; Duarte, M.S.L.; Pessoa, M.C.; Franceschini, S.D.C.C.; Ribeiro, A.Q. Evaluation of diet quality of the elderly and associated factors. *Arch. Gerontol. Geriatr.* **2017**, *72*, 174–180. [CrossRef] [PubMed]
63. Mercille, G.; Richard, L.; Gauvin, L.; Kestens, Y.; Shatenstein, B.; Daniel, M.; Payette, H. The food environment and diet quality of urban-dwelling older women and men: Assessing the moderating role of diet knowledge. *Can. J. Public Health* **2016**, *107*, 5309. [CrossRef] [PubMed]
64. Mendonça, N.; Hill, T.R.; Granic, A.; Davies, K.; Collerton, J.; Mathers, J.C.; Siervo, M.; Wrieden, W.L.; Seal, C.J.; Kirkwood, T.B.; et al. Micronutrient intake and food sources in the very old: Analysis of the Newcastle 85+ Study. *Br. J. Nutr.* **2016**, *116*, 751–761. [CrossRef] [PubMed]

65. Schoufour, J.D.; de Jonge, E.A.; Kiefte-de Jong, J.C.; van Lenthe, F.J.; Hofman, A.; Nunn, S.P.; Franco, O.H. Socio-economic indicators and diet quality in an older population. *Maturitas* **2018**, *107*, 71–77. [CrossRef] [PubMed]
66. Arbucias, J.S. The evolution of internal migration in Spain: An assessment of available demographic sources. *Papers* **2011**, *96*, 853–881.
67. (INE) INE. Estadística de Variaciones Regionales en España. Variaciones Residenciales Interiores. Serie 1998–2017. Available online: https://www.ine.es/dynt3/inebase/es/index.htm?type=pcaxis&path=/t20/p307/serie&file=pcaxis&dh=0&capsel=02018 (accessed on 11 October 2018).

Table S1. Intake of food groups (g/day) in both sexes divided by geographical areas and age

					55-70 years					
	Men					Women				
	North area (n=724)	Central area (n=245)	East area (n=1269)	South area (n=774)	*P value*	North area (n=479)	Central area (n=199)	East area (n=1209)	South area (n=774)	*P value*
Vegetables	277.1 ±95.3	304.4 ±155.8	317.5 ±141.9	314.1±141.4	<0.001	301.2 ±106.8	357.2 ±163.9	358.6 ±144.7	352.3 ±146.0	<0.001
Fruits	354.8±204.8	346.5±259.1	315.5±184.3	339.5±195.9	0.001	412.2±225.2	369.1±242.6	343.2±187.4	387.5±215.6	<0.001
Legumes	18.9±8.2	20.6±10.9	20.2±11.5	23.0±10.6	<0.001	17.7±7.8	20.8±13.9	19.2±10.9	23.7±11.5	<0.001
Cereals	190.5±100.0	156.9±92.3	153.4±76.5	152.1±75.9	<0.001	152.8±77.3	142.6±87.4	132.5±66.7	135.0±63.7	<0.001
Milk/dairy products	333.9±206.3	379.3±220.1	306.4±188.7	337.1±200.1	<0.001	401.0±208.4	377.9±177.9	334.6±193.1	375.7±214.8	<0.001
Meat/meat products	155.7±54.8	153.4±58.7	163.0±63.0	137.7±57.4	<0.001	147.7±51.0	134.8±51.3	150.1±56.1	117.7±48.5	<0.001
Olive oil	43.2±13.5	35.4±20.5	41.1±16.7	39.6±19.0	<0.001	43.3±14.7	36.8±18.6	39.9±16.7	33.4±17.5	<0.001
Fish/seafood	92.9±40.6	107.8±53.6	99.0±48.1	102.3±48.9	<0.001	99.8±38.1	114.2±67.5	106.3±45.8	99.0±46.1	<0.001
Nuts	13.2±16.1	16.3±20.9	15.5±17.3	15.3±16.5	0.018	12.0±16.5	15.5±23.1	15.0±17.3	16.0±18.2	0.001
Sugar/sweets	34.3±37.6	31.8±30.6	27.8±30.2	23.3±24.1	<0.001	31.0±34.1	27.7±31.0	23.5±24.9	22.8±24.9	<0.001
Eggs	27.7±14.8	24.9±14.1	23.7±12.4	23.7±12.8	<0.001	24.1±11.4	23.2±14.7	21.8±9.2	22.4±10.8	0.006
					More than 70 years					
	Men					**Women**				
Vegetables	298.6±113.7	308.6±120.0	325.0±143.7	326.9±128.3	0.368	304.9±105.7	333.3±137.6	332.1±141.7	330.0±136.2	0.245
Fruits	403.6±191.9	330.4±219.9	353.0±195.8	342.8±164.6	0.087	466.5±194.9	481.3±383.6	359.4±198.9	429.2±235.1	<0.001
Legumes	21.1±8.6	25.8±18.1	21.0±12.9	22.7±10.5	0.280	20.8±15.3	17.1±11.9	18.3±9.4	22.1±11.5	0.008
Cereals	187.0±95.9	152.7±82.7	154.6±76.4	147.6±82.7	0.004	158.8±88.0	153.0±98.1	124.8±58.5	135.7±69.1	0.001
Milk/dairy products	321.7±185.4	409.3±234.8	295.5±172.4	334.2±172.3	0.035	432.7±197.5	465.5±221.1	356.3±196.8	403.6±220.2	0.001
Meat/meat products	149.2±55.3	151.4±46.6	153.5±55.2	109.7±41.6	<0.001	143.3±50.6	127.2±45.5	141.5±53.0	111.9±47.2	<0.001
Olive oil	42.6±13.8	36.5±21.0	40.7±16.6	35.1±17.5	0.064	41.0±14.1	35.7±17.5	41.2±15.6	33.4±17.5	<0.001
Fish/seafood	94.6±41.5	105.2±52.8	102.3±45.0	94.2±47.3	0.327	94.2±38.5	101.6±62.6	102.9±48.4	92.4±40.3	0.104
Nuts	14.6±17.9	17.6±19.2	15.5±16.2	14.8±15.3	0.891	13.2±14.5	21.6±27.7	12.0±13.5	14.2±14.8	0.001
Sugar/sweets	35.2±39.1	29.9±57.5	26.7±31.5	28.6±43.7	0.324	29.9±32.0	23.6±20.5	22.0±24.5	20.3±22.5	0.012
Eggs	25.8±16.7	25.3±14.6	21.6±9.6	23.4±10.4	0.036	23.9±9.9	24.4±10.3	21.3±9.6	22.3±9.2	0.056

Data are expressed as means ± SD. ANOVA test was performed

Table S2. MedDiet adherence, total energy intake and profile of macronutrients, fiber and alcohol intake by geographical areas (total population *n = 6646*) among 55-75 years population

					55-70 years					
	Men					**Women**				
	North area (n=724)	**Central area (n=245)**	**East area (n=1269)**	**South area (n=774)**	***P value***	**North area (n=479)**	**Central area (n=199)**	**East area (n=1209)**	**South area (n=774)**	***P value***
MedDiet adherence Mean ±SD	8.1±2.7	9.0±2.4	7.7±2.6	8.5±2.6	<0.001	9.0±2.7	9.4±2.4	8.5±2.6	9.2±2.5	<0.001
Low adherence, n (%)	307 (42.4)	77 (31.4)	621 (48.9)	269 (34.8)		146 (30.5)	43 (21.6)	435 (35.6)	186 (24.0)	
Medium adherence, n (%)	272 (37.6)	106 (43.3)	466 (36.7)	330 (42.7)	<0.001	188 (39.3)	89 (44.7)	502 (41.5)	356 (46.09	<0.001
High adherence, n (%)	145 (20.0)	62 (25.3)	182 (14.3)	175 (22.6)		145 (30.3)	67 (33.7)	272 (22.5)	232 (30.0)	
Total energy intake, mean ±sd	2575±533	2507±629	2524±5446	2456±572	0.001	2262±501	2293±519	2205±485	2173±501	0.002
%Total fat intake,mean ±sd	37.6±5.9	38.0±6.5	40.0±6.0	39.5±6.9	<0.001	39.4±6.3	39.1±7.1	40.8±6.4	38.9±7.1	<0.001
% Monounsaturated fat,mean ±sd	19.4±4.0	19.0±4.5	20.8±4.3	20.6±5.1	<0.001	20.8±4.3	20.1±5.3	21.3±4.7	20.3±5.1	<0.001
% Polyunsaturated fat,mean ±sd	6.0±1.9	6.3±2.0	6.3±1.7	6.5±1.6	<0.001	6.1±2.0	6.3±1.9	6.5±1.9	6.5±1.8	0.002
% Saturated fat, mean ±sd	9.4±1.8	10.1±2.1	10.3±2.0	9.7±1.8	<0.001	9.7±2.0	10.1±2.2	10.3±2.0	9.5±1.9	<0.001
% Carbohydrate intake,mean ±sd	41.2±6.6	41.0±6.3	39.5±6.5	40.4±7.1	<0.001	41.9±6.4	42.2±7.2	40.1±6.6	42.9±7.2	<0.001
Protein intake (%),mean ±sd	15.5±2.4	16.6±3.2	16.0±2.7	15.8±2.7	<0.001	17.2±2.5	17.3±3.0	17.7±2.8	17.0±2.6	<0.001
Alcohol intake (g/d),mean ±sd	21.3±20.9	16.3±17.6	16.2±16.4	15.5±15.7	<0.001	5.1±10.2	4.7±7.6	4.5±6.9	4.1±6.9	0.162
Fiber intake (g/d),mean ±sd	25.1±8.6	25.3±9.2	25.2±8.5	24.9±8.6	0.883	25.9±8.3	27.2±9.7	26.3±8.5	27.6±9.4	0.003
					More than 70 years					
	Men					**Women**				
MedDiet Q-P17[a] adherence Mean ±SD	8.5±3.1	8.5±2.4	8.3±2.6	9.0±2.5	0.275	9.3±2.6	9.5±2.0	8.5±21	9.4±2.5	0.002
Low adherence, n (%)	38 (38.4)	5 (26.3)	80 (30.3)	30 (32.6)		32 (23.9)	5 (16.7)	89 (35.5)	33 (23.7)	
Medium adherence, n (%)	33 (33.3)	10 (52.6)	89 (42.6)	41 (44.6)	0.622	59 (44.0)	16 (53.3)	103 (41.0)	54 (38.9)	0.004
High adherence, n (%)	28 (28.3)	4 (21.1)	40 (19.1)	21 (22.8)		43 (32.1)	9 (30.0)	59 (23.5)	52 (37.4)	
Total energy intake, mean ±sd	2574.5±602.3	2439.1±534.9	2444.4±527.7	2257.4±548.4	0.001	2264.2±527.9	2338.7±575.1	2127.1±461.6	2085.3±484.5	0.003
%Total fat intake,mean ±sd	37.7±6.1	38.3±8.3	39.5±6.4	38.9±7.0	0.154	38.0±6.7	38.9±7.7	40.5±6.0	37.7±7.3	0.001
% Monounsaturate fat, mean ±sd	19.3±3.5	19.4±4.9	20.5±4.6	20.1±5.2	0.182	19.7±4.4	20.2±5.8	21.1±4.2	19.5±5.1	0.002
% Polyunsaturate fat, mean ±sd	6.3±2.3	6.4±2.5	6.4±1.8	6.7±2.0	0.671	6.2±1.9	6.7±2.2	6.3±1.7	6.4±1.9	0.429
% Saturated fat,mean ±sd	9.4±1.8	10.0±2.5	10.1±2.0	9.5±1.7	0.008	9.3±1.9	9.6±2.3	10.2±2.0	9.1±1.9	<0.001
% Carbohydrate intake,mean ±sd	41.6±6.8	40.5±8.2	39.9±6.4	41.4±7.1	0.148	43.6±7.0	43.0±8.2	40.5±6.4	44.3±7.1	<0.001
Protein intake (%),mean ±sd	15.5±2.0	17.2±3.2	16.1±2.4	15.7±2.6	0.015	17.3±2.3	16.9±2.6	17.6±2.9	17.1±2.6	0.255
Alcohol intake (g/d),mean ±sd	20.2±18.7	12.2±12.7	15.9±15.9	12.9±12.6	0.010	3.5±6.7	3.6±3.8	4.5±7.6	2.7±5.0	0.064
Fiber intake (g/d),mean ±sd	26.9±8.1	27.5±9.8	26.7±9.2	25.3±8.5	0.511	28.2±9.0	29.3±11.5	25.5±8.0	27.1±8.5	0.010

Values are means ± SD for continuous variables and percentages (n) for categorical variables unless otherwise indicated. Abbreviations: (MedDietQ-P17[b]), Mediterranean diet questionnaire 17 point cut off.

Table S3. Participants with nutrient intake below AR/AI proposed by EFSA by geographical areas, age and sex

Nutrient	*Group*	*AR/AI*[a]	*North area*	*Central area*	*East area*	*South area*	*P value*[1]
Dietary fiber	Male	*25g /d*	55.3	53.3	54.2	58.9	0.183
	Female	*25g /d*	49.8	48.5	48.7	45.2	0.273
P ***value***[2]			0.037	0.313	0.003	<0.001	
Vitamin A	Male	*570 μg/d*	23.5	19.2	14.2	14.5	<0.001
	Female	*490 μg/d*	9.8	7.4	7.8	6.6	0.154
P ***value***[2]			<0.001	<0.001	<0.001	<0.001	
Vitamin B_9	Male	*250 μg/d*	13.6	15.4	16.5	17.1	0.201
	Female	*250 μg/d*	11.3	13.4	14.5	14.8	0.196
P ***value***[2]			0.189	0.542	0.123	0.202	
Vitamin D	Male	*15 μg/d*	99.3	95.0	99.1	99.1	<0.001
	Female	*15 μg/d*	99.5	96.5	99.0	99.1	0.004
P ***value***[2]			0.562	0.428	0.680	0.914	
Vitamin E	Male	*13 mg/d*	86.4	77.5	75.5	75.7	<0.001
	Female	*11 mg/d*	76.0	60.4	65.0	63.2	<0.001
P ***value***[2]			<0.001	<0.001	<0.001	<0.001	
Calcium	Male	*950 mg/d*	48.6	37.5	46.5	45.8	0.026
	Female	*950 mg/d*	43.4	37.1	46.7	43.5	0.045
P ***value***[2]			0.051	0.936	0.871	0.336	
Magnesium	Male	*350 mg/d*	34.9	29.2	31.3	32.4	0.233
	Female	*350 mg/d*	18.8	12.9	16.2	16.3	0.232
P ***value***[2]			<0.001	<0.001	<0.001	<0.001	

[a]AR/AI: Average Requirements/Adequate intake according to EFSA criteria. Pearson`s Chi Square test was used to estimate differences among prevalence of inadequate nutrient intakes according to geographical area for sex strata (*p value*[1]) and also to estimate differences among prevalence of inadequate nutrient intakes according to sex, for each geographical area (*p value*[2]).

Table S4. Logistic regression model of micronutrients inadequate intake according to EFSA by geographical areas

Nutrient		*North area*	*Central area*	*East area*	*South area*
Dietary fiber	Model 1	1 (Ref.)	0.93 (0.75-1.15)	0.94 (0.83-1.08)	0.95 (0.83-1.10)
	Model 2	1 (Ref.)	0.92 (0.71-1.19)	0.72 (0.62-0.84)	0.78 (0.66-0.91)
Vitamin A	Model 1	1 (Ref.)	0.75 (0.55-1.01)	0.58 (0.48-0.69)	0.54 (0.44-0.67)
	Model 2	1 (Ref.)	0.68 (0.49-0.96)	0.49 (0.40-0.59)	0.45 (0.36-0.56)
Vitamin B9	Model 1	1 (Ref.)	1.18 (0.86-1.60)	1.27 (1.06-1.53)	1.32 (1.08-1.61)
	Model 2	1 (Ref.)	1.05 (0.73-1.51)	1.02 (0.83-1.26)	1.06 (0.84-1.34)
Vitamin E	Model 1	1 (Ref.)	0.51 (0.40-0.65)	0.52 (0.44-0.61)	0.50 (0.42-0.59)
	Model 2	1 (Ref.)	0.45 (0.34-0.61)	0.36 (0.30-0.43)	0.33 (0.27-0.40)
Calcium	Model 1	1 (Ref.)	0.69 (0.55-0.86)	1.01 (0.89-1.15)	0.93 (0.81-1.07)
	Model 2	1 (Ref.)	0.56 (0.43-0.73)	0.87 (0.75-1.00)	0.70 (0.59-0.82)
Magnesium	Model 1	1 (Ref.)	0.71 (0.55-0.92)	0.80 (0.70-0.93)	0.82 (0.70-0.96)
	Model 2	1 (Ref.)	0.55 (0.38-0.80)	0.47 (0.39-0.58)	0.45 (0.36-0.56)

Values are presented as OR and 95% CI for the inadequacy intake of micronutrients as categorical variable according to area of residence. Model 1: This model has not been adjusted for any variable. Model 2: has been adjusted by sex, age, smoking habits, physical activity, educational status, diabetic status, living alone, total energy intake and adherence to MedDiet.

Table S5. Logistic regression model of micronutrients deficiency intake according to 2/3 DRIs by areas

	DIETARY FIBER		*VITAMIN A*		*VITAMIN B_9*		*VITAMIN E*		*CALCIUM*		*MAGNESIUM*	
	OR (CI 95%)	***p value***	**OR (CI 95%)**	***p value***	**OR (CI 95%)**	***p value***	**OR (CI 95%)**	***p value***	**OR (CO 95%)**	***p value***	**OR (CI 95%)**	***p value***
Geographical areas												
North area	1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)	
Central area	1.03 (0.72-1.46)	0.874	0.57 (0.41-0.80)	0.001	0.98 (0.70-1.36)	0.889	0.47 (0.36-0.61)	<0.001	0.53 (0.38-0.76)	<0.001	0.39 (0.21-0.75)	0.005
East area	0.80 (0.65-0.98)	0.033	0.43 (0.35-0.52)	<0.001	0.97 (0.80-1.17)	0.721	0.30 (0.26-0.35)	<0.001	0.86 (0.72-1.04)	0.112	0.35 (0.25-0.50)	<0.001
South area	0.92 (0.73-1.15)	0.454	0.40 (0.32-0.50)	<0.001	1.09 (0.88-1.34)	0.437	0.30 (0.25-0.36)	<0.001	0.80 (0.65-0.98)	0.029	0.33 (0.22-0.49)	<0.001
Age	0.83 (0.67-1.06)	0.133	1.04 (0.84-1.30)	0.706	0.93 (0.77-1.14)	0.507	1.25 (1.06-1.48)	0.010	1.41 (1.17-1.70)	<0.001	0.92 (0.62-1.38)	0.713
Sex												
Men	1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)	
Female	0.05 (0.04-0.07)	<0.001	0.19 (0.16-0.23)	<0.001	0.49 (0.42-0.58)	<0.001	0.66 (0.58-0.76)	<0.001	1.36 (1.15-1.60)	<0.001	0.93 (0.62-1.38)	0.713
MedDiet adherence												
Low adherence	1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)	
Moderate adherence	0.41 (0.35-0.49)	<0.001	0.71 (0.60-0.84)	<0.001	0.47 (0.40-0.54)	<0.001	0.58 (0.51-0.67)	<0.001	0.78 (0.66-0.91)	0.002	0.25 (0.18-0.35)	<0.001
High adherence	0.14 (0.11-0.18)	<0.001	0.44 (0.35-0.55)	<0.001	0.19 (0.16-0.24)	<0.001	0.35 (0.30-0.41)	<0.001	0.58 (0.48-0.71)	<0.001	0.09 (0.06-0.15)	<0.001
Energy intake (kcal/day)	0.99 (0.99-0.99)	<0.001	0.99 (0.99-0.99)	<0.001	0.99 (0.99-0.99)	<0.001	0.99 (0.99-0.99)	<0.001	0.99 (0.99-0.99)	<0.001	0.99 (0.99-0.99)	<0.001
Smoking habits												
Current smoker	1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)	
Former smoker	0.71 (0.57-0.88)	0.002	1.09 (0.86-1.38)	0.472	0.69 (0.56-0.86)	0.001	0.84 (0.69-1.01)	0.119	0.84 (0.67-1.06)	0.125	0.60 (0.41-0.87)	0.007
Never smoker	0.67 (0.52-0.85)	0.001	0.97 (0.75-1.25)	0.798	0.60 (0.48-0.75)	<0.001	0.82 (0.67-1.00)	0.047	0.68 (0.54-0.86)	0.001	0.51 (0.33-0.79)	0.003
Physical activity												
Less active	1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)	
Moderate active	0.58 (0.47-0.72)	<0.001	0.82 (0.67-1.01)	0.064	0.65 (0.53-0.79)	<0.001	0.96 (0.82-1.12)	0.578	0.83 (0.69-1.00)	0.056	0.52 (0.35-0.77)	0.001
Active	0.83 (0.67-1.01)	0.065	0.88 (0.72-1.07)	0.187	0.88 (0.74-1.06)	0.187	0.93 (0.79-1.08)	0.323	1.00 (0.84-1.20)	0.982	0.83 (0.58-1.19)	0.306
Education level												
Tertiary level	1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)	
Secondary level	0.91 (0.74-1.12)	0.376	0.81 (0.66-1.01)	0.048	1.02 (0.84-1.24)	0.829	1.20 (1.01-1.42)	0.035	1.02 (0.83-1.25)	0.869	1.00 (0.68-1.46)	0.984
Primary level	0.75 (0.62-0.92)	0.006	0.88 (0.73-1.08)	0.221	0.80 (0.67-0.97)	0.022	1.12 (0.95-1.31)	0.177	1.04 (0.85-1.25)	0.725	1.22 (0.85-1.76)	0.277
Non diabetic	0.79 (0.66-0.94)	0.008	0.81 (0.68-0.97)	0.019	0.95 (0.80-1.10)	0.481	0.85 (0.75-0.97)	0.019	0.79 (0.68-0.93)	0.004	0.81 (0.59-1.10)	0.176
Living alone	0.84 (0.64-1.10)	0.193	0.91 (0.71-1.17)	0.466	0.82 (0.67-1.01)	0.068	0.93 (0.77-1.11)	0.426	1.09 (0.89-1.35)	0.376	1.31 (0.80-2.13)	0.285

OR, p value and 95% CI for the inadequacy intake of micronutrients as categorical variable according to area. Model has been adjusted by sex, age, smoking habits, physical activity, educational status, diabetic status, living alone, total energy intake and adherence into MedDiet Q-P17.

Table S6. Logistic regression model of micronutrients deficiency intake according to EFSA by areas

	DIETARY FIBER		*VITAMIN A*		*VITAMIN B_9*		*VITAMIN E*		*CALCIUM*		*MAGNESIUM*	
	OR (CI 95%)	**p value**	**OR (CI 95%)**	**p value**	**OR (CI 95%)**	**p value**	**OR (CI 95%)**	**p value**	**OR (CO 95%)**	**p value**	**OR (CI 95%)**	**p value**
Geographical areas												
North area	1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)	
Central area	0.92 (0.71-1.19)	0.518	0.68 (0.49-0.96)	0.026	1.05 (0.73-1.50)	0.798	0.48 (0.34-0.61)	<0.001	0.56 (0.44-0.73)	<0.001	0.51 (0.36-0.74)	>0.001
East area	0.72 (0.62-0.84)	<0.001	0.49 (0.40-0.59)	<0.001	1.02 (0.83-1.26)	0.859	0.36 (0.30-0.43)	<0.001	0.87 (0.75-1.00)	0.051	0.48 (0.39-0.59)	<0.001
South area	0.78 (0.66-0.92)	0.003	0.45 (0.36-0.56)	<0.001	1.06 (0.84-1.34)	0.615	0.33 (0.27-0.40)	<0.001	0.70 (0.59-0.82)	<0.001	0.43 (0.35-0.54)	<0.001
Age	0.79 (0.67-0.93)	0.005	0.11 (0.76-1.20)	0.703	0.92 (0.73-1.14)	0.432	1.16 (0.96-1.39)	0.125	0.95 (0.81-1.12)	0.544	0.96 (0.77-1.20)	0.715
Sex												
Men	1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)	
Female	0.47 (0.41-0.54)	<0.001	0.27 (0.23-0.33)	<0.001	0.53 (0.44-0.63)	<0.001	0.21 (0.18-0.25)	<0.001	0.52 (0.46-0.60)	<0.001	0.08 (0.07-0.10)	<0.001
MedDiet adherence												
Low adherence	(Ref.)		(Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)	
Moderate adherence	0.37 (0.33-0.43)	<0.001	0.68 (0.57-0.81)	<0.001	0.46 (0.39-0.55)	<0.001	0.66 (0.56-0.76)	<0.001	0.90 (0.79-1.02)	0.108	0.35 (0.29-0.42)	<0.001
High adherence	0.14 (0.12-0.17)	<0.001	0.40 (0.31-0.50)	<0.001	0.18 (0.14-0.23)	<0.001	0.43 (0.36-0.51)	<0.001	0.68 (0.59-0.80)	<0.001	0.10 (0.08-0.13)	<0.001
Energy intake (kcal/day)	0.99 (0.99-0.99)	<0.001	0.99 (0.99-0.99)	<0.001	0.99 (0.99-0.99)	<0.001	0.99 (0.99-0.99)	<0.001	0.99 (0.99-0.99)	<0.001	0.99 (0.99-0.99)	<0.001
Smoking habits												
Current smoker	1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)	
Former smoker	0.70 (0.58-0.85)	<0.001	1.16 (0.91-1.48)	0.241	0.67 (0.53-0.85)	0.001	0.87 (0.70-1.08)	0.204	0.81 (0.67-0.97)	0.020	0.67 (0.53-0.85)	0.001
Never smoker	0.66 (0.54-0.80)	0.002	1.06 (0.81-1.40)	0.670	0.57 (0.45-0.73)	<0.001	0.89 (0.71-1.12)	0.324	0.69 (0.57-0.84)	<0.001	0.60 (0.47-0.78)	<0.001
Physical activity												
Less active	1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)	
Moderate active	0.74 (0.64-0.86)	<0.001	0.80 (0.65-1.00)	0.045	0.68 (0.55-0.80)	<0.001	0.83 (0.70-0.98)	0.029	0.81 (0.70-0.93)	0.004	0.73 (0.59-0.89)	0.002
Active	0.80 (0.69-0.92)	0.003	0.95 (0.78-1.16)	0.636	0.86 (0.71-1.06)	0.157	0.93 (0.79-1.10)	0.425	0.85 (0.74-0.98)	0.029	0.86 (0.70-1.05)	0.132
Education level												
Tertiary level	1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)		1 (Ref.)	
Secondary level	0.94 (0.80-1.11)	0.491	0.93 (0.75-1.15)	0.488	1.06 (0.85-1.31)	0.599	1.20 (1.00-1.45)	0.047	0.99 (0.85-1.16)	0.930	1.02 (0.82-1.27)	0.846
Primary level	0.86 (0.74-1.00)	0.054	0.97 (0.79-1.20)	0.804	0.79 (0.64-0.97)	0.026	1.11 (0.94-1.32)	0.218	1.04 (0.90-1.21)	0.598	1.15 (0.94-1.41)	0.181
Non diabetic	0.91 (0.80-1.03)	0.141	0.78 (0.65-0.94)	0.008	0.94 (0.79-1.11)	0.468	0.79 (0.69-0.92)	0.002	0.74 (0.65-0.84)	<0.001	0.87 (0.73-1.03)	0.110
Living alone	1.16 (0.97-1.38)	0.101	0.89 (0.70-1.14)	0.353	0.78 (0.62-0.98)	0.032	0.88 (0.72-1.07)	0.191	0.96 (0.81-1.14)	0.664	1.15 (0.90-1.47)	0.252

OR, p value and 95% CI for the inadequacy intake of micronutrients as categorical variable according to area. Model has been adjusted by sex, age, smoking habits, physical activity, educational status, diabetic status, living alone, total energy intake and adherence into MedDiet Q-P17

Table S7. Multivariable logistic regression model for inadequate intake of 3 or more out 6 micronutrients in accordance with criteria by EFSA according to geographical area

	≥3 inadequate intake % Prevalence (95% CI)	*Odds Ratio (95% CI)*	*P value*
Geographical area			
North area	40.8 (38.2-43.3)	1 (Ref.)	
Central area	33.5 (29.1-37.9)	0.59 (0.44-0.80)	0.001
East area	36.6 (34.8-38.3)	0.59 (0.50-0.69)	<0.001
South area	37.4 (35.1-39.7)	0.59 (0.49-0.71)	<0.001

Results are expressed as OR and 95% CI for the inadequacy intake of ≥3 micronutrients as categorical variable according to geographical area. The model has been adjusted by sex, age, smoking habits, physical activity, educational status, diabetic status, living alone, total energy intake and adherence to MedDiet.

nutrients

IMPACT FACTOR 4.196

an Open Access Journal by MDPI

Message from the Editorial Board

Nutrients is an on-line open access journal that was first published in 2009. *Nutrients* adheres to rigorous peer-review and editorial processes and publishes only high quality manuscripts that address important issues related to the impacts of nutrients on human health. The Impact Factor of *Nutrients* has risen rapidly since its establishment and it is now ranked in the first quartile of journals publishing in the field of nutrition and dietetics research.

Author Benefits

- **Open Access** Unlimited and free access for readers
- **No Copyright Constraints** Retain copyright of your work and make free use of your article
- **Impact Factor 4.196 (2017 Journal Citation Reports®)**
- **Thorough Peer-Review**
- **Coverage by Leading Indexing Services** SCIE-Science Citation Index Expanded (Clarivate Analytics), MEDLINE (NLM), Pubmed (NLM), Scopus (Elsevier)
- **No Space Constraints, No Extra Space or Color Charges** No restriction on the length of the papers, number of figures or colors
- **Discounts on Article Processing Charges (APC)** If you belong to an institute that participates with the MDPI Institutional Open Access Program (IOAP)

TRABAJOS REALIZADOS

Artículo 3. Cano-Ibáñez N, Gea A, Martínez-González MA, Salas-Salvadó J, Corella D, Zomeño MD, et al. Dietary Diversity and Nutritional Adequacy among an Older Spanish Population with Metabolic Syndrome in the PREDIMED-Plus Study: A Cross-Sectional Analysis. Nutrients [Internet]. MDPI AG; 2019 Apr 26; 11 (5):958. Available from: http://dx.doi.org/10.3390/nu11050958.

Este trabajo titulado *"Dietary diversity and nutritional adequacy among an older Spanish population with Metabolic Syndrome in the PREDIMED-Plus study: A Cross-Sectional Analysis",* da respuesta al objetivo específico 3 de la Tesis Doctoral. Los hallazgos obtenidos ponen de manifiesto que la diversidad dietética lejos de los resultados obtenidos por otros autores, ejerce un factor protector en la inadecuación nutricional. Así pues, tras la realización de regresiones logísticas ajustadas, se observó que la ingesta inadecuada de nutrientes alcanzaba valores máximos en aquellos sujetos situados en el cuartil de menor diversidad dietética total. De forma análoga, el análisis de los componentes de cada uno de los grupos alimentarios que conformaban este índice reflejaron la misma tendencia, excepto para el grupo de los cereales. Teniendo en cuenta la importancia de esta variable en el riesgo de presentar ingestas deficitarias de nutrientes, se analizaron qué factores sociodemográficos y de estilo de vida se vinculaban con una mayor diversidad dietética, encontrándose que ser mujer, no fumar y presentar un mayor nivel de adherencia a la Dieta Mediterránea estaba asociado de forma directa y significativa. Por el contrario, no estar casado y el consumo de alcohol se asociaron de forma inversa.

6.1.3. Dietary Diversity and Nutritional Adequacy among an Older Spanish Population with Metabolic Syndrome in the PREDIMED-Plus Study: A Cross-Sectional Analysis

[Cano-Ibáñez N, Gea A, Martínez-González MA, Salas-Salvadó J, Corella D, Zomeño MD, et al. Dietary Diversity and Nutritional Adequacy among an Older Spanish Population with Metabolic Syndrome in the PREDIMED-Plus Study: A Cross-Sectional Analysis. Nutrients [Internet]. MDPI AG; 2019 Apr 26; 11 (5):958. Available from: http://dx.doi.org/10.3390/nu11050958].

Datos de la Publicación:

- Factor de impacto en JCR 2017: 4.196
- Ránking: 18/83
- Categoría: *Nutrition & Dietetics*
- Cuartil: Q1.

nutrients

MDPI

Article

Dietary Diversity and Nutritional Adequacy among an Older Spanish Population with Metabolic Syndrome in the PREDIMED-Plus Study: A Cross-Sectional Analysis

Naomi Cano-Ibáñez [1,2,3], Alfredo Gea [4,5,6], Miguel A. Martínez-González [4,5,6,7], Jordi Salas-Salvadó [6,8,9,10], Dolores Corella [6,11], M. Dolors Zomeño [12,13], Dora Romaguera [6,14], Jesús Vioque [2,15], Fernando Aros [6,16], Julia Wärnberg [6,17], J. Alfredo Martínez [6,18,19], Lluis Serra-Majem [6,20], Ramón Estruch [6,21], Francisco J. Tinahones [6,22], José Lapetra [6,23], Xavier Pintó [6,24], Josep A. Tur [6,25], Antonio García-Ríos [6,26], Blanca Riquelme-Gallego [1], Miguel Delgado-Rodríguez [2,27], Pilar Matía [6,28], Lidia Daimiel [19], Vicente Martín [2,29], Josep Vidal [30,31], Clotilde Vázquez [6,32], Emilio Ros [6,33], Pilar Buil-Cosiales [4,6,34], Andrés Díaz-López [6,8,9,10], Rebeca Fernández-Carrión [6,11], Montserrat Fitó [6,12,13], Jadwiga Konieczna [6,14], Leyre Notario-Barandiaran [2,15], Ángel M. Alonso-Gómez [6,16], Eugenio Contreras-Fernández [35], Itziar Abete [6,18], Almudena Sánchez-Villegas [6,20], Rosa Casas [6,21], Araceli Muñoz-Garach [6,22], José Manuel Santos-Lozano [6,23,36], Laura Gallardo-Alfaro [25], Josep Basora [6,8,9,10], Olga Portoles [6,11], Miguel Ángel Muñoz [37], Manuel Moñino [6,14], Salvador Miralles Gisbert [2,15], Anai Moreno Rodríguez [16], Miguel Ruiz-Canela [4,5,6], Antoni Palau Galindo [6,8,9,38], Karla Alejandra Pérez-Vega [12] and Aurora Bueno-Cavanillas [1,2,3,*]

1. Department of Preventive Medicine and Public Health, University of Granada, 18011 Granada, Spain; ncaiba@ugr.es (N.C.-I.); blanca.riquel@gmail.com (B.R.-G.)
2. CIBER Epidemiología y Salud Pública (CIBERESP). Instituto de Salud Carlos III (ISCIII), 28029 Madrid, Spain; vioque@umh.es (J.V.); mdelgado@ujaen.es (M.D.-R.); vicente.martin@unileon.es (V.M.); lnotario@umh.es (L.N.-B.); sjmirallesgis@gmail.com (S.M.G.)
3. Instituto de Investigación Biosanitaria de Granada (ibs.GRANADA), 18012 Granada, Spain
4. University of Navarre, Department of Preventive Medicine and Public Health, Medical School, 31008 Pamplona, Spain; ageas@unav.es (A.G.); mamartinez@unav.es (M.A.M.-G.); pilarbuilc@gmail.com (P.B.-C.); mcanela@unav.es (M.R.-C.)
5. Navarra institute for health research (IdisNa), 31008 Pamplona, Spain
6. CIBER Fisiopatología de la Obesidad y Nutrición (CIBEROBN), Instituto de Salud Carlos III (ISCIII), 28029 Madrid, Spain; jordi.salas@urv.cat (J.S.-S.); dolores.corella@uv.es (D.C.); doraromaguera@yahoo.es (D.R.); luisfernando.aros@ehu.eus (F.A.); jwarnberg@uma.es (J.W.); jalfmtz@unav.es (J.A.M.); lluis.serra@ulpgc.es (L.S.-M.); restruch@clinic.ub.es (R.E.); fjtinahones@hotmail.com (F.J.T.); jlapetra@ono.com (J.L.); xpinto@bellvitgehospital.cat (X.P.); pep.tur@uib.es (J.A.T.); angarios2004@yahoo.es (A.G.-R.); pilar.matia@gmail.com (P.M.); clotilde.vazquez@fjd.es (C.V.); eros@clinic.ub.es (E.R.); andres.diaz@urv.cat (A.D.-L.); rebeca.fernandez@uv.es (R.F.-C.); mfito@imim.es (M.F.); jadzia.konieczna@gmail.com (J.K.); angelmago13@gmail.com (Á.M.A.-G.); iabetego@unav.es (I.A.); almudena.sanchez@ulpgc.es (A.S.-V.); rcasas1@clinic.cat (R.C.); araceli.munoz.garach.sspa@juntadeandalucia.es (A.M.-G.); josemanuel.santos@ono.com (J.M.S.-L.); jbasora.tarte.ics@gencat.cat (J.B.); Olga.portoles@uv.es (O.P.); mmonyino@gmail.com (M.M.); apalau@grupsagessa.com (A.P.G.)
7. Department of Nutrition, Harvard T.H. Chan School of Public Health, Boston, MA 02115, USA
8. Universitat Rovira i Virgili, Departament de Bioquímica i Biotecnologia, Unitat de Nutrició, 43002 Reus, Spain
9. Institut d'Investigació Sanitària Pere Virgili (IISPV), 43204 Reus, Spain
10. University Hospital of Sant Joan de Reus, Nutrition Unit, 43204 Reus, Spain
11. Department of Preventive Medicine, University of Valencia, 46010 Valencia, Spain

[12] Unit of Cardiovascular Risk and Nutrition, Institut Mar d´Investigacions Mèdiques (IMIM), 08003 Barcelona, Spain; mariadoloreszf@blanquerna.edu (M.D.Z.); kperez@imim.es (K.A.P.-V.)
[13] Human Nutrition Unit, Blanquerna-Ramon Llull University, 08001 Barcelona, Spain
[14] Health Research Institute of the Balearic Islands (IdISBa), 07120 Palma de Mallorca, Spain
[15] Nutritional Epidemiology Unit, Miguel Hernández University, ISABIAL-FISABIO, 03202 Alicante, Spain
[16] Department of Cardiology, OSI ARABA, University Hospital Araba, University of the Basque Country UPV/EHU, 48940 Vitoria-Gasteiz, Spain; anai.m.rodriguez@gmail.com
[17] Department of Nursing, School of Health Sciences. University of Malaga- Instituto de Investigación Biomédica de Málaga (IBIMA), 29010 Málaga, Spain
[18] Department of Nutrition, Food Sciences, and Physiology, Center for Nutrition Research, University of Navarra, 31008 Pamplona, Spain
[19] Nutritional Genomics and Epigenomics Group, IMDEA Food, CEI UAM + CSIC, 28049 Madrid, Spain; lidia.daimiel@imdea.org
[20] Research Institute of Biomedical and Health Sciences. University of Las Palmas de Gran Canaria, 35016 Las Palmas de Gran Canaria, Spain
[21] Department of Internal Medicine, Institut d´Investigacion Biomèdiques August Pi Sunyer (IDIBAPS), Hospital Clinic, University of Barcelona, 08036 Barcelona, Spain
[22] Virgen de la Victoria Hospital, Department of Endocrinology, Instituto de Investigación Biomédica de Málaga (IBIMA), University of Málaga, 29016 Málaga, Spain
[23] Department of Family Medicine, Research Unit, Distrito Sanitario Atención Primaria Sevilla, 41013 Sevilla, Spain
[24] Lipids and Vascular Risk Unit, Internal Medicine, Hospital Universitario de Bellvitge, Hospitalet de Llobregat, 08907 Barcelona, Spain
[25] Research Group on Community Nutrition & Oxidative Stress, University of Balearic Islands, 07122 Palma de Mallorca, Spain; laura.gallardo@uib.es
[26] Lipids and Atherosclerosis Unit, Department of Internal Medicine, Maimonides Biomedical Research Institute of Córdoba (IMIBIC), Reina Sofía University Hospital, University of Córdoba, 14004 Córdoba, Spain
[27] Department of Health Sciences, University of Jaen, 23071 Jaen, Spain
[28] Department of Endocrinology and Nutrition, Instituto de Investigación Sanitaria Hospital Clínico San Carlos (IdISSC), 28040 Madrid, Spain
[29] Institute of Biomedicine (IBIOMED), University of León, 24071 León, Spain
[30] Department of Endocrinology, Institut d' Investigacions Biomédiques August Pi Sunyer (IDIBAPS), Hospital Clinic, University of Barcelona, 08036 Barcelona, Spain; jovidal@clinic.cat
[31] CIBER Diabetes y enfermedades metabólicas (CIBERDEM), ISCIII, 28029 Madrid, Spain
[32] Department of Endocrinology, Fundación Jiménez-Díaz, 28040 Madrid, Spain
[33] Lipid Clinic, Department of Endocrinology and Nutrition, IDIBAPS, Hospital Clinic, 08036 Barcelona, Spain
[34] Primary Care, Health Service of Navarra-Osasunbidea, 31002 Pamplona, Spain
[35] Unidad Gestión Clínica de Prevención, Promoción y Vigilancia de la Salud, Distrito Atención Primaria Costa del Sol, Servicio Andaluz de Salud. Red de Investigación Servicios De Salud en Enfermedades Crónicas (REDISSEC), 29651 Málaga, Spain; eugenio.contreras.sspa@juntadeandalucia.es
[36] Department of Medicine. University of Sevilla, 41004 Sevilla, Spain
[37] Primary Care Division of Barcelona, Institut Català de la Salud-IDIAP Jordi Gol, 08007 Barcelona, Spain; mamunoz.bcn.ics@gencat.cat
[38] ABS Reus V. Centre d'Assistència Primària Marià Fortuny, SAGESSA, 43203 Reus, Spain
* Correspondence: abueno@ugr.es; Tel.:+34-958-24-66-58

Received: 16 March 2019; Accepted: 24 April 2019; Published: 26 April 2019

Abstract: Dietary guidelines emphasize the importance of a varied diet to provide an adequate nutrient intake. However, an older age is often associated with consumption of monotonous diets that can be nutritionally inadequate, increasing the risk for the development or progression of diet-related chronic diseases, such as metabolic syndrome (MetS). To assess the association between dietary diversity (DD) and nutrient intake adequacy and to identify demographic variables associated with DD, we cross-sectionally analyzed baseline data from the PREDIMED-Plus trial: 6587 Spanish adults aged 55–75 years, with overweight/obesity who also had MetS. An energy-adjusted dietary diversity score (DDS) was calculated using a 143-item validated semi-quantitative food frequency questionnaire (FFQ). Nutrient inadequacy was defined as an intake below 2/3 of the dietary reference intake (DRI) forat least four of 17 nutrients proposed by the Institute of Medicine (IOM). Logistic regression models were used to evaluate the association between DDS and the risk of nutritionally inadequate intakes. In the higher DDS quartile there were more women and less current smokers. Compared with subjects in the highest DDS quartile, those in the lowest DDS quartile had a higher risk of inadequate nutrient intake: odds ratio (OR) = 28.56 (95% confidence interval (CI) 20.80–39.21). When we estimated food varietyfor each of the food groups, participants in the lowest quartile had a higher risk of inadequate nutrient intake for the groups of vegetables, OR = 14.03 (95% CI 10.55–18.65), fruits OR = 11.62 (95% CI 6.81–19.81), dairy products OR = 6.54 (95% CI 4.64–9.22) and protein foods OR = 6.60 (95% CI 1.96–22.24). As DDS decreased, the risk of inadequate nutrients intake rose. Given the impact of nutrient intake adequacy on the prevention of non-communicable diseases, health policies should focus on the promotion of a healthy varied diet, specifically promoting the intake of vegetables and fruit among population groups with lower DDS such as men, smokers or widow(er)s.

Keywords: dietary diversity; nutrient adequacy; metabolic syndrome; aging; PREDIMED-Plus study

1. Introduction

Metabolic syndrome (MetS), a clustering of risk factors (central obesity, insulin resistance, dyslipidemia and hypertension) [1], is a well-known condition in the causal pathway of cardiovascular disease (CVD). MetS has also been associated with a higher risk of other chronic diseases, such as cancer [2] and neurodegenerative diseases [3]. In recent years, the prevalence of MetS has increased worldwide to the point that presently it is considered as a major public health problem [4]. This trend has also been observed in Spain, where the current prevalence of MetS is approximately 22.7% and increases with age [5]. Typically subjects with MetS have a higher use of health care services, incrementing costs [6].

MetS is a multifactorial disease that may be associated with some modifiable risk behaviors, such as unhealthy lifestyles and dietary patterns [7]. Among these factors, dietary intake plays a critical role in the prevention and treatment of MetS. Thus, dietary patterns that include healthy varied food groups and which provide adequate nutrient intake have been shown to be beneficial in the progression of MetS [8]. In this sense, the Mediterranean dietary pattern (MedDiet) has been related, not only to a delay in the progression and a lower mortality of MetS [9], but also to an adequate nutritional intake [10]. This can be explained by the great variety of food products that characterize the MedDiet. These foods, such as fruit and vegetables, nuts, legumes, fish and whole grain cereals, have a relatively low caloric value but a high nutrient content, increasing the probability to meet nutritional requirements [11].

Spanish dietary guidelines have emphasized the importance of a varied, balanced and moderated diet to reduce the risk of diet-related chronic diseases [12]. However, the role of a varied diet on chronic disease development is still uncertain. Some studies have suggested that dietary diversity (DD) contributes to high energy consumption and has a positive association with a poor quality diet, increasing the risk of MetS in older adults [13–16]; other researchers have reported that DD is a key component of high-quality diets, being associated with nutrient adequacy [17] and reducing the rates of CVD [18] and MetS [19] in the overall population.

Older adult populations with chronic diseases are considered vulnerable groups, as they are at greater nutritional risk due to a higher prevalence of inadequate nutrient intakes [20]. This could be a consequence of the consumption of monotonous and nutritionally inadequate diets, influenced by several factors, including loneliness, low socioeconomic status and functional quality [21].

There is evidence that nutritional inadequacy is prevalent in the older Spanish population [22], likely related to a monotonous diet and which could accelerate the progression of chronic diseases such as MetS. In this study we examined DD among PREDIMED-Plus participants, an older adult population with MetS, with the aim of assessing the association between DD and nutrient adequacy and to identify demographic variables associated with DD.

2. Materials and Methods

2.1. Design of the Study

A cross-sectional analysis on baseline data of the PREDIMED-Plus study was conducted. The PREDIMED-Plus study is an ongoing multicenter, randomized and parallel-group primary cardiovascular prevention trial. The PREDIMED-Plus study aims to assess the potential advantages of the synergy of a high-quality energy reduced MedDiet plus a weight-loss intervention and behavioral support on the incidence of CVD, in comparison to standard MedDiet advice (control group). The participant recruitment methods and data collection process have been described previously [23]. The Institutional Review Boards of all participating centers approved the study protocol. The clinical trial was registered in 2014 at the International Standard Randomized Controlled Trial (www.isrctn.com/ISRCTN89898870). All participants provided written informed consent.

2.2. Study Population

The study participants were men and women (55–75 years old and 60–75 years old, respectively), with overweight or obesity (body mass index (BMI) ≥27 and ≤40 kg/m^2), who at baseline met at least three of the MetS criteria. The MetS criteria used have been previously described [24].

A total of 6874 subjects were recruited and randomized in 23 centers of the PREDIMED-Plus clinical trial from October 2013 to December 2016, from different universities, hospitals and research institutes across Spain. Of these, 287 participants were excluded for the present study (Figure 1): 47 participants because they did not complete the food frequency questionnaire (FFQ), and 240 participants because they reported values for total energy intake outside predefined limits (<3347 kJ <800 kcal/day or >17,573 kJ >4000 kcal/day for men); (<2510 kJ <500 kcal/day or >14,644 kJ >3500 kcal)/day for women) [25]. A final sample of 6587 participants was analyzed.

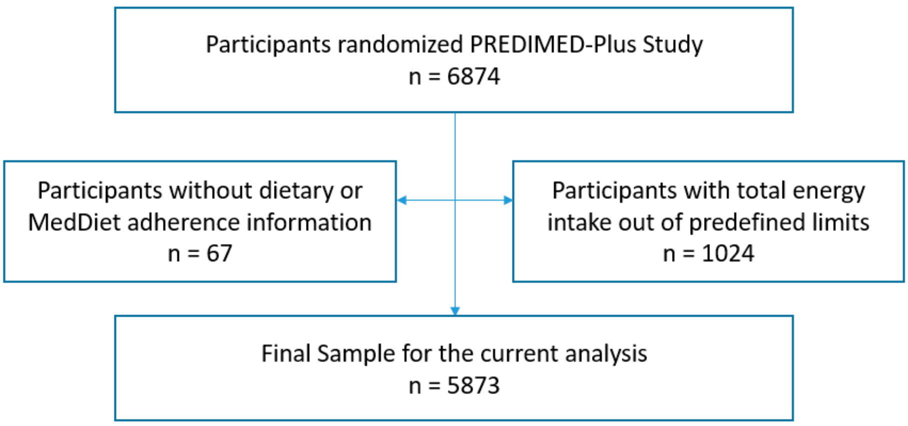


Figure 1. Flow-chart of participants.

2.3. Dietary Intake Assessment

Trained dieticians collected data on dietary intake at baseline in a face-to-face interview. Dietary intake was assessed using a 143 item semi-quantitative FFQ previously and repeatedly validated in Spain [26]. The FFQ provides a list of foods commonly used by the Spanish population and asks about the consumption of these foods during the previous year. It includes nine response options (never or almost never, 1–3 times a month, once a week, 2–4 times a week, 5–6 times a week, once a day, 2–3 times a week day, 4–6 times a day and more than 6 times a day). The indicated frequencies of consumption were converted to intakes per day and multiplied by the weight of the standard serving size in order to estimate the intake in grams per day. Nutrient information was derived from Spanish food composition tables [27,28].

2.4. Dietary Diversity Score Construction

Using the 143-item validated FFQ mentioned above, we calculated an energy-adjusted DD score (DDS). This DDS was calculated by the method originally developed by Kant et al. [29] and recently used by Farhangi et al. [30]. We included five food groups: Vegetables, fruits, cereals, dairy products and protein food groups (legumes, meat, fish, eggs and nuts), based on the food groups recommended by the Spanish guidelines' pyramid [12]. The vegetable group was divided into four subgroups, including: Green vegetables, tomatoes, yellow vegetables and mushrooms. The cereal group included potatoes and refined or whole grain cereals (bread, pasta, rice and breakfast cereals). The fruit group included all fresh fruit products divided in three categories: Citrus fruits, tropical fruits and other seasonal fruits. The dairy group included all kinds of milk, yogurt and cheese. Protein food groups included legumes (peas, beans, lentils and chickpeas), white meats (poultry and rabbit), fish (oily fish, white fish and other shellfish/seafood), eggs and nuts. Non-recommended food groups (that should be consumed as little as possible) [27], including sugar food groups (pastries, pies, biscuits, chocolate, fruit in sugar syrup and fruit juices) and food groups with high salt and/or saturated fats (butter, margarine, unhealthy vegetable fats, red meat, processed meats, sauces, pre-cooked dishes, condiments and snacks) were not included in the analysis as they are less healthy products and their variety is not desirable. These groups were used to define food variety groups. Therefore, we only analyzed diversity of recommended food groups, because the more important question was the percentage of total energy supplied by these food groups and our analyses were adjusted for total energy intake.

To be counted as a consumer for any of the food group categories reported previously, a subject should consume at least half of the recommended serving during one day (for example, if the Spanish nutritional recommendation advises a usual protein intake of three servings per week, for each protein item, participants should consume at least 1.5/7 servings/day). Within each food group, we summed up the number of items consumed. Each of the five predefined food categories received a maximum diversity score of 2 points, therefore the sum was rescaled to a 0-to-2 score by multiplying the score by 2 and dividing by the maximum score in that food group. Total DDS is the sum of the scores of the five main groups, theoretically ranging between 0 and 10 points. The score was adjusted for total energy intake, due to the general concern that high food variety might be a consequence of overconsumption of energy [14]. Finally, DDS was categorized in quartiles (Q) and the cutoff points were 3.8, 4.6 and 5.4. The variety in each food group was classified into four categories (C): C1 = 0 points, C2 ≥0–≤0.5 points, C3 ≥0.5–<1 points and C4 ≥1 point.

Subjects were asked about MedDiet adherence using a 17-item screening questionnaire used to both evaluate compliance with the intervention and guide the motivational interviews during the study follow-up. This screener is a modification of a previously validated 14-item MedDiet adherence questionnaire [31]. Compliance with each of the 17 items relating to characteristic food habits was scored with 1 point, and 0 points otherwise, so that the total score range was 0–17, with 0 meaning no adherence and 17 meaning maximum adherence. Adherence to the MedDiet, was categorized in tertiles as lower level (1st tertile, ≤7 points), medium (2nd tertile, 8–10 points) or higher level of adherence (3rd tertile, ≥11 points).

2.5. Nutrient Adequate Intake

The dietary intake of 17 selected nutrients, including vitamins A, B_1, B_6, B_9, B_{12}, C, D, E, minerals such as calcium, phosphorus, magnesium, iron, iodine, potassium, selenium and zinc and dietary fiber, was compared with age and sex-specific recommended intakes for these nutrients according to the established dietary reference intake (DRI) recommendations for the North-American population [32]. DRI is the general term for a set of reference values used to plan and assess nutrient intakes for healthy people. These values vary by age and sex. Intake levels above DRI imply a low likelihood of inadequate intake. To decrease potential measurement errors derived from the use of the FFQ, we calculated the proportion of individuals with intakes below two thirds (2/3) of the DRIs [33]. Furthermore, we estimated the proportion of inadequate intake according to European Food Safety Agency (EFSA) average requirements (ARs), taking as reference adequate intake (AI) when ARs were not available [34]. Results were based on dietary intake data only, excluding supplements.

2.6. Assessment of Non-Dietary Variables

At the baseline visit, trained PREDIMED-Plus staff collected information on lifestyle variables, educational achievement and socioeconomic status. The variables collected were sex, age (55–70 years and >70 years), educational level (primary, secondary and tertiary level, which includes university studies), civil status (married, widowed, divorced/single or other, which includes single participants and those who are priests or nuns who were categorized as "religious") and whether they lived alone or not. Other lifestyle variables such as smoking habit (non-smoker, current smoker or never smoker), alcohol intake (measured as a continuous variable and expressed as intake in g/day) and physical activity (less active, moderately active and active) were taken into account. Individuals were classified based on their level of physical activity using a validated Spanish version of the Minnesota questionnaire: Less active (<4 MET), moderately active (4–5.5 MET) and active (≥6 MET) physical activity level [35,36]. Anthropometric variables (weight, height and waist circumference) were determined by trained staff in accordance with the PREDIMED-Plus operations protocol. Weight and height were measured with calibrated scales and a wall-mounted stadiometer, respectively. BMI was calculated as the weight in kilograms divided by the height in meters squared. Waist circumference (WC) was measured midway between the lowest rib and the iliac crest using an anthropometric tape.

2.7. Statistical Analysis

Data were analyzed using Stata (12.0, StataCorp LP, College Station, TX, USA). We used the PREDIMED-Plus baseline database generated in August 2017. Participants were classified according to DDS quartiles. Baseline characteristics of participants were described as means ± standard deviations (SD) for continuous variables or number and percentages for categorical variables. Comparison of quantitative variables across DDS quartiles was performed using ANOVA. Pearson χ^2 test was used to compare the distribution of qualitative variables among DDS quartiles. A linear regression model was fitted to estimate the association of sociodemographic and lifestyle variables (sex, age, educational level, civil status, living alone, physical activity, smoking and drinking status) with DDS. Logistic regression models were used to evaluate the association between nutritional inadequate intakes (≥4 nutrients) as dependent variable and total DDS or food variety groups as the main independent variables. All analyses were adjusted for potential confounders based on prior knowledge: Sex, age, energy intake, BMI, WC, level of education, smoking status, physical activity, MedDiet adherence, marital status and living alone. We used a significance level of 0.05 for all analyses.

3. Results

3.1. Baseline Characteristics of PREDIMED-Plus Participants by Quartiles of DDS

Table 1 shows the comparison of demographic, anthropometric and lifestyle variables according to quartiles of DDS. We found significant differences for age, sex, smoking habits, marital status, educational level and WC ($p < 0.001$), but not for physical activity or BMI. Participants in the top DDS quartile (Q4) were older (65.8 ± 4.7) and more likely to be women (63.6%), never smokers (54.3%) and married (77.8%, $p < 0.05$) in comparison with the lower DDS quartiles. Moreover, participants in the top DDS quartile had a lower WC (106.3 ± 9.6) and lower educational level. However the magnitude of the differences across quartiles was small and should be interpreted in the light of the large power and sample size of the study.

Table 1. Baseline characteristics of PREDIMED-Plus participants by quartiles of an energy-adjusted dietary diversity score (DDS, total population = 6587).

	Q1 (*n* = 1647)	Q2 (*n* = 1647)	Q3 (*n* = 1647)	Q4 (*n* = 1646)	*p* Value
Age (Year), *n* (%)					
55–70 years	1442 (87.6)	1416 (86.0)	1403 (85.2)	1356 (82.4)	<0.001
>70 years	205 (12.5)	231 (14.0)	244 (14.8)	290 (17.6)	
Mean ± SD	64.1 ± 5.1	64.8 ± 4.9	65.3 ± 4.8	65.8 ± 4.7	<0.001
Sex, *n* (%)					
Male	1116 (67.8)	916 (55.6)	770 (46.8)	600 (36.5)	<0.001
Female	531 (32.2)	731 (44.4)	877 (53.3)	1046 (63.6)	
Smoking Habits, *n* (%)					
Current Smoker	297 (18.0)	195 (11.8)	171 (10.4)	152 (9.2)	<0.001
Former Smoker	793 (48.2)	747 (45.4)	722 (43.8)	593 (36.0)	
Never Smoker	548 (33.3)	699 (42.4)	749 (45.5)	893 (54.3)	
Without information	9 (0.6)	6 (0.4)	5 (0.3)	8 (0.5)	
Physical Activity, *n* (%)					
Less active	1014 (61.7)	985 (59.9)	983 (59.9)	940 (57.4)	0.29
Moderately active	294 (17.9)	304 (18.5)	319 (19.4)	326 (19.9)	
Active	335 (20.4)	355 (21.6)	340 (20.7)	373 (22.8)	
Educational Level, *n* (%)					
Tertiary level	421 (25.6)	360 (21.9)	340 (20.6)	320 (19.5)	<0.001
Secondary level	534 (32.4)	480 (29.2)	449 (27.3)	435 (26.4)	
Primary level	679 (41.3)	796 (48.4)	842 (51.1)	873 (53.1)	
Without information	13 (0.7)	11 (0.6)	16 (1.0)	18 (1.0)	
Civil Status, *n* (%)					
Married	1258 (76.7)	1254 (76.4)	1243 (75.7)	1278 (77.8)	0.030
Widowed	151 (9.2)	162 (9.9)	182 (11.1)	186 (11.3)	
Divorced/Separated	145 (8.8)	123 (7.5)	130 (7.9)	117 (7.1)	
Others [a]	93 (5.2)	108 (6.2)	92 (5.3)	65 (3.8)	
Living alone, n (%)	193 (11.8)	189 (11.5)	220 (13.4)	212 (12.9)	0.29
BMI (kg/m^2), Mean ± SD	32.6 ± 3.4	32.5 ± 3.4	32.5 ± 3.5	32.5 ± 3.5	0.82
WC (cm), Mean ± SD	109.3 ± 9.5	108.1 ± 9.5	107.0 ± 9.7	106.3 ± 9.6	<0.001

Values are presented as means ± SD for continuous variables and *n* (%) for categorical variables. Pearson's chi-square test was performed for categorical variables and ANOVA test for continuous variables. [a] includes religious and single status. Abbreviations: BMI, body mass index; DDS, dietary diversity score; Q, quartile; SD, standard deviation; WC, waist circumference.

3.2. Associations Between Demographic and Lifestyle Variables with DDS

The associations between these demographic and lifestyle variables with DDS as a continuous variable are presented in Table 2. We observed that DDS was significantly higher among women (mean difference = 0.26, 95% CI 0.18, 0.33), non-smokers (mean differences = 0.18, 95% CI 0.09, 0.27) and participants with higher adherence to the MedDiet (mean difference = 0.65, 95% CI 0.58, 0.73), whereas alcohol intake (mean difference = −0.01, 95% CI −0.01, −0.01) and being widowed (mean difference = −0.15, 95% CI −0.26, −0.05) were inversely associated with higher DDS.

Table 2. Linear regression model to evaluate demographic and lifestyle variables associated with DDS (DDS measure as continuous variable).

	Total DDS	
	Mean Differences (95% CI)	***p* Value**
Sex		
Men	0 (ref)	
Women	0.26 (0.18, 0.33)	<0.001
Age		
≤70 years	0 (ref)	
More 70 years	0.06 (−0.15, 0.14)	0.12
Smoking Habits		
Current smoker	0 (ref)	
Former smoker	0.14 (0.06, 0.23)	0.001
Never smoker	0.18 (0.09, 0.27)	<0.001
Physical Activity Status		
Less active	0 (ref)	
Moderate active	0.06 (−0.01, 0.13)	0.11
Active	0.03 (−0.04, 0.10)	0.34
Educational Status		
Tertiary Level	0 (ref)	
Secondary Level	0.02 (−0.05, 0.09)	0.59
Primary Le	0.07 (0.03, 0.14)	0.041
MedDiet Adherence		
Low Adherence	0 (ref)	
Medium Adherence	0.34 (0.28, 0.40)	<0.001
High Adherence	0.65 (0.58, 0.73)	<0.001
Civil Status		
Married	0 (ref)	
Widowed	−0.15 (−0.26, −0.05)	0.004
Divorced/Separated	−0.12 (−0.23, −0.02)	0.026
Others [a]	−0.21 (−0.34, −0.08)	0.002
Living alone	−0.31 (−0.14, 0.07)	0.57
WC (cm) [b]	−0.01 (−0.01, 0.01)	0.57
BMI (kg/m^2) [b]	−0.01 (−0.01, 0.01)	0.75
Alcohol intake (g) [b]	−0.01 (−0.02, −0.01)	<0.001

Linear regression model (95% CI) for the DDS as a dependent variable according to baseline characteristics of participants. [a] Others: Includes religious and single status. [b] 1-unit increase. Abbreviations: BMI, body mass index; CI, confidence interval; DDS, dietary diversity score; SD, standard deviation; WC, waist circumference.

3.3. Adherence to MedDiet and Dietary Intake of PREDIMED-Plus Participants by Quartiles of DDS Adjusted by Energy

Comparing across DDS quartiles, individuals in Q4 had significantly higher MedDiet adherence, higher intake of dietary fiber, carbohydrates, proteins and polyunsaturated fat, but lower saturated fat intake (Table 3). Vitamin and mineral intake increased progressively across DDS quartiles ($p < 0.001$). However the magnitude of these differences across quartiles is small and should be interpreted in the light of the large power and sample size of the study. On the other hand, participants in the bottom DDS quartile (Q1) reported higher alcohol intake. Total energy intake followed a U-shaped line, higher in Q1 and Q4 than in Q2–Q3. Supplementary Table 1 (Table S1) shows the proportion of participants with an intake below 2/3 of DRIs by DDS quartiles and is stratified by sex and group of age. The prevalence of inadequate intake of all nutrients decreased across DDS quartiles in all age and sex strata, except for vitamin D in older individuals. Vitamins B1, B12, C, phosphorus, iron, potassium, selenium and zinc presented high number of categories with zero cases, as nearly all the prevalent cases of deficient intake were at Q1 of DDS (Table S2.). These results were similar when the EFSA recommendations were used instead (Table S3.).

Table 3. Adherence to MedDiet, mean energy, alcohol and nutrient intakes of PREDIMED-Plus participants by quartiles of DDS adjusted by energy.

	Q1 (*n* = 1647)	Q2 (*n* = 1647)	Q3 (*n* = 1647)	Q4 (*n* = 1646)	*p* Value
MedDiet Adherence, *n* (%)					
Low adherence	857 (52.0)	638 (38.7)	507 (30.8)	372 (22.6)	
Medium adherence	602 (36.7)	686 (41.7)	717 (43.5)	684 (41.6)	<0.001
High adherence	188 (11.4)	323 (19.6)	423 (25.7)	590 (35.8)	
Mean ± SD	7.4 ± 2.5	8.3 ± 2.6	8.8 ± 2.5	9.5 ± 2.6	<0.001
Nutrient Intake, Mean ± SD					
Total energy (Kcal/day)	2382.3 ± 612.8	2345.0 ± 557.9	2340.7 ± 527.0	2397.1 ± 502.6	0.006
Total fat intake (%)	39.9 ± 7.1	39.9 ± 6.6	39.5 ± 6.3	38.9 ± 5.9	<0.001
Monounsaturated fat (%)	20.7 ± 4.9	20.8 ± 4.7	20.5 ± 4.6	20.1 ± 4.3	0.002
Polyunsaturated fat (%)	6.2 ± 1.9	6.3 ± 1.9	6.4 ± 1.8	6.6 ± 1.8	<0.001
Saturated fat (%)	10.1 ± 2.2	10.1 ± 2.1	9.9 ± 1.9	9.7 ± 1.8	<0.001
Carbohydrate intake (%)	40.1 ± 7.5	40.2 ± 7.0	40.7 ± 6.5	41.3 ± 6.1	<0.001
Protein intake (%)	15.4 ± 2.6	16.6 ± 2.7	17.2 ± 2.8	17.9 ± 2.6	<0.001
Fiber intake (g/day)	21.4 ± 7.8	24.8 ± 7.7	27.1 ± 7.8	31.3 ± 8.8	<0.001
Vitamin A (μg/day)	909.3 ± 624.6	1075.1 ± 648.9	1133.2 ± 587.7	1302.9 ± 650.3	<0.001
Vitamin B1 (mg/day)	1.5 ± 0.4	1.6 ± 0.4	1.7 ± 0.4	1.8 ± 0.4	<0.001
Vitamin B6 (mg/day)	2.0 ± 0.5	2.2 ± 0.5	2.4 ± 0.5	2.7 ± 0.6	<0.001
Vitamin B9 (μg/day)	290.7 ± 82.3	335.6 ± 88.9	363.6 ± 90.9	416.1 ± 102.0	<0.001
Vitamin B12 (μg/day)	9.0 ± 4.5	9.7 ± 4.5	10.1 ± 4.3	10.9 ± 4.5	<0.001
Vitamin C (mg/day)	147.5 ± 66.4	189.0 ± 74.3	216.5 ± 78.3	255.7 ± 83.2	<0.001
Vitamin D (μg/day)	5.3 ± 3.2	5.9 ± 3.3	6.4 ± 3.4	7.1 ± 3.6	<0.001
Vitamin E (mg/day)	9.6 ± 4.1	10.4 ± 3.9	10.7 ± 3.7	11.7 ± 3.8	<0.001
Calcium (mg/day)	876.6 ± 325.3	987.2 ± 325.1	1071.8 ± 320.3	1201.5 ± 326.2	<0.001
Phosphorus (mg/day)	1556.4 ± 389.7	1699.4 ± 388.3	1796.7 ± 389.7	1985.6 ± 397.1	<0.001
Magnesium (mg/day)	371.0 ± 99.3	403.7 ± 98.4	428.2 ± 98.8	479.4 ± 108.5	<0.001
Iron (mg/day)	15.2 ± 3.9	16.0 ± 3.8	16.6 ± 3.7	18.1 ± 3.9	<0.001
Iodine (μg/day)	242.9 ± 163.6	274.7 ± 153.1	297.0 ± 155.3	327.2 ± 151.1	<0.001
Potassium (mg/day)	3767.9 ± 858.1	4262.1 ± 880.0	4619.6 ± 929.3	5256.5 ± 1053.4	<0.001
Selenium (μg/day)	113.6 ± 36.8	115.9 ± 32.9	116.4 ± 31.3	122.5 ± 30.9	<0.001
Zinc (mg/day)	12.5 ± 3.5	13.0 ± 3.2	13.2 ± 3.1	14.1 ± 3.1	<0.001
Alcohol intake (g/day), Mean ± SD	16.5 ± 19.4	11.7 ± 15.0	9.1 ± 12.4	6.8 ± 9.8	<0.001

Values are presented as means ± SD for continuous variables and *n* (%) for categorical variables. Pearson's chi-square test was performed for categorical variables and ANOVA test for continuous variables. Abbreviations: DDS, dietary diversity score; Q, quartile; SD, standard deviation.

3.4. Distribution of Participants ny Number of Nutrients below Adequate Intake According to the DDS by Age and Sex

Table 4 shows the prevalence of four or more inadequacies in nutrient intake according to DDS quartiles, stratified by sex and age. Independently of age and sex, we observed that participants with the highest DDS (Q4) showed a lower number of nutrient inadequacies ($p < 0.001$). Also the prevalence of four or more inadequacies in nutrient intake decreased across DDS quartiles ($p < 0.001$) regardless of age or sex. When we used the EFSA dietary recommendations, we obtained similar results (Table S4.).

Table 4. Number of inadequacies and distribution of participants with ≥4 nutrients below 2/3 of the dietary reference intake (DRI) according to DDS by age and sex.

	MEN: ≤70 years				
	Q1 (*n* = 787)	**Q2 (*n* = 763)**	**Q3 (*n* = 973)**	**Q4 (*n* = 489)**	***p* Value**
Inadequacies, mean ± SD	3.0 ± 1.1	2.3 ± 1.1	2.0 ± 0.1	1.7 ± 0.7	<0.001 [1]
Participants, *n* (%)	468 (46.8)	156 (19.3)	78 (11.7)	12 (2.4)	<0.001 [2]
	WOMEN: ≤70 years				
	Q1 (*n* = 630)	**Q2 (*n* = 610)**	**Q3 (*n* = 884)**	**Q4 (*n* = 529)**	***p* Value**
Inadequacies, mean (SD)	2.9 ± 1.0	2.5 ± 1.1	2.1 ± 1.0	1.7 ± 0.8	<0.001 [1]
Participants, *n* (%)	169 (38.2)	145 (23.8)	81 (11.0)	23 (2.7)	<0.001 [2]
	MEN: >70 years				
	Q1 (*n* = 124)	**Q2 (*n* = 136)**	**Q3 (*n* = 111)**	**Q1 (*n* = 48)**	***p* Value**
Inadequacies, mean (SD)	2.9 ± 1.1	2.6 ± 1.2	2.0 ± 1.0	1.6 ± 0.9	<0.001 [1]
Participants, n (%)	51 (44.0)	37 (33.9)	11 (10.9)	5 (5.5)	<0.001 [2]
	WOMEN: >70 years				
	Q1 (*n* = 138)	**Q2 (*n* = 137)**	**Q1 (*n* = 177)**	**Q1 (*n* = 103)**	***p* Value**
Inadequacies, mean (SD)	3.0 ± 1.1	2.5 ± 1.1	2.0 ± 0.9	1.7 ± 0.8	<0.001 [1]
Participants, n (%)	38 (42.7)	30 (24.6)	14 (9.8)	6 (3.0)	<0.001 [2]

[1] *p* value: Pearson's Chi-Square test was used to estimate differences among prevalence of inadequate nutrient intake according to quartiles of DDS for sex strata. [2] *p* value: ANOVA test was performed to estimate differences among mean of inadequate nutrient intakes according to sex, for each DDS quartile. Abbreviations: DDS, dietary diversity score; DRI, dietary reference intake; Q, quartile; SD, standard deviation.

3.5. Multivariable Logistic Regression Model for Inadequate Intake of Four or More out Eight Micronutrients According to Food Group's Diversity Intake and Total DDS Quartiles

The risk of inadequate intake of four or more nutrients increased in the lower DDS quartiles, regardless of the model we chose to adjust by (Table 5). The adjusted odds ratio (OR) of inadequate intake was 28.56 (95% CI 20.80–39.21) for Q1 compared to Q4. We analyzed the prevalence of inadequate intake according to the category of DD for each one of the included food groups and found the same trend for all of them except for the cereal food group. The groups showing the strongest association were vegetables and fruit. These results were comparable if the EFSA criteria were used to define inadequate intake (Table S5.). The adjustment by age as a quantitative variable did not change the results (data not shown).

Table 5. Multivariable logistic regression models for inadequate intake of four or more out eight micronutrients according to food group's diversity intake and total DDS quartiles in the PREDIMED-Plus study participants. Odds ratios (95% Confidence intervals).

	Q1 (*n* = 1647)	**Q2 (*n* = 1647)**	**Q3 (*n* = 1647)**	**Q4 (*n* = 1646)**
	Total DDS			
Model 1	27.42 (20.13−37.34)	10.00 (7.30−13.72)	4.37 (3.14−6.09)	1 (Ref.)
Model 2	28.56 (20.80−39.21)	9.97 (7.25−13.70)	4.33 (3.11−6.04)	1 (Ref.)
	C1 (*n* = 550)	**C2 (*n* = 1315)**	**C3 (*n* = 2482)**	**C4 (*n* = 2240)**
	Vegetable Group			
Model 1	19.82 (15.19−25.85)	7.28 (5.85−9.10)	2.74 (2.22−3.38)	1 (Ref.)
Model 2	14.03 (10.55−18.65)	6.21 (4.92−7.83)	2.52 (2.02−3.14)	1 (Ref.)

Table 5. *Cont.*

	C1 (*n* = 845)	C2 (*n* = 4497)	C3 (*n* = 779)	C4 (v466)
		Fruit Group		
Model 1	19.75 (11.87–32.86)	3.76 (2.30–6.15)	2.23 (1.29–3.84)	1 (Ref.)
Model 2	11.62 (6.81–19.81)	2.71 (1.62–4.53)	2.02 (1.15–3.57)	1 (Ref.)
	C1 (*n* = 350)	**C2 (*n* = 4767)**	**C3 (*n* = 1390)**	**C4 (*n* = 80)**
		Cereal Group		
Model 1	1.33 (0.54–3.31)	1.13 (0.47–2.71)	0.90 (0.37–2.19)	1 (Ref.)
Model 2	0.83 (0.32–2.19)	0.84 (0.33–2.14)	0.71 (0.28–1.82)	1 (Ref.)
	C1 (*n* = 26)	**C2 (*n* = 1254)**	**C3 (*n* = 2770)**	**C4 (*n* = 2537)**
		Proteins group		
Model 1	12.33 (4.10–37.19)	3.00 (2.48–3.62)	2.00 (1.69–2.37)	1 (Ref.)
Model 2	6.60 (1.96–22.24)	2.02 (1.64–2.48)	1.63 (1.36–1.96)	1 (Ref.)
	C1 (*n* = 686)	**C2 (*n* = 2447)**	**C3 (*n* = 2600)**	**C4 (*n* = 854)**
		Dairy Group		
Model 1	9.51 (6.88–13.14)	3.35 (2.50–4.49)	1.52 (1.12–2.06)	1 (Ref.)
Model 2	6.54 (4.64–9.22)	2.40 (1.76–3.27)	1.24 (0.90–1.71)	1 (Ref.)

Values are presented as OR and 95% CI for inadequate intake of micronutrients as categorical variable according to total DDS and food's group diversity. Model 1: Adjusted for energy intake. Model 2: Adjusted for energy intake, sex, age, smoking habits, physical activity, educational level, MedDiet adherence, BMI, alcohol intake, living alone and civil status. Abbreviations: BMI, body mass index; C, category; DDS, dietary diversity score; Q, quartile.

4. Discussion

The present study, conducted among older individuals with MetS, showed that the greater the DDS the lower the risk of inadequate nutrient intake. Characteristics associated with a lower DDS are male sex, any marital status other than married, smoking habit and alcohol intake. Special attention should be paid to patients with these characteristics as they are likely to have a lower DDS.

It is known that demographic characteristics influence diet quality. The influence of age and sex on DDS could be attributable to multiple factors, including psychological and mental health issues, poorer nutritional knowledge, lack of cooking skills and increased loneliness [21,37]. Our results are in line with other studies regarding the impact of sex on the variety of food choices: Women consume more varied diets than men, presumably due to the traditional role as housewives and culinary knowledge [38]. Regarding age, despite other authors noting that dietary variety declined with age [39], we have not found the same trend, probably because the percentage of participants with >70 years old was small in our sample. Living alone has also been traditionally considered as a risk factor for poor dietary habits, mainly due to lower diversity of food intake [40,41]. We found lower DDS for widowed and divorced people, but not for people living alone.

In addition, some studies have highlighted that lower levels of education and economic status predict lower dietary variety [42,43]. Our results are not consistent on this point. According to socioeconomic level, the economic factors could explain low consumption of foods such as fish, fruits and vegetables, which require more frequent purchase and consumption and can also be more expensive. The discrepancy might be attributed to the fact that these studies have been carried out in non-European countries with heterogeneous socioeconomic levels. In our study, most participants had similar economic capacity (they were mostly retired) with the economic differences among them being small. Furthermore, the distribution of our population reflects the social and demographic characteristics of the Spanish population born in the 1940s–1960s. In that context, women had limited opportunity to pursue high levels of formal education. As the percentage of women is greater in the top quartile of DDS, this could be an attributable factor that explains that subjects with a higher DDS have a lower educational level.

In literature, smoking status and alcohol intake are the most important lifestyles variables related to food choices among older adults. In our study, non-smokers and drinkers of low quantities of alcohol showed higher DDS. Several studies have reported that smoking and drinking status are directly associated with less variety of food choices and poor nutrient intakes, consistent with our results [44,45]. However these findings have not been supported by a study carried out in middle-aged adults in Japan, probably because of socio-cultural differences and small sample size [46].

Dietary guidelines worldwide have promulgated the benefits of a variety of dietary intake, mainly because it is easier to provide the necessary amount of nutrients with a highly diverse diet. This could be especially important for obesity and chronic disease management [47,48]. In this regard, monotonous diets usually imply unhealthy eating habits, as well as the worsening in the progression of certain diseases, for example CVD [49]. In spite of this, some observational studies have related the diversity of food intake to higher rates of obesity and poor nutritional adequacy in adults [13,16]. However, in the case-control study of Karimbeiki et al. [16], cases were chosen from participants attending an obesity treatment group and dietary intake referred to the previous year, hence it is difficult to know whether it was cause or consequence. The study of Jayawardena et al. [13] estimate a DDS from a 24-h food record and not from a FFQ, and their results are not adjusted for total energy intake. Thus, their findings are not comparable to our results.

A recent non-systematic review concluded that "the scientific evidence to date does not support benefits of greater dietary diversity for optimal diet quality or healthy weight" [50] pointing out a need for standardized, reliable measures defining what diet diversity is. In the current study, high DDS level (Q4) was directly associated with adequate nutrient intake (≥4 nutrients out of 8) even after adjustment for confounders such as sociodemographic and lifestyle variables. This association corroborates findings reported by other authors [17,51,52], emphasizing the need to increase diet variety, specifically in older adult populations, in order to achieve adequate nutrient intakes in these vulnerable groups. A variety of recommended foods, such as vegetables, fruit, cereals and dairy products, decreases the risk of inadequate nutrient intake, mainly because these foods group are rich in vitamins and minerals and other healthy nutrients such as dietary fiber [53].

Based on results obtained from the adjusted binary logistic regression analyses, the higher DDS of the majority of the food groups analyzed was inversely associated with the risk of inadequate intake of nutrients (≥4 nutrients), except for cereals. Probably because the cereal group included not only whole grains, but also potatoes and refined grains. These findings are consistent with previous studies reporting a low probability of inadequate nutrient intakes in consumers of a high variety of foods groups, including vegetables and fruit [54], dairy products and protein-rich foods [51,55,56]. The notion is that for people who eat less variety of the healthy food groups, the intake of several nutrients might be endangered. For example, although vegetables provide a considerable amount of dietary fiber and water, green vegetables provide vitamins B_9, while yellow ones are rich in vitamin A and carotenes. Another example of variety within the same group is the protein group, which includes eggs, white meat, legumes, fish and nuts. This group is an excellent source of high-quality protein, minerals and vitamins. In particular, white meat is high in B-vitamins, while oily fish is rich in polyunsaturated fat and eggs provide vitamins D and E and minerals such as zinc, iron and iodine [27,28].

Our study has some limitations. First, the study sample is not representative of the general population. Due to the trial inclusion and exclusion criteria, only older adults with MetS were included. Second, we did not have data about income status; however, we recorded the education level and employment status, which are both reasonable "proxy" indicators of socioeconomic status. Third, the cross-sectional design of the study does not allow for inferring causality. Irrespective of the direction of the associations, the variables included in the analysis have a high potential to improve the nutrient intake in older populations and allow the detection of groups of individuals more prone to nutrient deficiencies (those with lower DDS). Fourth, we used a FFQ to measure dietary intakes. Despite that the FFQ used has been validated in an adult Spanish population and has a good reproducibility and validity [26], it might not be the ideal tool to measure micronutrient intake [57]. For this reason, we considered that there was an inadequacy only when the intake did not reach 2/3 of the DRIs, correcting the possible bias introduced by the FFQ and assuming in any case that the inadequate micronutrient intake would be higher than the estimated figures. Fifth, it is important to consider that, besides pharmacological treatments, chronic diseases entail changes in dietary habits and nutrient metabolism, which have not been assessed. Last, we have estimated a DDS following the methodology of Kant et al. [29]. However, we excluded non-recommended foods such as sweets, snacks, juices and sweet beverages and processed foods because these products are high-energy density foods, rich in sodium, sugar and saturated fat, and also low-nutrient density foods, thus we considered that the intake of these food groups could not increase dietary diversity [58]. A culinary fat group was also not taken into account because Spanish individuals consume olive oil almost exclusively [59].

Some strengths of our study are its large sample size (n = 6587) and the considerable amount of baseline information collected in a large ongoing primary prevention trial, using a standardized protocol that reduces information bias regarding reported food intakes, sociodemographic characteristics and lifestyles. The individual analysis of each food group's diversity can help to determine which aspects may maximize diet quality. The follow-up of this cohort will allow for the identification of any association between dietary diversity and clinical, metabolic and cardiovascular outcomes. Our results focus on the promotion of a healthy varied diet, specifically promoting the intake of a variety of vegetables and fruits among population groups with lower DDS such as men, smokers or widow(er)s people.

5. Conclusions

According to our findings, older Spanish adults with MetS had a high risk of inadequate nutrient intake. As DDS decreased, risk of inadequate nutrients intake increased. The impact of nutrient intake adequacy on the prevention of chronic non-communicable diseases, mainly among population groups with lower DDS such as men, older or widow people is very likely to play a crucial role from a public health perspective.

Supplementary Materials: The following are available online at http://www.mdpi.com/2072-6643/11/5/958/s1. Table S1: Percentage of participants of PREDIMED-Plus study with nutrient intake below 2/3 of DRIs according to DDS, Table S2: Percentage of participants in the PREDIMED-Plus study with nutrient intake below 2/3 of DRIs according to DDS, Table S3: Participants of PREDIMED-Plus study with nutrient intake below AR/AI proposed by EFSA according to DDS, Table S4: Number of inadequacies and distribution of participants with ≥4 nutrients below EFSA criteria according to DDS stratified by sex, Table S5: Multivariable logistic regression models for inadequate intake of 4 or more out 8 micronutrients according to EFSA AR/AI by food group's diversity intake and total DDS quartiles in the PREDIMED-Plus study participants. Odds ratios (95% Confidence intervals).

Author Contributions: N.C.-I., A.G., M.A.M.-G., J.S.-S., D.C., M.D.Z., J.V., F.A., J.W., J.A.M., L.S.-M., R.E., F.T., J.L., X.P., J.A.T., A.G.-R., M.D.-R., P.M., L.D., V.M., J.V., C.V., E.R., M.F. and M.R.-C. collected all the data from the PREDIMED-Plus trial. N.C.-I., A.G. and A.B.-C. designed the study; performed the analysis; and wrote the first draft of the manuscript. All authors contributed to the editing of the manuscript. All authors have read and approved the final version of the manuscript.

Funding: The PREDIMED-Plus trial was supported by the official funding agency for biomedical research of the Spanish government, ISCIII through the Fondo de Investigación para la Salud (FIS), which is co-funded by the European Regional Development Fund (three coordinated FIS projects led by J.S.-S. and J.V., 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, 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), the Especial Action Project entitled: Implementación y evaluación de una intervención intensiva sobre la actividad física Cohorte PREDIMED-Plus grant to J.S.-S., the European Research Council (Advanced Research Grant 2013-2018; 340918) grant to M.A.M.-G., the Recercaixa grant to J.S.-S. (2013ACUP00194), the grant from the Consejería de Salud de la Junta de Andalucía (PI0458/2013; PS0358/2016), the PROMETEO/2017/017 grant from the Generalitat Valenciana, the SEMERGEN grant and FEDER funds (CB06/03). None of the funding sources took part in the design, collection, analysis or interpretation of the

data, or in the decision to submit the manuscript for publication. The corresponding author had full access to all the data in the study and had final responsibility to submit for publication.

Acknowledgments: The first author would like to acknowledge support by the Ministry of Education of Spain (FPU14/03630). The authors especially thank the PREDIMED-Plus participants for their collaboration and the PREDIMED-Plus staff for their support and effort. The authors also wish to thank Ingrid de Ruiter, MBChB, PhD, for English language support.

Conflicts of Interest: J.S.-S. reports serving on the board of and receiving grant support through his institution from International Nut and Dried Fruit Council; receiving consulting personal fees from Danone, Font Vella Lanjarón, Nuts for Life, and Eroski; and receiving grant support through his institution from Nut and Dried Fruit Foundation and Eroski. E.R., reports grants, non-financial support, and other fees from California Walnut Commission and Alexion; personal fees and non-financial support from Merck, Sharp & Dohme; personal fees, non-financial support and other fees from Aegerion, and Ferrer International; grants and personal fees from Sanofi Aventis; grants from Amgen and Pfizer and; personal fees from Akcea, outside of the submitted work. X.P., reports serving on the board of and receiving consulting personal fees from Sanofi Aventis, Amgen, and Abbott laboratories; receiving lecture personal fees from Esteve, Lacer and Rubio laboratories. L.D. reports grants from Fundación Cerveza y Salud. All other authors declare no competing interests.

References

1. DeBoer, M.D.; Gurka, M.J.; Golden, S.H.; Musani, S.K.; Sims, M.; Vishnu, A.; Guo, Y.; Pearson, T.A. Independent associations between metabolic syndrome severity and future coronary heart disease by sex and race. *J. Am. Cardiol.* **2017**, *69*, 1204–1205. [CrossRef]
2. Micucci, C.; Valli, D.; Matacchione, G.; Catalano, A. Current perspectives between metabolic syndrome and cancer. *Oncotarget* **2016**, *7*, 38959–38972. [CrossRef]
3. Zhang, P.; Tian, B. Metabolic syndrome: An important risk factor for parkinson's disease. *Oxid. Med. Cell. Longev.* **2014**, *2014*, 729194. [CrossRef] [PubMed]
4. O'Neill, S.; O'Driscoll, L. Metabolic syndrome: A closer look at the growing epidemic and its associated pathologies. *Obes. Rev.* **2015**, *16*, 1–12. [CrossRef] [PubMed]
5. Guallar-Castillon, P.; Pérez, R.F.; García, E.L.; León-Muñoz, L.M.; Aguilera, M.T.; Graciani, A.; Gutiérrez-Fisac, J.L.; Banegas, J.R.; Rodríguez-Artalejo, F. Magnitude and management of metabolic syndrome in Spain in 2008–2010: The ENRICA Study. *Rev. Española Cardiol. (Engl. Ed.)* **2014**, *67*, 367–373. [CrossRef]
6. Boudreau, D.; Malone, D.; Raebel, M.; Fishman, P.; Nichols, G.; Feldstein, A.; Boscoe, A.; Ben-Joseph, R.; Magid, D.; Okamoto, L. Health care utilization and costs by metabolic syndrome risk factors. *Metab. Syndr. Relat. Disord.* **2009**, *7*, 305–314. [CrossRef] [PubMed]
7. De La Iglesia, R.; Loria-Kohen, V.; Zulet, M.A.; Martínez, J.A.; Reglero, G.; De Molina, A.R. Dietary strategies implicated in the prevention and treatment of metabolic syndrome. *Int. J. Mol. Sci.* **2016**, *17*, 1877. [CrossRef] [PubMed]
8. Calton, E.K.; James, A.P.; Pannu, P.K.; Soares, M.J. Certain dietary patterns are beneficial for the metabolic syndrome: Reviewing the evidence. *Nutr. Res.* **2014**, *34*, 559–568. [CrossRef] [PubMed]
9. Salas-Salvadó, J.; Guasch-Ferre, M.; Lee, C.-H.; Estruch, R.; Clish, C.B.; Ros, E. Protective effects of the mediterranean diet on type 2 diabetes and metabolic syndrome123. *J. Nutr.* **2016**, *146*, 920S–927S. [CrossRef] [PubMed]
10. Castro-Quezada, I.; Román-Viñas, B.; Serra-Majem, L. The mediterranean diet and nutritional adequacy: A review. *Nutrients* **2014**, *6*, 231–248. [CrossRef]
11. Martinez-Gonzalez, M.A.; Martín-Calvo, N. The major European dietary patterns and metabolic syndrome. *Rev. Endocr. Metab. Disord.* **2013**, *14*, 265–271. [CrossRef] [PubMed]
12. Aranceta Bartrina, J.; Arija Val, V.V.; Maíz Aldalur, E.; Martínez de Victoria Muñoz, E.; Ortega Anta, R.M.; Pérez-Rodrigo, C.; Quiles Izquierdo, J.; Rodríguez Martín, A.; Román Viñas, B.; Salvador Castell, G.; et al. Dietary guidelines for the Spanish population (SENC; diciembre 2016); the new graphic icon of healthy food. *Nutr. Hosp.* **2016**, *33*, 1–48. [CrossRef]
13. Jayawardena, R.; Byrne, N.M.; Soares, M.J.; Katulanda, P.; Yadav, B.; Hills, A.P. High dietary diversity is associated with obesity in Sri Lankan adults: An evaluation of three dietary scores. *BMC Public Health* **2013**, *13*, 314. [CrossRef]
14. Kennedy, E. Dietary diversity, diet quality, and body weight regulation. *Nutr. Rev.* **2004**, *62*, 78–81. [CrossRef]

15. Tian, X.; Xu, X.; Zhang, K.; Wang, H. Gender difference of metabolic syndrome and its association with dietary diversity at different ages. *Oncotarget* **2017**, *8*, 73568–73578. [CrossRef]
16. Karimbeiki, R.; Pourmasoumi, M.; Feizi, A.; Abbasi, B.; Hadi, A.; Rafie, N.; Safavi, S. Higher dietary diversity score is associated with obesity: A case–control study. *Public Health* **2018**, *157*, 127–134. [CrossRef] [PubMed]
17. Murphy, S.P.; Wilkens, L.R.; Basiotis, P.P.; Foote, J.A.; Carlson, A. Dietary variety increases the probability of nutrient adequacy among adults. *J. Nutr.* **2004**, *134*, 1779–1785.
18. Azadbakht, L.; Mirmiran, P.; Esmaillzadeh, A.; Azizi, F. Dietary diversity score and cardiovascular risk factors in Tehranian adults. *Public Health Nutr.* **2006**, *9*, 728–736. [CrossRef]
19. Gholizadeh, F.; Moludi, J.; Yagin, N.L.; Alizadeh, M.; Nachvak, S.M.; Abdollahzad, H.; Mirzaei, K.; Mostafazadeh, M. The relation of Dietary diversity score and food insecurity to metabolic syndrome features and glucose level among pre-diabetes subjects. *Prim. Care Diabetes* **2018**, *12*, 338–344. [CrossRef] [PubMed]
20. Barba, L.R.; Cavelaars, A.; Veer, P.V.; Viñas, B.R.; Ngo, J.; Gurinovic, M.; Novakovic, R.; De Groot, L.C.; Matthys, C.; Majem, L.S. Projected Prevalence of Inadequate Nutrient Intakes in Europe. *Ann. Nutr. Metab.* **2011**, *59*, 84–95.
21. Dean, M.; Raats, M.M.; Grunert, K.G.; Lumbers, M. The Food in Later Life Team Factors influencing eating a varied diet in old age. *Public Health Nutr.* **2009**, *12*, 2421. [CrossRef]
22. Serra-Majem, L.; Bes-Rastrollo, M.; Román-Viñas, B.; Pfrimer, K.; Sánchez-Villegas, A.; Martinez-Gonzalez, M.A. Dietary patterns and nutritional adequacy in a Mediterranean country. *Br. J. Nutr.* **2009**, *101*, S21–S28. [CrossRef]
23. Buil-Cosiales, P.; Vioque, J.; Romaguera, D.; Martínez, J.A.; López-Miranda, J.; Bueno-Cavanillas, A.; A Tur, J.; Serra-Majem, L.; Martín, V.; Lapetra, J.; et al. Cohort Profile: Design and methods of the PREDIMED-Plus randomized trial. *Int. J. Epidemiol.* **2018**, *48*, 387–388.
24. Alberti, K.G.M.M.; Eckel, R.H.; Grundy, S.M.; Zimmet, P.Z.; Cleeman, J.I.; Donato, K.A.; Fruchart, J.C.; James, W.P.T.; Loria, C.M.; Smith, S.C. 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 atherosclerosis society; and international association for the study of obesity. *Circulation* **2009**, *16*, 1640–1645. [CrossRef]
25. Willet, W. *Nutritional Epidemiology*, 3rd ed.; Oxford University Press: New York, NY, USA, 2013.
26. Martin-Moreno, J.M.; Boyle, P.; Gorgojo, L.; Maisonneuve, P.; Fernandez-Rodriguez, J.C.; Salvini, S.; Willett, W.C. Development and validation of a food frequency questionnaire in Spain. *Int. J. Epidemiol.* **1993**, *22*, 512–519. [CrossRef]
27. Moreiras, O.C.A.; Cabrera, L.; Cuadrado, C. *Tablas de Composición de alimentos. (Spanish Food Composition Tables)*, 7th ed.; Pirámide: Madrid, Spain, 2003.
28. Mataix-Verdú, J.; García diz, L.; Mañas Almendros, M.; Emilio, M.d.V.; Llopis González, J. *Tablas de Composición de Alimentos*, 4th ed.; Universidad de Granada: Granada, Spain, 2009.
29. Kant, A.K.; Schatzkin, A.; Harris, T.B.; Ziegler, R.G.; Block, G. Dietary diversity and subsequent mortality in the First National Health and Nutrition Examination Survey Epidemiologic Follow-up Study. *Am. J. Clin. Nutr.* **1993**, *57*, 434–440. [CrossRef]
30. Farhangi, M.A.; Jahangiry, L. Dietary diversity score is associated with cardiovascular risk factors and serum adiponectin concentrations in patients with metabolic syndrome. *BMC Cardiovasc. Disord.* **2018**, *18*, 68. [CrossRef]
31. Schroder, H.; Fíto, M.; Estruch, R.; Martínez-González, M.A.; Corella, D.; Salas-Salvadó, J.; Lamuela-Raventos, R.M.; Ros, E.; Salaverría, I.; Fiol, M.; et al. A Short Screener Is Valid for Assessing Mediterranean Diet Adherence among Older Spanish Men and Women. *J. Nutr.* **2011**, *141*, 1140–1145. [CrossRef]
32. IOM Nutrient Recommendations: Dietary Reference Intakes. Available online: https://ods.od.nih.gov/Health_Information/Dietary_Reference_Intakes.aspx (accessed on 4 May 2018).
33. Aranceta, J.; Serra-Majem, L.; Pérez-Rodrigo, C.; Llopis, J.; Mataix, J.; Ribas, L.; Tojo, R.; A Tur, J. Vitamins in Spanish food patterns: The eVe Study. *Public Health Nutr.* **2001**, *4*, 1317–1323. [CrossRef]
34. EFSA Dietary Reference Values and Dietary Guidelines. Available online: https://www.efsa.europa.eu/en/topics/topic/dietary-reference-values (accessed on 1 October 2018).
35. Elosua, R.; García, M.; Aguilar, A.; Molina, L.; Covas, M.-I.; Marrugat, J. Validation of the Minnesota Leisure Time Physical Activity Questionnaire in Spanish Women. *Med. Sci. Sports Exerc.* **2000**, *32*, 1431–1437. [CrossRef]

36. Elosua, R.; Marrugat, J.; Molina, L.; Pons, S.; Pujol, E. Validation of the Minnesota leisure time physical activity questionnaire in Spanish men. *Am. J. Epidemiol.* **1994**, *139*, 1197–1209. [CrossRef] [PubMed]
37. Larrieu, S.; Letenneur, L.; Berr, C.; Dartigues, J.F.; Ritchie, K.; Alperovitch, A.; Tavernier, B.; Barberger-Gateau, P. Sociodemographic differences in dietary habits in a population-based sample of elderly subjects: The 3C study. *J. Nutr. Health Aging* **2004**, *8*, 497–502.
38. Conklin, A.I.; Forouhi, N.G.; Surtees, P.; Wareham, N.J.; Monsivais, P. Gender and the double burden of economic and social disadvantages on healthy eating: Cross-sectional study of older adults in the EPIC-Norfolk cohort. *BMC Public Health* **2015**, *15*, 692. [CrossRef]
39. Westenhoefer, J. Age and gender dependent profile of food choice. *Nutr. Oppor. Asia* **2005**, *57*, 44–51.
40. Hanna, K.L.; Collins, P.F. Relationship between living alone and food and nutrient intake. *Nutr. Rev.* **2015**, *73*, 594–611. [CrossRef] [PubMed]
41. Vinther, J.L.; Conklin, A.I.; Wareham, N.J.; Monsivais, P. Marital transitions and associated changes in fruit and vegetable intake: Findings from the population-based prospective EPIC-Norfolk cohort; UK. *Soc. Sci. Med.* **2016**, *157*, 120–126. [CrossRef]
42. Ochieng, J.; Afari-Sefa, V.; Lukumay, P.J.; Dubois, T. Determinants of dietary diversity and the potential role of men in improving household nutrition in Tanzania. *PLoS ONE* **2017**, *12*, e0189022. [CrossRef]
43. Fukuda, Y.; Ishikawa, M.; Yokoyama, T.; Hayashi, T.; Nakaya, T.; Takemi, Y.; Kusama, K.; Yoshiike, N.; Nozue, M.; Yoshiba, K.; et al. Physical and social determinants of dietary variety among older adults living alone in Japan. *Geriatr. Gerontol. Int.* **2017**, *17*, 2232–2238. [CrossRef]
44. Hampl, J.S.; Ma, J.; Betts, N.M. Clustering of Lifestyle Behaviors: The Relationship between Cigarette Smoking, Alcohol Consumption, and Dietary Intake. *Am. J. Health Promot.* **2000**, *15*, 107–117. [CrossRef] [PubMed]
45. De Freitas, T.I.; Previdelli, Á.N.; Ferreira, M.P.N.; Marques, K.M.; Goulart, R.M.M.; de Aquino, R.C. Factors associated with diet quality of older adults. *Rev. Nutr.* **2017**, *30*, 297–306. [CrossRef]
46. Kobayashi, M.; Iwasaki, M.; Tsugane, S. Relationship between the variety of food consumed and sufficient nutrition in middle—Aged Japanese. *Nutr. Food Sci.* **2013**, *43*, 344–355. [CrossRef]
47. Vadiveloo, M.K.; Parekh, N. Dietary variety: An overlooked strategy for obesity and chronic disease control. *Am. J. Prev. Med.* **2015**, *49*, 974–979. [CrossRef] [PubMed]
48. Adebukola, C.O.; Ugwunna, U.M.; Ekerette, N.N. Dietary diversity and nutrient intake adequacy among women in Iwo Local Government Area; Osun State Nigeria. *Afr. J. Food Agr. Nutr. Dev.* **2017**, *17*, 12641–12656. [CrossRef]
49. Wirt, A.; E Collins, C. Diet quality—What is it and does it matter? *Public Health Nutr.* **2009**, *12*, 2473. [CrossRef]
50. De Oliveira Otto, M.C.; Anderson, C.A.M.; Dearborn, J.L.; Ferranti, E.P.; Mozaffarian, D.; Rao, G.; Wylie-Rosett, J.; Lichtenstein, A.H.; On behalf of the American Heart Association Behavioral Change for Improving Health Factors Committee of the Council on Lifestyle and Cardiometabolic Health and Council on Epidemiology and Prevention; Council on Cardiovascular and Stroke Nursing; et al. Dietary diversity: Implications for obesity prevention in adult populations: A science advisory from the American Heart Association. *Circulation* **2018**, *138*, e160–e168. [CrossRef] [PubMed]
51. Tavakoli, S.; Dorosty-Motlagh, A.R.; Hoshiar-Rad, A.; Eshraghian, M.R.; Sotoudeh, G.; Azadbakht, L.; Karimi, M.; Jalali-Farahani, S. Is dietary diversity a proxy measurement of nutrient adequacy in Iranian elderly women? *Appetite* **2016**, *105*, 468–476. [CrossRef] [PubMed]
52. Marshall, T.A.; Stumbo, P.J.; Warren, J.J.; Xie, X.J. Inadequate nutrient intakes are common and are associated with low diet variety in rural; community-dwelling elderly. *J. Nutr.* **2001**, *131*, 2192–2196. [CrossRef] [PubMed]
53. Masset, G.; Scarborough, P.; Rayner, M.; Mishra, G.; Brunner, E.J. Can nutrient profiling help to identify foods which diet variety should be encouraged? Results from the Whitehall II cohort. *Br. J. Nutr.* **2015**, *113*, 1800–1809. [CrossRef] [PubMed]
54. Meng, L.; Wang, Y.; Li, T.; Loo-Bouwman, C.A.V.; Zhang, Y.; Man-Yau Szeto, I. Dietary diversity and food variety in chinese children aged 3–17 years: Are they negatively associated with dietary micronutrient inadequacy? *Nutrients* **2018**, *10*, 1674. [CrossRef]
55. De Gavelle, E.; Huneau, J.F.; Mariotti, F. Patterns of protein food intake are associated with nutrient adequacy in the general french adult population. *Nutrients* **2018**, *10*, 226. [CrossRef]

56. Azadbakht, L.; Mirmiran, P.; Azizi, F. Variety scores of food groups contribute to the specific nutrient adequacy in Tehranian men. *Eur. J. Clin. Nutr.* **2005**, *59*, 1233–1240. [CrossRef]
57. Ortiz-Andrellucchi, A.; Sánchez-Villegas, A.; Doreste-Alonso, J.; De Vries, J.; De Groot, L.; Serra-Majem, L. Dietary assessment methods for micronutrient intake in elderly people: A systematic review. *Br. J. Nutr.* **2009**, *102*, S118. [CrossRef] [PubMed]
58. Kant, A.K. Consumption of energy-dense, nutrient-poor foods by adult Americans: Nutritional and health implications. The third National Health and Nutrition Examination Survey, 1988–1994. *Am. J. Clin. Nutr.* **2000**, *72*, 929–936. [CrossRef] [PubMed]
59. Ruiz, E.; Ávila, J.M.; Valero, T.; Del Pozo, S.; Rodriguez, P.; Aranceta-Bartrina, J.; Gil, Á.; González-Gross, M.; Ortega, R.M.; Serra-Majem, L.; et al. Macronutrient Distribution and Dietary Sources in the Spanish Population: Findings from the ANIBES Study. *Nutrients* **2016**, *8*, 177. [CrossRef] [PubMed]

Table S1. Percentage of participants of PREDIMED-Plus study with nutrient intake below 2/3 of DRIs according to DDS.

Nutrient	Group	DRI[a]	Q1 (n=1647)	Q2 (n=1647)	Q3 (n=1647)	Q4 (n=1646)	P value[1]
Dietary fiber	Male 55-70	30g /d	49.6	25.9	12.0	4.7	<0.001
	Male >70	30g /d	38.8	32.1	12.9	5.5	<0.001
	Female 60-70	21 g/d	13.4	4.6	1.2	0.4	<0.001
	Female >70	21 g/d	18.0	5.7	0.7	0	<0.001
P value[2]			<0.001	<0.001	<0.001	<0.001	
Vitamin A	Male 55-70	900 µg/d	33.8	15.7	12.0	3.5	<0.001
	Male >70	900 µg/d	31.9	20.2	9.9	7.7	<0.001
	Female 60-70	700 µg/d	14.9	8.4	3.4	0.7	<0.001
	Female >70	700 µg/d	22.5	12.3	6.3	0	<0.001
P value[2]			<0.001	<0.001	<0.001	<0.001	
Vitamin B_9	Male 55-70	400 µg/d	40.6	15.7	8.8	3.0	<0.001
	Male >70	400 µg/d	33.6	25.7	6.9	5.5	<0.001
	Female 60-70	400 µg/d	39.4	24.8	13.5	3.1	<0.001
	Female >70	400 µg/d	46.1	27.9	12.6	5.0	<0.001
P value[2]			0.31	<0.001	0.020	0.33	
Vitamin D	Male 60-70	15 µg/d	88.5	84.0	80.1	72.5	<0.001
	Male >70	20 µg/d	98.3	99.1	97.0	95.6	0.401
	Female 60-70	15 µg/d	89.1	84.2	82.3	76.2	<0.001
	Female >70	20 µg/d	96.6	98.4	98.6	97.0	0.66
P value[2]			0.001	<0.001	<0.001	<0.001	
Vitamin E	Male 55-70	15 mg/d	61.7	46.6	42.5	29.3	<0.001
	Male >70	15 mg/d	62.1	56.0	43.6	30.8	<0.001
	Female 60-70	15 mg/d	67.2	57.8	53.1	35.3	<0.001
	Female >70	15 mg/d	79.8	69.7	59.4	50.3	<0.001
P value[2]			0.003	<0.001	<0.001	<0.001	
Calcium	Male 55-70	1000 mg/d	24.4	9.4	4.8	0.1	<0.001
	Male >70	1200 mg/d	48.3	26.6	18.8	9.9	<0.001
	Female 60-70	1200 mg/d	49.1	35.6	20.7	7.1	<0.001
	Female >70	1200 mg/d	41.6	36.1	18.9	10.6	<0.001
P value[2]			<0.001	<0.001	<0.001	<0.001	

Magnesium	Male 55-70	420 mg/d	14.6	4.1	1.8	0.4	<0.001
	Male >70	420 mg/d	15.5	6.4	2.0	1.1	<0.001
	Female 60-70	320 mg/d	3.2	1.2	0.3	0	<0.001
	Female >70	320 mg/d	3.4	0.8	0	0	0.011
P value[2]			<0.001	0.001	0.012	0.06	
Iodine	Male 55-70	150 µg/d	17.7	9.4	7.6	3.3	<0.001
	Male >70	150 µg/d	24.1	11.0	9.9	3.3	<0.001
	Female 60-70	150 µg/d	22.6	14.5	8.3	4.5	<0.001
	Female >70	150 µg/d	13.5	9.8	6.3	3.0	0.007
P value[2]			0.037	0.029	0.73	0.63	

DRI[a]: Dietary Reference Intake. Pearson´s Chi-Square test was used to estimate differences among prevalence of inadequate nutrient intakes according to quartiles of DDS for each age and sex strata (*p value[1]*) and also to estimate differences among prevalence of inadequate nutrient intakes according to age and sex, for each DDS quartile (*p value[2]*).

Abbreviations: DDS, dietary diversity score; DRI, dietary reference intake.

Table S2. Percentage of participants in the PREDIMED-Plus study with nutrient intake below 2/3 of DRIs according to DDS

Nutrient	Group	DRI[a]	Q1 (n=1647)	Q2 (n=1647)	Q3 (n=1647)	Q4 (n=1646)	P value[1]
Vitamin B_1	Male 55-70	1.2 mg/d	1.3	0	0	0	<0.001
	Male >70	1.2 mg/d	2.6	0	0	0	0.049
	Female 60-70	1.1 mg/	2.3	0	0	0	<0.001
	Female >70	1.1 mg/d	2.3	0.82	0	0	<0.001
P value[2]			0.48	0.006	-	-	
Vitamin B_6	Male 60-70	1.7 mg/d	1.9	0	0	0	<0.001
	Male >70	1.7 mg/d	3.5	0	0	0	0.015
	Female 60-70	1.5 mg/d	2.3	0.2	0	0	<0.001
	Female >70	1.5 mg/d	3.4	0.8	0	0	0.011
P value[2]			0.61	0.11	-	-	
Vitamin B^{12}	Male 60-70	2.4 µg/d	0.2	0	0	0	0.26
	Male >70	2.4 µg/d	0	0	0	0	-
	Female 60-70	2.4 µg/d	0.2	0	0	0	0.18
	Female >70	2.4 µg/d	0	0.8	0	0	0.32
P value[2]			0.93	0.006	-	-	
Vitamin C	Male 60-70	90 mg/d	3.7	0	0	0	<0.001
	Male >70	90 mg/d	5.2	0	0	0	0.001
	Female 60-70	75 mg/d	1.8	0	0	0	<0.001
	Female >70	75 mg/d	1.1	0	0	0	0.16
P value[2]			0.09	-	-	-	
Phosphorus	Male 55-70	700 mg/d	0	0	0	0	-
	Male >70	700 mg/d	0	0	0	0	-
	Female 60-70	700 mg/d	0.2	0	0	0	0.18
	Female >70	700 mg/d	0	0	0	0	-
P value[2]			0.44	-	-	-	
Iron	Male 55-70	8 mg /d	0	0	0	0	-
	Male >70	8 mg /d	0	0	0	0	-
	Female 60-70	8 mg /d	0.2	0	0	0	0.18
	Female >70	8 mg /d	0	0	0	0	-
P value[2]			0.44	-	-	-	
Potassium	Male 55-70	4 g/d	0	0	0	0	-
	Male >70	4 g/d	0	0	0	0	-
	Female 60-70	4 g/d	0	0	0	0	-
	Female >70	4 g/d	0	0	0	0	-
P value[2]			-	-	-	-	
Selenium	Male 60-70	55 µg/d	0.2	0	0	0	0.26
	Male >70	55 µg/d	0	0	0	0	-
	Female 60-70	55 µg/d	1.1	0.8	0	0.4	<0.001
	Female >70	55 µg/d	1.1	0	0	0	0.34
P value[2]			0.08	0.006	-	-	
Zinc	Male 55-70	11 mg/d	3.3	0.7	0.8	0.2	<0.001
	Male >70	11 mg/d	2.6	0.9	0	0	0.17
	Female 60-70	8 mg/d	1.1	0	0	0	<0.001
	Female >70	8 mg/d	2.3	0	0	0	0.015
P value[2]			0.13	0.13	0.06	0.53	

DRI[a]: Dietary Reference Intake. Pearson´s Chi-Square test was used to estimate differences among prevalence of inadequate nutrient intakes according to quartiles of DDS for each age and sex strata (*p value*[1]) and also to estimate differences among prevalence of inadequate nutrient intakes according to age and sex, for each DDS quartile (*p value*[2]). Abbreviations: DDS, dietary diversity score; DRI, dietary reference intake; Q, quartile.

Table S3. Participants of PREDIMED-Plus study with nutrient intake below AR/AI proposed by EFSA according to DDS

Nutrient	Group	AR/AI[a]	Q1 (n=1647)	Q2 (n=1647)	Q3 (n=1647)	Q4 (n=1646)	P value[1]
Dietary fiber	Male	25g /d	74.8	58.5	43.4	24.7	<0.001
	Female	25 g/d	72.1	59.2	46.5	25.5	<0.001
P value[2]			0.25	0.77	0.20	0.70	
Vitamin A	Male	570 µg/d	30.6	12.9	9.6	3.0	<0.001
	Female	490 µg/d	19.8	11.1	5.0	0.7	<0.001
P value[2]			<0.001	0.27	<0.001	<0.001	
Vitamin B_1	Male	0.072 mg/d	0	0	0	0	-
	Female	0.072 mg/d	0	0	0	0	-
P value[2]			-	-	-	-	
Vitamin B_6	Male	1.5 mg/d	13.9	3.0	1.8	0.7	<0.001
	Female	1.3 mg/d	8.9	2.3	0.2	0	<0.001
P value[2]			0.004	0.44	0.001	0.008	
Vitamin B_9	Male	250 µg/d	31.6	11.9	5.5	1.8	<0.001
	Female	250 µg/d	34.7	19.0	8.9	1.9	<0.001
P value[2]			0.22	<0.001	0.007	0.91	
Vitamin B^{12}	Male	4 µg/d	4.8	2.2	2.0	0.3	<0.001
	Female	4 µg/d	9.0	3.7	3.0	0.7	<0.001
P value[2]			0.001	0.07	0.19	0.37	
Vitamin C	Male	90 mg/d	19.0	3.8	0.7	0.2	<0.001
	Female	80 mg/d	11.1	1.4	0.2	0	<0.001
P value[2]			<0.001	0.002	0.19	0.19	
Vitamin D	Male	15 µg/d	99.5	98.8	98.3	97.3	0.003
	Female	15 µg/d	98.7	99.0	99.3	98.3	0.19
P value[2]			0.09	0.64	0.06	0.19	
Vitamin E	Male	13 mg/d	85.4	78.7	74.2	65.0	<0.001
	Female	11 mg/d	79.1	70.6	68.2	52.9	<0.001
P value[2]			0.001	<0.001	0.008	<0.001	
Calcium	Male	950 mg/d	64.6	45.7	36.9	19.0	<0.001
	Female	950 mg/d	65.9	55.5	43.0	25.1	<0.001
P value[2]			0.60	<0.001	0.012	0.005	
Phosphorus	Male	550 mg/d	0.1	0	0	0	0.56
	Female	550 mg/d	0.2	0	0	0	0.17
P value[2]			0.591	-	-	-	
Magnesium	Male	350 mg/d	43.2	27.4	16.5	6.5	<0.001
	Female	300 mg/d	29.2	17.1	10.0	1.9	<0.001
P value[2]			<0.001	<0.001	<0.001	<0.001	

AR/AI[a]: Average Requirements/Adequate intake according to EFSA criteria. DDS: dietary diversity score. EFSA: European Food Safety Authority. Q: Quartile.

Pearson´s Chi-Square test was used to estimate differences among prevalence of inadequate nutrient intakes according to quartiles of DDS for each age and sex strata (*p value[1]*) and also to estimate differences among prevalence of inadequate nutrient intakes according to age and sex, for each DDS quartile (*p value[2]*).

Table S3. (Continued). Participants of PREDIMED-Plus study with nutrient intake below AR/AI proposed by EFSA according to DDS

Nutrient	Group	DRI[a]	Q1 (n=1647)	Q2 (n=1647)	Q3 (n=1647)	Q4 (n=1646)	P value[1]
Iron	Male	6 mg /d	0.3	0	0	0	0.11
	Female	6 mg /d	0.6	0	0	0	0.002
P value[2]			0.35	-	-	-	
Iodine	Male	150 µg/d	34.2	19.7	16.8	10.2	<0.001
	Female	150 µg/d	33.2	23.3	15.2	8.4	<0.001
P value[2]			0.66	0.08	0.38	0.23	
Potassium	Male	3.5 g/d	0	0	0	0	-
	Female	3.5 g/d	0	0	0	0	-
P value[2]			-	-	-	-	
Selenium	Male	70 µg/d	9.4	4.9	3.1	2.0	<0.001
	Female	70 µg/d	14.3	7.9	6.0	1.9	<0.001
P value[2]			0.003	0.012	0.005	0.90	
Zinc	Male	11 mg/d	31.3	22.4	19.4	10.8	<0.001
	Female	8.9 mg/d	20.0	11.8	7.3	2.9	<0.001
P value[2]			<0.001	<0.001	<0.001	<0.001	

AR/AI[a]: Average Requirements/Adequate intake according to EFSA criteria. Pearson´s Chi-Square test was used to estimate differences among prevalence of inadequate nutrient intakes according to quartiles of DDS for each age and sex strata (*p value*[1]) and also to estimate differences among prevalence of inadequate nutrient intakes according to age and sex, for each DDS quartile (*p value*[2]).

Table S4. Number of inadequacies and distribution of participants with ≥4 nutrients below EFSA criteria according to DDS stratified by sex

	MEN				
	Q1 (n=787)	**Q2 (n=763)**	**Q3 (n=973)**	**Q4 (n=489)**	**P value**
Inadequacies, mean ±SD	3.5±0.8	3.1±1.0	2.8±1.1	2.2±1.0	<0.001[1]
Participants, n (%)	778 (69.7)	432 (47.2)	253 (32.9)	81 (13.5)	<0.001[2]
	WOMEN				
	Q1 (n=630)	**Q2 (n=610)**	**Q3 (n=884)**	**Q4 (n=529)**	**P value**
Inadequacies, mean (SD)	3.4±0.8	3.1±1.0	2.7±1.1	2.1±1.1	<0.001[1]
Participants, n (%)	335 (63.1)	330 (45.1)	284 (32.4)	136 (13.0)	<0.001[2]

[1]P value: Pearson´s Chi-Square test was used to estimate differences among prevalence of inadequate nutrient intake according to quartiles of DDS for sex strata. [2]P value: ANOVA test was performed to estimate differences among mean of inadequate nutrient intakes according for each DDS quartile**.**

Abbreviations: AR/AI, Average Requirements/Adequate intake according to EFSA criteria; DDS, dietary diversity score; EFSA, European Food Safety Authority; Q, quartile.

Table S5. Multivariable logistic regression models for inadequate intake of 4 or more out 8 micronutrients according to EFSA AR/AI by food group's diversity intake and total DDS quartiles in the PREDIMED-Plus study participants. Odds ratios (95% Confidence intervals).

	Q1 (n=1647)	**Q2 (n=1647)**	**Q3 (n=1647)**	**Q4 (n=1646)**
Total DDS				
Model 1	13.73 (11.51-16.37)	5.67 (4.77-6.74)	3.19 (2.67-3.80)	1 (Ref.)
Model 2	14.48 (11.93-17.57)	5.50 (4.57-6.60)	3.17 (2.64-3.82)	1 (Ref.)
	C1 (n=550)	**C2 (n=1315)**	**C3 (n=2482)**	**C4 (n=2240)**
Vegetable food group				
Model 1	10.73 (8.41-13.71)	5.47 (4.62-6.48)	2.34 (2.03-2.70)	1 (Ref.)
Model 2	8.11 (6.13-10.73)	4.90 (4.01-5.93)	2.15 (1.83-2.53)	1 (Ref.)
	C1 (n=845)	**C2 (n=4497)**	**C3 (n=779)**	**C4 (n=466)**
Fruit food group				
Model 1	12.31 (8.89-17.01)	2.88 (2.17-3.84)	1.68 (1.21-2.33)	1 (Ref.)
Model 2	6.66 (4.61-9.62)	2.05 (1.49-2.84)	1.45 (1.00-2.10)	1 (Ref.)
	C1 (n=350)	**C2 (n=4767)**	**C3 (n=1390)**	**C4 (n=80)**
Cereal food group				
Model 1	1.30 (0.68-2.52)	1.13 (0.61-2.07)	1.07 (0.57-1.98)	1 (Ref.)
Model 2	0.71 (0.34-1.49)	0.74 (0.37-1.47)	0.77 (0.38-1.55)	1 (Ref.)
	C1 (n=26)	**C2 (n=1254)**	**C3 (n=2770)**	**C4 (n=2537)**
Protein food group				
Model 1	7.19 (1.94-26.67)	3.00 (2.56-3.53)	1.89 (1.66-2.15)	1 (Ref.)
Model 2	3.91 (0.77-19.72)	1.93 (1.61-2.32)	1.48 (1.28-1.72)	1 (Ref.)
	C1 (n=686)	**C2 (n=2447)**	**C3 (n=2600)**	**C4 (n=854)**
Dairy food group				
Model 1	23.13 (17.18-31.13)	6.61 (5.23-8.36)	2.67 (2.11-3.38)	1 (Ref.)
Model 2	17.88 (12.84-24.90)	5.14 (3.96-6.67)	2.19 (1.69-2.85)	1 (Ref.)

Model 1: Adjusted for energy intake. Model 2: Adjusted for energy intake, sex, age, smoking habits, physical activity, educational level, MedDiet adherence, BMI, WC, alcohol intake, living alone and civil status.
Abbreviations: AR/AI, Average Requirements/Adequate intake according to EFSA criteria; C, category; DDS, dietary diversity score; EFSA, European Food Safety Authority; Q, quartile.

Artículo 4. Cano-Ibáñez N, Bueno-Cavanillas A, Martínez-González MA, Salas-Salvadó J, Corella D, Freixer G, et al. Effect of changes in adherence to Mediterranean diet on nutrient density after one-year of follow-up: Results from the PREDIMED-Plus Study. Ahead of print. 2019.

Finalmente, en el cuarto artículo titulado *"Effect of changes in adherence to Mediterranean Diet on nutrient density after one-year of follow-up: Results from the PREDIMED-Plus Study"* enviado a publicación, se partió del precepto de que la adherencia a la Dieta Mediterránea promulgada en un estudio de intervención nutricional como es el estudio PREDIMED-Plus, mejoraría la calidad dietética de todos los participantes, independientemente del grupo de aleatorización. Se estimó la densidad nutricional basal y al año de los participantes del estudio; y se tuvo en cuenta como variable independiente en los modelos de regresión lineal ejecutados los cambios en la adherencia a la Dieta Mediterránea. De los resultados obtenidos, se puede destacar que los participantes, independientemente del grupo de aleatorización, mostraron un incremento en la densidad nutricional de todos los nutrientes analizados (medido como % de cambio en la densidad nutricional), excepto para la cantidad total de hidratos de carbono, ácidos grasos saturados e ingesta calórica, que sufrieron un descenso conforme se incrementaba la adherencia a la Dieta Mediterránea. Los modelos de regresión lineal múltiple ajustados mostraron una asociación directa entre las mejoras en la adherencia a la Dieta Mediterránea y el incremento en la densidad nutricional después de un año de intervención en el estudio PREDIMED-Plus. Principalmente, puede destacarse que aquellos nutrientes que experimentaron mayores incrementos en su densidad nutricional (>20%) fueron: la fibra dietética, los ácidos grasos monoinsaturados, polinsaturados, vitaminas A, B_9, B_{12}, C, D, E, potasio, yodo y magnesio.

6.1.4. Effect of changes in adherence to Mediterranean diet on nutrient density after one-year of follow-up: Results from the PREDIMED-Plus Study

[Cano-Ibáñez N, Bueno-Cavanillas A, Martínez-González MA, Salas-Salvadó J, Corella D, Freixer G, et al. Effect of changes in adherence to Mediterranean diet on nutrient density after one-year of follow-up: results from the PREDIMED-Plus Study. Submitted. 2019].

[MANUSCRITO EN PROCESO DE REVISIÓN]

TITLE PAGE

Title: Effect of changes in adherence to Mediterranean diet on nutrient density after one-year of follow-up: results from the PREDIMED-Plus Study

Authors: Naomi Cano-Ibáñez[1,2,3*], Aurora Bueno-Cavanillas[1,2,3], Miguel Ángel Martínez-González[4,5,6,7], Jordi Salas Salvadó[7,8,9,10], Dolores Corella[7,11], Gal-la Freixer[12], Dora Romaguera[7,13], Jesús Vioque[2,14], Ángel M. Alonso-Gómez[7,15], Julia Wärnberg[7,16], J. Alfredo Martínez[7,17,18], Lluis Serra-Majem[7,19], Ramón Estruch[7,20], Francisco J. Tinahones[7,21], José Lapetra[7,22], Xavier Pintó[7,23], Josep A. Tur[7,13,24], Antonio García-Ríos[7,25], Laura García-Molina[1,2], Miguel Delgado-Rodríguez[2,26], Pilar Matía-Martín[27], Lidia Daimiel[18], Vicente Martín Sánchez[2,28], Josep Vidal[29,30], Clotilde Vázquez[7,31], Emili Ros[7,32], Javier Bartolomé-Resano[4,33], Antoni Palau-Galindo[7,8,9,34], Olga Portoles[7,11], Laura Torres[12], Miquel-Fiol[7,13], María Teresa Cano Sánchez[35], Carolina Sorto-Sánchez[7,15], Noelia Moreno-Morales[36], Itziar Abete[5,17], Jacqueline Álvarez-Pérez[7,19], Emilio Sacanella[7,20], María Rosa Bernal-López[7,37], José Manuel Santos-Lozano[7,22,38], Marta Fanlo-Maresma[23], Cristina Bouzas[7,13,24], Cristina Razquin[4,5,7], Nerea Becerra-Tomás[7,8,9], Carolina Ortega-Azorin[7,11], Regina LLimona[12], Marga Morey[7,13], Josefa Román-Maciá[35], Leire Goicolea-Güemez[7,15], Zenaida Vázquez-Ruiz[4,5,7], Laura Barrubés[7,8,9], Montse Fitó[7,12], Alfredo Gea[4,5,7].

Affiliations:

[1]Department of Preventive Medicine and Public Health, University of Granada, Granada, Spain.
[2]CIBER Epidemiología y Salud Pública (CIBERESP). Instituto de Salud Carlos III (ISCIII), Madrid, Spain.
[3]Instituto de Investigación Biosanitaria de Granada (ibs.GRANADA), Granada, Spain.
[4]Department of Preventive Medicine and Public Health, Medical School, University of Navarre, Pamplona, Spain.
[5]Navarra institute for health research (IdisNa), Pamplona, Spain.
[6]Department of Nutrition, Harvard T.H. Chan School of Public Health, Boston, MA, USA
[7]CIBER Physiopathology of Obesity and Nutrition (CIBEROBN), Carlos III Institute of Health, Madrid, Spain.
[8]Human Nutrition Unit, Biochemistry and Biotechnology Department, IISPV, Universitat Rovira i Virgili, Reus, Spain.
[9]Institut d'Investigació Sanitària Pere Virgili (IISPV), Reus, Spain.
[10]University Hospital of Sant Joan de Reus, Nutrition Unit, Reus, Spain.
[11] Department of Preventive Medicine, University of Valencia, 46010 Valencia, Spain
[12]Unit of Cardiovascular Risk and Nutrition, Hospital del Mar, Institut Municipal d'Investigació Médica (IMIM), Barcelona, Spain.
[13]Health Research Institute of the Balearic Islands (IdISBa), 07120 Palma de Mallorca, Spain.
[14]Nutritional Epidemiology Unit, Miguel Hernández University, ISABIAL-FISABIO, Alicante, Spain.
[15]Department of Cardiology, OSI ARABA, University Hospital Araba, University of the Basque Country UPV/EHU, Vitoria-Gasteiz, Spain.
[16]Department of Nursing, School of Health Sciences. University of Malaga- Instituto de Investigación Biomédica de Málaga (IBIMA), Málaga, Spain.
[17]Department of Nutrition, Food Sciences and Physiology, Center for Nutrition Research,University of Navarra, Pamplona, Spain.
[18]Nutritional Genomics and Epigenomics Group, IMDEA Food, CEI UAM + CSIC, Madrid, Spain.
[19]Institute for Biomedical Research, University of Las Palmas de Gran Canaria, Las Palmas, Spain.
[20]Department of Internal Medicine, IDIBAPS, Hospital Clinic, University of Barcelona, Barcelona, Spain.
[21]Virgen de la Victoria Hospital, Department of Endocrinology, University of Málaga, Málaga, Spain.
[22]Department of Family Medicine, Research Unit, Distrito Sanitario Atención Primaria Sevilla, Sevilla, Spain.
[23]Lipids and Vascular Risk Unit, Internal Medicine, Hospital Universitario de Bellvitge, IDIBELL, Hospitalet de Llobregat, Barcelona, Spain.
[24]Research Group on Community Nutrition & Oxidative Stress, University of Balearic Islands, Palma de Mallorca, Spain.

[25]Lipids and Atherosclerosis Unit, Department of Internal Medicine, Maimonides Biomedical Research Institute of Córdoba (IMIBIC), Reina Sofía University Hospital, University of Córdoba, Córdoba, Spain.
[26]Department of Health Sciences, University of Jaen, Jaen, Spain.
[27]Department of Endocrinology and Nutrition, Instituto de Investigación Sanitaria Hospital Clínico San Carlos (IdISSC), Madrid, Spain.
[28]Institute of Biomedicine (IBIOMED), University of León, León, Spain.
[29]Department of Endocrinology, IDIBAPS, Hospital Clinic, University of Barcelona, Barcelona, Spain;
[30]CIBER Diabetes y Enfermedades Metabólicas (CIBERDEM), Instituto de Salud Carlos III (ISCIII), Madrid, Spain.
[31]Department of Endocrinology, Fundación Jiménez-Díaz, Madrid, Spain.
[32]Lipid Clinic, Department of Endocrinology and Nutrition, Institut d'Investigació Biomédiques August Pi Sunyer (IDIBAPS), Hospital Clinic, Barcelona, Spain.
[33]Navarra Health Service-Osasunbidea, Pamplona, Spain.
[34]ABS Reus V. Centre d'Assistència Primària Marià Fortuny, SAGESSA, Reus, Spain.
[35]Centro de Salud Santa Pola, Alicante, Spain.
[36]Department of Physiotherapy, School of Health Sciences, University of Malaga- Instituto de Investigación Biomédica de Málaga (IBIMA), Málaga, Spain.
[37]Department of Internal Medicine, Regional University Hospital of Malaga, Instituto de Investigación Biomédica de Malaga (IBIMA), Malaga, Spain.
[38]Department of Medicine, Facultad de Medicina, University of Sevilla, Sevilla, Spain.

***Corresponding Author:**
Naomi Cano-Ibáñez. Department of Preventive Medicine and Public Health, University of Granada, Avda. De la Investigación 11, 18016 Granada, Spain. Tel +34958240000 Ext-20439. Email: ncaiba@ugr.es

Last names listed (PubMed) and 16-digit ORCID:
Cano-Ibáñez N: ORCID: 0000-0002-3640-5486, Bueno-Cavanillas A: ORCID: 0000-0002-0649-3016, Martínez-González MA: ORCID: 0000-0002-3917-9808, Salas-Salvadó J: ORCID: 0000-0003-2700-7459, Corella D: ORCID: 0000-0002-2366-4104, Freixer G: No, Romaguera D: ORCID: 0000-0002-5762-8558, Vioque J: ORCID: 0000-0002-2284-148X, Alonso-Gómez AM: ORCID: 0000-0003-2945-7509, Wärnberg J: ORCID: 0000-0002-8408-316X, Martínez JA: ORCID: 0000-0001-5218-6941, Serra-Majem L: ORCID: 0000-0002-9658-9061, Estruch R: ORCID: 0000-0003-1260-4445, Tinahones FJ: ORCID: 0000-0001-6871-4403, Lapetra J: ORCID: 0000-0002-3873-5737, Pintó X: ORCID: 0000-0002-2216-2444, Tur JA: ORCID: 0000-0002-6940-0761, García-Ríos A: ORCID: No, García-Molina L.: ORCID: 0000-0002-8730-0434, Delgado-Rodríguez M: ORCID: 0000-0002-3838-2548, Matía P: ORCID: 0000-0002-1424-8352, Daimiel L: ORCID: 0000-0001-9898-6629, Martín Sánchez V: ORCID: No, Vidal J: ORCID: 0000-0002-4564-4518, Vázquez C: ORCID: 0000-0003-1629-2143, Ros E: ORCID: 0000-0002-2573-1294, Bartolomé-Resano J: ORCID: 0000-0003-1818-3370, Palau-Galindo A: ORCID: No, Portoles O: ORCID: No, Torres L: ORCID: No, Fiol M: ORCID: 0000-0002-5370-1391, Cano-Sánchez MT: ORCID: No, Sorto-Sánchez C: ORCID: No, Moreno-Morales N: ORCID: 0000-0001-5907-9735, Abete I: ORCID: 0000-0002-6475-5387, Álvarez-Pérez J: ORCID: 0000-0001-5726-3731, Sacanella E: ORCID: No, Bernal-López MR: ORCID: 0000-0002-0238-0890, Santos-Lozano JM: ORCID: 0000-0001-7097-5653, Fanlo-Maresma M: ORCID: No, Bouzas C: ORCID: 0000-0002-1407-8641, Razquin C: ORCID: 0000-0003-3480-2645, Becerra-Tomás N: ORCID: 0000-0002-4429-6507, Ortega-Azorin C: ORCID: No, LLimona R: ORCID: No, Morey M: ORCID: No, Román-Maciá J: ORCID: No, Goicolea-Güemez L: ORCID: No, Vázquez-Ruiz Z: ORCID: 0000-0002-6828-9627, Barrubés L: ORCID: No, Fitó M: ORCID: 0000-0002-1817-483X, Gea A: ORCID: 0000-0002-2229-4690,

Word Count: 3302
Number of figures: 4
Number of tables: 3
Supplemental material: Supplementary table 1
Running Title: Improvements into Mediterranean diet adherence and nutrient density

Footnotes:

(i) Existence of **Supplementary data** (We have included a supplementary table, supplementary table 1).

(ii) **List of abbreviations:** (ANOVA): Analysis of Variance, (BMI): Body Mass Index, (CI): Confidence intervals, (CVD): Cardiovascular disease, (FFQ): Food Frequency Questionnaire, (MedDiet): Mediterranean Diet, (MetS): Metabolic Syndrome, Monounsaturated Fatty Acids (MUFAs), Polyunsaturated Fatty Acids (PUFAs), Saturated Fatty Acids (SFAs), (SD): Standard deviations, (WC): Waist Circumference.

(iii) **All sources of financial support**: Ministry of Education of Spain (FPU14/3630) grant Naomi Cano-Ibáñez. Ministry of Education of Spain (FPU16/00165) grant Laura Barrubés. The PREDIMED-Plus trial was supported by the European Research Council (Advanced Research Grant 2013-2018; 340918) grant to Miguel Ángel Martínez-González, and by the official funding agency for biomedical research of the Spanish Government, ISCIII through the Fondo de Investigación para la Salud (FIS), which is co-funded by the European Regional Development Fund (four coordinated FIS projects led by Jordi Salas-Salvadó and Josep 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, 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, The Especial Action Project entitled: "Implementación y Evaluación de una intervención intensiva sobre la actividad física Cohorte PREDIMED-Plus" grant to Jordi Salas-Salvadó, the Recercaixa grant to Jordi Salas-Salvadó (2013ACUP00194), grants from the Consejería de Salud de la Junta de Andalucía (PI0458/2013; PS0358/2016; PI0137/2018), the PROMETEO/2017/017 grant from the Generalitat Valenciana, the SEMERGEN grant, and CIBEROBN and FEDER funds (CB06/03), ISCIII. International Nut&Dried Fruit Council- FESNAD Nº201302: Miguel Ángel Martínez-González (PI). None of the funding sources took part in the design, collection, analysis or interpretation of the data, or in the decision to submit the manuscript for publication. The corresponding author had full access to all the data in the study and had final responsibility to submit for publication.

(iv) Conflict of Interest: Jordi Salas-Salvadó reports serving on the board of and receiving grant support through his institution from International Nut and Dried Fruit Council; receiving consulting personal fees from Danone, Font Vella Lanjarón, Nuts for Life and Eroski; and receiving grant support through his institution from Nut and Dried Fruit Foundation and Eroski. Emilio Ros reports grants, non-financial support and other fees from California Walnut Commission and Alexion; personal fees from California Walnut Commission and Alexion; personal fees, non-financial support and other fees from Aegerion and Ferrer International; grants and personal fees from Sanofi Aventis; grants from Amgen and Pfizer and personal fees from Akcea and Amarin, outside of the submitted work. Xavier Pintó reports serving on the board and receiving consulting personal fees from Sanofi Aventis, Amgen and Abbott laboratories; receiving lecture personal fees from Esteve, Lacer and Rubio laboratories. Miguel Delgado-Rodríguez reports receiving grants from the Diputación Provincial de Jaén and the Caja Rural de Jaén. Lidia Daimiel reports grants from Fundación Cerveza y Salud. All other authors declare no competing interests.

Acknowledgements

The principal author (N.C-I), wish to express her gratitude to the Ministry of Education of Spain for the grant received (FPU14/3630). L.B. has also received a grant from the Ministry of Education of Spain (FPU16/00165). The authors especially thank the PREDIMED-Plus participants for their collaboration and the PREDIMED-Plus staff for their support and effort. CIBEROBN is an initiative of ISCIII, Spain.

ABSTRACT

Background: The prevalence of overweight and obesity and related manifestations such as Metabolic Syndrome (MetS) is increasing worldwide. High energy density diets, usually with low nutrient density, are among the main causes. Some high-quality dietary patterns like the Mediterranean diet (MedDiet) have been linked to the prevention and better control of MetS. However, it is needed to show that nutritional interventions promoting the MedDiet are able to improve nutrient intake.

Objective: To assess the effect of improving MedDiet adherence on nutrient density after one year of follow-up at the PREDIMED-Plus trial.

Methods: We assessed 5783 men (55-75 years) and women (60-75 years) with overweight or obesity and MetS at baseline from the PREDIMED-Plus trial. Dietary changes and MedDiet adherence were evaluated at baseline and after one year. The primary outcome was the change in nutrient density (measured as nutrient intake per 1000 kcal). Multivariable-adjusted linear regression models were fitted to analyse longitudinal changes in adherence to the MedDiet and concurrent changes in nutrient density.

Results: During 1-y follow-up, participants showed clinically relevant improvements in nutrient density for all micronutrients assessed. The density of carbohydrates (CHO) (-9.0%), saturated fatty acids (SFA) (-10.3%) and total energy intake (-6.4%) decreased. These changes were more pronounced in the subset of participants with higher improvements in MedDiet adherence.

Conclusions: The PREDIMED-Plus dietary intervention, based on MedDiet recommendations for older adults, may be a feasible strategy to improve nutrient density in Spanish population at high risk of cardiovascular disease with overweight or obesity.

Keywords: Mediterranean Diet; nutrient density; Metabolic Syndrome.

INTRODUCTION

Global obesity rates have reached epidemic proportions. In the United States, the prevalence of obesity has increased progressively among adults, achieving figures of 39.6% [1]. A similar trend has been described in Spain, with growing rates of obesity in the last decades, particularly among males [2].

Diet and lifestyle changes that lead to an energy imbalance are among the main causes of the increased prevalence of obesity [3]. Usually, the ratio of nutrient intake related to energy is poor in obese people despite the increasingly energy-rich diet [4]. Reducing dietary energy intake has shown to improve weight maintenance and weight loss. However, restrictive diets jeopardize micronutrient intake and could worsen underlying metabolic diseases [5].

For the prevention and treatment of obesity and its related conditions such as Metabolic Syndrome (MetS) we must recommend high-quality overall dietary patterns. A high-quality dietary pattern should provide a low energy density but a high nutrient density. Mediterranean Diet (MedDiet) outmatches other high-quality patterns because of the growing evidence about its role in the management of weight and adiposity [6,7], and the prevention of cardiovascular diseases (CVD) and other chronic conditions such as cancer or neurodegenerative diseases [8,9]. MedDiet is characterized by the consumption of a wide variety of vegetables and fruits, legumes, whole-grains, nuts and olive oil, instead of sugar-sweetened beverages and other energy-dense foods, providing the necessary amount of vitamins and minerals but with a low energy content [10].

Peng et al. [11] showed an association between MedDiet adherence and an increase in nutrient density and we have been able to reproduce the same association among the PREDIMED-Plus participants (cross-sectional article) [12]. In Spain, some observational studies carried out in non-obese population showed that subjects with low adherence to the MedDiet exhibited a higher prevalence of inadequate intake of some nutrients such as zinc, iodine, magnesium, iron, selenium and vitamins B1, B9 and E [10,13]. However, to our knowledge no large clinical trial has assessed whether nutrient density also increases when MedDiet adherence does. We hypothesized that changes in dietary pattern toward greater MedDiet adherence might be associated to an improvement in nutrients intake (measured as nutrient density). The PREvención con DIeta MEditerránea (PREDIMED-Plus) is a large trial which randomize high CVD-risk individuals to follow a MedDiet (a usual or an energy-restricted MedDiet diet, respectively for control and intervention group) for primary cardiovascular prevention. The aim of the PREDIMED-Plus study is to improve MedDiet adherence in order to reduce CVD, supporting a causal association between adherence to MedDiet and diet quality independently of randomization group.

Therefore, with the present study, we aimed to assess the effect of improving MedDiet adherence over dietary nutrient density after one year of follow-up in the cohort integrated by the PREDIMED-Plus participants at the trial.

METHODS

Design of the Study

A detailed description of the design and methods of the PREDIMED-Plus trial can be found elsewhere [14]. Briefly, the PREDIMED-Plus trial is an ongoing 6-year multicentre, randomized, parallel-group, primary prevention trial conducted in Spain, to compare 2 interventions: a) an intensive weight loss intervention program based on an energy-restricted traditional Mediterranean diet, physical activity promotion behavioural support (intervention group), versus b) usual care and dietary counselling intervention recommending energy unrestricted MedDiet (control group). The primary end-point is CVD morbidity and mortality after 6-y follow-up.

Ethics Approval

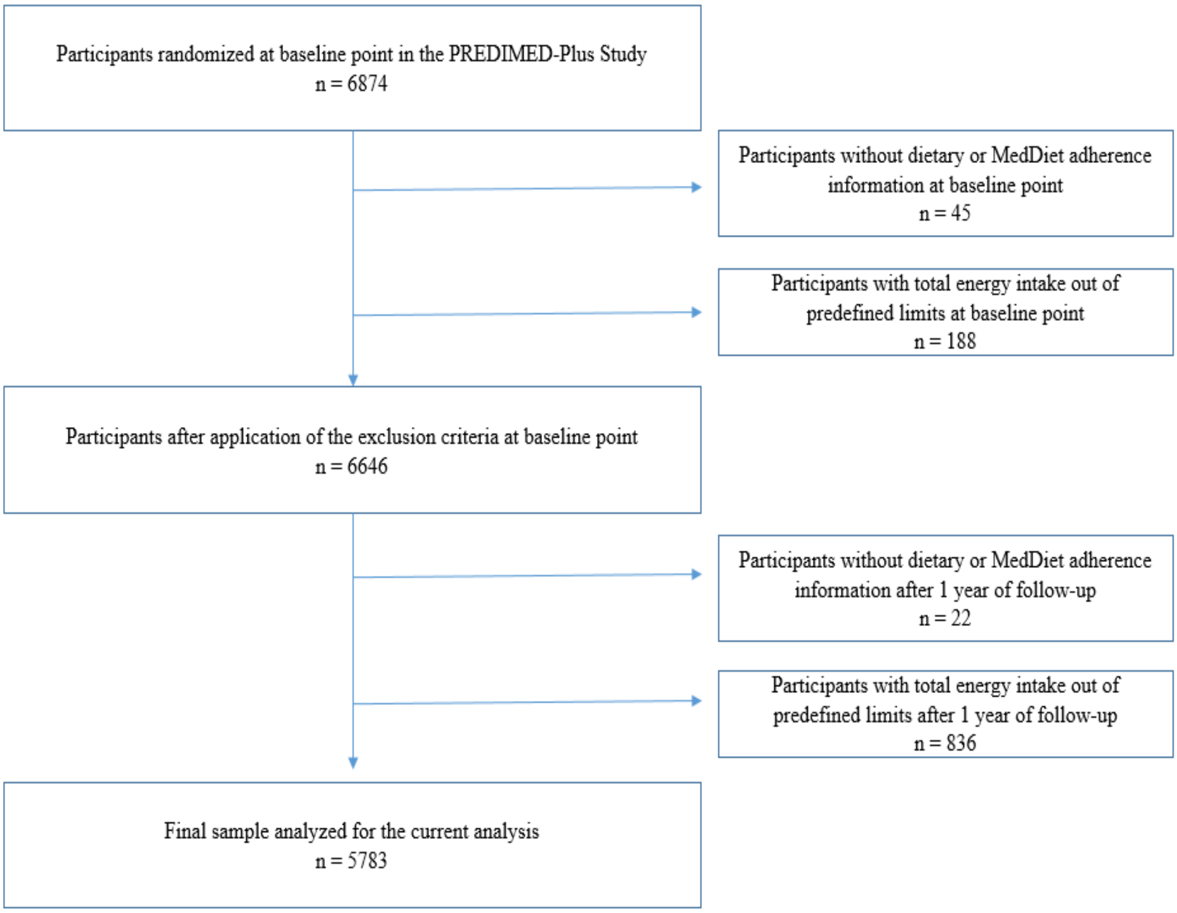
The protocol was written in accordance with the principles of the Declaration of Helsinki. The respective Institutional Review Board (IRB) of all study centres approved the study protocol. The trial was registered in 2014 at the International Standard Randomized Controlled Trial (www.isrctn.com/ISRCTN89898870). All participants provided written informed consent.

Participants and data collection procedures.

Eligible participants were men (aged 55-75 years) and women (aged 60-75 years) with overweight or obesity (body mass index (BMI) ≥27 and <40 kg/m^2) who were free of CVD at study recruitment, but with MetS according to the harmonized criteria of the International Diabetes Federation and the American Heart Association and National [15].

From the 6874 participants enrolled to the PREDIMED-Plus study, we selected for the present longitudinal analysis those participants who completed at baseline and at 1-year of follow-up a Food Frequency Questionnaire (FFQ) and a MedDiet adherence questionnaire. Those who failed to complete the FFQ (n=40) and MedDiet questionnaire (n=27), were excluded from this sub-study. Among the available 6807 participants, we also excluded those individuals with extreme values for total energy intake in FFQ (<800 kcal/day or >4000 kcal/day for men); (<500 kcal/day or >3500 kcal)/day for women) [16] (n=1024). Finally, data from 5783 participants were included in our analyses ***(Figure 1).***

Figure 1. Flow chart of the study participants



Dietary Assessment

Baseline adherence to the energy-reduced MedDiet (er-MedDiet) was appraised by a 17 item score, a modified form of a previously validated tool [17]. This tool was used to evaluate compliance with the intervention and as a key element to guide the motivation interviews during the follow-up study. Compliance with each of the 17 items relating to characteristic food habits was scored with 1 point if the goal was met or 0 points otherwise. Therefore, the total er-MedDiet score range was 0-17, with 0 meaning no adherence and 17 meaning maximum adherence to MedDiet. The study participants completed the questionnaire prior the randomization and also after 1 year of follow-up. As the main independent variable, we used changes in er-MedDiet adherence after 1 year of follow-up. The changes in adherence to er-MedDiet, were categorised in tertiles as follows: small changes of er-MedDiet adherence (1st tertile, ≤1 points, including negative values), medium (2nd tertile, 2-4 points) or large changes of adherence (3rd tertile, ≥5 points).

Data on dietary intake were collected at baseline and once yearly thereafter by trained dieticians. All participants were asked to complete a 143-item semi-quantitative FFQ previously validated in Spain [18]. The questionnaire included 9 frequency options for a specified serving size (never or almost never, 1-3 times a month, once a week, 2-4 times a week, 5-6 times a week, once a day, 2-3 times per day, 4-6 times a day, and more than 6 times a day). Nutrient intakes and food consumptions were obtained by multiplying serving sizes by consumption frequency. Energy and nutrient intakes were calculated as frequency multiplied by nutrient composition of specified portion size for each food item, using a computer program based on information available in Spanish food composition tables [19,20]. Thus, the dietary intake of a selection of nutrients including carbohydrates (CHO), total fat, monounsaturated (MUFAs), polyunsaturated (PUFAs) and saturated fatty acids (SFAs), protein, dietary fiber, vitamins A, B1, B6, B9, B12, C, D and E, calcium, magnesium, iron, iodine, potassium, selenium and zinc was assessed. To evaluate the nutrient density of the diet, density intake of all nutrients was calculated by dividing absolute nutrient intake by total energy intake. The nutrient density was expressed as nutrient intake per 1000 kcal [21]. For the present analysis, we have included the changes in nutrient density after 1 year of follow-up as the dependent variable in order to ascertain the effect of changes in er-MedDiet adherence (independent variable) on this variable.

Statistical Analysis

We used the PREDIMED-Plus database generated in March, 2019 including 1-y follow-up. All analyses were performed in the entire cohort, without taking into account the trial allocation group, as all participants were recommended to follow a MedDiet. All analyses were performed using Stata software (13.0, StataCorp LP, Tx. USA). Qualitative variables were described as frequencies and percentages, n (%), whereas the quantitative variables were expressed as means and standard deviations (SD). The significance level was set at 5%. ANOVA was used to test differences in nutrient density across tertiles of changes in er-MedDiet adherence. Mean percentage change was estimated for each nutrient as follows:

100*((baseline nutrient density - nutrient density at 1 year)/ baseline nutrient density). A multiple linear regression model was fitted to evaluate changes in mean nutrient density (dependent variables) of all the nutrients assessed across tertiles of changes in adherence to the er-MedDiet (compared with the lowest tertile) (as main independent variable). After the crude model, we fitted a sex- and age (55-70 years or more than 70 years)-adjusted model (model 1) and a model 2 additionally adjusted for other confounding variables (smoking habit (current smoker, former smoker, never smoker), physical activity (less active, moderately active and active), educational level (primary, secondary, tertiary, insufficient data), living alone (yes/no), marital status (married, widowed, divorced/separated, and other category which includes single participants and those who are priests or nuns who were categorized as “religious”), baseline BMI (kg/m^2), and allocation group of the participant (model 2). In order to evaluate the effect that the recruitment centre exerts on the dietary intervention and assuming in any case that the results could be heterogeneous, we performed a third model (model 3, supplementary table 1). To fit this model we performed a linear regression adjusted for the same confounding factors that in model 2 for each centre and nutrient, and then we obtained pooled results with a random-effects meta-analysis. As members of the same household were recruited for the study, we used robust variance estimators to account for intracluster correlation in all models.

RESULTS

Table 1 shows the baseline characteristics of participants across levels of changes in er-MedDiet adherence after 1-year follow-up: small (≤1 point), moderate (≥2 point - 4 point) and large (≥5 point). The following baseline characteristics were associated with smaller changes in er-MedDiet adherence after 1 year: female sex, higher levels of physical activity and higher educational level. Higher BMI and WC were associated with larger changes.

Table 1. Baseline characteristics of the PREDIMED-Plus trial participants according to tertiles of MedDiet adherence changes after 1 year of follow-up (n=5783)

	Small changes in MedDiet Adherence (≤1 point)	Moderate changes in MedDiet Adherence (≥2 - 4 point)	High changes in MedDiet Adherence (≥5 point)	P value
Age (y), n (%)				
≤70 y[a]	2016 (83.2)	1653 (85.5)	1260 (88.1)	<0.001
>70 y	407 (16.8)	280 (14.5)	170 (11.9)	
Mean ±SD	65 (4.9)	65 (4.9)	64 (4.8)	<0.001
Female sex, n (%)	1225 (50.6)	935 (48.4)	627 (43.9)	<0.001
Smoking Habit, n (%)				
Current smoker	307 (12.7)	230 (11.9)	178 (12.5)	0.384
Former smoker	1002 (41.4)	852 (44.1)	636 (44.5)	
Never smoker	1105 (45.6)	840 (43.5)	610 (42.7)	
Insufficient Data	9 (0.4)	11 (0.6)	6 (0.4)	
Physical activity				
Less active	1409 (58.4)	1172 (60.7)	857 (60.1)	0.187
Moderately active	445 (18.4)	368 (19.1)	272 (19.1)	
Active	559 (23.2)	391 (20.3)	296 (20.8)	
Educational level, n (%)				
Tertiary School	544 (22.5)	413 (21.4)	294 (20.6)	0.087
Secondary School	650 (26.8)	569 (29.5)	440 (30.8)	
Primary School	1211 (50.0)	935 (48.4)	679 (47.5)	
Insufficient Data	17 (0.7)	14 (0.7)	16 (1.1)	
Marital status, n (%)				
Married	1837 (76.1)	1456 (75.5)	1146 (80.4)	0.005
Widowed	249 (10.3)	224 (11.6)	133 (9.3)	

Divorced/Separated	207 (8.6)	139 (7.2)	83 (5.8)	
Others[b]	120 (5.0)	109 (5.7)	64 (4.5)	
Living alone, n (%)	306 (12.6)	260 (13.5)	140 (9.8)	0.016
Employment status, n (%)				
Retired	1395 (57.8)	1125 (58.5)	778 (54.5)	0.008
Employed	450 (18.6)	384 (20.0)	327 (22.9)	
Housekeeper	373 (15.5)	258 (13.4)	188 (13.2)	
Others[c]	197 (8.2)	155 (8.1)	135 (9.5)	
BMI (Kg/m²)	32.4 (3.4)	32.5 (3.4)	32.6 (3.5)	0.100
WC (cm)	107.1 (9.4)	107.4 (9.6)	108.3 (9.8)	0.001

Values are presented as means and standard deviations (SD) for continuous variables and number and percentages, n (%) for categorical variables. Pearson's chi-square test was performed for categorical variables and ANOVA test for continuous variables. [a]This age category includes 55-70years for males, and 60-70 years for females [b] Includes religious and single participants [c]Includes unemployed (with/without salary) incapacity, and students participants. Abbreviations: (BMI): Body Mass Index, (WC): Waist Circumference.

Changes from baseline to 1 year of follow-up in selected nutrient density intake per 1000 kcal are shown in **Table 2**. Participants showed a significant ($p<0.001$) increasing trend in nutrient density of all nutrients analyzed (% mean change), except for total CHO (-9.0 g/1000 kcal) and SFA (-10.3g/1000 kcal) that showed a marked decrease after 1 year of follow-up. Caloric intake at baseline point was higher between those who showed higher improvements in er-MedDiet adherence. At the same time, these participants showed lesser caloric intake after 1 year of follow-up. A similar result was observed for total fiber, vitamin B9, vitamin C, phosphorus and magnesium**.** The greater increase in total fat, PUFA and MUFA and decrease in SFA was found among those who showed higher increases in er-MedDiet adherence during the follow-up.

Table 2. One-year follow-up changes in total energy intake and nutrient density (mean and (SD)) by changes in MedDiet adherence in the PREDIMED-Plus study (n=5783).

	Changes in MedDiet Adherence	**Baseline**	**1 year of follow-up**	**% Mean Change (95% CI)**	**P value**
Total energy (Kcal/d)	≤1 point	2336.9 (549.3)	2274.7 (498.4)	-0.5 (-1.4, 0.44)	0.305
	≥2 point - 4 point	2362.7 (547.3)	2230.8 (471.6)	-2.5 (-1.4, -3.5)	<0.001
	≥5 point	2421.0 (545.2)	2193.8 (430.2)	-6.4 (-5.1, -7.6)	<0.001
CHO (g/1000 kcal)	≤1 point	100.2 (17.3)	95.5 (15.6)	-3.0 (-3.7, -2.3)	<0.001
	≥2 point - 4 point	101.3 (17.1)	93.0 (14.8)	-6.4 (-7.2, -5.6)	<0.001
	≥5 point	102.9 (16.4)	91.9 (13.6)	-9.0 (-9.9, -8.1)	<0.001

Protein (g/1000 kcal)	≤1 point	42.4 (7.1)	42.2 (6.9)	0.8 (0.1, 1.5)	0.020
	≥2 point - 4 point	42.2 (7.2)	43.7 (6.8)	5.2 (4.4, 6.0)	<0.001
	≥5 point	40.8 (6.6)	44.4 (6.2)	10.8 (9.9, 11.7)	<0.001
Total Fat (g/1000 kcal)	≤1 point	44.3 (7.3)	46.7 (6.7)	7.5 (6.7, 8.3)	<0.001
	≥2 point - 4 point	43.9 (7.3)	47.1 (6.4)	9.4 (8.5, 10.3)	<0.001
	≥5 point	43.6 (7.0)	47.1 (6.1)	10.1 (9.1, 11.1)	<0.001
MUFA (g/1000 kcal)	≤1 point	23.2 (5.3)	26.3 (5.2)	18.3 (17.0, 19.6)	<0.001
	≥2 point - 4 point	22.8 (5.2)	26.8 (5.1)	22.8 (21.3, 24.2)	<0.001
	≥5 point	22.5 (4.8)	27.1 (4.8)	24.9 (23.2, 26.6)	<0.001
PUFA (g/1000 kcal)	≤1 point	7.2 (2.0)	7.9 (1.9)	16.1 (14.5, 17.6)	<0.001
	≥2 point - 4 point	7.1 (2.1)	8.3 (1.9)	24.6 (22.9, 26.3)	<0.001
	≥5 point	6.8 (1.9)	8.6 (1.8)	33.9 (31.9, 36.)	<0.001
SFA (g/1000 kcal)	≤1 point	11.0 (2.3)	10.5 (2.0)	-1.9 (-2.7, -1.2)	<0.001
	≥2 point - 4 point	11.0 (2.2)	10.1 (1.8)	-5.7 (-6.6, -4.8)	<0.001
	≥5 point	11.2 (2.2)	9.8 (1.7)	-10.3 (-11.4, -9.3)	<0.001
Total fiber (g/1000 kcal)	≤1 point	11.7 (3.6)	12.7 (3.6)	12.9 (11.4, 14.4)	<0.001
	≥2 point - 4 point	11.3 (3.5)	13.8 (3.4)	29.2 (27.5, 30.9)	<0.001
	≥5 point	10.5 (3.1)	15.0 (3.1)	52.3 (50.3, 54.3)	<0.001

Values are presented as means and standard deviations (SD) at baseline point and at 1 year of follow-up. ANOVA test was performed to assess differences in dietary intake. Abbreviations: (CHO): Carbohydrates, (MUFA): Monounsaturated Fatty Acids, (PUFA): Polyunsaturated Fatty Acids, (SFA): Saturated Fatty Acids.

Multivariate adjusted-linear regression models (**table 3**) showed a direct association between improvements in adherence to er-MedDiet and the increase of the nutrient density after 1 year of follow-up (P for trend <0.05). This association persisted after adjusting for several confounding factors. We obtained similar findings after performed pooled results with a random-effects meta-analysis in order to evaluate the effect of the recruitment centre (**supplementary table 1**).

Table 3. β-coefficients and 95%CI for changes in nutrient density across categories of MedDiet adherence changes after 1 year of follow-up in the PREDIMED-Plus trial (n=5783)

	Small changes in MedDiet Adherence (≤1 point)	Medium changes in MedDiet Adherence (≥2 point - 4 point)	High changes in MedDiet Adherence (≥5 point)
CHO			
Model 1	1 (Ref.)	-3.5 (-4.5, -2.4)	-6.1 (-7.2, -4.9)
Model 2	1 (Ref.)	-3.2 (-4.2, -2.1)	-5.3 (-6.5, -4.0)
Protein			
Model 1	1 (Ref.)	4.3 (3.3, 5.4)	9.9 (8.7, 11.0)
Model 2	1 (Ref.)	3.3 (2.2, 4.3)	7.6 (6.4, 8.9)
Total Fat			
Model 1	1 (Ref.)	1.9 (0.8, 3.1)	2.7 (1.4, 4.0)
Model 2	1 (Ref.)	1.7 (0.5, 2.9)	2.2 (0.8, 3.6)
MUFAs			
Model 1	1 (Ref.)	4.5 (2.6, 6.4)	6.7 (4.6, 8.8)
Model 2	1 (Ref.)	3.7 (1.7, 5.7)	5.1 (2.8, 7.3)
PUFAs			
Model 1	1 (Ref.)	8.6 (6.3, 10.9)	18.0 (15.5, 20.6)
Model 2	1 (Ref.)	7.9 (5.5, 10.3)	16.6 (13.9, 19.3)
SFAs			
Model 1	1 (Ref.)	-3.7 (-4.9, -2.6)	-8.4 (-9.6, -7.1)
Model 2	1 (Ref.)	-3.5 (-4.7, -2.3)	-7.8 (-9.2, -6.5)
Dietary Fiber			
Model 1	1 (Ref.)	16.1 (13.8, 18.3)	38.6 (36.1, 41.1)
Model 2	1 (Ref.)	14.0 (11.7, 16.3)	34.7 (32.0, 37.3)
Vitamin A			
Model 1	1 (Ref.)	7.1 (3.1, 11.0)	17.3 (12.9, 21.7)
Model 2	1 (Ref.)	5.8 (1.7, 9.9)	15.2 (10.5, 19.8)
Vitamin B1			
Model 1	1 (Ref.)	6.2 (5.0, 7.5)	15.1 (13.7, 16.5)
Model 2	1 (Ref.)	4.9 (3.6, 6.1)	12.3 (10.8, 13.7)
Vitamin B6			
Model 1	1 (Ref.)	10.1 (8.6, 11.5)	22.8 (21.2, 24.4)
Model 2	1 (Ref.)	8.7 (7.2, 10.2)	19.8 (18.2, 21.5)

Model 1: Adjusted for sex and age. Model 2: Additionally adjusted for smoking habits, physical activity, educational level, BMI, living alone, civil status and allocation group in the trial.

Regarding nutrient density, the largest changes after 1-year of follow-up (more than 20%) were observed for the intakes of dietary fiber, MUFAs, PUFAs (*Figure 2*), vitamin A, B9, B12, C, D, E (*Figure 3*), potassium, iodine and magnesium (*Figure 4*). For all these dietary variables, we observed an increased intake as compared to baseline, although the increase was larger among participants who experimented large or moderate changes in er-MedDiet adherence. We also observed a relative decrease in total energy intake, CHO and SFA, particularly intense among participants with the largest change in er-MedDiet adherence (*Figure 2*).

Figure 2. Changes in percentage of total energy and nutrient intake after 1-year of follow up baseline according to changes in MedDiet adherence

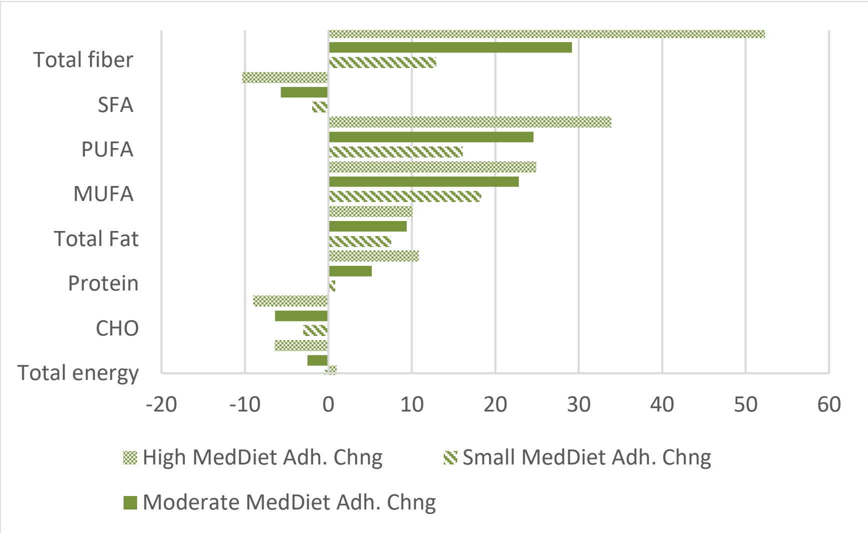


Figure 3. Changes in percentage of nutrients intake (vitamins) after 1-year of follow up baseline according to changes in MedDiet adherence

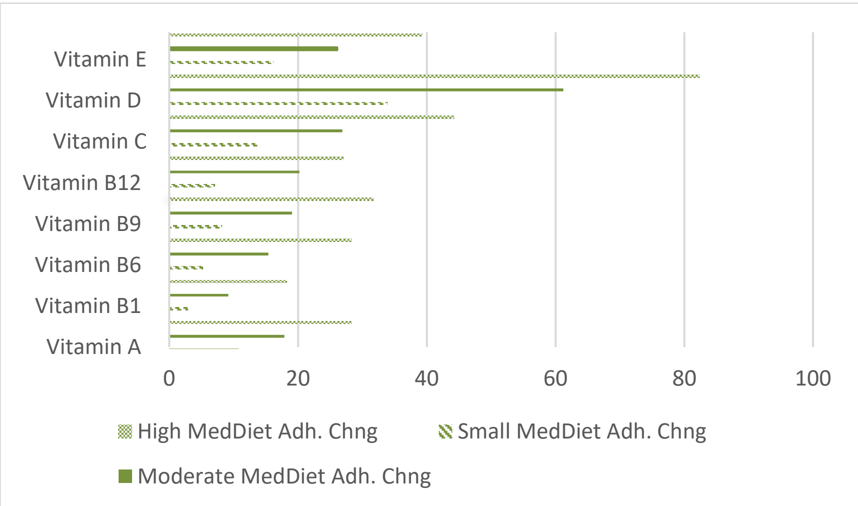
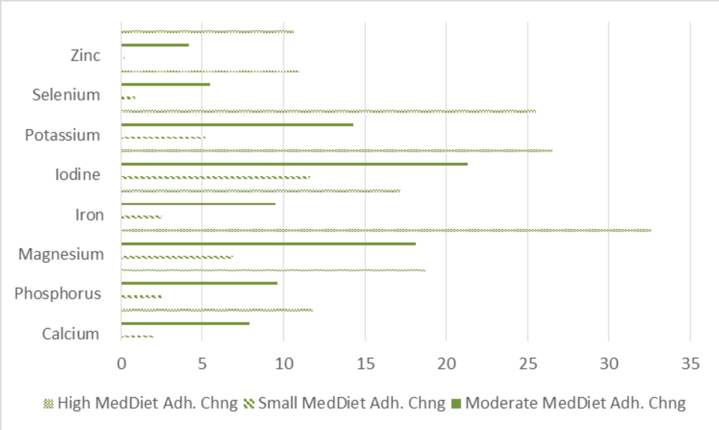


Figure 4. Changes in percentage of nutrients intake (minerals) after 1-year of follow up baseline according to changes in MedDiet adherence



DISCUSSION

The results of the present analysis showed an association between an increase in the adherence to the er-MedDiet after one year of follow up in the PREDIMED-Plus study and better dietary nutrient density. Although there are studies that have associated dietary patterns and nutrient adequacy [10,22], to our knowledge no large observational prospective study has assessed if nutrient density also increases when MedDiet adherence does over 1 year of follow-up in participants of a large cohort of free living aged adults with MetS.

In our sample, the highest MedDiet adherence changes were observed among male and younger population and in contrast with other studies [23], failure to increase postulated dietary goals by the MedDiet, was usually found among women and older participants. Furthermore, although other authors found a positive association between better anthropometric values and physical activity levels [24,25] in subjects with better MedDiet adherence, we found that people with lesser physical activity level but with high values of BMI and WC were more likely to achieve the intended MedDiet adherence changes.

A reason that may explain our contradictory results, is that having baseline dietary habits which are farther away from the dietary study goals could predict a higher success rate in reaching the intended dietary adherence [26]. That is, if the baseline dietary patterns of participants were closer to the MedDiet, the changes in dietary habits were small, meanwhile the participants with worst dietary habits at baseline tend to improve their dietary intake after 1 year of follow-up. In fact, when we stratified our sample by baseline MedDiet adherence, those who scored below 9 points (low adherence) showed higher changes in

MedDiet adherence after 1 year of follow up (4.7±3.1 points of adherence) compared to participants with good adherence into MedDiet (≥9 points) (1.7±2.8 points).

Dietary energy intake and dietary nutrient density are inversely linked [27]. Our data showed a negative association between MedDiet adherence and total energy intake, at the same time that the nutrient density of the majority of the vitamins and minerals increased with MedDiet adherence. The suggested lower energy density but higher micronutrient density of the MedDiet adds value to the health benefits of the MedDiet hypothesis. According to it, and considering the prevalence of suboptimal micronutrient intakes worldwide in overall population [28] and specifically in older adults [29], promoting MedDiet could be a plausible solution to the major global public health problems such as obesity and MetS [30,31] due to the low energy density and high quality nutrient of this dietary pattern.

In relation to dietary macronutrient, we observed that subjects with higher changes in adherence to the MedDiet after 1 year of follow-up, presented lower percentage of energy coming from SFAs and total CHO. Meanwhile the protein, MUFA and dietary fiber density increased throughout the tertiles of changes in MedDiet adherence. A review by Castro-Quezada et al. [32] evaluating the nutritional adequacy of the MedDiet reported similar findings. However, these results should be carefully interpreted, because they used repeated cross-sectional study designs, with different populations, and did not examine the same cohort over time.

Few studies have specifically examined longitudinal intra-individual changes in diet quality in adult populations [33-35]. The reported nutrient intake trends from these studies differ from our findings. The NHANES study (National Health and Nutrition Examination Survey) (1988-2012) found a decreased intake of dietary fiber and protein, meanwhile the SFAs intake among older adults (aged 20 years and over) increased significantly over the study period [34]. In addition, in a German cohort (14-80 years old), the total energy intake remained steady over 6 years of follow-up, although the CHO intake decreased [33]. The SUN (Seguimiento Universidad de Navarra) a Spanish study (average age of the participants at baseline: 35.0 years old), showed that intakes of CHO increased, whereas intakes of MUFA and PUFA decreased [35]. However, all these studies were observational. Our results support that the intervention promoting MedDiet is able to achieve better diet quality, in spite that social and population temporal trends go toward increased SFA and decreased fiber intakes as these observational studies have demonstrated.

Finally, several factors may contribute to explain the reported beneficial changes in the overall diet quality. One of them could be attributable to the personal characteristic of participants who accepted to be included in the study. It is possible that PREDIMED-Plus participants were aware of their metabolic problems and its relationship with poor food habits, and thus, firmly motivated to comply with dietary advices. However, the nutritional intervention was designed to improve MedDiet adherence, increasing knowledge and skills of participants and improving their dietary intake [36]. What is particularly relevant is that all the participants got some profit from their inclusion in the study, regardless the allocation group of the trial. This positive effect has been previously shown by other authors [37].

These findings highlight that the changes in dietary quality are presents after a nutritional intervention. These changes will be a part of the mechanism that explains a possible effect in health. The effect should be similar in both allocation groups. Therefore, anyone who participates in the PREDIMED-Plus study, even if they have been randomized into the control group, will obtain a nutritional benefit.

Our study has some limitations. First, the study sample is not representative of the general population since only aged adults with MetS were included. Second, other possible determinants of dietary quality might have not been evaluated in this study. Nevertheless, the most prominent sociodemographic and lifestyle factors in the literature have been analyzed. Third, although we used a FFQ to measure dietary intakes validated in adult Spanish individuals with good reproducibility and validity [38] , it might not be the ideal tool to measure micronutrient intake [39]. Furthermore, the use of FFQ could include a memory bias and, we could not rule out the possibility that intake of some nutrients have been misclassified. However, we have used the same FFQ with the same participants one year after and if there was some degree of misclassification it would be the same. Some strengths of our study include the large sample size (n=5783), the use of a standardized protocol which reduces the possibility of information bias about food intake and sociodemographic and lifestyles variables, as well as the inclusion of community-dwelling aged population, and the vast amount of baseline information collected in a large ongoing primary prevention trial. Finally, in the PREDIMED-Plus study, the same participants were evaluated over a period of time (1-year of follow-up). Therefore, the observed changes are less likely to be the result of differences in the sample characteristics. Last, we have dealt with all the study population like an entire cohort, independently of the intervention group. Previous analysis have shown the intervention effectiveness to improve MedDiet adherence [36], better in intervention group than in control one.

However, regardless of the allocation group, a greater MedDiet adherence implies better diet nutrient density.

In conclusion, this study showed that as MedDiet adherence increases the nutrient density also does. Thus diet quality could be easily enhanced addressing simple dietary advice to improve MedDiet adherence.

Statement of authors ‘contributions to manuscript

N.C.-I., A.B.-C., M.A.M.-G., J.S.-S., D.C., M.F., D.R., J.V., A.M.A-G., J.W., J.A.M., L.S-M., R.E., F.J.T., J.L., X.P., J.A.T., A.G.-R., M. D.-R., P.M.-M., L.D., V.M.S., J.V., C.V., E.R., and A.G. collected all the data from the PREDIMED-Plus trial. N.C.-I., A.B.-C and A.G., designed the study; performed the analysis; and wrote the first draft of the manuscript. All authors contributed to the editing of the manuscript. All authors have read and approved the final version of the manuscript.

REFERENCES

1. Hales CM, Fryar CD, Carroll MD, Freedman DS, Ogden CL (2018) Trends in obesity and severe obesity prevalence in us youth and adults by sex and age, 2007-2008 to 2015-2016. JAMA 319 (16):1723-1725. doi:10.1001/jama.2018.3060
2. Basterra-Gortari FJ, Bes-Rastrollo M, Ruiz-Canela M, Gea A, Martinez-Gonzalez MÁ (2017) Prevalence of obesity and diabetes in Spanish adults 1987-2012. Medicina Clinica 148 (6):250-256. doi:10.1016/j.medcli.2016.11.022
3. Malik VS, Willett WC, Hu FB (2013) Global obesity: Trends, risk factors and policy implications. Nature Reviews Endocrinology 9 (1):13-27. doi:10.1038/nrendo.2012.199
4. Hruby A, Hu FB (2015) The Epidemiology of Obesity: A Big Picture. PharmacoEconomics 33 (7):673-689. doi:10.1007/s40273-014-0243-x
5. Darmon P, Kaiser MJ, Bauer JM, Sieber CC, Pichard C (2010) Restrictive diets in the elderly: Never say never again? Clinical Nutrition 29 (2):170-174. doi:10.1016/j.clnu.2009.11.002
6. Schröder H, Marrugat J, Vila J, Covas MI, Elosua R (2004) Adherence to the traditional mediterranean diet is inversely associated with body mass index and obesity in a Spanish population. Journal of Nutrition 134 (12):3355-3361
7. Salas-Salvadó J, Díaz-López A, Ruiz-Canela M, Basora J, Fitó M, Corella D, Serra-Majem L, Wärnberg J, Romaguera D, Estruch R, Vidal J, Alfredo M, Borau F, Vázquez C, Ros E, Vioque J, López-Miranda J, Bueno-Cavanillas A, Tur JA, Martínez-González M (2018) Effect of a Lifestyle Intervention Program With Energy-Restricted Mediterranean Diet and Exercise on Weight Loss and Cardiovascular Risk Factors: One-Year Results of the PREDIMED-Plus Trial. doi:10.2337/dc18-0836
8. Martínez-González MA, Salas-Salvadó J, Estruch R, Corella D, Fitó M, Ros E (2015) Benefits of the Mediterranean Diet: Insights From the PREDIMED Study. Progress in Cardiovascular Diseases 58 (1):50-60. doi:10.1016/j.pcad.2015.04.003
9. Babio N, Toledo E, Estruch R, Ros E, Martínez-González MA, Castañer O, Bulló M, Corella D, Arós F, Gómez-Gracia E, Ruiz-Gutiérrez V, Fiol M, Lapetra J, Lamuela-Raventos RM, Serra-Majem L, Pintó X, Basora J, Sorlí JV, Salas-Salvadó J (2014) Mediterranean diets and metabolic syndrome status in the PREDIMED randomized trial. CMAJ 186 (17):E649-E657. doi:10.1503/cmaj.140764
10. Serra-Majem L, Bes-Rastrollo M, Román-Viñas B, Pfrimer K, Sánchez-Villegas A, Martínez-González MA (2009) Dietary patterns and nutritional adequacy in a Mediterranean country. British Journal of Nutrition 101 (S2):S21-S28. doi:10.1017/S0007114509990559
11. Peng W, Berry EM, Goldsmith R (2019) Adherence to the Mediterranean diet was positively associated with micronutrient adequacy and negatively associated with dietary energy density among adolescents. Journal of Human Nutrition and Dietetics 32 (1):41-52. doi:10.1111/jhn.12602
12. Cano-Ibáñez N, Gea A, Ruiz-Canela M, Corella D, Salas-Salvadó J, Schröeder H, Navarrete-Muñoz EM, Romaguera D, Martínez JA, Barón-López FJ, López-Miranda J, Estruch R, Riquelme-Gallego B, Alonso-Gómez Á, Tur JA, Tinahones F, Serra-Majem L, Martín V, Lapetra J, Vázquez C, Pintó X, Vidal J, Daimiel L, Gaforio JJ, Matía P, Ros E, Fernández-Carrión R, Díaz-López A, Zomeño MD, Candela I, Konieczna J, Abete I, Buil-Cosiales P, Basora J, Fitó M, Martínez-González MA, Bueno-Cavanillas A (2019) Diet quality and nutrient density in subjects with metabolic syndrome: influence of socioeconomic status and lifestyle factors. A cross-sectional assessment in the PREDIMED-Plus study. Clinical Nutrition. doi:https://doi.org/10.1016/j.clnu.2019.04.032
13. Sanchez-Tainta A, Zazpe I, Bes-Rastrollo M, Salas-Salvado J, Bullo M, Vicente Sorli J, Corella D, Isabel Covas M, Aros F, Gutierrez-Bedmar M, Fiol M, Garcia de la Corte F, Serra-Majem L, Pinto X, Schroeeder H, Ros E, Carmen Lopez-Sabater M, Estruch R, Angel Martinez-

Gonzalez M, Investigators PS (2016) Nutritional adequacy according to carbohydrates and fat quality. European Journal of Nutrition 55 (1):93-106. doi:10.1007/s00394-014-0828-3
14. Martínez-González MA, Buil-Cosiales P, Corella D, Bulló M, Fitó M, Vioque J, Romaguera D, Martínez JA, Wärnberg J, López-Miranda J, Estruch R, Bueno-Cavanillas A, Arós F, Tur JA, Tinahones F, Serra-Majem L, Martín V, Lapetra J, Vázquez C, Pintó X, Vidal J, Daimiel L, Delgado-Rodríguez M, Matía P, Ros E, Fernández-Aranda F, Botella C, Portillo-Baquedano MP, Lamuela-Raventós RM, Marcos A, Sáez G, Gómez-Gracia E, Ruiz-Canela M, Toledo E, Alvarez-Alvarez I, Díez-Espino J, Sorlí JV, Basora J, Castañer O, Schröder H, Navarrete-Muñoz EM, Zulet MA, García-Rios A, Salas-Salvadó J, Investigators PR-P (2018) Cohort Profile: Design and methods of the PREDIMED-Plus randomized trial. International Journal of Epidemiology:dyy225-dyy225. doi:10.1093/ije/dyy225
15. Alberti KGMM, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, Fruchart JC, James WPT, Loria CM, Smith SC (2009) 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 atherosclerosis society; And international association for the study of obesity. Circulation 120 (16):1640-1645. doi:10.1161/CIRCULATIONAHA.109.192644
16. Willet W (2013) Nutritional Epidemiology. 3rd Edition edn. Oxford University Press, New York
17. Schröder H, Fitó M, Estruch R, Martínez-González MA, Corella D, Salas-Salvadó J, Lamuela-Raventós R, Ros E, Salaverría I, Fiol M, Lapetra J, Vinyoles E, Gómez-Gracia E, Lahoz C, Serra-Majem L, Pintó X, Ruiz-Gutierrez V, Covas MI (2011) A Short screener is valid for assessing mediterranean diet adherence among older spanish men and women. Journal of Nutrition 141 (6):1140-1145. doi:10.3945/jn.110.135566
18. Martin-moreno JM, Boyle P, Gorgojo L, Maisonneuve P, Fernandez-rodriguez JC, Salvini S, Willett WC (1993) Development and validation of a food frequency questionnaire in Spain. International Journal of Epidemiology 22 (3):512-519. doi:10.1093/ije/22.3.512
19. Moreiras O CA, Cabrera L, Cuadrado C (2003) Tablas de Composición de alimentos. (Spanish food composition tables), vol 7 th ed. Pirámide, Madrid, Spain
20. J MV (2003) Tabla de composición de alimentos españoles. (Spanish food composition tables), vol 4 th ed. Universidad de Granada, Granada
21. Nicklas TA, Drewnowski A, O'Neil CE (2013) The nutrient density approach to healthy eating: Challenges and opportunities. Public Health Nutrition 17 (12):2626-2636. doi:10.1017/S136898001400158X
22. Schröder H, Vila J, Marrugat J, Covas MI (2008) Low energy density diets are associated with favorable nutrient intake profile and adequacy in free-living elderly men and women. Journal of Nutrition 138 (8):1476-1481
23. Sánchez-Villegas A, Martínez JA, De Irala J, Martínez-González MA (2002) Determinants of the adherence to an "a priori" defined Mediterranean dietary pattern. European Journal of Nutrition 41 (6):249-257. doi:10.1007/s00394-002-0382-2
24. Vitale M, Racca E, Izzo A, Giacco A, Parente E, Riccardi G, Giacco R (2019) Adherence to the traditional Mediterranean diet in a population of South of Italy: factors involved and proposal of an educational field-based survey tool. International Journal of Food Sciences and Nutrition 70 (2):195-201. doi:10.1080/09637486.2018.1481202
25. Agnoli C, Sieri S, Ricceri F, Giraudo MT, Masala G, Assedi M, Panico S, Mattiello A, Tumino R, Giurdanella MC, Krogh V (2018) Adherence to a Mediterranean diet and long-term changes in weight and waist circumference in the EPIC-Italy cohort. Nutrition and Diabetes 8 (1). doi:10.1038/s41387-018-0023-3
26. Zazpe I, Estruch R, Toledo E, Sánchez-Taínta A, Corella D, Bulló M, Fiol M, Iglesias P, Gómez-Gracia E, Arós F, Ros E, Schröder H, Serra-Majem L, Pintó X, Lamuela-Raventós R, Ruiz-Gutiérrez V, Martínez-González MÁ (2010) Predictors of adherence to a Mediterranean-type

diet in the PREDIMED trial. European Journal of Nutrition 49 (2):91-99. doi:10.1007/s00394-009-0053-7
27. Drewnowski A (2018) Nutrient density: Addressing the challenge of obesity. British Journal of Nutrition 120 (s1):S8-S14. doi:10.1017/S0007114517002240
28. Roman Viñas B, Ribas Barba L, Ngo J, Gurinovic M, Novakovic R, Cavelaars A, De Groot LCPGM, Van'T Veer P, Matthys C, Serra Majem L (2011) Projected prevalence of inadequate nutrient intakes in Europe. Annals of Nutrition and Metabolism 59 (2-4):84-95. doi:10.1159/000332762
29. Ter Borg S, Verlaan S, Mijnarends DM, Schols JMGA, De Groot LCPGM, Luiking YC (2015) Macronutrient Intake and Inadequacies of Community-Dwelling Older Adults, a Systematic Review. Annals of Nutrition and Metabolism 66 (4):242-255. doi:10.1159/000435862
30. Guasch-Ferré M, Salas-Salvadó J, Ros E, Estruch R, Corella D, Fitó M, Martínez-González MA, Arós F, Gómez-Gracia E, Fiol M, Lapetra J, Lamuela-Raventos RM, Tur J, Martinez JA, Serra-Majem L, Pintó X (2017) The PREDIMED trial, Mediterranean diet and health outcomes: How strong is the evidence? Nutrition, Metabolism and Cardiovascular Diseases 27 (7):624-632. doi:10.1016/j.numecd.2017.05.004
31. Salas-Salvadó J, Guasch-Ferré M, Lee CH, Estruch R, Clish CB, Ros E (2016) Protective effects of the mediterranean diet on type 2 diabetes and metabolic syndrome. Journal of Nutrition 146 (4):920S-927S. doi:10.3945/jn.115.218487
32. Castro-Quezada I, Román-Viñas B, Serra-Majem L (2014) The mediterranean diet and nutritional adequacy: A review. Nutrients 6 (1):231-248. doi:10.3390/nu6010231
33. Gose M, Krems C, Heuer T, Hoffmann I (2016) Trends in food consumption and nutrient intake in Germany between 2006 and 2012: Results of the German National Nutrition Monitoring (NEMONIT). British Journal of Nutrition 115 (8):1498-1507. doi:10.1017/S0007114516000544
34. Casagrande SS, Cowie CC (2017) Trends in dietary intake among adults with type 2 diabetes: NHANES 1988–2012. Journal of Human Nutrition and Dietetics 30 (4):479-489. doi:10.1111/jhn.12443
35. De La Fuente-Arrillaga C, Zazpe I, Santiago S, Bes-Rastrollo M, Ruiz-Canela M, Gea A, Martinez-Gonzalez MA (2016) Beneficial changes in food consumption and nutrient intake after 10 years of follow-up in a Mediterranean cohort: The SUN project. BMC Public Health 16 (1). doi:10.1186/s12889-016-2739-0
36. Zazpe I, Sanchez-Tainta A, Estruch R, Lamuela-Raventos RM, Schröder H, Salas-Salvado J, Corella D, Fiol M, Gomez-Gracia E, Aros F, Ros E, Ruíz-Gutierrez V, Iglesias P, Conde-Herrera M, Martinez-Gonzalez MA (2008) A Large Randomized Individual and Group Intervention Conducted by Registered Dietitians Increased Adherence to Mediterranean-Type Diets: The PREDIMED Study. Journal of the American Dietetic Association 108 (7):1134-1144. doi:10.1016/j.jada.2008.04.011
37. Nijjar SK, D'Amico MI, Wimalaweera NA, Cooper NAM, Zamora J, Khan KS (2017) Participation in clinical trials improves outcomes in women's health: a systematic review and meta-analysis. BJOG: An International Journal of Obstetrics and Gynaecology 124 (6):863-871. doi:10.1111/1471-0528.14528
38. Fernández-Ballart JD, Piñol JL, Zazpe I, Corella D, Carrasco P, Toledo E, Perez-Bauer M, Martínez-González MA, Salas-Salvadó J, Martn-Moreno JM (2010) Relative validity of a semi-quantitative food-frequency questionnaire in an elderly Mediterranean population of Spain. British Journal of Nutrition 103 (12):1808-1816. doi:10.1017/S0007114509993837
39. Ortiz-Andrellucchi A, Sánchez-Villegas A, Doreste-Alonso J, de Vries J, de Groot L, Serra-Majem L (2009) Dietary assessment methods for micronutrient intake in elderly people: a systematic review. The British journal of nutrition 102 Suppl 1:S118-149. doi:10.1017/S0007114509993175

Supplementary Table 1. Linear Regression of pooled results obtained with a random-effects meta-analysis in order to evaluate the effect of recruitment centre on the dietary intervention in the PREDIMED-Plus trial (n=5783) (β-coefficients and 95%CI for changes in nutrient density across categories of MedDiet adherence changes after 1 year of follow-up)

	Small changes in MedDiet Adherence (≤1 point)	Medium changes in MedDiet Adherence (≥2 point - 4 point)	High changes in MedDiet Adherence (≥5 point)
CHO			
Model 3	1 (Ref.)	-3.1 (-4.3,-2.0)	-5.1 (-6.9, -3.3)
Protein			
Model 3	1 (Ref.)	2.9 (1.8, 4.1)	6.3 (4.6, 7.9)
Total Fat			
Model 3	1 (Ref.)	1.3 (-0.2, 2.5)	2.4 (0.2, 4.7)
MUFAs			
Model 3	1 (Ref.)	3.2 (1.3, 5.2)	5.8 (2.4, 9.1)
PUFAs			
Model 3	1 (Ref.)	6.4 (3.8, 9.0)	13.0 (8.2, 17.7)
SFAs			
Model 3	1 (Ref.)	-3.0 (-4.4, -1.6)	-6.2 (-7.9, -4.5)
Dietary Fiber			
Model 3	1 (Ref.)	11.6 (8.4, 14.8)	28.9 (24.8, 32.9)

Model 3: Adjusted for sex, age, smoking habits, physical activity, educational level, BMI, living alone, civil status and allocation group in the trial.

Table Supplementary 1. (Continued) Linear Regression of pooled results obtained with a random-effects meta-analysis in order to evaluate the effect of recruitment centre on the dietary intervention in the PREDIMED-Plus trial (n=5783) (β-coefficients and 95%CI for changes in nutrient density across categories of MedDiet adherence changes after 1 year of follow-up)

	Small changes in MedDiet Adherence (≤1 point)	Medium changes in MedDiet Adherence (≥2 point - 4 point)	High changes in MedDiet Adherence (≥5 point)
Vitamin A			
Model 3	1 (Ref.)	4.1 (-1.5, 9.7)	10.9 (3.2, 18.6)
Vitamin B1	**Vitamin B1**	**Vitamin B1**	**Vitamin B1**
Model 3	Model 3	Model 3	Model 3
Vitamin B6			
Model 3	1 (Ref.)	7.5 (5.8, 9.1)	15.9 (14.1, 17.7)
Vitamin B9			
Model 3	1 (Ref.)	7.5 (4.8, 10.2)	15.8 (12.6, 18.9)
Vitamin B12			
Model 3	1 (Ref.)	8.4 (5.1, 11.8)	13.9 (8.3, 19.6)
Vitamin C			
Model 3	1 (Ref.)	9.5 (5.0, 14.0)	19.3 (14.2, 24.4)
Vitamin D			
Model 3	1 (Ref.)	15.6 (7.1, 24.2)	28.8 (18.6, 39.0)
Vitamin E			
Model 3	1 (Ref.)	7.9 (5.0, 10.7)	16.4 (13.6, 19.1)
Calcium			
Model 3	1 (Ref.)	4.8 (2.7, 6.9)	6.0 (2.7, 9.4)
Phosphorus			
Model 3	1 (Ref.)	5.3 (4.1, 6.4)	11.0 (9.0, 13.1)
Magnesium			
Model 3	1 (Ref.)	8.4 (6.6, 10.2)	19.4 (16.8, 22.1)
Iron			
Model 3	1 (Ref.)	5.1 (3.4, 6.8)	10.7 (9.1, 12.4)
Iodine			
Model 3	1 (Ref.)	7.9 (2.4, 13.5)	8.7 (0.9, 16.5)
Potassium			
Model 3	1 (Ref.)	6.5 (4.7, 8.2)	14.3 (11.9, 16.7)
Selenium			
Model 3	1 (Ref.)	3.3 (1.8, 4.9)	6.7 (4.8, 8.5)
Zinc			
Model 3	1 (Ref.)	3.0 (1.8, 4.1)	7.4 (5.9, 8.9)

Model 3: Adjusted for sex, age, smoking habits, physical activity, educational level, BMI, living alone, civil status and allocation group in the trial.

7. DISCUSIÓN

7. DISCUSIÓN

La realización de esta Tesis Doctoral ha permitido estudiar de forma pormenorizada la dieta de un colectivo creciente poblacional en nuestro país: población adulta mayor, no institucionalizada, con sobrepeso/obesidad y Síndrome Metabólico. Población vulnerable cuyo número se está viendo incrementado debido a la occidentalización de los estilos de vida y al aumento de la esperanza de vida a nivel mundial. Lo realmente novedoso de la aproximación realizada en este trabajo es el enfoque por el que se ha abordado la temática, obviando la perspectiva tradicional de la sobreingesta energética para centrarse en la deficiencia de nutrientes.

El proceso de investigación realizado permitió obtener os resultados presentados en cada una de las publicaciones que configuran esta Tesis Doctoral, en concreto:

1. Evaluar el porcentaje de población con ingesta adecuada de nutrientes de acuerdo a las ingestas dietéticas de referencia teniendo en cuenta tanto las recomendaciones europeas como internacionales en función del sexo y la edad; así como investigar la influencia que los factores socioeconómicos, demográficos y de estilo de vida ejercen sobre la calidad dietética, definida tanto por la densidad nutricional como por la ingesta inadecuada de nutrientes.

2. Comparar la ingesta alimentaria y el perfil nutricional en función del área geográfica de residencia de los individuos; así como analizar la influencia de esta variable sobre la frecuencia de ingesta inadecuada de nutrientes.

3. Identificar los factores socioeconómicos, demográficos y de estilo de vida asociados con la diversidad dietética; y cuantificar el efecto de esta variable sobre la ingesta inadecuada de nutrientes, tanto de la diversidad dietética total como de la referida a cada uno de los grupos alimentarios que se incluyen al estimar la variedad de la dieta.

4. Cuantificar el efecto que la mejora de la calidad de la dieta (medida en función del aumento de la adherencia a la Dieta Mediterránea) después de un año de seguimiento en el estudio PREDIMED-Plus ejerce sobre la densidad nutricional, independientemente del grupo de estudio al que se asignan aleatoriamente los participantes del ensayo.

Los resultados obtenidos en cada uno de los trabajos fueron discutidos individualmente en cada una de las publicaciones que componen esta Tesis Doctoral. En este apartado se procederá a resaltar los principales hallazgos y se destacarán las fortalezas y limitaciones encontradas. Finalmente se realizará una valoración de la utilidad práctica de los resultados obtenidos y de las nuevas líneas de investigación que las evidencias derivadas de esta investigación permitirán construir.

7.1. Principales hallazgos

Los resultados más destacables que se han obtenido se resumen de forma esquemática a continuación. Los análisis descriptivos señalan una frecuencia elevada de ingesta deficitaria en población adulta mayor con Síndrome Metabólico, a pesar de presentar sobrepeso u obesidad. Al utilizar un índice sintético (déficits en la ingesta de al menos 4 nutrientes), se encontró una prevalencia de ingesta deficitaria de aproximadamente el 17%, esto supone que 1 de cada 6 adultos con Síndrome Metabólico, sobrepeso u obesidad está afectado por un déficit importante de nutrientes. Cuando se analizó cada nutriente por separado, la ingesta deficitaria osciló entre el 98% para la Vitamina D y el 8% para el magnesio. Los factores asociados con una menor probabilidad de presentar una ingesta deficitaria fueron el sexo, en concreto ser mujer, tener un mayor nivel de estudios, y mejor adherencia a la Dieta Mediterránea. Hábitos como el tabaquismo activo o la vida sedentaria se asociaron por el contrario a un mayor riesgo de déficit nutricional.

Existen diferencias significativas en la ingesta de macro y micronutrientes en relación al área geográfica de residencia, sin embargo, y en contra de lo esperado inicialmente, la mayor frecuencia de ingesta deficitaria se encontró en las regiones del Norte de España, en particular para la ingesta de vitaminas A y E, calcio y magnesio.

Cuanto mayor es la diversidad de la dieta menor frecuente es el déficit nutricional. Además, la diversidad de la dieta se asocia de forma independiente y estadísticamente significativa con ser mujer y con otros estilos de vida saludables, destacando principalmente la mayor adherencia a la Dieta Mediterránea y el ser no fumador.

Una vez corroborado que la densidad nutricional y la adherencia a la Dieta Mediterránea están estrechamente asociadas a la ingesta deficitaria de nutrientes, y que no necesariamente presenta la misma intensidad en sujetos de diferentes puntos de la población española, nos planteamos si la intervención realizada, centrada en el fomento de la Dieta Mediterránea, consigue no sólo mejorar la adherencia, sino también aumentar la densidad nutricional de la dieta y disminuir la ingesta deficitaria de los micronutrientes analizados. Los resultados muestran que al año de intervención existe una mejora global neta, que beneficia a todos los participantes en el estudio, pero que es significativamente mayor en el grupo de intervención.

7.1.1. La adecuación de la ingesta nutricional y la influencia de los factores socioeconómicos, demográficos y de estilo de vida sobre la calidad dietética

El análisis de la ingesta nutricional en términos de macronutrientes de la población de nuestro estudio mostró que la ingesta total procedente de grasas estaba por encima de las ingestas recomendadas (<30%) (Health, 2018). Sin embargo, esto no debería suponer ningún problema ya que las pautas dietéticas actuales enfatizan la necesidad de mejorar la calidad más que la cantidad de este nutriente. Así, el estudio PREDIMED demostró que la sustitución del consumo de ácidos grasos saturados por la ingesta de ácidos grasos mono/poliinstaurados resultó ser beneficiosa en la prevención de la enfermedad cardiovascular (Guasch-Ferré et al., 2015). En nuestra población, se encontró un perfil de ingesta de grasa saturada inferior al 10%, mientras que la ingesta de ácidos grasos polinsaturados fue de aproximadamente el 6%, ambos valores refrendan por tanto que el exceso de grasa dietética se produce a expensas de grasa dietética saludable. Además, la ingesta de proteínas también fue superior a la ingesta recomendadas (<15%), mientras que la ingesta de hidratos de carbono fue ligeramente inferior a la recomendada. Esta tendencia ha sido también reportada por otros autores que evaluaron la distribución de los macronutrientes y sus fuentes alimentarias en la población Española recientemente (Ruiz et al., 2016).

Precisamente en esa cohorte poblacional (Ruiz et al., 2015) se estimó la ingesta energética, en el estudio PREDIMED-Plus la ingesta media fue superior para los mismos estratos de edad y sexo. A pesar de la elevada ingesta energética, y que nuestra estimación fue penalizada considerando ingesta deficitaria solo cuando un sujeto presentaba ingestas inferiores a 2/3 de las recomendadas, el 16.6% (21.3% de los hombres, 11.7% de las mujeres) de los individuos presentaron una ingesta inadecuada en al menos 4 de los 10 nutrientes analizados en este estudio. Para estas estimaciones se tomaron como referencia las ingestas dietéticas internacionales, cuando se tuvieron en cuenta las recomendaciones para población europea dichas cifras se incrementan de forma notoria (44.0 % de los hombres, 32.0 % de las mujeres).

La desnutrición en países desarrollados ha sido poco estudiada hasta la fecha, sin embargo, son notorios los datos aportados por algunas revisiones publicadas sobre la alta prevalencia de ingesta inadecuada en países europeos, especialmente en población no mediterránea de edad avanzada (Mensink et al., 2013). Así pues uno de los principales hallazgos de este estudio fue encontrar que la población adulta mayor Española con sobrepeso/obesidad y Síndrome Metabólico está expuesta a riesgos dietéticos debido a las deficiencias encontradas en términos de consumo inadecuado de los siguientes nutrientes: fibra, vitaminas B_9, B_{12}, calcio y magnesio. Todos estos nutrientes parecen tener un rol protector fundamental en el tratamiento de la obesidad/sobrepeso y el Síndrome Metabólico (Hosseinpour Niazi, Mirmiran, Sohrab, Hosseini Esfahani, & Azizi, 2012; Moore-Schiltz, Albert, Singer, Swain, & Nock, 2015).

También resulta llamativo el hecho de que a pesar de la elevada ingesta de grasa en la dieta de la población analizada, se encontraron deficiencias en numerosas vitaminas liposolubles (vitaminas A, D y E). Esta tendencia ha sido sustentada por otros estudios que muestran resultados similares (Toffanello et al., 2011). Una posible explicación a este fenómeno podría venir derivada de una baja frecuencia de consumo de productos lácteos, por debajo de las ingestas recomendadas (Ruiz et al., 2016).

La ingesta inadecuada de nutrientes puede estar relacionada con una disminución de la ingesta energética vinculada al proceso de envejecimiento o por una dieta restrictiva (Ter Borg et al., 2015), para obviar esta dualidad se estimó la densidad nutricional. Así, a pesar de que respecto a la ingesta energética se encontró un descenso en el consumo energético con la edad en ambos sexos, la densidad nutricional fue significativamente superior en los mayores de 70 años, especialmente en mujeres.

El hecho de que la densidad nutricional y la ingesta adecuada de nutrientes fuesen superiores en mujeres puede ser atribuible al fenómeno encontrado por otros autores en el que se sugiere que una elección alimentaria está mediada por el género. El interés no radica en cuestiones puramente biológicas, sino que se sustenta en los tradicionales roles impuestos a la mujer y que están estrechamente relacionados con la alimentación (Hsiao et al., 2013). Otros factores, como los asociados al estilo de vida, en particular fumar y ser poco activo se asociaron también de forma independiente con menor densidad nutricional y mayor riesgo de presentar ingesta inadecuada de nutrientes. Ambos factores se relacionaron también de forma significativa y similar a la aquí referida en un estudio realizado en población europea (Alkerwi et al., 2017), es decir, aquellos individuos que se preocupan más por su salud, adoptando estilos de vida saludables, también cuidan más su alimentación. Respecto a la Dieta Mediterránea, nuestros resultados mostraron que aquellos sujetos que presentaban una mayor adherencia a este patrón dietético también tuvieron una mayor calidad nutricional, lo que sustenta la continuidad de la promoción de este modelo de alimentación como herramienta para la mejora de la calidad de la dieta.

En cuanto a los factores sociodemográficos, la evidencia actual indica que el estado civil es un fuerte predictor en la calidad dietética, así estar casado o convivir en pareja se ha asociado directamente con una mayor densidad nutricional (Deierlein, Morland, Scanlin, Wong, & Spark, 2014). La soledad, específicamente en hombres mayores, se vincula de forma negativa con la adopción de una dieta saludable. Este hecho puede estar fundamentado directamente con los roles de género tradicionales y con la interrupción de la vida cotidiana sufrida tras quedar viudo (Charlton, 1999). Sin embargo, en nuestro análisis no se observó una asociación significativa entre este factor y la densidad nutricional. Probablemente porque la mayoría de los participantes de nuestro estudio estaban casados y no vivían solos por lo que el escaso tamaño muestral de este colectivo no ha sido suficiente para ser representativo. Finalmente, factores socioeconómicos como el nivel educativo y la ocupación se han vinculado con una mayor calidad dietética (Fekete & Weyers, 2016; Shatenstein et al., 2016) en estudios internacionales, este hecho vendría derivado de la idea de que un alto poder adquisitivo y un mayor nivel de conocimiento mediarían en la elección de alimentos con un mejor perfil nutricional. Sin embargo, de nuestros hallazgos tampoco puede desprenderse esa idea, principalmente porque la mayoría de los participantes estaban jubilados y partían del mismo nivel educativo oficial (estudios primarios). Es interesante señalar que la población de estudio abarca una cohorte generacional nacida en las décadas de 1940 y 1950, arrastrando sin duda alguna las peculiaridades socioeconómicas y culturales de la época en la que les tocó vivir.

7.1.2. Influencia del Área Geográfica en la ingesta alimentaria e inadecuación nutricional

El patrón dietético tradicional de la población española está sufriendo un deterioro progresivo, en el sentido de que cada vez se parece menos a un modelo de Dieta Mediterránea. Así, la dieta en España se caracteriza por un elevada consumo de cereales refinados, azúcares y productos cárnicos en detrimento de alimentos tales como las verduras, las frutas, las legumbres y el pescado (Ruiz et al., 2015). En nuestros resultados, aunque la ingesta media estimada de verduras y frutas fue menor que la reportada en el Estudio ANIBES, la ingesta de legumbres y pescados fue ligeramente superior. Llamativamente, aunque esperable debido a las características del colectivo poblacional estudiado, el consumo de huevo se encontró muy por debajo de los niveles recomendados de ingesta, probablemente debido a la extendida creencia (pero infundada) de que el huevo incrementa los niveles de colesterol (Vázquez-Ruiz et al., 2018).

Tal y como se planteaba en la hipótesis de partida de este trabajo, el área geográfica ejerce una impronta significativa en los modelos de ingesta alimentaria. Así, se encontraron diferencias estadísticamente significativas en relación al consumo alimentario y por ende en el perfil nutricional. Los habitantes del Norte de España, específicamente los hombres, consumen más azúcares y alcohol que en las otras áreas analizadas. Estos resultados fueron similares a los encontrados en un reciente estudio que examinó la influencia del lugar de residencia en la alimentación española (Samaniego-Vaesken et al., 2018). Sin embargo y lejos de lo que esperábamos encontrar, los participantes reclutados en las áreas geográficas Este y Sur, principales regiones españolas exportadoras de frutas y aceite de oliva, registraron las ingestas más bajas de estos productos respectivamente. Curiosamente estos resultados son consistentes con los referidos por Alemán (Alemán et al., 2016) en un estudio publicado recientemente.

La adherencia a la Dieta Mediterránea medida a nivel global fue moderada. Sin embargo cuando se estratifica por área geográfica de residencia se comprueba que en el Área Este, específicamente entre los hombres de menor edad, apenas se alcanza una puntuación de 8 puntos sobre 17 en el cuestionario de adherencia, y aproximadamente la mitad de esta población se encuentra en el tercil más bajo de adherencia la Dieta Mediterránea. Probablemente influenciado por el hecho de que en este colectivo se registró la ingesta más baja de pescado y frutas.

También resultó llamativa la baja ingesta de hidratos de carbono totales, ligada al escaso consumo de cereales, verduras y frutas. Las diferencias en el perfil nutricional detectadas en función de la edad avalan el abandono progresivo de la Dieta Mediterránea reflejado por otros autores (Naska & Trichopoulou, 2014), más agudizado en algunas áreas geográficas españolas que en otras.

El área geográfica de residencia se comportó como un factor independiente asociado a la adecuación nutricional. Los patrones dietéticos de las diferentes áreas geográficas españolas están caracterizados por factores culturales, económicos y gastronómicos diversos, diferencias que se mantienen en todos los estratos de sexo y edad. Resultados equivalentes se han descrito en otros países, concretamente en mujeres norteamericanas, entre las que se ha demostrado que existen diferencias significativas en la ingesta dietética influenciadas por el ambiente y las costumbres alimentarias propias de cada región del país (Newby et al., 2012).

7.1.3. Influencia de la diversidad dietética en la inadecuación nutricional y factores asociados a esta variable

Aunque las guías dietéticas nacionales han promulgado los beneficios de la variedad dietética en la salud (Aranceta Bartrina et al., 2016), algunos estudios observacionales han asociado la diversidad dietética con el desarrollo de enfermedades crónicas como la obesidad y el Síndrome Metabólico (Azadbakht, Mirmiran, Esmaillzadeh, & Azizi, 2006; Karimbeiki et al., 2018; Kennedy,

2004) y una peor adecuación nutricional (Jayawardena et al., 2013). Sin embargo, estos estudios utilizaron poblaciones no europeas, distintas herramientas para medir la ingesta alimentaria y además la alimentación no fue ajustada por la ingesta energética total, por lo que los resultados de los citados estudios no son comparables a los nuestros. Así pues, una reciente revisión no sistemática concluyó en que "Es necesario definir qué es la diversidad dietética y el uso de herramientas estandarizadas para evaluarla" (de Oliveira Otto et al., 2018).

El índice de diversidad dietética utilizado se derivó del cuestionario de frecuencia alimentaria previamente validado para población española, utilizando la metodología propuesta por Kant et al. (Kant et al., 1993), con ligeras modificaciones, acordes a las recomendaciones propuestas por la *Sociedad Española de Nutrición Comunitaria* (Aranceta Bartrina et al., 2016). Los resultados nos permiten comprobar que la diversidad dietética se asocia positivamente con la ingesta adecuada de nutrientes, incluso después de ajustar por factores de confusión, realzando por tanto la necesidad de aconsejar el consumo de alimentos variados, específicamente en poblaciones de edades avanzadas (Foote, Murphy, Wilkens, Basiotis, & Carlson, 2004), en las que, por el contrario, la tendencia generalizada es a disminuir el espectro de alimentos consumidos. El análisis individualizado de los componentes de este índice de diversidad dietética, mostró que una mayor variedad de alimentos recomendados en cada grupo (verduras, frutas y productos lácteos) era capaz por sí mismo de disminuir el riesgo de presentar una ingesta inadecuada de nutrientes. Esto no pudo comprobarse para el grupo de cereales. Probablemente porque el grupo de cereales incluido en el análisis, no solo incluía cereales integrales, sino también cereales refinados y patatas.

El análisis de los factores asociados a la adopción de una dieta variada destacó nuevamente la ventaja del sexo (ser mujer). Este hallazgo, y en la misma dirección, también ha sido constatado por otros autores (Ochieng, Afari-Sefa, Lukumay, & Dubois, 2017). Respecto a la edad, ya se ha comentado anteriormente que la dieta de los mayores tiende a hacerse monótona, posiblemente por las características que acompañan el proceso de envejecimiento (soledad, pérdida de ingresos, limitación de movimientos y capacidades, etc.) y que condicionan la alimentación del individuos (Westenhoefer, 2005); no obstante no se encontraron diferencias por edad estadísticamente significativas, seguramente porque el porcentaje de participantes mayores de 70 años fue escaso. Otros factores como el estado civil y/o el vivir solo también se han asociado a una menor diversidad alimentaria, específicamente para la ingesta de frutas y verduras (Hanna & Collins, 2015; Vinther, Conklin, Wareham, & Monsivais, 2016).

Además de los factores mencionados anteriormente, bajos niveles educativos y económicos se relacionan con una menor diversidad dietética (Fukuda et al., 2017; Ochieng et al., 2017). Parece lógico pensar que los factores económicos podrían explicar el bajo consumo de alimentos que requieren una mayor inversión económica como es el caso de pescado, frutos secos, frutas y verduras en comparación con productos ultrapocesados que suelen ser más asequibles y accesibles (De Roos, Binacchi, Whybrow, & Sneddon, 2017). Paradójicamente y lejos de los resultados que se esperaban obtener, el nivel socioeconómico (medido a partir de la ocupación de los participantes) no mostró asociación significativa alguna. Hay que considerar que la mayoría de los participantes en el estudio PREDIMED-Plus tienen un nivel sociocultural y una capacidad económica media o media-baja, por lo que el espectro de diferencias en esta variable fue limitado. En este sentido destacó una asociación significativa entre nivel educativo bajo y mayor diversidad dietética. Las características de la cohorte estudiada pueden explicar este resultado, dado que en España, entre los años 40 y 50 del siglo pasado, las mujeres tuvieron un acceso a la educación secundaria y superior bastante limitado.

7.1.4. Efecto de la intervención dirigida a incrementar la adherencia a la Dieta Mediterránea sobre la Densidad Nutricional

Algunos estudios observacionales han examinado los cambios en la calidad de la dieta en población adulta (Casagrande & Cowie, 2017; De La Fuente-Arrillaga et al., 2016; Gose, Krems, Heuer, & Hoffmann, 2016), y son varios los autores que constatan una relación positiva entre la Dieta Mediterránea y la adecuación nutricional (Castro-Quezada, Román-Viñas, & Serra-Majem, 2014; Serra-Majem et al., 2009), sin embargo no tenemos constancia de que se haya evaluado esta asociación de forma prospectiva en una población de adultos mayores no institucionalizados.

Los mejores resultados en cuanto al incremento de la adherencia al patrón dietético mediterráneo se observaron entre los hombres y en la población más joven, entre los sujetos con menor nivel de actividad física y peores valores antropométricos, resultados en principio contrarios a los referidos en otros estudios llevados a cabo en población española (Agnoli et al., 2018; Vitale et al., 2019; Zazpe et al., 2010). A priori, los sujetos que presentan mejor adherencia a la Dieta Mediterránea al inicio del estudio son los que van a cambiar menos sus hábitos alimenticios, mientras que aquellos participantes con peores hábitos a nivel basal deberían ser los que con mayor frecuencia introducen mejoras en su ingesta alimentaria. Esto pudo comprobarse al estratificar por adherencia basal a la Dieta Mediterránea.

Los resultados obtenidos han confirmado la existencia de una asociación negativa entre el grado de adherencia a Dieta Mediterránea y la ingesta energética total, la densidad nutricional de ácidos grasos saturados e hidratos de carbono y positiva con la densidad nutricional del resto de nutrientes, específicamente vitaminas y minerales. Es decir, conforme la adherencia a la Dieta Mediterránea aumenta, se incrementa también la calidad nutricional, al mismo tiempo que disminuye el aporte de energía total. De acuerdo a esto, y considerando la elevada prevalencia de ingesta nutricional inadecuada encontrada en la población de adultos con sobrepeso u obesidad y Síndrome Metabólico (Cano-Ibáñez et al., 2019), la promoción de una alimentación basada en los preceptos tradicionales de la Dieta Mediterránea sería una solución factible y plausible para suavizar los déficits nutricionales y por ende atenuar las enfermedades no transmisibles relacionadas con una ingesta nutricional inadecuada (Salas-Salvadó et al., 2016).

Así mismo, los resultados incluidos en esta tesis avalan el efecto positivo de la participación en un ensayo comunitario de prevención primaria. Todos los participantes en este estudio obtuvieron algún beneficio nutricional derivado de su inclusión, independientemente del grupo de asignación dentro del estudio. Un metaanálisis centrado en el efecto sobre la salud de las mujeres en diferentes ensayos clínicos destacó igualmente los beneficios netos de dicha participación, independientemente del grupo de asignación de la participante (Nijjar et al., 2017). No obstante, hay que señalar que son los participantes asignados al grupo de intervención, aquellos que reciben un consejo nutricional intensivo, los que presentan los mayores incrementos de la densidad nutricional.

7.2. Limitaciones de la Tesis Doctoral

Este trabajo no está exento de limitaciones, que deben afrontarse, tanto para interpretar correctamente los resultados como para diseñar estrategias que permitan superarlas. Pueden ser agrupadas en grandes bloques:

- Extrapolación de los resultados obtenidos a la población general
- Factores asociados a la ingesta dietética no incluidos en los análisis
- Diseño del estudio
- Fuentes de información utilizadas para estimar la ingesta alimentaria
- Otros factores

7.2.1. Extrapolación de los resultados obtenidos a la población general

Debido a los criterios de inclusión de la población de estudio en el ensayo clínico PREDIMED-Plus, puede decirse que se trata de una población altamente seleccionada, ya que únicamente se incluyen adultos mayores con sobrepeso/obesidad y Síndrome Metabólico, sin otras patologías cardiovasculares, neurológicas o metabólicas. Se trata además de sujetos que aceptan participar en el estudio tras ser informados de sus objetivos, y que por tanto, en general, son conscientes de la necesidad de mejorar su alimentación y perder algo de peso. Es por ello, que la muestra analizada no es representativa de la población general, por lo que los resultados obtenidos deben interpretarse con cautela y no pueden extrapolarse a toda la población española. Sin embargo, el hecho de ser una cohorte de más de 6000 sujetos, reclutados en puntos muy distantes de la geografía española, y afectados por un problema de elevada prevalencia en nuestra población y enorme trascendencia, el Síndrome Metabólico, supone que la información recogida es altamente relevante para este grupo específico de población.

7.2.2. Factores asociados a la ingesta dietética no incluidos en los análisis

Aunque se han incluido los principales factores asociados a la ingesta dietética que la literatura científica sugiere, es probable que existan otros determinantes no evaluados en este estudio. Por ejemplo, el seguimiento cercano de nuestros participantes nos ha permitido comprobar cómo las habilidades culinarias influyen en el cumplimiento de los consejos nutricionales, o cómo la efectividad de la intervención aumenta cuando se cambian las dietas por recetas, con instrucciones claras de cómo preparar los diferentes platos recomendados.

Al tratarse de una población de edad avanzada, hay que valorar la prevalencia de otras enfermedades, y en particular el consumo de fármacos, que pueden inducir cambios en los hábitos dietéticos y en el metabolismo nutricional, factores que no han sido contemplados en los análisis realizados. No obstante, dada la homogeneidad de la población analizada, es presumible que tengan un efecto limitado.

Por otra parte, para algunas de las variables recogidas no se dispone de mediciones directas, sino sólo de variables “proxy”. Por ejemplo, para evaluar los factores socioeconómicos no se cuenta con datos sobre ingresos económicos, sino que se hace una estimación indirecta a partir del nivel educativo y el estatus ocupacional.

7.2.3. Diseño del estudio

A pesar de que trabajamos sobre la población seleccionada para un gran ensayo comunitario, los análisis realizados en los tres primeros artículos utilizan un diseño transversal. Epidemiológicamente, este diseño no permite inferir relaciones causales. Independientemente de la dirección de la asociación, los factores incluidos en el análisis poseen un gran potencial para mejorar la calidad de la dieta en población de semejantes características, permitiendo detectar grupos poblacionales de alto riesgo. En el cuarto artículo se ha podido acceder a datos longitudinales, con ello hemos podido consolidar algunas de las asociaciones detectadas previamente. En concreto, confirmar que la adherencia a la Dieta Mediterránea no sólo se asocia a una mejor calidad nutricional, sino que su aumento se acompaña de un incremento significativo en dicha calidad nutricional.

7.2.4. Fuentes de información utilizadas para estimar la ingesta alimentaria

Para la evaluación de la ingesta dietética, se utilizó un cuestionario de frecuencia alimentaria previamente validado para población española. Sin embargo, a pesar de que esta herramienta posee una adecuada reproducibilidad y validez, no es la herramienta más eficaz para medir déficits nutricionales. Por esta razón, y asumiendo que un cuestionario de frecuencia infraestima la ingesta de micronutrientes, se consideró que existía un aporte inadecuado de un nutriente dado solo cuando la ingesta estimada para dicho nutriente no alcanzaba al menos dos terceras partes de la ingesta dietética recomendada. De esta manera se pretendió corregir, al menos en parte, el posible sesgo introducido por el cuestionario. En cualquier caso, tanto este sesgo como el posible sesgo de memoria, son no diferenciales, al menos para los datos basales, recogidos antes de la aleatorización. Los cuestionarios de frecuencia cumplimentados al año de estudio pudieran estar afectados por un sesgo de observación diferencial, a pesar de ello podemos comprobar un beneficio neto de la intervención, manifestado en un incremento de la adherencia a la Dieta Mediterránea y de la densidad nutricional incluso en el grupo control. Estudios posteriores basados en marcadores bioquímicos de la dieta permitirán constatar o desmentir las asociaciones detectadas.

En relación a los índices de calidad de la dieta, tanto el índice de adherencia a la Dieta Mediterránea cómo el índice de diversidad dietética, estimados a partir del cuestionario de frecuencia de alimentos, e igualmente para la estimación de ingestas adecuadas de acuerdo a las referencias, hay que destacar su dependencia de la cantidad de alimentos consumida. Es por ello, que de acuerdo con las recomendaciones de los expertos en epidemiología nutricional (Willet, 2013), todos los análisis realizados están ajustados por consumo energético total.

7.2.5. Otros factores

Finalmente, debemos considerar las diferencias en los criterios de inclusión de participantes. Dado que la población de estudio se recluta para un ensayo de prevención primaria de enfermedad cardiovascular, es lógico entender que se pretenda seleccionar población de alto riesgo de enfermedad cardiovascular, y por tanto que existan diferencias en los criterios de edad aplicados a hombres y mujeres, así se incluyeron hombres de 55 a 75 años, y mujeres de 60-75 años. Estas diferencias por edad podrían explicar ligeramente las diferencias detectadas en la ingesta dietética. Para descartar o confirmar este argumento, en el primer artículo se realizó un análisis de sensibilidad excluyendo a la población de hombres de 55-59 años, sin que se observaran variaciones relevantes en los resultados originales.

En relación con la clasificación del área geográfica de residencia utilizada en el segundo artículo, es importante destacar que se basó en la localización del nodo que reclutaba al participante. En ningún momento se ha dispuesto de información sobre el origen geográfico del participante o sus posibles movimientos geográficos a lo largo de su historia vital. No obstante, es importante destacar que el flujo de migraciones internas en España ha sido bastante escaso en los últimos 20 años y que ha afectado principalmente a los grupos poblacionales más jóvenes (Arbucias, 2011).

7.3. Utilidad Práctica de los Resultados Obtenidos

Las cifras de obesidad en España se han duplicado en los últimos 40 años, de forma paralela aumenta la prevalencia de diabetes, hipertensión e hiperlipemia, la enfermedad cardiovascular continua siendo la primera causa de muerte y los problemas osteomusculares constituyen una de las primeras causas de perdida de salud y calidad de vida. La evidencia científica que apoya la importancia de un estilo de vida saludable (dieta sana, actividad física, evitar alcohol, no fumar, controlar el estrés) para la prevención primaria y secundaria de las enfermedades no transmisibles es cada día mayor y más fuerte. Los resultados discutidos ponen de manifiesto una vez más que la dieta de nuestra población ofrece muchas oportunidades de mejora, no sólo porque la ingesta es muy superior al gasto, sino fundamentalmente porque los alimentos que se están consumiendo no son los adecuados para lograr un buen equilibrio nutricional.

Somos plenamente conscientes de que los cambios en la dieta y los patrones de actividad son el resultado de cambios ambientales y sociales, asociados con el desarrollo, y favorecidos por la ausencia o la debilidad de políticas sanitarias, agrícolas, de transporte, planificación urbana, medioambientales, comerciales (procesamiento, distribución y publicidad de alimentos), y educativas. En Andalucía, el proyecto de Ley para la Promoción de una Vida Saludable y una Alimentación Equilibrada, anunciado como una estrategia rompedora y novedosa, a día de hoy no aún no ha sido ejecutado. Y aunque sin duda se han intentado hacer grandes esfuerzos en materia de legislación alimentaria e información al consumidor, por ejemplo con la implementación del *NutriScore*, las medidas legislativas han sido laxas, condicionadas por la posible disminución del consumo de ciertos alimentos, y los intereses económicos de la industria alimentaria. Así, asistimos con estupor a situaciones como las derivadas del Plan de Colaboración para la Mejora de la Composición de Alimentos y Bebidas y Otras Medidas 2020 (AECOSAN, 2018) que recoge los compromisos de reformulación de los sectores de la Fabricación y de la Distribución, para varios tipos de alimentos y bebidas de consumo habitual en las niños, jóvenes y familias y se centra en la reducción de azúcares añadidos, sal y grasas saturadas. A modo de ejemplo, una reducción del 5% en el contenido de sal de los productos de aperitivo, que supone pasar de 2.02 a 1.92 gramos por cada 100 gramos de producto, permitirá promocionar estos productos como "contenido reducido de sal". De la misma manera, una reducción del 5% en el contenido de azúcares de la bollería industrial implica para un dulce pasar de 39 a 37.1 gramos por cada 100 gramos de producto y con ello alegar "contenido reducido de azúcares". Estos ejemplos pueden inducir a pensar al consumidor que son saludables, a pesar de que los beneficios nutricionales son insignificantes.

Ante situaciones de este tipo, desde el sector sanitario, además de implantar medidas radicales, apoyadas en una evidencia científica clara y contundente, deben utilizarse una y otra vez los resultados de la investigación para exigir a los gobiernos, y a la industria alimentaria, un cambio en la orientación de las políticas de producción, distribución y comercialización de alimentos (Bes-Rastrollo & Ruiz-Canela, 2013), y concienciar a la población en general sobre la necesidad de controlar sus estilos de vida, evitando el consumo de productos de alimentación y transporte que poco a poco van minando la salud de igual o peor forma que el tabaco u otras drogas.

En este sentido es alentador el 1º Accésit en los premios de la Estrategia NAOS de 2019 logrado por el proyecto "Efecto de un programa de intervención del estilo de vida con Dieta Mediterránea restringida en energía y promoción del ejercicio físico sobre la pérdida de peso y los factores de riesgo cardiovascular: Resultados de un año del ensayo clínico PREDIMED-PLUS" a iniciativa de la Facultad de Medicina y Ciencias de la Salud. Universidad Rovira i Virgili (URV). Reus. Cataluña.

Los resultados que se presentan en esta Tesis Doctoral constituyen un empujón adicional en la lucha hercúlea contra los estilos de vida nocivos que impone la occidentalización de la vida diaria. No cabe la menor duda de que una ingesta dietética adecuada, equilibrada, variada y saludable es el mejor cimiento para lograr una vida plena. Esta premisa, válida a cualquier edad, es particularmente significativa en sujetos de edad avanzada, en los que no solo contribuye a la prevención primaria de enfermedades crónicas, sino que es fundamental para un control adecuado de dichas enfermedades y la prevención de sus complicaciones.

En este sentido, nuestros resultados permiten llamar la atención sobre el peligro de una dieta restrictiva, cuyos efectos directos serán disminuir aún más la diversidad de la dieta y el aporte de nutrientes. Por otra parte, nos permiten confirmar la repercusión positiva de una intervención dietética centrada en el fomento de la Dieta Mediterránea. Cuando se incrementa la adherencia a la Dieta Mediterránea mejora significativamente el aporte de macro y micronutrientes a pesar de que se reduce la ingesta calórica total.

De los resultados aquí presentados y discutidos se deriva la necesidad de diseñar y desarrollar estrategias nutricionales orientadas a mejorar la densidad nutricional de la dieta en la población con sobrepeso u obesidad. Las autoridades sanitarias deben asumir las riendas de la prevención primaria y poner los recursos necesarios para una actuación efectiva sobre la conducta alimentaria de nuestra población en lugar de focalizar todos los recursos en poner parches farmacológicos para controlar los efectos de una mala alimentación.

La selección de una población diana adecuada es fundamental para las estrategias centradas en la intervención directa sobre los individuos. De ahí la importancia de analizar las variables que identifican los grupos más vulnerables, sobre quienes se deben priorizar las intervenciones nutricionales. Finalmente, debemos destacar la necesidad de adaptar las estrategias de intervención a la idiosincrasia de cada una de las regiones españolas, partiendo de su entorno sociocultural y su antropología gastronómica, e identificando en cada caso los objetivos concretos sobre los que trabajar para conseguir una mejor adaptación a los preceptos generales de la Dieta Mediterránea.

7.4. Estrategias Futuras de Investigación

Cada pregunta a la que se contesta abre nuevos interrogantes. Tras una aproximación transversal que permitió caracterizar la situación de partida, hemos comprobado que la intervención nutricional permite aumentar la calidad de la dieta, mejorando el aporte de nutrientes y al mismo tiempo disminuyendo la ingesta calórica. El paso siguiente debe ser valorar si un aporte de nutrientes más acorde con las recomendaciones dietéticas realmente se relaciona con una evolución positiva de los marcadores bioquímicos y en definitiva del proceso de enfermar.

He tenido la fortuna de iniciar mi andadura en el mundo de la investigación en el seno del proyecto PREDIMED-Plus. Un proyecto ambicioso, con gran amplitud de miras, y que me ha puesto al alcance una cohorte de 6.874 pacientes, aleatorizada y controlada, y hasta la fecha seguida entre 3 y 5 años. A pesar de que son muchos y muy buenos los investigadores que trabajan sobre esta cohorte, son muchas más las respuestas que, gracias a la generosidad de nuestros participantes, esta gran muestra guarda para quién sepa hacer las preguntas adecuadas. Mi ambición es poner un granito de arena para hacer realidad esa frase atribuida a Thomas Alba Edison: “*El médico del futuro no tratará el cuerpo humano con medicamentos, más bien curará y prevendrá las enfermedades con la nutrición*.”

8. CONCLUSIONS/CONCLUSIONES

8. CONCLUSIONS

1. Adult Spanish with Metabolic Syndrome have a moderate adherence into Mediterranean Diet. However, they show a high prevalence of inadequate intake of several nutrients, particularly vitamin A, D, E, B_9 and calcium. The nutrient density intake is related to sex (higher for women). A better lifestyle (not smoking intake and practice of physical activity) is associated with raised nutrient density intake. The results found, stress the importance of focusing on nutritional education in those vulnerable population, taking into account the nutrients requirements.

2. Even within the same country, the place of residence was significantly associated with nutrients inadequacy intake. Aged adult dietary pattern leave room from improvement related to Mediterranean Diet adherence as well as to micronutrients intake. The effect of geographical area on diet quality should be taken into account when planning food policies.

3. Greater dietary diversity is directly associated with adequate nutrient intake even after adjustment for confounders such as sociodemographic and lifestyle variables. The food groups with higher contribution in the prevention of the nutritional inadequateness are vegetables and fruits. Our results focus on the promotion of a healthy varied diet, specifically promoting the intake of a variety of recommended foods, such as vegetables, fruit, cereals and dairy products. On the long time, the nutrient intake adequacy impacts on the prevention of chronic non-communicable diseases is very likely to play a crucial role from a public health perspective.

4. The Mediterranean Diet is an important factor linked to diet quality. As Mediterranean Diet adherence increases the nutrient density also does. This means that diet quality can be easily enhanced addressing simple dietary advice to improve Mediterranean Diet adherence. In other words, we can conclude that the PREDIMED-Plus dietary intervention, based on Mediterranean Diet recommendations for older adults, is a feasible strategy to improve nutrient density in Spanish population at high risk of cardiovascular disease with overweight or obesity

8. CONCLUSIONES

1. La población adulta Española con Síndrome metabólico tiene una adherencia a la Dieta Mediterránea moderada. A pesar de ello muestra una elevada prevalencia de ingesta deficiente de varios nutrientes, en particular Vitaminas A, D, E y B_9 y Calcio. La densidad de nutrientes en la dieta está relacionada con el sexo (mayor en mujeres). Un estilo de vida saludable (no fumar y realizar alguna actividad física) se asocia con mayor densidad nutricional. Los resultados obtenidos enfatizan la necesidad de centrar la educación nutricional en la población más vulnerable, teniendo siempre en cuenta los requerimientos nutricionales mínimos.

2. Incluso dentro del mismo país, el lugar de residencia influye significativamente sobre la ingesta deficiente de nutrientes. El patrón dietético de los adultos mayores tiene un amplio margen de mejora, relacionado tanto con el incremento de la adherencia a la Dieta Mediterránea como con la ingesta de micronutrientes. El efecto del área geográfica de residencia debe considerarse cuando se planifican las políticas alimentarias.

3. La diversidad de la dieta se asocia directamente con la ingesta adecuada de nutrientes, incluso tras ajustar por factores de confusión cómo variables sociodemográficas y otras relacionadas con el estilo de vida. Los grupos de alimentos con mayor contribución a la inadecuación nutricional son las verduras y frutas. Nuestros resultados alientan la promoción de una dieta saludable, específicamente promocionando la ingesta tan variada como sea posible de los alimentos recomendados: verduras, frutas, cereales integrales y lácteos. A largo plazo, y desde una perspectiva de salud pública, es más que probable que el impacto de la ingesta adecuada de nutrientes sobre la prevención de enfermedades crónicas transmisibles sea fundamental.

4. El patrón de Dieta Mediterránea está estrechamente vinculado a la calidad de la dieta. A medida que aumenta la adherencia a la Dieta Mediterránea aumenta también la densidad de nutrientes en la dieta. Esto significa que la calidad de la dieta puede mejorarse fácilmente mediante consejos dietéticos simples para mejorar la adherencia a la Dieta Mediterránea. En otras palabras, podemos concluir que la intervención nutricional del ensayo PREDIMED-Plus, basada en la Dieta Mediterránea, es una estrategia factible para mejorar la densidad nutricional de la población española con sobrepeso u obesidad, y alto riesgo de enfermedad Cardiovascular.

9. REFERENCIAS BIBLIOGRÁFICAS

9. REFERENCIAS BIBLIOGRÁFICAS

AECOSAN. (2018). Plan de Colaboración para la Mejora de la Composición de Alimentos y Bebidas y Otras Medidas 2020. Retrieved 7 June, 2019, from http://www.aecosan.msssi.gob.es/AECOSAN/docs/documentos/nutricion/PLAN_COLABORACION_2020.pdf

AESAN. (2017). ENIDE, Evaluación Nutricional de la Dieta Española. Retrieved 2 May, 2018, from http://www.cibr.es/ka/apps/cibr/docs/estudio-enide-1.pdf

Afshin, A., Sur, P. J., Fay, K. A., Cornaby, L., Ferrara, G., Salama, J. S., et al. (2019). Health effects of dietary risks in 195 countries, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. [Article]. *The Lancet, 393*(10184), 1958-1972.

Agarwal, S., Reider, C., Brooks, J. R., & Fulgoni, V. L. (2015). Comparison of Prevalence of Inadequate Nutrient Intake Based on Body Weight Status of Adults in the United States: An Analysis of NHANES 2001–2008. [Article]. *Journal of the American College of Nutrition, 34*(2), 126-134.

Agnoli, C., Sieri, S., Ricceri, F., Giraudo, M. T., Masala, G., Assedi, M., et al. (2018). Adherence to a Mediterranean diet and long-term changes in weight and waist circumference in the EPIC-Italy cohort. [Article]. *Nutrition and Diabetes, 8*(1).

Alberti, K. G. M. M., Eckel, R. H., Grundy, S. M., Zimmet, P. Z., Cleeman, J. I., Donato, K. A., et al. (2009). 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 atherosclerosis society; And international association for the study of obesity. [Review]. *Circulation, 120*(16), 1640-1645.

Alberti, K. G. M. M., Zimmet, P., & Shaw, J. (2005). The metabolic syndrome - A new worldwide definition. [Note]. *Lancet, 366*(9491), 1059-1062.

Alemán, J. A., Rentero, M. P. Z., Montoro-García, S., Mulero, J., Garrido, A. P., Leal, M., et al. (2016). Adherence to the "Mediterranean diet" in Spain and its relationship with cardiovascular risk (DIMERICA study). [Article]. *Nutrients, 8*(11).

Alkerwi, A., Baydarlioglu, B., Sauvageot, N., Stranges, S., Lemmens, P., Shivappa, N., et al. (2017). Smoking status is inversely associated with overall diet quality: Findings from the ORISCAV-LUX study. [Article]. *Clinical Nutrition, 36*(5), 1275-1282.

Andreeva, V. A., Allès, B., Feron, G., Gonzalez, R., Sulmont-Rossé, C., Galan, P., et al. (2016). Sex-specific sociodemographic correlates of dietary patterns in a large sample of French elderly individuals. [Article]. *Nutrients, 8*(8).

Aranceta Bartrina, J., Arija Val, V. V., Maíz Aldalur, E., Martínez de Victoria Muñoz, E., Ortega Anta, R. M., Pérez-Rodrigo, C., et al. (2016). Dietary Guidelines for the Spanish population (SENC, diciembre 2016); the new graphic icon of healthy food. [Article]. *Nutricion hospitalaria, 33*, 1-48.

Aranceta, J., Serra-Majem, L., Pérez-Rodrigo, C., Llopis, J., Mataix, J., Ribas, L., et al. (2001). Vitamins in Spanish food patterns: The eVe study. [Article]. *Public Health Nutrition, 4*(6A), 1317-1323.

Arbucias, J. S. (2011). The evolution of internal migration in Spain: An assessment of available demographic sources. [Review]. *Papers, 96*(3), 853-881.

Atkins, J. L., Ramsay, S. E., Whincup, P. H., Morris, R. W., Lennon, L. T., & Wannamethee, S. G. (2015). Diet quality in older age: The influence of childhood and adult socio-economic circumstances. [Article]. *British Journal of Nutrition, 113*(9), 1441-1452.

Azadbakht, L., Mirmiran, P., Esmaillzadeh, A., & Azizi, F. (2006). Dietary diversity score and cardiovascular risk factors in Tehranian adults. [Article]. *Public Health Nutrition, 9*(6), 728-736.

Bamia, C., Trichopoulos, D., Ferrari, P., Overvad, K., Bjerregaard, L., Tjønneland, A., et al. (2007). Dietary patterns and survival of older Europeans: The EPIC-Elderly Study (European Prospective Investigation into Cancer and Nutrition). [Article]. *Public Health Nutrition, 10*(6), 590-598.

Beaglehole, R., Epping-Jordan, J., Patel, V., Chopra, M., Ebrahim, S., Kidd, M., et al. (2008). Improving the prevention and management of chronic disease in low-income and middle-income countries: a priority for primary health care. [Review]. *The Lancet, 372*(9642), 940-949.

Beaglehole, R., & Yach, D. (2003). Globalisation and the prevention and control of non-communicable disease: The neglected chronic diseases of adults. [Article]. *Lancet, 362*(9387), 903-908.

Benhammou, S., Heras-González, L., Ibáñez-Peinado, D., Barceló, C., Hamdan, M., Rivas, A., et al. (2016). Comparison of Mediterranean diet compliance between European and non-European populations in the Mediterranean basin. [Article]. *Appetite, 107*, 521-526.

Benjamin, E. J., Blaha, M. J., Chiuve, S. E., Cushman, M., Das, S. R., Deo, R., et al. (2017). Heart Disease and Stroke Statistics'2017 Update: A Report from the American Heart Association. [Review]. *Circulation, 135*(10), e146-e603.

Bes-Rastrollo, M., & Ruiz-Canela, M. (2013). Regulation and the food industry. *The Lancet, 381*(9881), 1902.

Bloom, D. E., Cafiero, E. T., & Jané-Llopis, E. (2011). *The Global Economic Burden of Non-communicable Diseases*.

Blüher, M. (2019). Obesity: global epidemiology and pathogenesis. [Review]. *Nature Reviews Endocrinology, 15*(5), 288-298.

Cano-Ibáñez, N., Gea, A., Ruiz-Canela, M., Corella, D., Salas-Salvadó, J., Schröeder, H., et al. (2019). Diet quality and nutrient density in subjects with metabolic syndrome: influence of socioeconomic status and lifestyle factors. A cross-sectional assessment in the PREDIMED-Plus study. *Clinical Nutrition*.

Carlos, S., De La Fuente-Arrillaga, C., Bes-Rastrollo, M., Razquin, C., Rico-Campà, A., Martínez-González, M. A., et al. (2018). Mediterranean diet and health outcomes in the SUN cohort. [Article]. *Nutrients, 10*(4).

Casagrande, S. S., & Cowie, C. C. (2017). Trends in dietary intake among adults with type 2 diabetes: NHANES 1988–2012. [Article]. *Journal of Human Nutrition and Dietetics, 30*(4), 479-489.

Castro-Quezada, I., Román-Viñas, B., & Serra-Majem, L. (2014). The mediterranean diet and nutritional adequacy: A review. [Review]. *Nutrients, 6*(1), 231-248.

Charlton, K. E. (1999). Elderly men living alone: Are they at high nutritional risk? [Article]. *Journal of Nutrition, Health and Aging, 3*(1), 46-47.

Conklin, A. I., Forouhi, N. G., Surtees, P., Wareham, N. J., & Monsivais, P. (2015). Gender and the double burden of economic and social disadvantages on healthy eating: Cross-sectional study of older adults in the EPIC-Norfolk cohort. [Article]. *BMC Public Health, 15*(1).

de Freitas, T. I., Previdelli, Á. N., Ferreira, M. P. N., Marques, K. M., Goulart, R. M. M., & de Aquino, R. C. (2017). Factors associated with diet quality of older adults. [Article]. *Revista de Nutricao, 30*(3), 297-306.

De Groot, L. C. P. M. G., Verheijden, M. W., De Henauw, S., Schroll, M., & Van Staveren, W. A. (2004). Lifestyle, nutritional status, health, and mortality in elderly people across Europe: A review of the longitudinal results of the SENECA study. [Review]. *Journals of Gerontology - Series A Biological Sciences and Medical Sciences, 59*(12), 1277-1284.

De La Fuente-Arrillaga, C., Zazpe, I., Santiago, S., Bes-Rastrollo, M., Ruiz-Canela, M., Gea, A., et al. (2016). Beneficial changes in food consumption and nutrient intake after 10 years of follow-up in a Mediterranean cohort: The SUN project. [Article]. *BMC Public Health, 16*(1).

de Oliveira Otto, M. C., Anderson, C. A. M., Dearborn, J. L., Ferranti, E. P., Mozaffarian, D., Rao, G., et al. (2018). Dietary Diversity: Implications for Obesity Prevention in Adult Populations: A Science Advisory From the American Heart Association. [Article]. *Circulation, 138*(11), e160-e168.

De Onis, M., & Habicht, J. P. (1996). Anthropometric reference data for international use: Recommendations from a World Health Organization Expert Committee. [Article]. *American Journal of Clinical Nutrition, 64*(4), 650-658.

De Roos, B., Binacchi, F., Whybrow, S., & Sneddon, A. A. (2017). Differences in expenditure and amounts of fresh foods, fruits and vegetables, and fish purchased in urban and rural Scotland. [Article]. *Public Health Nutrition, 20*(3), 524-533.

Dean, M., Raats, M. M., Grunert, K. G., & Lumbers, M. (2009). Factors influencing eating a varied diet in old age. [Article]. *Public Health Nutrition, 12*(12), 2421-2427.

Deierlein, A. L., Morland, K. B., Scanlin, K., Wong, S., & Spark, A. (2014). Diet Quality of Urban Older Adults Age 60 to 99 Years: The Cardiovascular Health of Seniors and Built Environment Study. [Article]. *Journal of the Academy of Nutrition and Dietetics, 114*(2), 279-187.

Dent, E., Hoogendijk, E. O., & Wright, O. R. L. (2019). New insights into the anorexia of ageing: from prevention to treatment. [Article]. *Current opinion in clinical nutrition and metabolic care, 22*(1), 44-51.

Doyle, I. M., Borrmann, B., Grosser, A., Razum, O., & Spallek, J. (2017). Determinants of dietary patterns and diet quality during pregnancy: A systematic review with narrative synthesis. [Review]. *Public Health Nutrition, 20*(6), 1009-1028.

Drewnowski, A. (2018). Nutrient density: Addressing the challenge of obesity. [Article]. *British Journal of Nutrition, 120*(s1), S8-S14.

EFSA. (2018). Dietary Reference Values and Dietary Guidelines. Retrieved 1 October 2018, from https://www.efsa.europa.eu/en/topics/topic/dietary-reference-values

Elosua, R., Garcia, M., Aguilar, A., Molina, L., Covas, M. I., & Marrugat, J. (2000). Validation of the Minnesota leisure time physical activity questionnaire in Spanish women. [Article]. *Medicine and Science in Sports and Exercise, 32*(8), 1431-1437.

Elosua, R., Marrugat, J., Molina, L., Pons, S., & Pujol, E. (1994). Validation of the minnesota leisure time physical activity questionnaire in Spanish men. [Article]. *American Journal of Epidemiology, 139*(12), 1197-1209.

Estruch, R., Ros, E., Salas-Salvadó, J., Covas, M.-I., Corella, D., Arós, F., et al. (2013). Primary Prevention of Cardiovascular Disease with a Mediterranean Diet. *New England Journal of Medicine, 368*(14), 1279-1290.

Eveleth, P. B., Andres, R., Chumlea, W. C., Eiben, O., Ge, K., Harris, T., et al. (1998). Uses and interpretation of anthropometry in the elderly for the assessment of physical status report to the Nutrition Unit of the World Health Organization: The expert subcommittee on the use and interpretation of anthropometry in the elderly. [Article]. *Journal of Nutrition, Health and Aging, 2*(1), 5-17.

Fekete, C., & Weyers, S. (2016). Social inequalities in nutrition: Evidence, causes and interventions. [Article]. *Bundesgesundheitsblatt - Gesundheitsforschung - Gesundheitsschutz, 59*(2), 197-205.

Fernández-Ballart, J. D., Piñol, J. L., Zazpe, I., Corella, D., Carrasco, P., Toledo, E., et al. (2010). Relative validity of a semi-quantitative food-frequency questionnaire in an elderly Mediterranean population of Spain. [Article]. *British Journal of Nutrition, 103*(12), 1808-1816.

Foote, J. A., Murphy, S. P., Wilkens, L. R., Basiotis, P. P., & Carlson, A. (2004). Dietary variety increases the probability of nutrient adequacy among adults. [Article]. *Journal of Nutrition, 134*(7), 1779-1785.

Forouzanfar, M. H., Alexander, L., Bachman, V. F., Biryukov, S., Brauer, M., Casey, D., et al. (2015). Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990-2013: A systematic analysis for the Global Burden of Disease Study 2013. [Review]. *The Lancet, 386*(10010), 2287-2323.

Freisling, H., Knaze, V., & Slimani, N. (2013). A systematic review of peer-reviewed studies on diet quality indexes applied to old age: A multitude of predictors of diet quality *Diet Quality: An Evidence-Based Approach* (Vol. 2, pp. 365-381).

Fukuda, Y., Ishikawa, M., Yokoyama, T., Hayashi, T., Nakaya, T., Takemi, Y., et al. (2017). Physical and social determinants of dietary variety among older adults living alone in Japan. [Article]. *Geriatrics and Gerontology International, 17*(11), 2232-2238.

Fullman, N., Barber, R. M., Abajobir, A. A., Abate, K. H., Abbafati, C., Abbas, K. M., et al. (2017). Measuring progress and projecting attainment on the basis of past trends of the health-related Sustainable Development Goals in 188 countries: An analysis from the Global Burden of Disease Study 2016. [Article]. *The Lancet, 390*(10100), 1423-1459.

Gabhainn, S. N., Nolan, G., Kelleher, C., & Friel, S. (2002). Dieting patterns and related lifestyles of school-aged children in the Republic of Ireland. [Article]. *Public Health Nutrition, 5*(3), 457-462.

Gillum, R. F., & Sempos, C. T. (2005). Ethnic variation in validity of classification of overweight and obesity using self-reported weight and height in American women and men: The Third National Health and Nutrition Examination Survey. [Article]. *Nutrition Journal, 4*.

Goncalves, A., & Amiot, M. J. (2017). Fat-soluble micronutrients and metabolic syndrome. [Review]. *Current Opinion in Clinical Nutrition and Metabolic Care, 20*(6), 492-497.

Gose, M., Krems, C., Heuer, T., & Hoffmann, I. (2016). Trends in food consumption and nutrient intake in Germany between 2006 and 2012: Results of the German National Nutrition Monitoring (NEMONIT). [Article]. *British Journal of Nutrition, 115*(8), 1498-1507.

Grundy, S. M., Cleeman, J. I., Daniels, S. R., Donato, K. A., Eckel, R. H., Franklin, B. A., et al. (2005). Diagnosis and management of the metabolic syndrome: An American Heart Association/National Heart, Lung, and Blood Institute scientific statement. [Review]. *Circulation, 112*(17), 2735-2752.

Guasch-Ferré, M., Babio, N., Martínez-González, M. A., Corella, D., Ros, E., Martín-Peláez, S., et al. (2015). Dietary fat intake and risk of cardiovascular disease and all-cause mortality in a population at high risk of cardiovascular disease. [Article]. *American Journal of Clinical Nutrition, 102*(6), 1563-1573.

Guasch-Ferré, M., Merino, J., Sun, Q., Fitó, M., & Salas-Salvadó, J. (2017). Dietary Polyphenols, Mediterranean Diet, Prediabetes, and Type 2 Diabetes: A Narrative Review of the Evidence. [Review]. *Oxidative Medicine and Cellular Longevity, 2017*.

Guilbert, J. J. (2003). The world health report 2002 - reducing risks, promoting healthy life. *Educ Health (Abingdon), 16*.

Hanna, K. L., & Collins, P. F. (2015). Relationship between living alone and food and nutrient intake. [Article]. *Nutrition Reviews, 73*(9), 594-611.

Haro, J. M., Tyrovolas, S., Garin, N., Diaz-Torne, C., Carmona, L., Sanchez-Riera, L., et al. (2014). The burden of disease in Spain: Results from the global burden of disease study 2010. [Article]. *BMC Medicine, 12*(1).

Health, N. I. o. (2018). Nutrient Recommendations: Dietary Reference Intakes (DRI). Retrieved 24 October, 2018, 2018, from https://ods.od.nih.gov/Health_Information/Dietary_Reference_Intakes.aspx

Hiza, H. A. B., Casavale, K. O., Guenther, P. M., & Davis, C. A. (2013). Diet Quality of Americans Differs by Age, Sex, Race/Ethnicity, Income, and Education Level. [Article]. *Journal of the Academy of Nutrition and Dietetics, 113*(2), 297-306.

Hosseinpour Niazi, S., Mirmiran, P., Sohrab, G., Hosseini Esfahani, F., & Azizi, F. (2012). Association between dietary fiber intake and metabolic syndrome: Tehran lipid and glucose study. [Article]. *Iranian Journal of Epidemiology, 7*(4), 19-28.

Hruby, A., & Hu, F. B. (2015). The Epidemiology of Obesity: A Big Picture. [Review]. *PharmacoEconomics, 33*(7), 673-689.

Hsiao, P. Y., Mitchell, D. C., Coffman, D. L., Allman, R. M., Locher, J. L., Sawyer, P., et al. (2013). Dietary patterns and diet quality among diverse older adults: The university of Alabama at Birmingham study of aging. [Article]. *Journal of Nutrition, Health and Aging, 17*(1), 19-25.

Hu, F. B. (2002). Dietary pattern analysis: A new direction in nutritional epidemiology. [Review]. *Current Opinion in Lipidology, 13*(1), 3-9.

Hu, F. B. (2011). Globalization of diabetes: The role of diet, lifestyle, and genes. [Conference Paper]. *Diabetes Care, 34*(6), 1249-1257.

IOM. Nutrient Recommendations: Dietary Reference Intakes. Retrieved 4 May, 2018, from https://ods.od.nih.gov/Health_Information/Dietary_Reference_Intakes.aspx

Jayawardena, R., Byrne, N. M., Soares, M. J., Katulanda, P., Yadav, B., & Hills, A. P. (2013). High dietary diversity is associated with obesity in Sri Lankan adults: An evaluation of three dietary scores. [Article]. *BMC Public Health, 13*(1).

Jenkins, D. J. A., Spence, J. D., Giovannucci, E. L., Kim, Y. I., Josse, R., Vieth, R., et al. (2018). Supplemental Vitamins and Minerals for CVD Prevention and Treatment. [Review]. *Journal of the American College of Cardiology, 71*(22), 2570-2584.

Kant, A. K., Schatzkin, A., Harris, T. B., Ziegler, R. G., & Block, G. (1993). Dietary diversity and subsequent mortality in the First National Health and Nutrition Examination Survey Epidemiologic Follow-up Study. [Article]. *American Journal of Clinical Nutrition, 57*(3), 434-440.

Karimbeiki, R., Pourmasoumi, M., Feizi, A., Abbasi, B., Hadi, A., Rafie, N., et al. (2018). Higher dietary diversity score is associated with obesity: a case–control study. [Article]. *Public Health, 157*, 127-134.

Kehoe, L., Walton, J., & Flynn, A. (2019). Nutritional challenges for older adults in Europe: Current status and future directions. [Conference Paper]. *Proceedings of the Nutrition Society, 78*(2), 221-233.

Kennedy, E. (2004). Dietary diversity, diet quality, and body weight regulation. [Conference Paper]. *Nutrition Reviews, 62*(7 II), S78-S81.

Keys, A., Aravanis, C., Blackburn, H. W., Van Buchem, F. S., Buzina, R., Djordjević, B. D., et al. (1966). Epidemiological studies related to coronary heart disease: characteristics of men aged 40-59 in seven countries. [Article]. *Acta Medica Scandinavica, Supplement, 460*, 1-392.

Kiefer, I., Rathmanner, T., & Kunze, M. (2005). Eating and dieting differences in men and women. [Review]. *Journal of Men's Health and Gender, 2*(2), 194-201.

Kimokoti, R. W., & Millen, B. E. (2016). Nutrition for the Prevention of Chronic Diseases. [Review]. *Medical Clinics of North America, 100*(6), 1185-1198.

Lalonde, M. (1974). *A New Perspective on the Health of Canadians*.

Lammes, E., Törner, A., & Akner, G. (2009). Nutrient density and variation in nutrient intake with changing energy intake in multimorbid nursing home residents. [Article]. *Journal of Human Nutrition and Dietetics, 22*(3), 210-218.

León-Muñoz, L. M., Guallar-Castillón, P., Graciani, A., López-García, E., Mesas, A. E., Aguilera, M. T., et al. (2012). Adherence to the mediterranean diet pattern has declined in Spanish adults. [Article]. *Journal of Nutrition, 142*(10), 1843-1850.

Lozano, R., Fullman, N., Abate, D., Abay, S. M., Abbafati, C., Abbasi, N., et al. (2018). Measuring progress from 1990 to 2017 and projecting attainment to 2030 of the health-related Sustainable Development Goals for 195 countries and territories: a systematic analysis for the Global Burden of Disease Study 2017. [Article]. *The Lancet*, 2091-2138.

Malik, V. S., Willett, W. C., & Hu, F. B. (2013). Global obesity: Trends, risk factors and policy implications. [Review]. *Nature Reviews Endocrinology, 9*(1), 13-27.

MAPAMA. (2018). Informe de Consumo Alimentario en España. Retrieved 10 May, 2018, from https://www.mapa.gob.es/es/alimentacion/temas/consumo-y-comercializacion-y-distribucion-alimentaria/panel-de-consumo-alimentario/ultimos-datos/

Martinez-Gonzalez, M. A., Corella, D., Salas-Salvado, J., Ros, E., Covas, M. I., Fiol, M., et al. (2012). Cohort profile: design and methods of the PREDIMED study. *Int J Epidemiol, 41*(2), 377-385.

Martinez-Gonzalez, M. A., Garcia-Arellano, A., Toledo, E., Salas-Salvado, J., Buil-Cosiales, P., Corella, D., et al. (2012). A 14-item Mediterranean diet assessment tool and obesity indexes among high-risk subjects: the PREDIMED trial. *PLoS One, 7*(8), e43134.

Martínez Cía, N., Pérez Pérez, M., Heras-Mosteiro, J., Gutiérrez Ávila, G., Díaz-Olalla, J. M., & Ruiz-Giménez Aguilar, J. L. (2018). Agreements and disagreements between community health and the Spanish health system. SESPAS Report 2018. [Short Survey]. *Gaceta Sanitaria, 32*, 17-21.

Martínez-González, M. A., Buil-Cosiales, P., Corella, D., Bulló, M., Fitó, M., Vioque, J., et al. (2018). Cohort Profile: Design and methods of the PREDIMED-Plus randomized trial. *International Journal of Epidemiology*, dyy225-dyy225.

Martínez-González, M. A., Salas-Salvadó, J., Estruch, R., Corella, D., Fitó, M., & Ros, E. (2015). Benefits of the Mediterranean Diet: Insights From the PREDIMED Study. [Article]. *Progress in Cardiovascular Diseases, 58*(1), 50-60.

Martínez-González, M. Á., Hershey, M. S., Zazpe, I., & Trichopoulou, A. (2017). Transferability of the Mediterranean diet to non-Mediterranean countries. What is and what is not the Mediterranean diet. [Article]. *Nutrients, 9*(11).

Mayén, A. L., Stringhini, S., Ford, N. D., Martorell, R., Stein, A. D., Paccaud, F., et al. (2016). Socioeconomic predictors of dietary patterns among Guatemalan adults. [Article]. *International Journal of Public Health, 61*(9), 1069-1077.

Medina-Remón, A., Casas, R., Tressserra-Rimbau, A., Ros, E., Martínez-González, M. A., Fitó, M., et al. (2016). Polyphenol intake from a Mediterranean diet decreases inflammatory biomarkers related to atherosclerosis: A substudy of the PREDIMED trial. *British Journal of Clinical Pharmacology*.

Mendonça, R. D., Carvalho, N. C., Martin-Moreno, J. M., Pimenta, A. M., Lopes, A. C. S., Gea, A., et al. (2019). Total polyphenol intake, polyphenol subtypes and incidence of cardiovascular disease: The SUN cohort study. *Nutrition, Metabolism and Cardiovascular Diseases, 29*(1), 69-78.

Mensink, G. B. M., Fletcher, R., Gurinovic, M., Huybrechts, I., Lafay, L., Serra-Majem, L., et al. (2013). Mapping low intake of micronutrients across Europe. *British Journal of Nutrition, 110*(4), 755-773.

Moore-Schiltz, L., Albert, J. M., Singer, M. E., Swain, J., & Nock, N. L. (2015). Dietary intake of calcium and magnesium and the metabolic syndrome in the National Health and Nutrition Examination (NHANES) 2001-2010 data. [Article]. *British Journal of Nutrition, 114*(6), 924-935.

Moreiras, O., Carbajal, A., Cabrera, L., & Cuadrado, C. (2013). Tablas de composición

de alimentos/Guía de Prácticas (16th Edition ed.). Madrid: Edici ones Pirámide

Moreno, L. A., Sarría, A., & Popkin, B. M. (2002). The nutrition transition in Spain: A European Mediterranean country. [Article]. *European Journal of Clinical Nutrition, 56*(10), 992-1003.

Muka, T., Imo, D., Jaspers, L., Colpani, V., Chaker, L., van der Lee, S. J., et al. (2015). The global impact of non-communicable diseases on healthcare spending and national income: a systematic review. [Review]. *European Journal of Epidemiology, 30*(4), 251-277.

Murphy, S. P., Foote, J. A., Wilkens, L. R., Basiotis, P. P., Carlson, A., White, K. K. L., et al. (2006). Simple measures of dietary variety are associated with improved dietary quality. [Article]. *Journal of the American Dietetic Association, 106*(3), 425-429.

Murphy, S. P., & Poos, M. I. (2002). Dietary reference intakes: Summary of applications in dietary assessment. [Conference Paper]. *Public Health Nutrition, 5*(6 A), 843-849.

Murray, C. J. L., & Lopez, A. D. (2013). Measuring the global burden of disease. [Review]. *New England Journal of Medicine, 369*(5), 448-457.

Naska, A., & Trichopoulou, A. (2014). Back to the future: The Mediterranean diet paradigm. [Short Survey]. *Nutrition, Metabolism and Cardiovascular Diseases, 24*(3), 216-219.

Newby, P. K., Noel, S. E., Grant, R., Judd, S., Shikany, J. M., & Ard, J. (2012). Race and region have independent and synergistic effects on dietary intakes in black and white women. [Article]. *Nutrition Journal, 11*(1).

Nicklas, T. A., Drewnowski, A., & O'Neil, C. E. (2013). The nutrient density approach to healthy eating: Challenges and opportunities. [Review]. *Public Health Nutrition, 17*(12), 2626-2636.

Nijjar, S. K., D'Amico, M. I., Wimalaweera, N. A., Cooper, N. A. M., Zamora, J., & Khan, K. S. (2017). Participation in clinical trials improves outcomes in women's health: a systematic review and meta-analysis. [Review]. *BJOG: An International Journal of Obstetrics and Gynaecology, 124*(6), 863-871.

Nishtar, S., Niinistö, S., Sirisena, M., Vázquez, T., Skvortsova, V., Rubinstein, A., et al. (2018). Time to deliver: report of the WHO Independent High-Level Commission on NCDs. [Review]. *The Lancet, 392*(10143), 245-252.

Oberlander, L., Disdier, A. C., & Etilé, F. (2017). Globalisation and national trends in nutrition and health: A grouped fixed-effects approach to intercountry heterogeneity. [Article]. *Health Economics (United Kingdom), 26*(9), 1146-1161.

Ochieng, J., Afari-Sefa, V., Lukumay, P. J., & Dubois, T. (2017). Determinants of dietary diversity and the potential role of men in improving household nutrition in Tanzania. [Article]. *PLoS ONE, 12*(12).

Passi, S. J. (2017). Prevention of non-communicable diseases by balanced nutrition: Population-specific effective public health approaches in developing Countries. [Review]. *Current Diabetes Reviews, 13*(5), 461-476.

Peng, W., Berry, E. M., & Goldsmith, R. (2019). Adherence to the Mediterranean diet was positively associated with micronutrient adequacy and negatively associated with dietary energy density among adolescents. [Article]. *Journal of Human Nutrition and Dietetics, 32*(1), 41-52.

Ramos, P., Brooks, F., García-Moya, I., Rivera, F., & Moreno, C. (2013). Eating habits and physical activity in dieter and non-dieter youth: A gender analysis of English and Spanish adolescents. [Article]. *Social Science Journal, 50*(4), 575-582.

Ruiz, E., Ávila, J. M., Valero, T., del Pozo, S., Rodriguez, P., Aranceta-Bartrina, J., et al. (2016). Macronutrient distribution and dietary sources in the spanish population: Findings from the ANIBES study. [Article]. *Nutrients, 8*(3).

Ruiz, E., Ávila, J. M., Valero, T., Pozo, S. D., Rodriguez, P., Aranceta-Bartrina, J., et al. (2015). Energy intake, profile, and dietary sources in the spanish population: Findings of the ANIBES study. [Article]. *Nutrients, 7*(6), 4739-4762.

Salas-Salvadó, J., Becerra-Tomás, N., García-Gavilán, J. F., Bulló, M., & Barrubés, L. (2018). Mediterranean Diet and Cardiovascular Disease Prevention: What Do We Know? [Review]. *Progress in Cardiovascular Diseases, 61*(1), 62-67.

Salas-Salvadó, J., Fernández-Ballart, J., Ros, E., Martínez-González, M. A., Fitó, M., Estruch, R., et al. (2008). Effect of a Mediterranean diet supplemented with nuts on metabolic syndrome status: One-year results of the PREDIMED randomized trial. [Article]. *Archives of Internal Medicine, 168*(22), 2449-2458.

Salas-Salvadó, J., Guasch-Ferré, M., Lee, C. H., Estruch, R., Clish, C. B., & Ros, E. (2016). Protective effects of the mediterranean diet on type 2 diabetes and metabolic syndrome. [Article]. *Journal of Nutrition, 146*(4), 920S-927S.

Samaniego-Vaesken, M. L., Partearroyo, T., Ruiz, E., Aranceta-Bartrina, J., Gil, Á., González-Gross, M., et al. (2018). The influence of place of residence, gender and age influence on food group choices in the Spanish population: Findings from the ANIBES study. [Article]. *Nutrients, 10*(4).

Samieri, C. (2018) Epidemiology and risk factors of Alzheimer's disease: A focus on diet. *Vol. 137. Neuromethods* (pp. 15-42).

Sauerland, S., Angrisani, L., Belachew, M., Chevallier, J. M., Favretti, F., Finer, N., et al. (2005). Obesity surgery: Evidence-based guidelines of the European Association for Endoscopic Surgery (E.A.E.S.). [Article]. *Surgical Endoscopy and Other Interventional Techniques, 19*(2), 200-221.

Schneider, E. L., & Guralnik, J. M. (1990). The Aging of America: Impact on Health Care Costs. [Article]. *JAMA: The Journal of the American Medical Association, 263*(17), 2335-2340.

Schoufour, J. D., de Jonge, E. A. L., Kiefte-de Jong, J. C., van Lenthe, F. J., Hofman, A., Nunn, S. P. T., et al. (2018). Socio-economic indicators and diet quality in an older population. [Article]. *Maturitas, 107*, 71-77.

Schröder, H., Marrugat, J., Covas, M., Elosua, R., Pena, A., Weinbrenner, T., et al. (2004). Population dietary habits and physical activity modification with age. [Article]. *European Journal of Clinical Nutrition, 58*(2), 302-311.

Schröder, H., Vila, J., Marrugat, J., & Covas, M. I. (2008). Low energy density diets are associated with favorable nutrient intake profile and adequacy in free-living elderly men and women. [Article]. *Journal of Nutrition, 138*(8), 1476-1481.

Schulze, M. B., Hoffmann, K., Kroke, A., & Boeing, H. (2003). An approach to construct simplified measures of dietary patterns from exploratory factor analysis. *British Journal of Nutrition, 89*(3), 409-418.

Serra-Majem, L., Bes-Rastrollo, M., Román-Viñas, B., Pfrimer, K., Sánchez-Villegas, A., & Martínez-González, M. A. (2009). Dietary patterns and nutritional adequacy in a Mediterranean country. *British Journal of Nutrition, 101*(S2), S21-S28.

Shatenstein, B., Gauvin, L., Keller, H., Richard, L., Gaudreau, P., Giroux, F., et al. (2016). Individual and collective factors predicting change in diet quality over 3 years in a subset of older men and women from the NuAge cohort. *European Journal of Nutrition, 55*(4), 1671-1681.

Ter Borg, S., Verlaan, S., Mijnarends, D. M., Schols, J. M. G. A., De Groot, L. C. P. G. M., & Luiking, Y. C. (2015). Macronutrient Intake and Inadequacies of Community-Dwelling Older Adults, a Systematic Review. [Review]. *Annals of Nutrition and Metabolism, 66*(4), 242-255.

Tian, X., Xu, X., Zhang, K., & Wang, H. (2017). Gender difference of metabolic syndrome and its association with dietary diversity at different ages. [Article]. *Oncotarget, 8*(43), 73568-73578.

Toffanello, E. D., Inelmen, E. M., Minicuci, N., Campigotto, F., Sergi, G., Coin, A., et al. (2011). Ten-year trends in vitamin intake in free-living healthy elderly people: The risk of subclinical malnutrition. [Article]. *Journal of Nutrition, Health and Aging, 15*(2), 99-103.

Toledo, E., Salas-Salvado, J., Donat-Vargas, C., Buil-Cosiales, P., Estruch, R., Ros, E., et al. (2015). Mediterranean diet and invasive breast cancer risk among women at high cardiovascular risk in the predimed trial a randomized clinical trial. [Article]. *JAMA Internal Medicine, 175*(11), 1752-1760.

Toth, F. (2010). Is there a Southern European healthcare model? [Article]. *West European Politics, 33*(2), 325-343.

Trichopoulou, A., Martínez-González, M. A., Tong, T. Y. N., Forouhi, N. G., Khandelwal, S., Prabhakaran, D., et al. (2014). Definitions and potential health benefits of the Mediterranean diet: Views from experts around the world. [Article]. *BMC Medicine, 12*(1).

Tucker, K. L. (2010). Dietary patterns, approaches, and multicultural perspective. [Article]. *Applied Physiology, Nutrition and Metabolism, 35*(2), 211-218.

Vineis, P. (2017). *Health without borders: Epidemics in the era of globalization*.

Vinther, J. L., Conklin, A. I., Wareham, N. J., & Monsivais, P. (2016). Marital transitions and associated changes in fruit and vegetable intake: Findings from the population-based prospective EPIC-Norfolk cohort, UK. [Article]. *Social Science and Medicine, 157*, 120-126.

Visser, M., Volkert, D., Corish, C., Geisler, C., de Groot, L. C., Cruz-Jentoft, A. J., et al. (2017). Tackling the increasing problem of malnutrition in older persons: The Malnutrition in the Elderly (MaNuEL) Knowledge Hub. [Article]. *Nutrition Bulletin, 42*(2), 178-186.

Vitale, M., Racca, E., Izzo, A., Giacco, A., Parente, E., Riccardi, G., et al. (2019). Adherence to the traditional Mediterranean diet in a population of South of Italy: factors involved and proposal of an educational field-based survey tool. [Article]. *International Journal of Food Sciences and Nutrition, 70*(2), 195-201.

Vos, T., Allen, C., Arora, M., Barber, R. M., Brown, A., Carter, A., et al. (2016). Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. [Article]. *The Lancet, 388*(10053), 1545-1602.

Vázquez-Ruiz, Z., De La Fuente-Arrillaga, C., Bes-Rastrollo, M., Zazpe, I., Santiago, S., Razquin, C., et al. (2018). Egg consumption and dyslipidemia in a mediterranean cohort. [Article]. *Nutricion Hospitalaria, 35*(1), 153-161.

Westenhoefer, J. (2005) Age and gender dependent profile of food choice. *Vol. 57. Forum of Nutrition* (pp. 44-51).

WHO. (2003). Dieta, Nutrición y Prevención de Enfermedades Crónicas. Retrieved 27 May, 2019, from http://www.fao.org/3/a-ac911s.pdf

WHO. (2018a). Global Health Observatory. Retrieved 3 June, 2019, from http://apps.who.int/gho/data/node.imr

WHO. (2018b). Riesgo de mortalidad prematura debido a enfermedades no transmisibles en España. Retrieved 31 May, 2019, from https://www.who.int/nmh/countries/esp_es.pdf?ua=1

Willet, W. (2013). *Nutritional Epidemiology* (3rd Edition ed.). New York: Oxford University Press.

Zazpe, I., Estruch, R., Toledo, E., Sánchez-Taínta, A., Corella, D., Bulló, M., et al. (2010). Predictors of adherence to a Mediterranean-type diet in the PREDIMED trial. *European Journal of Nutrition, 49*(2), 91-99.