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Dietary patterns and cardiometabolic health

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Dietary patterns and cardiometabolic health

Memòria presentada per Míriam Rodríguez Monforte per optar al títol de doctor en el Programa de Doctorat d'Alimentació i Nutrició de la Facultat de Farmàcia i Ciències de l'Alimentació, Universitat de Barcelona.

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List of publications arising from the thesis work

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CONTENTS

GLOSSARY OF ABBREVIATIONS AND ACRONYMS

AACE	American Association of Clinical Endocrinologists
AHA	American Heart Association
AMI	Acute myocardial infarction
ApoB	Apolipoprotein B
ATP III	Adult Treatment Panel III
BMI	Body mass index
BP	Blood pressure
CC	Colorectal cancer
CHD	Coronary heart disease
CKD	Chronic kidney disease
COPD	Chronic obstructive pulmonary disease
CV	Cardiovascular
CVD	Cardiovascular disease
DALY	Disability-adjusted life year
DASH	Dietary Approaches to Stop Hypertension
DBP	Diastolic blood pressure
DII	Dietary inflammatory index
DP	Dietary pattern
DVT	Deep vein thrombosis
EC	Endometrial cancer
EGIR	European Group for the study of Insulin Resistance
FFQ	Food Frequency Questionnaire
GC	Gastric cancer
HbA1c	Glycated haemoglobin
HDL-C	High-density lipoprotein cholesterol
HEI	Healthy eating index
HF	Heart Failure
IDF	International Diabetes Federation
IFG	Impaired fasting glucose
INE	Instituto Nacional de Estadística
IGT	Impaired glucose tolerance
MDS	Med diet score
MetS	Metabolic syndrome
MI	Myocardial infarction
NCD	Non-communicable disease
PA	Physical activity
PAD	Peripheral artery disease
PE	Pulmonary embolism
Rx	Prescription medication
SBP	Systolic blood pressure
T2DM	Type 2 diabetes mellitus
TG	Triglycerides
WC	Waist circumference
WHO	World Health Organization

1. INTRODUCTION

Cardiometabolic diseases are the principal cause of mortality and morbidity in the world. They are considered a global health burden, accounting for more than 17 million deaths annually. The combination of cardiovascular and metabolic diseases leads to a far greater cardiovascular risk, an inferior life expectancy, and a poorer quality of life. Despite the implementation of specific health policies with the aim of lowering incidence, cardiometabolic diseases still account for millions of deaths each year in countries such as Spain, Finland, or the USA.

Primary prevention is a key approach to reducing the prevalence of both conditions. The acquisition of healthy habits, starting from childhood, is the general recommendation from worldwide organizations. The link between bad habits during early years and future adult disease is clear. Therefore, exercise and diet, the basic components for a healthy lifestyle, should be prescribed and taught from birth.

Population-based preventive interventions must be low-cost, minimally invasive, and avoid discomfort and pain. Patient-centered care prevention, tailored to the needs of a population in order to focus on specific health targets, has been shown to be successful and cost-effective.

Analysis of dietary patterns (as opposed to any one food or nutrient alone) has become a critical way of evaluating the composition of a diet, and may be more predictive of overall health status and disease risk than individual nutritional factors. The *a posteriori* dietary pattern approach leads to a realistic and robust description of the eating habits of a population, taking into account their food preferences. A great deal of research has used this approach in order to analyze the link between diet and disease; in particular, the incidence of cardiovascular disease (CVD) and metabolic syndrome (MetS) associated with following a specific dietary pattern. However, some results are contradictory.

Based on the importance of diet as a key preventive element for cardio-metabolic disease and the volume of research carried out to date, we decided to conduct two systematic reviews and meta-analyses: one exploring the relationship between dietary patterns and CVD, and the other focusing on the associations between dietary patterns and MetS. Furthermore, we decided to explore the influence of dietary patterns on the emergence of MetS (a main risk factor for CVD) and type 2 diabetes (T2DM), within a sample of individuals in Catalonia.

The PhD dissertation presented herein is a compilation of three papers, two of which have been peer-reviewed, published in international journals, and indexed in international databases. The present compilation relates to one research topic: the study of how dietary patterns are associated with CVD and MetS, two important health outcomes.

The first study assessed the relationship between *a posteriori* dietary patterns and the risk of experiencing a cardiovascular event or mortality; more specifically, their associations with coronary heart disease (including myocardial infarction and ischemic heart disease), stroke (cerebrovascular disease and ischemic stroke), and overall CVD were assessed. The second study evaluated the relationship between *a posteriori* dietary patterns and the risk of developing MetS. In the third study, the aim was to investigate the dietary patterns of individuals at high diabetes risk in Catalonia, within a primary healthcare setting. Furthermore, we assessed whether following these patterns was associated with a MetS' and T2DM risk.

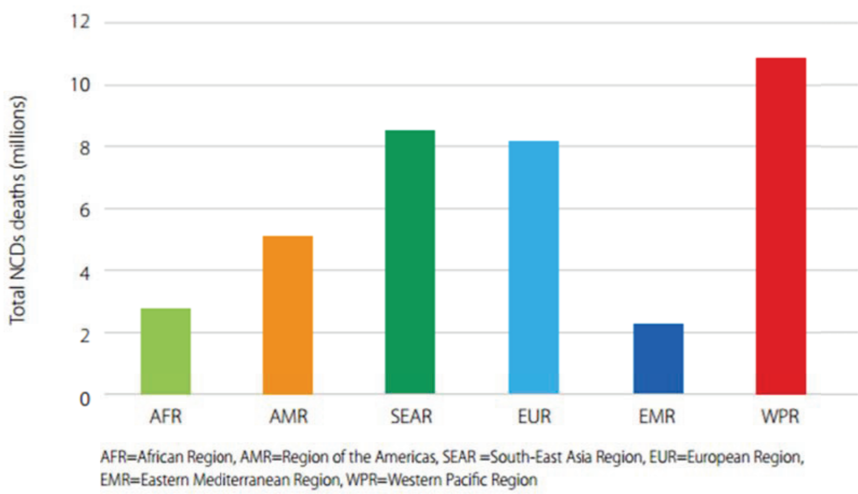
2. LITERATURE REVIEW

2.1 Non-communicable diseases

Non-communicable diseases (NCDs; also referred to as chronic diseases) can be defined as health conditions that are non-infectious and non-transmissible among individuals (Beaglehole et al. 2011; WHO, 2016). Nowadays, NCDs are the leading cause of death and disease worldwide, and include CVDs, cancer, chronic lung diseases, and diabetes mellitus (WHO, 2014).

Mortality figures suggest that NCDs account for more than 38 million deaths each year, of which 16 million occur in individuals under the age of 70. Since 2000, the number of deaths has increased every year on a worldwide scale (WHO, 2014). Models suggest that this trend will persist, with a projected 52 million deaths worldwide by the year 2030 (WHO, 2015).

Figure 1. Comparative mortality estimates between different world regions, 2012



Adapted from WHO Global Status Report on Non-Communicable Diseases, 2014 (WHO, 2014)

In the year 2010, the World Health Organization (WHO) published the first Global Status Report on NCDs (WHO, 2010), which brought NCDs to the forefront as a common target for governments and organizations globally.

In 2013, a Global Action Plan for NCD was created. This essentially consists of a monitoring framework including a set of nine voluntary global targets and 25 indicators that will need to be attained by 2025 (WHO, 2013). Its aim is to translate the different countries' commitments into tangible action points, and to address the overall NCD-related burden. The same Action Plan describes particularly cost-effective interventions (termed "best-buys"), which have been determined to be high-impact and feasible for implementation, even in resource-constrained settings. These interventions include the management of modifiable risk factors (such as tobacco use, alcohol abuse, diet and physical activity), drug therapy for diabetes and CVD, and prevention of cancer through immunization and early screening (WHO, 2011).

Table 1. Voluntary global targets for prevention and control of non-communicable diseases to be attained by 2025

1. A 25% relative reduction in the risk of premature death from CVD, cancer, diabetes, or chronic respiratory diseases
2. At least 10% relative reduction in the harmful use of alcohol, as appropriate within the national context
3. A 10% relative reduction in the prevalence of insufficient PA
4. A 30% relative reduction in the population's mean intake of salt/sodium
5. A 30% relative reduction in the prevalence of current tobacco use in persons aged 15 or older
6. A 25% relative reduction in the prevalence of raised BP or contain the prevalence or raised BP, according to national circumstances
7. Halt the rise in diabetes and obesity
8. At least 50% of eligible individuals receiving drug therapy (including glycemic control) and counseling to prevent heart attacks and strokes
9. An 80% availability of the affordable basic technologies and essential medicines, including generics, required to treat major non-communicable diseases in both public and private facilities

Legend: CVD: cardiovascular disease; PA: physical activity; BP: blood pressure.
Adapted from WHO Global Status Report on Non-Communicable Diseases, 2014 (WHO,2014)

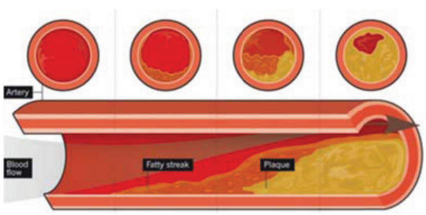
In the year 2012, the four major NCDs (CVD, cancer, chronic lung diseases, and diabetes mellitus) accounted for 82% of all NCD-related deaths, with CVD the leading cause (proportional mortality rate: 46.2%). Furthermore, diabetes accounted for 4% of mortalities (WHO, 2012).

2.2 Cardiovascular disease

CVD can be defined as a group of disorders affecting the heart and blood vessels, including CHD, cerebrovascular disease, peripheral arterial disease (PAD), rheumatic heart disease, congenital heart disease, deep vein thrombosis (DVT), and pulmonary embolism (PE) (World Heart Federation, 2016).

Atherosclerosis is the major cause of CVD. It is a chronic inflammatory disorder, driven by risk factors (mainly hypercholesterolemia, hypertension and cigarette smoking) that activate and exacerbate oxidative and inflammatory mechanisms in the artery wall. The development of atherosclerosis is slow and lasts for many years. The balance between atherosclerotic plaque stability (facilitated by enhanced vascular smooth muscle cell proliferation and matrix formation) and plaque instability (produced by excessive inflammation, cellular apoptosis and secretion of matrix metalloproteases) determines plaque fate and the risk of clinical events (Scott, 2004).

Figure 2. Plaque formation in the vascular lumen



Adapted from Cardiovascular disease: biochemistry to behavior, 2013 (Cannon, 2013)

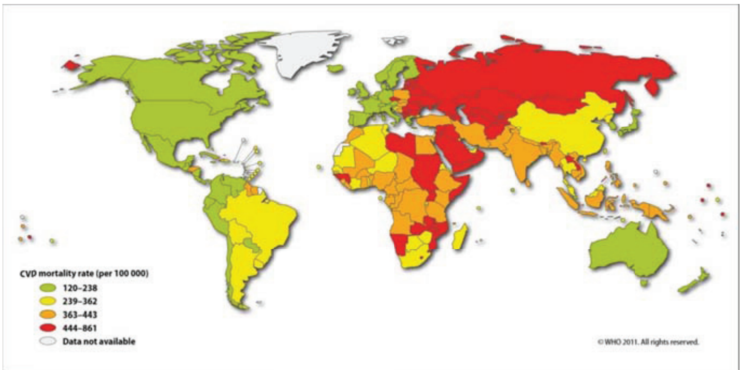
CVD is the leading cause of morbidity and mortality worldwide. In the year 2012, 17.5 million people died from CVD, representing 31% of all deaths globally. Of these deaths, an estimated 7.4 million were attributable to CHD and 6.7 million to stroke (WHO, 2014). The highest prevalence of CVD was found in low and middle-income countries, accounting for more than 37% of NCD-related deaths and affecting men and women equally (WHO, World Heart Federation, World Stroke Organization; 2011). CVD also represents a heavy burden for the individuals and the economies, especially in low-and middle-income countries, accounting for more than 5% of expenses. One of the main reasons for this is the lack of primary healthcare programs for the early detection and treatment of risk factors (WHO, 2014).

In the year 2013, 30.9% of all deaths in Spain were due to CVD; the primary cause of death in the country. Galicia, Andalucia and Asturias reported the highest mortality rates, with 9% more women dying than men (INE, 2016). The annual National Health System cost derived from CVD is around €9,000 per person, or €6,122 per patient (7.1% of the total healthcare budget) (Ministerio de Sanidad, Servicios Sociales e Igualdad, 2013).

CHD and stroke are the main clinical manifestations of CVD, and are considered leading causes of disability and mortality in many worldwide populations (Nichols et al., 2014; Ohira et al., 2013; CDC, 2015). In the case of CHD, acute myocardial infarction (AMI) accounts for approximately 36% of the population-attributable risk worldwide (44% in men). Moreover, eating fruit and vegetables, doing physical exercise, and avoiding smoking could lead to around an 80% lower relative risk of AMI. (Stampfer et al., 2000; Yusuf et al., 2004; Eriksen et al., 2015; de Lorgeril et al., 1999).

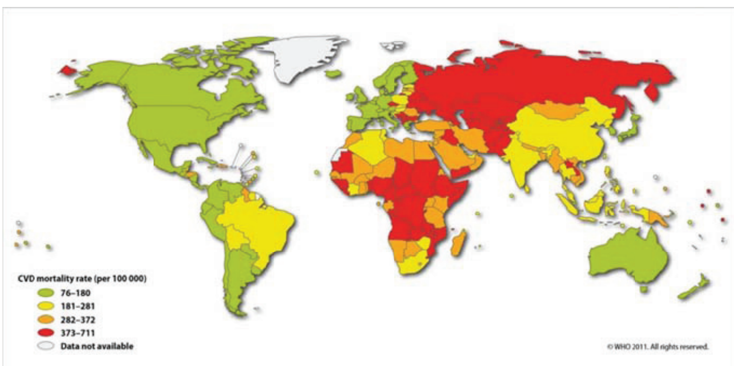
Stroke is the leading cause of functional impairment. Six months after a stroke, only 26% of patients who are ≥65 years of age are dependent in their activities of daily living, and 46% have cognitive deficits. Risk factor modification remains the principal approach to stroke prevention (Go et al., 2014). Medications to control blood pressure (BP) and lipids, anticoagulants for at-risk individuals with atrial fibrillation, revascularization, cessation of cigarette smoking, diet modification, and exercise are among the interventions broadly applicable to the general public (Meschia et al., 2014).

Figure 3. CVD mortality rates in men (age standardized, per 100,000)



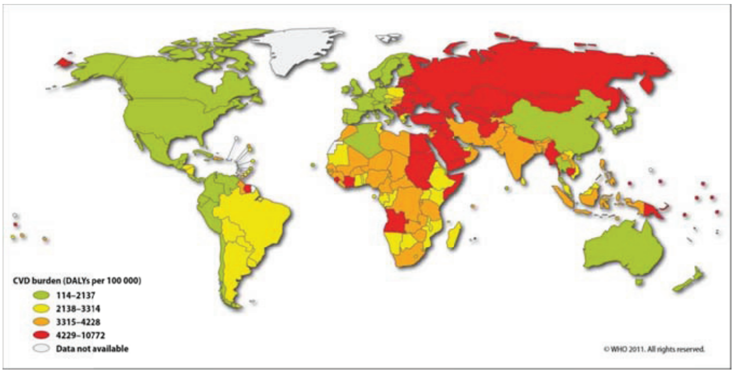
Adapted from *Global Atlas on Cardiovascular Disease Prevention and Control* (WHO, 2011)

Figure 4. CVD mortality rates in women (age standardized, per 100,000)



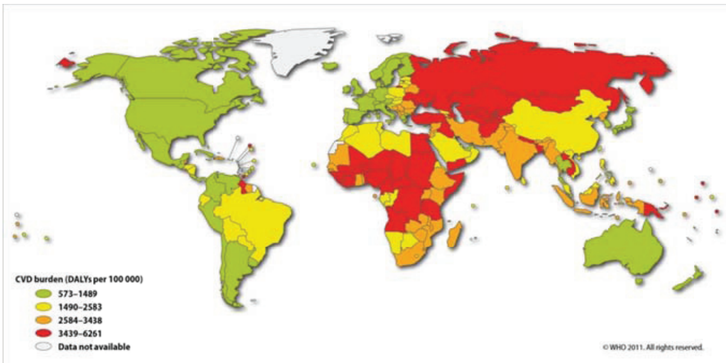
Adapted from *Global Atlas on Cardiovascular Disease Prevention and Control* (WHO, 2011)

Figure 5. CVD burden in men (age standardized, per 100,000)



Adapted from *Global Atlas on Cardiovascular Disease Prevention and Control* (WHO, 2011)

Figure 6. CVD burden in women (age standardized, per 100,000)



Adapted from *Global Atlas on Cardiovascular Disease Prevention and Control* (WHO, 2011)

2.3 Metabolic syndrome

MetS can be defined as a constellation of different factors, involving physiological, biochemical, clinical and metabolic mechanisms (Alberti et al., 2005; Reilly, 2003). It is characterized by insulin resistance, type 2 diabetes mellitus (T2DM) or impaired glucose tolerance (IGT), hypertension, dyslipidemia, and central obesity (Grundy et al., 2004). The presence of MetS has been related to an increased risk of developing CVD or T2DM in future; however, it cannot be used as a tool to predict absolute cardiometabolic risk (Alberti et al., 2009; Mottillo et al., 2010).

The predominant underlying risk factors for MetS appear to be abdominal obesity (Lemieux et al., 2000; Carr et al., 2004) and insulin resistance (Reaven, 1988; Ferrannini et al., 1991). Insulin resistance predisposes an individual to development of hyperglycemia, which accompanies T2DM. Although insulin-resistant individuals need not be clinically obese, they commonly have an abnormal fat distribution characterized by upper body fat, which correlates strongly with the degree of insulin resistance (especially visceral fat) (Carr et al., 2004; Brochu et al., 2000; Hayashi et al., 2004). Adipose tissue in obese individuals is insulin-resistant, which raises non-esterified fatty acid levels, exacerbating insulin resistance in muscle and altering hepatic metabolism (Petersen et al., 2002; Bergman et al., 2001; Yu et al., 2002). MetS has also been associated with a state of chronic, low-grade inflammation (Hu et al., 2004; Hanley et al., 2004). It is likely that the expression of each metabolic risk factor falls partially under its own genetic control, which influences an individual's response to different environmental factors (Martin et al., 2003).

Despite having an ICD-9 diagnostic code (277.7), there is ongoing controversy about whether MetS is a homogeneous disorder or disease, and whether it merits recognition as a syndrome (Grundy et al., 2005). Taking this into account, the diagnosis of MetS has been a challenge in the clinical field, and different classifications have appeared with the objective of helping clinicians identify affected patients (Gustat et al., 2002; Ford et al., 2002).

Table 2. Criteria for the diagnosis of MetS

Clinical measure	WHO (1998)	EGIR (1999)	ATPIII (2001)	AACE (2003)	IDF (2005)	AHA (2005)
Insulin Resistance	IGT, IFG, T2DM, or lowered insulin sensitivity, plus any 2 of the following:	Plasma insulin >75th percentile plus any 2 of the following:	None, but any 3 of the following:	IGT or IFG plus any of the following (based on clinical judgment):	None	None, but any 3 of the following:
Body weight	Men: waist-to-hip ratio >0.90; women: waist-to-hip ratio >0.85 and/or BMI >30 kg/m^2	WC ≥ 94 cm in men or ≥80 cm in women	WC ≥102 cm in men or ≥88 cm in women	BMI ≥25 kg/m^2	Increased WC (population-specific) plus any 2 of the following:	Elevated WC (≥102 cm in men and ≥88 cm in women)
Lipid	TG ≥150 mg/dL and/or HDL-C <35 mg/dL in men or <39 mg/dL in women	TG ≥150 mg/dL and/or HDL-C <39 mg/dL in men or women	TG ≥150 mg/dL; HDL-C <40 mg/dL in men or <50 mg/dL in women	TG ≥150 mg/dL; HDL-C <40 mg/dL in men or <50 mg/dL in women	TG ≥150 mg/dL; HDL-C <40 mg/dL in men or <50 mg/dL in women, or on HDL-C Rx	TG ≥ 150 mg/dL or drug treatment for elevated triglycerides; HDL-C <40 mg/dL in men and <50 mg/dL in women, or drug treatment for reduced HDL
Blood Pressure	≥140/90 mmHg	≥140/90 mmHg or on hypertension Rx	≥130/85 mmHg	≥130/85 mmHg	≥130 mmHg systolic or ≥85 mmHg diastolic or on hypertension Rx	SBP ≥130 mmHg or DBP ≥85 mmHg. If history of hypertension, on antihypertensive drug treatment
Glucose	IGT, IFG, or T2DM	IGT or IFG (but not diabetes)	>110 mg/dL (includes diabetes)	IGT or IFG (but not diabetes)	≥100 mg/dL (includes diabetes)	Elevated fasting glucose ≥100 mg/dL or on drug treatment for elevated glucose
Other	Microalbuminuria			Other features of IR		

Legend: IGT: impaired glucose intolerance; IFG: impaired fasting glucose; T2DM: type 2 diabetes mellitus; BMI: body mass index; TG: triglycerides; WC: waist circumference; HDL-C: high-density lipoprotein cholesterol; IR: insulin resistance; SBP: systolic blood pressure; DBP, diastolic blood pressure; Rx: prescription medication.

Adapted from AHA Diagnosis and Management of the MetS, 2005 (Grundy et al., 2005)

According to the International Diabetes Federation, a quarter of the world's adults have MetS (IDF, 2016). In Europe, data from the BioSHaRE-EU Healthy Obese Project, which includes 163,517 individuals from ten population-based cohorts (Estonia, Finland, Germany, Italy, the

Netherlands, Norway, and the United Kingdom), suggest that MetS can occur in between 24% (Italy) and 65% (Finland) of women, and between 43% (Italy) and 78% (Finland) of men (van Vliet-Ostaptchouk et al., 2014).

One of the latest publications analyzing data from the Framingham Cohort shows a clear progression of obesity, diabetes mellitus and other metabolic diseases in the past century, with abdominal adiposity (most robustly visceral adipose tissue) identified as one of the strongest predictors of CVD and cancer. In the Framingham Cohort, MetS was found to be a strong predictor of incident T2DM, associated with a nearly seven-fold increase in risk among those fulfilling the definition of MetS (Long et al., 2016).

Most of the different diagnostic criteria include abdominal obesity as a requisite for the diagnosis of the syndrome, however MetS can be diagnosed without the presence of this factor. It has been suggested that abdominal obesity has a crucial impact on the incidence of CVD; however, this impact can be attenuated after adjustment for hypertension, dyslipidemia and diabetes mellitus, indicating that abdominal obesity increases CVD risk mainly via its associated metabolic abnormalities (Browning et al., 2010; Czernichow et al., 2011; de Koning et al., 2011; Wornser et al., 2011).

All individuals with MetS should be categorized according to absolute risk using a validated CV risk-assessment system. These are intuitive easy-to-use tools that assess total risk up to 10 years. As examples, the Framingham risk score or the SCORE chart can be used to achieve this classification. Preventative measures against CVD or MetS in an individual should be adapted according to their overall CV risk; the higher the risk, the more intensive the measures required (D'Agostino et al., 2008; Conroy et al., 2003).

2.4 Cardiometabolic health: health promotion and disease prevention

Health promotion is the process of empowering people to increase control over their own health and its determinants. This is achieved through health literacy efforts and multi-sectoral action to increase healthy behaviors. Disease prevention can be defined as population-based and individual-based interventions which aim to minimize the burden of diseases and their associated risk factors (WHO, 2016).

The scope of prevention has changed over time. In general, primary prevention focuses on the promotion of health prior to the development of disease or injuries; secondary prevention centers on the detection and treatment of the disease in its early stages; and tertiary prevention focuses on reversing, arresting or delaying the progression of an existing disease. Additionally, primordial prevention consists of taking action to minimize future health hazards. The latter inhibits the establishment of factors (environmental, economic, social, behavioral, and cultural) known to increase the risk of disease by addressing health determinants, rather than preventing personal exposure to risk factors (Gillman, 2015). Nowadays, a further preventative strategy classified as quaternary prevention is in use. This is defined as the action taken to identify a patient at risk of over medicalization, protect him/her from new medical invasion, and suggest interventions which are ethically acceptable (WHO, 2016; Tengland, 2010).

The definition of “ideal cardiovascular health” in an adult population was presented by the American Heart Association in 2010. This definition refers to the simultaneous presence of four model health behaviors: never smoked or ceased to smoke ≥12 months previously; body mass index (BMI) ≤25 kg/m^2; physical activity at goal levels; and diet consistent with current guideline recommendations. In addition, ideal values for three specific health parameters were also described: untreated total cholesterol levels of 5.17 mmol/L (200 mg/dL); untreated BP at 120/80 mmHg; and untreated fasting plasma glucose levels of 5.6 mmol/L (100 mg/dL) (Lloyd-Jones et al., 2010).

The interrelationship between CVD and MetS has been explored in several studies, each drawing the conclusion that the presence of MetS increases the risk of CV events (Gami et al., 2007; Galassi et al., 2006). In an 11-year cohort study (the ARIC study), individuals without CVD or diabetes at baseline, but with MetS, were at higher risk of negative CV health outcomes in general, and were 1.5 to 2 times more likely to develop CHD and stroke. The MetS components elevated BP and lowered high-density lipoprotein cholesterol (HDL-C) (McNeill et al., 2005).

In a cohort study conducted in the USA, MetS was associated with an increased risk of death from CHD, CVD, or all causes in adults. Although diabetes is defined as a CHD risk equivalent, individuals with MetS but without diabetes had a wide spectrum of risk. In those with MetS who did not have diabetes, increased risk of CVD and CHD mortality remained. Even those with 1 or 2 MetS risk factors were at a 2-fold greater risk of CHD and CVD mortality, suggesting that risk is not “optimal” unless all MetS risk factors are entirely absent. Finally, MetS predicted CHD, CVD, and total mortality more strongly than individual MetS risk factors, consistent with previous reports (Malik et al., 2004).

The life-course perspective towards chronic disease recognizes that CVD and other chronic conditions are the result of risk factors that accumulate throughout an individual's lifetime. The perspective further recognizes that these risks can (and must) be reduced and prevented at all stages of life. In keeping with this principle, risk factors for CVD begin to accumulate as early as the fetal stage, and continue to do so throughout infancy, childhood, adolescence, and adult life (Aboderi et al., 2002).

A healthy lifestyle (i.e. the acquisition of healthy habits) has been a matter of much research and debate, and is a challenge both for patients and healthcare professionals alike. Several strategies have been established, mainly focusing on a healthy diet and regular physical activity. Lifestyle modification itself is a foundational strategy for visceral CV reduction, and can be carried out in different healthcare settings, mainly in primary care. Consequently, a large number of patients can benefit from these programs and avoid the adverse effects of surgery or pharmacological treatments, with the additional advantage of being cost-effective (Ryo et al., 2011).

Expert consensus publications identify the need to avoid the advancement of CVD and MetS through a key strategy: prevention (Grundy et al., 2005). CV or MetS risk factors, defined as elements or measurable characteristics that have a causal relationship with the growing frequency of an illness and constitute independent predictive factors for its development, are core targets for the primary prevention of CVD and MetS (O'Donnell et al., 2008). Risk factors can be classified as *non-modifiable*, (those that cannot be changed), and *modifiable* (those that can be treated or changed).

There is evidence to support the fact that lifestyle changes are the cornerstone for reducing the effect of modifiable risk factors. In the last three decades, more than half of the reduction in CV mortality has been attributed to changes in risk factor levels within the population; primarily the lowering of cholesterol, BP, and the prevalence of smoking. This favorable trend is partly offset by an increase in other risk factors; mainly obesity and T2DM (Mason et al., 2014; O'Keeffe et al., 2013).

Table 3. Modifiable and non-modifiable risk factors for CVD and MetS

NON-MODIFIABLE RISK FACTORS	CVD	MetS
AGE	Most important CVD risk factor; risk increases with age (Wilson et al., 1998; Roth et al., 2015)	The prevalence increases strongly with age (Hildrum et al., 2007)
GENDER	Men are at more risk of a CV event than women. When women reach menopause, their risk is elevated (Mercuro et al., 2010; Rossouw et al., 2007)	Men are more at risk of MetS than women. When women reach menopause, the prevalence increases. Younger men and women have a higher mortality risk than older men and women with MetS (Kuk et al., 2010)
ETHNICITY	CVD risk varies considerably between immigrant groups. South Asians and sub-Saharan Africans have a higher risk, while Chinese and South Americans have a lower risk (Bohpal et al., 2012; Bansal et al., 2013)	The prevalence of MetS varies between ethnic groups. It is more prevalent among individuals of a Hispanic or African origin than those of a Caucasian origin (Crossrow et al., 2004)
FAMILY HISTORY	A family history of premature CVD (before 55 years of age in men and 65 years of age in women) in first-degree relatives increases the risk of CVD (ESC CVD guidelines, 2016)	Familial segregation and heredity studies clearly support the genetic basis of MetS and its components. Of these components, HDL-C has shown the highest estimated heritability (50% to 60%) (Lin et al., 2005)

MODIFIABLE RISK FACTORS		
DYSLIPIDEMIA	There is a gradual and continuum relationship between cholesterol blood levels and mortality due to ischemic heart disease. High total LDL-C levels are related to a higher CVD risk, whereas high total HDL-C levels are protective (Kannel et al., 1979; Klag et al., 1993)	This condition consists of abnormal levels of ApoB, small LDL particles, and low HDL-C. Lowering LDL-C levels is a primary target in MetS (NCEP-ATPIII, 2002)
HYPERTENSION	Most prevalent CVD risk factor; higher hypertensive values are related to a higher probability of a coronary event (Lewington et al., 2007; McMahon et al., 1990; van den Hoogen et al., 2000)	The target is to achieve values <140/90 mmHg (without presence of T2DM or CKD) (Chobanian et al., 2003)
DIABETES MELLITUS	The increment in this risk factor has occurred in parallel with the increment in obesity. The probability of suffering a CV event increases 2-3 times overall, with a greater increase in women (Flores-Mateo et al., 2010; Fox et al., 2007)	In individuals with T2DM, the coexistence of other MetS factors denotes a higher risk for future development of CVD (Alexander et al., 2003). Fasting plasma glucose carries the greatest predictive power for diabetes (Liao et al., 2004)
SMOKING STATUS	First cause of premature and preventable death in developed countries. The rate of mortality due to ischemic pathology is 70% higher in smokers than in non-smokers (WHO, 2016)	Smokers are at greater risk of developing insulin resistance and CVD than non-smokers (Hu et al., 2001)
OVERWEIGHT AND OBESITY	The presence of obesity, especially with a BMI >30 kg/m^2, has been related to a higher CVrisk. It has also been related to other comorbidities such as CHD, T2DM, and hypertension (Manson et al., 1995; Hubert et al., 1983; Eckel et al., 2006; Stamler et al., 1978)	Weight reduction deserves first priority; abdominal obesity is an important underlying risk factor of MetS (Yumuk et al., 2015; Klein et al., 2004)
SEDENTARISM	Sedentary lifestyle has been related to CVD, with the risk 1.9 times higher in individuals that do not partake in any PA (Berlin et al., 1990; Sofi et al., 2008; Wahid et al., 2016)	Increasing PA assists in weight reduction, is beneficial in terms of metabolic risk factors, and lowers total CV risk (Franklin et al., 2004)
DIET	The consumption of saturated fat as a predominant nutrient has been related to a higher CVD risk (Astrup et al., 2010). The Mediterranean diet has shown a trend towards protection from the development of CVD (Estruch et al., 2013)	Diets should be low in saturated fats, cholesterol, sodium, and simple sugars (US Dietary Guidelines, 2015). The Mediterranean diet has been related to an improvement in MetS (García-Fernández et al., 2014)

Legend: CVD: cardiovascular disease; MetS: metabolic syndrome; CV: cardiovascular; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; ApoB: apolipoprotein B; T2DM: type 2 diabetes mellitus; CKD: chronic kidney disease; BMI: body mass index; CHD: coronary heart disease; PA: physical activity.

There has been a strong movement worldwide to implement health promotion and CVD preventive strategies in both children and adult populations, especially in high-income countries (Health and Ageing Asutralian Department, 2009; Euroheart: European Heart Health Strategy, 2007; Healthy Living and Chronic Disease in Canada, 2010).

Scientific societies have focused on bringing together the different recommendations for achieving good cardiometabolic health. In the following tables, some of the recommendations are briefly described, mainly focusing on lifestyle modifications.

Table 4. Therapeutic goals and recommendations for the clinical management of CVD

LIFESTYLE RISK FACTORS	THERAPEUTIC TARGETS
LDL- C	Consume a DP that emphasizes intake of vegetables, fruits, and whole grains; includes low-fat dairy products, poultry, fish, legumes, non-tropical vegetable oils and nuts; and limits intake of sweets, sugar-sweetened beverages, and red meats.
	Aim to consume only 5-6% of calories from saturated fat
	Reduce the proportion of calories from saturated fat
	Reduce the proportion of calories from trans fat
BP	Target is <140/90 mmHg. Consume a DP that emphasizes intake of vegetables, fruits, and whole grains; includes low-fat dairy products, poultry, fish, legumes, non-tropical vegetable oils, and nuts, and limits intake of sweets, sugar-sweetened beverages, and red meats
	Reduce sodium intake
	Consume no more than 2,400 mg of sodium/day, with a further reduction to 1,500 mg/day. Reduce intake by at least 1,000 mg/day
	Combine the DASH DP with lower sodium intake
PA	Target is at least 150 min/wk of moderate aerobic PA (30 min for 5 days/wk) or 75 min/wk of vigorous aerobic PA (15 minutes for 5 days/wk, or a combination thereof)
	Lipids: advise adults to engage in aerobic PA to reduce LDL-C and non-HDL-C: 3 to 4 sessions per week, lasting an average of 40 mins per session, and involving moderate-to-vigorous intensity PA
	BP: advise adults to engage in aerobic PA to reduce BP: 3 to 4 sessions per week, lasting an average of 40 minutes per session, and involving moderate-to-vigorous intensity PA
Body weight	BMI 20-25 kg/m^2; WC <94 cm (men) or <80 cm (women)
Diabetes	HbA_{1c} <7%

Legend: DP: dietary pattern; LDL-C: low-density lipoprotein cholesterol; BP: blood pressure; DASH: Dietary Approaches to Stop Hypertension; PA: physical activity; HDL-C: high-density lipoprotein cholesterol; BMI: body mass index; WC: waist circumference; HbA_{1c}: glycated hemoglobin.

Adapted from the AHA Guideline on Lifestyle management to reduce CV risk, 2013; ESC CVD Guidelines, 2016 (Eckel et al., 2013; ESC CVD Guidelines, 2016)

In table 4, the therapeutic goals and recommendations for CVD prevention are specified and defined as a coordinated set of actions, both at a population level (by promoting healthy lifestyle behaviors) and when targeted towards a particular individual at moderate-to-high risk (by tackling unhealthy lifestyle behaviors). They aim to eliminate or minimize the impact of CVDs and their associated disabilities (NCEP-ATPIII, 2002). There is evidence to suggest that prevention is effective: the elimination of behaviors which pose a risk to health would make it possible to prevent (at least) 80% of CVDs (Liu et al., 2012; ESC CVD guidelines, 2016).

Table 5. Therapeutic goals and recommendations for the clinical management of MetS

LIFESTYLE RISK FACTORS	THERAPEUTIC TARGETS	LONG-TERM PREVENTION (CVD and T2DM)
Abdominal obesity	Reduce body weight by 7-10% during year 1 and continue until achievement of BMI <25 kg/m^2	Weight maintenance/reduction though balanced PA, caloric intake, and WC <102/<88 cm in men/women. Even small amounts of weight loss are associated with significant health benefits.
Physical activity	Regular moderate-intensity PA; at least 30 min of continuous or intermittent PA (preferably ≥60 min) on 5d/wk (preferably daily)	30-60 min moderate-intensity aerobic PA: brisk walking (preferably daily) supplemented by an increase in daily lifestyle activities (pedometer step tracking, walking breaks at work, gardening, housework). Longer exercise times can be achieved by accumulating exercise throughout the day. Advise medically supervised programs for high-risk patients.
Atherogenic diet	Reduced intake of saturated fat, trans fat, and cholesterol	Saturated fat <7% of total calories; reduce trans fat; dietary cholesterol <200 mg/dL; total fat 25%-35% of all calories. Most dietary fat should be unsaturated; simple sugars should be limited.

METABOLIC RISK FACTORS	THERAPEUTIC TARGETS	SHORT-TERM PREVENTION (CVD or treatment of T2DM)
Atherogenic dyslipidemia	Primary target: elevated LDL-C Secondary target: elevated non-HDL-C Tertiary target: reduced HDL-C	Primary target: elevated LDL-C Secondary target: elevated non-HDL-C Tertiary target: reduced HDL-C
Elevated BP	Reduce BP to achieve <140/90 mmHg (<130/80 mmHg if T2DM present). Reduce BP further to the extent possible through lifestyle changes	For BP ≥120/80 mmHg: initiate or maintain lifestyle modification: weight control, increased PA, alcohol moderation, sodium reduction, increased consumption of fresh fruits, vegetables, and low-fat dairy For BP ≥140/90 mmHg (≥130/80 mmHg for CKD or diabetes): as tolerated, add BP medication as needed to achieve goal BP
Elevated glucose	For IFG, delay progression of T2DM. For patients with T2DM, HbA_{1C} <7.0%	For IFG, encourage weight reduction and increased PA For T2DM, lifestyle therapy, and pharmacotherapy
Prothrombotic state	Reduce thrombotic and fibrinolytic risk factors	For high-risk patients: low-dose aspirin therapy; clopidogrel if aspirin contraindicated. Moderately high-risk patients: low-dose aspirin prophylaxis
Proinflammatory state	Lifestyle therapies	Lifestyle therapies

Legend: BMI: body mass index; PA: physical activity; WC: waist circumference; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; BP: blood pressure; T2DM: type 2 diabetes mellitus; CKD: chronic kidney disease; IFG: impaired fasting glucose; HbA_{1c}: glycated hemoglobin.

Adapted from AHA Diagnosis and Management of the MetS, 2005 (Grundy et al., 2005)

Table 5 shows the therapeutic goals and recommendations for the clinical management of MetS. The primary aim is to reduce the underlying risk factors (obesity, physical inactivity, and atherogenic diet) through lifestyle changes intended to decrease all of the metabolic risk factors. Subsequently, if absolute risk remains significantly elevated, consideration can be given to incorporating drug therapy into the regimen. Moreover, efforts should be made to bring about smoking cessation (Grundy et al., 2005).

The 2016 ESC Guidelines highlight that lifestyle interventions act on several CV risk factors, and should be applied prior to (or in conjunction with) drug therapies (ESC CVD guidelines, 2016). As seen in the different tables, CVD and MetS share many of the goals recommended by a wide range of research. Lifestyle improvements that are linked to the achievement of normalized body weight, increased physical activity, and following a healthy diet are the principle approaches in both conditions.

2.5 The dietary patterns approach

A healthy diet is essential for human well-being throughout life (including during pregnancy, child development, adulthood, and later life) as it prevents the emergence and development of disease. The traditional approach to studying the associations between individual nutrients/food groups and risk factors/outcomes related to chronic conditions is being modified or complemented by the dietary patterns approach, which takes into account the combinations of foods and nutrients.

The main reason why this approach has been incorporated into the nutrition epidemiology field is the consideration of diet as a multidimensional aspect. Accordingly, the food combinations consumed reflect individual preferences, modulated by a mixture of genetic, cultural, social, health, environmental, lifestyle, and economic determinants (Quandt, 1999; Krondl et al., 1986; van den Bree et al., 1999). The first authors to describe the implementation of dietary patterns in nutrition were Jacobson and Stanton in 1986 (Jacobson et al., 1986). Since then, other researchers have implemented this approach in their studies (Peñalvo et al., 2016).

A dietary pattern can be defined as the quantities, proportions, variety, and combinations of different foods and beverages in a particular diet, and the frequency with which they are habitually consumed (US Dietary Guidelines, 2015). There are several possible advantages to this approach.

Firstly, understanding the selection of dietary patterns within a population and identifying their respective nutrient qualities allows a more complete characterization of individual eating behaviors and enables researchers to examine their relationship to diverse health outcomes. Secondly, dietary patterns reflect a population's life experiences and wide-ranging personal, socio-cultural, and other environmental influences that are related to dietary intake. Thirdly, meals generally include complex combinations of nutrients that are likely to be interactive or synergistic, and many nutrients are highly correlated, making it difficult to examine their separate effects. Accordingly, though the effect of a single nutrient may be difficult to determine when considered alone, the cumulative effects of nutrients included in a dietary pattern may be sufficiently large to allow detection. However, analyses of a large number of nutrients or food groups may produce statistically significant associations simply by chance, and have been criticized for using too many tests. Furthermore, analyses of single nutrients may be confounded by the effect of dietary patterns. Regardless, results from clinical trials have shown positive health outcomes associated with changes in several types of dietary behaviors (Michels et al., 2004; Newby et al., 2004; Kant et al., 2004; Hu, 2002; Dixon et al., 2001; Jacobs et al., 2003; Moeller et al., 2007).

Several scientific associations have adopted dietary patterns as part of their guidelines, highlighting their ease of translation into dietary recommendations in daily practice (van Horn et al., 2016, Liese et al., 2015; US Dietary Guidelines, 2015).

When defining a population's dietary patterns, two different approaches may be followed (Hu, 2002; Newby et al., 2004; Moeller et al., 2007):

1) "*a priori*", which focuses on the construction of patterns that reflect hypothesis-oriented combinations of foods and nutrients

2) "*a posteriori*", which builds on exploratory statistical methods and uses the observed dietary data in order to extract dietary patterns

Both of these approaches have positive and negative aspects.

A priori methods (or investigator-defined approaches) employ predefined diet quality indices or dietary recommendations based on current nutritional knowledge. They identify a desirable pattern which, if adhered to, could maximize health benefits, with the aim of creating general recommendations to reduce the risk of chronic diseases. This approach, which is limited by the available knowledge and present understanding of the diet-disease relationship, can be fraught by uncertainties regarding the selection of individual score components and subjectivity when defining cut-off points. Additionally, it is based on the prevailing dietary recommendations, which may not represent the best available scientific evidence (Hu, 2002; Newby et al., 2004). The *a priori* approach generally falls into three categories: nutrient adequacy or density scores, variety or diversity scores, and food-group patterning.

Table 6. Summary of diet indices, scores, and dietary patterns

Name of Index/Score/Pattern	Main findings related to CVD or MetS
Healthy Eating Index (HEI) (Kennedy et al., 1995)	Little or no association with the risk of chronic diseases (McCullough et al., 2000; McCullough et al., 2000)
Canadian HEI (Shatenstein et al., 2005)	-
Alternative HEI (AHEI) (McCullough et al., 2002)	Low level of correlation with CVD risk and other chronic diseases (McCullough et al., 2002)
HEI-2005 (HEI-05) (Guenther et al., 2007)	-
Alternative HEI (AHEI)-2010 (Chiuve et al.,2012)	Strongly associated with chronic disease risk, particularly CHD and diabetes (Chiuve et al.,2012)
Diet Quality Index (DQI) (Patterson et al., 1994)	Correlation with overall and CVD mortality (Seymour et al., 2003)
Diet Quality Index Revised (DQI-R) (Haines et al., 1999)	No correlation with biochemical indices of CVD (Fung et al., 2005)
Diet Quality Index-International (DQI-I) (Kim et al., 2003)	-
Dietary Guidelines Index (DGI) (Harnack et al., 2002)	-
Overall dietary Index-revised (ODI-R) (Lee et al., 2008)	Association with the risk of obesity (Lee et al., 2008)
Dietary Quality Score (DQS) (Toft et al., 2007)	No association with serum lipids, homocysteine or absolute risk of ischemic heart disease (Toft et al., 2007)
Mediterranean Diet Quality Index (MDQI) (Gerber et al., 2002)	-
Mediterranean Diet Scale (MDS) (Trichopoulou et al., 1995)	Inverse relationship with overall mortality (Trichopoulou et al., 1995)
Modified Mediterranean Diet Score (MMDS) (Trichopoulou, 2003)	Significant association with all-cause mortality (Trichopoulou, 2003)
A priori Mediterranean dietary pattern (Martínez-González et al., 2002)	Correlation with risk of MI (Martínez-González et al., 2002)
Mediterranean Score (Martínez-González et al., 2004)	Correlation with risk of MI (Martínez-González et al., 2004)
Relative Med Diet Score (rMED) (Buckland et al., 2009)	High degree of adherence to an rMED is associated with a 40% reduction in the risk of CHD (Buckland et al., 2009)
Alternative Med Diet Score (aMed) (Fung et al., 2009)	High degree of adherence to aMed is associated with a lower risk of incident CHD and stroke in women (Fung et al., 2009)
Mediterranen Style Diet Pattern Score (MSDPS) (Rumawas et al., 2009)	Application of this score in a case–control study (CARDIO2000) suggested it was inversely associated with the odds of having an acute coronary syndrome (Panagiotakos et al., 2006)
Food Based Quality Index (FBQI) (Lowik et al., 1999)	-
Healthy Food Index (HFI) (Osler et al., 2001)	No association with incidence of CHD or overall mortality (Osler et al., 2001 and 2002)

DASH Score (Levitan et al., 2009)	Diets consistent with the DASH diet are associated with lower rates of HF in the Swedish mammography cohort and Swedish men cohort (Levitan et al., 2009)
Vegetarian-style dietary pattern (Orlich, 2013)	Vegetarian diets are associated with lower all-cause mortality and with some reductions in cause-specific mortality. Results appeared to be more robust in males (Orlich, 2013)

Legend: CVD: cardiovascular disease; MetS: metabolic syndrome; CHD: coronary heart disease; MI: myocardial infarction; DASH: Dietary Approaches to Stop Hypertension; HF: heart failure.

Adapted from Healthy indexes in public health practice and research: a review (Kourlaba et al., 2008)

"A posteriori" methods (or data-driven approaches) use mathematics to empirically derive eating behavior patterns using data collected from Food Frequency Questionnaires (FFQs), 24-hour recalls, or diet records. Some negative aspects include the fact that dietary data in-hand may lack robustness for relating diet and disease; the extracted dietary patterns may have little relation to morbidity and mortality if nutrients or foods relevant to the etiology of disease are not included. In cohort studies, this pattern is usually based upon qualitative self-reported behaviors, rather than detailed questionnaires. In order to analyze "*a posteriori*" dietary patterns, data-driven techniques are used, including factor analysis, cluster analysis or reduced rank regression. Occasionally, all of these approaches are combined. Once the different dietary patterns have been analyzed, they are labeled according to the specific food items or food groups included. Some examples of labels are as follows: healthy, prudent, unhealthy, western, meat-based, vegetable-based, fast-food-based, etc. No one method of dietary pattern analysis is regarded as better than all of the others; in fact, there is little consensus as to which approach should be applied for any given purpose (Hu, 2002; Moeller 2007; Tucker, 2001).

Table 7. Dietary assessment methods in *a posteriori* dietary patterns

Method	Characteristics	Strengths and weaknesses
FFQ	Represents long-range intake (6 months to 1 year) Subjective measure using pre-defined, self- or interviewer-administered format	Cost-effective due to its simplicity Cognitively difficult, so accuracy is reduced Traditionally, only affordable method for large scale studies
24-hour dietary recall	Represents short-term intake (24 hours) Subjective measure using open-ended questionnaires administered by a trained interviewer	Captures detail Relatively small respondent burden New tools make them affordable Requires modeling to estimate usual intake Possible recall bias Trained interviewer required (with their possible inherent bias) Expensive and time-consuming Multiple days required to assess usual intake Possible changes to diet if repeated measures
Diet record	Actual intake information during a specific period Subjective measure using open-ended, self-administered questionnaires	Provides detailed intake data No recall bias Relatively large respondent burden Literacy and high motivation required Expensive and time-consuming Multiple days required to assess usual intake Possible changes to diet if repeated measures

Legend: FFQ: Food Frequency Questionnaire.

Adapted from Dietary assessment methods in epidemiological studies (Shim et al., 2014)

Research has been carried out with the aim of comparing both approaches to dietary patterns and minimizing the potential bias linked to either methodology (Barbaresko, 2014; Bédard, 2015). Several evaluations of the different approaches are shown in Table 8.

Table 8. Strengths and limitations of different dietary pattern analysis approaches

Method	Strengths	Limitations
Score-based methods (*a priori*) Density scores, variety or diversity scores, food-group pattering scores, index-based summary scores	Characterize total diet Intuitively appealing Analytically simple to compute Easily reproducible and comparable Results can be meaningful, interpretable, and associated with health outcomes	In dichotomizations (e.g. meat vs. no meat), the full range of foods consumed is not taken into account When including a range of points for each component, variability of intake is considered, but not values for the extremes Dependent on the selected dietary guidelines, which are generally not specific to one type of disease Subjectivity is introduced in the interpretation of the guidelines and construction of the scores (foods selected for inclusion) The summation of equally weighted dietary component scores implies that each component is equally important and additively related to health status
Data-driven methods (*a posteriori*) Factor analysis, principal components analysis, cluster analysis	Characterize total diet Allow for biological interactions among nutrients Results can be meaningful, interpretable, associated with health outcomes, and show some reproducibility across populations Patterns can be a starting point for modeling different types of interactions because they describe eating behavior Factor analysis describes the variation in food intake in the population based upon correlations between dietary items; a continuous variable Cluster analysis separates individuals into mutually exclusive groups based upon dietary intake; a categorical variable	Few rigorous statistical tests have been used to examine the validity of derived conditions Subjectivity is introduced at: ▪ grouping of dietary items ▪ form of the input variable (i.e. grams, servings, etc.) ▪ analytic choices and options (i.e. statistical algorithms, use of rotation) ▪ selection of a final pattern solution

Adapted from Dietary from Patterns: Challenges and Opportunities in Dietary Patterns Research: An Experimental Biology Workshop (Moeller, 2006)

The overall aim of dietary pattern classification arises from the existence of a specific and prevalent health problem. The patterns identified should ultimately be an informative and powerful means to augment the understanding of the role of diet in chronic disease. Their appropriate use should provide assurance that existing dietary recommendations do indeed have tangible health results and, in the process, may lead to new hypotheses (Tucker, 2001).

As previously mentioned, there has been increasing interest over the past years regarding the management of chronic illnesses through lifestyle modification. Diet is one of the central tools, as many of these conditions have been labeled as chronic diet-related diseases. The effect of dietary patterns on cancer and lung diseases (two of the four conditions described as priorities by the NCD classification) have been analyzed in the past five years, with special consideration given to colorectal cancers.

In the following table, a summary of systematic reviews from the past five years regarding dietary patterns and cancer can be found.

Table 9. Systematic reviews of dietary patterns, by type of cancer or disease (2011-2016)

Outcome	Type of DP approach	General results
Colorectal cancer (Feng et al., 2016)	*A posteriori* DP	A healthy DP may decrease the risk of CC, whereas Western-style DPs and those including alcohol consumption may increase the risk
Colorectal cancer (Steck et al., 2015)	*A priori* DP (HEI, MDS, DII)	Association between higher overall diet quality and lower risk of CC. Increasing MDS, HEI and anti-inflammatory DII scores are characterized by a high intake of plant-based foods and a low intake of animal products
Colorectal cancer (Yusof et al., 2012)	*A posteriori* DP	The Western DP, which mainly consists of red and processed meat and refined grains, is associated with

		an elevated risk of development of CC
Colorectal cancer (Magalhães et al., 2012)	*A posteriori* DP	The risk of CC was increased in DPs characterized by a high intake of red and processed meat and decreased with those labeled as healthy
Gastric cancer (Liu et al., 2014)	*A posteriori* DP	Some DPs may be associated with the risk of esophageal squamous cell carcinoma
Gastric cancer (Bertuccio et al., 2013)	*A posteriori* DP	There is a ~2-fold difference in GC risk between a 'prudent/healthy' diet (rich in fruits and vegetables), and a 'Western/unhealthy' diet (rich in starchy foods, meat and fats)
Gastric cancer (Shu et al., 2013)	*A posteriori* DP	Healthy DPs may decrease the risk of stomach cancer, whereas Western-style DPs and those including alcohol consumption may increase the risk
Gastric cancer (Bravi et al., 2012)	*A priori* and *a posteriori*	Diets rich in fruit and vegetables and low in alcohol and animal products are favorable for preventing upper aerodigestive tract cancers
Breast cancer (Alburquerque et al., 2014)	*A posteriori* DP	The Mediterranean DP and diets composed largely of vegetables, fruit, fish, and soy are associated with a decreased risk of breast cancer. There was no evidence of an association between traditional DPs and risk of breast cancer, and only one study showed a significant increase in risk associated with the Western DP. Diets that include alcoholic beverages may be associated with increased risk.
Endometrial cancer (Si et al., 2016)	*A posteriori* DP	No significant association with the risk of EC was found when comparing DPs with the highest versus the lowest category of alcohol-consumption
COPD (Zheng et al., 2016)	*A posteriori* DP	An increase in the risk of COPD was shown for the highest compared to the lowest categories of "unhealthy/Western-style" DP

DP: dietary pattern; COPD: chronic obstructive pulmonary disease; CC: colorectal cancer; GC: gastric cancer; EC: endometrial cancer; MDS: Med diet score; HEI: healthy eating index; DII: dietary inflammatory index

2.6 Dietary patterns and cardiometabolic health

Following an *a priori*- or *a posteriori*-defined dietary pattern has been shown to be positive for achieving better CVD and MetS outcomes. In the case of *a priori*, examples include the Mediterranean Dietary Pattern (Sánchez-Villegas et al., 2002), the Healthy Eating Index (HEI) (Kennedy et al., 1995), and the Dietary Approaches to Stop Hypertension (DASH) diet (Appel, 1997).

Other studies using the *a posteriori* approach have found an association between dietary patterns and CVD/MetS in several geographical regions and population age ranges (Heidemann et al., 2008; Fung et al., 2004; Mohammadifard et al., 2014; Denova-Gutiérrez et al., 2016 ; Atkins et al., 2016); however, some of the results appear contradictory, especially in children (Bull et al., 2016), the elderly (Nobbs et al., 2016), and within the dietary patterns labeled unhealthy (Osler et al., 2001; Akter et al., 2013; Naja et al., 2013). Some studies have highlighted the need for the analysis of dietary patterns to include all types of populations, as diets can vary significantly depending on culture (Green, 2016).

Moreover, secondary prevention strategies using the dietary patterns approach are being considered. A recent study conducted in Spain, which included 4,052 adults who work in a business environment, showed a higher prevalence of subclinical atherosclerosis (assessed via computed tomography) in the participants who followed the social-business eating pattern (rich in red meat, shellfish, pre-made foods, snacks, sugar-sweetened beverages, and excessive alcohol) and a lower prevalence amongst those consuming a Mediterranean-style diet (high in fruits, vegetables, whole grains, olive oil, low-fat dairy, lean meat and fish, and low in processed food) (Peñalvo et al., 2016).

The more recent American Guidelines for the Study of Nutrition implement the dietary pattern approach, including three main patterns: HEI, Mediterranean Dietary Pattern and Vegetarian Dietary Pattern (US Dietary Guidelines, 2015). Conversely, the up-to-date guidelines from the European Society of Cardiology for the prevention of CVD describe the relationships between single nutrients and CVD, giving only a brief description of the benefits of the Mediterranean Dietary Pattern for the prevention of CVD (ESC CVD Guidelines, 2016).

The American Guidelines were based on a systematic review in which the relationships between prevalent diet-based pathologies (specifically, obesity, CVD, and T2DM) and the different dietary patterns were analyzed. The results showed that, across the methodologies, the most consistent evidence was from cohort studies using an *a priori* index or score and randomized controlled trials testing specific patterns. From studies using factor or cluster analyses, limited conclusions were drawn, primarily due to the variability in the dietary patterns identified making comparisons difficult. Overall, no one specific dietary pattern was found to be more favorably associated with health outcomes. Rather, several dietary patterns were shown to be beneficial in reducing the risk of CVD, obesity, and/or T2DM: Mediterranean-style, DASH, and Dietary Guideline-related patterns (Systematic review US Guidelines; 2014).

Therefore, it may be concluded that optimal nutrition can be attained through several dietary patterns, and that a single dietary pattern approach or prescription is unnecessary (US Dietary Guidelines, 2015). Notwithstanding, a dietary pattern to support optimal nutrition and health should be based not only on biological and medical needs, but also on the preferences of the individual. Based on this idea, analyzing the current eating patterns from a specific population based on their basic choices is key, as it will permit exploration of many other factors linked to a specific eating behavior. Following a Mediterranean dietary pattern is clearly a healthy option, but this is unlikely to be the pattern that someone from India or Mexico would follow. Thus, as a result of globalization, thousands of different cultures and, consequently, thousands of diverse eating habits coexist in many cities worldwide. In addition, diets are multidimensional and dynamic; they include complex combinations of foods and nutrients consumed in varying formulations and contexts that change with age, disease onset, mood, and other milestones experienced throughout life (Hu, 2016).

The INTERHEART study provided some evidence for the effects of globalization on human nutrition and chronic disease risk; however, this evidence was indirect as the study did not specifically assess the impact of global trade and marketing on food consumption patterns across different countries. Nevertheless, the study suggested that the current trend of dietary convergence toward a typical Western diet is likely to play a role in the global epidemics of obesity and CHD (Iqbal et al., 2008; Hu, 2008).

2.7 Evidence-based nutrition for health professionals

Evidence-based practice was first defined by Sackett in 1996 as “the conscientious, explicit and judicious use of current best evidence in making decisions about the care of the individual patient. It means integrating individual clinical expertise with the best available external clinical evidence from systematic research” (Sackett, 1996). In 2002, the definition was improved by adding further detail and considering the following predictors when making a clinical decision: clinical expertise, patient values, and best research evidence. Furthermore, including the patient as an active figure in the clinical decision-making process was advocated. The definition also described best research practice as that having been conducted using accurate methodology (Sackett, 2002).

Unfortunately, in daily clinical practice, many nutritional recommendations have been (and continue to be) given which have no supporting scientific evidence. This highlights the need for the development of rigorous and precise studies in the field of nutrition (Franz, 2002).

In the area of dietary patterns, there is also the need to place an emphasis on carrying out high-quality, original research and systematic reviews which follow a structured process to objectively select and evaluate studies. These are necessary in order to ensure a strong future knowledge base regarding dietary patterns and chronic disease (Wirfält, 2013).

Clinicians need to be regularly updated about scientific novelties within their field of interest. In the case on nutrition, systematic reviews and meta-analyses summarizing the research of other studies are a valuable tool in daily practice. Exploring the relationship between diverse eating habits and the development of disease should help to adapt and tailor clinical and nutritional advice. Considering the large volume of research that has been carried out to date and the heterogeneity of results pertaining to *a posteriori* dietary patterns, there is a clear need for a systematic review and meta-analysis of observational studies to explore the associations between *a posteriori* dietary patterns and CVD/MetS.

3. HYPOTHESES AND OBJECTIVES

3.1 Hypotheses

3.1.1 Dietary patterns are associated with the risk of developing cardio metabolic diseases. “Healthy” dietary patterns play a protective role, whereas “Western-style” dietary patterns increase the risk.

3.1.2 Dietary patterns in individuals from Catalonia at high diabetes risk are related to the development of MetS and T2DM. Healthy and Mediterranean-style dietary patterns play a protective role, whereas Westernized dietary patterns increase the risk.

3.2 General objectives

3.2.1 To assess the relationship between dietary patterns and cardiometabolic diseases, using the *a posteriori* approach.

3.2.2 To analyze the dietary patterns of individuals at high diabetes risk in Catalonia, within a primary healthcare setting.

3.3 Specific objectives

3.3.1 To assess the relationship between *a posteriori* dietary patterns and the risk of experiencing CVD events or mortality; more specifically, their associations with coronary heart disease (CHD; including myocardial infarction and ischaemic heart disease), stroke (cerebrovascular disease and ischemic stroke), and overall CVD.

3.3.2 To evaluate the association between *a posteriori* dietary patterns and the risk of developing MetS.

3.3.3 To investigate the link between *a posteriori* dietary patterns and MetS and T2DM within a Mediterranean population of individuals with a high diabetes risk.

4. METHODS

In order to conduct the two systematic reviews and meta-analysis of the present thesis a specific methodology based on predefined steps was followed (Egger et al., 2007; Stroup et al., 2011).

4.1 Dietary patterns and CVD: a systematic review and meta-analysis of observational studies

4.1.1 Literature review

The search had no time limit or language restriction and was conducted on Pubmed, with the following Medical Subject Heading (MeSH) terms and text words: ("dietary patterns"[All Fields] OR "dietary intake"[All Fields]) AND (("mortality"[Subheading] OR "mortality"[All Fields] OR "mortality"[MeSH Terms]) OR ("myocardial infarction"[MeSH Terms] OR ("myocardial"[All Fields] AND "infarction"[All Fields]) OR "myocardial infarction"[All Fields]) OR ("stroke"[MeSH Terms] OR "stroke"[All Fields]) OR ("peripheral vascular diseases"[MeSH Terms] OR ("peripheral"[All Fields] AND "vascular"[All Fields] AND "diseases"[All Fields]) OR "peripheral vascular diseases"[All Fields] OR ("peripheral"[All Fields] AND "arterial"[All Fields] AND "disease"[All Fields]) OR "peripheral arterial disease"[All Fields]) OR (("hypertension"[MeSH Terms] OR "hypertension"[All Fields]) OR "elevated blood pressure"[All Fields])).

The search strategy retrieved 1,578 citations. After retrieval of articles from the search, the reference lists of all selected articles were checked for other potentially relevant articles; 6 additional papers were identified.

The *inclusion criteria* were as follows:

-Observational studies: cohort or case-control studies

-Assessment of the association of dietary patterns with clinical CVD, defined a priori as CHD (including myocardial infarction and ischemic heart disease), stroke (cerebrovascular disease and ischemic stroke) and overall CVD.

-Dietary patterns derived by cluster analysis, factor analysis or PCA

The *exclusion criteria* were as follows:

-No original research (i.e., reviews, editorials, nonresearch letters)

-Case reports or case series

-Ecological studies

-Studies not conducted in humans or adult population

-Studies without measures of association (hazard ratios, odds ratios, relative risks)

4.1.2 Data extraction of the included studies

Two investigators independently abstracted the articles that met the selection criteria, resolving any discrepancies by consensus. The investigators of the original studies were contacted if relevant information on eligibility or key study data were not available in the published report. The following information was recorded from all studies: study design, geographic region, gender, sample size, dietary assessment method, dietary patterns identified and by which *a posteriori* method, factors adjusted for in each study, outcome and outcome assessment, population age range and follow-up time (cohort studies), naming of patterns, factor loadings per pattern and total variance, measures of association (odds ratios, relative risks, hazard ratios) and their 95% confidence intervals (CIs).

We defined as prudent/healthy those patterns having generally healthy characteristics and as unhealthy/western those patterns having generally less-healthy characteristics, based on the food loading reported within individual studies. When several healthy and unhealthy patterns were reported, we first selected the pattern that explained the maximum of variation in food groups and then the pattern that fulfilled the most healthy or unhealthy criteria, determined by the highest factor loadings.

4.1.3 Quality assessment of the included studies

The quality assessment was based on the Newcastle-Ottawa assessment scale (NOS), using a star system for cohort and case-control studies. The 8-item instrument consists of three subscales: selection of subjects (4 items), comparability of subjects (1 item), and assessment of outcome/exposure (3 items). High-quality responses earn a star and the comparability question earns up to two stars, yielding a maximum total of 9 stars. The present study dichotomized the NOS scores, considering ≥7 points an indication of high methodological quality (Wells et al., 2012).

4.1.4 Statistical analysis

Cohort studies and case-control studies were analysed separately. The results of dietary patterns were variously reported as quintiles, quartiles or dietary factor scores and CVD risk or outcomes. A meta-analysis was conducted to combine the results and evaluate the risk of CVD in the highest compared to the lowest categories of prudent/healthy and western/unhealthy dietary patterns. Heterogeneity was quantified using the I^2 statistic, which describes the proportion of total variation in study estimates that is due to heterogeneity (Higgins et al., 2002). Each study's estimate and standard error (SE) was used to produce a forest plot that yielded a pooled estimate.

To explore sources of heterogeneity, we performed a subgroup analysis to evaluate whether results differed depending on the number of food frequency questionnaire (FFQ) items (categorized as median number of <101 or ≥101 FFQ items, or other information source), geographic area (Asia or other countries), *a posteriori* approach (PCA, factor analysis or cluster analysis), sex (men, women or both), sample size (categorized as <40,011 or ≥40,011 participants, according to median sample size in the meta-analysis), adjustment or non-adjustment for all key confounders (considering as key confounders age, sex, family history of CVD, CHD or stroke, diabetes, hypertension and body mass index) and incidence or mortality outcomes. We did not perform subgroup analysis of case-control studies because of the limited number of such studies that reported an association between dietary patterns and CVD outcomes.

Assessment of the relative influence of each study was based on pooled estimates, omitting one study at a time (sensitivity analysis). Finally, publication bias was assessed using the Egger test and funnel plots. Statistical analyses were conducted using Stata software (version 11; StataCorp LP).

4.2 Metabolic syndrome and dietary patterns: a systematic review and meta-analysis of observational studies

4.2.1 Literature review

The search had no time limit or language restriction and was conducted on Pubmed, CINAHL and Scopus databases. For Pubmed, the combination of Medical Subject Heading (MeSH) terms and text words was: ("diet"[MeSH Terms] OR "diet"[All Fields] OR "dietary"[All Fields] OR "dietary patterns"[All Fields] OR “food patterns”[All Fields]) AND (“Metabolic syndrome”[All Fields] OR "Metabolic Syndrome X"[Mesh] OR "Metabolic Syndrome X"[All Fields]).

For Scopus and CINAHL, the search terms were Diet OR dietary OR dietary patterns OR food patterns AND Metabolic syndrome OR syndrome X OR metabolic syndrome X.

The search strategy retrieved 3,730 citations. After retrieval of articles from the search, the reference lists of all selected articles were checked for other potentially relevant articles; 8 additional papers were identified.

The *inclusion criteria* were as follows:

-Observational studies

-Assessment of the association of dietary patterns with MetS (any existent definition)

-Dietary patterns derived by cluster analysis, factor analysis or PCA

The *exclusion criteria* were as follows:

-No original research (i.e., reviews, editorials, non-research letters)

-Case reports or case series

-Ecological studies

-Studies not conducted in humans or adult population

-Studies without measures of association (hazard ratios, odds ratios, relative risks)

4.2.2 Data extraction of the included studies

Two investigators independently abstracted the articles that met the selection criteria, resolving any discrepancies by consensus. The investigators of the original studies were contacted if relevant information on eligibility or key study data were not available in the published report. The following information was recorded from all studies: study design, geographic region, sample size, dietary assessment method, dietary patterns identified and by which *a posteriori* method, factors adjusted for in each study, outcomes and outcome assessment, health status, criteria for defining MetS, population, sex of participants, age range, follow-up time (cohort studies), naming of patterns, factor loadings per pattern, total variance and main conclusions of each study, measures of association (odds ratios, relative risks or hazard ratios) and their 95% CIs.

We defined as prudent/healthy those patterns having generally healthy characteristics and as unhealthy/western those patterns perceived to have generally less-healthy characteristics, based on the food loading reported within individual studies. When several healthy and unhealthy patterns were reported, we first selected the pattern that explained the maximum of variation in food groups and then the pattern that fulfilled the most healthy or unhealthy criteria, determined by the highest factor loadings. The classification of each food was based on the recommendations of different consensus dietary guidelines such as the Eighth Edition of the Dietary Guidelines for Americans and The Guidelines for a Healthy Diet from Sociedad Española de Nutrición Comunitaria (US Dietary Guidelines, 2015; Guías SENC, 2011).

4.2.3 Quality assessment of the included studies

As the studies were observational, their quality was assessed according to the following: (1) study design and method; (2) attrition; (3) measurement of dietary patterns; (4) measurement of MetS and (5) statistical analysis. Sixteen criteria were chosen and adapted from a detailed checklist developed for observational longitudinal studies (Tooth et al., 2005) including the six areas of potential study bias recommended for consideration in any quality-appraisal component of systematic reviews (Hayden et al., 2006) Each criterion was scored as yes (1), no (0) or partially achieved (0.5), based on the available information. The scores were totalled to give an overall indication of study quality (Crichton et al, 2011).

The review was registered at PROSPERO with registration number CRD42015029807.

4.2.4 Statistical analysis

Cohort studies and cross-sectional studies were analysed separately. The results of dietary patterns were variously reported as quintiles, quartiles, or dietary factor scores and MetS incidence or prevalence. A meta-analysis was conducted to combine the results and compare the risk/prevalence of MetS in the highest categories of prudent/healthy and western/unhealthy dietary patterns, compared to the lowest category. To pool odds ratio (OR) or relative risk (RR) estimates from individual studies, we used an inverse variance weighted random-effects model. Heterogeneity was quantified using the I^2 statistic, which describes the proportion of total variation in study estimates that is due to heterogeneity (Higgins et al., 2002). Each study's estimate and standard error (SE) was used to produce a forest plot that yielded a pooled estimate.

To explore sources of heterogeneity, we performed subgroup analysis and meta-regression in both dietary patterns to evaluate whether results differed. Several factors were analysed according to geographic area (Asia, Europe, America and Australia), *a posteriori* approach (PCA, factor analysis, cluster analysis or other assessment), sex (men, women or both), MetS definition (NCEP-ATP III, IDF or others), adjustment or not for all key confounders (age, sex, body mass index, energy intake and physical activity), age of participants (young adults 18-35, adults 36-70, mixed of younger adults, adults and older adults, mixed of young adults and adults or not reported) and health status (not having CVD and/or metabolic diseases, having CVD and/or metabolic diseases or general population) .

Assessment of the relative influence of each study was based on pooled estimates, omitting one study at a time (sensitivity analysis). Finally, publication bias was assessed using funnel plots. All statistical analyses were conducted using Stata software (version 12; StataCorp LP).

4.3 Dietary patterns in adults with high risk diabetes in Catalonia Primary Health Care settings: a cohort revisited

The third study consisted on the analysis of dietary patterns from a pre-existing cohort of high risk diabetes individuals related to the development of MetS and T2DM.

The DE-PLAN-CAT study was a prospective cohort designed to investigate the prevention of diabetes in Primary Health Care (PHC) settings in high-risk populations using lifestyle, physical activity and nutritional interventions (Costa et al., 2012). Participants, aged 45-75 years, were recruited from 18 PHC centers in Catalonia (Spain). In order to select the participants with high risk for diabetes firstly, 2,054 individuals were screened with the Finnish Diabetes Risk Score (FINDRISC). The follow-up period began in 2006 and finished in 2010.

4.3.1 Assessment of dietary intake and dietary patterns derivation

At baseline and in every follow-up intervention's examination usual dietary intake was assessed by a 46-item FFQ provided by the European DE-PLAN/IMAGE project, adapted to the Spanish language and habits, and focused on dietary and physical exercise behavior. Food and beverages from the FFQ were categorized into 21 food groups that were used to derive dietary patterns via PCA and to determine factor loadings for each of those groups.

4.3.2 Assessment of MetS and T2DM

MetS and its components were defined according to the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) guidelines, which characterizes MetS by the presence of, at least, 3 of the following conditions: *central obesity* (waist circumference >102 cm in men and >88 cm in women), *high serum triglycerides* (≥150mg/dL (≥1.695 mmol/L)), *low serum HDL cholesterol* (<40mg/dL (<1.036 mmol/L) in men and <50mg/dL (< 1.295 mmol/L) in women), *high blood pressure* (PAS ≥130 mmHg, PAD ≥ 85mmHg), and *high fasting glucose* (≥100mg/dL (≥5.6 mmol/L)) (23). The assessment of the association between dietary patterns and MetS and MetS components excluded those participants that had the syndrome at baseline. The diagnostic of T2DM was categorized according to the WHO criteria based on the results of 2h post-load glucose and being > 11.1 mmol/L.

4.3.3 Statistical analysis

In order to derive the different dietary patterns, PCA was performed considering factors with eigenvalues >1.5 and scree tests. In addition, the identified factors were orthogonally rotated to simplify the factor structure and to enhance their interpretability. For each factor, foods with factor loadings ≥0.30 were considered to contribute significantly to the pattern. Afterwards, factors were numbered and given provisional labels according to the food groups that loaded highly on the pattern.

A descriptive analysis was first performed on the baseline characteristics of study participants and categorized into tertiles. ANOVA analysis was used to determine the difference on the characteristics among them; the distribution of qualitative variables across tertiles was evaluated with chi-square tests.

To ascertain associations between dietary patterns and MetS, MetS components, or T2DM, Cox regression models were performed, being each dietary pattern the independent variable and MetS, type 2 diabetes or components of MetS the dependent variable. We controlled for potential confounders for each dependent variable. In the case of MetS and MetS components we adjusted for age, sex, smoking, and physical activity. In type 2 diabetes we adjusted for age, sex, smoking, physical activity, BMI, and hypertension. Hazard ratios and 95% confidence intervals are presented. New cases of both MetS and T2DM across the four intervention years, and cumulative incidence rates were also assessed. For all analyses, SPSS version 22 was used.

5. RESULTS

The dissertation is based on the results of three different projects. The following two first articles have been published in international journals, as a result of the work performed.

1. Rodríguez-Monforte M, Flores-Mateo G, Sánchez E. Dietary patterns and CVD: a systematic review and meta-analysis of observational studies. Br J Nutr 2015;114:1341-59.

2. Rodríguez-Monforte M, Sánchez E, Barrio F, Costa B, Flores-Mateo G. Metabolic syndrome and dietary patterns: a systematic review and meta-analysis of observational studies. Eur J Nutr 2016 [Epub ahead of print].

3. Rodríguez-Monforte M, Sánchez E, Barrio F, Costa B, Delagneau J, Benadero I, Flores-Mateo G. Dietary patterns in adults with high diabetes risk in primary healthcare settings in Catalonia: a cohort revisited. Draft.

5.1 Publication one

Dietary patterns and CVD: a systematic review and meta-analysis of observational studies

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British Journal of Nutrition 2015; 114:1341-59.

Impact Factor (JCR): 3.311

ABSTRACT

Introduction: Epidemiologic studies show that diet is linked to the risk of developing cardiovascular diseases (CVD). The objective of this meta-analysis was to estimate the association between empirically derived dietary patterns and CVD.

Materials and Methods: PubMed was searched for observational studies of data-driven dietary patterns that reported outcomes of cardiovascular events. The association between dietary patterns and CVD was estimated using a random-effects meta-analysis with 95% confidence intervals (CIs).

Results: Twenty-two observational studies met the inclusion criteria. The pooled relative risk (RR) for CVD, coronary heart disease (CHD) and stroke in a comparison of the highest to the lowest category of prudent/healthy dietary patterns in cohort studies were: 0.69 (95% CI: 0.60, 0.78; I^2 = 0%), 0.83 (95% CI: 0.75, 0.92; I^2 = 44.6%), 0.86 (95% CI: 0.74, 1.01; I^2 = 59.5%), respectively. The pooled RR of CHD in a case-control comparison of the highest to the lowest category of prudent/healthy dietary patterns was 0.71 (95% CI: 0.63, 0.80; I^2 = 0%). The pooled RR for CVD, CHD and stroke in a comparison of the highest to the lowest category of western dietary patterns in cohort studies was 1.14 (95% CI: 0.92, 1.42; I^2 =56.9%), 1.03 (95% CI: 0.90, 1.17; I^2 =59.4%), and 1.05 (95% CI: 0.91, 1.22; I^2 =27.6%), respectively; in case-control studies there was evidence of increased CHD risk.

Conclusions: Our results support the evidence of the prudent/healthy pattern as a protective factor for CVD.

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Dietary patterns and CVD: a systematic review and meta-analysis of observational studies

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Abstract

Epidemiological studies show that diet is linked to the risk of developing CVD. The objective of this meta-analysis was to estimate the association between empirically derived dietary patterns and CVD. PubMed was searched for observational studies of data-driven dietary patterns that reported outcomes of cardiovascular events. The association between dietary patterns and CVD was estimated using a random-effects meta-analysis with 95 % CI. Totally, twenty-two observational studies met the inclusion criteria. The pooled relative risk (RR) for CVD, CHD and stroke in a comparison of the highest to the lowest category of prudent/healthy dietary patterns in cohort studies was 0·69 (95 % CI 0·60, 0·78; $I^2 = 0$ %), 0·83 (95 % CI 0·75, 0·92; $I^2 = 44·6$ %) and 0·86 (95 % CI 0·74, 1·01; $I^2 = 59·5$ %), respectively. The pooled RR of CHD in a case–control comparison of the highest to the lowest category of prudent/healthy dietary patterns was 0·71 (95 % CI 0·63, 0·80; $I^2 = 0$ %). The pooled RR for CVD, CHD and stroke in a comparison of the highest to the lowest category of western dietary patterns in cohort studies was 1·14 (95 % CI 0·92, 1·42; $I^2 = 56·9$ %), 1·03 (95 % CI 0·90, 1·17; $I^2 = 59·4$ %) and 1·05 (95 % CI 0·91, 1·22; $I^2 = 27·6$ %), respectively; in case–control studies, there was evidence of increased CHD risk. Our results support the evidence of the prudent/healthy pattern as a protective factor for CVD.

Key words: **Dietary patterns: CVD: Systematic reviews: Meta-analyses**

CVD is the world's leading cause of morbidity and mortality, affecting millions of people in developed and developing countries[1,2]. In Europe, a decline in CVD deaths has been observed, particularly in affluent countries[3]. Analysis from the WHO MONICA (Multinational MONitoring of trends and determinants in CArdiovascular disease) project attributed this lower CVD incidence and more than two-thirds of the decline in CHD deaths to a reduced exposure to risk factors, such as smoking or high blood cholesterol levels[4]. Nevertheless, CVD remains the major cause of overall death and premature deaths in Europe, especially in people younger than 75 years, accounting for 42 and 38 % of all deaths in women and men, respectively. In addition to 4·3 million deaths every year, there is an enormous individual and societal burden of cardiovascular ill-health[5]. Similarly, some studies have found that a large proportion of the decline in mortality – from approximately 44 % in the USA, Italy, England and Spain, for example, to as much as 72 % in Finland – can be attributed to reduced exposure to risk factors[6–9]. The interrelationship between many chronic conditions and their risk factors also means that targeting key CVD risk factors may help prevent cancer and diabetes[10].

Multiple risk factors for CVD, such as family history, obesity, diabetes, hypertension and hypercholesterolaemia, are well established[11]. Furthermore, the evolution of the disease depends on how many factors can be modified throughout life. The existing research shows the importance of dietary and lifestyle changes in the prevention of CVD[12,13].

The multiple ways of studying relationships between CVD and diet, specific nutrients, food groups or dietary patterns offer the possibility to study the association of foods and nutrients of a specific type of diet with the risk of disease. The link between diet and the risk of a specific disease can be analysed by evaluating dietary patterns. A technique known as dietary pattern analysis has evolved in nutritional epidemiology as a complementary approach to the study of individual foods. Furthermore, there are two different ways to define dietary patterns: '*a priori*', focusing on the construction of patterns that reflect hypothesis-oriented combinations of foods and nutrients, and '*a posteriori*', which builds on exploratory statistical methods and uses the observed dietary data in order to extract dietary patterns. Both ways show positive and negative aspects; '*a priori*'

Abbreviation: RR, relative risk.

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methods are based on predefined diet quality indices, using current nutrition knowledge, and identify a desirable pattern adherence to which could maximise health benefits. On the contrary, '*a posteriori*' methods use dietary data in-hand but might be debatable in relating diet and disease; the extracted dietary patterns may have little relation to morbidity and mortality when nutrients or foods relevant to the aetiology of diseases are not included in their definition. However, focus on '*a posteriori*' dietary patterns helps avoid increased heterogeneity[14,15]. Diverse classifications have been used to group the different dietary patterns, primarily categorising them as healthy or prudent *v.* unhealthy or western[16,17]. The Mediterranean dietary pattern approach, classified as a prudent or healthy dietary pattern, is one of the best established[18–21]. Several studies have reported a weak association between dietary patterns and CVD risk, especially those dietary patterns with high fat, dairy products, fried foods and meat intake classified as western or unhealthy. Our systematic review and meta-analysis complements the latest meta-analysis on this topic by analysing a larger population (610 691 participants), adding studies that identified dietary patterns by cluster analysis and considering not only CVD or stroke mortality but also CVD outcomes such as clinical CVD, CHD, stroke and overall CVD[22–32].

The objective of this study was to systematically review and synthesise the results from observational studies and to clarify the association between empirically defined (*a posteriori*) dietary patterns and CVD outcomes.

Methods

Search strategy

We searched PubMed for relevant studies published through September 2014 using the following combination of Medical Subject Heading (MeSH) terms and text words, with no language limitations: ('dietary patterns'[All Fields] OR 'dietary intake'[All Fields]) AND (('mortality'[Subheading] OR 'mortality'[All Fields] OR 'mortality'[MeSH Terms]) OR ('myocardial infarction'[MeSH Terms] OR ('myocardial'[All Fields] AND 'infarction'[All Fields]) OR 'myocardial infarction'[All Fields]) OR ('stroke'[MeSH Terms] OR 'stroke'[All Fields]) OR ('peripheral vascular diseases'[MeSH Terms] OR ('peripheral'[All Fields] AND 'vascular'[All Fields] AND 'diseases'[All Fields]) OR 'peripheral vascular diseases'[All Fields] OR ('peripheral'[All Fields] AND 'arterial'[All Fields] AND 'disease'[All Fields]) OR 'peripheral arterial disease'[All Fields]) OR (('hypertension'[MeSH Terms] OR 'hypertension'[All Fields]) OR 'elevated blood pressure'[All Fields])).The search strategy retrieved 1578 citations (Fig. 1). We included all observational studies that assessed the association of dietary patterns analysed by cluster analysis, factor analysis or principal component

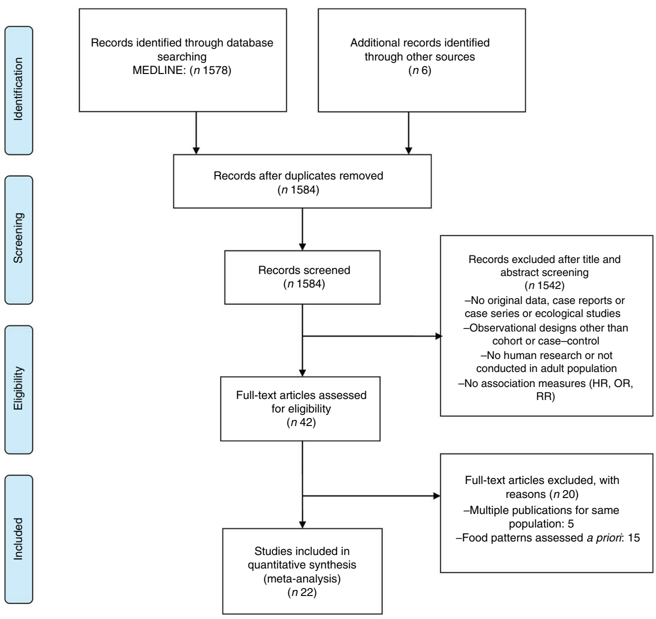

Fig. 1. Flow diagram of the study selection process. HR, hazard ratio; OR, odds ratio; RR, relative risk.

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analysis (PCA) with CVD outcomes. We limited the search to clinical CVD, defined *a priori* as CHD (including myocardial infarction and ischaemic heart disease), stroke (cerebrovascular disease and ischaemic stroke) and overall CVD.

Two investigators (M. R.-M and G. F.-M.) independently reviewed each of the 1578 papers identified and applied the following exclusion criteria: (a) no original research (i.e. reviews, editorials, non-research letters); (b) case reports or case series; (c) ecological studies; (d) lack of data on dietary patterns; (e) studies without CVD, cardiovascular death or cardiovascular events as the end point; (f) studies not conducted in humans or adult population; (g) studies without measures of association (hazard ratios, OR, relative risks (RR)); and (h) observational designs other than cohort or case–control. Fig. 1 summarises the study selection process. Any discrepancies were resolved by consensus.

After retrieval of articles from the search, the reference lists of all selected articles were checked for other potentially relevant articles; six additional papers were identified.

Data extraction and quality assessment

Two investigators (M. R.-M. and G. F.-M.) independently abstracted the articles that met the selection criteria. They resolved discrepancies by consensus. The investigators of the original studies were contacted if relevant information on eligibility or key study data were not available in the published report. The following information was recorded from all studies: study design, geographic region, sex, sample size, dietary assessment method, dietary patterns identified and by which *a posteriori* method, factors adjusted for in each study, outcome and outcome assessment, population age range and follow-up time (cohort studies), naming of patterns, factor loadings per pattern and total variance (Tables 1 and 2, and see online Supplementary Material). Measures of association (OR, RR, hazard ratios) and their 95 % CI were abstracted.

We defined those patterns having generally healthy characteristics as prudent/healthy and those patterns having generally less-healthy characteristics as unhealthy/western, on the basis of the food loading reported within individual studies. The prudent/healthy pattern tended to have high-factor loading for food such as fruit, vegetables, whole grains, fish and poultry. The unhealthy/western pattern was characterised by high-factor loadings for foods such as meat, processed meat, refined grains, sweets, sugar drinks and fried foods. When several healthy and unhealthy patterns were reported, we first selected the pattern that explained the maximum of variation in food groups[25,26,28,31,39] and then the pattern that fulfilled the most healthy or unhealthy criteria, determined by the highest factor loadings[30,37,43,44,47].

As the studies were observational, the quality assessment was based on the Newcastle–Ottawa Assessment Scale (NOS), using a star system for cohort and case–control studies. The NOS is one of the more comprehensive instruments for assessing the quality of non-randomised studies in meta-analyses. The eight-item instrument consists of three subscales: selection of subjects (four items), comparability of subjects (one item) and assessment of outcome/exposure (three items). High-quality responses earn a star and the comparability question earns up to two stars, yielding a maximum total of nine stars. The present study dichotomised the NOS scores, considering ≥7 points an indication of high methodological quality[33] (Appendices 1 and 2).

Statistical analysis

Cohort studies and case–control studies were analysed separately. The results of dietary patterns were variously reported as quintiles, quartiles or dietary factor scores and CVD risk or outcomes. A meta-analysis was conducted to combine the results and evaluate the risk of CVD in the highest compared with the lowest categories of prudent/healthy and western/unhealthy dietary patterns. Heterogeneity was quantified using the I^2 statistic, which describes the proportion of total variation in study estimates that is due to heterogeneity[34]. Each study's estimate and SE was used to produce a forest plot that yielded a pooled estimate.

To explore sources of heterogeneity, we performed a subgroup analysis to evaluate whether results differed depending on the number of FFQ items (categorised as median number of <101 or ≥101 FFQ items or other information source), geographic area (Asia or other countries), *a posteriori* approach (PCA, factor analysis or cluster analysis), sex (men, women or both), sample size (categorised as >40 011 or ≥40 011 participants, according to median sample size in the meta-analysis), adjustment or non-adjustment for all key confounders (considering as key confounders age, sex, family history of CVD, CHD or stroke, diabetes, hypertension and BMI) and incidence or mortality outcomes. We did not perform subgroup analysis of case–control studies because of the limited number of such studies that reported an association between dietary patterns and CVD outcomes.

Assessment of the relative influence of each study was based on pooled estimates, omitting one study at a time (sensitivity analysis). Finally, publication bias was assessed using the Egger test and funnel plots. Statistical analyses were conducted using the Stata software (version 11; StataCorp LP).

Results

Study selection

The search strategy retrieved 1578 articles in the PubMed index. Of these citations, 1542 publications were excluded on the basis of title and abstract and twenty were excluded after full-text review. The remaining twenty-two observational studies, all published between 2000 and 2014, were included in the meta-analysis[23–31,35–47] (Fig. 1). The studies were conducted in Europe[23,26,28,31,38,39,41], America[35,36,40,44,45], Asia[25,27,30,37,43,47] and Australia[24]. There were nineteen cohort studies[23–31,35–44] (Table 1) and three case–control studies[45–47] (Table 2). The number of cases ranged from 449[29] to 74 942[37]. All the selected studies assessed total CVD, CVD mortality, CHD and stroke as the end point; Nettleton *et al.*[42] also assessed revascularisation. All of these papers met most of the present study's quality criteria (Tables 1 and 2).

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Table 1. Prospective cohort studies of dietary patterns and CVD
(Hazard ratios, risk ratios and 95 % confidence intervals)

References, country	Population	Sample size (sex)	Age range (years)	Outcome ascertainment	Diet-assessment method (items)	Follow-up (years)	Outcome	Hazard ratio/risk ratio	95 % CI	Dietary pattern identified and method used	Factors adjusted for in analyses	NOS quality score/number of stars/9*
Hu *et al.*[35], USA	US health professionals	44 875 (men)	40–75	Medical records	FFQ (131)	8	CHD incidence	Prudent Q1:1·0 Q2:0·90 Q3:0·83 Q4:0·79 Q5:0·75 Western Q1:1·0 Q2:1·21 Q3:1·27 Q4:1·27 Q5:1·43	 0·74, 1·08 0·68, 1·01 0·64, 0·98 0·59, 0·95 0·98, 1·50 0·99, 1·63 0·99, 1·69 1·01, 2·01	Prudent/healthy, western/unhealthy FA	Age, BMI, smoking alcohol consumption, physical activity, parental history of AMI before 60 years, multivitamin and vitamin E supplements use, BP, diabetes, hypercholesterolaemia, total energy and nutrient intake	8
Osler *et al.*[23], Denmark	Copenhagen county	7316 (both)	30–60	Medical records and National Board of Health	FFQ (26)	1	CHD incidence	–		Western-unhealthy FA	Age, sex, BMI, smoking, alcohol consumption, physical activity, education	8
Fung *et al.*[36], USA	Boston, Nurses' Health Study	71 768 (women)	38–63	Interview, medical records or/and National Death Index	FFQ (116)	14	Stroke incidence	Prudent Q1:1·0 Q2:0·89 Q3:1·02 Q4:0·85 Q5:0·74 Western Q1:1·0 Q2:1·16 Q3:1·30 Q4:1·26 Q5:1·56	 0·54, 1·02 1·05, 2·33	Prudent/healthy, western/unhealthy FA	Age, BMI, alcohol consumption, smoking, physical activity, family history of AMI, BP, hypercholesterolaemia, diabetes, menopausal status, aspirin use, multivitamin use, food and nutrient intake	8
Cai *et al.*[37], China	Shanghai Women's Health Study	74 942 (women)	40–70	Medical records and National Death Index	FFQ (71)	5·7	CHD and stroke mortality	Prudent CHD Q1:1·0 Q2:0·51 Q3:0·91 Q4:1·10 Western CHD Q1:1·0 Q2:0·99 Q3:1·14 Q4:1·58 Prudent stroke Q1:1·0 Q2:1·20 Q3:1·09 Q4:1·35 Western stroke Q1:1·0 Q2:1·03 Q3:0·94 Q4:0·76	 0·25,1·02 0·50, 1·65 0·61, 1·99 0·56, 1·78 0·61, 2·14 0·81, 3·08 0·83, 1·75 0·74, 1·61 0·92, 1·97 0·75, 1·43 0·65, 1·35 048, 1·19	Prudent/healthy, western/unhealthy FA	Age, BMI, smoking, alcohol consumption, physical activity, WHR, education, marital status, income, tea consumption, ginseng intake	8
Harriss *et al.*[24], Australia	Melbourne Collaborative study	40 653 (both)	40–69	Medical records or/and National Death Index	FFQ (121)	10·4	CVD mortality	Prudent Q1:1·0 Q2:0·92 Q3:0·89 Q4:0·70 Western Q1:1·0 Q2:0·84 Q3:0·99 Q4:0·91	 0·75,1·14 0·69, 1·14 0·51, 0·96 0·67, 1·06 0·79, 1·24 0·70, 1·18	Prudent/healthy, western/unhealthy FA	Age, sex, BMI, smoking, physical activity, country of birth, family history of CVD, diabetes and BP, education, social isolation, WHR, energy intake	8

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British Journal of Nutrition

Table 1. *Continued*

References, country	Population	Sample size (sex)	Age range (years)	Outcome ascertainment	Diet-assessment method (items)	Follow-up (years)	Outcome	Hazard ratio/risk ratio	95 % CI	Dietary pattern identified and method used	Factors adjusted for in analyses	NOS quality score/number of stars/9*
Shimazu *et al.*[24], Japan	Ohsaki National Health Insurance study	40 547 (both)	40–79	Death certificates filed	FFQ (40)	7	Stroke and CHD mortality	Prudent CHD Q1:1·0 Q2:0·86 Q3:0·71 Q4:0·82 Western CHD Q1:1·0 Q2:1·10 Q3:1·39 Q4:1·50 Prudent stroke Q1:1·0 Q2:0·71 Q3:0·67 Q4:0·64 Western stroke Q1:1·0 Q2:0·89 Q3:1·11 Q4:1·00	 0·57, 1·29 0·46, 1·11 0·52, 1·29 0·72, 1·70 0·89, 2·16 0·95, 2·37 0·54, 0·92 0·51, 0·88 0·48, 0·86 0·69, 1·15 0·85, 1·45 0·74, 1·35	Prudent/healthy, western/unhealthy FA	Age, sex, BMI, smoking, alcohol consumption, walking duration, energy intake, BP, education	9
Akesson *et al.*[38], Sweden	Swedish mammography cohort	24 444 (women)	43–83	Medical records or/and National Death Index	FFQ (96)	6·2	CHD incidence	Prudent Q1:1·71 Q2:1·50 Q3:1·28 Q4:1·22 Q5:1·0	 1·14, 2·55 1·00, 2·25 0·85, 1·94 0·80, 1·84	Prudent/healthy FA	Age, smoking, alcohol consumption, physical activity, family history of AMI, hypercholesterolaemia, hypertension, hormone therapy use, aspirin use, WHR, energy and nutrient intake, education	8
Brunner *et al.*[41], UK	Whitehall II study	7731 (both)	50	Medical records or/and National Death Index	FFQ (127)	15	CHD incidence		–	Prudent/healthy CA	Sex, BMI, smoking, physical activity, waist circumference, systolic BP, cholesterol, TAG, employment grade	9
Heidemann *et al.*[40], USA	Nurses' Health Study	72 113 (women)	30–55	Family reports or/and National Death Index	FFQ (116)	18	CVD mortality	Prudent Q1:1·0 Q2:0·78 Q3:0·85 Q4:0·69 Q5:0·72 Western Q1:1·0 Q2:0·98 Q3:1·13 Q4:1·20 Q5:1·22	 0·65, 0·93 0·71, 1·01 0·57, 0·83 0·60, 0·87 0·81, 1·19 0·93, 1·36 0·99, 1·45 1·01, 1·48	Prudent/healthy, western/unhealthy FA	Age, BMI, smoking, physical activity, hormone therapy, BP, multivitamin supplement, dietary intake	9
Panagiotakos *et al.*[39], Greece	ATTICA study	3042 (both)	18–89	Medical records	FFQ (156)	5	CVD incidence	–		Prudent/healthy, western/unhealthy PCA	Age, sex, years of school, physical activity, BP, cholesterol, fasting glucose, diabetes, family history of CHD, BMI, obesity, abnormal waist	9
Nettleton *et al.*[42], USA	MESA study	5316 (both)	45–84	Medical records and/or National Death Index	FFQ (120)	7	CVD incidence	Prudent Q1:1·0 Q2:0·81 Q3:0·82 Q4:0·67 Q5:0·54	 0·52, 1·27 0·52, 1·30 0·41, 1·08 0·33, 0·91	Prudent/healthy PCA	Age, sex, BMI, smoking, physical activity, ethnicity, supplement use, waist circumference, BP, CRP, IL-6, fibrinogen, homocysteine, HDL, LDL, energy intake, education	8

British Journal of Nutrition

Table 1. *Continued*

References, country	Population	Sample size (sex)	Age range (years)	Outcome ascertainment	Diet-assessment method (items)	Follow-up (years)	Outcome	Hazard ratio/ risk ratio	95 % CI	Dietary pattern identified and method used	Factors adjusted for in analyses	NOS quality score/number of stars/9*
Guallar-Castillon *et al.*[26], Spain	EPIC study	40 757 (both)	29–69	Medical records, population-based AMI registries and National Death Index	Interview	11	CHD incidence	Prudent		Prudent/ healthy, western/ unhealthy FA	Age, sex, BMI, smoking, physical activity, diabetes, hypertension, hypercholesterolaemia, cancer, waist circumference, oral contraceptives, menopausal status, hormone therapy, energy and nutrient intake, education	9
								Q1:1·0				
								Q2:0·77	0·61, 0·98			
								Q3:0·64	0·50, 0·83			
								Q4:0·56	0·43, 0·73			
								Q5:0·73	0·57, 0·94			
								Western				
								Q1:1·0				
								Q2:0·96	0·75, 1·24			
								Q3:0·81	0·61, 1·09			
								Q4:0·98	0·72, 1·34			
								Q5:0·86	0·60, 1·24			
Maruyama *et al.*[27], Japan	JACC study	64 037 (both)	40–79	Medical records and/or National Death Index	FFQ (40)	12·6	Stroke and CHD mortality	Prudent CHD men		Prudent/ healthy, western-unhealthy FA	Age, sex, BMI, current smoker, physical activity, mental stress, sleep duration, total energy intake, BP and diabetes, education	8
								Q1:1·0				
								Q2:0·81	0·56, 1·19			
								Q3:0·77	0·53, 1·14			
								Q4:0·79	0·54, 1·16			
								Q5:0·73	0·49, 1·08			
								Western CHD men				
								Q1:1·0				
								Q2:0·73	0·51, 1·06			
								Q3:0·89	0·63, 1·27			
								Q4:0·72	0·49, 1·06			
								Q5:0·72	0·48, 1·08			
								Prudent stroke men				
								Q1:1·0				
								Q2:1·11	0·83, 1·49			
								Q3:1·07	0·80, 1·43			
								Q4:1·19	0·90, 1·58			
								Q5:1·13	0·85, 1·51			
								Western stroke men				
								Q1:1·0				
								Q2:0·79	0·61, 1·03			
								Q3:0·84	0·65, 1·09			
								Q4:0·93	0·71, 1·21			
								Q5:0·97	0·74, 1·27			
								Prudent CHD women				
								Q1:1·0				
								Q2:0·87	0·57, 1·43			
								Q3:0·88	0·57, 1·33			
								Q4:0·66	0·42, 1·05			
								Q5:0·67	0·43, 1·06			
								Western CHD women				
								Q1:1·0				
								Q2:0·85	0·57, 1·26			
								Q3:0·93	0·61, 1·41			
								Q4:0·96	0·61, 1·50			
								Q5:0·73	0·42, 1·26			
								Prudent stroke women				
								Q1:1·0				
								Q2:0·93	0·70, 1·24			
								Q3:0·80	0·59, 1·08			
								Q4:0·89	0·66, 1·19			
								Q5:0·91	0·68, 1·22			
								Western stroke women				
								Q1:1·0				
								Q2:0·91	0·70, 1·18			
								Q3:0·98	0·75, 1·30			
								Q4:0·87	0·64, 1·18			
								Q5:1·03	0·75, 1·41			

Table 1. *Continued*

References, country	Population	Sample size (sex)	Age range (years)	Outcome ascertainment	Diet-assessment method (items)	Follow-up (years)	Outcome	Hazard ratio/risk ratio	95 % CI	Dietary pattern identified and method used	Factors adjusted for in analyses	NOS quality score/number of stars/9*
Stricker *et al.*[28], The Netherlands	EPIC study	35 910 (both)	20–69	Medical records and/or National Death Index	FFQ (79)	13	Stroke and CHD incidence	Prudent CHD		Prudent/ healthy, western/ unhealthy PCA	Age, sex, BMI smoking, physical activity, energy intake, diabetes, WHR, BP, education	8
								Q1:1·0				
								Q2:0·99	0·87, 1·12			
								Q3:0·96	0·85, 1·10			
								Q4:0·87	0·75, 1·00			
								Western CHD				
								Q1:1·0				
								Q2:0·89	0·78, 1·01			
								Q3:0·94	0·81, 1·09			
								Q4:0·91	0·76, 1·08			
								Prudent stroke				
								Q1:1·0				
								Q2:0·85	0·69, 1·05			
								Q3:0·78	0·62, 0·98			
								Q4:0·69	0·53, 0·88			
								Western stroke				
								Q1:1·0				
								Q2:0·81	0·65, 1·01			
								Q3:0·94	0·73, 1·52			
								Q4:1·11	1·81, 1·52			
Chen *et al.*[43], India	HEALS	11 116 (both)	18–75	Proxy reports, medical records,	FFQ (39)	6·6	Stroke and CHD mortality	Prudent CHD		Prudent/ healthy, western/ unhealthy PCA	Age, sex, BMI, current smoker, BP, education, energy intake, own a land, own a television	8
								Q1:1·0				
								Q2:1·01	0·57, 1·80			
								Q3:1·06	0·61, 1·85			
								Q4:0·79	0·44, 1·40			
								Western CHD				
								Q1:1·0				
								Q2:1·38	0·63, 3·04			
								Q3:1·76	0·84, 3·71			
								Q4:1·94	0·95,·4·00			
								Prudent stroke				
								Q1:1·0				
								Q2:1·88	1·03, 3·46			
								Q3:0·87	0·43, 1·75			
								Q4:1·05	0·56, 1·99			
								Western stroke				
								Q1:1·0				
								Q2:0·80	0·41, 1·56			
								Q3:0·69	0·36, 1·36			
								Q4:0·74	0·39, 1·41			
Judd *et al.*[44], USA	REGARDS	28 151 (both)	>65	Telephone contact, medical records, National Death Index	FFQ (107)	5·7	Stroke incidence	Prudent		Prudent/ healthy, western/ unhealthy PCA	Age, sex, BMI, smoking, sedentary, race, residence, education, income	9
								Q1:1·0				
								Q2:0·80	0·62, 1·02			
								Q3:0·74	0·57, 0·96			
								Q4:0·85	0·65, 1·12			
								Western				
								Q1:1·0				
								Q2:0·93	0·71, 1·22			
								Q3:1·12	0·86, 1·47			
								Q4:1·30	0·97, 1·76			

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Table 1. *Continued*

References, country	Population	Sample size (sex)	Age range (years)	Outcome ascertainment	Diet-assessment method (items)	Follow-up (years)	Outcome	Hazard ratio/ risk ratio	95 % CI	Dietary pattern identified and method used	Factors adjusted for in analyses	NOS quality score/number of stars/9*
Hsiao *et al.*[29], USA	GRAS	449 (both)	>75	Medical records	Dietary recalls	5	CVD incidence	–		Western-unhealthy CA	Age, sex, BMI, smoking, waist circumference, PASE, prescribed medication, MMSE, GDS, marital status, education	7
Chan *et al.*[30], China	Osteoporosis Hong Kong	2735 (both)	>65	Medical records	FFQ (280)	2	Stroke incidence	Prudent men Q2:0·63 Q3:0·41 Q4:0·70 Western men Q1:1·0 Q2:0·87 Q3:0·86 Q4:1·05 Prudent women Q1:1·0 Q2:0·61 Q3:0·66 Q4:0·88 Western women Q1:1·0 Q2:0·59 Q3:1·39 Q4:0·99	 0·36, 1·09 0·22, 0·76 0·71, 1·20 0·49, 1·56 0·48, 1·55 0·59, 1·88 0·28, 1·31 0·30, 1·45 0·43, 1·82 0·29, 1·65 0·66, 2·92 0·44, 2·23	Prudent/ healthy, western/ unhealthy FA	Age, BMI, smoking, current drinker, PASE, BP, education, energy intake, community ladder	9
Zazpe *et al.*[31], Spain	SUN project	16 008 (both)	>18	Medical records and/or National Death Index	FFQ (136)	7	CVD mortality	–		Prudent/ healthy, western/ unhealthy PCA	Age, sex, current smoker, alcohol consumption, BMI, physical activity, BP, self-report depression, hypercholesterolaemia, special diet, energy and nutrient intake, profession	9

NOS, Newcastle–Ottawa Scale; AMI, acute myocardial infarction; FA, factor analyses; BP, blood pressure; WHR, waist:hip ratio; CA, cluster analyses; MMSE, Mini-Mental State Examination; GDS, Geriatric Depression Scale; PASE, activity score for the elderly; PCA, principal component analyses. Currently, mortality is included; MESA, Multi-Ethnic Study of Atherosclerosis; CRP, C-reactive protein; EPIC, European Prospective Investigation into Cancer and Nutrition; JACC, Japan Collaborative Cohort Study; HEALS, Health Effects of Arsenic Longitudinal Study; REGARDS, Reasons for Geographic and Racial Differences in Stroke; GRAS, Geisinger Rural Aging Study; SUN, Seguimiento Universidad de Navarra.

* Quality assessment of cohort studies with the NOS. The full NOS score is 9 points. Scores ≥7 were considered high-quality.

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British Journal of Nutrition

Table 2. Case–control studies of dietary patterns and CVD
(Hazard ratios, risk ratios and 95 % confidence intervals)

References, country	Population (sex)	Age range (years)	Type of controls	Source of cases	Outcome	Number of cases/non-cases	Dietary pattern and method used	Dietary pattern categorisation: Hazard ratio/risk ratio	Dietary pattern categorisation: 95 % CI	Factors adjusted for in analyses	NOS quality score/number of stars (9)*
Martinez-Ortiz *et al.*(45), Costa Rica	1062 (both)	≥75	Survivors of a first AMI between 1994 and 1998	Hospital	CHD incidence (AMI)	496/518	Prudent/healthy, western/unhealthy FA	Prudent Q1:1·0 Q2:0·89 Q3:1·08 Q4:1·17 Q5:0·92 Western Q1:1·0 Q2:2·42 Q3:3·55 Q4:3·21 Q5:3·53	 0·58, 1·37 0·69, 1·70 0·72, 1·92 0·57, 1·50 1·44, 4·08 2·05, 6·15 1·85, 5·57 1·98, 6·31	Age, sex, current smoker, physical activity, WHR, self-reported history of diabetes, self-reported history of BP, income	7
Iqbal *et al.*(46), 52 countries worldwide	16 407 (both)	53–57	General population	Hospital	CHD incidence (AMI)	5761/10 646	Prudent/healthy, western/unhealthy FA	–		Age, sex, BMI, current smoker, alcohol consumption, physical activity, psychosocial factors, education, household income, region, ApoB/ApoA1 tertiles	9
Guo *et al.*(47), China	1312 (both)	≥18	Survivors of a first AMI	Hospital	CHD incidence (AMI)	1312/2235	Prudent/healthy, western/unhealthy FA	Prudent Q1:1·0 Q2:0·81 Q3:0·67 Q4:0·70 Western Q1:1·0 Q2:0·96 Q3:0·94 Q4:1·36	 0·66, 1·00 0·54, 0·82 0·56, 0·88 0·78, 1·19 0·75, 1·17 1·09, 1·69	Age, sex, BMI, current smoker, alcohol consumption, physical activity, WHR, educational level, marital status, general stress, depression region	7

NOS, Newcastle–Ottawa Scale; AMI, acute myocardial infarction; FA, factor analyses; WHR, waist:hip ratio; BP, blood pressure.
* Quality assessment of case–control studies with the NOS. The full NOS score is 9 points. Scores ≥7 were considered with high-quality.

BJN (2015) - 114
No of pages 19
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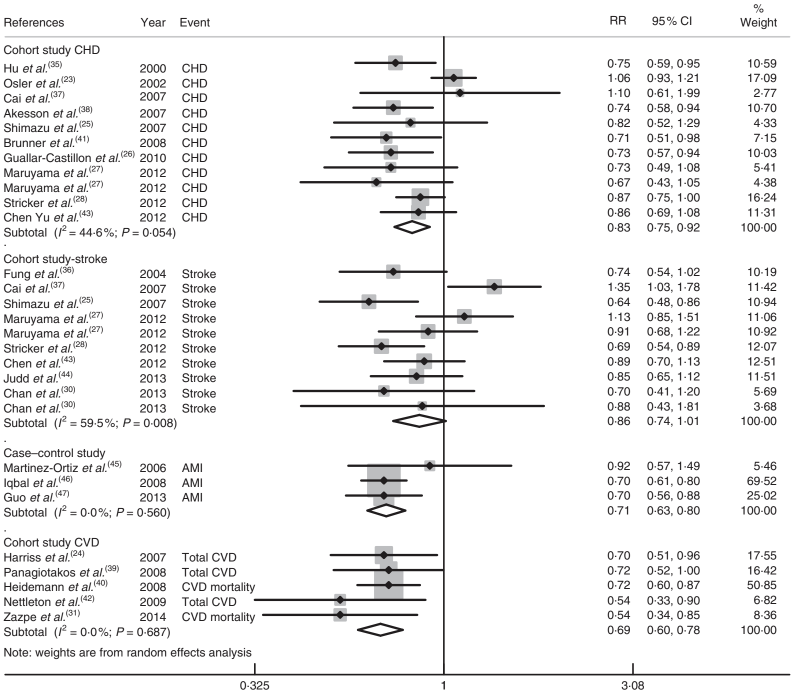

Fig. 2. Meta-analysis of prudent/healthy dietary pattern and CVD in observational studies. Relative risks (RR) correspond to comparisons of extreme categories of exposure within each study. The area of each square is proportional to the inverse of the variance of the log RR. Horizontal lines represent 95 % confidence intervals. Diamonds represent pooled estimates from inverse-variance-weighted random-effects models. AMI, acute myocardial infarction.

Meta-analysis of prudent/healthy dietary pattern

Totally, eighteen cohort studies[23–28,29,31,35–44] and three case–control studies[45–47] were included in the meta-analysis of prudent/healthy dietary pattern and CVD outcomes. Ten cohort studies analysed the association between the prudent/healthy dietary pattern and CHD risk[23,25–28,35,37,38,41,43]. Five studies also analysed the association between a prudent/healthy dietary pattern and total CVD risk and CVD mortality[24,31,39,40,42]. Eight cohort studies[25,27,28,30,36,37,43,44] described the relationship between prudent/healthy dietary pattern and the risk of stroke.

The association between dietary pattern and CVD was estimated using a random-effects meta-analysis with 95 % CI. In all, twenty-one observational studies met the inclusion criteria. Overall, in a comparison of the highest to the lowest category of prudent/healthy dietary patterns in cohort studies, the pooled RR for CVD, CHD and stroke was 0·69 (95 % CI 0·60, 0·78; $P_{heterogeneity}=0·687$; and $I^2=0\,\%$), 0·83 (95 % CI 0·75, 0·92; $P_{heterogeneity}=0·054$; and $I^2=44·6\,\%$) and 0·86 (95 % CI 0·74, 1·01; $P_{heterogeneity}=0·008$; $I^2=59·5\,\%$), respectively. In case–control studies, the pooled RR for CHD was 0·71 (95 % CI 0·63, 0·80; $P_{heterogeneity}=0·560$; $I^2=0\,\%$) (Fig. 2).

To further explore the reasons for heterogeneity, we performed subgroup analysis according to sex, geographic area, sample size, number of FFQ items, incidence or mortality outcomes, *a posteriori* approach and adjustments for confounders (Table 3). As shown in Table 4, most subgroups showed no significant association with heterogeneity between dietary patterns and CVD outcomes.

In sensitivity analyses, exclusion of individual studies did not modify the estimates substantially, with pooled RR of CVD, CHD and stroke in cohort studies ranging from 0·65 to 0·70, 0·80 to 0·84 and 0·82 to 0·89, respectively. In case–control studies, the pooled RR of CHD in case–control studies ranged from 0·70 to 0·73. The funnel plot showed reasonable symmetry and a non-significant Egger test for publication bias ($P=0·278$) (Appendix 3).

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Table 3. Subgroup analyses for prudent/healthy dietary pattern
(Pooled relative risk values and 95 % confidence intervals)

	Cohort studies CHD					Cohort studies stroke					Cohort studies CVD				
				Heterogeneity					Heterogeneity					Heterogeneity	
	Number of studies	Relative risk	95 % CI	I^2 (%)	*P*	Number of studies	Relative risk	95 % CI	I^2 (%)	*P*	Number of studies	Relative risk	95 % CI	I^2 (%)	*P*
Geographic area															
Other countries	6	0·82	0·71, 0·95	67·3	0·009	3	0·75	0·64, 0·88	0·0	0·541	5	0·69	0·60, 0·78	0·0	0·687
Asia	4	0·82	0·70, 0·96	0·0	0·694	7	0·92	0·75, 1·12	63·3	0·012	–	–		–	–
Sample size															
≥40 011	6	0·81	0·73, 0·89	0·0	0·015	5	0·87	0·68, 1·11	76·8	0·069	2	0·71	0·61, 0·84	0·0	0·880
<40 011	4	0·85	0·69, 1·04	71·4	0·029	3	0·85	0·72, 1·00	0·0	0·000	3	0·63	0·50, 0·79	0·0	0·489
Incidence or mortality outcome															
Mortality	4	0·82	0·71, 0·96	0·0	0·694	4	0·95	0·75, 1·21	73·5	0·005	3	0·69	0·60, 0·81	0·0	0·521
Incidence	6	0·82	0·71, 0·95	67·3	0·009	4	0·75	0·65, 0·87	0·0	0·831	2	0·66	0·50, 0·87	0·0	0·350
FFQ items															
≥101 items	3	0·73	0·63, 0·85	0·0	0·964	3	0·79	0·65, 0·95	0·0	0·869	5	0·68	0·60, 0·78	0·0	0·687
<101 items	7	0·87	0·77, 0·98	42·9	0·092	5	0·90	0·72, 1·12	75·3	0·001	–	–		–	–
Sex															
Men	2	0·74	0·61, 0·91	0·0	0·909	2	0·94	0·59, 1·48	57·9	0·123	–	–		–	–
Women	2	0·81	0·58, 1·15	32·9	0·222	4	0·96	0·71, 1·3	64·8	0·036	2	0·71	0·60, 0·84	0·0	0·772
Both	6	0·86	0·75, 0·98	55·2	0·048	4	0·76	0·65, 0·89	28·2	0·243	4	0·65	0·54, 0·78	0·0	0·631
A posteriori approach															
PCA	3	0·82	0·70, 0·96	57·6	0·021	3	0·80	0·69, 0·94	11·0	0·325	3	0·63	0·50, 0·79	0·0	0·489
FA	6	0·84	0·70, 1·00	64·6	0·015	5	0·89	0·71, 1·12	67·0	0·006	2	0·71	0·61, 0·84	0·0	0·880
CA	1	0·71	0·51, 0·98	–	–										
Adjustment for key confounding factors*															
Adjusted for all	2	0·74	0·63, 0·88	0·0	0·937	1	0·74	0·53, 1·01	–	–	1	0·72	0·51, 0·99	–	–
Not adjusted	8	0·85	0·76, 0·96	44·1	0·074	7	0·88	0·74, 1·04	62·2	0·007	4	0·68	0·59, 0·79	0·0	0·539

PCA, principal component analysis; FA, factor analysis; CA, cluster analysis.
* Key confounding factors are age, sex, family history of CVD, CHD or stroke, diabetes, hypertension and BMI.

British Journal of Nutrition

Table 4. Subgroup analyses for western/unhealthy dietary pattern
(Pooled relative risk values and 95 % confidence intervals)

	Cohort studies CHD					Cohort studies stroke					Cohort studies CVD				
				Heterogeneity					Heterogeneity					Heterogeneity	
	Number of studies	Relative risk	95 % CI	I^2 (%)	*P*	Number of studies	Relative risk	95 % CI	I^2 (%)	*P*	Number of studies	Relative risk	95 % CI	I^2 (%)	*P*
Geographic area															
Other countries	4	1·02	0·89, 1·59	54·1	0·088	3	1·28	1·06, 1·55	0·0	0·418	5	1·14	0·92, 1·42	56·9	0·055
Asia	4	1·13	0·81, 1·59	67·5	0·015	5	0·93	0·80, 1·09	0·0	0·616	–	–		–	–
Sample size															
≥40 011	6	1·14	0·88, 1·48	62·0	0·032	4	1·05	0·87, 1·27	31·2	0·201	2	1·06	0·80, 1·42	68·3	0·076
<40 011	2	1·27	0·71, 2·26	65·3	0·089	1	1·30	0·96, 1·75	–	–	3	1·25	0·79, 1·98	59·2	0·086
Incidence or mortality outcome															
Mortality	4	1·13	0·80, 1·59	54·1	0·088	4	0·95	0·80, 1·13	0·0	0·674	3	1·01	0·78, 1·31	55·5	0·106
Incidence	4	1·02	0·88, 1·17	67·5	0·015	4	1·15	0·90, 1·47	42·9	0·136	2	1·49	0·95, 2·33	35·8	0·212
FFQ items															
≥101 items	1	1·43	1·01, 2·01			3	1·14	0·81, 1·60	55·6	0·080	4	1·10	0·90, 1·35	54·9	0·084
<101 items	6	1·00	0·87, 1·16	60·8	0·018	5	0·98	0·85, 1·14	0·0	0·698					
Other information sources	1	0·86	0·59, 1·23	–	–	–	–		–	–	1	2·28	0·99, 5·21	–	–
Sex															
Men	2	1·02	0·52, 2·00	84·4	0·011	2	0·91	0·72, 1·17	5·2	0·348					
Women	2	1·07	0·62, 1·85	63·6	0·097	3	1·07	0·74, 1·57	64·6	0·059	1	1·22	1·00, 1·47	–	–
Both	5	1·03	0·88, 1·20	53·5	0·072	4	1·14	0·95, 1·38	0·0	0·474	4	1·12	0·80, 1·56	66·0	0·032
A posteriori approach															
PCA	2	1·22	0·59, 2·52	75·1	0·045	3	1·13	0·89, 1·43	20·2	0·285	3	1·03	0·75, 1·41	69·5	0·053
Factor analysis	6	1·03	0·88, 1·20	59·1	0·023	5	1·01	0·83, 1·22	33·7	0·171	1	1·22	1·00, 1·47	–	–
Cluster analysis											1	2·28	0·99, 5·21	–	–
Adjustment for key confounding factors*															
Adjusted for all	1	1·43	1·01, 2·01			1	1·59	1·04, 2·32	–	–	1	1·32	1·05, 1·66	–	–
Not adjusted	7	0·99	0·86, 1·13	57·0	0·023	7	1·01	0·89, 1·16	5·5	0·389	4	1·08	0·81, 1·45	60·3	0·056

PCA, principal component analysis.
* Key confounding are age, sex, family history of CVD, CHD or stroke, diabetes, hypertension and BMI.

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British Journal of Nutrition

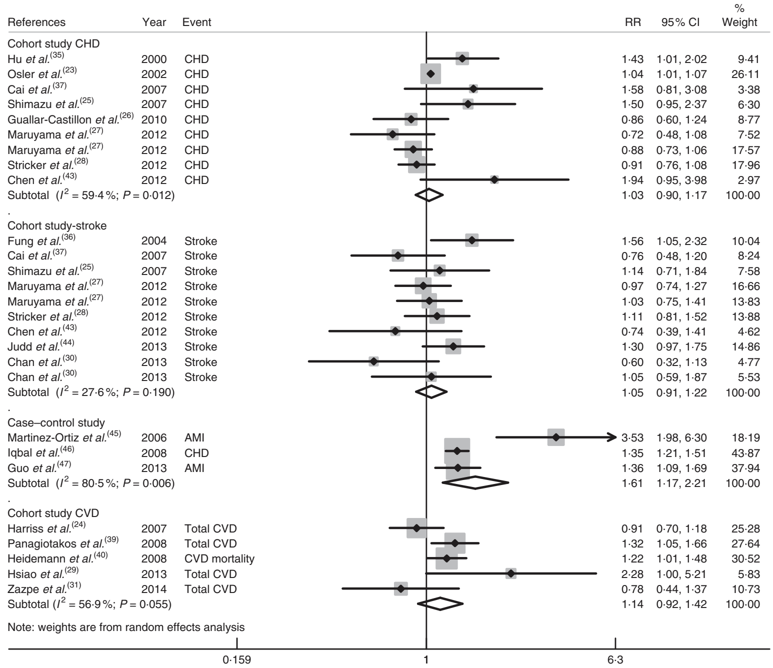

Fig. 3. Meta-analysis of western/unhealthy dietary pattern and CVD in observational studies. Relative risks (RR) correspond to comparisons of extreme categories of exposure within each study. The area of each square is proportional to the inverse of the variance of the log RR. Horizontal lines represent 95 % confidence intervals. Diamonds represent pooled estimates from inverse-variance-weighted random-effects models. AMI, acute myocardial infarction.

Meta-analysis of western/unhealthy dietary pattern

In all, sixteen cohort studies[23–31,35–37,39,40,43,44] were included in the meta-analysis of western/unhealthy dietary pattern and CVD. Eight studies[23,25–28,35,37,43] analysed the relationship between a western/unhealthy dietary pattern and CHD incidence. Five studies[24,29,31,39,40] analysed the relationship between a western/unhealthy dietary pattern and CVD and CVD mortality risk. Eight studies[25,27,28,30,36,37,43,44] also analysed the relationship between a western/unhealthy dietary pattern and the risk of stroke. Three case–control studies[45–47] were also included.

Totally, nineteen observational studies met the inclusion criteria. Overall, the pooled RR for CVD, CHD and stroke in a comparison of the highest to the lowest category of western/unhealthy dietary patterns in cohort studies was 1·14 (95 % CI 0·92, 1·42; $P_{heterogeneity} = 0·055$; and $I^2 = 56·9\,\%$), 1·03 (95 % CI 0·90, 1·17; $P_{heterogeneity} = 0·012$; and $I^2 = 59·4\,\%$) and 1·05 (95 % CI 0·91, 1·22; $P_{heterogeneity} = 0·190$; $I^2 = 27·6\,\%$), respectively (Fig. 3).

The pooled RR for CHD in case–control studies was 1·61 (95 % CI 1·17, 2·21), with statistically significant heterogeneity between studies ($P_{heterogeneity} = 0·006$; $I^2 = 80·5\,\%$). The sensitivity analysis indicates that a single study was the main origin of heterogeneity among studies (forty-five). The heterogeneity decreased ($I^2 = 0\,\%$; $P = 0·953$) after Martinez study was excluded; however, the association remained was significant (the pooled RR was 1·35 (95 % CI 1·22, 1·49). Other sources of heterogeneity produced only non-significant differences (Table 4).

In sensitivity analyses, exclusion of individual studies did not modify pooled RR substantially: CHD risk ranged from 0·99 to 1·06, stroke risk from 1·01 to 1·08 and CVD risk from 1·08 to 1·23 in cohort studies, and CVD risk ranged from 1·35 to 2·10 in case–control studies. The funnel plot was reasonably symmetric and the Egger test for publication bias did not reach statistical significance ($P = 0·219$) (Appendix 4).

Discussion

Our meta-analysis evaluated the results from published cohort and case–control studies involving approximately 610 691 participants, all of which investigated the association between *a posteriori* dietary patterns and CVD. The findings indicated that healthier patterns are associated with a lower risk for all clinical cardiovascular end points, except for stroke. When we pooled the results of cohort or case–control studies, the association between unhealthy/western dietary patterns and an increased risk of CHD, CVD mortality and stroke was not clearly established. Because there was significant heterogeneity among case–control studies, a sensitivity analysis was conducted to explore possible explanations for heterogeneity. After deleting the study that was the main origin of the heterogeneity, the summary ranged from 1·61 (95 % CI 1·7, 2·21) to 1·21 (95 % CI 1·22, 1·49), which suggested that the association remained significant and our findings were reliable and robust.

Despite a statistically significant association between unhealthy dietary patterns and CVD risk in some studies, the pooled estimation was non-significant. According to our findings, following an unhealthy pattern is not always synonymous with developing CVD. There are several reasons why the unhealthy/western pattern may not necessarily represent the food choices that pose the highest CVD risk. Maruyama *et al.*[27] studied an unhealthy pattern defined by milk and dairy products, butter, margarine, fruits, coffee and tea that was protective against stroke risk. Judd *et al.*[44] also included a pattern defined by high intake of sweets and saturated fats that was associated with a reduction in stroke risk. In both cases, adherence to that pattern could be associated with a higher risk of cancer or some kind of CHD that might lead to death before a stroke could occur.

The adjusted confounding factors differed in the included studies. All of the studies were adjusted for age and sex. Most of them also were adjusted for BMI, diabetes or hypertension[24,25,27,28,30,31,38,39,41–43,45,46]. However, family history as a non-modifiable risk factor for CVD and high cholesterol levels as a modifiable risk factor for CVD[48] were not considered[23,25,27,29–31,37,41–47], and it should be taken into account in future research. Only four studies adjusted for all key confounding factors[35,36,38,39]. The subgroup analysis by adjusted confounders in CHD cohort studies showed low heterogeneity, but the association remained significant, which confirmed our findings.

We identified two prominent general dietary patterns: a healthy/prudent and an unhealthy/western pattern. Following a healthy or unhealthy dietary pattern is also culturally and socially mediated. The factor loadings per pattern analysis reflected the foods most commonly consumed within the healthy dietary patterns, considering cultural differences. Authors from Asian countries study dietary patterns very divergent from those of Europe or America[25,27,30,35–37,40,43–45,47]. In the subgroup analysis by country, the studies conducted in Europe and America showed that the unhealthy/western dietary pattern was a risk factor for stroke but was not associated with CHD, and the pooled results from studies of Asian countries showed a non-significant association. The studies from China or Japan defined other dietary patterns as normal for the general population; for example, Chen *et al.*[43] includes a pattern named ‘gourd and root vegetable’ in China and Shimazu *et al.*[25] includes a Japanese dietary pattern represented by high intake of soyabean products, fish, seaweed, vegetables and green tea.

Many reports have shown that the association of diet with CVD is plausible[12,49,50]. One of the most representative examples is the association with cardiovascular risk prevention linked to the Mediterranean dietary pattern, based on fish and plant foods such as fruits, vegetables, cereals, legumes, wholegrain products, nuts and olive oil and the moderate consumption of red wine, along with low consumption of red meat, dairy products and SFA[19–21].

Different biological mechanisms might explain the results of the meta-analysis regarding the effect on CVD outcome of following a healthy or an unhealthy dietary pattern. The prudent/healthy dietary pattern included high-factor loadings for vegetables, fruit, legumes, whole grains, fish and poultry, whereas the western/unhealthy pattern included high-factor loadings for red and processed meat, refined grains, French fries, sweets, desserts, high-fat dairy products and alcohol. The consumption of vegetables and fruits is protective: the more the better, and no upper limit has been found. The higher proposed population goal of 600 g/d is in line with the most recent global population goal proposed by the World Cancer Research Fund in 2009[51,52]. Several systematic reviews on this subject[53,54] have shown that the consumption of fruit (>2 servings/d, 200 g) and vegetables (>2 servings/d, 200 g) significantly reduces the risk of CHD and stroke. Furthermore, the intake of fruit, vegetables, whole grains and legumes increases the amount of fibre, which can have protective value against CVD[55,56]. Antioxidants – such as vitamin C, flavonoids, K and folates – that can be found in fruits and vegetables also might influence the decrease in CVD risk[50].

In addition, oily fish and nuts contain PUFA (*n*-3 fatty acid), which reduce the risk of CHD[57]. Some studies have provided evidence that a modest increase (1–2 servings/week) in fish consumption reduces CHD mortality by 36 %[58,59], and that 2–4 servings/week can decrease the risk of stroke by 18 %[60]. Nevertheless, fish was included as a component in the unhealthy pattern in some studies, and related to an increased acute myocardial infarction, stroke and CVD risk[26,29,43,44,47].

On the other hand, the intake of refined grains, deep-fried potatoes, sweets (especially sugar-sweetened soft drinks), desserts and high-fat dairy products increases the amount of saturated and *trans*-saturated fat, dietary sugars and salt consumed. These three dietary components have been shown to directly or indirectly increase CVD risk[61–63]. Moderate alcohol consumption might be protective against CVD according to different epidemiological studies because of the content of polyphenols. However, increasing the intake above 10 g/d for women and 20 g/d for men may increase the risk of CVD[64].

According to our results, alcohol seems to have an important role in the studies included in the unhealthy pattern, especially in European and American cultures. According to Zazpe *et al.*[31] and Judd *et al.*[44], it was considered a negative predisposing factor.

The main limitation of our study is that factor loadings for individual foods in the different dietary patterns were not identical between the included studies, which may result in a misclassification bias. Descriptions of the factor loadings for

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individual food items for the dietary patterns analysed in our meta-analysis were not exactly equal between studies, and included different food items. Despite this, there were similarities in the type of foods that generally featured within the healthy patterns (fruit, vegetables, whole grains, fish and poultry) and the western patterns (meat, processed meat, refined grains, sweets, sugar drinks and fried foods) (see online Supplementary Material)[32]. Depending on the predominant factor loadings per food in each pattern, the influence of that pattern would generally be considered healthy or unhealthy. This means that, commonly, dietary patterns mix different kinds of foods, but the ones that are more predominant will define the final influence of that pattern.

Another limitation could be the inclusion of *a posteriori* dietary patterns, which can vary depending on the population and are more complex to standardise and compare across cohorts and population groups.

Confounding factors within the different studies also had an important role in the final results.

Another limitation of this meta-analysis is related to the heterogeneity found. However, this heterogeneity was not explained by the study design, number of FFQ items, geographic area, type of *a posteriori* approach, quality assessment, sex or sample size. Our study population was rather heterogeneous, which can increase residual confounding, biasing the estimate to the null, but it leads to generalisability[40].

Finally, dietary patterns may represent a lifestyle in general and, even the adjustment for known and suspected confounders, residual confounding cannot be ruled out because of the observational nature of the studies included[65,66].

To the best of our knowledge, this is the first meta-analysis of empirically derived dietary patterns to relate dietary patterns and CVD outcomes. Dietary patterns are becoming an essential approach to discovering the association of diet with the risk of a specific pathology. These patterns may be a consequence of cultural and ethnic heritage and of many environmental factors, including the availability of foods, the ability to purchase and prepare foods, the numerous advertisements for foods and the efforts of the government and the nutrition community to foster healthy diets[16].

Four meta-analyses relating dietary patterns to different CVD events are also in line with our results and conclude that, despite a need for further studies to confirm the findings, adherence to a prudent/healthy dietary pattern is associated with a lower risk of CVD mortality but not significantly associated with stroke mortality or CHD risk and, furthermore, that a western/unhealthy dietary pattern is not associated with CHD or stroke mortality[22,32,67,68]. Our meta-analysis adds to these findings a similar conclusion about other outcomes such as CVD or stroke incidence and mortality in cohort and case–control studies.

In summary, this meta-analysis strengthens the evidence in support of a prudent/healthy dietary pattern as a protective factor for CVD, especially CHD, but it fails to demonstrate a direct association between adherence to unhealthy dietary patterns and CVD incidence. These results may help reaffirm the clinical advice from health professionals such as physicians, nurses or dietitians in this field.

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There are no conflicts of interest.

Supplementary material

For supplementary material/s referred to in this article, please visit http://dx.doi.org/doi:10.1017/S0007114515003177

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Appendix 1. Quality assessment scheme for cohort studies (Newcastle–Ottawa Scale (NOS))

Study (author and year)							
Selection				Comparability	Outcome		
Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur?	Adequacy of follow-up cohorts
⋆ (a) Truly representative of the average of CVD events in the community	⋆ (a) Drawn from the same community as the exposed cohort	⋆ (a) Secure record (e.g. clinical records)	⋆ (a) Yes	⋆ (a) Most important adjustment factors (age, sex, BMI, diabetes mellitus, hypertension)	⋆ (a) Independent blind assessment	⋆ (a) Yes (minimum of 1 year of follow-up)	⋆ (a) Complete follow-up – all subjects accounted for
⋆ (b) Somewhat representative of the average of CVD events in the community	(b) Drawn from a different source	⋆ (b) Structured interview or questionnaire	(b) No	(b) Any additional factor (family history, cholesterol levels)	⋆ (b) Record linkage	(b) No (<1 year of follow-up)	⋆ (b) Subjects lost to follow-up unlikely to introduce bias (lost to follow-up ≤5 %)
(c) Selected group of users	(c) No description of the derivation of the non-exposed cohort	(c) Written self-report			(c) Self-report		(c) Subjects lost to follow-up >5 % and description provided of those lost
(d) No description of the derivation of the cohort		(d) No description			(d) No description		(d) No statement

A study can be awarded a maximum of one star for each numbered item within the selection and outcome categories. A maximum of two stars can be given for comparability.

Appendix 2. Quality assessment scheme for case–control studies (Newcastle–Ottawa Scale (NOS))

Study (author and year)							
Selection				Comparability	Exposure		
Is the case definition adequate?	Representativeness of cases	Selection of controls	Definition of controls	Comparability of cohorts on the basis of the design or analysis	Ascertainment of exposure	Same method of ascertainment for cases and controls	Non-response rate
⋆ (a) Yes, with independent validation	⋆ (a) Consecutive or obviously representative series of cases	⋆ (a) Community controls	⋆ (a) No history of CVD	⋆ (a) Most important adjustment factors (age, sex, BMI, diabetes mellitus, hypertension)	⋆ (a) Secure record (e.g. clinical records)	⋆ (a) Yes	⋆ (a) Same rate for both groups
(b) Yes, for example, record linkage	(b) Potential for selection biases or not stated	⋆ (b) Hospital controls	(b) No description of source	⋆ (b) Any additional factor (family history, cholesterol levels)	⋆ b) Structured interview or questionnaire where blind to case–control status	(b) No	(b) Non-respondents described
(c) No description		(c) No description			(c) Interview not blinded to case/ control status		(c) Rate different and no designation
					(d) No description		

A study can be awarded a maximum of one star for each numbered item within the selection and outcome categories. A maximum of two stars can be given for comparability.

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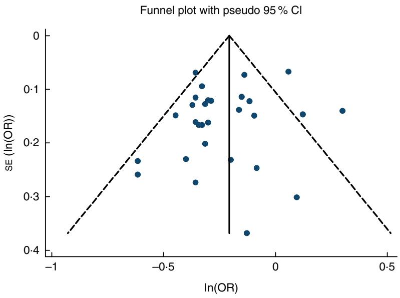
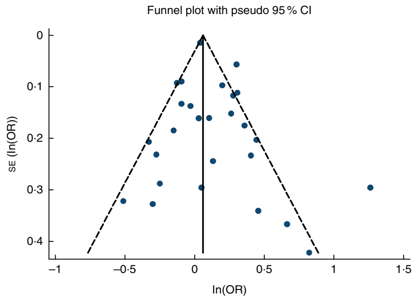
Appendix 3. Publication bias, prudent/healthy dietary pattern.



Appendix 4. Publication bias, western/unhealthy dietary pattern.



5.2 Publication two

Metabolic syndrome and dietary patterns: a systematic review and meta-analysis of observational studies

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ABSTRACT

Introduction: Lifestyle is linked to the risk of developing metabolic syndrome (MetS), however its relationship with dietary patterns remains unclear. This systematic review and meta-analysis aims to analyze the association of *a posteriori* dietary patterns with the metabolic syndrome.

Materials and Methods: The PubMed, CINAHL and Scopus databases were searched for epidemiological studies of dietary patterns and MetS. The association between dietary patterns and MetS was estimated using a random-effects meta-analysis with 95% confidence intervals (CIs).

Results: A total of 28 cross-sectional studies and 3 cohort studies were included in the meta-analysis. In a comparison of the highest to the lowest category of prudent/healthy dietary patterns the pooled odds ratio (OR) for MetS was 0.83 (95% CI: 0.76, 0.90; *P* for heterogeneity = 0.0; and I^2 = 72.1%) in cross-sectional studies, and the pooled relative risk (RR) for MetS in cohort studies was 0.91 (95% CI: 0.68, 1.21; *P* for heterogeneity = 0.005; I^2 = 81.1%). The pooled OR for MetS in a comparison of the highest to the lowest category of western dietary patterns was 1.28 (95% CI: 1.17, 1.40; *P* for heterogeneity = 0.0; and I^2 = 72.0%) in cross-sectional studies, and the RR was 0.96 (95% CI: 0.53, 1.73; *P* for heterogeneity = 0.102; I^2 = 62.6%) in cohort studies.

Conclusions: The results from cross-sectional studies showed that a prudent/healthy pattern is associated with a lower prevalence of MetS whereas a western/unhealthy is associated with an increased risk for MetS. Additional prospective studies are needed to confirm the association between dietary patterns and MetS.

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REVIEW

Metabolic syndrome and dietary patterns: a systematic review and meta-analysis of observational studies

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Abstract
Purpose Lifestyle is linked to the risk of developing metabolic syndrome (MetS); however, its relationship with dietary patterns remains unclear. This systematic review and meta-analysis aims to analyse the association of a posteriori dietary patterns with the metabolic syndrome.
Methods The PubMed, CINAHL and Scopus databases were searched for epidemiological studies of dietary patterns and MetS. The association between dietary patterns and MetS was estimated using a random-effects meta-analysis with 95 % confidence intervals (CIs).
Results A total of 28 cross-sectional studies and three cohort studies were included in the meta-analysis. In a comparison of the highest to the lowest category of prudent/healthy dietary patterns, the pooled odds ratio (OR) for MetS was 0.83 (95 % CI 0.76, 0.90; *P* for heterogeneity =0.0; and $I^2 = 72.1$ %) in cross-sectional studies, and the pooled relative risk (RR) for MetS in cohort studies was 0.91 (95 % CI 0.68, 1.21; *P* for heterogeneity =0.005; $I^2 = 81.1$ %). The pooled OR for MetS in a comparison of the highest to the lowest category of Western dietary patterns was 1.28 (95 % CI 1.17, 1.40; *P* for heterogeneity =0.0; and $I^2 = 72.0$ %) in cross-sectional studies, and the RR was 0.96 (95 % CI 0.53, 1.73; *P* for heterogeneity =0.102; $I^2 = 62.6$ %) in cohort studies.
Conclusions The results from cross-sectional studies showed that a prudent/healthy pattern is associated with a lower prevalence of MetS, whereas a Western/unhealthy is associated with an increased risk for MetS. Additional prospective studies are needed to confirm the association between dietary patterns and MetS.

Keywords Dietary patterns · Metabolic syndrome · Systematic review · Meta-analysis

Electronic supplementary material The online version of this article (doi:10.1007/s00394-016-1305-y) contains supplementary material, which is available to authorized users.

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Introduction

Metabolic syndrome (MetS) can be defined as a constellation of physiological, biochemical, clinical and metabolic factors that directly increase the risk of cardiovascular disease and diabetes greater than that of its individual components [1, 2]. These factors include insulin resistance, type 2 diabetes or impaired glucose tolerance, hypertension, dyslipidaemia and central obesity [3]. Multiple classifications exist for the diagnosis of MetS, which can be explained by gaps in knowledge about some of the underlying mechanisms that lead to the development of the syndrome [1, 4–6]; however, in clinical practice, the most widely used diagnostic criteria [7] are those developed by the United States Adult Treatment Panel III of the National Cholesterol Education Program (NCEP-ATP III) [8] and by the International Diabetes Federation (IDF) [9].

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In recent decades, the worldwide prevalence of MetS has increased in parallel with other cardiovascular risk factors. In fact, when the prevalence of the individual components of the syndrome varies between populations, so does the prevalence of MetS itself [10]. These differences have been attributed to lifestyle influences, genetic factors and the age and sex structures of the populations under study. Prevalence can vary depending on the definition used for its diagnosis [11].

The prime emphasis in the management of MetS is to mitigate the modifiable, underlying risk factors (obesity, physical inactivity and atherogenic diet) through lifestyle changes [12]. Diet is one of the most important tools available to improve the factors linked to MetS, as well as, in other chronic conditions. However, the diet for the prevention and treatment of MetS remains unspecified beyond weight control and reduction in total calories. Several evidences show that it should generally be low in saturated fats, *trans* fats, cholesterol, sodium and simple sugars [13, 14].

The analysis of dietary patterns aims to explore the influence in health that the combination of foods have in a specific population. There are two approaches when analysing dietary patterns: "a priori", focusing on the construction of patterns that reflect hypothesis-oriented combinations of foods and nutrients (e.g. Mediterranean diet), and "a posteriori", which builds on exploratory statistical methods and uses the observed dietary data in order to extract dietary patterns [15, 16].

The link between the Mediterranean diet, categorized as a prudent dietary pattern, and MetS has been analysed in several publications [17, 18] as well as its adherence and the risk of developing diabetes mellitus [19]. Results show an inverse association between following the Mediterranean pattern and the development of MetS or diabetes mellitus, which leads to the recommendation of the pattern for primary prevention of *type 2 diabetes* and its adoption in countries where MetS is prevalent. However, other dietary patterns and its relation with MetS should be analysed, considering that following a specific dietary pattern can be influenced by several factors such as age, sex, culture or society [20]. Consequently, to clarify the association between empirically defined (a posteriori*)* dietary patterns and MetS, we conducted a systematic review and meta-analysis of observational studies.

Methods

The PubMed, CINAHL and Scopus databases were searched for epidemiological studies of dietary patterns and MetS published through May 2016. The following combination of Medical Subject Heading (MeSH) terms and text words, with no language limitations, was used in PubMed: *("diet"[MeSH Terms] OR "diet"[All Fields] OR "dietary"[All Fields] OR "dietary patterns"[All Fields] OR "food patterns"[All Fields]) AND ("Metabolic syndrome"[All Fields] OR "Metabolic Syndrome X"[Mesh] OR "Metabolic Syndrome X"[All Fields]).* For Scopus and CINAHL, the search terms were *Diet OR dietary OR dietary patterns OR food patterns AND Metabolic syndrome OR syndrome X OR metabolic syndrome X*. Observational studies that assessed the association of dietary patterns with MetS analysed by cluster analysis, factor analysis or principal component analysis (PCA) were selected. All MetS existent definitions were considered. After retrieval of articles from the search, the reference lists of all selected articles were checked and any relevant published reviews were inspected for other potentially pertinent articles.

Two investigators (MR-M and GF-M) independently searched the literature, selected the studies, and extracted the data applying to the following exclusion criteria: no original research (i.e. reviews, editorials, non-research letters); case reports or case series; ecological studies; lack of data on dietary patterns; studies without MetS as the endpoint; studies not conducted in humans or adult populations; studies without measures of association (hazard ratios, odds ratios, or relative risks); (Fig. 1). They resolved any discrepancies by consensus. The authors of the original studies were contacted if relevant information on eligibility or key study data were not available in the published report. The MOOSE (Meta-analysis Of Observational Studies in Epidemiology) guidelines were followed in the meta-analysis of the selected studies [21].

The following information was recorded from all studies: study design, geographic region, sample size, dietary assessment method, dietary patterns identified and by which a posteriori method, factors adjusted for in each study, outcomes and outcome assessment, health status, criteria for defining MetS, population, sex of participants, age range, follow-up time (cohort studies), naming of patterns, factor loadings per pattern, total variance and main conclusions of each study (Tables 1 and 2 and online supplement). Measures of association (odds ratios, relative risks or hazard ratios) and their 95 % confidence intervals (CIs) also were abstracted.

We defined as prudent/healthy those patterns having generally healthy characteristics and as unhealthy/Western those patterns perceived to have generally less healthy characteristics, based on the food loading reported within individual studies. When several healthy and unhealthy patterns were reported, we first selected the pattern that explained the maximum of variation in food groups [22–38] and then the pattern that fulfilled the most healthy or unhealthy criteria, determined by the highest factor

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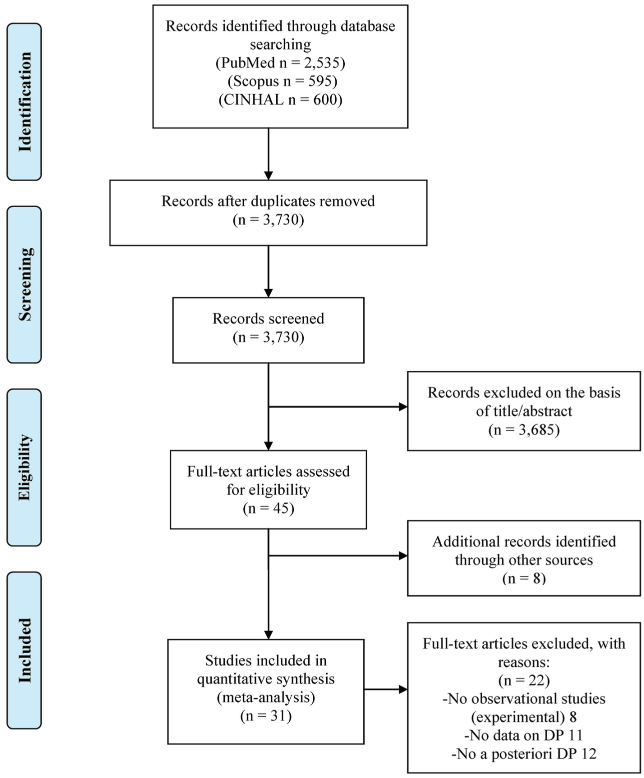
Fig. 1 Flow diagram of study selection process



loadings [39–52]. The prudent/healthy pattern tended to have high factor loading for food such as fruit, vegetables, whole grains, fish and seafood, legumes, poultry, olive oil, nuts, seeds and fat-free and low-fat dairy. The unhealthy/Western pattern was characterized by high factor loadings for foods such as meat, processed meat and poultry, refined grains, sweets, desserts, fast food, snack foods and soda and sweetened beverages. The classification of each food was based on the recommendations of different consensus dietary guidelines such as the Eighth Edition of the Dietary Guidelines for Americans and The Guidelines for a Healthy diet from Sociedad Española de Nutrición Comunitaria [53, 54].

As the studies were observational, their quality was assessed according to the following: (1) study design and method; (2) attrition; (3) measurement of dietary patterns; (4) measurement of MetS and (5) statistical analysis. Sixteen criteria were chosen and adapted from a detailed checklist developed for observational longitudinal studies [55], including the six areas of potential study bias recommended for consideration in any quality appraisal component of systematic reviews (online supplement 2) [56]. Each criterion was scored as yes (1), no (0) or partially achieved (0.5), based on the available information. The scores were totalled to give an overall indication of study quality [57].

The review was registered at PROPSERO with registration number CRD42015029807.

Cohort studies and cross-sectional studies were analysed separately. The results of dietary patterns were variously reported as quintiles, quartiles, or dietary factor scores and MetS incidence or prevalence. A meta-analysis was conducted to combine the results and compare the risk/prevalence of MetS in the highest categories of prudent/healthy and Western/unhealthy dietary patterns, compared with the lowest category. To pool odds ratio (OR) or relative risk

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(RR) estimates from individual studies, we used an inverse variance weighted random-effects model. Heterogeneity was quantified using the I^2 statistic, which describes the proportion of total variation in study estimates that is due to heterogeneity [58]. Each study's estimate and standard error (SE) was used to produce a forest plot that yielded a pooled estimate.

To explore sources of heterogeneity, we performed subgroup analysis and meta-regression in both dietary patterns to evaluate whether results differed. Several factors were analysed according to geographic area (Asia, Europe, America and Australia), a posteriori approach (PCA, factor analysis, cluster analysis or other assessment), sex (men, women or both), MetS definition (NCEP-ATP III, IDF or others), adjustment or not for all key confounders (age, sex, body mass index, energy intake and physical activity), age of participants (young adults 18–35, adults 36–70, mixed of younger adults, adults and older adults, mixed of young adults and adults or not reported) and health status (not having CVD and/or metabolic diseases, having CVD and/or metabolic diseases or general population) .

Assessment of the relative influence of each study was based on pooled estimates, omitting one study at a time (sensitivity analysis). Finally, publication bias was assessed using funnel plots. All statistical analysis were conducted using Stata software (version 12; StataCorp LP).

Results

The search strategy retrieved 3730 articles. Of these citations, 3693 publications were excluded on the basis of title and abstract and 14 after full-text review. After retrieval of articles from the search, the reference lists of all selected articles were checked for other potentially relevant review articles; eight additional papers were identified.

A total of 28 cross-sectional studies [22–49] (Table 1) and three cohort studies (Table 2) [50–52] all published between 2007 and 2015 were included in the meta-analysis (Fig. 1). Eight studies were performed in Europe [22, 30, 34, 37, 40, 41, 43, 44], eight in America [23, 24, 37, 42, 47, 50–52], 14 in Asia [25–29, 31–33, 35, 36, 39, 45, 46, 48] and one in Australia [38]. The number of cases ranged from 107 [33] to 16,734 [48]. All the selected studies assessed frequency of MetS as the endpoint.

The majority of studies provided detailed descriptions and data for the baseline characteristics of the population, the criteria used to define MetS (NCEP-ATPIII was most commonly used), the dietary assessment method (the majority of studies used a Food Frequency Questionnaire, FFQ), the statistical analysis used to identify dietary patterns (PCA was most frequently used), as well as the potential confounding variables and measures of association between dietary patterns and MetS. One study included only younger adults (age range 18–30) [52]; however, the majority of the studies included populations with a wider age range [22, 24, 28–30, 34, 36, 40, 43, 45–48, 51].

Meta-analysis of prudent/healthy dietary pattern

Twenty-seven observational studies met the inclusion criteria. Twenty-four cross-sectional studies [22–33, 35–39, 41, 43–52] and three cohort studies [50–52] were included in the meta-analysis of prudent/healthy dietary pattern and MetS outcomes. The food groups included in this pattern were the following: vegetables (leafy vegetables, roots, cruciferous, yellow and red vegetables, tomatoes, mushrooms, and carotenoid vegetables), fruits, dried fruits, whole grains, dairy (low-fat milk, low-fat cheese and yogurt), protein (fish, poultry, nuts, legumes, eggs and soy products), oils (olive oil and other vegetable oils) and tea.

Overall, in a comparison of the highest to the lowest category of prudent/healthy dietary patterns in cross-sectional studies, the pooled OR (95 % CI) for MetS was 0.83 (95 % CI 0.76, 0.90; P for heterogeneity =0.0; and $I^2 = 72.1$ %) (Fig. 2). The pooled RR (95 % CI) for MetS in cohort studies was 0.91 (95 % CI 0.68, 1.21; P for heterogeneity =0.005; $I^2 = 81.1$ %) (Fig. 3).

Potential sources of heterogeneity, such as sex ($P = 0.487$), geographic area ($P = 0.595$), a posteriori approach ($P = 0.722$), adjustment for key confounders ($P = 0.950$), MetS definition ($P = 0.551$), age ($P = 0.429$) or health status ($P = 0.226$) produced only minor, non-significant differences (Table 3). As only three cohort studies were included in the meta-analysis, the subgroup analyses were conducted using cross-sectional data.

In sensitivity analyses, exclusion of individual studies did not modify the estimates substantially, with pooled ORs of MetS in cross-sectional studies ranging from 0.81 to 0.84. In cohort studies, the pooled RRs of MetS ranged from 0.77 to 1.06. The funnel plot showed reasonable symmetry ("Appendix").

Meta-analysis of Western/unhealthy dietary pattern

Twenty-nine observational studies met the inclusion criteria. Twenty-seven cross-sectional studies [22–45, 47, 49–51] and two cohort studies [50, 51] were included in the meta-analysis of Western/unhealthy dietary pattern and MetS.

The food groups included in this pattern were, as follows: fruits (canned fruits), refined grains (pasta, rice, white bread, and breakfast cereal), dairy (whole milk, high-fat cheese), protein (red meat, processed meat, organ meat), oils and fats (butter, margarine, fat sauces, high-fat salad dressings), alcohol drinks (beer, spirits), soft drinks, coffee,

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Table 1 Cross-sectional studies of dietary patterns and metabolic syndrome

References	Country	Population	Sample size (sex)	Age (year)	Outcome ascertainment	Diet assessment method (items) and method to identify DP	Criteria for defining MetS
Esmaillzadeh et al. [39]	Iran	Female teachers in Tehran	486 (women)	40–60	Interview	FFQ (168) PCA	NCEP-ATPIII
Panagiotakos et al. [22]	Greece	ATTICA study	3,042 (both)	18–87	Interviews and questionnaires	FFQ (156) PCA	NCEP-ATPIII
Berg et al. [40]	Sweden	INTERGENE study	3,542 (both)	25–74	Questionnaires, health examination	FFQ (93) CA	NCEP-ATPIII
Leite et al. [41]	Italy	Italian Bollate Eye Study	1,052 (both)	40–47	Interview	FFQ (166) CA	NCEP-ATPIII
Deshmukh-Taskar et al. [23]	USA	Bogalusa Heart Study	995 (both)	19–39	Data from survey	FFQ (131) FA	NCEP-ATPIII
Noel et al. [42]	USA	Boston Puerto Rican Health Study	1167 (both)	45–75	Interviews	FFQ (126) FA	NCEP-ATP III (modified to reflect recommendations by ADA)
Denova-Gutiérrez et al. [24]	Mexico	Workers cohort study	524 (both)	20–70	Data from survey	FFQ (116) FA	NCEP-ATPIII
Amini et al. [25]	Iran	Isfahan Diabetes Prevention study	425 (both)	35–55	Data from survey	FFQ (39) FA	NCEP-ATPIII
Cho et al. [26]	Korea	Cancer-screening at National Cancer Center in South Korea	4,984 (women)	30–79	Self-administered questionnaire	FFQ (16) FA	NCEP-ATPIII
Heidemann et al. [43]	Germany	German Health Interview and Examination Survey	4,025 (both)	18–79	Data from survey	24-h recall, 3-day food records PCA	NCEP-ATPIII
Kim et al. [27]	Korea	Korean National Health and Examination Survey (KNHANES)	9,850 (both)	≥19	Data from survey FA	24-h recall	IDF/AHA
Wagner et al. [44]	France	MONA LISA Study	3,091 (both)	35–74	National Survey PCA	3-day food diary	NCEP-ATPIII
Hong et al. [28]	Korea	Health Examination Center, Internal Medicine Department of 2 general hospitals in Seoul	406 (both)	22–78	Interviews PCA	24-h recall, 3-day food records	NCEP-ATPIII
Song et al. [45]	Korea	Korean National Health and Examination Survey (KNHANES III)	473 (both)	≥20	National Survey CA	24-h recall	NCEP-ATPIII
Naja et al. [29]	Lebanon	Nation-wide nutrition and Non-Communicable Disease Risk Factors cross-sectional survey	323 (both)	>18	National Survey FA	FFQ (61)	IDF

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Table 1 continued

References	Country	Population	Sample size (sex)	Age (year)	Outcome ascertainment	Diet assessment method (items) and method to identify DP	Criteria for defining MetS
Akter et al. [46]	Japan	Health survey of employees of two municipal offices in Kyushu	460 (both)	21–67	Questionnaire and health examination PCA	FFQ (52)	NCEP-ATPIII
Liu et al. [47]	USA	Jackson Heart Study	1775 (both)	21–94	Dietary assessment interviews and multi detector computed tomography scan PCA	FFQ (158)	NCEP-ATPIII (modified)
Sahay et al. [30]	Croatia	Surveys from eight villages on the island of Hvar (eastern Adriatic coast of Croatia)	1442 (both)	20–94	Interviews PCA	FFQ (74)	IDF
Yoo, Ki-Bong et al. [48]	Korea	Korean National Health and Examination Survey (KNHANES)	16,734 (both)	≥18	Data from survey FA	24-h recall	NCEP-ATPIII
Hae Dong Woo et al. [31]	Korea	Participants in health screening at National Cancer Center, South Korea	1,257 (both)	31–70	Self-administered question-naire PCA	FFQ (103)	NCEP-ATPIII
Arisawa et al. [32]	Japan	J-MICC study	513 (both)	35–70	Self-administered question-naire PCA	FFQ (46)	NCEP-ATPIII
Sun et al. [33]	China	Patients from Changshu and Beijing Fangshan Centers for Disease Control and Prevention	107 (both)	≥50	Health check-up, medical records, interviews CA	FFQ (34)	IDF
Barbaresko et al. [34]	Germany	PopGen Biobank cohort	905 (both)	19–77	Data from follow-up examina-tions (self-administered questionnaire) PCA	FFQ (112)	IDF
Choi et al. [35]	Korea	Patients from health screening examination at the National Cancer Center	5189 (women)	31–70	Self-administered question-naire and medical records PCA	FFQ (106)	NCEP-ATPIII
He et al. [36]	China	5th Nationwide Nutrition and Health Survey	2196 (both)	≥18	Questionnaire FA	24-h recall, 3-day food records	NCEP-ATPIII
Suliga et al. [37]	Poland	PONS Project	2479 (both)	45–64	Questionnaire interview PCA	FFQ (31)	IDF
Gadgil et al. [49]	USA	MASALA community based cohorts study	892 (both)	40–84	In-person interviews PCA	FFQ (163)	NCEP-ATPIII
Bell et al. [38]	Australia	Australian Health Survey	2415 (both)	≥45	Data from survey FA	24-h recall	Self-categorization (metabolic phenotype)

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Table 1 continued

References	Health status	Healthy DP and food components	Unhealthy DP and food components	Factors adjusted for in analysis	Qlty. score/15*
Esmaillzadeh et al. [39]	Women without history of CVD, diabetes, cancer or stroke. TEI outside the range of 800–4200 kcal, and with >70 items in blank in FFQ	Healthy DP: fish 0.22, poultry 0.53, butter −0.31 low-fat dairy products 0.26, high-fat dairy products −0.23, tea 0.39, fruit 0.74, fruit juices 0.37, cruciferous vegetables 0.47, yellow vegetables 0.21, tomatoes 0.63, green leafy vegetables 0.41, other vegetables 0.71, legumes 0.52, potatoes 0.29, whole grains 0.34, hydrogenated fats −0.20	Western DP: processed meats 0.39, red meats 0.56, fish −0.29, eggs 0.35, butter 0.43, low-fat dairy products −0.37, high-fat dairy products 0.39, coffee 0.23, fruit −0.29, fruit juices 0.21, other vegetables −0.31, French fries 0.24, potatoes 0.35, refined grains 0.66, pizza 0.36, snacks 0.29, mayonnaise 0.22, sweets and desserts 0.37, hydrogenated fats 0.34, vegetable oils 0.20, soft drinks 0.33	Age, sex, BMI, current smoker, physical activity, current oestrogen use, menopausal status, family history of diabetes and stroke, energy intake	13.5
Panagiotakos et al. [22]	Adults without clinical evidence for CV disease	Healthful DP: cereals 0.71, small fish (e.g. sardine) 0.59, big fish (e.g. sword fish) 0.58, greens 0.65, legumes 0.56, fruits 0.53, vegetables 0.70	High glycaemic index and high-fat DP: beef 0.57, pork 0.47, other meat 0.41, meat products 0.71, poultry 0.54, fried potatoes 0.45, boiled–baked potatoes 0.36	Age, sex, BMI, current smoker, years of school, income, use of medication	14
Berg et al. [40]	Unspecified general population	–	Fast energy DP. soft drinks, white bread, fast food, full-fat milk, cheese, beer, spirits, sweets and snacks	Age, sex, current smoker, physical activity, education	14
Leite et al. [41]	Non-diabetic participants	Vitamin/fibre DP: vegetables, legumes, fruit	Starch DP: refined grain products (bread, rice and pasta)	Age, sex, current smoker, alcohol consumption, physical activity, education	13
Deshmukh-Taskar et al. [23]	Young adults from general population excluding pregnant or lactating women, females with energy intake <500 kcal, or >3500 kcal; males with energy intake 800 kcal or >4000 kcal	Prudent DP: whole grains 0.46, legumes 0.61, cruciferous vegetables 0.70, other vegetables 0.74, green leafy vegetables 0.69, dark-yellow vegetables 0.70, tomatoes 0.58, fruits 0.64, 100 % fruit juices 0.43, low-fat dairy products 0.36, poultry 0.40, clear subs 0.36, low-fat salad dressings 0.49	Western DP: refined grains 0.43, French fries 0.53, high-fat dairy products 0.53, dishes with cheese 0.58, red meats 0.50, processed meats 0.59, eggs 0.39, snacks 0.53, sweets and desserts 0.54, sweetened beverages 0.44, condiments 0.40	Age, sex, BMI, current smoker, alcohol intake, physical activity, energy intake, ethnicity and ethnicity per gender, socio-economic status	13.5
Noel et al. [42]	Puerto Ricans from Boston area, excluding individuals unable to answer study questions due to serious health condition/advanced dementia, planning to move from the area within 2y, not having a permanent address	–	Meat, processed meat, and French Fries DP: meat 0.58, processed meat 0.45, French fries 0.38, pizza/Mexican 0.36, eggs 0.35, alcohol 0.25, other grains/pasta 0.25, rice 0.24, oils 0.21, refined grains 0.20, whole grains −0.23, sweetened beverages −0.24, vegetables −0.25, poultry −0.25, citrus fruit and juice −0.30, cold cereal −0.37, hot cereal −0.40, other fruit and juice −0.48, reduced fat dairy −0.53	Age, sex, BMI, current smoker, alcohol intake, physical activity, energy intake, acculturation, multivitamin and medication use	14

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Table 1 continued

References	Health status	Healthy DP and food components	Unhealthy DP and food components	Factors adjusted for in analysis	Qlty. score/15*
Denova-Gutiérrez et al. [24]	Working population, excluding participants with DM2, High BP, dyslipidaemia, rheumatoid arthritis and those taking medication that would affect serum lipoprotein concentrations, BP and CH metabolism	Prudent DP: processed vegetable juices 0.55, potatoes 0.40, fresh fruits 0.57, fresh vegetables 0.70, legumes 0.39, pastry −0.37, fruit juice 0.30	Western DP: legumes 0.35, refined cereals 0.31, whole cereals −0.54, seafood −0.35, high-fat dairy products −0.39, low-fat dairy products −0.35, corn tortillas 0.66, sodas 0.39	Age, sex, current smoker, physical activity, weight change, place of residence, oestrogen use, menopausal status, energy intake	13.5
Amini et al. [25]	Adult population with IGT	Prudent DP: hydrogenated fat −0.32, vegetable oil 0.36, liver and organic meat 0.34, coconut 0.30, juice 0.38, peas 0.50, barley 0.28, fish 0.56, non-leafy vegetables 0.30, dry fruits 0.36, nuts 0.41, honey 0.42	Western DP: sweets 0.60, butter 0.59, soda 0.53, mayonnaise 0.45, sugar 0.44, cookies 0.44, tail 0.34, hydrogenated fat 0.33, egg 0.29, macaroni 0.25, vegetable oil −0.25, liver and organic meat 0.23, coconut 0.22, mutton 0.22, juice 0.22	Age, sex, physical activity, education	13
Cho et al. [26]	Women who underwent cancer-screening examinations	Healthy DP: fried foods 0.21, cholesterol rich foods 0.33, green yellow vegetables 0.58, healthy protein foods 0.58, seaweeds 0.55, bone fish 0.54, fruits 0.47, dairy products 0.34, light coloured vegetables 0.34	Western DP: fast foods 0.72, animal fat rich foods 0.71, fried foods 0.61, grilled meat and sea foods 0.54, sweet foods 0.54, cholesterol rich foods 0.51, caffeinated drinks 0.35	Age, menopausal status	13
Heidemann et al. [43]	Adult general population	Health-conscious DP: red meat 0.34, high sugar beverages −0.16, eggs 0.23, potatoes 0.32, butter 0.16, tea 0.18, cruciferous vegetables 0.65, fruity root vegetables 0.58, other vegetables 0.55, leafy vegetables 0.55, vegetable oils 0.52, legumes 0.39, fruits 0.39, fish 0.34, whole grains 0.31, other animal fats 0.31, poultry 0.26, nuts and seeds 0.17, olives, olive oil 0.17, wine 0.16	Processed foods DP: refined grains 0.72, processed meat 0.66, red meat 0.57, high sugar beverages 0.50, eggs 0.41, potatoes 0.38, beer 0.38, sweets, cakes 0.37, snacks 0.37, butter 0.37, organ meats 0.19, margarine 0.19, coffee 0.16, tea −0.24, fruity and root vegetables −0.19, vegetable oils 0.16, fruits −0.32, whole grains −0.30, other animal fats 0.26, olives, olive oil 0.16	Age, sex, current smoker, BMI, sport activity, total energy intake, socio-economic status	14
Kim et al. [27]	Adult general population	Grains, vegetables and fish DP: white rice −0.26, grains 0.38, noodle and dumplings −0.26, nuts 0.24, vegetables 0.67, kimchi −0.32, fish and shellfish 0.29, milk and dairy products 0.02, oils 0.26, other beverages 0.58	Meat and alcohol DP: white rice −0.41, grains −0.24, noodle and dumplings 0.33, sugar and sweets −0.34, vegetables −0.28, mushrooms −0.23, meat and its products 0.65, fish and shellfish −0.24, milk and dairy products −0.17, alcohol 0.53, other beverages 0.09	Age, sex, current smoker, alcohol intake, BMI, physical activity, energy intake, carbohydrate intake	12

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Table 1 continued

References	Health status	Healthy DP and food components	Unhealthy DP and food components	Factors adjusted for in analysis	Qlty. score/15*
Wagner et al. [44]	General population	–	Energy-dense DP: delicatessen foods 0.39, red meat 0.61, fruits −0.48, potatoes 0.56, yoghourt −0.40, animal fat (butter) 0.55, sauce and condiments 0.20, water −0.28, sodas 0.21, alcohol 0.50	Age, sex, current smoker, BMI, total calories intake, heart rate (physical activity), educational level, menopause	14
Hong et al. [28]	Patients from health examination centres or internal medicine departments with all the records for DM diagnosis; excluding patients taking medications other than to decrease BP or glucose	Fruit and dairy DP: refined grains −0.33, kimchi −0.31, beef 0.25, fruits 0.49, pork −0.49, ramen (instant noodles) −0.48, dairy products 0.47, rice cakes 0.43, nuts 0.32	Korean traditional DP: soy sauce 0.69, refined grains 0.59, onion and garlic 0.58, vegetable oil 0.55, soy products 0.51, red pepper and soybean paste 0.45, starch syrup and sugar 0.45, kimchi 0.44, seaweed 0.43, fish 0.39, whole grains 0.32, vegetables 0.28, pork 0.26	Age, sex, current smoker, BMI, physical activity, medications	12
Song et al. [45]	General population	Korean healthy DP: noodle, bred, eggs and tea	Meat and alcohol DP: processed meat and alcohol	Age, sex, current smoker, physical activity, education, region	13
Naja et al. [29]	No prior history of chronic diseases	Traditional Lebanese DP: desserts 0.23, dairy products full-fat 0.58, olives 0.56, fruits 0.49, legumes 0.47, grains 0.47, eggs 0.45, vegetable oil 0.43, nuts and dried fruits 0.40, traditional sweets 0.37, vegetables 0.34, dairy products low-fat −0.29	Fast Food/Desserts DP: Hamburger 0.76, shawarma 0.72, pizza and pies 0.70, falafel sandwiches 0.61, desserts 0.41, carbonated beverages and juices 0.40, mayonnaise 0.35, butter 0.22, alcoholic beverages 0.20, fruits −0.22, grains 0.27, eggs 0.21, nuts and dried fruits 0.27, chicken 0.21, meat 0.22	Age, sex, current smoker, physical activity, marital status, education, crowding index	13
Akter et al. [46]	Adults without history of CVD or cancer 2	Healthy Japanese DP: carrots and pumpkin 0.78, mushrooms 0.73, green leafs vegetables 0.69, cabbage/Chinese cabbage 0.68, Japanese radish/turnip 0.68, other root vegetables 0.67, tofu/atsuage 0.50, seaweeds 0.48, potatoes 0.46, other fruit 0.37, persimmons/strawberries/kiwi fruit 0.31, natto 0.30, citrus fruit 0.25, green tea 0.22, 100 % fruit and vegetable juice −0.19, buckwheat noodles −0.25, cola drink/soft drink −0.29, Chinese noodles −0.44, squid/octopus/shrimp/shellfish −0.16, lean fish 0.15, lettuces/cabbage (raw) 0.21, tomatoes 0.19, small fish with bones 0.20, ice cream −0.19, pickled green leaves vegetables 0.18	–	Age, sex, current smoker, occupational physical activity, non-occupational physical activity, workplace, marital status, job position	14

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Table 1 continued

References	Health status	Healthy DP and food components	Unhealthy DP and food components	Factors adjusted for in analysis	Qlty. score/15*
Liu et al. [47]	Adults excluding those with presence of CVD, hypertension or DM or without dietary assessment	Prudent DP: cold cereal 0.47, dairy desserts 0.36, fruit juice 0.31, fruit 0.63, hot cereal 0.49, milk and dairy 0.30, nuts and seeds 0.33	Southern DP: beans and legumes 0.59, bread 0.42, chicken and turkey 0.34, corn and corn products 0.52, eggs 0.46, fast food 0.32, margarine and butter 0.58, meat 0.44, miscellaneous fats 0.52, organ meats 0.45, vegetables 0.45, processed meats and poultry 0.47, rice and pasta 0.67, sea food 0.31, soups 0.36, potato 0.63	Age, sex, current smoker, alcohol consumption, physical activity, education	14
Sahay et al. [30]	All adults excluding those with missing dietary information, implausible total calories (≥ 7500 kcal/day), missing metabolic measurements	Olive oil, vegetables and fruits DP: bacon, sausage, salami −0.24, leafy, roots, cruciferous, onion, garlic, tomato, eggplant, squash, mushroom 0.25, mixed nuts 0.24, eggs −0.24, olive oil 0.41, canola and vegetable oil −0.33	Meat, alcohol and fish DP: pork, beef, veal and lamb 0.24, haddock, salmon, sardines, shrimp, squid, octopus 0.21, beer, red wine, white wine, and spirit 0.22	Age, sex, BMI, physical activity, energy intake	13
Yoo, Ki-Bong et al. [48]	Adults excluding those with diabetes or those who were on dietary therapy	Dairy-cereal DP: refined grains −0.55, kimchi 0.39, dairy 0.77, fruit 0.25, cereal snack 0.53, bread 0.52, jam 0.31	–	Age, sex, current smoker, alcohol consumption, physical activity, education, household income, obesity variables, energy intake, nutrient intake (carbohydrate, protein, fat, crude fibre, sodium)	11
Hae Dong Woo et al. [31]	Adults from National Cancer Center, South Korea	Traditional DP : condiments 0.78, green and yellow vegetables 0.74, light coloured vegetables 0.71, tubers 0.67, clams 0.63, tofu, soy milk 0.61, seaweeds 0.60, bonefish 0.54, kimchi 0.49, leanfish 0.46, mushrooms 0.42, fruits 0.40, nuts 0.37, legumes 0.29, yogurt 0.27, eggs 0.27, pickled vegetables 0.24, milk 0.20, red meat 0.23, other seafood 0.25	Meat DP: light coloured vegetables 0.40, clams 0.22, leanfish 0.37, mushrooms 0.36, red meat 0.79, red meat by-products 0.74, other seafood 0.67, high-fat red meat 0.60, oil, 0.50, salted fermented seafood 0.44, noodles 0.43, poultry 0.43, fatty fish 0.37, carbonated beverages 0.36, dairy products 0.30, processed meats 0.29, sweets 0.28, coffee, tea 0.20	Age, sex, current smoker, alcohol consumption, physical activity, total energy intake	13.5

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Table 1 continued

References	Health status	Healthy DP and food components	Unhealthy DP and food components	Factors adjusted for in analysis	Qlty. score/15*
Arisawa et al. [32]	Adults without treatment for diabetes	Prudent DP: milk 0.23, miso soup 0.29, bean curd 0.22, soy beans, fermented soy beans 0.43, eggs 0.30, chicken 0.29, beef, pork 0.40, ham, sausage, salami, bacon 0.29, fish (raw, boiled, grilled) 0.48, small fish with bones 0.46, canned tuna 0.24, squid, shrimp, crab, octopus 0.21, shell-fish (cram, oyster) 0.27, tube-shaped fish paste cake, boiled fish paste 0.30, deep-fried bean curd 0.50, potatoes, taro, sweet potatoes 0.63, pumpkin 0.52, carrot 0.69, broccoli 0.52, green leafy vegetables (spinach, komatsuna, garland chrysanthemum 0.67, other green and yellow vegetables (bell peppers, string beans) 0.66, cabbage 0.65, Japanese white radish 0.66, kiriboshi-daikon 0.37, burdock, bamboo shoot 0.56, other vegetables (cucumber, onion, bean sprouts, Chinese cabbage, lettuce) 0.68, mushrooms 0.68, seaweed 0.53, mayonnaise 0.28, fried foods 0.30, fried dishes 0.49, mandarin orange, orange, grape fruit 0.55, other fruits (strawberry, kiwi, apple, watermelon) 0.53, peanuts, almond 0.26, Japanese confectionery 0.28, green tea 0.30	High-fat/Western DP: rice −0.23, bread 0.25, noodles 0.24, miso soup −0.38, soy beans, fermented soy beans −0.35, eggs 0.39, chicken 0.46, beef, pork 0.46, ham, sausage, salami, bacon 0.46, small fish with bones −0.40, canned tuna 0.28, squid, shrimp, crab, octopus 0.21, salted cod roe, salmon roe 0.29, mayonnaise 0.47, fried foods 0.57, fried dishes 0.47, Western style confectionery 0.41, green tea −0.25	Age, sex, current smoker, alcohol consumption, physical activity, total energy intake	12
Sun et al. [33]	Older adults with one or more CV risk factors or a history of CVD	Balanced diet DP: foods from all four factors	Western DP: flour 0.69, light vegetable 0.60, grains 0.59, beans 0.57, soy beans 0.54, potatoes 0.43, water 0.38, peanuts sunflower 0.37, fresh milk 0.36, red meats 0.35	Age, sex, physical activity. education, employment, income	9.5
Barbaresko et al. [34]	All participants excluding those with missing data on dietary intake, characteristics of MetS or potential confounders or implausible energy intake (8000 kcal/day)	–	PCA derived DP. leafy vegetables, fruiting vegetables, root vegetables, cabbage, other vegetables, beef, pork, processed meat, vegetable oil, other fats, sauce and bouillon	Age, sex, current smoker, physical activity, energy intake, education	14

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Table 1 continued

References	Health status	Healthy DP and food components	Unhealthy DP and food components	Factors adjusted for in analysis	Qlty. score/15*
Choi et al. [35]	All adults from health screening. Participants were excluded if medical records were not available or with implausible energy intakes (< 500 or ≥ 4000 kcal)	Prudent DP: bread, dairy products, nuts, milk, eggs, grains, fruit products, fruits	Traditional DP: light coloured vegetables, green/yellow vegetables, condiments, shellfish, mushrooms, tofu/soymilk, seaweeds, lean fish, tubers, fatty fish, bonefish, other seafood, kimchi	Age, current smoker, alcohol intake, BMI, physical activity, WC, BP, triglyceride, fasting glucose, HDL-CT, marital status, education level, income	14
He et al. [36]	All adults from survey	Diary and eggs DP: refined grains 0.02, vegetables 0.20, livestock meat 0.08, milk and dairy products 0.70, eggs 0.60, fruits, marine products 0.54, organ meats 0.16, poultry −0.03, coarse food grains 0.07, soybean and bean products −0.06	Refined grains and vegetables DP: refined grains 0.67, vegetables 0.64, livestock meat 0.63, milk and dairy products −0.12, eggs 0.16, fruits 0.02, marine products 0.25, organ meats 0.04, poultry 0.14, coarse food grains −0.25, soybean and bean products 0.33	Age, sex, BMI, occupation, type of area	14
Suliga et al. [37]	All adults from PONS project excluding the ones with a history of CVD, strokes, DM or cancer	Healthy DP: low-fat milk 0.36, cottage cheese 0.53, yogurt 0.44, fruit 0.66, vegetables 0.62, whole grains 0.32	Fat, meat and alcohol DP: eggs 0.59, red meat 0.45, cold cured meat 0.33, lard 0.44, fried foods 0.49, vegetable oils 0.38, mayonnaise 0.39	Age, current smoker, physical activity, education level, place of residence	13.5
Gadgil et al. [49]	South Asians ancestry, excluding those with CVD, nitroglycerin, cancer, impaired cognitive ability, or a life expectancy < 5y, living in a nursing home or planning to relocate	Fruits, vegetables, nuts, and legumes DP	Fried snacks, sweets and high-fat dairy DP	Age, sex, BMI, current smoker, alcohol intake, physical activity, energy intake, study site, income, education	13.5
Bell et al. [38]	All participants from survey	Healthy DP: whole grains 0.36, fresh fruit 0.35, low-fat dairy products 0.33, dried fruit 0.32, legumes 0.29, unsaturated spreads 0.25, takeaway foods −0.28, soft drinks −0.33, alcoholic drinks −0.40, fried potatoes −0.42	Refined and processed DP: added sugar 0.56, full-fat dairy products 0.41, unsaturated spreads 0.36, cakes, biscuits and sweet pastries 0.32, processed meat 0.25, canned fruit 0.25, soft drinks 0.25, other vegetables −0.26, fresh fruit −0.32	Age, sex, current smoker, physical activity, energy intake, income	13

DP dietary pattern, *FFQ* food frequency questionnaire, *BMI* body mass index, *Qlty*. quality, *CHD* coronary heart disease, *CVD* cardiovascular disease, *CV* cardiovascular, *FA* factor analyses, *CA* cluster analyses, *PCA* principal component analyses, *WC* waist circumference, *IGT* Impaired Glucose Tolerance, *BP* systolic and diastolic blood pressure, *PASE* activity score for the elderly, *MMSE* mini-mental state examination, *GDS* geriatric depression scale, *DM* diabetes mellitus, *NCEP-ATP III* United States Adult Treatment Panel III of the National Cholesterol Education Program, *IDF* International Diabetes Federation, *ADA* American Diabetes Association, *J-MICC* The Japan Multi-Institutional Collaborative Cohort Study, *HDL-CT* high-density lipoprotein cholesterol

* Quality score was calculated on 16 criteria based on the reporting of the study design and method, study attrition, measurement of dietary patterns, measurement of CVD, and statistical analysis

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Table 2 Cohort studies of dietary patterns and metabolic syndrome

Author, Year	Country	Population	Sample size (sex)	Age range (year)	Outcome ascertainment	Diet assessment Method (items) and method to identify DP	Follow-up, years	Health status	DP identified and method used	Factors adjusted for in analysis Criteria for defining MetS	Quality score/15*
Lutsey et al. [50]	USA	ARIC study	9,514 (both)	45–64	Medical records, interviews	FFQ (66) PCA	9	Middle aged adults without CVD, MetS, missing diet data, or energy intakes women: <500 to >3500 kcal and men <700 to >4500 kcal	Prudent DP (healthy): cruciferous vegetables 0.62, carotenoid vegetables 0.60, fruit (no juice) 0.58, other vegetables 0.52, fish and seafood 0.46, poultry 0.43, dark leafy vegetables 0.43, whole grains 0.40, tomatoes 0.39, legumes 0.34, low-fat dairy 0.31, yogurt 0.27, nuts and peanut butter 0.26, fruit juice 0.24, potatoes 0.24, fat 0.21 Western DP (unhealthy): refined grain bread/cereal/rice/pasta 0.63, processed meat 0.63, fried foods 0.61, red meat 0.57, eggs 0.48, refined grain desserts 0.43, soda and sweetened beverages 0.41, cheese and whole milk 0.38, legumes 0.35, sweets/candy 0.30, fat 0.30, other vegetables 0.29, potatoes 0.28, ice cream 0.27, yogurt −0.21	Age, sex, current smoker (packs/year), physical activity, race, centre, education, energy intake, behavioural characteristics. AHA guidelines	14.5
Kimokoti et al. [51]	USA	Framingham Offspring/Spouse cohort	1,146 (women)	25–77	Medical records	FFQ (145), 3-d dietary records, 24-h recall CA	7	Women from the Framingham Heart cohort study without CVD, DM, cancer, MetS who had attended exams 4–6.	Higher fat DP (unhealthy): sweets and animal fats 4.6, refined grains, soft margarine and oils 3.6, diet beverages and firm vegetable fats 4.2, desserts 1.3 Heart Healthier DP (healthy): vegetables 3.8, fruits and low-fat milk 4.4, other low-fat foods 4.6, legumes, soups and miscellaneous foods 0.36	Age, current smoker, BMI, physical activity, WC, BP, glucose, HDL-cholesterol, TG, postmenopausal status, hypertension medication, lipid-lowering medication, elevated WC, elevated BP, low HDL-cholesterol, elevated TG Joint Scientific Statement	14

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Eur J Nutr (2016)
No of pages 23
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Table 2 continued

Author, Year	Country	Population	Sample size (sex)	Age range (year)	Outcome ascertainment	Diet assessment Method (items) and method to identify DP	Follow-up, years	Health status	DP identified and method used	Factors adjusted for in analysis Criteria for defining MetS	Quality score/15*
Duffey et al. [52]	USA	CARDIA study	3,728 (both)	18–30	Interviews, questionnaires	CARDIA Diet History questionnaire CA	20	Young adults who had complete outcome and covariate data; excluded those who in year 0 indicated high prevalent WC, elevated BP, low HDL-CT, high TG and MetS	Prudent DP (healthy): fruit, whole grains, milk, nuts and seeds.	Sex, age, smoking status, total physical activity, CARDIA exam centre, baseline weight, total energy intake, family structure, maximum years of educational attained ever during the study NCEP-ATPIII	14.5

DP dietary pattern, *FFQ* food frequency questionnaire, *BMI* body mass index, *MetS* metabolic syndrome, *AHA* American Heart Association, *CHD* coronary heart disease, *CVD* cardiovascular disease, *CV* cardiovascular, *TG* triglycerides, *FA* factor analyses, *CA* cluster analyses, *PCA* principal component analyses, *BMI* body mass index, *WC* waist circumference, *BP* systolic and diastolic blood pressure, *DM* diabetes mellitus

* Quality score was calculated on 16 criteria based on the reporting of the study design and method, study attrition, measurement of dietary patterns, measurement of CVD, and statistical analysis

sweets (ice cream, cakes, cookies, biscuits, chocolate) and fast food (pizza, snacks, French fries).

Overall, the pooled OR (95 % CI) for MetS in a comparison of the highest to the lowest category of Western/unhealthy dietary patterns in cross-sectional studies was 1.28 (95 % CI 1.17, 1.40; *P* for heterogeneity =0.0; and $I^2 = 72$ %) (Fig. 4). The pooled RR (95 % CI) for MetS in cohort studies was 0.96 (95 % CI 0.53, 1.73; *P* for heterogeneity =0.102; $I^2 = 62.6$ %) (Fig. 5).

Potential sources of heterogeneity, such as sex ($P = 0.956$), geographic area ($P = 0.588$), a posteriori approach ($P = 0.578$), adjustment for key confounders ($P = 0.978$), MetS definition ($P = 0.531$), age ($P = 0.925$) or health status ($P = 0.150$) produced only minor, non-significant differences (Table 4). As only two cohort studies were included in the meta-analysis, the subgroup analyses were conducted using cross-sectional data.

In sensitivity analyses, exclusion of individual studies did not modify pooled estimates substantially: MetS ORs ranged from 1.25 to 1.31 in cross-sectional studies. The funnel plot was reasonably symmetric ("Appendix").

Quality score

The scores for quality assessment ranged from 9.5 to 14 out of 16 points. Overall, there were no obvious differences in quality scores between the 31 studies that found an inverse association between the different dietary patterns and MetS and those that reported either a positive association or not.

Discussion

The results of our meta-analysis, involving 85,137 participants, assessed the results from published cohort and cross-sectional studies that investigated the association between a posteriori dietary patterns and MetS. In cross-sectional studies, a healthy/prudent dietary pattern was associated with a lower prevalence of MetS, and an unhealthy/Western pattern was associated with an increased risk of the MetS. The pooled estimate from the three prospective cohort studies seems to agree with the cross-sectional study findings, although the 95 % CI does not confirm the protective role of the prudent/healthy dietary pattern. In the study with the longest follow-up, however, Duffey et al. [52] show a clear link between the exposure to that pattern and reduced incidence of MetS.

The initial results of the meta-analysis were consistent when tested for sensitivity analysis. Previous reviews have analysed the influence of diet on MetS, showing a positive effect of the Mediterranean diet on decreasing the prevalence and development of MetS [18, 59, 60]. As Calton et al. [60] point out in his 2014 review, other worldwide

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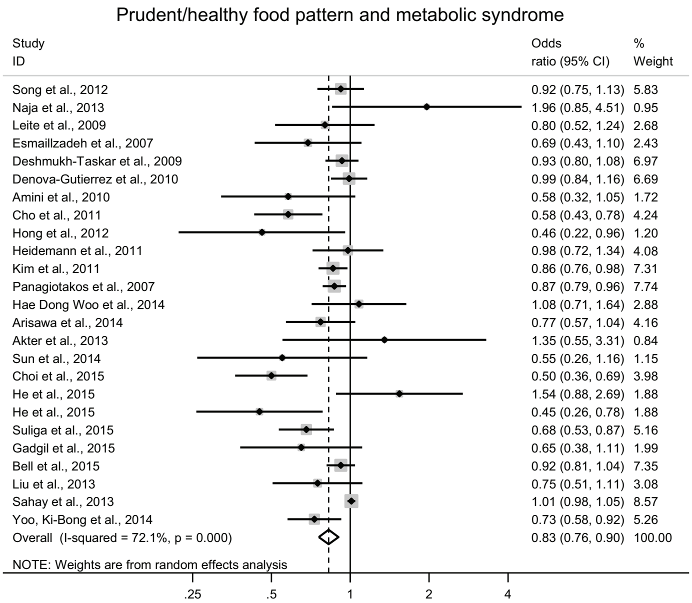

Fig. 2 Meta-analysis of prudent/healthy dietary pattern and metabolic syndrome in cross-sectional studies. Odds ratios and relative risks correspond to comparisons of extreme categories of exposure within each study. The area of each square is proportional to the inverse of the variance of the log estimate. Horizontal lines represent 95 % confidence intervals. Diamonds represent pooled estimates from inverse-variance weighted random effects models. *CI* confidence interval, *OR* odds ratio, *RR* relative risk

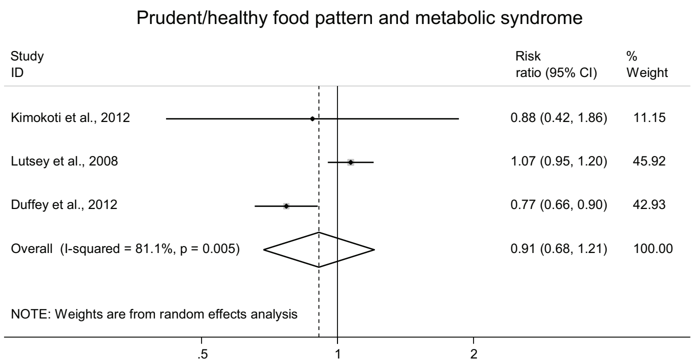

Fig. 3 Meta-analysis of prudent/healthy dietary pattern and metabolic syndrome in cohort studies. Odds ratios and relative risks correspond to comparisons of extreme categories of exposure within each study. The area of each square is proportional to the inverse of the variance of the log estimate. Horizontal lines represent 95 % confidence intervals. *Diamonds* represent pooled estimates from inverse-variance weighted random effects models. *CI* confidence interval, *OR* odds ratio, *RR* relative risk

pre-defined representative dietary patterns such as the DASH diet (high intake of fruits, vegetables, whole grains and dairy) [61] or Northern Europe dietary pattern (fruits, vegetables, legumes, low-fat dairy, fatty fish, oats, barley and almonds) [62] can improve MetS and should be taken into account when establishing a general statement about protection or risk of developing MetS, considering that following a healthy or unhealthy dietary pattern is influenced

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Table 3 Subgroup analyses and meta-regression for prudent/healthy dietary pattern

Subgroup	Number of studies	Odds ratio (95 % CI)	I^2 (%)	*P* value
Adjustment for key confounders				
Yes	8	0.87 (0.77, 0.98)	75.9	
No	16	0.80 (0.71, 0.90)	54.7	0.950
Geographic area				
Asia	14	0.76 (0.65, 0.89)	63.4	
Europe	5	0.88 (0.77, 1. 20)	77.2	
America	4	0.92 (0.82, 1. 04)	13	
Australia	1	0.92 (0.81, 1. 04)	–	0.595
Pattern design				
PCA	12	0.80 (0.69, 0.92)	76.7	
Factor analysis	9	0.85 (0.74, 0.97)	67.9	
Cluster analysis	3	0.87 (0.73, 1.04)	0.0	0.722
Sex				
Men	1	1.54 (0.88, 2.69)	–	
Women	4	0.55 (0.46, 0.66)	0.0	
Both sexes	20	0.88 (1.81, 0.94)	59.9	0.487
Metabolic syndrome definition				
NCEP-ATPIII	18	0.80 (0.72, 0.89)	58.8	
IDF	4	0.90 (0.74, 1.09)	83.2	
Other	2	0.82 (0.53, 1.25)	43.5	0.551
Age				
Young adults 18–35	–	–	–	
Adults 36–70	5	0.71 (0.59, 0.85)	0.0	
Mixed young adults, adults and older adults	15	0.84 (0.75, 0.93)	77.8	
Mixed young adults and adults	1	0.93 (0.80, 1.08)	–	
Mixed adults and older adults	3	0.80 (0.59, 1.07)	37.1	0.429
Health status				
Metabolic disease and/or CVD	3	0.53 (0.36, 0.79)	0.0	
No metabolic disease and/or CVD	12	0.79 (0.70, 0.89)	49.7	
General population	9	0.89 (0.80, 1.00)	75.2	0.226

PCA principal component analysis, *NCEP-ATP III* United States Adult Treatment Panel III of the National Cholesterol Education Program, *IDF* International Diabetes Federation, *CVD* cardiovascular disease

by culture and society. Our study combined different a posteriori dietary patterns derived from very diverse worldwide eating habits, such as traditional dietary patterns from eastern Asian countries (Japan, China, Korea), the Mediterranean area (Greece, Italy, France, Lebanon, Croatia), Northern Europe (Sweden, Germany), eastern/middle Europe (France and Poland), North America (USA, Mexico) and Australia. The factor loadings per pattern analysis reflected the foods most commonly consumed, showing the cultural diversity linked to food consumption [20, 63]. According to this, and when grouping the different foods, there were similarities and differences among geographical areas. The vegetable and fruit groups appear to be the most common ones in the healthy pattern with foods such as leafy vegetables, yellow vegetables or mushrooms. Whole grains and low-fat dairy are also common among the different countries as well as fish, legumes and poultry. Vegetable oils are also usual as healthy oils. On the other side, in the Western/unhealthy dietary pattern, the foods most commonly consumed are cakes, cookies, soft drinks, red and processed meat, fast food, butter, margarine, and coffee. Certain foods were only consumed in specific geographical areas; some examples are kimchi, from Korea, corn tortillas from Mexico, miso soup from Japan, shawarma and falafel from Iran, lamb and garlic, goat milk and cheese from the Mediterranean area. Despite including a posteriori dietary patterns leads to a more realistic approach to the population dietary habits it also brings difficulties aiming for the homogenization of results. Some foods, such as cheese, wine, potatoes, rice or milk, were categorized as healthy as well as unhealthy, depending on the studies. Therefore, the need for a rank/grading when

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Table 4 Subgroup analyses and meta-regression for Western/unhealthy dietary pattern

Subgroup	Number of studies	Odds ratio (95 % CI)	I^2	*P*-value
Adjustment for key confounders				
Yes	9	1.24 (1.04, 1.47)	73.1 %	
No	17	1.31 (1.18, 1.47)	72.7 %	0.978
Geographic area				
Asia	12	1.28 (1.06, 1.55)	67.7 %	
Europe	8	1.33 (1.16, 1.51)	70.6 %	
America	5	1.28 (0.91, 1.79)	86.4 %	
Australia	1	1.16 (1.04, 1.29)	–	0.781
Pattern design				
PCA	13	1.30 (1.15, 1.46)	69.2 %	
Factor analysis	9	1.16 (0.97, 1.38)	79.0 %	
Cluster analysis	4	1.61 (1.23, 2.09)	34.4 %	0.578
Sex				
Men	3	1.27 (0.65, 2.49)	76.8 %	
Women	6	1.23 (0.93, 1.63)	46.0 %	
Both sexes	20	1.29 (1.17, 1.42)	76.5 %	0.956
Metabolic syndrome definition				
NCEP-ATPIII	19	1.34 (1.17, 1.52)	71.4 %	
IDF	5	1.19 (1.01, 1.41)	72.4 %	
Other	2	1.26 (0.96, 1.66)	46.1 %	0.531
Age				
Young adults 18–35 years	–	–	–	
Adults 36–70 years	4	1.55 (1.11, 2.15)	37.9 %	
Mixed young adults, adults and older adults	18	1.31 (1.18, 1.47)	75.5 %	
Mixed young adults and adults	1	0.93 (0.80, 1.08)	–	
Mixed adults and older adults	3	1.19 (0.99, 1.42)	19.9 %	0.925
Health status				
Metabolic disease and/or CVD	3	2.34 (1.40, 3.89)	59.2 %	
No metabolic disease and/or CVD	11	1.35 (1.14, 1.59)	71.1 %	
General population	12	1.15 (1.05, 1.27)	58.0 %	0.150

PCA principal component analysis, *NCEP-ATP III* United States Adult Treatment Panel III of the National Cholesterol Education Program, *IDF* International Diabetes Federation, *CVD* cardiovascular disease

considering the categorization of a pattern arises: from pure unhealthy to pure healthy, based on worldwide recommendations. Moreover, the more specific the dietary assessment is made, the better the dietary pattern categorization can be achieved. Consequently, the assessment with FFQ with little questions should be avoided. Additionally, the assessment by other methods such as 3-day food records could be considered.

The tool used to assess dietary intake in most of the studies was a FFQ, notwithstanding eight studies used different dietary assessment tools such as 24-h recall [27, 38, 45, 48], 3-day food records [44], the sum of 24-h recall and 3-days food records [28, 36, 43, 51] and a specific diet history questionnaire (CARDIA diet history questionnaire) [52].

Furthermore, Akter et al. [46] and Yoo et al. [48] also maintain that eating breakfast is associated with a reduced prevalence of MetS, even if the breakfast characteristics could be considered unhealthy. Our outcomes are also consistent with recent recommendations contained in the European Society of Cardiology Guidelines on diabetes, pre-diabetes and cardiovascular diseases developed in collaboration with the European Association for the Study of Diabetes [64] and the Dietary Guidelines for Americans related to risk of MetS [65]. It is also noteworthy that red meat and processed meat, included in the unhealthy pattern, have been labelled by the World Health Organization as a carcinogenic product [66]. It is remarkable that regardless of how MetS is defined and without including established risk factors (age, gender, smoking), it has been associated with a twofold increase in cardiovascular outcomes and a 5-fold increase in the development of type 2 diabetes [67–69].

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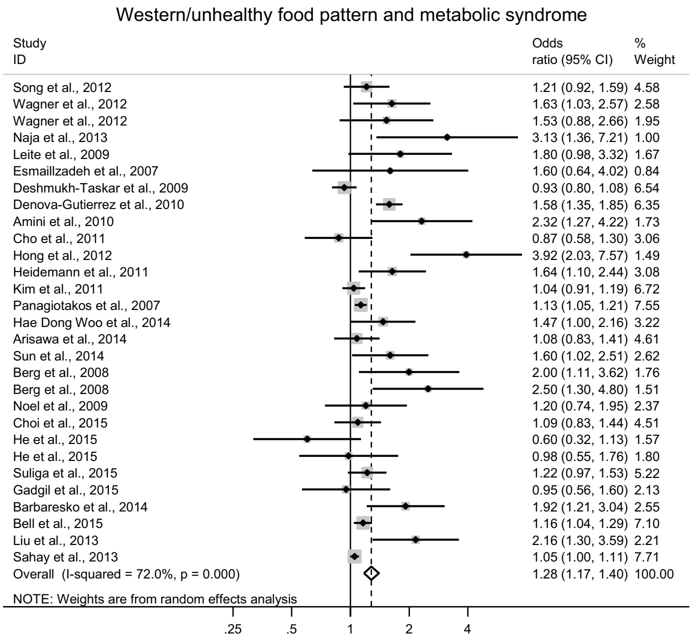

Fig. 4 Meta-analysis of Western/unhealthy dietary pattern and metabolic syndrome in cross-sectional studies. Odds ratios and relative risks correspond to comparisons of extreme categories of exposure within each study. The area of each square is proportional to the inverse of the variance of the log estimate. Horizontal lines represent 95 % confidence intervals. *Diamonds* represent pooled estimates from inverse-variance weighted random effects models. *CI* confidence interval, *OR* odds ratio, *RR* relative risk

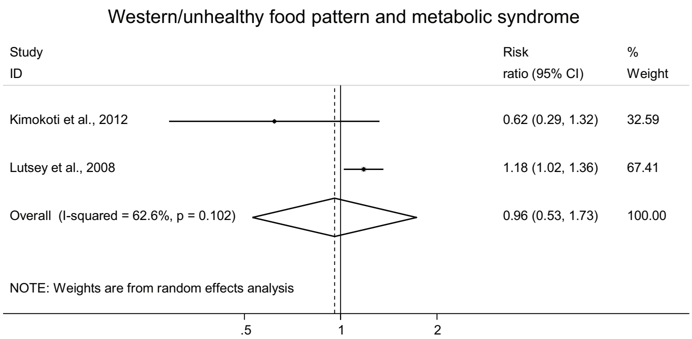

Fig. 5 Meta-analysis of Western/unhealthy dietary pattern and metabolic syndrome in cohort studies. Odds ratios and relative risks correspond to comparisons of extreme categories of exposure within each study. The area of each square is proportional to the inverse of the variance of the log estimate. Horizontal lines represent 95 % confidence intervals. *Diamonds* represent pooled estimates from inverse-variance weighted random effects models. *CI* confidence interval, *OR* odds ratio, *RR* relative risk

Various biological mechanisms might explain the results of the meta-analysis regarding the effects on MetS risk of following a healthy or an unhealthy dietary pattern. Considering the food items included in the healthy dietary patterns, vegetable and fruit consumption play a protective role and there is no upper limit for its intake. The proposed population goal of, a minimum, 600 g/day is in line with the most recent global population goal proposed by the World Cancer Research Fund in 2009 [70, 71]. Higher intakes of fruits and vegetables are associated with a lower MetS risk, perhaps due to lower C-reactive protein concentrations, and have also been inversely associated with

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diastolic blood pressure in MetS patients [72, 73]. Furthermore, the intake of fruit, vegetables, whole grains and legumes increases the amount of fibre, which can have a protective value against cardiometabolic diseases due to its antioxidant content [74–77]. In addition, the consumption of whole grains shows an inverse trend with MetS [78], whereas refined grains intake is positively associated with the risk of having MetS [79]. Moreover, in a cohort of Spanish graduates (the SUN project), nut consumption was significantly associated with lower risk of developing MetS after a 6-year follow-up period [80]. In addition, nut consumption does not increase body weight, body mass index or waist circumference [81]. In regard to the unhealthy dietary patterns, the consumption of soft drinks and sweets, which was a common food within the included studies, has been linked to the development of MetS in the literature [82–84]. Dietary sugars have been related to providing excess energy and large amounts of rapidly absorbable sugars [85, 86]. The intake of fast food, has been also related to MetS [87], even in children and adolescents [88], increasing the amount of saturated and trans-saturated fat and salt. In our study, mostly represented by Asiatic dietary patterns, white rice and noodles were widely consumed and have been related to MetS in some studies [89, 90]. Despite being a controverted research topic, moderate alcohol consumption (the intake below 10 g/day for women and 20 g/day for men) might not increase the risk of developing MetS [91], notwithstanding moderate red wine consumption was associated with a lower prevalence of the MetS in an elderly Mediterranean population at a high cardiovascular risk [92]. According to our results, alcohol seems to play an important role in the studies included, being classified, predominantly, as an unhealthy food or related to an unhealthy lifestyle [22, 27, 30, 38, 40, 42, 44, 45]. Dairy products have appeared in some of the analysed studies as a protective food group for some components of MetS [36, 48]. Crichton et al. [57] pointed this out in a 2011 review, concluding that the majority of the existing literature suggested a benefit of low-fat dairy consumption in lowering the odds of having MetS.

The main limitation of our study is that factor loadings for individual foods in the different dietary patterns were not exactly equal between the previously published studies, and they included different food items, being especially diverse in the Western/unhealthy dietary pattern. Nonetheless, there were similarities in the types of foods generally featured in the healthy patterns and the unhealthy patterns [93]. Despite the fact that dietary patterns combine different kinds and amount of foods, the ones that are more predominant will define the final influence of that pattern. Without discounting the possibility of finding other kinds of dietary patterns, our study included those most commonly identified in the observational studies reviewed. Despite the fact that heterogeneity is accounted as a weakness of our study, it was not explained by geographic area, type of a posteriori approach, quality assessment, sex, MetS definition, age, health status or adjustment for key confounders. In cohort studies, the difference among studies was important: the age range of the population included in the studies differed notably. Duffey et al. included a population of younger adults (18–30), Lutsey included adults (45–64) and Kimokoti a wider age range including younger adults, adults and older adults (25–77). Moreover, the different sample sizes between them could also have played an important role in the heterogeneity showed (Lutsey 9514; Kimokoti 1146; Duffey 3728). Our study population was rather heterogeneous, which can increase residual confounding, biasing the estimate to the null, but leads to generalizability [94].

The confounding factors within the different studies also played an important role in the final results. All of the studies were adjusted for age and sex, and most also were adjusted for physical activity [22, 25, 26, 28–34, 36–38, 40, 41, 45–48, 50, 52]. However, body mass index (BMI) or energy intake, well-defined risk factors for developing MetS, was not considered in most of the studies [excepting 23, 24, 27, 30, 35, 39, 42–44, 49, 51]. Other confounding factors such as income or ethnicity should be considered in future research [95]. The results of meta-analyses of observational studies must be interpreted with caution because of the potential for confounding. Moreover, dietary patterns may represent a general lifestyle and, even with the adjustment for known and suspected confounders, residual confounding cannot be ruled out because of the observational nature of the studies included [96, 97]. Finally, most of the studies included are cross-sectional; therefore, they cannot be used to infer a causal role of dietary patterns with the risk of developing MetS.

Although more research about the topic should be held, practitioners, nurses or dieticians could benefit from these results and consider them in the recommendations of their daily clinical practice.

In conclusion, this meta-analysis showed that a prudent/healthy dietary pattern is a protective factor for MetS and that an unhealthy dietary pattern could be associated with an increased risk of developing MetS. Additional prospective studies are needed to confirm the association between dietary patterns and MetS.

Authors' contributions Míriam Rodríguez-Monforte and Gemma Flores-Mateo formulated the research question, designed the study and carried it out, and analysed the data. Míriam

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Rodríguez-Monforte and Emília Sánchez discussed the results. Míriam Rodríguez-Monforte, Gemma Flores-Mateo, Emília Sánchez, Francisco Barrio and Bernardo Costa wrote the paper. All authors contributed to the revision of the manuscript and read and approved the final version.

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Compliance with ethical standards

Conflict of interest The authors have no relevant interests to declare.

Appendix

See Figs. 6 and 7.

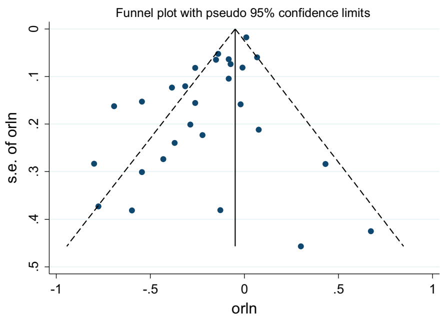

Fig. 6 Publication bias, prudent/healthy dietary pattern

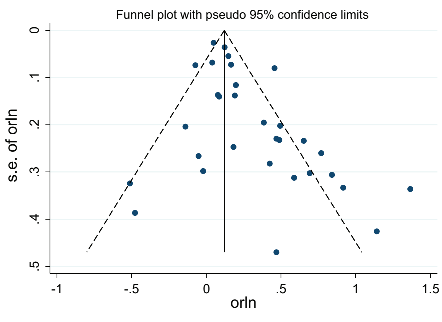

Fig. 7 Publication bias, Western/unhealthy dietary pattern

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5.3 Publication three

Dietary patterns in adults with high diabetes risk in primary healthcare settings in Catalonia: a cohort revisited

Míriam Rodríguez-Monforte, Emília Sánchez, Francisco Barrio, Bernardo Costa, Jorge Delagneau, Iris Benadero, Gemma Flores-Mateo

ABSTRACT

Background: Analysis of dietary patterns in high diabetes risk individuals living in a Mediterranean area may help understand which lifestyle modifications are needed in order to tailor interventions and achieve better health outcomes.

The **aim** of this study was to describe the dietary patterns and adherence in adults in community care settings (DE-PLAN cohort). The association of dietary patterns with metabolic syndrome and type 2 diabetes also was assessed.

Research design and methods: Participants completed a 46-item basic food frequency questionnaire. Foods and beverages were categorized to derive dietary patterns via Principal Component Analysis (PCA). The distribution of qualitative variables across tertiles was evaluated with chi-square tests. Cox regression models were used to estimate multivariable-adjusted hazard ratios and 95% CIs for MetS and type 2 diabetes.

Results: The study population consisted of 552 individuals. Three major dietary patterns were derived and named after their major foods or food groups: *1) Rice, potatoes and legumes, 2) Alcohol, sausages, 3) Protein, vegetables*. The 4-year progression in adherence to the dietary patterns, represented by the food factor loadings, remained stable. After adjustment for potential confounders, there was no significant association between dietary pattern adherence and MetS or type 2 diabetes. Cumulative incidence rates of MetS and type 2 diabetes were 49.4% and 18.1%, respectively. A significant trend to decrease over time was observed in both conditions ($p<0.001$ and $p=0.007$, correspondingly).

Conclusions: The derivation of dietary patterns in a Mediterranean population with high diabetes risk allows analysis of food consumption taking into account personal choices. Our study describes the dietary patterns followed by a sample of adults with high-diabetes risk in PHC settings in Catalonia and highlights the need to continuously improve nutritional habits by more intensive, long-lasting and professional-supported interventions in order to enhance the adherence to a healthy dietary pattern, such as the Mediterranean diet, and thereby achieve better health status and quality of life.

Dietary patterns in adults with high diabetes risk in primary healthcare settings in Catalonia: a cohort revisited

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Dietary patterns; metabolic syndrome; type 2 diabetes; Mediterranean population

Running title:

Dietary patterns and metabolic syndrome

Abbreviations:

MS, Metabolic Syndrome

CI, Confidence Interval

IDF, International Diabetes Federation

NCEP-ATPIII, Adult Treatment Panel III of the National Cholesterol Education Program

FFQ, Food Frequency Questionnaire

ABSTRACT

Background: Analysis of dietary patterns in high diabetes risk individuals living in a Mediterranean area may help understand which lifestyle modifications are needed in order to tailor interventions and achieve better health outcomes.

The **aim** of this study was to describe the dietary patterns and adherence in adults in community care settings (DE-PLAN cohort). The association of dietary patterns with metabolic syndrome and type 2 diabetes also was assessed.

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healthy dietary pattern, such as the Mediterranean diet, and thereby achieve better health status and quality of life.

INTRODUCTION

Diet is an important predictor of health outcomes in the general population (1), and becomes essential in the case of adults with high diabetes risk (2-3). Metabolic syndrome (MetS) is the clustering of physiological, biochemical, clinical and metabolic factors that directly increase the risk for cardiovascular disease and diabetes beyond that of its individual components (5,6). Regardless of how MetS is defined, and without including established risk factors (age, sex, smoking), it has been associated with a 2-fold increase in cardiovascular outcomes and a 5-fold increase in the development of type 2 diabetes (7-9). According to the International Diabetes Federations (IDF), the primary intervention for the management of MetS is a healthy lifestyle, including moderate calorie restriction, moderate increase in physical activity and attention to dietary composition (10).

The link between diet and the risk of a specific disease can be analyzed by evaluating dietary patterns, developed in nutritional epidemiology as a complementary approach to the study of individual foods (11). Although the Mediterranean dietary pattern has been related to good cardiovascular health (12), the prevalence of MetS in the Mediterranean area (Spain, Italy, Greece) is not significantly lower than in other worldwide regions. This means that following a healthy dietary pattern is not always related with belonging to a specific geographical region or culture. As Anagnostis points out in his review (13), MetS prevalence in Mediterranean countries varies from 23.6% (both sexes) in Greece (14) to 18% (women) in Italy (15). Moreover, the results from a Spanish cohort showed that the prevalence of MetS was much higher in patients with diabetes mellitus, and even greater in sedentary diabetic patients (16).

Diets are multidimensional and dynamic; they include complex combinations of foods and nutrients consumed in varying preparations and contexts that change with age, disease onset, mood, and other life-course events. Little research has analyzed dietary patterns over time, which is especially relevant when conducting a lifestyle intervention (17,18).

The general aim of this study was to analyze dietary patterns and progressive adherence to them in adults with high diabetes risk in community care settings within the Diabetes in Europe-Prevention using Lifestyle, Physical Activity and Nutritional Intervention in Catalonia cohort (DE-PLAN-CAT). We also described the association of the different dietary patterns observed with the risk of MetS and type 2 diabetes in the same population.

METHODS

Study population

The DE-PLAN-CAT study was a prospective cohort designed to investigate the prevention of diabetes in Primary Health Care (PHC) settings in high-risk populations using lifestyle, physical activity and nutritional interventions (19). The nutritional intervention had several targets: to limit daily energy intake from fat to no more than 30%, from saturated fat to no more than 10%, to obtain at least 15 g/1,000 kcal of fiber, and achieve at least 30 min/day of moderate physical activity and at least an arbitrary realistic 3% weight reduction. The Mediterranean diet and nutritional advice based on the Prevención con Dieta Mediterránea-Mediterranean Diet Adherence Screener (PREDIMED-MEDAS) questionnaire was used as a tool to increase adherence to the Mediterranean diet during the follow-up (20).

Participants aged 45-75 years were recruited from 18 PHC centers in Catalonia (Spain) in 2006. To select participants with high risk for diabetes, 2,054 individuals were screened with the Finnish Diabetes Risk Score (FINDRISC) (21). Of these, 1,192 were screened using a 2h 75g Oral Glucose Tolerance Test (OGTT). Participants were eligible only if they had an OGTT, did not have diabetes, and had a FINDRISC score >14 or pre-diabetes defined using World Health Organization (WHO) criteria for fasting or 2h post-load plasma glucose (or both). The study cohort included 552 men and women in 2006; data collection on dietary habits and follow-up testing were assessed each year through 2010. Eligible individuals with severe psychiatric disease, chronic kidney disease, liver disease or blood disorders were excluded.

The research ethics committee at the Jordi Gol Research Institute approved the protocol and all participants gave written informed consent.

Assessment of dietary intake and dietary patterns derivation

At baseline and in every follow-up examination (year 1, 2, 3 and 4), usual dietary intake was assessed by a 46-item food frequency questionnaire (FFQ) provided by the European DE-PLAN/IMAGE project, adapted to the Spanish language, and focused on dietary and physical exercise behaviors. Health professionals from the PHC centers were responsible for the assessment and available for consultation if additional information was needed. Food and beverages from the FFQ were categorized into 21 food groups that were used to derive dietary patterns via Principal Component Analysis (PCA) and to determine factor loadings for each of those groups. Food groups and subgroups in the dietary patterns analysis included consumption of meats, fish, dairy, fruit and vegetables, grains, sugar, fat, alcohol, fast-food and caffeinated drinks (TABLE 1).

Assessment of anthropometric, sociodemographic and lifestyle factors

In the first screening, age, sex, hypertension, smoking status, history of high blood glucose disorders, physical activity, weight, height, body mass index (BMI) and waist circumference were collected by the FINDRISC questionnaire or from the clinical records. Body weight and height were measured in light clothing, without shoes. Waist circumference was measured midway between the lowest rib and the iliac crest. Both measurements were done by trained nurses. BMI was calculated as weight (in Kg) divided by height (in m^2).

Assessment of other variables

In the second screening, a 2h 75g OGTT with measurements of fasting and 2h post load plasma glucose was carried out according to WHO standards. Lipid profile and

HbA_{1c} tests were performed simultaneously. The plasma glucose and lipid profile were carried out using a uniform glucose oxidase-peroxidase and a cholesterol oxidase-phenol aminophenazone (CHOD-PAP) method, respectively. The HbA_{1c} was a standardized HPLC assay aligned to the Diabetes Control and Complications Trial in all laboratories (22).

MetS and type 2 diabetes definition

MetS and its components were defined according to the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) guidelines, which characterizes MetS by the presence of at least 3 of the following conditions: *central obesity* (waist circumference >102 cm in men and >88 cm in women), *high serum triglycerides* (≥150mg/dL (≥1.695 mmol/L)), *low serum HDL cholesterol* (<40mg/dL (<1.036 mmol/L) in men and <50mg/dL (< 1.295 mmol/L) in women), *high blood pressure* (PAS ≥130 mmHg, PAD ≥ 85mmHg), and *high fasting glucose* (≥100mg/dL (≥5.6 mmol/L)) (23). The assessment of the association between dietary patterns and MetS and MetS components excluded those participants that had the syndrome at baseline. The diagnosis of type 2 diabetes was categorized according to the WHO criteria based on the results of 2h post-load glucose and being > 11.1 mmol/L.

Statistical analysis

Dietary patterns were derived by PCA, which provides a large number of factor solutions. This makes it very important to define the dietary patterns that will finally be included. Factors with eigenvalues >1.5 were considered along with scree testing, which involves plotting the eigenvalues in descending order of their magnitude against their factor numbers and determining where they level off, in order to determine the number of factors to retain in PCA (24). In addition, the identified factors were orthogonally rotated to simplify the factor structure and to enhance their interpretability. For each factor, foods with factor loadings ≥0.30 were considered to contribute significantly to the pattern. Afterwards, factors were numbered and given provisional labels according to the food groups that loaded highly on the pattern.

A descriptive analysis was first performed on the baseline characteristics of study participants and categorized into tertiles. ANOVA analysis was used to determine the difference between their characteristics; the distribution of qualitative variables across tertiles was evaluated with chi-square tests.

To ascertain associations between dietary patterns and MetS, MetS components, or type 2 diabetes, Cox regression models were performed, with each dietary pattern as the independent variable and MetS, type 2 diabetes or components of MetS the dependent variable. We controlled for potential confounders for each dependent variable, adjusting for age, sex, smoking, and physical activity in the case of MetS and MetS components and adding BMI and hypertension in type 2 diabetes. Hazard ratios (HR) and 95% confidence intervals (CI) are presented. New cases of both MetS and type 2 diabetes across the four intervention years, and cumulative incidence rates were also assessed. For all analyses, SPSS version 22 was used.

RESULTS

The PCA revealed three major dietary patterns named after the foods that had higher loadings on that specific pattern: *Rice, potatoes and legumees dietary pattern* (percentage of variance from baseline to fourth year of 10.6%, 11.5%, 9.5%, and 10.5%, respectively) characterized by high intake of rice, potatoes, and legumes; *Alcohol, sausages dietary pattern* (percentage of variance from baseline to fourth year of 8.9%, 9.7%, 7.7%, 7.8%, and 9.7%, respectively) with a predominant intake of all types of alcohol, sausages and nuts; and a *Protein, vegetables dietary pattern* (percentage of variance from baseline to fourth year of 7.8%, 8.1%, 8.6%, 8.8%, and 8.1%, respectively) with high factor loadings on fish, meat, poultry, and vegetables (TABLE 2).

Overall, the foods most widely consumed in the three dietary patterns and accounting for factor loadings ≥0.3 were fish, poultry, red and processed meat, sausages, vegetables, fruit, nuts and dried fruits, potatoes, legumes, rice, wine, beer and distilled drinks.

Our study population included 552 participants (368 women and 184 men) with a median age of 61.6 years. Participants were followed up for an average of 3.8 years. At baseline, all participants were at risk of developing type 2 diabetes and 129 participants already had MetS. During this period, 100 participants were diagnosed with type 2 diabetes and 209 with MetS.

At baseline, participants with a higher score for the *Alcohol, sausages dietary pattern* tended to be younger men, weigh more, have high levels of basal glucose and triglycerides and low HDL-cholesterol values, and were currently smokers. No significant differences in adherence to the *Rice, potatoes, legumes* or *Protein, vegetables dietary patterns* were found at baseline in our population (TABLE 3).

Despite being very constant along the four years, progression in the adherence to dietary patterns during the intervention period, represented by the food factor loadings, varied for some food components. In the *Rice, potatoes and legumes dietary pattern* the consumption of these foods remained high, with no significant changes during the intervention years (from baseline to year 4: rice: 0.83, 0.83, 0.82 0.81, 0.78; potatoes: 0.77, 0.82, 0.79, 0.80, 0.76; legumes: 0.76, 0.79, 0.82, 0.66, 0.70, respectively). In year 1, 3, and 4, the consumption of sweets and desserts (0.11, 0.17, 0.13) and distilled drinks (0.27, 0.15) began, as well as the consumption of fruit in the fourth year (0.31).

Data from the *Alcohol, sausages dietary pattern* showed a high alcohol consumption (wine, beer and distilled drinks), especially at baseline and in years 1, 2, and 4 (wine: 0.79, 0.67, 0.67, 0.75; beer: 0.59, 0.22, 0.18, 0.12; distilled drinks: 0.64, 0.73, 0.27, 0.14, respectively). In year 3, the consumption was reduced, increasing again in year 4; the trend was similar to previous years for wine, and was lower in beer and distilled drinks (year 4 for wine: <0.15, 0.75; beer: -0.48, 0.12; distilled drinks: <0.15, 0.14). The consumption of sausages increased from baseline until year 2, held steady in year 3, and increased again in year 4 (from baseline to year 4: 0.18, 0.35, 0.46, <0.15, 0.22). The consumption of nuts and dried fruits was high during years 1 and 3 (0.62; 0.61), lowering in year 4 (0.16). The consumption of fruit increased from year

1 to year 3 (0.24, 0.68), remaining equal to year 1 in year 4 (0.23). On the third year of this pattern, there was a substantial change with higher consumption of foods considered healthy (dairy products 0.26; vegetables 0.11; fruit 0.68; nuts and dried fruit 0.61; legumes 0.23, bread 0.10), and reducing those labeled as unhealthy (red and processed meat -0.31; beer -0.48, caffeinated drinks -0.20).

In the *Protein and vegetables dietary pattern*, the consumption of protein products remained high from baseline and during the four intervention years (fish 0.57, 0.18, 0.74, 0.71, 0.67; poultry 0.66, 0.71, 0.45, 0.71 0.65); red and processed meat consumption decreased in year 3, increasing again in year 4 (0.31, 0.71, -0.30, 0.24, 0.13). The consumption of vegetables was also high from baseline and along the four years of follow-up (0.67, 0.45, 0.72, 0.69, 0.62).

The HR and 95% CI for total MetS and MetS components and type 2 diabetes, according to baseline adherence to the three dietary patterns, are shown in Tables 4 and 5. No association was evident between the highest tertile of adherence to any of the three dietary patterns and total MetS (*Rice, potatoes, legumes dietary pattern*: (HR: 0.89; 95% CI: 0.39-2.06); *Alcohol, sausages dietary pattern*: (HR: 1.16; 95% CI: 0.42-3.21); *Protein, vegetables dietary pattern*: (HR: 1.03; 95% CI: 0.49-2.17) and type 2 diabetes (*Rice, potatoes, legumes dietary pattern*: (HR: 1.07; 95% CI: 0.49-2.29); *Alcohol, sausages dietary pattern*: (HR: 0.70; 95% CI: 0.29-1.68); *Protein, vegetables dietary pattern*: (HR: 2.03; 95% CI: 0.88-4.68). In addition, no significant trend was evident in MetS (*P* for trend=0.79; 0.76; 0.92 in the *Rice, potatoes, legumes*; *Alcohol, sausages*, and *Protein, vegetables* dietary patterns, respectively) or in type 2 diabetes (*P* for trend=0.86; 0.43; 0.09, respectively). The new cases of MetS and type 2 diabetes according to dietary pattern score and year of follow-up are shown in tables 6 and 7. Cumulative incidence rates of MetS and type 2 diabetes were 49.4% and 18.1%, respectively. A significant trend to decrease over time was observed in both conditions ($p<0.001$ and $p=0.007$, correspondingly).

DISCUSSION

Overall, our research identified three main dietary patterns in the eating habits of a Mediterranean cohort at high risk for diabetes. We named the patterns after the foods or food groups that loaded more heavily on that specific pattern: *Rice, potatoes and legumes*; *Alcohol, sausages* and *Protein, vegetables*. Rather than focusing on specific nutrients or foods, the dietary patterns approach considers overall food consumption patterns, which leads to a better recognition of the complexities of dietary intake (25). Since 2006, the cohort study has aimed to assess whether an intensive lifestyle intervention delayed progression of type 2 diabetes (a diet-related disease); the present study aimed to consider a new approach by analyzing the dietary patterns of that same population and assessing its association with MetS and type 2 diabetes incidences.

The Mediterranean diet, considered a prudent dietary pattern, is characterized by high consumption of plant foods, breads, legumes, nuts, seeds, fresh fruit, olive oil, poultry, fresh fish, seafood, low consumption of red and processed meat, moderate consumption of dairy products and frequent but moderate intake of wine (26). It could be considered surprising that not a single pattern in this Mediterranean population could be labeled as Mediterranean. Only a combination of all three dietary patterns could achieve a Mediterranean-like diet. However, this is not an isolated case; other researchers have previously described a dangerous departure in Spain, and in the Mediterranean area in general, from the traditional Mediterranean diet to more Western-type diets characterized by higher intake of processed meat, red meat, alcohol, butter, high-fat dairy products and refined grains (27-29).

To the best of our knowledge, this is the first study to categorize the dietary patterns of adults with high diabetes risk in PHC settings in Catalonia. Our analysis was conducted within the frame of a 4-year longitudinal study, which included the option of describing and comparing dietary patterns in consecutive years. Despite the framework of an intensive lifestyle intervention, the stability in dietary habits, with no major changes in dietary intake trends, is remarkable, especially in the *Rice, potatoes, legumes* and *Protein, vegetables* dietary patterns. In the *Alcohol, sausages dietary pattern*, major dietary improvements were observed in year 3 but didn’t persist in year 4. Evidence shows that improving dietary habits is challenging, both for patients and are mainly effective in highly motivated individuals (31), during the first years after an intervention (32-34). Some research has shown that individuals with high cardiovascular risk are more motivated than other patients, especially after a cardiovascular event, when the need to improve their health status becomes a stronger motivation than the preventive approach (35). Thus, the explanation for the dietary improvement in year 3 in the population following the *Alcohol, sausages dietary pattern* (young, cigarette smoking, high basal glucose, low HDL-C levels, and hypertriglyceridemia) could be related to their higher baseline risk characteristics.

Our study supports the need for dietary interventions in high-risk populations, which should be designed and tailored to individual characteristics, taking into consideration their baseline habits. Despite the positive influence of achieving a healthy dietary score, such as the Mediterranean diet score (36), intensive follow-up and the support of a trained health professional should be considered in order to achieve an optimal adherence (32). Throughout the past few years, new technologies have been applied to increase adherence during and after interventions, but their effectiveness remains a pending topic (37).

The alcohol most predominantly consumed in the *Alcohol, sausages dietary pattern* was wine (factor loadings at baseline: 0.79; year 1: 0.67; year 2: 0.75; year 4: 0.75). The French Paradox highlighted the relationship between wine consumption and health more than 25 years ago, and other researchers have added evidence (38). The observed benefit is closely related to quantities consumed per day, with a maximum of 1 drink (12 g ethanol) per day in women, and up to 2 in men, not considered harmful (39).

In the case of beer, research has shown a protective role for vascular risk, a J-shaped relationship similar to the protection derived from wine (40). However, no significant association with vascular events has been apparent for the intake of spirits; this type of distillate has the highest alcohol concentration but the lowest polyphenol concentration, suggesting that the polyphenol present in wine and beer could contribute to the beneficial effect of alcoholic beverages (41-43).

In Mediterranean populations, the consumption of wine and beer is widely spread and is culturally accepted in everyday meals. In our study population, the consumption of wine and distilled drinks was high in the *Alcohol, sausages dietary pattern*, which could have played a negative role; this population showed high triglyceride levels and low HDL-C levels (44).

Our study also describes the relationship between a specific dietary pattern and the risk of disease, specifically the MetS and its components and type 2 diabetes, common health conditions in Mediterranean populations. Despite not reaching statistical significance (*P* for trend=0.76), the results of our study show a slight tendency among individuals within the *Alcohol, sausages dietary pattern* to develop MetS (HR: 1.16; 95% CI: 0.42-3.21). Conversely, when analyzing the new cases of MetS and type 2 diabetes according to dietary pattern score and year of follow-up, a significant trend to incidence rate decrease in both conditions over time was observed. An explanation might be that other factors would have had a positive influence in the study population, not being diet the primary one.

Several explanations are possible for the unexpected lack of significant associations between the *Alcohol, nuts dietary pattern* and the *Protein, vegetables dietary pattern* and MetS in our analysis. First, unmeasured or uncontrolled residual confounders not taken into account could explain this association. Moreover, both of these patterns differed from the so-called western dietary pattern found in other cohorts; our sample also adhered to beneficial foods such as nuts and vegetables, which could have had a beneficial influence. Depending on the predominant factor loadings per food in each pattern, the influence of the pattern would generally be considered healthy or unhealthy. This means that dietary patterns mix different kinds of foods but the ones that are more predominant will define the final influence of that pattern (44). Higher intakes of fruits and vegetables are associated with a lower MetS risk, perhaps due to lower C-reactive protein concentrations, and have also been inversely associated with diastolic blood pressure in MetS patients (45,46).

Moreover, in the SUN project in Spain, nut consumption was significantly associated with lower risk of developing MetS after a 6-year follow-up period (48). Nut consumption does not increase body weight, BMI or waist circumference (49,50). A FFQ should feature the main characteristics of the dietary variety of the population under analysis; we acknowledge that some healthy eating habits common in the Mediterranean area were not fully collected in the FFQ. This can be considered a limitation of our research (29). In addition, the follow-up period lasted for 4 years, which could have been insufficient for MetS or type 2 diabetes to develop.

Our study consisted of Catalan adults merely, thus presenting limitations regarding inference to other ethnic populations. The analysis was only adjusted by sex, age, current smoking and physical activity (plus BMI and hypertension in type 2 diabetes). The PCA method itself also has some weaknesses that stem from subjective decisions that must be made to determine the nature of the components that have been extracted (29).

As our population was made up of high-risk individuals, results must be interpreted with caution and can only be extrapolated to similar populations. In addition, more research on the topic should be conducted in healthy populations in order to enhance primary prevention of cardiovascular risk factors.

In conclusion, our study describes the dietary patterns followed by a sample of adults with high-diabetes risk in PHC settings in Catalonia and highlights the need to continuously improve nutritional habits by more intensive, long-lasting and professional-supported interventions in order to enhance the adherence to a healthy dietary pattern, such as the Mediterranean diet, and thereby achieve better health status and quality of life.

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CONFLICT OF INTEREST

None.

AUTHORS' CONTRIBUTIONS TO MANUSCRIPT

Míriam Rodríguez-Monforte, Gemma Flores-Mateo, Emília Sánchez, Jorge Delagneau and Iris Benadero formulated the research question, designed the study, carried it out and analyzed the data. Míriam Rodríguez-Monforte, Emília Sánchez and Gemma Flores-Mateo reviewed and discussed the results. Míriam Rodríguez-Monforte, Gemma Flores-Mateo, Emília Sánchez, Francisco Barrio and Bernardo Costa wrote the paper. All authors contributed to the revision of the manuscript, read and approved the final version.

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FIGURE LEGENDS

Table 1. Food groups and subgroups in the dietary patterns analysis.

Table 2. Factor loading matrix for major dietary patterns.

Table 3. Characteristics of study participants by tertile (T) categories of dietary patterns. ANOVA for quantitative variables and chi-square test for qualitative variables.

Table 4. **Multivariate adjusted HR (95% CI) for MetS and type 2 diabetes across tertile (T) categories of dietary patterns.** Adjusted for sex, age, current smoking and physical acitivity. Type 2 diabetes was also adjusted for BMI, and hypertension. MetS was defined according to NCEP-ATPIII criteria (HBP: ≥130/85; central obesity as >88cm for women and >102 cm for men; hyperglycemia ≥100 mg/dL; low HDL-C as <50 mg/dL for women and <40 mg/dL for men; hypertriglyceridemia as ≥ 150 mg/dL). Type 2 diabetes was defined according to the WHO criteria based on the results of 2h postload glucose > 11.1 mmol/L.

HR: hazard ratio; CI: confidence interval.

Table 5. Multivariate adjusted HR (95% CI) for components of MetS across tertile (T) categories of dietary patterns. Adjusted for sex, age, current smoking and physical acitivity. Components of the MS were defined according to NCEP-ATPIII criteria (HBP: ≥130/85; central obesity as >88cm for women and >102 cm for men; hyperglycemia ≥100 mg/dL; low HDL-C as <50 mg/dL for women and <40 mg/dL for men; hypertriglyceridemia as ≥ 150 mg/dL). HR: hazard ratio; CI: confidence interval.

Table 6. Number of new cases of type 2 diabetes across tertile (T) per year and dietary pattern score, and cumulative incidence.

Table 7. Number of new cases of MetS across tertile (T) per year and dietary pattern score, and cumulative incidence.

TABLE 1. Food groups and subgroups in the dietary patterns analysis

Main food group	Food groups	Food items
Meats	1)Red meat	Beef, pork, lamb
	2)Poultry	Chicken, turkey, rabbit
	3)Processed meat: high-fat, low-fat and sausages	Frankfurters,“butifarra”, “fuet”,”sobrassada”, smoked ham and turkey, cured ham
Fish	4)Fish: blue and white	Tuna, salmon, hake
Dairy	5)Low-fat and high-fat dairy products	Whole milk, skimmed milk, low-fat yoghurts, enriched yoghurts, high-fat cheese, low-fat cheese
Fruits and vegetables	6)Fruit and natural juices	Mandarins, strawberries, apples, orange juice, apple juice
	7)Vegetables	Salads, cooked vegetables, vegetable soups
	8)Legumes	Peas, lentils
	9)Potatoes	
	10)Nuts and dried fruits	
Grains	11)Refined grains	Breakfast cereal, muesli and oats
	12)Bread	Cereal bread, high-fiber bread, white bread
	13)Pasta and rice	
Sugar	14)Sugary drinks and processed juices	Sodas, diet sodas, processed juices
	15)Sweets and desserts	Cakes, sweet bread, ice cream, doughnuts, cookies, chocolate, sugar, honey, candies
Oil and fat	16)Salad dressings and cooking fat	Olive oil, sunflower oil, margarine, butter, mayonnaise, vinegar
Alcohol	17)Wine	White and black wine, cider
	18)Beer and light beer	
	19)Distilled drinks	Whiskey, vodka, liquors, gin, cider
Caffeinated drinks	20)Tea and coffee	Plain coffee, decaffeinated coffee, tea, rooibos
Fast-food	21)Fast-food	Hamburgers, pizza, French fries, sandwiches

TABLE 2. Factor loadings for the three major dietary patterns

	Rice, potatoes, legumes dietary pattern					Alcohol, sausages dietary pattern					Protein, vegetables dietary pattern				
Foods or food groups	Baseline	Year 1	Year 2	Year 3	Year 4	Baseline	Year 1	Year 2	Year 3	Year 4	Baseline	Year 1	Year 2	Year 3	Year 4
	Factor loading														
Fish	-	-	-	-	-	-	-	-	-	-0.13	**0.57**	0.18	**0.74**	**0.71**	**0.67**
Sausages	-	-	-	-	-	0.18	**0.35**	**0.46**	-	0.22	-	**0.34**	**-0.39**	-	-0.16
Poultry	-	-	-	-	-	-0.12	-0.12	**0.12**	-	-	**0.66**	**0.71**	**0.45**	**0.71**	**0.65**
Red and processed meat	-	-	-	-	**-0.12**	0.16	-	-	**-0.31**	-	**0.31**	**0.71**	**-0.30**	0.24	0.13
Dairy products	0.18	-	**0.31**	-	-	-0.17	-	0.17	0.26	**-0.39**	-	-	-	-	-
Vegetables	-	-0.11	-	-	-	-	-	-	0.11	0.18	**0.67**	**0.45**	**0.72**	**0.69**	**0.62**
Fruit	-	-	-	-	**0.31**	-	0.24	-	**0.68**	0.23	0.16	0.11	-	-	0.11
Nuts and dried food	-	-	**0.30**	-0.13	-	-	**0.62**	-	**0.61**	0.16	-	-	-	-0.14	-0.11
Potatoes	**0.77**	**0.82**	**0.79**	**0.80**	**0.76**	-	-	-	-	0.14	-	-	-	-	-
Legumes	**0.76**	**0.79**	**0.82**	**0.66**	**0.70**	-	-	-	0.23	-0.27	-	-	-	-	0.11
Cereals	-	-	-	-	-0.19	-	-	-	-	-0.25	-	-	0.13	-	-0.13
Rice	**0.83**	**0.83**	**0.82**	**0.81**	**0.78**	-	-	-	-	-	0.10	-	-	-	-
Bread	0.20	-	-	-	-	0.15	-	-	0.10	**0.62**	0.19	0.11	-	-	0.19
Wine	-	-	-	-	-	**0.79**	**0.67**	**0.67**	-	**0.75**	-	-	-	-0.11	-
Beer	-	-	-	-	-	**0.59**	0.22	0.18	**-0.48**	0.12	-	-	-	-0.18	-0.16
Distilled drinks	-	-	-	0.27	0.15	**0.64**	**0.73**	0.27	-	0.14	-	-0.12	-	-	-0.18
Caffeinated drinks	0.11	-	-	-	-	0.26	0.10	**0.76**	-0.20	-	0.13	0.16	-	-	-
Sweets and desserts	-	0.11	-	0.17	0.13	-	-	-	-	-	-0.25	0.18	-0.26	-0.25	-
Sugary drinks	-	-	-	-	-	-	-	-	-0.25	-	-	-	-	-0.13	-
Vegetable oil	-	-	-	-	-	-	-	-	-	-	0.12	-	-	0.11	-
Percentage of variance explained (%)	10.6%	11.5%	12.4%	9.5%	10.5%	8.9%	9.7%	7.7%	7.8%	9.7%	7.8%	8.1%	8.6%	8.8%	8.1%

Coefficients 0.30 or greater in absolute value are highlighted in boldface.

TABLE 3. Baseline characteristics of study participants by tertile (T) categories of dietary patterns

	Rice, potatoes, legumes dietary pattern				Alcohol, sausages dietary pattern				Protein, vegetables dietary pattern			
	T1	T2	T3	P_t^*	T1	T2	T3	P_t^*	T1	T2	T3	P_t^*
Age, ***years***	61.2 ± 7.9	62.7 ± 7.9	61.9 ± 8	0.7	62.1 ± 7.4	62.3 ± 7.9	60.4 ± 8.3	**0.04**	61.8 ± 8.4	61.5 ± 7.5	61.5 ± 7.9	0.9
Sex, ***% women***	69	69	62	0.2	85.3	72.8	41.8	**0.00**	63	69.6	67.4	0.4
Weight, ***kg***	78.5 ± 12.2	78.3 ± 12.6	78.8 ± 14	0.8	78 ± 12.4	77.4 ± 11.8	81.2 ± 14.1	**0.01**	78.7 ± 12.6	78.2 ± 13	79.6 ± 13.2	0.5
BMI, ***kg/m^2***	31.2 ± 4.4	31.6 ± 4.6	30.7 ± 4.8	0.2	32 ± 4.8	31 ± 4.4	30.5 ± 4.6	0.07	31 ± 4.3	31.2 ± 4.8	31.2 ± 4.8	0.8
Central obesity, ***cm***	100.5 ± 10.3	100.8 ± 10.6	100.4 ± 11	0.9	100.28 ± 11.1	101.13 ± 9.5	100.4 ± 11.2	0.2	100.5 ± 10.6	101 ± 10.9	100.2 ± 10.4	0.7
Basal glucose, ***mg/dL***	94.3 ± 12.7	93.7 ± 12.7	94.4 ± 12.7	0.8	92.3 ± 12	93.4 ± 12.7	96.7 ± 12.9	**0.02**	94.5 ± 13	94.5 ± 12.4	93.4 ± 12.6	0.6
Systolic BP, ***mmHg***	134.3 ± 14.1	134.1 ± 15	133.5 ± 13.8	0.8	133.4 ± 14	133.7 ± 14.4	134.7 ± 14.5	0.6	133.2 ± 15	134.5 ± 14.4	134.1±13.4	0.6
Diastolic BP, ***mmHg***	79.9 ± 9.4	80.7 ± 9	79.7 ± 9.1	0.5	80.4 ± 8.9	79.6 ± 8.5	80.3 ± 10	0.6	80.6 ± 9.8	80.1 ± 9.1	79.6 ± 8.5	0.5
Total C, ***mg/dL***	209 ± 33.5	210.9 ± 36.6	213.8 ± 38.5	0.4	209 ± 34.5	211 ± 35.8	213.6 ± 38.3	0.4	215.9 ± 39	209.9 ± 33.8	208 ± 35.5	0.09
HDL-C, ***mg/dL***	59 ± 14.8	56.9 ± 15.1	58.8 ± 14.7	0.3	58.8 ± 13.9	60.1 ± 15.3	55.8 ± 15.1	**0.01**	57.8 ± 15.5	58.2 ± 14.3	58.6 ± 14.9	0.8
TG, ***mg/dL***	122.3 ± 59.1	127.9 ± 79.1	130.5 ± 64.7	0.5	125.9 ± 68.6	118.1 ± 54.4	136.7 ± 78.4	**0.03**	129.3 ± 64.7	120.4 ± 55.8	131.1 ± 81.4	0.2
Currently smoking, ***%***	11.1	11.4	11.5	0.9	6.7	8.7	18.4	**0.04**	12.1	12.5	9.2	0.8
Physical activity, ***%***	49.7	50.6	55.1	0.8	57.4	50	48.3	0.3	46.2	54.9	54.4	0.1
Metabolic syndrome, ***%***	22.5	21.2	22.5	0.9	18.7	17.5	30.1	0.06	22.5	23	20.8	0.8

BP: blood pressure; C: cholesterol; HDL: high-density lipoproteins; TG: triglycerides.
ANOVA for quantitative variables and chi-square test for qualitative variables
*P values for trend

TABLE 4. Multivariate adjusted HR (95% CI) for MetS across tertile (T) categories of dietary patterns

	MetS				Type 2 diabetes			
	T1	T2	T3	*P* value	T1	T2	T3	*P* value
Rice, potatoes, legumes dietary pattern								
Number of cases (n)	64	76	69	-	32	34	34	-
Multivariable model[a,b]	1.0[c]	0.82 (0.38-1.79)	0.89 (0.39-2.06)	0.79	1.0[c]	0.40 (0.15-1.08)	1.07 (0.49-2.29)	0.86
Alcohol, sausages dietary pattern								
Number of cases (n)	62	66	81	-	35	28	37	-
Multivariable model[a,b]	1.0[c]	1.01 (0.39-2.55)	1.16 (0.42-3.21)	0.76	1.0[c]	0.58 (0.22-1.47)	0.70 (0.29-1.68)	0.43
Protein, vegetables dietary pattern								
Number of cases (n)	67	69	73	-	31	34	35	-
Multivariable model[a,b]	1.0[c]	1.37 (0.60-3.14)	1.03 (0.49-2.17)	0.92	1.0[c]	0.92 (0.35-2.36)	2.03 (0.88-4.68)	0.09

[a]Multivariable model of MetS adjusted for sex, age and current smoking; MetS was defined according to NCEP-ATPIII criteria (HBP: ≥130/85; central obesity as >88cm for women and >102 cm for men; hyperglycaemia ≥100 mg/dL; Low HDL-C as <50 mg/dL for women and <40 mg/dL for men
[b]Multivariable model of type 2 diabetes adjusted for sex, age, current smoking, hypertension and body mass index (BMI)
HBP: high blood pressure; HDL-C: high density lipoprotein-cholesterol. T: tertile; MetS: metabolic syndrome
[c]Reference category

TABLE 5. Multivariate adjusted[a] HR (95% CI) for components of MetS across tertile (T) categories of dietary pattern

	HBP				Central Obesity				Hyperglycemia				Low HDL-C				Hypertriglyceridemia			
	T1	T2	T3	*P* value	T1	T2	T3	*P* value	T1	T2	T3	*P* value	T1	T2	T3	*P* value	T1	T2	T3	*P* value
Rice, potatoes, legumes dietary pattern																				
Number of cases (n)	64	76	69		64	76	69	-	64	76	69		64	76	69	-	64	76	69	-
Multivariable model[a]	1.0[b]	0.73 (0.19-2.78)	0.51 (0.10-2.64)	0.43	1.0[b]	0.82 (0.38-1.79)	0.89 (0.39-2)	0.79	1.0[b]	1.12 (0.33-3.83)	0.61 (0.15-2.56)	0.50	1.0[b]	0.33 (0.10-1.03)	0.69 (0.24-1.98)	0.49	1.0[b]	0.71 (0.23-2.19)	1.29 (0.41-4.07)	0.65
Alcohol, sausages dietary pattern																				
Number of cases (n)	62	66	81		62	66	81	-	62	66	81		62	66	81	-	62	66	81	-
Multivariable model[a]	1.0[b]	0.41 (0.06-2.79)	0.75 (0.12-4.72)	0.76	1.0[b]	1.01 (0.39-2.55)	1.16 (0.42-3.2)	0.76	1.0[b]	1.07 (0.21-5.26)	1.61 (0.29-8.98)	0.58	1.0[b]	0.95 (0.32-2.85)	0.52 (0.13-2.02)	0.34	1.0[b]	1.28 (0.32-5.09)	3.68 (0.87-15.45)	0.075
Protein, vegetables dietary pattern																				
Number of cases (n)	67	69	73		67	69	73	-	67	69	73		67	69	73	-	67	69	73	-
Multivariable model[a]	1.0[b]	0.56 (0.10-3.01)	0.84 (0.22-3.15)	0.79	1.0[b]	1.37 (0.60-3.14)	1.03 (0.49-2.17)	0.92	1.0[b]	1.61 (0.45-5.78)	0.84 (0.25-2.84)	0.78	1.0[b]	0.61 (0.16-2.35)	0.95 (0.37-2.43)	0.91	1.0[b]	1.29(0.39-4.26)	1.30 (0.47-3.57)	0.60

[a]Multivariable model of MetS adjusted for sex, age and current smoking; MetS defined according to NCEP-ATPIII criteria (HBP: ≥130/85; central obesity as >88cm for women and >102 cm for men; hyperglycaemia ≥100 mg/dL; Low HDL-C as <50 mg/dL for women and <40 mg/dL for men; hypertrygliceridemia as ≥ 150 mg/dL).
HBP: high blood pressure; HDL-C: high density lipoprotein-cholesterol
[b]Reference category

TABLE 6. Number of new cases of type 2 diabetes across tertile (T) and cumulative incidence rates, per year and dietary pattern score

	YEAR 1	YEAR 2	YEAR 3	YEAR 4	*P*-value for lineal trend
New cases of type 2 diabetes / individuals at risk	45/478 (9.4 %)	30/384 (7.8 %)	13/293 (4.4 %)	12/233 (5.1 %)	0.007
Cumulative incidence rate		100/552 (18.1%)			
Rice, potatoes, legumes dietary pattern					
T1	16	7	5	4	
T2	10	17	5	2	
T3	19	6	3	6	
Alcohol, sausages dietary pattern					
T1	22	7	2	4	
T2	7	14	4	3	
T3	16	9	7	5	
Protein, vegetables dietary pattern					
T1	11	12	3	5	
T2	14	11	5	4	
T3	20	7	5	3	

TABLE 7. Number of new cases of MetS across tertile (T) and cumulative incidence rates, per year and dietary pattern score

	YEAR 1	YEAR 2	YEAR 3	YEAR 4	*P*-value for lineal trend
New cases of MetS / individuals at risk	**142/349 (40 %)**	**43/255 (16.8 %)**	**23/164 (14 %)**	**11/104 (10.5%)**	**<0.001**
Cumulative incidence rate		**209/423 (49.4%)**			
Rice, potatoes, legumes dietary pattern					
T1	42	10	9	3	
T2	42	19	11	4	
T3	48	14	3	4	
Alcohol, sausages dietary pattern					
T1	40	11	8	3	
T2	38	15	7	6	
T3	54	17	8	2	
Protein, vegetables dietary pattern					
T1	44	14	4	5	
T2	45	10	11	3	
T3	43	19	8	3	

6. DISCUSSION

6.1 Meta-analyses (first and second studies)

In terms of the first specific objective of the present thesis, the first study provides evidence that following a prudent/healthy dietary pattern is protective against all clinical cardiovascular endpoints, except for stroke. In the case of a Western/unhealthy dietary pattern, no direct associations with any of the cardiovascular outcomes were seen.

Concerning the second specific objective of the thesis, findings from the second study demonstrate that a prudent/healthy dietary pattern is associated with a lower prevalence of MetS in cross-sectional studies, and an unhealthy pattern is linked to an increased risk of developing the syndrome. The pooled estimates from the three included prospective cohort studies generally agree with the findings from the cross-sectional studies; however, the protective role of the prudent/healthy dietary pattern was not supported by the 95% confidence interval (95% CI).

The protective role of diet has been a matter of research and debate for decades. Moreover, studies aiming to understand the influence of daily dietary consumption on health outcomes emerged alongside the identification of modifiable risk factors as major contributors to chronic diseases and mortality. This was particularly the case in developed countries. The Framingham cohort study was extremely influential when considering the concept of risk factors for CVD. It was carried out in 1961, when hypertension, elevated serum cholesterol levels, and left ventricular hypertrophy were first related to the development of CHD, highlighting prevention as a key approach to controlling CVD (Kannel et al., 1961). Nowadays, prevention remains a core tool for the management of CVD and MetS, with reports suggesting that the elimination of health risk behaviors would make it possible to avoid (at least) 80% of all CVD (Liu et al., 2012; NICE Guidelines, 2010).

In the last three decades, other researchers have analyzed the role of risk factors in the emergence CVDs and their related disabilities (Hubert et al., 1983; Stamler et al., 1993). More than half of the reduction in cardiovascular mortality has been primarily attributed to a reduction in cholesterol, blood pressure levels, and smoking. However, this favorable trend has been partly offset by an increase in other risk factors, predominantly obesity, T2DM, and aging (Mason et al., 2014; O'Keeffe et al., 2013; Roth et al., 2015).

In our first study, we aimed to assess the relationship between diet and the risk of developing CHD (including MI and ischemic heart disease), stroke (cerebrovascular disease and ischemic stroke), and overall CVD, using data from observational studies. This is based on the idea that disease emergence reflects the cumulative effects of unhealthy lifestyles and the resulting presence of risk factors during an individual's lifespan. This can be analyzed, principally in long-term follow-up studies. Consequently, we were able to include nineteen cohort studies and three case-control studies in our systematic review and meta-analysis, representing a total of 610,691 individuals.

In our second study we aimed to evaluate the role of diet in the development of MetS, based on results from observational studies. In this case, studies with long-term follow-ups were scarce, and most had cross-sectional designs. In total, we were able to incorporate 28 cross-sectional studies and 3 cohort studies in our analysis, with a total sample of 85,137 subjects.

Two main dietary categories were described: a prudent/healthy dietary pattern and a Western/unhealthy dietary pattern. Based on the food loading reported within individual studies, we defined patterns which had generally healthy characteristics as prudent/healthy and those which had generally less-healthy characteristics as Western/unhealthy. Where several healthy and unhealthy patterns were reported within the same study, we first selected the pattern that contained the maximum variation in food groups, followed by the pattern that fulfilled the most healthy or most unhealthy criteria (as determined by the highest factor loadings). In order to determine which foods were healthy or unhealthy, we followed the recommendations given by The Guidelines for a Healthy Diet from the Sociedad Española de Nutrición Comunitaria (Guía Sociedad Española de Nutrición Comunitaria, 2011) [9] (first and second studies) and the Eighth Edition of the Dietary Guidelines for Americans (US Dietary Guidelines, 2015) (second study only).

The prudent/healthy dietary pattern included foods and food groups such as fruit, dried fruit, vegetables and vegetable oils, legumes, whole grains, fish, poultry, and low-fat dairy. Meanwhile, the Western/unhealthy dietary pattern included foods or food groups such as red and processed meant, offal, refined grains, sweets, fried foods, high-fat dairy, oils and fats, alcoholic drinks, soft drinks, and fast-food.

The statistical approaches used to derive dietary patterns in the different studies were factor analysis, PCA, and cluster analysis. Heterogeneity was present when assessing *a posteriori* dietary patterns, as factor loadings for individual food items were never exact between studies. In order to solve this issue, we conducted subgroup analysis for the results showing greater heterogeneity.

Results from the first meta-analysis indicated that, when considering both cohort and case-control studies, the prudent/healthy dietary pattern had a protective effect against the risk of CHD (risk ratio [RR]: 0.83; 95% CI: 0.75–0.92; p=0.054; I^2=44.6%), total CVD (RR: 0.71; 95% CI: 0.63–0.80; p=0.560; I^2=0.0%), and CVD-related mortality (RR: 0.69; 95% CI: 0.60–0.78; p=0.687; I^2=0.0%). Each of these findings remained significant following sensitivity analysis.

In the second analysis, results also showed a negative association between adherence to a prudent/healthy dietary pattern and MetS, which also remained significant after sensitivity analysis (odds ratio [OR]: 0.83; 95% CI: 0.76–0.90; p=0.0; I^2=72.1%). However, the pooled risk ratio for MetS in cohort studies was 0.91, with a 95% CI of 0.68–1.21 (p=0.005; I^2=81.1%). To further explore the reasons for heterogeneity, we performed subgroup analysis according to gender, geographic area, and *a posteriori* approach. Adjustment for the key confounding variables (MetS definition, age and health status) produced only minor, non-significant differences.

The protective role of a prudent/healthy diet against CVD and MetS has been described in other studies using different approaches. Observational studies have provided evidence of this association, taking into account different geographical regions and preventive approaches (primary, secondary or tertiary), with similar findings to ours (Aljefree et al., 2015; Stewart et al., 2016 ;Hu et al., 2000). The present analysis included studies conducted in a range of geographical regions: Eastern, Central and Northern Europe; Mediterranean Europe; North America; Eastern Asia; and Australia. The factor loadings per pattern analysis in each of the studies reflected the foods most commonly consumed, showing the cultural diversity linked to food consumption. Randomized control trials have also assessed the influence of a healthy eating pattern on CVD and MetS outcomes, the Mediterranean diet being one of the most robust examples (Levitan et al., 2009; Estruch et al., 2013; Kastorini et al., 2011; Esposito et al., 2013; Calton et al., 2014).

Several biological mechanisms related to the nutrient composition of the foods and food groups that are considered healthy may explain these results. Firstly, the consumption of vegetables and fruit is protective, with no maximum cut-off point. The quantity required in order to achieve a risk reduction is between 5 to 7 portions per day, with fiber, flavonoids, vitamin C, lower-C reactive protein concentrations, and folates described as the nutrients responsible for the protective effect (Dauchet et al., 2006; Buil-Cosales et al., 2016; Oyebode et al., 2014; Esmalziadehet al., 2006; European Heart Network, 2001; Pereira et al., 2004; Threapleton et al., 2013).

Early epidemiologic studies in the 1960s first demonstrated the lower incidence of coronary atherosclerosis and lower plasma lipid levels in particular ethnic groups, such as the Greenland Eskimos. Since then, the consumption of fish has been established as a healthy habit. This is particularly true in the case of blue fish, mainly due to its omega-3 fatty acid content; though recent research indicates that long-chain monounsaturated fatty acids may also play a role (Bang et al., 1980; Dyerberg et al., 1975; Yang ZH et al., 2016).

Furthermore, in different cohort studies, nut consumption has been associated with a lower risk of CVD mortality and MetS. In addition, nut consumption does not increase body weight, BMI or waist circumference (Fernández-Montero et al., 2013; Flores-Mateo et al., 2013; Van den Brandt et al., 2015)[26-28]. Nuts are characterized by a hard shell and dry seed, the latter of which is rich in unsaturated fatty acids, high-quality protein, fiber, vitamins (folate, niacin, and vitamin E), minerals (potassium, calcium, and magnesium), carotenoids, phytosterols, and phenolic compounds (Estruch et al., 2015).

In some studies, dairy has been labeled as a protective food, while in others, it is considered a risk food. In the most recent systematic review and meta-analysis, results showed a trend towards these products being protective against CVD and MetS (Alexander et al., 2016; Chen et al., 2015). In light of such findings, more studies involving dairy products are required to establish its true role in disease.

Olive oil and vegetable oils have, in general, been related to better CVD and MetS outcomes. This is principally due to their monounsaturated fatty acid content (primarily oleic acid) and other minor bioactive compounds. In a recent systematic review, it was stated that virgin olive oil significantly reduces the risk of CVD clinical events. This conclusion was based on the results of the PREDIMED study, a large randomized trial that included a recommendation for the use of large quantities of virgin olive oil (even when frying foods) as part of the intervention (Estruch et al., 2013; Sayon-Orea et al., 2015; Buckland et al., 2015).

The present two studies also assessed the association between following a Western/unhealthy dietary pattern and the risk of developing CVD and MetS. Our findings suggest that, despite a statistically significant association between Western/unhealthy dietary patterns and CVD risk, the pooled estimates were non-significant for CVD (RR: 1.14; 95% CI: 0.92–1.42; p= 0.055 for heterogeneity; I^2=56.9%), CHD (RR: 1.03; 95% CI: 0.90–1.17; p=0.012 for heterogeneity; I^2=59.4%) or stroke (RR: 1.05; 95% CI: 0.91–1.22; p=0.190 for heterogeneity; I^2=27.6%). The heterogeneity for this dietary pattern was, overall, much higher than for the prudent/healthy dietary pattern. The assessment of sources of heterogeneity (FFQ items, geographic area, *a posteriroi* approach, gender, sample size, adjustment [or not] for key confounders, incidence, and mortality) produced only minor, non-significant differences.

In MetS, following a Western/unhealthy dietary pattern produced statistically significant results in cross-sectional studies (OR: 1.28; 95% CI: 1.17–1.40; p=0.0 for heterogeneity; I^2=72%), but not in cohort studies (RR: 0.96; 95% CI: 0.53–1.73; p=0.102 for heterogeneity; I^2=62.6%). Similarly to the prudent/healthy dietary pattern, potential sources of heterogeneity also produced only minor, non-significant differences for the Western/unhealthy pattern.

Foods or food groups labeled as Western/unhealthy show a specific composition that may partly explain why they are considered negative for different health outcomes. Dietary sugars (included in soft drinks, sweets and desserts) provide a source of rapidly absorbable glucose and fructose, and have been related to excess energy production (Bernstein et al., 2010; Malik et al., 2010; Johnson et al., 2009;). The consumption of fast-food, which contains a high quantity of salt, saturated and trans-saturated fat, has also been associated with MetS and CVD (Denova-Gutiérrez et al., 2010; Nettleton et al., 2009; Bahadoran et al., 2013).

Conversely, moderate alcohol consumption (<10 g/day for women and <20 g/day for men) may not increase the risk of developing MetS or CVD (Fan et al., 2008). Indeed, moderate red wine consumption was associated with a lower prevalence of MetS in an elderly, Mediterranean population at high cardiovascular risk (Tresserra-Rimbau et al., 2015; Opie et al., 2007). Alcohol seems to play an important role in the studies included in the present report, classified predominantly as a Western/unhealthy dietary element or as being related to an unhealthy lifestyle, especially in Europe and America.

Consumption of red and processed meat was labeled as a carcinogenic product by the World Health Organization, and has also been associated with an increased risk of several major chronic diseases and preterm mortality (Bouvard et al., 2015; Wolk, 2016).

There is ongoing controversy about the association between so called "unhealthy" dietary patterns and the risk of developing CVD or MetS. Previous authors have already highlighted this, reporting findings ranging from a lack of significance to identifying unhealthy patterns as protective (Judd et al., 2013; Osler et al., 2001; Maruyama et al., 2012; Zazpe et al., 2014; Akter et al., 2013; Yoo et al., 2014). A plausible explanation for this "unexpected" association may be the existence of unmeasured or uncontrolled residual confounding variables. In addition, Western patterns are extremely variable and heterogeneous between studies. Accordingly, strong adherence to a Western dietary pattern can occur in parallel with the consumption of beneficial foods or food groups. Furthermore, some foods (such as cheese, wine, potatoes, rice or milk) have been categorized as healthy as well as unhealthy, depending on the study in question. This underlines the need for a universal, graduated scale ranging from purely unhealthy to purely healthy (based on worldwide recommendations) for the categorization of dietary patterns. Moreover, several publications have reported that to reduce chronic conditions and/or their associated mortality, it is more important to increase the number and variety of healthy foods than to reduce the consumption of regularly consumed unhealthy foods (Michels et al., 2002 from Zazpe et al., 2014). In any case, adherence to a Western dietary pattern may be associated with a higher risk of cancer or some kind of CHD, which may result in death before a CV event or MetS can emerge (Agurs-Collins et al., 2009; Satagopan et al., 2004).

Overall, the *a posteriori* approach to dietary patterns may lead to a more realistic overview of a population's dietary habits, but is also associated with inherent difficulties relating to the homogenization of results. However, the more specific the initial dietary assessment, the better the categorization of dietary patterns. Consequently, assessment using a FFQ with only a limited number of questions should be avoided. In addition, assessment using other methods such as 3-day food records should be taken into consideration.

In general, the influence of a dietary pattern can generally be considered healthy or unhealthy depending on the predominant factor loadings per food within the pattern. This means that although dietary patterns commonly combine different kinds of foods, the ones that are more predominant will define the final influence of a particular pattern on an individual's health.

6.2 Spanish cohort study (third study)

In terms of the third specific objective of this thesis, evidence from the third study shows that the dietary patterns of a Mediterranean population at high risk of diabetes can be analyzed in order to tailor interventions and achieve better health outcomes. However, no association between dietary patterns and MetS or T2DM was found amongst these individuals.

Chronic diseases usually emerge around middle-age, following a prolonged exposure to an unhealthy lifestyle. The population analyzed in the third study was a cohort of 552 individuals with diabetes risk factors (368 women and 184 men) aged between 45 and 75 years. The assessment for their inclusion was made using the Finnish Diabetes Risk Score (FINDRISC) in primary healthcare centers across Catalonia (Spain). The primary objective was to assess whether an intensive lifestyle intervention could delay the progression of T2DM in this population, who were followed-up over 4 years (from 2006 to 2010). Initial results from this study showed a substantial reduction in the incidence of T2DM amongst high-risk individuals (Costa et al., 2012).

Subsequently, this cohort was re-visited in order to analyze their eating habits using an *a posteriori* approach. The motivation for this second analysis was the emergence of dietary pattern assessment as an alternative and more realistic approach to the analysis of dietary habits (especially in populations at risk of developing diet-related diseases) and its adoption as part of the general framework comprising dietary recommendations in diverse national contexts. Dietary patterns were derived using PCA, and revealed the existence of three main patterns, each labeled according to their highest loadings, as follows: *1) rice, potatoes and legumes dietary pattern; 2) alcohol and sausages dietary pattern; and 3) protein and vegetables dietary pattern*.

Surprisingly, despite our population being from a Mediterranean area, none of the three derived patterns showed Mediterranean diet characteristics when considered individually. Previous studies have reported similar findings. ENRICA, a cross-sectional study conducted between 2008 and 2010 in 12,948 Spanish individuals aged ≥18 years, reached the conclusion that the Spanish population is drifting away from Mediterranean dietary patterns and towards a less healthy diet typical of Western countries. In ENRICA, the departure from the Mediterranean pattern mostly affected the socially disadvantaged, and was clustered with other unhealthy lifestyle behaviors which may have had undesirable synergistic health effects (León-Muñoz et al., 2012). These results were echoed by the SUN cohort study in 2014 (Zape et al., 2014). Previously, Sofi et al. had also highlighted this trend in two articles published in 2005 and 2008 (Sofi et al., 2005 and 2008). These reported findings in an Italian population, and claimed to have identified effective preventive strategies for decreasing the risk related to dietary habits in the general population. The population in the present study had characteristics associated with a high risk of diabetes, which increased the need for adopting a healthy diet in order to minimize the risk of developing chronic conditions.

A secondary objective of the third study was to analyze the degree of adherence to the three derived dietary patterns over the four interventional years. In general, changes within patterns were minor or insignificant, with the exception of the a*lcohol and sausages dietary pattern.* In the latter case, a progression towards a healthier food intake was seen in year three, with a reversion to initial tendencies noted in year four.

Changing dietary habits is challenging for several reasons. The stages-of-change spiral model describes the different phases an individual goes through when modifying any given habit, beginning with pre-contemplation and progressing through to action and maintenance stages. The model also includes a phase that indicates failure and relapse (ProChaska i DiClemente, 1984). According to cognitive theories of psychology, individuals process messages in accordance with their existing values, beliefs, and behavior (Glanz et al., 1990). Correspondingly, it would appear that messages intended to change a person's perception of the importance of nutrition are also interpreted from this standpoint. A more promising strategy may be to emphasize the tastiness of healthy foods, as people are more likely to consume flavors and dishes that they perceive as being pleasing to the palate. Other factors that may influence dietary choices are the cost of foods, convenience and concerns over weight control (Glanz et al., 1998).

In the third study, the results from the Cox regression analysis showed no significant association between any of the dietary patterns and MetS or MetS components. Despite being non-significant, patients accounted for by the a*lcohol and sausages dietary pattern* had a nominally higher risk of developing MetS (hazard ratio [HR]: 1.16; 95% CI: 0.42–3.21). Similarly to other studies, though our dietary patterns were mainly unhealthy, they also included healthy items such as vegetables, nuts and fruit, which could have offset the overall negative effect.

6.3 Considerations for the future

Data from the Organization for Economic Cooperation and Development (OECD) database show an overall increase in life expectancy worldwide. In Spain, the life expectancy in 1960 was 72.2 years, whereas nowadays it is 86.2 years (OECD, 2016). A study published in 2013 using the same database concluded that, for the USA population, diet was the most important factor related to disease burden, even more so than physical inactivity or high BMI. The study also claimed that, from a public healthcare perspective, the best investments for improving the health of a population were programs and multi-sectoral action plans to address risks such as physical inactivity, poor diet, ambient particulate matter, and alcohol and tobacco consumption (US Burden disease collaborators, 2013).

Dietary pattern changes are paralleled by major changes in health status and by key demographic and socioeconomic changes. The latter include changes in economic resources, demographic patterns, disease patterns, various cultural factors, knowledge associated with food choice, and sociological considerations. As a world population, we have undergone an extensive transition from the early dietary patterns associated with hunter-gatherer societies to the present pattern, which is linked to the behavioral changes intended to reverse NCDs and aging. Trends show that diets are becoming increasingly sweeter and more energy-dense globally, with many higher-fiber foods being replaced with processed versions. Globalization has had profound effects on lifestyle, and subsequent imbalances have led to an epidemic of diet-related disease. So far, few countries have tackled these issues at a national level (Popkin, 2006).

With the aim of addressing the global trend described above, the assessment of dietary patterns within individual populations is a key step towards designing tailored and effective strategies to achieve better health outcomes.

7. CONCLUSIONS

- **Conclusions of study 1**

According to the analysis of observational studies,

- Prudent/healthy dietary patterns appear to be inversely associated with the risk of CHD and CVD; however, such patterns have no apparent association with stroke risk.
- Conversely, Western/unhealthy dietary patterns do not appear to be directly associated with CHD, stroke or CVD.
- In order to reduce the prevalence of cardiovascular outcomes, an emphasis should be placed on increasing a population’s intake of dietary elements considered to be healthy.

- **Conclusions of study 2**

According to the analysis of observational studies,

- Prudent/healthy dietary patterns appear to be inversely associated with the risk of developing MetS.
- Correspondingly, Western/unhealthy dietary patterns may be associated with an increased risk of developing MetS; though this was shown only in cross-sectional studies.
- Taken together, these findings suggest that in order to reduce a population's risk of developing MetS, both an increase in healthy and decrease in unhealthy dietary elements may be beneficial.

- **Conclusions of study 3**

From a sample of individuals at high risk of diabetes living in the Mediterranean region,

- Three dietary patterns were derived (*1) rice, potatoes and legumes dietary pattern; 2) alcohol and sausages dietary pattern; 3) protein and vegetables dietary pattern*) which, surprisingly, did not show the typical characteristics of a Mediterranean diet.
- This finding adds weight to the growing body of evidence suggesting a global deviation away from the traditional diet of a particular culture and towards a more Western-style diet.

Despite their participation in a lifestyle intervention aiming to improve the dietary habits,

- Individuals at high diabetic risk showed a high degree of adherence to the three non-Mediterranean dietary patterns throughout the four-year follow-up.
- None of the dietary patterns identified in the study appeared to be significantly associated with the development of MetS or T2DM.
- These facts are illustrative of the difficulty individuals commonly encounter when attempting to change any habit, and beg the need for alternative strategies to aid the switch to a healthier dietary pattern.

Future research directions

The studies of dietary patterns reported in this thesis have highlighted several aspects which may merit future research.

1. The underlying mechanisms that cause an individual to establish and adhere to a specific kind of dietary pattern do not appear to have been characterized. This becomes an essential topic when, as seen, pre-defined dietary patterns that have been widely recognized as healthy are being abandoned.
2. As previously mentioned, new strategies to help patients switch and adhere to healthy dietary patterns should be studied, such as apps, social media, blogs, and so on. This investigation will likely follow on from future research direction 1 (above).
3. Dietary patterns in vulnerable populations (such as elderly people living alone or individuals with mental disease) should also be analyzed in order to relate them to the development of cognitive disorders and other health outcomes that are specific to these populations.
4. The analysis of dietary patterns should be conducted in low and middle income countries (as CVD and MetS rates are the highest worldwide) with the aim of assessing diet related-disease and defining preventive strategies adapted to the population's characteristics.
5. Establishing the relationship between dietary patterns in non-risk populations (such as children or teenagers) and academic results, social development/interactions and psychological outcomes could also be interesting, and results may be used to develop relevant preventative strategies.

6. Apart from predicting disease risk, trends in adherence to a specific dietary pattern could also provide useful information regarding other variables, as diet is not only linked to nutrition, but is also a holistic representation of how we feel or interrelate with others. This warrants investigation.

Taken together with findings from the present studies, these future research directions may provide interesting information with which to advance the field of preventative medicine and attenuate the rising global health burden.

8. SUMMARY (Catalan version)

8.1 Resum del primer estudi

Introducció: Diferents estudis epidemiològics han demostrat que el consum dietètic està vinculat amb al risc de desenvolupar malalties cardiovasculars. L'objectiu de la present meta-anàlisi va ser estimar l'associació entre els patrons dietètics derivats "a posteriori" i les malalties cardiovasculars.

Materials i Mètodes: Es van realitzar una cerca, a la base de dades PubMed, d'estudis observacionals que descrivissin els patrons dietètics relacionats amb diferents esdeveniments cardiovasculars. L'associació entre els patrons dietètics i les malalties cardiovasculars es va estimar utilitzant una meta-anàlisi amb intervals de confiança del 95% (IC 95%).

Resultats: Vint-i-dos estudis observacionals van complir els criteris d'inclusió. El risc relatiu (RR) per a les malalties cardiovasculars, la malaltia coronària i els accidents cerebrovasculars en una comparació de la més alta a la més baixa categoria dels patró dietètic prudent/sà en estudis de cohorts va ser: 0.69 (IC del 95%: 0.60, 0.78; I^2 = 0%), 0.83 (IC del 95%: 0.75, 0.92; I^2 = 44.6%), 0.86 (IC del 95%: 0,74, 1,01; I^2 = 59.5%), respectivament. El RR combinat de malaltia coronària en els estudis de casos i controls comparant la categoria més alta amb la més baixa del patró dietètic prudent/sà va ser de 0.71 (IC del 95%: 0.63, 0.80; I^2 = 0%). El RR combinat per a les malalties cardiovasculars, les malalties coronàries i els accidents cerebrovascular en una comparació de la categoria més alta a la categoria més baixa del patró dietètic no prudent/no sa en els estudis de cohorts va ser de 1,14 (IC del 95%: 0.92, 1.42; I^2 = 56.9%), 1.03 (IC del 95%: 0.90, 1.17; I^2 =59.4%) i 1.05 (IC del 95%; 0.90, 1.17: 0.91, 1.22; I^2 = 27.6%), respectivament; en els estudis de casos i controls no hi va haver evidència d'augment de risc de malaltia coronària.

Conclusions: Els nostres resultats donen suport l'evidència que el seguiment d'un patró dietètic prudent/sà és un factor protector per a les malalties cardiovasculars.

8.2 Resum del segon estudi

Introducció: Determinats estils de vida estan vinculats amb el risc de desenvolupar síndrome metabòlica (SM); no osbtant, la seva relació amb els patrons dietètics segueix essent poc clara. Aquesta revisió sistemàtica i metanàlisi té com a objectiu analitzar l'associació de patrons dietètics derivats -"a posteriori" amb la SM.

Materials i Mètodes: Es va realitzar una cerca a les bases de dades PubMed, CINAHL i Scopus d'estudis epidemiològics sobre patrons dietètics i la SM. L'associació entre els patrons dietètics i la SM es va estimar utilitzant una meta-anàlisi amb intervals de confiança del 95% (IC).

Resultats: Un total de 28 estudis transversals i 3 estudis de cohorts van ser inclosos en la meta-anàlisi. Pel que fa al patró prudent/sà la odds ratio (OR) per a la SM va ser de 0.83 (IC del 95%: 0.76, 0.90; P= 0,0; I^2= 72.1%) en el cas dels estudis tranvsersals. En els estudis de cohorts del mateix patró, el risc relatiu (RR) va ser de 0.91 (IC del 95%: 0.68, 1.21; P = 0.005; I^2 = 81,1%). En el patró no prudent/no sà, la OR va ser de 1,28 (IC del 95%: 1.17, 1.40; P= 0,0; i I^2= 72,0%) en els estudis transversals, i en els estudis de cohorts el RR va ser de 0,96 (IC del 95%: 0.53-1.73; P = 0,102; I^2 = 62,6%).

Conclusions: Els resultats dels estudis transversals van demostrar que un patró prudent/saludable s'associa amb una menor prevalença de SM, mentre que un patrò no prudent/no sà s'associa amb un major risc de SM.

Caldria realitzar estudis prospectius addicionals per confirmar l'associació entre els patrons dietètics i la SM.

8.3 Resum del tercer estudi

Introducció: l'Anàlisi dels patrons dietètics en individus d'alt risc metabòlic que viuen en una zona mediterrània, pot ajudar a entendre que es necessiten realizar modificacions en l'estil de vida per tal d'adaptar les intervencions dietètiques i aconseguir millors resultats de salut. L'objectiu d'aquest estudi va ser descriure els patrons dietètics i la seva adherència per part d'adults amb alt risc per desenvolupar diabetis tipus 2, en Centres d'Atenció Primària de Catalunya en la cohort DE-PLAN (DE-PLAN- CAT). També es va avaluar l'associació de patrons dietètics amb la síndrome metabòlica i la diabetis tipus 2.

Materials i Mètodes: Els participants van completar un qüestionari de freqüència alimentària de 46 ítems. Els patrons alimentaris es van derivar mitjançant l'anàlisi de components prinicpals. La distribució de les variables qualitatives mitjançant tercils es va avaluar amb proves de chi-quadrat. Els models de regressió de Cox es van utilitzar per estimar els coeficients de risc multivariable, per la síndrome metabòlica i la diabetis tipus 2 (IC 95%).

Resultats: La població de l'estudi va consistir en 552 individus. Tres patrons dietètics es van derivar i anomenar en funció del principals aliments o grups d'aliments que contenien: 1) Arròs, patates i llegums, 2) Alcohol i salsitxes (embotits) 3) Proteïnes, verdures. La progressió en l'adhesió als patrons dietètics al llarg dels 4 anys de durada de la intervenció, representada pel pes de cada factor alimentari, es va mantenir

estable. Després de l'ajust per variables confusores, no es va obervar cap associació significativa entre l'adherència dietètica al diversos patrons i la síndrome metabòlica o la diabetis tipus 2. Les taxes d'incidència acumulada de la síndrome metabòlica i la diabetis tipus 2 van ser del 49,4% i 18,1%, respectivament; observant-se una tendència significativa a disminuir amb el temps en les dues malalties (p <0,001 i p = 0,007, respectivament).

Conclusions: La derivació dels patrons alimentaris en una població mediterrània amb alt risc de diabetis permet l'anàlisi del consum d'aliments tenint en compte les opcions personals. El nostre estudi descriu els patrons dietètics d'una mostra d'adults amb alt risc de diabetis en l'Atenció Primària de Salut a Catalunya i posa en relleu la necessitat de millorar els hàbits nutricionals de la població amb intervencions intensives, de llarga durada i que comptin amb el suport professional d'experts. Aquest fet podria millorar l'adherència a un patró dietètic saludable, com la dieta mediterrània, per tal d'aconseguir un millor estat de salut i qualitat de vida.

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10. APPENDIX

ONLINE SUPPLEMENT 1 (ARTICLE 1)

Author	Dietary patterns (DP) identified, as named	Factor loadings per pattern and total variance (%)*
Hu	Prudent DP, western DP	<u>**Prudent DP (10%) (healthy)**:**</u> Other vegetables 0.75, Green, leafy vegetables 0.64, Dark-yellow vegetables 0.63, cruciferous vegetables 0.63, legumes 0.61, fruit 0.57, tomatoes 0.56, fish 0.51, garlic 0.42, poultry 0.36, whole grains 0.35. <u>**Western DP (7.4%) (unhealthy)**:</u> red meat 0.63, processed meat 0.59, refined grains 0.49, sweets and dessert 0.47, French fries 0.46, high fat dairy products 0.43, eggs 0.39, high sugar drinks 0.38, snacks, 0.37, condiments 0.36, margarine 0.34, potatoes 0.33, butter 0.31.
Osler	Prudent DP, western DP	<u>**Prudent DP (20%) (healthy)**:</u> white bread -0.38, whole meal breads 0.61, white rye bread -0.46, whole meal rye bread 0.56, oatmeal 0.30, pasta 0.35, rice 0.41, fruit 0.51, vegetables raw 0.53, vegetables boiled 0.39, juice 0.36, jam and honey 0.33, cakes and biscuits 0.36, candy and chocolate 0.31, milk products 0.24, fish 0.27, diet margarine 0.22, tea 0.36, coffee -0.26. <u>**Western DP (20%) (unhealthy)**:</u> white bread 0.51, white rye bread 0.38, potatoes 0.28, juice 0.21, jam and honey 0.32, cakes and biscuits 0.43, candy and chocolate 0.44, ice cream 0.43, milk products 0.21, eggs 0.28, meat 0.36, sausages 0.49, meat for sandwiches 0.53, butter/lard 0.41, vegetable margarine 0.24.
Fung	Prudent DP, western DP	<u>**Prudent DP (healthy)**:</u> other vegetables 0.68, leafy vegetables 0.60, cruciferous vegetables 0.63, yellow vegetables 0.66, fruits 0.62, fish 0.43, legumes 0.60, tomatoes 0.46, poultry 0.32, garlic 0.26, salad dressings 0.24, whole grains 0.42, potatoes 0.25, cereal 0.20, low-fat dairy products 0.37, fruit juice 0.26, water 0.35, olive oil 0.21. <u>**Western DP (unhealthy)**:</u> legumes 0.15, processed meats 0.57, red meats 0.61, refined grains 0.44, French fries 0.47, condiments 0.29, sweets and desserts 0.46, potatoes 0.34, full fat dairy products 0.43, pizza 0.33, sweetened beverages 0.33, margarine 0.34, mayonnaise 0.27, eggs 0.41, snacks 0.33, butter 0.27, cream soups 0.35, fruit juice 0.15, nuts 0.29.

Cai Hui	Vegetable-rich DP (prudent), Fruit-rich DP (prudent), meat-rich DP (western)	**Vegetable-rich DP (healthy)**: green beans 0.54, yard long beans 0.52, wild rice stems 0.49, eggplant 0.48, celery 0.47, cucumber/luffa 0.46, cauliflower 0.43, green cabbage 0.42, Chinese cabbage 0.42, wax gourd 0.41, asparagus lettuce 0.40, potatoes 0.40, Chinese greens 0.38, spinach 0.37, fresh peppers 0.37, hyacinth beans/snow peas 0.37, tomatoes 0.37, white turnips 0.33, fresh mushrooms 0.32, lotus roots 0.23, bamboo shoots 0.31 **Meat-rich DP (unhealthy)**: chicken 0.47, animal parts 0.42, liver 0.36, rice 0.36, pig's feet 0.34, pork chops 0.33, pork ribs 0.33, beef/lamb 0.32, duck/goose 0.32, fresh pork 0.31, shrimp/crab 0.29, rice -0.43. **Fruit-rich DP (healthy)*****: oranges/grape fruit 0.67, apples 0.66, pears 0.63, bananas 0.54, watermelon 0.52, peaches 0.50, other fruits 0.50, grapes 0.49, tomatoes 0.29, shrimp/crab 0.28, bamboo shoots 0.26, rice field eel or river eel -0.40.
Harriss	Mediterranean DP (prudent), vegetable DP (prudent) fresh fruit DP (prudent) and meat DP (western)	**Mediterranean DP (69%) (healthy)**: garlic 0.44, cucumber 0.41, olive oil 0.41, salad greens 0.38, capsicum 0.35, cooked dried legumes 0.32, legume soups 0.31, tomatoes 0.29, pasta dish 0.29, olives 0.28, celery or fennel 0.28, feta cheese 0.28, beef or veal schnitzel 0.27, ricotta cheese 0.27, steamed fish 0.26, onion or leek 0.25, boiled or steamed chicken 0.23, leafy greens 0.23, game 0.23, hard cheese 0.23, watermelon 0.22, cream or sour cream -0.20, lamb roast or chops -0.21, other cereal -0.21, ice cream -0.23, chocolate -0.23, sausage or frankfurter -0.25, jam or honey -0.26, potatoes cooked without fat -0.26, pudding -0.28, cakes or sweet pastries -0.31, sweet biscuits -0.31, margarine -0.36, tea -0.37. **Meat DP (69%) (unhealthy)**: beef or veal schnitzel 0.34, beef rissoles 0.40, beef or veal roast 0.39, potatoes cooked in fat 0.36, savory pastries 0.34, mixed dishes with lamb 0.33, fried eggs 0.33, beef steaks 0.33, fried dish 0.31, bacon 0.31, pork roast 0.29, white bread 0.29, beef dish 0.28, roast or fried chicken 0.27, egg dish 0.25, corned beef 0.22, fried rice 0.22, lamb roast or chops 0.29, sausage or frankfurter 0.29. **Vegetable DP (69%) (healthy)*****: cucumber 0.32, salad greens 0.32, capsicum 0.31, cooked dried legumes 0.27, tomatoes 0.23, celery or fennel 0.43, steamed fish 0.21, onion or leek 0.29, leafy greens 0.46, cauliflower 0.60, broccoli 0.59, carrot 0.58, cabbage 0.57, pumpkin 0.56, green beans 0.48, beetroot 0.42, zucchini or eggplant 0.34, coleslaw 0.33, whole meal bread 0.26, banana 0.26, mushroom 0.24, yogurt 0.24, vegetable dish 0.23,sweet corn 0.23, pineapple 0.22, fruit salad 0.22, chicken dish 0.21, potatoes cooked without fat 0.43. **Fresh fruit DP (69%) (healthy)*****: cucumber 0.23, salad greens 0.21, olives 0.28, banana 0.27, apricots 0.68, peaches/nectarine 0.66, plums 0.64, cantaloupe 0.55, grapes 0.55, watermelon 0.55, pears 0.53, strawberries 0.46, oranges/mandarins 0.43, figs 0.42, apples, 0.40, pineapple 0.31, fruit salad 0.21.

Shimazu	Japanese DP (prudent), animal food DP (western), high dairy, fruit, vegetable and low alcohol DP (prudent)	**Japanese DP (26.2%) (healthy)**: miso soup 0.25, egg 0.34, milk 0.26, deep fried dishes/tempura 0.28, fried vegetable 0.43, raw fish/fish boiled with soy/roast fish 0.51, boiled fish paste 0.39, dried fish 0.37, green vegetables 0.64, carrot/pumpkin 0.59, tomatoes 0.45, cabbage/lettuce 0.59, Chinese cabbage 0.62, wild plant 0.27, mushrooms (shiitake, enokitake) 0.42, potatoes 0.61, pickles (radish, Chinese cabbage) 0.41, soybean (tofu, fermented soybeans) 0.57, orange 0.50, other fruits 0.49, confectioneries 0.27 fish, seaweed 0.59, green tea 0.29. **Animal food DP (26.2%) (unhealthy)**: beef 0.48, pork (excluding ham, sausage) 0.55, ham/sausage 0.56, chicken 0.49, liver 0.43, egg 0.32, cheese 0.44, butter 0.50, margarine 0.37, deep-fried dishes tempura 0.39, boiled fish paste 0.32, coffee 0.29, alcohol beverages 0.27. **High dairy, fruit, vegetable and low alcohol DP (26.2%) (healthy)*****: rice -0.59, miso soup -0.39, milk 0.28, yoghurt 0.50, margarine 0.40, carrot/pumpkin 0.36, tomato 0.32, seaweeds 0.26, orange 0.42, other fruits 0.47, alcohol beverages -0.50.
Akesson	Healthy dietary DP (prudent), western/Swedish DP (western), alcohol DP (western) and sweets DP (western)	**Healthy dietary DP (healthy)**: vegetables 0.67, fruit 0.65, legumes 0.45, soy products 0.39, fruit juice 0.35, cereal 0.31, whole grains 0.29, refined grains -0.26. **Western/Swedish DP (unhealthy)*****: meat 0.63, processed meat 0.58, fish 0.52, liver 0.50, poultry 0.47, rice, pasta, eggs 0.45, potatoes 0.42, vegetables 0.32, refined grains 0.24. **Alcohol DP (unhealthy)*****: wine 0.68, spirits 0.61, beer 0.49, salty snacks 0.39, chocolate 0.26, fruit soup -0.26. **Sweets DP (unhealthy)*****: sweet baked goods 0.59, chocolate 0.49, dairy desserts 0.44, fruit soup 0.42, sugary foods 0.33, refined grains 0.33, soda 0.30, high-fat dairy 0.22, salty snacks 0.2, processed meat 0.21.
Brunner	Unhealthy DP (western), sweet DP (western), Mediterranean-like DP (western), healthy DP (healthy)	**Healthy DP (healthy)**: fruit, vegetables, whole-meal bread, low-fat dairy, little alcohol. **Unhealthy DP (unhealthy)*****: white bread, processed meat, fries, full-cream milk. **Sweet DP (unhealthy)*****: white bread, biscuits, cakes, processed meat and high fat dairy products. **Mediterranean-like DP (healthy)*****: fruit, vegetables, rice, pasta and wine.
Heidemann	High prudent DP, western DP	**High prudent DP (healthy):** other vegetables 0.71, green/leafy vegetables 0.63, cruciferous vegetables 0.62, legumes 0.57, dark-yellow vegetables 0.62, fruit 0.59, fish 0.50, tomatoes 0.53, poultry 0.40, whole grains 0.40, salad dressing 0.33, low-fat diary 0.28, fruit juice 0.22, nuts 0.19, egg white 0.22, olive oil 0.39, tea 0.19, potatoes 0.21, mayonnaise 0.23, snacks 0.16. **Western DP (unhealthy)**: poultry 0.17, nuts 0.21, low sugar beverages 0.21, refined grains 0.50, red meat 0.62, processed meat 0.58, French fries 0.48, condiments 0.36, sweets/desserts 0.36, potatoes 0.33, high fat dairy 0.45, pizza 0.39, mayonnaise 0.33, high-sugar beverages 0.30, eggs 0.40, margarine 0.25, snacks 0.32, butter 0.31, soups 0.32, coffee 0.19.
Panagiotakos	Prudent DP, western DP	**Prudent DP (healthy)**: cereals, small fish, hardtack and olive oil. **Western DP (unhealthy)**: sweets, red meat, margarine, salty nuts, hard cheese and alcohol.

Nettleton	Fats and processed meat DP, whole grains and fruit DP, vegetables and fish DP, beans, tomatoes and refined grains DP	**<u>Whole grains and fruit DP (healthy)</u>**: added fats and oils 0.18, processed meat -0.12, fried potatoes -0.09, salty snacks 0.08, desserts 0.10, high fat cheese/cream sauce 0.16, red meat -0.13, pizza 0.08, sweet breads 0.11, pasta or potatoes salad 0.29, ice cream 0.15, white potatoes 0.04, poultry 0.01, sugar-sweetened soda -0.16, sweets 0.13, eggs/omelet's -0.08, chicken, tuna or egg salad 0.30, coffee 0.16, cream-based soup 0.11, refined grain bread, rice, cereal, pasta -0.19, cream in coffee or tea 0.08, beer -0.03, fish 0.13, whole milk -0.07, seeds or nuts 0.46, cottage or ricotta cheese 0.30, tomatoes 0.25, other alcohol 0.16, diet soda 0.10, other soups -0.09, hot chocolate 0.08, high- fat Chinese dishes -0.21, fruit juice 0.24, low-fat dairy desserts 0.28, other vegetables 0.27, meal replacement drinks 0.10, green, leafy vegetables 0.38, low-fat milk 0.33, yogurt 0.21, whole grain bread, rice, cereal, pasta 0.59, tea 0.09, beans 0.09, dark-yellow vegetables 0.21, soy foods/soy milk 0.05, avocados or guacamole 0.10, fruit 0.55, cruciferous -0.13. **Fats and processed meat DP (unhealthy)*****: added fats and oils 0.65, processed meat 0.63, fried potatoes 0.60, salty snacks 0.50, desserts 0.48, high fat cheese/cream sauce 0.42, red meat 0.42, pizza 0.42, sweet breads 0.41, pasta or potatoes salad 0.41, ice cream 0.40, white potatoes 0.37, poultry 0.36, sugar-sweetened soda 0.36, sweets 0.36, eggs/omelet's 0.34, chicken, tuna or egg salad 0.30, coffee 0.29, cream-based soup 0.28, refined grain bread, rice, cereal, pasta 0.28, cream in coffee or tea 0.23, beer 0.19, fish 0.14, whole milk 0.13, seeds or nuts 0.13, cottage or ricotta cheese 0.12, tomatoes 0.12, other alcohol 0.11, diet soda 0.10, other soups 0.09, hot chocolate 0.09, high-fat Chinese dishes 0.05, fruit juice 0.05, low-fat dairy desserts 0.04, other vegetables 0.04, meal replacement drinks 0.03, green, leafy vegetables 0.01, low-fat milk 0.01, yogurt 0.01, whole grain bread, rice, cereal, pasta 0.01, tea -0.03, beans -0.04, dark-yellow vegetables -0.15, soy foods/soy milk -0.15, avocados or guacamole -0.15, fruit -0.17, cruciferous -0.18. **Vegetables and fish DP (healthy)*****: added fats and oils -0.01, processed meat -0.02, fried potatoes 0.004, salty snacks -0.01, desserts -0.09, high fat cheese/cream sauce -0.05, red meat 0.42, pizza -0.07, sweet breads 0.08, pasta or potatoes salad 0.12, ice cream -0.07, white potatoes 0.14, poultry 0.38, sugar-sweetened soda -0.04, sweets -0.07, eggs/omelet's 0.14, chicken, tuna or egg salad 0.16, coffee -0.08, cream-based soup 0.13, refined grain bread, rice, cereal, pasta 0.30, cream in coffee or tea -0.08, beer –0.09, fish 0.60, whole milk -0.03, seeds or nuts 0.14, cottage or ricotta cheese -0.04, tomatoes 0.06, other alcohol -0.09, diet soda -0.06, other soups 0.58, hot chocolate -0.02, high- fat Chinese dishes 0.42, fruit juice 0.002, low-fat dairy desserts 0.10, other vegetables 0.62, meal replacement drinks 0.02, green, leafy vegetables 0.13, low-fat milk -0.04, yogurt -0.02, whole grain bread, rice, cereal, pasta 0.01, tea 0.25, beans 0.02, dark-yellow vegetables 0.77, soy foods/soy milk 0.37, avocados or guacamole 0.004, fruit 0.21, cruciferous 0.75. **Beans, tomatoes and refined grains DP (unhealthy)*****: added fats and oils 0.05, processed meat 0.04, fried potatoes 0.14, salty snacks 0.02, desserts 0.04, high fat cheese/cream sauce 0.57, red meat 0.46, pizza 0.14, sweet breads -0.02, pasta or potatoes salad 0.01, ice cream -0.01, white potatoes 0.02, poultry 0.32, sugar-sweetened soda 0.11, sweets 0.06, eggs/omelet's 0.10, chicken, tuna or egg salad -0.03, coffee 0.05, cream-based soup 0.05, refined grain bread, rice, cereal, pasta 0.60, cream in coffee or tea -0.05, beer 0.05, fish -0.03, whole milk 0.20, seeds or nuts 0.02, cottage or ricotta cheese 0.14, tomatoes 0.73, other alcohol -0.03, diet soda 0.11, other soups 0.10, hot chocolate 0.10, high- fat Chinese dishes 0.22, fruit juice 0.15, low-fat dairy desserts -0.08, other vegetables 0.18, meal replacement drinks -0.004, green, leafy vegetables 0.01, low-fat milk 0.03, yogurt 0.16, whole grain bread, rice, cereal, pasta -0.001, tea -0.12, beans 0.76, dark-yellow vegetables 0.07, soy foods/soy milk -0.11, avocados or guacamole 0.53, fruit 0.10, cruciferous -0.05.

Guallar	Mediterranean DP and westernized DP	**Mediterranean DP (6%) (healthy)**: vegetables oils (not including olive oil) -0.26, sugar, chocolate and ice cream -0.19, fat-free dairy products 0.28, vegetables 0.64, olive oil 0.61, non-oily fish 0.44, fruits 0.35, whole grains 0.27, cheese 0.23, oily fish 0.22, tea 0.21, shell fish 0.20, nuts 0.19, fruit and vegetable juices 0.16, poultry and other unprocessed white meat 0.16, pastries -0.16, coffee -0.26, whole dairy products -0.42. **Westernized DP (11%) (unhealthy)**: refined grains 0.66, fried potatoes 0.66, potatoes 0.64, unprocessed red meat 0.57, wine 0.53, eggs 0.53, legumes 0.52, processed red meat 0.48, liquors 0.41, sauces and mayonnaise 0.40, vegetable oils (not including olive oil) 0.38, beer and cider 0.24, appetizers 0.21, soups 0.20, sugar, chocolate and ice cream 0.19, fat-free dairy products -0.35, olive oil 0.19, whole grains -0.23, oily fish 0.17, tea -0.16, shellfish 0.17, whole dairy products 0.15.
Chan	Vegetables-fruits DP, snacks-drinks-milk products DP, meat-fish DP	**Vegetables-fruits DP (6.2%) (healthy):** other vegetables 0.52, tomatoes 0.47, starchy vegetables 0.45, fruits 0.43, dark green and leafy vegetables 0.42, soy 0.42, cruciferous vegetables 0.39, legumes 0.36, mushroom and fungi 0.23, fats and oils -0.39, condiments -0.07, coffee -0.13, milk and milk-products 0.05, fast food -0.04, sweets and desserts 0.01, nuts 0.13, French fries and potato chips -0.06, wholegrain 0.19, cakes, cookies, pies and biscuits 0.06, eggs 0.09, beverages -0.02, dim sum -0.18, red and processed meats -0.07, poultry 0.04, fish and seafood 0.20, wine -0.15, refined grains -0.25, organ meats -0.10,n others 0.01, preserved vegetables 0.13, soups 0.00, tea -0.02. **Snacks-drinks-milk products DP (5.5%) (unhealthy):** other vegetables -0.05, tomatoes 0.02, starchy vegetables 0.00, fruits 0.06, dark green and leafy vegetables -0.27, soy 0.09, cruciferous vegetables -0.03, legumes -0.07, mushroom and fungi 0.05, fats and oils -0.23, condiments 0.52, coffee 0.40, milk and milk-products 0.37, fast food 0.36, sweets and desserts 0.33, nuts 0.32, French fries and potato chips 0.29, wholegrain 0.29, cakes, cookies, pies and biscuits 0.24, eggs 0.21, beverages 0.20, dim sum -0.07, red and processed meats 0.07, poultry 0.11, fish and seafood -0.20, wine 0.08, refined grains -0.51, organ meats 0.13, others 0.10, preserved vegetables -0.03, soups 0.00, tea 0.19. **Meat-fish DP (5.1%) (unhealthy)***:** other vegetables 0.03, tomatoes 0.00, starchy vegetables 0.01, fruits -0.03, dark green and leafy vegetables -0.03, soy 0.10, cruciferous vegetables -0.05, legumes 0.01, mushroom and fungi -0.05, fats and oils 0.13, condiments -0.12, coffee -0.19, milk and milk-products -0.17, fast food 0.01, sweets and desserts 0.13, nuts -0.03, French fries and potato chips 0.08, wholegrain -0.14, cakes, cookies, pies and biscuits 0.19, eggs 0.08, beverages 0.09, dim sum 0.52, red and processed meats 0.50, poultry 0.49, fish and seafood 0.36, wine 0.22, refined grains -0.68, organ meats 0.09, others 0.02, preserved vegetables 0.18, soups -0.01, tea 0.02.

Maruyama	Vegetable DP, animal food DP and dairy product patterns DP	<u>**Men (24.5%):**</u> <u>**Vegetable DP (11.9%) (healthy):**</u> boiled rice 0.05, miso-soup 0.35, beef -0.12, pork (excluding ham or sausage) 0.16, ham or sausage 0.07, chicken 0.14, liver 0.00, eggs 0.32, fresh fish 0.42, kamaboko (fish paste) 0.10, dried fish or salted fish 0.27, milk 0.23, yogurt 0.08, cheese 0.08, butter -0.02, margarine -0.02, deep-fried food or tempura 0.19, fried vegetable 0.35, spinach or garland chrysanthemum 0.59, carrot or pumpkin 0.64, tomatoes 0.42, cabbage or head lettuce 0.60, Chinese cabbage 0.59, edible wild plants 0.25, fungi (enokidake, shiitake mushroom) 0.50, potatoes 0.64, algae (seaweeds) 0.63, pickles 0.35, preserve food using soy sauce 0.21, boiled beans 0.35, tofu (soy bean curd) 0.54, citrus fruits 0.49, fresh fruits juice (in summer) 0.22, fruits (excluding citrus variety) 0.54, sweets 0.23, coffee 0.03, tea 0.00, green tea 0.12, oolong tea 0.05, alcohol beverage -0.03. <u>**Animal food DP (7.0%) (unhealthy):**</u> boiled rice 0.18, miso-soup 0.03, beef 0.34, pork (excluding ham or sausage) 0.46, ham or sausage 0.53, chicken 0.55, liver 0.47, eggs 0.23, fresh fish 0.21, kamaboko (fish paste) 0.49, dried fish or salted fish 0.40, milk -0.01, yogurt 0.10, cheese 0.23, butter 0.27, margarine 0.17, deep-fried food or tempura 0.54, fried vegetable 0.45, spinach or garland chrysanthemum 0.14, carrot or pumpkin 0.14, tomatoes 0.18, cabbage or head lettuce 0.15, Chinese cabbage 0.12, edible wild plants 0.32, fungi (enokidake, shiitake mushroom) 0.17, potatoes 0.05, algae (seaweeds) 0.08, pickles 0.07, preserve food using soy sauce 0.32, boiled beans 0.20, tofu (soy bean curd) 0.11, citrus fruits -0.06, fresh fruits juice (in summer) 0.17, fruits (excluding citrus variety) -0.06, sweets 0.16, coffee -0.14, tea 0.07, green tea 0.00, oolong tea -0.04, alcohol beverage -0.01. **Dairy product DP (5.6%) (unhealthy)***:** boiled rice -0.39, miso-soup -0.24, beef 0.21, pork (excluding ham or sausage) 0.08, ham or sausage 0.19, chicken 0.02, liver 0.04, eggs 0.08, fresh fish -0.11, kamaboko (fish paste) 0.00, dried fish or salted fish -0.16, milk 0.35, yogurt 0.40, cheese 0.47, butter 0.51, margarine 0.56, deep-fried food or tempura -0.01, fried vegetable -0.08, spinach or garland chrysanthemum 0.00, carrot or pumpkin 0.07, tomatoes 0.00, cabbage or head lettuce 0.11, Chinese cabbage 0.02, edible wild plants -0.11, fungi (enokidake, shiitake mushroom) 0.09, potatoes 0.14, algae (seaweeds) 0.06, pickles -0.08, preserve food using soy sauce 0.04, boiled beans 0.15, tofu (soy bean curd) -0.04, citrus fruits 0.33, fresh fruits juice (in summer) 0.22, fruits (excluding citrus variety) 0.39, sweets 0.15, coffee 0.45, tea 0.34, green tea 0.04, oolong tea 0.27, alcohol beverage 0.03. <u>**Women (23.7%):**</u> <u>**Vegetable DP (10.7%) (healthy):**</u> boiled rice -0.05, miso-soup 0.35, beef -0.10, pork (excluding ham or sausage) 0.08, ham or sausage 0.03, chicken 0.11, liver 0.02, eggs 0.30, fresh fish 0.43, kamaboko (fish paste) 0.10, dried fish or salted fish 0.26, milk 0.24, yogurt 0.15, cheese 0.12, butter 0.02, margarine -0.04, deep-fried food or tempura 0.15, fried vegetable 0.34, spinach or garland chrysanthemum 0.59, carrot or pumpkin 0.64, tomatoes 0.40, cabbage or head lettuce 0.57, Chinese cabbage 0.52, edible wild plants 0.25, fungi (enokidake, shiitake mushroom) 0.51, potatoes 0.61, algae (seaweeds) 0.61, pickles 0.24, preserve food using soy sauce 0.16, boiled beans 0.36, tofu (soy bean curd) 0.56, citrus fruits 0.39, fresh fruits juice (in summer) 0.16, fruits (excluding citrus variety) 0.45, sweets 0.16, coffee -0.03, tea 0.01, green tea 0.11, oolong tea 0.09, alcohol beverage -0.07. <u>**Animal food DP (7.0%) (unhealthy):**</u> boiled rice 0.22, miso-soup 0.07, beef 0.34, pork (excluding ham or sausage) 0.53, ham or sausage 0.56, chicken 0.52, liver 0.36, eggs 0.30, fresh fish 0.16, kamaboko (fish paste) 0.47, dried fish or salted fish 0.38, milk 0.00, yogurt 0.07, cheese 0.22, butter 0.31, margarine 0.15, deep-fried food or tempura 0.57, fried vegetable 0.42, spinach or garland chrysanthemum 0.06, carrot or pumpkin 0.10, tomatoes 0.13, cabbage or head lettuce 0.14, Chinese cabbage 0.10, edible wild plants 0.25, fungi (enokidake, shiitake

		mushroom) 0.09, potatoes 0.08, algae (seaweeds) 0.08, pickles 0.15, preserve food using soy sauce 0.35, boiled beans 0.17, tofu (soy bean curd) 0.06, citrus fruits -0.05, fresh fruits juice (in summer) 0.22, fruits (excluding citrus variety) -0.03, sweets 0.25, coffee -0.01, tea 0.05, green tea 0.05, oolong tea -0.08, alcohol beverage 0.04. **Dairy product DP (6.0%) (unhealthy)***:** boiled rice -0.44, miso-soup -0.27, beef 0.28, pork (excluding ham or sausage) 0.14, ham or sausage 0.20, chicken 0.05, liver 0.07, eggs 0.15, fresh fish -0.08, kamaboko (fish paste) -0.06, dried fish or salted fish -0.21, milk 0.36, yogurt 0.40, cheese 0.47, butter 0.44, margarine 0.59, deep-fried food or tempura -0.08, fried vegetable -0.10, spinach or garland chrysanthemum 0.05, carrot or pumpkin 0.07, tomatoes -0.04, cabbage or head lettuce 0.13, Chinese cabbage -0.02, edible wild plants -0.19, fungi (enokidake, shiitake mushroom) 0.13, potatoes 0.10, algae (seaweeds) 0.09, pickles -0.12, preserve food using soy sauce -0.05, boiled beans 0.05, tofu (soy bean curd) -0.01, citrus fruits 0.32, fresh fruits juice (in summer) 0.14, fruits (excluding citrus variety) 0.38, sweets 0.05, coffee 0.47, tea 0.37, green tea 0.03, oolong tea 0.28, alcohol beverage 0.16.
Stricker	Prudent DP, western DP	**<u>Prudent DP (20.8%) (healthy):</u>** chicken 0.21, processed meat -0.22, red meat -0.25, low-fat fish 0.62, high-fat fish 0.64, shellfish 0.74, fruit juices 0.28, wine 0.48, high-fiber bread 0.24, low-fiber bread -0.33, high-fiber cereal 0.36, low-fiber cereal 0.27, potatoes -0.43, raw vegetables 0.66, fruit 0.28, nuts and seeds, soy products and peanut butter 0.23, fat and butter -0.33, sugar and sweets -0.33. **<u>Western DP (20.8%) (unhealthy):</u>** processed meat 0.25, other alcoholic drinks (excluding wine) 0.35, soft drinks with sugar 0.52, other non-alcoholic drinks 0.29, high-fiber bread -0.36, low-fiber bread 0.35, low-fiber cereal 0.43, boiled vegetables and legumes -0.36, raw vegetables -0.21, fruit -0.55, French fries 0.70, fast food 0.65, cakes and cookies -0.42, low-fat dairy products -0.52, high-fat dairy products -0.33, cheese -0.29.
Chen Yu	Balanced DP, gourd and root vegetable DP, animal protein DP	**<u>Balanced DP (healthy):</u>** wheat bread (brown) -0.16, beef or mutton 0.21, bitter gourd 0.43, banana 0.16, jack fruit 0.30, watermelon 0.20, mango 0.39, steam rice 0.24, guava 0.27, beans (scarlet runner) 0.62, potatoes 0.22, bottle gourd 0.46, small fish (fresh water) 0.39, eggplant 0.33, cauliflower 0.64, parwar/patol (a kind of squash) 0.22, green papaya 0.22, cabbage 0.51, okra 0.29, yam 0.31, spinach 0.24. **<u>Animal protein DP (unhealthy)</u>**: tea 0.48, big fish (fresh water 0.44, eggs, hane eggs) 0.49, milk 0.49, poultry (fowl) 0.47, puffed rice 0.22, lentil 0.37, wheat bread (brown) 0.49, beef or mutton 0.45, bitter gourd 0.18, banana 0.47, jack fruit 0.22, watermelon 0.29, mango 0.22, steamed rice -0.29, parwar/patol (a kind of squash) 0.17. **Gourd and root vegetable DP (healthy)*****: bitter gourd 0.28, eggplant 0.17, cauliflower 0.16, parwar/patol (a kind of squash) 0.37, green papaya 0.35, cabbage 0.24, okra 0.37, yam 0.26, spinach 0.25, dried fish 0.22, ridge gourd/jhinga (a kind of squash) 0.53, snake gourd/chachinga 0.57, ghosala/dhundal (a kind of squash) 0.51, radish 0.48, spinach stalks 0.48, sweet potatoes 0.29, water rice 0.17, pumpkin 0.39.

Judd	Convenience DP, Healthy DP, sweets/fats DP southern DP, alcohol/salads DP	**<u>Healthy DP (healthy)</u>:** fruit juice 0.25, beans 0.38, beer -0.16, bread: whole grain 0.30, cereal 0.38, high fiber cereal 0.24, fish 0.38, fruit 0.58, low-fat dairy 0.20, milk alternatives 0.18, milk low fat 0.16, pizza -0.18, poultry 0.31, refined grains 0.17, salad dressing/sauces 0.30, seeds, nuts 0.26, soda -0.23, soup 0.32, cruciferous 0.59, dark yellow vegetable 0.41, green leafy vegetables 0.49, other vegetables 0.48, tomatoes 0.32, mixed dishes with vegetables 0.31, water 0.32, yogurt 0.31. **<u>Southern DP (unhealthy)</u>:** fruit juice 0.17, added fats 0.38, bread 0.37, high fiber cereal -0.25, coffee -0.16, eggs and egg dishes 0.42, fried food 0.56, fried potatoes 0.16, low fat dairy -0.19, high fat milk 0.24, low fat milk -0.42, miscellaneous sugar 0.19, organ meat 0.47, processed meats 0.45, red meat 0.26, refined grains 0.20, shellfish 0.23, soda 0.24, sugar sweetened beverages 0.37, green leafy vegetables -0.22, yogurt -0.25. **Convenience DP (unhealthy)*****: beans 0.36, Chinese food 0.44, condiments 0.25, desserts 0.20, fish 0.27, fried food 0.24, fried potatoes 0.37, high-fat dairy 0.18, Mexican dishes 0.48, mixed dishes with meat 0.61, organ meat 0.17, pasta 0.59, pizza 0.45, potatoes 0.36, poultry 0.29, processed meats 0.25, red meat 0.45, refined grains 0.31, salty snacks 0.32, shellfish 0.28, soup 0.44, sweet breakfast foods 0.19, green leafy vegetables 0.16, mixed dishes of vegetables 0.35. **Sweets/fats DP (unhealthy)*****: added fats 0.40, bread 0.47, whole grain bread 0.18, butter 0.17, candy 0.40, chocolate 0.46, coffee 0.22, condiments 0.31, desserts 0.53, fried potatoes 0.28, high-fat dairy 0.37, margarine 0.37, high fat milk 0.18, miscellaneous sugar 0.54, pasta 0.17, pizza 0.20, potatoes 0.26, processed meat 0.26, red meat 0.18, refined grains 0.20, salty snacks 0.30, seeds, nuts 0.19, sweet breakfast foods 0.39, tea 0.31. **Alcohol/salads DP (unhealthy)*****: fruit juice -0.17, added fats 0.25, beer 0.23, butter 0.32, cereal -0.20, coffee 0.30, condiments 0.29, desserts -0.17, eggs and egg dishes 0.29, fish 0.21, high fat dairy 0.21, liquor 0.31, processed meats 0.22, red meats 0.26, salad dressings/sauces 0.55, seeds, nuts 0.19, shellfish 0.24, sugar sweetened beverages -0.15, dark yellow vegetables -0.17, green leafy vegetables 0.48, tomatoes 0.27, mixed dishes -0.25, wine 0.36.
Martinez	Vegetable DP, staple DP	**<u>Vegetable DP (9.12%) (healthy)</u>:** vegetables and other 0.65, green and leafy vegetables 0.59, dark yellow vegetables 0.58, cruciferous 0.56, fruits 0.44, tomatoes 0.37, meat, chicken, lean 0.36, root starchy vegetables 0.34, saccharine 0.30, beverages tea and water 0.29, snacks 0.25, whole grains 0.22, liquors -0.23, meat, chicken 0.28, sugar -0.37, refined grains -0.20, fresh condiments 0.25, coffee -0.25, fruit juices 0.22, skinless and lean chicken, saccharin, low intake of added sugar, chicken and coffee. **<u>Staple DP (5.44%) (unhealthy)</u>:** meat, chicken and lean -0.26, meat, chicken 0.24, sugar 0.30, palm oil 0.73, legumes 0.58, refined grains 0.51, fresh condiments 0.44, coffee 0.33, red meat 0.30, organ meat 0.27, high energy beverages 0.22, nuts -0.21, other whole grains -0.23, no energy beverages -0.23, low-fat dairy products -0.26, pizza -0.31, whole breakfast cereal -0.33, dressings -0.39, fruit juices -0.41, unsaturated oil -0.42.

Iqbal	Oriental DP, western DP, prudent DP	**Prudent DP (healthy):** dairy 0.56, nuts 0.29, green leafy vegetables 0.32, raw vegetables other than green leafy 0.63, fruits 0.68, desserts 0.40. **Western DP (unhealthy)**: eggs 0.44, meats 0.39, fried foods 0.63, salty foods 0.61, sugar 0.32, nuts 0.28, desserts 0.41. **Oriental DP (unhealthy)*****: eggs 0.32, soy sauce 0.65, pickle foods 0.41, sugar -0.53, tofu 0.70, green leafy vegetables 0.58.
Hsiao	Sweets and dairy DP, health-conscious DP, western DP	**Western DP (unhealthy)**: bread, eggs, fats, fried vegetables, miscellaneous (sauces, condiments), alcohol, soft drinks and lowest intakes of milk and whole fruit. **Sweets and dairy DP (unhealthy)*****: baked goods, milk, sweetened coffee and tea, dairy based desserts food groups and lowest intakes of poultry. **Health-conscious DP (healthy)*****: pasta, noodles, rice, whole fruit, poultry, nuts, fish, vegetables, lower intake of fried vegetables, processed meats and soft drinks.
Guo	Vitamin and microelement DP, carbohydrate DP, fat and protein DP	**Vitamin and microelement DP (healthy)**: refined grains 0.33, soy sauce 0.19, salty foods 0.26, tofu 0.29, legumes 0.30, green vegetables 0.15, other raw vegetables 0.46, other cooked vegetables 0.77, fruits 0.35, desserts 0.22. **Fat and protein DP (unhealthy)**: eggs 0.35, grains 0.16, meats 0.52, fish 0.51, diary 0.27, fried foods 0.28, salty foods 0.26, sugar 0.19, nuts 0.24. **Carbohydrate DP (unhealthy)*****: refined grains 0.76, salty foods 0.20, other cooked vegetables 0.28.
Zazpe	Western DP, Mediterranean DP, alcoholic beverages DP	**Mediterranean DP (6.1%) (healthy)**: whole-wheat bread 0.30, poultry 0.34, virgin olive oil 0.37, low-fat dairy 0.38, fruits 0.55, fish and seafood 0.56, vegetables 0.67. **Western DP (8.5%) (unhealthy)**: red meat 0.50, processed meats 0.47, potatoes 0.47, processed meals 0.45, fast food 0.43, whole fat dairy products 0.42, sauces 0.42, commercial bakery 0.42, eggs 0.38, sugar-sweetened sodas 0.33, refined grains 0.31. **Alcoholic beverages DP (5.1%) (unhealthy)*****: wine 0.63, beer 0.63, liqueurs 0.63.

*Some studies did not have the information requested.

**The information about how the pattern was categorized is situated between brackets.

***Patterns not included in the meta-analysis. The patterns included are underlined.

ONLINE SUPPLEMENT 1 (ARTICLE 2)

Author	Main conclusions of study	Dietary patterns (DP) identified, as named	Factor loadings per pattern and total variance (%)
Song*	Meat and alcohol DP is negatively associated with MS, compared with Traditional DP. Korean Healthy DP is positive against MS.	Traditional DP, Meat and alcohol DP, Korean Healthy DP	**Traditional DP (healthy):** rice and kimchi. **Korean healthy DP (healthy):** noodle, bread, eggs and tea. **Meat and alcohol DP (unhealthy):** processed meat and alcohol.
Wagner*	The energy-dense DP was positively associated with MS. No association was found between the convenience-food pattern and MS risk.	Energy-dense DP, Convenience-food DP	**Convenience-food DP (unhealthy)***:** grains, pasta, rice 0.24, fruits -0.29, vegetables -0.39, cheese 0.20, cream 0.40, cake 0.47, junk food 0.21, water -0.28, fruit and vegetable juices 0.25, sodas 0.22, diet sodas 0.22, prepared dishes 0.48, fresh products prepared at home -0.52, pizza, quiches, sausage rolls, pies 0.49. **Energy-dense DP (unhealthy):** delicatessen foods 0.39, red meat 0.61, fruits -0.48, potatoes 0.56, yoghourt -0.40, animal fat (butter) 0.55, sauce and condiments 0.20, water -0.28, sodas 0.21, alcohol 0.50.
Naja	Fast food/Desserts DP is associated with a higher prevalence of MS. Traditional Lebanese DP was no associated with MS.	Fast food/Desserts DP, Traditional Lebanese DP, High Protein DP	**High Protein DP (7.80%) (unhealthy)***:** fruits 0.23, fish 0.70, chicken 0.69, meat 0.60, dairy products low-fat 0.54, breakfast cereals 0.23. **Traditional Lebanese DP (9.71%) (healthy)**: desserts 0.23, dairy products full-fat 0.58, olives 0.56, fruits 0.49, legumes 0.47, grains 0.47, eggs 0.45, vegetable oil 0.43, nuts and dried fruits 0.40, traditional sweets 0.37, vegetables 0.34, dairy products low-fat -0.29. **Fast Food/Desserts DP (13.11%) (unhealthy):** Hamburger 0.76, shawarma 0.72, pizza and pies 0.70, falafel sandwiches 0.61, desserts 0.41, carbonated beverages and juices 0.40, mayonnaise 0.35, butter 0.22, alcoholic beverages 0.20, fruits -0.22, grains 0.27, eggs 0.21, nuts and dried fruits 0.27, chicken 0.21, meat 0.22.

Leite*	Starch DP (very low fat diet rich in refined CH on lipid profile) had the highest prevalence for MS. Vegetable/fat DP (rich in unsaturated fats, fruits and vegetables) had the lowest MS prevalence.	Common DP, Animal products DP, Starch DP, Vegetable/fat DP, Vitamin/fibre DP	**Common DP***: -.** **Animal products DP (unhealthy)***:** meat, eggs, dairy. **Vegetable/fat DP (healthy):** olive oil, fat sauces made with seed oil and butter, dry fruits. **Vitamin/fibre DP (healthy):** vegetables, legumes, fruit. **Starch DP (unhealthy):** refined-grain products (bread, rice and pasta).
Esmaillzadeh*	Healthy DP is associated with reduced risk for MS, whereas Western DP is associetad with greater risk.	Healthy DP, Western DP, Traditional DP	**Traditional DP (unhealthy)***:** tea 0.42, legumes 0.26, potatoes 0.46, whole grains 0.40, refined grains 0.51, hydrogenated fats 0.28, broth 0.23. **Healthy DP (healthy):** fish 0.22, poultry 0.53, butter -0.31 low-fat dairy products 0.26, high-fat dairy products -0.23, tea 0.39, fruit 0.74, fruit juices 0.37, cruciferous vegetables 0.47, yellow vegetables 0.21, tomatoes 0.63, green leafy vegetables 0.41, other vegetables 0.71, legumes 0.52, potatoes 0.29, whole grains 0.34, hydrogenated fats -0.20. **Western DP (unhealthy):** processed meats 0.39, red meats 0.56, fish -0.29, eggs 0.35, butter 0.43, low-fat dairy products -0.37, high-fat dairy products 0.39, coffee, 0.23, fruit -0.29, fruit juices 0.21, other vegetables -0.31, French fries 0.24, potatoes 0.35, refined grains 0.66, pizza 0.36, snacks 0.29, mayonnaise 0.22, sweets and desserts 0.37, hydrogenated fats 0.34, vegetable oils 0.20, soft drinks 0.33.
Deshmuck-Taskar	Prudent DP may be helpful in preventing MS. No association was found between Western DP and MS.	Prudent DP, Western DP	**Prudent DP (12%) (healthy):** whole grains 0.46, legumes 0.61, cruciferous vegetables 0.70, other vegetables 0.74, green leafy vegetables 0.69, dark-yellow vegetables 0.70, tomatoes 0.58, fruits 0.64, 100% fruit juices 0.43, low-fat dairy products 0.36, poultry 0.40, clear subs 0.36, low-fat salad dressings 0.49. **Western DP (19%) (unhealthy):** refined grains 0.43, French fries 0.53, high fat dairy products 0.53, dishes with cheese 0.58, red meats 0.50, processed meats 0.59, eggs 0.39, snacks 0.53, sweets and desserts 0.54, sweetened beverages 0.44, condiments 0.40.

Denova-Gutiérrez	Western DP had a positive association with MS. The Prudent DP was not associated with MS.	Prudent DP, Western DP, High-protein/fat DP	**High-protein/fat DP (6%)***:** pastry -0.34, seafood 0.32, poultry 0.35, processed meat 0.57, red meat 0.59, butter 0.44, eggs 0.38. **Prudent DP (7.8%) (healthy):** processed vegetable juices 0.55, potatoes 0.40, fresh fruits 0.57, fresh vegetables 0.70, legumes 0.39, pastry -0.37, fruit juice 0.30. **Western DP (6.6%) (unhealthy):** legumes 0.35, refined cereals 0.31, whole cereals -0.54, seafood -0.35, high fat dairy products -0.39, low-fat dairy products -0.35, corn tortillas 0.66, sodas 0.39.
Amini	Western DP promotes the risk of MS. Prudent DP was associated with high HDL Cholesterol levels.	Prudent DP, western DP, Vegetarian DP, High-fat DP, Chicken and plant DP	**Vegetarian DP (5%) (healthy)***:** sugar 0.33, cookies 0.20, rice 0.51, legume 0.54, potatoes 0.59, low-fat milk 0.20, green leafy vegetables 0.46, non-leafy vegetables 0.20, fruits rich in vitamin-C 0.51, fruits rich in vitamin A 0.27. **High-fat dairy DP (4.2%) (unhealthy)***:** bread -0.20, peas -0.20, cheese -0.20, high-fat milk 0.62, low-fat yoghurt -0.63, high-fat yoghurt 0.63, other fruits 0.25. **Chicken and plant DP (5.1% (unhealthy))***:** mayonnaise 0.34, liver and organic meat -0.20, beef -0.35, chicken 0.65, green leafy vegetables 0.37, fruits rich in vitamin A 0.39, candy 0.33, tea 0.40. **Prudent DP (5.3%) (healthy):** hydrogenated fat -0.32, vegetable oil 0.36, liver and organic meat 0.34, coconut 0.30, juice 0.38. **Western DP (6.8%) (unhealthy):** sweets 0.60, butter 0.59, soda 0.53, mayonnaise 0.45, sugar 0.44, cookies 0.44, tail 0.34, hydrogenated fat 0.33, egg 0.29, macaroni 0.25, vegetable oil -0.25, liver and organic meat 0.23, coconut 0.22, mutton 0.22, juice 0.22.
Cho	Prudent DP is associated with a reduced risk of MS. Western DP and Traditional DP were not associated with MS.	Healthy DP, western DP, Traditional DP	**Traditional DP (8.3%) (healthy)***:** green yellow vegetables 0.30, seaweeds 0.21, salted vegetables and seafood 0.66, cereals 0.60, light colored vegetables 0.56. **Healthy DP (12.2%) (healthy):** fried foods 0.21, cholesterol rich foods 0.33, green yellow vegetables 0.58, healthy protein foods 0.58, seaweeds 0.55, bone fish 0.54, fruits 0.47, dairy products 0.34, light colored vegetables 0.34. **Western DP (15.3%) (unhealthy):** fast-foods 0.72, animal fat rich foods 0.71, fried foods 0.61, grilled meat and sea-foods 0.54, sweet foods 0.54, cholesterol rich foods 0.51, caffeinated drinks 0.35.

Hong	Fruit and dairy DP was associated with a reduced risk of MS. The Korean traditional DP was associated with an increased likelihood of having MS. Alcohol and meat or Sweets and fast-foods DP were not associated with MS.	Korean traditional DP, alcohol and meat DP, sweets and fast-foods DP, fruit and dairy DP	**Alcohol and meat DP (7.1%) (unhealthy)***:** onion and garlic 0.40, vegetable oil 0.36, soy products -0.42, fish 0.26, alcohol 0.65, processed meat 0.50, poultry and eggs 0.46, beef 0.41, boiled fish paste 0.40, animal fat 0.33, organ meat 0.30, coffee 0.27, sauce 0.26. **Sweets and fast-foods DP (6.5%) (unhealthy)***:** fruits juice and canned fruits 0.61, chocolate and ice-cream 0.55, pizza and hamburgers 0.53, spaghetti 0.48, carbonated beverages 0.43, sauce 0.41, ramen (instant noodles) 0.27, dairy products 0.27. **<u>Korean traditional DP (9.3%) (unhealthy):</u>** soy sauce 0.69, refined grains 0.59, onion and garlic 0.58, vegetable oil 0.55, soy products 0.51, red pepper and soybean paste 0.45, starch syrup and sugar 0.45, kimchi 0.44, seaweed 0.43, fish 0.39, whole grains 0.32, vegetables 0.28, pork 0.26. **<u>Fruit and dairy DP (5.6%) (healthy):</u>** refined grains -0.33, kimchi -0.31, beef 0.25, fruits 0.49, pork -0.49, ramen (instant noodles) -0.48, dairy products 0.47, rice cakes 0.43, nuts 0.32.
Heidemann*	Processed foods DP was related to a higher prevalence of MS. Higher adherence to health-conscious DP was related to a lower prevalence of HBP and favorable levels of folate, homocysteine and fibrinogen.	Processed foods DP, Health-conscious DP	**<u>Processed foods DP (unhealthy):</u>** refined grains 0.72, processed meat 0.66, red meat 0.57, high sugar beverages 0.50, eggs 0.41, potatoes 0.38, beer 0.38, sweets and cakes 0.37, snacks 0.37, butter 0.37, organ meats 0.19, margarine 0.19, coffee 0.16, tea -0.24, fruity and root vegetables -0.19, vegetable oils 0.16, fruits -0.32, wholegrain -0.30, other animal fats 0.26, olives and olive oil 0.16. **<u>Health-conscious DP (healthy):</u>** red meat 0.34, high sugar beverages -0.16, eggs 0.23, potatoes 0.32, butter 0.16, tea 0.18, cruciferous vegetables 0.65, fruity and root vegetables 0.58, other vegetables 0.55, leafy vegetables 0.55, vegetable oils 0.52, legumes 0.39, fruits 0.39, fish 0.34, whole grains 0.31, other animal fats 0.31, poultry 0.26, nuts and seeds 0.17, olives and olive oil 0.17, wine 0.16.

Kim	Grains, vegetables, fish DP was associated with a reduced risk of MS. Meat and alcohol DP was associated with hypertriglyceridemia and HBP.	White rice and Kimchi DP, Meat and alcohol DP, High fat, sweets, and coffee DP, Grains, vegetables and fish DP	**White rice and Kimchi DP (8.6%) (healthy)***:** white rice 0.74, grains -0.25, noodles and dumplings -0.27, flour and bread -0.56, cereal and snacks -0.25, vegetables 0.23, kimchi 0.33, fruits -0.32, milk and dairy products -0.46, other beverages -0.27. **High fat, sweets, and coffee DP (5.7%) (unhealthy)***:** grains -0.29, sugar and sweets 0.70, legumes -0.22, eggs 0.22, oils 0.72, coffee 0.40. **Meat and alcohol DP (6.7%) (unhealthy):** white rice -0.41, grains -0.24, noodle and dumplings 0.33, sugar and sweets -0.34, vegetables -0.28, mushrooms -0.23, meat and its products 0.65, fish and shellfish -0.24, milk and dairy products -0.17, alcohol 0.53, other beverages 0.09. **Grains, vegetables and fish DP (5.7%) (healthy):** white rice -0.26, grains 0.38, noodle and dumplings -0.26, nuts 0.24, vegetables 0.67, kimchi -0.32, fish and shellfish 0.29, milk and dairy products 0.02, oils 0.26, other beverages 0.58.
Kimokoti*	Heart healthier DP was not associated with a lower risk for MS or its components. None of the clusters was associated with MS or other MS components.	Empty calories DP, Higher fat DP, Wine and moderate eating DP, Lighter eating DP, Heart Healthier DP	**Wine and moderate eating DP (unhealthy):** wine 2.75, organ meats, eggs, high-fat dairy and snack foods 0.94. **Lighter eating DP (unhealthy):** fat poultry and beer 0.20. **Empty calories DP (unhealthy):** sweetened beverages 2.58, meats and mixed dishes 1.16. **Higher fat DP (unhealthy):** sweets and animal fats 4.6, refined grains, soft margarine and oils 3.6, diet beverages and firm vegetable fats 4.2, desserts 1.3. **Heart Healthier DP (healthy):** vegetables 3.8, fruits and low-fat milk 4.4, other low-fat foods 4.6, legumes, soups and miscellaneous foods 0.36.
Lutsey*	Consumption of a Western DP promotes the incidence of MS, whereas dairy consumption provides some protection. Following a Prudent DP was not associated with MS risk.	Prudent DP, western DP	**Prudent DP (healthy):** cruciferous vegetables 0.62, carotenoid vegetables 0.60, fruit (no juice) 0.58, other vegetables 0.52, fish and sefood 0.46, poultry 0.43, dark leafy vegetables 0.43, whole grains 0.40, tomatoes 0.39, legumes 0.34, low-fat dairy 0.31, yogurt 0.27, nuts and peanut butter 0.26, fruit juice 0.24, potatoes 0.24, fat 0.21. **Western DP (unhealthy):** refined-grain bread/cereal/rice/pasta 0.63, processed-meat 0.63, fried foods 0.61, red meat 0.57, eggs 0.48, refined grain desserts 0.43, soda and sweetened beverages 0.41, cheese and whole milk 0.38, legumes 0.35, sweets/candy 0.30, fat 0.30, other vegetables 0.29, potatoes 0.28, ice cream 0.27, yogurt -0.21.

Yoo, Ki-Bong*	Eating breakfast itself reduced the risk for MS. Eating either a dairy cereal breakfast or high energy and fiber breakfast are associated with reduced risk of MS.	Traditional Korean DP, dairy-cereal DP	**Traditional Korean DP (unhealthy)*****: refined grains 0.26, vegetable oil 0.31, syrup and sugar 0.36, red pepper, soy sauce, soy bean paste 0.60, legumes 0.36, vegetables 0.50, garlic and onion 0.59, potatoe 0.25, kimchi (traditional fermented cabbage) 0.23, pork 0.41, organ meat -0.24, fish 0.35, salt 0.24. **Dairy-cereal DP (healthy):** refined grains -0.55, kimchi -0.39, dairy 0.77, fruit 0.25, cereal snack 0.53, bread 0.52, jam 0.31.
Duffey*	Prudent DP showed a lower risk of incident MS and each of its components than did a western DP.	Prudent DP, Western DP	**Western DP (unhealthy)***:** fast food, meat, poultry, pizza and snacks. **Prudent DP (healthy):** fruit, whole grains, milk, nuts and seeds.
Panagiotakos	Healthful DP is strongly associated with reduced levels of clinical and biological markers linked to MS, whereas High glycemic index and high fat DP showed opposite results.	Healthful DP, high glycemic index and high-fat DP, pasta DP, dairy products and eggs DP, sweets DP, alcohol DP	**Pasta DP (8.6%)***:** bread, pasta, biscuits -0.21. **Dairy products and eggs DP (6.2%)***:** whole milk 0.56, whole yoghurt 0.51, feta cheese 0.54, other cheese 0.44, egg 0.51. **Sweets DP (5%)***:** sweets 0.59. **Alcohol DP (4.8%)***:** alcoholic beverages -0.40. **Healthful DP (19.7%) (healthy):** cereals 0.71, small fish (e.g sardine) 0.59, big fish (e.g, sword fish) 0.58, greens 0.65, legumes 0.56, fruits 0.53, vegetables 0.70. **High glycemic index and high-fat DP (11.7%) (unhealthy):** beef 0.57, pork 0.47, other meat 0.41, meat products 0.71, poultry 0.54, fried potatoes 0.45, boiled-baked potatoes 0.36.

Hae Dong Woo	Traditional and Snack DP were not associated with an increased prevalence of MS. The meat DP was associated with a higher prevalence of MS in male adults.	Traditional DP, meat DP, snack DP	**Snack DP (5.6%) (unhealthy)***:** condiments 0.26, tubers 0.32, clams 0.26, tofu and soymilk 0.22, eggs 0.28, oil 0.20, fatty fish 0.29, carbonated beverages 0.27, dairy products 0.25, cakes and pizza 0.81, snacks 0.68, bread 0.60, processed meats 0.50, sweets 0.36, rice cake 0.23. **<u>Traditional DP (18.8%) (healthy):</u>** condiments 0.78, green and yellow vegetables 0.74, light colored vegetables 0.71, tubers 0.67, clams 0.63, tofu, soy milk 0.61, seaweeds 0.60, bonefish 0.54, kimchi 0.49, lean fish 0.46, mushrooms 0.42, fruits 0.40, nuts 0.37, legumes 0.29, yoghurt 0.27, eggs 0.27, pickled vegetables 0.24, milk 0.20, red meat 0.23, other seafood 0.25. **<u>Meat DP (7.5%) (unhealthy):</u>** light colored vegetables 0.40, clams 0.22, lean fish 0.37, mushrooms 0.36, red meat 0.79, red meat by-products 0.74, other seafood 0.67, high fat red meat 0.60, oil, 0.50, salted fermented seafood 0.44, noodles 0.43, poultry 0.43, fatty fish 0.37, carbonated beverages 0.36, dairy products 0.30, processed meats 0.29, sweets 0.28, coffee, tea 0.20.
Arisawa	Prudent DP and Bread and dairy products DP were associated with lower prevalence of some components of MS. A high fat/western DP was positively correlated with insulin resistance.	Prudent DP, high fat/western DP, bread and dairy products DP, seafood DP	**Bread and dairy products DP (29%)***:** rice -0.47, bread 0.62, margarine 0.52, milk 0.37, yoghurt 0.46, miso soup -0.32, liver -0.24, shell fish (cram, oyster) -0.31, salted cod roe, salmon roe -0.23, potatoes, taro, sweet potatoes 0.24, carrot 0.22, kiriboshi-daikon -0.20, mayonnaise -0.23, mandarine orange, orange, grape fruit 0.20, other fruits (strawberry, kiwi, apple, watermelon) 0.28, western-style confectionery 0.21. **Seafood DP (33%)***:** butter 0.28, liver 0.49, fish (raw, boiled, grilled) 0.36, small fish with bones 0.20, squid-shrimp-crab-octopus 0.44, shellfish (cram, oyster) 0.52, salted cod roe, salmon roe 0.55, other green and yellow vegetables (bell peppers, string beans) -0.21, cabbage -0.23, other vegetables (cucumber, onion, beans sprouts, chinese cabbage, lettuce) -0.28, fried foods -0.22, fried dishes -0.27, peanuts, almond 0.20, Japanese confectionary 0.31. **<u>Prudent DP (17%) (healthy):</u>** milk 0.23, miso soup 0.29, bean curd 0.22, soy beans, fermented soy beans 0.43, eggs 0.30, chicken 0.29, beef, pork 0.40, ham, sausage, salami, bacon 0.29, fish (raw, boiled, grilled) 0.48, small fish with bones 0.46, canned tuna 0.24, squid, shrimp, crab, octopus 0.21, shellfish (cram, oyster) 0.27, tube-shaped fish paste cake, boiled fish paste 0.30, deep-fried bean curd 0.50, potatoes, taro, sweet potatoes 0.63, pumpkin 0.52, carrot 0.69, broccoli 0.52, green leafy vegetables (spinach, komatsuna, garland chrysanthemum 0.67, other green and yellow vegetables (bell peppers, string beans) 0.66, cabbage 0.65, Japanese white radish 0.66, kiriboshi-daicon 0.37, burdock, bamboo shoot 0.56, other vegetables (cucumber, onion, bean sprouts, chinese cabbage, lettuce) 0.68, mushrooms 0.68, seaweed 0.53, mayonnaise 0.28, fried foods 0.30, fried dishes 0.49, mandarin orange, orange, grape fruit 0.55, other fruits (strawberry, kiwi, apple, watermelon) 0.53, peanuts, almond 0.26, Japanese confectionery 0.28, green tea 0.30. **<u>High fat/western DP (24%) (unhealthy):</u>** rice -0.23, bread 0.25, noodles 0.24, miso soup -0.38, soy beans, fermented soy beans -0.35, eggs 0.39, chicken 0.46, beef, pork 0.46, ham, sausage, salami, bacon 0.46, small fish with bones -0.40, canned tuna 0.28, squid, shrimp, crab, octopus 0.21, salted cod roe, salmon roe 0.29, mayonnaise 0.47, fried foods 0.57, fried dishes 0.47, western style confectionery 0.41, green tea -0.25.

Akter*	Westernized breakfast DP may confer some protection against MS.	Westernized breakfast DP, animal food DP, healthy Japanese DP	**Animal food DP (unhealthy)***:** cabbage/chinese cabbage 0.17, seaweeds 0.16, buckwheat noodles 0.18, squid/octopus/shrimp/shellfish 0.47, canned tuna 0.44, lean fish 0.43, pork/beef 0.43, dried fish/salted fish 0.41, ham/sausage/bacon 0.37, chicken 0.37, oily fish 0.33, lettuces/cabbage (raw) 0.30, tomatoes 0.29, mayonnaise/dressing 0.29, small fish with bones 0.28, liver 0.27, egg 0.21, black tea/oolong tea 0.19, other pickles 0.18, rice -0.67, pickled green leafy vegetables 0.18. **Healthy Japanese DP (healthy)***:** carrots and pumpkin 0.78, mushrooms 0.73, green leafs vegetables 0.69, cabbage/chinese cabbage 0.68, Japanese raddish/turnip 0.68, other root vegetables 0.67, tofu/atsuage 0.50, seaweeds 0.48, potatoes 0.46, other fruit 0.37, persimmons/strawberries/kiwi fruit 0.31, natto 0.30, citrus fruit 0.25, green tea 0.22, 100% fruit and vegetable juice -0.19, buckwheat noodles -0.25, cola drink/soft drink -0.29, chinese noodles -0.44, squid/octopus/shrimp/shellfish -0.16, lean fish 0.15, lettuces/cabbage (raw) 0.21, tomatoes 0.19, small fish with bones 0.20, ice cream -0.19, pickled green leaves vegetables 0.18. **Westernized breakfast DP (unhealthy):** tofu/atsuage -0.16, seaweeds -0.16, other fruit 0.21, 100% fruit and vegetable juice 0.17, cola drink/soft drink 0.15, squid/octopus/shrimp/shellfish -0.21, dried fish/salted fish -0.23, oily fish -0.29, lettuces/cabbage (raw) 0.17, mayonnaise/dressing 0.28, small fish with bones -0.23, egg 0.21, rice -0.34, bread 0.57, western type confectioneries 0.56, milk and yogurt 0.36, rice crackers/rice cake/okonomiyaki 0.36, Japanese confectioneries 0.36, ice-cream 0.32, miso soup -0.18, pickled green leaf vegetables -0.24.
Sun	Healthy DP descrease the chance of developing MS.	Healthy diet DP, western DP, balanced diet DP	**Healthy diet DP ***** **Western DP (8.66%) (unhealthy):** flour 0.69, light vegetable 0.60, grains 0.59, beans 0.57, soy beans 0.54, potatoes 0.43, water 0.38, peanuts sunflower 0.37, fresh milk 0.36, red meats 0.35. **Balanced diet DP (15.16%) (healthy):** fish 0.66, pork 0.55, poultry 0.38, vegetables 0.53, fruits 0.12, nuts , soybeans 0.32, rice 0.65.
Berg*	Fast energy DP was associated with MS.	Healthy DP, sweet DP, coffee DP, traditional DP, fast energy DP	**Healthy DP (healthy)***:** high-fiber cereals, fruits and vegetables, low-fat milk products, tea, fish. **Sweet DP (unhealthy)***:** sugar, soft drinks, white bread, tea, sweets and snacks. **Coffee DP (unhealthy)***:** coffee and alcoholic drinks. **Traditional DP***:** medium-fat milk, offal, boiled coffee, potatoes. **Fast energy DP (unhealthy):** soft drinks, white bread, fast food, full-fat milk, cheese, beer, spirits, sweets and snacks.

Noel*	A traditional pattern (high in beans, rice, oil) and a sweets patterns (high in sugar, sugary beverages and dairy desserts) were associated with MetS, and lower HDL-cholesterol.	Meat and French-Fries DP,traditional DP, sweets DP	**Sweets DP (unhealthy)***:** candy, sugar, and chocolate candy 0.53, soda 0.43, sweetened beverages 0.40, sweet baked goods 0.40, dairy desserts 0.37, salty snacks 0.26, French fries 0.21, reduced-fat dairy -0.21, whole grains -0.24, soups -0.29, oils -0.29, vegetables -0.37, poultry -0.38, fish -0.42 **Traditional DP (unhealthy)***:** oils 0.77, rice 0.76, beans/legumes 0.55, vegetables 0.21, reduced fat-dairy -0.20, solid fats -0.20, cold cereal -0.20, eggs -0.20, soups -0.20, pizza and Mexican -0.21, fish -0.22, nuts and seeds -0.27, condiments -0.30, high-fat diary -0.38 **Meat and French-Fries DP (unhealthy):** meat 0.58, processed meat 0.45, French fries 0.38, Pizza/Mexican 0.36, eggs, 0.35, alcohol 0.25, other grains/pasta 0.25, rice 0.24, oils 0.21, refined grains 0.20, whole grains -0.23, sweetened beverages -0.24, vegetables -0.25, poultry -0.25, citrus fruit and juice -0.30, cold cereal -0.37, hot cereal -0.40, other fruit and juce -0.48, reduced fat dairy -0.53
Liu*	Southern DP was associated with adverse risk factor profiles, including a larger WC, more VAT, elevated DBP, lower HDL-cholesterol and a greater likelihood of MetS. Prudent pattern was significantly associated, in a protective direction, with liver fat and hypertension.	Southern DP, fast food DP, prudent DP	**Fast food DP (unhealthy)***:** baked desserts 0.48, sugar and candy 0.60, fast food 0.62, fruit drinks 0.42, meat 0.47, milk and dairy 0.35, oils and salad dressing 0.39, processed meat and poultry 0.39, soda 0.42, salty snacks 0.61 **Prudent DP (healthy):** cold cereal 0.47, dairy desserts 0.36, fruit juice 0.31, fruit 0.63, hot cereal 0.49, milk and dairy 0.30, nuts and seeds 0.33 **Southern DP (unhealthy):** beans and legumes 0.59, bread 0.42, chicken and turkey 0.34, corn and corn products 0.52, eggs 0.46, fast food 0.32, margarine and butter 0.58, meat 0.44, miscellaneous fats 0.52, organ meats 0.45, vegetables 0.45, processed meats and poultry 0.47, rice and pasta 0.67, sea food 0.31, soups 0.36, potatoe 0.63

Sahay	The meat, alcohol and fish DP showed a strong association with metabolic disturbances, suggesting that higher intakes of meat and alcohol, despite fish consumption, may have detrimental health consequences.	Meat, alcohol and fish DP, sweets, grains and fats DP, olive oil, vegetables and fruits DP	**Sweets, grains and fats DP (unhealthy) (7.8%)***:** whole milk, goat milk, yogurt, cream, cottage cheese, mozzarella cheese, goat cheese 0.26, muesli, rice and pasta 0.21, cake, pastry and rolls 0.27, sugar cookie, compotes, chocolate, candy and jam and jelly 0.30, fruit juice and orange drink 0.22, margarine and butter 0.20 **Meat, alcohol and fish DP (unhealthy) (15.6%):** pork, beef, veal and lamb 0.24, haddock, salmon, sardines, shrimp, squid, octopus 0.21, beer, red wine, white wine, and spirit 0.22 **Olive oil, vegetables and fruits DP (healthy) (7.2%):** bacon, sausage, salami -0.24, leafy, roots, crouciferous, onion, garlic, tomato, eggplant, squash, mushroom 0.25, mixed nuts 0.24, eggs -0.24, olive oil 0.41, canola and vegetable oil -0.33
Barbaresko*	PCA derived DP showed statistically significant positive associations with BMI and WC.	PCA derived pattern (traditional German diet)	**PCA derived pattern (unhealthy) (5.1%):** leafy vegetables, fruiting vegetables, root vegetables, cabbage, other vegetables, beef, pork, processed meat, vegetable oil, other fats, sauce and bouillon.
Choi*	Prudent DP was negatively associated with the likelihood of having MetS, however the traditional and western DP did not significantly influence on the likelihood of developing MetS.	Traditional DP, western DP, Prudent DP	**Western DP (unhealthy) (7.8%)***:** red meat, high-fat red meat, oil, cakes/pizza, noodles, poultry, processed meats, sweets, red meat products, cracker/cookie, seafood products, carbonated beverages, legumes **Traditional DP (unhealthy) (11.5%):** light colored vegetables, green/yellow vegetables, condiments, shellfish, mushrooms, tofu/soymilk, seaweeds, lean fish, tubers, fatty fish, bonefish, other seafood, kimchi **Prudent DP (healthy) (5.4%):** bread, dairy products, nuts, milk, eggs, grains, fruit products, fruits

He	In female subjects, dairy and eggs DP was negatively associated with the odds of MetS and a 55% reduction in likelihood of having MetS. Refined grains and vegetables DP and organ meat and poultry DP were not associated with MetS.	Refined grains and vegetables DP, diary and eggs DP, organ meat and poultry DP, coarse grains and beans DP	**Organ meat and poultry DP (unhealthy) (10.30%)***:** refined grains 0.10 , vegetables -0.12, livestock meat 0.29, milk and dairy products 0.24, eggs -0.05, fruits -0.40, marine products 0.10, organ meats 0.68, poultry 0.52, coarse food grains 0.17, soybean and bean products -0.06 **Coarse grains and beans DP (healthy) (9.95%)***:** refined grains -0.05, vegetables 0.08, livestock meat 0.04, milk and dairy products -0.02, eggs -0.03, fruits 0.30, marine products 0.00, organ meats -0.06, poultry 0.25, coarse food grains 0.69, soybean and bean products 0.66 **<u>Refined grains and vegetables DP (unhealthy) (14.35%)</u>:** refined grains 0.67, vegetables 0.64, livestock meat 0.63, milk and dairy products -0.12, eggs 0.16, fruits 0.02, marine products 0.25, organ meats 0.04, poultry 0.14, coarse food grains -0.25, soybean and bean products 0.33 **<u>Diary and eggs DP (healthy) (14.04%):</u>** refined grains 0.02, vegetables 0.20, livestock meat 0.08, milk and dairy products 0.70, eggs 0.60, fruits, marine products 0.54, organ meats 0.16, poultry -0.03, coarse food grains 0.07, soybean and bean products -0.06
Suliga	The DP characterized by high consumption of fish as well as food with whole grains and a low consumption of refined products, sugar, and seeds as well as cured meat is connected with a lower risk of MetS, lower HDL cholesterol and increased glucose concentration.	Healthy DP, fat, meat and alcohol DP, prudent DP, coca-cola, hard cheese, French-fries DP	**Prudent DP (healthy) (5.5%)***:** fish 0.34, cold cured meat -0.41, bolied potatoes -0.62, whole grains 0.58, refined grains -0.70, sugar and sweets -0.55 **Coca-cola, hard cheese, French-fries DP (unhealthy) (5.02%)***** **<u>Healthy DP (healthy) (12.74%):</u>** low-fat milk 0.36, cottage cheese 0.53, yogurt 0.44, fruit 0.66, vegetables 0.62, whole grains 0.32 **<u>Fat, meat and alcohol DP (unhealthy) (9.69%):</u>** eggs 0.59, red meat 0.45, cold cured meat 0.33, lard 0.44, fried foods 0.49, vegetable oils 0.38, mayonnaise 0.39

Gadgil*	The animal protein DP and the fried snacks, sweets and high fat dairy DP were associated with adverse metabolic risk factors in South Asians whereas the fruit, vegetables, nuts and legumes DP was linked with a decreased prevalence of hypertension and MetS.	Animal protein DP, fried snacks, sweets, and high-fat dairy DP, fruits, vegetables, nuts, and legumes DP	**Animal protein DP (unhealthy)***** **Fried snacks, sweets, and high-fat dairy DP (unhealthy)** **Fruits, vegetables, nuts, and legumes DP (healthy)**
Bell	A healthy DP increased the odds of having a metabolically healthy profile.	Red meat and vegetable DP, refined and processed DP, healthy DP	**Red meat and vegetable DP (unhealthy) (9.8%)***:** yellow or red vegetables 0.59, potatoes 0.57, red meats 0.50, other vegetables 0.33, cruciferous vegetables 0.29, meat based mixed dishes -0.40 **Refined and processed DP (unhealthy) (7.5%):** added sugar 0.56, full-fat dairy products 0.41, unsaturated spreads 0.36, cakes, biscuits and sweet pastries 0.32, processed meat 0.25, canned fruit 0.25, soft drinks 0.25, other vegetables -0.26, fresh fruit -0.32 **Healthy DP (healthy) (4.6%):** whole grains 0.36, fresh fruit 0.35, low-fat dairy products 0.33, dried fruit 0.32, legumes 0.29, unsaturated spreads 0.25, take-away foods -0.28, soft drinks -0.33, alcoholic drinks -0.40, fried potatoes -0.42

*Some studies did not have the information requested.
**The information about how the pattern was categorized is situated between brackets.
***Patterns not included in the meta-analysis. The patterns included are underlined.

ONLINE SUPPLEMENT 2 (ARTICLE 2)

CHECKLIST for methodological assessment of cross-sectional and prospective studies included in review adapted from Tooth et al., Hayden et al., and Crichton et al.

STUDY DESIGN & METHOD

1.Sampling, recruitment methods, time and place of recruitment adequately described.

2.Inclusion and exclusion criteria adequately described.

3.Baseline characteristics of study sample adequately described (number of participants, age, gender, health status).

STUDY ATTRITION

Cross-sectional	*Prospective*
4.Justification or explanation for the number of participants.	4.Specification of number at each follow-up period and duration of follow-up.
5.Explanation of how missing data was dealt.	5.Analyses conducted to determine whether participants lost to follow-up do not significantly differ in key-characteristics/outcomes from those who completed the study.

MEASUREMENT OF PREDICTOR VARIABLE

6.Method used to assess dietary intake adequately described and reference provided.

7.Reliability and validity of measurement tool(s) mentioned.

8.Dietary patterns adequately described in sample.

9.Dietary patterns associated with outcome measure of interest clearly described.

MEASUREMENT OF OUTCOME VARIABLE

10.Criteria used to define MS provided and any modifications to criteria adequately described.

11.Number of participants with MS provided at baseline (and follow-up for prospective studies).

ANALYSIS

12.Potential confounders mentioned and accounted for in analyses.

13.Specific type of analyses adequately described.

14.Measure of association provided with confidence intervals.

15.The impact of biases/limitations to study assessed qualitatively.

Methodological appraisal scores for the included studies in the primary review

Study	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	T
Cross-sectional																
Song; 2012	1	1	0.5	1	0	1	0.5	1	1	1	1	1	1	1	1	**13**
Wagner; 2012	1	1	1	1	1	0.5	0.5	1	1	1	1	1	1	1	1	**14**
Naja; 2013	1	0.5	1	0.5	0	1	1	1	1	1	1	1	1	1	1	**13**
Leite; 2009	1	1	0.5	0.5	0	1	1	1	1	1	1	1	1	1	1	**13**
Esmaillzadeh; 2007	1	1	0.5	1	0	1	1	1	1	1	1	1	1	1	1	**13.5**
Desmukh-Taskar; 2009	1	1	1	0.5	0	1	1	1	1	1	1	1	1	1	1	**13.5**
Denova-Gutiérrez; 2010	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	**13.5**
Amini; 2010	1	1	1	0.5	0	0.5	1	1	1	1	1	1	1	1	1	**13**
Cho; 2011	1	1	0.5	0.5	0	1	1	1	1	1	1	1	1	1	1	**13**
Hong; 2012	1	1	0.5	0.5	0	0.5	0.5	1	1	1	1	1	1	1	1	**12**
Heidemann; 2011	1	1	1	1	0.5	1	1	1	1	1	0.5	1	1	1	1	**14**
Kim; 2011	1	1	0.5	0.5	0	1	0.5	1	1	1	1	1	1	1	0.5	**12**
Yoo, Ki-Bong; 2014	1	0.5	0.5	0.5	0	0.5	0.5	1	1	1	1	0.5	1	1	1	**11**
Panagiotakos; 2007	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	**14**
Hae Dong Woo; 2014	1	1	1	1	0	1	1	1	1	1	1	0.5	1	1	1	**13.5**
Arisawa; 2014	1	1	1	0.5	0	0.5	0.5	1	1	1	1	0.5	1	1	1	**12**
Akter; 2013	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	**14**
Sun; 2014	0.5	0.5	1	1	0	0.5	0.5	0.5	0.5	0.5	1	0.5	1	1	0.5	**9.5**
Berg; 2008	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	**14**
Noel; 2009	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	**14**
Liu; 2013	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	**14**
Sahay; 2013	1	1	1	1	0	1	1	1	1	1	1	1	1	0	1	**13**
Barbaresko; 2014	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	**14**
Choi; 2015	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	**14**
He; 2015	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	**14**
Suliga; 2015	1	1	1	1	0	0.5	1	1	1	1	1	1	1	1	1	**13.5**
Gadgil; 2015	1	1	1	1	0	1	1	1	1	0.5	1	1	1	1	1	**13.5**
Bell; 2015	1	1	1	1	0	1	0.5	1	1	0.5	1	1	1	1	1	**13**
Cohort																
Kimokoti; 2012	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	**14**
Lutsey; 2008	1	1	1	1	0.5	1	1	1	1	1	1	1	1	1	1	**14.5**
Duffey;2012	1	1	1	1	0.5	1	1	1	1	1	1	1	1	1	1	**14.5**