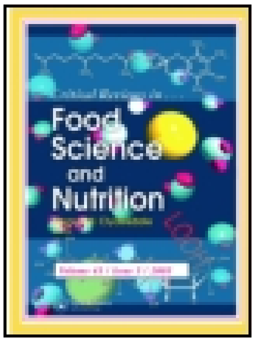

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Dietary Patterns and the Risk of Obesity, Type 2 Diabetes Mellitus, Cardiovascular Diseases, Asthma, and Mental Health Problems.

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ABSTRACT

Diet and lifestyle play a significant role in the development chronic diseases; however the full complexity of this relationship is not yet understood. Dietary pattern investigation, which reflects the complexity of dietary intake, has emerged as an alternative and complementary approach to examining the association between diet and chronic diseases. Literature on this association has largely focused on individual nutrients, with conflicting outcomes, but individuals consume a combination of foods from many groups that form dietary patterns. Our objective was to

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systematically review the current findings on the effects of dietary patterns on chronic diseases. In this review, we describe and discuss the relationships between dietary patterns, such as the Mediterranean, the Dietary Approach to Stop Hypertension, Prudent, Seventh-day Adventists, and Western, with risk of obesity, type-2 diabetes mellitus, cardiovascular diseases, asthma, and mental health problems. Evidence is increasing from both observational and clinical studies that plant-based dietary patterns, which are rich in fruits, vegetables, and whole grains, are valuable in preventing various chronic diseases, whereas a diet high in red and processed meat, refined grains and added sugar seems to increase said risk. Dietary pattern analysis might be especially valuable to the development and evaluation of food-based dietary guidelines.

Keywords

Mediterranean diet; DASH diet; Prudent diet; Seventh-day Adventists diet; Western diet.

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INTRODUCTION

Diet-related chronic diseases, frequently referred to as “lifestyle diseases” include obesity, coronary heart disease, type 2 diabetes mellitus, various inflammatory conditions and certain cancers, and are believed to be caused both by dietary changes and reduced physical activity (World-Health-Organization, 1990). Currently, levels of obesity in the US adult population stand at 34.9% (Ogden et al., 2014), diabetes levels stand at 9.3% (US-Department-of-health-and-human-services, 2014), more than one third of the population suffers from some form of cardiovascular disease (CVD) (Lloyd-Jones et al., 2010), and rates of metabolic syndrome (MetS), a cluster of clinical conditions including impaired glucose metabolism, central obesity, elevated triglycerides, reduced HDL-cholesterol and hypertension (Alberti et al., 2006; Alberti et al., 1998) have reached 25%. However, these conditions are considered to be preventable by dietary/lifestyle interventions (Franz et al., 2002; Stampfer et al., 2000; World-Health-Organization-UNAIDS, 2007; World-Health-Organization, 2000), thus, highlighting the importance of research on the role of nutrition in disease prevention.

Nutritional epidemiology has traditionally focused on the relationship of specific foods and nutrients with disease outcomes (Mozaffarian et al., 2011). However, an individual’s diet is made up of a complex mix of different foods and not individual nutrients (National-Research-Council, 1989), which makes identification of the role of individual foods or nutrients in specific health outcomes difficult to ascertain (Ursin et al., 1993). In recent years the study of overall dietary patterns, which takes into account both the complexity and cumulative/synergistic effect of the foods that make up a diet, has emerged as a useful tool in the study of how diet affects health (Kant, 1996; Millen et al., 2001; Millen et al., 2005). For example, accumulating evidence

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from dietary intervention studies has proven the efficacy of the Mediterranean dietary pattern in both the primary and secondary prevention of cardiovascular disease (de Lorgeril et al., 2006a, 2006b; Estruch et al., 2013). Other population-based studies have associated the consumption of a traditional Okinawan dietary pattern with reduced incidence of cardiovascular disease, some cancers, and other chronic diseases (Willcox et al., 2009). Additionally, the use of the Dietary Approaches to Stop Hypertension (DASH) dietary pattern has been shown to be effective in protecting against CVDs (Salehi-Abargouei et al., 2013).

Thus, not only are dietary patterns effective for the prevention of certain conditions but also are more easily translatable into actionable changes by the general population (Ammerman et al., 2002; Hulshof et al., 2001; Krauss et al., 2000), thus potentially improving their public health-impact.

In this review we analyze the current evidence relating the adherence to a number of different dietary patterns with the risk of certain diet-related chronic conditions including obesity, type 2 diabetes mellitus, cardiovascular disease, asthma and various mental health problems.

Dietary patterns investigated in this review

For the purposes of this review the following 5 dietary patterns were investigated:

The “Western pattern” characterized by higher intake of processed meat, red meat, butter, high-fat dairy products, eggs and refined grains (Hu, 2002), the “prudent pattern” characterized by higher intakes of fruits, vegetables, whole grains, legumes and fish (Hu, 2002), the Mediterranean diet (Med-Diet) characterized by a high consumption of plant foods (fruits,

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vegetables, breads, other forms of cereals, legumes, nuts, and seeds), fresh fruit as the typical daily dessert, abundant use of olive oil as the major culinary fat, moderate consumption of dairy products (mainly cheese and yogurt), poultry fresh fish, seafood, and eggs, low consumption of red and processed meat, and frequent but moderate intake of wine, usually with meals (Willett et al., 1995), the Dietary Approaches to Stop Hypertension (DASH) diet which is high in fruits, vegetables, whole cereal products, low-fat dairy products, fish, chicken, and lean meats designed to be low in saturated fat and cholesterol, moderately high in protein and high in minerals and fiber (Sacks et al., 2001), and the Seventh-Day Adventist diet which is characterized as a mostly lacto-ovo vegetarian diet with followers abstaining from alcohol, pork products and tobacco (Beeson et al., 1989).

MEDITERRANEAN DIET PATTERN

The Med-Diet is defined as the traditional dietary pattern found in Greece, Southern Italy, Spain and other olive-growing countries of the Mediterranean basin in the early 1960s (Willett et al., 1995). Recently, in 2010, the Med-Diet was recognized by UNESCO as a cultural heritage of Humanity, incorporating in its definition other aspects, such as conviviality, socialization, biodiversity and seasonality, Figure 1 (Bach-Faig et al., 2011).

Obesity

Regarding the association between adherence to the Med-Diet pattern and obesity, some cohort studies reported that adherence to the Med-Diet pattern was significantly associated with reduced weight gain, and also reduced risk of developing overweight or obesity. Mendez *et al.* determined whether a Med-Diet pattern was associated with a reduced incidence of obesity over

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3 years using data from the Spanish cohort of the EPIC-Spain study. High Med-Diet adherence was associated with significantly lower likelihood of becoming obese among overweight subjects, observing similar association in women (OR = 0.69; 95% CI: 0.54 to 0.89) and men (0.68; CI: 0.53 to 0.89) (Mendez et al., 2006). However, Med-Diet adherence was not associated with incidence of overweight in initially normal-weight subjects.

Another Spanish cohort (Beunza et al., 2010) studied the association between adherence to Med-Diet and weight change, as well as assessing the risk of relevant weight gain or the risk of developing overweight or obesity. Participants with the lowest score of adherence to the Med-Diet exhibited the highest average yearly weight gain, while those with the highest adherence exhibited the lowest weight gain (−0.059 kg/y; $P = 0.02$). The group with the highest adherence to the Med-Diet also showed the lowest risk of relevant weight gain (≥5 kg) during the first 4-y of follow-up (OR = 0.76; CI: 0.64 to 0.90). In 373,803 individuals from EPIC-PANACEA project (Romaguera et al., 2010), from 10 European countries; individuals with a high adherence to the Med-Diet pattern showed a 5-y weight change of -0.16 kg and were 10% less likely to develop overweight or obesity than individuals with a low adherence to the Med-Diet pattern.

Three interventional dietary studies (Andreoli et al., 2008; Goulet et al., 2003; Martínez-González et al., 2012) found that adherence to a Med-Diet significantly decreased weight/BMI and, specifically, abdominal obesity. A strong inverse linear association between the 14-item tool and all adiposity indexes was found in 7,447 participants from the PREDIMED study (Martínez-González et al., 2012), the multivariable-adjusted OR for the waist-to-height ratio >0.6 was 0.68 (CI: 0.57 to 0.80) for women and 0.66 (CI: 0.54 to 0.80) for men, in participants with a higher

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Med-Diet score compared with those with a lower score. In 47 obese women (Andreoli et al., 2008) body weight, BMI, and fat mass, significantly decreased after 2 and 4 months with a moderately hypoenergetic Med-Diet and exercise program. Goulet *et al.* examined the effect of a nutritional intervention promoting the Med-Diet pattern in uncontrolled “real life” conditions among a group of 77 French-Canadian women. Small but significant decreases in BMI were observed after 6 weeks of intervention with a Med-Diet (Goulet et al., 2003).

The EPIC-PANACEA study by Romaguera *et al*. found that higher adherence to the Med-Diet was significantly associated with lower abdominal adiposity for a given BMI, measured by waist circumference, in both men and women. This association was stronger in men (−0.20; CI: −0.23 to −0.17) and women (−0.17; CI: −0.21 to −0.13) from Northern European countries, while the Med-Diet was not significantly associated with BMI (Romaguera et al., 2009).

Other cross-sectional studies (Lazarou et al., 2010; Panagiotakos et al., 2006; Schröder et al., 2004) found that greater adherence to a Med-Diet had a significantly negative association with overweight/obesity. The strongest association was reported in the ATTICA study by Panagiatakos *et al.* in this study greater adherence to the Med-Diet was associated with a 51% lower odds of being obese (OR = 0.49; CI: 0.42 to 0.56) and a 59% lower odds of having central obesity (OR = 0.41; 0.35 to 0.47) compared with a non-Med-Diet, after adjustment for potential confounders (Panagiotakos et al., 2006). In other cross-sectional Spanish population study (Schröder et al., 2004) an increase of 5-units in the Med-Diet score was associated with a statistically significant reduction in the BMI of 0.43 kg/m^2 and 0.68 kg/m^2, in men and women, respectively, and consequently, the obesity risk decreased in men (P = 0.010) and women (P =

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0.013) with increasing adherence to the traditional Med-Diet pattern. In the CYKIDS study (Lazarou et al., 2010) children with a high KIDMED score were 80% less likely to be overweight or obese, although, when physical activity was taken into account, this relationship became less significant. Moreover, children with higher adherence to a Med-Diet reported following a healthier diet and also having higher physical activity levels (Farajian et al., 2011). In contrast, Tripocholou *et al.* did not find any association between Med-Diet adherence and weight (Trichopoulou et al., 2005).

In conclusion, these studies show that promoting the Med-Diet pattern as a model of healthy eating may help to prevent weight gain and the development of overweight, obesity and central obesity.

Type 2 diabetes mellitus

The Med-Diet has been suggested to have a beneficial effect in the primary prevention of diabetes, although results have not been consistent. The relationship between type 2 diabetes and the Med-Diet has been confirmed by the recent results of the PREDIMED study (Estruch et al., 2006; Salas-Salvadó et al., 2014). In this trial, that included 3,541 high-risk participants who were followed-up a mean of 4.8 years, the group treated with a Med-Diet supplemented with extra virgin olive oil had the lowest incidence of diabetes, and a significantly decreased HR (0.60; CI: 0.43 to 0.85) compared with the control diet group. In the Med-Diet supplemented with nuts, the decreased HR did not achieve statistical significance (0.82; CI: 0.61 to 1.10) when compared with the control diet (Salas-Salvadó et al., 2014). In fact, in the analysis of the pilot study of this trial, evaluated the short-term effects of two Med-diets versus those of a low-fat diet in 772 high cardiovascular risk persons, including 421 (54.5%) diabetic patients: after 3 months, the Med-diet groups had lower fasting glucose than the low-fat diet group (Estruch et al., 2006). Thus, Med-Diets without calorie restriction appear to be helpful in the prevention of diabetes in subjects at high cardiovascular risk.

In the large GISSI-Prevenzione study including 8291 Italian patients with recent myocardial infarction, followed up for 3.5 years and who were free of diabetes at baseline, a Med-diet protected against new diabetes (OR = 0.65, CI: 0.49 to 0.85) in the highest quintile *vs* lowest quintile of adherence (Mozaffarian et al., 2007). The Med-Diet score was significantly associated with reduced risk of type 2 diabetes in 41, 615 Men from the Health Professionals Follow-Up Study, followed over ≤ 20 years. The participants in the top quintile of the Med-Diet score had a 25% lower risk than those in the bottom quintile, HR = 0.75; (CI: 0.66 to 0.86) (de Koning et al., 2011) and the reduction in the incidence of diabetes achieved 83% in the top tertile of Med-Diet score among 13,380 Spanish university graduates from the SUN project ("Seguimiento Universidad de Navarra") (Martínez-González et al., 2008). Other large cohort studies such as and European Prospective Investigation into Cancer and Nutrition (EPIC) study (Romaguera et al., 2011; Rossi et al., 2013) have obtained similar results. However, the Med-Diet was not significantly related to the risk of incident diabetes (*P* for trend = 0. 64) in Multi-Ethnic Study of Atherosclerosis (Abiemo et al., 2013).

Intervention trials have also evaluated the effects of different Med-Diets on glucose metabolism and incidence of diabetes. Shai *et al*. compared 3 weight-loss diets in 322 moderately obese subjects, including 46 diabetic patients, in a 2-year trial. Among the participants with diabetes,

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there was a significant decrease in fasting glucose concentration (−32.8 mg/dl) in the Med-diet group and an increase (12.1 mg/dl) in the low-fat diet group (Shai et al., 2008).

Esposito *et al.* evaluated the metabolic effects of a Med-diet and a low fat diet in 215 patients with newly diagnosed type 2 diabetes. Fasting glucose decreased more in the Med-diet group than in low-fat diet group after one year of intervention (−21 mg/dl, CI: −30 to −13 mg/dl); additionally, hemoglobin A1c (HbA1c) levels were lower in the Med-diet group than the low fat diet group (−0.6%, CI: −0.9 to −0.3%) (Esposito et al., 2009). In other comparative study of a low-carbohydrate Med-diet *vs*. the American Diabetes Association diet in 259 overweight type 2 diabetic patients, Elhayany *et al.* found a non-significant decrease in fasting glucose. The reduction in HbA1c was significantly greater in the low-carbohydrate Med-diet than in the American Diabetes Association diet (−2% *vs* −1.6%, respectively, $P = 0.022$) (Elhayany et al., 2010).

Adherence to the Med-Diet pattern is associated with lower type 2 diabetes mellitus risk among women with a history of gestational diabetes mellitus. Tobias *et al*. evaluated 4413 participants from the Nurses' Health Study II cohort, in this study an alternate Med-Diet pattern was associated with 40% lower risk of type 2 diabetes mellitus, HR = 0.60 (CI: 0.44 to 0.82) (Tobias et al., 2012a). Previously, a Med-Diet pattern was inversely associated with gestational diabetes mellitus risk after adjustment for several covariables, in 21,376 singleton live births reported from 15,254 participants of the Nurses' Health Study II cohort. In a comparison of the multivariable risk of gestational diabetes mellitus in participants in the fourth and first quartiles

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of dietary pattern adherence scores, the Med-Diet was associated with a 24% lower risk, RR = 0.76; (CI: 0.60 to 0.95) (Tobias et al., 2012b).

Two recent meta-analyses have evaluated the effects of Med-Diets on the development of type 2 diabetes. Koloverou *et al.* obtained a significant 23% reduction in the risk of developing type 2 diabetes mellitus for the highest versus the lowest centile of the score used to evaluate adherence to the Med-Diet (combined effect, RR = 0.77; CI: 0.66 to 0.89) (Koloverou et al., 2014).

Another recent meta-analysis of randomized controlled trials and cohort studies showed that greater adherence to a Med-Diet is associated with a significant reduction in the risk of diabetes (19%; moderate quality evidence), the pooled risk ratio for highest adherence to the Med-Diet was 0.81 (CI: 0.73 to 0.90), compared with lowest adherence. The relative risk for developing type 2 diabetes according to adherence to a Med-Diet was significantly different when comparing European and US studies. Interestingly, there was a significant association in the European analysis (RR = 0.81; CI: 0.71 to 0.93) but not in the US analysis (RR = 0.82; CI: 0.68 to 1.00) with the US analysis not being considered significant (Schwingshackl et al., 2015).

Cardiovascular diseases

The relationship between dietary factors and coronary heart disease (CHD) has been a major focus of health research for the last 50 years. The first step in the management of hypertension and other coronary risk factors is to follow a healthy diet such as the traditional Med-Diet and/or to improve lifestyle, for instance, by reducing body weight and increasing physical activity (Mancia et al., 2007). Consequently, several studies have pointed out that a higher adherence to the Med-Diet improves CHD prognosis and inversely reduces CHD mortality.

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The PREvención con DIeta MEDiterránea (PREDIMED) study is the first large randomized trial to show that a Med-Diet is able to reduce clinical events in primary cardiovascular prevention (Estruch et al., 2013). Participants in this trial were men and women from 55 to 80 years at high cardiovascular risk. They were randomly allocated to one of the following three diets: a Med-Diet rich in mixed nuts, a Med-Diet rich in extra virgin olive oil, and a control group, which consumed a low-fat American Heart Association type diet. A 30% reduction in the risk of a combined cardiovascular end-point (myocardial infarction, stroke or cardiovascular death) was observed for both groups allocated to the Med-Diet. Compared with the control group, the hazard ratio was 0.70 (CI: 0.54 to 0.92) for the Med-Diet with extra-virgin olive oil and 0.72 (CI: 0.54 to 0.96) for the Med-Diet with nuts. The trial was stopped after a median follow-up of 4.8 years because of the early evidence of benefit. A random effect meta-analysis combining this trial and a randomized trial (the Lyon Diet Heart Study) showed a relative 38% reduction in the risk of CVD after intervention with a Med-Diet with a pooled risk ratio of 0.62 (CI: 0.45 to 0.85) (Martinez-Gonzalez et al., 2014).

The pooled analyses of cohort studies showed that an increased adherence to a Med-Diet RR = 0.63 (CI: 0.53 to 0.72) and high-quality diet patterns RR = 0.63 (CI: 0.45 to 0.81) were each associated with a significantly lower risk of CHD. The pooled analysis of randomized controlled trials showed that Med-Diet pattern was associated with a significantly lower risk of CHD, RR = 0.32 (CI: 0.15 to 0.48) (Mente et al., 2009). Kastorini *et al.* evaluated the association between adherence to the Med-Diet and the development of an acute coronary syndrome or ischemic stroke and noted that for each one unit increase of a Med-Diet score (with a scale of 1-55), the corresponding OR for having an acute coronary syndrome was 0.91 (CI: 0.87 to 0.96), whereas concerning stroke, it was 0.88 (CI: 0.82 to 0.94) (Kastorini et al., 2011). In another case-control study (Yau et al., 2011), the Med-Diet was significantly and negatively associated with ischaemic stroke (OR = 0.1; CI: 0.02 to 0.4). Some longitudinal cohort studies merit to be commented separately. In the Nurses' Health Study, a greater adherence to the Med-Diet was associated with a lower risk of stroke in 74,886 women from the Nurses' Health Study. Women in the top Med-Diet score quintile were at lower risk of stroke compared with those in the bottom quintile (RR = 0.87; CI: 0.73 to 1.02) (Fung et al., 2009). In the EPICOR study, Agnoli *et al.* investigated the association between stroke and adherence to a Greek and Italian Mediterranean Index, during a mean follow-up of 7.9 y. The Italian Mediterranean Index was significantly inversely associated with risk of all types of stroke (HR = 0.47; CI: 0.30 to 0.75; third vs. first tertile) and with ischemic stroke (HR = 0.37; CI: 0.19 to 0.70), and tended to be inversely associated with hemorrhagic stroke (HR = 0.51; CI: 0.22 to 1.20) (Agnoli et al., 2011).

In the Greek EPIC cohort, adherence to the Med-Diet was associated with a non-significant lower CHD incidence, and a statistically significant reduction in CHD mortality of 25% among women and 19% among men (Dilis et al., 2012). Other results from this same cohort, during a median follow-up period of 10.6 years, reported a significant inverse association with cerebrovascular disease incidence (HR = 0.85; CI: 0.74 to 0.96) and mortality (HR = 0.88; CI: 0.73 to 1.06) (Misirli et al., 2012).

In the Spanish EPIC Cohort Study, 41,078 participants aged 29-69 years, with a mean follow-up of 10.4 years, showed that a high Med-Diet score was associated with a 40% reduction in CHD risk when compared with a low Med-Diet score. A 1-unit increase in relative Med-Diet score

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was associated with a 6% reduced risk of CHD (Buckland et al., 2009) and in another Spanish cohort study, for each 2-point increment in the score of adherence to Med-Diet, the adjusted HR were 0.80 (CI: 0.62 to 1.02) for total CVD and 0.74 (CI: 0.55 to 0.99) for CHD (Martínez-González et al., 2011).

Tognon *et al.* determined whether three distinct variations of the Med-Diet Score (which varied according to the method of 7-d food record assessment) were associated with reduced total mortality, cardiovascular incidence and mortality in 1849 men and women, from the Danish multinational MONItoring of trends and determinants in CArdiovascular disease (MONICA) cohort. All three Med-Diet scores were inversely associated with the endpoints, although associations with score 1 did not reach statistical significance (Tognon et al., 2014). In an Italian middle-aged male population, from the Seven Countries Study, Mediterranean Adequacy Index showed a significant 26% relative reduction in CHD mortality for each 2.7-point increment, after 20 years of follow-up, and 21% after 40 years of follow-up (Menotti et al., 2012). Similar results were observed in the Monitoring Project on Risk Factors and Chronic Diseases in the Netherlands (MORGEN) study (Hoevenaar-Blom et al., 2014).

In studies performed in USA, in the Northern Manhattan Study Med-Diet was also inversely associated with risk of the composite outcome of CVD (ischemic stroke, myocardial infarction or vascular death) (Gardener et al., 2011) and, in the Nurses' Health Study, women in the top Med-Diet score quintile were at lower risk for CHD compared with those in the bottom quintile (RR = 0.71; CI: 0.62 to 0.82). Cardiovascular disease mortality was significantly lower among women in the top quintile of the Med-Diet score (RR = 0.61; CI: 0.49 to 0.76) (Fung et al., 2009).

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Martínez-González MA *et al.* in a recent systematic review, showed that each 2-point increment in a 0--9 score of adherence to the Med-Diet was associated with a 13% relative reduction in the incidence of CVD (RR = 0.87; CI: 0.85 to 0.90) (Martinez-Gonzalez et al., 2014). These results were highly consistent with the previous reported by Sofi *et al.* (Sofi et al., 2010). All this evidence suggests that the promotion of the Mediterranean dietary pattern can be a successful and feasible tool for the prevention of CVD.

Other studies have analyzed the effects of Med-Diet on main cardiovascular risk factors. In the SUN study, adherence to the Med-Diet was associated with reduced changes in mean levels of systolic blood pressure (BP) (moderate adherence, --2.4 mm Hg; high adherence, --3.1 mm Hg) and diastolic BP (moderate adherence, --1.3 mm Hg; high adherence, --1.9 mm Hg) after a 6-year follow-up, suggesting that adherence to a Mediterranean-type diet could contribute to the prevention of age-related changes in BP (Nuñez-Córdoba et al., 2008). Estruch *et al.* compared the short-term effects of two Med-diets versus those of a low-fat diet and after 3-months of intervention participants included in the Med-Diet groups showed a significant decrease in systolic and diastolic BP measurements compared to the low-fat diet group (Estruch et al., 2006). Epidemiological evidence suggests that a polyphenol-rich diet may help to prevent BP from increasing and reduce high BP levels in people with normal-to-high BP or hypertension (Whelton et al., 2002). In another PREDIMED trial, the Med-Diet significantly reduced BP compared with the control group after a 4-year intervention (Toledo et al., 2013). Recently, in elderly participants at high cardiovascular risk included in the PREDIMED trial, we observed that the changes in plasma nitric oxide were associated with significantly lower systolic and diastolic BP after one-year interventions with Med-Diets supplemented with extra virgin olive oil

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or nuts, compared with the control diet (Medina-Remón et al., 2015). In another PREDIMED sub-study, Med-Diets reduced 24-hour ambulatory systolic and diastolic BP after a 1-year intervention (Doménech et al., 2014). Part of the effects of Med-Diet on BP has been attributed to its high polyphenol content (Medina-Remón et al., 2011).

Asthma

Healthy dietary habits such as Med-Diet may influence incidence and severity of bronchial asthma. Several cross sectional studies (Arvaniti et al., 2011; Barros et al., 2008; Castro-Rodriguez et al., 2008; de Batlle et al., 2008; Garcia-Marcos et al., 2007; Grigoropoulou et al., 2011; Miyake et al., 2011; Nagel et al., 2010), but not all (Chatzi et al., 2007; Gonzalez Barcala et al., 2010) have observed a negative association between adherence to Med-Diet and incidence of asthma. Thus, high adherence to a Med-Diet reduced the risk of uncontrolled asthma by 78% (OR = 0.22; CI: 0.05 to 0.85) in 174 asthmatics. The higher intake of fresh fruit decreased the probability of having non-controlled asthma (OR = 0.29; CI: 0.10 to 0.83), while the higher intake of ethanol had the opposite effect (OR = 3.16; CI: 1.10 to 9.11) (Barros et al., 2008).

Higher Mediterranean score was associated with a lower prevalence of ever-asthma (incidence of asthma at some time) (OR = 0.84; CI: 0.77 to 0.91) in 10- to 12-year-old children from Greece. When stratifying the analysis by area of living, adherence to the Med-Diet was associated with lower probability of asthma in both urban and rural areas (urban, OR = 0.81; CI: 0.73 to 0.91; rural, OR = 0.87; CI: 0.75 to 1.00) (Grigoropoulou et al., 2011). In other study that measure the adherence to Med-Diet using the KIDMED score, a one-unit increase in this score was associated with a 14% lower likelihood of having asthma symptoms (OR = 0.86; CI: 0.75 to

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0.98), after adjusting for various confounders (Arvaniti et al., 2011). In fact, several studies performed different countries have observed that, greater adherence to a Med-Diet was associated with a lower prevalence of ever-asthma and current wheezing (Castro-Rodriguez et al., 2008; de Batlle et al., 2008; Garcia-Marcos et al., 2007; Nagel et al., 2010).

In addition, Sexton *et al.* who evaluated the benefits of a Med-Diet on 38 adults with symptomatic asthma in a 12-week open-label randomized trial, observed that the intervention group with a higher Med-Diet score achieved a small but non-significant improvement in asthma-related quality of life (Sexton et al., 2013).

During pregnancy, higher adherence to a Med-Diet was a protective factor against persistent wheeze (OR 0.22; CI: 0.08 to 0.58) and atopic wheeze (OR = 0.30; CI: 0.10 to 0.90) in offspring at age 6.5 years (Chatzi et al., 2008). However, recently the adherence to a Med-Diet during pregnancy was not associated with wheeze in the first year of life (Chatzi et al., 2013), nor was the Med-Diet score associated with ever-wheezing during the first year, in other study conducted in 1,409 healthy infants from Spain. Interestingly, in this study olive oil was protective against ever-wheezing (OR = 0.57; CI: 0.4 to 0.9) (Castro-Rodriguez et al., 2010). Thus, this issue is still open and new studies are needed.

A recent meta-analysis showed that adherence to the Med-Diet was negatively associated with current wheeze (OR = 0.79; CI: 0.66 to 0.94; $P = 0.009$) and current severe wheeze (OR = 0.66; CI: 0.48 to 0.90; $P = 0.008$) in Mediterranean regions, and with ever-asthma (OR = 0.86; CI: 0.75 to 0.98; $P = 0.027$) in non-Mediterranean regions. Considering all regions together, the

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Med-Diet tended to have a protective effect on current wheeze and ever-asthma but not on current, severe wheeze (Lv et al., 2014).

These conclusion was confirmed by the results of another recent meta-analysis of eight cross-sectional studies in children that concluded that the Med-diet might protect against ever-asthma and current wheeze (Garcia-Marcos et al., 2013). Thus, these meta-analyses and other additional studies suggest that the Med-Diet is potentially protective against childhood asthma.

Mental health problems

Greater adherence to a Med-Diet is linked to lower risk of chronic diseases, and now we have additional evidence showing the protective effects of Med-Diet on cognitive decline and dementia.

In relation to cognitive decline and dementia, in a case-control study within a community-based cohort in New York, higher adherence to the Med-Diet was associated with lower risk of Alzheimer's disease (OR = 0.76; CI: 0.67 to 0.87). Compared with subjects in the lowest Med-Diet tertile, subjects in the middle Med-Diet tertile had an OR of 0.47 (CI: 0.29 to 0.76) and those at the highest tertile an OR of 0.32 (CI: 0.17 to 0.59) for Alzheimer disease (Scarmeas et al., 2006).

In cohort studies such as a multiethnic community study from New York, higher adherence to the Med-Diet was associated with a trend for reduced risk of developing mild cognitive impairment and with reduced risk of mild cognitive impairment conversion to Alzheimer's disease. Compared with subjects in the lowest Med-Diet adherence tertile, subjects in the highest

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tertile had 28% less risk (HR = 0.72; CI: 0.52 to 1.00) of developing mild cognitive impairment. Subjects in the highest Med-Diet adherence tertile had 48% less risk (HR = 0.52; CI: 0.30 to 0.91) of developing Alzheimer's disease, compared with subjects in the lowest tertile (Scarmeas et al., 2009b). Feart *et al.* also investigated the association of a Med-Diet with changes in cognitive performance and risk of dementia in elderly French persons and, found that higher adherence to a Med-Diet was associated with slower Mini-Mental State Examination (MMSE) cognitive decline but although no such observations were made with other cognitive tests (Feart et al., 2009).

In another prospective cohort study of 2 groups comprising of 1880 community-dwelling elders without dementia living in New York, moderate (HR = 0.98; CI: 0.72 to 1.33), and high Med-Diet scores (HR = 0.60; CI: 0.42 to 0.87), were associated with lower Alzheimer's disease risk when compared with low diet scores (Scarmeas et al., 2009a). Another longitudinal study showed a 21% reduced risk of mild cognitive impairment or dementia in subjects in the second tertile of the Med-Diet score, and 25% for subjects in the upper tertile at baseline although the association did not reach statistical significance (Roberts et al., 2010). Similar results were obtained by Gardener *et al.* in an Australian cohort (Gardener et al., 2012) and by Tangney *et al.* in a biracial Midwest population of older adults (Tangney et al., 2011). However, other cohort studies failed to find a significant association between adherence to Med-diet and better cognitive function (Feart et al., 2009; Psaltopoulou et al., 2008; Vercambre et al., 2012).

Regarding this issue, of particular note are the results of the randomized PREDIMED trial that also investigated whether a Med-Diet supplemented with anti-oxidant-rich foods influences cognitive function compared to a control diet in 447 participants from Barcelona, Spain (Valls-Pedret et al., 2015). After a mean follow-up of 4.1 years, participants in two Med-Diet groups (one with extra-virgin olive oil and the other with nuts) scored better on the Rey Auditory Verbal Learning test (RAVLT), Color Trail test and tests for global cognition compared with controls ($P < 0.05$; all). These results confirm with the highest level of scientific evidence that the Med-Diet protects against age-related cognitive decline.

In a recent meta-analysis, Psaltopoulou *et al.* evaluated the association between adherence to a Med-Diet and risk of depression, cognitive impairment, and Parkinson disease. High adherence to a Med-Diet was consistently associated with reduced risk of cognitive impairment (RR = 0.60; CI: 0.43 to 0.83). Moderate adherence was similarly associated with reduced risk cognitive impairment (Psaltopoulou et al., 2013).

In a systematic review by Lourida et al. higher adherence to a Med-Diet was associated with better cognitive function, lower rates of cognitive decline, and reduced risk of Alzheimer disease, whereas results for mild cognitive impairment were inconsistent (Lourida et al., 2013). Furthermore, a 2-point increase in adherence to the Med-Diet was associated with a significant reduction in neurodegenerative diseases (RR = 0.87; CI: 0.81 to 0.94) (Sofi et al., 2010). Finally, in another systematic review, higher adherence to the Med-Diet was associated with reduced risk of mild cognitive impairment and Alzheimer’s disease. Those in the highest Med-Diet tertile had a 33% less risk of cognitive impairment (HR = 0.67; CI: 0.55 to 0.81) compared to the lowest Med-Diet score tertile. Among cognitively normal individuals, higher adherence to the Med-Diet

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was associated with a reduced risk of mild cognitive impairment (HR = 0.73; CI: 0.56 to 0.96) and Alzheimer's disease (HR = 0.64; CI: 0.46 to 0.89) (Singh et al., 2014).

DIETARY APPROACH TO STOP HYPERTENSION PATTERN

The Dietary Approaches to Stop Hypertension (DASH) diet is characterized by high intake of fruits and vegetables, moderate low-fat dairy products, poultry and fish, with substantial amount of plant protein from legumes and nuts, and low red meat, sweets, and sugar-containing beverages, combined with sodium restriction. This eating pattern was basically designed to normalize BP in patients with hypertension. In comparison with standard diets the DASH diet provides lower amounts of total fat, saturated fat, and dietary cholesterol, while providing higher amounts of potassium, calcium, magnesium, fiber, and protein.

Obesity

The article by Champagne *et al*. provides a welcome examination of dietary intake changes associated with successful initial weight loss and subsequent weight loss maintenance. In this study, they examine which changes in diet are associated with greater weight loss and weight loss maintenance. The study was conducted in two phases. Phase I was a 6-month intensive behavioral weight loss period, and Phase II was a 36-month maintenance period in those who achieved an initial 4-kg weight loss during Phase I. The participants in Phase I were instructed on the basic DASH diet and particularly asked to increase their consumption of fruits and vegetables, low-fat dairy and whole grains. The authors founded that those who replaced fat with protein sources, or replaced carbohydrates with fat or protein, or those who increased their intake of fruits and vegetables had greater weight loss in both study phases (Champagne et al., 2011).

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Promoting food choices consistent with the DASH diet was related to significantly less weight regain in this randomized controlled trial.

The Exercise and Nutritional Intervention for Cardiovascular Health study examined the effects of the DASH diet in combination with exercise in 144 overweight or obese subjects with elevated BP who were not taking hypertensive medications. The subjects were randomized to the DASH diet, the DASH diet combined with a weight management intervention and aerobic exercise, and a standard diet as the control. Participants in the DASH diet plus weight management group lost on average 8.7 kg over 4 months. The DASH diet alone intervention lost 0.3 kg, and the usual care control group gained 0.9 kg over that same time period. Relative to the control diet, the DASH diet combined with exercise and caloric reduction was effective for helping individuals to lose weight (Blumenthal et al., 2010a). In other study, 124 participants with hypertension who were sedentary and overweight or obese were randomized to the DASH diet alone, DASH combined with a behavioral weight management program including exercise and caloric restriction, or a standard diet (control group). Participants on the DASH diet combined with a behavioral weight management program exhibited greater improvements in executive function-memory-learning and psychomotor speed, and DASH diet alone participants exhibited better psychomotor speed compared with the standard diet control (Smith et al., 2010).

In obese and overweight adults, from The Latino Health Project, an intervention during 20 weeks with a DASH dietary pattern, increasing physical activity, and reducing caloric intake, produced an average weight loss of 5.1 lbs, and a reduction in BMI of 1.3 kg/m^2 (Corsino et al., 2012). In the Prospective National Growth and Health Study, adolescent girls whose diet more closely

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resembled the DASH eating pattern had smaller gains in BMI over 10 years (Berz et al., 2011). Thus, a DASH-type diet seems helpful for weight maintenance (Soeliman et al., 2014) although the need for more study remains.

Type 2 diabetes mellitus

Adherence to the DASH dietary pattern may have the potential improve insulin sensitivity and to prevent appearance of type 2 diabetes. After following the DASH eating pattern over 8 weeks, fasting blood glucose levels were reduced significantly (−29.4 ± 6.3 mg/dl), in 31 type 2 diabetic patients (Azadbakht et al., 2011). Insulin sensitivity using the frequently sampled intravenous glucose tolerance test with minimal model analysis was assessed in 55 participants from the PREMIER study. Based on the results of this small study, including the DASH dietary pattern in combination with a comprehensive lifestyle modification program for hypertension, lead to significant improvements of up to 50% in insulin sensitivity, from baseline over the 6-month intervention period (Ard et al., 2004). In another secondary analysis of PREMIER, the established and established-plus-DASH interventions both led to significant decreases in fasting insulin levels and in the homeostasis model index of insulin resistance (Lien et al., 2007).

On the other hand, Blumenthal *et al.* examined the effects of the DASH diet and a weight loss program on insulin sensitivity in a randomized control trial, after 4 months. The DASH diet with aerobic exercise and caloric restriction demonstrated lower glucose levels after the oral glucose load, and improved insulin sensitivity, compared with both the DASH diet alone and a standard diet, in addition to lower fasting glucose compared with the standard diet (Blumenthal et al., 2010b). Hinderliter *et al.* also examined the independent and combined effects of the DASH diet and weight loss plus exercise on fasting glucose and insulin sensitivity, with a focus on data from the ENCORE (Exercise and Nutritional Interventions for Cardiovascular Health) study. Participants who completed the DASH plus weight management intervention, compared with usual-care participants showed lower fasting glucose and insulin levels and lower values for area under the glucose concentration curve, as well as exhibiting greater insulin sensitivity compared with either DASH-alone or standard-care participants (Hinderliter et al., 2011). Consequently, even though participants in the DASH plus weight management group showed significant improvements in glucose tolerance and insulin sensitivity, no change in these metabolic parameters was observed after the DASH diet alone. This data suggest that the DASH eating plan significantly improves insulin sensitivity only when the DASH diet is implemented as part of a more comprehensive lifestyle modification program that includes exercise and weight loss. These results have been confirmed in other studies (Ard et al., 2004; Liese et al., 2009b; Yazici et al., 2009).

Additionally, diet may prevent the development of diabetes in some individuals. The DASH diet was significantly associated with a reduced risk of type 2 diabetes in 41,615 men from the Health Professionals Follow-Up Study, followed over ≤ 20 years. The participants in the top quintile of the DASH score had a 25% lower risk than those in the bottom quintile HR = 0.75 (CI: 0.65 to 0.85) (de Koning et al., 2011). Adherence to the DASH pattern was associated with lower type 2 diabetes mellitus risk among women with a history of gestational diabetes mellitus. Tobias *et al*. evaluated 4,413 participants from the Nurses' Health Study II cohort and found the DASH pattern was associated with a 46% lower risk of type 2 diabetes mellitus, HR = 0.54 (CI: 0.39 to 0.73) (Tobias et al., 2012a). Previously, the DASH pattern was inversely associated with

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gestational diabetes mellitus risk. In a comparison of the multivariable risk of gestational diabetes mellitus in participants in the fourth and first quartiles of DASH pattern adherence scores, it was associated with a 34% lower risk, RR = 0.66; (CI: 0.53 to 0.82) (Tobias et al., 2012b). Likewise, over 5 years of follow-up an inverse association between the DASH diet and incidence of type 2 diabetes was observed in white participants from the Insulin Resistance Atherosclerosis Study (IRAS) [OR = 0.31; CI: 0.13 to 0.75 (tertile 3 vs. tertile 1)], whereas no association was observed in blacks or Hispanics (OR = 1.34; CI: 0.70 to 2.58), nor in the study cohort as a whole (Liese et al., 2009a).

Shirani *et al.* showed in a meta-analysis that the DASH diet can significantly reduce fasting insulin concentrations compared with a control diet (mean difference −0.15; CI: −0.22 to −0.08) and it could significantly reduce fasting insulin levels when prescribed for more than 16 wk (mean difference −0.16; CI: −0.23 to −0.08). In this meta-analysis adherence to the DASH diet was associated with lower fasting blood glucose levels in two studies, but overall, this meta-analysis could not show the beneficial effects of the DASH diet on fasting blood glucose. Also, this meta-analysis could not show a significant effect of the DASH diet on Homeostatic Model Assessment insulin resistance (HOMA-IR) levels (Shirani et al., 2013).

Cardiovascular diseases

The DASH diet is widely promoted by the National Heart, Lung, and Blood Institute for the prevention and treatment of hypertension in the USA (Appel et al., 2006). This diet significantly reduced systolic and diastolic BP by 5.5 mm Hg and 3.0 mm Hg, respectively, compared with a control diet; with the reductions even greater (11.4 mm Hg/5.5 mm Hg) in those subjects with

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hypertension. Among those without hypertension, the corresponding reductions were 3.5 mm Hg and 2.1 mm Hg (Appel et al., 1997). The BP-lowering effect of the DASH diet is mentioned as the diet's major characteristic because hypertension is found to be a main risk factor for most CVDs (Bhupathiraju et al., 2011). The DASH eating plan has been shown to be effective in lowering BP in a series of well-designed clinical trials. The DASH pattern over 8 weeks, had beneficial effects on systolic (−13.6 ± 3.5 mm Hg) and diastolic BP (−9.5 ± 2.6) (Azadbakht et al., 2011).

Persons with above-optimal BP, including stage 1 hypertension, could make additional lifestyle changes that lower BP and decrease their CVD risk. In the PREMIER trial 810 adults with higher-than-optimal BP were randomized to one of 3 interventions groups: 1) an "established" group, a behavioral intervention that implemented established recommendations, 2) "established plus DASH" group which implemented the established lifestyle modifications plus the DASH diet; and 3) an advice only group. The net reduction in systolic BP was 3.7 mm Hg in the established group and 4.3 mm Hg in the established plus DASH group, relative to advice only. The prevalence of hypertension at 6 months, compared with baseline hypertension was 26% in the advice only group, 17% in the established group, and 12% in the established plus DASH group. The prevalence of optimal BP (<120 mm Hg systolic and <80 mm Hg diastolic) was 19% in the advice only group, 30% in the established group, and 35% in the established plus DASH group (Appel et al., 2003).

For overweight or obese persons with above-normal BP, the addition of exercise and weight loss to the DASH diet resulted in even larger BP reductions, as shown in the ENCORE study, which

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examined the independent and combined effects of the DASH diet and weight loss plus exercise on BP, among participants with pre-hypertension or stage 1 hypertension. Clinic-measured BP was reduced in DASH plus weight management, and DASH alone, by 16.1/9.9 mm Hg, and 11.2/7.5 mm Hg, respectively; a similar pattern was observed for ambulatory BP (Blumenthal et al., 2010a).

These effects of the DASH dietary pattern have been confirmed in a free-living UK population (Harnden et al., 2010). Systolic and diastolic BP decreased significantly by 4.6 and 3.9 mm Hg, respectively, in those who followed a DASH-style diet.

Accordingly, adherence to the DASH-style diet was associated with a lower risk of CHD and stroke among middle-aged women during 24 years of follow-up, in the Nurses' Health Study cohort. Women in the top quintile of the DASH score, compared with those in the bottom quintile, had a RR of 0.76 (CI: 0.67 to 0.85) for CHD, after adjustment for potential confounders. DASH score appeared stronger among normal weight women than among overweight women. For total stroke, the RR comparing the top to bottom quintiles of the DASH score was 0.82 (CI: 0.71 to 0.94) (Fung et al., 2008). Likewise, in the EPICOR study, Agnoli *et al.* investigated the association between stroke and adherence to the DASH diet, during a mean follow-up of 7.9 y, in an Italian population. In this study, the DASH diet was significantly inversely associated with risk of ischemic stroke (HR = 0.53; CI: 0.30 to 0.91), but not significantly associated with hemorrhagic stroke (HR = 0.97; CI: 0.45 to 2.07) (Agnoli et al., 2011). In the Iowa Women's Health Study, greater concordance with DASH-style diet did not have an independent long-term association with hypertension or cardiovascular mortality (Folsom et al., 2007).

Greater adherence to the DASH diet was associated with lower rates of heart failure events in 38,987 participants in a Cohort of Swedish Men aged 45 to 79 years. Those in the greatest quartile of the DASH component score had a 22% lower rate of heart failure events than those in the lowest quartile (Levitan et al., 2009b). The same authors conducted a prospective observational study in 36,019 participants in the Swedish Mammography Cohort who were aged 48 to 83 years. Women in the top quartile of the DASH diet score had a 37% lower rate of heart failure (Levitan et al., 2009a).

Consumption of a DASH-like diet was associated with lower all-cause mortality (HR = 0.69; CI: 0.52 to 0.92) and stroke (HR = 0.11; CI: 0.03 to 0.47) in 5,532 hypertensive adults from the Third National Health and Nutrition Examination Survey, during an average of 8.2 person-years of follow-up (Parikh et al., 2009).

The results of a recent meta-analysis performed by Salehi-Abargouei *et al.* confirmed that high adherence to a DASH-style diet can significantly reduce by 20%, 21%, 19% and 29%, incidence of CVDs (RR = 0.80; CI: 0.74 to 0.86), CHD (RR = 0.79; CI: 0.71 to 0.88), stroke (RR = 0.81; CI: 0.72 to 0.92), and heart failure (RR = 0.71; CI: 0.58 to 0.88) risk, respectively (Salehi-Abargouei et al., 2013).

Asthma

There are a limited number of intervention studies, on the effect of DASH diet on asthma in adults. Reduction in bodyweight has previously been linked to improved asthma symptoms in obese adults with asthma (Aaron et al., 2004; Stenius-Aarniala et al., 2000) and as has been previously mentioned in this section, the DASH dietary pattern is effective as a weightloss/anti-

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obesity strategy and thus may indeed be indirectly useful in the alleviation of asthma symptoms in obese subjects. Indeed, one pilot study of the DASH diet aims to provide critical data on the feasibility and potential efficacy of the DASH diet among adults with uncontrolled asthma. According to this study, the DASH diet could provide a practical, safe, and acceptable public health intervention in the form of dietary modification to reduce the burden of asthma (Ma et al., 2013)..

Mental health problems

In a 4-month clinical trial, the effects of DASH adherence on a modification of the Folsom score were evaluated. Participants on the DASH diet combined with a behavioral weight management program exhibited greater improvements in executive function-memory-learning (Smith et al., 2010).

Some cohort studies have evaluated the effects of DASH diet on incidence of cognitive decline and dementia. A significant reduction in rates of global cognitive decline was observed with higher DASH scores in elderly men and women (Norton et al., 2012; Wengreen et al., 2013). Higher DASH diet score was associated with higher average Modified Mini-Mental State Examination scores. Thus, subjects in the highest quintile of DASH scores had 0.97 Modified Mini-Mental State Examination points higher than subjects in the lowest quintile ($P = 0.001$) (Wengreen et al., 2013). Similarly, in a cohort of the Chicago based Memory and Aging Project, a 1-unit increase in DASH dietary adherence score was associated with a slower rate of cognitive decline by 0.007 units (SE = 0.03, P = 0.03) in older persons (Tangney et al., 2014). Recently, Morris *et al.* evaluated the relationship between diet and Alzheimer’s disease in a prospective study of 923 participants, ages 58 to 98 years, followed on average for 4.5 years (Morris et al., 2015). Only the third tertile of the DASH diet (HR = 0.61; CI: 0.38 to 0.97) diet was associated with lower Alzheimer's disease rates. This evidence supporting the association between dietary patterns and cognitive decline, dementia and Alzheimer's disease has been recently reviewed (Alles et al., 2012).

PRUDENT DIET AND HEALTH OUTCOMES

Obesity

Some studies have evaluated the relationship between Prudent Western diet and adiposity parameters. In a study in women (Tucker et al., 2015), higher adherence to a prudent diet was associated with a lower body fat percentage (P = 0.0038) and BMI (P = 0.0363) when compared with other dietary patterns defined as "low-fat milk" and "meat" patterns. Likewise, in the Health Professionals Follow-Up study (Fung et al., 2001) a Prudent dietary pattern was inversely associated with adiposity parameters, fasting insulin, homocysteine and positively associated with folate concentration. Case-control studies (Murtaugh et al., 2007; Paradis et al., 2009) have found that consumption of a Prudent dietary pattern was also associated with a 29% lower prevalence of overweight and a halving of the prevalence of obesity similarly in Hispanic and non-Hispanic white women.

Furthermore, in a study in a Mexican population (Donova-Gutiérrez et al., 2011), individuals in the highest quintile of a prudent dietary pattern were found to be less likely to have high-body fat (OR = 0.82; CI: 0.70 to 0.98) and in other study conducted in a Northern European population with normal weight (Suliga et al., 2015), individuals found to be in the highest tertile of

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adherence to a prudent dietary pattern were found to have a lower OR for metabolic obesity with normal weight (MONW) (0.69; CI: 0.53 to 0.89; $P < 0.01$) when compared to second and third tertiles.

Type 2 diabetes mellitus

Since the incidence of diabetes increases with rising obesity (Mokdad et al., 2001) the effects of the Prudent dietary pattern on preventing obesity, as mentioned in the previous section should be taken into account as potentially beneficial in the prevention of diabetes. Numerous studies have also shown the specific benefits of a Prudent dietary pattern in regards to diabetes. In a study by Villegas *et al.* subjects following a Prudent diet (defined as higher intake of foods typically recommended in health promotion programs and a lower intake of meat, meat products, sweets, high fat dairy and unrefined cereal products) was found to have lower HOMA scores and to show lower levels of insulin resistance (OR = 0.53; 95% CI: 0.33 to 0.85) when compared to a traditional diet (Villegas et al., 2004). In the prospective cohort of Health Professionals Follow-up study, a Prudent dietary pattern was associated with a modestly lower risk for type 2 diabetes (RR for extreme quintiles, 0.84; CI: 0.70 to 1.00) (van Dam et al., 2002). A further study in women similarly found a modest inverse association between the prudent pattern and type 2 diabetes with women in the highest quintile of the prudent pattern having a RR of 0.8 (CI: 0.67 to 0.95) (Fung et al., 2004). This was in contrast to the highest quintile of a Western diet pattern. Finally, Malik *et al.* evaluated the relationship between dietary patterns during adolescence and risk of type 2 diabetes in midlife. They examined the 7-year incidence of type 2 diabetes in relation to dietary patterns during high school among 37,038 participants in the Nurses' Health

Study II cohort. In this case, the Prudent dietary pattern, characterized by healthy foods, was not associated with risk of type 2 diabetes (Malik et al., 2012) although it should be noted that this study involved the recall of adolescent diet which may limit the validity of the findings.

Cardiovascular diseases

Heidemann *et al.* evaluated the relationship between dietary patterns and risk of CVD, cancer, and all-cause mortality among 72,113 women who were free of myocardial infarction, angina, coronary artery surgery, stroke, diabetes mellitus, or cancer (Heidemann et al., 2008). Comparing the highest with the lowest quintile of the prudent diet score (high scores represented high intakes of vegetables, fruit, legumes, fish, poultry, and whole grains), the prudent diet was associated with a 28% lower risk of cardiovascular mortality (RR = 0.72; 95%CI: 0.60 to 0.87) and a 17% lower risk of all-cause mortality (RR = 0.83; 95%CI: 0.76 to 0.90). In addition, in a recent meta-analysis of prospective cohort studies, an inverse association was observed between the prudent/healthy dietary pattern, and the risk of all-cause and CVD mortality, but an absence of association between this dietary pattern and stroke mortality was also observed (Li et al., 2014).

Some studies have also evaluated the relationship of dietary patterns with biochemical markers of CVD (Ko et al., 2015) high prudent diet scores were found to be inversely correlated with leptin, sICAM-1, and CRP, indicators of inflammation in CVD. Furthermore, in a study with participants from the Nurses' Health Study the prudent pattern was shown to be inversely associated with plasma concentrations of CRP and E-selectin (Lopez-Garcia et al., 2004) which are indicators of endothelial dysfunction found in the early stages of CVD (Ross, 1999). As

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mentioned previously, the Prudent diet was also inversely associated with fasting insulin and homocysteine and positively associated with folate concentration, also biomarkers of CVD (Fung et al., 2001). A similar trend in plasma CRP, E-selectin and soluble vascular cell adhesion molecule-1 (sVCAM-1) levels was observed in a study by Esmailzadeh *et al.* with a "healthy" diet pattern (high in fruits, vegetables, tomato, poultry, legumes, tea, fruit juices, and whole grains) similar to the definition of the prudent pattern (Esmaillzadeh et al., 2007a).

Asthma

Evidence relating the consumption of any particular dietary pattern with asthma is currently rather sparse but there do exist a few studies investigating this topic. For example, one case-control study in the UK (Bakolis et al., 2010) found that a prudent diet was actually positively associated with chronic bronchitis (not asthma) (OR = 2.61; CI: 1.13 to 6.05), whereas a study by Varraso *et al.* found no association between dietary patterns (including the prudent diet) and incidence of asthma (Varraso et al., 2009).

Mental health problems

Similarly to asthma, few studies have evaluated the relationship between dietary patterns to mental health issues. However, one longitudinal study of older adults found that high adherence to a prudent diet was inversely associated with cognitive decline compared to high adherence to a western dietary pattern which was positively associated with cognitive decline (Shakersain et al., 2015). Indeed high prudent diet adherence was also found to attenuate the effects of high adherence to a western diet on cognitive decline.

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SEVENTH DAY ADVENTIST DIET AND HEALTH OUTCOMES

Obesity

Seventh Day Adventists are known for following "healthier" diets, free from alcohol and tobacco and it is known that a large proportion of seventh day Adventists are vegetarians (Beeson et al., 1989). It has been observed that adherence to a vegetarian diet amongst Adventists is inversely associated with obesity (Brathwaite et al., 2003). Similarly, another study of Adventists found that BMI increased with increasing meat consumption (Fraser, 1999). Interestingly, increasing mean BMI were also observed with increasing meat consumption from vegans (23.6 kg/m^2) to lacto-ovo vegetarians (25.7 kg/m^2), pesco-vegetarians (26.3 kg/m^2), semi-vegetarians (27.3 kg/m^2), and nonvegetarians (28.8 kg/m^2) (Tonstad et al., 2009), which potentially highlights the advantages of diets with low meat content.

Type 2 diabetes mellitus

Similarly vegans (OR 0.51; CI: 0.40 to 0.66), lacto-ovo vegetarians (OR 0.54; CI: 0.49 to 0.60), pesco-vegetarians (OR 0.70; CI: 0.61 to 0.80), and semi-vegetarians (OR 0.76; CI: 0.65 to 0.90) had a lower risk of type 2 diabetes than non-vegetarians (Tonstad et al., 2009). Similar studies in Adventist populations have also shown this tendency for lower risk of diabetes with increasing adherence to vegetarianism (Tonstad et al., 2013). Another study found a positive association between meat consumption (but not other animal products) and diabetes related mortality, especially amongst males (Snowdon, 1988).

Cardiovascular diseases

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Both obesity and diabetes are considered risk factors for CVD (Malik et al., 2004) and thus the evidence from the previous sections would indicate that lower meat consumption in the Adventist population would also confer protection from CVD. One study found a particularly strong association between beef consumption and fatal ischemic heart disease, once again in men only (Fraser, 1999). This trend was also seen in the study by Snowdon (Snowdon, 1988) which positively associated meat consumption with CHD in both male and female Adventists. Interestingly, in a systematic review and meta-analysis vegetarian Adventist diet was found to reduce the risk of both CHD (RR = 0.60; CI: 0.43 to 0.80 *vs* RR = 0.84; CI: 0.74 to 0.96) and stroke (RR = 0.71; CI: 0.41 to 1.20 *vs* RR = 1.05; CI: 0.89 to 1.24) when compared to a non Adventist population (Kwok et al., 2014).

Asthma

Studies specifically relating the Adventist dietary pattern with asthma are virtually non-existent however, as hinted at in a previously mentioned study, increasing adherence to a vegetarian dietary pattern was weakly and positively associated with ever asthma (OR = 1.43; CI: 0.93 to 2.20) and no association was found with asthma severity (Bakolis et al., 2010). While not specifically investigating the Adventist dietary pattern, one study of Australian adults found that increasing meat/cheese was associated with increased risk of lifetime asthma (AOR = 1.18, 95%CI: 1.08 to 1.28; P for trend = 0.001) in men (Rosenkranz et al., 2012).

Mental health problems

Studies analyzing the relationship between mental health problems and the Seventh Day Adventist Diet are similarly scarce however preliminary findings from one investigation in the

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Adventist Health Study analyzed the incidence of dementia in two cohorts of meat and non-meat eaters, one cohort consisting of age, sex and location matched subjects and the other cohort consisting of unmatched subjects residing in the Loma Linda region of California. It found, in the matched cohort, that meat eaters had twice the risk of developing dementia compared to non-meat eaters (RR = 2.18, $P = 0.065$). Additionally a trend towards delayed onset of dementia was observed in non-meat eaters in both cohorts (Giem et al., 1993).

WESTERN PATTERN

Obesity

The Western dietary pattern was suggested to be associated with an elevated risk of general and central obesity. This is consistent with a body of literature conducted in different countries and ethnicities.

The "Western/new affluence" dietary pattern was associated with a significantly elevated risk of metabolic syndrome (OR = 1.37; CI: 1.13 to 1.67). Subjects who followed-up a "Western" dietary pattern had significantly higher BMI, and waist circumference, compared with people with the "Green Water" dietary pattern, characterized by high intakes of rice and vegetables and moderate intakes in animal foods. Participants with a combination of sedentary activity with the "Western" dietary pattern had more than three times (CI: 2.8 to 6.1) higher risk of metabolic syndrome than those with higher activity levels and the "Green Water" dietary pattern (He et al., 2013).

In the Atherosclerosis Risk in Communities (ARIC) study (Lutsey et al., 2008), and the Health Workers Cohort Study (Denova-Gutiérrez et al., 2010; Donova-Gutiérrez et al., 2011), participants in the highest tertile of the Western pattern had a higher OR for metabolic syndrome, central obesity, and fasting glucose than those in the lowest tertile, after adjustment for potential confounders (Denova-Gutiérrez et al., 2010). Other studies have also observed a significant association between Western dietary pattern and prevalence of overweight/obesity and other adiposity parameters in adults (Esmaillzadeh et al., 2008; Murtaugh et al., 2007; Paradis et al., 2009; Yu et al., 2015) and in children, compared with the individuals following the traditional southern dietary pattern.

Type 2 diabetes mellitus

A diet high in sugar-sweetened soft drinks, refined grains, diet soft drinks, and processed meat and low in wine, coffee, cruciferous vegetables, and yellow vegetables may increase the risk of developing type 2 diabetes, probably by exacerbating inflammatory processes. This pattern was strongly associated with diabetes risk in a nested case-control study (OR = 3.09; CI: 1.99 to 4.79), comparing extreme quintiles. The multivariate RR comparing extreme quintiles of the Western pattern were 2.56 (CI: 2.10 to 3.12) in the Nurses' Health Study and 2.93 (CI: 2.18 to 3.92) in the Nurses' Health Study II (Schulze et al., 2005). Other studies have also evaluated the association between dietary patterns and biomarkers of type 2 diabetes. In a study of 5 ethnic groups living in Amsterdam, Netherlands, the “meat-and-snack” pattern derived within the native Dutch population was significantly associated with glycated hemoglobin and fasting glucose concentrations (Dekker et al., 2015). In addition, cross-sectional studies performed in

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Iran (Darani et al., 2015; Esmaillzadeh et al., 2007b), the Netherlands (van Dam et al., 2003), Japan (Arisawa et al., 2014), USA (Lutsey et al., 2008; van Dam et al., 2002) and Sweden (Wirfalt et al., 2001) observed a positive association between higher adherence to Western dietary pattern and higher incidence of insulin resistance and increased risk of type 2 diabetes mellitus.

Malik *et al.* also evaluated the relationship between dietary patterns during adolescence and risk of type 2 diabetes in midlife. They examined the 7-year incidence of type 2 diabetes in relation to dietary patterns during high school among 37,038 participants in the Nurses' Health Study II cohort. The western pattern, characterized by desserts, processed meats, and refined grains, was associated with 29% greater risk of type 2 diabetes (RR = 1.29; CI: 1.00 to 1.66). Women who had high Western pattern scores in high school and adulthood had an elevated risk of type 2 diabetes compared with women who had consistent low scores (RR = 1.82; CI: 1.35 to 2.45), this association was partly mediated by adult BMI (RR = 1.15; CI: 0.85 to 1.56) (Malik et al., 2012). A similar study in women found an association between the western diet pattern and type 2 diabetes, with women in the highest quintile of the western pattern having a RR of 1.49 (CI: 1.26 to 1.76). This was in contrast to the highest quintile of a Prudent dietary pattern (Fung et al., 2004).

Cardiovascular diseases

Western diet patterns, among studies of higher methodological quality, were significantly associated with CHD, with a pooled RR of 1.55 (CI: 1.27 to 1.83) (Mente et al., 2009). Heidemann *et al.* evaluated the relation between dietary patterns and risk of cardiovascular

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disease, cancer, and all-cause mortality among 72,113 women who were asymptomatic at baseline. The Western pattern was associated with a higher risk of mortality from cardiovascular disease (22%; CI: 1 to 48), and mortality for all causes (21%; CI: 12 to 32) when the highest quintile was compared with the lowest quintile (Heidemann et al., 2008).

In the Health Professionals Follow-up Study, the Western dietary pattern, characterized by higher intakes of red meats, high-fat dairy products, and refined grains, was significantly positively correlated with C-peptide, plasma leptin, and homocysteine concentrations, and an inverse correlation was observed with plasma folate concentrations, all biomarkers of CVD risk (Fung et al., 2001). In healthy US adults, the Western pattern was also associated ($P < 0.05$) positively with serum C-peptide, and glycated hemoglobin and inversely with red blood cell folate concentrations after adjustment for confounding variables (Kerver et al., 2003). Participants from the Strong Heart Study who followed the Western pattern had higher LDL cholesterol, slightly higher systolic BP, and lower HDL cholesterol, in the lowest *vs.* highest deciles of adherence to this pattern (Eilat-Adar et al., 2013).

Ambrosini *et al.* examined dietary patterns, CVD risk factors, and the clustering of these risk factors in 1139 14-year-olds living in Western Australia. In this study, higher Western dietary pattern scores were associated with greater risk of the “high risk metabolic cluster” and greater mean values for total cholesterol, waist circumference and BMI in girls, but not boys (Ambrosini et al., 2010).

However, other recent studies (Labonté et al., 2014; Martínez-González et al., 2014; Zazpe et al., 2014) showed no association between Western dietary patterns with any CVD outcome. In a

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recent meta-analysis of prospective cohort studies, no significant associations were observed between the Western/unhealthy dietary pattern and the risk of all-cause, CVD and stroke mortality (Li et al., 2014).

Asthma

Varrasco *et al.* investigated the association between dietary patterns and asthma incidence, current asthma and frequent asthma exacerbations, from the large E3N study in France. In this study the Western dietary pattern, that included pizza, salty pies, desserts, and cured meat, was associated with an increased risk of reporting frequent asthma attacks (highest *vs* lowest tertile, OR = 1.79; CI: 1.11 to 3.73), while the "nuts and wine pattern" was protective (highest *vs* lowest tertile, OR = 0.65; CI: 0.31 to 0.96) (Varraso et al., 2009). However, a population-based case-control study of asthma in adults aged between 16 and 50 in South London, UK (Bakolis et al., 2010) observed no clear relation between the dietary patterns and adult asthma outcomes.

The influence of dietary patterns on the prevalence of wheezing in the child and adolescent population in Northeastern Brazil was evaluated by de Cássia Ribeiro Silva *et al.* They found a positive statistically significant association between the Western pattern and wheeze (OR = 1.77; CI: 1.10 to 2.84) after adjustment for total energy intake and controlling for potential confounders (de Cássia Ribeiro Silva et al., 2013). Similar results were observed in Dutch pre-school children (Tromp et al., 2012) and in 763 Japanese mother-child pairs (Miyake et al., 2011).

CONCLUSIONS

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A personalized diet consists of combinations of foods which contain a complex mixture of nutrients which potentially have a synergistic effect on one's health. Previous research into the effects of specific nutrients on health outcomes, essential to further scientific knowledge relating to the health effects of individual nutrients, does not take this synergism into consideration. In contrast, the recent focus on dietary patterns can be seen as a more holistic approach to the investigation of how long term consumption of certain food combinations can affect health. This "dietary pattern" approach also lends itself more readily to practical application in the area of public health promotion due to the fact that it is easier for people to adopt whole dietary patterns instead of incorporating or eliminating specific nutrients from their diets.

In this review we have presented evidence from a number of studies which show the potential benefits of four "healthy" dietary patterns (Mediterranean, DASH, Prudent and Seventh Day Adventist) regarding obesity, diabetes, CVD, asthma and mental health disorders. For the purpose of comparison, studies revealing the negative effects of the Western dietary pattern were also reviewed. The first three of the conditions mentioned, obesity, diabetes and CVD are considered to be components of metabolic syndrome which currently affects 25% of certain populations. All these conditions are preventable by dietary/lifestyle intervention, further highlighting the importance of research into dietary patterns and health outcomes.

The evidence provided in this review highlights the effectiveness of higher adherence to the four dietary patterns mentioned in reducing prevalence levels of obesity, diabetes and CVD when compared to lower adherence to these diets. Regarding asthma, evidence for the benefit of any particular dietary pattern is inconclusive although the Med-Diet has been inversely associated with asthmatic symptoms. The otherwise inconclusive evidence may be due to the lower number of studies available investigating dietary links to asthma, when compared to those linking diet with obesity, diabetes and CVD. Regarding mental health conditions, adherence to the four healthy dietary patterns in this review was consistently associated with either low incidence of depression, cognitive decline and/or dementia in subjects with high adherence to these diets.

While the four 'healthy' patterns mentioned in this review do have some distinguishing features, it is their common components that should be of particular interest in this field of dietary pattern analysis. These similarities include: high consumption of plant-based foods including fruit, vegetables and whole grains; moderate consumption of dairy products, fish and poultry; and low consumption of processed foods, refined grains and sugars, red and processed meats. Polices or nutritional recommendations focusing on these dietary patterns could potentially prove effective in reducing the incidence of the chronic, lifestyle diseases discussed in this review.

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AUTHOR CONTRIBUTIONS

A. M.-R., R.K., R.M.L.-R. and R.E. interpreted data and wrote the first draft of the manuscript. All authors contributed to the writing and revision of the manuscript and approval of the final version to be published.

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Table 1: General characteristics of the studies reporting the association between mediterranean patterns and Obesity.

Authors (year of study)	Country	Type of study	Sample Size	Age range (years)	Gender	Follow up	Main Outcome	Results	Adjustments
Mendez et al. (2006)	Spain	Cohort	27,827	29–65	♂ 10,589 ♀ 17,238	3.3 year	Obesity	♀ (OR= 0.69; 95% CI: 0.54 to 0.89); ♂ (0.68; CI: 0.53 to 0.89)	Age, special diets related to obesity or related disorders, categorical activity index, education, center, height, parity (in women), smoking status, winter season, follow-up time, health status

									and changes in lifestyle or health during follow-up.
Beunza et al. (2010)	Spain	Cohort	10,376	Mean 38	Men and women	5.7 ± 2.2 year	Overweight and Obesity	↑ Med-Diet, ↓ weight –0.059 kg/year 95% CI: –0.111 to –0.008 kg/year, *P* = 0.02; lowest risk weight gain 4-year OR=0.76 (95% CI: 0.64 to	Age, sex, baseline BMI, physical activity, sedentary behaviors, smoking, between-meals snacking, total energy intake.

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								0.90)	
Romaguera et al. (2010)	10 European countries	Cohort	373,803	25–70	♂ 103,455 ♀ 270,348	5 year	Overweight and Obesity	↑ rMED, ↓ weight gain 5–year –0.16 kg (95% CI: –0.24 to –0.07 kg); less likelihood of overweight or obesity 10% (95% CI: 4% to18%)	Sex, age, baseline BMI, follow-up, educational level, physical activity, smoking status, menopausal status, total energy intake, misreporting of total energy intake.
Martínez-González et al. (2012)	Spain	RCT	7,447	55–80	♂3,165 ♀4,282	4.8 year	Obesity	Waist-to-height ratio >0.6 ♀ OR=0.68	Age, smoking, diabetes status, hypertensive status, physical

								(CI: 0.57 to 0.80) ♂ OR=0.66 (CI: 0.54 to 0.80)	activity, educational level, marital status, center, total energy intake.
Andreoli et al. (2008)	Italy	RCT	47	25–70	♀47	4 month	Cardiovascular disease risk factors in obese women	↑ Med-Diet, ↓ weight (m0 80.4 ± 15.8 kg to m4 75.2 ± 14.7 kg) $p < 0.001$; ↑ Med-Diet, ↓ BMI (m0 30.7 ± 6.0 kg to m4 28.7 ± 5.6 kg) $p < 0.001$	/

Goulet et al. (2003)	Canada	RCT	77	30–65	♀77	12 week	Overweight and Obesity	↑ Med-Diet, ↓ BMI (mean week0: 25.8 ± 3.9 kg/m^2 to mean week12 25.6 ± 3.8 kg/m^2) $p <$ 0.01; and less weight (week0: 67.7 ± 11.9 kg to week12: 67.3 ± 11 kg) $p <$ 0.01	/
Romaguera	10	Cross-	497,30	25–70	♂145,7	/	Obesity	↑ Med-	Age,

et al. (2009)	European countries	sectional	8		11 ♀351,597			Diet, ↓ WC, for a given BMI ♂ –0.09 (95% CI: –0.14 to –0.04), ♀ –0.06 (95% CI: –0.10 to –0.01); Northern European countries ♂ –0.20 (95% CI: –0.23 to –0.17), ♀ –0.17 (95% CI: –0.21 to –	educational level, physical activity level, smoking status, height, and menopausal status.

								0.13)	
Lazarou et al. (2010)	Cyprus	Cross-sectional	1,140	9.72–11.68	children	/	Obesity	↑ KIDMED, ↓ likelihood of overweight or obesity, 80% (95% CI: 0.041 to 0.976)	Age, gender, parental obesity status, parental educational level, dietary beliefs and behaviors
Panagiotakos et al. (2006)	Greece	Cross-sectional	3,042		♂1514 ♀1528	/	Overweight and Obesity	Reduced obesity (OR= 0.49; CI: 0.42 to 0.56); reduced central obesity(O	Age, sex, physical activity, metabolism, educational level, smoking status

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								R= 0.41; 0.35 to 0.47) with 5 point increased score. ↑ Med-Diet, ↓ BMI (−4 kg) *P* = 0.001	
Schröder et al. (2004)	Spain	Cross-sectional	3,162	25–74	♂1403 ♀1468	/	Obesity	↓ BMI 0.43 kg/m^2 in ♂ and 0.68 kg/m^2 in ♀ with 5 point increased score ↑ Med-Diet, ↓ OB (OR=	Age, total energy intake, educational level, smoking, leisure-time physical activity, smoking and alcohol consumption

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								0.61, *P*= 0.010)	
Trichopoulou et al. (2005)	Greece	Cross-sectional	23,597	20–86	♂9612 ♀13,985	/	Obesity	With 2 point increased score and control of total energy intake ♂ OR 0.08 (95% CI −0.03 to 0.20), ♀ OR −0.06 (95% CI −0.16 to 0.04); With 2 point	Age, years of schooling, smoking, physical activity, total energy intake

								increased score without control of total energy intake ♂ OR 0.21 (95% CI 0.10 to 0.32), ♀ OR 0.05 (95% CI −0.04to 0.15)	

♂ men

♀ women

BMI: body mass index

CI: confidence interval

Med-Diet: Mediterranean Diet

OR: odd ratio

RCT: Randomized Controlled Trial

rMED: relative Med-Diet Score

WC: waist circumference

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Table 2: General characteristics of the studies reporting the association between mediterranean patterns and Type 2 diabetes mellitus.

Authors (year of study)	**Country**	**Type of study**	**Sample Size**	**Age range (years)**	**Gender**	**Follow up**	**Main Outcome**	**Results**	**Adjustments**
Estruch et al. (2006)	Spain	RCT	772	55-80	Men and women	3 month	Fasting glucose level	Lower fasting glucose level: Med-Diet supplemented with EVOO (−7 mg/dl, CI: −13 to −1.3 mg/dl; *P*=0.017) and, Med-Diet supplemente	Age, sex, and baseline body weight.

								d with nuts (–5.4 mg/dl, CI: –10.5 to –0.2, *P*=0.039) compared with low-fat diet group.	
Salas-Salvadó et al. (2014)	Spain	RCT	3,541	55-80	Men and women	4.8 year	T2DM	Med-Diet supplemented with EVOO (HR=0.60; 95% CI: 0.43 to 0.85) and Med-Diet supplemented with nuts (HR=0.82; CI: 0.61 to	Energy intake, BMI, WC, physical activity, smoking status, fasting plasma glucose, use of lipid-lowering drugs, MD Score.

								1.10), compared with control diet group.	
Mozaffarian et al. (2007)	Italy	RCT	8,291	48–70	♂ 7,216 ♀1,075	3.5 years	T2DM	Highest quintile of Med-diet *vs* lowest quintile (OR= 0.65, CI: 0.49 to 0.85)	Age, sex, smoking, time from myocardial infarction to enrolment, treatment assignment, BMI, maximum exercise tolerance during stress testing, ischaemia during stress testing, New

									York Heart Association heart failure symptoms, Canadian Cardiovascular Society angina symptoms, history of hypertension, prior myocardial infarction previous to index myocardial infarction, angiotensin-converting-enzyme

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									inhibitor use, β -blocker use, diuretic use, lipid-lowering medication use and, consumption of cheese, wine, and coffee.
Martínez-González et al. (2008)	Spain	RCT	13,380	23–55	♂5,312 ♀8,068	4.4 years	T2DM	RR= 0.40 (95% CI: 0.18 to 0.90) for moderate adherence (score 3-6) and RR= 0.17 (0.04	Sex, age, years of university education, BMI, family history of diabetes, hypertension at baseline,

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								to 0.72)for those with the highest adherence (score 7-9) compared with those with low adherence (score <3).	physical activity, hours/week sitting down, smoking and , total energy intake.
Abiemo et al. (2013)	USA	RCT	5,390	45–84	♂2479 ♀2911	6 years	T2DM	HR= 1.09 (95% CI: 0.80, 1.49) for highest quintiles of the Med-Diet Score.	Age, gender, race/ethnicity , study site, educational level, family income, physical activity, smoking status, total caloric intake

									and waist circumference.
de Koning et al. (2011)	USA	Longitudinal	41,615	8–40	♂ 41,615	≤ 20 years	T2DM	Top quintile of the Med-Diet score had a 25% lower risk than those in the bottom quintile, HR= 0.75; (CI: 0.66 to 0.86).	Smoking, physical activity, coffee intake, family history of type 2 diabetes, BMI, and total energy intake.
Romaguera et al. (2011)	Eight European cohorts	Longitudinal	15,798	25–70	♂ 5,968 ♀ 9,830	8 years	T2DM	Medium adherence to Med-Diet pattern (7-10 points) HR=0.93	Sex, BMI, educational level, physical activity, smoking

								(95% CI: 0.86 to 1.01) and high adherence (11-18 points) HR=0.88 (0.79 to 0.97), compared with the lowest category	status, and total calorie intake.
Rossi et al. (2013)	Greece	Longitudinal	22,295	40–64	Men and women	11.34 years	T2DM	Higher Med-Diet score was inversely associated with diabetes	Age, sex, education, BMI, physical activity, WHR and total energy

								risk, HR=0.88, 95% CI: 0.78 to 0.99.	intake.
Shai et al. (2008)	Israel	intervention study	322	40–65	♂277 ♀45	2 years	Fasting plasma glucose	↓ (−32.8 mg/dl) in the Med-diet group and ↑ (12.1 mg/dl) in the low-fat diet group.	/
Esposito et al. (2009)	Italy	RCT	215	30–75	♂106 ♀109	1 year	Fasting plasma glucose	Greater reduction in the Med-diet group (−21 mg/dl, CI: −30 to −13 mg/dl) than in low-	/

								fat diet group	
Tobias et al. (2012a)	USA	Longitudinal	4,413	24–44	♀4413	16 years	T2DM	HR= 0.60 (CI: 0.44 to 0.82) for highest quartiles of dietary pattern adherence scores.	Age, total energy intake, parity, age at first birth, race/ethnicity, parental history of T2DM, oral contraceptive use, menopausal status, smoking status, total physical activity.
Tobias et al. (2012b)	USA	Longitudinal	15,254	24–44	♀15,254	11 years	T2DM	Med-Diet was	Age, total energy

								associated with a 24% lower risk, RR= 0.76; (CI: 0.60 to 0.95)	intake, gravidity, smoking status, physical activity, sedentary time, parental history of T2DM, and, prepregnancy BMI.

♂ men

♀ women

BMI: body mass index;

CI: confidence interval

EVOO: extra virgin olive oil

HR: Hazard ratio

Med-Diet: Mediterranean Diet;

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OR: odds ratio

RCT: Randomized Controlled Trial;

rMED: relative Med-Diet Score;

RR: rate ratio

T2DM: Type 2 diabetes mellitus

WC: waist circumference;

WHR: Waist-to-hip ratio

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Table 3: General characteristics of the studies reporting the association between mediterranean patterns and cardiovascular disease.

Authors (year of study)	**Country**	**Type of study**	**Sample size**	**Age range (years)**	**Gender**	**Follow up**	**Main Outcome**	**Results**	**Adjustments**
Estruch et al. (2013)	Spain	RCT	7447	55–80	Men and women	4.8 year	Cardiovascular end-point	HR= 0.70 (CI: 0.54 to 0.92) for the Med-Diet with extra-virgin olive oil and HR= 0.72 (CI: 0.54 to 0.96) for the Med-Diet with nuts	Sex, age, family history of premature coronary heart disease, smoking status, BMI, waist-to-height ratio, hypertension at baseline, dyslipidemia at baseline, and diabetes at baseline.

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Kastorini et al. (2011)	Greece	Longitudinal	1,000	48–86	♂694 ♀306	/	Acute coronary syndrome and, ischemic stroke	For each 1-of-55-unit increase in the Med-Diet Score, OR= 0.91; CI: 0.87 to 0.96 for acute coronary syndrome, and OR= 0.88; CI: 0.82 to 0.94 for ischemic stroke.	Physical activity, ever smoker vs no smoker, family history of CVD, hypertension, hypercholesterolemia, diabetes mellitus, BMI, education years and financial status satisfaction
Yau et al. (2011)	Australia	Longitudinal	95	23–92	♂67 ♀28	/	Ischaemic stroke	Med-Diet was significantly and negatively associated with ischaemic stroke (OR= 0.1; CI: 0.02 to 0.4)	/

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Fung et al. (2009)	USA	Longitudinal	74,886	38–63	♀74,886	20 years	CHD and stroke	Those in the top Med-Diet score quintile were at lower risk compared with those in the bottom quintile; RR= 0.71; 95% CI: 0.62 to 0.82 for CHD; RR= 0.87; 95% CI: 0.73 to 1.02 for stroke.	Age, smoking, BMI, menopausal status and postmenopausal hormone use, energy intake, multivitamin intake, alcohol intake, family history, physical activity, and aspirin use
Agnoli et al. (2011)	Italy	Longitudinal	40,681	35–64	♂14,863 ♀32,158	7.9 years	Stroke	The Italian Mediterranean Index was significantly inversely associated with risk of all types	Sex, smoking status, education, nonalcoholic energy intake, and BMI.

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								of stroke (HR= 0.47; CI: 0.30 to 0.75; third vs. first tertile) and with ischemic stroke (HR= 0.37; CI: 0.19 to 0.70), and tended to be inversely associated with hemorrhagic stroke (HR= 0.51; CI: 0.22 to 1.20)	
Dilis et al. (2012)	Greece	Longitudinal	23,929	20–86	Men and women	10 years	CHD and mortality	A two-point increase in the Med-Diet score was associated with lower CHD mo	Age, BMI, height, physical activity, years of schooling and energy intake, smoking status,

								rtality by 25% (95% CI: 0.57 to 0.98) among women and 19 % (95% CI: 0.67 to 0.99) among men. Med-Diet was associated with a non-significant lower CHD incidence; HR= 0.85 (95% CI: 0.71 to 1.02) among women and 0.98 (95% CI. 0.87 to 1.10) among men).	arterial blood pressure and, use of antihypertensive medication.

Misirli et al. (2012)	Greece	Longitudinal	23,601	20–86	Men and women	10.6 years	Cerebrovascular disease and mortality	Med-Diet was significantly inversely associated with cerebrovascular disease incidence (HR= 0.85; CI: 0.74 to 0.96) and mortality (HR= 0.88; CI: 0.73 to 1.06)	Sex, age, education, smoking status, BMI, level of physical activity as measured in metabolic equivalents, hypertension, diabetes, and total energy intake.
Buckland et al. (2009)	Spain	Longitudinal	41,078	29–69	♂ 15,632 ♀ 25,446	10.4 years	CHD	High Med-Diet score was associated with a 40 % reduction in CHD risk when compared with a low Med-Diet score. (HR =	BMI, educational level, smoking status, physical activity, energy intake, and the presence of diabetes, hyperlipidemia,

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								0.60; 95% CI: 0.47 to 0.77)	and hypertension.
Martínez-González et al. (2011)	Spain	Longitudinal	13,609	mean age: 38 y	♂5,444 ♀8,165	4.9 years	CVD and CHD	For each 2-point increment in the score of adherence to Med-Diet, HR= 0.80 (CI: 0.62 to 1.02) for total CVD and 0.74 (CI: 0.55 to 0.99) for CHD.	Age, sex, total energy intake, family history of coronary heart disease, smoking, physical activity, baseline BMI, a history of hypertension or use of medication for hypertension at baseline, use of aspirin, diabetes at baseline and dyslipidaemia at baseline.

Menotti et al. (2012)	Italy	Longitudinal	1,139	45–64	♂1139	40 years	CHD mortality	Mediterranean Adequacy Index showed a significant 26% relative reduction in CHD mortality for each 2.7-point increment, after 20 years of follow-up, and 21% relative reduction after 40 years of follow-up.	Age, cigarette smoking, systolic blood pressure, serum cholesterol, physical activity and BMI
Hoevenaar-Blom et al. (2014)	Netherlands	Longitudinal	17,887	20–65	♂8,128 ♀9,759	10-14 years	CVD, fatal CVD	Med-Diet Score 5–8 (range 0–8) had lower risk of composite	Age, sex, educational level, and BMI with the number of healthy

								CVD (HR= 0.88; 95%CI: 0.74 to 1.05) and lower risk of fatal CVD (HR= 0.73; 95%CI: 0.50 to 1.08) compared with unhealthy diet.	lifestyle factors in relation to composite and fatal CVD.
Gardener et al. (2011)	USA	Longitudinal	2,568	59–79	♂924 ♀1,644	9 years	CVD (ischemic stroke, myocardial infarction or vascular death)	Med-Diet Score 6-9 (range 0-9) had lower risk of composite outcome of ischemic stroke, myocardial infarction, or	Age at baseline, sex, race-ethnicity, completion of high school education, moderate-to-heavy physical activity, kilocalories, and

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								vascular death. HR =0.75; 95%CI: 0.56 to 0.99; P-trend = 0.04	cigarette smoking
Fung et al. (2009)	USA	Longitudinal	74,886	38–63	♀74,886	20 years	CHD, stroke, and CVD mortality	Women in the top Med-Diet score quintile were at lower risk for CHD (RR= 0.71; 95%CI: 0.62 to 0.82) and stroke (RR= 0.87; 95%CI: 0.73 to 1.02) compared with those in the bottom quintile CVD mortality was	Age, smoking, BMI, menopausal status and postmenopausal hormone use, energy intake, multivitamin intake, alcohol intake, family history, physical activity, and aspirin use.

								significantly lower among women in the top quintile of the Med-Diet score (RR= 0.61; 95%CI: 0.49 to 0.76)	
Nuñez-Córdoba et al. (2008)	Spain	Longitudinal	2,990	20–90	Men and women	6 years	BP	Adherence to the Med-Diet ↓ SBP (moderate adherence, –2.4 mm Hg; high adherence, –3.1 mm Hg) and DBP (moderate adherence, –1.3 mm Hg; high adherence, –1.9 mm Hg).	Age, sex, body mass index, family history of hypertension, hypercholesterolemia, basal blood pressure, caffeine intake, total energy intake, physical activity, and smoking.
Estruch	Spain	RCT	772	55–	Men	3	SBP	Mean changes	Age, sex, and

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et al. (2006)				80	and women	month		in the Med-Diet supplemented with EVOO, –5.9 mm Hg (95%CI: –8.7 to –3.1 mm Hg) and, Med-Diet supplemented with nuts, –7.1 mm Hg (95%CI: –10.0 to –4.1 mm Hg) compared with low-fat diet group.	baseline body weight.
Toledo et al. (2013)	Spain	RCT	7,447	55–80	♂3,346 ♀4,101	4 years	SBP and DBP	DBP: changes in the Med-Diet supplemented with EVOO, –1.53 mm Hg (95%CI: –2.01	Centre, age, sex, baseline T2DM, baseline number of anti-hypertensive drugs and

								to –1.04 mm Hg) and, Med-Diet supplemented with nuts, –0.65 mm Hg (95%CI: –1.15 to –0.15 mm Hg) compared with low-fat diet group. Between-group differences in SBP were not observed.	baseline SBP or DBP.
Medina-Remón et al. (2015)	Spain	RCT	200	55–80	♂87 ♀113	1 year	SBP and DBP	↓SBP: –5.79 mm Hg and –7.26 mm Hg; after the Med-EVOO and Med-nuts	Baseline BP, change in plasma nitric oxide, sex, age, BMI, smoking status, physical

								interventions, respectively, compared with the control diet. ↓DBP: –3.43 mm Hg and –3.26 mm Hg; after the Med-EVOO and Med-nuts interventions, respectively, compared with the control diet.	activity, medication use (antihypertensive, statins or other hypolipidemic drugs, insulin, oral hypoglycemic drugs and aspirin or other antiplatelet drugs) supplements taken in the last month, sodium, potassium, and total energy intake.
Doménech et al.	Spain	RCT	235	55–80	♂102 ♀133	1 year	24-hour ambulatory	Changes in mean SBP: –	/

(2014)							BP	2.3 (95%CI: –4.0 to –0.5) mm Hg and –2.6 (95% CI: –4.3 to –0.9) mm Hg in the Med-Diets supplemented with EVOO and supplemented with nuts, respectively. Respective changes in mean DBP: –1.2 (95% CI: –2.2 to –0.2), and –1.2 (95% CI: –2.2 to –0.2).	

♂ men

♀ women

BMI: body mass index;

BP: blood pressure

CHD: coronary heart disease

CI: confidence interval

CVD: cardiovascular disease

DBP: diastolic blood pressure

EVOO: extra virgin olive oil

HR: Hazard ratio

Med-Diet: Mediterranean Diet;

OR: odd ratio

RCT: Randomized Controlled Trial;

RR: rate ratio

SBP: systolic blood pressure

T2DM: Type 2 diabetes mellitus

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Table 4: General characteristics of the studies reporting the association between mediterranean patterns and Asthma.

Authors (year of study)	**Country**	**Type of study**	**Sample size**	**Age ranger (years)**	**Gender**	**Follow up**	**Main Outcome**	**Results**	**Adjustments**
Arvaniti et al. (2011)	Greece	Cross sectional	700	10–12	Children (323 boys)	/	Asthma symptom	Higher adherence to Med-Diet was associated with a lower prevalence of any asthma symptom (OR= 0.86; 95%CI: 0.75 to 0.98).	Age, sex, BMI, physical activity status, energy intake.

Barros et al. (2008)	Portugal	Cross sectional	174	25–55	♂ 32 ♀142	/	Asthma	High adherence to a Med-Diet ↓the risk of uncontrolled asthma by 78% (OR= 0.22; 95%CI: 0.05 to 0.85). Higher intake of fresh fruit ↓ the probability of having non-controlled asthma (OR= 0.29; 95%CI: 0.10 to 0.83),	Gender, age, education, energy intake and current use of inhaled corticosteroid.

								while a higher intake of ethanol had the opposite effect (OR= 3.16; 95%CI: 1.10 to 9.11)	
Castro-Rodriguez et al. (2008)	Spain	Cross sectional	1,784	3.28–4.88	Children	/	Current wheeze	Med-Diet was a protective factor for current wheezing (OR= 0.54; 95%CI: 0.33 to 0.88).	Age, birth weight, livestock during pregnancy, delivery by cesarean, antibiotic consumption during the first year, acetaminophen consumption

									during the previous 12 months, rhinoconjunctivitis, dermatitis, paternal asthma, maternal asthma, maternal age, maternal education level, current paternal smoking, current maternal smoking, vigorous physical activity frequency, cats at home in the

									last 12 months.
de Batlle et al. (2008)	Mexico	Cross sectional	1,476	6–7	Children	/	Ever asthma, ever wheezing, current wheezing	Adherence to Med-Diet was negatively associated with ever asthma (OR= 0.60; 95% CI: 0.40 to 0.91) and ever wheezing (OR= 0.64; 95% CI: 0.47 to 0.87).	Sex, maternal education, exercise, current tobacco smoking at home, maternal asthma, maternal rhinitis.
Garcia-Marcos et al. (2007)	Spain	Cross sectional	20,106	6–7	Children	/	Current occasional asthma,	Med-Diet was a protective factor for	Older and younger siblings, maternal

							current severe asthma	current severe asthma in girls (OR= 0.90; 95% CI: 0.82 to 0.98).	smoking.
Grigoropoulou et al. (2011)	Greece	Cross sectional	1125	10–12	Children (529 boys)	/	Ever asthma	Higher Mediterranean score was associated with a lower prevalence of ever-asthma (OR= 0.84; CI: 0.77 to 0.91). Urban areas, OR= 0.81; CI: 0.73 to	Environmental factors (details unknown).

								0.91; rural areas OR= 0.87; CI: 0.75 to 1.00	
Nagel et al. (2010)	20 countries	Cross sectional	50,004	8–12	Children	/	Ever asthma, current wheeze, and atopic wheeze	Higher adherence to Med-Diet was associated with a lower prevalence of ever asthma (OR= 0.95; 95% CI: 0.92 to 0.99) and current wheezing (OR= 0.97; 95% CI: 0.94 to	Age, sex, environmental tobacco smoke, parental atopy, exercise, number of siblings.

								0.99).	
Chatzi et al. (2007)	Spain	Longitudinal	967	6.5	507 pregnant women and 460 children	6.5 years	Persistent wheeze, atopic wheeze	Higher adherence to Med-Diet was a protective factor of persistent wheeze (OR= 0.22; CI: 0.08 to 0.58) and atopic wheeze (OR= 0.30; CI: 0.10 to 0.90).	Sex, maternal and paternal asthma, maternal social class and education, BMI, total energy intake, children adherence to Med-Diet at age 6.5.
Chatzi et al. (2013)	Spain, Greece	Longitudinal	2,516	29–33	2,516 pregnant	1 year	Wheeze in the first	Adherence to Med-Diet during	Maternal age; education; maternal history

					woman-infant pairs		year of life	pregnancy was not associated with wheeze in the first year of life	of asthma; smoking during pregnancy; parity; duration of breastfeeding; child's age at assessment; child's sex.
Castro-Rodriguez et al. (2010)	Spain	Longitudinal	1,409	14.1–19.1 months	1,409 pregnant woman-infant pairs	1 year	Ever wheezing during the first year	Med-diet score (excluding olive oil) was not associated with infants' ever wheezing during the first year. However, ol	Sex, exclusive breastfeeding, day care attendance, eczema, maternal asthma, smoking during pregnancy, siblings, mold on household wall, preterm

								ive oil was protective against ever-wheezing (OR= 0.57; CI: 0.4 to 0.9)	birth, olive oil.

♂ men

♀ women

BMI: body mass index

CI: confidence interval

Med-Diet: Mediterranean Diet

OR: odd ratio

Table 5: General characteristics of the studies reporting the association between mediterranean patterns and mental health problems.

Author (year of study)	Country	Type of study	Sample size	Age range (years)	Gender	Follow up	Main Outcome	Results	Adjustments
Scarmeas et al. (2006)	USA	Cross-sectiona	1,984	69–83	♂630 ♀1354	/	Prevalence AD	Higher adherence to the Med-Diet was associated with lower risk of Alzheimer's disease (OR=0.76; CI: 0.67 to 0.87) Subjects in middle Med-Diet tertile	Age, sex, education, ethnicity, cohort, caloric intake, apolipoprotein E genotype, BMI, smoking and, medical comorbidity index.

								OR= 0.47 (CI: 0.29 to 0.76); highest tertile OR=0.32 (CI: 0.17 to 0.59), compared with the lowest tertile.	
Scarmeas et al. (2009b)	USA	Longitudinal	1,393	70–83	♂603 ♀790	4.5 years	Mild cognitive impairment risk, conversion to AD	Subjects in the highest tertile had 28% less risk of developing mild cognitive impairment (HR= 0.72; CI: 0.52 to 1.00). Subjects in the highest Med-Diet	Age, sex, education, ethnicity, cohort, caloric intake, apolipoprotein E genotype, BMI, and time between 1st dietary and 1st cognitive assessment.

								adherence tertile had 48% less risk of developing Alzheimer's disease (HR= 0.52; CI: 0.30 to 0.91).	
Feart et al. (2009)	France	Longitudinal	1,410	67.7 – 94.9	♂527 ♀883	4.1 years	Cognitive decline, Dementia risk	Higher adherence to a Med-Diet was associated with slower MMSE. Med-diet adherence was not associated with the risk for incident dementia	Age, sex, education, marital status, energy intake, physical activity, depressive symptomatology, taking 5 medications/d or more, apolipoprotein E genotype, cardiovascular risk factors, and

									stroke.
Psaltopoulou et al. (2008)	Greece	Longitudinal	732	≥60	♂257 ♀475	8 years	Cognitive decline	Each unit increase in the Med-Diet score at baseline corresponds to 0.05 (95% CI: −0.09 to 0.19; P = 0.49) higher cognitive function on MMSE at follow-up.	Age, sex, education, marital status, caloric intake, height, physical activity, alcohol intake, smoking, depression, BMI, diabetes, hypertension
Vercambre et al. (2012)	USA	Longitudinal	2,504	66.1 – 91.2	♀2,504	5.4 years	Cognitive decline	Med-Diet style was not related to cognitive decline. 0.00 (95% CI:	Age, education, energy from diet, marital status, physical activity, use of multivitamin

								−0.02 to 0.01; $P = 0.88$	supplements, smoking status, body mass index, postmenopausal hormone therapy use, aspirin use exceeding 10 days during the previous month, nonsteroidal anti-inflammatory drug use exceeding 10 days during the previous month, history of depression, cardiovascular profile at baseline, diabetes, hypertension, hyperlipidemia and randomization

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									assignment for vitamin E, vitamin C, beta carotene and folate.
Scarmeas et al. (2009a)	USA	Longitudinal	1,880	70–83	♂587 ♀1293	5.4 years	AD risk	Moderate (HR=0.98; 95%CI: 0.72 to 1.33), and high Med-Diet scores (HR=0.60; 95%CI: 0.42 to 0.87), were associated with lower Alzheimer's disease risk when compared with low diet scores	Age, sex, education, ethnicity, cohort, caloric intake, apolipoprotein E genotype, BMI, smoking, comorbidity, depression, leisure activities, CDR score

Roberts et al. (2010)	USA	Cross-sectiona/longitudinal	1,233	70–89	♂641 ♀592	2.2 years	Mild cognitive impairment and Dementia risk	Prevalence mild cognitive impairment: OR= 0.80; 95% CI: 0.52 to1.25; *P* = 0.33) for highest tertile compared with lowest on Med-Diet score. Dementia: HR= 0.75; 95% CI: 0.46 to 1.21; *P* = 0.24) for highest tertile compared with lowest on Med-Diet	Age, sex, education, caloric intake, apolipoprotein E genotype, stroke, CHD and, depressive symptoms

								score.	
Tangney et al. (2011)	USA	Cross-sectional/longitudinal	3,790	69.2–81.6	♂1452 ♀2338	7.6 years	Cognitive function /cognitive decline	Each unit increase in the Med-Diet score corresponds to 0.007 (95% CI: 0.003 to 0.011; $P <$ 0.001) increase on the global cognitive Z score at baseline. Each unit increase in the Med-Diet score corresponds to 0.0014 (95% CI: 0.0006 to	Age, sex, education, race, total energy intake, participation in cognitive activities, interaction between time and dietary quality score

								0.0022; *P* < 0.001) less cognitive decline per year on the global cognitive Z score.	
Valls-Pedret et al. (2015)	Spain	RCT	447	66.9	♂214 ♀233	4.1 years	Cognitive function	Med-Diet groups scored better on the Rey Auditory Verbal Learning test (RAVLT), Color Trail test and tests for global cognition compared with controls	Sex, baseline age, years of education, apolipoprotein E genotype, smoking, body mass index, energy intake, physical activity, diabetes, hyperlipidemia, the ratio of total cholesterol to high-density lipoprotein

								(P< 0.05; all).	cholesterol, statin treatment, hypertension, and use of anticholinergic drugs.

♂ men

♀ women

AD: Alzheimer disease

BMI: body mass index

CI: confidence interval

HR: Hazard ratio

Med-Diet: Mediterranean Diet

MMSE: Mini-Mental State Examination test

OR: odd ratio

RCT: Randomized Controlled Trial

Table 6: General characteristics of the studies reporting the association between Dietary Approaches to Stop Hypertension (DASH) patterns and obesity.

Authors and years	**Country**	**Type of study**	**Sample size**	**Age range years**	**Gender**	**Follow up**	**Main Outcome**	**Results**	**Adjustments**
Champagne et al. (2011)	USA	RCT	828	28–83	♂311 ♀517	6 month	Weight loss	All participants in this substudy experienced a minimum 4 kg weight loss during Phase I and were randomized to weight maintenance (i.e., Phase	Site, age, race, sex, and race-by-sex interaction

								II). From baseline to 6 months (Phase I weight loss period), participants experienced significant decreases in weight (8.4 ± 0.1 kg)	
Blumenthal et al. (2010a)	USA	RCT	144	42–62	♂47 ♀97	4 months	Weight loss	Participants in the DASH diet plus weight management group lost on average 8.7 kg over 4 months.	Age, sex, ethnicity, posture in the analysis of ambulatory BP and for arterial diameter at rest in the

								The DASH diet alone intervention lost 0.3 kg.	FMD analysis.
Smith et al. (2010)	USA	RCT	124	42.7 – 61.9	♂45 ♀79	4month	Sychomotor speed	Participants on the DASH diet combined with a behavioral weight management program exhibited greater improvements in psychomotor speed (Cohen's D=0.480;	Age, years of education, intima-medial thickness (IMT), Framingham Stroke Risk Profile (FSRP), and abdominal adiposity.

								P=0.023)	
Corsino et al. (2012)	USA	Intervention study	56	28.8 – 47.2	♂9 ♀47	20 weeks	Weight loss	An average weight loss of 5.1 lbs (95%CI: -8.7 to -1.5; *P* = 0.006), and a reduction in BMI of 1.3 kg/m^2 (95%CI: -2.2 to -0.5; *P* =0.002)	/
Berz et al. (2011)	USA	Longitudinal	2,327	9–10	♀2,327	9 year	BMI	Girls in the highest vs lowest quintile of the DASH score had an adjusted	Race, height, socioeconomic status, television viewing and video game playing

								mean BMI of 24.4 *vs* 26.3 ($P < 0.05$)	hours, physical activity level, and total energy intake.

♂ men

♀ women

BMI: body mass index

BP: blood pressure

CI: confidence interval

DASH: Dietary Approaches to Stop Hypertension

FMD: flow-mediated dilation

RCT: Randomized Controlled Trial

Table 7: General characteristics of the studies reporting the association between DASH patterns and type 2 diabetes mellitus.

Authors (year of study)	Country	Type of study	Sample Size	Age range (years)	Gender	Follow up	Main Outcome	Results	Adjustments
Azadbakht et al. (2011)	USA	RCT	31	/	♂13 ♀18	8 weeks	FBG	FBG levels were reduced significantly (−29.4 ± 6.3 mg/dl; *P* = 0.04)	/
Ard et al. (2004)	USA	RCT	52	42.5 – 60.9	♂16 ♀36	6 month	Insulin sensitivity, FBG and insulin concentration	Significant improvements of up to 50% in insulin sensitivity. FBG levels and insulin concentration did not change significantly.	Baseline differences.
Lien et al.	USA	RCT	397	40.9 –	♂137 ♀260	24 wee	Fasting insulin	Significant decreases in fasting insulin levels and	Race, sex, age, the

(2007)				58.9		ks	levels, insulin resistance	in the homeostasis model index of insulin resistance.	baseline measure, site, and cohort.
Blumenthal et al. (2010b)	USA	RCT	144	42–62	♂ 47 ♀97	16 weeks	FBG, insulin sensitivity	DASH diet with aerobic exercise and caloric restriction demonstrated lower glucose levels after the oral glucose load and improved insulin sensitivity.	The corresponding pretreatment value of the outcome, age, sex, and ethnicity.
de Koning et al. (2011)	USA	Longitudinal	41,615	8–40	♂ 41,615	≤ 20 years	T2DM	The participants in the top quintile of the DASH score had a 25% lower risk than those in the bottom quintile (HR= 0.75; 95%CI: 0.65 to 0.85).	Smoking, physical activity, coffee intake, family history of type 2 diabetes, BMI, and total energy

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									intake.
Tobias et al. (2012a)	USA	Longitudinal	4,413	24–44	♀4413	16 years	T2DM	DASH pattern was associated with a 46% lower risk. (HR= 0.54; 95%CI: 0.39 to 0.73).	Age, total energy intake, parity, age at first birth, race/ethnicity, parental history of T2DM, oral contraceptive use, menopausal status, smoking status, total physical activity.
Tobias et al. (2012b)	USA	Longitudinal	15,254	24–44	♀15,254	11 years	Gestational diabetes mellitus	DASH pattern was associated with a 34% lower risk, RR= 0.66; (CI: 0.53 to 0.82).	Age, total energy intake, gravidity, smoking

									status, physical activity, sedentary time, parental history of T2DM, and, prepregnancy BMI.
Liese et al. (2009a)	USA	Longitudinal	862	40–69	Men and women	5 years	T2DM	DASH pattern was associated with a 69% lower risk in white participants [OR= 0.31; 95%CI: 0.13 to 0.75 (tertile 3 vs. tertile 1)], whereas no association was observed in blacks or Hispanics (OR= 1.34; 95%CI: 0.70 to 2.58)	Age, sex, BMI, race/ethnicity/clinic, glucose tolerance status, family history of diabetes, education, smoking status, energy intake, and

									energy expenditure.

♂ men

♀ women

BMI: body mass index

CI: confidence interval

DASH: Dietary Approaches to Stop Hypertension

FBG: fasting blood glucose

RCT: Randomized Controlled Trial

RR: relative risk

T2DM: Type 2 diabetes mellitus

Table 8: General characteristics of the studies reporting the association between DASH patterns and cardiovascular diseases.

Authors (year of study)	**Country**	**Type of study**	**Sample Size**	**Age range (years)**	**Gender**	**Follow up**	**Main Outcome**	**Results**	**Adjustments**
Appel et al. (1997)	USA	RCT	459	34–55	♂234 ♀225	8 weeks	SBP and DBP	Adherence to the DASH ↓ SBP and DBP, −5.5 mm Hg (−7.4 to −3.7) and −3.0 mm Hg (−4.3 to −1.6), respectively (P<0.001 for each). For subjects with hypertension: −11.4 mm Hg (−15.9 to −6.9)	Clinical center.

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								and −5.5 mm Hg (−8.2 to −2.7); and without hypertension: −3.5 mm Hg (−5.3 to −1.6) and −2.1 mm Hg (−3.6 to −0.5)	
Azadbakht et al. (2011)	USA	RCT	31	/	♂13 ♀18	8 weeks	SBP and DBP	Adherence to the DASH patterns ↓ SBP (−13.6 ± 3.5 mm Hg) and DBP BP (−9.5 ± 2.6)	/
Appel et al. (2003)	USA	RCT	810	41.1–58.9	♂308 ♀502	6 months	SBP and DBP	SBP ↓ “established” group −3.7 mm Hg (−5.3 to −2.1) "established plus DASH" group ↓	/

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								−4.3 mm Hg(−5.9 to −2.8) DBP ↓ “established” group −1.7 mm Hg (−2.8 to −0.6) "established plus DASH" group ↓ −2.6 mm Hg(−3.7 to −1.5)	
Blumenthal et al. (2010a)	USA	RCT	144	42–62	♂ 47 ♀97	4 months	SBP and DBP	DASH plus weight management: SBP ↓ 16.1 mm Hg/ DBP ↓ 9.9 mm Hg DASH diet: SBP ↓ 11.2mm Hg/ DBP ↓ 7.5 mm Hg.	Age, sex, ethnicity, posture in the analysis of ambulatory BP and for arterial diameter at rest in the

									FMD analysis.
Harnden et al. (2010)	UK	Intervention study	14	39–58	♂ 8 ♀6	30 days	SBP and DBP	SBP ↓ 4.6 mm Hg and DBP↓ 3.9 mm Hg	/
Fung et al. (2008)	USA	Longitudinal	88,517	30–55 34–59	♀88,517	24 years	Fatal and nonfatal CHD	The participants in the top quintile of the DASH score, CHD: RR= 0.76; 95% CI: 0.67 to 0.85). Stroke: RR= 0.82; 95%CI: 0.71 to 0.94).	Age, smoking, BMI, menopausal status and postmenopausal hormone use, energy intake, multivitamin intake, alcohol intake, family history, physical

									activity, and aspirin use
Agnoli et al. (2011)	Italy	Longitudinal	40,681	35–74	♂ 14,863 ♀ 32,158	7.9 years	Stroke	DASH score was not significantly inversely associated with risk of all types of stroke: HR = 0.75; 95%CI: 0.51 to 1.1; third vs. first tertile. But, it was significantly inversely associated with Ischemic stroke: HR = 0.53; 95%CI: 0.30 to 0.9	Sex, smoking status, education, nonalcoholic energy intake, and BMI.
Folsom et	USA	Longitudi	20,99	55–	♀20,99	17	All CVD	All CVD death:	Age, energy

al. (2007)		nal	3	69	3	years	death, Stroke death, Hypertension	HR = 0.93 (95%CI: 0.76 to 1.12) CHD death: 0.86; 95%CI: 0.67 to 1.12) Stroke death: HR = 0.82; 95%CI: 0.55 to 1.23) Hypertension: HR = 0.97; 95%CI: 0.87 to 1.07).	intake, education, BMI, waist/hip, smoking status, and pack-years, estrogen use, alcohol intake, physical activity and multivitamin use.
Levitan et al. (2009b)	Sweden	Longitudinal	38,947	45–79	♂ 38,947	9 years	Heart failure	RR= 0.78; 95%CI: 0.65 to 0.95	Age, physical activity, energy intake, education, family

									history of MI at age < 60 y, cigarette smoking, marital status, self-reported history of hypertension and high cholesterol, BMI, and incident MI.
Levitan et al. (2009a)	Sweden	Longitudinal	36,019	48–83	♀ 36,019	7 years	Heart failure	RR= 0.63; 95%CI: 0.48 to 0.81	Age, physical activity, energy intake, education status, family

									history of MI at age < 60 y, cigarette smoking, living alone, postmenopausal hormone use, self-reported history of hypertension and high cholesterol concentration, BMI, and incident MI
Parikh et al. (2009)	USA	Longitudinal	5,532	63.0–67.5	Men and women	8.2 person-years	All-cause mortality, stroke	DASH-like diet was associated with lower mortality from all-cause	Multiple confounders.

								mortality (HR= 0.69; CI: 0.52 to 0.92) and stroke (HR= 0.11; CI: 0.03 to 0.47)	

♂ men

♀ women

BMI: body mass index

BP: blood pressure

CHD: coronary heart disease

CI: confidence interval

DASH: Dietary Approaches to Stop Hypertension

DBP: diastolic blood pressure

FMD: flow-mediated dilation

HR: Hazard ratio

MI, myocardial infarction

RCT: Randomized Controlled Trial

RR: relative risk

SBP: systolic blood pressure

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Table 9: General characteristics of the studies reporting the association between DASH patterns and mental health problems.

Authors (year of study)	Country	Type of study	Sample Size	Age range (years)	Gender	Follow up	Main Outcome	Results	Adjustments
Smith et al. (2010)	USA	RCT	124	42.7–61.9	♂ 45 ♀79	4 month	Battery of neurocognitive tests for executive function, memory and learning	DASH diet + weight management: greater improvement in executive function, memory and learning (Cohen's d = 0.562; *P*=0.008).	Age, years of education, intima-medial thickness (IMT), Framingham Stroke Risk Profile (FSRP), and abdominal adiposity.

Norton et al. (2012)	USA	Longitudinal	2491	67.3–78.7	♂1270 ♀1221	6.3 years	Cognitive decline and dementia	Unhealthy - nonreligious (HR = 0.54; 95%CI: 0.31 to 0.93), healthy-moderately religious (HR = 0.56; 95%CI: 0.38 to 0.84), and healthy-very religious (HR = 0.58; 95%CI:	Age, sex, education, and apolipoprotein E status.

								0.40 to 0.84) had significantly lower dementia risk than Unhealthy-religious.	
Tangney et al. (2014)	USA	Longitudinal	826	74.4–88.6	Men and women	4.1 years	Cognitive decline	A 1-unit increase in DASH dietary adherence score was associated with a slower rate of cognitive decline by 0.007 units	Different covariates.

								(SE = 0.03, *P*= 0.03) in older persons	
Morris et al. (2015)	USA	Longitudinal	923	58–98	♂ 225 ♀698	4.5 years	Alzheimer's disease	The third tertile of the DASH diet (HR= 0.61; 95%CI: 0.38 to 0.97)	Age, sex, education, apolipoprotein E (any), participation in cognitively stimulating activities, physical activity, and total energy intake.

♂ men

♀ women

BMI: body mass index

CI: confidence interval

DASH: Dietary Approaches to Stop Hypertension

HR: Hazard ratio

RCT: Randomized Controlled Trial

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Table 10: Main studies in the context of prudent diet and health outcomes.

Authors (year of study)	**Country**	**Type of study**	**Sample Size**	**Age range (years)**	**Gender**	**Follow up**	**Main Outcome**	**Results**	**Adjustments**
Tucker et al. (2015)	USA	Cross-sectional	281	/	♀281	/	Obesity	Higher adherence to a prudent diet was associated with a lower body fat percentage (F = 8.5, P= 0.0038) and BMI (F = 4.4, P= 0.0363).	/
Murtaugh et al. (2007v)	USA	Cross-sectional	2470	25–79	♀2470	/	Overweight and obesity	Prudent dietary pattern was associated with a 29% lower prevalence of overweight and a halving of the	Age, center, physical activity level, total energy intake, and ethnicity.

								prevalence of obesity similarly in Hispanic and non-Hispanic white women.	
Paradis et al. (2009)	USA	Cross-sectional	664	18–55	♂272 ♀392	/	Obesity	Individuals in the upper tertile of the prudent pattern were less likely to be obese (OR=0.62; 95%CI: 0.40 to 0.96).	Age, gender and energy intakes.
Donova-Gutiérrez et al. (2011)	Mexico	Cross-sectional	6070	20–70	Men and women	/	Obesity	Individuals in the highest quintile of a prudent dietary pattern were less likely to have high-body fat (OR= 0.82; 95%CI: 0.70 to 0.98)	Age, sex, cigarette smoking, physical, weight change within last year, place of residence, estrogen use, and menopausal status.

Suliga et al. (2015)	Poland – Norway	Cross-sectional	2479	37–66	♂590 ♀1889	/	Obesity	Individuals in the highest tertile of prudent dietary pattern were found to have a lower OR for metabolic obesity normal weight (0.69; 95%CI: 0.53 to 0.89; $P< 0.01$)	Age, sex, place of residence, education, smoking and total physical activity.
Villegas et al. (2004)	Ireland	Cross-sectional	1018	50–69	♂491 ♀527	/	Insulin resistance	The prevalence of insulin resistance in the prudent diet was lower than that in the traditional diet (OR= 0.53; 95%CI: 0.33 to 0.85).	Age, sex, total daily energy intake, BMI, physical activity, smoking and socio-economic status.
van Dam et al. (2002)	USA	Longitudinal	42 504	40–75	♂42 504	12 years	T2DM	Prudent dietary pattern was associated with a	Age, BMI, total energy intake, time period,

								modestly lower risk (RR= 0.84; 95%CI: 0.70 to 1.00).	physical activity, cigarette smoking, alcohol consumption, ancestry, hypercholesterolemia, hypertension, and family history of type 2 diabetes mellitus.
Fung et al. (2004)	USA	Longitudinal	69,554	38–63	♀69,554	14 years	T2DM	RR = 0.8; 95%CI: 0.67 to 0.95 when comparing the highest to lowest quintiles of the prudent pattern.	Age, BMI, family history of diabetes, history of hypercholesterolemia, smoking , hormone therapy use, caloric intake, history of hypertension, physical activity,

									alcohol intake, and missing FFQ.
Malik et al. 2012	USA	Longitudinal	37,038	24–44	♀37,038	7 year	T2DM	Prudent pattern was not associated with risk of T2DM. RR = 0.98; 95%CI: 0.76 to 1.27 when comparing the highest to lowest quintiles of the prudent pattern.	BMI at age 18 years, total energy intake in high school, smoking between ages 15 and 19 years, and high school physical activity.
Ko et al. (2015)	USA	Cross-sectional	196	35–55	Men and women	/	CVD inflammation	Prudent diet pattern was negatively related to leptin, soluble intracellular adhesion molecule 1 (sICAM-1), and C-reactive protein (CRP).	BMI and total energy intake.

Lopez-Garcia et al. (2004)	USA	Cross-sectional	732	43–69	♀732	/	CVD inflammation	The prudent pattern was inversely associated with plasma concentrations of CRP (*P* = 0.02) and E-selectin (*P* = 0.001).	Age, BMI, physical activity, smoking status, and alcohol consumption.
Esmaillzadeh et al. (2007a)	Iran	Cross-sectional	486	40–60	♀486	/	CVD inflammation	The healthy pattern was inversely related to plasma concentrations of C-reactive protein (CRP) (beta = -0.09, *P* < 0.001), E-selectin (beta = -0.07, *P* < 0.05), and soluble vascular cell adhesion molecule-1 (sVCAM-1)	Age, cigarette smoking, physical activity, current estrogen use, menopausal status, family history of diabetes and stroke, energy intake, BMI and waist circumference
Heidemann et al.	USA	Longitudinal	72,113	30–55	♀72,113	18 year	CVD and all-	Prudent diet was associated with a	Age, BMI, follow-up,

(2008)						s	cause mortality	28% lower risk of cardiovascular mortality (RR= 0.72; 95%CI: 0.60 to 0.87) and a 17% lower risk of all-cause mortality (RR= 0.83; 95%CI: 0.76 to 0.90).	physical activity, smoking, hormone replacement therapy, history of hypertension, use of multivitamin supplements, missing FFQ during follow-up, and total energy intake.
Bakolis et al. (2010)	UK	Cross-sectional	1,453	16–50	♂587 ♀866	/	Chronic bronchitis, asthma	Prudent dietary pattern was positively associated with chronic bronchitis (OR= 2.61; CI: 1.13 to 6.05), but not with asthma (OR= 0.91; 95%CI: 0.53 to	For all other dietary patterns, age, sex, body mass index, social class, housing tenure, employment status, whether a single parent,

								1.56).	smoking, passive smoke exposure at home, total energy intake, ethnicity, number of siblings, paracetamol and supplement use.
Varraso et al. (2009)	France	Cross-sectional	54,672	40–65	♀54,672	/	Asthma	Prudent dietary pattern was not associated with current asthma (OR=1.02; 95%CI: 0.87 to 1.20), adult-onset asthma (RR=0.98; 95%CI: 0.81 to 1.19) or asthma attacks in asthmatic females (OR= 1.01; 95%CI: 0.65 to1.57).	Age, total energy intake, BMI, physical activity, smoking status, menopausal status, education and dietary supplementation.

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Shakersain et al. (2015)	Sweden	Longitudinal	2,223	≥60	♂871 ♀1352	6 years	Cognitive decline	The highest adherence to prudent pattern was related to less mini-mental state examination decline (β = 0.106, *P*= 0.011).	Age, sex, education, total energy intake, civil status, smoking, physical activity, BMI, vitamin or mineral supplement intakes, vascular disorders, diabetes, cancer, depression, apolipoprotein E genotype, and the other dietary pattern score

♂ men

♀ women

BMI: body mass index

CI: confidence interval

CRP: C-reactive protein

HOMA score: glucose homeostasis model

HR: Hazard ratio

OR: odd ratio

RCT: Randomized Controlled Trial

RR: relative risk

sICAM-1: soluble intracellular adhesion molecule 1

T2DM: Type 2 diabetes mellitus

(HOMA scores)

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Table 11: Main studies in the context of Seventh-Day Adventists diet and health outcomes.

Authors (year of study)	**Country**	**Type of study**	**Sample Size**	**Age range (years)**	**Gender**	**Follow up**	**Main Outcome**	**Results**	**Adjustments**
Brathwaite et al. (2003)	Barbados	Cross-sectional	407	25–74	♂153 ♀254	/	Obesity	Adherence to a vegetarian diet amongst Adventists is inversely associated with obesity.	/
Fraser, (1999)	USA	Longitudinal	34,192	≥25	♂13,857 ♀20,341	6 years	Obesity, ischemic heart disease	BMI increased with increasing meat consumption. Significant associations between beef consumption and fatal ischemic heart disease in men (RR= 2.31 for subjects who ate beef > or =3 times/wk compared with vegetarians). No	Age, smoking, exercise, BMI, hypertension, and consumption of bread, nuts, fish, cheese,

								associations were found between in women.	coffee, legumes, and fruit.
Tonstad et al. (2009)	USA and Canada	Cross-sectional	60,903	50.7–74.3	♂22,434 ♀38,469	/	T2DM	Vegans (OR= 0.51; 95%CI: 0.40 to 0.66), lacto-ovo vegetarians (OR= 0.54; CI: 0.49 to 0.60), pesco-vegetarians (OR= 0.70; 95%CI: 0.61 to 0.80), and semi-vegetarians (OR= 0.76; 95%CI: 0.65 to 0.90) had a lower risk of T2DM than non-vegetarians.	Age, sex, ethnicity, education, income, physical activity, television watching, sleep habits, alcohol use, and BMI.
Tonstad et al. (2013)	USA and Canada	Cross-sectional	41,387	44.4–75.1	♂15,200 ♀26,187	/	T2DM	Vegans (OR= 0.38; 95% CI: 0.24 to 0.62), lacto ovo vegetarians (OR= 0.618; 95% CI: 0.50 to 0.76) and semi-	Age, gender, education, income, television

								vegetarians (OR= 0.49, 95%CI: 0.31 to 0.75) had a lower risk of T2DM than non-vegetarians.	watching, physical activity, sleep, alcohol use, smoking and BMI.

♂ men

♀ women

BMI: body mass index

CI: confidence interval

OR: odd ratio

RR: relative risk

T2DM: Type 2 diabetes mellitus

(HOMA scores)

Table 12: Main studies in the context of Western dietary pattern and health outcomes.

Authors (year of study)	Country	Type of study	Sample Size	Age range (years)	Gender	Follow up	Main Outcome	Results	Adjustments
He et al. (2013)	China	Cross-sectional	20,827	45–69	♂9,936 ♀10,891	/	Metabolic syndrome	"Western/new affluence" dietary pattern was associated with a significantly elevated risk of metabolic syndrome (OR= 1.37; 95%CI: 1.13 to 1.67)	Age, sex, rural/urban, family income, educational level, current smoking, drinking, physical activity level, cooking salt and salted vegetable consumption,

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									dietary energy intake, family history of hypertension, and family history of diabetes.
Denova-Gutiérrez et al. (2010)	México	Cross-sectional	5,240	20–70	♂1,485 ♀3,755	/	Metabolic syndrome, fasting glucose, central obesity	Those in the highest tertile of Western pattern had higher OR for high fasting glucose (OR= 1.71; 95%CI: 1.40 to 2.10), metabolic syndrome	Age, sex, physical activity, place of residence, and weight changes, cigarette smoking, estrogen use, menopausal status and, energy intake.

								(OR= 1.58; 95%CI: 1.35 to 1.85), and central obesity (OR= 1.43; 95%CI: 1.23 to 1.67).	
Esmail lzadeh et al. (2008)	Iran	Cross-sectional	486	40–60	♀ 486	/	Obesity	Individuals in the upper quintile of western pattern had greater OR for general o besity: 2.48; 95% CI: 1.20 to 4.61 and for central obesity:	Age, smoking, current estrogen use, socioeconomic status, physical activity and energy intake.

								OR= 5.33; 95%CI: 2.85 to 10.6).	
Murtaugh et al. (2007)	USA	Cross-sectional	2,470	25–79	♀ 2,470	/	Overweight and obesity	Western patterns were associated with higher prevalence of overweight (OR= 2.07; 95%CI: 1.39 to 3.10) and obesity (OR= 2.11; 95%CI: 1.38 to 3.24) particularly among non-Hispanic	Age, center, physical activity level, total energy intake, and ethnicity.

								white women.	
Paradis et al. (2009)	USA	Cross-sectional	664	18–55	♂272 ♀392	/	Obesity	Individuals in the upper tertile of the Western pattern were more likely to be obese (OR=1.82; 95% CI: 1.16 to 2.87)	Age, gender and energy intakes.
Yu et al. (2015)	China	Cross-sectional	107,472	30–79	♂44,708 ♀62,764	/	Obesity	Individuals following a Western/new affluence dietary pattern had a significantly increased	Age, sex, study, marital status education level, household income, alcohol

								risk of general obesity PR: 1.06; 95%CI: 1.03 to1.08 and central obesity, PR: 1.07; 95%CI: 1.06 to 1.08).	consumption, tobacco smoking, and physical activity level in MET-hours/day.
Schulze et al. (2005)	USA	Cross-sectional/Longitudinal/Longitudinal	1,350/ 5,340/ 89,311	43–69/ 30–55/ 24–44/	♀1,350/ ♀35,340/ ♀89,311	/458,991 person-years /701,155 person-years	T2DM	Western dietary pattern was associated with an increased risk of diabetes (OR=3.09; 95%CI: 1.99	Age, BMI, physical activity, family history of diabetes in a first-degree relative, smoking, postmenopausal hormone

								to 4.79). RR= 2.56 (95%CI: 2.10 to 3.12) in the Nurses' Health Study and RR= 2.93 (95%CI: 2.18 to 3.92) in the Nurses' Health Study II, comparing extreme quintiles of the Western pattern.	use, total energy intake, and fasting status.
Darani	Iran	Cross-sectional	400	40–	Men	/	Fasting blood	Fasting	Age, sex,

et al. (2015)				60	and women		glucose	blood glucose was positively associated with western dietary pattern (b=0.014, *p*<0.05).	education, household income, occupation, marital status, smoking and physical activity, duration of diabetes mellitus, treatment of diabetes mellitus, family history of diabetes, hypertension, energy intake, and BMI.
Esmaillzadeh	Iran	Cross-sectional	486	40–60	♀486	/	Metabolic syndrome and	Women in the highest	Age, cigarette smoking,

et al. (2007b)							insulin resistance	quintile of Western dietary pattern scores had greater odds for the metabolic syndrome (OR=1.68; 95%CI: 1.10 to 1.95) and insulin resistance (OR=1.26; 95%CI: 1.00, 1.78).	physical activity, current estrogen use, menopausal status, and family history of diabetes, stroke and, energy intake,
Arisawa et al. (2014)	Japan	Cross-sectional	513	35–70	♂377 ♀136	/	Insulin Resistance	The high fat/Western pattern was positively correlated	Age, sex, total energy intake, physical activity, and smoking and

								with Homeostasis Model of Assessment-Insulin Resistance (HOMA-IR) (*P*=0.04)	drinking habits.
Lutsey et al. (2008)	USA	Longitudinal	9,514	45–64	♂4,196 ♀5,318	9 years	Metabolic syndrome	Participants in the highest quintile of Western dietary pattern scores had an 18% greater risk (HR= 1.18; 95% CI: 1.03 to 1.37)	Age, sex, race, education, center, total energy intake. Smoking, pack-years, and physical activity.

								of developing metabolic syndrome than those in the lowest quintile.	
van Dam et al. (2002)	USA	Longitudinal	42,504	40–75	♂ 42,504	12 years	T2DM	The western dietary pattern score was associated with an increased risk for T2DM (RR= 1.59; 95%CI: 1.32 to 1.93).	Age, BMI, total energy intake, time period, physical activity, cigarette smoking, alcohol consumption, ancestry, hypercholesterolemia, hypertension,

									and family history of type 2 diabetes mellitus.
Malik et al. (2012)	USA	Longitudinal	37,038	24–44	♀37,038	7 years	T2DM	The Western pattern was associated with 29% greater risk of T2DM (RR= 1.29; 95%CI: 1.00 to 1.66).	BMI at age 18 years, total energy intake in high school, smoking between ages 15 and 19 years, and high school physical activity.
Fung et al. (2004)	USA	Longitudinal	69,554	38–63	♀69,554	14 years	T2DM	Western pattern was associated with risk of T2DM. RR= 1.49;	Age, BMI, family history of diabetes, history of hypercholesterolemia,

								95%CI: 1.26 to1.76, when comparing the highest to lowest quintiles of the Western pattern.	smoking , hormone therapy use, caloric intake, history of hypertension, physical activity, alcohol intake, and missing FFQ.
Heidemann et al. (2008)	USA	Longitudinal	72,113	30–55	♀72,113	18 years	CVD and all-cause mortality	Western pattern was associated with a higher risk of mortality from CVD (RR= 1.22; 95%CI: 1.01 to 1.48) and	Age, BMI, follow-up, physical activity, smoking, hormone replacement therapy, history of hypertension,

								mortality for all causes (RR=1.21; 95%CI: 1.12 to 1.32) when the highest quintile was compared with the lowest quintile.	use of multivitamin supplements, missing FFQ during follow-up, and total energy intake.
Ambrosini et al. (2010)	Australia	Longitudinal	1,139	0–14	♂593 ♀546	14 years	High risk metabolic cluster,	Higher Western dietary pattern scores were associated with greater risk of the "high risk	Total energy intake, television viewing time, aerobic fitness, single parent status and maternal education.

								metabolic cluster" OR= 2.50; (1.05 to 5.98) in girls, but not boys OR= 0.66 (0.30 to 1.49).	
Labonté et al. (2014)	Canada	cross-sectional	666	22.8–50	♂666	/	CVD	Western patterns showed no association with any CVD risk factor.	Sex, age, waist circumference, physical activity, smoking status, drinking habits, education level, diabetes, and use of lipid-lowering

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									medication.
Martínez-González et al. (2014)	Spain	RCT	7216	60.8–73.2	♂3076 ♀4140	4.3 years	CVD, death	No significant association was found between the upper quartile of Western dietary pattern and the risk of cardiovascular events (HR= 1.05; 95%CI: 0.73 to 1.51), and death (HR= 1.04; 95%CI: 0.74 to 1.47).	Sex, age, intervention group and recruitment center, smoking status, baseline BMI, physical activity during leisure time, baseline self-reported hypertension, hypercholesterolemia, diabetes, history of previous depression and educational

									level.
Zazpe et al. (2014)	Spain	Longitudinal	16,008	25.8–50.4	♂6467 ♀9541	6.96 years	Death	No association between the highest tertile of adherence to the Western dietary pattern and total mortality was observed (HR= 0.79; 95%CI: 0.45 to 1.38)	Age, sex, total energy intake, total alcohol intake, smoking status, baseline BMI, physical activity during leisure time, self-reported hypertension, self-reported hypercholesterolemia, self-reported depression, years of university education, prescription of

									a special diet at baseline, and daily hours of television watching.
Varraso et al. (2009)	France	Cross-sectional	54,672	40–65	♀54,672	/	Asthma	Western dietary pattern was associated with an increased risk of reporting frequent asthma attacks (highest vs lowest tertile OR= 1.79; 95%CI: 1.11	Age, total energy intake, BMI, physical activity, smoking status, menopausal status, education and dietary supplementation.

								to 3.73) but not with current asthma OR= 0.98; 95%CI: 0.76 to 1.26).	
de Cássia Ribeiro Silva et al. (2013)	Brazil	Cross-sectional	1,187	6–12	child and adolescent	/	Wheeze	A positive statistically significant association between the Western pattern and wheeze was observed (OR= 1.77; 95%CI: 1.10 to 2.84).	Age, gender, education of caregivers, per capita income, number of people living in the household, presence of smokers in the house, BMI, stages of sexual maturity, and

									physical activity
Tromp et al. (2012)	Germany	Longitudinal	2,173	≤ 4	children	Post-natal follow-up	Wheeze	High adherence to the Western dietary pattern was significantly associated with frequent wheeze (≥4) at 3 years of age (RR= 1.47; 95%CI: 1.04 to 2.07).	Maternal age, maternal socioeconomic status, smoking during pregnancy, parental history of atopy, multiple parities, standard deviation score birthweight, sex, breastfeeding, vitamin D supplementation at 6–12

									months, daycare attendance in the first 2 yrs of life, and history of cow's milk allergy in the first year and total energy intake.
Miyake *et al.* (2011)	Japan	Cross-sectional	763	16–24 months	Mother-child pairs	/	Wheeze	Western pattern during pregnancy was inversely associated with the risk of childhood wheeze.	Maternal age, gestation, residential municipality, family income, maternal and paternal education, maternal and paternal

								(OR=0.59; 95%CI: 0.35 to 0.98)	history of allergic disorders, changes in maternal diet in pregnancy, season at baseline, maternal smoking during pregnancy, baby's older siblings, sex, birth weight, age at the third survey, household smoking, and breastfeeding duration.

♂ men

♀ women

BMI: body mass index

CI: confidence interval

FFQ: food frequency questionnaires.

HR: Hazard ratio

OR: odd ratio

PR: prevalence ratio.

RCT: Randomized Controlled Trial

RR: relative risk

T2DM: Type 2 diabetes mellitus

(HOMA scores)

 ACCEPTED MANUSCRIPT

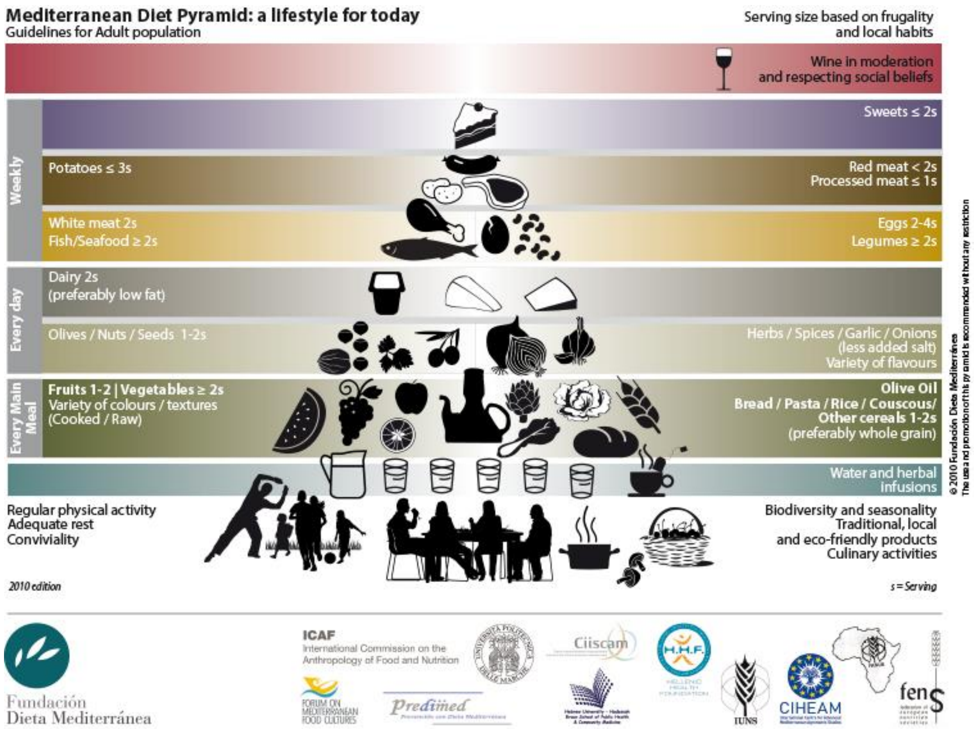

Figure 1. Mediterranean diet pyramid: a lifestyle for today.