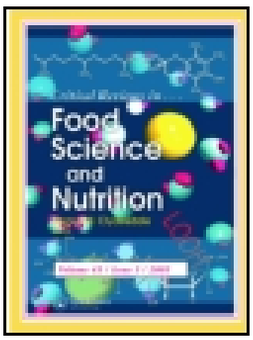

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REVIEW

Dietary habits, lipoprotein metabolism and cardiovascular disease: From individual foods to dietary patterns

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ABSTRACT

Cardiovascular disease (CVD) remains the first cause of mortality in Western countries. Among cardiometabolic risk factors, dyslipidemia, and especially high low-density lipoprotein cholesterol (LDL-C) concentrations, have been extensively linked to the development and progression of atherosclerosis and to CVD events. Recent evidence has shown that the prevention of unhealthy dietary habits and sedentarism is crucial in the management of dyslipidemia. In this sense, a number of scientific societies recommend the adherence to certain healthy dietary patterns (DPs), such as the Mediterranean diet (MedDiet), the Dietary Approaches to Stop Hypertension (DASH), the Portfolio diet, the Vegetarian diet, the Nordic diet and low-carbohydrate diets, as well as increased physical activity between others. This nutritional and lifestyle advice could be adopted by government bodies and implemented in different health programs as a reliable way of providing healthcare professionals with efficient tools to manage cardiometabolic risk factors and thus, prevent CVD. In this narrative review, we will discuss recent data about the effects of nutrition on dyslipidemia, mainly focusing on high LDL-C concentrations and other lipid particles related to atherogenic dyslipidemia such as triglycerides (TG) and non-high density lipoprotein cholesterol (non-HDL-C), that are related to CVD. On the other hand, we also comment on other cardiometabolic risk factors such as type 2 diabetes mellitus (T2DM), high blood pressure (HBP), inflammation and endothelial dysfunction. This review includes food groups as well as different healthy DPs.

KEYWORDS

Mediterranean diet; low-density lipoprotein cholesterol; healthy diet; cardiovascular disease; cardiometabolic risk factors

Introduction

Despite changes in lifestyle and intensive treatments to manage cardiometabolic risk factors, cardiovascular disease (CVD) currently remains the first cause of mortality in the world (Hartley et al. 2016, Writing Group Members et al. 2016). In particular, coronary heart disease (CHD) is now the most common cause of death worldwide (Cardiovascular disease in Europe 2016: an epidemiological update 2016, Ibanez et al. 2018).

Among cardiometabolic risk factors, dyslipidemia is one of the key modifiable factors related with CHD and CVD (Jellinger et al. 2017). Several lipoproteins have been related to atherosclerosis due to the cholesterol accumulation that they favor in the arterial wall; among them, low-density lipoprotein cholesterol (LDL-C) constitutes the cornerstone of treatment to prevent CVD events bringing an extensively evidence in this sense (Varbo and Nordestgaard 2016). However, high-density lipoprotein cholesterol (HDL-C) and triglycerides (TG) are also strong and independent predictors of CVD risk (Varbo and Nordestgaard 2016). Non-HDL-C has therefore been recognized as a secondary therapeutic target for CHD prevention. Furthermore, it has been suggested that non-HDL-C may provide a more accurate estimate of atherogenic particles, especially in patients with type 2 diabetes mellitus (T2DM) or metabolic syndrome (MetS) (Catapano et al. 2011).

Unhealthy dietary habits, such as the high consumption of saturated fatty acids (SFA), trans fatty acids (tFA), soft drinks and other refined carbohydrates, as well as tobacco and alcohol consumption are closely linked to obesity and dyslipidemia (Siri-Tarino and Krauss 2016). The management of dyslipidemia, and especially high LDL-C and total cholesterol (TC) concentrations, could be achieved by means of certain changes in the macronutrient composition of the diet: 1) replacement of tFA and SFA by monounsaturated (MUFA) and polyunsaturated fatty acids (PUFA), as recommended by scientific societies, e.g. the European Society of Cardiology and the European Atherosclerosis Society (ESC/EAS) (Catapano et al. 2016) or the Canadian Cardiovascular Society (CCS) (Anderson et al. 2016), 2) consumption of specific food groups (whole-grains, nuts and fruits etc.) and 3) intake of functional foods or nutraceuticals (fish oil, soluble fiber or phytosterols, etc.) (Eckel et al. 2014, Anand et al. 2015, Catapano et al. 2016, DeSalvo 2016). These dietary advices are summarized in Table 1.

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Dietary patterns (DPs) are highly heterogeneous between regions and countries, and public bodies have a part to play in helping to reduce the economic burden of unhealthy dietary habits and, consequently, of the increased incidence and prevalence of CVD (Imamura et al. 2015). Physical activity, avoidance of alcohol abuse and smoking cessation may also improve dyslipidemia and decrease CVD risk (Catapano et al. 2016). The implementation of healthy habits could be easier through adherence to certain DPs rather than specific advices about concrete nutrients or foods, since it can be better adopted irrespective of individual's biological, physical, physiological and socioeconomic factors (Nestle et al. 1998). Following the emerging role of dietary guidelines proposed by the different Scientific Societies mentioned in this review, we have therefore evaluated a number of different DPs which promote adherence and implementation of these healthy habits, including the Mediterranean Diet (MedDiet) (Willett et al. 1995), the dietary approaches to stop hypertension (DASH) (Appel et al. 2003), the Portfolio diet (Jenkins et al. 2011), the Vegetarian diet (Expert Panel on Detection, Evaluation, and and Treatment of High Blood Cholesterol in Adults 2001), the Nordic diet (Becker et al. 2004) (Nordisk Ra˚d and Nordisk Ministerra˚d 2005) and low-carbohydrate diets (Oh and Uppaluri 2019); and we have assessed their usefulness in managing dyslipidemia, including others cardiometabolic risk factors and CVD risk.

In this narrative review, we will discuss recent data on the effects of food groups and specific DPs on lipid metabolism and especially on LDL-C, TG and non-HDL-C, as well as different cardiometabolic risk factors, including type 2 diabetes mellitus (T2DM), high blood pressure (HBP), inflammation and endothelial dysfunction with a key impact on CVD risk.

Literature search strategy

To collect the data included in prospective cohort studies (PCS), randomized clinical trials (RCTs) and meta-analyses, we searched databases in Health Sciences, specifically: PubMed, Cochrane and data repository PubMed Central through the governmental website of Junta de Andalucía and Servicio Andaluz de Salud (http://www.bvsspa.es/profesionales/). MesH terms (http://www.ncbi.nlm.nih.gov/mesh) used for literature search were *"food"*, *"diet"*, *"cardiovascular diseases"*, *"lipid metabolism disorder"* and cardiometabolic risk factors such as: *"Diabetes Mellitus"* or *"Blood Pressure"*

Table 1. Recommended dietary changes to manage dyslipidemia according to different scientific societies.

Scientific society (year)	LIFESTYLE CHANGES			Ref.
	Fat (% of total cal.)	*Carbohydrates (% of total cal.)*	*Foods /others*	
AACE (2017)	– Total: 30-35%. - SFA: < 7%. – tFA: < 1%. – Cholesterol: < 200 mg/day. (level of evidence: A).	< 60% (level of evidence: A).	– Fruits and vegetables (combined ≥5 servings/day), grains (primarily whole grains), fish, and lean meats (level of evidence: A). – Phytosterols (~2 g/day), soluble fiber (10-25 g/day) and fish oil (2-4 g/day) (level of evidence: A).	(Jellinger et al. 2017)
ESC/EAS (2016)	– Total: < 35%. – SFA: < 10% or < 7% in dyslipidemia. – tFA: < 1%. – Cholesterol: < 300 mg/day). – n-6 PUFA: < 10%. (level of evidence: A). – Change SFA by MUFA and PUFA (level of evidence: A; B: TG)*.	– 45-55% – Sugar: < 10% of total cal. (level of evidence A). – Replace carbohydrates by MUFA or PUFA (level of evidence A).	– Phytosterols (~2 g/day), soluble fiber (7-13 g/day) and fish oil (2-4 g/day) (level of evidence: A).	(Catapano et al. 2016)
CCS (2016)	– SFA: < 7%. – Cholesterol: < 200 mg/day. (level of evidence: A).		– Nuts (>30 g/day), Phytosterols (>2 g/day), soluble fiber (>10 g/day) and fish oil (2-4 g/day) (level of evidence: A).	(Anderson et al. 2016)
AHA/ACC (2018)	– SFA: < 5-6%. – tFA: < 1%.		– Emphasize intake of vegetables, fruits, and whole grains; include low-fat dairy products, poultry, fish, legumes, non-tropical vegetable oils, and nuts; and limit the intake of sweets, sugar-sweetened beverages and red meats.	(Grundy et al. 2019)

Abbreviations: AACE, American Association of Clinical Endocrinologists; AHA/ACC, American Heart Association and American College of Cardiology; CCS, Canadian Cardiovascular Society, cal., calories; Canadian Cardiovascular Society; ESC/EAS, European Society of Cardiology and European Atherosclerosis Society; HDL-C, high density lipoprotein cholesterol; MUFA, monounsaturated fatty acid; LDL-C, low density lipoprotein cholesterol; PUFA; polyunsaturated fatty acid; Ref., reference; SFA, saturated fatty acid: tFA, trans fatty acid; TG; triglycerides.

Level of evidence is indicated in parentheses:

A: Data derived from multiple randomized clinical trials or meta-analyses.

B: Data derived from a single randomized clinical trial or large non-randomized studies.

*Level of evidence A for TC, LDL-C and HDL-C; level of evidence B for TG.

which were subsequently added to PubMed Search Builder to find the different studies. Furthermore, in PubMed Tools, we selected therapy, etiology and prognosis Clinical Study Categories in the Clinical Queries (accessible from: http://www.ncbi.nlm.nih.gov/pubmed/clinical). This literature search was performed with no time restriction up to 31 March 2020.

Food groups

Fish and marine omega-3 fatty acids

Fish and mainly oily fish are rich in PUFA, especially omega-3 (n-3) docosahexanoic acid (DHA) and eicosapentanoic acid (EPA) (Essential Fatty Acids | Linus Pauling Institute | Essential Fatty Acids | Linus Pauling Institute | Oregon State University 2018). The main sources of these n-3 PUFA are anchovy, herring, salmon and sardines. The ESC/EAS guidelines recommend a fish intake at least twice a week for the general population (Catapano et al. 2016). Similar advices have been recommended by the American Heart Association (AHA) (American Heart Association Nutrition Committee et al. 2006) and the CCS (Anderson et al. 2016). Nevertheless, given the increase of global per capita fish consumption over the last few years, it is important to assess its effects on health, food safety and sustainability.

Due to its content in n-3 PUFA, oily fish has been linked with a positive effect in dyslipidemia and specifically in patients with hypertriglyceridemia. A meta-analysis from 14 RCTs including 1378 subjects and published by Alhassan et al. (2007) showed a significant reduction in TG (-0.11 mmol/L; 95% CI -0.18 to -0.04; $p = 0.002$) and a significant increase in HDL-C (0.06 mmol/L, 95% CI 0.02 to -0.11; $p = 0.008$). Several mechanisms such as changes in phospholipid cellular synthesis and the regulation of sterol regulatory element-binding transcription factor-1 (SREBP-1) and lipoprotein lipase, may contribute to enhance TG clearance improving hypertriglyceridemia (López-Miranda et al. 2004, Delgado-Lista et al. 2010). On the other hand, a recent meta-analysis from 7 RCTs (Ursoniu et al. 2017), showed that the intake of Krill oil (a small crustacean from the Antarctic ocean, rich in n-3 PUFA) significantly reduced TG (-14.03 mg/dL; 95%CI: − 21.38 to -6.67; $p < 0.001$) and LDL-C concentrations (- 15.52 mg/dL; 95% CI: − 28.43 to -2.61; $p = 0.018$). The benefits of fish and concretely fish oil must be attributed to n-3 DHA and EPA. In relation to dyslipidemia, DHA has showed better outcomes in increasing HDL-C and Apo-AI concentrations, decreasing very low-density lipoprotein cholesterol (VLDL-C) and increasing the number of large LDL-C and HDL-C particles (Mori et al. 2000, Mikhailidis et al. 2011, Neff et al. 2011, Nikolic et al. 2013, Katsiki et al. 2014). Nonetheless, other nutrients included in this food (proteins, vitamins, minerals, etc.) may also play a positive role in managing dyslipidemia (Tørris, Småstuen, and Molin 2018).

A previous meta-analysis from PCS and case-control studies (Leung Yinko et al. 2014) showed an inverse association between fish consumption and CHD risk [relative risk (RR) 0.79; 95% confidence interval (CI): 0.70 to 0.89]. On the other hand, fish consumption may also be associated with a reduction in ischemic stroke (IS) risk as reported by (Qin et al. 2018) with a meta-analysis from PCS. Furthermore, a positive effect of fish intake on CVD mortality has been supported by a meta-analysis from PCS published by Jayedi et al. (2018) in which fish consumption was inversely associated with the risk of CVD death; in brief, a 20 g/d increase in fish consumption was inversely related to CVD mortality (RR 0.96; 95% CI: 0.94 to 0.98).

Based on the above, scientific advice from the AHA in 2018 included new recommendations to consume fish with n-3 PUFA twice a week, with benefits in the secondary prevention of heart failure (HF), IS and cardiac death risk, in addition to the secondary prevention of CHD, especially, if fish replaces the intake of unhealthy foods (Rimm et al. 2018). In contrast, the AHA scientific advisory board does not include specific advices in relation to fish and n-3 PUFA intake for the primary prevention of CVD and atrial fibrillation due to the lack of solid evidence of any beneficial effects in these endpoints. However, not all results in relation to fish consumption and n-3 PUFA have shown positive results. In 2012, a meta-analysis from RCTs published by Rizos et al. (2012) with more than 60,000 patients, evaluated the effect of n-3 PUFA on all-cause mortality, cardiac death, sudden death, MI and IS without significant results. Similar results were obtained in the meta-analysis published by Kwak et al. (2012) even in patients in secondary cardiovascular prevention after analyzing data from 14 RCTs with inconclusive effect of n-3 PUFA in CVD risk reduction. A subsequent meta-analysis from RCTs as published by Aung et al. (2018) do not support current recommendations for n-3 PUFA supplementation to lower CVD risk. In the same sense, although recent RCTs as the REDUCE-IT trial (Bhatt et al. 2018) showed that a certain amount and type of n-3 PUFA decreased CVD events, other subsequent RCTs such as the ASCEND (Bowman et al. 2018) and the VITAL (Manson et al. 2019) did not find any significant impact of n-3 PUFA on CVD morbidity and mortality. Obviously, specific therapeutic strategies and certain populations that would benefit more with n-3 fatty acid supplementation remain to be established (Perez-Martinez et al. 2020).

Since available data are controversial, long-term and RCTs are needed to clarify the potential health effects of fish and n-3 PUFA consumption.

Vegetable oils

Vegetable oils can vary widely in their MUFA, PUFA and SFA content. They are obtained from seeds such as sunflower, soy and rapeseed or fruits such as olives (Orsavova et al. 2015). Vegetable oils rich in MUFA (e.g. olive and canola oils) and PUFA (e.g. sunflower and soy oils) may beneficially affect dyslipidemia and CVD risk as showed a meta-analysis from 60 RCTs published by Mensik et al. (2003). In this context, olive oil has a high nutritional quality due to its components such as polyphenols. However, olive oil processing and storage may reduce the amounts of these components, thus minimizing their beneficial health effects. It should be noted that only extra virgin olive oil (EVOO) extraction techniques preserve these minor

components, thus maintaining its health benefits (Lorenzo et al. 2019). EVOO has been shown to reduce LDL-C (Lapointe, Couillard, and Lemieux 2006, Fitó et al. 2007) oxidation and inflammation during the postprandial state with different RCTs in this sense (Jiménez-Gómez et al. 2009). In a previous meta-analysis of PCS, a high intake of MUFA from EVOO was associated with a decrease in all-cause death (by 11%), CVD mortality (by 12%), CVD events (by 9%) and IS (by 17%) when compared with a low MUFA intake (Schwingshackl and Hoffmann 2014). One of the main advantages of EVOO compared with other vegetable oils lies in the extraction of the oil from the olives, which avoids certain chemical and mechanical procedures which could adversely affect the polyphenol content (Pérez-Jiménez et al. 2018). Polyphenols are a large group of phytochemicals with several subgroups including flavonoids, phenolic acids, lignans, stilbens between others (Tangney and Rasmussen 2013). Oxidative stress, chronic inflammation, postprandial lipemia and LDL-C oxidation may be differentially affected by these dietary components (Kishimoto, Tani, and Kondo 2013). In this context, the consumption of different foods containing polyphenols [tea (Ohmori et al. 2005) or EVOO (Covas et al. 2006)] has been shown to significantly decrease LDL-C oxidation. Furthermore, in a RCT published by Covas et al. (2006) showed a dose-dependent increase in HDL-C concentrations after a low-, medium-, and high-polyphenol EVOO intake: mean change = 0.025 mmol/L (95% CI: 0.003 to 0.05 mmol/L), 0.032 mmol/L (95% CI: 0.005 to 0.05 mmol/L), and 0.045 mmol/L (95% CI: 0.02 to 0.06 mmol/L), respectively. Similar findings from RCTs were observed in different populations, such as elderly or postmenopausal women, where EVOO consumption led to a decrease in TC, LDL-C and TG concentrations and a rise in HDL-C concentrations (Oliveras-López et al. 2013, Filip et al. 2015).

A daily intake of EVOO ranging from 20 to 40 g has been associated with improved lipid profile and CVD risk (Scientific Opinion on the substantiation of health claims related to olive oil and maintenance of normal blood LDL-cholesterol concentrations (ID 1316, 1332), maintenance of normal (fasting) blood concentrations of triglycerides (ID 1316, 1332), maintenan 2011, Pérez-Martínez et al. 2017). Nevertheless, the effects of EVOO on human health should be also considered in relation to the MedDiet (see below).

Besides EVOO, others vegetable oils differ in their PUFA, MUFA and SFA content, thus differentially affecting lipid metabolism and CVD. Vegetable oils rich in PUFA are obtained mainly from nuts (e.g. almonds), seeds (e.g. sunflower) and leafy vegetables (e.g. soybeans) (De Caterina et al. 2001). The most abundant PUFA in these vegetable oils is linoleic acid (n-6 LA) (Orsavova et al. 2015a) which demonstrated a positive effect in dyslipidemia (Bjermo et al. 2012). Indeed, PUFA and n-6 LA intake and especially when replacing SFA, reduced liver fat, TC, LDL-C and TG concentrations. Meta-analyses of RCTs failed to support a role of n-6 PUFA in the prevention of CHD events (Hamley et al. 2017), and therefore, the cardiovascular effects of n-6 PUFA needs to be better explored. On the other hand, n-3 PUFAs, represented mainly by α-linolenic acid (n-3 ALA), are present in less than 2% of fat in these vegetable oils (Orsavova et al. 2015b). As mentioned in the previous section, the n-3 marine PUFAs (DHA and EPA) possess most of the scientific evidence in the relationship of the n-3 PUFAs with cardiometabolic risk factors and CVD. However, various studies have explored the effect of n-3 ALA with CVD, also presenting contradictory results. A previous meta-analysis of PCS and RCTs by (Mente et al. 2009) reported no significant association of n-3 ALA with CHD, whereas others found a lower CVD risk with n-3 ALA (Pan et al. 2012). Given the uncertainty of the relation between n-6 and n-3 PUFA with cardiometabolic risk factors and CVD risk, the n-3/n-6 PUFA ratio has been proposed as a suitable CVD. In this context, it has been suggested that the reversal of the n-3/n-6 PUFA ratio by increasing n-3 intake could achieve a benefit in CVD risk. However, this positive effect could be related only with n-3 EPA and DHA from fish, rather than n-3 ALA from plants. Therefore, there is a heterogeneity in the role of each n-3 PUFA (Marventano et al. 2015).

Based on this knowledge, the importance of vegetable oils, and especially their MUFA and PUFA content, constitute a great way to improve plasma lipids and potential CVD risk. Above all, the majority of data support the healthy effects of MUFA vegetable oils and mainly EVOO, followed by PUFA vegetable oils such as those from sunflower, nuts and soybeans.

Nuts

Almonds, hazelnuts and walnuts are vegetable foods with over half their content in fat, predominantly MUFA (oleic acid) and PUFA (n-3 linolenic and n-6 linoleic acids) (Sabaté et al. 1993). Nut consumption with a minimum daily intake of 30 g (Anderson et al. 2016) exerts beneficial effects on lipids, with significant decreases in TC, LDL-C, TC/HDL-C ratio and LDL-C/HDL-C ratio (Sabaté, Oda, and Ros 2010). In this context, a previous meta-analysis by Del Gobbo et al. (2015) including 2,582 patients from 61 RCTs, showed that an approximate daily nut intake of 30 g led to a reduction of 5 mg/dL in TC and LDL-C concentrations, as well as a decrease of 4 mg/dL in apolipoprotein B (apoB) and 2 mg/dL in TG concentrations. Furthermore, as showed PCS, other cardiometabolic risk factors such as BP (Zhou et al. 2014), oxidative stress, inflammation and endothelial function (Ros 2015) may be improved by nut consumption. These benefits could further reduce an individual's CVD risk. In this context, nut consumption is associated with a decrease in CHD events and mortality, all-cause death, CVD morbidity and mortality and type 2 diabetes mellitus (T2DM), as shown in previous meta-analyses from PCS (Aune et al. 2016a, Mayhew et al. 2016, Chen et al. 2017). These findings strongly reinforce the role of nuts as an essential food in the diet.

Legumes and grains

Legumes are mainly composed of complex carbohydrates, as well as proteins, fiber and some micronutrients that may

affect lipids and CVD risk. Two meta-analyses of RCTs published by Anderson et al. (2002) and Bazzano et al. (2011) found that consumption of a large amount of legumes was associated with a significant decrease in TC (by 7.2%), LDL-C (by 6.2%) and TG concentrations (by 16.6%). These benefits may be attributed to the low quantity of fat, as well as to certain micronutrients including phytosterols and polyphenols, which inhibit cholesterol absorption in the small intestine (Sala-Vila, Estruch, and Ros 2015). Furthermore, data from PCS showed that legume consumption (4 weekly 100 g servings) has been associated with a 14% CHD risk reduction (Afshin et al. 2014).

Whole grains, such as corn, barley, oats and rice, have a similar macronutrient composition with a high quantity of complex carbohydrates as well as protein and a low quantity of fat (Rebello, Greenway, and Finley 2014). Whitehead et al. (2014) in their meta-analysis from RCTs concluded that consumption of >3 g/day of oat beta-glucan significantly decreased TC and LDL-C. Another meta-analysis of RCTs by Ho et al. (2016) showed that barley beta-glucan intake significantly reduced LDL-C and non-HDL-C. Furthermore, meta-analysis from PCS published by Aune et al. (2016b) reported that a high daily intake of whole grains was associated with a decrease in the risk of CHD (by 12%), IS (by 19%) and total CVD (by 22%), as well as reductions in all-cause death (by 15%) and T2DM (by 26%) risk. Similar findings were obtained by Chen et al. (2016) with a risk reduction of 12% for total mortality, 30% for CVD mortality and 32% for CHD mortality.

In contrast, refined grains have shown inconsistent results in relation to CVD. In 2006, the meta-analysis by Flight and Clifton (2006) concluded that the intake of refined grains had no effect on CVD risk. Later, Mellen et al. (2008) reached the same conclusion in the light of results obtained from seven PCS, reporting that refined grain intake was not associated with CVD incidence. Furthermore, the effect on CVD risk after replacing SFA with refined grains was previously investigated without significant results, as showed in the meta-analysis by Siri-Tarino et al. (2010). In contrast, a previous meta-analysis of PCS (in 2017) performed by Bechthold et al. (2017) showed a trend for a positive association between refined grain intake and CHD risk; however, no associations were observed with IS or HF. Data from a PCS (Li et al. 2015) showed a slight increase in CHD risk [RR 1.10; 95% CI: 1.00 to 1.21] following the replacement of 5% of the energy intake from SFA with refined grains. Based on the above data, we can conclude that the consumption of a minimum of 3 daily servings of legumes and grains, preferably whole grains, could improve CVD risk (Anderson et al. 2016).

Other food groups

Recommendations from scientific societies (Anderson et al. 2016, Catapano et al. 2016) and panels of experts (Pérez-Martínez et al. 2017, Pérez-Jiménez et al. 2018) include advices related to the consumption of other food groups, including fruits, eggs and dairy foods due to their effects in CVD risk factors.

Fruits

The daily intake of fruits reflects adherence to a plant-based DP characterized also by a replacement of red meat and animal source foods by whole grains, legumes and nuts, between others, with a consequent lipid-lowering effect due to a reduction in fat content and especially in SFA as showed in RCTs (Guasch-Ferré et al. 2019). Furthermore, there is evidence that a higher consumption of fruits is linked with an improvement in other cardiometabolic risk factors with data of PCS which showed a positive effect in high BP (HBP) (Wada, Urashima, and Fukumoto 2007) and T2DM (Cooper et al. 2012); as well as inflammation, oxidative stress and endothelial dysfunction as showed McCall et al. in a short-term intervention study (McCall et al. 2011). Such effects of fruit intake could lead to a reduction in CVD risk (Buil-Cosiales et al. 2016) beyond its effect on lipid metabolism. These benefits may be attributed to certain nutrients found in fruits, including soluble fiber, polyphenols and vitamins as we will discuss throughout the manuscript.

Eggs

Eggs fit into every DP and contain proteins (55 % ovalbumin) with all the essential amino acids and certain nutrients (vitamins, carotenoids and choline) which play a key role in cellular biology. On the other hand, fat content constitutes the 11% of each serving with a considerable content of MUFA (5 g/100g) but less content of PUFA (1,2 g/100g) and SFA (3 g/100g) (Pérez-Jiménez et al. 2018). For several decades, general dietary advices limited the consumption of eggs due to its cholesterol content. However, egg intake has not been associated with dyslipidemia (Kritchevsky 2004), whereas it could even improve the lipid profile (Blesso et al. 2013). Moreover, recent data support the absence of adverse effects in cardiometabolic risk factors after an intervention with a diet rich in eggs (Fuller et al. 2018). A previous meta-analysis of PCS by (Alexander, Miller, et al. 2016) showed that a daily egg intake may be related to a decreased IS risk, without affecting CHD risk. In this context, a consumption of no more than one egg per day does not negatively affect health status (Pérez-Jiménez et al. 2018), being even reported to reduce CVD risk as showed a meta-analysis from PCS (Bechthold et al. 2017).

Dairy foods

There are different and inconclusive results regarding the impact of dairy foods on the lipid profile. In this context, a meta-analysis of RCTs by Benatar et al. (Benatar, Sidhu, and Stewart 2013) did not find any significant effects of dairy foods on cardiometabolic risk factors, including LDL-C and HDL-C concentrations. Similarly, neutral effects on LDL-C were reported by two randomized crossover trials in relation to the intake of specific dairy foods, such as milk and cheese (Drouin-Chartier et al. 2015, Thorning et al. 2015). Of note, cheese

contains a moderate/high content of SFA. Furthermore, dairy food consumption did not affect HDL-C in the light of results published in a meta-analysis from RCTs (de Goede et al. 2015) and TG concentrations as showed by Crichton et al. in a 12-month crossover trial (Crichton et al. 2012). In contrast, Abdullah et al. reported in a multi-center crossover study that dairy intake increased LDL-C concentrations in healthy individuals (Abdullah et al. 2015). Furthermore, PCS with different dairy products, such as butter and cheese, may modify differently the lipid profile (Brassard et al. 2017). For example, butter can increase LDL-C to a greater extent than cheese (Brassard et al. 2017). Similarly, HDL-C concentrations were differentially affected after an intervention study with two isocaloric SFAs rich diets with butter or cheese (Brassard et al. 2018).

Full- and low-fat dairy products may also impact CVD risk differently. Two-meta-analysis of PCS showed that consumption of low-fat dairy products reduces the risk of T2DM (Chen et al. 2014) and MetS (as well as each MetS component) (Lee, Lee, and Kim 2018). In contrast, full-fat dairy products have a neutral effect on CVD risk as showed different meta-analysis from PCS (Alexander, Bylsma, et al. 2016, Pimpin et al. 2016) CCrichton and Alkerwi 2014, Drehmer et al. 2016). Thus, there is a need for further research to clarify what dairy products are better in terms of health benefits and whether low-fat dairy products should be recommended rather than full-fat (Drouin-Chartier et al. 2016).

Alcohol

Low and moderate alcohol intake (<2 daily drinks men): < 20-30 g alcohol and < 1 daily drink (women): < 20 g alcohol) (Alcohol and Heart Health | American Heart Association 2019) has often been postulated as beneficial in improving lipid metabolism, and especially increasing HDL-C concentrations (Tabara et al. 2017), among other cardiometabolic risk factors. Recently, research from the *Atherosclerosis Risk in Communities (ARIC) study* showed that alcohol consumption was associated with an increase in HDL-C concentrations and a reduction in TG, TC, LDL-C and apoB concentrations (Vu et al. 2016). However, the beneficial effects of alcohol also include its antioxidant (Park, Febbraio, and Silverstein 2009), antithrombotic (Mukamal et al. 2001) and anti-inflammatory (Maraldi et al. 2006) properties, which help produce the familiar J-Shaped relationship between alcohol intake and CVD exhibited in several PCS (Ronksley et al. 2011, Mostofsky et al. 2016, Xi et al. 2017). Nevertheless, recent meta-analyses from different PCS have cast doubts on this relationship (Stockwell et al. 2016, GBD 2016 Alcohol Collaborators et al. 2018, Wood et al. 2018). Further RCTs are therefore needed to clarify the effects of alcohol on health and general health advice in this area should be revised and refocused in order to attempt to decrease alcohol intake in the general population. In relation to beverage types, some PCS exhibit a greater benefit with red wine versus other types. In particular, the superiority of red wine is largely due to its content in polyphenols (Haseeb, Alexander, and Baranchuk 2017). Lippi et al. (2010) reported a positive effect of moderate consumption of red wine (1-2 daily drinks: 10-30 g alcohol) on cardiovascular health. In this context, an inverse association between low and moderate red wine intake and CVD risk was found in a meta-analysis by Di Castelnuovo et al. (2002).

Fried and processed

Fried and processed foods need to be considered in relation to cardiovascular health. Frying is a cook method that adversely modifies food (vegetables, potatoes, fish, shellfish, meat and poultry) by promoting oxidation and hydrogeneration, as well as increasing fat content (Guallar-Castillón et al. 2012). This cooking method makes the food much more palatable, but simultaneously increases energy intake, thus favoring obesity (Guallar-Castillón et al. 2007). Furthermore, when fried foods are consumed >2-4 times/week, PCS have been showed that the risk for dyslipidemia is increased (Ng et al. 2014), as well as for HBP by 18%(Sayon-Orea et al. 2014) and for T2DM by 27% (Odegaard et al. 2012). Consequently, an association between fried foods consumption and CVD risk have been reported by Cahill et al. (Cahill et al. 2014) in a PCS with 70,842 women from the *Nurses' Health Study* and 40,789 men from the *Health Professionals Follow-Up Study* obtaining a 23% increased CHD risk when fried foods are consumed >4 times/week. Furthermore, Djoussé et al. (2015) found a positive association between fried food intake and incident HF in a PCS from the *Physicians' Health Study*.

Processed foods exert adverse health effects due to changes in their nutritional composition with high sodium, SFA and tFA content, as well as lower fiber and vitamin content (Adams and White 2015). Processed foods have different ingredients that are used exclusively in food manufacturing. Thus, a meta-analysis of PCS (Wang et al. 2016, Micha et al. 2017, Zganiacz et al. 2017) and another one of PCS and RCTs (Micha et al. 2017), reported an association between processed foods intake and CVD risk. On the other hand, a PCS recently published (Srour et al. 2019), also found that the consumption of processed foods correlated with total CVD risk, as well as CHD and IS risk separately. Based on these data, it is advisable for the general population to reduce the consumption of fried and processed foods. It is necessary to include this recommendation in nutritional management guidelines.

Sweetened beverages

In relation to sweetened beverages (SBs), different exploratory outcomes have been obtained a linear association between their intake and cardiometabolic risk factors. As a first step, the relationship between consumption of SBs with alterations in the lipid profile has been confirmed in this PCS by Van Rompay et al. (2015) where these alterations appeared even in a population of children and adolescents after consumption of SBs over 12 months with a positively association with high TG concentrations and low HDL-c concentrations. Inside lipid profile, we have mentioned high TG concentrations and low HDL-c as the main fractions altered by SBs consumption as subsequent results recently showed by Haslam et al. (2020) with data from *Framingham Offspring Study* and *Generation Three cohorts* including more than 7,000 patients analyzed. In this PCS, SBs

consumption was associated with a greater decrease in HDL-c and an increase in TG concentrations respectively; even, regular low-calorie SBs consumption was associated with high no-HDL-c and LDL-c concentrations. On the other hand, SBs consumption have shown an association with other cardiovascular risk factors through different systematic reviews and meta-analyses from cross-sectional and PCS that showed: an increase in BP (Kim and Je 2016), a greater incidence in T2DM (Tong et al. 2018, (Imamura, O'Connor, et al. 2015) and obviously, an increased risk of MetS (Narain et al. 2017). Consequently with theses evidences, different meta-analyses from PCS support an association between SBs consumption and CVD risk (Narain et al. 2016, Malik and Hu 2019).

Dietary patterns

Beyond of 20 % of premature deaths globally are attributed to poor diet (Gakidou et al. 2017). As mentioned previously in Table 1, scientific societies recommend dietary changes and, in particular, increase in the intake of fruits, vegetables, whole grains, nuts and legumes, as well as moderate consumption of poultry and seafood with a reduction in sugar-sweetened beverages and red meat. These dietary advices are related to the effects of different foods on cardiometabolic risk factors, lipid metabolism and CVD risk. In this section, we reviewed different DPs included in these recommendations, such as the MedDiet, the DASH diet, the Portfolio diet, the Vegetarian diet, the Nordic and low-carbohydrate diets.

Mediterranean diet (MedDiet)

This DP, advocated by Willett et al. (Willett et al. 1995) in the early 1960s, is characterized by an increased consumption of vegetables, fruits, whole grain, legumes, nuts and seeds. The fat content ranges between 25 and >45%, depending on the country (Willett et al. 1995, Bach-Faig et al. 2011). This DP represents a healthy high-fat diet due to its limited SFA content (<7-10%) and the use of MUFA as the main source of fat from EVOO. The beneficial effects of EVOO have been widely reported; in particular, the minor components of EVOO (polyphenols, plant sterols etc.) may play an additional role in the health effects of this fat (Camargo et al. 2014). Furthermore, the MedDiet is characterized by the consumption of fish, poultry, eggs, red meat and wine (in low to moderate amounts) (Willett et al. 1995).

Short-term intervention studies have showed that MedDiet can improve glycemic control, dyslipidemia, chronic inflammation, oxidative stress and endothelial dysfunction (Delgado-Lista, Perez-Martinez, Garcia-Rios, Perez-Caballero, et al. 2016), constituting a valuable DP to reduce CVD risk, especially in "high-risk" patients (Chiva-Blanch, Badimon, and Estruch 2014).

There is evidence from clinical studies supporting the cardiometabolic benefits of this DP in terms of its favorable effects on obesity, HBP, T2DM and dyslipidemia (Gotsis et al. 2015). In this context, a meta-analysis by Nordmann et al. (Nordmann et al. 2011) (6 RCTs, 2,650 patients, 35-68 years) showed that the MedDiet significantly reduced body weight (- 2.2 kg; 95% CI: − 3.9 to - 0.6 kg), body mass index (BMI) (- 0.6 kg/m2; 95% CI: − 1 to - 0.1 kg/m^2), systolic BP (SBP; − 1.7 mmHg; 95% CI: − 3.3 to - 0.05 mmHg), diastolic BP (DBP; − 1.5 mmHg; 95% CI: − 2.1 to - 0.8 mmHg), fasting plasma glucose (FPG: − 3.8 mg/dL, 95% CI: − 7 to - 0.6 mg/dL), TC (- 7.4 mg/dL: 95% CI, − 10.3 to - 4.4 mg/dL), and high-sensitivity C-reactive protein (hsCRP; − 1.0 mg/L; 95% CI: − 1.5 to - 0.5 mg/L) compared with low-fat diets. No effects were observed in relation to LDL-C and HDL-C concentrations. In contrast, Quian et al. (2016) found that MedDiet favorably affected the lipid profile in a meta-analysis of RCTs with T2DM patients. Briefly, significant reductions in FPG (- 0.57 mmol/L; 95% CI: − 0.76 to - 0.39 mmol/L), TG (- 0.31 mmol/L; 95% CI: − 0.44 to - 0.18 mmol/L), body weight (- 1.56 kg; 95% CI: − 2.89 to - 0.23 kg) and SBP (- 2.31 mmHg; 95% CI: − 4.13, − 0.49 mmHg), as well as a significant increase in HDL-C concentrations (0.06 mmol/L; 95% CI: 0.02 to 0.10 mmol/L) were observed with high-MUFA compared with a high-carbohydrate DP. More recently, a cross-sectional study published by Vitale et al. (2018) confirmed that the MedDiet is a highly suitable DP for T2DM patients, leading to improvements in lipid profile, BMI, BP and glycated hemoglobin (HbA1c). Cross-sectional studies (Paletas et al. 2010) and retrospective cohort studies (Salvia et al. 2017), have demonstrated that the MedDiet is associated with a decrease in LDL-C concentrations, obesity and MetS prevalence, thus preventing CVD. MedDiet also reduced LDL-C oxidation compared with a low-fat diet (Fitó et al. 2007).

A high intake of fruits, legumes, nuts and whole grains (similar to those consumed in the MedDiet) has been associated with reduced CVD and CHD risk (Akesson et al. 2007). In this context, a meta-analysis of RCTs by Liyanage et al. (Liyanage et al. 2016) showed that consumption of the MedDiet was associated with a significant decrease in CVD (by 31%) and IS risk (by 34%). Similar findings were observed in the meta-analyses published by Rosato et al. (2019) with data obtained from PCS reporting an inverse association between MedDiet adherence and IS (RR 0.82; 95% CI: 0.73 to 0.92) risk. Finally, a meta-analysis performed with data from PCS and RCTs published by Grosso et al. (2017) obtained a reduction in CHD (RR 0.72; 95% CI: 0.60 to 0.86), MI (RR 0.67; 95% CI: 0.54 to 0.83) and IS (RR: 0.76; 95% CI: 0.60 to 0.96) risk in subjects with high MedDiet adherence compared with subjects with low adherence.

The Primary Prevention of Cardiovascular Disease with a Mediterranean Diet (PREDIMED) trial (Estruch et al. 2013) provided important evidence on the role of MedDiet in CVD prevention, further supporting the data provided by PCS. This multicentre clinical trial included 7,447 men and women (57%), 55 to 80 years of age, at high CVD risk but without established CVD at baseline. These patients were randomized to 3 DP: 1) MedDiet supplemented with EVOO, 2) MedDiet supplemented with mixed nuts, or, 3) control group (advised to decrease dietary fat). The trial ended in early 2013, with a median follow-up of 4.8 years.

The main results, published in 2013, were withdrawn recently, due to protocol deviations in the randomization process (Estruch et al. 2013). However, after removing from the analysis those patients with protocol deviations, significant results were obtained, with a reduction in major cardiovascular events with the MedDiet (supplemented with EVOO or nuts) compared with a reduced-fat diet (Estruch et al. 2013). Furthermore, HDL-C concentrations and LDL-C particle size significantly increased in the MedDiet groups (Damasceno et al. 2013).

The links between the MedDiet and CVD risk should be further elucidated in future trials, and there are currently 2 ongoing clinical trials, the PREDIMED-PLUS (ISRCTN89898870) and the CORonary Diet Intervention With Olive Oil and Cardiovascular PREVention trial (CORDIOPREV; NCT00924937), which will provide further data on these health effects. The PREDIMED-PLUS clinical trial (http://predimed-plus.com/) focuses on CVD prevention in MetS (BMI 27 to < 40 kg/m^2). Participants have been randomized to a MedDiet supplemented with EVOO and nuts, or to a hypocaloric MedDiet with similar supplementation and an intensive program of physical activity and weight-loss with CVD morbidity or mortality as primary endpoint. The CORDIOPREV study (Delgado-Lista, Perez-Martinez, Garcia-Rios, Alcala-Diaz, et al. 2016) evaluates the effect of 2 healthy DPs (MedDiet enriched with EVOO and a low-fat diet proposed by the AHA (Grundy et al. 2019) on CVD recurrence after a long-term intervention lasting 7 years. This is an ongoing prospective, randomized, open-label, controlled trial, including 1,002 patients with established CVD.

With this extensive evidence, MedDiet has been recently recognized as one of the most important DPs related to human health (Mediterranean Edges Out DASH for Best Diet of 2019 2019). Of note, a recent systematic review by Dinu et al. (2018), including 29 meta-analyses with 12,800,000 individuals that explored 37 health outcomes, showed that adherence to the MedDiet was correlated with a significant risk reduction in all-cause mortality and CVD, CHD, MI, cancer, neurodegenerative diseases and T2DM incidence. The ESC/EAS guidelines mention that the MedDiet may effectively reduce CVD risk factors, thus contributing to CVD prevention (Catapano et al. 2016). Similarly, the CCS recommends the implementation of the MedDiet to lower CVD risk (Anderson et al. 2016). Finally, the American Diabetes Association guidelines suggest adherence to the MedDiet to prevent T2DM development (American Diabetes Association 2018).

Dietary approaches to stop hypertension (DASH)

The Dietary Approaches to Stop Hypertension (DASH) has been extensively related to significant improvements in BP (Appel et al. 2003, Saneei et al. 2013, 2014). The DASH DP contains fruits and vegetables that provide high amounts of fiber and some micronutrients, such as potassium, calcium and magnesium. The main feature of this DP is its low-fat content, including dairy foods with reduced amounts of SFA, total fat and cholesterol (Appel et al. 1997). In recent years, the effects of DASH DP on other cardiometabolic risk factors such as dyslipidemia have been investigated and presented as guidelines to manage CVD risk (Grundy et al. 2019). The benefits of DASH DP in relation to the lipid profile do not change, even when the amount of fat in the diet is modified. In this context, a RCT published by Chiu et al. (2016) showed that a high-fat (HF) DASH DP significantly decreased TG and large and medium VLDL-C, without affecting LDL-C concentrations compared with a standard DASH DP. In the same study, the standard DASH DP led to a significant reduction in LDL-C, HDL-C, apolipoprotein A-I (apo A-I) and intermediate-density lipoprotein cholesterol (IDL-C) concentrations. Similarly, in a meta-analysis of RCTs (n = 1,917 subjects), DASH DP significantly lowered TC (- 0.20 mmol/L; 95% CI: − 0.31 to - 0.10 mmol/L; $p < 0.001$) and LDL-C concentrations (- 0.10 mmol/L; 95% CI: −0.20 to −0.01 mmol/L; $p = 0.03$) (Siervo et al. 2015).

Based on the beneficial effects of DASH DP on traditional cardiometabolic risk factors (BP and lipids), it has been suggested that this DP can contribute to CVD risk reduction. In a recent study involving data from 1,409 participants of the Medical Research Council (MRC) National Survey of Health and Development (Maddock et al. 2018), a high adherence to DASH DP was correlated with lower BP ($p \leq 0.08$), higher HDL-C ($p < 0.001$) and lower TG ($p < 0.001$) concentrations, as well as lower PWV (− 0.28 standard deviation; 95% CI: − 0.50 to − 0.07, p trend = 0.01) and carotid intima-media thickness (cIMT) (− 0.24 standard deviation; 95% CI: − 0.44 to − 0.04, p trend = 0.02) compared with those with low adherence to this DP.

In terms of CVD prevention, Fung et al. (2008) followed 88,517 female nurses with established CVD for 24 years and showed that adherence to the DASH DP was associated with lower risks of CHD (RR across quintiles of increasing adherence 1.0, 0.99, 0.86, 0.87 and 0.76; $p < 0.001$ for trend) and IS (RR across quintiles 1.0, 0.92, 0.91, 0.89 and 0.82; $p = 0.002$ for trend).

The DASH DP represents an effective nutritional strategy to manage cardiometabolic risk factors and CVD risk. Nevertheless, certain components of this DP (e.g. high fruit and vegetable intake and reduced SFA consumption through the low-fat dairy products intake) can also beneficially affect health disorders other than CVD. In this context, a meta-analysis of observational studies by Schwingshackl, Bogensberger, and Hoffmann (2018) (n = 1,670,179 subjects, 68 PCS) reported that the DASH DP was associated with a reduction in all-cause mortality (by 12%), T2DM (by 18%) and CVD (incidence or mortality; by 22%).

Portfolio diet

The Portfolio diet has been established as a healthy DP and has been progressively recognized over the last decade in different guidelines (Anderson et al. 2016, Catapano et al. 2016). This is a plant-based DP with 4 foods (nuts, soy protein, soluble fiber and phytosterols), mainly focused on managing the lipid profile (Jenkins et al. 2011). The main lipid particle that the Portfolio diet can affect is LDL-C. An intervention study by Jenkins et al. (2010) showed that the

Portfolio diet enriched with MUFA significantly decreased LDL-C and hsCRP concentrations, and increased HDL-C and apo A-I concentrations. In another intervention study, the Portfolio diet led to a significant decrease in LDL-C concentrations (by 28.6%) in hyperlipidemic patients, while a low-fat diet plus lovastatin 20 mg/d reduced LDL-C by 30.9% (Jenkins et al. 2003).

The 4 dietary components included in the Portfolio diet demonstrated benefits in BP, oxidative stress, inflammation and CVD risk. Keith, M. et al. (Keith et al. 2015) reported that the consumption of the Portfolio diet decreased homocysteine concentrations, as well as increased flow mediated dilatation and the number of endothelial progenitor cells (CD34+, CD 133+ and UEA-1+) in T2DM patients with CHD. A recent meta-analysis (Chiavaroli et al. 2018) (n = 439 hyperlipidemic patients, 7 RCTss) showed that the Portfolio diet significantly decreased LDL-C, non-HDL-C, apolipoprotein B, TC, TG, BP and hsCRP, thus reducing CHD risk. Further studies are needed to establish the role of the Portfolio diet in CVD risk management.

Vegetarian diet

In 2001, the NCEP ATP-III guidelines for the management of dyslipidemia recommended the limitation of total fat (and especially SFA) and an increase in the intake of vegetables and foods such as phytosterols, fiber and nuts, to prevent and/or manage dyslipidemia (Expert Panel on Detection, Evaluation, and and Treatment of High Blood Cholesterol in Adults 2001). These dietary recommendations, among others, are included in the Vegetarian DP, which favorably affects the lipid profile. In 2009, Ferdowsian and Barnard (2009) published a systematic review (n = 27 RCTs and PCS) defining 4 primary variants of the vegetarian DP: 1) vegan (containing no animal products), 2) ovolactovegetarian (including eggs and dairy products), 3) primary plant (similar to the ovolactovegetarian diet but allowing small amounts of lean meat), and 4) combination (a vegetarian or vegan diet combined with nuts, soy, and/or fiber). The 'combination' variant of the Vegetarian DP was associated with the greatest LDL-C reduction (up to 35%), followed by the vegan and the ovolactovegetarian variants. In another meta-analysis of RCTs by Wang et al. (2015), the Vegetarian diet achieved significant decreases in TC (− 0.36 mmol/L; 95% CI: − 0.55 to - 0.17 mmol/L; $p < 0.001$), LDL-C (− 0.34 mmol/L; 95% CI: − 0.57 to -0.11 mmol/L; $p < 0.001$), HDL-C (− 0.10 mmol/L; 95% CI: − 0.14 to − 0.06 mmol/L; $p < 0.001$) and non HDL-C concentrations (− 0.30 mmol/L; 95% CI: − 0.50 to - 0.10 mmol/L; $p = 0.04$).

The 2015 Dietary Guidelines Advisory Committee (2015-2020 Dietary Guidelines - health.gov 2018) highlighted the role of the Vegetarian diet in the management of dyslipidemia. Also, PCS such as published by Orlich et al. (Orlich et al. 2013) showed that Vegetarian diet decrease CHD and all-cause mortality. On the other hand, a recent meta-analysis published in Dinu et al. (2017) showed a reduction in CHD incidence and/or mortality risk (RR 0.75; 95% CI: 0.68 to 0.82). Further research is required to elucidate to elucidate whether the beneficial effect of this DP is extendable to other diseases and vascular territories.

Nordic diet

This emerging DP includes typical foods consumed in the Nordic countries, and features a high intake of fatty fish (e.g. salmon), low-fat dairy products, fruits (e.g. apples and pears), legumes, almonds or psyllium seeds, and berries (Becker et al. 2004) (Nordisk Ra˚d and Nordisk Ministerra˚d 2005). However, only a few studies have reported significant results for the Nordic diet in managing several cardiometabolic risk factors, in particular dyslipidemia, due to the high intake of LDL-C lowering foods (e.g. almonds or psyllium seeds). Adamsson et al. (2011) showed that consumption of the Nordic diet for 6 weeks achieved significant reductions in TC (by 16%, $p < 0.001$), LDL-C (by 21%, $p < 0.001$) and HDL-C concentrations (by 5%, $p < 0.01$), LDL-C/HDL-C ratio (by 14%, $p < 0.01$) and apoB/apoA-I ratio (by 1%, $p < 0.05$); insulin sensitivity and BP were also significantly improved. Similar results in the lipid profile were observed in MetS patients, with significant changes in non-HDL-C concentrations, LDL-C/HDL-C and apoB/apoAI ratios (Uusitupa et al. 2013). A recent review including 513 patients from 5 RCTs also reported that the Nordic diet significantly lowered BP and lipids, with decreased TC (- 0.38 mmol/L; 95% CI: − 0.76 to - 0.01; $p = 0.04$) and LDL-C (- 0.30 mmol/L; 95% CI: − 0.54 to - 0.06; $p = 0.013$) but without changes in HDL-C and TG concentrations. The Nordic diet also significantly reduced SBP (- 3.97 mmHg; 95% CI: − 6.40 to - 1.54; $p = 0.001$) and DBP (- 2.08 mmHg; 95% CI: − 3.43 to - 0.72; $p = 0.003$) (Ramezani-Jolfaie, Mohammadi, and Salehi-Abargouei 2019).

The long-term effects of the Nordic diet on CVD risk have not been clearly demonstrated. The *Swedish Women's Lifestyle and Health cohort* (n = 43,310 women, follow-up = 20 years) (Roswall et al. 2015) and the *EPIC-Potsdam cohort* (n = 27,548 patients, follow-up = 10.6 years) (Galbete et al. 2018) failed to show that the Nordic diet could prevent CVD. Therefore, further studies are necessary to clarify the effects of long-term dietary interventions with the Nordic diet on CVD risk.

Low-carbohydrate diets

Low-carbohydrate diet has been classically defined as a DP with a carbohydrate content <26% of the overall macronutrient composition or total carbohydrate intake <130 g/day (Oh and Uppaluri 2019). The main benefit of this diet is the promotion of weight loss (Bueno et al. 2013, Mansoor et al. 2016). Nonetheless, this DP generally includes a high protein and fat (even SFA) content, thus being less appropriate for dyslipidemia management as supported by studies showing an increase in TC and LDL-C concentrations in relation to this DP (Tay et al. 2008). However, beneficial effects have also been observed with this DP in lipid metabolism markers with greater decreases in TG, TC and LDL-C, as well as greater increases in HDL-C concentrations.

Table 2. Effects of different dietary patterns on cardiometabolic risk factors, cardiovascular disease, cancer and mortality.

AUTHOR	DIET	YEAR	MA (No of studies)	N	RESULTS	REF.
Nordmann	MedDiet	2011	YES (6)[a]	2,650	− 2.2 kg weight; − 0.6 kg/m^2 BMI; SBP - 1.7 mmHg; DBP - 1.5 mmHg; FPG - 3.8 mg/dL; TC - 7.4 mg/dL; hsCRP - 1.0 mg/L compared with low-fat diets.	(Nordmann et al. 2011)
Qian	MedDiet	2016	YES (24)[a]	2,460	− 1.56 kg weight; − 0.57 mmol/L FPG; − 0.31 mmol/L TG; + 0.06 mmol/L HDL-C; − 2.31 mmHg SBP compared with CHO-diets.	(Qian et al. 2016)
Liyanage	MedDiet	2016	YES (6)[a]	10,950	A decrease of: 31% in CVD risk and 34% in IS risk.	(Liyanage et al. 2016)
Grosso	MedDiet	2017	YES (29)[a]	–	A decrease of: 28% in CHD risk and 24% in IS risk.	(Grosso et al. 2017)
Dinu	MedDiet	2018	YES (29)[a,b]	12,800,000	Significant ($p < 0.001$) risk reductions in all-cause mortality, CVD, CHD, MI, and T2D incidence. Significant ($p < 0.05$) risk reduction in certain site-specific cancers and inflammatory/metabolic parameters.	(Dinu et al. 2018)
Siervo	DASH	2015	YES (20)[a]	1,917	− 0.2 mmol/L TC; − 0.10 mml/L LDL-C; − 5.2 mmHg SBP; − 2.6 DBP mmHg.	(Siervo et al. 2015)
Maddock	DASH	2018	NO	1,409	High adherence led to lower BP ($p \leq 0.08$), higher HDL-C ($p < 0.001$) and lower TG ($p < 0.001$) levels, as well as reduced - 0.28 PWV and - 0.24 cIMT.	(Maddock et al. 2018)
Schwingshackl	DASH	2018	YES (68)[b]	1,670,179	Association with a decrease of: 22% in CVD risk (incidence or mortality) and 22% in all-cause mortality.	(Schwingshackl, Bogensberger, and Hoffmann 2018)
Chiavaroli	Portfolio	2018	YES (7)[a]	439	A decrease of: 12% TC,17% LDL-C, 16% TG, 14% non-HDL-C; 15% apoB; 1% SBP; 2% DBP; 32% hsCRP and 10% 10-year CHD risk combined with a NCEP step-II dietary pattern.	(Chiavaroli et al. 2018)
Wang	Vegetarian	2015	YES (11)[a]	832	− 0.36 mmol/L TC; − 0.34 L mmol/L LDL-C; − 0.10 mmol/L HDL-C; − 0.30 mmol/L non HDL-C.	(Wang et al. 2015)
Dinu	Vegetarian	2017	YES (10)[b]	–	Association with a decrease of: 25% in CHD mortality.	(Dinu et al. 2017)
Ramezani-Jolfaie	Nordic	2018	YES (15)[a]	513	− 0.38 mmol/L TC; − 0.30 mmol/L LDL-C; − 3.97 mmHg SBP; − 2.08 mmHg DBP.	(Ramezani-Jolfaie, Mohammadi, and Salehi-Abargouei 2019)
Hu	Low-carbohydrate	2012	YES (23)[a]	2,788	− 2.7 mg/dL TC; − 3.7 mg/dL LDL-C; + 3.3 mg/dL HDL-C; − 14.0 mg/dL TG.	(Hu et al. 2012)
Gjuladin-Hellon	Low-carbohydrate	2019	YES (8)[a]	1,633	+ 0.08 mmol/L HDL-C; −0.13 mmol/L TG compared with low-fat diet.	(Gjuladin-Hellon et al. 2019).

Abbreviations: apo A-I, apolipoprotein A1; apoB, apolipoprotein B; BMI, body mass index; CHD, coronary heart disease; CHO, carbohydrates; cIMT, carotid intima-media thickness; CVD, cardiovascular disease; DASH, dietary approaches to stop hypertension; DBP, diastolic blood pressure; FPG, plasma glucose; HDL-C, high density lipoprotein cholesterol; hsCRP, high sensitivity C reactive protein; IS, ischemic stroke; kg, kilograms; LDL-C, low density lipoprotein cholesterol; MA, meta-analysis; MedDiet, Mediterranean diet; MI: myocardial infarction;NCEP, national cholesterol education program; PWV, pulse wave velocity; REF., reference; SBP, systolic blood pressure; SFA, saturated fatty acid; T2D, type 2 diabetes mellitus; TC, total cholesterol; TG, triglycerides.

MA (No. of studies): This column shows if the evidence presented comes from a meta-analysis or not, with the number of studies included in each case in parentheses. [a]Meta-analysis of clinical trials; [b]Meta-analysis of observational studies.

Specifically, a RCT published in Yancy et al. (2004) showed that this DP favored a weight loss compared with a low-fat diet (mean change: −12.9% vs. −6.7%; $p < 0.001$) and also a decrease in TG (change: −74.2 mg/dL vs. −27.9 mg/dL; $p = 0.004$) and a greater increase in HDL-C (5.5 mg/dL vs. −1.6 mg/dL; $p < 0.001$). In 2012, a meta-analysis of RCTs (Hu et al. 2012) showed a reduction in TC, LDL-C, a greater increase HDL-C and a greater decrease TG concentrations. The positive effect of this DP on dyslipidemia has been recently confirmed in a meta-analysis (Gjuladin-Hellon et al. 2019). This DP may also lead to increases in LDL-C particle size (Morgan et al. 2009).

Low-carbohydrate diets may also improve glucose metabolism (Tay et al. 2018), as well as other cardiometabolic risk factors in patients with T2DM (Bhanpuri et al. 2018), thus representing an attractive therapeutic option in these patients (American Diabetes Association 2019). In 2009, a short-term dietary intervention showed a reduction in LDL-C concentration and TC/HDL-C and apoB/apoAI ratios were greater for this DP compared with a high-carbohydrate diet (Jenkins et al. 2009). Recently, a meta-analysis of PCS showed that low-carbohydrate diet health benefits even more consistent in the presence of increased fat content with PUFA and MUFA from vegetables and plant foods (Seidelmann et al. 2018). However, there is no clear evidence up-to-date to link a low-carbohydrate DP with CVD risk reduction (Clar et al. 2017). Obviously, large, randomized clinical trials need to be conducted to obtain direct conclusions regarding the benefits of this DP on CVD risk. Until then, dietary guidelines could consider this DP as an

alternative for the management of dyslipidemia in the light of these evidences.

The different DPs reviewed above have been beneficial on lipid metabolism, cardiometabolic risk factors and CVD risk. Among them, the MedDiet and the DASH diet constitute the best DPs to improve cardiovascular health. However, it is necessary to highlight that adherence to DPs have been primarily measured by food frequency questionnaires (FFQ) (for example the 137-item FFQ) (Fernández-Ballart et al. 2010). On the other hand, in each specific DP the adherence is measured by specific scores as the 14-item dietary screener to assess adherence to the MedDiet (Martínez-González et al. 2002) or the DASH score based on 8 food and nutrient components (Fung 2008). These questionnaires include items related to food habits and frequency of food consumption. However, this method of data collection may have certain limitations, such as the subjectivity of the information expressed by the patient and the need to recall specific dietary habits over a relatively long follow-up period.

Obviously, this is a key feature in order to collect information on dietary habits in PCS as well as obtaining rigorous and reliable results in those researches in which a specific dietary intervention is carried out. New methods to measure the adherence to DPs could avoid biases derived from the subjective assessment. Among them, the measurement of specific urine metabolites to ascertain the intake of specific foods (Landberg et al. 2018) or DPs using metabolomics (Almanza-Aguilera et al. 2017) and even, the dietary self-monitoring using apps with multiple indicators of adherence (Patel et al. 2019), could improve the assessment of these DPs and foods

The effects of different DPs on cardiometabolic risk factors, CVD, cancer and mortality are summarized in Table 2.

Conclusions

In summary, to adequately control cardiometabolic risk factors such as dyslipidemia, T2DM and HBP, it is necessary to increase the consumption of fish and plant-based foods such as fruits, legumes, EVOO, nuts and whole-grains, whereas minimize the intake of fried and processed foods, as well as refined grains. On the other hand, a moderate intake of eggs and dairy products should be recommended based on their cardiometabolic benefits.

Certain DPs demonstrated lipid-lowering and CVD preventive effects. Based on such data by epidemiological studies and clinical trials, dietary advice from some scientific societies has been progressively changed, supporting adherence to specific DPs rather than the consumption of specific foods. The MedDiet and the DASH diet, and to a lesser extent the Portfolio, Vegetarian, Nordic and low-carbohydrate DPs, were also shown to improve cardiometabolic risks factors and reduce the risk of CVD morbidity or mortality. The MedDiet and the DASH diet seem to represent the best dietary tools to improve cardiovascular health, although further large-scale randomized clinical trials are necessary to confirm this. In particular, the MedDiet is the most recommended DP to reduce CVD risk in different populations by some scientific societies. On the other hand, the DASH DP also showed a significant reduction in CVD risk, especially in terms of HBP prevention and management. Nevertheless, certain barriers limit the implementation of these DP in the general population, including the popularity of poor quality take-away food with a high content in SFA and total energy (Zang et al. 2018), the high economic cost of these healthy DP compared with Western diets (Tong et al. 2018) and the socioeconomic status of some food types in certain populations (Fitzpatrick et al. 2018). Clinicians should adapt their advice regarding the most appropriate DP for each individual according to the factors mentioned above.

Age, gender, genetics, BMI and health status are crucial predictors in the response to lifestyle changes, and specifically to diet. Therefore, the benefits of DPs may differ between individuals. In this context, the emerging field of research in nutrigenetics has shown that nutritional advice could be tailored to the individual's genetic background (Garcia-Rios et al. 2012, Gomez-Delgado et al. 2014). Data from long-term dietary interventions and nutrigenetics could provide us with an effective health tool to improve cardiometabolic risk factors, thus treating, or even preventing, cardiometabolic diseases such as dyslipidemia, hypertension and CVD; choosing in each patient the best DP and foods to obtain the most benefit on health.

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