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Reduction of Low-Density Lipoprotein Cholesterol through Plant-Based Diets: A Scoping Review

Supervisor
Prof. Valerie Tikhonoff

Submitted by
Monika Kim
Student no.
2108084

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Abstract

Background: Cardiovascular disease (CVD) is the leading cause of death in the world. High levels of low-density lipoprotein cholesterol (LDL-C) are recognized as a key modifiable factor of CVD and currently managed by pharmacological therapies such as statins. There is an increasing interest in applying dietary interventions as a non-drug approach for lowering LDL-C. Recent research demonstrated that a plant-based diet characterized by high intake of vegetables and fruits, legumes, nuts, whole grains and limited amount of meat products can substantially reduce LDL-C levels.

Objective: This review aims to summarize the available evidence on the association between various plant-based diets and LDL-C, highlight current knowledge gaps in this developing field, and suggest areas for future research.

Methods: A comprehensive search was conducted to identify relevant studies describing plant-based diets and LDL-C using PubMed, Scopus and Web of Science databases over the last 10 years. An independent reviewer screened studies for eligibility and then charted data. Extracted data included study characteristics, dietary intervention, and outcome measures.

Results: Out of 900 studies, 18 eligible studies were identified including 11 RCTs, 3 cohorts, and 4 systematic reviews with meta-analysis. The collective evidence demonstrated that plant-based diets are associated with decreased levels of LDL-C levels, where vegan diets had the most consistent results while others had an effect depending on adherence and duration.

Conclusion: This scoping review highlighted the potential of plant-based diets in management of cardiovascular health.

1. Introduction

Cardiovascular diseases (CVDs) are the predominant cause of mortality worldwide, accounting for one third of deaths (1). Nearly half of adults aged 20 years and older in the US have CVD, which includes conditions such as coronary heart disease (CHD), heart failure, stroke and hypertension, and the prevalence of CVD increases with age for both males and females (2). Beyond this, the high prevalence of CVD places an enormous economic burden on patients and health care systems, € 282 billion in the EU in 2021 and $423.3 billion in the US between 2019 and 2020, including healthcare services, prescribed medications, and lost productivity years (2,3). This issue underscores the need for effective strategies aimed at the risk factors of CVD that can improve this issue.

The development of CVD is substantially driven by modifiable and non-modifiable risk factors. Three high-profile modifiable risk factors of CVD are hypertension, high cholesterol levels, and overweight/obesity (4). Other significant factors are diabetes mellitus, smoking, unhealthy dietary patterns, low physical activity and consumption of alcohol (5). Non-modifiable risk factors include age, gender, family history of heart disease and ethnicity (6). In most cases, risk factors cluster with each other, increasing significantly the risk for CHD, stroke and all-cause mortality (7). Among them, dyslipidemia is one of the major risk factors and characterized by high levels of plasma total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), and low levels of high-density lipoprotein cholesterol (HDL-C) (8). The management of modifiable risk factors can prevent major CVD events.

Atherosclerosis is a well-established disease and major cause of CVD involving the inflammatory cells and lipid accumulation in the inner wall of arteries (9). LDL-C plays a central role in the development of atherosclerosis and CVD (10). The effect of LDL on atherosclerotic cardiovascular disease (ASCVD) risk depends on both the magnitude of LDL-C levels and the duration of exposure which were addressed in the LDL cumulative exposure hypothesis (11). This hypothesis states that the total accumulated plaque, its speed of progression and absolute risk of cardiovascular events are determined by the

cumulative exposure to LDL over lifetime (11). Therefore, reducing LDL-C and maintaining low levels decreases the risk of ASCVD events.

Guidelines from the American College of Cardiology and American Heart Association suggest to have LDL-C less than 100 mg/dL for generally healthy people and less than 70 mg/dL for high risk ASCVD individuals (12). One of the effective pharmacological approaches is statin therapy which reduces cardiovascular risk among individuals at high risk as primary prevention and patients for whom moderate or high-intensity statin therapy were recommended based on guidelines (13). Statin is a competitive inhibitor of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, which is the rate-limiting step of cholesterol biosynthesis (14). Although the risk is low, statins like all drugs have side effects such as mild muscle pain and weakness during the first year after treatment (15). Based on adverse effects or clinically significant abnormalities in liver or muscle function markers, patients can develop statin intolerance, the inability to continue statin therapy either partially (specific statins or doses) or completely (all statins at any dose) (16). It is also important to understand patients' preference, where they may favor pharmacology-free approaches. Moreover, access to statin therapy in low- and middle-income countries can be challenging due to several factors, including restricted availability in public healthcare facilities, the high cost of medication not covered by public health insurance and insufficient supply of free-of-charge statins, forcing people to pay out-of pocket or travel to higher-level healthcare facility (17). Therefore, non-drug approaches, particularly healthy diets have been focused on as the potential approach in the prevention of CVDs.

Diet is recognized as a modifiable factor in disease prevention and management. While numerous studies have shown a beneficial cardioprotective impact, their narrow therapeutic focus and regional specificity limit their overall efficacy. Considering that CVD rarely appears alone and it is often linked with hyperglycemia, inflammation and adiposity, a more holistic dietary approach is needed (18). In the search for an effective dietary pattern, plant-based diets (PBDs) have taken attention which can be adapted to various cultural and ethnic contexts. Broadly defined, PBDs emphasize a high intake of fruits and vegetables, whole grains, legumes, and nuts, while restricting or avoiding

animal products (19). According to the 2021 European Society of Cardiology guidelines on CVD prevention in clinical practice, healthy diet is also more based on plants and less on animals, particularly low in saturated fatty acids (SFA), salt, red and processed meat, alcohol, added sugar, but emphasize intake of fibers, fruits and vegetables, nuts (20). Vegan, vegetarian, Portfolio, Mediterranean, Dietary Approaches to Stop Hypertension (DASH), Nordic and many more other diets can be considered plant-based dietary patterns (21–23). These dietary patterns are gaining attention due to both health benefits and increasing awareness of the environmental impact of food production systems (24). Therefore, PBDs are extensively studied for its association with cardiovascular health.

Preliminary evidence from observational studies, clinical trials and systematic reviews with meta-analysis suggested that adherence to various types of PBDs may induce positive effects on cardiovascular health. In a cohort study of female nurses, women with a greater adherence to the Mediterranean diet were associated with significantly reduced risk of CHD, stroke and cardiovascular mortality compared to women with lower adherence (25). One large primary prevention study of more than 7000 participants, the PREDIMED, demonstrated that individuals at high risk of CVD following a Mediterranean diet enriched with either extra virgin olive oil or nuts had 30 % lower incidence of major cardiovascular events compared to those who adhered to a low-fat diet (26). Particularly, several studies reported a beneficial effect of PBDs on reducing LDL-C levels. Study by Fremont et al. showed that polyphenolic antioxidants, resveratrol and flavonoids protected LDL particles from oxidation by free radicals (27). Other systematic review with meta-analysis found that vegan and vegetarian diets which were characterized as PBDs reduced blood levels of TC, LDL-C, apolipoprotein B by 0.34mmol/L, 0.3 mmol/L and 12.92 mg/dL respectively (28). In contrast, saturated fats and dietary cholesterol consumption were associated with increase in serum cholesterol levels (29). The various studies showed that red meat is associated with a high risk of CVDs (30,31). The systematic review and meta-analysis found that both unprocessed and processed red meat consumption is linked to a greater risk of CVD and diabetes, particularly in Western countries (32). Consequently, numerous studies were conducted to investigate the relationship between PBDs, blood lipids, and CVD

outcomes. These studies have provided valuable results, often indicating the favorable association between certain PBDs and cardiovascular health.

However, several limitations and gaps exist in the current evidence base. Current research continues to explore the importance of dietary components such as macronutrient imbalances and specific nutrient substitution on health outcomes, focusing narrowly on single nutrient or specific food items, whereas shifting toward overall dietary patterns may open a more comprehensive understanding of the interactive and cumulative effects of various food components (33,34). Moreover, PBD does not have a clear definition and composition, ranging from strict vegan diet to flexi-vegetarian which can lead to significant variability in their effects on CVD risk factors, including LDL-C (35). Another limitation is that prospective cohort studies are focused on association of PBDs with the cardiovascular risk, while the effect of PBD on lipid profile is presented by either cross-sectional studies or short-term RCTs. The evidence of the long-term adherence to PBDs and its impact on LDL-C reduction is currently lacking. In addition, most studies include heterogeneous populations such as healthy individuals, those at-risk or those with established CVD. These variabilities make synthesis of evidence difficult and a clear overview of the current evidence base regarding the impact of PBDs on LDL-C can be challenging for clinicians, researchers and public health workers. Therefore, there is a need for a comprehensive overview map for the existing complex knowledge which examines changes of LDL-C levels across diverse PBDs over time. The aim of this scoping review is to systematically map and synthesize the available evidence regarding the effect of various types of PBDs on LDL cholesterol over the last 10 years.

The objectives are:

- To identify the range of PBDs that have been investigated regarding LDL-C levels;
- To describe the characteristics of the included studies such as designs, population, duration, geographical settings;
- To summarize the LDL-C outcomes;
- To determine key knowledge gaps for future research;

2. Background

2.1 Cardiovascular diseases

CVDs is a group of conditions that affect the heart and blood vessels including CHD, coronary artery disease (CAD), cerebrovascular diseases, peripheral artery disease (PAD), heart failure, rheumatic heart disease, congenital heart disease and other conditions(36,37). The underlying cause for most common forms of CVD is atherosclerosis.

Atherosclerosis is a chronic inflammatory process characterized by the gradual accumulation of fatty deposits within the inner walls of large and medium size arteries (38). Fatty deposits also known as plaques are complex lesions which contain cholesterol particularly from LDL, cellular debris, smooth muscle cells and calcium (39). Under normal conditions, LDL particles penetrate into the intima of the arterial wall and eventually re-enter to the blood circulation, but the effect of cardiovascular risk factors make them adherent to proteoglycans and be retained (40). The underlying mechanism can be seen in Figure 1, where it begins with endothelial dysfunction and retention of modified LDL and other apo B lipoproteins in the intima which with other atherogenic stimuli activate pro-inflammatory mechanisms (41). This triggers monocytes attaching to the endothelial layer and moving into the intimal space, where they transform into macrophages (42). These macrophages engulf oxidized LDL, accumulated at subendothelial level, turning into foam cells and forming fatty streaks (42,43). Fatty streaks represent an early stage of atherosclerosis and evolve into fibrous lesions characterized by lipid-rich necrotic core and a fibrous cap consisting of smooth muscle cells and extracellular matrix (44). Retained macrophages and other cells release more pro-atherogenic particles including enzymes, tissue factors and signaling molecules that amplify the inflammatory process (40). When plaques become unstable and ruptures, a highly thrombogenic lipid core is exposed to the bloodstream which triggers a blood clot formation (45). Thrombus development leads to plaque growth which reduces the blood flow causing severe cardiovascular complications (41). The atherosclerosis develops

silently, and severe damage can occur before clinical symptoms are manifested (46). Therefore, it is critically important to identify and manage risk factors as early as possible.

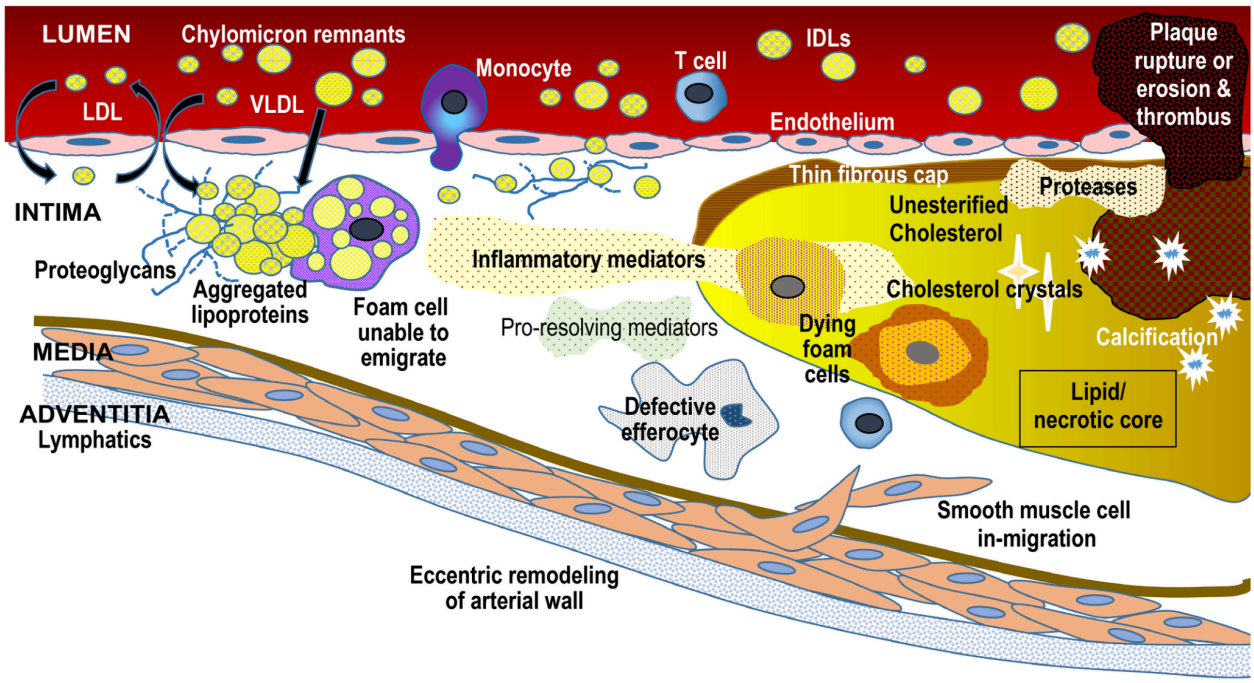

Figure 1. The mechanism of atherosclerosis development (40)

2.2 LDL cholesterol

Cholesterol is an essential lipid for cell membrane structure and hormone synthesis, which is mostly synthesized endogenously by the liver via the mevalonate pathway or obtained from the diet (47). Due to its insolubility, it requires carrier particles, lipoproteins (48). Lipoproteins are protein-containing complexes transporting cholesterol and TG in the bloodstream (49). These particles have a hydrophobic core of cholesterol esters and TG while the outer layer is constructed by phospholipids, free cholesterol and apolipoproteins (50,51). Lipoproteins classified into categories based on density, diameter and apolipoprotein composition: chylomicrons, very low-density lipoprotein (VLDL), intermediate density lipoproteins (IDL), low-density lipoprotein (LDL), high-density lipoprotein (HDL) and Lp(a) (52). Except for HDL, others are considered atherogenic (51). For example, dietary cholesterol, absorbed in duodenum and jejunum,

is packaged into chylomicrons, which become remnants in blood circulation that can penetrate the endothelial layer and participate in atherosclerosis (47). However, LDL serves as the primary transporter of cholesterol in the bloodstream (53). In the liver, cholesterol and TG are assembled with apolipoproteins into VLDL particles which transport lipids to peripheral tissues such as adipose tissue and muscle (54). When TG is metabolized, VLDL transforms into LDL, rich in cholesterol and containing ApoB-100 (54). The clearance of LDL mostly is performed by hepatocyte LDL receptors, while the remaining is removed by extrahepatic tissue and non-receptor-mediated mechanisms (55). An increased number of receptors remove LDL particles whereas the reduction leads to decreased LDL clearance and elevated plasma LDL levels (56). Statins decrease hepatic cholesterol level causing upregulation of hepatic LDL-receptors which remove LDL (57).

LDL particles can be categorized according to size and density like small-dense LDL (sdLDL) and large buoyant LDL (lbLDL) (58). sdLDL particles have greater atherogenicity than lbLDL due to prolonged residence time in plasma, leading to oxidative and structural modifications, which enhance endothelial wall penetration (59). The long residence time can occur because the binding domain of apolipoprotein B on sdLDL, which binds to LDL receptors, is less exposed making LDL clearance difficult (60).

Initially, native LDL undergoes multiple physical-chemical modifications where it is desialylated, decreased in size and major lipid content, became more negatively charged, denser, and oxidized (61). Oxidized LDL (oxLDL) plays a pivotal role in dysfunction of endothelial cells during atherosclerosis development (62). Figure 2 shows two mechanisms of lipid peroxidation: enzymatic and non-enzymatic. Under normal conditions, cells maintain prooxidant-antioxidant balance and reactive oxygen species (ROS) act as signaling molecules, but during exposure to exogenous (e.g. environmental toxins, radiation, smoking, alcohol) or endogenous particles (e.g. mitochondria, inflammation, peroxisomes), ROS production is increased causing oxidative stress (63,64). Consequently, ROS triggers LDL oxidation by phospholipid peroxidation resulting in oxLDL which attracts monocytes and serves as a strong ligand

for macrophage scavenger receptors (65). Another pathway involves enzymes such as lipoxygenases, cytochrome P450, myeloperoxidase and cyclooxygenases (66). The modification of LDL causes the production of specific epitopes recognized by macrophage scavenger receptors, Toll-like receptors and others, triggering a pro-inflammatory process (67). Therefore, there are two strategies to prevent atherosclerosis via LDL-C: either reduce LDL-C concentration or remove inflammation and oxidative stress. PBDs can solve both problems because it is abundant in phytonutrients, anti-inflammatory compounds, phytosterols and low in fat (68).

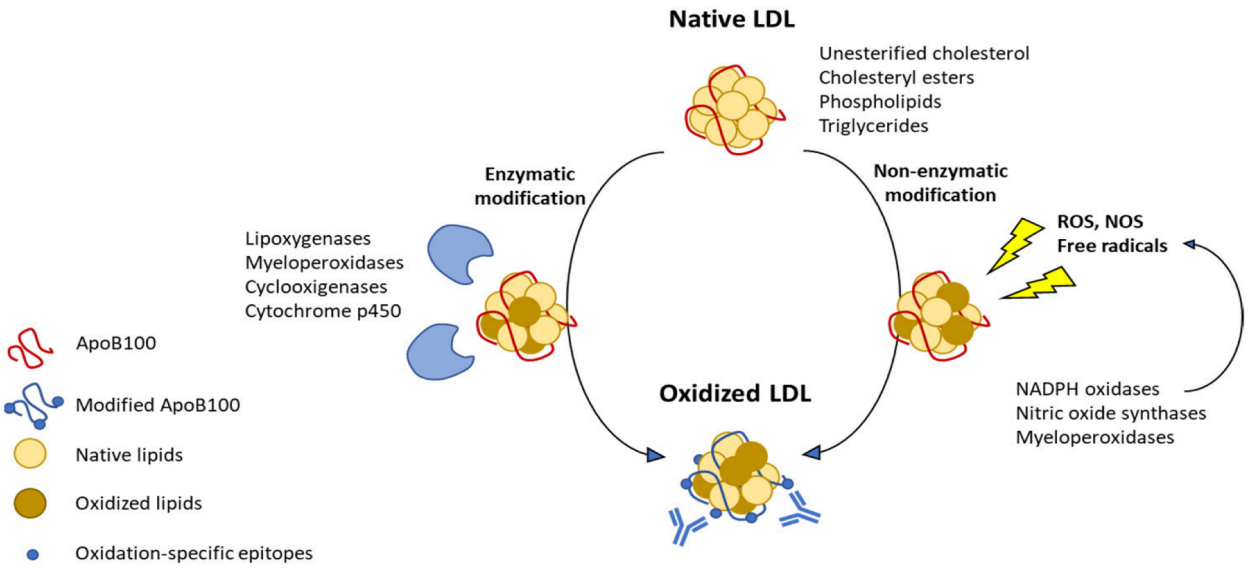

Figure 2. The mechanisms of LDL oxidation (66)

2.3 Plant-based diets

The concept of PBDs varies broadly from absolute exclusion of meat products to minimization of all animal food (19,69). Some studies consider PBD and vegan as the same diets while others highlight PBD in terms of traditional diets such as Mediterranean diet or DASH (35,70). These cause confusion in the definition of PBDs. In this review, PBD is an umbrella term for diets (e.g., Mediterranean, DASH, Nordic, Portfolio, vegetarian), illustrated in Figure 3, that contain a higher amount of plant foods and lower amount of animal food.

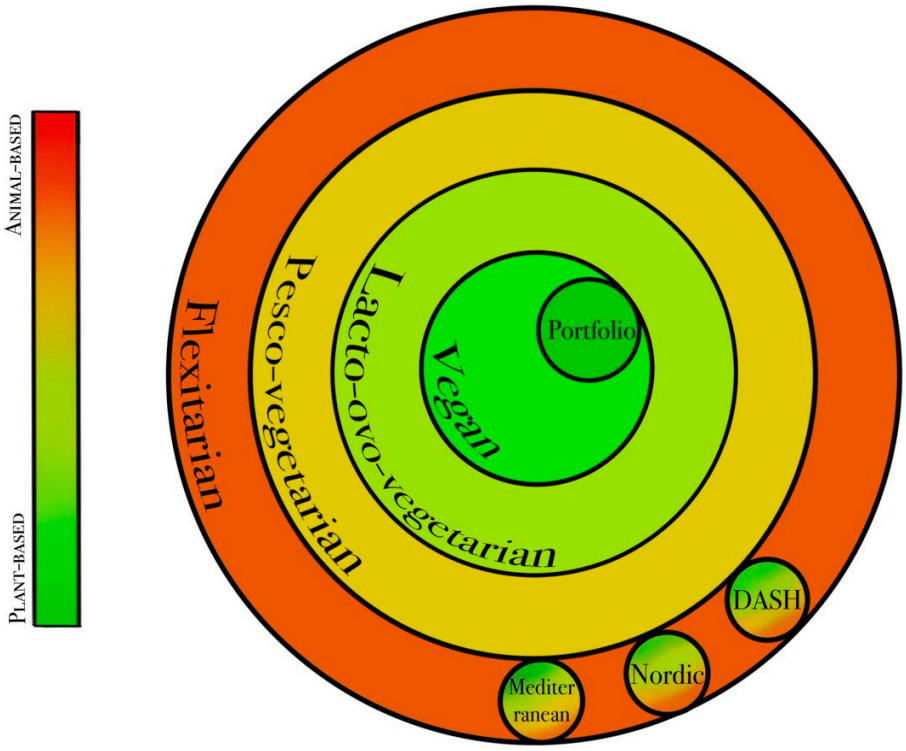

Figure 3. Spectrum of dietary patterns based on plant and animal food proportions

2.3.1 Vegan and Vegetarian diets

Vegetarian diets are defined as the diet which exclude all types of meats or meat products and can be classified into subgroups such as vegans, lacto-ovo vegetarians, flexi-vegetarians, pesco-vegetarians (35). Strict vegan diet is considered as the purest form of PBD due to elimination of all animal food (23). Lacto-ovo vegetarian diets include dairy products and eggs, while pesco-vegetarians in addition to eggs and milk products can consume fish and seafood (71,72). Semi-vegetarians, also called flexitarians, consume all foods including dairy products, eggs but limit the frequency of meat consumption such as red meat and poultry (e.g., no more than once a week) (35,72). The limitation of vegetarian diets is the deficiency of key nutrients such as iron, calcium, vitamin D, vitamin B12, and zinc (73). They should be obtained from supplementation or through fortified food (74).

2.3.2 Mediterranean diet

The traditional Mediterranean diet is not only a list of foods but the lifestyle coming from the Mediterranean region where olives are grown (22). The initial scientific evidence about health benefits from the Mediterranean diet were identified by Ancel Keys who performed the Seven countries study, investigating the effect of diet on CVD risk (23). He found that the mortality from CVD in the Mediterranean region was the lowest despite consuming high amounts of fat among the included countries (75). This diet is rich in plant-origin foods (fruits, vegetables, cereals, legumes, nuts) with olive oil as the primary source of fat (76). It also includes moderate amounts of seafood and fish, eggs, poultry and dairy products, but red meat and sweets consumption is low (76). The unique feature of this diet is high intake of olive oil and nuts, alongside moderate wine consumption (22). The Mediterranean diet is associated with low risk of chronic diseases and high life expectancy (77,78).

2.3.3 Dietary Approaches to Stop Hypertension (DASH) diet

DASH is the beneficial PBD for hypertension treatment and prevention (79). It includes high intake of fruits and vegetables, low-fat dairy products, fish and low consumption of red meat, sweets and refined carbohydrates (80). The DASH diet has features of lower amounts of total fat, saturated fat and cholesterol while providing higher levels of potassium, calcium, magnesium, fiber and protein (81).

2.3.4 Portfolio diet

Another PBD is the Portfolio diet with the cholesterol-lowering effect. The four main food products in the diet are nuts (tree nuts or peanuts), plant protein (soy products or dietary pulses), viscous soluble fiber from fruit, grains, vegetables and plant sterols (82). These elements in combination decrease LDL-C levels comparably to the initial dose of first-generation statins (83). According to its name “Portfolio”, this diet is supposed to collect cholesterol-lowering foods as new evidence appears (84).

2.3.5 Nordic diet

Nordic diet is the predominantly PBD emphasizing traditional Nordic foods. It includes high intake of fruits, vegetables and root vegetables, berries, cereals, legumes, fish, and low intake of meat products, dairy products, sweet, and alcoholic beverages (85). Instead of olive oil, the Nordic diet uses canola oil (86). It follows three principles: 1) prioritizing calories from plant foods over meat, 2) increasing intake of food from sea and lakes, 3) incorporating more wild countryside food (87). Healthy Nordic diet has beneficial effects on cardiovascular risk factors (88).

2.3.6 The Planetary Health diet

The current food systems promote a more westernized diet, characterized by overconsumption of animal products, refined grains, added sugars, and ultra-processed food, leading to high prevalence of chronic diseases such as obesity, type 2 diabetes, hypertension, cancer and CVD (89,90). Consequently, food systems significantly contribute to poor health and environmental issues, using 70% of global freshwater for agriculture and accounting for 26% of global greenhouse gas emissions, where almost half of which are related to livestock and its land use, making meat production to have a high impact on climate change, land degradation, water pollution and loss of biodiversity (91). The intake of red meat exceeds safe operating space, the limit of Earth that maintains sustainability. Therefore, there is a need for healthy diets from sustainable food systems. In 2019, the EAT-Lancet Commission proposed a healthy reference diet, called the Planetary Health diet, which considers both human and planet boundaries and aims to provide a healthy diet for 10 billion people by 2050 (92). It mostly consists of diverse plant-based foods, favoring unsaturated rather than saturated fats and allows small to moderate intake of seafood and poultry, but limits red and processed meats, added sugar and refined grains (93).

2.3.6 Predominant PBD indexes

A few recent studies have shifted from exclusionary definitions of PBD towards gradations of adherence to predominant PBD. In this regard, Martinez-Gonzalez et al. made a pro-vegetarian diet score which gives positive weights to plant foods and

negative to animal foods (94). However, not all plant foods have the same beneficial effect. Satija et al. created three indices: an overall plant-based diet index (PDI), which positively scores plant derived foods and negatively scores animal-derived foods; the healthful plant-based diet index (hPDI), which favors healthy plant-foods (whole grains, fruits and vegetables, nuts, legumes, vegetable oils) while giving reverse scores to unhealthy plant (refined grains, potatoes, sweets, sweetened beverages) and animal foods; and unhealthful plant-based diet index (uPDI), which assigns positive scores to unhealthy plant foods and negative scores to health plant and animal products (95). The PDI is a flexible tool that can be adapted in different populations because it does not consider specific food and it helps researchers to better understand the quality of PBDs (96).

2.3.7 Cardioprotective components of PBD

Animal foods are rich in SFA, cholesterol, L-carnitine and choline, which contribute to CVD (97,98). Particularly, L-carnitine/choline produce trimethylamine-N-oxide (TMAO) which participates in development of atherosclerosis by activating macrophages that form foam cells (33). However, healthy plant foods have high content of nutrients such as dietary fibers, antioxidants, phytosterols and phytostanols which contribute to LDL-C lowering and improvement of cardiovascular health. (99).

2.3.7.1 Dietary fibers

Dietary fiber is a carbohydrate or plant wall substance found in plant-based foods that the human digestive system cannot digest or absorb with complete or partial fermentation (100). They are divided into several types: non-starch polysaccharides (cellulose, hemicellulose, pectins and hydrocolloids), resistant oligosaccharides and resistant starch (101). Also, these dietary fibers can be classified as soluble (β-glucan, galactomannan, pectin, psyllium, inulin and resistant starch) and insoluble (cellulose, hemicellulose, chitosan, lignin) in water (102).

High consumption of dietary fibers is associated with decreasing the risk of CVD (103). In general, dietary fibers improve insulin sensitivity, plasma lipids and chronic

inflammation (104). They help with weight management by increasing satiety, consequently decreasing energy intake and promoting weight loss (105). Moreover, dietary fibers provide nutrients for gut microbiota thus modulating its composition (106). Insoluble fibers have a bulking effect whereas soluble fibers are fermented and produce beneficial short-chain fatty acids (SCFA) (107). Particularly, soluble viscous fibers reduce serum cholesterol level via bile acids excretion mechanism and decrease hepatic cholesterol synthesis (Figure 4) (108).

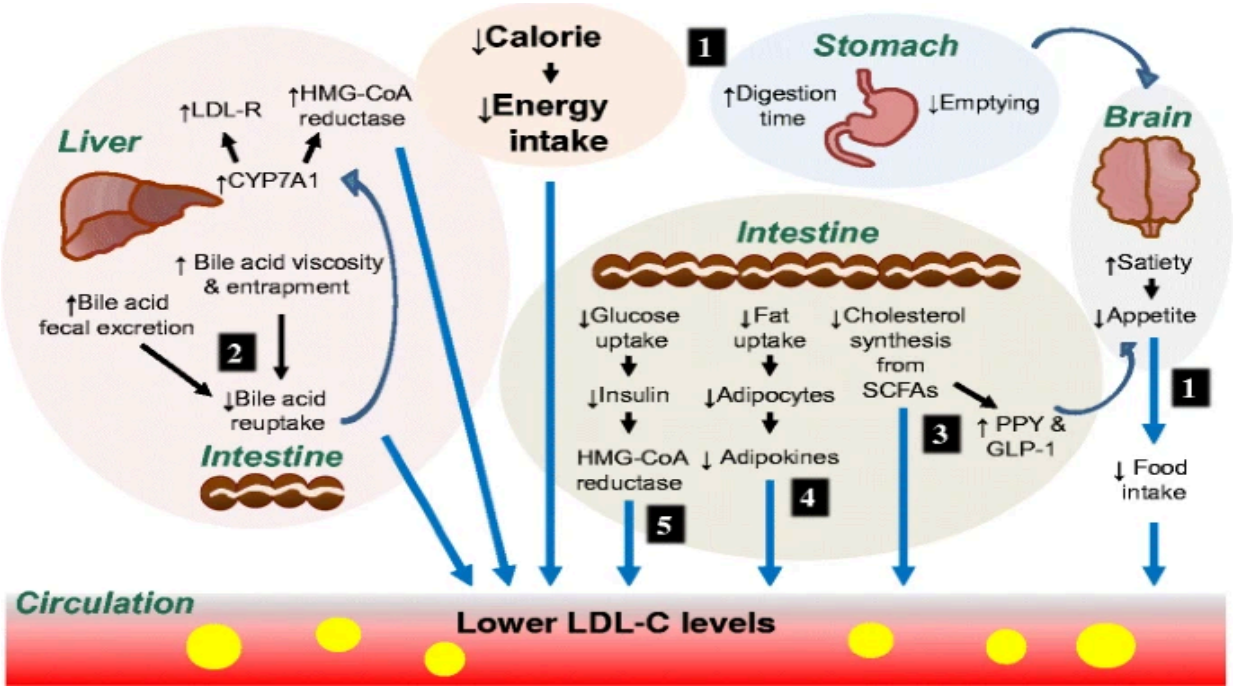

Figure 4. The mechanism of dietary fiber impact on LDL-C levels (109)

The current recommended intake of dietary fibers is approximately 25-30 g for adults to maintain optimal health but the values can vary depending on countries and age group (110). The European Food Safety Authority (EFSA) recommends adults to consume 25 g for normal laxation and more than 25 g for health benefits (111).

2.3.7.2 Polyphenols

Polyphenols are secondary plant metabolites with phenol groups found in fruits and vegetables, chocolate, legumes, tea and wine, and categorized into flavonoid and non-flavonoid (112,113). Dietary polyphenols demonstrate beneficial cardioprotective

effects, particularly anti-inflammatory, antioxidant and antiplatelet aggregation properties (68,114,115). Moreover, flavonoids support vascular homeostasis by neutralizing ROS, which increase nitric oxide (NO) bioavailability, inducing endothelium-dependent relaxation (116).

2.3.7.3 Phytosterols

Phytosterols are triterpenes that play a structural role in plant cell membranes(117). Phytostanols are 5α-saturated derivatives of phytosterols (118). Naturally, the main sources of phytosterols and phytostanols are vegetable oils, nuts, cereals and grains (119). The intake of both phytosterols and stanols inhibits dietary cholesterol absorption in the intestine, consequently reducing serum TC and LDL-C levels (120). The National Cholesterol Education Program recommends consuming 2 grams per day of plant sterols/stanols to decrease LDL cholesterol (121).

3. Materials and Methods

The guidelines published by the Preferred Reporting Items for Systematic review and Meta-Analysis (PRISMA) extension for scoping reviews were followed in this scoping review (122).

3.1 Eligibility criteria

Eligibility criteria are based on the PICOS (Population, Intervention, Comparison, Outcomes, Study Design) approach.

Studies were included in the review if:

(1) Participants were adults (≥18 years) and generally healthy, at the risk of CVD or adults with a history of major CVD (e.g., myocardial infarction, stroke, those who have undergone revascularization procedures);
(2) The intervention (≥12 weeks) was plant-based dietary patterns (e.g. Mediterranean, Nordic, DASH, portfolio diet, vegan and vegetarian type diet

patterns) and studies with or without physical activity, if physical activity is equally promoted in both the intervention and control groups;

(3) The comparison group followed an active diet (other dietary pattern different from intervention) or passive diet (a usual diet or dietary advice)

(4) Studies reported LDL-C either as a primary or secondary outcome;

(5) The study type was RCT, non-randomized controlled trial, systematic reviews with meta-analyses that align with the inclusion criteria and cohort studies;

Studies were excluded in the review if:

(1) Population included children under 18 years, pregnant and lactating women, non-human studies such as animal or in vitro research, and individuals with serious conditions unrelated to cardiovascular health;

(2) Studies had unclear definitions of dietary exposure or measurements, diets that are not plant-based, mixed dietary interventions lacking adequate subgroup data on plant-based dietary patterns, studies focusing solely on dietary supplements or single-food interventions that do not reflect an overall dietary pattern, and research investigating the replacement of individual food components rather than assessing a dietary pattern;

(3) Studies did not measure or report LDL-C in any form;

(4) The study type was generic review, case studies, cross-sectional studies and articles not published in English;

3.2 Databases and search strategy

A comprehensive search was conducted using Scopus, PubMed, Web of Science databases. All searches were run on March 14, 2025. The search strategy was designed to identify potentially relevant studies published between January 1, 2015 and March 14, 2025. Briefly, the search combined key terms related to CVD, PBDs, LDL cholesterol, and various study designs (Table 1). Database-specific filters were applied to refine the results, including publication date range, document types, language restrictions, and human studies.

Table 1. Search terms categorized by PICOS criteria

Category	Search terms
Population	“cardiovascular disease*”, “CVD”, “heart disease*”, “coronary artery disease”, “CAD”, “myocardial infarction”, “stroke”, “revascularization”, “healthy”, “at risk”
Intervention	“plant-based diet*”, “vegetarian*”, “vegan*”, “Mediterranean diet*”, “Nordic diet*”, “DASH diet*”, “Dietary Approaches to Stop Hypertension”, “portfolio diet*”, “plant-forward diet*”, “flexitarian*”
Outcome	“LDL cholesterol”, “LDL-C”, “low density lipoprotein cholesterol”, “low-density lipoprotein cholesterol”, “lipid profile”, “blood lipid*”, “cholesterol level*”
Study designs	“cohort stud*”, “prospective stud*”, “longitudinal stud*”, “randomized controlled trial*”, “RCT*”, “controlled trial*”, “systematic review*”, “meta-analys*”

3.3 Selection process and data collection

All results were exported and organized by using a systematic review management software, Zotero. The study selection process involved two stages:

- **Title and abstract screening:** A reviewer screened all identified studies against the predefined criteria. An abstract was used to gather information on study type, participants, interventions, comparisons, and outcome measures. If any of the characteristics did not comply with criteria, the study was not included in the full-text search.
- **Full-text assessment:** The reviewer screened full-text studies for eligibility using predefined inclusion and exclusion criteria.

Risk of bias assessment was not conducted because it is not necessary for scoping review according to guidelines of PRISMA-ScR (122).

3.4 Data charting process

A data charting form was constructed by one reviewer and implemented in Google Sheets to systematically extract and organize information from each study. Data items include author, country, study design, aims, study population, sample size, diet intervention (type of PBD, diet composition, duration, comparison diet), outcome (change in LDL-C, statistical significance vs. baseline, statistical significance vs. comparator), and key findings.

3.5 Synthesis of results

The collected evidence from eligible studies were organized to address the research question of this scoping review. Studies were grouped based on the type of PBD used as an intervention. Following this, each group was divided into several subgroups according to significant or non-significant effect on LDL-C levels. The synthesized evidence was presented in a narrative format. It provided a summary of the characteristics of the included studies and clearly reported similarities and dissimilarities in statistical significance between intervention and baseline or comparison group across studies.

4. Results

4.1 Selection of sources of evidence

The search revealed 900 citations from which 218 were duplicates. After duplicates removal, the titles and abstracts were examined carefully for eligibility. A total of 633 studies were excluded. Four studied out of 49 were not retrieved. During full-text assessing, 27 studies were excluded for the following reasons: cross-sectional study (*n* = 8), intervention less than 12 weeks (*n* = 7), not PBD intervention (*n* = 4), lifestyle

intervention (n = 4), LDL-C outcomes not reported (*n* = 3), single food intervention (n=1) (Fig. 5, flow diagram). The remaining 18 studies were eligible for scoping review.

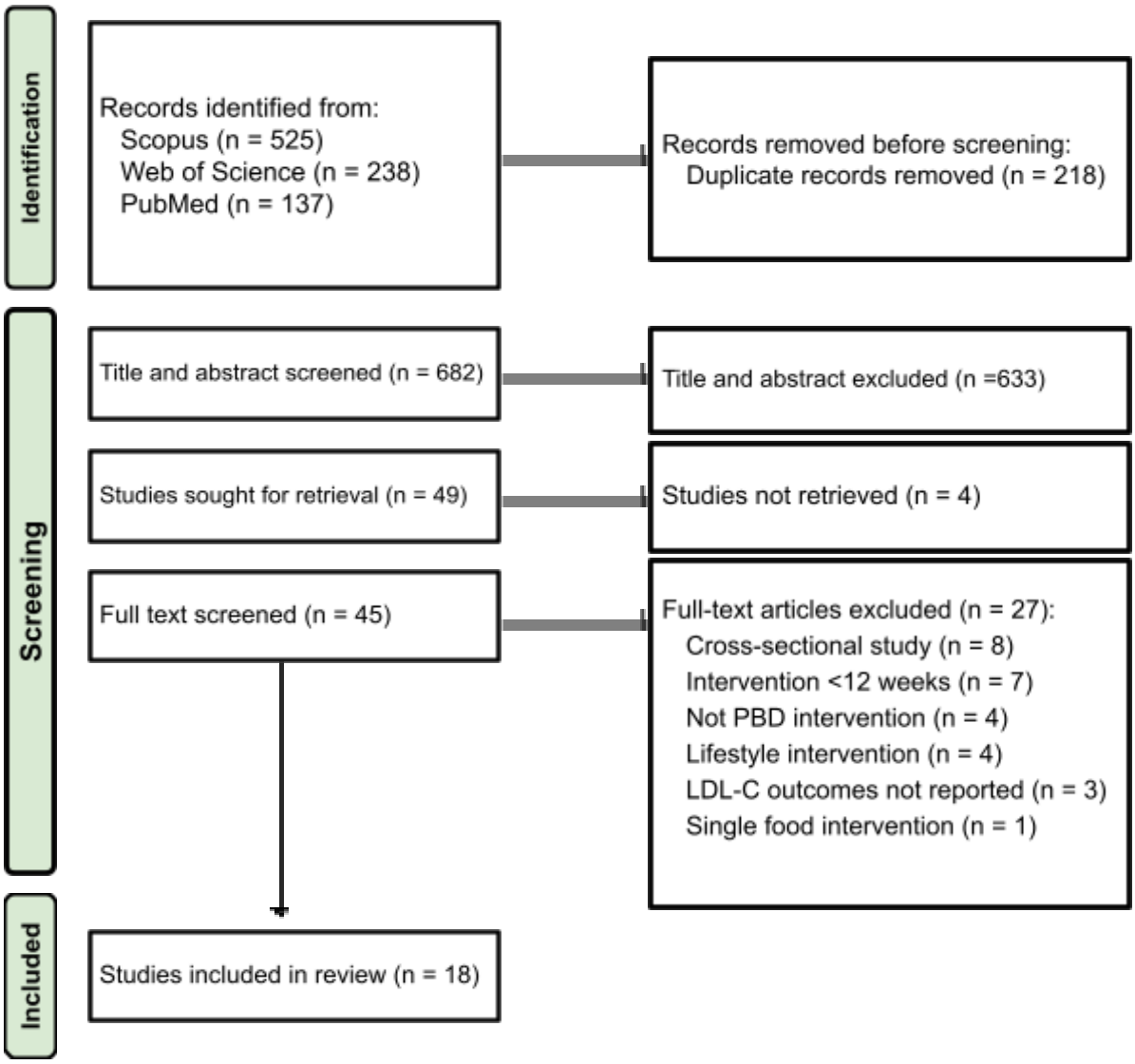

Figure 5. PRISMA flow diagram of study selection process

4.2 Characteristics of sources of evidence

The characteristics extracted from the 18 publications are summarized in Table 1 (Annex A). Research papers have a range of study designs, including randomized controlled trials (parallel and cross-over), systematic reviews with meta-analysis and prospective longitudinal observational studies. Research was conducted in various

regions including Europe, the United States, the Middle East and Asia. These studies assessed diverse populations such as generally healthy adults, overweight people, patients with type 2 diabetes, individuals at high CVD risk or with established CVD and those with metabolic syndrome. Sample size in RCTs ranged from approximately 60-300 people to over 6500 participants in meta-analysis and cohort studies. Dietary interventions particularly plant-based were interpreted broadly and embraced strict low-fat vegan diets, lacto-ovo vegetarian diets, Mediterranean diets (with varying compositions and enriched with olive oil or nuts), DASH diets, and dietary patterns identified via statistical analysis (vegetable pattern or plant-centered diets). Comparison or control groups were heterogeneous and generally fell into two categories: the first included usual or habitual diets and minimal dietary advice, while the second covered healthy diet advice, low-fat diets, and other active dietary interventions such as Mediterranean diet. The duration of RCTs varied from 12 weeks to two years, while observational studies followed participants from 3 to 20 years. Systematic review with meta-analysis assessed from 3 months to 7 years.

4.3 Results of individual sources of evidence

Table 2 presents the LDL-C outcomes reported in 18 studies.

Table 2. Summary of LDL-C outcomes reported in 18 studies

Author (year)	Study design	Type of PBD	Control/Comparison diet	Change in LDL-C	Statistical significance vs. baseline(123)	Statistical significance vs. comparator
Barbosa et al. (2024) (123)	RCT	Physical exercise + MD (Group 2)	No intervention group (Group 1a) Physical exercise group (Group 1b)	Group 1a: +5.42 mg/dL (rate of change = +6.14%) Group 1b: -6.94 mg/dL (rate of change = -10.47%) Group 2: -8.52 mg/dL(rate of change= −9.48%)	N/S ↑ in Group 1a (p=0.115) N/S ↓ in Group 1b (p=0.162) N/S ↓ in Group 2 (p=0.061)	S/D (p=0.01)
Barnard et al. (2021) (124)	RCT	LF vegan diet	MD	MD: -0.5 mg/dL Vegan diet: -15.3 mg/dL Treatment effect: -14.8 mg/dL	N/S ↓ in MD group S ↓ in Vegan group (p<0.001)	S/D (p=0.001)
Bonekamp et al. (2023) (125)	Systematic review with meta-analysis	Low GI diet, MD, PBD, high protein diet, low carbohydrate diet, LF diet	No dietary intervention	6 months High protein -0.2 mmol/L; Low carbohydrate -0.1 mmol/L; LF -0.2 mmol/L; Low GI -0.3 mmol/L; Moderate carbohydrate -0.1mmol/L; PBD -0.2mmol/L 12 months High protein 0.0 mmol/L; Low carbohydrate 0.1 mmol/L; LF 0.1 mmol/L; Low GI 0.0 mmol/L; MD -0.1 mmol/L; Moderate carbohydrate 0.0 mmol/L; PBD -0.1 mmol/L	NA	S/D in Low GI diet N/S in PBD
Bonekamp et al. (2024)(126)	Systematic review with meta-analysis	MD, LF diet, moderate carbohydrate diet, low GI diet	Minimal dietary intervention	Short-term changes: LF diet: 0.0 mmol/L; Low GI diet: -0.1 mmol/L; MD: 0.0 mmol/L; Moderate carbohydrate diet: 0.6 mmol/L Long-term changes: LF diet: 0.0 mmol/L; MD: 0.0 mmol/L; Moderate carbohydrate diet: 0.0 mmol/L	NA	N/S in all diets
Choi et al. (2022)(127)	Prospective observational study	Plant-centered diet	Cholesterol lowering diet	Adjusted Mean Change for Each 1 SD Increment APDQS: −0.05 ± 0.02 Keys score: −0.05 ± 0.01	S ↓ APDQS (p = 0.007) S ↓ Keys score (p < 0.001)	NA
Daidone et al. (2024) (128)	RCT	MD	LF diet	at 6 months: MD -1.2 mg/dL, LF -6.1 mg/dL at 12 months: MD -6.2 mg/dL, LF +3.9 mg/dL	S ↓ in MD at T2 vs T0 (p<0.005)	S/D at T2 (p = 0.009)
Hernaez et al. (2017)(129)	RCT	TMD-VOO, TMD-Nuts	LF diet	TMD-VOO: 1.35 mg/dL TMD-Nuts: 0.56 mg/dL LF diet: -10.5 mg/dL	S ↓ in LF (p=0.007) N/S ↑ in TMD-VOO (p=0.641) and TMD-Nuts (p=0.827)	S/D LF vs. TMD-VOO (p=0.003) N/S LF vs. TMD-Nuts (p=0.081)
Keshani et al. (2024) (130)	Systematic review with meta-analysis	TMD-VOO	Various control diets including LF diets and habitual diets	Weighted mean difference (WMD) = 6.304 mg/dl	NA	N/S (P = 0.200)
Li et al. (2016) (131)	Longitudinal observational study	Vegetable pattern (plant-forward)	Meat pattern and animal offal-dessert-alcohol pattern (ADA	The mean of changed LDL-C (low, middle, high) were in ADA: model 1 −0.02, 0.04, and 0.11; model 2 -0.01, 0.03, 0.12 ; in vegetable pattern: model 1 and 2 0.09, 0.06, and -0.01; in meat pattern: model 1 and 2 0.05, 0.05, and 0.04;	S ↑ in ADA (p<0.05) N/S ↓ in Vegetable and Meat patterns (p>0.05)	NA

Said et al. (2021)(132)	Prospective non-randomized controlled trial	DASH diet	Healthy Dietary Advice (HDA)	DASH group: -11.21 mg/dL (7.5% reduction) HDA group: -4.57 mg/dL (3.1% reduction)	S ↓ in DASH and HDA (p<0.001)	N/S (p=0.67)
Sangouni et al. (2024) (133)	RCT	DASH diet	Healthy diet	DASH group: -13.50±9.58 mg/dL; Control group: -4.90±18.28 mg/dL	S ↓ in DASH (p<0.001) N/S ↓ in Control (p=0.15)	S/D (p=0.02)
Sofi et al. (2018) (134)	RCT	Low-calorie lacto-ovo vegetarian diet (Vd)	Low-calorie MD	VD: -6.92 mg/dL MD: +2.12 mg/dL	S↓ in Vd (p<0.05) N/S ↑ in MD	S/D (p=0.01)
Termannsen et al. (2022)(135)	Systematic review with meta-analysis	Vegan diets	passive groups (habitual diet) or active groups (e.g., MD, LF diets)	Mean difference: -0.24 mmol/L	NA	S/D (p=0.005)
Tsaban et al. (2021) (136)	RCT	Green MD MD	Healthy dietary guidance (HDG)	Green-MD: -6.11 mg/dL (-3.7%) MD: -2.34 mg/dL (-0.8%) HDG: -0.21 mg/dL (+1.8%)	NA	S/D Green-MD vs. HDG (p=0.012); N/S MD vs. HDG (p=0.386) N/S MD vs. Green-MD (p=0.100)
Turner-McGrievy et al. (2023) (137)	RCT	Vegan diet (whole plant foods)	LF omnivorous diet (omni)	At 6 months: Vegan: -5.86 mg/dL Omni: -0.86 mg/dL At 12 months: Vegan: -2.56 mg/dL Omni: -0.79 mg/dL At 24 months: Vegan: 0.39 mg/dL Omni: 0.62 mg/dL	NA	N/S (P=0.73).
Waterplas et al. (2020) (138)	Prospective longitudinal cohort study	Plant-based diet indices (PDI, hPDI, uPDI)	Changes over time	Men: +2 mg/dL Women: +18 mg/dL	S ↑ in women (p<0.001) N/S ↑ in men (p=0.264)	N/S association between PDI,hPDI, uPDI and LDL-C in either men or women
Wright et al. (2017) (139)	RCT	LF whole food plant-based diet (WFPB)	Standard medical care without dietary intervention	Intervention 3 months: -0.9 mmol/L; 6 months: -0.8 mmol/L; 12 months: -0.6 mmol/L Control 3 months: -0.5 mmol/L; 6 months: -0.4 mmol/L;	S ↓ in WFPB at 3 months (p<0.0001), 6 months (p<0.001), and 12 months (p=0.01); S ↓ in control at 3 months (p<0.01), 6 months (p=0.02)	N/S at 3 (p=0.15) and 6 months (p=0.12)
Zahedi et al. (2020)(140)	RCT	MD	Routine diet	MD: -14.44 mg/dL Control: 1.02 mg/dL	S ↓ in MD (p=0.001) N/S in control (p=0.721)	S/D (p=0.040).

Abbreviations: MD (Mediterranean diet), LF (Low-fat), GI (Glycemic index), PBD (Plant-based diet), APDQS (A Priori Diet Quality Score,) TMD (Traditional Mediterranean diet), TMD-VOO (Traditional Mediterranean diet enriched with virgin olive oil), TMD-Nuts (Traditional Mediterranean diet enriched with nuts), DASH (Dietary Approaches to Stop Hypertension), SD (Standard deviation), RCT (Randomized controlled trial), S (Statistically significant), S/D (Statistically significant difference), N/S (Not statistically significant), NA (Not available), ↑ (Increase), ↓ (Decrease)

4.4 Synthesis of results

4.4.1 Effects of vegan and vegetarian diets on LDL-C level

Studies showing significant LDL-C reduction

Three studies including systematic review with meta-analysis in Table 2 reported significant LDL-C lowering effects with vegan or vegetarian diets.

A randomized cross-over trial by Barnard et al. reported that a low-fat vegan diet reduced LDL-C by 15.3 mg/dL ($p<0.001$), and it is significantly more effective than a Mediterranean diet (treatment effect -14.8 mg/dL, $p=0.001$) (124). Similarly, the CARDIVEG crossover study demonstrated a significant decrease of LDL-C (-5.44% from baseline, $p<0.05$) in a low-calorie lacto-ovo vegetarian diet, exceeding significantly a low-calorie Mediterranean diet (between diet difference: 9.10 mg/dL, $p=0.01$) (134). Supporting these findings, a systematic review with meta-analysis of 11 RCTs by Termannsen et al. concluded that vegan diets cause a significant mean reduction in LDL-C of 0.24 mmol/L compared to various control diets (135).

Studies showing non-significant LDL-C reduction

An individual study showed no significant difference in LDL-C outcomes between a vegan and low-fat omnivorous diets, highlighting the importance of the context (137).

4.4.2 Effects of Mediterranean-style diets on LDL-C level

Studies showing significant LDL-C reduction

Three RCTs demonstrated significant LDL-C reductions. Daidone et al. reported that a Mediterranean diet significantly decreases LDL-C in high risk individuals over 12 months compared to baseline ($p<0.005$) and compared to a low-fat diet ($p=0.009$) (128). Likewise, Zahedi et al. showed a significant reduction in patients with type 2 diabetes after 6 months compared to a routine diet (140). A modified diet called Green-Mediterranean diet, incorporating green tea and Mankai, significantly reduced LDL-C compared to healthy dietary guidance, but not significantly more than a traditional Mediterranean diet (136).

Studies showing non-significant LDL-C reduction

Other studies, including systematic-review with meta-analyses and specific RCTs, did not have statistically significant LDL-C lowering effect with Mediterranean-style diets. Barbosa et al. showed a substantial, non-significant towards reduced LDL-C with a Mediterranean-inspired diet plus exercise compared to baseline (-9.48%), although the difference between three groups was significant (p=0.01), demonstrating an effect of the Mediterranean-inspired diet plus exercise and only exercise compared to control (123). In a PREDIMED substudy, the Mediterranean diet enriched either with olive oil or nuts failed to lower significantly LDL-C over one year unlike low-fat diet vs. baseline (-10.5 md/dL, p=0.007) (129). Moreover, the systematic reviews with meta-analysis by Keshani et al., Bonekamp et al. (2023) and Bonekamp et al. (2024) reported no overall significant effect of Mediterranean diets on LDL-C levels compared to control (125,126,130). Barnard et al. showed that the Mediterranean diet did not significantly change LDL-C (-0.5 mg/dL) (124). The CARDIVEG crossover study also showed non-significant increase of LDL-C with Mediterranean diet (134).

4.4.3 Effects of DASH diets on LDL-C level

Two studies investigating DASH diets also found positive effects on LDL-C. The DASH diet significantly reduced LDL-C compared to baseline over 12 weeks (132,133). Also Sangouni et al. demonstrated statistically significant differences between groups (p=0.02) while Said et al. showed that the difference in reduction between groups was non-significant (132,133).

4.4.4 Effects of general plant-based or plant-forward diets on LDL-C level

Five studies examining associations between plant-based dietary patterns and LDL-C produced mixed results.

Studies showing significant LDL-C reduction

A prospective observational study by Choi et al. found that greater adherence to a high-quality plant-centered diet (every 1 SD increase in APDQS score) was significantly associated with reduced LDL-C over a 20-year period (−0.05 ± 0.02, p = 0.007) (127).

Furthermore, the BROAD study showed significant LDL-C reductions at 3, 6, and 12 months with a low-fat whole-food PBD compared to baseline, but it was not significantly different from changes in standard care control (139).

Studies showing non-significant LDL-C reduction

Two observational studies of Chinese women and Flemish adults did not identified significant associations between adherence to general vegetable pattern or PBD indices and longitudinal changes in LDL-C levels, despite observing increases of LDL-C in some subgroups over time (131,138). A systematic review with meta-analyses reported no significant effect on LDL-C levels (125).

5. Discussion

This scoping review identified 18 studies of PBDs associated with LDL-C levels over 10 years. Our findings demonstrate that individuals adhering to PBDs have lower blood LDL-C concentration, although the direct comparison across different studies was challenging.

According to results, vegan and vegetarian dietary patterns demonstrate the most consistent LDL-C lowering effects (124,134,135). The findings of the current study are in agreement with a previous meta-analysis which demonstrated that vegetarian diets had a significant lowering effect on blood lipids including LDL-C (141,142). The possible mechanisms explaining the effects of vegetarian diets may be related to diet composition which is rich in dietary fiber and various plant-based phytochemicals such as phytosterols, phenolics, flavonoids, carotenoids, saponins, sulfides (143–146). Phytosterols compete with dietary cholesterol for intestinal absorption, while flavonoids and saponins inhibit cholesterol micellization, resulting in decrease of cholesterol absorption (147,148). Phenolics prevent oxidation of LDL-C and sulfides or organosulfur compounds inhibit cholesterol production (149,150). Moreover, the exclusion of meat products, a substantial source of cholesterol and SFA likely explains a significant reduction in vegetarian groups compared to the Mediterranean diet and other dietary patterns (97,98). Vegans take 90% less of cholesterol compared to omnivores, which

contributes to 13% decrease in their LDL-C levels (151). However, it is important to note that not all studies have found significant differences such as the New soul study (137). The researchers suggested several potential reasons, including the impact of COVID-19 pandemic, and the design of diets which were based on the primarily plant-focused Oldways African Heritage diet, where the omnivorous diet was meat-reduced (137). This similarity could explain why no significant difference in LDL-C was observed.

The Mediterranean diet, the most frequently studied dietary pattern in this review, presents a more complex picture with mixed results on LDL-C reduction. While some studies reported significant reduction of LDL-C compared to baseline or control diets, others demonstrated a greater decrease in low-fat diets (128,129,140). Although, the low-fat diet reduced LDL-C, it was also associated with a decrease in LDL particle size which are considered pro-atherogenic, while adherence to the TMD, particularly enriched with olive oil was associated with improved atheroprotective changes beyond simple quantitative lowering such as LDL resistance to oxidation and increasing LDL particle size (129). This highlights the importance of considering qualitative aspects of LDL-C. Olive oil, the primary fat source in the Mediterranean diet, has anti-atherogenic effects due to its high content of MUFA (152). Beside this, a 3-year RCT demonstrated an increased plasma antioxidant capacity in subjects adhering to Mediterranean diet enriched with virgin olive oil, suggesting that this diet may protect LDL from oxidation, even if LDL-C levels do not decrease (153). In the Medi-RIVAGE study, when the Mediterranean diet was compared to a low-fat diet, it showed a higher decrease in LDL-C but non-significantly, which is consistent with findings in the current study (154). In comparison, a low-fat diet can reduce LDL-C because it decreases the total fat intake including SFA, but it also reduces HDL-C and increases TG level (155). The effect of dietary fat on cardiovascular health appears to depend more on the type than the total amount leading to a substantial reduction in CVD risk (156). A substitution of SFA by MUFA or PUFA from plant oils lowers LDL-C by inhibition of LDL receptor degradation and boosting LDL clearance (157). In addition, when the Mediterranean diet is enhanced by specific food ingredients (e.g., green tea and a *Wolffia globosa*) or combined with exercise, which also helps to transform sdLDL particles to lbLDL, it shows modest reduction in LDL-C and improvements in the lipid profile (123,136,158).

However, systematic reviews with meta-analyses did not demonstrate consistently that the Mediterranean diet had a significant LDL-C lowering effect (125,126,130). The discrepancy might arise from the heterogeneity of studies included in meta-analyses, variations in the amount or type of olive oil, baseline LDL levels, population characteristics, adherence rates, and control diet specifics. Overall, current evidence suggests that the Mediterranean diet appears favorable for LDL-C but generally less effective than vegetarian diets, where the magnitude and consistency are influenced by study contexts and specific dietary modifications.

The DASH diet, represented by fewer studies, consistently showed significant LDL-C reductions from baseline, aligning with a recent systematic review (132,133,159). However, findings were inconsistent when compared with control groups, potentially due to the effectiveness of the control diets, which were based on either the “Healthy eating plate” model (e.g., a well-designed healthy dietary advice group) or the composition of the control diet (e.g., lower fiber and micronutrients) (132,133). In general, the LDL-C lowering effects are attributed to high fiber content and bioactive compounds from fruits, vegetables, legumes and whole grains (160). The fermentation of dietary fibers produces SCFA such as acetate, propionate and butyrate, which can enhance the development of beneficial gut microbiota and inhibit cholesterol synthesis (47,161). Soluble dietary fiber, including psyllium, certain pectins, β-glucan, guar gum, can lower serum TC and LDL-C by slowing absorption of lipids and increasing bile acid excretion, which depletes liver cholesterol stores and enhances uptake from the bloodstream (162,163). In this case, the HDA encouraged participants to consume complex carbohydrates, which included starches, dietary fibers, and healthy oils, while minimizing low-nutrient dense food, which likely lowered LDL-C to the level observed with the DASH diet (164). Moreover, differences in study design (randomized vs. nonrandomized) may introduce unmeasured confounding which contributed to varied comparative outcomes (132,133,165). Nevertheless, the DASH diet demonstrated a beneficial association with reduction of LDL-C but further research is needed to comprehensively evaluate its long-term effects.

Several studies investigated general PBD but did not find strong or consistent effects on LDL-C. In some cases, the interchangeable use of “vegetarian diets” and “PBD” led to conflicting meta-analytic conclusions, seen in Bonekamp et al. study with non-significant LDL-C decrease, while previous meta-analysis showed greater LDL-C lowering, particularly with vegetarian diets in patients with type 2 diabetes (125,166). The inconsistency in meta-analysis could be due to mixed-quality RCTs and potential funding bias (125). However, low-GI diets, often high in fiber, demonstrated more consistent LDL-C reductions, probably by mitigating postprandial blood glucose spikes, which in turn may lower oxidative stress, inflammation, LDL oxidation, protein glycation and thrombus formation (167–169). In this review, the findings from long-term observational studies investigating habitual PBDs are mixed. The favorable association of APDQS score and LDL-C changes found by Choi et al. over 20 years, suggests that high adherence to beneficial for cardiovascular health plant foods and low to adverse can contribute to long-term low LDL-C levels (127). In contrast, the results from Li et al. over 3 years using “vegetable” pattern and Waterplas et al. over 10 years using PDI indexes, indicate that consuming plant foods or adhering to overall plant food proportions may not directly produce significant LDL-C reductions over time in observational settings (131,138). The strengths of observational design are long-term adherence, low cost and the availability of real-world data (170). However, factors such as limited dietary variation within the studied population, attenuation of adherence over time, residual confounding and selection of generally healthy population, probably contributed to discrepancies of results (138,171,172). Moreover, healthy people can have smaller LDL-C changes in comparison to individuals with diabetes, obesity or CVD who have higher LDL-C baseline (166,173). Nevertheless, the BROAD study also indicated pronounced LDL-C reduction at 3 months, with the effect diminishing after 6 and 12 months, although remaining significant versus baseline (139). This demonstrated the challenge in maintaining strict dietary adherence over a long time. Despite the heterogeneity, a general trend from the literature moves towards lower LDL-C.

Additionally, the observed modest LDL-C reduction in included studies may be related to two physiological factors. Firstly, cholesterol synthesis balance can counteract

significant drops in blood cholesterol by increasing endogenous synthesis of cholesterol (174). Secondly, individuals have dietary cholesterol absorption varying from 15 to 75 % depending on metabolism or genetics, which limits the effectiveness of dietary interventions (175). Therefore, future studies should consider this in their research methodology.

A strength of this scoping review lies in the use of a systematic search strategy combined with PRISMA-ScR reporting guidelines. This study covered a range of relevant PBDs and synthesized findings from various study designs. The current study includes a minimum of 12 weeks of dietary intervention, which is sufficient to observe the long-term cardiometabolic effects (176). A limitation of this review is that, although specific PBDs were identified such as Mediterranean diet and DASH, other relevant plant-based dietary patterns may have been overlooked. Moreover, title and abstracts were screened by a single reviewer for feasibility, which may result in the unintentional exclusion of eligible studies. Another limitation was a significant heterogeneity in dietary interventions, even within the same category such as Mediterranean diet, as well as in control diets, study populations, duration and study designs. Lastly, this scoping review is limited by the absence of quality appraisal and quantitative synthesis, thus it cannot assess the strength and reliability of results and it is not suitable for direct practice or policy recommendations, but it maps existing evidence based on the effectiveness of PBD in LDL-C reduction, identifies gaps and serves a precursor for systematic review (122).

This review reveals several gaps which require further investigation to better understand PBDs and LDL-C. Future research should focus on effective strategies to improve or maintain long-term dietary adherence, which is essential for consistent and significant outcomes. There is a need for an adoption of standardized definition and detailed characteristics of PBDs to enhance consistency and comparability across studies. Moreover, research should be expanded beyond LDL-C quantity by incorporating the qualitative aspects such as LDL-C size, density, oxidation across different dietary approaches. Finally, the emphasis should be put on mechanisms and synergistic effects of food components within PBDs which optimize LDL-C levels and reduce CVD burden.

6. Conclusion

To conclude, the evidence in this scoping review favors lower LDL-C effects of plant-based dietary patterns which offer promising non-pharmacological strategies for managing LDL cholesterol and contribute positively to well-being. The synthesized evidence suggests that the degree of LDL-C level depends on specific type and composition of the PBDs, with vegetarian diets appearing as the most consistently effective approach to study the impact on LDL-C, whereas the Mediterranean diet offers benefits regarding LDL particle quality, though its effect on the level of LDL-C is variable and potentially less evident than vegetarian approaches. The DASH diet is also a valuable intervention for cardiometabolic health but requires more comparative research. The general category of PBD suffers from heterogeneity, thus needs more clarification and precise research. Choosing the most appropriate approach requires consideration of study population, baseline lipid levels, overall dietary quality, and the maintenance of long-term adherence.

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Annexes

Annex A. Table 1: Summary of Study Characteristics

Author (year)	Country of origin	Study design	Aims	Study population	Sample size	Diet Intervention				Key findings
						Type of plant based diet	Diet composition	Duration	Control/Comparison diet	
Barbosa et al. (2024)(123)	Portugal	Randomized clinical trial	To investigate the effect of a Mediterranean-type diet in combination with physical exercise on cardiovascular disease risk factors in high-risk people	Adults (≥50 years) with high risk of CVD	88	Physical exercise + MD (Group 2)	Include: vegetables, fruits, seeds, and less processed meals (≤1, every 2-weeks); vegetable intake (at least 5 portions/day); maximum one low-fat dairy source per day; whole grains (whole pasta, whole rice, whole bread); at dinner,legumes and pulses, such as chickpeas, all types of beans, lentils, and broad beans; at lunch, fish, lean meat (chicken, poultry), or eggs; Exclude: red and/or processed meats Limit potato to twice a week	12 weeks	No intervention group (Group 1a) Physical exercise group (Group 1b)	Group 2 had significant decrease in WC, visceral fat, bicipital skinfold, TG
Barnard et al. (2021)(124)	USA	Randomized cross-over trial	To compare the impact of a Mediterranean diet and a vegan diet on body weight and cardiometabolic risk factors (plasma lipids, insulin sensitivity, and blood pressure)	Overweight adults (BMI 28 - 40 kg/m²) A mean age is 56-58 years	62 (52 completed)	LF vegan diet	Vegan Diet: Included vegetables, grains, legumes, and fruits; 75% of energy from carbs, 15% protein, 10% fat; Avoided animal products and added fats; Supplemented 500mg/day of Vitamin B12 MD (PREDIMED protocol): Included ≥2 daily servings of vegetables, ≥2-3 daily servings of fresh fruits, ≥3 weekly servings of legumes, ≥3 weekly servings of fish or shellfish, and ≥3 weekly servings of nuts or seeds, extra virgin olive oil (50g per day)	16 weeks per diet period 4-week washout period	MD	Vegan diet reduced BW, TC and LDL-C, improved HOMA-IR and OGIS but no effect in MD Both reduced BP but MD reduced greater systolic BP

Bonekamp et al. (2023) (125)	Netherlands, USA	Systematic review and network meta-analysis (73 RCTs)	To determine the most effective dietary pattern which improves cardiovascular risk factors in individuals with type 2 diabetes	Adults with type 2 diabetes A mean age is 58 years	5753	Low GI diet, MD, PBD, high protein diet, low carbohydrate diet, LF diet	Low GI diet: focusing on food items with a low GI and high fiber content MD: rich in whole grains, green vegetables, fruits, fish, lean meat and plant-based oils PBD: vegan or vegetarian diet High protein diet: ≥25 % of total energy from protein Low carbohydrate diet: <30E% from carbohydrates LF diet: <30E% from fat Moderate carbohydrate diet: >45E% from carbohydrates, >30E% from fat and <25E% from protein	Median 26 weeks (12 weeks - 7 years)	No dietary intervention	All diets significantly reduced BW, HbA1c, only low GI significantly reduced LDL-C. No significant effect on BP or other lipids. After 12 months effects attenuated. MD had the largest estimated risk reduction but Low GI had the significant estimated risk reduction
Bonekamp et al. (2024)(126)	Netherlands, USA	Systematic review and network meta-analysis design (17 RCT)	To compare the effects of different dietary patterns on cardiovascular risk factors in patients with established CVD, considering both short-term and long-term effects	Adult population with established cardiovascular disease. The median age is 61 years	6331	MD, LF diet, moderate carbohydrate diet, low GI diet	MD: Rich in whole grains, green vegetables, fruits, fish, lean meat, and plant-based oils LF diet: ≤30% of total energy intake from fat Moderate carbohydrate diet: 30-60% of energy from carbohydrates and 10-20% of energy from protein Low GI diet: NR Minimal dietary intervention: No changes in dietary pattern or intervention limited to pamphlet with dietary advice	Short-term (range 3-11 months), long-term (range 12-18 months)	Minimal dietary intervention	Moderate carbohydrate diets had the largest but non-significant reduction in BW and systolic BP. No dietary pattern had a significant effect on LDL-C. Effects attenuated after 12 months
Choi et al. (2022)(127)	USA	Prospective observational study	To investigate association between blood-cholesterol lowering diet vs. plant-centered diet and risk of coronary heart disease and stroke	Adults (18-30 years) without CVD	4701	Plant-centered diet	Plant centered diet: APDQS score. The 46 food groups were categorized into beneficial (n = 20), adverse (n = 13), and neutral (n = 13) groups based on their presumed influence on CVD. Cholesterol lowering diet: Keys score calculated by formula based on % energy from saturated fat and polyunsaturated fat, dietary cholesterol amount. Higher values related to higher plasma cholesterol	20 years	Cholesterol lowering diet	Both diets were associated with concurrent reduction in LDL-C and non-HDL-C. Only higher APDQS significantly predicted lower long-term CHD risk and stroke risk. LDL-C predicted CHD risk.

Daidone et al. (2024)(128)	Italy	Randomized clinical trial	To investigate the impact of Mediterranean-style diet on vascular health indices, lipid profiles, serum ceramide levels, and adipokine serum concentrations	Adults (male 55-80; female 60-80) with high risk level of cardiovascular disease	153	MD	MD: Abundant olive oil use, ≥2 daily servings of vegetables, >2-3 daily servings of fresh fruits, ≥3 weekly servings of legumes, ≥3 weekly servings of fish, ≥1 weekly serving of nuts or seeds, preference for white meats, regular cooking with tomato/garlic/onion, and moderate wine consumption with meals for usual drinkers. To minimize cream, butter, margarine, cold meat, pate, duck, carbonated and/or sugared beverages, pastries, industrial bakery products, industrial desserts, french fries or potato chips, and out-of-home pre-cooked cakes and sweets. LF diet: <30% of total calories from fat (12-14% MUFAs, 6-8% PUFAs, <10% SFAs), 55% from carbohydrates, 15% from protein, and cholesterol <300 mg/day.	12 months	LF diet	MD had significantly lower TC, better endothelial function, lower inflammatory adipokines, higher adiponectin, favorable changes in ceramide levels
Hernaez et al. (2017)(129)	Spain	Randomized controlled trial (subsample of the PREDIMED study)	To investigate the effect of long-term consumption of a Traditional Mediterranean Diet (TMD), enriched with either virgin olive oil or nuts on the atherogenicity of LDL particles	A random subsample of volunteers from the PREDIMED Study (Elders with high cardiovascular risk)	210	TMD-VOO, TMD-Nuts	TMD: rich in virgin olive oil, nuts, fruits, vegetables, whole grains, legumes, fish, poultry, and moderate wine consumption. TMD-VOO: 1L/week of virgin olive oil. TMD-Nuts: 210g/week of mixed nuts (walnuts, hazelnuts, almonds) LF diet (American Heart Association guidelines): reduced consumption of fatty foods (oils, nuts, butter, meat, fish, processed foods) and increased intake of vegetable foods	1 year	LF diet	TMD-VOO increased LDL resistance to oxidation, reduced oxidative modifications, increased LDL particle size, made LDL cholesterol rich, reduced LDL cytotoxicity for macrophages. TMD-Nuts did not have significant effect on LDL traits
Keshani et al. (2024) (130)	Iran, USA	Systematic review with meta-analysis (18 RCTs)	To investigate the effect of the Mediterranean diet enriched with olive oil on blood lipids, glycemic indices, blood pressure, and anthropometric indices	Adults (≥ 18 years)	3184	TMD-VOO	High consumption of fruit, nuts, vegetables, olive oil, and cereals; moderate consumption of poultry and fish; low consumption of processed meats, red meat, dairy foods, and sweets; with moderation in wine consumption. Enriched with olive oil (varying from 15-45 mL/day to 1L/week)	3 months - 5 years	Various control diets including LF diets and habitual diets	MD significantly reduced triglycerides but no effect on TC, LDL-C, HDL-C, glycemic indices, BP, BMI or BW

Li et al. (2016)(131)	China	Longitudinal observational study	To evaluate relationships between dietary patterns via principal component analysis and longitudinal changes in cardiovascular risk factors (CVRFs) in healthy Chinese women	Healthy Chinese women aged 39-48 years (mean)	1028	Vegetable pattern	Vegetable pattern were predominantly melon vegetables, starchy tubers, root vegetables, leafy and flowering vegetables, fungi and algae, lotus root, allium vegetables, fruits, fish, coarse cereals, tea, soybean, nuts, wheat, and dairy products Meat patterns included red meat, rice, poultry, and eggs. ADA pattern included a variety of animal offal, fish, shellfish and mollusks, condiments, convenience foods and desserts, alcohol and beverages, poultry, and red meat.	3 years	Meat pattern and animal offal-dessert-alcohol pattern	Higher adherence to vegetable patterns was linked to significant decreases in TC had FBG over 3 years. ADA pattern was linked to significant increases in diastolic BP, TC, LDL-C over 3 years. Meat pattern did not have significant association with changes in cardiovascular risk
Said et al. (2021) (132)	Egypt	Prospective non-randomized controlled trial	To investigate the effect of the DASH diet compared to usual healthy dietary advice (HDA) on the estimated risk of atherosclerotic cardiovascular disease (ASCVD)	Adults ≥40 years	92	DASH diet	DASH: Rich in fruits, vegetables, poultry, fish, nuts, and legumes; low-fat dairy products; whole grains rather than refined grains; limited sweets; contained 2400 mg Na per day (1 teaspoon) HDA encouraged complex healthy carbohydrates (whole grains, potatoes, beans); avoidance of processed food and sugary beverages; encouraged consumption of healthy oils	12 weeks	Healthy Dietary Advice (HDA)	Both groups had significant reductions in the estimated 10-year ASCVD risk and both showed significant improvements in BMI, systolic BP, FBS, lipid profiles, but the DASH group had larger % improvements.
Sangouni et al. (2024) (133)	Iran	Randomized controlled trial	To evaluate the impact of DASH diet on fatty liver and cardiovascular risk factors in individuals with metabolic syndrome	Adults (30-60 years) with metabolic syndrome	60 (59 completed)	DASH diet	DASH: Rich in fruits, vegetables, whole grains, low-fat dairy products; low in saturated fats, cholesterol, refined grains, and sugar-sweetened beverages. Macronutrient distribution: 50-55% carbohydrate, 15-20% protein, 30% total fat. Energy restriction: 500-700 kcal below requirement based on BMI Healthy diet: macronutrient distribution (50-55% carbohydrate, 15-20% protein, 30% total fat) but lower content of fibers and micronutrients than DASH diet; also energy-restricted	12 weeks	Healthy diet	DASH had greater reductions in fatty liver indices (FLI,HSI), WC, BW, BMI, systolic/diastolic BP, TG, TC, LDL-C

Sofi et al. (2018)(134)	Italy	Randomized crossover trial	To compare the effects of a 3-month low-calorie vegan diet (Vd) versus a low-calorie Mediterranean diet (MD) on cardiovascular disease risk markers	Adults (18-75 years) with a low-to-moderate cardiovascular risk	118	Low-calorie lacto-ovo vegetarian diet(Vd)	Vd: restrict consumption of meat and meat products, poultry, fish, and seafood, and the flesh of any other animal. Eggs and dairy products, as well as all the other food groups were included; MD: all food groups, including meat and meat products, poultry, and fish	3 months per diet period	Low-calorie MD	Both diets had significant reductions in BW, BMI, and fat mass. VD significantly reduced LDL-C, vitamin B12, uric acids, while MD lowered TG and improved interleukin-17
Termannsen et al. (2022)(135)	Denmark	Systematic review and meta-analysis (11 RCT)	To investigate the effects of vegan diets on cardiometabolic risk factors in individuals with overweight or type 2 diabetes	Adults (≥18 years) with overweight (BMI ≥25 kg/m²) or type 2 diabetes (including prediabetic state)	796	Vegan diets	The vegan diets varied substantially with regard to carbohydrate, protein, and fat content	19 weeks (12-26 weeks)	passive (habitual diet) or active (e.g., MD, LF diets)	Vegan diets reduced BW, BMI, HbA1c, TC and LDL-C but had no effects on BP, HDL-C and TG
Tsaban et al. (2021) (136)	Israel	Randomized controlled trial	To investigate the impact of a green Mediterranean diet enriched with green plant-based foods and lower meat intake on cardiometabolic risk	Adults (>30 years) with abdominal obesity/ dyslipidemia	294	Green MD MD	Green MD: Calorie restriction (1500-1800 kcal/day for men, 1200-1400 kcal/day for women). Enriched with 3-4 cups/day of green tea, 100g of Wolffia globosa (Mankai strain) frozen cubes as a plant-based protein shake replacing animal protein at dinner, and 28g/day of walnuts. Avoid red/processed meat consumption; MD: Similar calorie restriction as the Green-MED, rich in vegetables with poultry and fish replacing beef and lamb. Included 28g/day of walnuts; Healthy dietary guidance: Basic health-promoting guidelines for achieving a healthy diet without specific calorie restriction;	6 months	Healthy dietary guidance (HDG)	Both MDs reduced BW. Greed MD reduced WC, LDL-C, diastolic BP, insulin resistance, hsCRP and had greater absolute reduction in 10-year Framingham risk

Turner-Mc Grievy et al. (2023) (137)	USA	Randomized clinical trial	To investigate the effects of vegan diet versus low-fat omnivorous diet on body weight and lipids over a 2-year intervention period	African American adults with overweight/obesity (18-65 years)	159	Vegan diet (whole plant foods)	Vegan: whole plant foods, including fruits, vegetables, legumes, whole grains, nuts, and seeds; limit processed fats and oils in favor of whole plant fat sources such as nuts, seeds, and avocados; completely avoid all meat, fish, poultry, eggs, and dairy products Omnivorous:reduced animal product intake;limited meat consumption (≤5 oz/140 g of lean meat per day), limited egg consumption (≤2 yolks per week), and emphasized low-fat dairy, fish, fruits, vegetables, legumes, and whole grains	2 years	Low fat omnivorous diet	No significant differences between vegan and omni groups in body weight, TC, LDL-C
Waterplas et al. (2020) (138)	Belgium	Prospective longitudinal cohort study	To examine the 10-year associations between changes in plant-based diet indices with changes in BMI, waist circumference and blood lipids	Flemish adults (18-75 years)	650	Plant-based diet indices (PDI, hPDI, uPDI)	18 food groups classified into: Healthy plant foods (fruits, vegetables, nuts, whole grains, legumes, tea/coffee, vegetable oils) Unhealthy plant foods (potatoes, fruit juices, sugar-sweetened beverages, refined grains, sweets/desserts) Animal foods (egg, fish, dairy, meat, animal fats, miscellaneous animal-based foods)	10 years	Changes over time	No significant change in PDIs over time. Few associations between indices and BMI, WC, blood lipids; most disappeared after adjusting.
Wright et al. (2017) (139)	New Zealand	Randomized controlled trial	To evaluate the effect of a community-based whole food plant-based dietary programme on BMI and cholesterol levels	Adults (35-70 years) with obesity/ overweight and comorbidities	65	LF whole food plant-based diet (WFPB)	Low-fat (approximately 7-15% total energy from fat); included whole grains, legumes, vegetables and fruits; ad libitum with no restriction on total energy intake; avoidance of refined oils and animal products (meat, fish, eggs, and dairy); limit high-fat plant foods (nuts, avocados) and highly processed foods; minimize sugar, salt and caffeinated beverages; 50 µg daily vitamin B12 supplementation	12 week intervention and 12 months follow up	Standard medical care without dietary intervention	WFPB reduced BMI and BW, TC. Improvements in HbA1c, LDL-C and quality of life
Zahedi et al. (2020) (140)	Iran	Randomized controlled trial	To evaluate the effect of Mediterranean diet on blood biochemical factors in individuals with type II diabetes	Adults (40-60 years) with type II diabetes	228	MD	High intake of legumes, nuts, cereals, fruits and vegetables; higher intake of olive oil with less saturated fats; higher consumption of fish compared to meat and poultry; low to moderate dairy products intake; and moderate alcohol intake	6 months	Routine diet	MD had significantly lower FBS, HbA1c, LDL-C,systolic/diastolic BP compared to control. Also MD vs. baseline improved TC, HDL and BMI