The influence of a plant-based diet on cardiovascular risk factors

Annelies Van Cappellen, VUB

Promotor: Prof. Dr. Dirk Devroey, VUB

Co-promotoren: Dr. Lieve Goeman, VUB

Master of Family Medicine

Masterproef Huisartsgeneeskunde
Academiejaar: 2025 – 2026

Deze masterproef is een examendocument dat niet werd gecorrigeerd voor eventueel vastgestelde fouten. Zonder voorafgaande schriftelijke toestemming van zowel de promotor(en) als de auteur(s) is overnemen, kopiëren, gebruiken of realiseren van deze uitgave of gedeelten ervan verboden. Voor aanvragen tot of informatie i.v.m. het overnemen en/of gebruik en/of realisatie van gedeelten uit deze publicatie, wendt u tot de universiteit waaraan de auteur is ingeschreven.

Voorafgaande schriftelijke toestemming van de promotor(en) is eveneens vereist voor het aanwenden van de in dit afstudeerwerk beschreven (originele) methoden, producten, schakelingen en programma's voor industrieel of commercieel nut en voor de inzending van deze publicatie ter deelname aan wetenschappelijke prijzen of wedstrijden.

Dankwoord

Graag bedank ik mijn promotor Professor Dirk Devroey voor het begeleiden van deze thesis, alsook Katrien Alewaters en Lieve Goeman voor hun hulp.

CONTENT

Abstract **3**

1 Introduction **4**

2 Background **6**

3 Methods **7**

4 Results **13**

5 Discussion **20**

6 Strengths and limitations **26**

7 Conclusion **27**

8 References **28**

The influence of a plant-based diet on cardiovascular risk factors

Abstract

Cardiovascular disease continues to be the most significant cause of death around the world with more than 17.9 million deceased every year. Atherosclerotic cardiovascular disease is caused by a combination of multiple interrelated risk factors, some of which are in human control. These include abnormal cholesterol levels, high blood pressure, insulin resistance, obesity, injury to the blood vessel endothelium and low-level chronic activation of the immune system. Dietary patterns are among the most significant ways that nutrition can have an impact on cardiometabolic health. Of all the dietary patterns identified, plant-based diets are emerging as especially effective.

This paper aims to evaluate how plant-based eating patterns influence the intermediate risk factors that are linked most significantly to heart disease: blood cholesterol levels, blood pressure, insulin levels, weight, and metabolic health, by reviewing all available clinical trials and long-term cohort study results. This review is intended not only to highlight the effects of plant-based diets, but also to identify gaps within the current body of research that require further investigation.

To evaluate the effects of diet on cardiovascular health risk factors, the scientific literature on plant-based diets were systematically evaluated. The study methods and reporting followed the PRISMA guideline for systematic reviews and meta-analysis to promote transparency, reproducibility, and high-quality methodology.

603 articles were listed. After removing duplicates, 523 studies appeared eligible to be screened. 490 were excluded after title and abstract review (because of irrelevant PICO); 14 were not retrieved; and 2 were excluded after full text reviewing. Finally, 17 studies were retained for this systematic review, of which 0 systematic reviews, 9 randomised controlled trials (RCTs), but also controlled dietary studies and some large prospective cohort studies.

All of the studies included in this review, have shown consistent significant reduction of different intermediate cardiovascular risk factors in individuals following a plant-based diet. This reduction is combined, multi-level and multi-pathway.

1. Introduction

Cardiovascular disease (CVD) continues to be the most significant cause of death around the world with more than 17.9 million deceased every year. This represents an increasing burden on health care systems worldwide, equally in developed and developing countries. (1) Atherosclerotic cardiovascular disease is caused by a combination of multiple interrelated risk factors, some of which are in human control. These include abnormal cholesterol levels, high blood pressure, insulin resistance, obesity, injury to the blood vessel endothelium and low-level chronic activation of the immune system. (2,3) Despite significant progress in available pharmacological treatments to control these risk factors, the general population control of CVD-related risk factors continues to be largely inadequate. This indicates the need for effective, affordable, and preventive approaches, like community-based dietary solutions aimed to prevent CVD from occurring. (4)

Dietary patterns are among the most significant ways that nutrition can have an impact on cardiometabolic health; they directly influence lipid metabolism, glucose levels, blood pressure, inflammatory responses, oxidative stress, and gut microbiota. (4,5,6) Historically, recommendations for healthy diets focused primarily on changing the amount of macronutrients consumed like protein, fat, or carbohydrates (in addition to specific vitamins and minerals) - however, there is now evidence that dietary patterns can more effectively reflect the collective and synergistic biological impacts of dietary intake on the risk of cardiovascular disease. (7) Of all the dietary patterns identified, plant-based diets are emerging as especially effective. In general, a plant-based diet is based primarily on vegetables, fruits, whole grains, legumes, nuts, seeds, etc., while significantly reducing or eliminating any animal products from that diet.

The primary benefit of following a plant-based dietary pattern is that it results in lower levels of saturated fat and cholesterol than those seen in animal diet patterns and in higher levels of healthful fats (like omega-3 fatty acids) and many nutrients such as fibre, phytochemicals, and essential vitamins (8,9). Studies have shown that both soluble fibre and certain naturally occurring plant phytosterols limit the amount of cholesterol that the gut will absorb and lower the amount of low-density lipoprotein (LDL) produced by the liver. (10,11,12) Additionally, replacing saturated fats with unsaturated fats has a positive effect on both the blood lipids and the responsiveness of the blood vessels. (13)

Another benefit of a plant-based diet is that it promotes efficient blood sugar control by decreasing the accumulation of fats in muscle cells and increasing the way these cells utilize insulin. Plant-based diets are often associated with changes in the gut microbiota and those effects may extend beyond metabolism: short-chain fatty acids, produced when gut microbes ferment dietary fibre, appear to reduce inflammation and promote endothelial cell relaxation. That process might partly explain why people on plant-based diets tend to have healthier hearts. Markers such as C-reactive protein and interleukin-6, known to rise before heart problems occur, often show lower levels in those who eat mostly plants. (14)

Plant-based diets also seem to positively influence body weight and cardiometabolic disease risk. Clinical studies performed according to standardised protocols, as well as randomised controlled trials using vegetarian or plant-based diets show a statistically significant decrease in body weight, in addition to improvements to physiological parameters related to overall health. Improvements to energy balance and metabolic efficiency appear to be responsible for the increase in energy expenditure when subjects consume vegetarian or plant-based diets. (15) Because of statistically significant improvements to insulin sensitivity and lipid profiles, plant-based diets may reduce the risk of developing cardiometabolic disease. (16) Changes in the composition of gut microbiomes likely regulate cardiometabolic diseases via modulation of inflammation, lipid metabolism and endothelial function. (17) High-fibre plant-based diets produce short-chain fatty acids such as acetate, which lead to improved regulation of blood pressure and therefore reduce the risk of developing hypertension, as shown in both experimental and human clinical

trials. (18) The Mediterranean diet, which emphasises the consumption of a variety of plant foods, high levels of fibre and healthy unsaturated fats, is consistently associated with decreased systemic inflammation and improved cardiovascular outcomes. Increasingly, researchers are recognising the role that diets play as modifiable determinants of cardiometabolic health. (19)

The development of vegetarian dietary patterns has been correlated with enhanced health and decreased risk of several chronic diseases. Research has shown that individuals following these diets have superior cardiometabolic profiles and lower rates of developing cardiovascular diseases, hypertension, and type 2 diabetes than those following omnivorous dietary patterns (including animal products). Evidence supports that most of these benefits come from the increased consumption of plant-based foods such as fruits, vegetables, whole grains, and legumes, all of which contain more fibre, antioxidants, and unsaturated fats than animal products. Additionally, vegetarians typically consume less processed meat than omnivores. This consumption has been linked to several chronic diseases. (20,21)

According to extensive studies, those who primarily consume a plant-based diet live longer and are less prone to heart disease, hypertension, type 2 diabetes, obesity, and many other common diseases when compared with those whose diets are primarily composed of animal products. (18,19,20) While all plant-based diets do not provide the same health benefits, research indicates better outcomes are associated with meals based on whole, minimally processed plants versus sugary or refined foods. (21)

The relationship between plant-based diets and improved heart health occurs through various mechanisms simultaneously. The combination of these mechanisms is especially important to reduce cardiovascular risk factors, particularly when they coexist, in conditions such as metabolic syndrome. Medications are generally intended to treat a specific medical problem, whereas food has multiple effects on the body without causing adverse reactions to the body. (22, 23)

Evidence regarding effects of plant-based diets on heart disease risk factors remains inconclusive due to varying types of food classifications, diversity of participant cohorts, and varying trial results across studies. Additionally, it is difficult to clarify dietary impact on specific risk factors, both in controlled and long-term population-based studies, contributing to the lack of comparability and definitive conclusions from existing research. The main factor in determining heart health is the quality of the entire diet and not merely avoiding animal products; when a person eats nutritious foods, their overall food quality will have an impact on their heart. (24)

This paper aims to evaluate how plant-based eating patterns influence the intermediate risk factors that are linked most significantly to heart disease: blood cholesterol levels, blood pressure, insulin levels, weight, and metabolic health, by reviewing all available clinical trials and long-term cohort study results. This review is intended not only to highlight the effects of plant-based diets, but also to identify gaps within the current body of research that require further investigation.

2. Background

Atherosclerosis and vascular dysfunction are caused by interactions between metabolic, inflammatory, and vascular events that occur in a progressive manner, resulting in the development of cardiovascular disease. The development of atherosclerosis is the underlying pathology for most cardiovascular diseases, in which atherosclerotic plaque forms in the walls of arteries. The initiation of plaque formation occurs when endothelial cells become damaged, and atherogenic lipoproteins (e.g., low-density lipoprotein cholesterol) accumulate in the vascular intimal layer. Oxidation of the lipoproteins activates inflammatory pathways and recruits immune cells to form plaques that gradually narrow blood vessels. (2) Over time, these processes lead to the development of hypertension, coronary artery disease, stroke, and other cardiovascular-related diseases.

Cardiometabolic risk factors are associated with acceleration of this pathogenic process. Some of the most significant contributors to the progression of cardiovascular disease are elevated circulating lipids, insulin resistance, obesity, chronic low-grade inflammation, and endothelial dysfunction. (3) Most of these risk factors can be influenced by nutrition and dietary habits, which are highly modifiable determinants of cardiovascular health. (4)

The physiological mechanisms through which diet affects cardiovascular health are numerous. One lipid metabolism pathway known to be affected by dietary fat intake is the concentration of circulating low-density lipoprotein (LDL). Saturated fats increase LDL whereas unsaturated fats, plant sterols, and soluble fibre reduce LDL and improve lipid profiles in general. (12) Soluble fibres reduce cholesterol absorption in the intestine, while plant sterols compete with cholesterol for absorption from the intestine and reduce circulating concentrations of cholesterol. (11) These two mechanisms contribute to a decreased atherogenic load and a slower rate of development of atherosclerotic plaques.

Another important pathway is the influence of diet on glucose metabolism and insulin sensitivity. Insulin resistance is a primary contributor to the development of type 2 diabetes and to cardiometabolic disease. When insulin signalling is impaired, the amount of glucose taken up by skeletal muscle decreases, and the amount of glucose produced by the liver increases, leading to chronic hyperglycaemia and metabolic stress. (8) The composition of the dietary intake of carbohydrates affects insulin sensitivity significantly through the effect of dietary fat on the distribution of fatty acids between liver and muscle, and by an effect on energy metabolism. Whole plant-based diets have been inversely associated with the development of insulin resistance, due in part to increased fibre consumption and lower energy density. (25)

Recent research on gut bacteria indicates that they might be a key in which the foods we eat could influence our risk of heart disease. The food that we eat is known to contain carbohydrates such as fibre, starch and sugars that get fermented by the intestinal bacteria into short-chain fatty acids like acetate, propionate and butyrate. These short-chain fatty acids influence the way we metabolise energy from food by improving our ability to respond to insulin and regulating our immune system and blood vessel function. (26) Diets high in animal-based nutrients may increase the amount of a metabolite called trimethylamine N-oxide produced by the gut microbiota which has been linked to increased risk of atherosclerosis. (17)

Another major mechanism linking what we eat to our cardiovascular health is through endothelial dysfunction. The endothelium is the tissue that lines blood vessels and regulates blood flow, blood clotting and inflammation by secreting chemical messengers such as nitric oxide. Damage to the endothelium caused by oxidative stress and inflammation can reduce the amount of nitric oxide that is available to dilate blood vessels, leading to narrowing of the blood vessels and an increase in the stiffness of blood vessels. (27) Different types of foods, particularly foods rich in dietary antioxidants, polyphenols and unsaturated fats, can improve endothelial function and reduce the effects of oxidative stress on the vascular system. (28)

Various biological pathways are affected by and positively impacted by plant-based diets. Plant-based foods are predominately fruits, vegetables, whole grains, legumes, nuts, and seeds. The amount of animal-sourced products in plant-based diets is typically lower or absent. Because of this composition, plant-based diets typically contain a greater proportion of dietary fibres, antioxidants, phytochemicals, and unsaturated fats. Plant-based diets have also been shown to contain a lower proportion of saturated fat and cholesterol than animal-sourced diets. (8) Therefore, plant-based diets may have the potential to improve multiple risk factors simultaneously (lipid metabolism, glucose regulation, inflammatory markers, and endothelial function).

It is important to note that not all plant-based diets are nutritionally equal. Plant based diets that are high in refined carbohydrates (ex: white flour, sugar), added sugars, and/or heavily processed plant-based foods may not provide the same cardiometabolic benefits as those that are based on unrefined, whole plant foods. (9) Therefore, the health impact of a plant-based diet will depend on two factors; the absence of animal products and the overall quality of the plant-based diet.

3. Methods

3.1 Study design and reporting framework

To evaluate the effects of diet on cardiovascular health risk factors, the scientific literature on plant-based diets were systematically evaluated. The study methods and reporting followed the PRISMA guideline for systematic reviews and meta-analysis to promote transparency, reproducibility, and high-quality methodology. (29)

3.2 Literature search strategy

An extensive and methodical examination of the scientific literature was conducted through several digital databases: PubMed/MEDLINE, Scopus and Cochrane, from the beginning of their existence to the date of the final search. The technique for searching consisted of two separate ways: using controlled vocabulary MeSH terms and free-text keywords referring to "Plant-Based Diets" and "Cardiovascular Risk". The keyword table determined the search terms as follows:

- Plant-Based Diet
- Vegetarian Diet
- Vegan Diet
- Plant-Forward Diet
- Cardiovascular Disease
- Heart Disease
- Coronary Artery Disease
- Lipid Profile
- LDL Cholesterol
- Blood Pressure
- Glycaemic Control
- Metabolic Syndrome

To improve accuracy of searches, Boolean, “AND”, and “OR” operators were used in combining the keywords and terms. An examination of the references was conducted within the articles and reviews to find additional studies that met the criteria for inclusion. The search strategies were applied across each database to increase sensitivity.

Search strings of the search conducted on 02/10/2025:

Pubmed:

(“Diet, Vegan”[Mesh] OR ((“plant-based”[tiab] OR “plant based”[tiab] OR “vegan”[tiab] OR “fruitarian”[tiab]) AND (“diet”*[tiab] OR “nutrition”[tiab])) OR “vegan dietary pattern*” OR “vegan eating pattern*”[tiab] OR “Vegans”[Mesh] OR “vegans”[tiab]) AND (“Heart Disease Risk Factors”[Mesh] OR “Risk Factors”[Mesh] OR “cardiovascular risk*”[tiab] OR “cardiovascular effect*”[tiab] OR “cardiometabolic risk*” OR “cardiometabolic effect*”[tiab] OR “cardio metabolic outcome*”[tiab] OR “metabolic risk*”[tiab] OR “risk factor for cardiovascular disease*”[tiab] OR “risk factors for cardiovascular disease*”[tiab] OR “risk factor for heart disease*”[tiab] OR “risk factors for heart disease*”[tiab] OR "cardiovascular disease risk*”[tiab] OR "atherosclerotic disease risk*”[tiab] OR "biomarker cardiovascular risk*”[tiab] OR “biomarkers cardiovascular risk*”[tiab] OR “atherosclerosis”[tiab]) AND (“Body Weight”[Mesh] OR “body weight”[tiab] OR “weight gain”[tiab] OR “weight loss”[tiab] OR “obesity”[tiab] OR “overweight”[tiab]) OR “cholesterol”[Mesh] OR “hypercholesterolemia”[Mesh] OR “cholesterolemia”[tiab] OR “cholesteremia”[tiab] OR “hypercholesteremia”[tiab] OR “cholesterol”[tiab] OR “lipid level*”[tiab] OR “hyperlipidemia”[tiab] OR “Blood Glucose”[Mesh] OR “Hyperglycemia”[Mesh] OR “blood glucose”[tiab] OR “blood sugar”[tiab] OR “glycemia”[tiab] OR “glycemic control”[tiab] OR “fasting glucose”[tiab] OR “hyperglycaemia”[tiab] OR “hyperglycemia”[tiab]) OR “Blood Pressure”[Mesh] OR “Hypertension”[Mesh] OR “Arterial Pressure”[Mesh] OR “blood pressure”[tiab] OR “hypertension”[tiab] OR “hypertensive”[tiab] OR “arterial pressure”[tiab])

Scopus:

TITLE-ABS-KEY (("plant-based" OR "plant based” OR “vegan" OR "fruitarian" OR “vegetarian” OR “omnivorous”) AND (“diet” OR “nutrition”)) OR “vegan dietary pattern” OR “vegan eating pattern”) AND TITLE-ABS-KEY (“heart disease” OR “cardiovascular disease” OR “ cardiovascular risk” OR “cardiovascular effect” OR “cardiometabolic risk” OR “cardiometabolic effect” OR “cardio metabolic outcome” OR “metabolic risk” OR “metabolic syndrome” OR “atherosclerotic disease” OR “atherosclerosis” OR “risk factors for heart disease” OR "cardiovascular disease risk” OR "atherosclerotic disease”) AND TITLE-ABS-KEY (“body weight” OR “weight gain” OR “weight loss” OR “obesity” OR “overweight” OR “hypercholesterolemia” OR “cholesterolemia” OR “cholesteremia” OR “hypercholesteremia” OR “cholesterol” OR “lipid level” OR “triglycerides” OR “hyperlipidemia” OR “blood glucose” OR “hyperglycemia” OR “blood sugar” OR “glycemia” OR “glycemic control” OR “fasting glucose” OR “hyperglycaemia” OR “blood pressure” OR “hypertension” OR “arterial pressure” OR “blood pressure” OR “hypertensive” OR “arterial pressure”) AND TITLE-ABS-KEY ("cross-sectional" OR "observational study" OR “clinical trial” OR “intervention study”) AND NOT TITLE-ABS-KEY ("review")

Cochrane Library:

(("plant-based" OR "plant based” OR “vegan" OR "fruitarian" OR “vegetarian” OR “omnivorous”) AND (“diet” OR “nutrition”)) OR “vegan dietary pattern” OR “vegan eating pattern”) AND (“heart disease” OR “cardiovascular disease” OR “ cardiovascular risk” OR “cardiovascular effect” OR “cardiometabolic risk” OR “cardiometabolic effect” OR “cardio metabolic outcome” OR “metabolic risk” OR “metabolic syndrome” OR “atherosclerotic disease” OR “atherosclerosis” OR “risk factors for heart disease” OR "cardiovascular disease risk” OR "atherosclerotic disease”) AND (“body weight” OR “weight gain” OR “weight loss” OR “obesity” OR “overweight” OR “hypercholesterolemia” OR “cholesterolemia” OR “cholesteremia” OR “hypercholesteremia” OR “cholesterol” OR “lipid level” OR “triglycerides” OR “hyperlipidemia” OR “blood glucose” OR “hyperglycemia” OR “blood sugar” OR “glycemia” OR “glycemic control” OR “fasting glucose” OR “hyperglycaemia” OR “blood pressure” OR “hypertension” OR “arterial pressure” OR “blood pressure” OR “hypertensive” OR “arterial pressure”) AND ("cross-sectional" OR "observational study" OR “clinical trial” OR “intervention study”) AND (“humans”) NOT ("review")

3.2.1 Study selection and tools

All studies found during different searches were imported in Rayyan (QCRI), a web-based systematic review management system allowing to screen all records and removing duplicates with the help of artificial intelligence. (30,31) The reviewer also manually screened titles and abstracts of all records, to determine if they met inclusion or exclusion criteria. The eligible records were then manually full text reviewed according to the pre-determined criteria for inclusion/exclusion.

3.2.2 Eligibility criteria

Studies were eligible for inclusion if they met the following criteria:

- Human studies involving adult participants (≥18 years)
- Evaluation of a plant-based, vegetarian, vegan, or predominantly plant-based dietary pattern
- Assessment of one or more of the following intermediate cardiovascular risk factors: lipid levels, blood pressure, glycaemic indices, body weight, and/or metabolic syndrome risk
- Randomized controlled trials, controlled clinical trials, or prospective cohort studies
- Articles published in peer-reviewed journals and available in English

Studies were excluded if they:

- Included paediatric populations, pregnant or lactating women
- Were case reports, editorials, commentaries, narrative reviews, or conference abstracts
- Focused exclusively on single nutrients or supplements rather than dietary patterns
- Lacked relevant cardiovascular outcomes

3.2.3 Data extraction

Data extraction was performed using a standardized data extraction form, including following extracted variables:

1) Author and year of publication
2) Study design
3) Population characteristics
4) Sample size
5) Description of dietary intervention and comparator
6) Duration of follow-up
7) Primary cardiovascular outcomes
8) Direction and magnitude of effect

3.2.4 Risk of bias assessment

Included randomized controlled trials were evaluated for methodological quality, as well as their potential for bias, by applying the Cochrane Risk of Bias tool (RoB 2.0) for randomised controlled trials, and ROBINS-I tool (Risk Of Bias In Non-randomised Studies – of Interventions) for non-randomised studies. This evaluation included assessment of each trial's randomisation methodology, allocation concealment, blinding methodology, incomplete outcome data, and selective reporting. A prospective cohort study's methodological quality and risk of bias were evaluated by applying the Newcastle-Ottawa Scale (NOS), which evaluated the three domains of selection, comparability, and outcome assessment.

Table 1: Risk of Bias assessment

	First author (study)	Assessment tool	Risk of bias	Quality rating	Rationale for assessment
1	Jenkins et al. 2011 (32)	Cochrane RoB 2 (RCT)	Low	High	Adequate randomization, concealed allocation, objective lipid outcomes, low attrition.
2	Jenkins et al. 2003 (33)	Cochrane RoB 2 (RCT)	Moderate	Good	Short duration and small sample; strong biochemical endpoints and active comparator.
3	Barnard et al. 2006 (34)	Cochrane RoB 2 (RCT)	Low	High	Well-designed RCT with clinically meaningful endpoints and good adherence monitoring.
4	Turner-McGrievy et al. 2007 (35)	Cochrane RoB 2 (RCT)	Moderate	Good	Randomized design; reliance on self-reported dietary intake introduces some bias.
5	Wright et al. 2017 (36)	Cochrane RoB 2 (RCT)	Moderate	Fair	Small sample size and short intervention; objective blood pressure outcomes.
6	Mishra et al. 2013 (37)	Cochrane RoB 2 (RCT)	Moderate	Good	Adequate randomization; heterogeneous population and dietary adherence variability.
7	Kahleova et al. 2020 (38)	Cochrane RoB 2 (RCT)	Low	High	Strong internal validity, controlled intervention, objective metabolic outcomes.
8	Hall et al. 2021 (39)	Cochrane RoB 2 (Crossover RCT)	Low	High	Controlled feeding, crossover design minimizes confounding, excellent outcome ascertainment.
9	Bruns et al. 2023 (40)	ROBINS-I	Moderate	Good	Non-randomized but controlled intervention; residual confounding likely but outcomes objectively measured.
10	Esselstyn et al. 2014 (41)	ROBINS-I	Serious	Fair	No randomization or parallel control; strong adherence bias despite long-term follow-up.
11	Ornish et al. 1990 (42)	ROBINS-I	Serious	Fair	Multifactorial lifestyle intervention; difficult to isolate dietary effect, objective angiographic outcomes.
12	Satija et al. 2017 (23)	Newcastle–Ottawa Scale (NOS)	Moderate	High	Large prospective cohort with validated plant-based diet indices; residual confounding unavoidable.
13	Kim et al. 2020 (43)	Newcastle–Ottawa Scale (NOS)	Moderate	Good	Well-characterized cohort; dietary exposure assessed via questionnaires.
14	Baden et al. 2023 (44)	Newcastle–Ottawa Scale (NOS)	Moderate	High	Longitudinal dietary change analysis with repeated measures; strong follow-up.
15	Huo et al. 2023 (45)	Newcastle–Ottawa Scale (NOS)	Moderate	Good	Large Chinese cohort; cultural dietary patterns may limit external validity.
16	Orlich et al. 2013 (46)	Newcastle–Ottawa Scale (NOS)	Moderate	High	Robust cohort size and follow-up; potential misclassification of diet patterns.
17	Chiu et al. 2018 (47)	Newcastle–Ottawa Scale (NOS)	Moderate	Good	Clear vegetarian exposure definition; observational design limits causality.

3.2.5 Data analysis

The great heterogeneity of data within study populations, dietary definitions, outcome measures, and length of time for follow up made it impossible to perform a quantitative meta-analysis. Instead, a structured narrative synthesis of the information is presented in this paper. The results were grouped according to following categories of cardiovascular risk: lipid profiles, blood pressure, glycaemic control, body weight, and metabolic syndrome, with highlighting of the consistency and direction of effects from different designs.

However, in order to compare estimations of minimal and maximal effects of the different plant-based diets on the individual intermediate cardiovascular risk factors, exact Cohen's d was calculated whenever standard deviations of the change scores or post values were reported or available to compute a pooled standard deviation. When standard deviations were not available, means or medians and confidence intervals (to reconstruct standard errors), interquartile ranges, or assumed standard deviations derived from the study's power calculations were used to estimate approximal Cohen's d effect size ranges.

All data analyses were carried out using Python.

3.3 Definition of exposure

In order to define and categorise the different possible plant-based diets interventions, following definitions were used:

Table 2: Definition of exposure

Dietary pattern	Operational definition used in studies	Typical included foods	Typical excluded foods	Key references
Vegan diet	100% plant-derived foods	Whole grains, legumes, fruits, vegetables, nuts, seeds	All animal products	Craig et al. 2009 (8); Barnard et al. 2015 (15)
Vegetarian diet	Plant-based diet excluding meat; may include dairy/eggs	Grains, legumes, fruits, vegetables, dairy/eggs	Meat, fish	Fraser et al. 2009 (20); Tonstad et al. 2013 (48)
Whole-food plant-based diet (WFPB)	Predominantly unprocessed plant foods	Whole grains, legumes, vegetables, fruits	Refined grains, added sugars, animal foods	Wright et al. 2017 (36)
Healthful plant-based diet (hPDI)	Plant foods weighted positively based on quality	Whole grains, vegetables, fruits, nuts	Refined carbs, sweets	Satija et al. 2017 (23); Wang et al. 2026 (49)
Unhealthful plant-based diet (uPDI)	Plant foods weighted negatively based on refinement	Refined grains, sweets, fries	Whole plant foods	Satija et al. 2017 (23)
Portfolio diet	Plant-based diet emphasizing LDL-lowering components	Viscous fibre, nuts, soy, plant sterols	High-SFA foods	Jenkins et al. 2002 (50); Chiavaroli et al. 2018 (51)
Plant-forward diet	Flexible, health-focused eating style that prioritizes whole, plant-based foods	Fruits, vegetables, whole grains, legumes, nuts, and seeds—while minimizing but not eliminating animal products	None	Yokoyama et al. 2014 (52)

3.4 Outcome reporting heterogeneity

There was no means to combine quantitative data or to conduct a formal meta-analysis on the included studies because of important discrepancies and significant inconsistencies in how measures, outcomes and endpoints were defined and reported. Many aspects of the studies included varied not only in methodological ways, but also in clinical approach.

First, the populations that were studied varied widely. Some studies used populations of individuals with cardiometabolic related diseases (hyperlipidaemia, obesity, Type II Diabetes Mellitus, and/or arterial hypertension); other studies comprised healthy populations. Because of this great degree of variety among populations, a subject's initial corresponding baseline risk profile and medication usage may influence the degree of response to dietary interventions.

Second, the dietary intervention itself was different among each study. The studies that were reviewed were evaluating different types of plant-based dietary patterns (vegan, vegetarian, whole-food plant-based, portfolio, and plant-forward). These various plant-based dietary patterns differ in macronutrient composition (the relative proportions of fat, carbohydrate, and protein), fibre content, the quality of the fats consumed, and the processing of the foods consumed (unprocessed/whole foods and/or refined/unprocessed). All of these factors combined make it impossible to classify any of the studies into equivalent exposures.

Third, the duration of the dietary interventions was greatly different. They ranged from short-term controlled feeding studies of a few weeks to longer-term prospective cohort studies with follow-up periods lasting several years. These differences affect how outcomes are measured and how results are quantified.

Fourth, the ways of reporting cardiovascular risk factors and outcomes were too diverse. The included studies reported lipid fractions and lipid profiles, inflammatory markers, and composite scores associated with diabetes mellitus and high blood pressure, but they were not reported uniformly or consistently. Studies used different measures of lipids (various fractions), varying markers of glycaemia, blood pressure measurements, and indices of metabolism (composite metabolic scores). Additionally, the synthesis of evidence was complicated by the selective reporting of study endpoints in smaller studies that have not been preregistered.

In conclusion, due to this important methodological and clinical heterogeneity of the included studies, complicating comparison of findings across studies, a structured narrative synthesis approach was deemed more suitable than a quantitative pooling of the results. (53)

4. RESULTS

4.1 Main results

Using the search strings in all databases, 603 articles were listed. After removing duplicates, 523 studies appeared eligible to be screened. 490 were excluded after title and abstract review (because of irrelevant PICO); 14 were not retrieved; and 2 were excluded after full text reviewing. Finally, 17 studies were retained for this systematic review, of which 0 systematic reviews, 9 randomised controlled trials (RCTs), but also controlled dietary studies and some large prospective cohort studies.

Fig 1: PRISMA flowchart

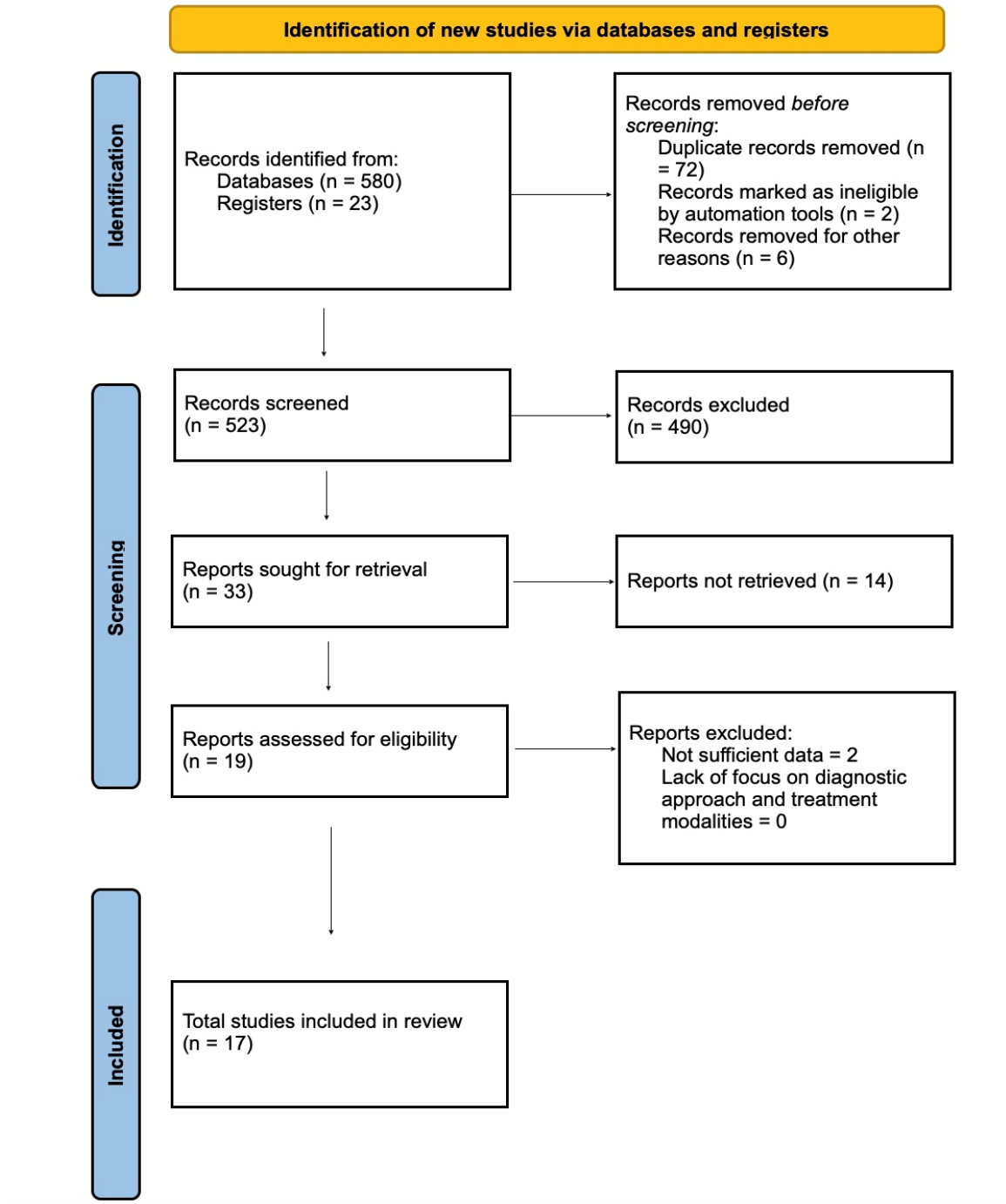


Table 3: Selected studies

	Author & year	Study Design	Population	Sample Size	Diet Intervention	Comparator	Duration	Primary Outcomes	Direction of Effect
1	Jenkins et al. 2011 (32)	RCT	Hyperlipidaemic adults	345	Portfolio diet	Low-fat control	24 wk	LDL-C, CRP	↓ LDL-C, ↓ CRP
2	Jenkins et al. 2003 (33)	RCT	Hypercholesterolemic adults	46	Portfolio diet	Lovastatin	4 wk	LDL-C, CRP	↓ LDL-C comparable to statin
3	Barnard et al. 2006 (34)	RCT	Type 2 diabetes	99	Low-fat vegan	ADA diet	22 wk	HbA1c, weight, lipids	↓ HbA1c, ↓ weight
4	Turner-McGrievy et al. 2007 (35)	RCT	Overweight adults	62	Vegan diet	Omnivorous	12 wk	Weight, TC	↓ weight, ↓ total cholesterol
5	Wright et al. 2017 (36)	RCT	Adults with hypertension	65	Plant-based diet	Usual diet	6 mo	BP	↓ SBP, ↓ DBP
6	Mishra et al. 2013 (37)	RCT	Adults with cardio-metabolic risk	291	Vegetarian diet	Non-vegetarian	NR	Lipids, glucose	↓ LDL-C, ↓ glucose
7	Kahleova et al. 2020 (38)	RCT	Overweight adults	244	Plant-based diet	Control diet	16 wk	Insulin sensitivity	↑ insulin sensitivity
8	Hall et al. 2021 (39)	Crossover RCT	Healthy adults	20	Plant-based diet	Animal-based diet	2 wk	Energy intake, weight	↓ energy intake, ↓ weight
9	Bruns et al. 2023 (40)	Controlled intervention	Adults with CVD risk	94	Plant-based diet	Standard care	NR	Lipids, BP	↓ LDL-C, ↓ BP
10	Esselstyn et al. 2014 (41)	Intervention	Coronary artery disease	198	Intensive plant-based	No control	4 yr	Cardiac events	↓ recurrent events
11	Ornish et al. 1990 (42)	RCT	CAD patients	48	Lifestyle + plant-based	Usual care	1 yr	Coronary stenosis	Regression of stenosis
12	Satija et al. 2017 (23)	Prospective cohort	US adults	>200,000	Healthful PBD index	Lowest adherence	Up to 20 yr	CVD risk	↓ CVD incidence
13	Kim et al. 2020 (43)	Prospective cohort	Korean adults	5646	Plant-based pattern	Omnivorous	10 yr	Metabolic syndrome	↓ MetS risk
14	Baden et al. 2019 (44)	Prospective cohort	US adults	75314	Improved PBD quality	Baseline diet	NR	Cardiometabolic markers	↓ cardiometabolic risk
15	Huo et al. 2023 (45)	Cohort	Chinese adults	10013	PBD indices	Lowest adherence	Longitudinal	Metabolic syndrome	↓ MetS prevalence
16	Orlich et al. 2013 (46)	Cohort	Adventist population	73308	Vegetarian diets	Non-vegetarian	NR	Metabolic risk	↓ diabetes, ↓ obesity
17	Chiu et al. 2018 (47)	Cohort	Taiwanese adults	2918	Vegetarian diet	Omnivorous	NR	Metabolic syndrome	↓ MetS

Legend: RCT Randomized Controlled Trial; NR not reported; CVD cardiovascular disease; PBD plant-based diet; MetS metabolic syndrome; US United States; CAD coronary artery disease; BP blood pressure

4.2 Study design, populations, and exposure structure

The RCTs focused mostly on participants with dyslipidaemia, overweight or obesity, type 2 diabetes, hypertension and coronary artery disease, while cohort studies assessed general populations and health-conscious groups over a longer period. The evaluated dietary exposures were primarily divided into two main criteria; one was the level of plant dominance (vegan, vegetarian, plant dominant, plant-based, and so on) and the second was the quality of the diet (whole food vs refined). The variability allowed for evaluating short term physiological reactions to controlled plant-based dietary interventions, along with long term relationships between plant-based diets and cardiometabolic trajectories and clinical outcomes.

4.3 Lipoprotein outcomes and atherogenic burden

Consistent results from randomized controlled trials (RCTs) indicate that plant-based dietary interventions lower blood levels of low-density lipoprotein cholesterol. However, the magnitude of these changes is determined by baseline lipid levels and the composition of the diets. Interventions using a "portfolio" approach to plant-based foods show similar reductions in serum LDL cholesterol over periods ranging from 4 to 24 weeks, compared to those achieved with pharmacological lipid-lowering therapies and showing better reductions than low-fat diets. (33,54)

Additionally, while LDL cholesterol reductions occurred with all plant-based approaches studied to date, the largest reductions were found where trials focused on decreasing saturated fat intake while increasing the intake of soluble fibre and plant sterols than those where interventions focused only on the exclusion of animal products. Little to no change was found in high-density lipoprotein cholesterol levels across studies, indicating that the improvements in atherogenic risk were primarily due to reductions in apoB-containing lipoprotein rather than global lipid remodelling. (23)

These data were also supported by prospective cohort studies, which found a more favourable longitudinal profile for lipoprotein levels in individuals following health-promoting plant-based dietary patterns. Longitudinal cohort studies that distinguished between whole-food plant-based diets and refined plant-based dietary patterns found that LDL cholesterol benefits occurred only when following whole food plant-based diets rich in minimally processed plant foods. These observations align with the trial data, reinforcing the importance of dietary quality within plant-based classifications. (55)

4.4 Blood pressure modulation across intervention and population settings

Intervention studies randomized to evaluate blood pressure endpoints showed modest, consistent improvements in blood pressure for both systolic and diastolic measurements after implementation of plant-based diets. However, the magnitude of change was greatest among those with blood pressure measured above average before starting an intervention, and among intervention groups exceeding 12 weeks in duration. (34) Intervention groups that were shorter in duration experienced smaller changes in absolute blood pressure, but they were also consistent in direction of effect. (56)

In addition to intervention research, observational cohorts also support these findings, with lower rates of hypertension and lower rates of increase in blood pressure with age associated with individuals who adhered more strictly to plant-forward diets, even after accounting for differences in body mass index (BMI) and levels of physical activity, which suggests the impact of dietary patterns on blood pressure is not limited to weight-related changes. (52)

4.5 Glycaemic control, insulin sensitivity, and diabetes risk

Improvements in fasting blood sugar levels, haemoglobin A1c, and insulin resistance were seen in trials of plant-based diets in subjects diagnosed with either Insulin Resistance or Type II Diabetes Mellitus. Also worth mentioning is the correlation identified in several of these studies whereby participants exhibited greater glucose control than could be expected based on weight loss alone. This indicates a direct relationship between the type of food consumed and the metabolic pathways regulated by the respective foods. (35,57)

Crossover studies have shown that plant-based diets were able to produce an increased energy intake when consumed ad libitum as well as a rapid increase in insulin sensitivity when used acutely, despite being isocaloric. These studies' findings therefore support the notion of the presence of specific acute diet-responsive metabolic mechanisms. (22)

Longitudinal cohorts have demonstrated a decrease in the number of individuals developing type 2 diabetes among those consuming either vegetarian-style or health-promoting plant-based diets. (48,58) Risk reductions for developing type 2 diabetes displayed a consistent, progressive pattern of association with dietary quality, whereby the less nutritious refined plant-based diets are found to have no significant association with reduced risk of developing type 2 diets whereas the more nutritious plant-based diets display an inverse association. (9)

4.6 Body weight dynamics and adiposity distribution

The outcomes of randomized trials indicate that adopting a plant-based diet is associated with a reduction in body weight over time, with no restrictions on energy intake. While both vegetarian and vegan diet patterns are less calorically dense than an omnivorous (meat-eating) pattern; however, the degree of weight loss between these vegan and vegetarian groups was found to be equal. Both groups demonstrated spontaneous regulation of their dietary intake without implementing strict caloric restrictions; this was further substantiated by evidence obtained from observational cohort studies. (15,42)

During long term follow-up of individuals adhering to a plant-based or vegan dietary pattern, the available evidence suggests that consuming more whole-food plant products provides a greater reduction in BMI and in the incidence of overweight and obesity. (20,59)

4.7 Inflammatory markers and integrated cardiometabolic profiles

Several randomized studies have shown a decrease in the amount of circulating inflammatory markers (including C-reactive protein) when individuals followed plant-based diets even when they were not losing vast amounts of fat or weight. The findings imply that inflammatory modulation is likely to be part of a separate response mechanism, although related to other variables in an individual's diet.

Several studies on the use of Community-Based Lifestyle Programs, conducted by Centers for Disease Control and Prevention (CDC), have shown a link between an individual's adherence to a healthy plant-based diet and reduced incidence of metabolic syndrome as well as lower incidences of individuals exhibiting co-occurrence of multiple cardiovascular risks. (60,45) At the same time, longitudinal studies have found that people who had made improvements in the quality of their plant-based food choices over time experienced coordinated improvements in several cardiovascular risk parameters (lipids, glycaemic levels, blood pressure, and adiposity) rather than simply one. (61)

4.8 Overview of outcomes

Table 4: Overview of outcomes

Outcome	Direction of association	Strength of evidence	Study designs supporting association	Representative references
LDL cholesterol	↓↓↓	Strong	RCTs, cohorts, Mendelian randomization	Jenkins et al. 2002 (50); Ference et al. 2017 (62)
Total cholesterol	↓↓	Strong	RCTs, cohorts	Barnard et al. 2015 (15)
Blood pressure	↓	Moderate–strong	Cohorts, RCTs	Yokoyama et al. 2014 (52); Appel et al. 1997 (63)
Body weight	↓	Strong	RCTs	Barnard et al. 2015 (15); Turner-McGrievy et al. 2007 (35)
Insulin resistance	↓	Moderate	RCTs	Kahleova et al. 2018 (82)
Type 2 diabetes incidence	↓	Strong	Prospective cohorts	Tonstad et al. 2013 (52); Cordova et al. 2025 (58)
Inflammatory markers (CRP)	↓	Moderate	Controlled feeding studies	O'Keefe et al. 2008 (64)
Subclinical atherosclerosis	↓ progression	Emerging	Imaging-based RCTs	Sala-Vila et al. 2014 (65)

Table 5: Estimations of effect sizes for intermediate cardiovascular risk factors per intervention

Risk factor	study	Intervention	duration	subanalysis	key effect (mean difference)	CI min	CI max	pooled SD	Cohen's d	min effect	max effect	used for analysis	effect size
LDL cholesterol	Jenkins et al. 2011 (32)	intensive portfolio vs control	6 months		-18mg/dL	-10mg/dL	-25mg/dL	28,4	**0,63**	0,59	1,06	CI, PA	moderate to large
	Jenkins et al. 2011 (32)	routine portfolio vs control	6 months		-16mg/dL	-9mg/dL	-23mg/dL	26,4	**0,61**		0,94	CI, PA	moderate to large
	Barnard et al. 2006 (34)	low fat vegan diet vs ADA diet (control)	22 weeks		-1mg/dL			23,1	**0,04**	0	0,52	CI, PA	very small
	Barnard et al. 2006 (34)	low fat vegan diet vs ADA diet (control)	22 weeks	medication stable subgroup	-11,9mg/dL	-22,2mg/dL	-1,7mg/dL	23,1	**0,52**			CI, PA	moderate
	Ornish et al. 1990 (42)	low fat vegetarian diet vs usual care (control)	1 year		-1,21 mmol/L			1,66	**0,73**	0,56	0,90	SD	moderate to large
Total cholesterol	Barnard et al. 2006 (34)	low fat vegan diet vs ADA diet (control)	22 weeks		-14,5 mg/dL	-25,8mg/dL	-3,2mg/dL	25,5	**0,57**			CI, PA	moderate
	Wright et al. 2017 (36)	WFPBD vs normal care	1 year		-0,45 mmol/L	-0,54mmol/L	+0,54mmol/L	0,97	**0,46**	-0,09	1,03	means, CI	moderate [1]
	Mishra et al. 2013 (37)	PBD vs no diet changes	18 weeks		-8,0mg/dL	-2,9mg/dL	-13,1mg/dL	22,2	**0,36**	0,13	0,59	means, SE, CI	small to moderate
	Kahlova et al. 2020 (38)	low fat vegan diet vs no diet changes	16 weeks		-0,6 mg/dL	-0,4 mg/dL	-0,9 mg/dL	1,02	**0.39**	0.59	0.88	means, CI	moderate
	Ornish et al. 1990 (42)	low fat vegetarian diet vs usual care control group	1 year		-1,09mg/dL			1,36	**0,80**	0,60	1,00	SD	moderate to large
Blood pressure systolic	Ornish et al. 1990 (42)	low fat vegetarian diet vs usual care control group	1 year		+ 2 mmHg			16,8	**0,12**	0	0,25	SD	very small
Blood pressure diastolic	Ornish et al. 1990 (42)	low fat vegetarian diet vs usual care control group	1 year		-9 mmHg			11	**0,82**	0,6	1,1	SD	moderate to large
HbA1c	Barnard et al. 2006 (34)	low fat vegan diet vs ADA diet (control)	22 weeks		-0,40%	-0,9%	+0,1%	1,26	**0,32**	0,08	0,35	CI, PA	small to moderate
	Barnard et al. 2006 (34)	low fat vegan diet vs ADA diet (control)	22 weeks	medication stable subgroup	-0,85%	-1,51%	-1,19%	1,26	**0,67**	0,15	0,70	CI, PA	moderate
	Mishra et al. 2013 (37)	PBD vs no diet changes	18 weeks	diabetes subgroup	-0,68%	-0,29%	-1,1%	0,69	**0,99**	0,42	1,59	means, SE, CI	moderate to very large

Risk factor	study	Intervention	duration	subanalysis	key effect (mean difference)	CI min	CI max	pooled SD	Cohen's d	min effect	max effect	used for analysis	effect size
Body weight	Barnard et al. 2006 (34)	low fat vegan diet vs ADA diet (control)	22 weeks		-1,5 kg	-3,3kg	+0,2kg	4,41	**0,34**			CI, SD	small to moderate
	Barnard et al. 2006 (34)	low fat vegan diet vs ADA diet (control)	23 weeks	medication stable subgroup	-3,4 kg	-5,5 kg	-1,4 kg	3,91	**0,87**			CI, SD	large
	Turner McGrievy et al. 2007 (35)	vegan diet vs NCEP	1 year		-3,1kg			4,33	**0,72**	0,4	0,8	IQR	moderate to large
	Turner McGrievy et al. 2007 (35)	vegan diet vs NCEP	2 years		-2,3kg			4,95	**0,46**	0,25	0,5	IQR	moderate
	Wright et al. 2017 (36)	WFPBD versus normal care	1 year		-10,6 kg	-7,7kg	-13,5kg	5,17	**2,05**	1,49	2,61	means, CI	very large
	Mishra et al. 2013 (37)	PBD vs no diet changes	18 weeks		-2,84kg	-2,0kg	-3,9kg	4,1	**0,69**	0,49	0,95	means, SE, CI	moderate to large
	Kahlova et al. 2020 (38)	low fat vegan diet vs no diet changes	16 weeks		-5,9kg	-5,0kg	-6,7kg	3,36	**1.49**	1.76	1.99	means, CI	very large
	Hall et al. 2021 (39)	plant-based low fat diet vs animal-based ketogenic diet	28 days		-0,68 kg	-2,11 kg	+0,75 kg	1,43	**0,48**	0,25	0,70	means, SE	moderate
	Esselstyn et al. 2014 (41)	plant-based nutrition mean	3,7 years		-8,5 kg	-4,5 kg	-12,5 kg	4	**1,55**	1,21	2,13	means, SD from other studies	very large [2]
	Ornish et al. 1990 (42)	low fat vegetarian diet vs usual care control group	1 year		-11,8 kg			8,7	**1,36**	1,00	1,70	SD	large to very large
BMI	Wright et al. 2017 (36)	WFPBD versus normal care	1 year		-3,9 kg/m^2	-2,9 kg/m^2	-4,9 kg/m^2	1,78	**2,19**	1,63	2,75	means, CI	extremely large
	Mishra et al. 2013 (37)	PBD vs no diet changes	18 weeks		-1,1kg/m^2	-0,7kg/m^2	-1,4kg/m^2	1,54	**0,71**	0,45	0,91	means, SE, CI	moderate to large
	Kahlova et al. 2020 (38)	low fat vegan diet vs no diet changes	16 weeks		-2,2 kg/m^2	-1,1 kg/m^2	-3,3 kg/m^2	4,38	**0.25**	0.50	0.75	means, CI	small to moderate
	Bruns et al. 2023 (40)	flexitarians vs omnivores	3 days		-3,0 kg/m^2	-5,96 kg/m^2	-0,04 kg/m^2	2,96	**1,01**	0,7	1,30	medians, IQR	large with uncertainty [3]
	Bruns et al. 2024 (40)	flexitarians vs vegans	3 days		-1,0 kg/m^2	-3,22 kg/m^2	+1,22 kg/m^2	2,6	**0,38**	0,2	0,6	medians, IQR	small to moderate [3]

Legend: CI Confidence interval; PA Power analysis assumed SD, SD Standard Deviation; IQR Interquartile Range; BMI Body Mass Index; WFPBD Whole Food Plant-based diet; PBD Plant-based diet; vs versus; ADA American Diabetes Association; NCEP National Cholesterol Program Diet.

Remarks: 1) Range uncertain; 2) Large within-cohort effect observed, but lack of comparator and variance data; 3) Cross-sectional study

5. Discussion

In this review, plant-based diets seem to be associated with coordinated and biologically plausible effects across multiple cardiovascular risk factors. Instead of just affecting individual biomarkers, these diets appear to change along with other processes to affect major upstream (metabolic and vascular) processes associated with cardiovascular disease. Therefore, a systems-level effect provides an explanation for the similarity of intermediate cardiovascular risk factor improvements found across many different types of populations and types of studies.

While the RCTs focused mostly on participants with an increased cardiovascular risk (in casu dyslipidemia, overweight or obesity, type 2 diabetes, hypertension and coronary artery disease), and compared plant-based diets as an intervention with alleged 'standard or normal cardiovascular care' (in casu low saturated fat therapeutic diet, a diet following the American Diabetes Association guidelines, no dietary changes to usual diet, minimally processes animal-based ketogenic low-carbohydrate diet, omnivorous and flexitarian diet, or unspecified 'standard care'), the included cohort studies generally assessed healthy or comorbidity-free populations and health-conscious groups over a longer period. The effects of plant-based diets may have been more expressed in the RCTs as their populations started with a higher cardiovascular risk.

5.1 Lipid modification as a causal anchor of cardiovascular benefit

The reduction of low-density lipoprotein cholesterol is the most consistently observed variable across studies demonstrating that plant-based diets are associated with reduced cardiovascular risk. Genetic studies have not only established that LDL cholesterol is a necessary driver of atherosclerotic cardiovascular disease, but also that cumulative exposure may determine the risk of this event. (66) The degree of LDL cholesterol reduction observed in individuals consuming a plant-based diet with high adherence appears to be at or near levels identified by both pharmacologic and Mendelian randomization studies as clinically meaningful for cardiovascular risk reduction. (67)

Additionally, while LDL cholesterol reductions are not uniform across all dietary patterns of a plant-based diet, cohort studies indicate that reductions in LDL cholesterol are dependent on the quality of fats consumed, the density of fibres in the diet, and the extent to which food products are processed, rather than solely on whether an individual consumes animal products. Therefore, the results of previous literature that have treated plant-based diets as an isolated exposure could not account for these variances. (68)

When unsaturated plant fats, intact fibres, and minimally processed foods define the dietary patterns, they result in greater lipid-lowering effects and reproducibility than when refined carbohydrates are dominant. (63) This finding has implications for the interpretation of cardioprotection. It suggests that it results from replacing atherogenic (cholesterol-raising) components of the diet rather than a dietary component of plant identity alone. Thus, the mechanisms by which a diet affects LDL cholesterol should now be viewed in the context of established lipid metabolic pathways.

5.2 Blood pressure effects beyond sodium restriction

Past research has often focused on sodium reduction as the primary mechanism by which plant-based foods lower blood pressure. However, recent studies have shown that several additional vascular and metabolic factors contribute to the decrease in blood pressure. For example, results from randomized controlled trials indicate that the reduction of blood pressure has been observed when sodium intake is

limited, as well as additional effects of other mechanisms, such as potassium mediated natriuresis, availability of endothelial nitric oxide and responsiveness of vascular smooth muscle. (69)

Observational studies show that the antihypertensive effects of plant-based diets are greater among individuals with elevated baseline blood pressure, suggesting a possible modification effect due to impaired vascular function. This pattern is similar to a pharmacological response curve for medication and provides evidence supporting the premise that improved vascular resilience is the outcome of plant-based diets, rather than merely improved electrolyte balance. These effects likely originate from both oxidative stress and inflammatory changes to endothelial cells, and chronic alteration of microvascular tone. (27)

5.3 Glycaemic regulation independent of energy balance

Across randomized trials, a key finding is that dietary composition improves glycaemic control and insulin sensitivity regardless of weight loss. This disconnect between dietary composition and weight loss is a challenge to current calorie-centric models of improving metabolism while providing further evidence of the direct physiological effect of food (diet) on insulin signalling mechanisms.

Furthermore, mechanistic studies provide robust evidence that consuming more plant-based foods decreases ectopic lipid storage within the liver and skeletal muscle, thereby reducing the harmful effects of lipotoxicity on the insulin receptor signalling pathway. (70) Additionally, the increased amount of fermentable fibre consumed alters the gut microflora and gut metabolite profile of the individual, ultimately resulting in increased quantity and quality of short-chain fatty acids. This increment in both the amount and quality of short-chain fatty acids is positively associated with improving hepatic and peripheral insulin sensitivity. (71) Collectively, the above examples offer biological support for observed reductions in both fasting glucose and glycosylated haemoglobin (HbA1c) in individuals with a degree of insulin resistance and type 2 diabetes.

The association between plant-based dietary patterns and reduced incidence of diabetes has been found in multiple cohort studies, suggesting evidence for the long-term effect of improved insulin sensitivity. (48)

5.4 Clustering of cardiometabolic risk factor improvement

Plant-based diets can improve multiple cardiovascular conditions in one individual. In many cases, when a person begins eating a plant-based diet, their LDL cholesterol levels, blood pressure, body fat percentage, glycaemic index, etc., all decrease. It appears that plant-based diets intervene at the "upstream" regulatory nodes of cardiometabolic homeostasis (for example how we metabolize things, respond to inflammation, function optimally and process what we consume), instead of at the "downstream" phenotypes (what can be measured in the clinic, such as biomarkers and disease risk itself) and thus influencing more than one downstream phenotype or pathway.

This cluster pattern stands in contrast to the pharmacological approach to the treatment of heart disease. Pharmacological approaches primarily target one pathway, thus requiring multiple drug combinations to obtain equivalent reductions in multi-faceted cardiovascular risk. The clustering effect also demonstrates that plant-based diets can be considered system-level "intervention networks" that create an environment that alters the course of human cardiovascular disease.

5.5 Reconciling heterogeneity across studies

The diversity of effect sizes across studies should not be interpreted as invalid results or as differences in the available evidence, but it reflects both biological and methodological differences across the different types of individual research studies.

Several factors influence the effect of diet on cardiometabolic risk, including: the baseline level of cardiometabolic risk in the research participants prior to dietary change; the type and quality of the food consumed during the dietary intervention versus the food consumed during the control; the participant's intensity of physical activity; and how dietary patterns were defined and recorded within each of the studies in question. The amount of compliance with the participants' dietary pattern during each research study can also greatly affect the results of that study. Finally, differences in the degree of dietary contrast between the dietary intervention and the control in each research study can also greatly influence the research outcome.

When the studies are classified and grouped based on diet type (e.g., quality of diet; degree of dietary contrast), there is a much greater level of consistency between the research findings from studies based on a randomized trial design and those based on an observational cohort design. Overall, both trial and cohort studies provide substantial support for the use of a plant-based diet as a means of protecting against cardiovascular disease. If those factors that can potentially affect the outcomes of each dietary study are not accounted for in the analysis of that study's results, the results may yield smaller and non-significant statistical values for the beneficial outcomes of the dietary contributions from each food. This warrants the emphatic recommendation of the stratification of all dietary studies based on biological and methodological modifiers to more accurately reflect the impact of nutritional patterns on health.

5.6 Comparative context with other cardioprotective dietary paradigms

Plant-based dietary patterns exhibit many of the same structural characteristics of other cardioprotective dietary patterns such as the Mediterranean diet, Dietary Approach to Stop Hypertension (DASH), and Portfolio Dietary Patterns, which include high levels of fibre (fibre density), predominant sources of unsaturated fats, and low-energy density. Compared with other dietary patterns, comparative cohort studies indicate that the degree of cardiovascular injury protection is more closely associated with the structural similarities among these dietary patterns than with each diet individually. (72)

This encourages the transition from culturally constructed definitions of dietary patterns to a categorisation based on their functional aspects (i.e., the ways they achieve specific biological outcomes), thereby clarifying for clinicians and public health practitioners the types of dietary patterns they recommend to patients and the general public.

5.7 Implications for causality assessment

The available evidence meets several standards for establishing a cause-and-effect connection with food (or food components) and health. It has shown the same associations across different populations, study designs, biological models of action, dosage-response relationships and timing to exposure through diet.

Observational research cannot eliminate all residual confounding factors, but the concordance of results obtained from biomarker data through randomised studies enhances the ability to ascertain causation. (73)

5.8 Remaining uncertainties and knowledge gaps

Although much evidence points towards successful modification of intermediate cardiovascular risk factors, the available randomized controlled trials have not yet provided a clear view of long-term cardiovascular outcomes.

Plant-based food habits have been shown by a large amount of available data to help decrease the risk for heart disease as measured by typical risk factors associated with getting heart disease (i.e., cholesterol

levels, blood pressure, body weight, and blood sugar). On the other hand, while there have been some randomised studies on people putting these food trends into practice for a short period of time (less than one year) and observing the change over time in interim measures associated with heart disease (above), there have been very few randomised trials looking at endpoints and hard outcomes (i.e., heart attack, stroke, heart failure, death from heart disease) for people following a prolonged plant-based dietary pattern. Most of the available randomised studies are typically of a shorter duration, with most not assessing the impact of plant-based diets on the incidence of cardiovascular disease but instead using interim measures (biomarkers) to measure biological changes associated with plant-based dietary patterns.

In addition, studies have shown substantial inter-individual variability among individual responders to plant-based dietary interventions (i.e., amount of weight lost, levels of cholesterol and blood sugar before and after changes in dietary practice). The variability seen in these studies may be due to genetic predispositions, the person's metabolic status at the time of the intervention, and/or the specific type of bacteria present in the person's digestive tract. These genetic, metabolic, and microbiome modifiers of dietary response remain poorly understood; therefore, this is an important area of future research. Recent studies suggest that baseline insulin sensitivity, microbiome composition and lipid phenotype may be important predictors of the response to primarily plant-based nutritional interventions. (15)

There are also still some uncertainties to be considered with respect to the sustainability, compliance, and generalisation of plant-based diets across a range of populations when evaluating the long-term maintenance of a plant-based diet, which can be affected by several factors. These may include but are not limited to cultural food preferences, socio-economic status (SES), access to food resources, and individual behavioural determinants. Additionally, while a well-planned plant-based diet is generally considered adequate in nutrition, the potential for inadequate or insufficient amounts of specific nutrients such as vitamin B12, iron, omega-3 fatty acids, and iodine (all of which are found in animal food) is a concern and has been raised; however, they are primarily discussed in terms of these issues being related to dietary adequacy/long-term adherence to plant-based diets. These issues are beyond the main scope of this paper which will only discuss plant-based diets and cardiovascular risk factors.

A better understanding of the mentioned genomic, metabolic, and microbiome-based modifications will contribute to improving dietary recommendations.

5.9 Translation to clinical practice

From a medical standpoint, plant-based nutrition can be classified into two categories of convergence: width and specificity. Unlike pharmacological agents, which target a specific biological pathway, a patient following a plant-based diet will experience simultaneous effects on lipid metabolism, glycaemic control, vascular health, and systemic inflammation. Such a broad-spectrum profile is particularly valuable in patients who present with cardiometabolic clustering or metabolic syndrome, in whom pharmacotherapy with a single agent produces only partial reduction in the patient’s risk factors.

Multiple randomized controlled trials in patients with dyslipidaemia and type 2 diabetes have shown that implementation of structured plant-based dietary programs can lead to significant reduction of LDL cholesterol and HbA1C, typically within a few weeks. (74) The findings are consistent across a wide variety of baseline risk profiles; accordingly, plant-based dietary patterns may be used for both primary and secondary prevention of cardiometabolic diseases. Intensive lifestyle intervention trials that included components of plant-based dietary patterns reported significant reductions in the use of antihypertensive medications and glucose-lowering medications in comparison with patients receiving standard care. Consequently, the use of plant-based diets may even offer opportunity for de-prescribing medications for

carefully selected patients. (51) Implications extend beyond traditional cardiovascular risk reduction and include improved medication adherence, fewer adverse effects from medications, and increased long-term patient engagement in their health care. (42)

5.10 Comparative effectiveness relative to pharmacologic strategies

Compared to drug interventions, using plant-based diets provides a higher estimated effect size. It has been shown in controlled trials, that reducing LDL cholesterol with a plant-based diet high in adherence is equal to the reduction caused by taking a first-line statin, especially in people who have a high baseline LDL. (54)

It's critical to note that dietary and drug treatment do not exclude one another. Some studies demonstrate that there is an additive effect when following a plant-based diet and taking lipid-lowering or anti-hypertensive drugs, and that patients who adhere to a plant-based diet can reduce their absolute risk factor by using a smaller amount of medication, which may indicate that they are more responsive to the drugs or experience less counter-regulatory metabolic stress. (75)

The relationship between dietary and drug treatments can have a significant impact on the practice of preventive care. Instead of positioning diet as an alternative to drug treatment, there is a strong argument for viewing diet as a means to modify risk and increase the effectiveness of the drug treatment by eliminating the residual cardiometabolic risk not being addressed by a single mechanism drug.

Table 6: Comparing dietary and drug treatments

Intervention	Primary target	Typical effect size	Advantages	Limitations
Plant-based diet (high adherence)	LDL-C, insulin resistance	LDL ↓ 20–30%	Multi-pathway benefit, low cost	Adherence variability
Statins (low–moderate dose)	LDL-C	LDL ↓ 30–50%	High efficacy	Side effects, lifelong use
Antihypertensives	Blood pressure	SBP ↓ 5–15 mmHg	Rapid effect	Single-risk-factor focus
Lifestyle intervention	Multiple	Moderate across domains	Holistic	Requires behaviour change

5.11 Implications for preventive care frameworks

At the population level, primordial and primary preventive health strategies correspond to the health-promoting elements of plant-rich dietary patterns. Modelling research utilising longitudinal data from large cohort studies indicates that adopting plant-centric diets earlier in life yields a greater lifetime reduction in cardiovascular disease risk than late-stage pharmacological treatments alone. Earlier implementation of diet-guided changes results in cumulative alterations to the physiological mechanisms underlying risk exposure (e.g., LDL cholesterol and insulin resistance). (76)

Not only do plant-based dietary approaches reduce disease incidence, but they also directly affect the trajectory of risk factors over the entire life course. Prospective data from studies that assessed the impacts of healthy plant-based diets suggest that individuals who consume these diets will have less

dramatic increases in blood pressure, bodyweight, and glycaemic loads as they age, therefore producing a flatter cardiometabolic risk curve over the course of their lives. (77) This trajectory effect is not achievable solely through pharmacological intervention started at a later stage of the disease process.

Dietary prevention has considerable capacity for scalability, compared to pharmacological prevention within healthcare systems; consequently, a shift towards healthier population-level dietary patterns could potentially decrease the total burden associated with cardiovascular diseases by a much larger degree than would result from marginal improvements in the amount of medications available, especially in resource-deprived settings. (3)

5.12 Feasibility, equity, and implementation considerations

Many authors cite concerns over the feasibility, affordability, and cultural acceptability of plant-based diets as obstacles to their widespread adoption. However, data show that this assumption is incorrect. Several studies have demonstrated that consuming diets composed primarily of legumes, whole grains, fruits, and vegetables, rather than animal-based foods, can yield similar or lower household food expenditures, accounting for caloric and nutrient density. (78)

Additionally, studies have found that plant-centric eating patterns can be adapted to local food systems worldwide while retaining their cardiometabolic benefits. Notably, the association between reduced cardiovascular risk and adherence to a plant-based diet was observed across all income classes, suggesting that the primary determinant of diet-related harm or benefit is not socioeconomic status but rather dietary quality. (79)

Moreover, research in implementation science indicates that gradual dietary change (i.e., reducing intake of higher-risk foods) produces measurable improvements in cardiovascular health, regardless of whether an individual fully adheres to an exceptionally restrictive diet. (54) This has implications for counselling strategies, reinforcing the idea that dietary approaches should be flexible and reflect individual patients' needs rather than imposing rigid guidelines based on societal expectations regarding nutrition.

5.13 Public health policy implications

Based on evidence collected over time, plant-based nutrition policies should be incorporated into national recommendations for preventing cardiovascular disease. Studies of various policy-based dietary interventions, including fruit and vegetable subsidies and institutionalized plant-based meal programs, show that these interventions are effective at the community level in reducing cardiometabolic risk. (80)

In addition, advocating for a plant-based diet promotes cardiovascular health while also achieving environmental sustainability. These dual benefits are essential in identifying common goals for both cardiovascular health and ecological sustainability. While the environment is not the primary focus of this review, the combination of health and sustainability provides policy support for implementing programs promoting plant-based diets. (81)

5.14 Lacking hard outcome measures

This review is primarily concerned with intermediate cardiovascular risk factors, as opposed to hard clinical outcomes. It is hard to establish a direct causal relationship between plant-based dietary patterns and long-term cardiovascular outcomes (myocardial infarction, stroke, cardiovascular mortality, or overall mortality) for several methodological reasons. Randomized controlled trials examining dietary interventions are typically limited in both their duration and sample size, which makes them insufficiently powered to detect rare clinical events. As a result, most trials are focused on measuring changes over the short to medium term in established risk factors, such as lipid levels, blood pressure, glycaemic control, and body weight—rather than clinical endpoints.

In contrast, long-term cohort studies are capable of assessing cardiovascular morbidity or mortality but depend upon observational designs and self-reports of dietary intake, thus introducing measurement error and residual confounding. Additionally, the nature of dietary patterns is such that they change over time, complicating an accurate measurement of long-term exposure. For these reasons, the majority of the existing evidence attributing plant-based diets with a decreased incidence of cardiovascular disease and/or prevention of cardiovascular disease is based on improvement in well-established intermediate risk factors (that have established causative relationships to cardiovascular outcomes) and not on direct evidence derived from clinical events.

6. Strengths and Limitations

A balanced evaluation of the present systematic review requires consideration of both its methodological strengths and its inherent constraints.

6.1 Strengths

One of the strengths of this review is that it synthesizes mechanistic, randomized, and observational studies within a single analytic framework. This review synthesizes evidence across all three study designs to ensure that both causal inference from RCTs and the long-term relevance of prospective cohort studies are represented. Because of this, the possibility that any observed association is an artefact of design-specific biases is reduced.

Another strong aspect of this review is that it provides an explicit comparison of the quality of plant-based dietary patterns rather than relying solely on the traditional categorical definitions. Empirical evidence indicates that the effects on cardiometabolic health of whole-foods plant-based diets differ considerably from those of refined plant-based diets; therefore, ignoring this distinction has led to many inconsistencies in the existing literature. By establishing a stratified body of evidence based on the food's component composition, biological coherence and interpretability are enhanced.

In addition, the review benefits from a mechanism-first interpretive approach, which enables evaluation of the clinical outcomes observed in the context of well-established mechanisms of lipid metabolism, insulin resistance, vascular biology, and inflammation. This approach increases confidence in establishing causal relationships between these areas of study by linking epidemiological associations to biologically validated mechanisms.

6.2 Limitations

First, misclassification of dietary exposure remains an unavoidable component of observational research. Although self-reported intake can be assessed using validated instruments, it suffers from the same limitations as all surveys in accurately recalling and classifying food processing and bio actives. Although this misclassification usually biases the relationship toward zero, it reduces the precision of effect-size estimation.

Second, because most randomised controlled trials are rather short-term, direct cardiovascular endpoints must be compared with reference to additional research on genetic and pharmacologic interventions using intermediate risk factors.

Third, residual confounding factors cannot be fully controlled in cohort studies. Analyses using cohorts of health-conscious individuals and studies validated by randomised controlled trials mitigate some of this risk; however, unmeasured psychosocial and behavioural factors may influence the association.

Fourth, considerable variability among studies in reporting outcomes hinders quantitative synthesis. There is variability across many of the risk factors used in the past, the statistical analyses, and the threshold

values selected for reporting. Therefore, many researchers believe that a mechanism-based narrative synthesis offers an alternative approach. However, a narrative synthesis lacks the statistical power of pooled estimates from the literature. Finally, the review is constrained by the current state of the literature, including the underrepresentation of low- and middle-income countries in long-term cardiovascular outcome studies and limited data on older adults with multimorbidity.

Fifth, when looking for correlations between diet interventions and cardiovascular risk factors, the studies included in this review did not consider all other real life possible confounders, like compliance and adherence to a diet of patients beyond study settings and follow up.

Finally, this review focused solely on intermediate risk factors that can be influenced by alternative diets, and thus excluded risk factors like smoking, body exercise, genetic predisposition among others. Those were beyond the scope of this review.

7. Conclusion

All of the studies included in this review, have shown consistent significant reduction of different intermediate cardiovascular risk factors in individuals following a plant-based diet. These risk factors include lipid profile levels, glycaemic control and insulin resistance, blood pressure, body weight and inflammatory markers.

The evidence suggests that plant-based diets do not only influence individual risk factors, but establish a combined multi-level and multi-pathway effect on multiple cardiovascular risk factors and overall cardiometabolic health.

Cohort and longitudinal studies show a decreased incidence of cardiovascular and metabolic disease in individuals following a plant-based diet, as well as reduced incidence of overweight individuals and obesity.

The similarities between plant-based diets and other comparable diets (mainly those focusing on whole foods, fibre, unsaturated fats and low-density energy) suggest that it is not solely the absence of animal-derived foods, but rather these specific properties of plant-based diets that support the beneficial outcomes.

Plant-based diets can yield similar results when compared to certain pharmacological treatments regarding singular risk reduction. But at the same time, plant-based diets also address an individual's residual cardiometabolic risk by reducing other risk factors, as opposed to pharmacological treatments.

To integrate the evidence that there is a relationship between plant-based dietary patterns and reductions in cardiovascular risk through the lens of plausibility, comparative effectiveness, scalability, and real-world feasibility, all must be evaluated together. Based on evaluations across these four dimensions, plant-based diets should not only be viewed as a lifestyle approach but could be a possible foundation of preventive or therapeutic interventions.

More research is needed on the long-term effects of plant-based diets, and their relation to hard outcome measures such as disease and mortality.

8. References

1. World Health Organization. Cardiovascular diseases (CVDs) [Internet]. Geneva: WHO; 2023 [cited 2026 Mar 8]. Available from: https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)
2. Libby P. Inflammation in atherosclerosis. Nature. 2002;420(6917):868–874.
3. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (INTERHEART study): case-control study. Lancet. 2004;364(9438):937–952.
4. Mozaffarian D. Dietary and policy priorities for cardiovascular disease, diabetes, and obesity: a comprehensive review. Circulation. 2016;133(2):187–225.
5. Hu FB. Dietary pattern analysis: a new direction in nutritional epidemiology. Curr Opin Lipidol. 2002;13(1):3–9.
6. Willett WC, Stampfer MJ. Current evidence on healthy eating. Annu Rev Public Health. 2013;34:77–95.
7. Jacobs DR Jr, Steffen LM. Nutrients, foods, and dietary patterns as exposures in research: a framework for food synergy. Am J Clin Nutr. 2003;78(3 Suppl):508S–513S.
8. Craig WJ. Health effects of vegan diets. Am J Clin Nutr. 2009;89(5):1627S–1633S.
9. Satija A, Hu FB. Plant-based diets and cardiovascular health. Trends Cardiovasc Med. 2018;28(7):437–441.
10. Brown L, Rosner B, Willett WC, Sacks FM. Cholesterol-lowering effects of dietary fiber: a meta-analysis. Am J Clin Nutr. 1999;69(1):30–42.
11. Demonty I, Ras RT, van der Knaap HC, Duchateau GS, Meijer L, Zock PL, et al. Continuous dose-response relationship of LDL-cholesterol-lowering effect of phytosterol intake. J Nutr. 2009;139(2):271–284.
12. Mensink RP, Zock PL, Kester AD, Katan MB. Effects of dietary fatty acids and carbohydrates on serum lipids: a meta-analysis. Am J Clin Nutr. 2003;77(5):1146–1155.
13. Vafeiadou K, Weech M, Altowaijri H, Todd S, Yaqoob P, Jackson KG, et al. Replacement of saturated with unsaturated fats and vascular function: DIVAS study. Am J Clin Nutr. 2015;102(1):40–48.
14. Haghighatdoost F, Bellissimo N, Totosy de Zepetnek JO, Rouhani MH. Vegetarian diet and inflammatory biomarkers: systematic review. Public Health Nutr. 2017;20(15):2713–2721.
15. Barnard ND, Levin SM, Yokoyama Y. Body weight changes in vegetarian diets: meta-analysis. J Acad Nutr Diet. 2015;115(6):954–969.
16. Semnani-Azad Z, Khan TA, Chiavaroli L, Chen V, Bhatt HA, Chen A, et al. Intermittent fasting and cardiometabolic risk factors: systematic review. BMJ. 2025;389:e082007.
17. Tang WH, Kitai T, Hazen SL. Gut microbiota in cardiovascular health and disease. Circ Res. 2017;120(7):1183–1196.
18. Marques FZ, Nelson E, Chu PY, Horlock D, Fiedler A, Ziemann M, et al. High-fiber diet and hypertension prevention. Circulation. 2017;135(10):964–977.

19. Kastorini CM, Milionis HJ, Esposito K, Giugliano D, Goudevenos JA, Panagiotakos DB. Mediterranean diet and metabolic syndrome: meta-analysis. J Am Coll Cardiol. 2011;57(11):1299–1313.

20. Fraser GE. Vegetarian diets and chronic disease. Am J Clin Nutr. 2009;89(5):1607S–1612S.

21. Dinu M, Abbate R, Gensini GF, Casini A, Sofi F. Vegetarian diets and health outcomes: systematic review. Crit Rev Food Sci Nutr. 2017;57(17):3640–3649.

22. Appleby PN, Key TJ. Long-term health of vegetarians and vegans. Proc Nutr Soc. 2016;75(3):287–293.

23. Satija A, Bhupathiraju SN, Spiegelman D, et al. Plant-based diets and coronary heart disease. J Am Coll Cardiol. 2017;70(4):411–422.

24. Estruch R, Ros E, Salas-Salvadó J, Covas MI, Corella D, Arós F, et al. Mediterranean diet and cardiovascular prevention (PREDIMED). N Engl J Med. 2018;378(25):e34.

25. Petersen KF, Dufour S, Befroy D, Garcia R, Shulman GI. Mitochondrial activity and insulin resistance. N Engl J Med. 2004;350(7):664–671.

26. Canfora EE, Jocken JW, Blaak EE. Short-chain fatty acids and metabolism. Nat Rev Endocrinol. 2015;11(10):577–591.

27. Förstermann U, Sessa WC. Nitric oxide synthases. Eur Heart J. 2012;33:829–837.

28. Tangney CC, Rasmussen HE. Polyphenols and cardiovascular disease. Curr Atheroscler Rep. 2013;15(5):324.

29. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. PRISMA 2020 statement. BMJ. 2021;372:n71.

30. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan systematic review tool. Syst Rev. 2016;5(1):210.

31. Rayyan. Rayyan – Intelligent Systematic Review [Internet]. 2022. [cited 2026 Apr 26] Available from: https://www.rayyan.ai/

32. Jenkins DJ, Jones PJ, Lamarche B, et al. Dietary portfolio trial. JAMA. 2011;306(8):831–839.

33. Jenkins DJ, Kendall CW, Marchie A, et al. Portfolio diet vs statin. JAMA. 2003;290(4):502–510.

34. Barnard ND, Cohen J, Jenkins DJ, et al. Vegan diet and diabetes. Diabetes Care. 2006;29(8):1777–1783.

35. Turner-McGrievy GM, Barnard ND, Scialli AR. Vegan vs low-fat diet. Obesity. 2007;15(9):2276–2281.

36. Wright N, Wilson L, Smith M, Duncan B, McHugh P. BROAD study. Nutr Diabetes. 2017;7(3):e256.

37. Mishra S, Xu J, Agarwal U, Gonzales J, Levin S, Barnard ND. GEICO study. Eur J Clin Nutr. 2013;67(7):718–724.

38. Kahleova H, Petersen KF, Shulman GI, et al. Vegan diet RCT. JAMA Netw Open. 2020;3(11):e2025454.

39. Hall KD, Guo J, Courville AB, et al. Plant vs ketogenic diet. Nat Med. 2021;27(2):344–353.

40. Bruns A, Nebl J, Jonas W, Hahn A, Schuchardt JP. Flexitarians vs vegans. BMC Nutr. 2023;9(1):140.

41. Esselstyn CB Jr, Gendy G, Doyle J, Golubic M, Roizen MF. Reversal of CAD. J Fam Pract. 2014;63(7):356–364.

42. Ornish D, Brown SE, Scherwitz LW, et al. Lifestyle Heart Trial. Lancet. 1990;336:129–133.

43. Kim H, Lee K, Rebholz CM, Kim J. Plant diets and metabolic syndrome. PLoS Med. 2020;17(11):e1003371.

44. Baden MY, Liu G, Satija A, et al. Plant diet quality and mortality. Circulation. 2019;140(12):979–991.

45. Huo Y, Cao S, Liu J, et al. Plant diet and metabolic syndrome. Nutrients. 2023;15(6):1341.

46. Orlich MJ, Singh PN, Sabaté J, et al. Vegetarian diets and mortality. JAMA Intern Med. 2013;173(13):1230–1238.

47. Chiu THT, Pan WH, Lin MN, Lin CL. Vegetarian diet and diabetes risk. Nutr Diabetes. 2018;8(1):12.

48. Tonstad S, Stewart K, Oda K, Batech M, Herring RP, Fraser GE. Vegetarian diets and diabetes incidence. Nutr Metab Cardiovasc Dis. 2013;23(4):292–299.

49. Wang XJ, Voortman T, Bos D, et al. Association between healthy plant-based diet-lifestyle (hPDI-Lifestyle) score and incidence of coronary heart disease, and effect modification by genetic predisposition: a prospective analysis in a population-based cohort. *Lancet Reg Health Eur*. 2026;64:101619.

50. Jenkins DJ, Kendall CW, Faulkner D, et al. A dietary portfolio approach to cholesterol reduction: combined effects of plant sterols, vegetable proteins, and viscous fibers in hypercholesterolemia. *Metabolism*. 2002;51(12):1596-1604.

51. Chiavaroli L, Mirrahimi A, Sievenpiper JL, et al. Portfolio diet and CVD. Prog Cardiovasc Dis. 2018;61(1):43–53.

52. Yokoyama Y, Nishimura K, Barnard ND, et al. Vegetarian diets and blood pressure. JAMA Intern Med. 2014;174:577–587.

53. Chan AW, Hróbjartsson A, Haahr MT, Gøtzsche PC, Altman DG. Empirical evidence for selective reporting of outcomes in randomized trials: comparison of protocols to published articles. JAMA. 2004;291(20):2457-2465.

54. Sacks FM, Lichtenstein AH, Wu JHY, et al. Dietary fats and cardiovascular disease. Circulation. 2017;136:e1–e23.

55. Kim H, Caulfield LE, Rebholz CM. Plant-based diets and dyslipidemia. Nutrients. 2018;10:1334.

56. Siervo M, Lara J, Chowdhury S, Ashor A, Oggioni C, Mathers JC. DASH diet and cardiovascular risk. Br J Nutr. 2015;113(1):1–15.

57. Kahleova H, Mari A, Nofrate V, Matoulek M, Kazdova L, Hill M, et al. β-cell function and diet-induced weight loss. J Diabetes Complications. 2012;26(5):442–449.

58. Córdova R, Kim J, Thompson AS, et al. Plant-based dietary patterns and age-specific risk of multimorbidity of cancer and cardiometabolic diseases: a prospective analysis. Lancet Healthy Longev. 2025;6(8):100742.

59. Newby PK, Tucker KL, Wolk A. Obesity among vegetarians. Int J Obes. 2005;29:292–298.

60. Chiu THT, Liu CH, Chang CC, et al. Vegetarian diet and gout risk. Clin Nutr. 2020;39(3):837–844.

61. Chen Z, Zuurmond MG, van der Schaft N, Nano J, Wijnhoven HAH, Ikram MA, et al. Plant diets and diabetes risk. Eur J Epidemiol. 2018;33(9):883–893.

62. Ference BA, Ginsberg HN, Graham I, et al. Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel. *Eur Heart J*. 2017;38(32):2459-2472.

63. Appel LJ, Moore TJ, Obarzanek E, et al. Dietary patterns and blood pressure. N Engl J Med. 1997;336:1117–1124.

64. O'Keefe JH, Gheewala NM, O'Keefe JO. Dietary strategies for improving post-prandial glucose, lipids, inflammation, and cardiovascular health. J Am Coll Cardiol. 2008;51(3):249-255.

65. 88 Sala-Vila A, Romero-Mamani ES, Gilabert R, et al. Changes in ultrasound-assessed carotid intima-media thickness and plaque with a Mediterranean diet: a substudy of the PREDIMED trial. Arterioscler Thromb Vasc Biol. 2014;34(2):439-445.

66. Nordestgaard BG, Nicholls SJ, Langsted A, Ray KK, Tybjærg-Hansen A. Lipid-lowering therapies. Eur Heart J. 2020;41(13):1189–1197.

67. Silverman MG, Ference BA, Im K, Wiviott SD, Giugliano RP, Grundy SM, et al. LDL-C lowering and risk reduction. JAMA. 2016;316(12):1289–1297.

68. Reynolds A, Mann J, Cummings J, Winter N, Mete E, Te Morenga L. Carbohydrates and health. Lancet. 2019;393(10170):434–445.

69. Petersen KF, Shulman GI. Mechanisms of insulin resistance. Am J Med. 2006;119:S10–S16.

70. De Vadder F, Kovatcheva-Datchary P, Zitoun C, et al. Microbiota-produced acetate. Nat Med. 2014;20:159–165.

71. Martínez-González MA, Gea A, Ruiz-Canela M. Mediterranean diet and cardiovascular health. Circ Res. 2019;124:779–798.

72. Hill AB. Environment and disease: association or causation? Proc R Soc Med. 1965;58:295–300.

73. Zeevi D, Korem T, Zmora N, et al. Personalized nutrition. Cell. 2015;163:1079–1094.

74. Huang T, Yang B, Zheng J, Li G, Wahlqvist ML, Li D. CVD mortality in vegetarians. Ann Nutr Metab. 2012;60(4):233–240.

75. Lloyd-Jones DM, Leip EP, Larson MG, et al. Lifetime risk for CVD. Circulation. 2006;113:791–798.

76. Baden MY, Liu G, Satija A, et al. Plant diet quality and CVD risk. J Am Coll Cardiol. 2019;73:2399–2407.

77. Rao M, Afshin A, Singh G, Mozaffarian D. Cost of healthy foods. BMJ Open. 2013;3:e004277.

78. Kim H, Hu EA, Rebholz CM. Plant-based diets and socioeconomic status. Am J Prev Med. 2020;58:106–115.

79. Mozaffarian D, Afshin A, Benowitz NL, et al. Population diet strategies. Circulation. 2018;138:231–244.

80. Ford I, Norrie J. Pragmatic trials. N Engl J Med. 2016;375:454–463.

81. Aleksandrowicz L, Green R, Joy EJ, Smith P, Haines A. Dietary change and sustainability. PLoS One. 2016;11(11):e0165797.

82. Kahleova H, Tura A, Hill M, Holubkov R, Barnard ND. A Plant-Based Dietary Intervention Improves Beta-Cell Function and Insulin Resistance in Overweight Adults: A 16-Week Randomized Clinical Trial. *Nutrients*. 2018;10(2):189.