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SYSTEMATIC REVIEWS AND META-ANALYSES

# A comprehensive review of healthy effects of vegetarian diets

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Type 2 diabetes;
Metabolic syndrome

**Abstract** *Aims:* A comprehensive review comparing the effect of vegetarian (V) and non-vegetarian (NV) diets on the major cardiometabolic diseases' outcomes was performed.
*Data synthesis:* We performed literature research (up to December 31, 2022) of the evidence separately for vascular disease (VD), obesity (OB), dyslipidemia (Dysl), hypertension (HPT), type 2 diabetes (T2D), metabolic syndrome (MetS), analyzing only cohort studies and randomized controlled studies (RCTs) and comparing the effect of V and NV diets. Cohort studies showed advantages of V diets compared to NV diets on incidence and/or mortality risk for ischemic heart disease, overweight and OB risk. Most cohort studies showed V had lower risk of HPT and lower blood pressure (BP) than NV and V diets had positive effects on T2D risk or plasma parameters. The few cohort studies on the risk of MetS reported mixed results. In RCTs, V diets, mainly low-fat-vegan ones, led to greater weight loss and improved glycemic control than NV diets and in the only one RCT a partial regression of coronary atherosclerosis. In most RCTs, V diets significantly reduced LDL-C levels (but also decreased HDL-C levels) and BP.
*Conclusions:* In this comprehensive review of the association between V diets and cardiometabolic outcomes, we found that following this type of diet may help to prevent most of these diseases. However, the non-uniformity of the studies, due to ethnic, cultural, and methodological differences, does not allow for generalizing the present results and drawing definitive conclusions. Further, well-designed studies are warranted to confirm the consistency of our conclusions.


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## 1. Introduction

Diets partially or totally deprived of animal food have long been considered as a health threat, owing to the potential deficiency of some essential nutrients. On the contrary, literature emerging from the last decades supports quite the opposite: plant-based diets are a healthier option than meat-based diets. As a matter of fact, the nutrient intake of vegetarian (V) diets is adequate [1], and the health benefits they provide largely overcome potential health problems related to nutritional deficiencies [2]. The real problem is that the term "vegetarian diets" is an umbrella that includes many different dietary patterns: the western vegetarian pattern, which can be categorized into vegan (VEG), lacto-ovo-vegetarian (LOV), lacto-vegetarian (LV), ovo-vegetarian (OV), semi-vegetarian (SV), low-fat (LF)-VEG or LF-LOV; some plant-based restrictive patterns, such as the fruitarian and the raw-food diet; other ethnical dietary patterns such as the Asian or Buddhist diets; other type of diets where animal food are absent or limited owing to socioeconomical reasons, as in developing countries. For these reasons, literature on health effects of V diets can give contrasting results, because of the incorrect categorization of the pattern or to the often very different socioeconomical status of the examined population. A V diet followed by people living in developed countries has more chances to be well-planned in respect to the V diet adopted in a developing country, where economic or cultural limits can affect its adequacy.

For these reasons, we performed a careful selection of the studies to be included in this review, excluding those where the dietary pattern was not adequately described or those where the adopted diet didn't fit with the current classification of "vegetarian", as highlighted also in a recent umbrella review [3]. Therefore, the aim of the present study was to perform a comprehensive review of the effect of V diets on the health outcomes including risk factors for the major non-communicable diseases.

## 2. Methods

Potentially relevant articles were identified through a computerized search in PubMed and Embase up to December 31, 2022. Additional searches were conducted by scanning the references of the thus identified articles, reviews and meta-analyses. The search terms used were nutritionally-based ("plant-based diet*", "lacto-vegetarian∗", "ovo-lacto vegetarian∗", "lacto-ovo vegetarian∗", "vegan∗", "macrobiotic", "veganism", "fruitarian", "Buddhist vegetarianism", "Jain vegetarianism", "Seventh-day Adventists", and "vegetarian∗"), used in combination with words relating to the topic of the different paragraphs.

- **vascular disease (VD)**: "cardiometabolic disorders", "atherosclerosis", "cardiovascular", "cerebrovascular", "cardiac", "coronary artery disease", "heart disease, "stroke", and "atherogen∗".
- **obesity (OB):** "obese∗", "overweight", "ponderal", "weight", "body mass index", "waist circumference", "skinfold∗", "fat mass", "adipose", "sarcopenic" and "body fat".
- **dyslipidemia (Dysl):** "dyslipidemia**"** or "cholesterol" or "hypercholesterolemia∗" or "hypertrygliceridemia∗" or "LDL" or "HDL" or "triglyceride∗" or "visceral fat" or "lipoprotein∗" or "apoprotein C-III" or "lipid abnormalities" or "fatty liver" or "steatosis" or "lipid metabolism" or "hepatic lipidosis" or "steatohepatitis" or "lipid profile".
- **hypertension (HPT):** "hypertension","eclampsia"," pressure", "vascular resistance".
- **type 2 diabetes (T2D)**: "diabet∗", "insulin∗", "hyperglycemia∗", "glycemic", "glucose", "glycation", "glycosylation", "glucosidase", "pancrea∗", "beta cell", "Langerhans".
- **metabolic syndrome (MetS)**: "metabolic syndrome", "metabolic disease", "metabolic disorders", "syndrome X", "MetS", "dysmetabolic syndrome", "visceral adiposity syndrome", "visceral obesity syndrome", and "metabolic-vascular syndrome".

The search was limited to human studies. Initially, articles were selected for the present study only by title and abstract. After this preliminary selection, the full-texts were read independently by two reviewers for each outcome. Any incongruity about the inclusion of a study was analyzed and resolved through discussion among all the authors, and a final decision was made about inclusion in the study.

Eligible studies included randomized controlled trials (RCTs) and observational studies (i.e., cohort), comparing the effects of a V diet to those of an omnivore (OMN) or non-vegetarian (NV) diet. Exclusion criteria for selected studies were: 1. dietary patterns not adequately described; 2. V diet that didn't fit with the current classification of "vegetarian" (i.e., VEG, LOV, LV, and OV) and 3. RCTs without a control omnivorous or non-vegetarian group.

Our search, performed separately for each disease, retrieved the following citations.

- **VD:** 918 unique citations (905 identified through database search, and 13 by scanning references of the identified articles). After review of title and abstract, we identified 81 citations as potentially relevant for analysis. After full-text screening, 32 articles were excluded: 10 were reviews or meta-analyses, 10 did not include people adhering to a V diet, 9 reported no data on VD, 2 reported no NV control group, and 1 reported data from the preliminary stage of an intervention trial. Of the included 49 articles, 48 were cohort studies and 1 a RCT. The search process is shown in Fig. 1A.
- **OB**: 1707 unique citations (1645 identified through database search, and 62 by scanning references of the identified articles). After reviewing title and abstract, we identified 155 citations as potentially relevant for the analysis. After full-text screening, 122 articles were

excluded: 64 were cross-sectional, 6 were reviews or meta-analyses, 11 did not include real vegetarians, 36 reported no data on weight status, 2 reported data already published and 3 were mechanistic studies. Of the 31 included, 2 were longitudinal studies, and 31 were RCTs. The search process is shown in Fig. 2A.

- **Dysl:** 740 unique citations (692 identified through database search, and 48 by scanning references of the selected articles) were identified. After reviewing title and abstract, we identified 151 citations as potentially relevant for analysis. After full-text screening, 120 articles were excluded: of these 13 were reviews, 11 meta-analyses, 84 were cross-sectional studies, and 12 reported no data on dyslipidemia or reported no NV control group. Of the 31 included articles, one was a cohort study and 30 were RCTs. The search process is shown in Fig. 3A.
- **HPT:** 280 unique citations (221 identified through database search, and 59 by scanning references of the selected articles). After reviewing title and abstract, we identified 172 citations as potentially relevant for analysis. After full-text screening, 160 articles were excluded: 34 were reviews or meta-analyses, 75 regarded cross-sectional studies, 42 reported no data on hypertension (n = 34) or reported no NV control group (n = 8), 6 did not include people adhering to a V diet and 3 were not in English. Of the included 13 articles, 2 articles concerned 1 cohort study and 13 articles concerned 11 RCTs (3 articles concerned the same intervention study). The search strategy is shown in Fig. 4A.
- **T2D:** 675 unique citations (621 identified through database search, and 54 by scanning references of the selected articles). After reviewing title and abstract, we identified 204 citations as potentially relevant for the analysis. After full-text screening, 172 articles were excluded for different reasons (26 were reviews or meta-analyses, 56 were cross-sectional studies, 28 were studies that did not include people adhering to a V diet, 49 studies reported no data on T2D, 8 were studies without NV control group, and 5 were studies that reported data already presented in other more recent studies). Of the included 32 studies, 6 were prospective (cohort) and 26 were RCTs. The search process is shown in Fig. 5A.
- **MetS:** 80 unique citations (77 identified through database searching and 3 by scanning the references of the selected articles). After reviewing title and abstract, 38 citations were identified as potentially relevant for analysis. After full-text screening, 37 articles were excluded: 11 were reviews or meta-analyses, 11 were cross-sectional studies, 6 did not include people following a V diet, 4 reported no data on MetS, 2 reported no NV control group, 2 were conference abstracts, and 1 was not in English. Thus, we only included one cohort study. The search process is shown in Fig. 6A.

Details of the protocol for this review were registered on PROSPERO and can be accessed at https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022342073.

## 3. Results

The through description of the relative results with the corresponding references for each health outcome and risk factors is reported in Appendixes 1–6. In this section, we shortly summarized the results.

**VD** (Appendix 1): a total of 10 cohort studies evaluated the association between V diets and risk of VD; their results were published in 48 manuscripts. In the studies, the various V dietary patterns were grouped together, except for the Adventist Health Study (AHS)-2, which analyzed the different dietary patterns from OMN to VEG. For studies conducted in the '70s–'80s, the Health Food Shoppers Study, the Oxford Vegetarian Study and the German Vegetarian Study in Europe found no significant difference in the mortality risk of V vs NV for circulatory, cerebrovascular, and ischemic heart diseases (IHD). On the contrary, for studies conducted in the USA on the Adventist population, V diets showed a reduction of the mortality of 26% for IHD and 35% for cerebrovascular disease in the Adventist Mortality Study (AMS), and a significantly lower lifetime risk of coronary disease than NV in men, with no difference among women, in the Adventist Health Study (AHS)-1.

In the more recent, ongoing, EPIC-Oxford Study, V vs NV had a reduced IHD risk of 32% and 22% in the two studies performed (with a mean follow-up of 11.6 years and 18.1 years, respectively). In the last, ongoing AHS-2, when compared to NV, if distinguishing between sexes, only VEG men showed a lower risk of IHD and cardiovascular disease (CVD) mortality, whereas a lower risk of CVD mortality was observed for LOV men.

The only one RCT showed a marked effect of a LF-V diet on coronary heart disease outcomes (e.g. stenosis).

Except for the results coming from the EPIC-Oxford cohort, which found a 20% higher rate of total stroke in V vs meat eaters (ME), the analysis from all the other studies we discussed in Appendix 1 found no significant differences or a reduced risk for cerebrovascular disease in V vs NV.

**OB** (Appendix 2): 2 cohort studies and 22 RCTs, of which results were published in 31 manuscripts, evaluated the association between V diets and risk of overweight and OB. The cohort studies found that, compared with NV, V and especially VEG were likely to gain significantly less adiposity.

In 17 of the 22 intervention studies we analyzed, V diets, mainly the LF-VEG type, led to a more significant weight loss compared to NV diets. Five studies found no differences in weight loss or BMI.

**Dysl** (Appendix 3): Only a cohort study evaluated the association between the consumption of V diets with several outcomes in plasma lipids compared with OMN diets. The study showed that V diets had significant beneficial effects on metabolic traits, in particular for TC and LDL-C, but not for HDL-C, which may be partly due to the lower BMI.

In most of the 30 RCTs we analyzed, V diets significantly affected TC level, mainly reducing LDL-C level, but also decreasing HDL-C level, compared to NV diets. Conversely, V diets had no effect on TG, even though in 4 studies a significant reduction was observed.

Only a few studies provided data on the effect of V diets on the ratio of TC (or LDL-C) to HDL-C or HDL-C/LDL-C or TG/HDL-C: data emerging from these few studies are still controversial.

**HPT** (Appendix 4): One cohort, of which the results were published in 2 manuscripts, and 11 RCTs evaluated the association between V diets and HPT.

The only cohort study that examined the incidence of HPT showed that V had a decreased risk of HPT compared with matched NV. RCTs showed that BP is lowered when animal foods are replaced with plant foods in both normotensive and hypertensive participants.

**T2D** (Appendix 5): A total of 32 articles evaluated the association between V diets and risk of T2D.

In the 6 cohort studies that we have included, two found positive effects of VEG or V diets with respect to NV diets. One study evaluated regular meat intake, but not its occasional consumption, as an important risk factor for diabetes relative to zero meat intake. In two studies V diets promoted a lower risk of T2D with respect to OMN diet, in part because of a lower BMI. In one study V diets were not associated with lower risk of T2D.

Among the 26 RCTs, 13 studies found a protective effect of a VEG or LF-VEG diet; 10 studies did not find any difference between the experimental group (EG) (LOV or VEG) and the control group (CG); in 1 study, the groups were too small to perform a statistical analysis; 2 were pilot studies (positive results, but low number of subjects).

**MetS** (Appendix 6): Only one cohort study evaluated the association between V diets and risk of MetS. It found that in comparison with VEG, NV, pescovegetarians (PV), and LOV were less likely to develop MetS.

## 4. Discussion

In the present comprehensive review, we evaluated cohort studies and RCTs that explored the association between V diets and multiple health outcomes, including risk factors for the major chronic diseases, as well as the risk of VD. In several of these studies, a positive effect was reported in following a V diet. The possible mechanisms involved in better health outcomes for V diets are sometimes specific for a disease, but more frequently, they are present in the etiopathogeneses of several diseases.

V diets do not contain meat and its derivatives, which can contribute to the harmful effects related to excess animal protein intake, saturated fats, heme-iron, and the formation of trimethylamine-N-oxide (TMAO), through the different mechanisms to be discussed later [9]. V diets generally have higher content of plant foods, hence of complex carbohydrate, fiber, polyunsaturated fatty acids, and several micronutrients (e.g., magnesium and potassium) and phytochemicals [10,11], whose beneficial synergistic combinations have been associated with a reduced incidence of many pathological conditions such as overweight, T2D, and hypercholesterolemia [12–16]. Diets emphasizing the consumption of whole plant foods have also been associated with lower oxidative stress, inflammation, better endothelial function, and increased insulin sensitivity [17–19].

Hence, it is possible that the beneficial effects of a plant-based diet derive from the increased content of healthy compounds, mainly present in plant foods, and the reduced or absent content of some harmful factors (mentioned above), mainly contained in animal foods. It is also worth emphasizing here that the *mitigation of the -often- coexisting pathological conditions,* can be considered among the most important mechanisms.

### 4.1. Energy

Subjects who followed a LF-VEG diet were found to have a 16% higher postprandial energy expenditure when compared to the CG [12]. An increase in the thermic effect of food may partially explain the favorable weight status and weight management of V, but further research is needed to confirm such results.

### 4.2. Fiber

The high fiber (and water) content of V diets [20] is responsible for lower energy density and earlier satiety, causing a drop in energy intake, than OMN diets [21–23].

Fibers can also help to reduce the intestinal absorption of carbohydrates and fats, improving glycemic and lipid control [24]. Moreover, viscous fiber can increase cholesterol removal by binding bile acids and cholesterol [25], and can interfere with the enterohepatic circulation of estradiol-17β, whose excess has been linked to the genesis of overweight [26]. As a matter of fact, plasma levels of this steroid hormone correlate inversely with fiber intake in V [26].

In addition, dietary fiber intake has been reported to be inversely associated with inflammatory markers such as interleukin-6 and tumor necrosis factor α [27] resulting beneficial for weight, lipid and glycemic control, inflammation modulation, and for VD risk.

### 4.3. Fats

Plant-based diets are typically low in saturated fat and cholesterol [28]. The lower fat content of V diets than OMN diets is responsible for a lower energy density and a drop in energy intake [21,23] and can also help to control blood lipid levels [29]. Monounsaturated fats have been associated with decreased LDL-C and increased resistance to oxidation of LDL-C [30]**.** Plant sterol intake reduces cholesterol absorption by binding cholesterol and bile acids [25]. The lower saturated fatty acid and higher polyunsaturated fatty acid consumption in V, compared with OMN diets, has also been associated with lower BP [21,31,32]. It has been suggested that the relatively low ratio of saturated to unsaturated fat in most V diets can exert a favorable impact on insulin sensitivity and beta-cell lipotoxicity [33].

### 4.4. Proteins and amino acids

Since ingested amino acids can modulate the secretion and balance of insulin and glucagon, plant-based diets can promote greater net glucagon activity than OMN diets [34]. It has been hypothesized that the absence of animal proteins can explain the lighter weight status of VEG in comparison to LOV and OMN, suggesting that the different aminoacidic profile of animal proteins might enhance insulin response to starchy food, and thus promote their conversion into fat [35].

Branched-chain amino acids (BCAAs), higher in OMN diets, could persistently activate the mammalian target of rapamycin complex 1 (mTORC1) signaling pathway, inhibiting glucose transport into insulin-sensitive tissues, including muscle and fat tissues [36]. BCAAs can promote the accumulation of myotoxic metabolites, that can increase β-cell mitochondrial dysfunction and stimulate stress kinase signaling, β-cell apoptosis and insulin resistance due to serine phosphorylation of insulin receptor substrate 1 [36]. Non-essential amino acids, which predominate in plant protein, have a greater impact on glucagon secretion than the essential ones. Acting on hepatocytes, glucagon can promote (and insulin inhibit) cAMP-dependent mechanisms that down-regulate lipogenic enzymes and cholesterol synthesis, while upregulating hepatic LDL receptors and production of the insulin-like growth factor-1 (IGF-I) antagonist [34]. Also, soy protein may slightly decrease cholesterol synthesis and increase LDL-C oxidation resistance through multiple mechanisms, such as triglyceride fatty acid fractional synthetic rate (TGFA-FSR) and free cholesterol fractional synthetic rate (FC-FSR) and by impairing cholesterol absorption or bile acid reabsorption and/or by effecting on gene expression and LDL receptor production [37].

Moreover, the quantity and quality of proteins of a plant-based diet can activate the kinase general control nonderepressible 2 (GCN2) in the liver, which in turn can increase the hepatic expression of fibroblast growth factor 21 (FGF21). This factor is involved in the regulation of energy homeostasis and promotes hepatic lipid oxidation while inhibiting lipogenesis and favorably affecting serum lipids [33,38]. Glucagon, whose secretion is stimulated by plant protein intake, may also increase FGF21 levels, through enhanced transcription of the FGF21 gene in hepatocytes [39]. FGF21 can also act directly on beta-cells to prevent apoptosis [33].

Oral administration of arginine, abundant in plant proteins, has been shown to improve insulin sensitivity in individuals with T2D in randomized, long-term trials [40]. A lower sulfur amino acid intake, which relies on plant-derived protein sources rather than meat-derived foods, has been associated with reduced risk for cardiometabolic diseases in a recent analysis from the Third National Examination and Nutritional Health Survey (NHANES III) Study (1988–1994) [41].

### 4.5. Carbohydrate

The abundance in complex carbohydrates, together with the quantity and quality of proteins of a plant-based diet, has been shown to enhance the production of FGF21 [38]. As seen above, FGF21 levels may also be increased by glucagon. The slower delivery of glucose to the blood, because of an increased consumption of complex carbohydrates and decreased sugars intake, can in turn result in reduced sympathetic stimulation and reduced BP [42] through a blood glucose-insulin, sympathoadrenal mechanism [43].

### 4.6. Iron

Plant iron (non-heme iron) is not as easily absorbed as iron from meat (heme iron), for which heme iron can lead to higher ferritin levels. High iron tissue concentration can contribute to increase glucose production, hepatic glucose output, and to decrease glucose utilization [44]. Iron can promote the formation of the highly reactive oxygen species (ROS), hence increasing cellular oxidative stress, which in turn can inhibit insulin binding. Moreover, ROS can damage pancreatic β-cells, impair insulin-stimulated IRS-1 tyrosine phosphorylation, decrease phosphoinositide 3-kinase, and inhibit the translocation of glucose transporter type 4 (GLUT4) to the plasma membrane. It has been shown that iron stores in pancreatic β-cells can lead to impaired insulin secretion. Moreover, high hepatic iron stores can interfere with hepatic insulin extraction and increased hepatic glucose output [44]. Evidence has emerged from cross-sectional studies of a link between increased serum ferritin concentrations and MetS [45]. In V, significantly lower (although still normal) concentrations of serum ferritin have been reported than in OMNs [46–48]. These factors may be beneficial for glycemic control and MetS risk as well.

### 4.7. Potassium and magnesium

Potassium increases vasodilation and glomerular filtration rate, while decreasing renin level, renal sodium reabsorption, ROS production, and platelet aggregation, thus improving vasodilation and reducing BP levels [49]. A high magnesium content in some plant foods, acting as an enzyme co-factor for insulin, can improve glucose metabolism [24].

### 4.8. Phytochemicals and vitamins

An abundance of epidemiological data has demonstrated the extensive health potential of phytochemicals in humans: a high dietary intake of vegetables, fruits, nuts, legumes, and whole grains, which are foods rich in phytochemicals, has been associated with a reduced risk for CVD (reviewed in Ref. [50]).

Compounds such as phenolics, flavonoids, saponins, sulfides and organosulfur compounds appear to affect cholesterol metabolism through multiple mechanisms, including inhibition of cholesterol biosynthesis and LDL oxidation, and reduction of cholesterol absorption by disrupting the solubility of micelles [28]. It has been hypothesized that soy isoflavones genistein and daidzein may inhibit thrombus formation [28].

A recent meta-analysis described the association of higher dietary intake and blood concentrations of vitamin C, carotenoids, and α-tocopherol (as markers of fruit, vegetable, and nut intake) with a reduced risk of CVD [51].

Moreover, higher circulating heme-oxygenase-1 (HO-1) concentrations (a marker of adaptive response) were found in OMN compared with V, suggesting it may indicate a pro-oxidative status, since heme oxygenase-1 is activated under oxidative stress, a state that was not seen in V [52].

### *4.9. Microbiota*

Trimethylamine (TMA) is synthetized by the gut microbiota from nutrient precursors mainly present in animal foods (choline, phosphatidylcholine, and L-carnitine). TMA is then converted to TMA N-oxide (TMAO) in the liver [53]. It has been shown that this metabolite, which has several harmful effects, is produced to a much lower extent in individuals following a plant-based diet [54–56] that, through various mechanisms, can promote a diverse ecosystem of beneficial microbes [55,56]. TMAO might increase fasting insulin levels and homeostatic model assessment for insulin resistance (HOMA-IR) and produce impaired glucose tolerance [57]. TMAO is also an atherogenic factor [54] and this can explain why in a recent Finnish prospective study higher animal-to-plant protein ratio and higher meat intake were associated with increased mortality, half of which was due to CVD [58]. A modified gut microbiota composition has been hypothesized to be responsible of low grade chronic inflammatory status. Plant-based diets have been associated with an increased cell motility for accessing nutrients, increased catalytic activities for carbohydrates and food proteins, the synthesis and release of bioactive metabolites and proteins, and potentially beneficial impacts on human health. These findings indicate that the microbiota of individuals consuming plant-based diets might have developed strategies to gain physical access to nutrients [59].

Studies have also demonstrated the presence of more protective bacterial species in the gut of VEGs than in NVs, which in turn can lead to a lower inflammation grade [60]. A V diet has been associated with a more favorable inflammatory profile in 2 recent meta-analysis [61,62]; a VEG diet resulted in a significant 32% lower high-sensitivity C-reactive protein when compared with the American Heart Association diet [63]. The reduction of other inflammatory markers associated with plant-based diets has been shown to be central for contrasting the initiation and progression of T2D (reviewed in Ref. [64]).

Moreover, intervention studies found that a V diet can reduce oxidized LDL-C thanks to a more favorable microbiota composition [65].

The above discussed factors may be beneficial for weight, glycemic, lipid and BP level control and for inflammation modulation and for reduction of VD risk. Furthermore, *blood rheology* [66] is improved, because of an enhancement of *vasorelaxation* deriving from the production of nitric oxide in endothelium [67].

The present review has several strengths. First, we included all available data, through a systematic search strategy, from both cohort studies and intervention trials. Second, we considered multiple health outcomes, including risk factors for the major chronic diseases, as well as the risk of VD, to explore the role of V diets on human health, in comparison with NV diets. Third, we choose to limit the analysis to the categories of studies with the highest strength of evidence.

Despite the above strengths have led to a good degree of consistency between the results of the studies reviewed, some limitations need to be highlighted. Although we tried to select only cohort studies that clearly defined the various patterns we discussed, there is a degree of uncertainty related to the recording and categorization of foods consumed, and to the variability of dietary habits across participants belonging to different cultures, which can influence on the composition of the dietary patterns we compared. This is a problem that shares all observational studies on nutrition. We didn't also perform a rigorous evaluation of the studies using the Population, Intervention, Comparator and Outcome (PICO) framework, and didn't use other tools to evaluate the risk of bias and the quality of the studies. In several RCTs, the control group was not well defined as well as the vegetarian one, and most studies included rather small sample size, having a duration shorter than 12 weeks. Moreover, we didn't distinguish between primary and secondary prevention, while a recent Cochrane review [68] found evidence only in primary prevention, although limited to the effect of VEG diets in CV disease.

For this reason, the results provided by our comprehensive review cannot be generalized and should be taken with caution.

## 5. Conclusion

In our comprehensive review on the association between V diets and cardiometabolic health, we found that following this type of diet may help to prevent most of these diseases. Moreover, the most recent "umbrella meta-analysis" by Oussalah [3] confirms a positive impact of V diets on blood lipids and a protective effect on unfavorable outcomes, including VD and T2D. Further studies, analyzing the quality of the diet, found that only a high adherence to a healthful plant-based diet is associated with significant benefits in cardiovascular health [69]. This aspect can be relevant when considering the different results of the studies performed on vegetarians.

Diet is one of the life-style habits whose effect on health should be implemented, in a view of improving public health and reducing medical costs. But, unlike the other life-style factors, diet has also an impact on the health of our planet, and the sustainability of a diet should become a dimension to consider when dietary recommendations are formulated [70]. In this view, a V diet can represent a valuable option to recommend for the health of the planet and of its inhabitants.

## Authors' contributions

CA, SS and LB designed the study; CA, LB, IB, SC, AF, SG, DM, MP, RS, MLS, NP, SS performed the literature review, analyzed the articles; LB, CA, SS wrote the first version and edited the manuscript; NP, SS coordinated and assisted the data collection and the analysis and the discussion of the results, and critically revised the manuscript. All authors read and agreed with the published version of the manuscript.

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## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.numecd.2023.04.005.

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