

8-9-2017

Cardio-Metabolic Benefits of Plant-Based Diets.

Hana Kahleova

Susan Levin

Neal Barnard

George Washington University

Follow this and additional works at: http://hsrc.himmelfarb.gwu.edu/smhs_medicine_facpubs

 Part of the [Cardiology Commons](#), [Dietetics and Clinical Nutrition Commons](#), and the [Nutrition Commons](#)

APA Citation

Kahleova, H., Levin, S., & Barnard, N. (2017). Cardio-Metabolic Benefits of Plant-Based Diets.. *Nutrients*, 9 (8). <http://dx.doi.org/10.3390/nu9080848>

This Journal Article is brought to you for free and open access by the Medicine at Health Sciences Research Commons. It has been accepted for inclusion in Medicine Faculty Publications by an authorized administrator of Health Sciences Research Commons. For more information, please contact hsrc@gwu.edu.

Review

Cardio-Metabolic Benefits of Plant-Based Diets

Hana Kahleova ^{1,*} , Susan Levin ¹ and Neal Barnard ^{1,2}

¹ Physicians Committee for Responsible Medicine, 5100 Wisconsin Ave, N.W. Ste.400, Washington, DC 20016, USA; slevin@pcrm.org (S.L.); nbarnard@pcrm.org (N.B.)

² George Washington University School of Medicine and Health Sciences, Washington, DC 20052, USA

* Correspondence: hKahleova@pcrm.org; Tel.: +1-202-527-7379

Received: 17 June 2017; Accepted: 3 August 2017; Published: 9 August 2017

Abstract: Cardio-metabolic disease, namely ischemic heart disease, stroke, obesity, and type 2 diabetes, represent substantial health and economic burdens. Almost one half of cardio-metabolic deaths in the U.S. might be prevented through proper nutrition. Plant-based (vegetarian and vegan) diets are an effective strategy for improving nutrient intake. At the same time, they are associated with decreased all-cause mortality and decreased risk of obesity, type 2 diabetes, and coronary heart disease. Evidence suggests that plant-based diets may reduce the risk of coronary heart disease events by an estimated 40% and the risk of cerebral vascular disease events by 29%. These diets also reduce the risk of developing metabolic syndrome and type 2 diabetes by about one half. Properly planned vegetarian diets are healthful, effective for weight and glycemic control, and provide metabolic and cardiovascular benefits, including reversing atherosclerosis and decreasing blood lipids and blood pressure. The use of plant-based diets as a means of prevention and treatment of cardio-metabolic disease should be promoted through dietary guidelines and recommendations.

Keywords: cardio-metabolic; diet; nutrition; plant-based; vegan; vegetarian

1. Introduction

Cardio-metabolic disease, namely ischemic heart disease, stroke, obesity, and type 2 diabetes, represent substantial health and economic burdens [1]. Suboptimal nutrition is a leading contributor to chronic disease and premature death in the United States and worldwide [2,3]. According to a recent analysis, certain dietary factors, including high intakes of sodium and processed meat products and low intakes of fruits and vegetables, were associated with 45.5% of cardio-metabolic deaths in the United States [4].

In this review, we present evidence that plant-based diets (for the purposes of this paper, “plant-based” will serve as a substitution for vegetarian and vegan diets only) may be an effective strategy for improving nutrient intake [5]. Plant-based diets are associated with decreased all-cause mortality and decreased risk of obesity, type 2 diabetes, and coronary heart disease [6].

Plant-based diets are characterized by a reduction or elimination of animal product consumption. They are typically based on the consumption of grains, legumes, vegetables, fruits, and nuts. Vegan diets contain only plant foods, while lacto-ovo-vegetarian diets include dairy and/or egg products.

In this narrative review, we summarize the most recent findings on the effect of plant-based diets on cardio-metabolic disease risk. For each section, we searched for papers with the following key words: plant-based, vegetarian and vegan, giving special attention to systematic reviews and meta-analyses, particularly those drawing on randomized clinical trials. Findings from observational studies were included as supporting evidence.

2. Plant-Based Diets and Cardiovascular Disease

Cardiovascular disease is the leading cause of mortality, accounting for one in four deaths worldwide [7]. The high prevalence of heart disease has been linked to lifestyle factors, namely smoking, the adoption of diets high in animal fat and refined foods, and a lack of exercise [8].

A low-fat, vegetarian diet is the only dietary pattern to have shown cessation and reversal of atherosclerotic plaque in clinical trials [9–11], when combined with exercise and stress management [10,12,13]. Vegetarian diets are associated with a reduced risk for cardiovascular disease in general [14,15], including a reduced risk for ischemic heart disease and cerebrovascular disease [16]. Risk factors associated with heart disease are also less frequent among those following vegetarian diets [17,18]. In the European Prospective Investigation into Cancer and Nutrition study, vegetarians had a 32% lower risk of developing coronary heart disease, compared with non-vegetarians [15].

In a systematic review and meta-analysis of 8 prospective studies among Seventh-day Adventists, vegetarian diets were associated with a 40% reduced risk of coronary heart disease events and a 29% reduction in cerebral vascular disease events, compared with non-vegetarians [16]. A recent systematic review and meta-analysis of 86 cross-sectional and 10 cohort prospective studies reported a significant protective effect of a vegetarian diet against the incidence and/or mortality from ischemic heart disease. The observed risk reduction, compared with non-vegetarian dietary patterns, was 25% [19].

In summary, strong and consistent evidence from randomized clinical trials and observational studies supports beneficial effects of plant-based diets for cardiovascular disease.

3. Plant-Based Diets, Body Weight, and Metabolic Syndrome

The prevalence of overweight and obesity is increasing worldwide. The World Health Organization estimates that more than 1.3 billion adults worldwide are overweight, and a further 600 million are obese [20,21]. Overweight and obesity are associated with higher all-cause mortality [22].

Vegetarians typically have lower BMI (body mass index) values, compared with non-vegetarians [23]. BMI values tend to increase with increasing frequency of animal product consumption. In the Adventist Health Study-2, BMIs were lowest among vegans (23.6 kg/m²), higher in lacto-ovo-vegetarians (25.7 kg/m²), and highest in nonvegetarians (28.8 kg/m²) [24–26]. The average individual yearly weight gain is reduced when people limit consumption of animal foods [27]. Vegetarian diets seem to increase resting energy expenditure [28], which may be partly responsible for the lower BMI values in vegetarians.

Plant-based diets have been shown to be a particularly effective dietary approach for weight loss [29,30]. A recent study showed a mean BMI reduction of 4.4 kg/m² with a 6-month, whole-food, plant-based diet with no energy restrictions, compared with usual care (0.4 kg/m²), in overweight or obese subjects [31].

In a meta-analysis of randomized trials by Huang et al., plant-based diets were associated with a mean weight reduction of −2.02 kg (95% confidence intervals (CI), −2.8 to −1.23 kg). A vegan diet had a more pronounced effect (−2.52 kg; 95% CI, −3.02 to −1.98 kg) than a lacto-ovo-vegetarian diet (−1.48 kg; 95% CI, −3.43 to 0.47 kg) [32]. Similarly, a meta-analysis of 15 clinical trials using vegetarian or vegan diets showed an average weight loss range of 4.6 kg among study completers [30].

Plant-based diets appear to reduce the risk of developing metabolic syndrome by about one half [33]. They reduce the risk of individual components of the metabolic syndrome (except for low high-density lipoprotein (HDL) cholesterol) and are associated with lower waist circumference [33], lower concentrations of triglycerides, total and low-density lipoprotein (LDL) cholesterol [33–35], blood sugar, and blood pressure [33,34].

Two recent meta-analyses of randomized clinical trials showed a benefit of plant-based diets for body weight. This is supported by the observational studies.

4. Plant-Based Diets and Glycemic Control

The prevalence of type 2 diabetes has been increasing worldwide. An estimated 382 million adults worldwide had diabetes in 2013; this number is expected to rise to 592 million by 2035 [36]. The economic burden associated with diabetes (both diagnosed and undiagnosed) exceeded \$322 billion in 2012 in the United States [37]. Therefore, interventions to prevent and manage type 2 diabetes and its complications are desirable.

Diabetes prevalence has been found to be the lowest among vegans (Odds ratio (OR) 0.51; 95% CI 0.40–0.66) and lacto-ovo-vegetarians (OR 0.54; 95% CI 0.49–0.60), compared with non-vegetarians [26]. Diabetes incidence has also been observed to be the lowest in vegans (OR 0.381; 95% CI 0.236–0.617), lacto-ovo vegetarians (OR 0.618; 95% CI 0.503–0.760) and semi-vegetarians (OR 0.486, 95% CI 0.312–0.755). They all had a lower risk of diabetes than non-vegetarians [38].

Vegetarian diets have been shown to be helpful not only in prevention but also in the treatment of type 2 diabetes in several clinical trials. Early studies reported a dramatic reduction in the use of glucose-lowering medications and in plasma glucose levels, in response to a plant-based diet combined with exercise [39,40]. A 2014 meta-analysis found that a plant-based diet significantly improves blood sugar control in type 2 diabetes. The benefit of omitting meat, cheese, and eggs was as much as 0.7 points in some studies, and averaged about 0.4 points overall [41].

Even without exercise, beneficial effects of vegetarian diets included reduced body weight, better glycemic control, and lower blood lipids, compared with more conventional diets in treatment of type 2 diabetes—vegetarian diets being almost twice as effective [42–44].

In a long-term intervention study, the positive effects of a vegetarian diet (compared to a conventional reduced-energy diet) were partially preserved one year after the end of the intervention, although the patients did not continue with their originally assigned diets and consumed a comparable diet during that year [45]. A 2007 study showed that overweight participants following a low-fat, vegan diet were able to lose weight and keep most of it off after two years, more so than those following a diet based on the National Cholesterol Education Program guidelines [46].

Management of glycemic control is one of the cornerstones of diabetes care [47]. It has been well established that improved glycemic control reduces the risk of microvascular complications, whereas the role of glycemic control in reducing macrovascular complications is less clear.

Most observational studies have demonstrated a positive association between poor glucose control and the risk of cardiovascular disease [48–54]. Patients with HbA1c (glycated hemoglobin) concentrations of 6.0–6.9% had 20% lower relative risk of fatal/nonfatal coronary heart disease than patients with HbA1c concentrations of 7.0–7.9%. Limited data from four large, randomized, controlled trials and their follow-ups also suggest that chronic hyperglycemia is associated with an increased risk for cardiovascular disease in patients with diabetes [55–64]. Meta-analyses of these trials demonstrated significantly reduced risks of fatal/nonfatal myocardial infarction (15%) and cardiovascular disease (11–15%) with HbA1c reductions of approximately 1 absolute percentage point [58,65,66].

A recent meta-analysis of six randomized controlled trials showed that consumption of vegetarian diets was associated with a significant reduction in HbA1c by 0.4 absolute percentage points, compared with conventional diets in patients with type 2 diabetes [41]. This reduction in HbA1c alone (i.e., independently from improvements in body weight, blood lipids, blood pressure, platelet aggregation, and other variables) would be expected to decrease risks of myocardial infarction and cardiovascular disease by about 6% and 4.4–6%, respectively, based on estimates drawn from large prospective studies. Other healthful lifestyle factors add further reduction in risk.

One of the mechanisms that is likely responsible for improved glycemic control is increased insulin sensitivity in response to plant-based diets demonstrated in controlled trials [42]. It has also been demonstrated that partial replacement of meat with soy products increased insulin sensitivity in a randomized crossover trial [67].

Another potential mechanism responsible for improved glycemic control is improved gastrointestinal hormone response. Gastrointestinal hormones, especially the incretins, play an

important role in postprandial increase in plasma insulin [68]. In patients with type 2 diabetes, the incretin effect is diminished [69], and it seems to be influenced by diet composition. Consumption of processed meat, for example, leads to impaired release of gastrointestinal hormones, including the incretins both in a fasting state and after a meal compared with an isocaloric vegan meal [70]. These results suggest that vegetarian diets may be beneficial for improvement in gastrointestinal hormone release in patients with type 2 diabetes.

In summary, the evidence for the beneficial effects of plant-based diets on glycemic control comes from six randomized controlled trials, summarized in a recent meta-analysis, as well as observational studies. Although the number of studies on this topic is limited, the concordance of results across studies is compelling.

5. Plant-Based Diets and Blood Pressure

It has been estimated that 874 million adults worldwide have a systolic blood pressure of 140 mm Hg or higher. In an analysis of data from 844 population-based studies in 154 countries between 1990 and 2015, 14% of all deaths and 143 million life-years of disability were attributable to hypertension [71].

In the United States, hypertension is associated with several leading causes of death, including heart disease, cancer, stroke, and diabetes [72]. Each 20 mm Hg increase in systolic blood pressure or each 10 mm Hg increase in diastolic blood pressure more than doubles the risk of death from stroke [73]. Conversely, a reduction of 5 mm Hg in systolic blood pressure leads to a 7 percent reduced risk of all-cause mortality, a 9 percent reduced risk of heart disease, and a 14 percent reduced risk of stroke [74]. High protein intake, especially from meat, increases blood pressure [75]. High potassium intake, however, lowers blood pressure among people with hypertension [76]. This may also be relevant in childhood in order to prevent hypertension in adulthood [77]. Vegetarian diets typically have higher fiber and potassium and lower fat, compared with omnivorous diets [5].

A meta-analysis of 7 randomized controlled trials and 32 observational studies found that vegetarian diets lower blood pressure (both systolic and diastolic), compared with omnivorous diets. In observational studies, vegetarian diets were associated with blood pressure readings that were, on average, 6.9 mm Hg and 4.7 mm Hg lower for systolic and diastolic blood pressure, respectively. In randomized controlled trials, vegetarian diets decreased both systolic and diastolic blood pressure by 4.8 and 2.2 mm Hg, respectively [78]. The blood pressure reduction was independent of salt intake, overweight, and exercise levels. The reduction in systolic blood pressure by 5 mm Hg is estimated to result in a 7% reduction in all-cause mortality, a 9% reduction in mortality due to coronary heart disease, and a 14% reduction in mortality due to stroke [74,78].

In summary, a recent meta-analysis of randomized clinical trials and observational studies showed clear benefits of plant-based diets for blood pressure. Given the consistent results between the studies, the evidence is strong.

6. Plant-Based Diets and Blood Lipids

Epidemiological studies have shown a high prevalence of hypercholesterolemia in Western countries (more than 50% adults have total cholesterol serum levels higher than 5 mmol/L), along with the high incidence of cardiovascular disease and related deaths [79–81]. Data from clinical studies indicate that for every 1% reduction in LDL-cholesterol, the risk for a major cardiac event, including heart attack and stroke, is reduced by approximately 1% [82]. Since lifestyle changes (especially diet and exercise) can lower LDL levels by 30–40% in people with or at risk for heart disease, reducing LDL-cholesterol to lower targets can play a significant role in disease prevention and possibly treatment [10,83].

Saturated fat increases plasma LDL cholesterol concentrations. According to a report published by the American Heart Association, replacing saturated fat in the diet and replacing it with polyunsaturated vegetable oil can reduce the risk of cardiovascular disease by about 30%, similar to

the effect of statins. The authors concluded that the incidence of cardiovascular disease (CVD) would decrease with such a dietary shift [84].

The effect of dietary cholesterol on plasma cholesterol concentrations is less pronounced than that of saturated fat. Nonetheless, a recent meta-analysis confirmed the longstanding observation that dietary cholesterol increases serum total and LDL-cholesterol concentrations [85]. Dietary cholesterol is found only in animal products including meat, dairy, and eggs. A meat-free diet can lead to a significant reduction in total and LDL cholesterol, which corresponded with about a 10% reduced risk of heart disease, according to a meta-analysis of randomized-controlled trials published by the American Heart Association [17].

Vegetarian and especially vegan dietary patterns improve both fasting and postprandial blood lipids compared with conventional therapeutic diets [18,86–91], with effects similar to those seen with statin therapy [92]. If combined with moderate physical exercise, smoking cessation and stress management, the reduction of blood lipids can be even higher [10].

In summary, the findings of interventional trials are in accordance with those of observational studies, and the evidence for improved blood lipid profiles in response to plant-based diets is strong.

7. Plant-Based Diets and Platelet Aggregation

Enhanced platelet adhesion, activation, and aggregation increase the risk of ischemic stroke. In addition, insulin resistance plays a role in the pathogenesis of ischemic stroke by encouraging atherosclerotic changes. Clinical studies have suggested that improving insulin resistance may be an effective way how to prevent or delay ischemic stroke [88].

Both platelet aggregation and insulin resistance are influenced by diet choices. Plant-based diets have been shown to reduce insulin resistance [42], as well as to reduce platelet aggregation and thus reduce cardiovascular risk [89]. Plant foods with low glycemic index like whole grains, vegetables, nuts, legumes, garlic, ginger, onion, purple grape juice, tomatoes, berries, and dark chocolate, are particularly efficient in reducing platelet aggregation [89].

Because of the paucity of studies examining the effect of plant-based diets on platelet aggregation, the evidence for its beneficial effects is limited.

8. Potential Mechanisms Responsible for Benefits Associated with Plant-Based Diets

Several possible mechanisms may explain the beneficial cardio-metabolic effects of plant-based diets: lower caloric intake, increased intake of fiber, reduced intake of saturated fat and cholesterol, higher intake of polyunsaturated and monounsaturated fatty acids, increased intake of antioxidants and micronutrients, higher intake of vegetable protein, and a higher intake of plant sterols.

A reduction in energy intake due to the lower energy density of plant foods [93] has been shown to yield cardio-metabolic benefits even before any changes in body weight occur [93].

The ideal percentage carbohydrate, protein, and fat in the diet is a subject of ongoing discussion and debate. Plant-based diets used in the treatment of cardio-metabolic disease in clinical trials are typically high in complex carbohydrates [10,91,92]. A low-carbohydrate vegan (“Eco-Atkins”) diet has also been shown to decrease body weight and cardio-metabolic risk factors [92]. However, a recent systematic review and meta-analysis of low-carbohydrate diets has not shown any superiority of these diets in the long term in terms of glycemic control, weight, or blood lipids [94]. Therefore, macronutrient distribution should be based on individualized assessment of current eating patterns, preferences, and metabolic goals [93]. Reducing the intake of saturated fat and added sugars while increasing the intake of fiber and complex carbohydrates seems to be a reasonable approach [95].

Fiber contributes to bulk in the diet without adding digestible calories, thus leading to satiety and weight loss. Additionally, soluble fiber binds with bile acids in the small intestines, increasing fecal bile salt excretion and thus reducing cholesterol [96], and reduces blood lipids and blood glucose. High fiber consumption has been linked to reduced body weight, lower blood pressure and blood lipids, reduced plaque formation and cardiovascular risk, and lower risk of type 2 diabetes [97–99].

Plant-based diets are also lower in saturated fat and dietary cholesterol. Replacing saturated fat with polyunsaturated and monounsaturated fat has been shown to decrease insulin sensitivity and reduce cardio-metabolic risk, independent of changes in body weight [100–106].

Vegetable proteins reduce the concentrations of blood lipids [107–110], reduce the risk of obesity and cardiovascular disease, and may have anti-inflammatory and anti-cancer effects [111,112]. High intake of antioxidants and micronutrients from whole plant foods represents another potential cardio-metabolic beneficial mechanism [113]. Plant sterols that have a structure similar to that of cholesterol reduce the cardiovascular risk and mortality [114,115], have anti-inflammatory effects, and positively affect coagulation, platelet function, and endothelial function [116], as well as glycemic control in patients with type 2 diabetes [117].

It appears that plant-based diets exert cardio-metabolic benefits via several independent mechanisms. When eating all whole plant foods, the synergistic effect may be greater than a mere additional effect of eating isolated nutrients.

9. Ensuring Complete Nutrition

Certain nutrients may be less abundant in plant-based diets, compared with diets including animal products, although there is considerable variation depending on specific diet choices. These nutrients include protein, fat (particularly saturated fat), zinc, vitamin D, and vitamin B₁₂. However, manifestations of deficiencies are not more common in vegetarian populations than in omnivorous populations [97].

Vitamin B₁₂ deserves special attention. It is made by neither plants nor animals but is found in animal products due to its formation by intestinal bacteria. For those following plant-based diets, B₁₂-fortified products or supplements ensure that needs for this essential nutrient are met. Other populations who should take a B₁₂ supplement, regardless of their dietary pattern, include those who are 50 years or older, those who have digestive disorders such as Crohn's disease that limit B₁₂ absorption, and those who take certain medications such as acid-blockers and metformin [118].

Plant-based diets merit inclusion in dietary recommendations. With guidance and support, such therapeutic diet changes are well-accepted and sustainable, as determined by data on long-term adherence and food acceptability questionnaires [119,120].

The Academy of Nutrition and Dietetics states that, "... appropriately planned vegetarian, including vegan, diets are healthful, nutritionally adequate, and may provide health benefits for the prevention and treatment of certain diseases." [97]. "Appropriately planned" means that it is important to keep the main sources of macro- and micro-nutrients in mind, and make sure the diet supplies one's need for all of them.

10. Conclusions

Vegetarian diets represent an effective means for the prevention and treatment of cardio-metabolic diseases.

Properly planned vegetarian diets are healthful and effective for weight and glycemic control, and provide metabolic and cardiovascular benefits, including reversing atherosclerosis and decreasing blood lipids and blood pressure. The cardio-metabolic benefits seem to be greater with vegan than lacto-ovo-vegetarian diets [121]. The use of plant-based diets as a means of prevention and treatment of cardio-metabolic disease deserves to be promoted through dietary guidelines and recommendations.

Acknowledgments: This work was funded by Physicians Committee for Responsible Medicine (PCRM).

Author Contributions: H.K. and S.L. designed the structure of the paper, performed the literature search, and wrote the paper. N.B. provided funding and revised the manuscript. All authors had full access to the final version of the manuscript and gave their approval before publishing.

Conflicts of Interest: The authors declare no conflict of interest related to this manuscript.

References

1. Mozaffarian, D. Dietary and policy priorities for cardiovascular disease, diabetes, and obesity: A comprehensive review. *Circulation* **2016**, *133*, 187–225. [[CrossRef](#)] [[PubMed](#)]
2. Murray, C.J.L.; Atkinson, C.; Bhalla, K.; Birbeck, G.; Burstein, R.; Chou, D.; Dellavalle, R.; Danaei, G.; Ezzati, M.; Fahimi, A.; et al. The state of US health, 1990–2010: Burden of diseases, injuries, and risk factors. *JAMA* **2013**, *310*, 591–608. [[CrossRef](#)] [[PubMed](#)]
3. GBD 2015 Risk Factors Collaborators. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2015: A systematic analysis for the Global Burden of Disease Study 2015. *Lancet (Lond. Engl.)* **2016**, *388*, 1659–1724. [[CrossRef](#)]
4. Micha, R.; Peñalvo, J.L.; Cudhea, F.; Imamura, F.; Rehm, C.D.; Mozaffarian, D. Association between dietary factors and mortality from heart disease, stroke, and type 2 diabetes in the United States. *JAMA* **2017**, *317*, 912–924. [[CrossRef](#)] [[PubMed](#)]
5. Rizzo, N.S.; Jaceldo-Siegl, K.; Sabate, J.; Fraser, G.E. Nutrient profiles of vegetarian and nonvegetarian dietary patterns. *J. Acad. Nutr. Diet.* **2013**, *113*, 1610–1619. [[CrossRef](#)] [[PubMed](#)]
6. Fraser, G.E. Vegetarian diets: What do we know of their effects on common chronic diseases? *Am. J. Clin. Nutr.* **2009**, *89*, 1607S–1612S. [[CrossRef](#)] [[PubMed](#)]
7. Lozano, R.; Naghavi, M.; Foreman, K.; Lim, S.; Shibuya, K.; Aboyans, V.; Abraham, J.; Adair, T.; Aggarwal, R.; Ahn, S.Y.; et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: A systematic analysis for the Global Burden of Disease Study 2010. *Lancet (Lond. Engl.)* **2012**, *380*, 2095–2128. [[CrossRef](#)]
8. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation* **2002**, *106*, 3143–3421.
9. Ornish, D.; Scherwitz, L.W.; Billings, J.H.; Brown, S.E.; Gould, K.L.; Merritt, T.A.; Sparler, S.; Armstrong, W.T.; Ports, T.A.; Kirkeeide, R.L.; et al. Intensive lifestyle changes for reversal of coronary heart disease. *JAMA J. Am. Med. Assoc.* **1998**, *280*, 2001–2007. [[CrossRef](#)]
10. Ornish, D.; Brown, S.E.; Scherwitz, L.W.; Billings, J.H.; Armstrong, W.T.; Ports, T.A.; McLanahan, S.M.; Kirkeeide, R.L.; Brand, R.J.; Gould, K.L. Can lifestyle changes reverse coronary heart disease? The Lifestyle Heart Trial. *Lancet* **1990**, *336*, 129–133. [[CrossRef](#)]
11. Esselstyn, C.B., Jr. Updating a 12-year experience with arrest and reversal therapy for coronary heart disease (an overdue requiem for palliative cardiology). *Am. J. Cardiol.* **1999**, *84*, 339–341. [[CrossRef](#)]
12. Daubenmier, J.J.; Weidner, G.; Sumner, M.D.; Mendell, N.; Merritt-Worden, T.; Studley, J.; Ornish, D. The contribution of changes in diet, exercise, and stress management to changes in coronary risk in women and men in the multisite cardiac lifestyle intervention program. *Ann. Behav. Med. Publ. Soc. Behav. Med.* **2007**, *33*, 57–68. [[CrossRef](#)] [[PubMed](#)]
13. Frattaroli, J.; Weidner, G.; Merritt-Worden, T.A.; Frenda, S.; Ornish, D. Angina pectoris and atherosclerotic risk factors in the multisite cardiac lifestyle intervention program. *Am. J. Cardiol.* **2008**, *101*, 911–918. [[CrossRef](#)] [[PubMed](#)]
14. Orlich, M.J.; Singh, P.N.; Sabaté, J.; Jaceldo-Siegl, K.; Fan, J.; Knutsen, S.; Beeson, W.L.; Fraser, G.E. Vegetarian dietary patterns and mortality in Adventist Health Study 2. *JAMA Intern. Med.* **2013**, *173*, 1230–1238. [[CrossRef](#)] [[PubMed](#)]
15. Crowe, F.L.; Appleby, P.N.; Travis, R.C.; Key, T.J. Risk of hospitalization or death from ischemic heart disease among British vegetarians and nonvegetarians: Results from the EPIC-Oxford cohort study. *Am. J. Clin. Nutr.* **2013**, *97*, 597–603. [[CrossRef](#)] [[PubMed](#)]
16. Kwok, C.S.; Umar, S.; Myint, P.K.; Mamas, M.A.; Loke, Y.K. Vegetarian diet, Seventh Day Adventists and risk of cardiovascular mortality: A systematic review and meta-analysis. *Int. J. Cardiol.* **2014**, *176*, 680–686. [[CrossRef](#)] [[PubMed](#)]
17. Wang, F.; Zheng, J.; Yang, B.; Jiang, J.; Fu, Y.; Li, D. Effects of vegetarian diets on blood lipids: A systematic review and meta-analysis of randomized controlled trials. *J. Am. Heart Assoc.* **2015**, *4*, e002408. [[CrossRef](#)] [[PubMed](#)]

18. Bradbury, K.E.; Crowe, F.L.; Appleby, P.N.; Schmidt, J.A.; Travis, R.C.; Key, T.J. Serum concentrations of cholesterol, apolipoprotein A-I and apolipoprotein B in a total of 1694 meat-eaters, fish-eaters, vegetarians and vegans. *Eur. J. Clin. Nutr.* **2014**, *68*, 178–183. [[CrossRef](#)] [[PubMed](#)]
19. Dinu, M.; Abbate, R.; Gensini, G.F.; Casini, A.; Sofi, F. Vegetarian, vegan diets and multiple health outcomes: A systematic review with meta-analysis of observational studies. *Crit. Rev. Food Sci. Nutr.* **2017**, *57*, 3640–3649. [[CrossRef](#)] [[PubMed](#)]
20. NCD Risk Factor Collaboration (NCD-RisC). Trends in adult body-mass index in 200 countries from 1975 to 2014: A pooled analysis of 1698 population-based measurement studies with 19.2 million participants. *Lancet (Lond. Engl.)* **2016**, *387*, 1377–1396. [[CrossRef](#)]
21. Ng, M.; Fleming, T.; Robinson, M.; Thomson, B.; Graetz, N.; Margono, C.; Mullany, E.C.; Biryukov, S.; Abbafati, C.; Abera, S.F.; et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: A systematic analysis for the Global Burden of Disease Study 2013. *Lancet (Lond. Engl.)* **2014**, *384*, 766–781. [[CrossRef](#)]
22. The Global BMI Mortality Collaboration. Body-mass index and all-cause mortality: Individual-participant-data meta-analysis of 239 prospective studies in four continents. *Lancet (Lond. Engl.)* **2016**, *388*, 776–786. [[CrossRef](#)]
23. Berkow, S.E.; Barnard, N. Vegetarian diets and weight status. *Nutr. Rev.* **2006**, *64*, 175–188. [[CrossRef](#)] [[PubMed](#)]
24. Fraser, G.E. Associations between diet and cancer, ischemic heart disease, and all-cause mortality in non-Hispanic white California Seventh-day Adventists. *Am. J. Clin. Nutr.* **1999**, *70*, 532S–538S. [[PubMed](#)]
25. Appleby, P.N.; Thorogood, M.; Mann, J.I.; Key, T.J. The Oxford Vegetarian Study: An overview. *Am. J. Clin. Nutr.* **1999**, *70*, 525S–531S. [[PubMed](#)]
26. Tonstad, S.; Butler, T.; Yan, R.; Fraser, G.E. Type of vegetarian diet, body weight, and prevalence of type 2 diabetes. *Diabetes Care* **2009**, *32*, 791–796. [[CrossRef](#)] [[PubMed](#)]
27. Rosell, M.; Appleby, P.; Spencer, E.; Key, T. Weight gain over 5 years in 21,966 meat-eating, fish-eating, vegetarian, and vegan men and women in EPIC-Oxford. *Int. J. Obes.* **2006**, *30*, 1389–1396. [[CrossRef](#)] [[PubMed](#)]
28. Montalcini, T.; De Bonis, D.; Ferro, Y.; Carè, I.; Mazza, E.; Accattato, F.; Greco, M.; Foti, D.; Romeo, S.; Gulletta, E.; et al. High vegetable fats intake is associated with high resting energy expenditure in vegetarians. *Nutrients* **2015**, *7*, 5933–5947. [[CrossRef](#)] [[PubMed](#)]
29. Moore, W.J.; McGrievy, M.E.; Turner-McGrievy, G.M. Dietary adherence and acceptability of five different diets, including vegan and vegetarian diets, for weight loss: The New DIETs study. *Eat. Behav.* **2015**, *19*, 33–38. [[CrossRef](#)] [[PubMed](#)]
30. Barnard, N.D.; Levin, S.M.; Yokoyama, Y. A systematic review and meta-analysis of changes in body weight in clinical trials of vegetarian diets. *J. Acad. Nutr. Diet.* **2015**, *115*, 954–969. [[CrossRef](#)] [[PubMed](#)]
31. Wright, N.; Wilson, L.; Smith, M.; Duncan, B.; McHugh, P. The BROAD study: A randomised controlled trial using a whole food plant-based diet in the community for obesity, ischaemic heart disease or diabetes. *Nutr. Diabetes* **2017**, *7*, e256. [[CrossRef](#)] [[PubMed](#)]
32. Huang, R.-Y.; Huang, C.-C.; Hu, F.B.; Chavarro, J.E. Vegetarian diets and weight reduction: A meta-analysis of randomized controlled trials. *J. Gen. Intern. Med.* **2016**, *31*, 109–116. [[CrossRef](#)] [[PubMed](#)]
33. Rizzo, N.S.; Sabaté, J.; Jaceldo-Siegl, K.; Fraser, G.E. Vegetarian dietary patterns are associated with a lower risk of metabolic syndrome: The adventist health study 2. *Diabetes Care* **2011**, *34*, 1225–1227. [[CrossRef](#)] [[PubMed](#)]
34. Teixeira, R.C.; Molina, M.C.; Zandonade, E.; Mill, J.G. Cardiovascular risk in vegetarians and omnivores: A comparative study. *Arq. Bras. Cardiol.* **2007**, *89*, 237–244.
35. De Biase, S.G.; Fernandes, S.F.C.; Gianini, R.J.; Duarte, J.L.G. Vegetarian diet and cholesterol and triglycerides levels. *Arq. Bras. Cardiol.* **2007**, *88*, 35–39. [[CrossRef](#)] [[PubMed](#)]
36. Guariguata, L.; Whiting, D.R.; Hambleton, I.; Beagley, J.; Linnenkamp, U.; Shaw, J.E. Global estimates of diabetes prevalence for 2013 and projections for 2035. *Diabetes Res. Clin. Pract.* **2014**, *103*, 137–149. [[CrossRef](#)] [[PubMed](#)]
37. Dall, T.M.; Yang, W.; Halder, P.; Pang, B.; Massoudi, M.; Wintfeld, N.; Semilla, A.P.; Franz, J.; Hogan, P.F. The economic burden of elevated blood glucose levels in 2012: Diagnosed and undiagnosed diabetes, gestational diabetes mellitus, and prediabetes. *Diabetes Care* **2014**, *37*, 3172–3179. [[CrossRef](#)] [[PubMed](#)]

38. Tonstad, S.; Stewart, K.; Oda, K.; Batech, M.; Herring, R.P.; Fraser, G.E. Vegetarian diets and incidence of diabetes in the Adventist Health Study-2. *Nutr. Metab. Cardiovasc. Dis. NMCD* **2013**, *23*, 292–299. [[CrossRef](#)] [[PubMed](#)]
39. Anderson, J.W.; Ward, K. High-carbohydrate, high-fiber diets for insulin-treated men with diabetes mellitus. *Am. J. Clin. Nutr.* **1979**, *32*, 2312–2321. [[PubMed](#)]
40. Barnard, R.J.; Jung, T.; Inkeles, S.B. Diet and exercise in the treatment of NIDDM. The need for early emphasis. *Diabetes Care* **1994**, *17*, 1469–1472. [[CrossRef](#)] [[PubMed](#)]
41. Yokoyama, Y.; Barnard, N.D.; Levin, S.M.; Watanabe, M. Vegetarian diets and glycemic control in diabetes: A systematic review and meta-analysis. *Cardiovasc. Diagn. Ther.* **2014**, *4*, 373–382. [[CrossRef](#)] [[PubMed](#)]
42. Kahleova, H.; Matoulek, M.; Malinska, H.; Oliyarnik, O.; Kazdova, L.; Neskudla, T.; Skoch, A.; Hajek, M.; Hill, M.; Kahle, M.; et al. Vegetarian diet improves insulin resistance and oxidative stress markers more than conventional diet in subjects with type 2 diabetes. *Diabet. Med. J. Br. Diabet. Assoc.* **2011**, *28*, 549–559. [[CrossRef](#)] [[PubMed](#)]
43. Barnard, N.D.; Cohen, J.; Jenkins, D.J.A.; Turner-McGrievy, G.; Gloede, L.; Jaster, B.; Seidl, K.; Green, A.A.; Talpers, S. A low-fat vegan diet improves glycemic control and cardiovascular risk factors in a randomized clinical trial in individuals with type 2 diabetes. *Diabetes Care* **2006**, *29*, 1777–1783. [[CrossRef](#)] [[PubMed](#)]
44. Nicholson, A.S.; Sklar, M.; Barnard, N.D.; Gore, S.; Sullivan, R.; Browning, S. Toward improved management of NIDDM: A randomized, controlled, pilot intervention using a lowfat, vegetarian diet. *Prev. Med.* **1999**, *29*, 87–91. [[CrossRef](#)] [[PubMed](#)]
45. Kahleova, H.; Hill, M.; Pelikánová, T. Vegetarian vs. conventional diabetic diet—A 1-year-follow-up. *Cor Vasa* **2014**, *56*, e140–e144. [[CrossRef](#)]
46. Turner-McGrievy, G.M.; Barnard, N.D.; Scialli, A.R. A two-year randomized weight loss trial comparing a vegan diet to a more moderate low-fat diet. *Obesity (Silver Spring Md.)* **2007**, *15*, 2276–2281. [[CrossRef](#)] [[PubMed](#)]
47. American Diabetes Association. Standards of medical care in diabetes—2014. *Diabetes Care* **2014**, *37*, S14–S80. [[CrossRef](#)]
48. Avogaro, A.; Giorda, C.; Maggini, M.; Mannucci, E.; Raschetti, R.; Lombardo, F.; Spila-Alegiani, S.; Turco, S.; Velussi, M.; Ferrannini, E.; et al. Association of Clinical Diabetologists, Istituto Superiore di Sanità Incidence of coronary heart disease in type 2 diabetic men and women: Impact of microvascular complications, treatment, and geographic location. *Diabetes Care* **2007**, *30*, 1241–1247. [[CrossRef](#)] [[PubMed](#)]
49. Gerstein, H.C.; Pogue, J.; Mann, J.F.E.; Lonn, E.; Dagenais, G.R.; McQueen, M.; Yusuf, S.; HOPE Investigators. The relationship between dysglycaemia and cardiovascular and renal risk in diabetic and non-diabetic participants in the HOPE study: A prospective epidemiological analysis. *Diabetologia* **2005**, *48*, 1749–1755. [[CrossRef](#)] [[PubMed](#)]
50. Turner, R.C.; Millns, H.; Neil, H.A.; Stratton, I.M.; Manley, S.E.; Matthews, D.R.; Holman, R.R. Risk factors for coronary artery disease in non-insulin dependent diabetes mellitus: United Kingdom Prospective Diabetes Study (UKPDS: 23). *BMJ* **1998**, *316*, 823–828. [[CrossRef](#)] [[PubMed](#)]
51. Elley, C.R.; Kenealy, T.; Robinson, E.; Drury, P.L. Glycated haemoglobin and cardiovascular outcomes in people with type 2 diabetes: A large prospective cohort study. *Diabet. Med. J. Br. Diabet. Assoc.* **2008**, *25*, 1295–1301. [[CrossRef](#)] [[PubMed](#)]
52. Duckworth, W.C.; McCarren, M.; Abaira, C. Glucose control and cardiovascular complications: The VA Diabetes Trial. *Diabetes Care* **2001**, *24*, 942–945. [[CrossRef](#)] [[PubMed](#)]
53. Khaw, K.-T.; Wareham, N.; Bingham, S.; Luben, R.; Welch, A.; Day, N. Association of hemoglobin A1c with cardiovascular disease and mortality in adults: The European prospective investigation into cancer in Norfolk. *Ann. Intern. Med.* **2004**, *141*, 413–420. [[CrossRef](#)] [[PubMed](#)]
54. Kirkman, M.S.; McCarren, M.; Shah, J.; Duckworth, W.; Abaira, C. The association between metabolic control and prevalent macrovascular disease in type 2 diabetes: The VA Cooperative Study in diabetes. *J. Diabetes Complicat.* **2006**, *20*, 75–80. [[CrossRef](#)] [[PubMed](#)]
55. Selvin, E.; Marinopoulos, S.; Berkenblit, G.; Rami, T.; Brancati, F.L.; Powe, N.R.; Golden, S.H. Meta-analysis: Glycosylated hemoglobin and cardiovascular disease in diabetes mellitus. *Ann. Intern. Med.* **2004**, *141*, 421–431. [[CrossRef](#)] [[PubMed](#)]

56. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet* **1998**, *352*, 837–853.
57. UK Prospective Diabetes Study (UKPDS) Group. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). *Lancet (Lond. Engl.)* **1998**, *352*, 854–865.
58. Control Group; Turnbull, F.M.; Abraira, C.; Anderson, R.J.; Byington, R.P.; Chalmers, J.P.; Duckworth, W.C.; Evans, G.W.; Gerstein, H.C.; Holman, R.R.; et al. Intensive glucose control and macrovascular outcomes in type 2 diabetes. *Diabetologia* **2009**, *52*, 2288–2298. [[CrossRef](#)]
59. Duckworth, W.; Abraira, C.; Moritz, T.; Reda, D.; Emanuele, N.; Reaven, P.D.; Zieve, F.J.; Marks, J.; Davis, S.N.; Hayward, R.; et al. Glucose control and vascular complications in veterans with type 2 diabetes. *N. Engl. J. Med.* **2009**, *360*, 129–139. [[CrossRef](#)] [[PubMed](#)]
60. ADVANCE Collaborative Group; Patel, A.; MacMahon, S.; Chalmers, J.; Neal, B.; Billot, L.; Woodward, M.; Marre, M.; Cooper, M.; Glasziou, P.; et al. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. *N. Engl. J. Med.* **2008**, *358*, 2560–2572. [[CrossRef](#)] [[PubMed](#)]
61. Action to Control Cardiovascular Risk in Diabetes Study Group. Effects of intensive glucose lowering in type 2 diabetes. *N. Engl. J. Med.* **2008**, *358*, 2545–2559. [[CrossRef](#)]
62. Gerstein, H.C.; Miller, M.E.; Ismail-Beigi, F.; Largay, J.; McDonald, C.; Lochnan, H.A.; Booth, G.L.; ACCORD Study Group. Effects of intensive glycaemic control on ischaemic heart disease: Analysis of data from the randomised, controlled ACCORD trial. *Lancet (Lond. Engl.)* **2014**, *384*, 1936–1941. [[CrossRef](#)]
63. Zoungas, S.; Chalmers, J.; Neal, B.; Billot, L.; Li, Q.; Hirakawa, Y.; Arima, H.; Monaghan, H.; Joshi, R.; Colagiuri, S.; et al. ADVANCE-ON Collaborative Group Follow-up of blood-pressure lowering and glucose control in type 2 diabetes. *N. Engl. J. Med.* **2014**, *371*, 1392–1406. [[CrossRef](#)] [[PubMed](#)]
64. Hayward, R.A.; Reaven, P.D.; Emanuele, N.V.; VADT investigators. Follow-up of glycemic control and cardiovascular outcomes in type 2 diabetes. *N. Engl. J. Med.* **2015**, *373*, 978. [[CrossRef](#)] [[PubMed](#)]
65. Ray, K.K.; Seshasai, S.R.K.; Wijesuriya, S.; Sivakumaran, R.; Nethcott, S.; Preiss, D.; Erqou, S.; Sattar, N. Effect of intensive control of glucose on cardiovascular outcomes and death in patients with diabetes mellitus: A meta-analysis of randomised controlled trials. *Lancet (Lond. Engl.)* **2009**, *373*, 1765–1772. [[CrossRef](#)]
66. Mannucci, E.; Monami, M.; Lamanna, C.; Gori, F.; Marchionni, N. Prevention of cardiovascular disease through glycemic control in type 2 diabetes: A meta-analysis of randomized clinical trials. *Nutr. Metab. Cardiovasc. Dis. NMCD* **2009**, *19*, 604–612. [[CrossRef](#)] [[PubMed](#)]
67. Van Nielen, M.; Feskens, E.J.M.; Rietman, A.; Siebelink, E.; Mensink, M. Partly replacing meat protein with soy protein alters insulin resistance and blood lipids in postmenopausal women with abdominal obesity. *J. Nutr.* **2014**, *144*, 1423–1429. [[CrossRef](#)] [[PubMed](#)]
68. Nauck, M.A.; Homberger, E.; Siegel, E.G.; Allen, R.C.; Eaton, R.P.; Ebert, R.; Creutzfeldt, W. Incretin effects of increasing glucose loads in man calculated from venous insulin and C-peptide responses. *J. Clin. Endocrinol. Metab.* **1986**, *63*, 492–498. [[CrossRef](#)] [[PubMed](#)]
69. Nauck, M.; Stöckmann, F.; Ebert, R.; Creutzfeldt, W. Reduced incretin effect in type 2 (non-insulin-dependent) diabetes. *Diabetologia* **1986**, *29*, 46–52. [[CrossRef](#)] [[PubMed](#)]
70. Belinova, L.; Kahleova, H.; Malinska, H.; Topolcan, O.; Vrzalova, J.; Oliyarnyk, O.; Kazdova, L.; Hill, M.; Pelikanova, T. Differential acute postprandial effects of processed meat and isocaloric vegan meals on the gastrointestinal hormone response in subjects suffering from type 2 diabetes and healthy controls: A randomized crossover study. *PLoS ONE* **2014**, *9*, e107561. [[CrossRef](#)] [[PubMed](#)]
71. Forouzanfar, M.H.; Liu, P.; Roth, G.A.; Ng, M.; Biryukov, S.; Marczak, L.; Alexander, L.; Estep, K.; Hassen Abate, K.; Akinyemiju, T.F.; et al. Global burden of hypertension and systolic blood pressure of at least 110 to 115 mm Hg, 1990–2015. *JAMA* **2017**, *317*, 165–182. [[CrossRef](#)] [[PubMed](#)]
72. Kung, H.-C.; Xu, J. Hypertension-related mortality in the United States, 2000–2013. *NCHS Data Brief* **2015**, *193*, 1–8.
73. Lewington, S.; Clarke, R.; Qizilbash, N.; Peto, R.; Collins, R.; Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: A meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet* **2002**, *360*, 1903–1913. [[PubMed](#)]

74. Whelton, P.K.; He, J.; Appel, L.J.; Cutler, J.A.; Havas, S.; Kotchen, T.A.; Roccella, E.J.; Stout, R.; Vallbona, C.; Winston, M.C.; et al. Primary prevention of hypertension: Clinical and public health advisory from The National High Blood Pressure Education Program. *JAMA* **2002**, *288*, 1882–1888. [[CrossRef](#)] [[PubMed](#)]
75. Mattos, C.B.; Viana, L.V.; Paula, T.P.; Sarmiento, R.A.; Almeida, J.C.; Gross, J.L.; Azevedo, M.J. Increased protein intake is associated with uncontrolled blood pressure by 24-hour ambulatory blood pressure monitoring in patients with type 2 diabetes. *J. Am. Coll. Nutr.* **2015**, *34*, 232–239. [[CrossRef](#)] [[PubMed](#)]
76. Aburto, N.J.; Hanson, S.; Gutierrez, H.; Hooper, L.; Elliott, P.; Cappuccio, F.P. Effect of increased potassium intake on cardiovascular risk factors and disease: Systematic review and meta-analyses. *BMJ* **2013**, *346*, f1378. [[CrossRef](#)] [[PubMed](#)]
77. Buendia, J.R.; Bradlee, M.L.; Daniels, S.R.; Singer, M.R.; Moore, L.L. Longitudinal effects of dietary sodium and potassium on blood pressure in adolescent girls. *JAMA Pediatr.* **2015**, *169*, 560–568. [[CrossRef](#)] [[PubMed](#)]
78. Yokoyama, Y.; Nishimura, K.; Barnard, N.D.; Takegami, M.; Watanabe, M.; Sekikawa, A.; Okamura, T.; Miyamoto, Y. Vegetarian diets and blood pressure: A meta-analysis. *JAMA Intern. Med.* **2014**. [[CrossRef](#)] [[PubMed](#)]
79. Carroll, M.D.; Lacher, D.A.; Sorlie, P.D.; Cleeman, J.I.; Gordon, D.J.; Wolz, M.; Grundy, S.M.; Johnson, C.L. Trends in serum lipids and lipoproteins of adults, 1960–2002. *JAMA* **2005**, *294*, 1773–1781. [[CrossRef](#)] [[PubMed](#)]
80. Primatesta, P.; Poulter, N.R. Levels of dyslipidaemia and improvement in its management in England: Results from the Health Survey for England 2003. *Clin. Endocrinol. (Oxf.)* **2006**, *64*, 292–298. [[CrossRef](#)] [[PubMed](#)]
81. Guallar-Castillón, P.; Gil-Montero, M.; León-Muñoz, L.M.; Graciani, A.; Bayán-Bravo, A.; Taboada, J.M.; Banegas, J.R.; Rodríguez-Artalejo, F. Magnitude and management of hypercholesterolemia in the adult population of Spain, 2008–2010: The ENRICA Study. *Rev. Espanola Cardiol. (Engl. Ed.)* **2012**, *65*, 551–558. [[CrossRef](#)] [[PubMed](#)]
82. Grundy, S.M.; Cleeman, J.I.; Merz, C.N.B.; Brewer, H.B.; Clark, L.T.; Hunnigake, D.B.; Pasternak, R.C.; Smith, S.C.; Stone, N.J.; Coordinating Committee of the National Cholesterol Education Program. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III Guidelines. *J. Am. Coll. Cardiol.* **2004**, *44*, 720–732. [[CrossRef](#)] [[PubMed](#)]
83. Howard, B.V.; Roman, M.J.; Devereux, R.B.; Fleg, J.L.; Galloway, J.M.; Henderson, J.A.; Howard, W.J.; Lee, E.T.; Mete, M.; Poolaw, B.; et al. Effect of lower targets for blood pressure and LDL cholesterol on atherosclerosis in diabetes: The SANDS randomized trial. *JAMA* **2008**, *299*, 1678–1689. [[CrossRef](#)] [[PubMed](#)]
84. Sacks, F.M.; Lichtenstein, A.H.; Wu, J.H.Y.; Appel, L.J.; Creager, M.A.; Kris-Etherton, P.M.; Miller, M.; Rimm, E.B.; Rudel, L.L.; Robinson, J.G.; et al. Dietary fats and cardiovascular disease: A presidential advisory from the American Heart Association. *Circulation* **2017**. [[CrossRef](#)] [[PubMed](#)]
85. Berger, S.; Raman, G.; Vishwanathan, R.; Jacques, P.F.; Johnson, E.J. Dietary cholesterol and cardiovascular disease: A systematic review and meta-analysis. *Am. J. Clin. Nutr.* **2015**, *102*, 276–294. [[CrossRef](#)] [[PubMed](#)]
86. Riccardi, G.; Giacco, R.; Rivellese, A.A. Dietary fat, insulin sensitivity and the metabolic syndrome. *Clin. Nutr. (Edinb. Scotl.)* **2004**, *23*, 447–456. [[CrossRef](#)] [[PubMed](#)]
87. Jenkins, D.J.A.; Kendall, C.W.C.; Marchie, A.; Faulkner, D.A.; Wong, J.M.W.; De Souza, R.; Emam, A.; Parker, T.L.; Vidgen, E.; Trautwein, E.A.; et al. Direct comparison of a dietary portfolio of cholesterol-lowering foods with a statin in hypercholesterolemic participants. *Am. J. Clin. Nutr.* **2005**, *81*, 380–387. [[PubMed](#)]
88. Deng, X.-L.; Liu, Z.; Wang, C.; Li, Y.; Cai, Z. Insulin resistance in ischemic stroke. *Metab. Brain Dis.* **2017**. [[CrossRef](#)] [[PubMed](#)]
89. McEwen, B.J. The influence of diet and nutrients on platelet function. *Semin. Thromb. Hemost.* **2014**, *40*, 214–226. [[CrossRef](#)] [[PubMed](#)]
90. Trapp, C.B.; Barnard, N.D. Usefulness of vegetarian and vegan diets for treating type 2 diabetes. *Curr. Diabetes Rep.* **2010**, *10*, 152–158. [[CrossRef](#)] [[PubMed](#)]
91. Hughes, T.A.; Gwynne, J.T.; Switzer, B.R.; Herbst, C.; White, G. Effects of caloric restriction and weight loss on glycemic control, insulin release and resistance, and atherosclerotic risk in obese patients with type II diabetes mellitus. *Am. J. Med.* **1984**, *77*, 7–17. [[CrossRef](#)]

92. Jenkins, D.J.A.; Wong, J.M.W.; Kendall, C.W.C.; Esfahani, A.; Ng, V.W.Y.; Leong, T.C.K.; Faulkner, D.A.; Vidgen, E.; Paul, G.; Mukherjea, R.; et al. Effect of a 6-month vegan low-carbohydrate ('Eco-Atkins') diet on cardiovascular risk factors and body weight in hyperlipidaemic adults: A randomised controlled trial. *BMJ Open* **2014**, *4*, e003505. [[CrossRef](#)] [[PubMed](#)]
93. Evert, A.B.; Boucher, J.L.; Cypress, M.; Dunbar, S.A.; Franz, M.J.; Mayer-Davis, E.J.; Neumiller, J.J.; Nwankwo, R.; Verdi, C.L.; Urbanski, P.; et al. Nutrition therapy recommendations for the management of adults with diabetes. *Diabetes Care* **2014**, *37*, S120–S143. [[CrossRef](#)] [[PubMed](#)]
94. Snorgaard, O.; Poulsen, G.M.; Andersen, H.K.; Astrup, A. Systematic review and meta-analysis of dietary carbohydrate restriction in patients with type 2 diabetes. *BMJ Open Diabetes Res. Care* **2017**, *5*, e000354. [[CrossRef](#)] [[PubMed](#)]
95. Vitale, M.; Masulli, M.; Rivellese, A.A.; Babini, A.C.; Boemi, M.; Bonora, E.; Buzzetti, R.; Ciano, O.; Cignarelli, M.; Cigolini, M.; et al. Influence of dietary fat and carbohydrates proportions on plasma lipids, glucose control and low-grade inflammation in patients with type 2 diabetes-The TOSCA.IT Study. *Eur. J. Nutr.* **2016**, *55*, 1645–1651. [[CrossRef](#)] [[PubMed](#)]
96. Gunness, P.; Gidley, M.J. Mechanisms underlying the cholesterol-lowering properties of soluble dietary fibre polysaccharides. *Food Funct.* **2010**, *1*, 149–155. [[CrossRef](#)] [[PubMed](#)]
97. Melina, V.; Craig, W.; Levin, S. Position of the academy of nutrition and dietetics: Vegetarian diets. *J. Acad. Nutr. Diet.* **2016**, *116*, 1970–1980. [[CrossRef](#)] [[PubMed](#)]
98. Smit, E.; Nieto, F.J.; Crespo, C.J.; Mitchell, P. Estimates of animal and plant protein intake in US adults: Results from the Third National Health and Nutrition Examination Survey, 1988–1991. *J. Am. Diet. Assoc.* **1999**, *99*, 813–820. [[CrossRef](#)]
99. Pettersen, B.J.; Anousheh, R.; Fan, J.; Jaceldo-Siegl, K.; Fraser, G.E. Vegetarian diets and blood pressure among white subjects: Results from the Adventist Health Study-2 (AHS-2). *Public Health Nutr.* **2012**, *15*, 1909–1916. [[CrossRef](#)] [[PubMed](#)]
100. Lovejoy, J.C. The influence of dietary fat on insulin resistance. *Curr. Diabetes Rep.* **2002**, *2*, 435–440. [[CrossRef](#)]
101. Karlström, B.E.; Järvi, A.E.; Byberg, L.; Berglund, L.G.; Vessby, B.O.H. Fatty fish in the diet of patients with type 2 diabetes: Comparison of the metabolic effects of foods rich in n-3 and n-6 fatty acids. *Am. J. Clin. Nutr.* **2011**, *94*, 26–33. [[CrossRef](#)] [[PubMed](#)]
102. Shepherd, J.; Packard, C.J.; Grundy, S.M.; Yeshurun, D.; Gotto, A.M.; Taunton, O.D. Effects of saturated and polyunsaturated fat diets on the chemical composition and metabolism of low density lipoproteins in man. *J. Lipid Res.* **1980**, *21*, 91–99. [[PubMed](#)]
103. Hall, W.L. Dietary saturated and unsaturated fats as determinants of blood pressure and vascular function. *Nutr. Res. Rev.* **2009**, *22*, 18–38. [[CrossRef](#)] [[PubMed](#)]
104. Turpeinen, O.; Karvonen, M.J.; Pekkarinen, M.; Miettinen, M.; Elosuo, R.; Paavilainen, E. Dietary prevention of coronary heart disease: The Finnish mental hospital study. *Int. J. Epidemiol.* **1979**, *8*, 99–118. [[CrossRef](#)] [[PubMed](#)]
105. Miettinen, M.; Turpeinen, O.; Karvonen, M.J.; Pekkarinen, M.; Paavilainen, E.; Elosuo, R. Dietary prevention of coronary heart disease in women: The Finnish mental hospital study. *Int. J. Epidemiol.* **1983**, *12*, 17–25. [[CrossRef](#)] [[PubMed](#)]
106. Harris, W.S.; Mozaffarian, D.; Rimm, E.; Kris-Etherton, P.; Rudel, L.L.; Appel, L.J.; Engler, M.M.; Engler, M.B.; Sacks, F. Omega-6 fatty acids and risk for cardiovascular disease: A science advisory from the American Heart Association Nutrition Subcommittee of the Council on Nutrition, Physical Activity, and Metabolism; Council on Cardiovascular Nursing; and Council on Epidemiology and Prevention. *Circulation* **2009**, *119*, 902–907. [[CrossRef](#)] [[PubMed](#)]
107. Hodges, R.E.; Krehl, W.A.; Stone, D.B.; Lopez, A. Dietary carbohydrates and low cholesterol diets: Effects on serum lipids on man. *Am. J. Clin. Nutr.* **1967**, *20*, 198–208. [[PubMed](#)]
108. Anderson, J.W.; Johnstone, B.M.; Cook-Newell, M.E. Meta-analysis of the effects of soy protein intake on serum lipids. *N. Engl. J. Med.* **1995**, *333*, 276–282. [[CrossRef](#)] [[PubMed](#)]
109. Jenkins, D.J.; Wolever, T.M.; Spiller, G.; Buckley, G.; Lam, Y.; Jenkins, A.L.; Josse, R.G. Hypocholesterolemic effect of vegetable protein in a hypocaloric diet. *Atherosclerosis* **1989**, *78*, 99–107. [[CrossRef](#)]
110. Anderson, J.W.; Blake, J.E.; Turner, J.; Smith, B.M. Effects of soy protein on renal function and proteinuria in patients with type 2 diabetes. *Am. J. Clin. Nutr.* **1998**, *68*, 1347S–1353S. [[PubMed](#)]

111. McCarty, M.F. Vegan proteins may reduce risk of cancer, obesity, and cardiovascular disease by promoting increased glucagon activity. *Med. Hypotheses* **1999**, *53*, 459–485. [[CrossRef](#)] [[PubMed](#)]
112. Anderson, J.W.; Smith, B.M.; Washnock, C.S. Cardiovascular and renal benefits of dry bean and soybean intake. *Am. J. Clin. Nutr.* **1999**, *70*, 464S–474S. [[PubMed](#)]
113. Benzie, I.F.F.; Choi, S.-W. Antioxidants in food: Content, measurement, significance, action, cautions, caveats, and research needs. *Adv. Food Nutr. Res.* **2014**, *71*, 1–53. [[CrossRef](#)] [[PubMed](#)]
114. Derdemezis, C.S.; Filippatos, T.D.; Mikhailidis, D.P.; Elisaf, M.S. Review article: Effects of plant sterols and stanols beyond low-density lipoprotein cholesterol lowering. *J. Cardiovasc. Pharmacol. Ther.* **2010**, *15*, 120–134. [[CrossRef](#)] [[PubMed](#)]
115. Strandberg, T.E.; Gylling, H.; Tilvis, R.S.; Miettinen, T.A. Serum plant and other noncholesterol sterols, cholesterol metabolism and 22-year mortality among middle-aged men. *Atherosclerosis* **2009**. [[CrossRef](#)] [[PubMed](#)]
116. Othman, R.A.; Moghadasian, M.H. Beyond cholesterol-lowering effects of plant sterols: Clinical and experimental evidence of anti-inflammatory properties. *Nutr. Rev.* **2011**, *69*, 371–382. [[CrossRef](#)] [[PubMed](#)]
117. Smahelová, A.; Zadáč, Z.; Hyspler, R.; Haas, T. Significance of plant sterols in diabetes. *Vnitřní Lékařství* **2004**, *50*, 147–152. [[PubMed](#)]
118. Office of Dietary Supplements—Dietary Supplement Fact Sheet: Vitamin B₁₂. Available online: <https://ods.od.nih.gov/factsheets/VitaminB12-HealthProfessional/> (accessed on 6 July 2017).
119. Katcher, H.I.; Ferdowsian, H.R.; Hoover, V.J.; Cohen, J.L.; Barnard, N.D. A worksite vegan nutrition program is well-accepted and improves health-related quality of life and work productivity. *Ann. Nutr. Metab.* **2010**, *56*, 245–252. [[CrossRef](#)] [[PubMed](#)]
120. Berkow, S.E.; Barnard, N.; Eckart, J.; Katcher, H. Four therapeutic diets: Adherence and acceptability. *Can. J. Diet. Pract. Res.* **2010**, *71*, 199–204. [[CrossRef](#)] [[PubMed](#)]
121. Le, L.T.; Sabaté, J. Beyond meatless, the health effects of vegan diets: Findings from the Adventist cohorts. *Nutrients* **2014**, *6*, 2131–2147. [[CrossRef](#)] [[PubMed](#)]



© 2017 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<http://creativecommons.org/licenses/by/4.0/>).