

Perspective: Plant-Based Eating Pattern for Type 2 Diabetes Prevention and Treatment: Efficacy, Mechanisms, and Practical Considerations

Meghan A Jardine,¹ Hana Kahleova,² Susan M Levin,¹ Zeeshan Ali,¹ Caroline B Trapp,¹ and Neal D Barnard¹

¹Department of Nutrition, Physicians Committee for Responsible Medicine, Washington, DC, USA; and ²Department of Clinical Research, Physicians Committee for Responsible Medicine, Washington, DC, USA

ABSTRACT

A plant-based eating pattern is associated with a reduced risk of developing type 2 diabetes and is highly effective in its treatment. Diets that emphasize whole grains, vegetables, fruits, and legumes and exclude animal products improve blood glucose concentrations, body weight, plasma lipid concentrations, and blood pressure and play an important role in reducing the risk of cardiovascular and microvascular complications. This article reviews scientific evidence on the effects of plant-based diets for the prevention and treatment of type 2 diabetes. The mechanisms by which plant-based diets improve body weight, insulin sensitivity, and β -cell function are described. Practical considerations including education, nutrition adequacy, and adjusting medications will enhance the success of patients who have diabetes. *Adv Nutr* 2021;00:1–11.

Keywords: type 2 diabetes, plant-based nutrition, vegan diet, vegetarian diet, insulin resistance, diabetes, diet quality

Introduction

Diabetes is a major worldwide health challenge affecting individuals, families, communities, and governments. The International Diabetes Federation estimated that 463 million people (9.3% of the worldwide population) had diabetes in 2019. Prevalence is expected to increase to 578 million (10.4%) by 2030 (1). Globally, diabetes caused 15 million deaths and contributed to 12% of health care expenditures

in 2015 (2). In addition to contributing to mortality, macrovascular and microvascular complications of diabetes greatly reduce quality of life.

Diabetes prevalence has increased in recent decades in the context of significant diet changes, including reduced consumption of vegetables, fruits, and legumes, coupled with increased consumption of animal-derived and processed food products (3). A plant-based eating pattern is associated with a significantly lower prevalence of type 2 diabetes, compared with nonvegetarian diets (4), and there is strong evidence supporting the use of a plant-based eating pattern in clinical practice for individuals with type 2 diabetes. The American Association of Clinical Endocrinologists and the American College of Endocrinology, as well as the American College of Lifestyle Medicine, recommend a plant-based eating pattern as a key component of lifestyle therapy for patients with type 2 diabetes (5, 6). Both the American and Canadian Diabetes Associations include vegetarian and vegan eating patterns among those shown to improve glycemic control, body weight, and cardiovascular risk factors (6, 7). In addition to these organizations that support a plant-based diet for diabetes, the USDA lists a Healthy Vegetarian Dietary Pattern as an example of a healthy meal plan in the 2020–2025 Dietary Guidelines for Americans (8).

This article was funded by the Physicians Committee for Responsible Medicine, Washington DC, USA.

Author disclosures: MJ, HK, SL, ZA, and CT are employees of the Physicians Committee for Responsible Medicine in Washington, DC, a nonprofit organization providing education, research, and medical services related to nutrition. NDB is an Adjunct Professor of Medicine at the George Washington University School of Medicine. He serves without compensation as the President of the Physicians Committee for Responsible Medicine and the Barnard Medical Center in Washington, DC, nonprofit organizations providing educational, research, and medical services related to nutrition. He writes books and articles and gives lectures related to nutrition and health and has received royalties and honoraria from these sources.

Perspective articles allow authors to take a position on a topic of current major importance or controversy in the field of nutrition. As such, these articles could include statements based on author opinions or point of view. Opinions expressed in Perspective articles are those of the author and are not attributable to the funder(s) or the sponsor(s) or the publisher, Editor, or Editorial Board of *Advances in Nutrition*. Individuals with different positions on the topic of a Perspective are invited to submit their comments in the form of a Perspectives article or in a Letter to the Editor.

Address correspondence to MAJ (e-mail: meghan.jardine@sbcglobal.net).

Abbreviations used: AND, Academy of Nutrition and Dietetics; AHS-2, Adventist Health Study-2; CVD, cardiovascular disease; DASH, Dietary Approaches for Stopping Hypertension; HbA1c, glycated hemoglobin.

The aim of this article is to provide an overview of the evidence on the prevention and treatment of type 2 diabetes with a plant-based eating pattern, the mechanistic actions by which a plant-based eating pattern improves insulin sensitivity and weight management, and considerations in recommending a plant-based eating pattern. This article includes earlier evidence that provides a foundation for more current research. It also includes recent studies on the mechanistic actions that demonstrate a plant-based diet improves clinical outcomes for diabetes.

“Plant-based” is a generic term that may refer to diets consisting mainly of grains, vegetables, legumes, fruits, nuts, seeds, and products made from them. Vegetarian diets exclude meat. Subsets of vegetarian diets are lacto-ovo vegetarian diets, which include dairy products and eggs, and vegan diets, which exclude all animal products (9). Hereafter in this article, the term “plant-based” will refer to vegetarian (including lacto-ovo vegetarian and vegan) diets, unless otherwise indicated.

A Plant-Based Eating Pattern Is Associated with Reduced Risk of Type 2 Diabetes

Observational studies in widely diverse locales have identified large reductions in diabetes risk among populations consuming vegan and vegetarian eating patterns, compared with other dietary patterns.

Many Seventh-day Adventists limit or avoid meat and other animal products, whereas others do not, providing a unique opportunity to study the effects of different diet patterns (10). In 1985, Snowdon and Phillips first reported a strongly positive association between meat consumption and diabetes prevalence in 25,698 men and women from California who were followed for 21 y in the Adventist Mortality Study (11). Fifty per cent of this cohort reported following a vegetarian diet. Age-adjusted diabetes prevalence ratios in participants who consumed meat 6 or more times per week were 1.9 for men and 1.6 for women, compared with vegetarians (11). Fraser reported similar findings from the Adventist Health Study, in which men and women meat consumers reported a 97% (OR: 1.97; 95% CI: 1.56, 2.46, $P = 0.0001$) and 93% (OR: 1.93; 95% CI: 1.65, 2.25, $P = 0.0001$) greater diabetes risk, respectively, compared with vegetarian participants (10). Vang et al. (12) followed 8401 Adventists, all of whom were free of diabetes at study onset, for 17 y. After controlling for differences in body weight, those who consumed any type of meat (including poultry) at least once a week had a 38% increased risk of developing diabetes during the follow-up period, compared with those who consumed no meat (12).

The Adventist Health Study-2 (AHS-2), which started in 2002, included 22,434 men and 38,469 women living throughout the USA and Canada; 65.5% were non-Hispanic white and 26.9% were black (13). Compared with nonvegetarians, the OR for diabetes prevalence was 49% (0.51; 95% CI: 0.40, 0.66) less among vegans and 46% (0.54; 95% CI: 0.49, 0.60) less among lacto-ovo vegetarians, after adjustments for BMI and other lifestyle variables (13).

Diabetes prevalence among those limiting meat consumption to fish was 30% (0.70; 95% CI: 0.61, 0.80) less and those eating meat less than once per week was 24% (0.76; 95% CI: 0.65, 0.90) less compared with the nonvegetarians. The vegan participants consumed 33% more fruits and vegetables than the nonvegetarians and avoided animal products that are high in saturated fat and are associated with insulin resistance (13).

In a prospective analysis of this same cohort (AHS-2) of 15,200 men and 26,187 women (17% black) who did not have diabetes at baseline, vegan and lacto-ovo vegetarians had a 77% and 54% reduction in risk of developing diabetes, respectively (4). After controlling for BMI and other lifestyle factors, odds were 62% less for vegans and 38% less for the lacto-ovo vegetarians. The reduced risk was particularly pronounced among black vegans who, in the adjusted analysis, had a 70% reduced risk, and black lacto-ovo vegetarians (52% reduced risk), compared with nonvegetarians (4). The Adventist studies suggest a strong reduction in diabetes risk as a result of avoiding animal-derived products that is, in part, independent of the diet's beneficial effects on body weight.

Other cohort studies have reported similar findings. A Harvard study that included 26,357 men from the Health Professionals Follow-Up Study (1986–2006), 48,709 women from the Nurses' Health Study (1986–2006), and 74,077 women from the Nurses' Health Study II (1991–2007) found that increasing meat by half a serving per day was associated with a 48% (1.48; 95% CI: 1.37, 1.59) increase in diabetes risk over a 4-y period (14). Decreasing meat portions by half a serving a day was associated with a reported 14% (0.86; 95% CI: 0.80, 0.93) reduction in diabetes risk. In another report that included over 200,000 men and women health professionals from the same Harvard cohorts, 16,162 participants developed diabetes during 4,102,369 person-years of follow-up (15). It was reported that when participants followed a healthy plant-based diet that focused on whole grains, fruits, and vegetables, and was low in refined grains, sugar-sweetened beverages, and red and processed meats, there was an associated 34% reduction in diabetes risk (15).

Similarly, the European Prospective Investigation into Cancer and Nutrition (EPIC) study's InterAct Project followed 340,234 adults from 8 European countries for 11.7 y and reported significant associations between meat consumption and type 2 diabetes risk (16). For men, consumption of red and processed meat increased diabetes risk, whereas for women there was a positive association between total meat and poultry consumption (16).

In the Rotterdam study, a high intake of plant-derived products and a low intake of animal products was associated with lower insulin resistance, prediabetes, and type 2 diabetes (17). These outcomes remained significant after adjustment for body weight (17). The authors proposed that dietary guidelines should recommend a plant-based diet to reduce the burden of type 2 diabetes.

In Taiwan, the Tzu Chi Health Study found significant reductions in diabetes risk among vegetarian Buddhists.

Compared with the omnivore group (N = 2900), the vegetarian group (N = 1484) had a 51% lower risk in men (OR: 0.49; 95% CI: 0.28, 0.89) and a 75% lower risk in postmenopausal women (OR: 0.25; 95% CI: 0.15, 0.42) for type 2 diabetes after controlling for BMI and other lifestyle factors (18). It should be noted that “omnivores” in this population consume relatively little meat or fish by Western standards. The vegetarian group consumed more soy products, total and green leafy vegetables, nuts, and whole grains, less tea, and a similar amount of dairy products and fruits, compared with the omnivores (18). Within the vegetarian group were a small number of vegans (N = 69) among whom no cases of diabetes were found.

A Plant-Based Eating Pattern Is Effective for Treating Type 2 Diabetes

Plant-based diets, particularly vegan diets, improve glycemic control, body weight, and cardiovascular risk factors in individuals with type 2 diabetes. Each of these is central to diabetes management and is described below. A meta-analysis of 6 randomized controlled trials (N = 255) demonstrated that vegetarian diets were associated with a 0.4% greater reduction in glycated hemoglobin (HbA1c) when compared with other prescribed eating patterns for diabetes (19).

Low-fat, plant-based diets improve glycemic control. Various formulations have been tested for many years. In 1979, a 16-d, mainly plant-based, dietary intervention designed to maintain body weight was tested in a closed setting. Nine out of 20 men with type 2 diabetes were able to eliminate insulin, and the other 11 were able to reduce it by 60% after following a high-fiber, high-carbohydrate diet (65 g of fiber, 70% calories from carbohydrate, 21% from protein, 9% from fat) (20).

A 22-wk randomized controlled trial compared a low-fat, vegan diet (N = 49) to a conventional portion-controlled diet (N = 50). The vegan diet (~10% of energy from fat, 15% protein, and 75% carbohydrate) excluded animal products and favored low-fat, low-glycemic-index foods. The portion-controlled diet (15–20% protein, <7% saturated fat, 60–70% carbohydrate and monounsaturated fats) was individualized, based on body weight and plasma lipid concentrations, following 2003 American Diabetes Association guidelines (21). Those with a BMI >25 kg/m² were prescribed energy intake deficits of 500–1000 kcal/d. Among participants who made no medication changes, the vegan group had a significantly greater reduction in HbA1c (1.23% compared with 0.38%, [P = 0.01]) (22). The Pearson’s correlation of weight change with HbA1c change was $r = 0.51$, $P < 0.0001$ within the vegan group, suggesting that factors other than weight changes influence glycemic control. The authors proposed that high-fat diets increase lipid accumulation in the skeletal muscle, which contributes to insulin resistance by reducing mitochondrial activity.

Vegan diets have been shown to improve glycemic control in Asian populations that are already consuming diets that are generally rich in plant-derived foods. In a Korean

study, 93 volunteers with type 2 diabetes were randomly assigned to either a vegan diet (N = 46) or a conventional diet recommended by the Korean Diabetes Association (KDA) 2011 (N = 47) for 12 wk (23). The vegan diet consisted of whole grains, vegetables, fruit, and legumes. The mean HbA1c concentrations fell in both groups, however, the reductions were greater for the vegan group (–0.5% compared with –0.2%; P -interaction = 0.17). These results were greater in the participants who closely followed the prescribed eating patterns (–0.9% compared with –0.3%) (23).

Potential Mechanisms by Which Plant-Based Eating Patterns Affect Insulin Resistance and Weight Management

Insulin resistance

Insulin resistance and subsequent impairment in β -cell function are the hallmarks of type 2 diabetes pathophysiology (24). Plant-based eating patterns are beneficial for patients with diabetes by improving insulin sensitivity and improving body weight. Insulin resistance is caused by lipid accumulation within muscle and liver cells that typically begins many years before the diagnosis of type 2 diabetes. This lipid accumulation is highly responsive to diet changes. High-fat diets downregulate the genes required for mitochondrial oxidative phosphorylation in skeletal muscle (25). High-fat diets also appear to disrupt the normal intestinal barrier to bacterial endotoxins that, entering the bloodstream, may disrupt glucose oxidation processes (26). The effects of changes in fat intake on glycemic control can be observed, not only after long-term interventions, but after single meals; high-fat meals can cause postprandial elevations in plasma glucose that can remain high for a long period of time (27).

In a case-control study, Goff et al. (28) compared 24 healthy vegans to 25 healthy omnivores matched for sex, age, BMI, per cent body fat, energy intake, and physical activity levels. Individuals who followed a vegan diet had significantly lower intramyocellular lipid concentration, which was associated with 32% greater homeostatic model assessment of β -cell function (28). In a randomized trial in overweight nondiabetic individuals without limitations on energy or carbohydrate intake, a low-fat vegan diet reduced hepatocellular lipid concentrations by 34.4% and intramyocellular lipid concentrations by 10.4%. These changes in hepatocellular and intramyocellular lipid concentrations correlated with changes in insulin resistance (both $r = 0.51$; $P = 0.01$) (29). These findings suggest that low-fat, plant-based (especially vegan) diets improve glycemic control because of their ability to reduce lipid accumulation in muscle and liver, in addition to their effects on body weight.

Plant-based diets may also improve β -cell function. In a randomized trial, 75 participants who were overweight or obese were assigned to a low-fat plant-based diet or no diet changes for 16 wk. Meal-stimulated insulin secretion markedly increased in the intervention group compared

with controls (interaction between group and time, $G \times t$ [$P < 0.001$]) (30). This study demonstrates the potential that a plant-based eating pattern can play a role in reversing β -cell dysfunction and peripheral insulin resistance in patients with type 2 diabetes.

Weight management

Weight management plays an important role in improving insulin sensitivity and glycemic control and reducing cardiovascular disease (CVD) risk factors (31). Excess body weight is associated with risk of CVD and all-cause mortality among people with type 2 diabetes (32). Individuals following vegetarian, especially vegan, diets have lower mean BMIs, compared with nonvegetarians (33). Population studies have revealed that body weight increases progressively with increased meat consumption (10, 34).

In addition to preventing weight gain, a plant-based eating pattern is an effective weight management tool (35, 36). In randomized trials, plant-based interventions for patients with type 2 diabetes have resulted in greater weight loss compared with control diets containing animal products (22, 23, 37), with a major portion of weight loss attributable to a loss of visceral fat, a major advantage for reducing insulin resistance and inflammation (23, 37). The BROAD study demonstrated significant weight loss using a low-fat (~7–15% of calories from fat), plant-based diet in overweight individuals with ≥ 1 of the following comorbidities: type 2 diabetes, ischemic heart disease, hypertension, or hypercholesterolemia (38). Sixty-five adults (aged 35–70 y) were randomly assigned to the plant-based diet or usual care. The reduction in BMI at 6 mo was greater in the plant-based group compared with the usual-care group (4.4 compared with 0.4, difference: 3.9) (95% CI: ± 1 , $P < 0.0001$). At 12 mo, the reduction in BMI in the plant-based group was 4.2 (± 0.8). The program did not require restrictions on portion sizes, yet participants reported feeling satisfied, potentially enhancing compliance (38).

In a randomized trial of individuals with type 2 diabetes, a low-fat vegan diet prescribed with no energy-intake limits was associated with greater weight loss at 22 wk, compared with a conventional diet that required energy-intake restrictions (–6.5 kg compared with –3.1 kg [$P < 0.001$]) (22). At 74 wk, weight loss remained significant within each diet group but not significantly different between groups (–4.4 kg in the vegan group and –3.0 kg in the conventional diet group, $P = 0.25$) (39).

In a 24-wk trial, researchers tested the effects of plant-based diets when used in combination with other interventions, comparing an isocaloric vegetarian diet (animal products were limited to 1 serving of low-fat yogurt per day) with a conventional diabetes diet that followed the guidelines of the Diabetes and Nutrition Study Group of the European Association for the Study of Diabetes (37). Aerobic exercise was added to both study groups for the second 12 wk of the study. The macronutrient breakdown was 60% of kcal from carbohydrate, 15% protein, and 25% fat for the

vegetarian intervention and 50% from carbohydrate, 20% protein, and $<30\%$ fat ($\leq 7\%$ saturated fat, <200 mg/d of cholesterol) for the conventional group. Both diets restricted calories by 500 kcal/d, which was individualized based on indirect calorimetry (37). Meals were provided to the participants in both groups, supporting adherence to the prescribed diet interventions. The vegetarian intervention resulted in more weight loss (–6.2 kg; 95% CI: –6.6, –5.3 compared with –3.2 kg; 95% CI: –3.7, –2.5; interaction group \times time $P = 0.001$) and greater improvements in insulin sensitivity (30%; 95% CI: 24.5, 39 compared with 20%; 95% CI: 14, 25). Reductions in visceral and subcutaneous fat were significantly greater ($P = 0.007$ and $P = 0.02$, respectively) in the vegetarian group (37).

Weight loss on plant-based diets appears to be attributable to 2 main diet effects. First, increased fiber and carbohydrate intake and reduced fat intake lead to a reduction in the energy density of the diet. Second, plant-based diets have been shown to increase postprandial metabolism (the thermic effect of food) (36). In a randomized trial, participants with a diagnosis of overweight or obesity (BMI 28–40) were assigned to either a low-fat, vegan diet or to make no dietary changes for 16 wk. The vegan group lost 5.9 kg (95% CI: 5.0, 6.7 kg; $P < 0.001$) and its thermic effect of food (measured by indirect calorimetry) increased by 14.1% (95% CI: 6.5, 20.4; $P < 0.001$). These changes were associated with reductions in hepatocellular and intramyocellular fat and increased insulin sensitivity (29).

Plant-Based Eating Pattern for Macrovascular and Microvascular Complications of Diabetes

CVD

The effects of plant-based diets on glycemia, body weight, plasma lipids, and blood pressure collectively reduce the risk of CVD, the leading cause of morbidity and mortality in diabetes patients. CVD encompasses coronary heart disease, cerebrovascular disease, and peripheral arterial disease (32). A meta-analysis of 9 randomized controlled trials in patients with type 2 diabetes ($N = 664$), comparing vegetarian interventions with control diets, showed significant improvements in CVD risk factors, including lipids, blood pressure, glycemic control, body weight, and abdominal adiposity (40).

In addition to being associated with reduced CVD risk, a plant-based diet may help reverse atherosclerotic plaques. Ornish et al. demonstrated significant regression in coronary artery stenosis in patients with moderate to severe coronary artery disease. Participants were randomly assigned to usual care or a low-fat vegetarian diet combined with exercise, stress management, and smoking cessation. After 5 y there was a mean reduction in atherosclerotic stenosis in the vegetarian group, whereas there was a progression of atherosclerosis in the control group. The control group was also more likely to have required coronary angioplasty and bypass surgery than the vegetarian group (41).

Microvascular complications

Chronic kidney disease.

Chronic kidney disease is increasingly prevalent, and diabetes accounts for 44% of all new cases; 20–40% of patients with diabetes have chronic kidney disease (42). A Western dietary pattern, characterized by a high consumption of red meat, fat, salt, and sugar, is a major contributor to metabolic disturbances leading to the progression of kidney disease (43). In the Nurses' Health Study, women with mild renal insufficiency at baseline had a significantly greater reduction in renal function with greater consumption of animal protein (especially from meat) over an 11-y period (44). In contrast, a 24-y follow-up of 14,868 adults in the Atherosclerosis Risk and Communities Study found that a higher adherence to a healthy plant-based diet was associated with a lower risk of chronic kidney disease (45).

Several studies have reported a reduction of urinary albumin excretion in patients with diabetic nephropathy when consuming a plant-based or reduced-red-meat diet (46–48). One study showed a 54% decrease in urinary albumin in patients with type 1 diabetes after 8 wk of a plant-based diet (48). The study by Barnard et al. described above in which patients with type 2 diabetes followed a low-fat vegan diet, reported a significant reduction in urinary albumin in participants following a low-fat vegan diet, with no change in the control group following a portion-controlled diet (22).

Neuropathy.

More than 50% of individuals with diabetes suffer from neuropathy (49). Common clinical manifestations include pain, insensitivity to injury, orthostatic hypotension, cardiac autonomic neuropathy, gastroparesis, and erectile dysfunction (50). Diabetic neuropathy can lead to sleep disturbances, depression, and anxiety (51), and eventually amputations (52). Current treatment of diabetic neuropathy includes glycemic control to slow disease progression and medications for neuropathic pain (42). There is no pharmacological treatment that reverses nerve damage caused by neuropathy, apart from methods for improving glycemic control.

A 20-wk randomized, controlled trial using a low-fat, vegan intervention demonstrated improved nerve function, as measured by electrochemical skin conductance in the foot, and reduced pain, compared with an untreated control group. (53). These results are consistent with 2 smaller studies that used a vegan diet, one combined with exercise in which painful neuropathy symptoms were eliminated in 17 out of 21 patients (54) and another in which cutaneous reinnervation and reduced pain were reported in 30 individuals with impaired glucose tolerance (55).

Diabetic retinopathy.

The influence of a plant-based diet on diabetic retinopathy has not been studied. However, a plant-based diet is effective in controlling risk factors for diabetic retinopathy, including

glycemia (19), blood pressure (56), and lipids (57). Studies have also demonstrated that diets high in fruits, vegetables, and dietary fiber are associated with a reduction in diabetic retinopathy (58).

Comparing a Plant-Based Diet with Key Aspects of Other Dietary Approaches for Type 2 Diabetes

Very-low-calorie diets and metabolic surgery

Reversal of insulin resistance and β -cell dysfunction with associated reductions in pancreatic and hepatic triacylglycerol stores has been demonstrated in patients with type 2 diabetes with very-low-calorie diets (600 kcal/d) or bariatric surgery (59). These interventions are not free from clinical challenges or risk. Very-low-calorie diets require medical management by trained practitioners and may only be appropriate in select patients. Further, the long-term sustainability of such diets is limited; they are frequently followed by progressive weight gain (60, 61). Adverse effects of metabolic surgery include mortality (rates 0.1–0.5%), dumping syndrome, nutritional deficiencies, increased risk of depression, and substance abuse (62). A plant-based diet may provide improvements for diabetes without intentional caloric reduction and may do so independently of weight loss.

Mediterranean and Dietary Approaches for Stopping Hypertension

Mediterranean and Dietary Approaches for Stopping Hypertension (DASH) diets both emphasize the intake of plant-based foods with controlled portions of animal products. Mediterranean diets have been tested for the prevention and treatment of diabetes. Like a plant-based diet, Mediterranean diets emphasize the consumption of fruits, vegetables, whole grains, and legumes, and reduce meat, refined grains, and sugar, while allowing modest amounts of animal products. The term “Mediterranean diet” may be interpreted differently by different people. In research studies, the term refers to a diet that includes abundant plant-based foods, favors olive oil as the primary source of fat, and includes low to moderate amounts of meat, dairy products, eggs, and wine (63). A high score (range 0 to 9) for Mediterranean diet-style intake, measured by study participants' consumption of fruits, vegetables, whole grains, legumes, nuts, and fish, and the ratio of MUFAs to SFAs, was associated with a 30% reduced risk of developing diabetes in over 25,000 women followed for 20 y. The high Mediterranean diet scores were associated with lower biomarkers of insulin resistance (adiposity, lipoprotein metabolism, and inflammation) (64). A meta-analysis of 9 randomized controlled trials with 1178 patients with type 2 diabetes compared a Mediterranean diet with control diets resulting in a greater reduction in HbA1c (mean difference, -0.30 ; 95% CI: -0.46 , -0.14). There were also improvements in body weight and cardiovascular risk factors (65).

The outcomes for weight loss using a Mediterranean diet have been mixed. Although a 2016 systematic review reported that clinical trials using Mediterranean diets showed

TABLE 1 Dietary sources of key nutrients on a plant-based diet

Nutrient	Dietary sources	Importance for plant-based nutrition and diabetes
Protein	Legumes, whole grains, vegetables, nuts, and seeds	Consuming more animal protein may increase the risk of type 2 diabetes compared with consuming less and compared with replacing the animal sources with vegetable protein sources (66) (67)
ω -3 fatty acids	Seeds (hemp, chia, flax), walnuts, leafy green vegetables, microalgae, soybeans, wheat germ	A low-fat, plant-based diet will be lower in ω -6 fatty acids, thus allowing for a more ideal ratio to ω -3 fatty acids, with a lower ratio being preferable (68)
Iron	Legumes; leafy greens such as spinach, Swiss chard, kale, collards, and beet greens; raisins; blackstrap molasses; pumpkin seeds	Iron deficiencies do not manifest in those following a plant-based diet any more than in those following other diet patterns (9). Insulin resistance may be increased by heme iron found only in animal products (69)
Zinc	Legumes, soybeans, nuts, seeds, whole grains	Zinc deficiencies do not manifest in those following a plant-based diet any more than in those following other dietary patterns (9)
Iodine	Sea vegetables, iodized salt, supplements	Iodine is important for thyroid health
Calcium	Kale, collard greens, bok choy, broccoli, green cabbage, Brussels sprouts, fortified plant milks and juices, calcium-set tofu, almonds, sesame seeds	The absorption rate of calcium from greens is sometimes twice as high as calcium from cow milk, which has an absorption rate of ~30% (70)
Vitamin D	Sunshine exposure and supplements	Vitamin D status may improve inflammation and oxidative stress among diabetes patients (71)
Vitamin B-12	Fortified foods and supplements	Anyone over the age of 50 and taking certain medications, including metformin, could benefit from taking a vitamin B-12 supplement, regardless of eating pattern (72)

significant weight loss, all of the included studies used exercise or calorie restriction, confounding the effects of the dietary change (73). The well-controlled Lyon Diet Heart Study (74) and the Prevención con Dieta Mediterránea (PREDIMED) study (75) led to no clinically significant weight loss. In a crossover trial including 62 overweight adults, a low-fat vegan diet led to significantly greater weight loss over a 16-wk intervention period, compared with a Mediterranean diet (76).

The DASH diet was developed to lower blood pressure without medications. The eating pattern emphasizes fruit, vegetables, fat-free/low-fat dairy, whole grains, nuts, and legumes, and limits saturated fat, cholesterol, red and processed meats, sweets, added sugars, salt, and sugar-sweetened beverages. In an umbrella review of systematic reviews and meta-analyses on cardiometabolic outcomes, the DASH diet was associated with a significant reduced risk of diabetes (RR: 0.82; 95% CI: 0.74, 0.92) as well as significant reductions in CVD, coronary heart disease, and stroke, and reductions in blood pressure and body weight. There were no significant changes in HDL cholesterol, triglycerides, fasting blood glucose, HOMA-IR, or C-reactive protein. This review included 2 controlled trials evaluating the DASH diet in individuals with diabetes which resulted in a reduction in HbA1c (-0.53%; 95% CI: -0.62, -0.43) and fasting insulin (-0.15 μ U/mL; 95% CI: -0.22, -0.08) (77).

The absence of any need for portion control is an advantage of a low-fat vegan diet over Mediterranean and DASH eating patterns. The DASH diet does not appear to provide the reduction in inflammation and improvement in insulin sensitivity that has been documented in the vegan diet. Given that even small amounts of animal products may increase the risk of diabetes (in the AHS-2, the vegan diet provided

a major advantage in reducing the risk of diabetes compared with the lacto-ovo vegetarian or the semivegetarian where meat consumption was limited to ≥ 1 time a month and < 1 time/wk), there are theoretical advantages to avoiding animal products altogether.

Low-carbohydrate eating pattern

Low-carbohydrate diets cause weight loss in overweight individuals, although they are no more effective for weight loss than plant-based diets or other dietary approaches in 1-y comparisons (78, 79). The common idea that low-carbohydrate diets suppress appetite was challenged in a 2021 metabolic-ward study (80). Twenty young overweight adults were assigned to a low-fat, vegan diet (10% fat, 75% carbohydrate) or a low-carbohydrate diet (76% fat, 10% carbohydrate) for 2 wk, then switched to the opposite diet for an additional 2 wk (80). The vegan diet led to a much greater drop in calorie intake; energy intake was 689 (\pm 73) kcal/d lower during the vegan phase, compared with the low-carbohydrate phase ($P < 0.0001$) (80).

In individuals with diabetes, low-carbohydrate diets may cause an initial reduction in blood glucose values, but these benefits are often largely gone by 12 mo (81).

There may be some safety concerns with a low-carbohydrate diet. They often elevate plasma LDL cholesterol concentrations, with widely varying effects between individuals (82). Because low-carbohydrate diets restrict or eliminate fruits, whole grains, legumes, and other healthful foods, and are often high in saturated fats, they raise concerns about long-term risk of cancer, Alzheimer's disease, and other conditions. Long-term use of low-carbohydrate diets is associated with increased all-cause mortality (83).

TABLE 2 Guidelines for implementing plant-based nutrition in clinical practice**Consider patient referral**

Health care providers are encouraged to refer patients to a registered dietitian nutritionist (RDN) who specializes in plant-based nutrition. RDNs are trained to do a thorough nutrition assessment as well as education and counseling. Medicare and most insurance plans cover medical nutrition therapy (MNT)

Patient assessment for plant-based nutrition

- Readiness for change
- Assess current eating pattern
- Family and social support
- Cultural/religious beliefs
- Education and socioeconomic traits
- Lifestyle: sleep, exercise, tobacco, alcohol, and substance use
- Emotional well-being
- Use of glucose monitoring (self-monitoring of blood glucose/continuous glucose monitoring)
- Culinary skills
- Frequency of eating out and/or traveling
- Current dietary habits:
 - Plant-based eating habits: fiber, servings of fruit, vegetables, whole grains, legumes, nuts, and seeds
 - Intake of animal products and refined carbohydrates: chicken, fish, red meat, processed meat, eggs, dairy (including cheese), fried food, refined sugar, sugar-sweetened beverages, and processed and fast food

Note: this is in addition to a comprehensive medical evaluation described in the ADA Standards of Care that includes medical and family history, medications, vaccinations, and technology use (137).

Education: principles of plant-based nutrition

- Focus on the 4 food groups (see Table 3)
 - 2–4 servings of fruit
 - 3–5 servings of vegetables
 - 5–8 servings of whole grains
 - 2 or more servings of legumes
- Limit added oils, fried foods, and other high-fat foods
- Limit nuts and seeds to 1 ounce per day (scant $\frac{1}{4}$ cup or 2 tablespoons of nut butters)
- Aim to consume 40 g of fiber per day. A gradual intake may be necessary to minimize gastrointestinal symptoms
- Avoid all animal products including meats, fish, dairy, and eggs
- Supplement with vitamin B-12: 500–1000 μ 2–3 times per week (5)

Methods of intervention

- Meal planning
 - Grocery shopping and label reading
 - Cooking techniques
- Self-monitoring of blood glucose
- Concerns and treatment of changes in blood glucose with diet intervention (treatment of hypoglycemia)
- Have patient education materials:
 - Handouts
 - Books
 - Cookbooks
 - List of appropriate websites
- Consider using telehealth to provide care and education and send motivational messages to patients on a regular basis
- Provide group classes:
 - Ongoing support groups
 - Cooking classes

Topics to cover:

Follow-up and ongoing support

- Monitor body weight, self-monitoring of blood glucose, HbA1c, lipids, and blood pressure
- Assess for potential of medication-induced hypoglycemia or hypotension, and adjust medical therapy as needed
- Review diet records
- Use failures as opportunities for problem-solving and skill development

ADA, American Diabetes Association; HbA1c, glycated hemoglobin.

In terms of safety, plant-based diets reduce diabetes risk without untoward side effects. The same is true for treatment of diabetes with some precautions for hypoglycemia. In the study by Barnard et al., 43% of the subjects in the low-fat vegan group had to reduce or eliminate their diabetes

medications in response to hypoglycemia (22). Low blood glucose concentrations can be avoided by frequent glucose monitoring, patient education, and adjusting medications as needed. Plant-based eating patterns have been found to have a high diet quality and are nutritionally adequate.

TABLE 3 Plant-based nutrition food groups

Food group	Foods	Serving size	Servings per day
Vegetables: include a variety of colors from the rainbow: red, yellow, orange, green, and purple	Artichokes, asparagus, beets, bok choy, broccoli, Brussels sprouts, cabbage (all colors), carrots, cauliflower, celery, collards, cucumbers, eggplant, endive, garlic, ginger, green beans, kale, lettuce, mustard and turnip greens, okra, onions, parsnips, peppers, potatoes (all varieties), pumpkin, radishes, spinach, squash (all varieties), tomatoes, turnip, watercress	1 cup raw ½ cup cooked	≥3 to 5 or more servings or unlimited
Fruits	Apples, apricots, bananas, berries, citrus fruit, cherries, dates, grapes, kiwi fruit, kumquats, mangos, papayas, peaches, pears, pineapples, plums, pomegranates, melons, raisins	1 medium 1 cup chopped 2 tablespoons dried	2 to 4 or more servings
Whole grains: choose whole grain versus refined as much as possible	Amaranth, barley, bread, buckwheat, bulgur, cereal (hot or cold), corn, millet, oats (rolled, steel cut, or groats), pasta, popcorn (air-popped), quinoa and tortillas	½ cup any cooked grain ¾ cup dry cereal 1 slice bread 1 tortilla	5 to 8 or more servings
Legumes	Anasazi beans, adzuki beans, baked beans, black beans, chickpeas, dahl, hummus, lima beans, lentils, navy beans, peas, pinto beans, soy milk, tempeh, and tofu	½ cup hummus ¼ cup dry legumes ½ cup cooked beans, lentils, peas, tofu, tempeh 1 cup soy milk	2 or more servings
Nuts and seeds	Almonds, Brazil nuts, cashews, hazelnuts, macadamia, peanuts, pinons (pine nuts), pistachios, walnuts, and seeds: pumpkin, sunflower, hemp, flax, and chia	Limit to: 1 ounce 2 tablespoons nut butter	1 serving or less
Herbs and spices	Fresh or dried herbs and spices without salt added	unlimited	
Water and tea	Water or herbal teas without sugar added	8 ounces	8 servings

According to the Academy of Nutrition and Dietetics (AND), “appropriately planned vegetarian, including vegan, diets are healthful, nutritionally adequate (9).”

Considerations for the Use of a Plant-Based Diet for Diabetes

Caregivers should help patients who have (or are at risk of) diabetes to understand the benefits of a plant-based eating pattern and encourage a trial. Patients are typically willing to try a plant-based diet when its rationale has been explained, and they can adapt nutrition guidelines to suit their preferences (84). The fact that a plant-based diet does not require limits on calories, carbohydrates, or portions makes it appealing, and most patients find it to be no more challenging than other therapeutic diets (85). Further, the acceptability of a low-fat plant-based diet has been shown to be comparable to other therapeutic eating patterns in randomized trials with individuals with diabetes (85). Adopting a plant-based diet is often highly motivating due to the improvements with weight loss, glycemic control, and enhanced quality of life (86).

According to AND, vegan and vegetarian diets are nutritionally adequate and may provide health benefits for the prevention and treatment of certain diseases, including type 2 diabetes (9). Plants provide all required vitamins and minerals except vitamin B-12. Vitamin B-12 is made neither by plants nor animals but rather by microbes. Although cereals, plant-based milk, and other plant-based

foods may be fortified with vitamin B-12, a B-12 supplement will ensure adequacy. AND recommends adults following a plant-based diet take 500 to 1000 μg several times per week (9). Metformin use increases the risk of vitamin B-12 deficiency, which can contribute to symptoms of neuropathy. Periodic testing of vitamin B-12 status is suggested by the American Diabetes Association (ADA) (87). **Table 1** is a resource for dietary sources of key nutrients on a plant-based diet.

Once patients have a good list of meal possibilities, the next step is to adopt a fully vegan diet for 3 wk. This “test drive” is short enough to be readily approachable, particularly since patients have already drawn up a list of suitable foods, but it is long enough for health benefits to be noticed. For maximum impact, it is best to ask patients to (1) avoid all animal products, (2) minimize the use of oils and oily foods, and (3) favor foods that are high in fiber.

Involving the family will shore up support for the diet changes at home and diminish potential resistance. Teaching in groups is often particularly effective; groups bring added experiences, helpful questions, social support, and, as time goes on, validation for the effectiveness of the diet change. Additional guidance on how to deal with social situations and traveling will ensure success. Handouts, books, videos, and recipes should be readily available in waiting rooms and examination rooms or made accessible online. **Table 2** provides guidelines for implementing plant-based nutrition in clinical practice. **Table 3** has a list

of plant-based nutrition food groups and recommended servings.

Adjusting medications in response to a plant-based diet

It is essential to help patients anticipate blood glucose changes in response to the new eating pattern. Hypoglycemia is common among individuals treated with insulin or sulfonylureas as they improve their diets, often necessitating medication reduction or discontinuation. There is a need for the development of evidence-based deprescribing guidelines for patients with type 2 diabetes who need to reduce medication in response to episodes of hypoglycemia in the context of a plant-based diet.

Conclusion

Observational studies and randomized controlled trials support the benefits of plant-based nutrition for diabetes. The consumption of whole grains, legumes, fruits, and vegetables in conjunction with the elimination of animal products reduces the risk of developing type 2 diabetes. In individuals with type 2 diabetes, a low-fat, plant-based diet improves body weight, glycemic control, plasma lipid concentrations, and blood pressure, while reducing the risk of CVD and microvascular complications.

Health care providers should feel confident in counseling their patients to follow a plant-based eating pattern and should be prepared to provide education and support to improve their patients' diabetes outcomes, general health, and psychological well-being.

Further research on the effects of a plant-based diet for the prevention of nephropathy and retinopathy, as well as on their role in improving management of type 1 diabetes, would be helpful. High-quality studies comparing vegan and vegetarian eating patterns with DASH and or the Mediterranean eating patterns would provide more detail on how various eating patterns affect diabetes outcomes. Guidelines on reducing reliance on antihyperglycemic medications in response to plant-based lifestyle therapy would assist health care providers in reducing the risk of hypoglycemia and other untoward side effects associated with overmedication.

Acknowledgments

The authors' contributions were as follows: MAJ, developed the outline and focus of the article and was responsible for writing the final manuscript; HK, provided content on prevention, treatment, and complications of diabetes with a plant-based diet; SML, worked on the nutrition content as well as providing editing for each draft; ZA, researched and wrote content on the mechanisms section of the article; CBT, wrote section adjusting medications as well as editing to the final manuscript; NDB, added content on complications of diabetes, the mechanisms section as well as providing edits to the final manuscript; and all authors: read and approved the final manuscript.

References

1. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, Colagiuri S, Guariguata L, Motala AA, Ogurtsova K, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: results from the International Diabetes Federation Diabetes Atlas, 9th edition. *Diabetes Res Clin Pract* 2019;157:107843.
2. Papatheodorou K, Banach M, Bekiari E, Rizzo M, Edmonds M. Complications of diabetes 2017. *J Diabetes Res* 2018;2018:3086167.
3. Willett W, Rockström J, Loken B, Springmann M, Lang T, Vermeulen S, Garnett T, Tilman D, DeClerck F, Wood A, et al. Food in the Anthropocene: the EAT-Lancet Commission on healthy diets from sustainable food systems. *Lancet North Am Ed* 2019;393:447–92.
4. Tonstad S, Stewart K, Oda K, Batech M, Herring RP, Fraser GE. Vegetarian diets and incidence of diabetes in the Adventist Health Study-2. *Nutr Metab Cardiovasc Dis* 2013;23:292–9.
5. Garber AJ, Abrahamson MJ, Barzilay JL, Blonde L, Bloomgarden ZT, Bush MA, Dagogo-Jack S, DeFronzo RA, Einhorn D, Fonseca VA, et al. Consensus statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the comprehensive type 2 diabetes management algorithm – 2019 executive summary. *Endocr Pract* 2019;25:69–101.
6. Evert AB, Dennison M, Gardner CD, Garvey WT, Lau KHK, MacLeod J, Mitri J, Pereira RF, Rawlings K, Robinson S, et al. Nutrition therapy for adults with diabetes or prediabetes: a consensus report. *Diabetes Care* 2019;42:731–54.
7. Sievenpiper JL, Chan CB, Dworatzek PD, Freeze C, Williams SL. Nutrition therapy. *Can J Diabetes* 2018;42:S64–79.
8. U.S. Department of Agriculture. 2020–2025 Dietary Guidelines for Americans: We Want to Hear from You. [Internet]. 2 March, 2020. Accessed 12 April, 2021. Available from: <https://www.usda.gov/media/blog/2018/03/01/2020-2025-dietary-guidelines-americans-we-want-hear-you>.
9. Melina V, Craig W, Levin S. Position of the Academy of Nutrition and Dietetics: vegetarian diets. *J Acad Nutr Diet* 2016;116:1970–80.
10. Fraser GE. 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–8s.
11. Snowdon DA, Phillips RL. Does a vegetarian diet reduce the occurrence of diabetes? *Am J Public Health* 1985;75:507–12.
12. Vang A, Singh PN, Lee JW, Haddad EH, Brinegar CH. Meats, processed meats, obesity, weight gain and occurrence of diabetes among adults: findings from Adventist Health Studies. *Ann Nutr Metab* 2008;52:96–104.
13. Tonstad S, Butler T, Yan R, Fraser GE. Type of vegetarian diet, body weight, and prevalence of type 2 diabetes. *Diabetes Care* 2009;32:791–6.
14. Pan A, Sun Q, Bernstein AM, Manson JE, Willett WC, Hu FB. Changes in red meat consumption and subsequent risk of type 2 diabetes mellitus: three cohorts of US men and women. *JAMA Intern Med* 2013;173:1328–35.
15. Satija A, Bhupathiraju SN, Rimm EB, Spiegelman D, Chiuve SE, Borgi L, Willett WC, Manson JE, Sun Q, Hu FB. Plant-based dietary patterns and incidence of type 2 diabetes in US men and women: results from three prospective cohort studies. *PLoS Med* 2016;13:e1002039.
16. Consortium IA, Bendinelli B, Palli D, Masala G, Sharp SJ, Schulze MB, Guevara M, van der ADL, Sera F, Amiano P, et al. Association between dietary meat consumption and incident type 2 diabetes: the EPIC-InterAct study. *Diabetologia* 2013;56:47–59.
17. Chen Z, Zuurmond MG, van der Schaft N, Nano J, Wijnhoven HAH, Ikram MA, Franco OH, Voortman T. Plant versus animal based diets and insulin resistance, prediabetes and type 2 diabetes: the Rotterdam Study. *Eur J Epidemiol* 2018;33:883–93.
18. Chiu THT, Huang H-Y, Chiu Y-F, Pan W-H, Kao H-Y, Chiu JPC, Lin M-N, Lin C-L. Taiwanese vegetarians and omnivores: dietary composition, prevalence of diabetes and IFG. *PLoS One* 2014;9:e88547.
19. Yokoyama Y, Barnard ND, Levin SM, Watanabe M. Vegetarian diets and glycemic control in diabetes: a systematic review and meta-analysis. *Cardiovasc Diagn Ther* 2014;4:373–82.

20. Anderson JW, Ward K. High-carbohydrate, high-fiber diets for insulin-treated men with diabetes mellitus. *Am J Clin Nutr* 1979;32: 2312–21.
21. Franz MJ, Bantle JP, Beebe CA, Brunzell JD, Chiasson J-L, Garg A, Holzmeister LA, Hoogwerf B, Mayer-Davis E, Mooradian AD, et al. Evidence-based nutrition principles and recommendations for the treatment and prevention of diabetes and related complications. *Diabetes Care* 2003;26(Suppl 1):S51–61.
22. Barnard ND, Cohen J, Jenkins DJA, Turner-McGrievy G, Gloede L, Jaster B, Seidl K, Green AA, 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;29:1777–83.
23. Lee Y-M, Kim S-A, Lee I-K, Kim J-G, Park K-G, Jeong J-Y, Jeon J-H, Shin J-Y, Lee D-H. Effect of a brown rice based vegan diet and conventional diabetic diet on glycemic control of patients with type 2 diabetes: a 12-week randomized clinical trial. *PLoS One* 2016;11:e0155918.
24. American Diabetes Association. 2. Classification and diagnosis of diabetes: standards of medical care in diabetes – 2020. *Diabetes Care* 2020;43:S14–31.
25. Sparks LM, Xie H, Koza RA, Mynatt R, Hulver MW, Bray GA, Smith SR. A high-fat diet coordinately downregulates genes required for mitochondrial oxidative phosphorylation in skeletal muscle. *Diabetes* 2005;54:1926–33.
26. Anderson AS, Haynie KR, McMillan RP, Osterberg KL, Boutagy NE, Frisard MI, Davy BM, Davy KP, Hulver MW. Early skeletal muscle adaptations to short-term high-fat diet in humans before changes in insulin sensitivity. *Obesity* 2015;23:720–4.
27. Wolpert HA, Atakov-Castillo A, Smith SA, Steil GM. Dietary fat acutely increases glucose concentrations and insulin requirements in patients with type 1 diabetes: implications for carbohydrate-based bolus dose calculation and intensive diabetes management. *Diabetes Care* 2013;36:810–6.
28. Goff LM, Bell JD, So P-W, Dornhorst A, Frost GS. Veganism and its relationship with insulin resistance and intramyocellular lipid. *Eur J Clin Nutr* 2005;59:291–8.
29. Kahleova H, Petersen KF, Shulman GI, Alwarith J, Rembert E, Tura A, Hill M, Holubkov R, Barnard ND. Effect of a low-fat vegan diet on body weight, insulin sensitivity, postprandial metabolism, and intramyocellular and hepatocellular lipid levels in overweight adults. *JAMA Network Open* 2020;3:e2025454.
30. 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;10:189.
31. Wharton S, Pedersen SD, Lau DCW, Sharma AM. Weight management in diabetes. *Canadian Journal of Diabetes* 2018;42:S124–29.
32. American Diabetes Association. 10. Cardiovascular disease and risk management: standards of medical care in diabetes – 2020. *Diabetes Care* 2020;43(Suppl 1):S111–34.
33. Berkow SE, Barnard N. Vegetarian diets and weight status. *Nutr Rev* 2006;64:175–88.
34. Appleby PN, Thorogood M, Mann JI, Key TJ. The Oxford Vegetarian Study: an overview. *Am J Clin Nutr* 1999;70:525s–31s.
35. Moore WJ, McGrievy ME, Turner-McGrievy GM. Dietary adherence and acceptability of five different diets, including vegan and vegetarian diets, for weight loss: the New DIETs study. *Eat Behav* 2015;19: 33–8.
36. Barnard ND, Levin SM, Yokoyama Y. A systematic review and meta-analysis of changes in body weight in clinical trials of vegetarian diets. *J Acad Nutr Diet* 2015;115:954–69.
37. 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* 2011;28:549–59.
38. 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.
39. Barnard ND, Cohen J, Jenkins DJA, Turner-McGrievy G, Gloede L, Green A, Ferdowsian H. A low-fat vegan diet and a conventional diabetes diet in the treatment of type 2 diabetes: a randomized, controlled, 74-wk clinical trial. *Am J Clin Nutr* 2009;89:1588S–96S.
40. Vigiliouk E, Kendall CW, Kahleová H, Rahelić D, Salas-Salvadó J, Choo VL, Mejia SB, Stewart SE, Leiter LA, Jenkins DJ, et al. Effect of vegetarian dietary patterns on cardiometabolic risk factors in diabetes: a systematic review and meta-analysis of randomized controlled trials. *Clin Nutr* 2019;38:1133–45.
41. Ornish D, Scherwitz LW, Billings JH, Brown SE, Gould KL, Merritt TA, Sparler S, Armstrong WT, Ports TA, Kirkeeide RL, et al. Intensive lifestyle changes for reversal of coronary heart disease. *JAMA* 1998;280:2001–7.
42. American Diabetes Association. 11. Microvascular complications and foot care: standards of medical care in diabetes – 2020. *Diabetes Care* 2020;43(Suppl 1):S135–S151.
43. Odermatt A. The Western-style diet: a major risk factor for impaired kidney function and chronic kidney disease. *Am J Physiol Renal Physiol* 2011;301:F919–931.
44. Knight EL, Stampfer MJ, Hankinson SE, Spiegelman D, Curhan GC. The impact of protein intake on renal function decline in women with normal renal function or mild renal insufficiency. *Ann Intern Med* 2003;138:460–7.
45. Kim H, Caulfield LE, Garcia-Larsen V, Steffen LM, Grams ME, Coresh J, Rebholz CM. Plant-based diets and incident CKD and kidney function. *Clin J Am Soc Nephrol* 2019;14:682–91.
46. de Mello VDF, Zelmanovitz T, Perassolo MS, Azevedo MJ, Gross JL. Withdrawal of red meat from the usual diet reduces albuminuria and improves serum fatty acid profile in type 2 diabetes patients with macroalbuminuria. *Am J Clin Nutr* 2006;83:1032–8.
47. Barsotti G, Navalesi R, Giampietro O, Ciardella F, Morelli E, Cupisti A, Mantovanelli A, Giovannetti S. Effects of a vegetarian, supplemented diet on renal function, proteinuria, and glucose metabolism in patients with “overt” diabetic nephropathy and renal insufficiency. *Contrib Nephrol* 1988;65:87–94.
48. Jibani MM, Bloodworth LL, Foden E, Griffiths KD, Galpin OP. Predominantly vegetarian diet in patients with incipient and early clinical diabetic nephropathy: effects on albumin excretion rate and nutritional status. *Diabet Med* 1991;8:949–53.
49. Deli G, Bosnyak E, Pusch G, Komoly S, Feher G. Diabetic neuropathies: diagnosis and management. *Neuroendocrinology* 2013;98:267–80.
50. Boulton AJM, Vinik AI, Arezzo JC, Bril V, Feldman EL, Freeman R, Malik RA, Maser RE, Sosenko JM, Ziegler D, et al. Diabetic neuropathies: a statement by the American Diabetes Association. *Diabetes Care* 2005;28:956–62.
51. Alleman CJM, Westerhout KY, Hensen M, Chambers C, Stoker M, Long S, van Nooten FE. Humanistic and economic burden of painful diabetic peripheral neuropathy in Europe: a review of the literature. *Diabetes Res Clin Pract* 2015;109:215–25.
52. Lam T, Burns K, Dennis M, Cheung NW, Gunton JE. Assessment of cardiovascular risk in diabetes: risk scores and provocative testing. *World J Diabetes* 2015;6:634–41.
53. Bunner AE, Wells CL, Gonzales J, Agarwal U, Bayat E, Barnard ND. A dietary intervention for chronic diabetic neuropathy pain: a randomized controlled pilot study. *Nutr Diabetes* 2015;5:e158.
54. Crane MG, Sample C. Regression of diabetic neuropathy with total vegetarian (vegan) diet. *J Nutr Med* 1994;4:431–9.
55. Smith AG, Russell J, Feldman EL, Goldstein J, Peltier A, Smith S, Hamwi J, Pollari D, Bixby B, Howard J, et al. Lifestyle intervention for pre-diabetic neuropathy. *Diabetes Care* 2006;29:1294–9.
56. Yokoyama Y, Nishimura K, Barnard ND, Takegami M, Watanabe M, Sekikawa A, Okamura T, Miyamoto Y. Vegetarian diets and blood pressure: a meta-analysis. *JAMA Intern Med* 2014;174:577–87.

57. Ferdowsian HR, Barnard ND. Effects of plant-based diets on plasma lipids. *Am J Cardiol* 2009;104:947–56.
58. Wong MYZ, Man REK, Fenwick EK, Gupta P, Li L-J, van Dam RM, Chong MF, Lamoureux EL. Dietary intake and diabetic retinopathy: a systematic review. *PLoS One* 2018;13:e0186582.
59. Lim EL, Hollingsworth KG, Aribisala BS, Chen MJ, Mathers JC, Taylor R. Reversal of type 2 diabetes: normalisation of beta cell function in association with decreased pancreas and liver triacylglycerol. *Diabetologia* 2011;54:2506–14.
60. Weickert MO. Nutritional modulation of insulin resistance. *Scientifica* 2012;2012:424780.
61. Hall KD, Kahan S. Maintenance of lost weight and long-term management of obesity. *Med Clin North Am* 2018;102:183–97.
62. American Diabetes Association. 8. Obesity management for the treatment of type 2 diabetes: standards of medical care in diabetes – 2020. *Diabetes Care* 2020;43(Suppl 1):S89–97.
63. Serra-Majem L, Roman B, Estruch R. Scientific evidence of interventions using the Mediterranean diet: a systematic review. *Nutr Rev* 2006;64:S27–47.
64. Ahmad S, Demler OV, Sun Q, Moorthy MV, Li C, Lee I-M, Ridker PM, Manson JE, Hu FB, Fall T, et al. Association of the Mediterranean diet with onset of diabetes in the Women's Health Study. *JAMA Network Open* 2020;3:e2025466.
65. Huo R, Du T, Xu Y, Xu W, Chen X, Sun K, Yu X. Effects of Mediterranean-style diet on glycemic control, weight loss and cardiovascular risk factors among type 2 diabetes individuals: a meta-analysis. *Eur J Clin Nutr* 2015;69:1200–8.
66. Malik VS, Li Y, Tobias DK, Pan A, Hu FB. Dietary protein intake and risk of type 2 diabetes in US men and women. *Am J Epidemiol* 2016;183:715–28.
67. Sluijs I, Beulens JWJ, van der A DL, Spijkerman AMW, Grobbee DE, van der Schouw YT. Dietary intake of total, animal, and vegetable protein and risk of type 2 diabetes in the European Prospective Investigation into Cancer and Nutrition (EPIC)-NL study. *Diabetes Care* 2010;33:43–8.
68. Dietary Reference Intakes: The Essential Guide to Nutrient Requirements | The National Academies Press [Internet]. [cited 2 Mar, 2020]. Available from: <https://www.nap.edu/catalog/11537/dietary-reference-intakes-the-essential-guide-to-nutrient-requirements>.
69. Barnard N, Levin S, Trapp C. Meat consumption as a risk factor for type 2 diabetes. *Nutrients* 2014;6:897–910.
70. Weaver CM, Plawecki KL. Dietary calcium: adequacy of a vegetarian diet. *Am J Clin Nutr* 1994;59:1238S–41S.
71. Mansournia MA, Ostadmohammadi V, Doosti-Irani A, Ghayour-Mobarhan M, Ferns G, Akbari H, Ghaderi A, Talari HR, Asemi Z. The effects of vitamin D supplementation on biomarkers of inflammation and oxidative stress in diabetic patients: a systematic review and meta-analysis of randomized controlled trials. *Horm Metab Res* 2018;50:429–40.
72. Institute of Medicine (US) Standing Committee on the Scientific Evaluation of Dietary Reference Intakes and its Panel on Folate, Other B Vitamins, and Choline. Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B6, Folate, Vitamin B12, Pantothenic Acid, Biotin, and Choline. [Internet]. Washington (DC): National Academies Press (US); 1998 [cited 16 Apr, 2019]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK114310/>.
73. Mancini JG, Filion KB, Atallah R, Eisenberg MJ. Systematic review of the Mediterranean diet for long-term weight loss. *Am J Med* 2016;129:407–415.e4.
74. de Lorgeril M, Renaud S, Mamelle N, Salen P, Martin JL, Monjaud I, Guidollet J, Touboul P, Delaye J. Mediterranean alpha-linolenic acid-rich diet in secondary prevention of coronary heart disease. *Lancet North Am Ed* 1994;343:1454–9.
75. Estruch R, Ros E, Salas-Salvadó J, Covas M-I, Corella D, Arós F, Gómez-Gracia E, Ruiz-Gutiérrez V, Fiol M, Lapetra J, et al. Primary prevention of cardiovascular disease with a Mediterranean diet supplemented with extra-virgin olive oil or nuts. *N Engl J Med* 2018;378:e34.
76. Barnard ND, Alwarith J, Rembert E, Brandon L, Nguyen M, Goergen A, Horne T, do Nascimento GF, Lakkadi K, Tura A, et al. A Mediterranean diet and low-fat vegan diet to improve body weight and cardiometabolic risk factors: a randomized, cross-over trial. *J Am Coll Nutr* 2021;Feb 5:1–13.
77. Chiavaroli L, Vigiouk E, Nishi SK, Blanco Mejia S, Rahelić D, Kahleová H, Salas-Salvadó J, Kendall CW, Sievenpiper JL. DASH dietary pattern and cardiometabolic outcomes: an umbrella review of systematic reviews and meta-analyses. *Nutrients* 2019;11:338.
78. Gardner CD, Kiazand A, Alhassan S, Kim S, Stafford RS, Balise RR, Kraemer HC, King AC. Comparison of the Atkins, Zone, Ornish, and LEARN diets for change in weight and related risk factors among overweight premenopausal women: the A TO Z Weight Loss Study: a randomized trial. *JAMA* 2007;297:969–77.
79. Dansinger ML, Gleason JA, Griffith JL, Selker HP, Schaefer EJ. Comparison of the Atkins, Ornish, Weight Watchers, and Zone diets for weight loss and heart disease risk reduction: a randomized trial. *JAMA* 2005;293:43–53.
80. Hall KD, Guo J, Courville AB, Boring J, Brychta R, Chen KY, Darcey V, Forde CG, Gharib AM, Gallagher I, et al. Effect of a plant-based, low-fat diet versus an animal-based, ketogenic diet on ad libitum energy intake. *Nat Med* 2021;27:344–53.
81. Goldenberg JZ, Day A, Brinkworth GD, Sato J, Yamada S, Jönsson T, Beardsley J, Johnson JA, Thabane L, Johnston BC. Efficacy and safety of low and very low carbohydrate diets for type 2 diabetes remission: systematic review and meta-analysis of published and unpublished randomized trial data. *BMJ* 2021;372:m4743.
82. Foster GD, Wyatt HR, Hill JO, McGuckin BG, Brill C, Mohammed BS, Szapary PO, Rader DJ, Edman JS, Klein S. A randomized trial of a low-carbohydrate diet for obesity. *N Engl J Med* 2003;348:2082–90.
83. Noto H, Goto A, Tsujimoto T, Noda M. Low-carbohydrate diets and all-cause mortality: a systematic review and meta-analysis of observational studies. *PLoS One* 2013;8:e55030.
84. Lee V, McKay T, Ardern CI. Awareness and perception of plant-based diets for the treatment and management of type 2 diabetes in a community education clinic: a pilot study. *J Nutr Metab* 2015;2015:236234.
85. Barnard ND, Gloede L, Cohen J, Jenkins DJA, Turner-McGrievy G, Green AA, Ferdowsian H. A low-fat vegan diet elicits greater macronutrient changes, but is comparable in adherence and acceptability, compared with a more conventional diabetes diet among individuals with type 2 diabetes. *J Am Diet Assoc* 2009;109:263–72.
86. Trapp C, Barnard N, Katcher H. A plant-based diet for type 2 diabetes: scientific support and practical strategies. *Diabetes Educ* 2010;36:33–48.
87. American Diabetes Association. 9. Pharmacologic approaches to glycemic treatment: standards of medical care in diabetes – 2020. *Diabetes Care* 2020;43(Suppl 1):S98–S110.