Type 2 Diabetes Prevention and Management With a Low-Fat, Whole-Food, Plant-Based Diet

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INTRODUCTION

Quality care for people with type 2 diabetes (T2D) is a significant concern for family practice clinicians. Lifestyle medicine (LM) and, specifically, a whole-food, plant-based (WFPB)[1] dietary pattern are important therapeutic options, supported by a large body of evidence. This review examines the most current research on low-fat, plant-based diets and explores the mechanisms beyond glycemic control and weight loss by which the diet may improve health outcomes for individuals living with T2D and for those at risk for the disease. It also shares practical takeaways for family physicians, nurse practitioners, and the entire healthcare team.

According to the Centers for Disease Control and Prevention, as much as 10.5% of the US population has T2D and approximately one-third (34.5%) has prediabetes.[2] Many with diabetes are not diagnosed (26.9 million people diagnosed and 7.3 million underdiagnosed or not diagnosed).[2] Solutions for resolution of T2D are needed more urgently than ever.

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DISCLOSURES

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Current treatment guidelines for T2D recommend a target glycated hemoglobin level (HbA_{1c}) of 7% or less for most non-pregnant adults, with the important caveat that the target HbA_{1c} be individualized based on patient and disease factors (eg, age, duration, or vascular complications).[4,5] Major randomized clinical trials on the benefits of lowering HbA_{1c} with intensive glycemic control using medication combinations and/or multiple daily injections of insulin, generally defined as HbA_{1c} <7%,[6] have been disappointing in reducing the macrovascular and microvascular complications of diabetes.[6-9] In a meta-analysis of data from 13 randomized controlled trials, intensive glucose-lowering treatment showed no benefit on all-cause mortality or death from cardiovascular comorbidities in adults with T2D; in fact, a 19% increase in all-cause mortality and a 43% increase in death from cardiovascular events were revealed. The same meta-analysis showed that intensive glucose-lowering treatment was associated with a 10% absolute risk reduction of microalbuminuria; however, no significant benefit on microvascular endpoints of clinical significance, such as renal failure, neuropathy, retinopathy, or visual deterioration, were seen. Furthermore, intensive glucose-lowering treatment was associated with a significant 2-fold increased risk of severe hypoglycemic events.[10]

Current treatment for T2D in the United States usually includes ≥1 medications prescribed for glycemic control. Between 2010 and 2012, 88% of people with diabetes were taking ≥1 oral or injectable diabetes medications, or a combination of both.[11] Insulin, human or analog, has been used as the centerpiece of intensive antihyperglycemic therapy. The price of insulin increased by 353% over the 15-year period between 2001 and 2016.[12] Besides insulin, there are now 11 additional classes of medications available in the United States to manage hyperglycemia, with 170 new agents for diabetes and diabetes-related conditions in development.[13] Aggressively lowering HbA_{1c} with intensive medication use has not demonstrated the outcomes desired and expected by clinicians and patients. In response to the newly recognized risks and lack of significant benefits of intensive pharmacologic glucose lowering, especially in older adults, along with the demands and expense involved, the American Diabetes Association has called for shared decision-making with patients as well as a patient-centered approach with more emphasis on cardiovascular risk reduction through healthy habits, such as smoking cessation.[14] These initiatives are welcome and may help to promote a shift from a culture of medication primacy for T2D to one that embraces "intensive" therapeutic lifestyle and dietary changes. LM practice emphasizes informed consent with patient education and empowerment when setting a course of treatment[15]; family physicians and other healthcare team members can facilitate healthy behavior changes by fully discussing expected outcomes, risks, and benefits of both pharmaceutical and evidence-based LM interventions.

T2D is a largely preventable disease, and the epidemic rise in its incidence and prevalence calls for a paradigm shift in lifestyle and dietary patterns. As described in this paper, researchers have demonstrated that a low-fat, WFPB diet addresses the underlying pathophysiology of T2D and offers health benefits beyond glycemic control. A low-fat WFPB diet includes unrefined whole grains, legumes, vegetables, fruits, and nuts, and excludes all animal products (such as meat, poultry, fish, dairy, or eggs)[6] with no known negative side effects. This dietary pattern is consistent with recommendations from the American Association of Clinical Endocrinology (AACE) to follow a plant-based diet with higher polyunsaturated and monounsaturated fatty acids, avoid trans-fatty acids, and limit saturated fatty acids.[16] However, the WFPB diet discussed in this article aims to avoid all animal foods with an overall low-fat nutrient profile. Many LM nurses and physicians utilize a low-fat WFPB diet as first-line treatment for T2D[17-27]; this treatment option offers superior quality of life benefits in comparison to pharmacologic treatment. Low-fat, unprocessed diets with no animal foods have been found to be acceptable to patients and offer challenges in adherence no greater than any specific dietary change.[28]

DIETARY PATTERNS AND RISK FOR T2D

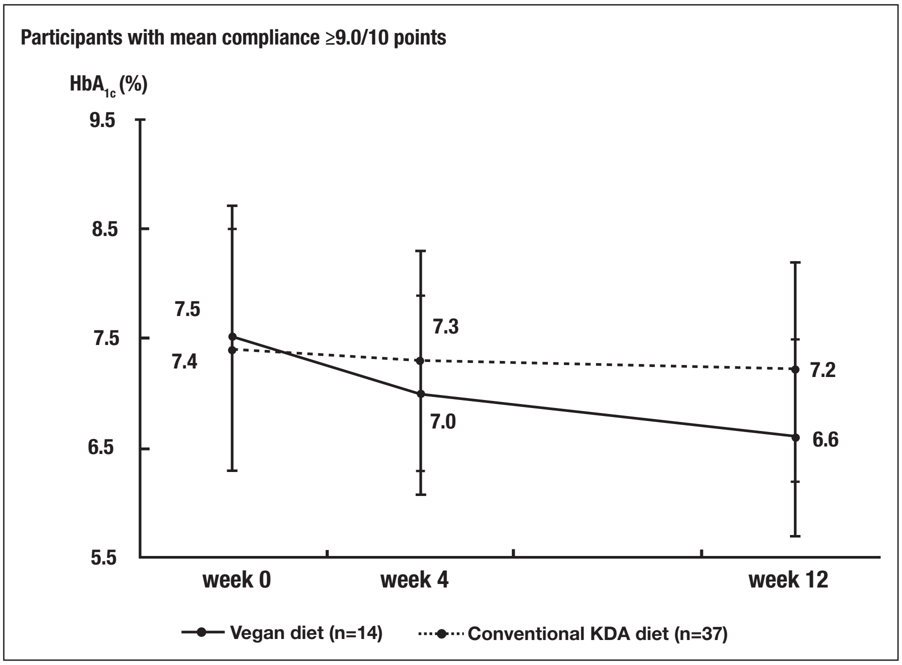
Gradations of adherence to different types of plant-based diets ("healthful" and "unhealthful") have been associated with diabetes risk. A diet that emphasized plant foods and that was low in animal foods was associated with a reduction of about 20% in the risk of diabetes; moreover, a "healthy" plant-based diet that mostly included whole grains, fruits, vegetables, and nuts had a 34% diabetes risk reduction. In contrast, individuals who followed an "unhealthy" plant-based diet (including large amounts of nutrient-poor, calorie-dense foods such as refined grains and sugar-sweetened beverages) had a 16% higher risk of diabetes. These associations were independent of body mass index (BMI) and other diabetes risk factors.[29] Other important work has focused on the Seventh-Day Adventist population. The Seventh-Day Adventist religious denomination exhibits a variety of dietary habits; while about half are omnivorous, many are vegetarian including vegans, lacto-ovo-vegetarians, semi-vegetarians, and pesco-vegetarians.[30] Church doctrines recommend vegetarian practices and abstinence from the use of tobacco and alcohol; hence, this presents an ideal opportunity to compare various vegetarian dietary patterns while controlling for known non-dietary confounders like alcohol and tobacco. Several findings relevant to T2D have been reported among the Adventist cohorts, including significantly lower body weight among vegans (mean BMI 23.1 kg/m^2) vs non-vegetarians (28.3 kg/m^2) (P=0.0001). Vegan Adventists were 49% less likely to have T2D compared to non-vegetarian Adventists, with analyses adjusted for age, sex, ethnicity, education, income, physical activity, television watching, sleep habits, alcohol use, and BMI (P=0.0001). Further, while both lacto-ovo-vegetarians and vegans had reduced risk for hypertension, T2D, and obesity, vegans experienced greater risk reduction for those diseases.[30]

INTERVENTION RESEARCH ON WFPB DIETS AND T2D

A plant-based nutrition program was implemented as a randomized controlled trial in the corporate setting (10 GEICO US-based offices) among employees >18 years of age with BMI ≥25 kg/m^2 and a previous diagnosis of T2D. The 142 participants in the intervention group were asked to follow a low-fat (<3 grams per serving) plant-based diet consisting of whole grains, vegetables, legumes, and fruits, and limiting added oils, with no restriction on energy intake for 18 weeks, and to avoid all animal products (meat, poultry, fish, dairy products, and eggs) while favoring foods low on the glycemic index.[31] Low-fat plant-based meal options were made available to participants at their worksites, along with educational classes, group support sessions, and cooking classes. Individuals at the control sites made no dietary changes, were given no dietary guidance or classes, and no plant-based meal option was made available to them during the study. All participants were asked not to alter their exercise patterns during the 18-week study period and to remain on their baseline medication regimen as prescribed by their primary care physicians, unless modified by those physicians.

Measurements taken at week 0 and week 18 included body weight, blood pressure, plasma cholesterol and triglycerides, high-density lipoprotein and low-density lipoprotein cholesterol, and HbA_{1c}. Mean body weight decreased by 2.9 kg in the intervention group vs 0.06 kg in the control group ($P<0.001$), BMI fell by 1.04 kg/m^2 in the intervention group vs 0.01 kg/m^2 in the control group ($P<0.001$), and weight loss of ≥5% of body weight was more frequent in the intervention group (37%) compared with the control group (11%; $P<0.001$).[31] Beyond body weight reduction, which has been proven to improve glycemic control, the intervention group experienced benefits in plasma lipid concentrations and blood pressure, which can help alleviate morbidity and mortality from cardiovascular events such a stroke and myocardial ischemia, for which T2D is a strong risk factor.[32]

FIGURE. **Participants with highest mean compliance to vegan diet**[33]



Another study compared a standard diabetic diet and a plant-based, brown-rice-centric diet and their effects on HbA_{1c} in 2 groups of adult Korean patients with diabetes on hypoglycemic medications with baseline HbA_{1c} levels between 6% and 11%. The plant-based diet group (n=47) was asked to consume whole grains, vegetables, fruits, and legumes; furthermore, they were instructed to eat brown rice and avoid white rice, avoid highly processed food made of rice or wheat flour, avoid all animal food products, and favor low–glycemic-index foods (ie, legumes, green vegetables, and seaweed). Amount and frequency of food consumption, caloric intake, and portion sizes were not restricted, and participants were monitored over a 12-week period.[33]

The control group (n=46) followed the treatment guidelines for diabetes recommended by the Korean Dietetic Association (KDA) in 2011, which include grains, meats, vegetables, fats and oils, milk, and fruits: participants were asked to (1) restrict their individualized daily energy intake based on body weight, physical activity, need for weight control, and compliance; and (2) achieve total calorie intake comprised of 50% to 60% carbohydrate, 15% to 20% protein (if renal function is normal), <25% fat, <7% saturated fat, minimal trans-fat intake, and ≤200 mg/day cholesterol. Participants were asked to maintain their baseline exercise regimens, to record their daily food intake, and to maintain their current medication(s), though dose reduction was permitted when it was necessary according to a physician's judgment. Glycemic control was the primary endpoint, and the HbA_{1c} levels of both groups significantly decreased over time: –0.5% in the vegan diet group ($P<0.01$) and –0.2% in the KDA diet group ($P<0.05$).[33]

Furthermore, dieters with high compliance (followed the diet strictly >90% of the time) had a larger effect, with HbA_{1c} decreased by –0.9% in the vegan group (n=14) and –0.3% in the KDA group (n=37) (interaction between group and time $P=0.010$; see **FIGURE**).[33] These differences remained significant after adjusting for energy intake or waist circumference.[30,34]

Two recent randomized controlled trials studied the effect of plant-based dietary intervention on insulin sensitivity and beta-cell function. Both demonstrated increased beta-cell glucose sensitivity in intervention groups along with decreased fasting insulin resistance (IR) compared to control groups.[35,36] A 16-week trial demonstrated that a plant-based dietary intervention elicited increased beta-cell glucose sensitivity and decreased fasting IR with a significant reduction in BMI in overweight participants assigned to the intervention group (n=38) compared to the control group (n=37), which showed no improvement in sensitivity. Visceral fat volume was reduced only in the intervention group (interaction between group and time $P<0.001$).[35]

Further, the second trial demonstrated that reduced body weight, improved glycemic control, and reduced insulin concentrations are feasible among overweight non-diabetic individuals using a plant-based dietary intervention (n=122), likely due to the reduction of lipid accumulation in muscle and liver cells from reduced energy intake. Participants' fasting plasma insulin concentrations decreased by 21.6 pmol/L compared to no significant change in the control group (n=122, 23.6 pmol/L; 95% CI: –5.0 to 54.3; between-group *P*=0.006).[36] Postprandial energy expenditure increased in the plant-based group as well, which is associated with decreased fat mass and increased insulin sensitivity.[37,38] These trials suggest that low-fat, plant-based diets have the potential to rapidly reduce lipid accumulation in muscle and liver cells, which can improve glycemic control and beta-cell function in those suffering from diabetes.[39,40]

BODY WEIGHT AND T2D RISK

Overweight and obesity continue to be strong risk factors for developing T2D, and an analysis of data from the Nurses' Health Study (NHS), with more than 200,000 participants followed up to 40 years, recently displayed the strength of that association. Through the first 8 years of NHS, the risk of diabetes incidence in women with high-normal BMI (23-23.9) was 3.6 times greater than those with BMI <22. Furthermore, weight gain after 18 years of age was a strong risk factor: compared with those who maintained a stable body weight through 1984, the relative risk (RR) of diabetes was higher than 17 for those who gained ≥35 kg.[41]

In the extended follow-up period, women with a BMI of ≥35 vs <22 had an age-adjusted RR of 93.2 for developing diabetes. Weight loss was actually shown to be protective against the development of diabetes: ≥5 kg of weight loss after 18 years of age was associated with an almost 50% lower risk of developing diabetes.[41]

WFPB diets offer an effective method for weight loss among overweight and obese adults. Researchers compared the effectiveness of 5 different diets in a 6-month, randomized controlled trial: totally plant-based/vegan diet (omitting all animal products), omnivorous diet (excluding no foods), semi-vegetarian diet (occasional meat intake), pesco-vegetarian diet (excludes meat except seafood), and vegetarian diet (excludes all meat and seafood but contains eggs and dairy products). The vegan group lost the most weight (–7.5% ± 4.5%), and lost significantly more than the omnivorous (3.1% ± 3.6%), semi-vegetarian (–3.2% ± 3.8%), and pesco-vegetarian (3.2% ± 3.4%) groups (*P*=0.03 for all).[42]

OTHER MECHANISMS FOR WFPB DIETS AND T2D TREATMENT

A low-fat WFPB diet has other potential qualities that can both prevent and manage T2D besides controlling blood glucose levels and mitigating risk factors like overweight and obesity. One possible alternative explanation for the success of this diet is the role of intramyocellular lipids (IMCL) in IR in skeletal muscle. It is widely accepted that IR, defined as impaired glucose uptake response to physiologic concentrations of insulin, precedes the clinical presentation of T2D.[43] Skeletal muscle, not a natural storage site for excess fat, accumulates lipids when the number and size of adipocytes, the normal storage site for excess fat, are inadequate to store excess fat.[43,44] IR in skeletal muscle has been a focus of much research and review: skeletal muscle is the largest organ in the body and plays a critical role in glucose homeostasis, accounting for up to 40% of body mass and up to 80% to 90% of insulin-stimulated glucose clearance.[43] Insulin promotes glucose control by enhancing glucose uptake in skeletal muscle and other tissues and by inhibiting glucose production in the liver.[45,46] The 2 most commonly cited IMCL lipid intermediates causing skeletal muscle IR are ceramides and diacylglycerol, but the role of these intermediates in IR is still debated.[43]

Skeletal muscle IR is detectable years before beta-cell failure and hyperglycemia, the hallmarks of T2D, and thus, understanding the development of IR and creating remedial mechanisms for affected populations could provide an early intervention to arrest the T2D epidemic.[43] It is undisputed that dietary fatty acid intake is central to lipid-induced IR in skeletal muscle, and that maintaining the dynamic lipid balance is key to human health.[43,47] As Kitessa and Abeywardena explain, "[Dietary fatty acid intake] is the one lever that can be dialed up/down to regulate the flow of lipid intermediates into organs not intended for lipid storage."[43]

In a study of early weight-loss intervention (from hypocaloric diets) on the IR offspring of individuals with T2D, the relationship between IMCL and skeletal muscle IR showed that weight loss produced a 30% reduction in IMCL with a 60% increase in insulin sensitivity.[48] In a Japanese study, 37 non-obese male participants were fed a high-fat diet (60% calories from fat, 45% of which was saturated fat). After 3 days, IMCL levels had increased by 30% (*P*<0.01).[49] Since vegan diets produce the most weight loss[42] and typically include very little saturated fat, a low-fat WFPB diet may act as a protective mechanism against the accumulation of IMCL in skeletal muscle, reducing IR and T2D.[50]

Another factor that offers protection against T2D for those who consume a low-fat WFPB diet is their minimized consumption of persistent organic pollutants (POPs), which are known to cause endocrine disruption.[51] POPs, which are either man-made or by-products of industrial processes, are hazardous chemicals that are resistant to environmental decay through chemical, biological, and photolytic means:

POPs, which are omnipresent in the environment and food chain, are capable of bioaccumulating in human and animal tissue and have a substantial impact on human health and the environment.[51,52]

Human exposure to POPs occurs primarily through the consumption of animal fats, including fatty fish, meat, and dairy products.[51] Initially, POPs were notorious for their ability to affect reproduction and promote cancer, but recent studies have highlighted their ability to amplify development of metabolic diseases like obesity and T2D.[52] Cross-sectional studies have shown the association between serum concentrations of POPs and prevalence of diabetes, and these studies are supported by prospective and experimental data.[51,53,54]

POPs have been described as "obesogens," functionally defined as chemicals that shift homeostatic metabolic set points, interrupt appetite controls, disturb lipid homeostasis to promote adipocyte hypertrophy, stimulate adipogenic pathways that encourage adipocyte hyperplasia, or otherwise alter adipocyte differentiation during development.[54] Animal products may be a double-edged sword to those at risk for T2D via dietary saturated fat and altered metabolic pathways from POPs.

Finally, an underlying mechanism foundational to the effects of healthy diet is the gut microbiota. A healthful WFPB diet can promote a gut microbiome environment that promotes the metabolism of fiber and polyphenols and discourages the metabolism of bile acids, choline, L-carnitine, and amino acids, further reducing T2D risk; a healthy gut microbiota can also help correct imbalances related to inflammation and metabolic dysfunction.[29,55]

TRANSLATING RESEARCH INTO PRACTICE: TAKEAWAYS FOR FAMILY PHYSICIANS AND NURSE PRACTITIONERS

Primary care clinicians have unique opportunities to support patients in creating their own culture of health and sustainable lifestyle habits to reduce risk for T2D, as well as to potentially improve glycemic control. The following strategies may be useful:

- **Consider prescribing a plant-based diet to all patients for diabetes prevention or treatment.**
  Nutrition prescriptions are increasingly used to formalize healthy lifestyle habits. For more information on prescribing a WFPB diet, supported with SMART goal setting, please see articles in this supplement by Campbell (eS117-eS123) and Hauser/McMacken (S5-S16).
- **Reframe treatment goals to focus on quality of life and medication reductions.**
  Patients may not be aware that aiming to reduce medications through lifestyle changes is possible. Improvements in quality of life may be appealing and motivating for patients to consider. Involving patients in a refreshed discussion about treatment goals may reinvigorate the patient-provider relationship and the treatment plan.
- **Reframe treatment strategies with a patient-centered approach to focus on lifestyle instead of medication.**
  Following a reframing of treatment goals, engaging in discussion with patients about the potential negative side effects of oral or injectable hypoglycemic drugs, as well as alternative options, may influence patients to be more open to lifestyle changes at any time across the disease spectrum. Important side effects for oral agents can include liver disease, fluid retention, weight gain, increased risk for fractures, increased risk for bladder cancer, hypoglycemia, headache, stomach upset, and diarrhea.[56-58] Important potential side effects of injectable medications include weight gain, inflammation, hypertension, dyslipidemia, atherosclerosis, heart failure, and arrhythmias.[59] In contrast, there are no known negative side effects to a low-fat WFPB diet.[60]
- **Provide education to patients on benefits and how to eat a WFPB diet.**
  As many as 89% of patients were not aware of using a plant-based diet for the prevention and management of T2D and many of them cited low confidence in adopting a plant-based eating pattern. However, two-thirds of the patients expressed willingness to follow a plant-based diet for the short term and interest in attending a vegetarian education program, contrary to the belief cited by most diabetes educators that patients would find a plant-based diet too difficult to follow and would not find it an acceptable recommendation.[61] Make referrals to clinicians, health coaches, and educational programs that specialize in plant-based nutrition (see references below).
- **Support long-term adherence with ad libitum recommendations.**
  Ad libitum intake of low-fat, whole, plant-based foods naturally causes a reduction in total calories,[62] allowing patients to still reap the benefits of weight loss: This factor can help motivate those who feel that diets are too difficult to follow due to hunger.[63] Patients who adjust insulin based on carbohydrate intake still need to count carbs; they may need support to recalculate carb-to-insulin ratios as they are likely to find that they need less insulin.[64]
- **Facilitate social support groups.**
  Worksite, plant-based nutrition programs have been

well accepted by participants, as was the case with the GEICO study. Worksites offer convenient and supportive environments for health promotion programs because there is no travel time and participants often have common interests and goals, as well as a preexisting camaraderie.[65] This satisfaction, along with the significant health benefits from the plant-based diet group mentioned previously, suggest that worksite interventions could offer a path forward in getting more people to try plant-based diets.[31] In addition to worksite programs, facilitating patient support groups with a medical practice, such as weekly or monthly potlucks, or referring patients to community resources provides important long-term social support.

- **Use resources that are now widely available.** The American College of Lifestyle Medicine (ACLM) offers a variety of patient-facing educational resources, available under the Practice Tools and Resources tab on lifestylemedicine.org, to support patients in transitioning toward and maintaining a WFPB diet, including the Food as Medicine Jumpstart, WFPB Plates for Adults and Children, Nutrition Myths, and other educational resources and infographics. The Physicians Committee for Responsible Medicine (PCRM) offers many resources, including a free 21-Day Vegan Kickstart App or online tool (https://kickstart.pcrm.org/en) that provides meal plans, recipes, and advice from plant-based nutrition experts. Continuing medical education on plant-based nutrition is available through ACLM and PCRM (www.NutritionCME.org).

CONCLUSION

As the incidence and prevalence of diabetes continues to rise, the time is now for clinicians to recommend a low-fat WFPB diet to all of their patients, but especially to those patients living with and at risk for T2D. WFPB diets can prevent T2D, as well as change the course of the disease, by controlling blood sugar naturally with no known negative side effects. The benefits of the diet are clear, but more education is needed for both clinicians and their patients on these benefits and how to promote dietary change effectively and sustainably. Practitioners can support patients in successful, long-term change by recommending useful resources and tools to facilitate adherence; practitioners can access resources for patient support through ACLM (lifestylemedicine.org). ●

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