THE EFFECTS OF PLANT-BASED DIETS ON DIABETES MELLITUS PREVENTION AND MANAGEMENT: A REVIEW OF THE LITERATURE

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ABSTRACT

The prevalence of diabetes has dramatically increased over the last few decades, and there are currently no indications of it slowing down. Additionally, there is no consensus on which dietary treatment is most appropriate to control blood glucose and facilitate long-term weight loss. This review analyzes how vegetarian diets may be viable options for certain individuals in reducing the risk of and managing diabetes mellitus (DM). Publications were evaluated for comparison of low-fat vegetarian and/or vegan diets and the effects on the prevention and management of DM. Findings from studies that measured blood glucose, HgA1C, and body weight indicate a strong association between reducing the risk of developing and managing DM by following a low-fat vegetarian or vegan diet. While some of the measured values did not reach statistical significance between the intervention and control groups, no harmful effects were noted by following a low-fat vegetarian diet. Although more research is needed, minimal harm has been shown in adopting a low-fat vegetarian diet. Therefore, this review concludes that clinicians may consider recommending a low-fat vegetarian diet to clients with diabetes as a way to manage the disease.
Introduction

Current type 2 diabetes mellitus (T2DM) rates indicate that 382 million adults aged 20-70 years worldwide are afflicted with the disease and projections for the future suggest that number will only increase, with some estimates at 592 million worldwide by 2035 (Ardisson, Korat, Willett, & Hu, 2014). In the US, T2DM is associated with increased morbidity, mortality, and healthcare costs, which increase concern for the economic burden of the disease. Type 2 diabetes mellitus is caused by the body’s ineffective use of insulin which has many etiologies such as lifestyle behaviors, genetics, and environmental factors.

Although lifestyle modification and medical nutrition therapy are considered the keystones of T2DM prevention and treatment, there is no consensus on which dietary treatment is most appropriate to control blood glucose and facilitate long-term weight loss. Several plant foods, such as whole grains, fruits, and vegetables, are associated with a lower risk of T2DM, while certain animal foods, such as red and processed meats, are positively associated with T2DM risk (Khazrai, Defeudis & Pozzilli, 2013). Additionally, the recently released 2015 Dietary Guidelines Advisory Committee report recommends shifting away from intake of certain animal foods and moving towards a plant-rich diet (Sitija et al., 2016). The purpose of this literature review is to examine the effectiveness of a vegetarian diet on the prevention and management of T2DM. This review is designed to evaluate the potential for recommending a vegetarian diet for effective T2DM prevention and management.

This literary review was conducted using PubMed’s MeSH database (keywords: type 2 diabetes mellitus and vegetarian diets). Original research papers were chosen based on study design, size of cohort, credibility and quality of research, and definition of “vegetarian diet.”
Type 2 Diabetes Mellitus Overview

Diabetes mellitus refers to a group of diseases characterized by chronic elevation of blood glucose. Glucose is the body’s preferred source of energy. There are several categories of the diabetes mellitus: type 1, type 2, gestational diabetes, and prediabetes. The former two are chronic conditions that are irreversible, while the latter two have the potential to be reversed under a change in status and/or proper management.

History of Diabetes:

Diabetes has a long history that dates back to the 14th century BCE. An Egyptian physician in 1552 BCE mentioned frequent urination as a symptom for somebody who presented with a diabetes-like condition (Swidorski, 2014). Further descriptions of “sugary” urine were noted from 500 BCE. In the 1st Century AD, the Greeks describe the disease as a “melting down of the flesh and limbs into urine,” (Swidorski, 2014). Until the 11th century, the diagnosis of diabetes (meaning “to go through, or siphon”) was often made by “water tasters” who drank the urine of those suspected of having diabetes. Mellitus, the Latin word for honey, was added to the term “diabetes” in the 11th century (Swidorski, 2014).

In 1776, a physician named Dobson observed that for some people, diabetes was fatal in less than five weeks and for others, it was a chronic condition (Swidorski, 2014). This was the first time that a distinction between type 1 and type 2 diabetes mellitus had been made (Swidorski, 2014). In 1921, insulin was “discovered” after a de-pancreatized dog was successfully treated with insulin (Swidorski, 2014). The following year, insulin began to be mass produced in North America, and by 1944, a uniform insulin syringe was developed and diabetes management became more standardized (Swidorski, 2014). In 1959, two major types of diabetes
were formally recognized: type 1 (insulin-dependent) diabetes and type 2 (non-insulin-dependent) diabetes (Swidorski, 2014).

Prevalence & Healthcare Costs

Since diabetes became a household name as early as the 1950’s, the disease has become more prevalent, resulting in consequential healthcare costs. Figure 1 depicts the population percentage by state of the prevalence of diabetes.

FIGURE 1. Map of the United States indicating age-adjusted percentage of adults with diagnosed diabetes. The categorical shadings of the states are as follows: the lightest shaded states have a population of 5.1-6.3% with diabetes (Montana, Idaho, Colorado, etc.). The next darkest shaded states have a population of 6.4-7.7% with diabetes (Alaska). The next darkest shaded states have a population of 7.8-9.4% with diabetes (Oregon, Washington, Arizona, Nevada, etc.). The darkest shaded states have a population between 9.5-15.2% with diabetes (California, Texas, Louisiana, etc.). From Centers for Disease Control and Prevention (2014).

Over the last 70 years, the prevalence of diabetes has skyrocketed in the United States (Centers for Disease Control and Prevention [CDC], 2014). As shown in Figure 2, fewer than 3
6 million people were diagnosed with diabetes in 1958 (CDC, 2016). In 2014, an estimated 26 million Americans had diabetes and over 8 million of those people were undiagnosed (CDC, 2014). Another 79 million Americans are categorized as “pre-diabetic” and are at risk of developing diabetes in the next ten years if appropriate lifestyle changes are not made (CDC, 2014). In the United States, diabetes effects 14.3% of the adult population with a disproportionate number of African American, Latino, Asian, and Native Americans effected by the disease (Papathakis, 2016a).

In congruence with the increase in diabetes over the last 70 years, a subsequent rise in healthcare costs has been associated with the disease. From 2007 to 2012, a 41% increase in total costs of diagnosed diabetes rose from $174 billion to $245 billion (American Diabetes Association [ADA], 2015). The total estimated costs in 2012 due to diabetes were estimated at
$245 billion dollars with $176 billion in direct medical costs and $69 billion in reduced productivity (ADA, 2015). Of those costs, the largest components of medical expenditures are hospital inpatient care (43% of total medical cost), prescription medications to treat complications of diabetes (18%), and anti-diabetic agents and diabetes supplies (12%) (ADA, 2015). People with diagnosed diabetes incur average medical expenditures approximately 2.3 times higher than those without diabetes (ADA, 2015). Diabetics spend an average of $13,700 per year in medical expenditures, of which about $7,900 is attributed directly to the disease (ADA, 2015).

Throughout the world, the prevalence of diabetes mellitus follows a similar pattern as in the United States. As shown in Figure 3, the top ten countries with the highest prevalence of diabetes based on population are India, China, and the United States. And the outlook seems

![Prevalence of diabetes](image)

FIGURE 3. The prevalence of diabetes throughout the world. The top three countries with the highest prevalence of diabetes based on population are India, China, and the United States. From Papathakis (2016a).
grim with estimates of the prevalence more than doubling in most regions of the world by 2030. These numbers are correlated with the rise in obesity of the last few decades. In the United States, more than 60% of the population is classified as overweight or obese. Figure 4 shows the rise in percentage of overweight and obesity among adults aged 20 years and over, by sex, in the United States from 1988-1994 and 2009-2012 (Papathakis, 2016a).

The complications that arise from obesity, including diabetes, cardiovascular disease, and stroke, further lead to increased healthcare costs and an overall burden on society and individuals.

Role of Insulin:

The pancreas plays a major role in maintaining blood glucose by hormone production in the islet cells. Alpha (α) cells produce glucagon which acts on the liver to stimulate glycolysis in order to raise the body’s blood sugar. Beta (β) cells in the pancreas produce insulin which counteracts the response of glucagon and initiates uptake of glucose into cells from the blood, thus lowering blood sugar. Cells that are non-insulin dependent include the brain, liver, and muscles; all other body cells rely on insulin to stimulate glucose uptake to be used in intracellular metabolic processes (Gropper, Groff & Smith, 2009).

The initial phases of digestion of food begin in the mouth with the breakdown of some carbohydrate (CHO) by salivary amylase. Once swallowed, the bolus of food enters the stomach
where most of the digestion process occurs. Enzymes such as pancreatic amylase, gastric lipase, and pepsinogen are secreted and further catabolize the bolus into the constituents of the macronutrients (amino acids, monosaccharides, and fatty acids). Upon digestion, the components are absorbed in the gastrointestinal tract and enter the blood stream. As shown in Figure 5, the absorbed glucose raises the blood sugar which stimulates the β-cells of the pancreas to secrete insulin, which binds to membrane-bound receptors on the cell surface.

![Mechanism of glucose uptake into a cell via insulin response. From McGuire & Beerman (2009).](image)

The binding of the insulin causes a conformational change in the receptor which initiates a signal cascade in the cell that prompts the GLUT-4 glucose transporters to translocate from the cytoplasm to the cell membrane (Gropper et al., 2009). The GLUT-4 transporter enables glucose to move from the extracellular space into the cytoplasm of the cell to be used in metabolic processes, subsequently lowering blood sugar levels and providing energy for the cells to function (Gropper et al., 2009).
Insulin is an anabolic hormone that controls CHO, protein, and fat storage. In CHO metabolism, glucose is transported in the cells when blood glucose is high. If the amount of glucose in the cells exceed the amount needed for metabolic processes, lipogenesis is triggered and the glucose is stored as fat in adipocytes (Gropper et al., 2009). The excess glucose can also be stored as glycogen in muscle and liver cells for use when metabolic needs exceed what is available in the body, such as during exercise, for example. In protein metabolism, insulin acts as an active transport of amino acids from blood to muscle cells and other tissues to promote protein synthesis and produce a positive nitrogen balance. During fat metabolism, insulin stimulates fatty acid synthesis in the liver and storage as triglycerides via the GLUT-4 transporter (Gropper et al., 2009).

Definitions, Risk Factors, and Diagnosis of Diabetes:

*Type 1 Diabetes Mellitus (T1DM).* Approximately 1.25 million Americans are living with type 1 diabetes mellitus (JDRF, 2017) and it accounts for 5-10% of all diagnosed cases of diabetes (Nelms, Sucher, & Lacey, 2016). This form of diabetes develops most frequently in adolescents and is usually diagnosed in early adulthood (Papathakis, P., 2016a; Nelms, Sucher, & Lacey, 2016). The development of T1DM is related to a cell-mediated autoimmune response causing a gradual decline in β-cell function in the pancreas, resulting in the insulin deficiency (Nelms, Sucher, & Lacey, 2016). Due to the lack of insulin production, glucose is unable to be transferred into cells for energy (Nelms, Sucher, & Lacey, 2016). The insufficient secretion of insulin can lead to chronic elevation of blood sugar, or hyperglycemia, which can result in complications such as cardiovascular disease, neuropathy, nephropathy, retinopathy, cataracts, and infections (Gropper, et al., 2009).
The initial signs and symptoms of the disorder are caused by uncontrolled high blood sugar and may include frequent urination (polyuria), excessive thirst (polydipsia), excessive hunger (polyphagia), fatigue, blurred vision, tingling or loss of sensation in the extremities, and weight loss (Papathakis, P., 2016a). If T1DM goes uncontrolled and undiagnosed, life-threatening consequences may occur, such as diabetic ketoacidosis (Papathakis, P., 2016a; Nelms, Sucher, & Lacey, 2016).

Type 2 Diabetes Mellitus (T2DM). In the United States and worldwide, about 90-95% of all diagnosed cases of diabetes are type T2DM (Nelms, Sucher, & Lacey, 2016). The disease occurs most frequently in adults, but is being diagnosed with increasing frequency in children and adolescents as well (Nelms, Sucher, & Lacey, 2016). Gender distribution of T2DM is equal, but prevalence increases with age (Nelms, Sucher, & Lacey, 2016). Other risk characteristics for T2DM include obesity, family history, history of festational DM, impaired glucose metabolism, and physical inactivity (Nelms, Sucher, & Lacey, 2016).

The development of T2DM is caused by a combination of abnormal insulin secretion and insulin resistance, and the condition is considered to be polygenic with multiple factors contributing to its development (Nelms, Sucher, & Lacey, 2016). Unlike T1DM, the pancreas in individuals with T2DM is fully functional in the early stages of the disease. The β-cells, however, may stop producing insulin after a certain point in the disease’s progression which could lead to insulin deficiency and thus glucose intolerance (PubMed Health, 2017).

Type 2 diabetes is often accompanied by severe and life-threatening complications similar to T1DM, particularly cardiovascular disease, retinopathy, nephropathy, and neuropathy (Nicholson, et al., 1999). The common treatments for T2DM often include prescriptions of oral medications, recommendations of physical activity, nutrition education, and diet management
guidance (National Institute of Diabetes and Digestive and Kidney Diseases [NIDDKD], 2017b). Additionally, individuals with T2DM are encouraged to lose weight as necessary, cease smoking, distribute carbohydrate intake throughout the day, engage in physical activity, decrease fat intake, monitor blood glucose, and add medications as needed (Papathakis, 2016b; PubMed Health, 2017; Khardoi, 2017).

**Diagnosis of Diabetes Mellitus:** One of four criteria must be met in order to diagnose an individual with diabetes, as shown in Figure 6.

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**Criteria for Diagnosis of Diabetes Mellitus**

- **HgbA1C ≥ 6.5% using standardized laboratory measures**  
  _OR_
- **Fasting plasma glucose ≥ 126 mg/dL (7.0 mmol/L)**  
  _OR_
- **Symptoms of diabetes plus random plasma glucose concentration ≥ 200 mg/dL (11.1 mmol/L)**  
  _OR_
- **2-hour post-prandial glucose ≥ 200 mg/dL (11.1 mmol/L) during an oral glucose tolerance test (OGTT)**

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Figure 6. Criteria for diagnosis of diabetes mellitus. Adapted from Nelms, Sucher, & Lacey (2016).

Glycosylated hemoglobin assays (HgbA1C) measure the amount of glucose bound to hemoglobin protein (Nelms, Sucher, & Lacey, 2016). The higher the glucose concentration in the blood, the more hemoglobin is glycated, thus making this a valid test to measure the degree of long-term hyperglycemia (Nelms, Sucher, & Lacey, 2016). Red blood cells have an average lifespan of 120 days, so a measure of HgbA1C can measure the average glucose concentration for the previous 2-3 months (Nelms, Sucher, & Lacey, 2016). With the standardization of the test, a HgbA1C of ≥ 6.5% is used as a mode of diagnosis (Nelms, Sucher, & Lacey, 2016). This test
serves not only as a diagnostic test of diabetes, but also as a crucial component of monitoring long-term glycemic control (Nelms, Sucher, & Lacey, 2016).

Controlling blood glucose levels is beneficial for individuals with diabetes. Hyperglycemia can cause inflammation in the blood vessels and result in the potentially fatal complications described briefly before. Hypoglycemia can also cause potential problems such as dizziness, confusion, or fainting (Spero, 2016). Table 1 highlights the recommendations for blood glucose levels for before and after meals for people with and without diabetes:

<table>
<thead>
<tr>
<th>TABLE 1. Blood Glucose Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fasting:</strong></td>
</tr>
<tr>
<td>Non-diabetic</td>
</tr>
<tr>
<td>ADA recommendation for diabetics</td>
</tr>
<tr>
<td><strong>2-Hours Post-Prandial</strong></td>
</tr>
<tr>
<td>Non-diabetic</td>
</tr>
<tr>
<td>ADA recommendation for diabetics</td>
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</table>

Adapted from Diabetes Self-Management (2017).

*Medical Treatment of Diabetes Mellitus:* For individuals with T1DM, they must depend on daily administration of exogenous insulin to survive in conjunction with nutrition therapy and physical activity (Nelms, Sucher, & Lacey, 2016). Treatment of T2DM utilizes a variety of medications (including insulin), nutrition therapy, and lifestyle changes (Nelms, Sucher, & Lacey, 2016). The initial steps in treating T2DM are weight loss and increased physical activity, with the addition of medication in latter stages of disease progression (Nelms, Sucher, & Lacey, 2016). The goals of treatment for both types of diabetes include avoiding hyperglycemia and inhibiting the development of complications within an acceptable level of treatment side effects.
The closer to the normal range of blood glucose can be maintained over the long term, the lower the risk of complications (Nelms, Sucher, & Lacey, 2016).

For nutrition therapy involving diabetes management, there are multiple goals that help manage diabetes: HgbA1C <7%, blood pressure <140/80 mgHg, LDL cholesterol <100 mg/dL, triglycerides <150 mg/dL; HDL cholesterol >40 mg/dL for men and >50 mg/dL for women, achieve and maintain body weight goals, and delay or prevent complication of diabetes (Nelms, Sucher, & Lacey, 2016). Current diet recommendations to achieve glycemic and metabolic control include the Mediterranean diet, the DASH diet, vegetarian or vegan diets, as well as low-fat and low-carbohydrate diets (Nelms, Sucher, & Lacey, 2016). This review focuses on the health benefits for diabetics by following a vegetarian diet.

*Exercise & body weight effect on Insulin Sensitivity:* With the correlation between a rise in obesity and diabetes, the correlation between body weight and insulin sensitivity has been heavily researched. In the 2011 study by Mason et al., the researchers found that dietary weight loss, with or without exercise, significantly improved insulin resistance (Mason et al., 2011). This conclusion has also been found by a growing body of researchers including Duncan et al (2003), Devlin et al (1987), and Goodyear & Kahn (1998). Exercise is a confounding variable when examining the effects of diet on the management of diabetes, and should be noted in this review as a potential contributor to success in reducing insulin resistance.

**Plant-Based Diets**

People adopt plant-based diets for a variety of reasons including health concerns, religious convictions, animal welfare, and environmental implications. Furthermore, some people follow a mostly vegetarian diet because they cannot afford to purchase and eat meat.
According to a Harris Interactive poll commissioned by the Vegetarian Resource Group, approximately six to eight million adults in the United States do not eat any meat, fish, or poultry. Several million more have eliminated red meat but still eat chicken or fish, and about two million people have adopted more restrictive vegan diets (Harvard Women’s Health Watch, 2016).

Definitions:

**Vegetarian Diets**: In general, vegetarianism excludes all animal flesh from the diet (Li, 2013). Foods such as dairy, cheese, eggs, and honey may still be included depending on the individual’s preference and tolerance. Within the vegetarian diet, there are further restrictions one may follow: lacto-ovo vegetarians consume diary and eggs, but no meat, poultry, or fish; lacto-vegetarians consume dairy, but no eggs, meat, poultry, or fish; and ovo-vegetarians consume eggs, but no meat, poultry, fish, or dairy. Vegan diets not only exclude all meat from the diet, but also all animal products including dairy, eggs, cheese, honey, and even certain foods that are processed with animal byproducts, such as gelatin (from animal bones and connective tissue) and some sugars that are whitened with bone char (Li, 2013).

For this literary analysis, inclusion criteria for clinical trials is established based on studies defining a vegetarian and/or vegan diet as an experimental variable on development and/or management of type 2 diabetes mellitus.

**History and Background of Vegetarian Diets**

Vegetarianism has a long history in most cultures around the world. In ancient Greece, the mathematician Pythagoras followed a vegetarian diet not only to avoid animal cruelty, but also because he experienced the health advantages of a meat-free diet (World History of Vegetarianism, 2016). In eastern religions, abstinence from meat is central to the religious
philosophies of Hinduism, Jainism, and Buddhism in addition to following non-violence practices (World History of Vegetarianism, 2016).

In western religions such as Christianity, vegetarian diets are also prevalent especially in the Seventh-Day Adventist community. According to the Seventh-Day Adventist church website, health is considered a gift from a “loving God,” and eating a well-balanced vegetarian diet that avoids the consumption of meat coupled with intake of legumes, whole grains, nuts, fruits and vegetables, along with a source of vitamin B$_{12}$, will promote vigorous health (Seventh-Day Adventist Church, 2017).

Now in the twenty-first century, vegetarian diets have been gaining popularity especially because of the environmental issues that have dominated headlines. The massive outbreaks of food-borne illnesses related to animal products, such as Mad Cow Disease and Salmonella, have also caused people to turn to vegetarianism as a “safe and healthy alternative” to consuming meat (World History of Vegetarianism, 2016).

**Overall Health Benefits and Concerns of a Vegetarian Diet**

Vegetarian diets are typically based on the consumption of whole grains, legumes, vegetables, fruits, and nuts. This general dietary pattern correlates to having a diet rich in fiber, magnesium, phytochemicals, antioxidants, vitamins C and E, F$^{3+}$, folic acid, and n-6 polyunsaturated fatty acids (PUFAs), but low in cholesterol, total fat and saturated fat, sodium, zinc, vitamins A, B$_{12}$ and D, and especially n-3 PUFAs (Li, 2013). Compared to omnivores, the low intake of cholesterol, total fat, sodium, and high intake of phytochemicals, antioxidants and fiber in vegetarians is associated with health advantages including decreased mortality and morbidity of non-communicable diseases such as diabetes (Li, 2013). Additionally, vegetarian diets are likely to have lower total and LDL cholesterol, lower blood pressure, and lower body
mass index (BMI), all of which are associated with longevity and a reduced risk for chronic diseases such as cardiovascular disease, stroke, cancer, and type 2 diabetes (Harvard Women’s Health Watch, 2016).

Conversely to the numerous health benefits of a vegetarian diet, there are also risks associated. The nutrients of concern in the diet of vegetarians include vitamin B$_{12}$, vitamin D, omega-3 fatty acids, calcium, iron, and zinc (Craig, 2010). According to Nutrition Concerns and Health Effects of Vegetarian Diets (2010), a vegetarian diet can meet current recommendations for all of the nutrients listed previously, however the use of supplements and fortified foods may provide a “useful shield” against deficiency (Craig, 2010).

Vitamin D plays an important role in bone health, immune function, reduction of inflammation, and reducing the risk of chronic diseases (Craig, 2010). Vitamin D insufficiency has also been linked to a wide variety of diseases including type 1 diabetes. The main sources of vitamin D include fatty fish, tuna, mackerel, fortified foods such as orange juice and dairy, cheese, liver, and egg yolks (National Institutes of Health [NIH], 2016a). These foods are mostly excluded from vegan and vegetarian diets and supplementation is generally recommended.

Vitamin B$_{12}$ is essential for DNA and RNA synthesis and is important in maintaining functional nerve cells (Ehrlich, 2015). Severe deficiency of vitamin B$_{12}$, which can occur in vegans and vegetarians if the diet is inadequately planned, may lead to long-term nerve damage (Ehrlich, 2015). Food sources of vitamin B$_{12}$ are all animal-based products, such as liver, fish, beef, milk, yogurt, and eggs (National Institutes of Health, 2016b).

**Plant-Based Diets and Type 2 Diabetes Mellitus**

As with most scientific trials, methodologies are often varying and therefore may produce varying results. Studies related to the effects of plant-based diets on diabetes are no exception.
However, most recent studies highlight the benefits of adopting a plant-based diet for diabetics and people at risk for developing diabetes.

**Plant-Based Diets and Prevention of T2DM**

One of the most notable studies for examining the prevention and development of T2DM based on diet is the follow up to the Adventist Health Study-2 (Tonstad et al., 2013). The Adventist Health Study-2 began in 2002 as a prospective study conducted among Adventist church members in the US and Canada with the purpose of investigating the role of foods in regard to various forms of cancer (Tonstad et al., 2013).

In the study conducted by Tonstad, et al. (2013), participants (15,200 men and 26,187 women) were grouped as vegan, lacto-ovo vegetarian, pescetarian, semi-vegetarian, or non-vegetarian as the reference group. A follow-up questionnaire after two years in the initial study elicited information on the development of diabetes (type 1 or 2 was not specified).

From these results, cases of diabetes developed in 0.54% of vegans, 1.08% of lacto-ovo vegetarians, 1.29% of pescetarians, 0.92% of semi-vegetarians, and 2.12% of non-vegetarians. The odds ratio (OR) for diabetes among vegans was 0.383 (95% CI 0.233, 0.629), lacto-ovo-vegetarians, 0.635 (95% CI: 0.511, 0.789), pescetarians, 0.791 (95% CI 0.572, 1.095), and semi-vegetarians, 0.477 (95% CI 0.277, 0.722) compared to the non-vegetarian reference group (Tonstad et al., 2013).

In the final model, adjustment was made for age, BMI, lifestyle, and sociodemographic factors including gender, ethnicity, income, and education. Vegan, lacto-ovo, and semi-vegetarian diets were associated with a lower incidence of diabetes, while pescetarian diets were not associated with lower incident (Tonstad et al., 2013) Table 2 includes the study’s data.
The main finding of this study was that vegan, lacto-ovo, and semi-vegetarian diets were associated with a statistical reduction in risk of diabetes compared to non-vegetarian diets, after adjusting for BMI and sociodemographic and lifestyle factors (Tonstad et al., 2013). In the study, there appeared to be an incremental protection as dietary pattern moved from non-vegetarian to semi-vegetarian to pescatarian to lacto-ovo vegetarian to vegan (Tonstad et al., 2013). The vegan diet appeared to afford the greatest protection against the development of diabetes, although the authors warn that the vegan results should be interpreted with care because there were only a small number of vegans who developed diabetes (Tonstad et al., 2013).

The study further notes that part of the protection associated with vegetarian diets may be due to the lower BMI of vegetarians compared to non-vegetarians (Tonstad et al., 2013). Plausible mechanisms have been proposed to explain the protection associated with vegetarian diets. Fruits and vegetables may contribute to a decreased incidence of T2DM through their low density, low glycemic load, and high fiber and micronutrient content. Other features of the vegetarian diet consist of whole grains and legumes which have been shown to improve

TABLE 2. Multiple logistic regression analysis of the relation between diet and diabetes in the total population (n = 41,387).

<table>
<thead>
<tr>
<th></th>
<th>Odds ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in 1-year increments</td>
<td>1.031</td>
<td>1.024–1.038</td>
</tr>
<tr>
<td>BMI per 1 kg/m²</td>
<td>1.109</td>
<td>1.096–1.122</td>
</tr>
<tr>
<td>Dietary status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vegan vs non-vegetarian</td>
<td>0.381</td>
<td>0.236–0.617</td>
</tr>
<tr>
<td>Lacto-ovo vegetarian vs non-vegetarian</td>
<td>0.618</td>
<td>0.503–0.760</td>
</tr>
<tr>
<td>Pesco-vegetarian vs non-vegetarian</td>
<td>0.790</td>
<td>0.575–1.086</td>
</tr>
<tr>
<td>Semi-vegetarian vs non-vegetarian</td>
<td>0.486</td>
<td>0.312–0.755</td>
</tr>
</tbody>
</table>

Adapted from Tonstad et al., (2013).
glycemic control, slow the rate of carbohydrate absorption, therefore decreasing the risk of diabetes (Tonstad et al., 2013).

Strengths of the study include that data were collected prospectively in a well-designed, established cohort study, which minimizes recall bias. Study results were strengthened due to measurement of several well-known confounders for diabetes, and after accounting for the confounders, the associations still remained strong (Tonstad et al., 2013).

Limitations of the study also must be considered when interpreting these findings. Because screening for blood glucose was not feasible for the large cohort, under-diagnosing of diabetes is likely. The data are also self-reported, however, the researchers attempted to assess the consistency of self-reports of diabetes. They confirmed consistency in 97.4% of those who reported diabetes (Tonstad et al., 2013). Additionally, dietary measurement error is inevitable and may have resulted in some misclassification. The vegetarian diet was also positively associated with some lifestyle-related factors (such as physical activity) and inversely associated with others (smoking), and residual confounding may have remained after adjustment due to inaccurate measurements (Tonstad et al., 2013).

Plant-Based Diets and Management of T2DM

Most of the studies delving into T2DM and plant-based diets focus on the management of the disease rather than the prevention. The following studies all identify various relationships with plant-based diets and their effect on blood glucose control, hemoglobin A1C, and body weight, all of which are correlated to management of T2DM.

Low-fat Vegan and Vegetarian Diet Studies. Multiple studies have looked into the effects of plant-based diets on blood glucose control. In the study conducted by Nicholson et al. (1999), the researchers investigated whether glycemic and lipid control in patients with non-insulin-
dependent diabetes (NIDDM) can be significantly improved using a low-fat vegan diet. Specifically, they intended to see the effects in the absence of recommendations regarding exercise or other lifestyle changes (Nicholson et al., 1999).

Table 3 indicates that eleven subjects with NIDDM were recruited from the Georgetown University Medical Center and local community were randomly assigned to a low-fat vegan diet (n = 7) or a conventional low-fat diet (n = 4) for 12 weeks of intervention (Nicholson et al., 1999). The researchers note that two additional subjects assigned to the control group failed to complete the study, and that data were not included in the analysis (Nicholson et al., 1999).

<table>
<thead>
<tr>
<th>TABLE 3. Baseline Demographic and Clinical Characteristics</th>
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<tbody>
<tr>
<td><strong>Experimental</strong> (n = 7)</td>
</tr>
<tr>
<td><strong>Mean age (years)</strong></td>
</tr>
<tr>
<td><strong>Age range</strong></td>
</tr>
<tr>
<td><strong>Women</strong></td>
</tr>
<tr>
<td><strong>On oral hypoglycemic agents</strong></td>
</tr>
<tr>
<td><strong>On insulin</strong></td>
</tr>
<tr>
<td><strong>History of hypertension</strong></td>
</tr>
<tr>
<td><strong>Receiving antihypertensives</strong></td>
</tr>
<tr>
<td><strong>History of coronary artery bypass graft surgery</strong></td>
</tr>
</tbody>
</table>


The inclusion criteria for the study were non-insulin-dependent diabetes mellitus, age greater than 25 years, willingness to attend all components of the study, and residence within commuting distance of Georgetown University (Nicholson et al., 1999). Exclusionary criteria included smoking, regular alcohol use, current or past drug abuse, pregnancy, psychiatric illness, and medical instability (Nicholson et al., 1999). Each subject then completed a medical history and physical examination, and laboratory specimens were collected for fasting serum glucose and hemoglobin A1C, among a few other measures irrelevant to this review.
The low-fat vegan diet excluded animal products, added oils, sugars, and refined carbohydrates. The dietary analysis indicated that 10-15% of calories were from protein, <10% of total calories were from fat, and the remaining calories (~75-80%) were from unrefined complex carbohydrates (Nicholson et al., 1999). The cholesterol content of the diet was zero. A vitamin B\textsubscript{12} supplement was recommended for subjects planning to continue the diet after the study’s conclusion, but was not mandatory for the study. The control diet emphasized the use of fish and poultry, rather than red meat. It was designed to derive 55-60% total calories from carbohydrate and <30% of calories from fat. Protein intake accounted for ~15% of the diet (Nicholson et al., 1999). The cholesterol content of the diet was approximately 200mg/day.

During the course of the 12-week study, subjects in both groups were offered prepared lunch and dinner meals conforming to their respective diets (Nicholson et al., 1999). Also of importance to the study design is that the diets were not designed to be isocaloric. Participants were responsible for preparing their own breakfast and were free to add any desired quantities of foods to their diets at any time of day without caloric restriction, provided they adhered to the prescribed guidelines (Nicholson et al., 1999). Subjects completed a 3-day dietary record, including two weekdays and one weekend day, at baseline and 12 weeks. This record served as a qualitative representation of nutrient intake. The study also included support groups, educational sessions, and shared meals (Nicholson et al., 1999).

Fasting serum glucose was measure at baseline and biweekly thereafter using an Abbott Spectrum analyzer, and hemoglobin A1C (HgA1C) was assayed at baseline and 12 weeks using affinity chromatography (Nicholson et al., 1999). As shown in Table 4, baseline diets were similar for the two groups. During the course of the study, fat, cholesterol, and protein intakes decreased substantially for the experimental group, while carbohydrate and fiber intake increased
(Nicholson et al., 1999). In the control group, total fat intake remained unchanged, fiber intake increased, and cholesterol intake decreased (Nicholson et al., 1999).

**TABLE 4. Dietary Characteristics of experimental and control groups at baseline and 12 weeks after intervention**

<table>
<thead>
<tr>
<th></th>
<th>Experimental (n = 7)</th>
<th>Control (n = 4)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Total energy (kcal/day)</td>
<td>1683 (435)</td>
<td>1409 (549)</td>
</tr>
<tr>
<td>Protein (% of energy)</td>
<td>20 (5.9)</td>
<td>14 (1.6)</td>
</tr>
<tr>
<td>Carbohydrate (% of energy)</td>
<td>46 (7.0)</td>
<td>75 (4.4)</td>
</tr>
<tr>
<td>Fiber (g)</td>
<td>14 (4.3)</td>
<td>26 (8.2)</td>
</tr>
<tr>
<td>Total fat (% of energy)</td>
<td>34 (5.3)</td>
<td>11 (4.7)</td>
</tr>
<tr>
<td>Saturated fat (% of energy)</td>
<td>10 (2.4)</td>
<td>3 (2.0)</td>
</tr>
<tr>
<td>Cholesterol (mg)</td>
<td>289 (86)</td>
<td>4.4 (7.4)</td>
</tr>
</tbody>
</table>

*Note. Standard deviations are indicated in parentheses.*


Additionally, fasting serum glucose values dropped 28% from baseline to the intervention mean for the experimental group, compared to a 12% decrease in the control group (Nicholson, et al., 1999). The effect of diet on HgA1C was insignificant. Furthermore, the differences in weight between baseline and 12 weeks was significant: the experimental group lost an average of 7.2kg over 12 weeks, compared to a mean weight loss of 3.8 kg in the control group (Nicholson et al., 1999). All of these values are highlighted in Table 5.

**TABLE 5. Clinical Changes from Baseline to 12 Weeks**

<table>
<thead>
<tr>
<th></th>
<th>Experimental (n = 7)</th>
<th>Control (n = 4)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Weight (kg)**</td>
<td>96.7 (13.3)</td>
<td>89.5 (14.4)</td>
</tr>
<tr>
<td>FSG (mmol/L)**</td>
<td>10.74 (2.85)</td>
<td>7.75 (2.07)</td>
</tr>
<tr>
<td>HbA1C (%)</td>
<td>8.3 (1.7)</td>
<td>6.9 (1.1)</td>
</tr>
</tbody>
</table>

*Note. Standard deviations are indicated in parentheses.*

*p < .005 for the effect of diet, controlling for baseline, on six biweekly measures.

**p < .05 for the effect of diet, controlling for baseline, on six biweekly measures (fasting serum glucose) or at 12 weeks (HDL). Adapted from Nicholson et al., (1999).
Despite the small sample size of this study, the differences between the treatment groups in the reductions of fasting serum glucose and body weight reached statistical significance (Nicholson et al., 1999). Additionally, the 7.2kg weight loss experienced by the experimental group was achieved with no attempt to limit energy intake (Nicholson et al., 1999). The results of this study are limited by its small sample size and by the fact that the participants may have been more motivated than other people with diabetes because they volunteered to enroll as study participants. In summary, the researchers found that use of a low-fat vegan diet was associated with reductions in fasting serum glucose concentrations and body weight in a 12-week trial (Nicholson et al., 1999).

The Nicholson study focused on a small cohort for a relatively short duration of intervention, however, a study similar in methodology, conducted by Barnard et al. (2009), focused on a larger cohort (n = 99) for 74 weeks. The study intended to compare the effects of a low-fat vegan diet and conventional diabetes diet recommendations on glycemia, weight, and plasma lipids (Barnard et al., 2009). Individuals with type 2 diabetes, defined by a fasting blood glucose concentration >125 mg/dL on two occasions or a prior diagnosis of T2DM treated with medications for blood glucose control for ≥6 months, in the Washington D.C. area were recruited to complete the study. Exclusionary criteria were a HgA1C <6.5% or >10.5%; use of insulin for >5 y; smoking, alcohol, or drug abuse; pregnancy; unstable medical status; and current use of a low-fat vegetarian diet. Hemoglobin A1C was measured with affinity chromatography (Barnard et al., 2009).

Study participants prescribed a vegan diet (n = 49) were asked to avoid animal products, “fatty foods” (such as added oils, fried foods, avocados, nuts, and seeds), and favor low-glycemic index foods, such as beans and green vegetables (Barnard et al., 2009). The vegan diet
also obtained ~10% energy from fat, 15% from protein, and 75% from carbohydrate and was unrestricted on energy intake (Barnard et al., 2009). Conversely, the conventional diabetic diet was about 15-20% total calories from protein, <7% saturated fat, and 60-70% carbohydrate, and was individualized based on body weight and blood lipid concentrations (Barnard et al., 2009). All participants were free living and no meals were provided, but a vitamin B₁₂ supplement was provided for all participants to be taken every other day (Barnard et al., 2009).

At seven points during the trial, a registered dietitian made unannounced phone calls to each participant to administer a 24-hour diet recall using a multiple-pass approach (Barnard et al., 2009). Additionally, multiple 3-day dietary records were completed by each participant using two weekdays and one weekend day.

From the data, both diets were associated with significant sustained weight reduction (~4.4 kg in the vegan group and -3.0 kg in the conventional diet group) (Barnard et al., 2009). Furthermore, both diets were associated with reductions in HgA₁C. The mean change was slightly but not significantly greater in the vegan group (Barnard et al., 2009). Among participants in the vegan group with no changes to diabetes medications, HgA₁C had fallen 1.23 by 22 weeks (n = 24) and 0.82 by 74 weeks (n = 14) (Barnard et al., 2009). Among medication-stable participants in the conventional diet group, the HgA₁C reduction was 0.38 at 22 weeks (n = 33) and 0.21 (n = 21) at 74 weeks (Barnard et al., 2009). The study’s authors concluded that much of the effect of the intervention diets on glycemia appear to be mediated by weight reduction (Barnard et al., 2009).

The strengths of this study include its randomized design, extended duration, inclusion of individuals with long-standing diabetes, analysis of dependent measures without regard to variations in dietary adherence, statistical methods aimed at reducing the effect of medication...
changes, and applicability outside the research setting (Barnard et al., 2009). The researchers also considered the study’s weaknesses: changing of medication for diabetics and a smaller sample size due to limiting analysis to those with no medication changes (Barnard et al., 2009).

In conclusion, individuals with T2DM participating in the study, both low-fat vegan diets and conventional diabetes diets based on the 2003 ADA guidelines facilitated long-term weight reduction (Barnard et al., 2009). In analyses controlling for medication changes, the vegan diet appeared to be more effective for control of blood glucose (Barnard et al., 2009).

The two previous studies highlighted the effects of low-fat vegan diets on T2DM. The following study compares the effects of a calorie-restricted vegetarian diet and conventional diabetic diets on subjects with T2DM. In the study conducted by Kahleova et al. (2010), the researchers directed a 24-week, randomized control trial in which 74 participants with T2DM were assigned to either the experimental group following a vegetarian diet (n = 37), or the control group following a conventional diabetic diet (n = 37). Inclusionary criteria were a diagnosis of T2DM, age 30-70 years, HgA1C between 6-11%, BMI between 25-53 kg/m², and willingness to change dietary habits and follow a prescribed exercise program (Kahleova et al., 2010). Exclusion criteria were HgA1C <6% or >11%, use of insulin, abuse of alcohol or drugs, pregnancy, lactation, or current use of vegetarian diet (Kahleova et al., 2010).

Both of the study’s diets were designed to be isocaloric and calorie restricted (-500 kcal/day), with calorie intakes based on the measurement or resting energy expenditure of each subject by indirect calorimetry (Kahleova et al., 2010). In the latter half of the study, the diets were combined with aerobic exercise. The researchers also incorporated educational sessions to teach the participants how to compose and prepare their diet, in addition to attending weekly one hour meetings with lectures and cooking classes (Kahleova et al., 2010). Of note, all meals
during the study were provided, and participants were examined at baseline, 12 weeks, and 24 weeks (Kahleova et al., 2010).

The vegetarian diet consisted of ~60% energy from carbohydrates, 15% protein and 25% fat and focused mostly on including vegetables, grains, legumes, fruits and nuts. Animal products were limited to a maximum of one portion of low-fat yogurt a day (Kahleova et al., 2010). This criterion allows for the diet to be classified as vegan since dairy was not heavily emphasized. The conventional diabetes diet was administered according to the dietary guidelines of the Diabetes and Nutrition Study Group (DNSG) of the European Association for the Study of Diabetes (EASD) (Kahleova et al., 2010). The diet contained 50% total energy from carbohydrates, 20% protein, <30% fat (≤7% saturated fat, <200 mg/day of cholesterol) (Kahleova et al., 2010). The vegetarian meals were provided in two vegetarian restaurants, whereas the conventional diabetic diet meals were provided at the Institute for Clinical and Experimental Medicine in Prague. Vitamin B\textsubscript{12} was supplemented in both the experimental group and the control group (50 µg/day) (Kahleova, et al., 2010).

During the first 12 weeks of the study, participants were asked not to alter their exercise habits, but from weeks 13-24, they were prescribed an individualized exercise plan based on their history of physical activity and initial examination (Kahleova et al., 2010). Additionally, participants were asked to continue their pre-existing medication regimens, except when hypoglycemia occurred repeatedly (Kahleova et al., 2010). In such cases, medications were reduced by a study physician (Kahleova et al., 2010). All participants were given an Accu-Chek Go glucometer and were instructed on how to use it. All measurements (plasma glucose, insulin, c-peptide, HgA1C, plasma lipids) were performed at 0, 12, and 24 weeks on an outpatient basis,
after 10- to 12-h overnight fasting with only tap water allowed *ad libitum* (Kahleova et al., 2010).

Ninety-two percent of the participants completed the first 12 weeks (95% in experimental groups and 89% in control group); 84% of participants in each group completed all 24 weeks (Kahleova et al., 2010). Adherence to the prescribed diet at 24 weeks was high among 55% participants in the experimental group and 32% in the control group (Kahleova et al., 2010). Diabetes medication was reduced in cases of repeated hypoglycemia in 43% of participants in the experimental group and in 5% of participants in the control group (P < 0.001); the difference between groups was 38% (95% CI 17-58%) (Kahleova et al., 2010).

Additionally, HgA1C fell in both groups during the first 12 weeks (P < 0.001) and remained reduced after implementation of the exercise program in weeks 13-24 (Kahleova, et al., 2010). The decrease from baseline to 24 weeks, however, was significant only in the experimental group (-0.65 ±1%; P = 0.002 vs -0.21 ± 1.1%); and not significant in the control group. The difference between groups was not statistically significant (Kahleova et al., 2010). Among participants whose diabetes medications remained unchanged, HgA1C fell by 0.9% in the experimental group from baseline to 24 weeks (P = 0.002) versus a non-significant decrease of 0.2% in the control group (P= 0.08) (Kahleova et al., 2010).

Furthermore, body weight decreased in both groups in response to the dietary interventions (P < 0.001) and it was maintained after the addition of exercise. Weight loss was greater in the experimental group than in the control group [-6.2 kg (95% CI -6.6 to -5.3) versus -3.2kg (95% CI -3.7 to -2.5)] (Kahleova et al., 2010). Waist circumference also decreased in both groups in response to the dietary interventions (P < 0.001), more in the experimental group than in the control group [-6.4cm (95% CI -7.1 to -5.7) versus -5.3cm (95% CI -5.9 to -4.5)]
(Kahleova et al., 2010). Volume of subcutaneous fat and visceral fat also decreased in both groups after the dietary interventions (P < 0.001), and further decreased in the experimental group after addition of exercise [4% (95% CI -5.8 to -0.2)] whereas it remained unchanged in the control group (P = 0.007) (Kahleova et al., 2010).

The study’s authors concluded that a calorie-restricted vegetarian diet increased insulin sensitivity, reduced body weight, and improved plasma concentrations of adipokines and oxidative stress markers (two values that were measured in the study, but are not directly relevant to this literary analysis). The researchers hypothesize that the advantageous effects of a vegetarian diet may be partly explained by weight loss, especially loss of visceral fat and the consequent increase in insulin sensitivity (Kahleova et al., 2010).

This study highlights the benefits of two calorie restricted diets, especially noting the benefits of the vegetarian diet. These benefits may be explained by several possible mechanisms: higher intake of fiber, lower intake of saturated fat (and higher polyunsaturated and saturated fatty acid ratio), higher intake of non-heme iron and reduction in iron stores, higher intake of vegetable protein in place of animal protein, high intake of antioxidants and plant sterols (Kahleova et al., 2010).

The strengths of this study include the parallel design (in which all participants started simultaneously), providing all meals for participants, relatively long study duration, and the measurement of several metabolic variables with results applicable outside of the research setting (Kahleova et al., 2010). There are limitations to the study design as well: small sample size and low adherence to diet in control group (Kahleova, et al., 2010).

In conclusion, the results of the study indicate that a vegetarian diet alone or in combination with exercise is more effective in increasing insulin sensitivity, reducing volume of
visceral fat and improving plasma concentrations of adipokines and oxidative stress markers than a conventional diabetic diet with or without the addition of exercise (Kahleova et al., 2010). Lastly, the researchers suggest that vegetarian diets may provide a beneficial alternative for nutritional therapy in T2DM, especially in combination with aerobic exercise (Kahleova et al., 2010).

**Summary and Suggestions for Future Research**

Diabetes is a growing pandemic. The rates of prevalence have been increasing for the last 70 years, and there is no indication that they will slow down any time soon (Ardisson, et al., 2014). Type 2 diabetes is largely attributable to lifestyle choices and behavioral practices that result in obesity, lack of physical activity, and undesirable food choices related to food and nutrition knowledge deficit. Behavior modification may be a starting point for management of T2DM, but the constructed modern environment does not allow for healthy choices to be the easy choices. A variety of research, however, is being conducted on the prevention and management of T2DM, especially relating to vegetarian diets.

From recent analysis, vegetarian diets may be viable options for certain individuals in reducing the risk of and managing diabetes. The studies evaluated in this review focused on mostly low-fat vegan diets that were implemented in a variety of populations either as part of a randomized, controlled trial, or a retrospective analysis. With relatively large sample sizes and applicability outside of the research setting, the results from the studies indicate that low-fat vegan and vegetarian diets maintain or improve certain biomarkers—such as HgA1C, blood glucose, insulin sensitivity, and body weight—all of which pertain to diabetes.

These results, however, do not mean that following a vegetarian or vegan diet should be recommended to all diabetics. Along with proper medications, exercise, and lifestyle factors,
adhering to a vegetarian diet may aid in managing the disease. Further evidence is needed in order to recommend a low-fat vegetarian or vegan diet as the most beneficial eating pattern for individuals with diabetes. Longer duration trials (> 52 weeks) that have a sample size of at least 100 participants may be beneficial in applying the results to the population at large. Furthermore, some recent studies include exercise as part of the intervention, which has been shown to increase insulin sensitivity (Kahleova, et al., 2010). More high-quality studies that reduce the effect of confounding variables would be beneficial in ascertaining the direct link between diet and disease state. Additional funding for plant-based diet-related research and the effects on diabetes would be valuable in order to make further dietary recommendations for individuals afflicted with the disease.
References


Beerman, K., & McGuire, M. (2014). [Figure illustration of insulin’s role in glucose uptake Figure 4-19, page 147]. *Nutritional Sciences: From Fundamentals to Food 2e*. Retrieved from Papathakis Diabetes Mellitus PowerPoint.


