Systematic Review of the Health Benefits of Vegetarian and Vegan Diets in the Management of Adults with Diabetes Mellitus Type 2

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Abstract

Introduction: The prevalence of type 2 diabetes mellitus (DM) is rapidly increasing and recent estimates rank type 2 DM as the 7th leading cause of death in the United States. Although some evidence suggests that consuming a vegetarian diet may lead to better glycemic control and improved metabolic outcomes compared with a conventional hypocaloric diet among persons with type 2 DM, there is uncertainty regarding the magnitude of benefit and the specific outcomes that show benefit. Medical costs associated with diabetes, overweight, heart disease, lipid disorders and hypertension are a significant cost to the healthcare system and employers. The need for reductions in these illnesses is driven by both medical and economic concerns and requires a targeted approach in both the patient-care and workplace settings. **Objective**: To conduct a systematic review of clinical trials evaluating the benefit of vegan and vegetarian diets for improving glycemic control and other metabolic outcomes in type 2 DM **Methods**: Data source: PubMed, EMBASE, Cochrane and the Clinical Trails databases were searched for trials published in the English language in the last ten years through April 4, 2018. The following criteria were used for study inclusion: (1) studies enrolling adults (18 years or older); (2) vegan or vegetarian diet as the intervention; and (3) participants had a previous diagnosis of type 2 DM. Main outcome measures were HbA1c, body weight and LDL levels. Critical appraisal and abstraction of relevant data from studies was performed by one author. **Results**: Eight studies met inclusion criteria (785 total participants, mean age 53 years). Vegan and vegetarian diets were shown to be associated with a significant reduction in HbA1c, body weight, and LDL levels. Consumption of a vegan or vegetarian diet yielded a decrease in HbA1c of -0.40% to -0.65% in the intervention arm of the four best studies. These same studies had an HbA1c change in the control arm of -0.08% to 0.21%. The difference between intervention and control groups mean change in HbA1c was reported with statistical significance in five studies with a range of -1.5% to -0.7 %. In the three of the studies reporting on BMI, differences between groups in mean changes from baseline were all statistically significant and

ranged from -1.0 kg/m^2 to -3.9 kg/m^2. In four of the studies reporting on weight change, differences between groups in mean changes from baseline were all statistically significant and ranged from -2.8 kg to -10.6 kg. In four of the studies reporting on LDL, differences between groups in mean changes from baseline were all statistically significant and ranged from -7.2 mg/dL to -0.54 mg/dL.

Conclusion: This systematic review supports the evidence from clinical trials that vegan and vegetarian diets reduce HbA1c levels and results in weight loss in adults with type 2 diabetes. The health benefits of introducing a vegan or vegetarian diet program, at home or in a corporate setting, can lead to improving the management of type 2 DM in adults, and reducing morbidity and mortality of type 2 DM.

Introduction

Diabetes mellitus, type2, is one of the fastest growing chronic diseases, with approximately 422 million cases worldwide in 2014.[16] In 2015, 30.3 million Americans (9.4% of the US population) were estimated to have diabetes; the estimated prevalence is higher among adults over 65 years of age (25.2%).[15] Diabetes accounts for $176 billion of direct medical costs in the US, including annual per capita costs of $7900, a number 2.3 times higher than costs for adults without diabetes. In 2015, type 2 DM was estimated to be the 7th leading cause of death in the United States.[16] The financial toll of type 2 DM is carried by the healthcare system and employers in the United States. An estimated 25–30% of medical costs incurred by employers are attributable to excess risk associated with specific factors, including diabetes, overweight, heart disease, lipid disorders and hypertension.[9, 26] The need for reductions in these illnesses is driven by both medical and economic concerns.

The burden of type 2 DM is growing, and globally, the number of people with diabetes is expected to exceed 430 million by 2030. Patients with diabetes are more than twice as likely to die from vascular causes, such as cardiovascular disease (CVD) and chronic kidney disease (CKD), as those without diabetes. CVD alone accounts for approximately 60% of the life years lost from diabetes. Diabetes is the leading cause of CKD in the United States with the Medicare expenditure on the US end-stage renal disease ESRD program alone reaching 33 billion dollars in 2010.[32] Among older adults, diabetes is associated with an increased risk of mortality, reduced functional status, and increased risk of institutionalization.[14]

The American Diabetes Association has made several recommendations regarding the medical nutrition therapy of diabetes, all of which emphasize the importance of minimizing macrovascular and microvascular complications in people with diabetes.[31] Diet and lifestyle interventions have been shown to be effective tools for type 2 DM prevention and management.[14] Dietary advice is one of the cornerstones in the management of type 2 DM, however, there is limited evidence on the optimal approaches to glycemic control and weight

loss in type 2 diabetics. In particular, vegan and vegetarian diets, plant-based diets that emphasize legumes, whole grains, vegetables, fruits, nuts, and seeds and discourage all animal products, may be particularly effective in preventing type 2 DM and lowering rates of obesity, hypertension, hyperlipidemia, cardiovascular mortality, and cancer.[14] Multiple potential mechanisms underlie the benefits of a plant-based diet in decreasing insulin resistance; including promotion of a healthy body weight; increases in fiber and phytonutrients; food-microbiome interactions; and decreases in saturated fat; advanced glycation end-products; nitrosamines; and heme iron.[14]

Although some evidence suggests that consuming a vegetarian diet may lead to a greater weight loss and greater reduction in fasting plasma glucose, hemoglobin A1c, plasma lipids, and hypoglycemic medication than a conventional hypocaloric diet in subjects with type 2 DM, there is uncertainty regarding the magnitude of benefit and the specific outcomes that show benefit.[4] This systematic review aims to examine the literature evaluating the health benefits of a vegan or vegetarian diet in the treatment of adults with DM type 2.

Methods

Data Sources and Searches

In order to review recent evidence related to the benefit of vegan or vegetarian diets among adults with diabetes, our literature search was limited to studies published in the last ten years. PubMed, EMBASE, Cochrane and the Clinical Trails databases were searched from April 2008 to April 2018 for English language articles. Eligible populations included adults previously diagnosed with DM type 2. Studies had to compare a dietary intervention focused on a vegan or vegetarian diet with another type of diet. Full inclusion and exclusion criteria and search terms are included in **Tables 1-3**. A research librarian at the University of North Carolina Health Sciences Library assisted in the formulation of the search strategy. Only randomized control trials were retained in the search results and one author independently reviewed all titles and abstracts identified by the search. In this review, the intervention of a vegan or vegetarian

diet included only those studies where the definition of vegan and vegetarian did not include any meat. This review outlines change in several blood levels that are used to monitor the management of a patient with type 2 diabetes. The outcome markers of interest included were body mass index (BMI), body weight, fasting glucose, hemoglobin A1c, and various lipid levels.

Data Abstraction

With the assistance of an experienced medical research librarian, searches in PubMed, EMBASE, Cochrane and Clinical Trials were completed and exported into a standardized data collection instrument called Covidence. The key question's focus was the health benefits of vegan or vegetarian diets on the management of type 2 DM. Articles were abstracted by evaluating the study design, the time frame of the study, population, sources of bias from selection, measurement, confounding, outcome measure and results. A full list of inclusion and exclusion criteria are listed in **Table 2**.

Results

Results of Literature Review

Details of the literature review, including reasons for excluding articles at the full-text stage are shown in **Figure 1**. A total of 898 unique citations were identified and screened by title and abstract. After abstract review, the full-texts of 181 potentially eligible citations were reviewed again for eligibility. Of these, 173 publications were excluded. Reasons for exclusion at the full-text stage are shown in Figure1. No additional studies were identified through ClinicalTrials.gov. In total, 8 studies met full inclusion criteria, as shown in **Figure 1**.[2,4,5,6,7,8,9,10]

Study Characteristics

Of eight studies identified, with 785 participants, all were randomized controlled trials (RCTs), and one trial was a crossover design.[5] All were open (non-masked) lasting at least eight weeks, with half of them lasting almost 6 months or more.[2, 4, 9, 10] The longest trial was 74-weeks.[2] Across all included RCTs, the sample size ranged from 18 to 291 participants, with the average number of participants being 98. The mean age of enrolled participants ranged from

44 to 59 years across all included studies. One study reported the age range but did not report the mean age of the participants.[7] Seven of the studies had a majority of female participants (ranging from 53 to 83%)[2, 4, 6, 7, 8, 9, 10], and one enrolled a minority of female participants (33%).[5] The most common results obtained by the studies were hemoglobin A1c, body weight or BMI, and LDL studies. Fasting glucose, blood pressure, hip and waist measurements and other lipid studies such as total cholesterol, HDL and triglycerides were also obtained in many of the studies.

The various studies included other outcomes such as blood pressure, albumin levels, insulin resistance, insulin sensitivity, and lipoprotein fractions, however, for consistency and closer comparisons, reviews were required to have at least one of the five outcome markers of interest. As shown in **Table 4**, five studies were conducted in the United States, one in South Korea, one in New Zealand and one in the Czech Republic.

Population Characteristics

The participants in all of the trials were 18 years or older and previously diagnosed with type 2 DM, with the exception of one study where patients could have one of the following diagnoses, type 2 diabetes, hypertension, hyperlipidemia, heart disease, in combination with being obese or overweight.[10] Participant recruitment was discussed in seven studies. [2, 4, 6, 7, 8, 9, 10] Advertisement in a newspaper or flier was used in five studies, two of which were within a corporation.[4, 9] Two studies used clinicians to select participants to invite to the study.[6, 8] In all studies, participants were willing to make dietary changes to be part of the studies. One study focused on Korean participants while another focused on Latino participants who lived in medically underserved areas.[7, 8] In the Korean study, a vegetarian diet was used, however, fish was also allowed.[8] All studies required that the participants were not previously on a vegan or vegetarian diet. Six of the studies used similar exclusion criteria for participants.[2, 4, 6, 8, 9, 10] This exclusion list included no drug or alcohol abuse, no pregnancy or lactation, no unstable medical

conditions, and no severe mental illness. One study also required participants not be using insulin medication.

Intervention Characteristics

Vegan diets were the identified intervention in five studies, and the other three used a vegetarian diet as the intervention. Two of the vegetarian interventions used a high fiber vegetarian diet.[5, 10] Five studies used a low-fat plant-based diet.[2, 4, 5, 9, 10] However, all of the intervention diets focused on legumes, whole grains, vegetables, and fruits. Two of the low fat vegan studies were done at corporate sites, focusing on workplace intervention with employees who had a BMI of 25 kg/m^2 or more.[4, 9] These corporate studies recruited geographically diverse participants from eight states across the country. The comparator diets included three studies using a typical American diet including meat, three studies used a conventional diabetic diet, one used the 2011 recommended Korean Diabetic Association Diet, and one used a plant-based diet with low carbohydrates and mono-unsaturated fat.

Five of the studies allowed participants to eat as much as they desired without any calorie restrictions.[4, 5, 7, 9, 10] Three of the studies restricted calories by 500 kcal in both intervention and control groups.[2, 6, 8] Of these three energy restricted diets, one chose to target only the participants that had a BMI greater than 25 mg/kg^2.[2] Six studies asked participants to not make any changes to their exercise routines.[2, 5, 6, 7, 8, 10] One study asked participants make no changes for the first half of a 24-week study, and then encouraged aerobic exercise for the second half of the study.[6] Exercise was not discussed in one study.[4] Vitamin B12 is a typical supplement in plant-based diet and was provided to participants in five of the eight studies.[2, 4, 6, 9, 10] Dietary education was provided on a scheduled and frequent basis in seven of the eight studies[2, 4, 6, 7, 8, 9, 10], six of the studies used a dietician to meet regularly with participants as well as make both scheduled and unscheduled calls to participants[2, 4, 6, 7, 8, 9], and five of these studies had participants keep a food diary for at least some portions of the study.[2, 4, 6, 8, 9] One of the studies did not use diet education, food diaries or a dietician.[5]

Study Quality

All eight studies used a method of randomization, however, none of the participants were blinded in the studies because the studies were dietary intervention trials. The process by which measurements were taken and the machines used for measurements were discussed in detail and standardized in five of the studies.[2, 6, 8, 9, 10] Three of the studies did not give any detail on how measurements were performed.[4, 5, 7] One study mentioned that the people doing the measurements were not blinded to the participant group, however, in this study the statistician was blinded to participant group.[10] One study noted that the persons performing the measurements were blinded to participant group.[5] The tables of characteristics within each study did not report any significant differences in characteristics of participants in the intervention and control arms. The different studies had variability with regards to the intervention diet proportion of carbohydrate, protein and fat ratios.

Baseline Data

The baseline data for all eight studies is listed in **Table 4**. Of the eight studies, five of the studies had very similar data and participants which made them easier to compare.[2, 4, 6, 9, 10] The remaining three studies provide good supporting information, however, have a more varied participant population and intervention, making it more difficult to directly compare the results.[5, 7, 8] The mean BMI of participants was 31.6 kg/m^2, with one study not providing baseline BMI information. In that study, the baseline average weight was 99.4 kg (219.1 lbs).[4] For the five most similar studies, the mean baseline BMI range was 34.4 – 35 kg/m^2.[2, 4, 6, 9, 10] These five studies also provided the average weight at baseline, and the mean weight was 98.2 kg (216.4 lbs.) at baseline. All eight studies reported HbA1c levels at baseline and at completion of the study. The HbA1c at baseline was an average of 7.64% (range of 6.9% – 9.1%) for the seven studies that reported HbA1c in percent versus mmol/mol.[2, 4, 5, 6, 7, 8, 9] Four of the five similar studies provided a baseline HbA1c range of 7.1% – 8.0%.[2, 4, 6, 9] Fasting glucose at baseline was only reported in three studies (mean 155 mg/dL)[2, 6, 8] and LDL at baseline was provided in

five studies.[2, 4, 6, 8, 9] Four of the studies reported LDL in mg/dL (versus mmol/L) and the average was 105.6 mg/dL. [2, 4, 8, 9]

Outcome Data of Included Studies

The outcome data for the eight studies are shown in **Table 5** and **Table 6**. Consumption of a vegan or vegetarian diet yielded a decrease in HbA1c of -0.40% to -0.65% in the intervention arm of the four best studies.[2, 4, 6, 9] These same studies had an HbA1c change in the control arm of -0.08% to 0.21%.[2, 4, 6, 9] One study used mmol/mol to report HbA1c and showed a HbA1c mean difference of 5 mmol/mol.[10] The difference between intervention and control groups mean change in HbA1c was reported with statistical significance in five studies with a range of -1.5% to -0.7 %.[2, 7, 8, 9, 10] In the study with the longest duration, when controlling for medication changes, the HbA1c levels went from 0.20% to 0.41% (p=0.03) difference between the means, and LDL difference between the means went from -4.1 mg/dL to -10.1 mg/dL (p=0.03).[2] Fasting glucose changes from baseline were not found to be statistically significant and were as high as 13.2 mg/dL lower on a vegan diet compared to a conventional diabetic diet.[8]

In the three of the studies reporting on BMI, differences between groups in mean changes from baseline were all statistically significant and ranged from -1.0 kg/m^2 to -3.9 kg/m^2.[6, 9, 10] In four of the studies reporting on weight change, differences between groups in mean changes from baseline were all statistically significant and ranged from -2.8 kg to -10.6 kg.[4, 6, 9, 10] The largest and longest study showed a mean BMI change from baseline of -1.6 kg/m^2 in the intervention group versus a -1.1 kg/m^2 in the control group. This same study showed a mean weight change from baseline of -4.4 kg in the intervention arm versus -3.0 kg in the control arm. Although not shown to be statistically significant, these changes are consistent with the other studies and were maintained for 74 weeks.[2]

Cholesterol was an outcome in all eight studies as this is an important factor in both diabetes treatment and morbidity and mortality of people with type 2 DM. While total

cholesterol, HDL and LDL were monitored in most studies, LDL was most similarly reported on in these studies. In four of the studies reporting on LDL, differences between groups in mean changes from baseline were all statistically significant and ranged from -7.2 mg/dL to -0.54 mg/dL.[2, 5, 6, 9] The remaining three studies that reported on LDL showed differences between groups in mean changes from baseline in a range of -7.2 mg/dL to -1.8 mg/dL.[4, 8, 10]

Five of these studies used low fat vegan or vegetarian diet as the intervention.[2, 4, 5, 9, 10] The comparator for these four studies was either a 2003 American Diabetic Association recommended diet or a regular meat diet. Despite the lower fat intake in these four studies, there was not an obvious difference in the results from the other studies. The two corporate studies, with a combined 404 participants, had almost identical baseline characteristics, both compared a low fat vegan diet to a meat diet, and both had statistically significant reductions in HbA1c and weight.[4, 9] For both studies, the intervention led to a 0.7% greater reduction in HbA1c and a 2.8 kg and 5.3 kg greater reduction in weight.[4, 9] One study that used low-fat vegetarian diet as the intervention had the highest weight loss and mean BMI changes from baseline.[10] This study was also unique in that it allowed the participants to have a diagnosis of either type 2 diabetes, hypertension, hyperlipidemia or heart disease, in combination with being obese or overweight. This study did not have any restriction on number of calories consumed. The focus of the intervention was on decreasing energy density of the food consumed, decreasing the fat intake and increasing the water and fiber intake, and, thus, increasing satiety.[10]

Compliance

The food diaries were used to write down what participants ate at different intervals in the study and this information was used to measure compliance. The dietician would also interview the participants to measure compliance with the prescribed diet. Six of the eight studies reported on diet compliance, using diaries, interviews, and questionnaires to assess compliance. The compliance ratings were 64% on average (range, 51% - 82%).[2, 4, 6, 8, 9, 10]

Discussion

Across all included studies, results of this review indicate that plant-based diets improve the management of type 2 DM in adults. The results reveal a pattern of improvement in glycemic control, weight loss, and improved lipid levels consistent with previous systematic reviews and meta-analyses showing statistically significant HbA1c improvements of 0.4% and 0.9%.[13, 17]

The most significant results from this review is the statistical significance in glycemic control and weight change; five of the eight studies showed statistical significance in improving HbA1c levels (-1.5% to -0.7 %).[2, 7, 8, 9, 10] HbA1c levels are a strong predictor of diabetes sequelae and cardiovascular events and, thus, these results show a clear benefit of vegan and vegetarian diets in the treatment of type 2 diabetes.[18] Weight loss and decrease in BMI was found to be statistically significant with four of 8 studies reporting weight outcomes, with as much at 10.6 kg greater weight loss in the intervention arm.[4, 6, 9, 10] Weight loss is important because weight loss alone has been shown to improve glycemic control. In addition, obesity alone is considered a major risk factor for type 2 diabetes and cardiovascular disease, and many studies suggest that weight management is the most important therapeutic tool for patients with type 2 diabetes.[24]

A low-fat vegan diet showed statistically and clinically significant improvements in body weight, plasma lipids and glycemic control, even without any caloric restriction or exercise.[4, 5, 7, 9, 10] In the study with the longest duration, when controlling for medication changes, hemoglobin A1c and plasma lipid levels reductions were more than double in the intervention group.[2] The low-fat vegetarian diet with no intake restrictions led to significant reductions in weight and BMI.[10] The high fiber/high carbohydrate plant-based diet with a low glycemic load led to significant reductions in postprandial lipoproteins, blunted post-prandial glucose and decreased late post-prandial hypoglycemia.[5] Post-prandial insulin decreased as a result of the decreased glucose levels, suggesting an improved insulin sensitivity.[5]

Dietary compliance is strongly correlated with weight loss. In one of the studies showing good compliance, the difference between the two arms doubled from 0.3% to 0.6%.[8] Having a supportive environment, health education and cooking demonstrations were found to increase the success and compliance.[4] This is important to note for both future study designs and for implementation of programs in primary care and the workplace, where dietary education and group support could be paired with a plant based diet.

Vegetarian and vegan diets improve glycemic control and weight loss in patients with type 2 diabetes by increasing fiber intake, decreasing saturated fat intake, increasing non-heme iron and reducing iron stores, increasing vegetable protein in place of animal protein, and increasing antioxidants and plant sterols.[6] All eight of these studies attribute this to a higher consumption of high dietary fiber with a low glycemic index, leading to a lower energy density in the food consumed.[31] The reduction in energy intake leads to weight loss, which is known to improve glycemic control.[22]

The decreased energy density, less fat and higher fiber and water content, lead to increased satiety, dietary adherence and lower overall intake. In addition, low-fat vegan diets increase insulin sensitivity in cells creating a thermic effect because the cells metabolize glucose more quickly rather than store it as body fat. This increases the post-prandial calorie burn by 16% up to three hours after a meal.[27] The plant-based diet is also typically lower in saturated fatty acid and is associated with improvements in plasma lipids.[31] A decrease in intramyocellular lipid concentrations and a decrease in visceral fat both lead to an increase in insulin sensitivity.[29]

The higher dietary fiber in plant-based diets can also reduce the risk of type 2 diabetes by several mechanisms. Dietary fiber may slow glucose absorption from the intestine, which lowers the glycemic index of carbohydrates.[30] Low-fat vegan diets decrease plasma lipid levels because of the absence of animal fat and the lipid-lowering effect of plant-based foods.[28] In addition, persistent organic pollutants (POPs), mainly found in fatty animal foods, are known to

disturb glucose and lipid metabolism.[25] Vegan diets have lower doses of POPs which may attribute to improvements in glycemic control as POPs are a risk factor in T2DM, poor glycemic control in T2DM and present an increased risk for cardiovascular diseases.[8]

Strengths

This review has several strengths. First, the studies were all randomized and published within the last ten years. Second, all of the studies were a minimum of eight weeks in duration which is adequate to observe meaningful changes in HbA1c. Third, this review looks at both plant-based diets in a variety of conditions and geographically diverse locations without tight control on the diet itself. This allows these results to be more broadly generalizable to many populations. A fourth strength is that within these studies, the intervention and control arms of the studies had no significant heterogeneity in their characteristics. A fifth strength is the parallel design in all studies, in which all participants started simultaneously, allowing the investigators to follow participants and perform measurements at the same time. Of note, these studies used diabetic participants that had long-standing diabetes and none of the studies reported any adverse outcomes, making this intervention little to no risk to employ.

Limitations

This body of literature has limitations. In terms of applicability, all enrolled a self-selected population and two of the studies were set in a corporate setting with relatively healthy employees. These factors may bias the results towards greater improvement with the intervention diet as participants who self-select or who are participating in an intervention at their worksite may be more motivated to participate and more likely to comply with the intervention. Two of the studies chose participants who were disadvantaged socioeconomically and medically underserved. Results from these studies may not be generalizable to a broader population. In terms of study design, there is a potential for measurement bias; investigators collecting data and performing analyses were generally not blinded, with the exception of one study. Implementation of diet changes typically benefit from multi-disciplinary approach to

support the patient. Education and dietician phone calls were more robust in the intervention groups and this type of addition to the intervention is also not typical of a person who may be embarking on a vegan or vegetarian diet outside of the study.

The studies had some inherent design limitations, such as small sample sizes and some with short durations with half of the studies being only 3 months or less. Also, the participants were predominantly female as is commonly found in these types of studies. It is not clear how that may affect the results. Several confounders were present such as the variations in the interventions, some with energy restrictions and others not, some performed outside the United States, one allowing fish, and most not monitoring the physical activity of participants.[4, 9]

Variations in the control diets were also a confounder as some were a standard meat diet and some a diabetic diet. Most studies did not report if the people doing measurements, laboratory work or statistical analysis were blinded. Another confounder was the independent effect of weight change on the other measured variables of glycemic control and lipid profile. It is difficult to isolate the effect of weight change on these markers of cardiovascular risk.[11] These factors limit the ability to attribute improvement in outcomes directly to a plant-based diet. Additionally, in these studies, most participants in both groups altered medications, often because of clinical success (low blood glucose values) in the intervention arms, and sometimes because of worsening blood glucose levels in the control arm.[10] This is a confounding variable that requires special statistical analysis.

Plant-based diets are a great adjunctive tool for primary care practitioners in the management adults with type 2 DM. While the studies in this review show relatively small improvements in the glycemic control, weight loss and cholesterol levels, these are relatively sizable considering the short durations of these studies. Introducing plant-based diets is a less expensive and at lower side effect profile than medications for type 2 DM. As noted above, these lifestyle changes are best implemented with dietary education support which is likely the most challenging aspect of implementation. Where possible, dietary coaching and cooking

support would assist the success of such changes. Supplying plant-based diets in corporate settings along with group dietary education and coaching is a great approach to cast a wide net, establishing a plant-based pattern of eating which may encourage similar changes away from the workplace.

Future Studies

To increase the applicability of these results, a good study design would include an intervention of a plant based diet with no calorie restriction, no exercise requirement, B12 supplementation, dietary education and food diary requirements. These study requirements would most similarly mirror someone attempting to make these diet changes and the food diary would allow for verification of compliance. Further studies are needed to explore the relationships between specific foods and glycemic control as the studies in this review did not have a clear guide for the proportions of fat to carbohydrate to protein within a vegan or vegetarian diet. Longer randomized controlled trials are needed to determine the long-term compliance and health effects of plant-based diets. It would also be beneficial to target employee interventions to clarify whether interventions that encourage plant-based diets are effective in a workplace setting.

Conclusions

This systematic review supports the evidence from clinical trials that vegan and vegetarian diets reduce HbA1c levels and result in weight loss in type 2 diabetics. These important tool for improving obesity, diabetes, and cardiovascular disease must be transferred to settings where people live and work. Providers, patients, and employers must be made aware of the benefits of nutritional therapy such as vegan and vegetarian diets. This systematic review demonstrates the health benefits of introducing a vegan or vegetarian diet program. These diet changes can lead to improving the management of type 2 DM in adults, and the long-term health benefits of reducing morbidity and mortality and the burden of type 2 DM.

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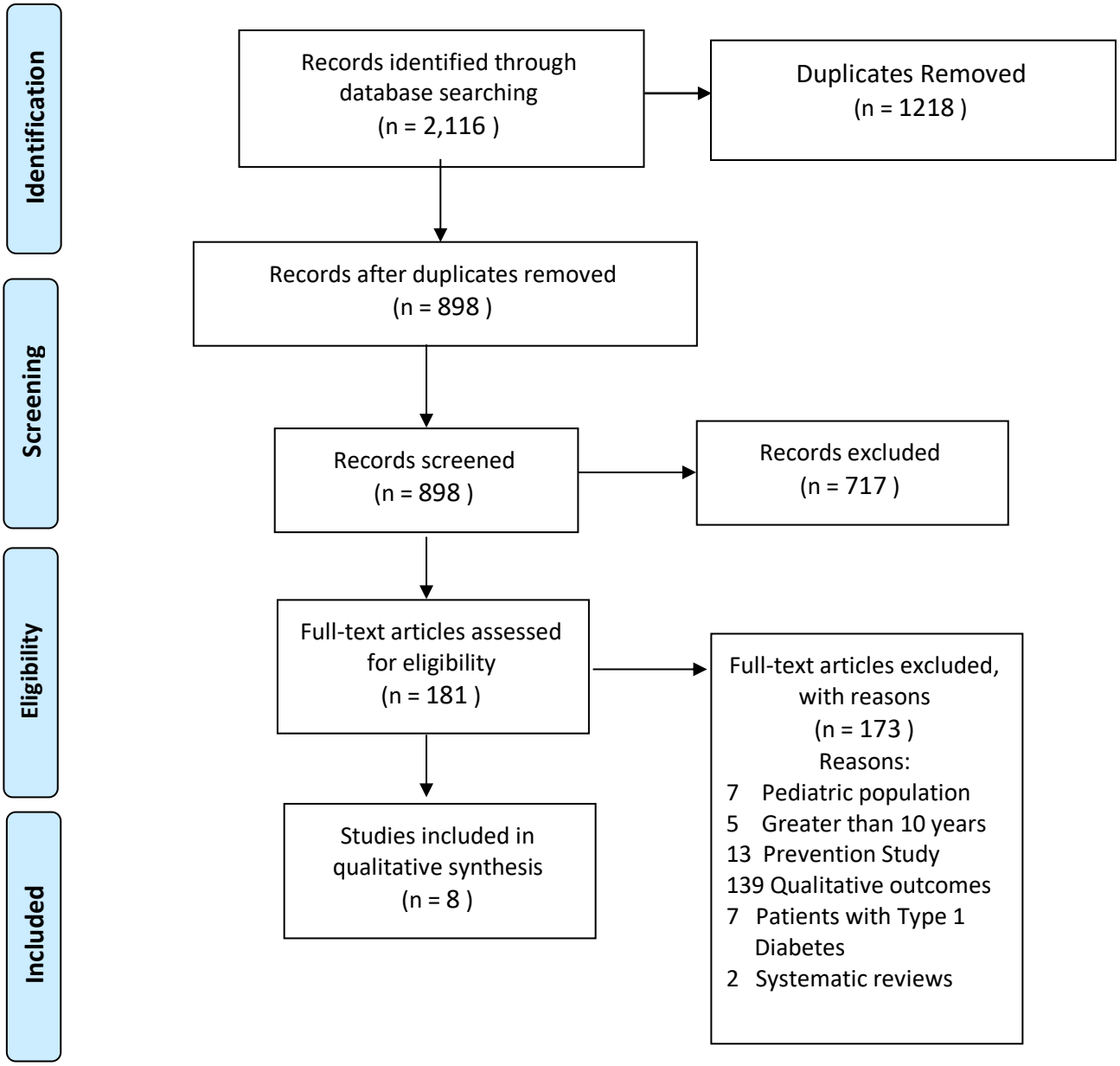

Figure 1. PRISMA Flow Diagram: database search (2008 – 2018)
Showing the number of studies screened, assessed for eligibility, and included in the review.

Table 1: Key Question

Key Questions	
1	Among adult patients with diabetes mellitus, type 2, do vegetarian or vegan diets improve the management of diabetes mellitus?

Table 2: Study Inclusion and Exclusion Criteria

Category	**Inclusion Criteria**	**Exclusion Criteria**
Population	Adults, > = 18 years old with diabetes mellitus type 2	Children (< 18 years old) Adults with diabetes mellitus type 1
Intervention	Vegetarian or Vegan Diet with or without dietary education	Diets containing meat
Comparator	Compared to another type of diet	No comparator
Outcomes	Fasting glucose, Hemoglobin A1c, Body weight, BMI, Lipid levels, management of diabetes mellitus type 2	Qualitative measures only Measures of prevention of diabetes
Timing	Studies within the last 10 years	Studies older than 10 years
Settings	Inpatient or outpatient, world-wide	None
Publication language	English	Language other than English
Admissible evidence (study design and other criteria)	Published in full Original research Cross-sectional studies Clinical trials completed Cohort studies Randomized Controlled Trials Controlled Trials	Studies not published in full Qualitative studies Results of cognitive interviews Clinical trials in progress Editorials Policy or Recommendation statements Case Reports Systematic Reviews

Table 3: PUBMED, EMBASE, Cochrane and Clinical Trials Search Strategy

PubMed

Search date: April 4, 2018

#1	Vegetarian* OR vegan* OR “plant-based diet” OR “plant-based dietary” OR “plant-based diets” OR “plant-based foods” OR “plant-based food” AND Diabetes	467
#2	Vegetarian* OR vegan* OR “plant-based diet” OR “plant-based dietary” OR “plant-based diets” OR “plant-based foods” OR “plant-based food” AND Diabetes Mellitus	227

EMBASE

Search date: April 4, 2018

#1	Vegetarian* OR vegan* OR “plant-based diet” OR “plant-based dietary” OR “plant-based diets” OR “plant-based foods” OR “plant-based food” AND Diabetes	790
#2	Vegetarian* OR vegan* OR “plant-based diet” OR “plant-based dietary” OR “plant-based diets” OR “plant-based foods” OR “plant-based food” AND Diabetes Mellitus	625

Cochrane

Search date: April 4, 2018

#1	Vegetarian* OR vegan* OR “plant-based diet” OR “plant-based dietary” OR “plant-based diets” OR “plant-based foods” OR “plant-based food” AND Diabetes	5
#2	Vegetarian* OR vegan* OR “plant-based diet” OR “plant-based dietary” OR “plant-based diets” OR “plant-based foods” OR “plant-based food” AND Diabetes Mellitus	5

Clinical Trials

Search date: April 4, 2018

#1	Vegetarian* OR vegan* OR “plant-based diet” OR “plant-based dietary” OR “plant-based diets” OR “plant-based foods” OR “plant-based food” AND Diabetes	5
#2	Vegetarian* OR vegan* OR “plant-based diet” OR “plant-based dietary” OR “plant-based diets” OR “plant-based foods” OR “plant-based food” AND Diabetes Mellitus	5

Table 4: Designs and characteristics of studies used in systematic review.

Study, year, reference	Country	Study Design	Intervention diet	Comparison diet	Duration (weeks)	Number (I/C)	Mean age (yrs.)	Female (%)	Mean BMI at Baseline (kg/m^2)	Fasting Glucose at Baseline	A1c at Baseline (%)	Weight at Baseline (kg)	LDL at Baseline
Barnard et al., 2009 (2)	US	RCT	Low-fat vegan	2003 American Diabetic Diet	74	99 (49, 50)	56	61	35	162 mg/dL	8	98	111 mg/dL
Ferdowsian et al., 2010 (4)	US	RCT	Low-fat vegan	Meat diet	22	113 (68, 45)	44	83	_	_	7.1	99.4	105.6 mg/dL
De Natale et al., 2009 (5)	US	R Cross-over	High fiber/High carbohydrate vegetarian	Low carb/Mono-unsaturated fat vegetarian	4 + 4	18	59	33	27	_	6.9	_	_
Kahleova et al., 2011 (6)	Czech Republic	RCT	Vegan	Conventional diabetic diet	12	74 (37, 37)	56	53	35	9.5 $mmol\ l^{-1}$	7.65	101	2.56 $mmol\ l^{-1}$
Mishra et al., 2013 (9)	US	RCT	Low-fat vegan	Meat diet	18	291 (143, 149)	45	83	35	_	7.30	96.5	108.2 mg/dL
Yu-Mi et al., 2016 (8)	South Korea	RCT	Vegan	2011 Korean Diabetic Association Diet	12	93 (47, 46)	58	81	23.5	132 mg/dL	7.5	_	97.7 mg/dL
Ramal et al., 2017 (7)	US	RCT	Vegetarian	Conventional diet	26	32 (17, 15)	_	78	31	_	9.05	_	_
Wright et al., 2017 (10)	New Zealand	RCT	Low-fat vegetarian	Meat diet	26	65 (33, 32)	56	60	34.4	_	39.5 mmol/mol	95.9	_

Table 5: Differences from baseline of studies used in systematic review.

Study, year, reference	Study Design	Intervention diet	Comparison diet	BMI change (kg/m^2) (I,C)	Fasting Glucose change (mg/dL) (I,C)	A1c change (%) (I,C)	Weight change (kg) (I,C)	LDL change (I,C)
Barnard et al., 2009 (2)	RCT	Low-fat vegan	2003 American Diabetic Diet	-1.6, -1.1	-14.1, -6.5	-0.40, +0.01	-4.4, -3.0	-13.5, -3.4 mg/dL
Ferdowsian et al., 2010 (4)	CT	Low-fat vegan	Meat diet	_	_	-1.0, -0.2	-5.1, +0.1	-5.2 -1.4 mg/dL
De Natale et al., 2009 (5)	R Cross-over	High fiber/High carbohydrate vegetarian	Low carb/Mono-unsaturated fat vegetarian	_	-6.6, --	0.0	0.0	-2.62, -0.4 mg/dL (P< 0.05)
Kahleova et al., 2011 (6)	RCT	Vegan	Conventional diabetic diet	-2.018, -0.98 (P< 0.001)	-1.49, -1.05 (P< 0.42)	-0.65, 0.21 (P< 0.375)	-6.2, -3.2 (P< 0.001)	-0.17, -0.14 mmol l^{-1} (P< 0.05)
Mishra et al., 2013 (9)	RCT	Low-fat vegan	Meat diet	-1.04, 0.01	_	-0.60, -0.08	-2.9, -0.06	-8.1, -0.9 mg/dL
Yu-Mi et al., 2016 (8)	RCT	Vegan	2011 Korean Diabetic Association Diet	-0.5, -0.1 (P< 0.092)	-13.2, 0.0 (P< 0.146)	-0.5, -0.2 (P< 0.017)	_	-2.8, -1.0 mg/dL (P< 0.732)
Ramal et al., 2017 (7)	RCT	Vegetarian	Conventional diet	+0.02, -0.16 (P< 0.478)	_	-1.24, -0.07 (P< 0.002)	_	_
Wright et al., 2017 (10)	RCT	Low-fat vegetarian	Meat diet	-4.4, -0.5	_	-3, +2 mmol/mol	-12.1, -1.6	-.08, -0.04 mmol l^{-1}

Table 5: Mean differences in selected studies used in systematic review.

Study, year, reference	Study Design	Intervention diet	Comparison diet	BMI change (kg/m^2)	Fasting Glucose change (mg/dL)	A1c change (%)	Weight change (kg)	LDL change (mg/dL)
				Between group difference in change score, mean (95% CI)				
Barnard et al., 2009 (2)	RCT	Low-fat vegan	2003 American Diabetic Diet	-0.5 (P 0.25)	-7.6 (P 0.44)	-0.41 (P 0.03)	-1.4 (P 0.25)	-1.1 (P 0.03)
Ferdowsian et al., 2010 (4)	RCT	Low-fat vegan	Meat diet	_	_	-0.7	-5.3 (P<0.0001)	-3.7 (P 0.45)
Mishra et al., 2013 (9)	RCT	Low-fat vegan	Meat diet	-1.0 (P 0.001)	_	-0.7 (P 0.004)	-2.8 (P 0.001)	-7.2 (P 0.001)
Kahleova et al., 2011 (6)	RCT	Vegan	Conventional diabetic diet	-1.03 (P< 0.001)	-0.44 (P< 0.42)	-0.66 (P< 0.375)	-3.0 (P< 0.001)	-0.54 (P< 0.05)
Wright et al., 2017 (10)	RCT	Low-fat vegetarian	Meat diet	-3.9 (P<0.0001)	_	-1.5 (P<0.0001)	-10.6 (P<0.0001)	-7.2 (P 0.12)