Improved Management of Type 2 Diabetes With a Plant-Based Diet Compared to a Conventional Diabetes Diet

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Improved Management of Type 2 Diabetes With a Plant-Based Diet Compared to a Conventional Diabetes Diet

Abstract

Background: Diabetes is a rapidly growing epidemic that, to a degree, is both caused by and managed with diet. Vegetarian and vegan diets are associated with a reduced risk of diabetes, and have been shown to increase insulin sensitivity and decrease body weight. This study sought to review trials that directly compare a vegetarian or vegan diet to a conventional diabetes diet with the outcome of improved management, as measured by weight loss, reduction in medication use and glycated hemoglobin (HbA1c).

Method: An extensive literature search was performed using MEDLINE-OVID, CINAHL, Evidence-Based Medicine Reviews Multifile and Web of Science to include randomized controlled trials (RCTs) directly comparing a vegetarian or vegan diet to a conventional diabetes diet. The following search terms were used: "Diabetes or Diabetes Mellitus or Diabetes Mellitus, Type 2" and "Vegan diet or Diet, vegetarian." The quality of evidence presented in each article was assessed using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) criteria.

Results: Three RCTs were included in the review. Diabetics assigned to the experimental group reduced or stopped hypoglycemic medications significantly more than those in the control group. The effect of diet on HbA1c was not significant in any study based on intention-to-treat analyses, but in sub-group analyses accounting for medication change, the vegan/vegetarian group indicated a greater reduction in two studies. Weight loss was significant within each diet group, and two studies found it to be significantly greater in the vegetarian group.

Conclusion: Individuals with type 2 diabetes who participate in vegan and vegetarian diets effectively lose weight and have better glycemic control as measured by medication reduction than those following a conventional diabetes diet.

Keywords: diabetes, type 2 diabetes, vegan diet, vegetarian diet, conventional diabetes diet, glycemic control, weight loss, management

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Improved Management of Type 2 Diabetes With a Plant-Based Diet Compared to a Conventional Diabetes Diet

Trisha Thoms

A Clinical Graduate Project Submitted to the Faculty of the School of Physician Assistant Studies Pacific University Hillsboro, OR For the Masters of Science Degree, September 20, 2012

Faculty Advisor: Annjenette Sommers, PA-C, MS Clinical Graduate Project Coordinator: Annjanette Sommers, PA-C, MS
Biography

Trisha Thoms was born and raised in rural Northern Wisconsin, where she adamantly opposed following in the footsteps of her mother to study medicine. She left the Midwest to attend Colorado College and major in Environmental Science: Concentration in Chemistry with a vision of pursuing ecosystem science research. After two years of working on a climate change study in the Olympic National Park, she decided medicine is where she belonged all along. She moved to Jackson, WY to acquire patient-care experience as a surgical assistant and medical assistant, while taking advantage of the Grand Tetons on her skis and bikes. After graduation from Pacific University, she hopes to practice in hospital medicine in the Northwest.
Abstract

Background: Diabetes is a rapidly growing epidemic that, to a degree, is both caused by and managed with diet. Vegetarian and vegan diets are associated with a reduced risk of diabetes, and have been shown to increase insulin sensitivity and decrease body weight. This study sought to review trials that directly compare a vegetarian or vegan diet to a conventional diabetes diet with the outcome of improved management, as measured by weight loss, reduction in medication use and glycated hemoglobin (HbA1c).

Method: An extensive literature search was performed using MEDLINE-OVID, CINAHL, Evidence-Based Medicine Reviews Multifile and Web of Science to include randomized controlled trials (RCTs) directly comparing a vegetarian or vegan diet to a conventional diabetes diet. The following search terms were used: “Diabetes or Diabetes Mellitus or Diabetes Mellitus, Type 2” and “Vegan diet or Diet, vegetarian.” The quality of evidence presented in each article was assessed using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) criteria.

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# Table of Contents

Biography ................................................................. 2  
Abstract ........................................................................ 3  
Acknowledgements ..................................................... 4  
Table of Contents ........................................................ 5  
List of Tables ............................................................ 6  
List of Abbreviations.................................................... 6  
Background ............................................................... 7  
Method ......................................................................... 8  
Results ......................................................................... 8  
Discussion ................................................................. 15  
Conclusion ................................................................. 21  
References ................................................................. 23  
Tables ......................................................................... 26
List of Tables

Table 1: Characteristics of Reviewed Studies
Table 2: Summary of Findings, GRADE Analyses

List of Abbreviations

DM………………………………………………………………………Diabetes Mellitus
HbA₁c………………………………………………………………...Glycated hemoglobin
RCT……………………………………………………………..Randomized Control Trial
BMI………………………………………………………………………Body Mass Index
SD……………………………………………………………………...Standard Deviation
CI………………………………………………………………………Confidence Interval
GRADE………Grading of Recommendations Assessment, Development and Evaluation
ADA.................................................................American Diabetes Association
Improved Management of Type 2 Diabetes With a Plant-Based Diet Compared to a Conventional Diabetes Diet

BACKGROUND

Type 2 diabetes is a rapidly growing epidemic, and according to a 2011 CDC report, it accounts for 90-95% of the 25.8 million cases of diabetes in the United States. The American Diabetes Association recommends weight loss and dietary strategies as integral components of diabetes management, with loose guidelines to individualize the macronutrient composition based on patient’s conditions and preferences, and to monitor carbohydrates, maintain saturated fat intake <7% of total calories and minimize intake of trans fat.

A large body of evidence suggests vegetarian and vegan diets are associated with a reduced risk of many chronic diseases, including diabetes. In two separate large-scale cohort studies of more than 86 000 Seventh-day Adventists, a population almost equally divided between vegetarians and omnivores who generally avoid alcohol, tobacco and caffeine, the prevalence of diabetes was significantly lower in vegetarians compared to omnivores. Researchers have also related vegetarian and vegan diets with increased insulin sensitivity, and a lower body weight. In contrast, other studies have linked diets that include meat, particularly processed and/or red meat, as positively correlated with incidence of diabetes. A variety of possible mechanisms have been proposed and studied to explain the beneficial effects of a plant-based diet, including increased fiber, reduced saturated fat, reduced total protein, and reduced heme-iron from animal protein in particular. Moreover, studies have shown acceptability of a vegan diet to be comparable with that of other therapeutic diets. On that account, a
plant-based diet with emphasis on fiber, whole grains, legumes, vegetables and fruit may provide benefit for management of type 2 diabetes over diets that include meat.

This study sought to review trials that directly compare a vegetarian or vegan diet to a conventional diabetes diet with the outcome of improved management, as measured by weight loss, reduction in medication use and HbA1c.

**METHODS**

An extensive literature search was performed using MEDLINE-OVID, CINAHL and Evidence-Based Medicine Reviews Multifile with the following keywords: “Diabetes or Diabetes Mellitus or Diabetes Mellitus, Type 2” and “Vegan diet or Diet, vegetarian.” The search was further limited to humans and English language. Inclusion criteria comprised of those studies directly comparing a vegetarian or vegan diet to a conventional diabetes diet conducted in a randomized controlled trial method. After eliminating duplicates and reviews, Web of Science was utilized for a cited reference search of remaining articles.

**RESULTS**

The searches identified 152 articles, of which all but 4 were excluded. The forward-cited reference search did not provide any additional studies that compared a vegan or vegetarian diet to a diabetes diet. Two of the 4 studies use the same participant population with one paper written after 22 weeks and the second after 74 weeks of the study, so for the purposes of this systematic review, the long-term data was selected for analysis and a total of 3 articles were reviewed (see Table 1). The following outcomes of
interest were examined based on clinical relevance and commonality among the studies: 1) medication reduction 2) HbA1c and 3) weight loss.

Nicholson et al

Methods—This study was intended as a 12-week pilot investigation to assess dietary intervention on management of DM II (Diabetes Mellitus Type 2), in a randomized, controlled design. Thirteen subjects were recruited through newspaper advertisements in the Washington, DC area. Individuals greater than 25 years of age with DM II willing to attend all components of the study were included. Exclusionary criteria included smoking, regular alcohol use, current or past drug abuse, pregnancy, psychiatric illness, and medical instability. Individuals were randomly assigned to either a low-fat vegan diet (n=7) or a control diet (n=6). Two control subjects dropped out and were not included in analyses. The vegan diet consisted of whole grains, vegetables, legumes, and fruit and excluded animal products, added oils, sugars and refined carbohydrates. Calories were divided among macronutrients in the following manner: 10-15% from protein, <10% from fat, and the remaining from carbohydrates. Cholesterol content was zero. The control diet was designed to derive 10-15% of calories from protein, <30% from fat, and 55-60% from carbohydrates. Cholesterol was limited to 200 mg per day. Participants had the option of eating provided lunches and dinners throughout the study period and attended twice-weekly cooking and nutrition classes. Adherence to the assigned diets was assessed with periodic submission of 3-day dietary records at baseline and again at 12 weeks, in addition to weekly self-report questionnaires handed out at group meals. Biweekly, participants met with the medical director or nurse-project coordinator to assess medication needs, which were altered according to protocol as
necessary. Exercise habits were collected by self-reports at baseline and again at 12 weeks, and no recommendations were made. The following were measured during the study: blood pressure, weight, fasting serum glucose, fasting serum lipids, glycosylated hemoglobin, and urinary microalbumin.21

**Results**—Although not included in outcome analyses, the authors reported good adherence by all subjects to their diet as monitored by verbal reports, with the exception of two experimental group participants who later indicated several lapses in compliance. Five out of 7 vegan participants had to reduce either oral hypoglycemic agents or insulin, whereas no changes were made in the control group. There was a reduction in mean HbA$_{1c}$ in the experimental group from 8.3 (SD 1.7) at baseline to 6.9 (SD 1.1) after 12 weeks. The control group started at an average HbA$_{1c}$ 8.0 (SD 1.1) and dropped to 7.0 (SD 0.6) after 12 weeks. Sub-analyses to control for medication changes were not performed, and raw data were not available. There was a mean weight loss of 7.2 kg in the experimental group, compared to an average loss of 3.8 kg in the control group (P<0.005).21

**Barnard et al**

**Methods**—The purpose of this 74-week RCT was to compare the long-term effect of diet on management of DM II by comparing individuals prescribed a vegan diet versus a diet based on 2003 American Diabetes Association (ADA) guidelines. Newspaper advertisements were used to recruit 99 participants in the Washington, DC area, a number decided upon from a statistical calculation indicating 49 participants per group were necessary in order to have an 80% chance of detecting a 0.8 difference of HbA$_{1c}$ between groups with a standard deviation (SD) of 1.3 and loss to follow-up of
33%. Inclusion criteria consisted of individuals who had been diagnosed with DM II and had used hypoglycemic medications for at least 6 months. Exclusion criteria included smoking, alcohol or drug abuse, pregnancy, medical instability, HbA1c <6.5 or >10.5%, use of insulin for >5 years, and current use of a low-fat vegetarian diet. Individuals were ranked in order of HbA1c concentrations and randomly assigned in sequential pairs, using a random-number table, to either a low-fat vegan diet (n=49) or a conventional diabetes diet following the 2003 guidelines of the ADA (n=50). The vegan diet consisted of whole grains, vegetables, legumes, and fruit and excluded animal products and fatty foods, such as added oils, fried foods, avocados, nuts and seeds. Subjects were asked to favor low-glycemic index foods, and no restrictions were placed on carbohydrates, calories or portion size. Calories were divided among macronutrients in the following manner: 15% from protein, 10% from fat, and 75% from carbohydrates. The control diet was designed to derive 15-20% of calories from protein, <7% from saturated fat, and 60-70% from carbohydrates and monounsaturated fats. Cholesterol was limited to 200 mg per day. The control diet was individualized, based on body weight and plasma lipid concentrations, and energy intake deficits of 500-1 000 kcal were prescribed for those with a BMI >25. No meals were provided. All subjects met for 1 h with a registered dietitian to establish a dietary plan, followed by weekly cooking and nutrition classes for the first 22 weeks, and optional biweekly meetings thereafter. Adherence to the assigned diets was assessed with periodic submission of 3-day dietary records, in addition to unannounced telephone calls by dieticians to collect a 24-h diet recall. Participants were to continue their preexisting medications, but in the event of hypoglycemia, medications were reduced according to protocol by a study endocrinologist, who remained blind to group assignment.
Participants were asked not to alter their exercise habits for the first 22 weeks of the study, but were free to change habits for the following 52 weeks. Physical activity was assessed over 3-d periods by pedometry. The following were measured during the study by technicians who remained blind to group assignment: blood pressure, body weight, waist circumference, hip circumference, fasting plasma glucose, fasting plasma lipids, HbA$_{1c}$, and urinary albumin.$^{22}$

**Results**—Loss to follow-up was reported separately for laboratory assessments (n=7 vegan, n=5 conventional diet) and dietary records (n=9 vegan, n=7 conventional diet). Dietary adherence criteria were met by 67% of vegan participants at 22 weeks compared to 44% of control participants, and at 74 weeks, dietary adherence criteria were met by 51% and 48% respectively. Medication reductions and increases were noted in both groups, but the net 74-week dosages were reduced in 17 (35%) participants in the vegan group and 10 (20%) participants in the conventional diet group. The observed change in HbA$_{1c}$ from baseline to 74 weeks was -0.34 (+/- 0.19) and -0.14 (+/- 0.17) for vegan and conventional diets, respectively (P=0.43). In two additional analyses controlling for medication changes, significantly greater reductions were seen in HbA$_{1c}$ values in the vegan group. Changes from baseline to 74 weeks or to the last available value before any medication adjustment, were -0.40 (vegan) and 0.01 (control) (P=0.03). Among participants whose medications remained unchanged throughout (14 vegan, 21 control), HbA$_{1c}$ changes for vegans were -0.82 and -0.21 for controls (P=0.14). Both groups sustained significant weight loss from baseline to 74 weeks, but there was no significant difference between diets (- 4.4 kg +/- 0.9 in vegan group, - 3.0 kg +/-0.8 in conventional diet group).$^{22}$
Kahleova et al

The aim of this 24-week RCT was to compare the effects of vegetarian and conventional diabetes diets alone (0-12 weeks) and in combination with exercise (12-24 weeks) on management of DM II as indicated by insulin resistance, visceral fat and oxidative stress markers. Individuals between the ages of 30 and 70 with DM II were pre-chosen by their endocrinologists in Prague, Czech Republic. Inclusion criteria included HbA1c between 6 and 11%, BMI between 25 and 53 kg/m^2, and a willingness to alter diet and exercise habits. Exclusion criteria included alcohol or drug abuse, pregnancy, lactation, HbA1c <6 or >11%, use of insulin, and current use of a vegetarian diet. Individuals were randomly assigned to either a vegetarian diet (n=37) or a conventional diabetes diet following the guidelines of the Diabetes and Nutrition Study Group of the European Association for the Study of Diabetes (n=37). Both diets were designed to be isocaloric and calorie-restricted. The vegetarian diet consisted of whole grains, vegetables, legumes, nuts and fruit. Animal products were limited to a portion of a low-fat yogurt a day. Calories were divided among macronutrients in the following manner: 15% from protein, 25% from fat, and 60% from carbohydrates. The control diet was designed to derive 20% of calories from protein, 30% from fat (<7% from saturated fat), and 50% from carbohydrates and monounsaturated fats. Cholesterol was limited to 200 mg per day. All meals were provided during the study period, and participants met weekly for cooking and nutrition classes. Adherence to the assigned diets was assessed with periodic submission of 3-day dietary records, in addition to unannounced telephone calls by dieticians to collect a 24-h diet recall. Participants were to continue their preexisting medications, but in the event of hypoglycemia, a study physician reduced
medications according to protocol. During the first 12 weeks, subjects were asked to keep their exercise habits constant, and during weeks 13-24 they were to follow a prescribed exercise program. Physical activity was assessed over 3-d periods by pedometry and questionnaires. The following were measured during the study: blood pressure, body weight, waist circumference, fasting plasma glucose, fasting plasma lipids, HbA1c, insulin sensitivity as estimated by the metabolic clearance rate of glucose calculated during a 3-hour hyperinsulinaemic isoglycaemic clamp, subcutaneous and visceral fat volume as measured by magnetic resonance imaging, oxidative stress markers and adipokines.23

**Results**—Loss to follow-up was reported as participant completion of the first 12 weeks (95% vegetarian, 89% control) and again after 24 weeks (84% in each group). Adherence at 24 weeks was high among 55% of vegetarians and 32% of controls, medium among 22.5% of vegetarians and 39% of controls, and low among 22.5% of vegetarians and 29% of controls. Forty-three percent of participants in the vegetarian group reduced medications, compared to 5% in the control group. The difference between groups was 38% (95% CI 17-58%). HbA1c fell significantly in both groups in the first 12 weeks prior to starting an exercise program [-0.68 (+/- 0.86) vegetarian, -0.59 (+/- 0.89) control, (P <0.001)], but the difference between groups was not significant (P=0.370). In sub-analysis including those whose medications remained constant, HbA1c fell significantly by 0.9% in the vegetarian group from baseline to 24 weeks vs. a non-significant decrease of 0.2% in the control group. There was significant weight loss in both groups in response to the first 12 weeks of dietary interventions (P<0.001), but with greater weight loss in the vegetarian group than in the control group [- 6.2 kg (95% CI -6.6 to -5.3) vs. - 3.2 kg (95% CI -3.7 to -2.5); P=0.001].23
I. DISCUSSION

In this systematic review, a search of the current literature found studies comparing a vegan or vegetarian diet to a conventional diabetes diet with the outcome of improved management of diabetes type 2 as measured by reduction in medications, HbA1c and weight loss. Of the three studies reviewed, the vegan/vegetarian groups consistently indicated better outcomes over the conventional diets, with a significant reduction in medications, mild but not significant greater mean change of HbA1c, and a mixed report of significant and non-significant weight loss over that of the controls.21-23

In analyses controlling for medications, the vegan diet appeared to be more effective for control of glycemia,22,23 suggesting that individuals with type 2 diabetes may be better managed on a plant-based diet.

The greater weight loss observed in the vegan and vegetarian groups by the three studies in this review is consistent with large-scale population studies comparing weight differences among vegetarians and non-vegetarians3,5, and previous clinical trials directly comparing effects of a plant-based diet to a conventional low-fat diet7,10. A systematic review by Berkow and Barnard (2006) examined the extent to which vegetarian diets are associated with reduced body weight, and identified 29 studies reporting that vegetarians weighed significantly less than non-vegetarians.9 Additionally, many studies have reported a consistent dose-dependent gradient that generally indicates BMI of vegans is lower than that of ovo-lacto-vegetarians, which is lower than that of individuals who eat moderate amounts of meat.3,5,24 Moreover, data suggest a greater ability to sustain weight reduction on a vegetarian diet. In a two-year randomized weight loss trial comparing a vegan diet to a National Cholesterol Education Program diet in overweight,
postmenopausal women, a vegan diet was associated with significant weight loss comparatively at 1 and 2 years.\textsuperscript{10}

The differences in weight loss between the two groups cannot fully be explained by differences in calorie consumption. Kahlova et al\textsuperscript{23} designed both groups to be isocaloric, and despite this, the vegetarian group lost more weight. Furthermore, regardless of the daily energy intake limits placed on the conventional diet groups, and lack thereof on the vegan groups, in the studies by Nicholson et al\textsuperscript{21} and Barnard et al,\textsuperscript{22} significant weight loss was observed in the intervention groups, which is consistent with previous studies.\textsuperscript{7}

The observed weight loss of the intervention groups consistently correlates with reduction in medications and HbA$_{1c}$ among the 3 studies examined, and there is evidence from previous trials to suggest the glycemic effect of the vegan/vegetarian diet is at least partially mediated by weight loss.\textsuperscript{3,7,8,10} Kahleova et al\textsuperscript{23} reported a strong association among weight loss, reduction of visceral fat, and insulin sensitivity (two additional outcomes not evaluated in this review), suggesting a correlation of the three. As insulin sensitivity increases, blood glucose levels over time decrease, thus it would be reasonable to expect to observe a decrease in HbA$_{1c}$ to follow. In an analysis at 22 weeks by Barnard et al\textsuperscript{22}, a regression model indicated a significant association with HbA$_{1c}$ and weight change, leading the authors to conclude the weight-reducing effect of the vegan diet was responsible for a substantial portion of its effect on HbA$_{1c}$.\textsuperscript{6}

Several studies have sought to explain the observed difference between vegetarians and non-vegetarians in regards to weight loss and glycemic control. Much of the variance in body weight likely lies in the macronutrient differences of the diets, with a
lower proportion of fat and protein in a vegetarian diet and a greater amount of fiber.9,25 Animal products are generally high in total and saturated fats, which, independent of body weight changes, have been associated with insulin resistance,8,14 a link that may be explained by lipid build-up in the cell membranes of skeletal muscle interfering with insulin receptor binding or affinity, and transport and cell signaling.26 Although a high-protein, low-carbohydrate diet has generally been advocated for weight loss, many longer-term studies have indicated a positive correlation with BMI.5,9 In a recent prospective cohort study of 38 084 participants with a 10-yr follow-up suggests that consumption of 5% energy from both red meat or total protein at the expense of carbohydrates or fat increases diabetes risk as much as 30%.17 Likewise, Weickert et al concluded that a very high protein intake may have unfavorable effects on insulin sensitivity compared to a high cereal fiber diet.15 The connection between protein and insulin sensitivity may be related to the heme-iron content of meat, versus the non-heme iron of plant proteins. A number of studies have associated dietary heme-iron from meat with promoting oxidative stress and insulin resistance,18 and by reducing total body stores of heme-iron, insulin sensitivity increases.27

Favorable patient-important outcomes of a plant-based diet include reducing medications, thereby reducing medical costs, in addition to lowering body weight and decreasing risk factors. Nonetheless, a vegan or vegetarian diet requires the patient to alter dietary habits, often in a radical way. Surprisingly, both Kahleova et al and Barnard et al demonstrated a higher adherence rate to the vegan/vegetarian diet over the conventional diabetes diet,22 particularly during exercise,23 and this has previously been documented.10 In a sub-analysis at the 22-week mark, Barnard et al concluded that the
vegan diet was as acceptable as the conventional diabetic diet, and although it requires greater effort initially, for some, it was simpler to follow without restrictions on calories, carbohydrates or portion size.28

**Limitations of the Studies**

It is important to note the limitations of the three studies analyzed in this review.

All studies had risk of recruitment bias. Nicholson et al21 and Barnard et al22 screened applicants who responded to newspaper advertisements, limiting their population to those who read the newspaper and were motivated enough to respond to an advertisement. Kahleova et al23 screened individuals who were pre-chosen by their endocrinologists without mention of any randomized method, inviting the possibility of bias by hand-selecting certain patients. Additionally, by nature of design, all three trials excluded individuals who were not willing to change their diet, and in the case of Kahleova et al23, enter an exercise program after 12 weeks, which narrows participants to those who are motivated and may not represent the larger population of diabetics.

Although all studies were randomized, only Barnard et al22 described the randomization procedure, which excluded the need for allocation concealment since assignment to groups was done simultaneously. Blinding of participants and dieticians was not possible for either group across studies, due to the nature of diet as the testing modality. In cases where participants needed to have medications reduced due to hypoglycemic events, Barnard et al22 describes using a study endocrinologist that remained blinded to group assignment, but the other two authors make no mention of blinding physicians who decided whether medication changes were necessary.
Two of the studies were limited by small sample size, thereby affecting precision. Nicholson et al\textsuperscript{21} recruited merely 13 patients, two of whom dropped out and were not included in final analyses. Kahleova et al\textsuperscript{23} included 37 participants in each group, which falls short of the calculation of by Barnard et al.\textsuperscript{22}

There were several confounding factors that affected all three studies. Firstly, there is no foolproof way to monitor adherence to diet for people living independently, and the method utilized by all authors—3-day dietary records and unannounced phone calls to elicit recall of diet in the previous 24 hours—invokes the possibility of recall bias. Additionally, adherence to the assigned diet as reported by Barnard et al\textsuperscript{22} after 74 weeks was approximately 50% for both groups, with a relatively similar finding from Kahleova et al,\textsuperscript{23} which makes data interpretation difficult when only half the participants followed treatment guidelines. Secondly, exercise habits can have an affect on the outcomes of interest. Nicholson et al\textsuperscript{21} reported the participants of the vegan group exercised somewhat more at baseline than those in the control group, and this trend remained unchanged throughout the study. The other two studies found no significant difference between groups with regard to exercise, as monitored by pedometry readings and self-reports. But again, self-reporting is not free from bias. Thirdly, the most profound confounder appears to be the medication changes required for patient safety, and the subsequent affect on HbA\textsubscript{1c}. In sub-group analyses, as demonstrated by Barnard et al\textsuperscript{22} and Kahleova et al,\textsuperscript{3} elimination of those participants whose medications were altered reduces the sample size and statistical power.

Finally, all studies reported averages for weight loss and HbA\textsubscript{1c} reductions without providing raw data. In this setting, if one participant makes a dramatic change the
entire mean score is influenced. It would have been more applicable for an endpoint if the studies had established a set value (pounds of weight lost or specific % drop in HbA1c) for participants to achieve, in order to calculate event rates.

**GRADE:**

The quality of evidence presented in each article was assessed using the GRADE criteria.29 In adults with Type 2 DM, a vegetarian or vegan diet was compared to a conventional diabetes diet by measuring three primary outcomes: medication reductions, HbA1c and weight loss (Table 2).

**Medication Reduction**—All three studies reported medication reduction as an outcome, and all found a significant reduction in the experimental group compared to the control. Following the GRADE protocol, the studies began as high quality as indicated for RCT design. The outcome was downgraded two levels based on serious limitations identified in each trial, namely the inability to blind participants and dieticians to treatment groups. Additionally, Nicholson et al21 reported a large loss to follow up and did not abide by intention-to-treat analysis. It is worth mentioning that medication reduction was not stated as a primary outcome of any study, thus is classified as ‘indirectness’ according to GRADE, however it is not considered a limitation because this is a patient-important outcome and confounds other primary outcomes. Imprecision, inconsistency and publication bias did not affect the quality assessment. The outcome was upgraded one level based on the large magnitude of effect as indicated in each study. Overall, the GRADE quality is moderate.

**HbA1c** —Without accounting for medication changes, no study found a significant difference between the treatment groups in regards to reduction of HbA1c.
Following the same reasoning above, the HbA1c outcome was downgraded from high to low for lack of blinding across studies. Additionally, HbA1c was not a primary outcome of Kahleova et al\textsuperscript{23}, and should be noted as an indirect measure, however it is not considered a factor that requires downgrading because it is universally utilized as an index of DM II management. Although the results from Barnard et al\textsuperscript{22} were precise, the other two studies were limited by imprecision, affecting the quality of the outcome by downgrading it one more level to very low. Further examination was not applicable, as a quality of ‘very low’ cannot be upgraded. However, it should be noted that confounding factors reduced the effect, as evidenced by sub-analyses performed by Barnard et al\textsuperscript{22} and Kahleova et al\textsuperscript{23} excluding those who had medication changes during the study period. Overall, the GRADE outcome is very low.

**Weight Loss**—Two studies found significant decreases in weight loss among the vegetarian/vegan participants over those on the conventional diabetes diet, and Barnard et al\textsuperscript{22} reported similar results, but without statistical significance. Accordingly, weight loss was considered inconsistent among trials, and the quality was downgraded one level. As above, the outcome was downgraded two levels for serious limitations regarding blinding. Although no further downgrading could be applied, Barnard et al\textsuperscript{22} was the only study that demonstrated precision. No upgrades were applicable, as such the quality of weight loss as an outcome is very low.

II. CONCLUSION

In conclusion, individuals with type 2 diabetes who participate in vegan and vegetarian diets effectively lose weight and have better glycemic control as measured by
medication reduction than those following a conventional diabetes diet. In analyses controlling for medication change, glycemic control is demonstrated further by reduction in HbA1c in the intervention group. Although motivating patients to change their dietary habits is certainly a challenge, a vegan or vegetarian diet without carbohydrate, caloric, or portion size restrictions may lend itself to patient-adherence and acceptability in the setting of long-term healthcare savings. Whether increased insulin sensitivity of the vegetarian group is strictly due to weight loss, or is a manifestation of specific properties of animal products has yet to be elucidated.
References


<table>
<thead>
<tr>
<th>Study Design</th>
<th>Blinding</th>
<th>Number of Participants</th>
<th>Age Range</th>
<th>Study Duration</th>
<th>Diet Classification</th>
<th>Diet Composition</th>
<th>Meals Provided</th>
<th>Adherence Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCT</td>
<td>None reported</td>
<td>13, 11 included in analyses</td>
<td>&gt;25</td>
<td>12 weeks</td>
<td>Vegan</td>
<td>Protein: 10-15%</td>
<td>Lunches, Dinners</td>
<td>3-day dietary records</td>
</tr>
<tr>
<td>RCT</td>
<td>Endocrinologist who evaluated medications who remained blind to group assignment</td>
<td>99</td>
<td>27-82</td>
<td>74 weeks</td>
<td>Vegan</td>
<td>Protein: 15%</td>
<td>None</td>
<td>3-day dietary records</td>
</tr>
<tr>
<td>RCT</td>
<td>Lab technicians remained blind</td>
<td>74</td>
<td>30-70</td>
<td>24 weeks</td>
<td>Vegetarian</td>
<td>Protein: 15%</td>
<td>Lunches, Dinners</td>
<td>Unannounced calls for 24-hour diet recall</td>
</tr>
</tbody>
</table>

- **Nicholson et al**
- **Barnard et al**
- **Kahleova et al**
Table 2. Summary of Findings, GRADE analyses

<table>
<thead>
<tr>
<th>Quality Assessment</th>
<th>Study</th>
<th>Number of Patients</th>
<th>Effect</th>
<th>Importance</th>
<th>Quality</th>
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<tr>
<td>Downgrade Criteria</td>
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<tr>
<td>Number of studies</td>
<td>Design</td>
<td>Limitations</td>
<td></td>
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<td>3</td>
<td>RCT</td>
<td>Serious limitations*</td>
<td>No</td>
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<td>Moderate</td>
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<td></td>
<td></td>
<td>No indirectness**</td>
<td>No</td>
<td></td>
<td>Moderate</td>
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<tr>
<td></td>
<td></td>
<td>Imprecision</td>
<td>None</td>
<td>Large</td>
<td>Moderate</td>
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<td></td>
<td></td>
<td>Inconsistency</td>
<td>None</td>
<td></td>
<td>Moderate</td>
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<td></td>
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<td>Publication bias</td>
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<td></td>
<td></td>
<td>Large magnitude of effect</td>
<td>None</td>
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<td></td>
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<td></td>
<td>Con founding factors reducing effect</td>
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<td>Moderate</td>
<td></td>
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<td></td>
<td></td>
<td>Dose-response gradient</td>
<td>None</td>
<td>Moderate</td>
<td></td>
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<td>Upgrade Criteria</td>
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<td>Design</td>
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<td>RCT</td>
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<td>Medication Reduction</td>
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<td>Summary of Findings</td>
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<td>Number of patients</td>
<td>Effect</td>
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<tr>
<td>Nicholson et al21</td>
<td>7 4</td>
<td>71</td>
<td>0</td>
<td>RR = 71; NNT = 1</td>
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<tr>
<td>Barnard et al22</td>
<td>49 50</td>
<td>35</td>
<td>20</td>
<td>RR = 1.8; NNT = 7</td>
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<tr>
<td>Kahleova et al23</td>
<td>37 37</td>
<td>43</td>
<td>51</td>
<td>RR = 8.6; NNT = 3</td>
<td>Moderate</td>
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<tr>
<td>HbA1c</td>
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<td>Mean change</td>
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<td></td>
<td></td>
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<tr>
<td>Study</td>
<td>Number of patients</td>
<td>Effect</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Nicholson et al21</td>
<td>7 4</td>
<td>-1.4</td>
<td>-1.0</td>
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</tr>
<tr>
<td>Barnard et al22</td>
<td>49 50</td>
<td>-0.34 (SD: 0.19)</td>
<td>-0.14 (SD: 0.17)</td>
<td>Very Low</td>
<td></td>
</tr>
<tr>
<td>Kahleova et al23</td>
<td>37 37</td>
<td>-0.68 (SD: 0.86)</td>
<td>-0.59 (SD: 0.89)</td>
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</tr>
<tr>
<td>Weight Loss</td>
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<td>Mean loss</td>
<td></td>
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<td>Number of patients</td>
<td>Effect</td>
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<tr>
<td>Nicholson et al21</td>
<td>7 4</td>
<td>7.2 kg</td>
<td>3.8 kg</td>
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<tr>
<td>Barnard et al22</td>
<td>49 50</td>
<td>4.4 kg (SD: 0.9)</td>
<td>3.0 kg (SD: 0.8)</td>
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<tr>
<td>Kahleova et al23</td>
<td>37 37</td>
<td>6.2 kg (CI: -6.6 to -5.3)</td>
<td>3.2 kg (CI: -3.7 to -2.5)</td>
<td>Very Low</td>
<td></td>
</tr>
</tbody>
</table>

* Participants were not blinded, and Nicholson et al21 had large loss to follow up and did not follow intention-to-treat analyses.
** Outcome is not primary outcome of some studies, but is patient-important.
+ Nicholson et al21 had a very small sample size, but this was incorporated into study limitations.
~ Nicholson et al21 and Kahleova et al23 had wide CI, in part due to small sample size.
\[\text{Barnard et al22 did not report a significant difference in weight loss between the two groups, unlike the other two studies.}\]
\[\text{~* Medication reduction is a confounding factor for HbA1c values, but once a study has been downgraded to very low, there is no opportunity to upgrade.}\]