

Low-carbohydrate vegan diets in diabetes for weight loss and sustainability: a randomized controlled trial

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ABSTRACT

Background: Low-carbohydrate, high animal fat and protein diets have been promoted for weight loss and diabetes treatment. We therefore tested the effect of a low-carbohydrate vegan diet in diabetes as a potentially healthier and more ecologically sustainable low-carbohydrate option.

Objectives: We sought to compare the effectiveness of a low-carbohydrate vegan diet with a moderate-carbohydrate vegetarian diet on weight loss and metabolic measures in diabetes.

Methods: One hundred and sixty-four male and female participants with type 2 diabetes were randomly assigned to advice on either a low-carbohydrate vegan diet, high in canola oil and plant proteins, or a vegetarian therapeutic diet, for 3 mo, with both diets recommended at 60% of calorie requirements. Body weight, fasting blood, blood pressure, and 7-d food records, to estimate potential greenhouse gas emissions, were obtained throughout the study with tests of cholesterol absorption undertaken at baseline and end of study on 50 participants.

Results: Both low-carbohydrate vegan and vegetarian diets similarly but markedly reduced body weight (−5.9 kg; 95% CI: −6.5, −5.28 kg; and −5.23 kg; 95% CI: −5.84, −4.62 kg), glycated hemoglobin (−0.99%; 95% CI: −1.07, −0.9%; and −0.88%; 95% CI: −0.97, −0.8%), systolic blood pressure (−4 mmHg; 95% CI: −7, −2 mmHg; and −6 mmHg; 95% CI: −8, −3 mmHg), and potential greenhouse gas emissions, but only for potential greenhouse gas emissions was there a significant treatment difference of −0.63 kgCO₂/d (95% CI: −0.99, −0.27 kgCO₂/d) favoring the low-carbohydrate vegan diet.

Conclusions: Low-carbohydrate vegan and vegetarian diets reduced body weight, improved glycemic control and blood pressure, but the more plant-based diet had greater potential reduction in greenhouse

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Introduction

The Atkins and other low-carbohydrate diets for weight loss and the treatment of type 2 diabetes have focused public and scientific attention on lower carbohydrate and higher fat and protein intakes (1) and raised concerns over processed carbohydrate foods in general (2, 3). The Dietary Approaches

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Supplemental Tables 1–11, Supplemental Text, and Supplemental Figure 1 are available from the “Supplementary data” link in the online posting of the article and from the same link in the online table of contents at <https://academic.oup.com/ajcn/>.

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Flow of participants through the study

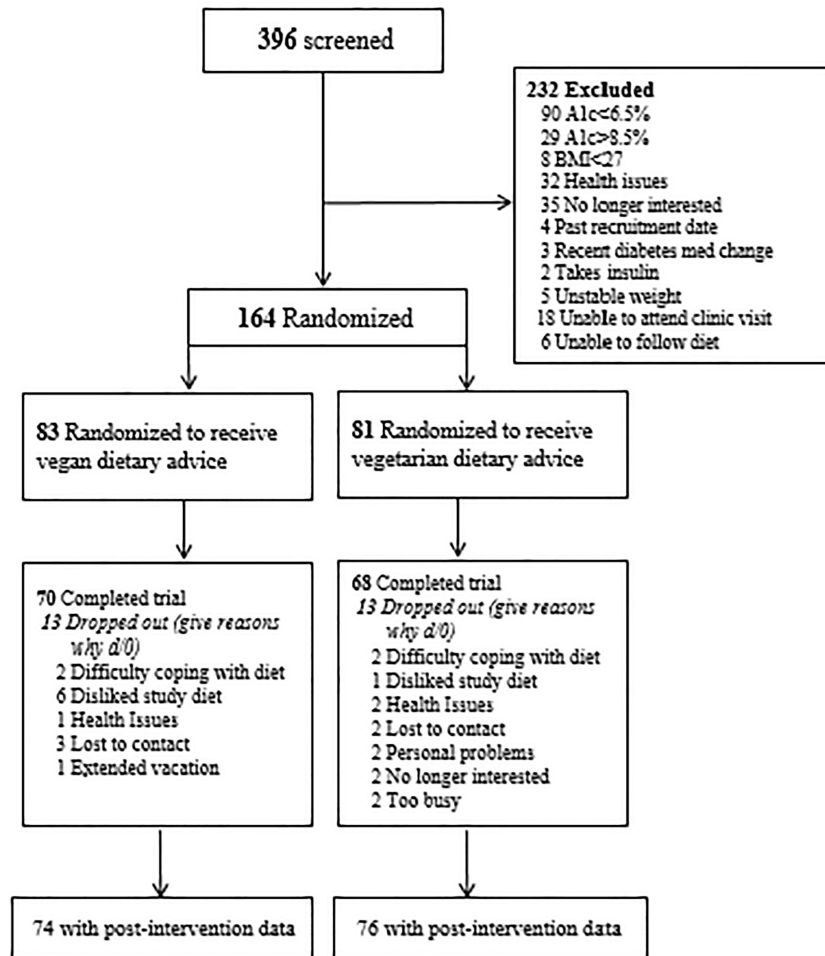


FIGURE 1 Study flow diagram.

to Stop Hypertension (DASH) and Mediterranean diets have emphasized the value of diets with higher fruit and vegetables, low in dairy foods, and reduced meat intake (4). These more plant-based diets are now acknowledged as appropriate dietary patterns for the general public and are advocated in clinical practice guidelines for hypertension control (5), diabetes management, and the reduction of cardiovascular disease risk (5, 6). By virtue of their promotion of increased fruit and vegetable intake, they are not low-carbohydrate diets. Although these more plant-based diets have gained scientific acceptance, the Atkins diet is now not generally advocated in its original form because it is a diet high in red meat and saturated fat from animal sources. However, the original low-carbohydrate goals of the diet continue to be popular as the “paleo” and “keto” diets (7, 8). To address concerns over high red meat and saturated fat consumption, and low levels of plant foods, fruit, and vegetables we have therefore developed a low-carbohydrate vegan approach to Atkins-type diets, using a diet high in plant proteins and unsaturated vegetable oils, such as canola, that we considered would be more in keeping with dietary guidelines and also potentially more ecologically sustainable. We compared this plant-based

low-carbohydrate vegan diet with a meat-free DASH-type vegetarian diet in type 2 diabetes and also assessed the sustainability of these 2 diets from their potential greenhouse gas emissions. We assessed potential greenhouse gas emissions related to diet, because agriculture, food processing, and transportation have important environmental impacts, increasingly recognized in international dietary guidelines and with outcomes that have warranted serious warnings of climate change from the Intergovernmental Panel on Climate Change (9). We believe that the more plant-based diet would result in improvements in cardiovascular risk factors and have lower potential greenhouse gas emissions.

Methods

Participants were recruited from newspaper, public transport, and hospital clinic advertisements. One hundred and sixty-four eligible participants were randomly assigned (Figure 1). Recruitment took place from September 2014 to September 2016, with the last study visit on December 14, 2016. Eligible participants had a ≥ 6 -mo history of type 2 diabetes, were

taking a stable dose of oral antihyperglycemic agents for at least the previous month, were not on insulin therapy, and had glycated hemoglobin (HbA1c) values that were between 6.5% and 8.5%. No participant had clinically significant cardiovascular disease, renal disease (creatinine $>150 \mu\text{mol/L}$), liver disease (alanine transaminase >3 times the upper limit of the laboratory normal range), or a history of cancer. Five participants were smokers. No participants took alcohol >2 drinks/d. Participation selection and reasons for exclusion are given in [Figure 1](#).

Protocol

The study followed a randomized, parallel design with two 3-mo treatment arms, consisting of a low-carbohydrate vegan and a vegetarian diet. Participants attended the Risk Factor Modification Center at St Michael's Hospital, a teaching hospital of the University of Toronto, for screening and weeks -1 , 0, 2, 4, 8, 10, and 12 of the study. Fasting blood, anthropometric measurements, and 7-d food diaries were obtained ([Supplemental Tables 1A–C and 2](#)).

Diet

On the low-carbohydrate vegan diet participants were provided with a canola oil-enriched bread and high-protein simulated meat products (Loblaws Companies; Gardein Protein foods). The vegetarian diet emphasized fruit, vegetables, and low-fat dairy products, with avoidance of meat and snack foods. Participants were also provided with wholewheat bread and with liquid egg whites to reduce dietary cholesterol intake (Blue Menu, Loblaws Companies). Diets were prescribed at 60% of energy requirement ([Supplemental Tables 1A–C](#)).

Cholesterol absorption studies were carried out on the first 50 participants in the week prior to the start and during the last week of the study period ([Supplemental Table 3](#)).

The study was approved by the Research Ethics Board of St Michael's Hospital and written consent was obtained from all participants. The trial was registered with [clinicaltrials.gov](#) (NCT02245399).

Blood pressure

Routine fasting blood pressure was measured with an automatic sphygmomanometer ([Supplemental Table 2](#)).

Biochemical analyses

HbA1c, blood glucose, serum lipids, and urine samples were measured in the hospital routine analytical laboratory ([Supplemental Table 2](#)) (10). Uric acid was measured at the beginning and end of the study (10).

LDL particle size and distribution was assessed by electrophoretic characteristics obtained by nondenaturing polyacrylamide gradient (2–16%) gel electrophoresis of serum (11).

Free cholesterol absorption test

Carbon-13 cholesterol absorption from an enriched test meal breakfast margarine was determined using stable isotope methodology pre study and during the last week of the 12-wk study on the first 50 participants (12). Plasma markers of cholesterol absorption and biosynthesis, including desmosterol, lathosterol, campesterol, sitosterol, and stigmastanol concentrations were assessed at the beginning and end of each diet by using GC (13) ([Supplemental Table 3](#)).

Potential greenhouse gas emission analyses

The greenhouse gas emission database was constructed with data from 6 greenhouse gas databases (14–19) and applied to the foods in the database. Mean values were obtained for each food and values were also ascribed to the components of mixed dishes. We attempted to use data with a complete life cycle analysis but these details were often not available.

Statistical process and analyses

Power calculation.

We expected similar weight reductions to those seen in our low-carbohydrate vegan trial with the test diet having shown a 6.9-kg reduction and a 5.8-kg reduction on the control diet (20). To calculate the sample size, we used as the effect size a treatment difference of 1.1 kg with an SD of the difference of 2 kg [rounded up from 1.8 kg SD from a previous low-carbohydrate vegan trial (20); the larger SD of 2 kg was used to ensure adequate power because other published weight loss studies suggest larger SDs]. We have used body weight for our power calculation due to the availability of the data rather than HbA1c, which was previously included in [clinicaltrials.gov](#). Using a 2-sided 2-sample z -test estimation of sample size approach with $\alpha = 0.05$, $1 - \beta = 0.80$, we would require 53 participants per arm to detect a significant difference between treatments (21). Therefore, allowing for a 30% dropout rate (higher than the 20–25% anticipated) we needed to recruit 160 participants.

Randomization and blinding.

After stratification by sex and HbA1c ($>7.1\%$ or $\leq 7.1\%$), but without a predetermined block size, participants were randomly assigned in a blinded fashion by a statistician who was geographically separate from the study center. Randomization assignments were computer generated and provided to study staff in opaque envelopes. Interventions were assigned by study dietitians. The dietitians and the participants could not be blinded but equal emphasis was placed on the potential importance for health of both diets. The analytical technicians were blinded to treatment, as was the statistician, up to and including analysis of the primary outcome.

Statistical analyses

Baseline characteristics were expressed as means $\pm$ SD for continuous variables and medians and IQRs for nonnormally distributed data, or as proportions for categorical variables. The primary outcome was the treatment difference as change from

TABLE 1 Baseline characteristics of study participants¹

Characteristics	No. of participants	
	Vegan (<i>n</i> = 83)	Vegetarian (<i>n</i> = 81)
Age, mean $\pm$ SD, y	59 $\pm$ 8.6	58 $\pm$ 11.7
Sex		
Men	38 (45.8)	37 (45.7)
Women	45 (54.2)	44 (54.3)
Race/ethnicity ²		
European	29 (34.9)	26 (32.1)
Other white/Caucasian	9 (10.8)	6 (7.4)
Indian/South Asian	15 (18.1)	16 (19.8)
Far Eastern	7 (8.4)	6 (7.4)
African	14 (16.9)	13 (16.1)
Hispanic	3 (3.6)	4 (4.9)
Native American	0 (0)	2 (2.5)
Other	6 (7.2)	8 (9.9)
Weight, mean $\pm$ SD, kg	95.0 $\pm$ 17.3	90.6 $\pm$ 16.9
BMI, mean $\pm$ SD, kg/m ²	34.5 $\pm$ 4.8	32.8 $\pm$ 4.5
Current smokers	4 (4.8)	1 (1.2)
HbA1c		
No. of participants <7.1%	38 (45.8)	37 (45.7)
No. of participants $\geq$ 7.1%	45 (54.2)	44 (54.3)
Duration of diabetes, mean $\pm$ SD, y	7.9 $\pm$ 6.2	6.7 $\pm$ 5.5
Medication use		
Total antihyperglycemic medications	83 (100)	81 (100)
Biguanide	83 (100)	79 (98)
Sulfonylurea	23 (28)	25 (31)
Dipeptidyl peptidase-4 inhibitors	31 (37)	34 (42)
Sodium-glucose transport protein 2 inhibitors	7 (8)	6 (7)
Glucagon-like peptide-1 agonists	0 (0)	3 (4)
Meglitinides (nonsulfonylurea)	1 (1)	0 (0)
α -Glucosidase inhibitors	0 (0)	0 (0)
Thiazolidinedione	0 (0)	0 (0)
Cholesterol-lowering medications	58 (70)	58 (72)
Blood pressure medications	64 (77)	62 (77)

¹Data are *n* (%) or mean $\pm$ SD. HbA1c, glycated hemoglobin.²Race was self-identified.

baseline in body weight between the low-carbohydrate vegan and vegetarian treatments at weeks 2 to 12. Secondary measures included HbA1c, blood lipids, and blood pressure. HbA1c was stated as our primary outcome in clinicaltrials.gov. However, because the power calculation was based on body weight change, this outcome is currently taken as the primary outcome. The significance of the treatment difference was assessed using a mixed model with repeated measures with a spatial linear covariance structure (PROC MIXED 9.4; SAS Institute Inc), including all postintervention time points in the calculation of the outcome (see **Supplemental Text**). The spatial power covariance structure was chosen to account for within-participant correlation and unequal spacing of observation times of repeated measures. The analysis was a modified intention-to-treat analysis that included all postintervention measures, with follow-up at weeks 2, 4, 8, 10, and 12 postbaseline. Fourteen participants had no postintervention data (9 low-carbohydrate vegan and 5 vegetarian). Covariates included sex, and HbA1c representing stratification factors. In the model, treatment, time, the treatment by time interaction, and baselines were treated as fixed effects whereas participant was considered a random effect. For LDL

particle size, serum uric acid, and cholesterol synthesis, where only baseline and week 12 samples were available, we used an ANCOVA model with change from baseline to week 12. Where changes across treatments were nonnormally distributed, treatment differences were assessed after log-transformation (ln) of data with the change from baseline calculated after log-transformation.

A post hoc analysis was undertaken to determine whether the change in body weight on the low-carbohydrate vegan diet met the criterion for noninferiority compared with the change on the DASH-like diet using 75%, 50%, and 25% of the prespecified treatment difference (1.1 kg) (22).

Spearman correlations were used to evaluate the associations of changes in potential greenhouse gas emissions with study outcomes (**Supplemental Table 4**).

Results

Baseline characteristics of participants are described in **Table 1**. Seventy of 83 participants (84%) completed the low-carbohydrate vegan diet (i.e., provided ≥ 1 blood sample in the

TABLE 2 Nutritional profiles at week 0 and week 12 for participants consuming a low-carbohydrate vegan diet and a vegetarian diet

	Week 0		Week 12		Between treatments	
	Vegan (n = 80)	Vegetarian (n = 81)	Vegan (n = 67)	Vegetarian (n = 66)	β	95% CI
Energy, ¹ kcal	1668 (722)	1719 (627)	1198 (493)	1231 (416)	93	−64, 250
Available carbohydrate, ² % energy	40.6 ± 6.1	42.3 ± 7.7	31 ± 6	48.4 ± 6.6	−16	−18.3, −12.8
Fiber, ¹ g/4.2 MJ	12.3 (5.8)	12.9 (7)	20.2 (6.3)	17.2 (4.9)	2.53	0.51, 4.54
Dietary cholesterol, ¹ mg/4.2 MJ	145 (69)	148 (64)	3 (42)	111 (112)	−2.18	−2.8, −1.55
Total protein, ¹ % energy	18.7 (4.9)	19 (6.5)	24.5 (7.4)	19 (4.5)	4.75	3.1, 6.39
Plant protein, ¹ % energy	6.45 (1.61)	6.93 (2.31)	21.92 (9.09)	7.01 (1.85)	1.04	0.94, 1.15
Animal protein, ¹ % energy	12 (6)	11.5 (6.8)	0.7 (3.4)	12.1 (4.2)	−10	−11.9, −7.6
Egg protein, ¹ % energy	0.69 (0.61)	0.63 (0.73)	0.35 (1.04)	3.45 (2.17)	−2.69	−3.43, −1.95
Dairy protein, ¹ % energy	2.61 (2.08)	2.32 (1.85)	0.44 (0.69)	4.11 (3.2)	−4.40	−5.47, −3.33
Total fat, ² % energy	35.1 ± 6.5	33.4 ± 5.9	40.1 ± 4.9	28.8 ± 6.7	10	7.3, 12.3
MUFAs, ¹ % energy	12.8 (4.6)	12.8 (3.6)	20.4 (4.1)	9.8 (3.4)	8.86	7.38, 10.34
PUFAs, ¹ % energy	6.6 (2.23)	6.96 (2.22)	11.47 (3.55)	6.95 (3.01)	4.24	3.18, 5.31
SFAs, ² % energy	10.8 ± 3.2	10.1 ± 2.5	5.4 ± 2.4	8.3 ± 2.8	−3.58	−4.61, −2.55
Sodium, ¹ mg/d	1349 (301)	1302 (343)	1399 (325)	1247 (337)	115	−16, 246
Potassium, ¹ mg/d	1578 (387)	1598 (330)	1954 (400)	2009 (394)	−86	−229, 58
Magnesium, ¹ mg/d	185 (64)	190 (59)	252 (63)	234 (48)	22	2.3, 41.9
Calcium, ¹ mg/d	422 (187)	386 (148)	369 (145)	501 (268)	−186	−250, −122

¹Data are medians (IQRs) for nonnormally distributed data.

²Data are means ± SD for normally distributed data.

^βDifference in change from baseline between treatments [shown with no adjustment (ln) for nonlinear distribution].

final month), and 68 of 81 (84%) completed the vegetarian diet (Figure 1). Significant treatment differences were seen in the macronutrient profiles between the low-carbohydrate vegan and vegetarian diets, with 16% less available carbohydrate and 10% more fat and 5% more protein as a percentage of total calories on the low-carbohydrate vegan diet (Table 2). Of note, our diets, especially the vegan diet, were low in calcium (Table 2).

Body weight and waist circumference

No treatment differences were seen in body weight or waist circumference, because on both low-carbohydrate vegan and vegetarian diets, body weight and waist circumference were reduced (Table 3) representing a −5.9 kg (95% CI: −6.5, −5.3 kg) and a −5.2 kg (95% CI: −5.8, −4.6 kg) reduction in body weight, respectively (Figure 2). Although the falls in body weight were similar for both treatments, noninferiority was not established for the low-carbohydrate vegan diet (Supplemental Figure 1).

Blood pressure

There were no changes in blood pressure medications and no treatment differences in blood pressure. However, within treatment, both diets showed significant reductions in systolic blood pressure: −4.12 mmHg (95% CI: −6.65, −1.59 mmHg) on the low-carbohydrate vegan and −5.91 mmHg (95% CI: −8.45, −3.38 mmHg) on the vegetarian diet. Similarly, the fasting diastolic blood pressure fell: −3.54 mmHg (95% CI: −5.29, −1.8 mmHg) and −4.13 mmHg (95% CI: −5.89, −2.38 mmHg), respectively (Table 3).

Potential greenhouse gas emissions

Based on self-reported dietary intakes, the predicted greenhouse gas emissions fell at week 2 and remained down on both diets for the period of weeks 2 to 12 (Figure 2). The average reduction for all intervention weeks on the low-carbohydrate vegan diet was −2.61 kgCO₂ per day (95% CI: −2.86, −2.35 kgCO₂) and on the vegetarian was −1.97 kgCO₂ (95% CI: −2.23, −1.72 kgCO₂). The treatment difference was significant, with the low-carbohydrate vegan diet potential greenhouse gas emissions value being lower than the vegetarian diet potential greenhouse gas emissions by −0.63 kgCO₂ (95% CI: −0.99, −0.27 kgCO₂) (Table 3). Expressed per 2000 kcal, the potential greenhouse gas emissions treatment difference was −0.39 (ln) (95% CI: −0.52, −0.25) (Supplemental Table 4).

HbA1c and blood lipids

No treatment differences were seen in changes in antihyperglycemic or lipid-lowering medications (Supplemental Table 5) nor in HbA1c or serum lipid measurements (Table 3). However, HbA1c fell on the low-carbohydrate vegan diet by −0.99% (95% CI: −1.07, −0.9%) and on the vegetarian diet by −0.88% (95% CI: −0.97, −0.8%); and LDL concentrations fell on the low-carbohydrate vegan diet by −0.21 mmol/L (95% CI: −0.31, −0.11 mmol/L) and on the vegetarian diet by −0.16 mmol/L (95% CI: −0.26, −0.06 mmol/L) (Table 3).

LDL cholesterol particle size

No between-treatment differences were seen in LDL cholesterol particle size distribution. However, small LDL cholesterol concentrations (log_e) fell on both low-carbohydrate vegan

TABLE 3 Treatment differences for anthropometric, blood, and potential greenhouse gas emission measurement in the modified intention-to-treat analysis ($n = 150/164$)¹

	Vegan			Vegetarian			Between treatments	
	Mean baseline $\pm$ SD	β	95% CI	Mean baseline $\pm$ SD	β	95% CI	β	95% CI
Weight, ² kg	95 $\pm$ 17	-5.89	-6.5, -5.28	91 $\pm$ 17	-5.23	-5.84, -4.62	-0.66	-1.53, 0.2
BMI, ² kg/m ²	34 $\pm$ 5	-2.07	-2.28, -1.86	33 $\pm$ 5	-1.95	-2.16, -1.74	-0.12	-0.42, 0.18
Waist, ^{2,3} cm	113 $\pm$ 12	-5.08	-6.38, -3.77	110 $\pm$ 12	-5.83	-7.14, -4.51	0.75	-1.1, 2.6
Hemoglobin A1c, ^{2,3} %	7.28 $\pm$ 0.55	-0.99	-1.07, -0.9	7.23 $\pm$ 0.47	-0.88	-0.97, -0.8	-0.10	-0.22, 0.02
Glucose, ^{2,3} mmol/L	7.59 $\pm$ 1.28	-1.02	-1.32, -0.72	7.6 $\pm$ 1.19	-1.21	-1.52, -0.91	0.19	-0.23, 0.61
Total cholesterol, ^{2,3} mmol/L	3.96 $\pm$ 0.82	-0.34	-0.46, -0.21	3.81 $\pm$ 0.82	-0.28	-0.4, -0.15	-0.06	-0.23, 0.12
LDL cholesterol, ^{2,3} mmol/L	2.15 $\pm$ 0.68	-0.21	-0.31, -0.11	2.03 $\pm$ 0.67	-0.16	-0.26, -0.06	-0.05	-0.19, 0.1
Small LDL cholesterol (<255 Å), ⁴ mmol/L	1.46 $\pm$ 0.57	-0.10	-0.18, -0.02	1.43 $\pm$ 0.47	-0.10	-0.18, -0.03	0.00	-0.11, 0.11
Medium LDL cholesterol (255–260 Å), ^{3,4} mmol/L	0.42 $\pm$ 0.26	-0.04	-0.08, -0.001	0.41 $\pm$ 0.24	-0.07	-0.11, -0.03	0.03	-0.03, 0.08
Large LDL cholesterol (>260 Å), ^{3,4} mmol/L	0.25 $\pm$ 0.26	-0.03	-0.07, 0.004	0.21 $\pm$ 0.16	-0.02	-0.06, 0.02	-0.02	-0.07, 0.04
HDL cholesterol, ^{2,3} mmol/L	1.13 $\pm$ 0.24	-0.02	-0.05, 0.02	1.14 $\pm$ 0.29	-0.01	-0.04, 0.02	-0.01	-0.05, 0.04
Triglyceride, ^{2,3} mmol/L	1.53 $\pm$ 0.82	-0.28	-0.42, -0.14	1.42 $\pm$ 0.63	-0.21	-0.35, -0.07	-0.07	-0.27, 0.13
Total cholesterol:HDL ratio ^{2,3}	3.64 $\pm$ 1.04	-0.27	-0.4, -0.15	3.51 $\pm$ 1.05	-0.22	-0.35, -0.09	-0.06	-0.24, 0.12
LDL:HDL ratio ^{2,3}	1.99 $\pm$ 0.79	-0.18	-0.28, -0.07	1.88 $\pm$ 0.78	-0.13	-0.24, -0.03	-0.05	-0.19, 0.1
Non-HDL cholesterol, ^{2,3} mmol/L	2.83 $\pm$ 0.82	-0.31	-0.42, -0.2	2.67 $\pm$ 0.79	-0.26	-0.37, -0.15	-0.05	-0.21, 0.1
Triglyceride:HDL ratio ^{2,3}	1.47 $\pm$ 1.01	-0.26	-0.43, -0.09	1.39 $\pm$ 0.86	-0.19	-0.35, -0.02	-0.08	-0.31, 0.16
Urea, ^{2,3} mmol/L	5.64 $\pm$ 1.69	0.16	-0.24, 0.56	5.47 $\pm$ 1.63	-0.30	-0.71, 0.1	0.46	-0.11, 1.03
Creatinine, ^{2,3} μ mol/L	73 $\pm$ 16	-5.31	-7.4, -3.22	74 $\pm$ 19	-3.51	-5.61, -1.41	-1.80	-4.75, 1.16
Uric acid, ⁴ μ mol/L	333 $\pm$ 87	6.35	-3.78, 16.47	318 $\pm$ 78	-7.74	-17.95, 2.47	14.09	-0.26, 28.44
Systolic blood pressure, ^{2,3} mmHg	118 $\pm$ 10	-4.12	-6.65, -1.59	120 $\pm$ 11	-5.91	-8.45, -3.38	1.79	-1.79, 5.37
Diastolic blood pressure, ² mmHg	72 $\pm$ 8	-3.54	-5.29, -1.8	71 $\pm$ 8	-4.13	-5.89, -2.38	0.59	-1.88, 3.06
Greenhouse gas emissions, ^{2,3} kgCO ₂ /d	4.39 $\pm$ 2.44	-2.61	-2.86, -2.35	4.33 $\pm$ 2.14	-1.97	-2.23, -1.72	-0.63	-0.99, -0.27

¹Fourteen participants (9 low-carbohydrate vegan, 5 vegetarian) without postintervention data, not captured in this analysis.

²The outcome is change from baseline to week 12 derived from a mixed model and repeated measures analysis (that included weeks 2, 4, 8, 10, and 12), with sex and baseline hemoglobin A1c as covariates.

³*P* values obtained by log transformation where data were not normally distributed.

⁴The same as for ² but using an ANCOVA model because only baseline and week 12 values were available.

(-0.10 mmol/L; 95% CI: -0.18, -0.02 mmol/L) and vegetarian diets (-0.10 mmol/L; 95% CI: -0.18, -0.03 mmol/L) (Table 3).

Other biochemical measures

No between-treatment differences were seen in other serum measures (Table 3); however, a higher urinary urea output was seen on the low-carbohydrate vegan diet, with a higher urinary potassium excretion on the vegetarian diet (Supplemental Tables 6 and 7) likely reflecting higher protein and fruit intakes, respectively.

Completer analyses

The completer analyses ($n = 138$) also showed no significant treatment differences between outcome measures (Supplemental Table 2).

Cholesterol absorption

No within- or between-treatment differences were seen in carbon-13 cholesterol absorption in the 48 participants who

completed this test (Supplemental Table 8). There were no differences in serum markers of cholesterol biosynthesis. The apparent difference in markers of cholesterol absorption simply demonstrates adherence to a diet that contained plant sterols (Supplemental Tables 3 and 9).

differences between outcome measures

A correlation matrix of potential greenhouse gas emissions with study outcomes is shown in Supplemental Table 10. Changes in greenhouse gas emissions related to changes in key risk factors: body weight ($r = 0.38$, $n = 146$, $P < 0.001$), HbA1c ($r = 0.23$, $n = 145$, $P = 0.005$), LDL cholesterol ($r = 0.25$, $n = 141$, $P = 0.003$) (Figure 3), systolic and diastolic blood pressure ($r = 0.25$, $n = 143$, $P = 0.003$ and $r = 0.23$, $n = 143$, $P = 0.005$) (Supplemental Table 10).

Adverse events

No serious adverse events were recorded.

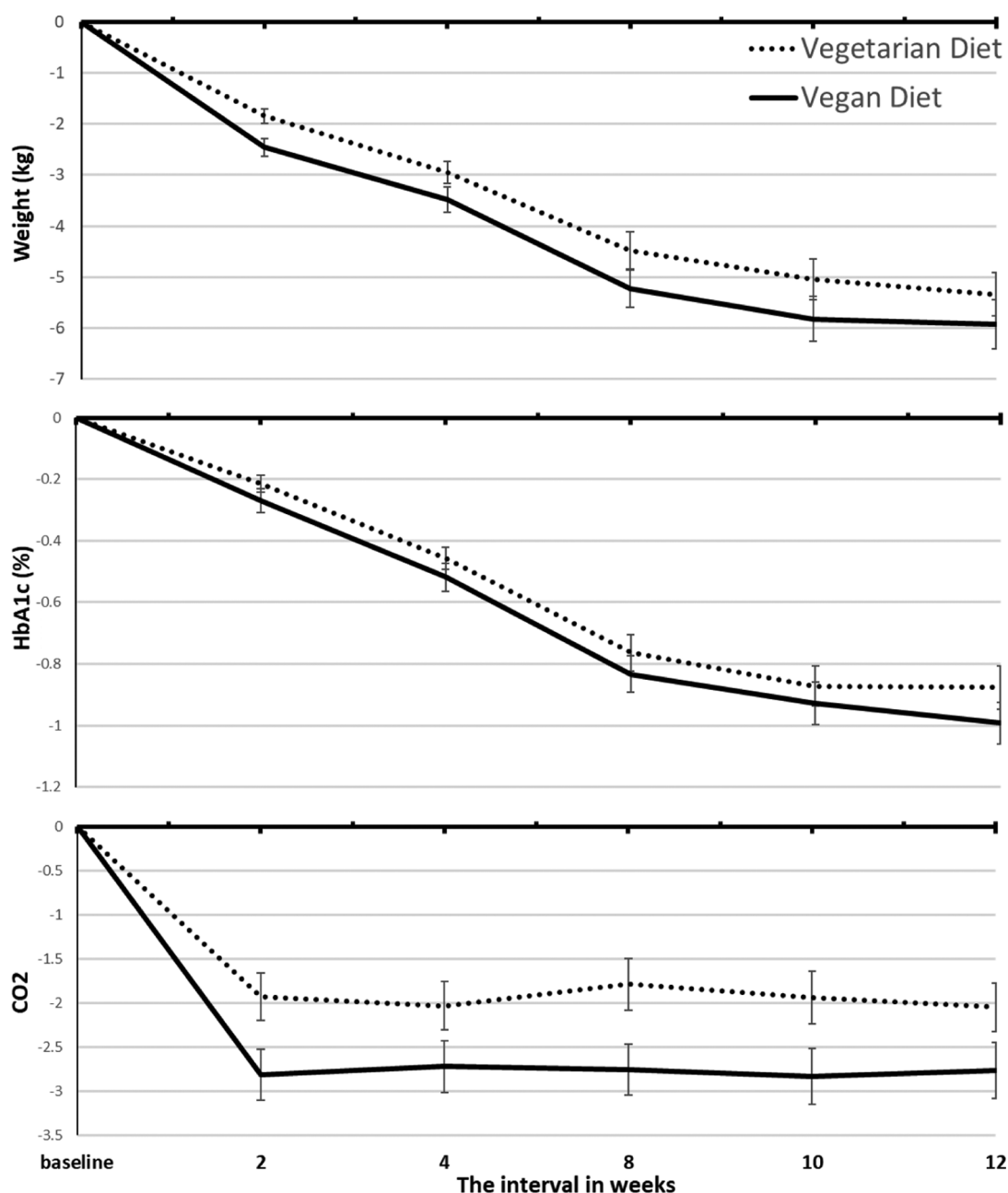


FIGURE 2 Change in body weight (vegan $n = 74$ and vegetarian $n = 76$), hemoglobin A1c (vegan $n = 74$ and vegetarian $n = 75$), and carbon dioxide (vegan $n = 70$ and vegetarian $n = 76$) over 12 wk.

Discussion

These data indicate that low-carbohydrate vegan diets or vegetarian diets without carbohydrate restrictions do not differ in their effectiveness for weight loss, glycemic control, or cardiovascular disease risk factor reduction in type 2 diabetes. The data also support previous findings that modest changes in carbohydrate content do not influence blood pressure (4). Similar findings were recorded by Gardner and colleagues (23) in a weight loss trial comparing diets with different macronutrient profiles. However, in a subsequent study, improvements in lipids and trimethylamine *N*-oxide, a novel cardiovascular risk

factor, were only seen on plant-based diets (24). Our study demonstrated that 10% more fat as canola oil (40% total fat) in the context of increased plant protein intake (22% of dietary calories) permitted weight loss as effectively as the DASH-type vegetarian diet (at 29% fat calories) (Table 2). There are, however, data to suggest that fat can have calorific advantages for weight loss in a healthy low-carbohydrate diet (25).

No significant treatment differences were seen in blood pressure between the 2 diets. The association of change in weight with blood pressure change suggested that 40% of the systolic

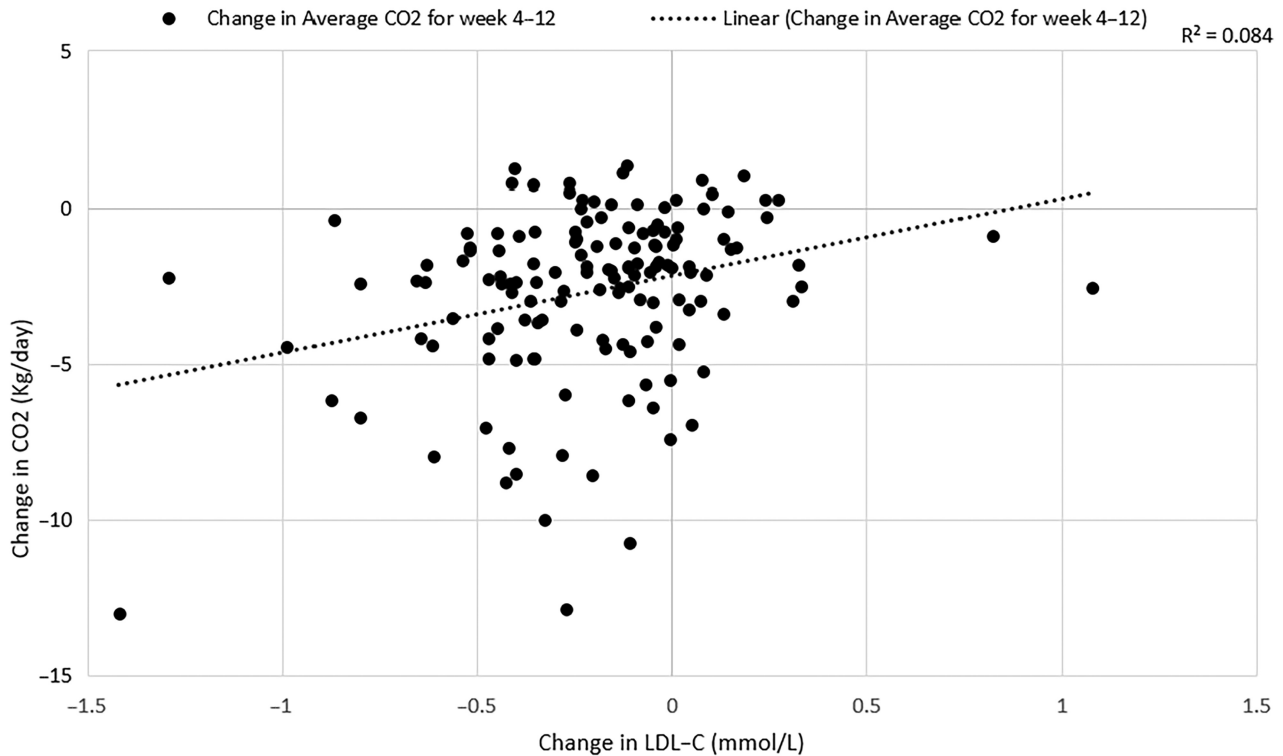


FIGURE 3 Average change over weeks 4 to 12 of the study in potential greenhouse gas emissions of the low-carbohydrate vegan and vegetarian diets against the change in LDL cholesterol (LDL-C) ($r = 0.25$, $n = 141$, $P = 0.003$).

blood pressure reduction was related to weight loss achieved on both diets.

We used a DASH-like vegetarian diet as a comparison group because the DASH diet, originally developed to reduce blood pressure, has become a recommended diet in many clinical practice guidelines for the treatment not only of hypertension but also of diabetes, hyperlipidemia, and cardiovascular disease (5, 6). Our DASH-like diet was vegetarian to increase its consistency with growing recommendations to consume more plant-based diets. The DASH diet is often paired with the Mediterranean diet as the ideal diet for the general population (5, 6). Common to both diets are increased fruit and vegetable consumption, and a reduction in red meat intake and therefore less saturated fat and dietary cholesterol.

Vegetarian and vegan diets have long been recognized to reduce LDL cholesterol concentrations (26) and other cardiovascular risk factors and to reduce cardiovascular disease risk (27). Increased intake of plant proteins and oils has been associated with low rates of diabetes and cardiovascular disease in cohort studies (28), and trial data indicate that increased vegetable oil as extra virgin olive oil reduces stroke (29). The current study indicates that major changes in macronutrients, as vegetable oil (canola) and plant proteins (palatable meat substitutes), are as effective as the more conventional and broadly accepted therapeutic dietary patterns of the vegetarian diet in achieving weight loss, improving glycemic control, and reducing cardiovascular disease risk factors.

The present study provided no evidence that changes in cholesterol absorption and synthesis differ between or within treatments.

Our assessment of the potential difference in the reduction in greenhouse gas emissions between these test diets is in line with the generally recognized reduction in potential greenhouse gas emissions from foods of plant origin as opposed to animal origin (30). Thus on the vegan diet the potential greenhouse gas emissions were reduced by >50% compared with the baseline diet. Considering that animal agriculture and therefore food production contribute 14% of annual anthropogenic greenhouse gas emissions (31), it has been estimated that phasing out livestock production would provide half of the net emissions reduction required to limit global warming to 2°C (32). We believe the greenhouse gas emissions relation to LDL cholesterol and blood pressure in this trial support the increased use of more plant-based diets for both human and environmental health.

Study limitations include its relatively short duration of 3 mo, the overall very good health of the participants, with risk factor levels close to target, making further reductions more difficult to achieve. Nevertheless, both low-carbohydrate vegan and vegetarian diets brought the HbA1c and serum LDL cholesterol below target, with HbA1c at 6.3% for both diets and LDL cholesterol at 1.94 mmol/L and 1.87 mmol/L for low-carbohydrate vegan and vegetarian diets, respectively. The systolic blood pressures achieved were 114 mmHg for both diets and were excellent for participants with a mean age of

59 y with type 2 diabetes for an average of 7 y. However, weight loss could prove a problem in interpreting the changes in risk factors because the observed treatment effects might be attributable to either or both the nature of the diets or energy restriction. Nevertheless, body weight changes plateaued during the final month. Previous studies with a low-carbohydrate vegan dietary approach in hyperlipidemic participants demonstrated maintenance of weight loss between 3 and 6 mo (20), over which time blood lipid reductions were also maintained. It has been concluded that 3 mo is adequate for metabolic adaptation (25). Rather than using standard intention-to-treat analysis, we used a modified intention-to-treat analysis that included only postrandomization data. We did not perform multiple imputation but relied on the use of the mixed model because the dropout rates were similar on both treatments. Further, we consider it likely that the missing data were missing completely at random because there were no differences in baseline characteristics between the completers and those with no postbaseline values in terms of defining characteristics such as age, sex, body weight, BMI, and duration of diabetes (Supplemental Table 11).

We cannot be sure that a full life cycle analysis was performed for all the greenhouse gas emission data used in our internationally derived greenhouse gas emissions database. However, by taking the mean values of foods from a number of databases, we believe our data are internationally relevant. In the long term attention must also focus on vitamin and mineral intake especially in those with low intake levels and baseline, although for calcium the currently stated requirements may be higher than actually needed (33).

The present study's strengths include testing a low-carbohydrate dietary strategy that was plant based rather than animal product based and assessing its potential greenhouse gas emissions.

We conclude that although noninferiority was not established for the low carbohydrate vegan diet, our data indicate that diets higher in vegetable oils and plant proteins appear suitable as weight-reducing diets in type 2 diabetes. More plant-based diets can also have the advantage of being more environmentally sustainable while reducing risk factors for cardiovascular disease and diabetes complications.

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of the Canadian Nutrition Society. MEK has received funding from a Toronto 3D Knowledge Synthesis and Clinical Trials foundation PhD scholarship award and is a part-time employee at INQUIS Clinical Research, a contract research organization. CWCK has received grants or research support from the Advanced Food Materials Network, Agriculture and Agri-Foods Canada (AAFC), Almond Board of California, Barilla, Canadian Institutes of Health Research (CIHR), Canola Council of Canada, International Nut and Dried Fruit Council, International Tree Nut Council Research and Education Foundation, Loblaw Brands Ltd, the Peanut Institute, Pulse Canada, and Unilever. He has received in-kind research support from the Almond Board of California, Barilla, California Walnut Commission, Kellogg Canada, Loblaw Companies, Nutrartis, Quaker (PepsiCo), the Peanut Institute, Primo, Unico, Unilever, WhiteWave Foods/Danone. He has received travel support and/or honoraria from Barilla, California Walnut Commission, Canola Council of Canada, General Mills, International Nut and Dried Fruit Council, International Pasta Organization, Lantmannen, Loblaw Brands Ltd, Nutrition Foundation of Italy, Oldways Preservation Trust, Paramount Farms, the Peanut Institute, Pulse Canada, Sun-Maid, Tate & Lyle, Unilever, and White Wave Foods/Danone. He has served on the scientific advisory board for the International Tree Nut Council, International Pasta Organization, McCormick Science Institute and Oldways Preservation Trust. He is a founding member of the International Carbohydrate Quality Consortium (ICQC), Executive Board Member of the Diabetes and Nutrition Study Group (DNSG) of the European Association for the Study of Diabetes (EASD), is on the Clinical Practice Guidelines Expert Committee for Nutrition Therapy of the EASD, and is a Director of Glycemic Consulting and the Toronto 3D Knowledge Synthesis and Clinical Trials foundation. JLS has received research support from the Canadian Foundation for Innovation, Ontario Research Fund, Province of Ontario Ministry of Research and Innovation and Science, Canadian Institutes of Health Research (CIHR), Diabetes Canada, PSI Foundation, Banting and Best Diabetes Centre (BBDC), American Society for Nutrition, INC International Nut and Dried Fruit Council Foundation, National Dried Fruit Trade Association, National Honey Board (the USDA honey "Checkoff" program), International Life Sciences Institute (ILSI), Pulse Canada, Quaker Oats Center of Excellence, United Soybean Board (the USDA soy "Checkoff" program), Tate & Lyle Nutritional Research Fund at the University of Toronto, the Glycemic Control and Cardiovascular Disease in Type 2 Diabetes Fund at the University of Toronto (a fund established by the Alberta Pulse Growers), and the Nutrition Trialists Fund at the University of Toronto (a fund established by an inaugural donation from the Calorie Control Council). He has received food donations to support randomized controlled trials from the Almond Board of California, California Walnut Commission, Peanut Institute, Barilla, Unilever/Upfield, Unico/Primo, Loblaw Companies, Quaker, Kellogg Canada, WhiteWave Foods/Danone, Nutrartis, and Dairy Farmers of Canada. He has received travel support, speaker fees, and/or honoraria from Diabetes Canada, Dairy Farmers of Canada, FoodMinds LLC, International Sweeteners Association, Nestlé, Pulse Canada, Canadian Society for Endocrinology and Metabolism (CSEM), GI Foundation, Abbott, General Mills, Biofortis, ASN, Northern Ontario School of Medicine, INC Nutrition Research & Education Foundation, European Food Safety Authority (EFSA), Comité Européen des Fabricants de Sucre (CEFS), Nutrition Communications, International Food Information Council (IFIC), Calorie Control Council, International Glutamate Technical Committee, and Physicians Committee for Responsible Medicine. He has or has had ad hoc consulting arrangements with Perkins Coie LLP, Tate & Lyle, Wirtschaftliche Vereinigung Zucker e.V., Danone, and INQUIS Clinical Research. He is a member of the European Fruit Juice Association Scientific Expert Panel and former member of the Soy Nutrition Institute (SNI) Scientific Advisory Committee. He is on the Clinical Practice Guidelines Expert Committees of Diabetes Canada, European Association for the study of Diabetes (EASD), Canadian Cardiovascular Society (CCS), and Obesity Canada/Canadian Association of Bariatric Physicians and Surgeons. He serves or has served as an unpaid scientific advisor for the Food, Nutrition, and Safety Program (FNSP) and the Technical Committee on Carbohydrates of ILSI North America. He is a member of the International Carbohydrate Quality Consortium (ICQC), Executive Board Member of the Diabetes and Nutrition Study Group (DNSG) of the EASD, and Director of the Toronto 3D

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Data Availability

Data described in the manuscript and analytic code will be made available upon approval by the local Research Ethics Board (REB) (internal review board).

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