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Original Research Article

Impact of a Low-Carbohydrate Compared with Low-Fat Breakfast on Blood Glucose Control in Type 2 Diabetes: A Randomized Trial

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A B S T R A C T

Background: In type 2 diabetes (T2D), consuming carbohydrates results in a rapid and large increase in blood glucose, particularly in the morning when glucose intolerance is highest.

Objectives: We investigated if a low-carbohydrate (LC) breakfast (~465 kcal: 25 g protein, 8 g carbohydrates, and 37 g fat) could improve glucose control in people with T2D when compared with a low-fat control (CTL) breakfast (~450 kcal:20 g protein, 56 g carbohydrates, and 15 g fat).

Methods: Participants with T2D ($N = 121$, 53% women, mean age 64 y) completed a remote 3-month parallel-group randomized controlled trial comparing a LC with standard low-fat guideline CTL breakfast. The change in HbA1c was the prespecified primary outcome. Continuous glucose monitoring, self-reported anthropometrics, and dietary information were collected for an intention-to-treat analysis.

Results: HbA1c was reduced (−0.3%; 95% CI: −0.4%, −0.1%) after 12 wks of a LC breakfast, but the between-group difference in HbA1c was of borderline statistical significance (−0.2; 95% CI: −0.4, 0.0; $P = 0.06$). Self-reported total daily energy (−242 kcal; 95% CI: −460, −24 kcal; $P = 0.03$) and carbohydrate (−73 g; 95% CI: −101, −44 g; $P < 0.01$) intake were lower in the LC group but the significance of this difference is unclear. Mean and maximum glucose, area under the curve, glycemic variability, standard deviation, and time above range were all significantly lower, and time in the range was significantly higher, in the LC group compared with CTL (all $P < 0.05$).

Conclusions: Advice and guidance to consume a LC breakfast appears to be a simple dietary strategy to reduce overall energy and carbohydrate intake and improve several continuous glucose monitoring variables when compared with a CTL breakfast in persons living with T2D.

The trial was registered at clinicaltrials.gov as NCT04550468.

Keywords: breakfast, chronobiology, glycemic control, low-carbohydrate diets, nutrition, type 2 diabetes

Introduction

Postprandial hyperglycemia and glycemic variability are independent risk factors for CVD and mortality in people living with type 2 diabetes (T2D) [1,2]. Postprandial hyperglycemia is characterized by a rapid and large increase in blood glucose levels after meals. Isolated postprandial hyperglycemia, even with normal fasting glucose and HbA1c is associated with a 2-fold increased risk of death from CVD [3]. Glycemic variability, daily blood glucose oscillations, including episodes of hyperglycemia and hypoglycemia [4], is now also recognized as a significant predictor of diabetes complications, in addition to HbA1c [5,6]. Exposure to daily glycemic excursions contributes to heightened oxidative stress and inflammation, linking postprandial hyperglycemia and glycemic variability to the pathogenesis of atherosclerosis [2]. Because CVD is the major cause of morbidity and mortality in patients with T2D, treatment strategies specifically directed toward lowering postprandial glucose swings and reducing glycemic variability are crucial.

Ingesting carbohydrates directly influence postprandial glucose levels and affect overall glycemic control in individuals with diabetes

Abbreviations: CGM, Continuous glucose monitoring; CTL, Control, low-fat; LC, Low-carbohydrate; iAUC, incremental Area Under the Curve; MAGE, Mean amplitude of glycemic excursion; RCT, Randomized controlled trial; T2D, Type 2 diabetes; CVD, Cardiovascular disease; EI, Energy intake.

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[7]. Reducing carbohydrate intake is recognized as a dietary strategy with substantial evidence for improving glucose control [8]. However, the benefits of a low-carbohydrate (LC) diet can be limited by poor dietary adherence [9]. One potential strategy to mitigate hyperglycemic excursions, without following a strict LC diet, is to manipulate only one of the daily meals. A low-fat (and high-carbohydrate) breakfast meal, in line with most dietary guidelines [10], appears to consistently incur the highest daily hyperglycemic spike in people with T2D and thus presents a crucial barrier to achieving good glycemic control [11]. Disruptions in the circadian rhythm in people with T2D result in higher levels of insulin resistance and greater glucose intolerance in the morning [12]. A higher carbohydrate intake in the morning leads to higher markers of glycemic variability, when compared with lower carbohydrate intake [13]. Reducing the carbohydrate content of the morning breakfast might be a simple way to improve glycemia in people with T2D, even without changing the macronutrient content of other meals [14].

In a recent proof-of-concept randomized crossover trial, we demonstrated that when participants with T2D completed two 24-h experimental days under fully controlled feeding conditions, there was a 74% reduction in the postprandial glucose response and significantly lower glycemic variability when an LC breakfast was consumed compared with a dietary guideline low-fat breakfast [15]. These findings suggest that eating an LC breakfast may better align with daytime variations in glucose tolerance and help mitigate overall exposure to postprandial hyperglycemia in people with T2D. However, the long-term or free-living impacts of regularly consuming a LC breakfast compared with a low-fat breakfast in people with T2D have yet to be established.

The aim of this randomized controlled trial (RCT) was to determine if advice and guidance to regularly consume an LC breakfast, when compared with a low-fat breakfast, could lead to clinically meaningful improvements in glycemic control in individuals with T2D. We hypothesized that consuming a LC breakfast over 3 mo would improve glycemic control assessed by HbA1c (primary outcome) and continuous glucose monitoring (CGM; secondary outcomes). We also explored whether the LC breakfast would impact overall dietary intake, hunger/satiety, body mass, physical activity, and breakfast intentions. Targeting the meal that leads to the largest postprandial hyperglycemic response of the day may represent a simple, feasible, and sustainable intervention that is aligned with daytime variation in glucose tolerance with potential to improve glycemic control and reduce risk of diabetes complications over time.

Methods

Study design and participants

This study was a 12-wk 2-site parallel-arm RCT conducted during the COVID-19 pandemic with participants randomly allocated (1:1, blocks of 6) to a LC breakfast (LC) or a low-fat control breakfast (CTL) on the basis of the dietary guidelines and breakfasts typically consumed. Individuals from Canada (British Columbia, Saskatchewan, and Ontario) and Australia (New South Wales, South Australia, Victoria, and Western Australia) responded to online advertisements between October 2020 and March 2022. Eligibility criteria included the following: *1*) physician-diagnosed T2D of $\geq$1 y; *2*) current HbA1c of $<$8.5% (69 mmol/L); *3*) BMI: $>$25 kg/m^2; *4*) blood pressure of $<$160/99 mmHg; and *5*) 20–79 y old. Participants were excluded if they were *1*) using exogenous insulin; *2*) taking $>$2 glucose-lowering medications; *3*) undergoing medical treatment of cancer, autoimmune or inflammatory disease, liver or kidney disorders; *4*) smokers; *5*) on HRT, corticosteroids, or antiinflammatory medications; *6*) allergic, intolerant or with aversion to eggs or any other dietary restrictions that would prevent them from following the intervention breakfasts; *7*) being unable to follow remote guidance by internet or smartphone; or *8*) unable to follow the prescribed diet instructions. After screening, participants met with a member of the research team over telephone or video conference where study procedures were explained in detail and digital informed consent was obtained via RedCAP (version 12.2.10, 2022 University of British Columbia, Advanced Research Computing) [16]. A research assistant then obtained randomization via Sealed Envelope, an online generator, with sex as a stratification factor and permuted block sizes of 6 [17]. The COVID-19 pandemic resulted in various lockdowns, limitations to close contact, and restrictions to in-person research that varied over time across both study sites, necessitating that this study was designed to be conducted completly remotely.

The trial was approved by the University of British Columbia Research Ethics Board and the University of Wollongong Ethics Board, registered at ClinicalTrials.gov (NCT04550468), and conducted in accordance with the Declaration of Helsinki.

Diet intervention

Each group was provided with a menu of 8–10 breakfast recipes designed by registered/accredited dietitians at each site to provide ~450 kcal. According to their randomization, participants were instructed to select from a menu of LC breakfasts (~25 g protein, 8 g carbohydrates, and 37 g fat; e.g., omelet with cheese and nonstarchy vegetables) or CTL breakfasts (~20 g protein, 56 g carbohydrates, and 15 g fat; e.g., oatmeal and fruit based) each morning (Supplemental Appendix 1A and B). No specific guidance or calorie restriction was oriented for the other meals.

To foster adherence over the 12 wk, we provided some autonomy and variety in the breakfast choices for each group while accounting for cultural differences between sites. The CTL group recipes, which reflect usual breakfasts consumed by the general population, were compared with a LC breakfast menu. Participants were able to choose their own breakfast options and were required to upload a photograph of their breakfast every morning via RedCap link. Breakfasts were reviewed by a study dietitian to confirm compliance. The conservative approach of counting only breakfasts that were from the recipe books (or minor variations thereof) as compliant was chosen; any missing photographs, breakfasts outside the recipe book, or consuming $<$50% of the proposed recipe were categorized as noncompliant.

Participants were also guided by a study dietitian to register three 3-d food records (2 wk d and 1 weekend d) within wk 1, at midpoint within wk 6 and within the last week of the intervention, wk 12, using a diet logbook provided. Diet records were entered into nutritional analysis software (the Food Processor, version 11.11.0, Esha Research) to determine macronutrient and energy content.

Anthropometry

Given the remote nature of the trial conducting during the COVID-19 pandemic, participants provided self-reported height, weight, and waist circumference measures at the beginning and end of the trial. They were advised to use the same scale for repeated measures and perform the measurements fasted in the morning. Participants received a measuring tape and printed guidelines for waist circumference self-measurement (2022, International Chair on Cardiometabolic Risk –

www.myhealthwaist.org) in study testing kits mailed before the start of the study.

Blood samples

Venous blood samples were collected at baseline and after 12 wk. For the primary outcome of HbA1c, participants were provided with blood requisitions to a local accredited laboratory nearest to their place of residence. At baseline, results from a recent physician-prescribed HbA1c test (measured at an accredited laboratory) were used if the blood sample was obtained within 1 mo from the study start date. Post blood samples were obtained within 1 wk of completion of the 12-wk intervention.

CGM

Participants inserted a blinded CGM device (FreeStyle Libre PRO, Abbott Diabetes Care) into the subcutaneous adipose tissue of the upper arm to collect continuous (every 15 min) interstitial glucose readings during the first and last 2 wk (14 d) of the trial. The CGM provided 24-h data on overall glucose control through fasting glucose concentrations, mean blood glucose concentrations, maximum and minimum glucose concentrations, AUC, incremental AUC (iAUC), MAGE, SD, time below range (time <3.9 mmol/L), time above range (time >10 mmol/L) and time in range (time between 3.9 and 10 mmol/L). The 6-h overnight data for mean, minimum, and maximum glucose concentrations were also explored. CGM data were downloaded via LibreView software. Each file was separated by date, beginning at midnight, and ending at 23:59. Data sets were included in the analyses if the file contained >3 d of data and ≥70% of data points per day. Mean, maximum, minimum, time in range, AUC and iAUC, SD, and MAGE values were calculated for each usable day and then averaged for the monitoring period. AUC and iAUC were calculated using the trapezoidal method [18] and glycemic variability (SD and MAGE) were calculated using the EasyGV

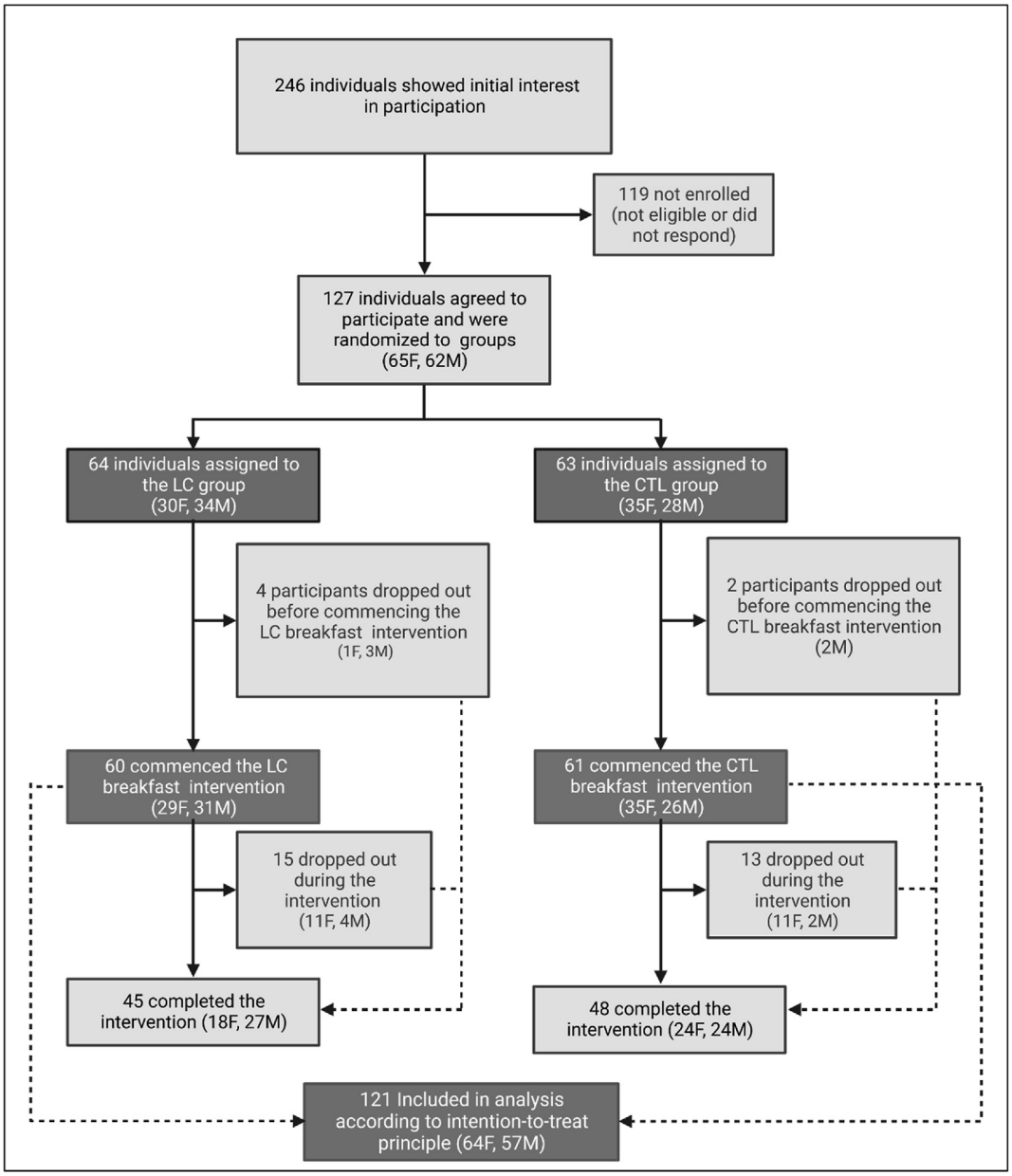

FIGURE 1. CONSORT study flow diagram. Consolidated standards of reporting trials; LC, low-carbohydrate breakfast; CTL, guideline low-fat control breakfast; F, females; M, male.

platform (Oxford University Innovation). Overnight (12:00–6:00) mean, maximum, and minimum values were calculated for each usable day and then averaged for the monitoring period. Postprandial breakfast glucose values (2 h mean, maximum, SD, iAUC) were calculated manually for each usable day where participants provided a breakfast start time and then averaged for the monitoring period using GraphPad Prism version 9.3.1 (GraphPad Software).

Questionnaires

The Godin Leisure-Time Exercise Questionnaire [19] was used to assess self-reported leisure-time physical activity and a 100-mm visual analog scale [20] was used to measure self-reported hunger and satiety at wk 1, 6, and 12 of the trial. Hunger and satiety questionnaires were sent to participants at the same time of day at each time point but given the remote and free-living nature of the trial were not explicitly controlled for time since the last meal. Participants' intentions to consume a breakfast consistent with their group assignment (that is, low-carbohydrate or low-fat) over the following 3 mos were assessed using a 2-item measure at baseline and on the last day of the study intervention period. These items were developed based on Ajzen's recommendations for developing scales to measure the theory of planned behavior constructs [21]. Item scores were averaged to provide an overall intentions score, and the internal consistency was acceptable at each administration (Cronbach's αs ≥.92) [22].

Statistical analyses

The sample size estimations originally revealed that $n = 34$ per group would be required to detect a between–within interaction using repeated measures ANOVA with an effect size of $d = 0.4$ (which corresponds to an ANOVA effect size of Cohen's $f = 0.2$) with 90% power and 5% type 1 error with a conservative correlation among repeated measures of $r = 0.5$ (calculated using G*Power v3.1.9.2). The effect size of $d = 0.4$ was based on our previous short-term controlled CGM study [15] and previous trials showing that manipulating breakfast size can impact HbA1c [23]. To account for a 20% dropout rate, we aimed to recruit a sample size of $n = 41$ per group. Sample size was expanded and recruitment reopened after 92 participants had originally been randomly assigned due to a higher than expected dropout rate. These calculations and adjustments are documented in the Statistical Analysis Plan (Supplemental Appendix 2).

The primary objective was to test the superiority of a LC breakfast intervention compared with a CTL breakfast intervention for reducing HbA1c after 12 wk. Blinded data were analyzed on an intention-to-treat basis. We used constrained baseline longitudinal [24] analysis via a linear mixed model with fixed effects for timepoint (baseline and after intervention), stratified allocation factor (sex), and the interaction between timepoint and dietary intervention group, and random effects for participants. Effect estimates with 95% CI for the between-group differences from the model are reported as the main analyses of interest. Effect estimates for within-group changes over time are also reported. Statistical significance was established at an α level of 0.05. Secondary end points were analyzed similarly. No α adjustments were applied to secondary and exploratory outcomes.

Measures that were assessed throughout the trial but not at baseline (e.g., CGM, dietary intake) were analyzed using a linear mixed model with fixed effects for dietary intervention group, time, and stratified allocation factors (sex), and a random intercept for participant. In this case, the main effects of group with 95% CI are presented as the main analyses of interest. Data on physical activity levels were analyzed analogously but using a Poisson mixed model [25]. All data were analyzed in R (version 4.1.3 "One Push-Up"). Further information on sample size and interim analyses are documented in the statistical analysis plan presented in (Supplemental Appendix 2).

Results

Study flow and participants

Two-hundred forty-six participants were prescreened; 127 met all inclusion criteria and were randomly assigned ($n = 64$ to LC and $n = 63$ to CTL breakfast groups). Following randomization, 4 participants dropped out or could not be contacted in the LC group and 2 participants were lost in the CTL group, leaving $n = 60$ who commenced the LC breakfast and $n = 61$ who commenced the CTL breakfast interventions. Fifteen participants from the LC group and 13 from the CTL group withdrew, dropped out or were not able to be contacted after starting the intervention (Figure 1, CONSORT diagram). Reasons were not related to adverse events or trial outcomes but rather to the study being remote and affected by the COVID-19 pandemic. The participants had a mean (SD) age of 64 y (9 y), BMI of 32.3 (7.3) kg/m^2, HbA1c of 7.0 (0.7%) and 53% were women. Baseline characteristics are presented in Table 1.

Dietary intake

Breakfast compliance was measured by the proportion of daily breakfast photographs uploaded that followed group allocation and recipe books while eating >50% of the meal. The LC group displayed a median of 79 (IQR = 9) and the CTL group a median of 75 (IQR = 13) compliant photographs out of a total of 84 breakfasts. Table 2 provides

TABLE 1
Participant baseline characteristics

	Total		LC		CTL	
N	121		60		61	
Age, mean (SD), y	64 (9)		65 (9)		64 (10)	
Female, *N* (%)	64 (53)		29 (48)		35 (57)	
Male, *N* (%)	57 (47)		31 (52)		26 (43)	
Duration of T2D, mean (SD), y	9 (7)		10 (8)		9 (6)	
HbA1c (%)	7.0 (0.7)		6.9 (0.8)		7.0 (0.7)	
HbA1c (mmol/mol)	52 (8.1)		52 (8.4)		53 (7.9)	
Weight (kg)	93.3 (22.9)		95.8 (26.3)		90.8 (18.8)	
BMI (kg/m^2)	32.3 (7.3)		33.2 (8.2)		31.4 (6.2)	
Waist circumference (cm)	110.2 (15.9)		111.0 (16.2)		109.6 (15.7)	
Glucose-lowering medication, *N* (%)						
Metformin	67 (55)		32 (53)		35 (57)	
DPP-4 inhibitors	3 (3)		2 (3)		1 (2)	
GLP-1 receptor agonists	12(10)		6 (10)		6 (10)	
SGLT2 inhibitors	20 (17)		10 (17)		10 (16)	
Sulfonylureas	5 (4)		3 (5)		2 (3)	
No medication	14 (12)		6 (10)		8 (13)	
Country of origin, *N* (%)	CAN	AUS	CAN	AUS	CAN	AUS
	75 (62)	46 (38)	38 (63)	22 (37)	37 (61)	24 (39)

Abbreviations: AUS, Australia; CAN, Canada; CTL, guideline low-fat control breakfast; LC, low-carbohydrate breakfast.
Data presented as mean (SD).

TABLE 2
Dietary intake across the intervention period by meal

	LC ($N = 60$)	CTL ($N = 61$)	Difference between groups	P value[1]
Daily total				
Energy (kcal)	1701 (510)	1927 (480)	−242 (−460 to −24)	0.03
Protein, g	87 (25)	81 (28)	5 (−7 to 17)	0.43
Protein, % EI	20.7 (3.6)	17.0 (4.2)	3.7 (2.0 to 5.5)	<0.001
Carbohydrates, g	150 (56)	221 (72)	−73 (−101 to −44)	<0.001
Carbohydrates, % EI	35.4 (7.2)	45.7 (8.6)	−10.4 (−14.0 to −6.8)	<0.001
Fat, g	84 (28)	80 (28)	3 (−9 to 16)	0.60
Fat, % EI	43.8 (6.6)	37.3 (8.2)	6.6 (3.3 to 10.0)	<0.001
Breakfast				
Energy, kcal	421 (112)	434 (98)	−14 (−62 to 35)	0.58
Protein, g	24 (6)	17 (5)	7 (4 to 9)	<0.001
Protein, % EI	23.0 (4.7)	16.1 (3.8)	7.0 (5.0 to 8.9)	<0.001
Carbohydrates, g	16 (10)	60 (19)	−44 (−51 to −37)	<0.001
Carbohydrates, % EI	16.6 (11.8)	55.2 (10.8)	−38.8 (−44.0 to −33.6)	<0.001
Fat, g	29 (11)	14 (7)	15 (11 to 19)	<0.001
Fat, % EI	60.4 (11.9)	28.8 (11.1)	31.8 (26.5 to 37.1)	<0.001
Lunch				
Energy, kcal	444 (176)	510 (153)	−76 (−151 to −2)	<0.05
Protein, g	23 (11)	23 (9)	0 (-5 to 5)	0.99
Protein, % EI	20.7 (5.9)	18.0 (5.6)	2.8 (0.0 to 5.5)	<0.05
Carbohydrates, g	44 (15)	56 (22)	−14 (−22 to −5)	<0.01
Carbohydrates, % EI	42.3 (13.0)	44.4 (11.7)	−2.7 (−8.4 to 3.0)	0.35
Fat, g	19 (11)	22 (10)	−2 (−7 to 2)	0.32
Fat, % EI	37.0 (10.9)	37.6 (9.8)	−0.1 (−4.8 to 4.7)	0.98
Dinner				
Energy, kcal	727 (237)	732 (279)	−7 (−129 to 115)	0.91
Protein, g	39 (15)	36 (11)	3 (−3 to 9)	0.36
Protein, % EI	21.6 (5.1)	20.5 (4.9)	1.1 (−1.3 to 3.4)	0.37
Carbohydrates, g	71 (30)	70 (28)	0 (−13 to 14)	0.97
Carbohydrates, % EI	39.0 (8.1)	39.2 (10.8)	−0.3 (−4.8 to 4.2)	0.90
Fat, g	32 (12)	34 (19)	−2 (−10 to 5)	0.57
Fat, % EI	39.4 (5.8)	40.3 (9.9)	−0.8 (−4.6 to 3.1)	0.69
Snacks				
Energy, kcal	293 (160)	348 (236)	−49 (−159 to 61)	0.38
Protein, g	7 (5)	10 (7)	−2 (−6 to 1)	0.15
Protein, % EI	9.9 (4.9)	11.9 (5.0)	−1.9 (−4.6 to 0.8)	0.17
Carbohydrates, g	39 (27)	46 (34)	−7 (−24 to 10)	0.39
Carbohydrates, % EI	53.4 (19.2)	54.6 (12.1)	−1.9 (−10.3 to 6.5)	0.65
Fat, g	12 (7)	13 (9)	−1 (−5 to 3)	0.67
Fat, % EI	36.7 (17.5)	33.5 (10.6)	3.8 (−3.7 to 11.3)	0.31

Abbreviations: CTL, guideline low-fat control breakfast; LC, low-carbohydrate breakfast; EI, energy intake.
Data by group presented as mean (SD), main effect of group presented as between-group effect estimate (95% CI).
[1] Data analyzed via linear model with fixed effects for dietary intervention group and stratified allocation factors (sex).

average daily dietary and macronutrient intake along with energy and macronutrient distribution for meals in the LC and CTL groups, estimated from the 3 separate 3-d self-reported dietary records. Self-reported total daily energy intake (EI) was lower in the LC compared with the CTL breakfast group (−242 kcal; 95% CI −460 to −24 kcal; $P = 0.03$) but the significance of this difference is unclear given the nature of the dietary assessments. The LC group had significantly lower daily carbohydrate intake when compared with the CTL group (−73 g; 95% CI: −101 to −44 g; $P < 0.01$). There were no significant differences in daily protein or fat intake, but rather a higher percent protein (3.7%; 95% CI: 2.0, 5.0%; $P < 0.001$) and fat (6.6%; 95% CI: 3.3, 10.0; $P < 0.001$) EI in the LC group between the 2 groups. The findings for the diet record data complement the breakfast photograph data showing participant compliance in following recipes as the LC group consumed lower carbohydrate (−44 g, 95% CI: −51, −37 g), as well as higher protein (7 g, 95% CI: 4, 9) and fat (15 g; 95% CI: 11, 19), at the breakfast meal when compared with the CTL group (all $P < 0.01$). Interestingly, the LC group had reduced energy (−76 kcal; 95% CI: −151, −2 kcal; $P < 0.05$), carbohydrate (−14g; 95% CI: −22, −5 g; $P < 0.01$) and percent of protein EI (2.8 %; 95% CI: 0.0, 5.5; $P < 0.05$) at lunch when compared with the CTL group. There were no significant differences in energy or macronutrient content in dinner and snacks between groups.

HbA1c (primary outcome) and anthropometrics (secondary outcomes)

Table 3 shows the results for the primary outcome (HbA1c) along with weight, BMI, and waist circumference. HbA1c was reduced at 12 wk in the LC group (−0.3%; 95% CI: −0.4%, −0.1%), whereas the between-group difference between the LC and CTL group did not reach statistical significance (−0.2; 95% CI: −0.4, 0.0; $P = 0.06$). There were no significant differences between the LC and CTL groups for weight, BMI, or waist circumference. At 12-wk, 5 participants in the LC group increased glucose-lowering medication compared with 4 in the CTL group, whereas 8 participants reduced glucose-lowering medication in the LC group compared with 1 in the CTL group. All others had no change in medication. Supplemental Table 1 shows HbA1c outcomes disaggregated by sex.

TABLE 3
Effect estimates for 12-wk changes in HbA1c (primary outcome) and body mass (secondary outcomes)

	LC (N = 60)	CTL (N = 61)	Difference between groups	P value[1]
Primary outcome				
HbA1c (%)	−0.3 (−0.4 to −0.1)	−0.1 (−0.2 to 0.1)	−0.2 (−0.4 to 0.0)	0.06
Secondary outcomes				
Weight (% change)[2]	−1.2 (−2.3 to −0.1)	−0.9 (−1.9 to 0.1)	−0.3 (−1.8 to 1.2)	0.68
BMI (% change)[2]	−1.2 (−2.3 to −0.1)	−1.1 (−2.2 to 0.0)	−0.1 (−1.6 to 1.5)	0.92
Waist circumference (cm)	−2.3 (−4.2 to −0.4)	−2.7 (−4.6 to −0.8)	0.4 (−2.2 to 3.1)	0.76

AbbreviationsLC, low-carbohydrate breakfast; CTL, guideline low-fat control breakfast.
All data are presented as (within-group or between-group) effect estimates (95% CI). Effect estimates are based on ITT analyses and included all participants that had a baseline or a follow-up value.
[1] Data analyzed via constrained longitudinal data analysis (cLDA) using a linear mixed model with fixed effects for timepoints (baseline, 12 wk), the interaction between timepoint and dietary intervention group, and stratified allocation factors (sex), and a random effect for participant.
[2] Log-transformed, interpret effect estimates as percent change.

Hunger and satiety, physical activity, and breakfast intentions

There were no significant differences in hunger and satiety or physical activity between the 2 groups across the intervention period (Supplemental Tables 2 and 3). There were statistically significant interaction effects for the first item assessing intention (1.0; 95% CI: 0.2, 1.7; $P = 0.01$) and the overall intention score (0.9; 95% CI: 0.1, 1.6; $P = 0.03$), indicating a greater decline in intentions to consume a CTL breakfast when compared with the group assigned to eat an LC breakfast (Supplemental Table 4).

CGM

Table 4 shows the CGM data for the LC and CTL groups, and Figure 2 shows CGM data averaged across all participants for the first and last 14 d of the trial. Supplemental Table 5 shows CGM data disaggregated by sex. For the 24-h CGM data, the mean glucose concentration was significantly lower in the LC group (−0.7 mmol/L; 95% CI: −1.4, −0.1 mmol/L; $P = 0.03$) compared with the CTL group. Compared with the CTL group, the LC group had reduced maximum glucose concentration (−1.3 mmol/L; 95% CI: −2.3, −0.4 mmol/L; $P = 0.01$) and reduced AUC (−1052 mmol/L; 95% CI: −1949, −155 mmol/L × 24 h; $P = 0.02$). The MAGE for the LC condition was significantly lower (−0.8 mmol/L; 95% CI: −1.2, −0.3 mmol/L; $P < 0.01$) compared with the CTL group. The SD of blood glucose with the LC was also significantly lower (−0.2 mmol/l; 95% CI: −0.4, −0.1 mmol/L; $P = 0.01$) than in the CTL, suggesting the benefits of an LC breakfast for glycemic variability. There was a 50% (95% CI: 9%, 72%) decrease in odds of experiencing time above range (time >10 mmol/L) in the LC group compared with CTL and a 77% (95% CI: 11%, 182%) increase in odds of experiencing time in the range (time between 3.9 and 10 mmol/L) in the LC group compared with CTL. Fasting glucose levels, minimum glucose concentration, iAUC, and time below range (i.e., time <3.9 mmol/L) were not significantly different between the LC and CTL groups.

The 2-h postprandial CGM data analyzed after breakfast showed that mean glucose was significantly lower in the LC group when

TABLE 4
Continuous glucose monitor data

	First 14 d		Last 14 d		Main effect of group	P value[1]
	LC	CTL	LC	CTL		
24-h data						
Fasting glucose (mmol/L)	6.5 (1.5)	7.0 (1.9)	6.5 (1.5)	6.8 (1.7)	−0.5 (−1.2 to 0.2)	0.15
Mean glucose (mmol/L)	7.0 (1.3)	7.6 (1.9)	7.0 (1.3)	7.6 (1.7)	−0.7 (−1.4 to −0.1)	0.03
Max glucose (mmol/L)	10.8 (2.1)	12.1 (2.5)	10.8 (2.1)	11.8 (2.2)	−1.3 (−2.3 to −0.4)	0.01
Min glucose (mmol/L)	4.5 (1.0)	4.8 (1.4)	4.6 (1.1)	4.8 (1.3)	−0.4 (−0.9 to 0.1)	0.15
AUC (mmol/L × 24 h)	9884 (1807)	10870 (2650)	9958 (1836)	10752 (2354)	−1052 (−1949 to −155)	0.02
iAUC (mmol/L × 24 h)	682 (402)	833 (380)	716 (461)	865 (399)	−160 (−324 to 4)	0.06
MAGE (mmol/L)	2.2 (1.2)	2.9 (1.4)	2.2 (1.1)	2.5 (0.8)	−0.8 (−1.2 to −0.3)	0.002
SD (mmol/L)	0.9 (0.4)	1.1 (0.4)	0.9 (0.4)	1.0 (0.3)	−0.2 (−0.4 to −0.1)	0.009
Time <3.9 mmol/L[2]	0.03 (0.04)	0.03 (0.04)	0.04 (0.08)	0.02 (0.04)	27 (−54 to 271)	0.64
Time >10 mmol/L[3]	0.09 (0.10)	0.18 (0.23)	0.10 (0.13)	0.16 (0.20)	−50 (−72 to −9)	0.02
TIR[3]	0.89 (0.10)	0.80 (0.22)	0.86 (0.14)	0.82 (0.19)	77 (11 to 182)	0.02
2-h breakfast postprandial data						
Mean glucose (mmol/L)	7.1 (1.1)	9.2 (2.1)	7.2 (1.5)	8.9 (2.1)	−2.2 (−3.0 to −1.4)	<0.001
SD (mmol/L)	0.4 (0.2)	0.9 (0.5)	0.4 (0.3)	0.9 (0.5)	−0.5 (−0.7 to −0.3)	<0.001
Max glucose (mmol/L)	7.9 (1.4)	10.7 (2.4)	8.1 (1.8)	10.4 (2.4)	−2.9 (−3.8 to −2.0)	<0.001
iAUC (mmol/L × 2 h)	53 (33)	127 (50)	54 (37)	117 (50)	−74 (−93 to −55)	<0.001

AbbreviationsCTL, guideline low-fat control breakfast group; iAUC, incremental area under the curve; LC, low-carbohydrate breakfast group, MAGE, mean amplitude of glycemic excursions; TIR, time between 3.9 and 10 mmol/L.
Data by group are presented as mean (SD), main effect of group is presented as effect estimates (95% CI).
[1] Data analyzed via linear mixed model with fixed effects for timepoints (first compared with last 14 d), dietary intervention group, the interaction between timepoint and dietary intervention group, and stratified allocation factors (sex), and a random effect for participant.
[2] Data were converted to and are presented as proportion of time in range and analyzed via mixed effects binomial. Interpret effect estimates as % change in odds.
[3] Data were converted to and are presented as proportion of time in range and analyzed via mixed effects beta model. Interpret effect estimates as % change in odds.

compared with the CTL group (−2.2 mmol/L; 95% CI: −3.0, −1.4 mmol/L; $P < 0.01$). The same was observed for SD (−0.5 mmol/L; 95% CI: −0.7, −0.3 mmol/L; $P < 0.01$), maximum glucose (−2.9 mmol/L; 95% CI: −3.8, −2.0 mmol/L; $P < 0.01$) and iAUC (−74 mmol/L; 95% CI: −93, −55 mmol/L × 2 h; $P < 0.01$). There were no significant differences between the groups in the overnight CGM data (Supplemental Table 6).

Discussion

The primary aim of this RCT was to examine if advice and guidance to consume a LC breakfast could improve glycemic control compared with a guideline-based low-fat breakfast. We also explored compliance to this relatively simple dietary change over 3 mos in free-living conditions and assessed CGM outcomes, self-reported dietary intake, and cardiometabolic health markers. The findings revealed that despite being conducted remotely and with minimum supervision, high compliance to the breakfast interventions could be achieved, demonstrating high feasibility and acceptability of the LC breakfast over 3 mo. There was reduction in HbA1c over time in the LC group, and although the between-group difference in HbA1c at 3 mo was not statistically significant ($P = 0.06$), there were consistent and statistically significant differences between the LC and CTL breakfast groups in CGM variables assessed over 2 14-d periods at the start and end of the intervention.

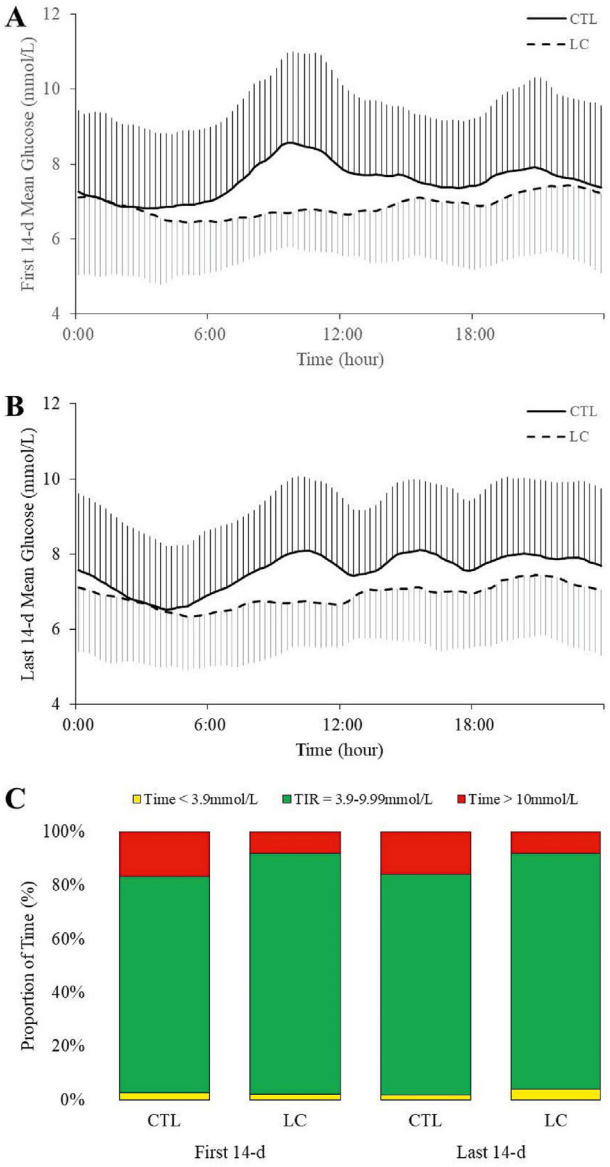

FIGURE 2. Continuous glucose monitor data. Continuous glucose monitoring (CGM) (mean ± SD for $n = 76$) during the first 14-d CGM period (A) and last 14-d CGM period (B) for the CTL (black line) and LC (dashed line) groups; (C) time in range, presented as a proportion of time across 24 h ($n = 72$), during the first and last 14-d CGM period for the CTL and LC groups.

Extensive research supports the carbohydrate restriction for improving glycemic control in people with T2D [26–28]. Although the primary outcome of HbA1c was not significantly different between groups ($P = 0.06$), many CGM metrics were better in the LC group compared with the CTL group across both 14-d monitoring periods. These metrics are more sensitive to detecting differences in postprandial hyperglycemia, and we speculate that a longer (or more controlled) intervention might be needed to see the corresponding significant reductions in HbA1c, which showed a clear trend to be reduced in the LC compared with CTL group. Mealtime hyperglycemia is the predominant factor associated with an increased risk of cardiovascular morbidity and mortality [29], and strategies to minimize postprandial glucose concentrations are important for reducing complications of diabetes [29,30]. Our findings indicate that consuming a LC breakfast can improve CGM-derived indices of overall and postprandial glucose control and highlight CGM as a useful tool to assess the impact of a dietary intervention on glycemic control in T2D.

Adherence to LC diets may be challenging when carbohydrate intake is severely restricted, whereas more moderate restrictions appear easier to comply with [31]. Our results demonstrate high compliance to the LC breakfast recipes over 12 wk (79 [IQR = 9] out of 84 breakfasts). It seems reasonable to assume that manipulating the carbohydrate content of one meal could generate higher adherence than at all meals. Consuming lower amounts of carbohydrates in the morning also aligns with diurnal variations in glucose tolerance for people with T2D, who experience the worst glucose tolerance in the morning and see improvements in glucose tolerance across the daytime [12]. Although intentions to adhere to the study breakfasts declined in both groups over time, this decline was mitigated in the LC group compared with the CTL group. In fact, it has been shown that there is stronger intentional control for restricted dietary patterns than there is for general healthy eating advice [32]. These findings support the idea that following an LC breakfast could be an achievable dietary intervention, aligned with daytime glucose tolerance rhythms, for people living with T2D.

The diet records showed that carbohydrate, fat, and protein intake for breakfast were significantly different between the LC and CTL groups, supporting successful manipulation of breakfast macronutrient contents. Additionally, participants from the LC group had reduced energy, carbohydrate, and protein %EI at lunch. The reduction in self-reported total EI could be a result of measurement error because self-reported EI is known to be unreliable [33] and accurate assessment of small-scale changes in EI or expenditure was beyond the scope of this trial. Therefore, the significance of these findings is unclear – particularly in the context of a short-term trial, in which corresponding changes in body mass would be challenging to assess. Nevertheless, it has been demonstrated that eating in the morning is particularly satiating and associated with lower total EI across the day [34], specifically with the consumption of foods high in fat content while low in carbohydrates [35]. This is particularly important for people with T2D because their highest glucose concentrations are usually seen in the

mornings. In fact, Han et al. [36] found that higher EI from fat and protein at dinner rather than breakfast was associated with diabetes, CVD, and all-cause mortality. The typical LC breakfasts consumed in this trial were higher in protein and fat and lower in processed food and refined carbohydrates when compared with the low-fat CTL breakfasts. It is known that the protein and fat content of breakfast could suppress breakfast postprandial glucose levels [37,38]. We showed that postprandial mean glucose after breakfast was significantly lower in the LC group when compared with the CTL group, which could be due not only to the LC per se but also the higher fat or protein content. Our results may give people living with T2D a simpler alternative to lowering the overall amount of energy and carbohydrates in their diets [39] as presumably it would be easier to lower the carbohydrate content of the breakfast meal than all meals simultaneously.

Previous studies have examined the relationship between postprandial glucose, macronutrient intake, and self-reported feelings of hunger and satiety following meals. Flint et al. [40] found that postprandial glucose concentration was unrelated to self-reported hunger and appetite, although it was positively associated with EI at the next meal. Ruddick-Collins et al. [32] also support the idea that a breakfast load generates greater satiety and may contribute to reduce calorie intake later in the d, and weight loss when compared with dinner. We previously saw lower hunger and greater satiety later in the day when people with T2D consumed an LC breakfast [15]. In the present study, there was no significant effect on hunger and satiety but a reduction in self-reported daily EI in the LC group, although weight loss was not detected. However, it is known that LC diets may provide benefit in the absence of weight loss [41,42], and our data support this notion of overall better glycemic control assessed by CGM with a LC breakfast despite no change in body mass or waist circumference. Weight loss or body composition changes may require longer or stricter interventions to generate a greater reduction in EI.

The COVID-19 pandemic imposed challenges to this trial (e.g., ethics approval received in December 2019 with in-person visits planned for the original study). Because of the public health guidelines (e.g., social distancing and limiting of social gathering) and university research curtailments, adaptations to the protocol were required. The study was adapted to be conducted remotely, enabling recruitment from multiple locations rather than being restricted to local participants. Although this likely includes a more diverse sample and increases the generalizability of the findings, it means that diet and anthropometric data are based on self-report, which has inherent limitations and that the dropout rate was higher than what was anticipated. Although breakfast was captured with photographs to assess compliance, the remaining daily meals were analyzed from self-reported data and therefore could be subject to known reporting inaccuracies [33,43]. In line with best practices [44], we report data disaggregated by sex as Supplemental Tables but the trial was not powered to detect sex or gender differences between groups and across time.

In conclusion, advice and guidance to consume a LC breakfast appears to be a simple dietary strategy that can be adhered to over 12 wk and results in better measures of glycemic control assessed by CGM when compared with a low-fat breakfast. The LC breakfast lowered HbA1c over time, but the effect was not statistically significant between groups in the context of this free-living remote trial. Consuming a LC breakfast also appeared to reduce overall energy and carbohydrate intake when compared with a traditional low-fat breakfast in adults living with T2D. Future studies that manipulate the macronutrient composition of meals are warranted and may consider CGM metrics as more informative than HbA1c as the primary outcome(s). This trial provides evidence that advice to consume a LC breakfast could be a simple, feasible, and effective approach to manage postprandial hyperglycemia and lower glycemic variability in people living with T2D.

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Author contributions

The authors' responsibilities were as follows – BFO, CRC, KC, MS, MH, TE, MEF, and JPL: designed the study; BFO, CRC, KO, KC, MEF, and JPL: coordinated the study; BFO, CRC, KO, and KC: conducted the trial, enrolled and managed the participants as well as collected samples and clinical data; CRC and KF: carried out data analyses; BFO, CRC, KO, KF, KC, MS, MEF, and JPL: contributed to data interpretation; all authors: contributed to critical reading and providing comments and edits to the manuscript for important intellectual content; all authors: gave final approval of the version to be published; and BFO, MEF, and JPL: are the guarantors of this work.

Conflicts of interest

The authors report no conflicts of interest.

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Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Disclaimers

JPL is Chief Scientific Officer for the Institute for Personalized Therapeutic Nutrition, a registered charity in Canada. JPL holds founders shares in Metabolic Insights Inc., a start-up company designing noninvasive metabolic monitoring devices. The authors declare that there are no relationships or activities that might bias, or be perceived to bias, their work.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajcnut.2023.04.032.

References

[1] H. Gin, V. Rigalleau, Post-prandial hyperglycemia post-prandial hyperglycemia and diabetes, Diabetes. Metab. 26 (2000) 265–272.
[2] A. Ceriello, Postprandial hyperglycemia and diabetes complications: is it time to treat? Diabetes 54 (2005) 1–7.
[3] D. Giugliano, A. Ceriello, K. Esposito, Glucose metabolism and hyperglycemia, Am. J. Clin. Nutr. 87 (2008) 217S–222S.
[4] N.F. Sheard, N.G. Clark, J.C. Brand-Miller, M.J. Franz, F.X. Pi-Sunyer, E. Mayer-Davis, et al., Dietary carbohydrate (amount and type) in the prevention and management of diabetes a statement by the American Diabetes Association, Diabetes 27 (2004) 2266–2271.
[5] T. Battelino, T. Danne, R.M. Bergenstal, S.A. Amiel, R. Beck, T. Biester, et al., Clinical targets for continuous glucose monitoring data interpretation: recommendations from the international consensus on time in range, Diabetes Care 42 (2019) 1593–1603.

[6] M. Martinez, J. Santamarina, A. Pavesi, C. Musso, G.E. Umpierrez, Glycemic variability and cardiovascular disease in patients with type 2 diabetes, BMJ, Open. Diabetes. Res. Care. 9 (2021), e002032.
[7] S. Suh, J.H. Kim, Glycemic variability: how do we measure it and why is it important? Diabetes. Metab. J. 39 (2015) 273–282.
[8] A.B. Evert, M. Dennison, C.D. Gardner, W.T. Garvey, K.H.K. Lau, J. MacLeod, et al., Nutrition therapy for adults with diabetes or prediabetes: a consensus report, Diabetes Care 42 (2019) 731–754.
[9] N.K. Kumar, J.D. Merrill, S. Carlson, J. German, W.S. Yancy, Adherence to low-carbohydrate diets in patients with diabetes: a narrative review, Diabetes Metab. Syndr. Obes. 15 (2022) 477–498.
[10] Health Canada, Canada's Food Guide [Internet], Healthy eating recommendations (2019) [date updated: 2023-may-11; date cited: 2022-july-10]. Available from: https://food-guide.canada.ca/en/healthy-eating-recommendations/.
[11] S. Franc, D. Dardari, C. Peschard, J.P. Riveline, M. Biedzinski, B. Boucherie, et al., Can postprandial blood glucose excursion be predicted in type 2 diabetes? Diabetes. Care. 33 (2010) 1913–1918.
[12] E. Van Cauter, K.S. Polonsky, A.J. Scheen, Roles of circadian rhythmicity and sleep in human glucose regulation, Endocr. Rev. 18 (1997) 716–738.
[13] L. Rasmussen, M.L. Christensen, C.W. Poulsen, C. Rud, A.S. Christensen, J.R. Andersen, et al., Effect of high versus low carbohydrate intake in the morning on glycemic variability and glycemic control measured by continuous blood glucose monitoring in women with gestational diabetes mellitus-a randomized crossover study, Nutrients 12 (2020) 475.
[14] D. Vlachos, S. Malisova, F.A. Lindberg, G. Karaniki, Glycemic index (GI) or glycemic load (GL) and dietary interventions for optimizing postprandial hyperglycemia in patients with T2 diabetes: a review, Nutrients 12 (2020) 1561.
[15] C.R. Chang, M.E. Francois, J.P. Little, Restricting carbohydrates at breakfast is sufficient to reduce 24-hour exposure to postprandial hyperglycemia and improve glycemic variability, Am. J. Clin. Nutr. 109 (2019) 1302–1309.
[16] P.A. Harris, R. Taylor, R. Thielke, J. Payne, N. Gonzalez, J.G. Conde, Research Electronic Data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support, J. Biomed. Inform. 42 (2009) 377–381.
[17] Sealed Envelope Ltd, Create a blocked randomisation list [Internet] [cited September 2, 2022]. Available from: www.sealedenvelope.com/simple-randomiser/v1/lists.
[18] J.P. Le Floch, P. Escuyer, E. Baudin, D. Baudon, L. Perlemuter, Blood glucose area under the curve: methodological aspects, Diabetes. Care. 13 (1990) 172–175.
[19] G. Godin, R.J. Shephard, A simple method to assess exercise behavior in the community, Can J. Appl. Sport Sci. 10 (1985) 141–146.
[20] A. Flint, A. Raben, J.E. Blundell, A. Astrup, Reproducibility, power and validity of visual analogue scales in assessment of appetite sensations in single test meal studies, Int. J. Obes. Relat. Metab. Disord. 24 (2000) 38–48.
[21] M. Fishbein, I. Ajzen, Predicting and Changing Behavior: the Reasoned Action Approach, Taylor & Francis, New York, 2011, pp. 1–518.
[22] M. Tavakol, R. Dennick, Making sense of Cronbach's alpha, Int. J. Med. Educ. 2 (2011) 53–55.
[23] H.R. Rabinovitz, M. Boaz, T. Ganz, D. Jakubowicz, Z. Matas, Z. Madar, et al., Big breakfast rich in protein and fat improves glycemic control in type 2 diabetics, Obesity. (Silver Spring). 22 (2014) E46–E54.
[24] C.J. Coffman, D. Edelman, R.F. Woolson, To condition or not condition? analysing 'change' in longitudinal randomised controlled trials, BMJ Open 6 (2016), e013096.
[25] M.J. Hayat, M. Higgins, Understanding poisson regression, J. Nurs. Educ. SLACK Inc. 53 (2014) 207–215.
[26] O. Snorgaard, G.M. Poulsen, H.K. Andersen, A. Astrup, Systematic review and meta-analysis of dietary carbohydrate restriction in patients with type 2 diabetes, BMJ, Open. Diabetes. Res. Care. 5 (2017), e000354.
[27] J.Z. Goldenberg, A. Day, G.D. Brinkworth, J. Sato, S. Yamada, T. Jönsson, et al., Efficacy and safety of low and very low carbohydrate diets for type 2 diabetes remission: systematic review and meta-analysis of published and unpublished randomized trial data, BMJ 372 (2021) m4743.
[28] P.D. McArdle, S.M. Greenfield, S.K. Rilstone, P. Narendran, M.S. Haque, P.S. Gill, Carbohydrate restriction for glycaemic control in Type 2 diabetes: a systematic review and meta-analysis, Diabet. Med. 36 (2019) 335–348.
[29] K.L. Pearce, M. Noakes, J. Keogh, P.M. Clifton, Effect of carbohydrate distribution on postprandial glucose peaks with the use of continuous glucose monitoring in type 2 diabetes, Am. J. Clin. Nutr. 87 (2008) 638–644.
[30] M. Drummond, A. Manca, M. Sculpher, Increasing the generalizability of economic evaluations: recommendations for the design, analysis, and reporting of studies, Int. J. Technol. Assess. Health. Care. 21 (2005) 165–171.
[31] M.N. Thomsen, M.J. Skytte, A. Samkani, M.H. Carl, P. Weber, A. Astrup, et al., Dietary carbohydrate restriction augments weight loss-induced improvements in glycaemic control and liver fat in individuals with type 2 diabetes: a randomised controlled trial, Diabetologia 65 (2022) 506–517.
[32] L.C. Ruddick-Collins, P.J. Morgan, C.L. Fyfe, J.A.N. Filipe, G.W. Horgan, K.R. Westerterp, Timing of daily calorie loading affects appetite and hunger responses without changes in energy metabolism in healthy subjects with obesity, Cell. Metab. 34 (2022) 1472–1485.e6.
[33] J. Guo, J.L. Robinson, C.D. Gardner, K.D. Hall, Objective versus self-reported energy intake changes during low-carbohydrate and low-fat diets, Obesity. (Silver Spring). 27 (2019) 420–426.
[34] J.M. De Castro, The time of day of food intake influences overall intake in humans, J. Nutr. 134 (2004) 104–111.
[35] J. Ratliff, J.O. Leite, R. de Ogburn, M.J. Puglisi, J. VanHeest, M.L. Fernandez, Consuming eggs for breakfast influences plasma glucose and ghrelin, while reducing energy intake during the next 24 hours in adult men, Nutr. Res. Elsevier. 30 (2010) 96–103.
[36] T. Han, J. Gao, L. Wang, C. Li, L. Qi, C. Sun, Y. Li, The association of energy and macronutrient intake at dinner versus breakfast with disease-specific and all-cause mortality among people with diabetes: the U.S. national health and nutrition examination survey, 2003–2014, Diabetes Care 43 (2020) 1442–1448.
[37] K. Xiao, A. Furutani, H. Sasaki, M. Takahashi, S. Shibata, Effect of a high protein diet at breakfast on postprandial glucose level at dinner time in healthy adults, Nutrients 15 (2022) 85.
[38] B. Ohlsson, P. Höglund, B. Roth, G. Darwiche, Modification of a traditional breakfast leads to increased satiety along with attenuated plasma increments of glucose, C-peptide, insulin, and glucose-dependent insulinotropic polypeptide in humans, Nutr. Res. Elsevier 36 (2016) 359–368.
[39] Diabetes Canada Position Statement on low-carbohydrate diets for adults with diabetes: a rapid review, Can. J. Diabetes. 44 (2020) 295–299.
[40] A. Flint, B.K. Møller, A. Raben, B. Sloth, D. Pedersen, I. Tetens, et al., Glycemic and insulinemic responses as determinants of appetite in humans, Am. J. Clin. Nutr. 84 (2006) 1365–1373.
[41] R.D. Feinman, W.K. Pogozelski, A. Astrup, R.K. Bernstein, E.J. Fine, E.C. Westman, et al., Dietary carbohydrate restriction as the first approach in diabetes management: critical review and evidence base, Nutrition 31 (2015) 1–13.
[42] M.C. Gannon, F.Q. Nuttall, Control of blood glucose in type 2 diabetes without weight loss by modification of diet composition, Nutr. Metab. (Lond). 3 (2006) 16.
[43] Y. Park, K.W. Dodd, V. Kipnis, F.E. Thompson, N. Potischman, D.A. Schoeller, et al., Comparison of self-reported dietary intakes from the automated self-administered 24-h recall, 4-d food records, and food-frequency questionnaires against recovery biomarkers, Am. J. Clin. Nutr. 107 (2018) 80–93.
[44] S. Heidari, T.F. Babor, P. De Castro, S. Tort, M. Curno, Sex and gender equity in research: rationale for the SAGER guidelines and recommended use, Res. Integr. Peer Rev. 1 (2016) 2.