Journal of Holistic Performance
ISSN: 2463-7238 DOI: 901.206.387
Published: 8/10/2019

Can Baseline Cardiometabolic Markers Predict the Efficacy of Carbohydrate Restriction in Healthy Adults? A Pilot Study

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Abstract

Background

Low-carbohydrate diets are frequently used and are effective for improving a range of health outcomes. There is some evidence to suggest that certain individuals will achieve greater results from higher- or lower-carbohydrate diets but at this time there is little evidence to indicate the relative 'appropriateness' of diets differing in carbohydrate content for an individual. This study explores associations between baseline and changes in blood measures of cardiometabolic health, relative to carbohydrate allocation.

Methods

Seventy-seven healthy, non-diabetic participants (25 males, 52 females [mean age: 39 years, range: 25 to 49; mean body mass index (BMI) 27 kg/m^2, range: 20-39]) participated in a 12-week, randomised, clinical intervention study. Participants completed baseline testing of blood measures and basic anthropometric measures and a lead-in week to identify habitual calorie intake. Participants were assigned to one of three low-carbohydrate diet plans which advised intakes of either 5%, 15%, or 25% of energy derived from carbohydrate, individualised to the participant and standardised for protein, at 1.4 g per kg of body weight (bw) per day. For the final nine weeks of the intervention they were advised to eat *ad libitum* but to adhere as closely as possible to the carbohydrate energy limit for their treatment group. Participants were instructed to continue habitual exercise patterns. Blood measures of cardiometabolic health (glucose, insulin, c-peptide, total cholesterol, high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol, triglycerides (TG)) and anthropometric measures (height, weight, and waist and hip girth) were measured at baseline and at the conclusion of the 12-week dietary intervention. The associations between baseline blood and anthropometric measures and the changes in these measures were made by undertaking

multiple linear regression for the baseline measure and treatment group as independent variables with the change in outcome measures as dependent variables.

Results

There was a greater improvement in participants who had more adverse baseline cardiometabolic measures from a greater carbohydrate restriction, with 7 of 11 measures most benefiting from a very low carbohydrate ketogenic diet (VLCKD) intervention relative to baseline measurements. Only HDL cholesterol reached between-group significance, with every 1 mmol/L higher HDL cholesterol at baseline associated with a 0.5 and 0.2 mmol/L improvement in HDL cholesterol for the moderate-low carbohydrate diet and low-carbohydrate diet groups respectively, and a 0.4 mmol/L worsening for VLCKD (p = 0.0006).

Conclusions

Overall, there is a consistent association between baseline markers of cardiometabolic health and changes in these markers relative to the amount of carbohydrate included in the diet. However, low HDL cholesterol might be improved most by a moderate restriction of carbohydrate to ~25% of TE when compared to greater carbohydrate restriction. Because most results were not significant due to the small sample size and preliminary nature of this study, further research is required with larger cohorts to investigate this hypothesis further.

Introduction

Low-carbohydrate diets (LCDs) and very-low-carbohydrate ketogenic diets (VLCKDs) are routinely used for the management of a range of health conditions, including neurological disorders, obesity, diabetes and metabolic syndrome, and various cancers.[1-11] They are also used widely for a range of outcomes in the general population including weight loss and maintenance,[12] and improved satiety.[13-15] Despite the potential offered by LCDs, and the common use of these diets, there is little evidence for the superiority of greater carbohydrate restriction compared to moderate restriction, and how benefits might play out for people of different metabolic status.

Systematic reviews show that, despite the greater loss of weight and fat initially from LCDs, over longer timeframes, when calories are equally restricted, there is little difference in outcomes for weight loss, and total or low-density lipoprotein (LDL) cholesterol.[16-20] However, there is a larger glucose-lowering effect,[19] and greater improvements in high-density lipoprotein (HDL) cholesterol and glycated haemoglobin (HbA1c) resulting from

greater carbohydrate restriction.[20] Additionally, those with greater insulin resistance might adhere better to a low-carbohydrate vs higher-carbohydrate diet,[21] but studies also show that adherence is more difficult with extreme carbohydrate restriction, i.e. <50 g of total carbohydrate per day.[20] Therefore, while there is overall little difference between diets containing greater or lesser amounts of carbohydrate, over time there are individuals who are likely to benefit from a greater carbohydrate restriction.

Currently, though, there are few studies that have explored the indicative value of baseline markers to outcomes achieved from differing diets, but several indicators have been proposed. For example, blood type is used by some practitioners as a way to determine food choices for individuals based on unproven allergic responses to lectins in foods,[22] but no effects of blood-type on the effectiveness of, or outcomes from, any diet has been observed.[23, 24]

Relative insulin homeostasis has also been investigated as a predictor of outcomes from diet. It has previously been demonstrated that those with above-median insulin response after an oral glucose challenge (i.e. more insulin resistant) lose more weight from a lower-carbohydrate diet, while those with below-median insulin responses (more insulin sensitive) lose more weight from a higher-carbohydrate, lower-fat diet.[25-28] A pilot trial to investigate these effects in an ad-libitum diet over six-months found increased weight loss resulting from low-carbohydrate diets in insulin-resistant participants and improved weight loss resulting from low-fat diets for insulin-sensitive participants. There were also non-significant improvements in HDL cholesterol, triglycerides (TG), fasting glucose and insulin, and blood pressure resulting from the low-carbohydrate diet versus the higher-carbohydrate diet in those more insulin resistant. In those more insulin sensitive, the low-carbohydrate diet improved HDL cholesterol and triglycerides more than that of the low-fat diet, whereas the low-fat diet resulted in improved fasted insulin and glucose.[29] A recent study by Gardner and colleagues demonstrated no significant difference in weight loss over 12 months between a moderate carbohydrate diet with 48% of total energy (TE) from carbohydrate versus a lower carbohydrate diet (30% TE) but significant improvements in HDL cholesterol and triglycerides in the lower-carbohydrate diet group.[30] However, baseline gene markers and insulin homeostasis were not associated with outcomes in either diet group in this study.

We hypothesised that blood and anthropometric measures associated with cardiometabolic health can predict anthropometric and cardiometabolic outcomes relative to diets differing in carbohydrate restriction. The present pilot

study compared baseline anthropometric and blood measures of cardiometabolic health, to changes in these markers, in individuals, relative to a twelve-week dietary intervention differing in the magnitude of carbohydrate restriction.

Materials and Methods

Population

Seventy-seven participants, 25 males, 52 females (mean age: 39 years, range: 25 to 49; mean BMI 27 kg/m^2, range: 20-39) were recruited between the 7th and 19th of August 2017 and gave written, informed consent to participate in a 12-week, randomised, clinical intervention study. The study took place between the 11th of September and the 10th of December 2017. Collection of data and analysis was performed at AUT Human Potential Centre, Auckland, New Zealand.

Inclusion and exclusion criteria

Participants were required to be healthy and between the ages of 25 and 49 years. Exclusion criteria were; underweight (<18.5 BMI kg/m^2), diagnosed with diabetes, diagnosed with any serious medical condition, having previously followed a ketogenic diet, or current or former clients of any of the researchers in clinical practice.

Ethical approval

The trial was registered by the Australia New Zealand Clinical Trial Registry. ACTRN12617000421336p. Ethics approval for this study was granted by the Southern Committee of the Health and Disability Ethics Committee of New Zealand. 17/STH/60

Dietary interventions and allocation

Participants completed baseline testing of blood and basic anthropometric measures and a lead-in dietary recording week to identify habitual calorie intake. Participants were randomised by the study statistician to one of three low-carbohydrate diet plans which advised intakes of either 5%, 15%, or 25% of TE from carbohydrate. The randomisation was stratified by gender, using a pre-prepared sequence, with investigators blinded to treatment allocation at baseline and follow-up. Participants were assigned to the next treatment group according to their order of recruitment. The primary researcher responsible for initial statistical analysis was blinded to the treatment group allocation until this analysis had been completed.

Diet plans were individualised per participant, with daily calories determined by the daily mean calories consumed during the lead-in week. Protein was controlled at 1.4 g.kg^{-1} bm.day^{-1}, consistent with International Society of Sports Nutrition (ISSN) guidelines for optimal protein intake for performance.[31] Participants were advised to adhere as strictly as possible to the energy and

macronutrient prescription for the first three weeks of the intervention. For the final nine weeks of the intervention, they were advised to eat *ad libitum* but to adhere as closely as possible to the carbohydrate energy limit for their treatment group as a percentage of their total energy intake. Usual exercise patterns were continued. Dietary intake was recorded by participants in a mobile application (Fat Secret) with the researchers able to obtain real-time entry on a partner mobile application (Fat Secret Pro*)*. Results were monitored for safety and compliance by the primary researcher and research assistants tasked with data-monitoring. Compliance to the dietary allocation was monitored daily by a data monitoring team. Where non-compliance to the dietary allocation, especially for carbohydrate, was noticed, the participant was notified and offered support and advice. Figure 1 profiles the instructions for the dietary allocations over the 13-week study course. Participants were instructed to contact either the clinical nutritionist or the registered dietitian in the research team for any assistance during the study duration.

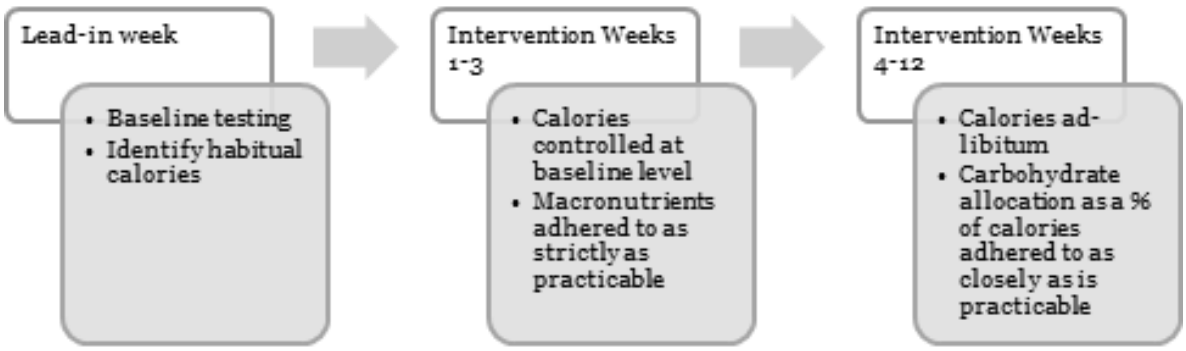

Figure 1. Participant flow of dietary interventions

Blood measures

Following an overnight fast, blood samples were obtained from participants, before the first meal, via venipuncture by a certified phlebotomist from an antecubital vein and collected into PST Vacutainer tubes using lithium-heparin as the anticoagulant (Becton Dickinson). Within 15 minutes of collection, tubes were centrifuged at 1500 revolutions per minute for 10 min at +4°C, and plasma samples were transferred into clean polypropylene tubes and frozen at −80°C until analyses were conducted using specific diagnostics assays on a Roche Modular analyser (P800 and E170). Blood samples were analysed for total cholesterol (Total-c), LDL cholesterol, HDL

cholesterol, TG, C-reactive protein (CRP), gamma-glutamyl transferase (GGT), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), glucose and uric acid on the P800 module. Insulin and C-peptide concentrations were measured on the E170 module. All analytical biomarkers were measured at baseline and immediately following the 12-week intervention. The total duration of the assay for each analyte was less than 20 min based on the electrochemiluminescence principle (ruthenium-conjugated monoclonal antibodies) for the E170 module and specific enzyme assay methods for the P800 module. Quantitative results were determined via instrument-specific full point calibration curves and validated with specific controls.

Anthropometry

The following measures were taken: height, weight, waist circumference at the narrowest point between the lowest rib and the iliac crest, and hip circumference at the widest point of the hips and buttocks. These measures were additionally used to derive body mass index (BMI) at baseline and during follow-up.

Statistical analyses

The associations between baseline blood and anthropometric measures and the changes in these measures were made by undertaking multiple linear regression for the baseline measure and treatment group as independent variables with change in outcome measures as dependent variables. The hypothesis that the linear relationship between baseline measures and outcome change varied by-group was tested for by including an interaction term in the model and evaluating the *p*-value from a likelihood ratio test. Whether or not this was statistically significant, the results of the model including the interaction term are presented, to explore the hypothesis of whether the baseline-to-change association varied by degree of carbohydrate restriction (treatment group), as the numbers of participants in each group are small and the likelihood ratio may be under-powered. A *p*-value of less than 0.05 was used as the threshold for significance. Beta coefficients from regression models, therefore, represent the mean change in outcome associated with a one-unit increase in baseline measure.

Results

A total of 283 people was assessed for eligibility with 206 excluded and 77 included for randomisation to the trial groups. Baseline characteristics of study participants are shown in Table 1.

Ten participants withdrew after they were randomised. Two failed to comply with guidelines to submit baseline data and withdrew from the study (one male, one female), and three females withdrew due to changes in personal circumstances, including two who became pregnant. A

further five withdrew due to challenges arising from following the diets: two female participants found the dietary allocation of carbohydrate too difficult to sustain (one each in the 5% and 15% allocation groups). One did not want to use the food app; one felt that she could not maintain her sports performance on 15% TE from carbohydrate; and one female in the 5% allocation group reported amenorrhea and reduced strength and power, despite improved mental clarity. A further 28 failed to present for post-intervention measurements. This left 39 participants with follow-up results available for analysis. (Figure 2.)

There were no significant differences in baseline characteristics between completers and non-completers and no meaningful difference in the number of non-completers by-group with 50%, 50%, and 48% of participants not completing post-intervention measures in the MCD, LCD, and VLCKD groups respectively. Mean baseline levels of TG were, however, 36% higher at baseline in those lost to follow-up compared to those who were not, even though the difference between the two distributions was not significant ($p = 0.08$). There was also no significant variation for age, gender, or ethnicity between the groups, in the participants analysed. At baseline, blood measures were all within reference ranges except for Total-c which had an overall mean of 5.31 mmol/L (SD = 1.29) for completers, and a significant between-group difference ($p = 0.005$). There was also a significant difference in weight between the groups at baseline ($p = 0.046$).

Overall changes in the outcome measures between intervention groups have been reported in a previously published paper.[32]

Table 1. Baseline characteristics of study participants

	Treatment group					
	MCD (n=12)	**LCD (n=13)**	**VLCKD (n=14)**	**Total (n=39)**	**Test**	***p*-value**
Age mean (SD)	39.1 (6.6)	38.9 (8.3)	38.7 (7.1)	38.9 (7.1)	ANOVA	0.992
Gender (%)					Fisher's	0.198
Female	10 (83.3)	6 (46.2)	9 (64.3)	25 (64.1)		
Male	2 (16.67)	7 (53.85)	5 (35.71)	14 (35.9)		
Ethnicity (%)					Fisher's	0.733
Asian	1 (8.3)	0 (0.0)	1 (7.1)	2 (5.1)		
European	8 (66.7)	11 (84.6)	10 (71.4)	29 (74.4)		
Maori	2 (16.7)	1 (7.7)	3 (21.4)	6 (15.4)		
Pacific	0 (0.0)	1 (7.7)	0 (0.0)	1 (2.6)		
Other ethnicity	1 (8.3)	0 (0.0)	0 (0.0)	1 (2.6)		
Total energy (Kcal) mean (SD)	1435 (293)	1567 (666)	1805 (857)	1603 (649)	ANOVA	0.378
Weight (kg) mean (SD)	76.3 (14.9)	90.4 (20.0)	76.8 (11.2)	81.2 (16.6)	ANOVA	0.046
Height (m) mean (SD)	1.70 (0.10)	1.76 (0.08)	1.74 (0.09)	1.73 (0.09)	ANOVA	0.245
BMI (kg/m^2) mean (SD)	26.4 (3.23)	29.1 (4.92)	25.5 (2.77)	27.0 (3.96)	ANOVA	0.050
Glucose (mmol/L) mean (SD)	5.54 (0.43)	5.38 (0.47)	5.44 (0.44)	5.45 (0.44)	ANOVA	0.673
Total cholesterol (mmol/L) mean (SD)	5.20 (1.3)	4.57 (0.61)	6.10 (1.37)	5.31 (1.29)	ANOVA	0.005
Triglyceride (mmol/L) mean (SD)	0.79 (0.2)	0.99 (0.36)	0.92 (0.22)	0.90 (0.27)	ANOVA	0.184
Insulin (pmol/L) mean (SD)	63.1 (37.3)	81.1 (39.4)	41.6 (17.6)	61.4 (35.8)	ANOVA	0.012

SD: standard deviation; BMI: body mass index

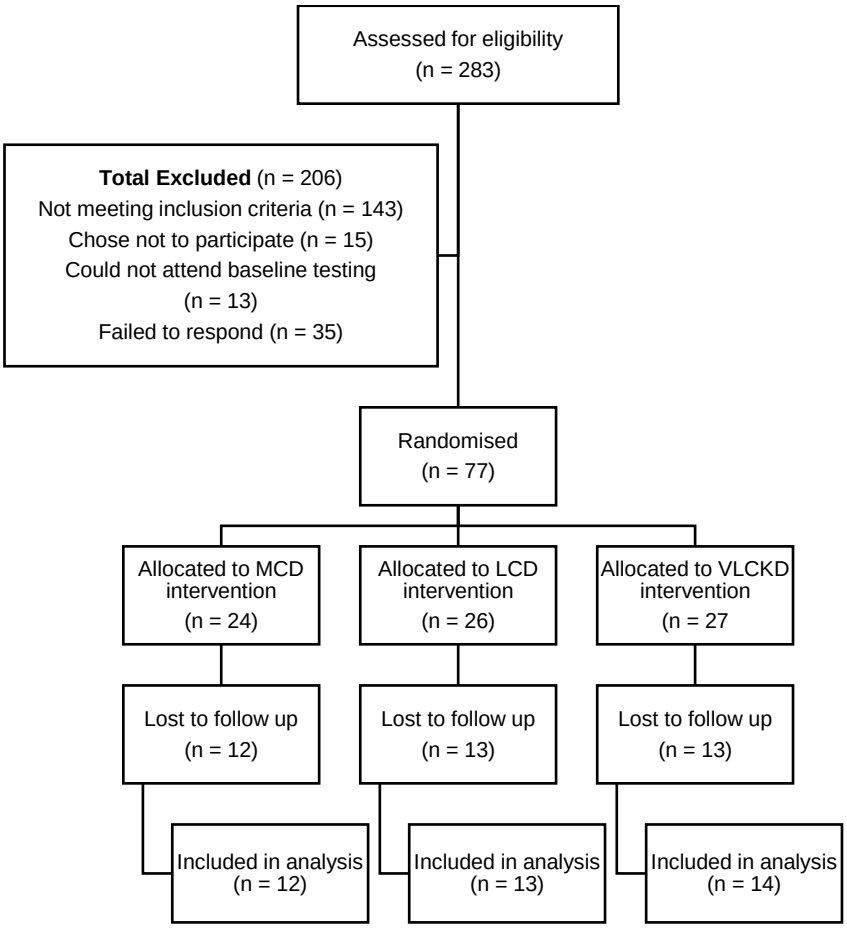

Figure 2. Flow-chart showing participant recruitment, randomisation, allocation and lost to follow-up

Associations between baseline and change in outcome measures

Overall, several measures showed significant associations between baseline and change in outcome, including HDL cholesterol, glucose, and weight and hip measurements. Of these measures, the higher the participant's baseline measure, the greater the reduction in HDL cholesterol, which is a less favourable outcome (Figure 3a). However, the higher the baseline glucose, weight, and hip, the greater the reduction (favourable outcomes). All results are presented in Tables 2 and 3. There was a trend towards more adverse baseline measures being improved more by greater carbohydrate restriction. Seven of 11 blood and anthropometric measures showed the strongest association between baseline and greatest improvement or least worsening in outcome measure, in the VLCKD intervention compared to more moderate carbohydrate restriction.

Only HDL cholesterol reached the threshold for significance between groups, with every 1 mmol/L higher HDL

cholesterol recorded at baseline associated with a 0.5 and 0.3 mmol/L decrease in HDL cholesterol for MCD and LCD respectively, and a 0.4 mmol/L increase for VLCKD (Figure 3b.) These results were also significant, within-group, for MCD and VLCKD (Table 2.)

Within-group changes were significant in the VLCKD group for glucose (Beta = -0.589, p = 0.020) and change in hip measurement (Beta = -0.418, p = 0.002).

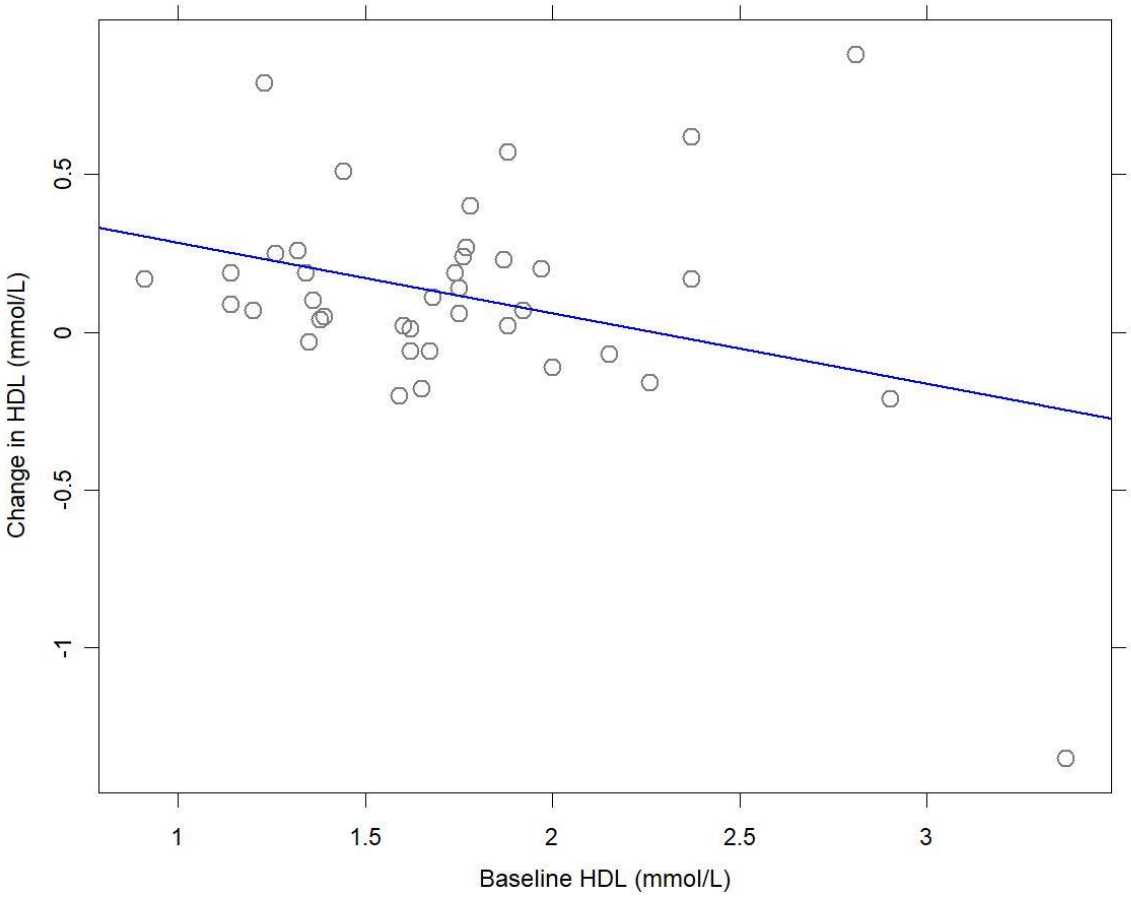

Figure 3a. Baseline HDL vs change in HDL. The blue line shows the linear regression. HDL: high-density lipoprotein cholesterol.

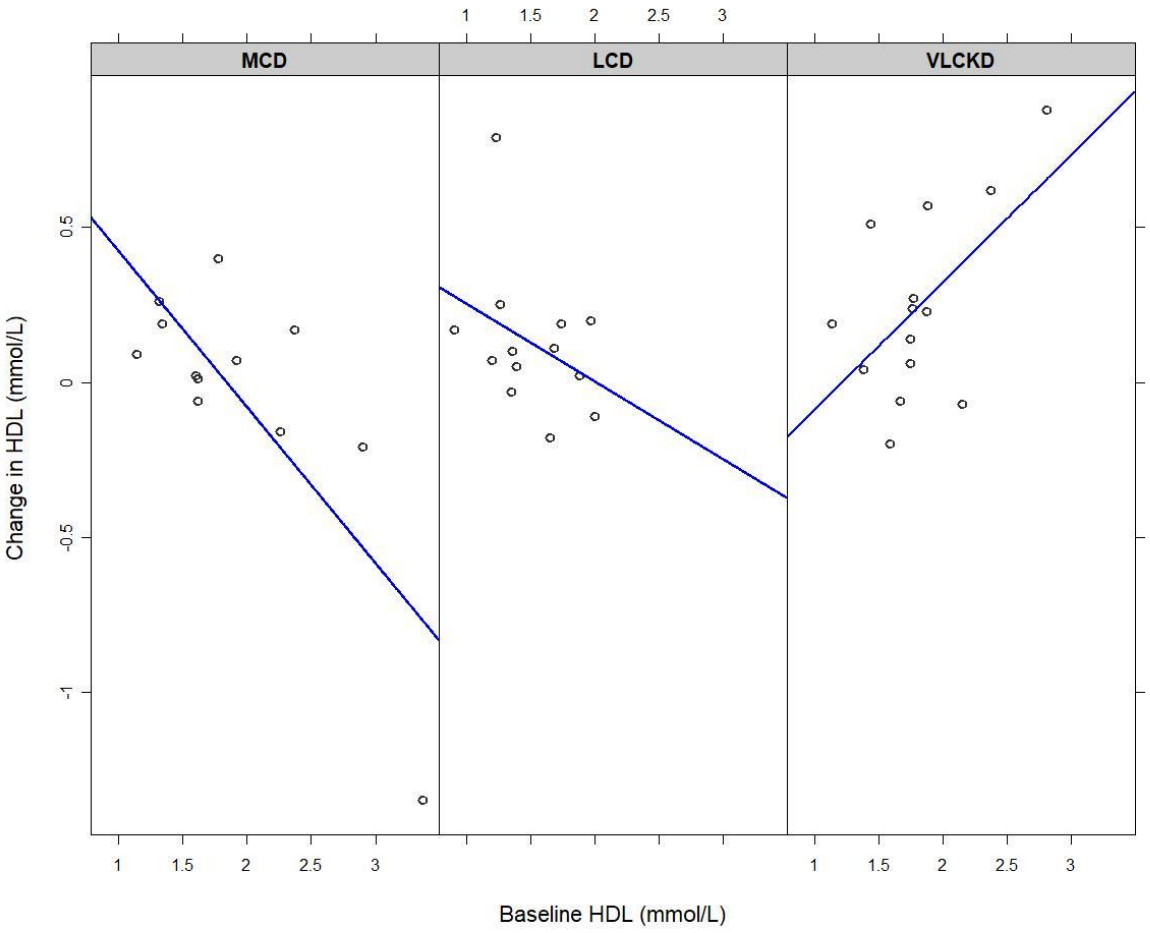

Figure 3b. Baseline HDL vs change in HDL by group. The blue line shows the linear regression. HDL: high-density lipoprotein cholesterol; MCD: Moderate-low carbohydrate diet; LCD: Low-carbohydrate diet; VLCKD: Very-low-carbohydrate ketogenic diet.

Table 2. Association between baseline blood measures and magnitude of change over 12 weeks by group.

	Treatment group Beta coefficient and *p*-value		
Baseline association to 12-week Δ	Moderate-Low Carbohydrate	Low Carbohydrate	Very Low Carbohydrate
Total cholesterol (mmol/L)	Overall β = -0.224† ; *p* = 0.225		
	-0.257 *p* = 0.30	-0.578 *p* = 0.41	-0.209 *p* = 0.58
	p = 0.887‡		
LDL cholesterol (mmol/L)	Overall β = -0.262† ; *p* = 0.173		
	0.042 *p* = 0.86	-0.866 *p* = 0.27	-0.532 *p* = 0.17
	p = 0.360‡		
HDL cholesterol (mmol/L)	Overall β = -0.224† ; *p* = 0.042**		
	-0.505 *p* = 0.004**	-0.252 *p* = 0.23	0.413 *p* = 0.034**
	p = 0.0006‡ **		
Triglycerides (mmol/L)	Overall β = -0.001† ; *p* = 0.99		
	0.715 *p* = 0.108	0.027 *p* = 0.92	-0.389 *p* = 0.21
	p = 0.135‡		
Insulin (pmol/L)	Overall β = -0.024† ; *p* = 0.83		
	0.261 *p* = 0.242	-0.052 *p* = 0.830	-0.215 *p* = 0.26
	p = 0.394‡		
C-peptide (nmol/L)	Overall β = -0.144† ; *p* = 0.160		
	0.083 *p* = 0.64	-0.122 *p* = 0.62	-0.346 *p* = 0.069*
	p = 0.448‡		
Glucose (mmol/L)	Overall β = -0.447† ; *p* = 0.008**		
	-0.301 *p* = 0.43	-0.353 *p* = 0.21	-0.589 *p* = 0.020**
	p = 0.745‡		

* = p < 0.1; ** = p < 0.05

† β refers to the beta coefficient of the overall linear regression between the measure at baseline and change in the outcome measure.

‡ This *p*-value relates to a regression model of the baseline measure and treatment group as independent variables and change in outcome as dependent variables. The *p*-value relates to the interaction term, testing for a significant difference in the baseline-change in outcome by treatment group.

Table 3. Association between baseline anthropometric measures and magnitude of change over 12 weeks by group.

	Treatment group Beta coefficient and *p*-value		
Baseline association to 12-week Δ	Moderate-Low Carbohydrate	Low Carbohydrate	Very Low Carbohydrate
BMI	Overall β = -0.031† ; *p* = 0.47		
	-0.058 *p* = 0.62	-0.004 *p* = 0.96	-0.123 *p* = 0.16
	p = 0.610†		
Weight (kg)	Overall β = -0.051† ; *p* = 0.095*		
	-0.077 *p* = 0.26	-0.053 *p* = 0.34	-0.030 *p* = 0.65
	p = 0.900†		
Waist (cm)	Overall β = 0.012† ; *p* = 0.79		
	0.118 *p* = 0.42	-0.004 *p* = 0.96	-0.061 *p* = 0.44
	p = 0.508†		
Hip (cm)	Overall β = -0.260† ; *p* = 0.003**		
	-0.130 *p* = 0.23	0.271 *p* = 0.12	-0.418 *p* = 0.002**
	p = 0.351†		

* = p < 0.1; ** = p < 0.05

† β refers to the beta coefficient of the overall linear regression between the measure at baseline and change in the outcome measure.

‡ This *p*-value relates to a regression model of the baseline measure and treatment group as independent variables and change in outcome as dependent variables. The *p*-value relates to the interaction term, testing for a significant difference in the baseline-change in outcome by treatment group.

Discussion

Principle findings

There were significant, greater overall improvements in cardiometabolic health markers occurred in those with more adverse measures at baseline. This association was more exaggerated in those who were allocated to the more restricted carbohydrate interventions. This suggests that those wanting to improve HDL cholesterol, blood glucose, weight, and hip measures especially benefit most from a reduced carbohydrate dietary intervention. There is also an overall trend towards the improvement of cardiometabolic measures of health relative to carbohydrate allocation and that those with poorer baseline markers of health, might improve these most effectively with greater reductions in carbohydrate, while those with 'better' baseline markers could benefit more from a lesser carbohydrate restriction. Of 11 measures, 7 were most improved relative to baseline by the VLCKD intervention and although these variables are not independent, if these effects were random, we would expect ~ 3-4 of 11 of these outcomes to show the

greatest improvements resulting from VLCKD. In the only measure to reach between-group statistical significance, poorer HDL cholesterol at baseline was most improved by MCD, followed by LCD and VLCKD. However, the greatest magnitude of improvements was observed in the VLCKD group and the number of participants to have worsened outcomes for HDL cholesterol were identical between the three groups.

Strengths and weaknesses of the study

The present study is one of the first to compare diets differing in the magnitude of carbohydrate restriction for cardiometabolic outcomes in healthy people and to investigate the possible predictive value of baseline blood measures for 'best-fit' to dietary prescription. As such, it provides an important addition to the literature to help inform clinical practice. There have been many comparisons between LCDs and usual care, high-carbohydrate, low-fat diets but, thus far, only one study comparing differing low-carbohydrate diets. In this study by Johnson et al., [33] the results between groups were equivocal. However, the 'ketogenic' diet contained only 60% TE from lipids, which based on the extant literature would not be considered ketogenic without the addition of MCTs and the non-ketogenic, low-carbohydrate diet consisted of a relatively modest reduction in carbohydrate to 40% of TE. Therefore, while an important study in the context of the literature, it doesn't adequately address the variation in outcomes between differing, low-carbohydrate diets, nor does it address the predictive value of markers of health at baseline on the efficacy of a lower-carbohydrate dietary intervention.

Our study was limited by relatively small sample size and by withdrawals. The sample size of 39 is likely to be too small to justify the use at this time of baseline cardiometabolic markers in isolation for the prescription of diets differing in carbohydrate content. However, the trend towards greater improvements resulting from very-low-carbohydrate diets for those with 'worse' baseline measures of cardiometabolic health suggests both their predictive, clinical use and the need for further research in this area.

The magnitude of any associations between baseline markers and changes could have also been affected by our chosen cohort as this was, according to our inclusion and exclusion criteria, a healthy cohort, absent from metabolic or other health conditions. Almost all participants began the study with anthropometric and blood measurements within the normal range, and in fact, many of these measures (such as triglycerides) were well within low-normal ranges for healthy populations. We would, therefore, not expect large changes for markers of health in a generally

'healthy' cohort. This was also a eucaloric intervention, designed to match habitual energy intake and was not designed as a 'weight loss' trial. The study also did not include a control group containing higher carbohydrate allocation consistent with existing dietary guidelines (i.e. 45-65 % of energy derived from carbohydrate) [34] and so, we cannot completely discount that higher-carbohydrate, lower-fat diets might exhibit differences to the trends shown in this study. This study was also not controlled for some variables that might affect outcomes such as the duration of the fasting vs feeding periods, physical activity, and sleep duration. These other factors deserve further study in other well-conducted human trials.

Meanings and implications of the study

The trend towards greater improvements in outcomes from lower-carbohydrate diets when compared to cardiometabolic measures at baseline suggests a potential role for the cardiometabolic profile as a predictor of efficacy of diets differing in carbohydrate content. Or, that the 'better' the baseline cardiometabolic markers, the more 'carbohydrate tolerant' someone might be.

Unanswered questions and directions for future research

Due to the small sample size, a healthy subject cohort, and results that failed to reach the threshold for statistical significance, additional research is warranted to validate this hypothesis, particularly in groups with poorer baseline measures who are both at greater risk and who may benefit most from reduced carbohydrate diets.

Conclusions

Overall, there is a consistent association between baseline markers of cardiometabolic health and changes in these markers relative to the amount of carbohydrate included in the diet. However, low HDL cholesterol might be improved most by a moderate restriction of carbohydrate to ~25% of TE when compared to greater carbohydrate restriction. Because most results were not significant due to the small sample size and preliminary nature of this study, further research is required with larger cohorts and subjects with adverse cardiometabolic measures of health, to investigate this hypothesis further.

Acknowledgements

We are grateful to the participants in this study. We acknowledge the support of our colleagues at the Human Potential Centre, AUT University, especially Catherine Crofts, Fabrice Merien, and Dee Holdsworth-Perks; and at the Holistic Performance Institute. Specifically, we would like to acknowledge the assistance of Amberleigh Jack, Bella Marinkovich, Emily White, and Lulu Caitcheon who assisted with data collection; phlebotomists, Brenda Costa-Scorse and Claudia Barclay; Kirsten Beynon for lab assistance during data collection and analysis, Dave Shaw for his co-operation during data-collection, and Eric Helms and Nigel Harris for advice about the study design and methods.

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Abbreviations

Very-low-carbohydrate ketogenic diet (VLCKD), moderate-low carbohydrate diet (MCD), low-carbohydrate diet (LCD), total cholesterol (Total-c), low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides (TG), C-reactive protein (CRP), gamma-glutamyl transferase (GGT), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP).

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Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

Authors' contribution

CJdCH, GMS, CZ, and SJT designed research; CJdCH conducted research; CJdCH, and SJT analysed data; CJdCH wrote the paper, with editing assistance from GMS, CZ and SJT. CJdCH had primary responsibility for final content. All authors read and approved the final manuscript.

Data availability

The raw, deidentified r-data files used to support the findings of this study are available from the corresponding author upon request.

Funding statement

All funding was provided by the Human Potential Centre, AUT.