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**Tay J, Luscombe-Marsh ND, Thompson CH, Noakes M, Buckley JD, Wittert GA, et al. A very low-carbohydrate, low-saturated fat diet for type 2 diabetes management: A randomized trial. Diabetes Care. 2014;37(11):2909–18.**

## What We Know, Think We Know, or Are Starting to Know

Low-carbohydrate diets have emerged as a popular dietary intervention for the management of Type-2 Diabetes [T2DM], based largely on the simple mechanism that dietary carbohydrate restriction leads to lower blood glucose levels, and effectively provides a dietary means to achieve blood glucose control [aka, glycaemic control]. This effect of carbohydrate restriction on glycaemic control has support in the literature, with a recent review by Snorgaard et al. in 2017 finding that low-carbohydrate [LC] diets lead to greater reductions in haemoglobin A1c, a marker of longer term [2-3 months] blood glucose regulation, in the short-term, which was defined as up to 6-months [(1)]. The reductions in blood glucose were linear to the degree of carbohydrate restriction, such that greater carbohydrate restriction resulted in greater reductions in blood glucose levels in the short-term [(1)]. However, over 1-year, these differences fell away, and there was no difference between higher or lower carbohydrate diets on glycaemic control, or cardiovascular risk factors, like LDL-cholesterol.

However, mean carbohydrate intake in these interventions was 30-35% energy, which is not reflective of a truly low-carbohydrate diet. n addition to the role of total carbohydrate level in the diet for T2DM management, two important dietary characteristics that influence insulin sensitivity and insulin action are often overlooked by advocates of LC diets [(2)]: a] dietary fibre intake, and; b] the composition of fats in the diet. Strong advocates for low-carbohydrate diets have defined LC diets as containing less than 26% energy, or <130g carbs per day [(2)]. Such advocates have called for LC diets to be front-line interventions for people with T2DM, on the basis that LC diets may lead to reductions or elimination in medications, and provide the best dietary option to achieve glycaemic control [(2)]. Certainly, there is support for post-prandial blood glucose levels being strong predictors of cardiovascular disease [CVD] events in people with moderate T2DM, while fasting blood glucose levels are a stronger predictor of CVD events in people with poorly controlled T2DM [(3)].

However, the metabolic effects of LC diets on T2DM may be over-exaggerated from certain studies. Differences in energy intake, higher protein content of LC diets, and only measuring HbA1c, may all influence results. In T2DM, insulin resistance in peripheral tissues, in particular skeletal muscle tissue, develops initially, and mediations like metformin target this process, leading to increased glucose disposal. The present study compared a true LC diet to a high-carbohydrate [HC] diet in T2DM.

## The Study

Obese adults with T2DM were randomised to a either an LC diet or HC diet, in a parallel design* intervention. Diets were individualised to a 30% energy deficit, which remained constant throughout the study. The LC diet was 14% carbohydrate [<50g/d], 28% protein, and 58% fat [of which 35% monounsaturated fat {MUFA}, 13% polyunsaturated fat {PUFA}, and <10% saturated fat {SFA}]. The HC diet was 53% carbohydrate, 17% protein, and 30% fat [15% MUFA, 9% PUFA, <10% SFA]. Mean fibre intake in the LC diet was 25.1g/d, and in the HC diet, 31.6g/d.

### *Geek Box: Parallel Design

*You've likely heard of randomised controlled trials referred to as the "gold standard" research design, and a parallel design is the gold standard in drug trials, because the study compares two treatments: drug vs. placebo. The essence of a parallel design is that participants only receive the intervention they are assigned to. This is contrast to crossover designs, which we had in a Geek Box in [INSERT STUDY], where the treatments are run in different order. So, in a crossover design, participants get Diet A followed by Diet B, while the other group may get Diet B followed by Diet A. A parallel study does not necessarily have to test the intervention against a placebo; it could have parallel groups of different types of intervention, as is the case in this study, where two different diets are being compared against each other. So, in a parallel study, participants only get the intervention they are assigned to, not all interventions. Therefore, participants assigned to Diet A are compared to participants assigned to Diet B.*

The intervention last 1-year, and participants met with a dietitian bi-weekly for the first three months, then monthly for the remainder of the study. Participants were provided with key foods, for example low-GI cereal, nuts, or legumes, to make up their diet for the first 12-weeks. Dietary intake was from 7-days of consecutive weighed food records were randomly assessed for each 14-day period during the study. Participants also undertook 3 circuit training sessions during the week, which mixed aerobic and resistance training, and for which attendance records were kept.

## *Geek Box: Glycaemic Variability

*Numerous blood glucose measures may be used in research, and if you have an interest in diabetes research, you're going to come across a head-spinning number of different measures, which fall under the broad definition of "glycaemic variability" [GV]. In simple terms, GV is the swings in blood glucose levels that occur throughout the day. GV includes the elevations in blood glucose that occur after a meal, the time spent with high or low blood glucose levels, as well as the difference in blood glucose responses at the same time of day, on different days. GV is a normal aspect of physiology; otherwise healthy people have blood glucose fluctuations throughout the day. However, in diabetes, the level of GV can be increased. Several measures have emerged. HbA1c is the most well-known, which is a marker of longer-term glycaemic control, over the preceding 2-3 months. The mean amplitude of glycaemic excursion [MAGE] is used as a measure of the glucose excursions in response to meals. There is also the continuous overall net glycaemic action [CONGA], which assesses the variability of glucose levels within a specified time window. These tools provide for a more thorough picture of glucose regulation, and this is important, because GV itself appears to be related to diabetic complications. However, while it is tempting to see GV as an important therapeutic target, the exact value of targeting GV specifically is yet to be fully determined.*

**Results:** There was no significant difference between the LC and HC diets in the primary outcome, HbA1c, which was reduced by 1% on average in both groups [from a baseline of 7.3-7.4%]. The LC diet resulted in twice the level of reductions in GV, compared to the HC diet, in the MAGE, CONGA-1 [which measured GV in windows 1-hour apart], and CONGA-4 [which measured GV in windows 4-hours apart]. Participants in the LC diet were more likely to spend a lower proportion of time during the day in a hyperglycaemic range. 52% of the LC group, compared to 21% of the HC group, achieved a reduction in medication doses of >20%. There were no changes in most lipid parameters, and blood pressure, with the exception of triglycerides [decreased] and HDL [increased] on the LC diet compared to the HC diet.

## The Critical Breakdown

**Pros:** The participants were matched for age, BMI, HbA1c, and medications, to ensure an equal distribution of these characteristics between the two groups. Key foods comprising the diet were provided to participants for the first 12-weeks, and the random assessment of weighed food records throughout the study may provide a more true reflection of dietary intake in a free-living intervention.

**Cons:** Protein intake between interventions was not matched, which may have influenced glycaemic outcomes, as increased dietary protein can improve blood glucose regulation [4]. The 1-year intervention meant diets were not fully controlled, despite the efforts to ensure high compliance. No intention-to-treat analysis was performed, however, this may not have influenced the results as both diet groups had similar numbers of dropouts, and therefore similar numbers completed the study.

## Key Characteristic

The difference between the diets was a test of the LC diet against a diet that reflected national guidelines for diabetes management [in Australia]. However, these studies are often interpreted to suggest that "low-carb is better than high-carb", when the reality is that the comparative HC diet in this study wasn' t really a "high-carb" diet, as they related to T2DM management. In effect, it is comparing carbohydrate restriction per se, which will result in improved BG measures, to a fibre intake that is not high enough to elicit significant improvements in these parameters, biasing the results toward the LC diet. Although this research reaches back, the metabolic ward studies by James W. Anderson and colleagues through the 1970' s and 1980' s in adults with T2DM using high-carbohydrate, high-fibre diets, had dietary fibre intakes of >60g/d. Not a typo: sixty grams per day. These diets resulted in significant reductions in medications, generally in subjects treated with insulin [5,6]. However, the use of these diets in research has fallen away somewhat, and have been replaced by a focus on LC diets. However, there is a suggestion that extremely high-fibre diets may have some capability to rejuvenate beta-cell function, but the data is limited [7]. A parallel study comparing a true LC diet [as in this study] to a true high-fibre, HC diet, low-fat diet…now that would be interesting.

## Interesting Finding

Despite the large differences in dietary composition, saturated fat was largely similar between both the LC and HC groups. Often, saturated fat levels increase in the context of LC diets. However, dietary fat composition is important for blood glucose regulation, and often overlooked. Higher saturated fat levels may lead to impaired glycaemic responses, and this effect has been shown in diabetics [8]. Experimental research also indicates that saturated fats induce insulin resistance, with one possible mechanism being an increase in ceramides, compounds that mediate insulin sensitivity, by inhibiting the glucose transporter responsible for shuttling glucose into the cell [9-11]. Conversely, unsaturated fats have not been shown to impact on ceramides in circulation [11], and are associated with more favourable impacts on blood glucose regulation. Thus, in addition to the carbohydrate restriction on the LC diet, the emphasis on unsaturated fats may also have provided a combination effect to improve glycaemic control on the LC diet.

## Relevance

These interventions don't really tell us much in terms of a true comparison between a high-fibre, higher carbohydrate diet vs. a low-carbohydrate diet, because the moderate-high carbohydrate diets are not really an intervention in themselves, but a generic control representative of typical healthy eating guidelines. Thus, the debate back and forth between the whole-foods plant-based sect and the low-carb/ketogenic sect over which dietary intervention may be more efficacious for T2DM will continue until better trials conduct true comparisons.

This isn't to say this is a bad trial. It's not. Both studies brought HbA1c just under the 6.5% target level for diabetics, and it is also important to remember that this study incorporate regular exercise in the intervention. Weight loss and body composition changes were similar for both the LC and HC diets. Arguably, the relevance of this study is that is demonstrates, again, that LC diets are better than generic national guideline diets for T2DM management. The study suggests that LC diets improve diurnal [i.e., over the course of the day] glycaemic variability to a significantly greater extent than the HC diet, however, it is important to bear in mind that there is still debate over the GV as a treatment target, and HbA1c was improved in both groups. A recent intervention comparing 3 meals to 6 meals in participants with T2DM, with diets containing 40% carbohydrate, found that consuming 3 meals with calories and carbohydrates front-loaded to the morning, led to reductions in daily hyperglycaemia of 5hrs 56mins, compared to energy and carbohydrate evenly spaced across 6-meals [(12)]. Therefore, daily GV may not be improved solely as a function of carbohydrate restriction, but also from distribution of energy and meal spacing (for which we don't have data in the present study). Nonetheless, the reductions in medications from the LC intervention in this study remain more pronounced.

In T2DM, insulin resistance in peripheral tissues, in particular skeletal muscle tissue, develops initially, and mediations like metformin target this process, leading to increased glucose disposal. However, **the hallmark of T2DM progression is continued decline in the function of pancreatic beta-cell function, which produce and secrete insulin, leading ultimately to a complete failure in the ability of beta-cells to secrete insulin** [(13)]. Thus, while LC diets lead to less requirement for peripheral glucose uptake [as there is lower blood glucose levels overall from carbohydrate restriction], they do not address the main underlying characteristic of T2DM progression, namely, beta-cell decline.

## Application to Practice

It is important to remember that this was a lifestyle intervention, incorporating both dietary change and an exercise intervention, and that improvements were found in both dietary interventions. However, the magnitude of improvement in glycaemic variability, and reduction in medication usage and dose, was significantly greater in the LC diet. The primary characteristic of the LC diet, which distinguishes it from previous research, was not only the carbohydrate restriction: it was the dietary fat composition. Often when discussing LC diets, there is a narrative that goes hand-in-hand that dietary fat can just be poured on the diet with relatively little consideration. In fact, this study provides strong support that consideration should be given to modifying dietary fat composition, in the context of LC diets, for managing T2DM.

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