

# Low Carbohydrate Diets in Type 2 Diabetes—A Translational Study

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## Abstract

Although intensive interventions with low carbohydrate diets compared with higher carbohydrate diets can reduce HbA1c in people with type 2 diabetes, it is not clear if simple advice to make modest reductions in carbohydrate is effective in clinical practice. Forty-three people with type 2 diabetes and poor control (HbA1c > 7.5%) were randomized to receive 2 short education sessions over 6 months with a non-dietitian researcher on how to reduce carbohydrate intake by about 25% or to 2 control sessions in which the Australian Guide to Healthy Eating was provided. HbA1c and fasting glucose and lipids were measured at baseline and 3 months and 6 months. 33 volunteers attended a baseline visit; 27 completed 3 months and 24 6 months. HbA1c was reduced by 0.6% - 0.7% in the low carbohydrate diet group compared with the control group (P = 0.1). Fasting glucose was reduced by 2.3 mmol/L compared with the control group at 3 months (P < 0.03) only. Changes in HbA1c at 6 months were related to baseline HbA1c in the intervention group only. Although we have obtained suggestive evidence that a low carbohydrate diet can be successfully implemented in normal practice without professional help, our results are limited by low participant numbers and further studies are required.

## Keywords

Translational Study, Low Carbohydrate Diet, HbA1c, Fasting Glucose

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## 1. Introduction

Intensive intervention with very low carbohydrate diets combined with weight loss could lead to lower HbA1c

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levels and reduced medication use [1] [2] in the low carbohydrate group while in a further study this difference in HbA1c was only seen in those with initially high HbA1c levels and only at 6 and not at 12 months [3] [4]. Low carbohydrate interventions without weight loss can lower HbA1c and glucose in untreated type 2 diabetes but trial numbers are small, and the interventions have been very intensive, and the volunteers were on no medication for diabetes [5]. Low carbohydrate diets are recommended as the first line therapy for both type 1 and type 2 diabetes by some authors [6] although diabetes associations currently do not recommend this and there is very little evidence of efficacy of the diet in patients on a variety of medications including insulin and in which contact is limited to usual clinical practice rather than the more intensive research contact. A 3 month very low carbohydrate intervention [7] with 4 education sessions in patients with very poor glycemic control (HbA1c 9%) led to 2.6 kg more weight loss than a low fat diet in 79 completers ( $P < 0.001$ ), but HbA1c was reduced by only 0.3% more than the control diet ( $P = 0.1$ ). A moderate intensity outpatient intervention aimed at lowering carbohydrate to  $<30$  g/day and comparing this to a low fat diet with a 500 kcal/day, energy deficit had 68 completers at 2 years out of 144 randomized. There were no differences in weight or glycemic control between the groups at 6, 12 or 24 months despite weekly visits for a month and monthly visits thereafter [8].

We hypothesized that a relatively flexible, straightforward and sustainable dietary regimen low in carbohydrate (replaced with protein and/or unsaturated fat) offered to poorly controlled type 2 diabetes patients (HbA1c  $> 7.5\%$ ), would significantly reduce HbA1c and fasting glucose over a period of 6 months in the absence of weight loss and without intensive contact compared with usual care.

## 2. Methods

### 2.1. Volunteers

Men and women aged 18 - 80 years with confirmed type 2 diabetes with an HbA1c of more than 7.5% were recruited from the BakerIDI Diabetes Clinics (a tertiary referral centre) by a direct mail out to individuals who indicated they wished to be involved in research or via public advertisement in the local newspaper. Volunteers could be on no medication or on multiple medications including insulin. Exclusion criteria were bariatric surgery, pregnancy or lactation or following a low carbohydrate diet within the last 3 months

Any changes of medication were at the discretion of the primary treating doctor and not the researchers. Information on medication changes was obtained after the volunteer completed the study. The study was approved by the Alfred Hospital Ethics committee approval number 228/12 and the study was recorded on the Australian and New Zealand Clinical Trial Registry ACTRN12612000676819.

### 2.2. Diet

Volunteers were randomized 1:1 by computer generated randomization code to a control diet (The Australian Guide to Healthy Eating) or to a low carbohydrate diet. Diets were pragmatic food based diets with no particular percentage of carbohydrate to be achieved and the amount of change depended on the amount of carbohydrate consumed in the pre-trial diet. They were not weight loss diets and the food substitution strategy was designed to ensure weight neutrality. This was a 6 month translational style study with dietary advice given to the intervention group on only two occasions (baseline and 3 months) in the form of  $2 \times 30$  min consultations with a researcher with take home information sheets. The dietary advice was to omit all salty snacks, sweets, cake and biscuits, pies and pasties and replace them with 2 - 3 pieces fruit/day or low fat dairy (e.g. yoghurts). Breakfast of cereal/toast was to be replaced on 2 mornings per week with lean meat (e.g. steak or fish) and eggs. Lunch was to be lean meat/fish/cheese/egg salad on 3 days per week with no bread/biscuits. Dinner was lean meat- steaks or casserole/lean beef/chicken/fish with unlimited green vegetables and pumpkin. Volunteers had the option of including small amounts of starchy carbohydrate in their main meal (e.g. rice/pasta/potato) for 1 - 2 meals per week. Potentially in a volunteer who consumed 45 g of breakfast cereal each day plus 2 slices of bread for lunch and a medium (250 g) potato each evening—the maximum reduction in carbohydrate would be about 100 g per day or about 350 - 400 g per week if the above scheme was adhered to. This would represent about a 25% reduction in typical carbohydrate intake and more if snack foods were consumed e.g. from a typical 55% of energy as carbohydrate to less than 45%. Food records were not kept as this is not part of routine clinical practice.

The Australian Guide to Healthy Eating includes: 1) enjoy a wide variety of nutritious foods from these five groups every day: plenty of vegetables, including different types and colors, and legumes/beans, fruit, grain (ce-

real) foods, mostly wholegrain and/or high cereal fibre varieties, such as breads, cereals, rice, pasta, noodles, polenta, couscous, oats, quinoa and barley, lean meats and poultry, fish, eggs, tofu, nuts and seeds, and legumes/beans, milk, yoghurt, cheese and/or their alternatives, mostly reduced fat and drink plenty of water; 2) limit intake of foods containing saturated fat, added salt, added sugars and alcohol.

### 2.3. Study Protocol

Volunteers were seen on 3 occasions at baseline, 3 and 6 months and had fasting blood samples taken for lipids, glucose and HbA1c. Spot urines were also collected on each occasion and sodium, potassium and creatinine measured in order to obtain an index of bread/cereal intake as well as fruit and vegetable intake. The tests were performed at the Alfred Hospital an accredited pathology supplier using standard laboratory tests.

### 2.4. Statistics

Data was analysed using repeated measures ANOVA and Pearson's correlations using SPSS 21. Data are shown as Mean and SD. We calculated with an SD of 1% we would be able to see a difference of 1% in HbA1c ( $P < 0.05$ , 80% power) with 16 completers in each group. Our primary end points were HbA1c and fasting glucose with secondary end points of lipids and weight. It was hypothesized that the secondary endpoints were not change. Analysis was based on completers only

## 3. Results

### 3.1. Volunteer Characteristics

Forty-three volunteers were randomized but only 33 attended a baseline visit. Of those who completed the baseline visit the medication profile was 20 on metformin, 9 on sulphonylureas, 9 on insulin, 7 on DPPIV inhibitors, 4 on GLP1 analogues and 3 on thiazolidinediones. Nine volunteers took 2 medications, 6 took 3 and one took 4 and one took 5 medications while the remainder took 1 medication. Only 3 volunteers were controlled with diet alone. Baseline characteristics are shown in **Table 1**. None of the baseline variables were different between groups.

### 3.2. Glycemic Control

16 control volunteers and 11 low carbohydrate diet volunteers attended the 3 month visit. At 6 months there were 15 control (83% of those randomized) and 9 low carbohydrate diet volunteers (56%). HbA1c at 3 months was 8.0% and 7.7% and at 6 months was 8.0% and 7.3% respectively. In the control group 6 volunteers had a decrease in HbA1c and 10 had an increase or no change while the low carbohydrate group had 8 decreases and 3 increases at 3 months. At 6 months there were 7 decreases and 8 increases in HbA1c in the control group and 5 decreases and 4 increases in the intervention group. The changes in HbA1c were not significant overall (**Table 2**)

**Table 1.** Baseline characteristics of volunteers.

	Low Carbohydrate Diet (n = 15)	Control Diet (n = 18)
Gender	7M, 8F	11M, 7F
Age	59	64
Weight	86.3 ± 14.1 (62 - 110.3)	95.8 ± 23.9 (47 - 139.6)
BMI	29 ± 5.0	31.8 ± 7.4
HbA1c%	8.1 ± 1.8 (6.0 - 12.2)	8.3 ± 1.2 (6.5 - 11.1)
Fasting glucose	8.7 ± 3.1 (5 - 16)	8.6 ± 3.9 (5 - 22)
Medications (total)	29	28
Insulin	4	5
Diet control	2	1

**Table 2.** Changes in glycaemic control and lipids at 3 and 6 months.

	Change at 3 months		Change at 6 months	
	Low Carbohydrate diet (11)	Control diet (16)	Low Carbohydrate diet (9)	Control diet (15)
HbA1c	-0.57 ± 1.4	0 ± 0.8	-0.73 ± 1.4	-0.04 ± 1.0
Fasting glucose	-1.4 ± 2.6*	0.93 ± 2.7	-0.07 ± 2.1	0.47 ± 1.9
TC	0.11 ± 0.57	-0.03 ± 0.75	0.26 ± 0.83	0.13 ± 1.0
TG	0.08 ± 0.38	-0.11 ± 0.43	0.08 ± 0.33	-0.06 ± 0.44
HDL	0.18 ± 0.06	0.02 ± 0.12	-0.03 ± 0.11	0.14 ± 0.19
Weight	0.05 ± 3.4	-0.95 ± 1.6	-1.6 ± 2.8	-0.61 ± 1.7

\*P &lt; 0.03 vs control.

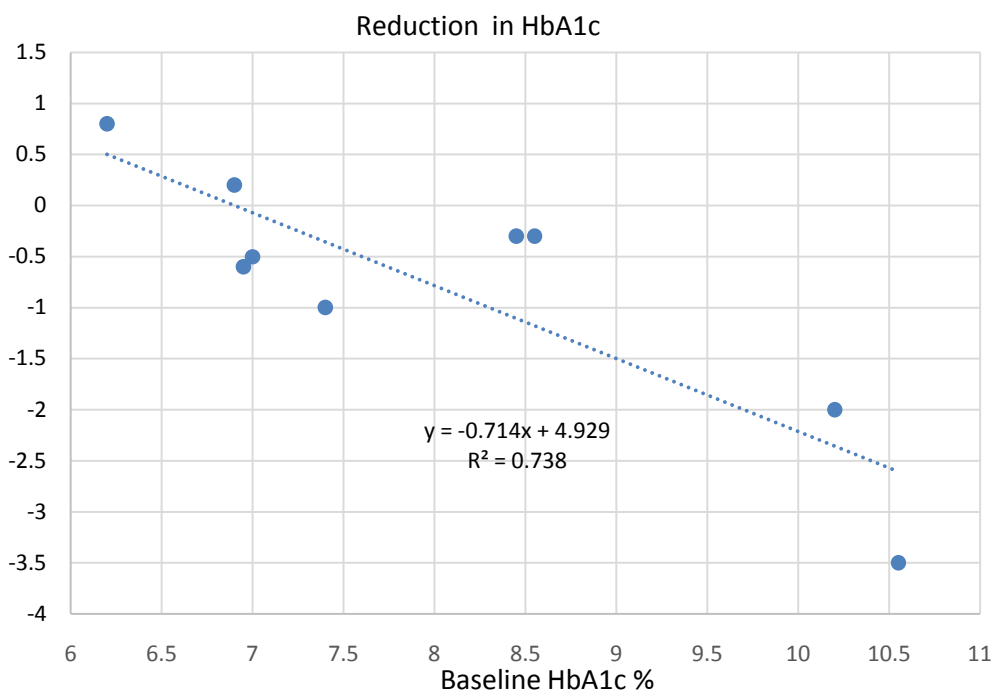
and were not different between diets ( $P = 0.1$ ) nor were the differences in the number of responders in each group. Only the change in glucose at 3 m was different between diets ( $P < 0.03$ ). Weight did not change significantly in either group with a decrease of 0.6 kg at 3 months in the control group and a 0.05 kg increase in the low carbohydrate group. Spot urine Na/Cr and N/K ratios did not change with time or between diets (data not shown). There was a modest correlation between baseline HbA1c and changes in HbA1c at 3 months ( $r = 0.52$ ,  $P = 0.1$ ) and 6 months ( $r = 0.76$ ,  $P < 0.02$ , [Figure 1](#)) in the low carbohydrate diet group. There was a correlation between the change in triglyceride and the change in weight at 3 months ( $r = 0.66$ ,  $P < 0.03$ ) only in the low carbohydrate group. There were no changes in medication recorded in this group over 6 months but this required patient notification at the end of the study and medication was not checked at each visit.

#### 4. Discussion

In this study advice to reduce carbohydrate appeared to have been followed by a majority of the group allocated to the diet but low numbers of participants prevented changes in HbA1c from being significant compared to the control group or compared to baseline. However fasting glucose was significantly different from the control diet at 3 months. Although a large number of volunteers expressed initial interest in the study only 43 were randomized and 33 attended a baseline visit with only 24 completing a 6 month visit. Thus although many people express an interest in a low carbohydrate diet the reality of following any kind of diet dramatically reduced the numbers of active participants despite recruitment being open to the study for 2 years and over 3000 patients per year being seen in the clinic. This reflects the reality in clinical practice where most patients with type 2 diabetes on multiple medications find it too difficult to follow lifestyle advice to any significant degree. Mayer *et al.* [2] reported on a 12 month weight loss study in which 37 people with type 2 diabetes achieved a weight loss of 2.5 BMI units. The low carbohydrate diet achieved a 0.7% reduction in HbA1c which was very similar to the size of the change seen in this study and was significantly different to the control diet (+0.2%  $P = 0.045$ ). Medications were also reduced in the low carbohydrate diet which initially aimed for a reduction to <20 g/day. Food records indicated that 75 g/day of carbohydrate was being consumed in the low carbohydrate group compared with 150 g/day in the low fat diet. Both groups were reasonably well controlled with a mean HbA1c of 7.6%

Although there have been two published low to moderate intensity clinic based dietary interventions in type 2 diabetes [7] [8] both were very low carbohydrate and aimed at weight loss as well as glycaemic control. Although more weight loss was achieved on the low carbohydrate diets in one of these studies neither produced significant benefits in glycaemic control. There have been no studies in a clinic setting aimed at reducing HbA1c by modest carbohydrate reduction without weight loss and without professional intervention which is usually not available in the average general practice clinic. Although most patients with type 2 diabetes are overweight and obese and would benefit from weight loss most find caloric restriction difficult and we reasoned that food substitution without caloric restriction may be more successful long term.

There have been several meta-analyses examining low and very low carbohydrate diets in type 2 diabetes. One analysis was restricted to 13 studies performed in the USA and Canada and reported that low carbohydrate diets improved HbA1c, fasting glucose and triglyceride but the effect was related to weight loss [9] while another meta-analysis restricted to studies of 12 weeks or more in duration found no effects of a low carbohydrate diet



**Figure 1.** Relationship between baseline HbA1c and change in HbA1c at 6 months in the intervention group.

[10]. Ajala *et al.* [11] examined 20 trials in type 2 diabetes and found that low carbohydrate, low GI, Mediterranean and high protein diets all led to significant reductions in HbA1c of 0.12%, 0.14%, 0.47% and 0.28% respectively. Our study was significantly more successful than these studies but numbers were limited. Weight loss may have accounted for the changes in the low carbohydrate and Mediterranean diets. Van Wyk *et al.* [12] examined 9 meta analyses with 153 trials and selected 12 studies from this group that had a duration of more than 4 weeks and had a carbohydrate intake of <45% from diet records at the end of the study. Overall there was no effect of a low carbohydrate diet on glycemic control and they concluded variable study quality accounted for the different results in each meta-analysis. Dyson [13] concluded that low carbohydrate diets were not superior to high carbohydrate diets and could not be recommended as the default diet.

### 5. Conclusion

Although we have obtained suggestive evidence that a low carbohydrate diet can be successfully implemented in normal practice without professional staff and lower fasting glucose and HbA1c, our results are limited by low participant numbers and further studies are required.

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### Authors' Contribution

Peter Clifton conceived the study, analyzed the data and wrote the manuscript. Claire Galbraith and Leah Coles designed the volunteer handout material and databases, saw the volunteers and supervised all logistical aspects of the trial.

### Conflict of Interest

The authors declare no conflict of interest.

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