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Inducing remission of Type 2 diabetes in the Caribbean: findings from a mixed methods feasibility study of a low-calorie liquid diet-based intervention in Barbados

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What's new?

- Studies of the remission of Type 2 diabetes through dietary means in people with a recent diagnosis have, to date, been conducted in predominantly white populations in the UK.
- In a predominantly black Caribbean population with Type 2 diabetes, diet-induced mean weight loss of 10 kg was associated with remission (fasting plasma glucose < 7.0 mmol/l) in 60% of participants at 8 weeks, and 38% at 8 months.
- Negative peer pressure in social situations was one of several challenges participants reported.
- Remission of Type 2 diabetes is possible in this population.
- Further support to achieve and maintain greater weight loss is desirable.

Abstract

Aim In a high proportion of people with recently diagnosed Type 2 diabetes, a short (2–3-month) low-calorie diet is able to restore normal glucose and insulin metabolism. The aim of this study was to determine the feasibility of this approach in Barbados.

Methods Twenty-five individuals with Type 2 diabetes diagnosed within past 6 years, not on insulin, BMI > 27 kg/m^2 were recruited. Hypoglycaemic medication was stopped on commencement of the 8-week liquid (760 calorie) diet. Insulin response was assessed in meal tests at baseline, 8 weeks and 8 months. Semi-structured interviews, analysed thematically, explored participants' experiences. 'Responders' were those with fasting plasma glucose (FPG) < 7 mmol/l at 8 weeks.

Results Ten men and 15 women (mean age 48, range 26–68 years) participated. Mean (SD) BMI was 34.2 kg/m^2 (6.0); FPG 9.2 mmol/l (2.2). Mean weight loss at 8 weeks and 8 months was 10.1 kg [95% confidence interval (CI) 8.1, 12.0] and 8.2 kg (95% CI 5.8, 10.6); FPG was lower by 2.2 mmol/l (95% CI 1.2, 3.2) and 1.7 mmol/l (95% CI 0.8, 2.7) respectively. Nine of 11 (82%) of those who lost ≥ 10 kg were 'responders' compared with 6 of 14 (43%) who lost < 10 kg ($P = 0.048$). The 30-min insulin increment was higher in responders at baseline and follow-up ($P \leq 0.01$). A food culture based on starchy foods and pressures to eat large amounts at social events were among the challenges identified by participants.

Conclusions The feasibility of this approach to weight loss and diabetes remission in a predominantly black population in Barbados was demonstrated.

<H1>Introduction

The Caribbean population, predominantly of African origin, has overall rates of Type 2 diabetes among the highest in the world [1,2]. In Barbados, the prevalence of diabetes in adults aged 25 years and over was 18.7% (21.0% in women, 15.9% in men) in 2012; with an obesity prevalence of 33.8% (43.4% women; 23.4% men) [3].

Historically, Type 2 diabetes has been regarded as a lifelong, steadily progressive disease [4,5]. However, recent understanding changes this. It is caused by excess accumulation of fat in the liver and pancreas in susceptible individuals, causing failure of control of hepatic glucose production in the liver and loss of insulin secretory capacity in the pancreas [6–8]. The former remains completely reversible, and the latter is reversible in a high proportion of people during the first 6 years after diagnosis. In the weight management for remission of Type 2 diabetes trial (DiRECT), remission was achieved in 46% of participants in the intervention group (compared with 4% in the control group). Weight loss was achieved through a low-calorie liquid diet, and remission success rates were associated with the degree of weight loss, being 73% in those who lost > 10 kg at 12 months [9] and 71% at 24 months [10].

The DiRECT study and associated proof of concept work were conducted in the England and Scotland, and < 2% of participants were of non-white ethnicity [7,9,11]. Successful application of this approach in populations and countries with different cultures and food systems cannot be assumed. Neither should it be assumed that the underlying physiology and metabolic responses to weight loss are the same in ethnically distinct populations [12]. The aim of this study was to examine, in people with Type 2 diabetes in Barbados, the feasibility and metabolic outcomes of the approach employed in the UK to bringing about remission of Type 2 diabetes.

<H1>Participants and methods

The overall design of this 8-month feasibility study followed that of similar work conducted in the UK [7,11] (Fig. 1). The study received ethical approval from the University of the West Indies Institutional Review Board, and from the Ministry of Health of the Government of Barbados.

<H2>Study participants

Twenty-five participants with Type 2 diabetes were recruited through a combination of publicity and contacts with local government and private healthcare providers. Participants had to be residents of Barbados with the following characteristics: aged 20–69 years; diagnosed with Type 2 diabetes (following World Health Organization criteria [13]) for 6 years or less; and with a BMI > 27 kg/m^2. Exclusion criteria were: current insulin use; HbA_{1c} > 12%; substance abuse; known cancer; myocardial infarction within the past 6 months; learning difficulties; current treatment with anti-obesity drugs; diagnosed eating disorder/purging; pregnant/considering pregnancy; evidence of liver disease (including liver enzymes more than three times above normal values) or renal disease (creatinine of > 150 μmol/l); and persons who have required hospitalization for depression or are on antipsychotic drugs.

<H2>Intervention

The intervention was delivered by a family practitioner (KB), following a detailed study protocol that included how to provide support to participants to address challenges in adhering to the dietary guidance. Participants were encouraged to phone KB between visits should they need advice.

Participants stopped any glucose-lowering medication on the day of starting the liquid diet (time 0). The liquid diet was supplied at no cost to participants and comprised four shakes per day, each shake containing 190 calories, 23 g carbohydrate, 10 g protein and 7 g fat. Participants were encouraged to consume 3 l of water, and three to four portions of high fibre low-carbohydrate vegetables per day. They were given a specially prepared recipe book for local low-carbohydrate vegetables. After 8 weeks on the liquid diet they transitioned over a 4-week period to a solid diet, with support and guidance from a local dietitian on eating healthily and taking regular exercise. Remission of diabetes was defined as achieving a fasting plasma glucose (FPG) < 7.0 mmol/l [11,14].

<H2>Data collection

Participants were seen weekly during the liquid diet phase, and monthly thereafter (Fig. 1). At each visit, weight, waist circumference, blood pressure and fasting glucose were measured following standard protocols. Height was measured at the first visit using a Seca 217 stadiometer. Weight was measured on a Seca 813 digital scale, waist and hip circumferences were measured twice, with a third measurement being taken if they differed by > 0.5 cm, and the mean of the two closest measurements used in analysis. Blood pressure was taken after the participant had been seated for at least 15 min. It was measured three times, at 3-min intervals, in the right arm using an Omron 705 CP digital monitor and an appropriate size cuff. The mean of the second and third measurements were used in analysis. Fasting glucose was measured on capillary blood using a Hemocue 201 RT analyser, with results given in plasma equivalent values.

Participants underwent three standard meal tests, each consisting of two wholegrain biscuits (Weetabix), 200 ml semi-skimmed milk, 200 ml orange juice, a white bread roll, 20 g grape jam, and 10 g margarine (equating to 575 calories, 72% carbohydrate, 15% protein, 13% fat). Venous blood

samples were taken when the participant was fasting and then at 10, 20, 30, 60, 90 and 120 min after the meal. At each time point, blood was taken for the measurement of glucose, and serum was stored at −80 °C for the subsequent measurement of C-peptide, insulin and non-esterified fatty acids (NEFA). Serum insulin was measured using the human insulin ELISA (EZHI-14K; Millipore, USA), C-peptide using the human C-peptide ELISA (EZHCP-20K; Millipore) and NEFA by NEFA-HR(2) (Wako Diagnostics, USA). In addition, the following were measured for the fasting sample: HbA_{1c} (Bayer DCA 2000+ analyser; Bayer Healthcare LLC, USA), total cholesterol, HDL cholesterol, triglycerides, calculated LDL cholesterol and alanine aminotransferase (ALT) (Roche Reflotron plus analyser; Roche Diagnostics GmbH, Germany). HbA_{1c} values were measured in NGSP units (%) and converted to IFCC (mmol/mol) units using the Master Equation [15].

<H2>β-Cell function

β-Cell function was assessed using the insulinogenic index [16], using the data from the meal tests, i.e. increment in insulin secretion between 30 min and baseline, divided by the equivalent increment in glucose. Assay results were available to calculate the insulinogenic index in 12 of 15 responders and 10 of 10 non-responders at baseline; 14 of 15 and 7 of 10 respectively at 8 weeks; and 15 of 15 and 9 of 10 respectively at 8 months.

<H2>Sample size and statistical analysis

The sample size of 25 was based on the experience of the study in Newcastle, UK [7], which demonstrated significant changes with a sample size of 11. It was estimated that 25, allowing for attrition, would provide adequate power for meaningful before and after analyses. For example, with 20 participants it is possible to demonstrate a 4 kg weight difference before vs. after, at $P < 0.05$ and with 90% power. In the Newcastle study, the mean weight loss was 15 kg. For fasting glucose, 20 participants would enable a difference 1.1 mmol/l to be detected. Similar considerations apply to other measures.

Data were analysed using STATA statistical software. Differences in continuous variables between baseline and follow-up were computed with paired *t*-tests. Independent *t*-tests were used to explore differences in continuous variables between 'responders' (fasting glucose, off medication, < 7 mmol/l by the end of 8 week diet phase) and 'non-responders' The Kruskal–Wallace test was used to compare insulin responses between these groups. The 'cs' command in STATA was used to calculate risk ratios. A 5% significance level was used and given the exploratory nature of these analyses no allowance was made for multiplicity of statistical tests.

<H2>Qualitative data collection and analysis

Individual semi-structured in-depth interviews were conducted with participants at three time points: baseline, end of the liquid diet phase (8 weeks) and end of the study (8 months). The interviews aimed to understand the experiences of participants, including the challenges they faced and the strategies they used to deal with them. All interviews with the exception of one were audio-taped and transcribed verbatim. Detailed notes were taken for the participant not wanting to be recorded. Interviews were analysed using ATLAS.ti v7 qualitative software (ATLAS.ti Scientific Software Development GmbH, Berlin Germany) and data were coded and then reviewed to extract any emerging themes.

<H1>Results

Twenty-five participants provided data at baseline, 8 weeks and 5 months. One participant failed to return for assessment at 8 months despite repeated attempts to encourage them to do so. Therefore, at 8 months data were provided by 24 participants.

<H2>Baseline clinical and metabolic characteristics

Mean BMI was 34.2 kg/m^2 (SD 6.0), age 48 (10) years, 60% were women and 88% classified themselves as black ethnicity, 8% as mixed, 4% as white. All males and 80% of females were taking

oral hypoglycaemic agents. The mean duration of diagnosed diabetes reflected the selection criteria, 3.0 (2.1) years. Details are shown in Table 1.

Mean FPG and HbA_{1c} were 9.2 (2.2) mmol/l and 65 mmol/mol (19) [8.1% (1.7)] respectively, and were similar in men and women. Mean plasma ALT was within the normal range and was higher in men than women (difference 10.8 U/l, 95% CI 2.0, 19.6) (Table 1).

<H2>Effect of intervention on weight and metabolic parameters

During the 8-week low-calorie diet phase, mean weight fell by 10.1 kg (95% CI 8.1, 12.0) (Table 2). The range of weight loss was 1.5 to 20.8 kg. Eleven of 25 (44%) people lost > 10 kg and 4 of 25 (16%) lost > 15 kg. Mean BMI fell by 3.4 kg/m^2 (95% CI 2.9, 4.0), and mean waist circumference reduced by 10.9 cm (95% CI 9.3, 12.5). Between the end of the low-calorie diet and month 8, mean weight increased by 1.8 kg (95% CI −0.3, 3.9; $P = 0.09$). On average, men lost more weight than women; 11.7% of their baseline body weight by 8 weeks compared with 8.6% in women (95% CI on difference: 0.8, 5.4; $P = 0.011$).

Following withdrawal of all hypoglycaemic agents and commencement of the low-calorie diet, FPG decreased by a mean of 1.5 mmol/l (95% CI 0.5, 2.5) by week 2, 2.0 mmol/l (95% CI 1.1, 3.0) by week 3, and 2.2 mmol/l (95% CI 1.2, 3.2) by week 8. Thus, mean fasting glucose at week 8 was 7.0 mmol/l (SD 1.4). At week 8, 60% (15/25) of the group achieved FPG < 7 mmol/l, and of those who lost > 10 kg, 82% (9 of 11) achieved FPG < 7.0 mmol/l. Between week 8 and the end of follow-up, mean fasting glucose increased by 0.6 mmol/l (95% CI −0.04, 1.15; $P = 0.07$). Six months after the end of the low-calorie diet phase, 9 of 24 participants (37.5%) who were followed up had a FPG < 7.0 mmol/l.

The decrease in mean HbA_{1c} was statistically significantly between baseline and week 8 [9 mmol/mol (95% CI 4, 15); 0.9% (95% CI 0.3, 1.4)]. It increased between week 8 and the end of the follow-up such that the mean decrease at month 8 compared with baseline was 7 mmol/mol (95% CI −4, 18; $P = 0.19$) [0.6% (95% CI −0.3, 1.6].

There was evidence of improvement in both triglycerides and HDL cholesterol levels. Compared with baseline, mean triglycerides showed a statistically significant decrease at week 8 (0.23 mmol/l, 95% CI 0.05, 0.41), and HDL cholesterol showed a statistically significant increase at the end of the follow-up period (0.17 mmol/l, 95% CI 0.01, 0.32). Fasting plasma NEFA did not change from baseline to 8 weeks (1.04 ± 0.14 and 1.17 ± 0.18 mmol/l) but fell to 0.68 ± 0.12 mmol/l ($P < 0.01$ compared with baseline) by 8 months. The post-meal suppression of plasma NEFA did not change during the study (0.56 ± 0.13, 0.73 ± 0.13 and 0.47 ± 0.23 mmol/l respectively).

<H2>Characteristics of responders vs. non-responders

Selected baseline characteristics of responders and non-responders are compared in Table 3. Responders and non-responders had a comparable age and duration of diabetes. A higher proportion of men were responders (8 of 10) than women (7 of 15), giving a relative risk of 1.7 in favour men but with a wide confidence interval (95% CI 0.9 to 3.2; $P = 0.10$). Mean baseline weight was 6.2 kg higher in responders, largely reflecting that mean baseline weight was 15 kg higher in men (Table 1). Baseline fasting glucose and HbA_{1c} were similar in responders and non-responders. All three participants who self-assigned their ethnicity as either white (1) or mixed (2) were responders, compared with 12 of 22 (55%) who self-assigned their ethnicity as black ($P = 0.32$).

Absolute and percentage mean weight loss at week 8 was slightly higher in responders vs. non-responders, being 10.7 vs. 9.2 kg and 10.1% vs. 9.4 % respectively, but neither group difference was statistically significant (Table 3). Nine of 11 (82%) of those who lost ≥ 10 kg responded, compared with 6 of 14 (42.9%) who lost < 10 kg, risk ratio 1.9 (95% CI 1.0 to 3.7; $P = 0.048$).

In responders, between baseline and week 8, fasting glucose fell by 3.2 mmol/l (95% CI 2.4, 4.5), compared with 0.8 mmol/l (95% CI −0.5, 2.1) in non-responders. There was no statistically significant change in fasting insulin in either group ($P \geq 0.2$) or in ALT ($P \geq 0.3$). A fall of borderline statistical significance was seen in mean triglyceride levels in the responders (0.27 mmol/l, 95% CI 0, 0.54; $P = 0.053$) but not in the non-responders (0.18 mmol/l, 95% CI −0.07, 0.42; $P = 0.14$).

There was no significant change in 0 to 30-min insulin increment between baseline and week 8 in either responders or non-responders ($P \geq 0.6$), nor in the 0 to 30-min C-peptide increment ($P > 0.1$).

<H2>Response to standard meal test

For the group as a whole, there was a marked improvement in meal tolerance after the weight loss period (Fig. 2). In addition to fasting glucose falling from 9.2 to 7.0 mmol/l (95% CI on the decrease: 1.2 to 3.2) between baseline and week 8, 60-min glucose fell from 13.3 to 10.4 mmol/l (95% CI 1.5 to 4.2) and 120-min glucose from 13.5 to 10.8 mmol/l (95% CI 0.9 to 4.5). At 8 months, mean fasting [7.5 mmol/l (SD 0.3)], 60-min [11.0 (0.6) mmol/l] and 120-min [10.5 (0.7) mmol/l] glucose were not significantly different from the 8 week values, and remained significantly lower ($P < 0.01$) than baseline values.

In the responders ($n = 15$), there was a significant increase in fasting plasma glucose ($P = 0.001$), but no significant change at 60 or 120 min during the meal test, between week 8 and 8 months (fasting +1.1 mmol/l, 95% CI 0.5 to 1.7; 60 min +0.8 mmol/l, 95% CI −0.1 to 1.6 and 120 min +0.1 mmol/l, 95% CI −1.4 to 1.5). In the non-responders there was no statistically significant change between baseline and 8 weeks (fasting +0.8 mmol/l, 60 min +1.6 mmol/l, and 120 min +1.1 mmol/l). Between 8 weeks and 8 months no further change occurred.

The 30-min increment in plasma insulin was statistically significantly greater at baseline in the responder group (70.2 vs. 32.0 pmol/l; difference 38.2 pmol, 95% CI 1.4 to 75.1). This difference persisted at 8 weeks (75.3 vs. 29.1 pmol/l; difference 46.2 pmol/l, 95% CI 14.6 to 77.9) and at 8 months (72.4 vs. 31.2 pmol/l; difference 41.2 pmol/l, 95% CI 8.0 to 74.4). The 30-min plasma C-peptide response was not statistically significantly higher in responders at baseline but was significantly higher in the responders at 8 weeks (3.7 vs. 1.5; difference 2.2, 95% CI 0.9 to 3.5) and at 8 months (3.4 vs. 1.3; difference 2.2, 95% CI 0.6 to 3.8).

The insulinogenic index was higher in responders than in non-responders at all meal test time points (Table 4), although this difference was only statistically significant at month 8 ($P = 0.031$).

Limiting the all the above analyses comparing responders to non-responders to the 22 black participants made only one difference of note to statistical significance. Six of eight (75%) who lost ≥ 10 kg responded compared with 6 of 14 (43%) who lost < 10 kg, risk ratio 1.8 (95% CI 0.8, 3.8; $P = 0.15$).

<H2>Participants' experiences

<H3>Structure of the low-calorie phase

At baseline, many participants were concerned that the low-calorie phase of the intervention would be the most difficult. They were surprised to realize that they were able to handle the low-calorie phase more easily than initially perceived and some reported having more energy when interviewed at 8 weeks. What most participants appreciated was the rigidity of the meal plan, which had very specific guidance on what they could or could not eat. In fact, most found the transition from the low-calorie phase to eating 'regular' foods the hardest as they attempted to navigate food choices.

<H3>Food environment and culture

The food environment proved to be a particularly difficult challenge due to temptations to consume foods not allowed during the intervention. For example, at social events it was expected that you would eat a lot of food, and if participants did not, they faced interrogation by peers. Additionally, cultural expectations dictate the acceptance of food that is offered to you: '… you can't go in people's house and not take what they offer you, they feel that you think what they have is not good enough' (Phase 1, woman), which leads to having to explain in detail why participants could not accept what was offered.

An associated challenge of the food environment was the availability and accessibility of healthy options such as fruit and vegetables. Culturally, Barbadians eat starchy and carbohydrate-heavy meals; it is not uncommon to see plates having a protein with two starches and a small amount of vegetables, so finding options when eating out was challenging, coupled with the higher cost of healthier foods compared to unhealthy foods.

<H3>Acceptability of rapid weight loss

Although rapid weight loss was a main goal of the intervention, the quick drop in weight loss was perceived in a positive light for women, but more negatively in men: '… it's sad to hear things "man you looking small, you looking bony. What wrong with you?". So, you just have to be strong mentally and laugh and say "look nothing aint really wrong". "But why you look so?" You know people say "man you look bad, something wrong with you…"' (Phase 2, man).

This perception that something may be wrong with men who were losing weight rapidly changed how some men continued to progress in the study as they were more likely to modify the intervention plan as to not lose too much weight too quickly, whereas for women the positive reinforcement spurred them on to continue the intervention.

<H3>Importance of social support

The main facilitator of success in following the intervention and losing weight that was identified in the qualitative analysis is social support. Those participants having a diverse network of informal support systems made up of family members, close friends, co-workers and other participants, as well as formal support systems including the project staff and their primary doctors, had least difficulty in following the intervention. What appeared key for many was support received from close family members, many of whom changed their dietary behaviours at the same time. However, some participants who did less well reported very different experiences, including being ridiculed at times by family members for their new food choices.

<H1>Discussion

This study demonstrates that non-diabetic levels of glucose control can be restored by dietary means in Barbadian people with Type 2 diabetes. At the end of the 8-week liquid diet, of those losing > 10 kg in weight, 82% (9 of 11) returned to non-diabetic levels of blood glucose control (FPG < 7 mmol/l). In the whole group, 38% had FPG < 7.0 mmol/l at the end of the study (8 months). The weight loss achieved in the whole group was substantial although less than that obtained by similar

methods in studies elsewhere [7,17]. Individuals who achieved non-diabetic blood glucose control were characterized at baseline by having better preserved β-cell function as indicated by a greater early insulin response to the standard test meal.

The definition of remission of diabetes used in this study is consistent with previous studies (achieving a non-diabetic level of HbA_{1c} or FPG after weight loss and off all hypoglycaemic agents) [9,11]. The threshold to diagnose diabetes remains that agreed by the American Diabetes Association and the World Health Organization (2002), as FPG ≥ 7.0 mmol/l [or subsequently, HbA_{1c} ≥ 48 mmol/mol (≥ 6.5%)]. In clinical practice, confirmation by a second test at least 2 months later is wise [14]. It is important to recognize that following weight loss, maintenance of a non-diabetic levels of FPG is associated with profound benefits in 10-year cardiovascular risk (QRISK® 23% to 7%) [8,11]. The state of 'post diabetes' is profoundly different to pre-diabetes in weight, plasma lipids and blood pressure, and even though plasma glucose levels may be above the defined normal range it is likely that this will impinge little upon their long-term health. Long-term follow-up after bariatric surgery demonstrates the low cardiovascular event rate consistent with the prognostic scores [18]. In other populations, HbA_{1c} is usually used to define overall degree of glucose control. However, we have previously demonstrated that HbA_{1c} tends to be higher in the Barbadian population for any given level of FPG giving a substantially higher prevalence of Type 2 diabetes than fasting glucose [19]. Similar findings have been reported in African Americans compared with white Americans [20–22]. The reasons for these differences are unclear and require further investigation, with hypotheses including that there are differences by ethnic group in the susceptibility to glycation of haemoglobin or that differences in underlying mean glucose concentrations are higher than reflected by fasting levels [23,24]. Given these uncertainties, in this study we have used FPG to define categories of glycaemic control.

It is notable that both plasma lipids (total and LDL cholesterol, and triglyceride) and blood pressure are lower than in comparable white European origin populations with Type 2 diabetes [7,8,11]. Nonetheless macrovascular disease is common, with mortality rates from ischaemic heart disease and

stroke in Barbados exceeding those in North America [25]. It may be that susceptibility to these factors is greater for any given measured level of exposure. This raises questions about the aetiological basis of Type 2 diabetes in the Barbadian population. For any given degree of adiposity, both liver and pancreas fat levels are lower in black populations [26]. This is reflected in the ALT levels observed in this study in comparison with our previous studies in largely white European origin groups [7,8,11]. Given the similarity of glycaemic response to weight loss, it appears likely that there are different levels of susceptibility to excess intra-organ triglyceride such that an increase from a lower baseline might be observed during the development of Type 2 diabetes in Afro-Caribbean populations. Direct study of liver and pancreas fat content is required in future studies of diabetes remission.

As noted above, mean weight loss in this study (10 kg) was less than that achieved in similar studies in the UK (15 kg). The results from the in-depth interviews with participants provide insight into the challenges they faced. Navigating social expectations around food consumption was a particular challenge. This included the fact that it is seen as normal to ‘load up’ one’s plate and not doing so was to leave oneself open to unwelcome questions. Even if participants wished to substitute starchy carbohydrates with vegetables, these typically were unavailable or available in only small quantities. This lack of availability at least in part the high price of fruit and vegetables in Barbados [27] and the fact that only 10% of the general population report eating five or more portions per day [3].

During the low-calorie diet phase, men lost significantly more weight than women and had a higher (non-significant) rate of diabetes remission. Data from the participant interviews suggest that overall men received greater support from close family members. In a society in which traditional gender roles around food preparation persist, men tended to be supported by a partner preparing their food, whereas women were more often in the position of preparing food for other family members while in parallel trying to follow the study diet.

This study has several limitations. It was a small non-randomized study to assess the feasibility in Barbados of an intervention found to be effective in the DiRECT trial [9]. The small numbers preclude meaningful subgroup analyses. Given the exploratory nature of the study the possibility of type 1 error is acknowledged. Our current follow-up of participants is to 8 months from baseline. Further follow-up will provide critical information on the potential longer term impacts of the intervention.

In conclusion, remission of Type 2 diabetes is possible in Barbados. The underlying biology of the condition in this predominantly black population appears to be similar to that demonstrated in largely white European origin populations, although we acknowledge the desirability of further work to investigate the relationships between glucose metabolism and intrahepatic and intrapancreatic fat. The qualitative findings identified the serious challenges faced by participants of adhering to the low-calorie diet and subsequently maintaining weight loss in what is a highly obesogenic environment, where two in three adults are overweight or obese and one in five has diabetes [3]. Our findings highlight the importance of social support and self-efficacy in navigating this environment and can guide improvements in the design of the intervention. However, major changes to the broader food environment in Barbados are likely to be necessary if this approach to diabetes remission is to be widely and successfully implemented.

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Competing interests

None declared.

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FIGURE 1 Overview of the study design, showing low-calorie diet (LCD), transition (T) and maintenance phases.

FIGURE 2 Change in response to the standard meal at baseline, after 8-week low-calorie diet and after 8 months' follow-up.

Table 1 Baseline characteristics of the study population

Characteristic	Men (*N* = 10)	Women (*N* = 15)	All (*N* = 25)
Age, years	51 (12)	46 (9)	48 (10)
Ethnicity, %			
Black	80	93	88
White	0	7	4
Mixed	20	0	8
Diabetes treatment, %			
Diet only	0	20	12
Oral medication	100	80	88
Time since diagnosis, years	3.0 (1.8)	3.1 (2.3)	3.0 (2.1)
Weight, kg	107.7 (22.3)	92.3 (17.6)	98.5 (20.7)
Height, cm	177.7 (8.9)	164.0 (5.6)	169.5 (9.7)
BMI, kg/m^2	33.9 (5.5)	34.4 (6.6)	34.2 (6.0)
Waist circumference, cm	110.4 (14.7)	102.0 (15.1)	105.4 (15.2)
Fasting plasma glucose, mmol/l	9.2 (2.2)	9.3 (2.2)	9.2 (2.2)
HbA_{1c}, mmol/mol	64 (21)	66 (17)	65 (19)
HbA_{1c}, %	8.0 (1.9)	8.2 (1.6)	8.1 (1.7)
Alanine aminotransferase, U/l	27.2 (14.4)	16.4 (6.7)	20.7 (11.5)
Total cholesterol, mmol/l	3.7 (0.8)	4.3 (0.7)	4.0 (0.8)
HDL cholesterol, mmol/l	0.77 (0.24)	0.86 (0.28)	0.82 (0.26)
LDL cholesterol, mmol/l	2.4 (0.8)	2.9 (0.7)	2.7 (0.8)
Triglycerides, mmol/l	1.30 (0.44)	1.04 (0.41)	1.15 (0.43)
Statin therapy, %	40	13	24
Systolic BP, mmHg	134.1 (15.6)	125.5 (11.3)	129.1 (13.7)
Diastolic BP, mmHg	79.3 (8.0)	79.7 (7.6)	79.5 (7.6)
On treatment for raised BP, %	60	40	48

Data are given as mean (SD) unless specified otherwise.

Table 2 Change in selected characteristics between baseline and follow-up

Characteristic	8 weeks *N* = 25	5 months *N* = 25	8 months *N* = 24
Weight, kg	10.1 (8.1, 12.0)§	9.9 (7.9, 12.0)§	8.2 (5.8, 10.6)§
BMI, kg/m^2	3.4 (2.9, 4.0)§	3.4 (2.8, 4.1)§	2.9 (2.1, 3.7)§
Waist circumference, cm	10.9 (9.3, 12.5)§	11.1 (9.2, 12.9)§	9.8 (7.5, 12.0)§
Fasting glucose, mmol/l	2.2 (1.2, 3.2)§	2.1 (1.0, 3.2)§	1.7 (0.8, 2.7)§
HbA_{1c}, mmol/mol*	9 (4, 15)		7 (−4, 18)
HbA_{1c}, %*	0.9 (0.3, 1.4)‡		0.6 (−0.3, 1.6)
HDL cholesterol, mmol/l*	−0.04 (−0.12, 0.05)		−0.17 (−0.32, −0.01)†
Triglycerides, mmol/l*	0.23 (0.05, 0.41)†		0.09 (−0.05, 0.22)
Systolic BP, mmHg	7.8 (−0.2, 15.7)	5.9 (−1.5, 13.2)	3.9 (−2.7, 10.6)
Diastolic BP, mmHg	7.8 (3.2, 12.4)‡	6.1 (2.6, 9.6)‡	4.3 (0.2, 8.4)†

Data are mean differences (95% confidence intervals): baseline values minus those at follow-up.

*Not measured at 5 months; †$P < 0.05$; ‡$P < 0.01$; §$P < 0.001$.

Table 3 Comparison of baseline characteristics and weight loss in responders (FPG < 7mmol/l at 8 weeks) and non-responders (FPG ≥ 7mmol/l at 8 weeks)

	Responders (*N* = 15)	Non-responders (*N* = 10)	Difference (95% CI)	*P*-value
Baseline characteristics				
Age, years	48.3 (11.3)	47.5 (9.2)	0.8 (−8.1, 9.6)	0.86
Men, %	80	20		
Women, %	46.7	53.3	1.7 (0.9, 3.2)*	0.10
Duration diabetes, years	2.9 (2.2)	3.2 (2.1)	−0.3 (−2.1, 1.6)	0.76
Weight, kg	101.0 (23.1)	94.8 (16.7)	6.2 (−11.4, 23.8)	0.47
BMI, kg/m^2	35.1 (6.7)	32.8 (4.9)	2.3 (−2.8, 7.4)	0.36
Waist circumference, cm	107.5 (16.4)	102.2 (13.3)	5.3 (−7.7, 18.2)	0.41
Fasting plasma glucose, mmol/l	9.3 (2.4)	9.1 (1.7)	0.2 (−1.6, 2.1)	0.79
HbA_{1c}, mmol/mol	63 (19)	70 (19)	−8 (−23, 8)	0.34
HbA_{1c}, %	7.9 (1.7)	8.6 (1.7)	−0.7 (−2.1, 0.8)	0.34
Insulin 30-min increment, pmol/l†	57.5 (46.1,92.2)	26.5 (21.5,39.5)	31.0 (8.4, 63.2)	0.01
HDL, mmol/l	0.76 (0.05)	0.91 (0.10)	−0.14 (−0.36, 0.08)	0.49
Triglycerides, mmol/l	1.22 (0.11)	1.03 (0.14)	0.19 (−0.17, 0.56)	0.27
Alanine aminotransferase, U/l	21.9 (13.7)	18.9 (7.4)	3.1 (−6.8, 12.9)	0.77
Systolic BP, mmHg	130.2 (13.5)	127.5 (14.5)	2.8 (−9.2, 14.7)	0.86
Weight loss at 8 weeks				
Weight loss, kg	10.7 (5.3)	9.2 (3.8)	1.5 (−2.5, 5.5)	0.18
Per cent change from baseline	10.1 (3.6)	9.4 (2.3)	0.7 (−2.0, 3.3)	0.32
Category of weight loss, %				
< 10 kg	42.9	57.1		
≥ 10 kg	81.8	18.2	1.9 (1.0, 3.7)‡	0.048

Values are means (SD) unless stated otherwise.

*Risk ratio: men vs. women. †Values are median (IQR). ‡Risk ratio ≥ 10 kg vs. < 10 kg.

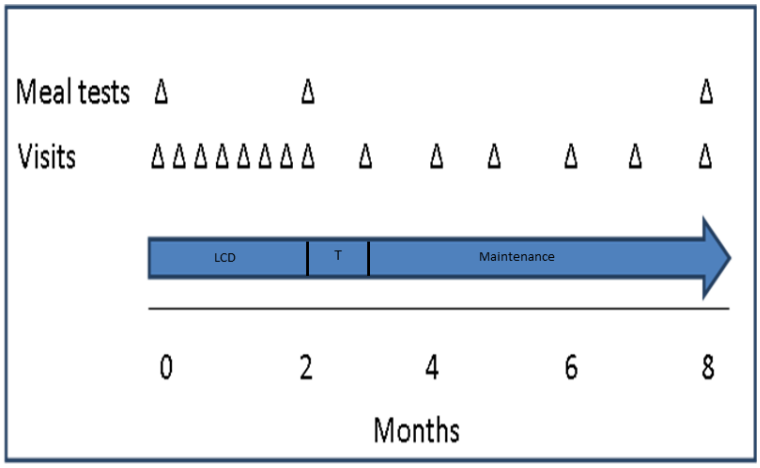
Table 4 Insulinogenic index in responders and non-responders at the three time points of the meal tests

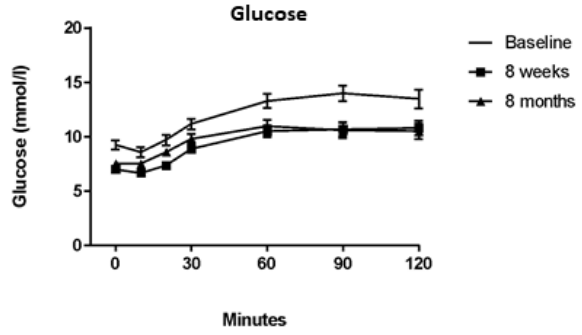
	Responders (*N* = 15)	Non-responders (N = 10)†	Difference (95% CI)	*P*-value
Baseline	576.6 (291.3)	120.9 (46.1)	455.67 (−218.45, 1129.79)	0.174
8 weeks	266.1 (67.5)	115.2 (36.2)	150.88 (−58.12, 359.88)	0.147
8 months	421.7 (106.4)	99.9 (20.3)	321.72 (32.49, 610.94)	0.031

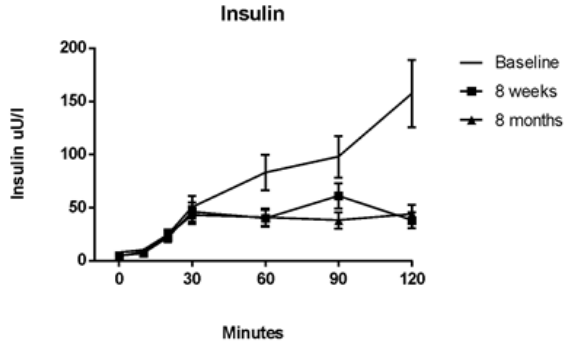
Values are given as means (SE) unless stated otherwise.

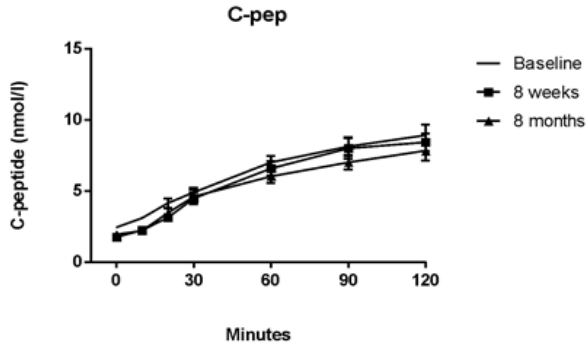
Insulinogenic index = 30-min increment in insulin (pmol/l) divided by 30-min increment in glucose (mmol/l).

†At 8 months, one participant was lost to follow-up and there were nine participants in this category.


Meal tests
Visits
LCD
T
Maintenance
0
2
4
6
8
Months


Glucose
Glucose (mmol/l)
20
15
10
5
0
0
30
60
90
120
Minutes
Baseline
8 weeks
8 months


Insulin
Insulin uU/l
200
150
100
50
0
0
30
60
90
120
Minutes
Baseline
8 weeks
8 months


C-pep
C-peptide (nmol/l)
15
10
5
0
0
30
60
90
120
Minutes
Baseline
8 weeks
8 months