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A Mixed Methods Pilot Study of a Low-Carbohydrate Diabetes Prevention Program Among Adults with Prediabetes

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ABSTRACT

Objective: (1) To evaluate the feasibility and acceptability of a Low-Carbohydrate Diabetes Prevention Program (LC-DPP) among adults with prediabetes; (2) To estimate weight loss from a LC-DPP.

Research Design and Methods: Single-arm mixed methods pilot study. We adapted the Center for Disease Control and Prevention's National Diabetes Prevention Program to teach participants to follow a very low-carbohydrate diet (VLCD). We recruited adults with body mass index ≥ 25 kg/m2 and prediabetes from one primary care clinic. Primary outcome measures were feasibility (e.g., enrollment, retention as measured by rates of survey completion) and acceptability (e.g., session attendance, qualitative feedback). Secondary outcome measures included change in weight and achievement of ≥5% weight loss. During semi-structured interviews, we explored facilitators of and barriers to VLCD adherence.

Results: 22/187 individuals (12%) enrolled. One person dropped out before a baseline weight was obtained; data from 21 individuals were analyzed. Fifteen individuals (71%) completed the 12-month survey. On average, participants attended 10.3/16 core sessions and 3.4/7 maintenance sessions. Mean (SD) percent weight change was 4.5 (5.0) at 6 months and 5.2 (6.0) at 12 months; 8/21 individuals (38%) achieved ≥ 5% weight loss at 12 months. Weight change was greater among survey completers (n=15) as compared to survey non-completers at 6 months (6.2% versus 4.5%) and 12 months (6.4% vs. 5.2%). Among interviewees (n=14), 3 factors facilitated VLCD adherence: (1) enjoyment of low-carbohydrate foods; (2) diminished hunger and cravings; and (3) health benefits beyond weight loss. Three factors hindered VLCD adherence: (1) enjoyment of high-carbohydrate foods; (2) lack of social support; and (3) difficulty pre-planning meals.

Conclusions: A LC-DPP is feasible, acceptable, and may be effective for weight loss among adults with prediabetes.

Strengths and Limitations

- This is the first study to explore a dietary strategy to augment the weight loss effectiveness of the Center for Disease Control and Prevention's National Diabetes Prevention Program (NDPP).
- A Low-Carbohydrate Diabetes Prevention Program (LC-DPP) was feasible and acceptable among participants.
- Mean weight loss among LC-DPP participants was greater than mean weight loss among historical NDPP controls.
- This was a single-arm pilot study.
- Outcomes beyond 12 months were not examined.

INTRODUCTION

An estimated 84 million U.S. adults have prediabetes and face an elevated risk of developing T2DM (1). Fortunately, individuals with prediabetes can prevent progression to T2DM. The landmark Diabetes Prevention Program (DPP) Trial demonstrated a 58 percent reduction in the 3-year incidence of T2DM among individuals with prediabetes who achieved at least 7 percent body weight loss through diet and physical activity changes (2). Accordingly, the Centers for Disease Control and Prevention (CDC) adapted the DPP's individual lifestyle intervention to a group-based program, which is now available in communities across the United States (3,4) and covered by a growing number of health plans, including Medicare (5).

Although the DPP is the prevailing public health strategy for T2DM, rates of program uptake and engagement are very low (6–8) and only 35% of real-world DPP participants achieve goal weight loss of at least 5% (4). A variety of efforts aim to augment DPP uptake and engagement, including public health campaigns to increase individuals' prediabetes risk awareness (9), initiatives to encourage primary care providers to identify and treat patients with prediabetes (10), and online and mobile health program adaptations to accommodate differences in individuals' needs and preferences (11). In contrast, no efforts, to our knowledge, specifically aim to increase the DPP's weight-loss effectiveness. Yet, doing so is critical, as weight loss is the key driver of T2DM risk reduction (12), and insurance payment hinges, in part, on participants' achievement and maintenance of at least 5% body weight loss (5).

One promising strategy to increase the DPP's weight loss effectiveness may be to change the program's dietary advice. The DPP was developed in the 1990s and thus teaches individuals to follow a low-fat, calorie-restricted diet, as this was the contemporaneous recommendation for healthy eating (15). However, the scientific merit of this recommendation has been criticized (15). Growing evidence supports the efficacy of low-carbohydrate diets (defined <26% total energy from carbohydrate per day) and VLCDs (defined as <10% of total energy from carbohydrate per day) (16) for short-term weight loss

(17–19), long-term weight maintenance (20–22), and improved glycemic control, particularly among individuals with T2DM and insulin resistance (16,23,24).

Several prior studies have effectively used VLCDs to promote weight loss among patients with prediabetes (25,26). However, these interventions are costly and often require specialty care, which limit their ability to be scaled. In contrast, the NDPP uses non-medical coaches to deliver the program in a variety of community-based settings (27). Accordingly, we hypothesized that a low-carbohydrate Diabetes Prevention Program (LC-DPP) may be better for weight loss and T2DM prevention than the traditional, low-fat DPP, and, if effective, a LC-DPP could be readily scaled using lay educators and existing DPP infrastructure and systems for monitoring and ensuring program fidelity (28). This mixed methods pilot study has two aims: (1) to test the feasibility (e.g., enrollment and retention rates) and acceptability (e.g., session attendance, qualitative feedback) of a LC-DPP; and (2) to estimate weight loss from the intervention.

METHODS

We conducted a single-arm pilot study to test the acceptability, feasibility and preliminary efficacy on weight loss of a LC-DPP among individuals with prediabetes (clinical trial reg. no. NCT03258918, ClinicalTrials.gov). The study was approved by the University of Michigan Institutional Review Board and conducted from August 2017 to October 2018. We used a mixed methods intervention design with quantitative data collected at baseline, 6-months, and 12-months and semi-structured interviews conducted at 6-months and 12-months. The purpose of embedded qualitative interviews was to better understand participants' experiences with the intervention and to help explain our quantitative findings (29) .

Setting and Participants

Individuals were recruited from one Michigan Medicine primary care clinic. Inclusion criteria were: (1) overweight, defined as body mass index (BMI) ≥ 25 kg/m^2 (30); (2) hemoglobin A1c (HbA1c) between 5.7-6.4% drawn within 6 months of the study start date; (3) willingness to participate in group-based classes; and (4) able to engage in at least light physical activity. Exclusion criteria were: (1) history

of type 1 diabetes or type 2 diabetes; (2) current participation in another lifestyle or behavior change program or research study; (3) following a vegetarian or vegan dietary pattern; (4) inability to read, write, or speak English; (5) inability to provide informed consent; or (6) pregnant or intention to become pregnant during the intervention period. We used an Electronic Health Record (EHR) reporting tool to identify individuals who met study eligibility criteria. A study invitation letter was sent to 187 individuals. Individuals interested in study participation emailed the study team and were then screened by telephone to ensure they met study eligibility criteria. Informed consent was obtained electronically using RedCap, a secure survey platform (31).

Intervention

The CDC offers two approved DPP curricula: (1) 2012 National Diabetes Prevention Program (NDPP) and (2) *Prevent T2* (28) . While *Prevent T2* is a newer program iteration, it has not been evaluated in peer-reviewed literature (4) and its effectiveness as compared to the 2012 NDPP is unknown. To facilitate comparison between our LC-DPP and published data on community-based DPPs, we modified the CDC's NDPP rather than *Prevent T2*.

The NDPP curriculum consists of 16-weekly sessions delivered over 6 months (i.e., core phase) followed by 6-8 bimonthly or monthly sessions (i.e., maintenance phase). In addition to teaching participants to follow a low-fat diet, the program also instructs individuals to engage in at least 150 minutes of moderate intensity physical activity per week and to use behavioral strategies (e.g., problem solving) to maintain lifestyle changes over time.

We adapted the NDPP's dietary advice to teach participants to follow a VLCD, restricting carbohydrate intake (not including fiber) to 20-35 grams per day during the program's core phase. Allowable foods included: meats, fish, poultry, eggs, cheese, seeds, nuts, leafy greens, non-starchy vegetables, and some fruits (e.g., berries). Participants were also taught to use low-carbohydrate substitutes when cooking or baking (e.g., almond flour in place of wheat flour). To minimize potential side effects (e.g. headache, constipation, muscle cramps, diarrhea, general weakness) participants were instructed to replace one meal a week with a low-carbohydrate alternative, starting with breakfast and

snacks. During the LC-DPP's maintenance phase, participants were instructed to gradually reintroduce carbohydrates (e.g., 5 non-fiber grams of carbohydrates per week) if: (1) they had met their weight loss target and (2) if they desired to liberalize their carbohydrate intake. Consistent with NDPP operating procedures, LC-DPP participants were asked to maintain daily food logs; these were submitted to the lifestyle coach at each session and then returned to participants with written feedback on food choices at the following session.

We partnered with the National Kidney Foundation of Michigan (NKFM), a local leader in community-based NDPP delivery. We trained an experienced NKFM lifestyle coach to deliver the LC-DPP. Training consisted of: (1) the coach's self-guided review of LC-DPP materials and online low-carbohydrate resources; (2) in-person training with the coach and study team, totaling approximately 4 hours; and (3) assessment of the coach's low-carbohydrate knowledge using a 22-item survey (Appendix 1). During the training period, our coach adapted her personal eating habits to adhere to a low-carbohydrate meal plan; she continued this eating pattern throughout the study period.

Participants' primary care physicians (PCPs) were notified via HIPPA-compliant messaging that their patient(s) was/were participating in this study. PCPs received written material about the study as well as potential side effects of low-carbohydrate diets and management strategies (e.g., magnesium for muscle cramps).

Primary Measures: Feasibility and Acceptability

Primary outcome measures were feasibility (e.g., uptake and retention rates) and acceptability (e.g., session attendance, qualitative feedback). LC-DPP uptake rate was defined as the number of participants recruited to the intervention divided by the total number of individuals invited to participate. LC-DPP retention rate was determined by calculating the rate of completion of the 6-month and 12-month surveys. Because some individuals remained engaged in the intervention (e.g., communicated via phone or email with the coach) despite personal barriers to in-person session attendance, we used survey

completion rate rather than a session attendance threshold (e.g., attendance at 9 core sessions) to measure study retention.

Intervention acceptability was determined by calculating the rate of attendance at core and maintenance sessions. Rates of session attendance were compared with the CDC's Diabetes Prevention Recognition Program (DPRP) standards (28). The DPRP monitors the fidelity and quality of community-based DPPs, and requires that at least 60% of program participants attend ≥9 core sessions and ≥3 core sessions. To further understand the program's acceptability, we conducted semi-structured interviews at 6 and 12 months. During interviews, we explored participants' general experiences with the intervention as well as specific facilitators of and barriers to VLCD adherence.

Secondary Measures:

Change in body weight: Body weight was measured and recorded at each attended session. We calculated average body weight change and percent body weight loss at the end of the program's core phase (6 months) and maintenance phase (12 months). Among session non-attendees, we attempted to schedule 6- and 12-month weigh-ins at participants' convenience within 2 weeks of the final core and maintenance sessions. All weights were obtained using the same calibrated scale.

Change in HbA1c: Baseline HbA1c was identified according to study inclusion criteria and abstracted from the electronic health record (EHR). Primary care physicians were notified that their patient(s) was/were participating in this intervention and they were asked to order HbA1c at 6 and 12 months. Change in HbA1c was calculated by subtracting participants' HbA1c at 6 and 12 months from baseline values.

Online Surveys: At baseline, 6 months, and 12 months, study participants were invited to complete an online survey via RedCap (31). At baseline, participants were asked to provide demographic and socioeconomic information. In each survey, we assessed participants' experiences of physical symptoms, which are known to be potential side effects of VLCDs. These include: bad breath, acne, gastrointestinal symptoms (e.g. constipation, diarrhea), dizziness, dry mouth, excessive thirst, headaches, and muscle

cramps. Survey response options were: not at all; 1 day a week; 2-3 days a week; 4-5 days a week; and 6-7 days a week.

Analysis

Quantitative analysis

Descriptive statistics were used for baseline survey response data including demographic and socioeconomic characteristics and self-reported side effects. For all continuous outcomes, mean change and standard deviation from baseline to 6 months and 12 months were calculated. We used paired *t*-tests to compare self-reported physical symptoms at 6 and 12 months compared to baseline. All analyses were conducted using Stata 14.

Qualitative analysis:

Semi-structured interviews were recorded and transcribed verbatim. Interviews were imported into qualitative analysis software. Two investigators independently read and coded transcribed interviews. Interviews were then coded jointly using consensus conferences. Interviews were analyzed using directed content analysis, meaning the codes were created to reflect the main topics in the interview guide and to characterize the patterns and themes that emerged from the data (32).

Integrated analysis

Integration—the mixing of quantitative and qualitative data (33)—occurred after the study period. We merged qualitative data with weight loss data to better understand the factors that might have influenced weight loss outcomes.

Patient and public involvement: There was no patient or public involvement with development of this pilot study. Rather, we sought feedback from study participants. These data will be used to refine the intervention for a larger-scale trial, which will also be informed by stakeholder groups including patients with prediabetes, primary care team members, and community partners (e.g., NKFM).

RESULTS

Intervention uptake: A total of 187 potentially eligible individuals were sent study invitation letters via postal mail. Thirty-two individuals (17%) expressed interest in study participation and 22 (12%) enrolled in the study within two weeks. Reasons for non-enrollment included: unable to reach (n=4); active participation in another weight loss intervention (n=2); unwilling or unable to participant in group classes or follow VLCD (n=3). One person was placed on a waitlist because we met our recruitment target (n=22), which was determined by room-size constraints. One participant dropped out of the study before a baseline weight could be obtained and she was therefore excluded from our analyses.

Baseline Characteristics

Demographic and socioeconomic characteristics were assessed at baseline (**Table 1**). Most participants were males (57%), white (86%), and educated, with 85% attaining education beyond high school. The mean age was 58.9 years (SD 11.0). At baseline, mean BMI was 34.1 kg/m^2 (SD 5.4) and mean HbA1c level was 5.9% (SD 0.22%).

Quantitative Analyses:

Retention: Eighteen out of 21 participants completed the 6-month survey and 15 completed the 12-month survey, resulting in a retention rates of 86% and 71%, respectively.

Session attendance: Participants attended a mean (SD) of 10.3 core sessions and 3.4 (2.7) maintenance sessions. Fourteen participants (67%) attended at least 9 core sessions and 11 participants (52%) attended at least 3 maintenance sessions.

Change in weight and HbA1c level: **Table 2** shows weight and HbA1c outcomes at 6 and 12 months among all participants (n=21) and among those who completed the 12-month survey (n=15). No participants progressed to T2DM, defined by HbA1c > 6.4%, during the study period.

Change in self-reported physical symptoms: There were no statistically significant differences in self-reported side effects at 6 or 12 months compared to baseline.

Adverse Events:

One participant suffered an ischemia stroke during the program's core phase.

Qualitative Analyses:

Participant Experiences with the Intervention

Fourteen participants participated in semi-structured interviews; 13 participated at 6 months and 12 participated at 12 months. During these interviews, we explored participants' experiences with the program, including barriers to and facilitators of adhering to a low-carbohydrate meal plan. At 12 months, we also explored participants' plans to continue to follow a low-carbohydrate meal-plan. These qualitative data were integrated with interviewees' weight change data to better elucidate factors that may influence participants' weight change.

Over half (n=8, 57%) of interviewees were female. Other baseline characteristics were similar between interviewees and non-interviewees (**Table 1**). At 12 months, mean (SD) percent body weight loss among interviewees was 7.0 (6.5) percent. Half (n=7) of interviewees achieved the program goal of ≥5% body weight loss at 12 months. **Table 3** shows key themes and representative quotes stratified by weight goal achievers and non-achievers.

Among weight goal achievers (n=7), three key themes emerged that facilitated adherence to the low-carbohydrate meal plan: (1) enjoyment of low-carbohydrate foods; (2) diminished hunger; and cravings (3) health benefits beyond weight loss.

The majority of weight goal achievers (n=5) found the meal plan easy to follow due to palatability of the diet and availability of low-carbohydrate substitutes for foods such as potatoes and rice. One participant noted, "In the lunch time, I'll substitute [sandwich bread] with a low-carb wrap. There's a 4-gram wrap that I could use…The only thing you're replacing at dinner time from a carb standpoint would be maybe some potatoes or pastas, and [there are] really great substitutes…there's a low-carb pasta option. And then of course [there's] cauliflower mashed potato. When you are doing something like a taco salad with cheese and meat and sour cream and salsa, all of that fits [in the meal plan]."

Over half (n=4) of weight goal achievers noted diminished hunger and cravings. For example, one participant commented, "I just love that I'm losing weight. It's the best diet I have ever been on, and I've been on a lot. And it seems effortless, it just seems like it's melting off. And I'm eating good and I'm

not hungry…" Another noted, "When I eat a higher fat diet, I'm not hungry. And that's been a big surprise to me." One weight goal non-achiever endorsed diminished hunger when she adhered to the low-carb meal plan; however, she also described social pressures to consume carbohydrates and non-adherence to the intervention at least 1-2 days per week.

Almost all (n=6) weight goal achievers experienced health benefits in addition to weight loss, which motivated their continued adherence to the low-carbohydrate meal plan. Several participants described increased energy levels and improved sleep. One stated, "[I was able] to decrease my blood pressure medications…[I'm] someone who's been on high blood pressure medication for probably 15, 20 years, now it's cut in half, so that's significant."

Among weight goal non-achievers (n=7), three key themes emerged that hindered adherence to the low-carbohydrate meal plan: (1) difficulty giving up high-carbohydrate foods; (2) lack of social support; and (3) difficulty planning ahead.

The majority of weight goal non-achievers (n=5) described difficulty giving up carbohydrates due to food preferences, and this was a particular challenge in the absence of social support. One participant commented, "The hardest [part is that] it's so much fun to go out for ice cream with my friends or just to go to a restaurant. And I don't like to have to order a salad or something... It's just kinda hard I guess, being around other people who are eating stuff that I shouldn't have." Another commented, "I live with somebody who eats things that I should not have. And it's become very difficult to resist those, especially as I go farther and farther into the program." In contrast, only one weight goal achiever noted difficulty giving up carbohydrates. However, this challenge was mitigated by the support of a spouse who also adhered to the meal plan: "The hardest thing for me, personally, is that I love bread, and I love potato, [but] as long as [my spouse an I] are working together on this, we're great."

Several weight goal non-achievers (n=3) described difficulty with planning low-carbohydrate meals. One noted, "Probably the [biggest challenge] is the pre-planning that you have to do…[when] I was going grocery shopping, I had meals planned, and…I was doing much better than if I run out of food and I'm hungry and I just want something now."

Almost half (n=6) the interviewees expressed concern about potential adverse health consequences of increased dietary fat intake, including heart disease and elevated cholesterol levels. One participant stated, "For years and years and years, I've heard eating red meats, cheeses, and nuts, and low carbohydrate foods…is not good for your coronary system, your heart. You gotta understand the last 50 years, [All I heard] was…sausage and steak and hamburger, and pork chops are not good for you. They're not good for your heart. But now it seems like things are changing. That's the only thing that bothers me. Otherwise, it's working great."

DISCUSSION

We tested the feasibility and acceptability of a Diabetes Prevention Program in which participants were taught to follow a carbohydrate-restricted rather than a fat-restricted meal plan. Twelve percent (n=22) of eligible individuals enrolled in our study within 2 weeks of receiving an invitation letter. LC-DPP participation was slightly higher than that observed in traditional DPPs (6–8), including those offered by our institution's self-funded health plan (34). Given room-size limitations and the pilot nature of this study, we ceased recruitment efforts once we met our enrollment target and we may therefore be underestimating potential LC-DPP participation. Over half of LC-DPP participants were male while the majority of NDPP participants are female (4). Study retention, as measured by survey completion, was high (85%, n=18) at 6 months and decreased at 12 months (71%, n=15). Similarly, attendance at LC-DPP core sessions was high, meeting CDC DPRP standards (28) with 67% (n=14) attending at least 9 core sessions; attendance decreased during the program's maintenance phase with only 52% (n=11) attending at least 3 maintenance sessions.

To our knowledge, this is the first study that aims to augment the weight loss effectiveness of the CDC's NDPP by modifying the program's dietary advice. At 12 months, percent body weight loss among all LC-DPP participants was greater than weight loss among historical NDPP controls (5.2% versus 4.2%) and an similar number of LC-DPP participants achieved at least 5% body weight loss (38% versus 35%) (4). Meta-analyses of NDPPs demonstrate a positive association between session attendance

and body weight loss (4,27). Due to sample size limitations, we were unable to evaluate the relationship between LC-DPP attendance and body weight change. However, among our sample, weight change was greater among survey completers (n=15) as compared to survey non-completers at 6 months (6.2% versus 4.5%) and 12 months (6.4% vs. 5.2%).

During qualitative interviews, we explored facilitators of and barriers to low-carbohydrate dietary adherence. These data not only provide insight into the factors that may influence individuals' weight change outcomes, but also reveal potential opportunities to refine and tailor the intervention. For example, consistent with prior literature (35), our participants identified social support as a key factor in dietary adherence, suggesting that LC-DPP partner classes and or peer-support programs may be one strategy to augment program adherence. Furthermore, interviewees that achieved goal weight loss described enjoyment of the low-carbohydrate diet as compared to weight goal non-achievers who struggled to give up the carbohydrate-rich foods that they loved. Participants that do not adhere to the low-carbohydrate meal plan due to non-enjoyment of allowable foods may benefit from other evidence-based interventions for T2DM prevention (e.g., traditional DPP, metformin) or weight loss (e.g., Weight Watchers, pharmacotherapy, bariatric surgery), and these alternatives should be readily offered.

The majority of interviewees expressed fear regarding the diet's fat content, reflecting the widely-held belief that dietary fat and cholesterol increase cardiovascular disease risk. While observational data demonstrating this association emerged in the 1950s (36), the causative role of dietary saturated fat and cholesterol in heart disease is not well-established (37). Furthermore, the Women's Health Initiative, the largest randomized controlled trial to evaluate health outcomes of low-fat diet adherence, showed no reduction in cardiovascular disease risk among intervention versus control group participants (38). Growing literature demonstrates favorable changes in cardiovascular disease risk factors (e.g., blood pressure) and serum biomarkers (e.g., LDL, HDL, and triglycerides) among individuals following low-carbohydrate, high-fat diets (16,17,19,22). Accordingly, the 2015-2020 U.S. Dietary Guidelines removed prior recommended limits on dietary fat and cholesterol intake, and clinical practice guidelines for T2DM (39) and obesity management (40) now endorse carbohydrate restriction as one evidence-based approach

to lifestyle modification. Despite these changes, however, pervasive fears regarding dietary fat remain one primary barrier to implementation of a LC-DPP. We plan to revise the LC-DPP curriculum to better address participants' concerns and we will test serum lipids in future program evaluations.

LIMITATIONS

First, we recruited individuals from one primary care clinic within an academic medical center, and our results are not generalizable to other populations. Second, we did not evaluate outcomes beyond 12 months, and are therefore unable to assess long-term adherence to a carbohydrate-restricted meal plan. Finally, because this was a pilot study designed to evaluate feasibility and acceptability, we cannot assess the intervention's weight loss effectiveness. A large-scale comparative effectiveness trial of the LC-DPP versus traditional DPP is warranted.

CONCLUSIONS

The CDC's NDPP is widely available throughout the United States. Yet, many program participants do not achieve the program's weight loss goal of at least 5%. A DPP adapted to teach participants to follow a low-carbohydrate rather than a low-fat diet may be one effective way to increase the program's weight loss effectiveness. In this study, we demonstrate that a LC-DPP is feasible and acceptable. Future work is needed to further evaluate the LC-DPP's weight loss effectiveness as compared to the NDPP. It is critical to explore issues concerning dietary adherence and sustainability as well as biomarker (e.g., lipid, HbA1c) changes and incident chronic disease (e.g., T2DM, cardiovascular disease) over time. Lastly, future work should explore the factors that facilitate or hinder LC-DPP weight loss success (e.g., presence or absence of social support) and develop tailored strategies that address these factors.

FOOTNOTES

Contributors: D.G., L.S., and C.R. designed the study. D.G., L.S., K.P., and A.T. developed the intervention. K.P., T.A., B.L., P.B., and S.S. collected the data. D.G. and C.R. analyzed the data; they take full responsibility for the integrity of data analyses. D.G. drafted the manuscript. All authors critically revised the manuscript.

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Data sharing: De-identified data may be shared pending University of Michigan Institutional Review Board review and approval. Please email dhafez@med.umich.edu.

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TABLES

Table 1. Baseline characteristics			
	All participants (n=21)	Program completers[1] (n=15)	Semi-structured interviewees (n=14)
Mean age in years, mean (SD)	58.9 (11.0)	60.5 (10.2)	58.7 (9.4)
Male, n (%)	12 (57.1)	8 (53.3)	6 (42.9)
White, n (%)	18 (85.7)	13 (86.7)	12 (85.7)
Education > high school, n (%)	17 (85.0)	12 (80.0)	13 (92.9)
Married / partnered, n (%)	15 (71.4)	12 (80.0)	10 (71.4)
Mean BMI in kg/m^2, mean (SD)	34.1 (5.4)	33.9 (4.2)	32.7 (3.1)
Baseline HbA1c, mean (SD)	5.9 (0.2)	6.0 (0.2)	5.9 (0.2)
[1]Defined has having completed the 12-month survey.			

Table 2. 6-month and 12-month results among all participants (n=21) and 12-month survey completers (n=15).				
Outcomes (mean (SD) or N (%))	6 months		12 months	
	All (n=21)	Completers (n=15)	All (n=21)	Completers[1] (n=15)
Weight change in kg	-4.3 (4.8)	-6.0 (4.7)	-4.9 (5.8)	-6.1 (6.1)
Percent weight change	4.5 (5.0)	6.2 (4.8)	5.2 (6.0)	6.4 (6.4)
At least 5% weight loss	9 (42.9)	9 (60.0)	8 (38.1)	7 (46.7)
At least 10% weight loss	3 (14.2)	3 (20.0)	6 (27.3)	5 (33.3)
HbA1c change	-0.1 (0.2)	-0.2 (0.2)	0.06 (0.3)	0.04 (0.4)
[1]Defined has having completed the 12-month survey.				

Table 3. Key themes and representative quotes stratified by percent body weight loss.	
Key Theme	**Representative Quotes**
≥5% body weight loss at 12 months (n=7)	
Enjoyment of low-carbohydrate foods	"[I'm eating] all the cheese and the meat and the vegetables I'm allowed. I'm enjoying all of it. And I found snacks like sugarless jello…beef sticks, salami with cheese…and I'm really enjoying it…If I have cake it'll be here and there, like for a party, but I know that I can get right back on this diet in the next day." *-14.5 kg (18% body weight) at 12 months*
Diminished hunger and cravings	"I don't have cravings. I like the fact that I'm not craving food and thinking about food all the time." *-8.6 kg (9.5% body weight) at 12 months*
Health benefits beyond weight loss	"By losing the weight, I feel more active. It seems like my joints don't hurt as bad." *-14.5 kg (14% body weight) at 12 months*

≤5% body weight loss at 12 months (n=6)	
Difficulty giving up high-carbohydrate foods	"The hardest thing is avoiding food that I like or love, like breads and mashed potatoes and potato chips and pasta and going out to dinner and having a nice, big juicy hamburger on a nice bun. Just taking the bun off, not having pasta, not having mashed potatoes, I miss that. But, if I see the weight loss keep going, I'm okay to tolerate that." *-3.6 kg (3.4% body weight) at 12 months*
Lack of social support	"It's very hard sometimes when you're traveling with friends, going on road trips, going to restaurants, watching everybody eat, the high carbohydrate food, being of a Mediterranean descent with pastas and stuff like that, spaghettis and pizzas and noodles, it's very hard to adhere to it at times." *-2.2 kg (2.3% body weight) at 12 months*
Trouble pre-planning meals	"I think just like with any sort of food awareness…there's time involved, and it's just hard to pre-plan and make meals that would benefit me and that my kids would like." *-0.63 kg (0.6% body weight) at 12 months*

Appendix 1. Quiz to assess LC-DPP teacher's knowledge about low-carbohydrate meal plan

Please choose all answers that are correct (by bolding or starring the right answer or by e-mailing me your choices in plain text). More than 1 answer will be correct.

1. Which of these fast-food restaurants reliably have standard low-carb options:
   a. Jimmy John's
   b. Chipotle
   c. Chinese restaurants

2. When making something low-carb at a restaurant make sure to consider:
   a. asking for extra butter pats or low-carb sides if they aren't serving you enough fat
   b. asking for lettuce-wrapped sandwiches and burgers
   c. checking for how salty the dressings are

3. Some low-carb flours include:
   a. almond flour
   b. cauliflower
   c. coconut flour
   d. rice flour

4. When someone is following a low-carb diet, we want their weight loss to be:
   a. more than 5 pounds a week at first
   b. less than 5 pounds a week at first
   c. generally we don't care how fast or slow their weight loss is, although if they're not at their ideal weight and they're still not losing weight, it's time to troubleshoot

5. Low-carb diets tend to make people:
   a. hungrier and less thirsty
   b. hungrier and more thirsty
   c. less hungry and less thirsty
   d. less hungry and more thirsty

6. If someone is constipated, they could try:
   a. taking a magnesium supplement
   b. drinking more water
   c. adding in more foods with potassium

7. When attending a party, how can someone prepare to stick to their low-cab meal plan?
   a. bring something low-carb
   b. eat before hand so they don't arrive very hungry
   c. give themselves a non low-carb treat at the party
   d. pre-think how they will deal with peer pressure at the party

8. What low-carb foods can often be found at convenience or corner stores?
   a. salted nuts (ideally lower carb like almonds, walnuts, and pecans and not higher carb like cashews and pistachios)
   b. hard boiled eggs
   c. string cheese
   d. pork rinds (make sure they don't include trans fats)

9. Net carbs:
   a. are total grams of carbohydrates minus grams of fiber
   b. are also called non-fiber grams of carbohydrates
   c. do not include naturally present sugars
   d. should be no more than about 20-35 grams a day for someone following a very low-carbohydrate diet

10. A very low-carb diet typically:
   a. includes fruit other than berries
   b. increases blood pressure
   c. includes saturated fat from animal and plant sources

11. Rare side effects of a low-carb diet include:
   a. insomnia
   b. hair loss
   c. more cavities
   d. diarrhea

12. A participant is facing a weight-loss plateau. What are some possible causes?
   a. eating too many calories
   b. consuming foods with artificial sweeteners most days
   c. poor sleep
   d. eating more than 40 grams of protein at once

13. A participant says they're feeling dizzy or woozy. What are some possible causes?
   a. Insufficient intake of water and salt
   b. Perceived or actual hypoglycemia
   c. Low blood pressure

14. A participant is worried about following a low-carb diet since they are very physically active and don't want it to hurt their performance. How might you respond?
   a. Weight loss on a low-carb diet is typically muscle-sparing, which can help preserve athletic performance
   b. Lots of athletes, especially those who do sports that require endurance, do quite well on a low-carb diet, since it prevents "hitting the wall" or "bonking."
   c. They should not exercise heavily while following a very low-carbohydrate diet.

15. What should participants know about alcohol?
   a. When on a low-carb diet, participants may get drunk more easily from less alcohol.
   b. Unsweetened and unflavored liquor has 0g net carbs.
   c. Alcohol may decrease fat burning and weight loss

16. What types of fats are preferred on a low-carb diet?
   a. Lard with partially hydrogenated oils added
   b. Coconut oil
   c. Olive oil
   d. Butter

17. Which of the following are true about sugar alcohols?
   a. Calculate net carbs by only counting half of the grams of sugar alcohols
   b. They can cause intestinal distress and flatulence

c. Erythritol is often considered to have the least amount of influence on blood sugar of all the sugar alcohols
d. They are an essential part of a low-carb diet.

18. A participant is complaining of intestinal distress. What might be causing it?
a. Cauliflower
b. Sugar-free gum
c. Erythritol
d. Broccoli

19. Which of these foods are potentially problematic on a low-carb diet because of their carb content?
a. Starchy vegetables like carrots
b. Butter
c. Chocolate with a cacao content less than 85%
d. Bacon and processed meats with added sugars

20. Which of the following typically improve when someone follows a low-carb meal plan?
a. triglycerides
b. weight
c. HbA1c

Amount Per Serving	
Calories 180	Calories from Fat 100
	Calories from Saturated Fat 15
	% Daily Value*
Total Fat 11g	**17 %**
Saturated Fat 2g	**9 %**
Trans Fat 0g	
Polyunsaturated Fat 3.5g	
Monounsaturated Fat 5g	
Cholesterol 0mg	**0 %**
Sodium 110mg	**5 %**
Potassium 150mg	**4 %**
Total Carbohydrate 17g	**6 %**
Dietary Fiber 14g	**54 %**
Sugars 2g	

21. How many net grams of carbohydrates are in the food to the left?

a. 17
b. 14
c. 3
d. 2

Amount per serving	
Calories	**230**
	% Daily Value*
Total Fat 8g	**10%**
Saturated Fat 1g	**5%**
Trans Fat 0g	
Cholesterol 0mg	**0%**
Sodium 160mg	**7%**
Total Carbohydrate 37g	**13%**
Dietary Fiber 4g	**14%**
Total Sugars 12g	
Includes 10g Added Sugars	**20%**
Protein 3g	

22. How many net grams of carbohydrates are in the food to the left?

a. 37
b. 34
c. 27
d. 25

A Mixed Methods Pilot Study of a Low-Carbohydrate Diabetes Prevention Program Among Individuals with Prediabetes

STUDY PROTOCOL

A. Background and Significance

An estimated 86 million US adults are have prediabetes [11], and, without intervention, many will develop T2DM over time [12]. Fortunately, T2DM can be prevented or delayed through modest lifestyle changes. The landmark Diabetes Prevention Program (DPP) Trial demonstrated a 58 percent reduction in the 3-year incidence of T2DM among individuals with prediabetes who achieved 7 percent body weight loss and engaged in routine physical activity [13]. Accordingly, the DPP lifestyle intervention has been translated to communities across the United States [14][15], and, on average, participant weight change is 4 percent at 12 months [16]. Thus, while group-based DPPs and can effectively promote weight loss among some participants, many DPP participants do not achieve the program goal of 5 to 7 percent body weight loss.

Novel strategies to help participants achieve DPP weight-loss goals are important for two key reasons. First, weight loss is the primary driver of T2DM risk reduction [17], and the potential population health impact of the intervention is diminished when participants do not lose weight. Second, a growing number of health plans including Medicare offer coverage for the DPP [18][19] and reimbursement is largely tied to weight loss of at least 5 percent at 6 months and 12 months [20] . The DPP costs approximately $400-$500 per participant per year [14]. Unfortunately, organizations that offer the DPP may be reimbursed for much less than this if participants do not meet weight loss goals, which could significantly compromise the program's long-term financial sustainability.

One promising approach to help DPP participants lose more weight may be through a low-carbohydrate (LC) dietary intervention. Consistent with United States Dietary Guidelines (USDG) [21], the original DPP Trial [13] and translational group-based curricula [22][23] recommend a low-fat (LF), calorie-restricted diet. However, there is growing controversy regarding the scientific merit of the Dietary Guidelines [21][1] as well as growing recognition that LC diets may be more effective than LF diets for short-term weight loss [2][3] and long-term weight maintenance [4][5]. Notably, weight loss occurs without calorie restriction [24] and LC diets improve blood glucose levels among individuals with T2DM and insulin resistance [24][25][26]. Thus, a LC dietary intervention for prediabetes may augment individual weight loss and T2DM risk reduction while also maximizing third-party reimbursement.

B. Objective

In this mixed methods pilot study, we aim to test whether a LC-DPP may lead to greater weight loss than the original DPP. In addition to objective measures of this program's preliminary efficacy (e.g. weight, HbA1c) we will also obtain qualitative participant feedback on the intervention. Taken together, these data will be used to improve the curriculum and inform a larger-scale intervention.

C. Specific Aims

Aim 1: To estimate weight loss from a Diabetes Prevention Program that is modified to incorporate a Low Carbohydrate (LC-DPP) rather than the traditional low fat diet among individuals with prediabetes. We will conduct a single-arm mixed methods pilot study to estimate weight loss as well as the percentage of participants who achieve 5% weight loss in a 16-week, LC-DPP. Weight loss from the pilot LC-DPP cohort will be compared to weight loss outcomes from previously published DPP studies. We will also evaluate secondary outcomes including change in physical activity, mental health, psychosocial functioning, and hemoglobin A1c over the 6-month study period.

Aim 2: To evaluate the acceptability of a LC-DPP among individuals with prediabetes. We will collect data on participant recruitment, session attendance, and intervention satisfaction to assess the acceptability of

LC-DPP. We will conduct qualitative, semi-structured interviews with a purposive sample of LC-DPP participants to solicit participant feedback on the LC-DPP curriculum and to better understand barriers to (e.g. food cravings, side effects) and facilitators of (e.g. satiety, energy) intervention adherence.

Aim 3: To integrate quantitative and qualitative data to better understand the mechanism(s) of change in weight, physical activity, mental health factors, psychosocial functioning factors, and hemoglobin A1c. This will allow us to determine which component(s) of the LC-DPP intervention were most and least effective. This information will be used to improve the LC-DPP curriculum and will inform a larger-scale intervention.

D. Research Design and Methodology

We will conduct a single-arm mixed methods pilot study to test the preliminary efficacy on weight loss of a LC-DPP among individuals with prediabetes (as defined by the American Diabetes Association [ADA] [10]). We hypothesize that at least 50% of LC-DPP participants will achieve greater than 5% weight and that the average weight loss in the LC-DPP will be greater than the average weight loss from traditional DPPs of the same duration (loss of 3.7 kg [27] or 4 percent of body weight [16]).

To do this, we will modify the Centers for Disease Control and Prevention's (CDC's) DPP curriculum, which consists of 16-weekly sessions delivered over 6 months (i.e. core phase) followed by 6 monthly sessions (i.e. maintenance phase). Importantly, our adapted curriculum will adhere to the CDC's Diabetes Prevention Recognition Program (DPRP) guidelines, which aim to maintain the integrity of the DPP in heterogeneous settings. The DPRP formally recognizes sites that achieve specific targets (e.g. session attendance, weight loss) through use of a CDC-approved curriculum. Therefore, our curriculum, if effective, may be eligible for CDC-approval, which would facilitate future dissemination of this intervention.

We will use a mixed-methods sequential explanatory design, which is to say that quantitative data and qualitative data will be collected in two consecutive phases within the study [28]. Specifically, in the first phase, we will collect and analyze the quantitative data (e.g. surveys, weight, HbA1c). In the second phase, we will collect and analyze qualitative data (e.g. semi-structured interviews). The rationale for this approach is that the quantitative data will provide a general overview of the intervention's efficacy and limitations, and the qualitative data will help to explain these findings by exploring participants' experiences and perspectives in more depth.

Intervention

We will recruit at least 20 individuals with prediabetes to participate in the LC-DPP. To deliver the intervention, we will partner with the National Kidney Foundation of Michigan's (NKFM's) Diabetes Prevention Research Center. NKFM delivers the DPP in communities throughout southern Michigan and is fully recognized by the CDC's DPRP. Further, NKFM has previously partnered with one of our study team members (DHG) to successfully deliver the DPP within a University of Michigan primary care clinic [29]. An experienced NKFM lifestyle coach will be trained to deliver the LC-DPP. The LC-DPP lifestyle coach will deliver 16-weekly one-hour sessions over the first 6 months and 6 maintenance sessions over the subsequent 6 months.

The CDC's Diabetes Prevention Program instructs participants to adhere to a fat-restricted diet with an explicit cap of less than 33-55 grams of fat per day depending on starting body weight. In contrast, LC-DPP participants will be initially instructed to follow *ad-libitum* very low-carbohydrate, ketogenic diet, which restricts carbohydrate intake (not including fiber) to 20-35 grams per day with the goal of achieving nutritional ketosis. Participants will be encouraged to eat a normal amount of protein (roughly 80-120 grams per day) and to derive the remaining calories from fat. Allowable foods include: meats, fish, poultry, eggs, cheese, seeds, nuts, leafy greens, non-starchy vegetables, and some fruits.

To minimize potential side effects (e.g. headache, constipation, muscle cramps, diarrhea, general weakness, and rash) participants will be instructed to replace one meal a week with a low-carbohydrate alternative, starting with breakfast. Participants will be counseled to drink sufficient water and to consume adequate sodium. Further, primary care providers will be notifed of their patients' involvement in this study, and they will be given a handout that describes the intervention, potential side effects, and strategies to minimize side

effects.

Study Population

We will recruit individuals based on the following inclusion criteria: (1) overweight, defined as BMI≥25 kg/m^2 [31]; (2) HbA1c between 5.7-6.4% drawn within 6 months of the study start date; (3) willingness to participate in group-based classes; and (4) able to engage in at least light physical activities such as walking.

We will exclude individuals based on the following criteria: (1) history of type 1 diabetes or type 2 diabetes; (2) current participation in another lifestyle or behavior change program or research study; (3) vegetarian or vegan lifestyle; (4) history of bariatric surgery; (5) inability to read, write, or speak English; (6) inability to provide informed consent; or (7) women who are pregnant or intend to become pregnant during the intervention period. We will also exclude individuals who are insured by Premier Care or Grad Care, as they have the opportunity to participate in a standard DPP, which is offered as a covered benefit through their health plan. Because the traditional DPP is currently standard-of-care for diabetes prevention and because most health plans do not cover the intervention, we will intentionally recruit individuals who do not otherwise have access to a lifestyle change program to prevent diabetes. If our intervention is successful, it may be made available to all individuals.

Recruitment

We will recruit individuals from a Michigan Medicine primary care clinic. We will use the Electronic Health Record (EHR) Reporting Tool to identify individuals who meet study eligibility criteria. A study invitation letter will be sent to at least 150 individuals. Two weeks after the letter is sent, a member of the study team will contact individuals who have not yet enrolled to directly invite them to take part this LC-DPP. Additionally, we will accept direct referrals to the program from primary care providers at Canton Health Center.

Setting

The intervention will be delivered in the conference room of the primary care clinic from which patients are recruited. In this way, we will ensure that the LC-DPP location is accessible to study participants.

Quantitative Data source

a) *Weight*

Participants will be encouraged to self-monitor weight using a home scale, if available, although this data will not be collected by the study team. In accordance with standard DPP operating procedure, participants will be weighed in a private room prior to each session and their weight will be recorded by a member of the study team.

b) *Physical activity*

In accordance with standard DPP operating procedure, participants will be encouraged to self-monitor physical activity minutes and to report this information to the lifestyle coach at the start of each session.

c) *Hemoglobin A1c*

We will evaluate change in hemoglobin A1c (HbA1c) over the study period. Baseline HbA1c will be abstracted from the electronic health record (EHR). Per study eligibility criteria, this HbA1c will be drawn within 6 months of the study start date. Primary care physicians will be notified via EHR communication (i.e. portal message) that their patient is participating in this intervention and they will be asked to obtain a repeat HbA1c at 6-months and 12-months. This laboratory test will not be billed to the study, as annual monitoring of HbA1c is standard-of-care for individuals with prediabetes.

d) *Session attendance*

Participants will be encouraged to attend all sessions and, in accordance with standard DPP operating procedure, attendance will be recorded by the lifestyle coach.

e) *RedCap surveys*

At baseline, 6 months, and 12 months study participants will be invited to complete an online RedCap survey. The survey will assess domains related to the following: global health and well-being; sleep; food cravings; stress eating; hunger; energy; mood; physical symptoms; side effects; and cost of food. At baseline, we will ask participants to provide sociodemographic characteristics. At 6 months and 12 months, participants will be asked to provide feedback about the study.

Qualitative Data Sources

Participants will be encouraged to maintain a log of food intake and physical activity. Each week, the lifestyle coach will review the logs and provide individual feedback. We will retain copies of participants' logs from their first 2 weeks in the study and their last 2 weeks in the study. In this way, we can qualitatively assess changes in dietary habits and physical activity.

We will conduct qualitative, semi-structured interviews with a purposive sample of LC-DPP participants to solicit participant feedback on the LC-DPP curriculum and to better understand barriers to (e.g. food cravings, side effects) and facilitators of (e.g. satiety, energy) intervention adherence.

Outcomes

The primary outcome for this study will be change in weight from baseline to 6 months. Secondary outcomes will include change in the following measures: weight, physical activity, hemoglobin A1c, and survey measures.

Analysis

Quantitative analysis

For all continuous outcomes, we calculate mean change and standard deviation from baseline to 6 months and 12 months. For all categorical outcomes, we will use chi-square or Fisher's exact tests to examine changes from baseline to 6 and 12 months. We will conduct all analyses using Stata 14.

Qualitative analysis:

Semi-structured interviews will be recorded and transcribed verbatim. Interviews will then be imported into qualitative analysis software. Two investigators will independently read and code transcribed interviews. Interviews will then be coded jointly using consensus conferences. Interviews will be analyzed using directed content analysis [33], which is to say that codes will be created to reflect the main topics in the interview guide and to characterize the patterns and themes that emerged from the data [34].

NOTE: ***We have a finalized Collaboration Agreement with the National Kidney Foundation of Michigan.***

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A Mixed Methods Pilot Study of a Low-Carbohydrate Diabetes Prevention Program Among Adults with Prediabetes in the US

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ABSTRACT

Objectives: (1) To estimate weight change from a Low-Carbohydrate Diabetes Prevention Program (LC-DPP); (2) To evaluate the feasibility and acceptability of a LC-DPP.

Research Design: Single-arm, mixed methods (i.e., integration of quantitative and qualitative data) pilot study.

Setting: Primary care clinic within a large academic medical center in the US.

Participants: Adults with prediabetes and body mass index ≥ 25 kg/m^2.

Intervention: We adapted the Center for Disease Control and Prevention's National Diabetes Prevention Program (NDPP)—an evidence-based, low-fat dietary intervention—to teach participants to follow a very low-carbohydrate diet (VLCD). Participants attended 23 group-based classes over 1 year.

Outcome Measures: Primary outcome measures were (1) weight change; (2) percentage of participants who achieved ≥5% weight loss. Secondary outcome measures included intervention feasibility and acceptability (e.g, attendance; qualitative interview feedback).

Results: Our enrollment target was 22. One person dropped out before a baseline weight was obtained; data from 21 individuals were analyzed. Mean (SD) weight loss in kilograms was 4.3(4.8) at 6 months and 4.9(5.8) at 12 months. Mean (SD) percent body weight change was 4.5 (5.0) at 6 months and 5.2 (6.0) at 12 months; 8/21 individuals (38%) achieved ≥ 5% weight loss at 12 months. Mean attendance was 10.3/16 weekly sessions and 3.4/7 bi-weekly or monthly sessions. Among interviewees (n=14), 3 factors facilitated VLCD adherence: (1) enjoyment of low-carbohydrate foods; (2) diminished hunger and cravings; and (3) health benefits beyond weight loss. Three factors hindered VLCD adherence: (1) enjoyment of high-carbohydrate foods; (2) lack of social support; and (3) difficulty pre-planning meals.

Conclusions: A LC-DPP is feasible, acceptable, and may be an effective option to help individuals with prediabetes to lose weight. Data from this pilot will be used to plan a fully-powered randomized controlled trial of weight loss among NDPP vs. LC-DPP participants.

Trial Registration: NCT03258918, ClinicalTrials.gov

Strengths and Limitations

- This is the first study to explore a dietary strategy to augment the weight loss effectiveness of the Center for Disease Control and Prevention's National Diabetes Prevention Program (NDPP).
- Mean weight loss among LC-DPP participants was greater than mean weight loss among historical NDPP controls.
- A Low-Carbohydrate Diabetes Prevention Program (LC-DPP) was feasible and acceptable among participants.
- This was a single-arm pilot study.
- Outcomes beyond 12 months were not examined.

INTRODUCTION

An estimated 84 million U.S. adults have prediabetes and face an elevated risk of developing Type 2 Diabetes Mellitus (T2DM) (1). Fortunately, individuals with prediabetes can prevent progression to T2DM. The landmark Diabetes Prevention Program (DPP) Trial demonstrated a 58 percent reduction in the 3-year incidence of T2DM among individuals with prediabetes who achieved at least 7 percent body weight loss through diet and physical activity changes (2). Accordingly, the Centers for Disease Control and Prevention (CDC) adapted the DPP's individual lifestyle intervention to a group-based program, which is now available in communities across the United States (3,4) and covered by a growing number of health plans, including Medicare (5).

Although the DPP is the prevailing public health strategy for T2DM, rates of program uptake and engagement are very low (6–8) and only 35% of real-world DPP participants achieve goal weight loss of at least 5% (4). A variety of efforts aim to augment DPP uptake and engagement, including public health campaigns to increase individuals' prediabetes risk awareness (9), initiatives to encourage primary care providers to identify and treat patients with prediabetes (10), and online and mobile health program adaptations to accommodate differences in individuals' needs and preferences (11). In contrast, no efforts, to our knowledge, specifically aim to increase the DPP's weight-loss effectiveness. Yet, doing so is critical, as weight loss is the key driver of T2DM risk reduction (12), and insurance payment hinges, in part, on participants' achievement and maintenance of at least 5% body weight loss (5).

One promising strategy to increase the DPP's weight loss effectiveness may be to change the program's dietary advice. The DPP was developed in the 1990s and thus teaches individuals to follow a low-fat, calorie-restricted diet, as this was the contemporaneous recommendation for healthy eating (13). However, the scientific merit of this recommendation has been criticized (14). Growing evidence supports the efficacy of low-carbohydrate diets (defined <26% total energy from carbohydrate per day) and very low-carbohydrate diets (VLCDs; defined as <10% of total energy from carbohydrate per day) (15) for

short-term weight loss (16–18), long-term weight maintenance (19–21), and improved glycemic control, particularly among individuals with T2DM and insulin resistance (15,22,23).

Several prior studies have effectively used VLCDs to promote weight loss among patients with prediabetes (24,25). Such interventions are often costly due to their use of individualized weight loss treatment and follow-up plans and subspecialty care, which limits their ability to be scaled. In contrast, the NDPP uses non-medical coaches to deliver the program in a variety of community-based settings (26). Accordingly, we hypothesized that a low-carbohydrate Diabetes Prevention Program (LC-DPP) may be better for weight loss and T2DM prevention than the traditional, low-fat DPP, and, if effective, a LC-DPP could be readily scaled using lay educators and existing DPP infrastructure and systems for monitoring and ensuring program fidelity (27). This mixed methods pilot study has two aims: (1) to estimate weight change from a LC-DPP; and (2) to test the feasibility and acceptability of the intervention. These data will enable us to refine both the LC-DPP intervention and the methods and procedures (e.g., recruitment, retention processes) in anticipation of conducting a fully-powered randomized controlled trial of weight loss among NDPP vs. LC-DPP participants.

METHODS

We conducted a single-arm pilot study to estimate weight change from a LC-DPP and to examine the intervention's feasibility and acceptability among adults with prediabetes. We used a mixed methods sequential explanatory study design (28); quantitative data were collected at baseline, 6-months, and 12-months; qualitative data were collected at 6-months and 12-months. Integration(29) of quantitative and qualitative data occurred after the study period when we merged our quantitative and qualitative data. The rationale for this approach is that quantitative data provides a general overview of the intervention's efficacy and limitations, and qualitative data help to explain these findings by exploring participants' experiences and perspectives in more depth (30).

The study was approved by the University of Michigan Institutional Review Board and conducted from August 2017 to October 2018.

Setting and Participants

Michigan Medicine has 14 adult primary care clinics throughout Southeast Michigan that serve approximately 240,000 patients with racial/ethnic characteristics similar to 2016 U.S. Census Data estimates for the state of Michigan (80% White, 14% African-American, 5% Latino, 3% Asian) (31). Approximately 70% of Michigan Medicine patients have commercial insurance and approximately 30% have federal insurance (e.g., Medicare, Medicaid). We conducted this study at one outpatient clinic with a demographic and payor mix similar to that of the health system.

Inclusion criteria were: (1) overweight, defined as body mass index (BMI) $\geq$ 25 kg/m^2 (32); (2) hemoglobin A1c (HbA1c) between 5.7-6.4% drawn within 6 months of the study start date; (3) willingness to participate in group-based classes; and (4) ability to engage in at least light physical activity. Exclusion criteria were: (1) history of type 1 diabetes or type 2 diabetes; (2) current participation in another lifestyle or behavior change program or research study; (3) following a vegetarian or vegan dietary pattern; (4) inability to read, write, or speak English; (5) inability to provide informed consent; or (6) pregnant or intention to become pregnant during the intervention period. We used an Electronic Health Record (EHR) reporting tool to identify individuals who met study eligibility criteria. A study invitation letter was sent to 187 individuals. Individuals interested in study participation emailed the study team and were then screened by telephone to ensure they met study eligibility criteria. Informed consent was obtained electronically using RedCap, a secure survey platform (33).

Intervention

The CDC offers two approved DPP curricula: (1) 2012 National Diabetes Prevention Program (NDPP) and (2) *Prevent T2* (27) . While *Prevent T2* is a newer program iteration, it has not been evaluated in peer-reviewed literature (4) and its effectiveness as compared to the 2012 NDPP is unknown. To facilitate comparison between our LC-DPP and published data on community-based DPPs, we modified the CDC's NDPP rather than *Prevent T2.*

The NDPP curriculum consists of 16-weekly sessions delivered over 6 months (i.e., core phase) followed by 6-8 bimonthly or monthly sessions (i.e., maintenance phase). In addition to teaching

participants to follow a low-fat diet, the program also instructs individuals to engage in at least 150 minutes of moderate intensity physical activity per week and to use behavioral strategies (e.g., problem solving) to maintain lifestyle changes over time.

We adapted the NDPP's dietary advice to teach participants to follow a VLCD, restricting carbohydrate intake (not including fiber) to 20-35 grams per day during the program's core phase (i.e. weeks 1-16). We did not substantially alter the content of NDPP sessions focused on non-dietary topics such as exercise. While the NDPP curriculum teaches to participants to initiate adherence to a low-fat diet during Session #2, we designed the curriculum to gradually ease individuals into the low-carbohydrate diet for two key reasons. First, we recognized that this dietary change may be drastic for individuals accustomed to consuming high-carbohydrate meals. Accordingly, we desired to increase individuals' competency and self-efficacy through step-by-step introduction of the meal plan, as these constructs have been associated with dietary adherence and favorable changes in health habits in other behavior change studies (34). Second, when transitioning to a very low carbohydrate meal plan, individuals may experience side effects such as headache, constipation, muscle cramps, diarrhea, general weakness (i.e., "keto flu"); a more gradual reduction in carbohydrate intake can reduce the likelihood that individuals experience these symptoms. During session #2, participants were instructed to replace typical breakfast and snack foods with low-carbohydrate options. During sessions #3 and #4, they were instructed to replace lunch and dinner foods, respectively, with low-carbohydrate options. As part of these sessions, participants were also advised about strategies to mitigate potential side effects (e.g., increase water and salt intake if experiencing headache; increase intake of water and non-starchy vegetables if experiencing constipation). Allowable foods included: meats, fish, poultry, eggs, cheese, seeds, nuts, leafy greens, non-starchy vegetables, and some fruits (e.g., berries). Participants were also taught to use low-carbohydrate substitutes when cooking or baking (e.g., almond flour in place of wheat flour).

During the LC-DPP's maintenance phase, participants were instructed to gradually reintroduce carbohydrates (e.g., 5 non-fiber grams of carbohydrates per week) if: (1) they had met their weight loss target and (2) if they desired to liberalize their carbohydrate intake. Consistent with NDPP operating

procedures, LC-DPP participants were asked to maintain daily food logs; these were submitted to the lifestyle coach at each session and then returned to participants with written feedback on food choices at the following session.

We partnered with the National Kidney Foundation of Michigan (NKFM), a local leader in community-based NDPP delivery. We trained an experienced NKFM lifestyle coach to deliver the LC-DPP. Training consisted of: (1) the coach's self-guided review of LC-DPP materials and online low-carbohydrate resources; (2) in-person training with the coach and study team, totaling approximately 4 hours; and (3) assessment of the coach's low-carbohydrate knowledge using a 22-item survey (Appendix 1). During the training period, our coach adapted her personal eating habits to adhere to a low-carbohydrate meal plan; she continued this eating pattern throughout the study period.

Participants' primary care physicians (PCPs) were notified via HIPPA-compliant messaging that their patient(s) was/were participating in this study. PCPs received written material about the study as well as potential side effects of low-carbohydrate diets and management strategies (e.g., magnesium for muscle cramps).

Primary Measures: Weight change

(1) Change in body weight at 6 months and 12 months: Body weight was measured and recorded at each attended session. Among session non-attendees, we attempted to schedule 6- and 12-month weigh-ins at participants' convenience. We calculated average body weight change and percent body weight change at 6 months and 12 months compared to baseline. All weights were obtained using a calibrated scale.

(2) Percentage of participants who achieved ≥5% body weight loss: At 6 months and 12 months, we determined the percentage of participants who achieved goal weight loss by dividing the number of individuals who achieved ≥5% body weight loss by the number of study enrollees with baseline weight data (n=21). We similarly calculated the percentage of participants who achieved 10% body weight loss at each time point.

Secondary Measures:

Intervention feasibility and acceptability: Measures of feasibility and acceptability were uptake, session attendance, and study retention rates. LC-DPP uptake rate was defined as the number of participants who enrolled in the intervention divided by the total number of individuals invited to participate.

Session attendance was determined by calculating the rate of attendance at core and maintenance sessions. Rates of session attendance were compared with the CDC's Diabetes Prevention Recognition Program (DPRP) standards (27). The DPRP monitors the fidelity and quality of community-based DPPs, and requires that at least 60% of program participants attend ≥9 core sessions and ≥3 maintenance sessions. We aimed to achieve these session attendance metrics to demonstrate LC-DPP feasibility.

LC-DPP retention rate was determined by calculating the rate of completion of the 6-month and 12-month surveys. Although session attendance is commonly used as a measure of intervention retention in larger trials, we observed that several participants in this small pilot study could not attend sessions due to personal and/or professional circumstances. However, they remained in periodic communication with the lifestyle coach, received course materials by e-mail, and completed assessments at 6 and 12 months. Accordingly, we felt that survey completion was the most accurate representation of study retention in this small sample.

To further understand the program's acceptability, we conducted semi-structured interviews at 6 and 12 months. During interviews, we explored participants' general experiences with the intervention as well as specific facilitators of and barriers to VLCD adherence. The 6-month interview guide is shown in Appendix 2.

Change in HbA1c: Baseline HbA1c was identified according to study inclusion criteria and abstracted from the electronic health record (EHR). Primary care physicians were notified that their patient(s) was/were participating in this intervention and they were asked to order HbA1c at 6 and 12 months. Change in HbA1c was calculated by subtracting participants' HbA1c at 6 and 12 months from baseline values.

Online Surveys: At baseline, 6 months, and 12 months, study participants were invited to complete an online survey via RedCap (33). At baseline, participants were asked to provide demographic and socioeconomic information. In each survey, we assessed participants' experiences of physical symptoms, which are known to be potential side effects of VLCDs. These include: bad breath, acne, gastrointestinal symptoms (e.g. constipation, diarrhea), dizziness, dry mouth, excessive thirst, headaches, and muscle cramps. Survey response options were: not at all; 1 day a week; 2-3 days a week; 4-5 days a week; and 6-7 days a week.

Exploratory Analysis

We examined participants' weight changes stratified by 12-month survey completion (i.e., study retention).

Sample Size

Consistent with CONSORT guidelines(35) and other expert recommendations for designing pilot studies (36–38), our sample size was selected based on pragmatic considerations with the goal of generating sufficient data to inform a fully powered RCT. Specifically, NKFM typically enrolls 15-20 individuals in their programs and the clinic's conference room has capacity for approximately 25 individuals. We specified an enrollment target to 22 individuals, as we believed this would maintain the group dynamic of NKFM's traditional DPPs while also allowing us to sufficiently test the feasibility of the methods and procedures (e.g., recruitment, retention) that we are likely to use in a fully powered RCT (35).

Analysis

Quantitative analysis

Descriptive statistics were used for baseline survey response data, including demographic and socioeconomic characteristics and self-reported side effects. For all continuous outcomes, including body weight and HbA1c, we calculated mean change and standard deviation from baseline to 6 months and 12 months. Given our small sample and non-normal distribution of the data, we used a nonparametric

statistical test, the Wilcoxon matched-pairs sign-rank test, to compare pre-post changes in the frequencies of participants' self-reported physical symptoms at 6 and 12 months compared to baseline. All analyses were conducted using Stata 14.

Qualitative analysis

Semi-structured interviews were recorded and transcribed verbatim. Interviews were imported into qualitative analysis software. Two investigators independently read and coded transcribed interviews. Interviews were then coded jointly using consensus conferences. Interviews were analyzed using directed content analysis, meaning the codes were created to reflect the main topics in the interview guide and to characterize the patterns and themes that emerged from the data (39).

Integrated analysis

Integration—the mixing of quantitative and qualitative data (29)—occurred after the study period. We merged qualitative data with weight loss data to better understand the factors that might have influenced weight loss outcomes.

Patient and public involvement

There was no patient or public involvement in the development of this pilot study. Rather, we sought feedback from study participants. These results will be used to refine the intervention for a larger-scale trial, which will also be informed by stakeholder groups, including patients with prediabetes, primary care team members, and community partners (e.g., NKFM).

RESULTS

Intervention uptake: A total of 187 potentially eligible individuals were sent study invitation letters via postal mail. Thirty-two individuals (17%) expressed interest in study participation and 22 (12%) enrolled in the study within two weeks. Reasons for non-enrollment included: unable to reach (n=4); active participation in another weight loss intervention (n=2); unwilling or unable to participate in group classes

or follow VLCD (n=3). One person was placed on a waitlist because we met our recruitment target (n=22), which was determined by room-size constraints. One participant dropped out of the study before a baseline weight could be obtained and was therefore excluded from our analyses.

Baseline Characteristics

Demographic and socioeconomic characteristics were assessed at baseline (**Table 1**). Most participants were males (57%), white (86%), and educated, with 85% attaining education beyond high school. The mean age was 58.9 years (SD 11.0). At baseline, mean BMI was 34.1 kg/m^2 (SD 5.4) and mean HbA1c level was 5.9% (SD 0.22%).

Quantitative Analyses:

Change in weight and HbA1c level: **Table 2** shows weight and HbA1c outcomes at 6 and 12 months among all participants (n=21) and among those who completed the 12-month survey (n=15). No participants progressed to T2DM, defined by HbA1c > 6.4%, during the study period.

Retention: Eighteen out of 21 participants completed the 6-month survey and 15 completed the 12-month survey, resulting in a retention rates of 86% and 71%, respectively.

Session attendance: Participants attended a mean (SD) of 10.3 core sessions and 3.4 (2.7) maintenance sessions. Fourteen participants (67%) attended at least 9 core sessions and 11 participants (52%) attended at least 3 maintenance sessions.

Change in self-reported physical symptoms: There was an increase in self-reported constipation from baseline to 6 months (p=0.006). There was a decrease in muscle cramps from baseline to 6 months (p=0.005) and a decrease in physical weakness from baseline to 6 months (p=0.05) and 12 months (p=0.05). There were no other statistically significant differences in self-reported side effects at 6 or 12 months compared to baseline.

Adverse Events:

One participant suffered an ischemia stroke during the program's core phase.

Qualitative Analyses:

Participant Experiences with the Intervention

Fourteen individuals participated in semi-structured interviews; 13 participated at 6 months and 12 participated at 12 months. During these interviews, we explored participants' experiences with the program, including barriers to and facilitators of adhering to a low-carbohydrate meal plan. At 12 months, we also explored participants' plans to continue to follow a low-carbohydrate meal plan. These qualitative data were integrated with interviewees' weight change data to better elucidate factors that may influence participants' weight change.

Over half (n=8, 57%) of interviewees were female. Other baseline characteristics were similar between interviewees and non-interviewees (**Table 1**). At 12 months, mean (SD) percent body weight loss among interviewees was 7.0 (6.5) percent. Half (n=7) of interviewees achieved the program goal of ≥5% body weight loss at 12 months. **Table 3** shows key themes and representative quotes stratified by weight goal achievers and non-achievers.

Among weight goal achievers (n=7), three key themes emerged that facilitated adherence to the low-carbohydrate meal plan: (1) enjoyment of low-carbohydrate foods; (2) diminished hunger; and cravings (3) health benefits beyond weight loss.

The majority of weight goal achievers (n=5) found the meal plan easy to follow due to palatability of the diet and availability of low-carbohydrate substitutes for foods such as potatoes and rice. One participant noted, "In the lunch time, I'll substitute [sandwich bread] with a low-carb wrap. There's a 4-gram wrap that I could use…The only thing you're replacing at dinner time from a carb standpoint would be maybe some potatoes or pastas, and [there are] really great substitutes…there's a low-carb pasta option. And then of course [there's] cauliflower mashed potato. When you are doing something like a taco salad with cheese and meat and sour cream and salsa, all of that fits [in the meal plan]."

Over half (n=4) of weight goal achievers noted diminished hunger and cravings. For example, one participant commented, "I just love that I'm losing weight. It's the best diet I have ever been on, and I've been on a lot. And it seems effortless, it just seems like it's melting off. And I'm eating good and I'm not hungry…" Another noted, "When I eat a higher fat diet, I'm not hungry. And that's been a big surprise to me." One weight goal non-achiever endorsed diminished hunger when she adhered to the low-carb

meal plan; however, she also described social pressures to consume carbohydrates and non-adherence to the intervention at least 1-2 days per week.

Almost all (n=6) weight goal achievers experienced health benefits in addition to weight loss, which motivated their continued adherence to the low-carbohydrate meal plan. Several participants described increased energy levels and improved sleep. One stated, "[I was able] to decrease my blood pressure medications…[I'm] someone who's been on high blood pressure medication for probably 15, 20 years, now it's cut in half, so that's significant."

Among weight goal non-achievers (n=7), three key themes emerged that hindered adherence to the low-carbohydrate meal plan: (1) difficulty giving up high-carbohydrate foods; (2) lack of social support; and (3) difficulty planning ahead.

The majority of weight goal non-achievers (n=5) described difficulty giving up carbohydrates due to food preferences, and this was a particular challenge in the absence of social support. One participant commented, "The hardest [part is that] it's so much fun to go out for ice cream with my friends or just to go to a restaurant. And I don't like to have to order a salad or something... It's just kinda hard I guess, being around other people who are eating stuff that I shouldn't have." Another commented, "I live with somebody who eats things that I should not have. And it's become very difficult to resist those, especially as I go farther and farther into the program." In contrast, only one weight goal achiever noted difficulty giving up carbohydrates. However, this challenge was mitigated by the support of a spouse who also adhered to the meal plan: "The hardest thing for me, personally, is that I love bread, and I love potato, [but] as long as [my spouse and I] are working together on this, we're great."

Several weight goal non-achievers (n=3) described difficulty with planning low-carbohydrate meals. One noted, "Probably the [biggest challenge] is the pre-planning that you have to do…[when] I was going grocery shopping, I had meals planned, and…I was doing much better than if I run out of food and I'm hungry and I just want something now."

Almost half (n=6) the interviewees expressed concern about potential adverse health consequences of increased dietary fat intake, including heart disease and elevated cholesterol levels. One

participant stated, “For years and years and years, I've heard eating red meats, cheeses, and nuts, and low carbohydrate foods…is not good for your coronary system, your heart. You gotta understand the last 50 years, [all I heard] was…sausage and steak and hamburger, and pork chops are not good for you. They're not good for your heart. But now it seems like things are changing. That's the only thing that bothers me. Otherwise, it's working great.”

DISCUSSION

This is the first study, to our knowledge, that aims to augment the weight loss effectiveness of the CDC’s NDPP by modifying the program’s dietary advice. Specifically, participants were taught to follow a carbohydrate-restricted rather than a fat-restricted meal plan. At 12 months, percent body weight loss among all LC-DPP participants was greater than weight loss among historical NDPP controls (5.2% versus 4.2%) and a similar number of LC-DPP participants achieved at least 5% body weight loss (38% versus 35%) (4). Meta-analyses of NDPPs demonstrate a positive association between session attendance and body weight loss (4,26). Due to sample size limitations, we were unable to evaluate the relationship between LC-DPP attendance and body weight change. However, among our sample, weight change was greater among survey completers (n=15) as compared to survey non-completers at 6 months (6.2% versus 4.5%) and 12 months (6.4% vs. 5.2%).

Twelve percent (n=22) of eligible individuals enrolled in our study within 2 weeks of receiving an invitation letter. LC-DPP participation was slightly higher than that observed in traditional DPPs (6–8), including those offered by our institution’s self-funded health plan (40). Given room-size limitations and the pilot nature of this study, we ceased recruitment efforts once we met our enrollment target and we may therefore be underestimating potential LC-DPP participation. Over half of LC-DPP participants were male while the majority of NDPP participants are female (4). Study retention, as measured by survey completion, was high (85%, n=18) at 6 months and decreased at 12 months (71%, n=15). Similarly, attendance at LC-DPP core sessions was high, meeting CDC DPRP standards (27) with 67% (n=14) attending at least 9 core sessions; attendance decreased during the program’s maintenance phase with

only 52% (n=11) attending at least 3 maintenance sessions. Notably, rates of attrition are often high in real-world behavioral health interventions, including traditional DPPs where approximately half of participants remain engaged with the intervention at 6 months (4,41). Accordingly, by CDC DPRP standards and in comparison to real-world DPPs, our findings suggest that an LC-DPP is feasible. Additional strategies (e.g., incentives, varied class times) could be explored to augment participants' session attendance.

During qualitative interviews, we explored facilitators of and barriers to low-carbohydrate dietary adherence. These data not only provide insight into the factors that may influence individuals' weight change outcomes, but also reveal potential opportunities to refine and tailor the intervention. For example, consistent with prior literature (42), our participants identified social support as a key factor in dietary adherence, suggesting that LC-DPP partner classes and/or peer-support programs may be one strategy to augment program adherence. Furthermore, interviewees that achieved goal weight loss described enjoyment of the low-carbohydrate diet as compared to weight goal non-achievers who struggled to give up the carbohydrate-rich foods that they loved. Participants that do not adhere to the low-carbohydrate meal plan due to non-enjoyment of allowable foods may benefit from other evidence-based interventions for T2DM prevention (e.g., traditional DPP, metformin) or for weight loss (e.g., Weight Watchers, pharmacotherapy, bariatric surgery), and these alternatives should be readily offered.

The majority of interviewees expressed fear regarding the diet's fat content, reflecting the widely-held belief that dietary fat and cholesterol increase cardiovascular disease risk. While observational data demonstrating this association emerged in the 1950s (43), the causative role of dietary saturated fat and cholesterol in heart disease is not well-established (44). Furthermore, the Women's Health Initiative, the largest randomized controlled trial to evaluate health outcomes of low-fat diet adherence, showed no reduction in cardiovascular disease risk among intervention versus control group participants (45). Growing literature demonstrates favorable changes in cardiovascular disease risk factors (e.g., blood pressure) and serum biomarkers (e.g., LDL, HDL, and triglycerides) among individuals following low-carbohydrate, high-fat diets (15,16,18,21). Accordingly, the 2015-2020 U.S. Dietary Guidelines removed

prior recommended limits on dietary fat and cholesterol intake, and clinical practice guidelines for T2DM (46) and obesity management (47) now endorse carbohydrate restriction as one evidence-based approach to lifestyle management. Despite these changes, however, pervasive fears regarding dietary fat remain one primary barrier to implementation of a LC-DPP. We plan to revise the LC-DPP curriculum to better address participants' concerns and we will test serum lipids in future program evaluations.

LIMITATIONS

First, we recruited individuals from one primary care clinic within a US academic medical center and our results may not be generalizable to other populations. Because the prevalence of prediabetes is increasing worldwide (48), there is a critical need to develop and test novel interventions for T2DM prevention among diverse populations and concomitantly explore what works for whom and under what circumstances (49,50). Second, we did not evaluate outcomes beyond 12 months, and are therefore unable to assess long-term adherence to a carbohydrate-restricted meal plan. Finally, because this was a pilot study, we cannot assess the intervention's weight loss effectiveness compared to the NDPP. A large-scale comparative effectiveness trial of the LC-DPP versus NDPP is warranted.

CONCLUSIONS

The CDC's NDPP is widely available throughout the United States. Yet, many program participants do not achieve the program's weight loss goal of at least 5%. A DPP adapted to teach participants to follow a low-carbohydrate rather than a low-fat diet may be one way to increase the program's weight loss effectiveness and broaden the range of available programs to help individuals with prediabetes. In future work, we aim to test the LC-DPP's weight loss effectiveness as compared to the NDPP in a randomized controlled trial. It is critical to explore issues concerning dietary adherence and sustainability as well as biomarker (e.g., lipid, HbA1c) changes and incident chronic disease (e.g., T2DM, cardiovascular disease) over time. Lastly, future work should explore the factors that facilitate or hinder LC-DPP weight loss success (e.g., presence or absence of social support) and develop tailored strategies that address these factors.

FOOTNOTES

Contributors: D.G., L.S., and C.R. designed the study. D.G., L.S., K.P., and A.T. developed the intervention. K.P., T.A., B.L., P.B., and S.S. collected the data. D.G. and C.R. analyzed the data; they take full responsibility for the integrity of data analyses. D.G. drafted the manuscript. All authors critically revised the manuscript.

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583 **TABLES**

Table 1. Baseline characteristics			
	All participants (n=21)	Program completers[1] (n=15)	Semi-structured interviewees (n=14)
Mean age in years, mean (SD)	58.9 (11.0)	60.5 (10.2)	58.7 (9.4)
Male, n (%)	12 (57.1)	8 (53.3)	6 (42.9)
White, n (%)	18 (85.7)	13 (86.7)	12 (85.7)
Education > high school, n (%)	17 (85.0)	12 (80.0)	13 (92.9)
Married / partnered, n (%)	15 (71.4)	12 (80.0)	10 (71.4)
Mean BMI in kg/m^2, mean (SD)	34.1 (5.4)	33.9 (4.2)	32.7 (3.1)
Baseline HbA1c, mean (SD)	5.9 (0.2)	6.0 (0.2)	5.9 (0.2)
[1]Defined has having completed the 12-month survey.			

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Table 2. 6-month and 12-month results among all participants (n=21) and 12-month survey completers (n=15).				
Outcomes (mean (SD) or N (%))	6 months		12 months	
	All (n=21)	Completers (n=15)	All (n=21)	Completers[1] (n=15)
Weight change in kg	-4.3 (4.8)	-6.0 (4.7)	-4.9 (5.8)	-6.1 (6.1)
Percent weight change	4.5 (5.0)	6.2 (4.8)	5.2 (6.0)	6.4 (6.4)
At least 5% weight loss	9 (42.9)	9 (60.0)	8 (38.1)	7 (46.7)
At least 10% weight loss	3 (14.2)	3 (20.0)	6 (27.3)	5 (33.3)
HbA1c change	-0.1 (0.2)	-0.2 (0.2)	0.06 (0.3)	0.04 (0.4)
[1]Defined has having completed the 12-month survey.				

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Table 3. Key themes and representative quotes stratified by percent body weight loss.	
Key Theme	**Representative Quotes**
≥5% body weight loss at 12 months (n=7)	
Enjoyment of low-carbohydrate foods	"[I'm eating] all the cheese and the meat and the vegetables I'm allowed. I'm enjoying all of it. And I found snacks like sugarless jello…beef sticks, salami with cheese…and I'm really enjoying it…If I have cake it'll be here and there, like for a party, but I know that I can get right back on this diet in the next day." *-14.5 kg (18% body weight) at 12 months*
Diminished hunger and cravings	"I don't have cravings. I like the fact that I'm not craving food and thinking about food all the time." *-8.6 kg (9.5% body weight) at 12 months*
Health benefits beyond weight loss	"By losing the weight, I feel more active. It seems like my joints don't hurt as bad." *-14.5 kg (14% body weight) at 12 months*

≤5% body weight loss at 12 months (n=6)	
Difficulty giving up high-carbohydrate foods	"The hardest thing is avoiding food that I like or love, like breads and mashed potatoes and potato chips and pasta and going out to dinner and having a nice, big juicy hamburger on a nice bun. Just taking the bun off, not having pasta, not having mashed potatoes, I miss that. But, if I see the weight loss keep going, I'm okay to tolerate that." *-3.6 kg (3.4% body weight) at 12 months*
Lack of social support	"It's very hard sometimes when you're traveling with friends, going on road trips, going to restaurants, watching everybody eat, the high carbohydrate food, being of a Mediterranean descent with pastas and stuff like that, spaghettis and pizzas and noodles, it's very hard to adhere to it at times." *-2.2 kg (2.3% body weight) at 12 months*
Trouble pre-planning meals	"I think just like with any sort of food awareness…there's time involved, and it's just hard to pre-plan and make meals that would benefit me and that my kids would like." *-0.63 kg (0.6% body weight) at 12 months*

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Appendix 1. Quiz to assess LC-DPP teacher's knowledge about low-carbohydrate meal plan

Please choose all answers that are correct (by bolding or starring the right answer or by e-mailing me your choices in plain text). More than 1 answer will be correct.

1. Which of these fast-food restaurants reliably have standard low-carb options:
   a. Jimmy John's
   b. Chipotle
   c. Chinese restaurants

2. When making something low-carb at a restaurant make sure to consider:
   a. asking for extra butter pats or low-carb sides if they aren't serving you enough fat
   b. asking for lettuce-wrapped sandwiches and burgers
   c. checking for how salty the dressings are

3. Some low-carb flours include:
   a. almond flour
   b. cauliflower
   c. coconut flour
   d. rice flour

4. When someone is following a low-carb diet, we want their weight loss to be:
   a. more than 5 pounds a week at first
   b. less than 5 pounds a week at first
   c. generally we don't care how fast or slow their weight loss is, although if they're not at their ideal weight and they're still not losing weight, it's time to troubleshoot

5. Low-carb diets tend to make people:
   a. hungrier and less thirsty
   b. hungrier and more thirsty
   c. less hungry and less thirsty
   d. less hungry and more thirsty

6. If someone is constipated, they could try:
   a. taking a magnesium supplement
   b. drinking more water
   c. adding in more foods with potassium

7. When attending a party, how can someone prepare to stick to their low-cab meal plan?
   a. bring something low-carb
   b. eat before hand so they don't arrive very hungry
   c. give themselves a non low-carb treat at the party
   d. pre-think how they will deal with peer pressure at the party

8. What low-carb foods can often be found at convenience or corner stores?
   a. salted nuts (ideally lower carb like almonds, walnuts, and pecans and not higher carb like cashews and pistachios)
   b. hard boiled eggs
   c. string cheese
   d. pork rinds (make sure they don't include trans fats)

9. Net carbs:
   a. are total grams of carbohydrates minus grams of fiber
   b. are also called non-fiber grams of carbohydrates
   c. do not include naturally present sugars
   d. should be no more than about 20-35 grams a day for someone following a very low-carbohydrate diet

10. A very low-carb diet typically:
   a. includes fruit other than berries
   b. increases blood pressure
   c. includes saturated fat from animal and plant sources

11. Rare side effects of a low-carb diet include:
   a. insomnia
   b. hair loss
   c. more cavities
   d. diarrhea

12. A participant is facing a weight-loss plateau. What are some possible causes?
   a. eating too many calories
   b. consuming foods with artificial sweeteners most days
   c. poor sleep
   d. eating more than 40 grams of protein at once

13. A participant says they're feeling dizzy or woozy. What are some possible causes?
   a. Insufficient intake of water and salt
   b. Perceived or actual hypoglycemia
   c. Low blood pressure

14. A participant is worried about following a low-carb diet since they are very physically active and don't want it to hurt their performance. How might you respond?
   a. Weight loss on a low-carb diet is typically muscle-sparing, which can help preserve athletic performance
   b. Lots of athletes, especially those who do sports that require endurance, do quite well on a low-carb diet, since it prevents "hitting the wall" or "bonking."
   c. They should not exercise heavily while following a very low-carbohydrate diet.

15. What should participants know about alcohol?
   a. When on a low-carb diet, participants may get drunk more easily from less alcohol.
   b. Unsweetened and unflavored liquor has 0g net carbs.
   c. Alcohol may decrease fat burning and weight loss

16. What types of fats are preferred on a low-carb diet?
   a. Lard with partially hydrogenated oils added
   b. Coconut oil
   c. Olive oil
   d. Butter

17. Which of the following are true about sugar alcohols?
   a. Calculate net carbs by only counting half of the grams of sugar alcohols
   b. They can cause intestinal distress and flatulence

c. Erythritol is often considered to have the least amount of influence on blood sugar of all the sugar alcohols
d. They are an essential part of a low-carb diet.

18. A participant is complaining of intestinal distress. What might be causing it?
a. Cauliflower
b. Sugar-free gum
c. Erythritol
d. Broccoli

19. Which of these foods are potentially problematic on a low-carb diet because of their carb content?
a. Starchy vegetables like carrots
b. Butter
c. Chocolate with a cacao content less than 85%
d. Bacon and processed meats with added sugars

20. Which of the following typically improve when someone follows a low-carb meal plan?
a. triglycerides
b. weight
c. HbA1c

Amount Per Serving	
Calories 180	Calories from Fat 100
	Calories from Saturated Fat 15
	% Daily Value*
Total Fat 11g	**17 %**
Saturated Fat 2g	**9 %**
Trans Fat 0g	
Polyunsaturated Fat 3.5g	
Monounsaturated Fat 5g	
Cholesterol 0mg	**0 %**
Sodium 110mg	**5 %**
Potassium 150mg	**4 %**
Total Carbohydrate 17g	**6 %**
Dietary Fiber 14g	**54 %**
Sugars 2g	

21. How many net grams of carbohydrates are in the food to the left?

a. 17
b. 14
c. 3
d. 2

Amount per serving	
Calories	**230**
	% Daily Value*
Total Fat 8g	**10%**
Saturated Fat 1g	**5%**
Trans Fat 0g	
Cholesterol 0mg	**0%**
Sodium 160mg	**7%**
Total Carbohydrate 37g	**13%**
Dietary Fiber 4g	**14%**
Total Sugars 12g	
Includes 10g Added Sugars	**20%**
Protein 3g	

22. How many net grams of carbohydrates are in the food to the left?

a. 37
b. 34
c. 27
d. 25

Low-Carbohydrate Diabetes Prevention Program: 6-month interview guide

Introduce self

Hello, my name is [name of interviewer].

Discuss purpose of the interview group

We are interested in understanding your experiences to date with the Low-Carbohydrate Diabetes Prevention Program. We want to understand how the program has changed your diet and physical activity habits, and we want to know your thoughts about what you liked about the program and ways that it could be improved.

I want to encourage you to answer honestly and share any thoughts you may have. There is no right or wrong answer, and you will not be penalized for anything you say. We care about your opinion, so that we can make an even better program that could benefit others.

You will receive a $20 gift card for participating in this interview.

Describe how we will assure confidentiality and answer any questions.

I want to take a minute to tell you what happens with the information you provide for us today. I am recording this conversation so that we don't miss any of the comments that you share. People working on this study will be the only ones who will use the interview recordings.

As a reminder, you are not obligated to answer any question you feel uncomfortable responding to, and you are not required to participate. You may leave the interview at any time.

Do you have any questions for me before you review and sign the consent form? (Answer questions and then give consent form).

I'm going to turn on the recorder and we will get started. ***Turn on recorder*** The rest of the conversation is being recorded for research purposes.

Interview

<u>General experience</u>

1. Tell me about how the program is going for you so far.
    a. Tell me more.
    b. Probe, if needed: what do you like about the program?
        i. Tell me more.
    c. Probe, if needed: what, if anything, has been hard or challenging about the program?
    d. Probe, if needed: Any side effects?
    e. Tell me more.

<u>Diet advice and experience</u>

2. Tell me specifically about how the low-carbohydrate diet is going for you.
    a. Tell me more.
    b. Probe, if needed: has anything surprised you about this meal plan?
    c. Probe, if needed: what, if anything, has been challenging about sticking to this meal plan?
3. Tell me about how your dietary habits and routines have changed with this program, if at all.
    a. Tell me more.

Physical activity advice and experience

4. Tell me about how your physical activity habits and routines have changed with this program, if at all.
    a. Tell me more.
    b. Probe, if needed: what, if anything, has been challenging about getting 30 minutes of physical activity, 5 days per week?

Motivation and expectations

5. Tell me about your motivation for joining the program?
    a. Tell me more.
    b. Probe, if needed: What made you decide to sign up for this program?
6. Before participating in this program, what other ways had you tried to lose weight or to prevent diabetes?
    a. If participant previously took part in traditional DPP:
        i. Tell me about how your experience with this low-carbohydrate DPP compares to your prior experience with the traditional low-fat DPP.
7. In what ways has this program met or not met your expectations?
    a. Tell me more.
    b. Probe, if needed: has your health improved in the ways that you hoped or expected?
        i. Tell me more.
    c. Probe, if needed: has your weight changed in the way you hoped or expected?
        i. Tell me more.

Outcomes and sustainability

8. Tell me about your plans, if any, to stick to this meal plan after the program ends.
    a. Tell me more.
    b. If plans to stick with it, ask: why might you stick with the program?
    c. If plans not to stick with it, as: why not?
    d. Probe, if needed: what might be some challenges, if any, of sticking to this meal plan after the program ends?

Changes to improve the program

We would like to improve this program to help more people to prevent diabetes.

9. What, if anything, could have made the low-carbohydrate meal plan easier for you to follow?
    a. Tell me more.
10. What suggestions do you have to improve this program so far?
    a. Tell me more.
    b. Probe, if needed: what changes would you make to help participants to better understand and follow the low-carbohydrate meal plan?
11. Are there particular topics that you would like to cover during the last 6 months of the program?
    a. Tell me more.

Support

We would like to understand how this program supports participants so that we can develop new ways, if needed, to help more people achieve their health and weight loss goals.

1. Tell me about the support you received from your lifestyle coach.
    a. Tell me more.
    b. Probe, if needed: was she available, responsive, able to answer questions?
2. Tell me about the support you received from your classmates.
    a. Tell me more.
3. Was there anyone else such as a friend or family member that provided you with support during this program?
    a. Tell me more.
4. Did you speak with your healthcare provider about your participation in this program?
    a. If yes: Tell me about what he or she said or advised.
        i. Probe, if needed: Did you feel supported by your healthcare provider?
5. Are there ways that this program could better support you in achieving your health goals?
    a. Tell me more.

Conclusion

6. Are there any other thoughts or experiences that you would like to share?

I want to thank you again for taking the time to discuss your thoughts and experiences. We will send you a $20 gift card in the mail. This concludes today's interview. Thank you and goodbye.
Turn off recorder