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Testing a Personalized Behavioral Weight Loss Approach Using Multifactor Prescriptions and Self-Experimentation: 12-Week mHealth Pilot Randomized Controlled Trial Results

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ABSTRACT

Background: Behavioral weight loss (WL) interventions typically follow standard diet and activity prescriptions for intervention duration to produce an energy deficit. Though average weight losses in these programs are clinically meaningful, there is heterogeneity in weight outcomes. Personalized diet and activity prescriptions may help increase the potency of WL programs by reducing this heterogeneity.

Methods: This 12-week pilot study randomized participants ($n = 35$; BMI 34.6 ± 4.9 kg/m^2, 34% with HbA1c 5.7%–6.4%) in a 3:1 ratio to a Personalized Behavioral Weight Loss (PBWL) or standard BWL and compared the feasibility and efficacy of these approaches. Both groups received a study mobile app, smart scale, activity tracker, and weekly telephone coaching sessions; PBWL participants received a continuous glucose monitoring device. PBWL participants had goals for 1) macronutrient composition (low fat or carbohydrate), 2) meal frequency (3 meals or meals and snacks), and 3) activity focus (daily or weekly goal); they experimented with different 3-part prescriptions, in random order and combination, for the first 4 weeks then picked their 3 goals to follow for weeks 5–12.

Results: Study retention (100%) and satisfaction were high. Mean 3-month weight loss (kg) was greater in PBWL (−7.08 (0.74)) than BWL (−3.79 (0.84), $P = 0.03$); 74% of PBWL and 63% of BWL participants were "optimizers" who achieved a 5% weight loss at 3 months. PBWL optimizers lost more weight (−8.66 (0.66)) than BWL optimizers (−4.76 (0.43), $p < 0.001$).

Conclusions: Experimentally-derived personalized prescriptions supported greater 12-week weight loss than standard recommendations.

Trial Registration: ClinicalTrials.gov NCT04639076.

Abbreviations: BMI, body mass index; BWL, behavioral weight loss; CGM, continuous glucose monitoring; HbA1c, hemoglobin A1c; mPWR, mobile personalized weight loss recommendations; PBWL, personalized behavioral weight loss; T2DM, Type II diabetes mellitus.

1 | Introduction

Obesity increases the risk of chronic diseases, with its relationship to type II diabetes mellitus (T2DM) being of particular public health concern. Though not all individuals with overweight or obesity develop T2DM, having a body mass index (BMI) that is clinically classified as "obese" or "very obese" is associated with a 20–40 fold increased risk of developing T2DM compared with having a BMI classified as "lean" [1]. In the United States, approximately 88 million adults (more than 1 out of 3) already have prediabetes. If current trends in conversion from prediabetes to T2DM continue, it is estimated that as many as one in three American adults could have T2DM by the year 2050 [2].

Fortunately, losing 5% of initial body weight can reduce T2DM risk by 56% [3]. Mean weight losses in clinical weight loss trials are often at or above this 5% goal, though the number of individuals who achieve a 5% weight loss ranges from 25% to 70% [4–7] and the standard deviation in weight loss is fairly large, indicating substantial heterogeneity of effects [8, 9]. Heterogeneity in risk factors for obesity likely drives heterogeneity in response to treatment [10, 11]. There is growing awareness that no one factor can explain individual risk or treatment response, but rather a complex and dynamic relationship between factors [11]. In other words, it is becoming clear that the search for the "ideal" weight loss approach across the population is less effective than identifying the "ideal" approach for the individual.

Personalizing obesity treatment based on a standard set of measured factors is the next step toward decreasing heterogeneity in treatment response [11]. Such "precision nutrition" involves considering biological, genetic, microbiome, and behavioral factors when prescribing an individualized treatment regimen that is predicted to maximize response [12, 13]. Ideally, predictors should be easily measured, including family history, physical measures such as adiposity and blood glucose, and psychosocial and cognitive factors that likely influence response to different types of weight loss plans.

To date, very few studies have tested weight loss interventions that prescribe a certain treatment based on a set of predictive factors to personalize intervention across multiple behaviors (i.e., more than just diet composition or therapy approach) [12]. Rather, many studies have been conducted to personalize interventions based on single factors, such as the presence of binge eating disorder, a phenotypic measurement such as elevated fasting glucose, or a specific genetic variant [13–15]. Unfortunately, while many studies have attempted to identify predictors of success in behavioral weight loss programs, few predictors have emerged as significant across studies [16]. As the field moves away from standard, one-size-fits-all prescriptions to "precision" or "personalized" approaches, there is a critical need to better understand feasible, personalized approaches to weight loss.

1.1 | Goal of This Study

The mobile Personalized Weight loss Recommendations (mPWR) pilot and feasibility trial was designed to fill this critical research gap. In mPWR, a standard Behavioral Weight Loss (BWL) intervention was compared to a Personalized Behavioral Weight Loss (PBWL) intervention. The PBWL approach explored three factors: diet prescription (calorie restriction with a low fat or low carbohydrate meal composition), meal frequency (3 meals or 3 meals plus snacks), and exercise frequency (daily or weekly activity goal). These factors were chosen because of their potential to result in differential weight loss and blood glucose based on individual characteristics [17–21]. To help participants see the effects of weight loss behaviors on blood glucose control, the PBWL group was also given a continuous glucose monitoring (CGM) device. The rationale was that the CGM may provide measures of blood glucose that more effectively and proximally provide information about the effects of different dietary and physical activity behaviors that could support better weight outcomes [22, 23].

The primary aim of this study was to test the feasibility and preliminary efficacy of using the PBWL approach in individuals with overweight or obesity—with or without impaired glucose at baseline. Specific objectives were to compare the PBWL and BWL groups on changes in: (i) weight and (ii) behaviors and factors that may influence intervention adherence and outcome (diet, physical activity, hunger and fullness). The hypothesis was that the PWBL intervention would result in greater weight loss compared with the BWL intervention. Exploratory analyses also compared outcomes in those who achieved a clinically meaningful 5% weight loss (weight loss "optimizers") and those who did not (weight loss "non-optimizers"), by study group.

2 | Materials & Methods

2.1 | Recruitment and Eligibility

The study was conducted in Chapel Hill, NC. Participants were recruited through informational listservs, letters to local primary care providers, and the UNC Health Care system using lists generated by the Carolina Data Warehouse. Individuals deemed eligible after a preliminary online screening and follow-up phone screen were invited to a study orientation, by video call, which provided further information about the study and allowed the potential participants to ask questions prior to enrolling. After that, potential study participants could review and electronically sign an online Informed Consent form.

Eligible participants were adults (20–65 years) with overweight or obesity (BMI 25–50 kg/m^2) who were normoglycemic (Hemoglobin A1c (HbA1c) < 5.7%) or had impaired glucose (HbA1c 5.7%—6.5%) at baseline, as determined by fingerstick. Individuals also had to own an iPhone with a data and text messaging plan, have home Wi-Fi access, be able to read, write, and speak English, have a baseline level of moderate to vigorous physical activity that was below the American College of Sports Medicine's recommendation of 150 min/week, be able to attend the two study assessments and weekly video calls, and obtain primary care provider consent if needed.

Exclusion criteria included: weight loss of 10 pounds or more in the past 6 months that was maintained; history of weight loss surgery, diabetes, a clinically diagnosed eating disorder,

schizophrenia or bipolar disorder, or pre-existing medical condition(s) that would preclude adherence to an unsupervised exercise program (determined by items endorsed on the Physical Activity Readiness Questionnaire [24]); use of medications to treat prediabetes or with known impact on metabolism or weight; current participation in another weight loss program; current or recent (past 6 months) pregnancy, or plans to become pregnant in the next 4 months; current treatment for cancer; plans to relocate within 4 months; hospitalization for a psychiatric diagnosis within the last year; a past diagnosis of or current symptoms of alcohol or substance dependence; current receipt of dialysis; or unwillingness or inability to wear the CGM device continuously for study duration.

2.2 | Study Design & Randomization

This was a single-site pilot study with a two-group randomized controlled trial design. Participants were randomly assigned by the study coordinator (KH) to either a Standard Behavioral Weight Loss (BWL) or Personalized Behavioral Weight Loss (PBWL) approach in a 1:3 ratio using a random numbers generator implemented in a REDCap randomization module. Due to the nature of the intervention, blinding was not possible. The sample size ($n = 35$) was driven by the funding available. The study was pre-registered (ClinicalTrials.gov NCT04639076).

All participants received a 12-week intervention. After the start of the study, a modification was approved by the Internal Review Board that gave participants the option to continue in the study for an additional 12 weeks to track longer-term outcomes. They received one coaching session between weeks 12 and 24 and completed a weight and short assessment after 24 weeks.

2.3 | Interventions

2.3.1 | All Groups

Table 1 outlines the key features of each study arm. All participants received a digital behavioral weight loss intervention that included a study-specific smartphone app, digital tools, and weekly counseling. Participants were instructed to self-monitor diet, activity, and weight daily and were given goals for daily calorie intake and physical activity. Goals were set to promote a one to two pound weight loss per week and at least 150 min of moderate-to-vigorous activity weekly by study end. All participants received a Wi-Fi-enabled smart scale (Withings Body Scale)

TABLE 1 | Intervention characteristics.

Intervention	Behavioral weight loss (BWL)	Personalized behavioral weight loss (PWBL)
Intervention components		
Daily self-monitoring of weight (via Bluetooth scale), diet (via Fitbit app), and activity (via Fitbit activity tracker)	Yes	Yes
Provision of a study app (mPWR), with tools to track progress with behavioral goals and weight outcome goal, lessons, and resources	Yes	Yes
Focus of the behavioral lessons and resources in the mPWR app	General	General, plus additional resources specific to their mPWR prescription
Continuous self-monitoring of blood glucose via a continuous glucose monitor	No	Yes
Weekly, one-on-one sessions with a study coach	Yes	Yes
Weekly feedback messages from a study coach	Yes	Yes
Intervention prescription		
Calorie goal	Based on starting weight: 1200 kcal for < 200 lbs 1500 kcal for 200–250 lbs 1800 kcal for 250–300 lbs	Based on BOD POD assessment. The prescribed calorie goal was set to 1000 calories below their estimated energy expenditure, but was never less than 1200 calories/day
4-Week experimentation period	No	Yes
Physical activity goal	Weekly goal; standard goal progression	Daily or weekly goal; goal progression only if goals are achieved
Macronutrient goal	None	Low-carbohydrate (≤ 25% calories from carbohydrate) or low-fat (≤ 25% calories from fat)
Eating frequency goal	None	3 meals or meals and snacks daily

and physical activity tracker (Fitbit Inspire) and were asked to track their diet using the Fitbit app. The custom mPWR study app displayed data from the tracking tools and summarized progress toward study goals, in addition to providing behavioral lessons and resources. During their in-person baseline assessment visit, all participants attended a 60-min in-person kick-off session during which they set up their study devices, learned about their randomly assigned program, and worked with a study coach to explore their motivations for weight loss.

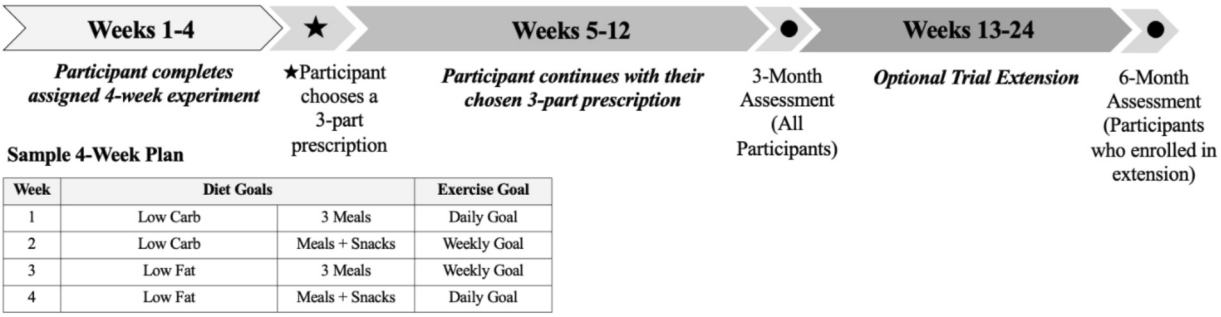
During the 12-week intervention, participants in both groups received weekly, one-on-one, 30-min, phone or video calls with a study coach. These sessions were semi-structured and led by interventionists with at least a Master's degree and trained in behavioral weight loss. Coaches could view food, weight, and activity progress through an online portal prior to that week's sessions. During the sessions, the coach reviewed self-monitoring records with the participant, set weekly goals, discussed behavioral lesson content introduced in the app that week, facilitated problem solving of any barriers to goal adherence, and adapted treatment recommendations based on the needs of the participant. Coaches sent a personalized feedback message after each weekly session.

2.3.2 | Differences Between Groups

The BWL program was consistent with standard weight loss programs that prescribe a daily calorie goal, a weekly physical activity goal, and goal for daily weighing. The weight loss "prescription" for BWL participants remained consistent throughout the 12-week intervention, with the exception of the physical activity goal. Participants started with a weekly activity goal based on their baseline physical activity and progressed to a weekly goal of 150 min, following a standard progression. As detailed in Table 1, BWL participants received a standard calorie goal based on starting weight (range: 1200–1800 calories).

The PBWL program prescribed a daily calorie goal based on baseline BOD POD (COSMED, USA) estimates of energy expenditure and self-reported physical activity. Over the 12-week intervention, PBWL participants followed a three-part weight loss prescription that specified goals for (1) macronutrient composition of the diet (low fat (≤ 25% calories from fat) or low carbohydrate (≤ 25% calories from carbohydrates)), (2) meal frequency (3 meals or 3 meals plus snacks), and (3) activity goal focus (daily or weekly active minutes goal). Participants in PBWL were also given an additional self-monitoring tool, a CGM monitor (Abbott Freestyle Libre). They were asked to wear the device continuously for the 12-week study and scan upon waking, before meals, before exercise, and before bedtime. They were taught to use the tool, interpret glucose readings, and make changes to their diet and activity to promote glycemic control. Both participants and study coaches could view the participant's glucose summary report online. During sessions, counselors helped PBWL participants explore possible reasons for elevated mean blood glucose readings, time outside of range, or glycemic excursions by highlighting possible relationships between CGM, diet, and activity data. Participants were encouraged to explore whether modifying their diet or activity could improve glucose control. For example, a participant whose CGM showed a glycemic excursion after a carbohydrate-rich meal might be challenged to try a modified meal with a lower carbohydrate content and higher protein content to explore its differential impact on blood glucose.

As seen in Figure 1, participants experimented with different prescriptions during the first 4 weeks before choosing a plan to follow for the remainder of the study. Participants were randomly assigned to the plan they followed in the first 4 weeks and were introduced to their assigned plan during their one-on-one kick-off session; that session included a discussion of how certain individuals may respond differently to different diet prescriptions and the possible benefit of identifying the prescription that was the best fit for them. All the plans were designed so that participants trialed each macronutrient prescription for two consecutive weeks (Weeks 1&2 or Weeks 3&4); the other factors were trialed for 2 weeks each, but not always consecutively. For example, their Week 1 plan may have been "low carbohydrate diet, 3 meals, weekly exercise goal" and their Week 2 plan may have been "low carbohydrate, 3 meals and snacks, daily exercise goal." To help with adherence to the diet prescriptions, the PBWL group received additional materials specific to the personalized prescriptions at study start, including sample meal plans consistent



Week	Diet Goals		Exercise Goal
1	Low Carb	3 Meals	Daily Goal
2	Low Carb	Meals + Snacks	Weekly Goal
3	Low Fat	3 Meals	Weekly Goal
4	Low Fat	Meals + Snacks	Daily Goal

FIGURE 1 | Overview of the Personalized Behavioral Weight Loss (PBWL) Intervention. This image depicts the PBWL intervention, which included a 4-week experiment during which participants trialed different 3-part prescriptions. Participants were randomly assigned to the plan they were asked to follow for the first 4 weeks. The table depicts a sample 4-week plan. After 4 weeks, they selected their 3-part prescription and followed it for 3 months (primary study end point). Most participants enrolled in an optional study extension and were followed up for an additional 3 months.

with the different macronutrient and meal frequency goals, as well as lists of lower-fat and lower-carbohydrate options from each food group.

During weekly sessions in the first 4 weeks, study coaches made note of the participant's experiences with the different prescriptions, and reviewed their relationships to weight and glucose outcomes. At the end of 4 weeks, participants then chose a three-part prescription to follow for the remainder of the program. The decision was made in consultation with their study coach and with consideration of measured blood glucose, weight loss, perceived hunger, and perceived ability to adhere to the prescription.

2.3.3 | Outcome Measures

The primary endpoint was change in body weight (kg) from baseline to 12 weeks. In-person weights were taken by trained study staff on a calibrated digital Tanita scale at baseline and 3 months. Two measures were completed, unless the difference between the measures exceeded 0.2 kg; in this case, a third measure was taken. Weight change and percent weight change were calculated using the average of weights taken at baseline and 3 months. Heights were measured at baseline using a wall-mounted stadiometer (Country Technology Inc, WI). Similarly, two measurements were taken and averaged unless the two measures were not within 0.5 cm, in which case a third measurement was taken and used in the average. Heights and weights were used to calculate BMI (kg/m^2).

Diet was assessed via two 24-h diet recalls collected with the Automated Self-Administered 24-h Dietary Assessment Tool [25]. At both baseline and 3 months, food consumption on one weekday and one weekend day were assessed and used to calculate daily calories, and percent of calories from carbohydrates, fat, protein, and alcohol. Physical activity was measured using the Paffenbarger Activity Scale, which was captured as energy expenditure from physical activity per week (kcal/week) [26]. Changes in diet and activity variables were calculated by subtracting baseline values from 3-month values. Hunger and satiety were assessed using a three item Visual Analog Scale measuring exactly 100 mm in length, anchored by word descriptors (ex:, Not at all hungry, Extremely hungry) at each end. Participants placed a mark on the line at the point they felt represented their response to the question. The three items asked about feelings of hunger over the past week, feeling of fullness after consuming meals in the past week, and feelings of fullness in general over the past week. Larger positive change numbers indicated a greater change in perceived hunger or fullness from baseline to 3 months.

Feasibility measures included self-monitoring adherence, study goal adherence, and attendance at coaching sessions. Adherence to the daily weighing, activity tracking, and diet monitoring goals was also assessed using data from the Fitbit app and study devices. Participants were adherent to self-monitoring goals on a given day if they weighed themselves at least once, tracked at least 500 calories, and tracked at least 1000 steps. In the PBWL, CGM engagement was captured as mean scans per day. They were adherent to their calorie goal if they tracked at least 500 calories but were below their daily calorie goal. Given that some participants had daily activity goals and others had weekly goals, average weekly active minutes are reported.

Program satisfaction was the primary acceptability measure and was assessed via one item on the 3-month questionnaire that asked them to rank their overall satisfaction with the intervention they received on a four-point Likert scale that ranged from “very dissatisfied” (1) to “very satisfied” (4). Adherence to study coaching was assessed via logs of how many sessions they attended (possible range: 0–12) and captured as the percent of sessions attended. Participant demographics were assessed at baseline via standard questionnaires. Additional health measures that were collected at baseline and 3 months included: waist circumference (per the National Health and Nutrition Examination survey anthropometry procedures manual), body composition (via BOD POD), and HbA1c (via fingerstick and analysis on a point of care unit (Aflinion Alere)).

2.3.4 | Statistical Methods

Analyses were conducted with SAS software version 9.4 (Cary, NC). Independent samples *t*-tests were used for between-group comparisons of continuous variables. For *t*-tests, the *F*-test of equal variances was performed. When the *p* value for the *F*-test was not statistically significant, the Pooled estimate was used; the Satterthwaite estimate was used when the *p* value for the *F*-test was statistically significant. Statistical significance was set at $p \leq 0.05$. Chi-square tests of independence or Fisher's exact tests were used for dichotomous variables, depending on cell frequencies. To meet the study's primary aim of testing the feasibility and preliminary efficacy of the PBWL, differences in outcomes in BWL and PBWL were compared. Additional exploratory analyses compared between-group differences in (a) 3-month outcomes in the sub-samples of participants who did and did not achieve at least 5% weight loss and (b) 6-month outcomes in BWL and PBWL. The 6-month analysis considered sub-samples of participants with a goal of continued weight loss or weight maintenance during the optional study extension. Given that research questions for this pilot and feasibility study were designed to be hypotheses-generating and not confirmatory, adjustments were not made for multiple comparisons [27].

2.4 | Ethical Considerations

The study was approved by the Internal Review Board at the University of North Carolina, Chapel Hill (IRB 19–2003).

3 | Results

3.1 | Participant Flow

A CONSORT diagram is presented in Figure 2. From October to December 2020, 122 participants were recruited, 81 of whom were eligible after an online screener and 44 of whom were eligible after a telephone screen. Ultimately, 35 participants

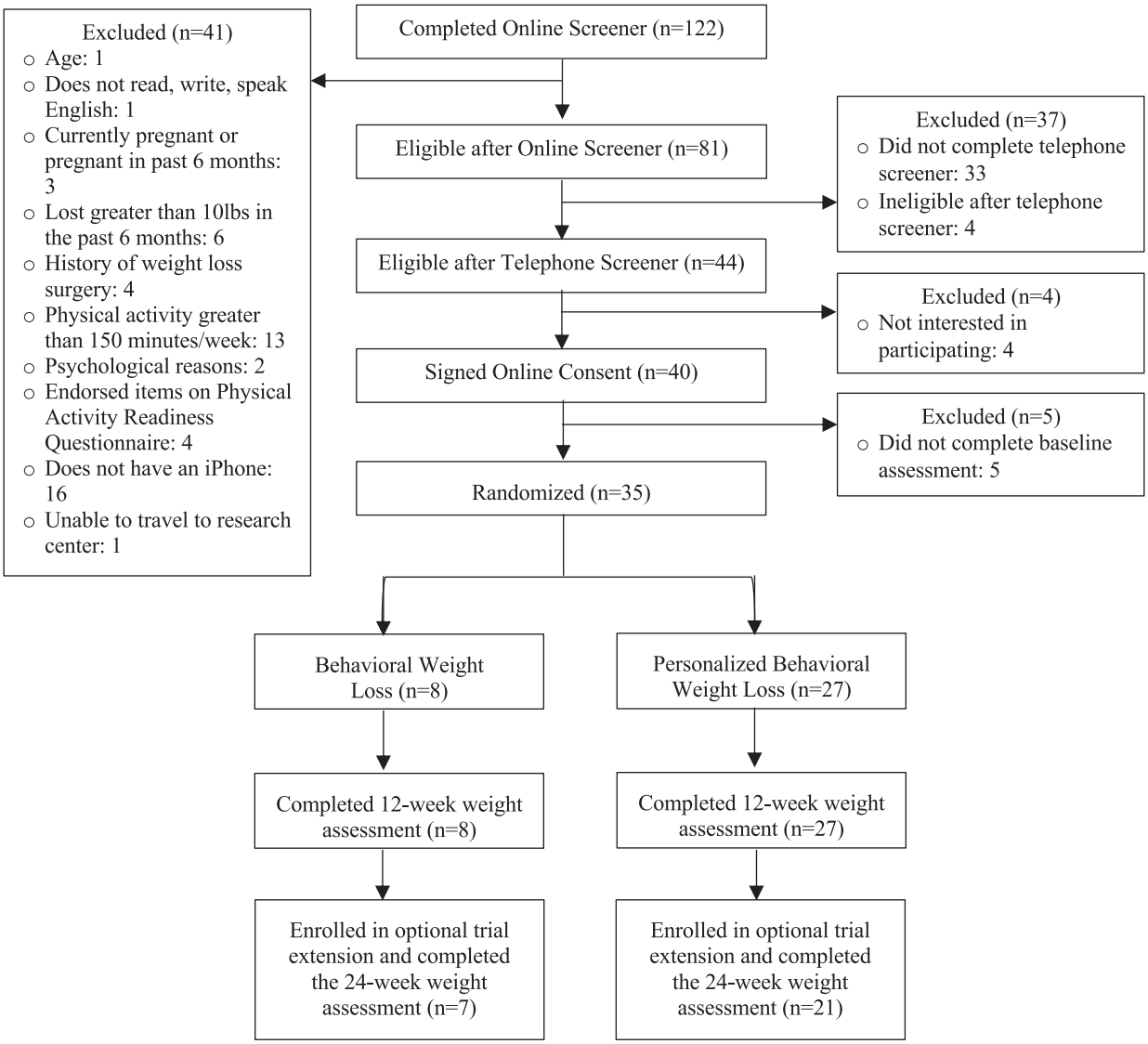


FIGURE 2 | CONSORT Diagram. This figure depicts the participant flow through the intervention, including the number of participants who were screened, consented, randomized, assessed at 3 months (study end), enrolled in the optional study extension, and assessed at 6 months (end of study extension).

were randomized; 8 were randomized to BWL and 27 to PBWL. Participants started the intervention between November 2020 and January 2021; the last participant finished the intervention in May 2021.

Of the 27 PBWL participants, all but one chose a 3-part prescription after the initial 4-week experiment. The participant requested to continue with her original personalized calorie goal but no goals for meal/snack pattern or macronutrient percentage. This request was honored by the study team given the nature of the study as a pilot and feasibility trial, as well as the importance of retention in this small sample. At the end of the 4-week trial, 65% (n = 17) of the remaining 26 PBWL participants chose a low carbohydrate diet, 88% (n = 23) chose meals and snacks, and 54% (n = 14) chose a weekly physical activity goal. Given the pilot nature of the intervention, PBWL participants were allowed to request changes to their 3-part prescription between Weeks 5 and 12; 6 elected to change at least one part of their prescription. At the end of 12 weeks, 59% (n = 16) of PBWL participants had a low carbohydrate diet prescription, 85% (n = 22) had a meal and snack prescription, and 54% (n = 14) had a weekly physical activity prescription.

All weights were available for assessment at 12 weeks. One participant from each group was missing a fasting glucose value and one participant from PBWL was missing additional questionnaire and anthropometric data. After 12 weeks, 77% (n = 28; n = 7 in BWL, n = 21 in PBWL) enrolled in the optional 12-week trial extension; all completed their weight and questionnaire at 24 weeks.

3.2 | Participant Characteristics

Participant characteristics are summarized in Table 2. On average (mean ± SD), participants (n = 35) were 49.2 ± 10.9 years old and had a BMI of 34.6 ± 4.99 kg/m^2; 85.7%

TABLE 2 | Baseline Participant Characteristics.

	All ($n = 35$)	BWL ($n = 8$)	PBWL ($n = 27$)
Sex			
Female	30 (85.71%)	8 (100.00%)	22 (81.48%)
Age (years)	49.20 ± 10.93	49.13 ± 10.74	49.22 ± 11.20
Race			
White	25 (71.43%)	3 (37.50%)	22 (81.48%)
Ethnicity			
Non-Hispanic	34 (97.14%)	8 (100.00%)	26 (96.30%)
Education			
High school graduate or G.E.D.	1 (2.86%)	0 (0.00%)	1 (3.70%)
Some college or associate degree	4 (11.43%)	0 (0.00%)	4 (14.81%)
College graduate or Baccalaureate degree	14 (40.00%)	3 (37.50%)	11 (40.74%)
Masters or Doctoral degree	16 (45.71%)	5 (62.50%)	11 (40.74%)
Weight (kg)	96.46 ± 20.46	84.44 ± 13.44	100.02 ± 21.01
HbA1c (%)	5.58 ± 0.35	5.51 ± 0.25	5.60 ± 0.38
Pre-diabetes status (% with HbA1c ≥ 5.7)	12 (34.29%)	3 (37.50%)	9 (33.33%)
Fasting glucose (mg/dL)	94.35 ± 10.97	94.14 ± 8.75	94.41 ± 11.62
BMI (kg/m^2)	34.65 ± 4.99	32.31 ± 3.30	35.34 ± 5.24
Overweight	5 (14.29%)	1 (12.50%)	4 (14.81%)
Class I Obesity	13 (37.14%)	5 (62.50%)	8 (29.63%)
Class II Obesity	13 (37.14%)	2 (25.00%)	11 (40.74%)
Class III Obesity	4 (11.43%)	0 (0.00%)	4 (14.81%)
Waist circumference (cm)	110.87 ± 11.52	103.24 ± 7.31	113.13 ± 11.66
Weekly energy expenditure (kcal/week)	268.44 ± 389.80	63.00 ± 136.33	329.31 ± 420.55
Daily calorie intake (kcal)	1988.41 ± 653.89	2092.53 ± 178.11	1957.56 ± 739.09
Percent calories from macronutrients (%)			
Fat	37.66 ± 6.89	36.91 ± 6.36	37.88 ± 7.14
Carbohydrates	45.06 ± 9.36	42.91 ± 10.38	45.69 ± 9.15
Protein	16.67 ± 4.38	16.47 ± 3.05	16.73 ± 4.76
Alcohol	1.97 ± 4.04	4.78 ± 6.62	1.14 ± 2.54

Note: Values are displayed as *n* (%) for categorical variables and mean ± standard deviation for continuous variables.

identified as female, 71.4% identified as White, and 85.71% had at least a Baccalaureate degree. At baseline, 34% had a HbA1c in the pre-diabetes range. There were no between-group differences except for race (37.5% White in BWL, 81.5% White in PBWL, $p = 0.027$).

3.3 | Acceptability & Feasibility

As seen in Table 3, tracking adherence for diet, activity, and weight was high in both BWL (77.25%, 95.83%, 86.01% of study days) and PBWL (86.73%, 96.65%, 86.46%); between-group differences in tracking adherence were not statistically significant. Average daily CGM scans (mean (SE)) in PBWL were 4.90 (0.30). PBWL participants stayed at or below their calorie goal on statistically significantly more days (70.86% (21.51) of study days) than BWL participants (53.13% (7.14), $t(33) = -2.07$, $p = 0.046$). Counseling session adherence was high with 95.83% of sessions completed in BWL (range: 50.00%–100.00%, percent who completed all 12 sessions: 75.00%) and 97.53% of sessions attended in PBWL (range: 83.33%–100.00%, percent who completed all 12 sessions: 92.59%). Average program satisfaction (on a scale of 1–4) was nearly identical in BWL (3.63) and PBWL (3.67, $t(33) = -0.17$, $p = 0.86$). Satisfaction was highest (3.85) among PBWL optimizers, but lowest in PBWL participants who did not optimize weight loss (3.14)—and lower in this group than the BWL sub-sample that did not optimize weight loss (3.67).

3.4 | Preliminary Efficacy

Table 3 also presents group means (SE) for primary and secondary clinical outcome variables. Weight change from baseline to 12 weeks (kg) was statistically significantly greater in the PBWL group (−7.08 (0.74)) than in the BWL group (−3.79

TABLE 3 | Study outcomes.

	BWL ($n = 8$)	PBWL ($n = 27$)	p
Acceptability & Feasibility			
Percent of days weighed (%)	86.01 (5.80)	86.46 (3.51)	0.95
Percent of days with complete calorie tracking (%)	77.25 (7.59)	86.73 (3.33)	0.21
Percent of days activity was tracked (%)	95.83 (2.33)	96.65 (1.51)	0.79
Mean daily scans		4.90 (0.30)	
Percent of days at calorie goal with complete tracking (%)	53.13 (7.14)	70.86 (21.51)	0.046
Average weekly active minutes (min)	219.80 (59.98)	222.50 (27.10)	0.96
Adherence to counseling sessions (% completed)	95.83 (2.73)	97.53 (1.93)	0.66
Overall program satisfaction	3.63 (0.18)	3.67 (0.12)	0.86
Primary Clinical Outcome			
Weight change (kg)	−3.79 (0.84)	−7.08 (0.74)	0.03
Secondary Outcomes			
Weight change (%)	−4.68 (1.08)	−7.27 (0.77)	0.10
BMI change (kg/m2)	−1.41 (0.37)	−2.50 (0.26)	0.04
Visual analog scale change (mm)			
Feeling hungry	−10.88 (9.88)	−12.67 (4.22)	0.85
Feeling full	−5.00 (9.98)	−2.41 (2.89)	0.81
Feeling full in general	3.88 (9.62)	−1.81 (2.85)	0.59
Change in percent of kcal from macronutrients (%)			
Fat	1.15 (3.32)	2.19 (1.58)	0.76
Carbohydrates	−3.97 (2.20)	−4.38 (1.99)	0.91
Protein	6.06 (1.85)	2.56 (1.09)	0.13
Alcohol	−2.77 (2.05)	−0.34 (0.51)	0.28
Weekly energy expenditure change (kcals)[a]	755.1 (143.5)	935.8 (171.9)	0.43
Average daily energy intake change (kcal)	−767.4 (169.7)	−520.3(120.5)	0.31
Additional Outcomes			
Lost 5%	5 (62.50%)	20 (74.07%)	0.66
Waist circumference change (cm)[a]	−1.78 (1.50)	−5.40 (1.53)	0.22
Fasting glucose change (mg/dL)[a,b]	−4.86 (2.72)	−3.27 (1.94)	0.70
HbA1c change (%)			
All participants[a]	−0.33 (0.06)	−0.45 (0.04)	0.13
HbA1c Normal at baseline (< 5.7%)[c]	−0.24 (0.05)	−0.38 (0.04)	0.09
HbA1c in Pre-DM range at baseline (5.7%–6.4%)[d]	−0.47 (0.09)	−0.59 (0.08)	0.45

Note: All values are listed as n (%) or mean (standard error).
[a]$n = 26$ for PBWL.
[b]$n = 7$ for BWL.
[c]Sample was 5 BWL and 17 PBWL.
[d]Sample was 3 for BWL and 9 for PBWL.

(0.84), $t(33) = -2.27$, $p = 0.03$). Participants in PBWL also lost a greater percentage of starting body weight (−7.27% (0.77)) than BWL (−4.68% (1.08)), though the between group difference did not reach statistical significance ($t(33) = 1.68$, $p = 0.10$). The between-group difference in change in BMI (kg/m^2) was statistically significant, with greater decreases from baseline to 12 weeks in PBWL (−2.50 (0.26)) than BWL (−1.41 (0.37), $t(33) = 2.09$, $p = 0.04$). There were slightly greater decreases in self-reported daily calorie intake in BWL (−767.4 (169.7)) than PBWL (−520.3 (120.5), $t(33) = -1.03$, $p = 0.31$) and slightly greater increases in weekly energy expenditure (kcals) in PBWL (935.8 (171.9)) than in BWL (755.1 (143.5), $t(26.32) = -0.81$, $p = 0.43$), though these differences did not reach statistical significance. Changes in Visual Analog Scale scores and percentage of calories from different macronutrients were similar between the groups. All participants with impaired glucose (HbA1c ≥ 5.7%) at baseline (34% of participants) had an HbA1c within normal range at (< 5.7%) at 12 weeks.

3.5 | Ancillary Analyses

At 12 weeks, 62.50% of BWL and 74.07% of PBWL participants had achieved a 5% weight loss and were considered to have optimized weight loss. As seen in Table 4, exploratory analyses showed that PBWL participants who optimized weight loss ($n = 20$) lost significantly more weight (−8.66 (0.66) kg) than BWL participants who optimized weight loss ($n = 5$, −4.76 (0.43) kg, $t(20.88) = 4.97$, $p < 0.001$) at 12 weeks; differences in percent weight change (%) in these two groups approached statistical significance (PBWL: −9.03 (0.67), BWL: −6.16 (0.70), $t(23) = 2.04$, $p = 0.05$) and the difference in BMI change (kg/m^2) was statistically significant (PBWL: −3.12 (0.20), BWL: −1.81 (0.21), $t(23) = 3.07$, $p = 0.005$). Other outcomes were similar in a) BWL participants who did not optimize weight loss and PBWL participants who did not optimize weight, as well as b) BWL and PBWL optimizers.

Among the 28 participants who completed the 12-week study extension and were assessed at 6 months, mean weight losses (kg) from month 3 to month 6 were −0.29 (1.05) in BWL and −1.38 (0.50) in PBWL (Table 5). Finally, 6-month weight losses (kg) in this sub-sample were −4.03 (1.38) in BWL and −9.19 (1.01) kg in PBWL; the between-group difference in weight loss was statistically significant ($t(26) = 2.67$, $p = 0.013$). The percentages of participants participating in the study extension who self-reported goals of continued weight loss from month 3 to month 6 (BWL: $n = 6$, 85.7%; PBWL: $n = 17$, 81.0%) or weight maintenance (BWL: $n = 1$, 14.3%; PBWL: $n = 4$, 19.0%) were similar in each group. Among participants with a goal of continued weight loss, the percentages of participants who achieved this goal (mean difference ≤ −1 kg; PBWL: 59%, BWL: 50%), maintained weight (mean difference −1 to 1 kg; PBWL: 29%, BWL: 17%), and regained weight (mean difference > 1 kg; PBWL: 12%; BWL: 33%) were also similar in each group.

4 | Discussion

Overall, the study found that a PBWL approach to weight loss—which included a 3-part energy balance prescription chosen after a 1-month period of experimenting with different diet and activity factors to monitor their impact on blood sugar and weight—resulted in greater weight loss than a standard BWL program. PBWL participants lost an average of −7.08 (0.74) kg after 12 weeks, while BWL lost an average of −3.79 (0.84) kg. Tracking adherence for diet, activity, and weight was high in both groups throughout the intervention, but PBWL participants had more days at or below their study calorie goal. Between-group comparisons of PBWL and BWL participants who achieved a 5% weight loss at study end showed greater weight losses in PBWL optimizers than BWL optimizers. All participants ($n = 11$) with elevated HbA1c at baseline (5.7%–6.4%) had an HbA1c within the normal range (< 5.7%) at 12 weeks.

It is encouraging that both remotely delivered interventions were able to support most participants with a 5% weight loss (74% in PBWL, 63% in BWL) while remaining acceptable and feasible. Though the PBWL intervention was more intensive for participants—requiring weekly changes to their 3-part prescription in the first 4 weeks, daily use of a CGM device, and close observation of the macronutrient composition of the diet—average program satisfaction in PBWL (3.67) was nearly identical to that in BWL (3.63). Though PBWL optimizers had the highest mean satisfaction scores (3.85) and the greatest mean weight losses (−8.66 kg), PBWL non-optimizers, on average, lost less weight (−2.57 kg) than PBWL optimizers and had the lowest satisfaction scores (3.14) of all sub-samples analyzed. This may suggest that the PBWL was exceptionally beneficial for most (80%), but not all (20%) PBWL participants. However, further investigation is needed given the small sample size and it should be noted that scores of "3" or greater on the satisfaction questionnaire still indicated satisfaction with the program.

Mean weight losses in PBWL were compelling (−7.08 (0.74) kg), and above what is typically seen in 12-week behavioral weight loss interventions that employ the combination of a mobile app and intensive behavior coaching by a human counselor. A recent meta-analysis found that such intervention groups lost −1.4 to −8.32 kg in 12 weeks, with an average mean difference of −2.03 kg [95% CI: −2.80, −1.26] in intervention participants, as compared to controls [28]. PBWL participants who continued with the study extension to 6 months were also successful with continued weight loss or maintenance during this time. Only 10% of PBWL regained weight from weeks 12–24, despite the fact that the intervention was primarily automated during that time; participants had access to their app, activity tracker, and smart scale—but not CGM—and had only one 30-min call with their study coach in Week 18.

The high adherence to self-monitoring in both study groups supports the feasibility of using wearable technologies to guide personalized treatment recommendations and participant decision-making in precision nutrition interventions [11]. High adherence also adds to the robustness of the study findings, as adherence is thought to be on the causal pathway to weight loss [29]. The greater adherence to diet study goals in PBWL may partially explain greater weight losses in that group [30]; participants in PBWL had complete calorie tracking on a greater percentage of study days (87%) than BWL participants (77%) and met their calorie goal on a greater percentage of study days (71%) than BWL participants (53%). However, the extent to which the more directive macronutrient and meal frequency goals in PBWL may have driven this greater adherence cannot be determined.

While both groups received a comprehensive core mHealth program and weekly calls with a study coach, there were multiple differences in the interventions delivered. Specifically, the PBWL intervention was different from the BWL intervention in its use of CGM, a three-part prescription, 4-week experimentation period, and participant autonomy in choice of prescription to follow for weeks 5–12. This individual components—and their combined use in the PBWL group—differentiate mPWR from past studies. The 4-week trial period was novel and may be important given that the prescription of a study diet congruent with food preferences and with a higher likelihood of adherence may be related to study outcomes [31, 32]. In mPWR, participants chose their prescription after 4 weeks of experimentation

TABLE 4 | Between-group differences in outcomes in the sub-samples of participants who did and did not optimize weight loss.

	Weight loss not optimized ($n = 10$)			Weight loss optimized ($n = 25$)		
	BWL ($n = 3$)	PBWL ($n = 7$)	p	BWL ($n = 5$)	PBWL ($n = 20$)	p
Acceptability & Feasibility						
Percent of days weighed (%)	76.59 (13.58)	73.81 (9.81)	0.88	91.67 (4.19)	90.89 (2.85)	0.90
Percent of days with complete calorie tracking (%)	61.53 (14.97)	77.06 (8.55)	0.37	86.68 (5.91)	90.12 (3.17)	0.63
Percent of days activity was tracked (%)	99.60 (0.40)	97.11 (1.47)	0.32	93.57 (3.42)	96.49 (1.99)	0.51
Percent of days at calorie goal with complete tracking (%)	41.27 (8.97)	62.07 (8.01)	0.17	60.24 (9.21)	73.93 (4.76)	0.21
Average weekly active minutes (min)	125.3 (23.66)	247.9 (86.88)	0.40	276.5 (88.10)	213.6 (22.50)	0.52
Overall program satisfaction	3.67 (0.22)	3.14 (0.26)	0.29	3.60 (0.24)	3.85 (0.11)	0.33
Primary clinical outcome						
Weight change (kg)	−2.17 (1.99)	−2.57 (0.87)	0.83	−4.76 (0.43)	−8.66 (0.66)	< 0.001
Secondary outcomes						
Weight change (%)	−2.20 (2.10)	−2.26 (0.50)	0.98	−6.16 (0.70)	−9.03 (0.67)	0.05
BMI change (kg/m2)	−0.74 (0.87)	−0.73 (0.24)	0.99	−1.81 (0.21)	−3.12 (0.20)	0.005
Visual analog scale change (mm)						
Feeling hungry	−26.67 (12.67)	−19.43 (7.02)	0.60	−1.40 (12.86)	−10.30 (5.14)	0.47
Feeling full	11.00 (8.33)	5.29 (5.98)	0.61	−14.60 (14.02)	−5.10 (3.17)	0.54
Feeling full in general	12.67 (9.39)	5.57 (5.03)	0.49	−1.40 (14.64)	−4.40 (3.29)	0.85
Change in percent of calories from macronutrients (%)						
Fat	0.180 (4.08)	0.51 (3.14)	0.95	1.73 (5.07)	2.78 (1.86)	0.82
Carbohydrates	−3.28 (2.94)	−2.84 (4.06)	0.95	−4.38 (3.29)	−4.93 (2.33)	0.91
Protein	5.66 (5.06)	1.22 (2.56)	0.41	6.29 (1.35)	3.03 (1.20)	0.21
Alcohol	−0.98 (4.10)	1.08 (1.08)	0.51	−3.85 (2.43)	−0.84 (0.55)	0.29
Weekly energy expenditure change (kcals)[a]	723.0 (327.4)	1116.0 (240.5)	0.37	774.3 (159.0)	881.7 (212.9)	0.81
Average daily kcal intake change	−716.4 (91.83)	−594.6 (258.9)	0.78	−798.0 (278.4)	−494.3 (138.9)	0.34
Additional Outcomes						
Waist circumference change[a]	−4.13 (1.46)	−2.98 (2.56)	0.77	−0.36 (2.08)	−6.13 (1.83)	0.15
Fasting glucose change[b]	0	−1.17 (3.00)	0.84	−6.80 (3.37)	−3.90 (2.38)	0.57
HbA1c change (%)						
All participants[a]	−0.33 (0.12)	−0.33 (0.07)	1.00	−0.32 (0.07)	−0.49 (0.05)	0.12
HbA1c Normal at baseline (< 5.7%)[c]	−0.25 (0.15)	−0.28 (0.09)	0.88	−0.23 (0.03)	−0.42 (0.04)	0.07
HbA1c in Pre-DM range at baseline (5.7%–6.4%)[d]	−0.50 A	−0.45 (0.05)		−0.45 (0.15)	−0.63 (0.10)	0.42

[a] $n = 6$ for weight loss not optimized in PBWL.
[b] $n = 2$ for weight loss not optimized in BWL and $n = 6$ for weight loss not optimized in PBWL.
[c] $n = 2$ for weight loss not optimized in BWL, $n = 4$ for weight loss not optimized in BWL, $n = 3$ for weight loss optimized in BWL, and $n = 13$ for weight loss optimized in PBWL.
[d] $n = 1$ for weight loss not optimized in BWL, $n = 2$ for weight loss not optimized in BWL, $n = 2$ for weight loss optimized in BWL, and $n = 7$ for weight loss optimized in PBWL.

with different prescriptions. In other studies that have explored the relationship between participant choice of a diet approach and weight loss—including those that have considered preference for a low-carb or low-fat diet—participants indicated their diet preference prior to intervention start and only one allowed participants to switch their prescription (after 12 weeks)

TABLE 5 | 6 Month outcomes.

	BWL	PBWL
All participants (n = 28)		
Sample size	7	21
Percent who had achieved a 5% weight loss at 3 months	4 (57.14%)	17 (80.95%)
Weight loss: 0–12 weeks (kg)	−3.74 (0.97)	−7.80 (0.79)
Weight loss: 12–24 Weeks (kg)	−0.29 (1.05)	−1.38 (0.50)
Weight loss: 0–24 Weeks (kg)	−4.03 (1.38)	−9.19 (1.01)
Participants with a goal of continued weight loss (n = 23)		
Sample size	6	17
Percent who had achieved a 5% weight loss at 3 months	4 (66.67%)	13 (76.47%)
Weight loss: 0–12 weeks (kg)	−3.65 (1.15)	−7.59 (0.95)
Weight loss: 12–24 Weeks (kg)	−0.37 (1.23)	−1.52 (0.60)
Weight loss: 0–24 Weeks (kg)	−4.02 (1.63)	−9.11 (1.21)
Participants with a goal of weight maintenance (n = 5)		
Sample size	1	4
Percent who had achieved a 5% weight loss at 3 months	0 (0.00%)	4 (100.00%)
Weight loss: 0–12 weeks (kg)	−4.30	−8.73 (1.10)
Weight loss: 12–24 Weeks (kg)	0.20	−0.80 (0.60)
Weight loss: 0–24 Weeks (kg)	−4.10	−9.53 (1.59)

[33, 34]. The 3-part prescription allowed for personalization of interventions across multiple behaviors instead of just one behavior (i.e., more than just diet composition or therapy approach) [12]. Lastly, few have used CGM to explore glucose regulation in normoglycemic individuals [23, 35].

The study was not designed to separate the individual effects of the PBWL intervention components on study outcomes, including weight and adherence. While this could be perceived as a limitation, it was an intentional decision in line with the study's underlying rationale that identifying the "ideal" weight loss approach for the population is less effective than identifying the "ideal" approach for the individual. Studies to date that have isolated single intervention characteristics have failed to find between-group differences in mean weight losses by diet composition prescribed [14, 36, 37] or by participant choice (or not) of intervention prescription [33, 34, 38]. It is possible that the combination of intervention components—including both the chance to test different evidence-based prescriptions and the provision of digital tools to provide multiple points of biofeedback for informed decision-making—drove weight losses in PBWL. It is also possible that only some of the PBWL intervention components were "active ingredients" in the PBWL approach. Future study designs could isolate individual components—such as monitoring with CGM—to see if they provide added benefit to the core personalized program.

Although the approach employed in this study was novel, there are some limitations that should be considered in the interpretation of these findings. The study's primary limitations were its pilot nature and small sample size, which limit its generalizability. The sample was also primarily female, which is notable given that one study that randomized participants to diet choice or not found a significant group by time by gender interaction in which men did better in the "No Choice" group and women did better in the "Choice" group [38]. Despite randomization, there were also a statistically significant between-group differences in self-identified race (37.5% White in BWL, 81.5% White in PBWL, $p = 0.027$). Last, it is only possible to estimate the percentage of calories from carbohydrates and fat in PBWL, due to limitations of data available through the Fitbit API.

5 | Conclusions

Combined, these findings suggest that personalized approaches that take into account early treatment response using weight and glucose monitoring show promise for optimizing weight loss. Given the compelling results but small sample size in the PBWL group, the PBWL approach should be tested in a larger trial. Future analyses may consider potential predictors of treatment choice and response—including the possible impact of genetic, microbiome, metabolomics, and psychosocial variables that were also collected as a part of this study. Such analyses may help generate testable hypotheses about the possible benefit of matching or personalizing the initial approach based on these predictors.

Author Contributions

All authors contributed to the study concept, design, and analysis. All authors were involved in writing the paper and had final approval of the submitted version.

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Conflicts of Interest

DFT is a member of the Scientific Advisory Board for WW. The other authors declare no conflict of interest.

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