doi: 10.1002/osp4.312

ORIGINAL ARTICLE

Randomized controlled trial assessing two commercial weight loss programs in adults with overweight or obesity

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Received 27 June 2018; revised 6 November 2018; accepted 11 November 2018

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CLINICAL TRIAL REGISTRATION: ClinicalTrials.gov identifier NCT02835092

Summary

Objective

Lifestyle interventions remain the cornerstone for obesity treatment. Commercial programs offer one weight loss approach, yet the efficacy of few such programs have been rigorously investigated. The purpose of this study was to evaluate the efficacy of two commercial weight-loss programs, both utilizing pre-portioned meal replacements (MRs) and different levels of behavioural support, compared to a self-directed control diet in adults with overweight and obesity.

Methods

In this 16-week study, participants were randomized to the low-calorie OPTAVIA® 5&1 Plan® with telephone coaching (OPT), the reduced-calorie Medifast® 4&2&1 self-guided plan (MED), or a self-directed, reduced-calorie control diet. Differences in weight, body composition (DXA) and body circumferences, all measured monthly, were assessed by analysis of covariance with sex and baseline measures as covariates.

Results

Of 198 participants randomized (80.8% female, BMI 34.2 kg/m^2, 45.7 years), 92.3% completed the study. The OPT and MED groups had significantly greater reductions in body weight (-5.7% and -5.0%, respectively, $p < 0.0001$), fat and abdominal fat mass ($p < 0.0001$) and waist and hip circumferences ($p \leq 0.003$) than control at 16 weeks. Weight change was correlated with MR usage and completion of coaching support calls.

Conclusions

Both structured commercial programs were more efficacious than a self-directed, reduced-calorie diet for weight loss and other anthropometric measures. Evidence-based commercial programs can be an important tool to help adults with overweight and obesity lose clinically relevant amounts of weight.

Keywords: Coaching, meal replacements, obesity, weight loss.

Introduction

Two-thirds of American adults struggle with overweight or obesity, and the burden of its sequelae, including cardiovascular disease and type 2 diabetes, make this one of the most pressing health issues of our time (1–3). In addition to the morbidity and mortality associated with obesity, the economic impact is also immense. The US spends an estimated $190 billion on obesity-related medical conditions, and the average annual medical costs for those with obesity are over $1,400 higher compared to people in a normal weight range (4,5).

Weight reduction strategies can help reduce both the medical and economic impact of obesity, as the risk of developing chronic diseases, especially cardiovascular disease and diabetes, is reduced in a clinically meaningfully way by modest weight loss in the 5–10% range (6,7). Lifestyle interventions have a minimal risk profile compared to pharmacotherapy or bariatric surgery, and remain the cornerstone treatment for obesity and

generally constitute the first line approach for weight management (1). The US Preventive Services Task Force (USPSTF) recently concluded that comprehensive lifestyle interventions in adults with obesity can lead to clinically meaningful weight loss and reduce the incidence of associated comorbidities while offering minimal risk of harm (8). In this context, commercial weight loss programs offer one such lifestyle approach. The joint guidelines issued by the American Heart Association, the American College of Cardiology and The Obesity Society for the management of overweight and obesity in adults recommend commercially available programs that promote a comprehensive lifestyle intervention can be prescribed as an option for weight loss provided there is peer-reviewed published evidence of their safety and efficacy (1). Many commercial programs, however, have not been rigorously tested for efficacy (9,10).

Given this backdrop, well-designed clinical studies can provide consumers and healthcare professionals alike with the evidence needed to confidently use specific commercial weight loss programs. These clinical studies can be particularly impactful when they are designed to mimic all aspects of the true consumer experience. The randomized, controlled study described herein was designed to test the efficacy of two commercial weight loss programs (Medifast and OPTAVIA), each compared to a self-directed, reduced-calorie control diet. The study arms mimicked the commercial experience through the utilization of the products (portion-controlled meal replacements), meal plans, educational materials and behavioural support provided to actual customers of these programs.

Methods

Study design

This was a randomized, controlled, 16-week, 3-arm parallel study conducted at a single clinical research center in the greater Chicago area between July 2016 and Feb 2017. After a screening visit, eligible participants were randomly assigned at baseline, in a 1:1:1 ratio stratified by sex, to one of three intervention groups: Medifast (MED), OPTAVIA (OPT), or Control. An independent biostatistician (not involved in data analysis) prepared the computer-generated randomization sequence (block size 6); group assignments were made sequentially by sealed envelope after each participant met eligibility criteria. Clinic visits occurred at screening, baseline, 2, 4, 8, 12 and 16 weeks. The study was approved by IntegReview Institutional Review Board (Austin, TX) and conducted according to the Declaration of Helsinki and Good Clinical Practice Guidelines (US 21CFR). Written informed consent was obtained from all participants prior to conducting protocol-specific procedures.

Study participants

Healthy adult (18–65 years) men and women, with a body mass index (BMI) of 27.0–42.0 kg/m^2, who were interested in losing weight and whose weight was stable ($\leq$ 5% change in the previous 6 months) were considered for the study. During the screening process fasting blood samples and vitals were taken and subjects were asked about their medical history and prior and current medication/supplement use. Subjects were excluded if they had clinically significant abnormal laboratory test results, had used medications, products, supplements or diet programs to try to lose weight in the past 6 months, previously had surgery or liposuction for weight reduction, were on unstable doses of medication(s) that can affect body weight, had a serious medical condition, including type 1 diabetes or type 2 diabetes requiring medication, had a history of eating disorders or alcohol abuse, were pregnant or lactating, or had an allergy, sensitivity or intolerance to ingredients or foods in the study diets. The study physician judged the health of the participant for inclusion in the study on the basis of the medical history and screening laboratory assessments. Stipends for attending clinic visits were provided to all study participants. To help with retention, participants in the Control group were offered up to 16 weeks of meal replacements (MRs) to continue their weight loss at the end of their intervention.

Interventions

The MED and OPT interventions in this study were designed to mimic as closely as possible the experiences of real-life users of these commercial weight loss programs.

Participants randomized to MED were meant to represent the typical self-guided, online Medifast customer. They received written program materials (meal plan guide, food journals, recipes, self-directed behavioural workbook) and were instructed to follow the Medifast 4&2&1 Plan® which consists of 4 Medifast Classic MRs, 2 lean and green meals (each self-prepared and consisting of 5–7 oz lean protein and 3 servings (~1 ½ cups) nonstarchy vegetables, and up to 2 healthy fat servings) and 1 healthy snack (i.e., a serving of fruit, dairy or whole grains). Each lean and green meal provides 250–400 kcals and $>$ 25 g protein, $\leq$ 15 g carbohydrate and 10–30 g fat. The 4&2&1 plan is intended to provide 1,100–1,300 kcal consisting of approximately 120–150 g protein, 85–100 g carbohydrate, 20–30 g fibre and 30–45 g

fat per day. Participants ordered MRs monthly from among 47 interchangeable options, including shakes, bars, soups, etc. Each MR was fortified with 24 vitamins/minerals and had 90–110 calories, 11–15 g protein (primarily from soy and/or dairy), 12–15 g of carbohydrate, and 0–3.5 g fat. Participants also had the option of ordering Medifast snacks and Flavors of Home® (prepackaged lean and green meals) for occasional use. Exercise as recommended by the American College of Sports Medicine was encouraged, but not required while following the Medifast 4&2&1 Plan®. All Medifast products were home-delivered to participants in their original commercial packaging and provided at no charge. Each participant had a 10–15 min introductory call with the Medifast Nutrition Support Team (NST) for an overview of the weight loss program, and like real customers, had telephone/email access to the NST throughout the study.

Participants randomized to OPT received written OPTAVIA® program materials (meal plan guide, food journals, recipes, Dr. A's Habits of Health book (11) and workbook (12)) and were instructed to follow the Optimal Weight 5&1 Plan®. This plan consists of 5 MRs and 1 lean and green meal (see above) and is intended to provide 800–1,000 kcal/day, consisting of 80–120 g protein, 80–100 g carbohydrate, 20–30 g fibre and 20–30 g fat. The OPT participants were given the same Medifast Classic MR, Medifast snack, and Flavors of Home® options as above, also home-delivered monthly and at no cost. Exercise was encouraged as part of the OPTAVIA® program, but not required, with a suggested limit of 45 minutes per day due to the caloric content of the meal plan. Consistent with the OPTAVIA customer experience, participants in OPT were each assigned a coach and received one-on-one telephonic coaching: one call the day before starting the program (lasting ~45 minutes and providing an overview of the program), four calls during week 1, two calls per week in weeks 2–4, and one call per week thereafter (weeks 5–16); these weekly check-in calls generally lasted 5–10 minutes and were focused on the participant's progress, overcoming challenges, etc. For the study, research assistants (not otherwise involved in the study) were trained to function as OPTAVIA coaches. The coach training, call content and schedule reflected the actual OPTAVIA coaching model. Additionally, like actual customers, participants also had access to online support tools and phone/email access to the NST throughout the study.

The Control group followed a self-directed, reduced-calorie diet, consistent with the 2015 Dietary Guidelines for Americans and based on the United States Department of Agricultural (USDA) ChooseMyPlate program. A daily calorie limit, targeting 7% weight loss over the 16-week study (consistent with the current guidelines for the management of overweight/obesity in adults (1)), was calculated for each participant (USDA Body Weight Planner; https://www.supertracker.usda.gov/bwp/). The daily caloric limit determined by the Body Weight Planner incorporated each participant's current physical activity level as well any planned increases in activity during the study period. Each participant received a one-on-one introduction session (10–15 min) with a trained study staff member during which they received their personalized calorie level recommendation, a corresponding meal plan (USDA, ChooseMyPlate), and other publicly-available information from ChooseMyPlate.com. Participants were instructed to use the SuperTracker (https://www.supertracker.usda.gov/) to track food, exercise, log progress, etc.

Assessments

Body weight (in gown, without shoes) was measured at each clinic visit on a medical quality digital scale (Health-o-meter 349KLX, Pelstar, McCook, IL) following a 10–14-hr fast. Body circumferences, measured using a stretch-resistant anthropometric tape (Gulick II Model 67020, Gays Mill, WI), and body composition, assessed using dual-energy x-ray absorptiometry (DXA) scans (GE Lunar Prodigy, enCORE software version 16, Madison, WI), were obtained at baseline and monthly. Quality of life (QOL) assessments (Impact of Weight on Quality of Life-Lite Questionnaire (IWQoL-Lite) and RAND-36 (13,14)) were electronically administered at baseline, week 8 and 16. Self-reported MR usage, program compliance (100-mm visual analog scale (VAS)), and degree of leisure time and work/school physical activity were collected electronically at monthly intervals throughout the study. Reported physical activity (i.e., degree of leisure time and work/school physical activity) was used to calculate physical activity level (PAL) which ranged from Very Light: 1.4 to Heavy: 2.3 (15). High sensitivity c-reactive protein (hsCRP) was measured at a CLIA-certified clinical laboratory (Elmhurst Memorial Reference Laboratory, Elmhurst, IL) from fasting plasma samples collected at baseline and week 16. All intervention-emergent adverse events (AEs) occurring after randomization were collected at each clinic visit for assessment of safety.

Statistics

The primary outcome was change in body weight (absolute and percent) from baseline to week 16. Secondary outcomes included proportion of participants achieving $\geq 5\%$ and $\geq 10\%$ loss of baseline body weight, changes in fat and lean mass, waist and hip circumference, hsCRP and QOL measures.

The sample size (198 randomized participants) was designed to provide 80% power to detect a 4-kg difference in body weight using a nominal $\alpha = 0.025$ (two-sided) to account for two primary comparisons (MED and OPT each compared separately to Control), maintaining an overall type I error of $\alpha = 0.05$.

A statistical analysis plan was generated prior to database lock. All statistical analyses were conducted using SAS (version 9.4, Cary, NC). Analyses were assessed on a modified Intent-to-Treat (mITT) population (all randomized participants with at least one post-baseline weight measurement). Analyses with and without single (last-observation carried forward, LOCF) and multiple imputation (MI, (16)) were also conducted for the primary endpoint.

Analysis of covariance (ANCOVA) was used to assess differences among intervention groups in the primary and continuous secondary outcome variables at each post-randomization visit. The ANCOVA model contained a term for intervention, with sex and baseline measures as covariates. Pairwise comparisons of MED and OPT each vs. Control were conducted. Differences in the proportion of participants in each intervention group achieving weight loss $\geq 5\%$ or $\geq 10\%$ were assessed using a generalized linear model with a logit link and binomial distribution specified. The model contained a term for intervention, with sex as a covariate. Pairwise comparisons at each post-randomization visit were conducted using step-down Dunnett's correction for multiple comparisons (MED and OPT each vs Control) for body weight, composition, and circumference parameters.

Results

Participants

Among 256 individuals screened for participation, 198 were randomized: 14 (7.1%) terminated early, 184 completed a 16-week assessment (92.3% retention), and of these, 179 (90.4%) completed all assigned clinic visits (Completers, see Figure 1). None withdrew due to an adverse event. Four participants (three Control and one OPT) withdrew consent prior to the week 2 visit (no longer interested in being in the study) and were excluded from the mITT population ($n = 194$).

Baseline characteristics for all randomized participants (Table 1) were similar across all three groups. Overall, the majority of participants were white (75.3%), female (80.8%), and had obesity (BMI ≥ 30 kg/m^2, 88.4%).

Weight loss

Both the MED and OPT groups lost significantly more absolute weight and a higher percentage of baseline body weight compared to Control at every time point ($p < 0.0001$) (Figure 2A, Figure 3, Table 2). Similar results

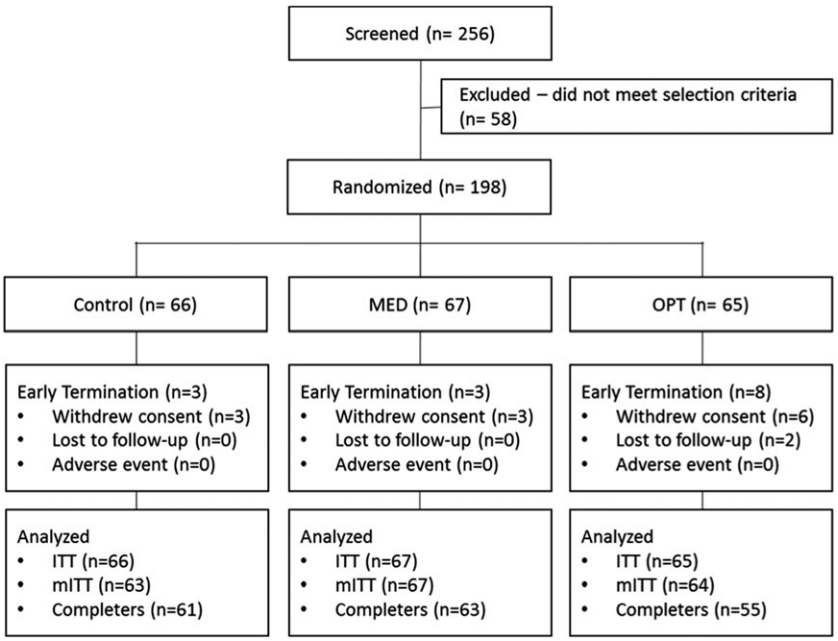

Figure 1 Disposition of Participants. ITT: Intent-to-Treat population, includes all participants randomized into the study. mITT: modified Intent-to-Treat population, includes all randomized participants with at least one post-baseline weight measurement. Completers: Includes all randomized participants that completed all clinic visits during the 16-week study.

Table 1 Baseline Characteristics

	Control	MED	OPT
Participants, n	66	67	65
Age, y	46.3±1.5	45.7 ± 1.7	45.2 ± 1.5
Sex, n (%)			
Male	12 (18.2)	13 (19.4)	13 (20.0)
Female	54 (81.8)	54 (80.6)	52 (80.0)
Race, n (%)			
White	50 (75.8)	54 (80.6)	45 (69.2)
African American	11 (16.7)	10 (14.9)	13 (20.0)
Multiracial Origin	2 (3.0)	0 (0.0)	3 (4.6)
Other	1 (1.5)	3 (4.5)	4 (6.2)
Ethnicity, n (%)			
Hispanic or Latino	4 (6.1)	8 (11.9)	6 (9.2)
Education, n (%)			
Some high school, no diploma	0 (0.0)	0 (0.0)	1 (1.5)
High school diploma or equivalent	6 (9.1)	7 (10.4)	11 (16.9)
Trade/technical/vocational training	3 (4.5)	2 (3.0)	1 (1.5)
Some college, no degree	20 (30.3)	18 (26.9)	18 (27.7)
College degree (Associate or Bachelor)	28 (42.4)	32 (47.8)	23 (35.4)
Graduate/professional degree	9 (13.6)	8 (11.9)	11 (16.9)
Smoking n (%)			
Current	4 (6.1)	5 (7.5)	4 (6.2)
Former	17 (25.8)	15 (22.4)	19 (29.2)
Never	45 (68.2)	47 (70.1)	42 (64.6)
Weight, kg	93.9±1.6	95.8 ± 1.6	95.5 ± 1.7
BMI, kg/m^2	33.8±0.4	34.2 ± 0.4	34.5 ± 0.4
BMI Category n (%)			
≥27.0 to ≤30.0 kg/m^2	9 (13.6)	8 (11.9)	6 (9.2)
>30.0 to <42.0 kg/m^2	57 (86.4)	59 (88.1)	59 (90.8)
	n = 63	*n = 67*	*n = 64*
Fat mass, kg	43.03±1.12	43.75 ± 1.10	43.39 ± 0.95
Lean mass, kg	48.27±1.11	49.60 ± 0.90	49.40 ± 1.26
Abdominal visceral fat, g	1426±89	1547 ± 113	1434 ± 96
Waist circumference, cm	109.0±1.3	109.7 ± 1.3	110.1 ± 1.4
Hip Circumference, cm	119.5±1.2	119.8 ± 1.1	119.9 ± 0.9
Waist to hip ratio	0.91±0.01	0.92 ± 0.01	0.92 ± 0.01
hsCRP, mg/L	5.71±0.64	5.28 ± 0.58	5.34 ± 0.60
Physical Activity Level (PAL)	1.69 (0.02)	1.65 (0.02)	1.69 (0.02)

Data are shown as Mean ± SEM except where indicated (e.g., n (%)). Data represent the ITT population except body composition, body circumferences hsCRP, and PAL data which are for the mITT population. Self-reported degree of leisure time and work/school physical activity was used to calculate PAL (from Very Light: 1.4 to Heavy: 2.3). There were no significant differences between either intervention and control for any baseline characteristic ($p > 0.05$).

were obtained regardless of whether missing data were imputed (by MI or LOCF) or not imputed (Figure 2A). Because of the high completion rate, results from the ITT and Completers populations were not materially different from the mITT population (Table 2). Close to half of the participants in each the MED and OPT groups lost ≥ 5% of baseline weight, and 14.9% in the MED group and 28.1% in the OPT group lost ≥10% of their body weight compared to 1.6% in the Control group ($p < 0.05$ each compared to Control) (Figure 2B).

Simple linear regression analysis using only the change in weight data from the MED and OPT groups showed a significant positive linear relationship between 4-week change in weight and 16-week change in weight (b = 2.0, $p < 0.0001$). The effect of baseline BMI on weight loss was explored (Figure 4). In MED, weight loss

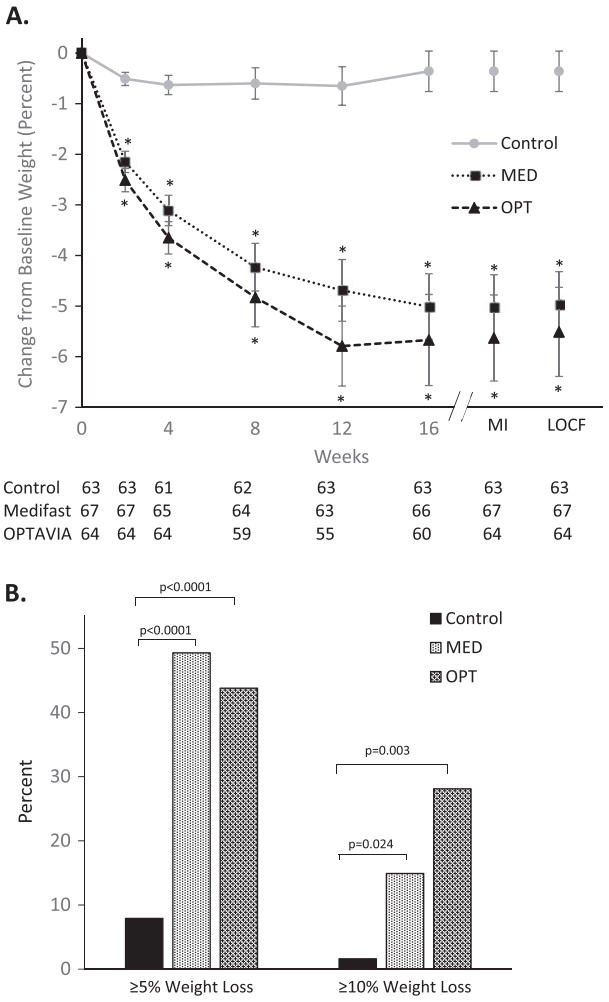

Figure 2 Changes in Body Weight. (A) Mean percentage change from baseline body weight by group. Error bars represent SEM. mITT population; the numbers of participants with weight data at each time point are shown below the graph. Mean weight change at 16 weeks was also calculated using multiple imputation (MI) or Last Observation Carried Forward (LOCF) to account for missing data. *$p < 0.0001$ compared to the Control group. **(B)** Proportion of participants achieving weight loss of ≥ 5% or ≥ 10% at 16 weeks. Between group p values are shown.

increased with increasing BMI class. In contrast, OPT participants in the overweight category lost more weight than those with Class 1 or Class 2 or 3 obesity, and recidivism was only evident in the cohort with Class 2 or 3 obesity.

Body composition

Both the MED and OPT groups lost significantly more absolute fat mass compared to Control at week 16 (Table 2) and all earlier time points ($p < 0.0001$, Figure 3), with fat making up the majority of the total body mass lost (75.0% and 87.1% for MED and OPT, respectively). Fat mass decreased by 8.17 ± 1.12% and 10.81 ± 1.92% at week 16 for the MED and OPT groups, respectively, which in both cases was significantly greater ($p < 0.0001$) than Control (−0.63 ± 0.80%). Both the MED and OPT groups also had a greater decline in abdominal visceral fat at week 16 compared to Control (Table 2). Consistent with the greater weight loss, the MED and OPT groups lost more lean mass than the Control (Table 2), representing 2.45 ± 0.43% and 1.49 ± 0.43% reductions from baseline in MED and OPT, respectively. These reductions occurred primarily in the first month (Figure 3).

Body circumferences

All groups had reductions in both waist and hip circumferences over the course of the study. Reductions in the MED and OPT groups were significantly greater than Control starting at week 4 ($p < 0.02$, not shown) through week 16 (Table 2). Waist-to-hip ratio decreased from baseline in all three groups, with no significant differences between the MED or OPT groups and Control (Table 2).

PAL, program adherence, and relationship to coaching and support

From baseline to week 16, PAL increased modestly in all three groups: from 1.65 to 1.70 (MED), from 1.69 to 1.73 (OPT), and from 1.69 to 1.72 (Control). Program adherence was higher at earlier time points compared to later ones. The mean self-reported adherence to the overall program based on VAS results declined between weeks 4 and 16 from 79.1 ± 2.1% to 59.5 ± 3.5% (MED), from 75.0 ± 2.9% to 62.7 ± 3.8% (OPT) and from 66.2 ± 2.7% to 55.8 ± 3.3% (Control). On average across the 16-week intervention, participants reported consuming 4.0 ± 0.2 of the assigned 4 MRs (MED) and 4.8 ± 0.1 of the assigned 5 MRs (OPT). Self-reported MR usage was inversely correlated with the 16-week change in body weight: MED $r = -0.31$ ($p = 0.012$), OPT $r = -0.30$ ($p = 0.022$), meaning that with increased usage of MRs, weight loss was greater.

OPT participants completed 16.1 ± 0.6 (mean ± SEM, median 17.5) of the 23 prescribed coaching calls. The degree of weight loss at week 16 was correlated with the number of completed coaching calls ($r = 0.37$, $p = 0.004$). Dividing the OPT group by the median number of calls completed, those who participated in at least 17 calls lost 2.3 times more weight than those participating in fewer calls (6.9 ± 1.1 vs 3.1 ± 1.3 kg at 16 weeks), and recidivism was only observed in the subgroup with

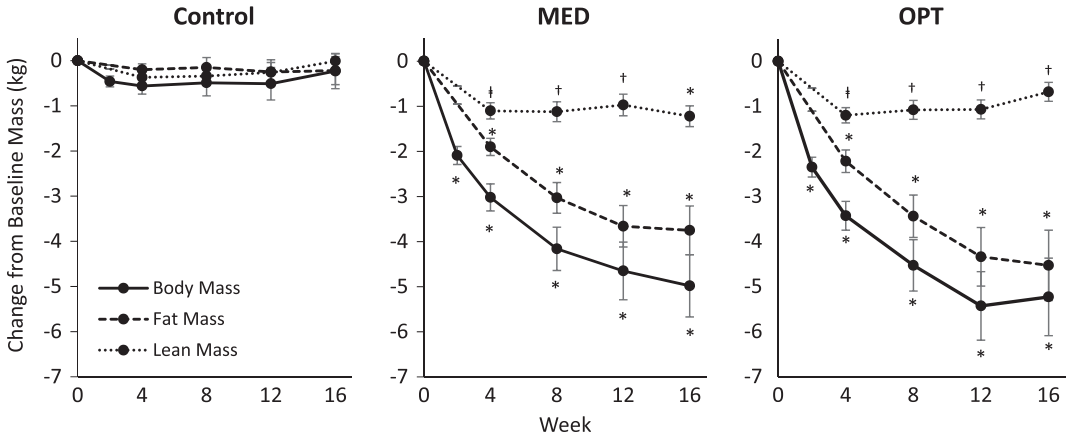

Figure 3 Body Mass and Body Composition for Each Study Group. Mean ± SEM, mITT population. See Figure 2A for sample sizes at each time point. Symbols represent differences in the commercial programs compared to the Control group. †$p < 0.05$; ‡$p < 0.01$; *$p < 0.0001$.

Table 2 Changes in Efficacy Endpoints from Baseline to 16 Weeks

Endpoint	Control	MED	OPT
Primary Endpoint			
Body Mass (kg)	n = 63	n = 67	n = 64
mITT Population	−0.2 ± 0.4	−5.0 ± 0.7	−5.2 ± 0.9
		p < 0.0001(r)	*p < 0.0001(r)*
ITT Population	*n* = 66	n = 67	*n* = 65
	−0.2 ± 0.4	−5.0 ± 0.7	−5.1 ± 0.9
		p < 0.0001	*p < 0.0001*
Completers Population	*n* = 61	n = 63	*n* = 55
	−0.2 ± 0.4	−5.2 ± 0.7	−5.4 ± 0.9
		p < 0.0001	*p < 0.0001*
Key Secondary Endpoints			
mITT Population	*n = 63*	*n = 67*	*n = 64*
Fat Mass (kg)	−0.22 ± 0.31	−3.75 ± 0.54	−4.53 ± 0.78
		p < 0.0001	*p < 0.0001*
Lean Mass (kg)	−0.01 ± 0.16	−1.22 ± 0.23	−0.68 ± 0.21
		p = 0.0205	*p < 0.0001*
Abdominal Visceral Fat Mass (g)	−8 ± 32	−236 ± 47	−239 ± 65
		p < 0.0001	*p < 0.0001*
Waist Circumference (cm)	−2.3 ± 0.7	−5.2 ± 0.7	−6.2 ± 0.9
		p = 0.0030	*p = 0.0009*
Hip Circumference (cm)	−0.3 ± 0.4	−3.6 ± 0.6	−4.1 ± 0.7
		p < 0.0001	*p < 0.0001*
Waist to Hip Ratio	−0.02 ± 0.01	−0.02 ± 0.01	−0.02 ± 0.01
		NS	*NS*
hsCRP (mg/L)	−0.03 ± 0.55	−0.38 ± 0.50	−1.14 ± 0.46
		NS	*NS*

Mean ± SEM. mITT: modified Intent-to-Treat (mITT) population; ITT: Intent-to-Treat (ITT) population. Completers population includes all randomized participants that completed all clinic visits during the 16-week study. NS – not significant ($p \geq 0.05$). P values pertain to differences from the Control group. (r) – indicates p-value was obtained from analysis applied on ranks.

poor coaching call adherence (Figure 5). OPT participants who contacted the NST for discretionary support were more likely to lose ≥ 5% of their body weight compared to those who did not (83.3% vs. 34.6%, $p = 0.002$).

hsCRP

The mean baseline hsCRP concentrations were in the high risk category (≥ 3 mg/L) for all three groups

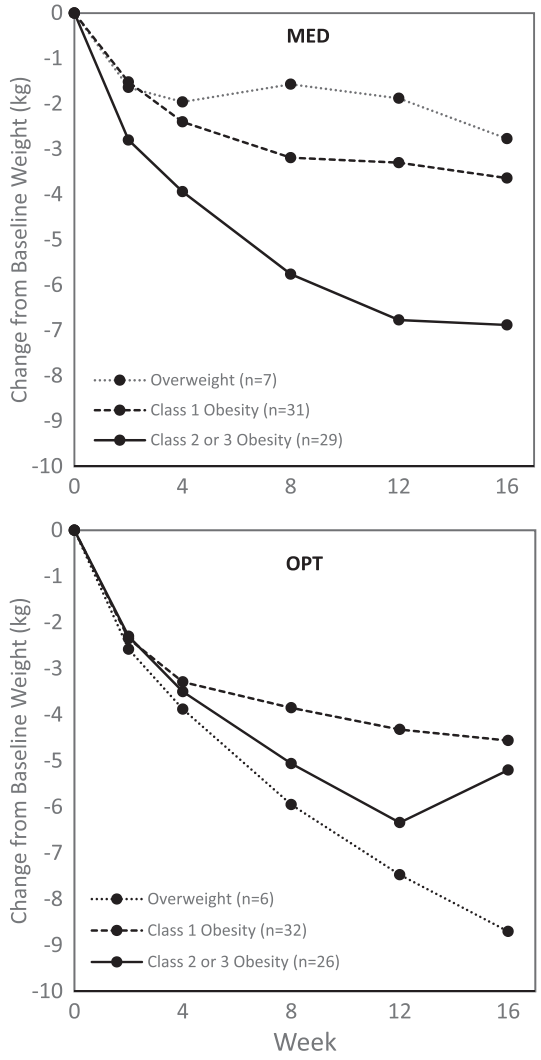

Figure 4 Mean Weight Change by BMI Category at Baseline. Overweight: BMI < 30.0 kg/m^2; Class 1: BMI ≥ 30 and < 35.0 kg/m^2; Class 2 or 3: BMI ≥ 35 kg/m^2.

(Table 1). The OPT group had a significantly greater decrease in hsCRP concentrations than Control in the Completers population (-1.33 ± 0.49 vs. 0.00 ± 0.57 mg/L, $p = 0.008$); this was not statistically significant in the mITT population (Table 2).

QOL

The IWQoL-Lite and RAND-36 scores improved in all groups during the study (Table S1; lower scores in the IWQoL and higher scores in the RAND-36, respectively, reflect improvements in QOL). The 16-week IWQoL-Lite total score ($p = 0.003$), and physical function sub-score ($p < 0.0001$), and the 8-week RAND-36 physical functioning score ($p = 0.001$) and 16-week role limitation due to physical health sub-scales ($p = 0.002$), all improved more in MED compared to Control. No other changes in QOL outcomes in MED or OPT were significantly different than the Control. In exploratory analyses, the 16-week IWQoL-Lite total score ($r = -0.271$, $p = 0.036$), and RAND-36 energy/fatigue ($r = 0.266$, $p = 0.040$) and emotional wellbeing ($r = 0.314$, $p = 0.015$) sub-scores were significantly correlated with the number of coaching contacts in the OPT group.

Safety

Similar numbers of mild or moderate AEs were reported in each group (Table 3). Of the AEs rated as mild or moderate, those deemed by the clinical investigator as definitely, probably or possibly related to the intervention, were generally gastrointestinal in nature. Only one AE (upper respiratory infection) occurred in over 5% of participants (Table 3). None of the four Serious Adverse Events (SAEs) that occurred during the study were deemed related to the interventions.

Discussion

This randomized, controlled trial (RCT) demonstrated that, in generally healthy adults with overweight or obesity, both the MED and OPT interventions (which were designed to closely mimic all aspects of actual customer experiences) were more effective for weight loss compared to a self-directed, reduced-calorie control diet. Participants in both the MED and OPT groups lost significantly more weight, body fat, abdominal visceral fat, and waist and hip circumferences than the Control group starting as early as 2 weeks and continuing for the duration of the 16-week study. On average, the MED and OPT groups lost 5.0% and 5.7% of baseline body weight, respectively. This magnitude of weight loss is similar to that reported with some pharmaceutical interventions (17–19). Weight loss in the range of 5–10% is associated with a reduced risk of developing cardiovascular disease and type 2 diabetes (6,7). Approximately 6 times more participants in the MED and OPT groups achieved clinically significant weight loss ($\geq$ 5%) compared to the Control group, and 9 times more MED and 18 times more OPT participants had $\geq$ 10% weight loss.

Weight declined in MED and OPT groups throughout the 16-week study period, except for a modest weight increase between weeks 12 and 16 in the OPT group. This weight increase in the OPT group was accompanied by a concomitant increase in lean mass and a continued decline in total and abdominal fat mass and waist circumference. Interestingly, nearly one-third of the OPT participants reported increasing their exercise (documented in coaching notes; data not reported) during this

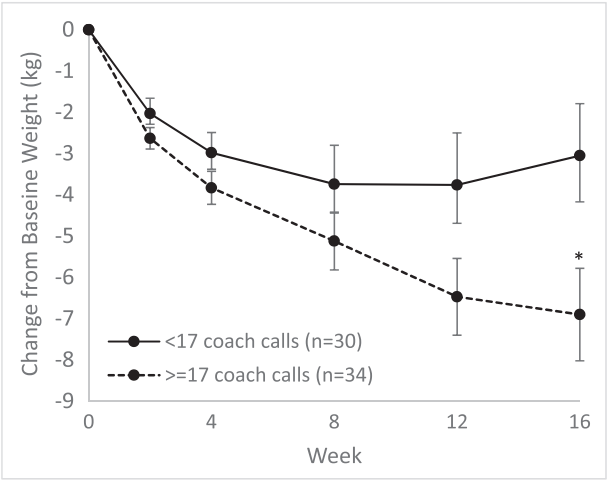

Figure 5 Weight Change Based on Participation in Coaching Sessions. Mean ± SEM. Participants in the OPT group were categorized by the number of coaching calls in which they participated ($<$ 17 vs $\geq$ 17 of the 23 assigned calls over the 16-week study period). *p = 0.019 based on an ANCOVA model, adjusted for sex and baseline value.

time frame which may have contributed to this increase in lean mass. Of note, the weight increase was only evident in participants $<$ 75% compliant with their coaching call schedule, suggesting coaching session adherence may help mitigate against weight increase (20,21).

Retention of lean mass was high with both commercial programs (97.55% in MED and 98.51% in OPT), likely because both meal plans incorporate adequate amounts of protein (120–160 g for MED and 80–120 g for OPT), which helps maintain lean mass during weight loss (22). In the OPT group, fat loss comprised 87.1% of the total weight lost, and while no formal exercise regimen was assigned, moderate physical activity is encouraged as part of the OPTAVIA program, which may have also contributed to lean mass retention.

The findings from this study are in alignment with previous research demonstrating the efficacy of portion-controlled MRs for weight loss and prior meta-analyses showing the efficacy of MRs for both weight loss and maintenance (23–32). Previous studies evaluating these commercial meal plans had similar (26) or somewhat greater weight loss results (23,31), possibly due to different study designs (longer intervention, different populations or level of support). Some studied real customers in a more intense weight control center setting (25,27,28). Retention was very high in this study (92.3%), perhaps because all participants were strongly encouraged to remain in this study (i.e., poor responders did not drop out), and at minimum, attend the final clinic visit for anthropometric measurements. The average weight loss values, therefore, reflect the high completion rate, and consequently, sensitivity analyses demonstrated nearly identical results regardless of whether missing data were imputed.

This study was designed to evaluate the commercially-available Medifast and OPTAVIA programs compared to a common self-directed, reduced-calorie control diet; there were no planned comparisons between the MED and OPT groups. In order to accurately mimic the Medifast and OPTAVIA programs, the MED and OPT groups were assigned different meal plans (of unequal calories) and levels of support representative of each commercial program; therefore, definitive conclusions about the relative impact of these independent variables were not possible. Nonetheless, a modest but significant relationship between MR use and weight loss was observed, suggesting the importance of this component of the programs. For OPT, coaching appeared to be an important factor as a significant correlation was found between the number of coaching calls completed and weight change (i.e., those who participated in more coaching sessions lost more weight). Those with the highest adherence ($\geq$ 75% completed coaching sessions) lost more than twice as much weight as those participating in fewer sessions, further affirming the role of coaching during weight loss. This is in agreement with a number of other studies that also found coaching/support, administered in-person or by telephone, improves weight loss outcomes relative to usual care and that better adherence with coaching sessions further enhances weight loss (21,33,34).

In exploratory analyses, early weight loss was correlated with weight loss at 16 weeks. This is similar to other studies (35–37) and emphasizes the importance of addressing weight loss issues early and making adjustments or employing alternative strategies for those not experiencing weight loss success in the first month. Other exploratory analyses evaluating the effect of baseline BMI

Table 3 Summary of Adverse Events

	Control (*n* = 66)	MED (*n* = 67)	OPT (*n* = 65)
Participants experiencing any adverse event n (% of group)	25 (37.8)	18 (26.9)	24 (36.9)
Number of Events			
Treatment-emergent adverse events			
Any	41	42	46
Serious[1]	1	1	2
Severity			
Mild	5	17	7
Moderate	36	25	41
Severe	1	1	0
Relatedness to the diet plan			
Definitely[2]	0	4	0
Probably[3]	0	2	0
Possibly[4]	0	4	11
Not Related	42	33	37
Gastrointestinal adverse events occurring in ≥2 participants			
Increased frequency of bowel movements	0	2	0
Decreased frequency of bowel movements	0	4	0
Diarrhoea	0	1	2
Constipation	0	0	3
Gastroenteritis	1	1	2
Other adverse events occurring in ≥5% of participants			
Upper respiratory tract infections	15	8	9

Data from the ITT population (n = 198). Relatedness to the diet plan was judged by the Clinical Investigator.

[1]The four Serious Adverse Events (knee surgery and tonsillectomy in OPT group, renal failure in MED group, and acute transient ischemic attack in Control) were judged to be not related to the study diet.

[2]Four mild adverse events judged to be definitely related to the study diet (more frequent, looser or softer bowel movements) occurred in two MED participants.

[3]Two mild AEs judged to be probably related to the study diet (abdominal bloating and decrease in bowel movement frequency) occurred in one MED participant.

[4]Fifteen mild or moderate adverse events judged as possibly related to the study diets, involving changes in bowel movements, dysmenorrhea or menorrhagia, urticaria, decreased energy, feelings of depression, lightheadedness, constipation/less frequent bowel movements, abdominal pain, increased flatulence or mouth sores, occurred in eight participants (three MED and five OPT participants).

on weight loss showed weight loss in the MED group increased with increasing BMI as expected. In the OPT group, however, those in the overweight category lost more weight than those in higher BMI categories. While subgroup sample size in this exploratory analysis may have been limiting, directionally, all OPT participants in the overweight category lost weight. One hypothesis is that the key tenets of the OPTAVIA program focus on lifestyle changes (e.g., better sleep, more activity) which may resonate more in adults with less weight to lose, and ultimately also contribute to weight loss. Further research would be needed to test this hypothesis.

The assigned caloric restriction in the Control arm was designed to reflect usual care and targeted a 7% weight loss goal, consistent with medical recommendations (5–10% in 6 months, (1)). Weight loss in the Control was minimal, but very similar to that observed in other RCTs employing self-directed control groups, suggesting a self-directed, slower approach that utilizes a balanced variety of foods, may not be a successful weight loss strategy for many individuals. Clinical trials studying different diets, exercise prescriptions, or lifestyle modifications face the unavoidable issue of being unable to mask study groups. Participants' expectations about not being assigned to what they perceive as a preferred program may have also contributed to the lower weight loss observed in control groups in this and other studies.

Safety was assessed through the collection of AEs. Some common gastrointestinal symptoms, mild or moderate in severity, may have been related to the commercial meal plans; no other AE assessments indicated concerns specific to safety. This is consistent with the USPSTF conclusions that interventions of this type are generally noninvasive and result in small to no harm, a stark contrast to their findings on pharmacotherapy-based weight loss interventions where adverse events are high and lead to greater dropout rates (8). This study thus contributes to the body of evidence (23–28,31,38) that the MRs and meal plans used in this study do not pose significant safety concerns for a generally healthy adult population with overweight or obesity.

A weakness of the study was the inability to mask study groups. The statistician, however, was blinded to intervention assignment during data analyses, eliminating any potential bias at this level. While the study strived to mimic the commercial programs, one aspect that could not be replicated in a clinic trial was the social network/community, particularly for OPT. Moreover, while coach training and materials reflected those offered commercially, the study personnel acting as coaches had no prior coaching experience. The actual OPTAVIA coach network includes all levels of coaching experience and many draw upon their own experiences from having lost weight on the program. In addition, study participants who receive compensation (monetary, food, support) may have different levels of motivation or commitment than real customers who have a greater financial investment. Open label studies in real customers are a reasonable option to augment RCTs to gain a broader indication of weight loss in the real world.

Strengths of the study include the randomized, controlled design, a relatively large sample size (*n* = 198),

careful and repeated measurement of weight and anthropometrics, and use of DXA for body composition assessments. The study also had a high completion rate (92.3%) and rigorous statistical methods, including a prespecified statistical analysis plan and adjustments for multiplicity, all contributing to robust, conservative estimates of weight loss.

In conclusion, both the Medifast and OPTAVIA programs were more efficacious than a self-directed, reduced-calorie diet for weight loss and other anthropometric outcomes. Adherence with MR usage and coaching sessions were associated with improved weight loss. Evidence-based commercial programs can be an important tool to help adults with overweight and obesity lose clinically relevant amounts of weight.

Acknowledgements

We thank study participants, study coaches (especially Peter Wojtowicz), Lindsey Provelengios and the Medifast Nutrition Support Team, and Alexandra Miller and the late Lori Andersen (coach training). We also thank Jessica Rusch (study coordinator), Liju George (data management) and DeAnn Liska (study advice).

Funding

This study was funded by Medifast, Inc.

Disclosure Statement

Dr. Arterburn, Mr. Coleman, Ms. Kiel, and Mr. Frye report personal fees from Medifast, Inc., during the conduct of the study. Dr. Kelley, Dr. Mantilla, Ms. Sanoshy, and Dr. Cook report personal fees from Biofortis, Inc., during the conduct of the study.

Author Contributions

LMA, CMC, CDC, JK, NF and KS designed the study, LM performed all statistical analyses, KK was the clinical investigator overseeing the study. All authors were involved in writing the paper and had final approval of the submitted and published versions.

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1
Quality of Life Scores