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REGULAR ARTICLE

BestFIT Sequential Multiple Assignment Randomized Trial Results: A SMART Approach to Developing Individualized Weight Loss Treatment Sequences

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Abstract

Background State-of-the-art behavioral weight loss treatment (SBT) can lead to clinically meaningful weight loss, but only 30–60% achieve this goal. Developing adaptive interventions that change based on individual progress could increase the number of people who benefit.

Purpose Conduct a Sequential Multiple Assignment Randomized Trial (SMART) to determine the optimal time to identify SBT suboptimal responders and whether it is better to switch to portion-controlled meals (PCM) or acceptance-based treatment (ABT).

Method The BestFIT trial enrolled 468 adults with obesity who started SBT and were randomized to treatment response assessment at Session 3 (Early TRA) or 7 (Late TRA). Suboptimal responders were re-randomized to PCM or ABT. Responders continued SBT. Primary outcomes were weight change at 6 and 18 months.

Results PCM participants lost more weight at 6 months (−18.4 lbs, 95% CI −20.5, −16.2) than ABT participants (−15.7 lbs, 95% CI: −18.0, −13.4), but this difference was not statistically significant (−2.7 lbs, 95% CI: −5.8, 0.5, p = .09). PCM and ABT participant 18 month weight loss did not differ. Early and Late TRA participants had similar weight losses (p = .96), however, Early TRA PCM participants lost more weight than Late TRA PCM participants (p = .03).

Conclusions Results suggest adaptive intervention sequences that warrant further research (e.g., identify suboptimal responders at Session 3, use PCMs as second-stage treatment). Utilizing the SMART methodology to develop an adaptive weight loss intervention that would outperform gold standard SBT in a randomized controlled trial is an important next step, but may require additional optimization work.

Clinical Trial information ClinicalTrials.gov identifier; NCT02368002

Keywords: Obesity · Intervention · Weight loss · Adults

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Introduction

Clinically meaningful weight loss (7–10%) can be achieved through state-of-the-art behavioral weight loss treatment (SBT) participation [1, 2] but only 30–60% of people achieve this goal [3]. Rather than continuing with "one size fits all" approaches, developing adaptive interventions that change over time based on an individual's progress could increase the number of people who benefit from treatment [4, 5]. Sequential Multiple Assignment Randomized Trials (SMART) use experimental design principles to answer whether, how, and when to alter treatment intensity, type or delivery method to build

adaptive interventions [6–8]. An additional strength of the SMART is the opportunity to develop more deeply tailored interventions that identify which individuals are likely to benefit the most from which sequence of treatments [4].

Suboptimal SBT responders may benefit from alternate treatments that address factors which impede weight loss [9–13]. One such factor is self-regulation, given that exercising calorie restraint in today's obesogenic environment is compromised by both food-specific [11, 14] and general self-regulation difficulties [15–18]. Augmenting SBT with portion-controlled meals (PCM) or acceptance and commitment therapy-derived skills could address self-regulation challenges through different mechanisms. PCMs immediately reduce the need for decision making and behavioral control by providing people with meals that are compliant with SBT caloric intake recommendations [19]. Alternatively, acceptance-based treatment (ABT) teaches skills, such as distress tolerance, that may boost self-regulation capacity [20]. Each approach has empirical support [19, 21–24], but may be best reserved as second-stage treatments since PCMs can be expensive and difficult to fit into a person's lifestyle, and ABT requires specialized training [23]. PCMs are effective because they are pre-planned and pre-packaged, however, this is accompanied by a level of inflexibility that may not easily fit into a person's lifestyle (e.g., family meals, parental responsibilities, work commitments, etc.) and may not be feasible over the long-term. Although treatment accompanying PCMs should help people develop other tools and strategies to support weight loss and maintenance, reliance on PCMs may impede the development of important behavioral strategies. In contrast, switching the therapeutic approach to ABT theoretically addresses the root problem of many weight loss challenges and boosts long-term capacity for self-regulation. Because ABT directly addresses the underlying causes of overeating, it may take longer to develop this skill set. Thus, these treatments may have differential short- and long-term effects, with PCMs being more effective short-term, and ABT skill development accelerating over time. Different individuals also may vary in their responsiveness to different treatment sequences. For example, suboptimal responders who experience greater food-specific self-regulation challenges such as binge eaters may respond differently to PCMs and ABT [4].

Establishing the best time to transition to second-stage treatment is important. Difficulty losing weight early in treatment predicts suboptimal response [25–27]. Stepped care interventions have intensified treatment to address suboptimal response as early as 3 and up until 12 weeks after initial treatment began, with limited empirical justification [28–31]. Weight loss trial data, [22, 32–35] using weekly weight loss to predict the likelihood of achieving weight loss success at 6 months (i.e., 10% weight loss), suggest that sessions 3 and 7 are good candidate time points for treatment transition. Participants who had not lost at least 2.5% of their starting body weight at session 3 or at least 5% by session 7, had a high likelihood of not being classified as successful weight losers at 6 months. However, it is unclear which of these two time points would be best. Switching at session 3 may "rescue" people before it's too late, but could be premature and subject to incorrect classification. Waiting until session 7, however, could be detrimental if people have started to experience a sense of futility.

This paper describes results of BestFIT, a SMART which addressed: (a) whether PCM or ABT was more effective for suboptimal responders; and (b) when to identify suboptimal responders. All participants began with SBT and were randomized to treatment response assessment at Session 3 (Early TRA) or 7 (Late TRA). Suboptimal responders were re-randomized to PCM or ABT and Responders continued SBT. We hypothesized that participants re-randomized to PCMs would lose more weight at 6 months (6m) than those re-randomized to ABT, but that ABT would outperform PCM at 18 months (18m). We hypothesized that participants randomized to Session 3 treatment response assessment (Early TRA) would lose more weight at 6m and 18m follow-up than those randomized to Session 7 treatment response assessment (Late TRA). Exploratory analyses examined 6m and 18m weight loss across the four embedded Adaptive Interventions that begin with SBT (Early PCM, Early ABT, Late PCM, Late ABT) and examined whether responses to the embedded Adaptive Interventions varied for participant subgroups (sex, BMI category, binge eating disorder status).

Methods

Study Design

BestFIT was a two-stage SMART. The study protocol was reported previously [36]. All treatment was provided with individual, in-person sessions. Participants all began by receiving state-of-the art behavioral weight loss treatment (SBT) sessions. Participants were randomized to treatment response assessment (TRA) at Session 3 (Early TRA) or 7 (Late TRA). Responders identified at the Early and Late TRA continued SBT while suboptimal responders were re-randomized to have SBT augmented with the provision of portion-controlled meals (PCM), or to switch to an acceptance-based version of behavioral treatment (ABT). This resulted in four adaptive interventions (AI) that begin with SBT, switch treatment for suboptimal responders,

and continue SBT for responders: Early Augment with PCM (Early PCM); Early Switch to ABT (Early ABT); Late Augment with PCM (Late PCM); Late Switch to ABT (Late ABT). Outcomes were assessed at 6m and 18m. The study was approved by the HealthPartners Institutional Review Board. The ClinicalTrials.gov identifier is NCT02368002.

Study Participants

Participants were enrolled between May 2015 and September 2017. Inclusion criteria were: (a) 21–70 years old; (b) BMI ≥ 30.0 and ≤ 45 kg/m^2; and (c) able to participate for 18 months. Exclusion criteria were: (a) pregnant, breastfeeding or planning a pregnancy;(b) diet intervention study or weight loss program involvement; (c) dietary restrictions (e.g., gluten-free); and (d) insulin-dependent diabetes.

Study Procedures

Participants recruited through radio, print, web-based advertisements, and direct mailings were screened by phone, invited to an orientation session, and scheduled for a visit during which informed consent was obtained and baseline measures were collected.

Randomization and Blinding

The first randomization (Early TRA or Late TRA) was stratified by sex and BMI category (30–<35 kg/m^2, 35–<40 kg/m^2, 40–<45 kg/m^2). The second randomization (PCM or ABT among suboptimal responders) was stratified by Early or Late TRA, sex, BMI category, and percent of weight lost prior to re-randomization (Early TRA: <1% or 1–2.49%; Late TRA: <2% or 2–4.9%). The decision to stratify by TRA timing was made to ensure that there were equal numbers of Session 3 and Session 7 TRA participants re-randomized to PCM and ABT. We also stratified by amount of weight lost prior to the TRA to ensure that there was a similar distribution of pre-TRA weight loss among participants re-randomized to PCM and ABT. Blocks of 10 and 6 were used within each stratum to ensure approximately equal numbers of participants randomized to Early and Late TRA and suboptimal responders re-randomized to PCM and ABT, respectively. Randomization allocation was concealed in the study database. An algorithm, triggered when the weight loss coach entered the participant's weight at weekly sessions, assessed whether the participant was due for TRA; if so, whether the participant was responding optimally; and if not, to which treatment the participant should be re-randomized. Weight loss coaches and participants were blinded to the first randomization (Early TRA vs. Late TRA), but not to the results of the second randomization for suboptimal responders. Study team members remained blinded to study outcomes until 18m measurements were completed.

Interventions

All participants were offered a total of 20 treatment sessions (45 minutes per session) delivered in-person at the Institute over an approximately 20-week time period. Of the six weight loss coaches, four were master's level registered dieticians and two had a psychology background (master's degree in counseling psychology, PhD in health behavior). Two supervision sessions per week were led by PhD-level clinical psychologists, with sessions focused on SBT and PCM led by Drs. Sherwood and Kunin-Batson and sessions focused on ABT led by Drs. Butryn and Forman. Intervention sessions were audio recorded to monitor quality assurance and for coach training and supervision. Five different counselor manuals were developed for each treatment arm (i.e., SBT, Early PCM, Late PCM, Early ABT and Late ABT) to promote adherence to the treatment protocols. The study database included treatment-specific cues for each participant. Session content in each treatment arm was reviewed throughout the study to ensure all coaches were delivering the content in a similar, consistent manner. Audio was provided by coaches for feedback on content delivery. Coaches completed case conceptualization forms and provided audio for participants who had recently been classified as a suboptimal responder and switched treatment arms and for participants who were struggling with their weight loss efforts.

State-of-the-art Behavioral Weight Loss Treatment (SBT)

Participants were offered 20 weekly in-person sessions over a 6m period and started with SBT which focused on self-monitoring, stimulus control, goal setting, problem-solving, cognitive reframing, addressing social situations, and relapse prevention [2, 34, 37]. Participants were assigned a calorie intake goal of 1200, 1500, or 1800 kcal/day based on body weight and worked on increasing their physical activity level to 1 hour per day. Participants were taught how to self-monitor their eating and physical activity using the MyFitnessPal™ smartphone application or a paper self-monitoring log based on their preference. Weight loss coaches reviewed self-monitoring records and provided feedback to participants at each session. The weight loss coach also measured and documented each participant's weight in the study treatment database

prior to delivering the weekly treatment session content. Additional detail about the interventions is provided in our study protocol paper [36].

Sub-optimal Response Definitions

Participants randomized to Early TRA were considered sub-optimal responders if they had lost less than 2.5% of their session 1 weight by Session 3 or 28 days following Session 1, which ever came first. Late TRA participants were considered sub-optimal responders if they had lost less than 5.0% of their session 1 weight by Session 7 or 63 days following Session 1, whichever came first. Participants classified as sub-optimal responders at Sessions 3 and 7 were re-randomized to either portion-controlled meals or ABT.

Portion-controlled Meals (PCM)

PCM participants completed the 20 sessions of SBT. Additionally, they received meals (17 weeks for Early TRA and 13 weeks for Late TRA) prepared by Healthy for Life Meals™ at different caloric levels (e.g., 1200, 1500 kcals/day) at no cost and included freshly prepared food with fruits and vegetables. The weight loss coach helped identify a convenient location for twice-weekly pick-up of the participant's meals.

Acceptance-based Behavioral Treatment (ABT)

ABT [38, 39] participants identified internal experiences that make weight control behaviors challenging and learned through several activities that adaptive behavior (e.g., eating less) often depends on the ability to tolerate unpleasant internal experiences (e.g., desire to eat tasty food) or experience a perceived or anticipated loss of pleasure (e.g., choosing a less, over a more, tasty food). ABT focused on increasing willingness to engage in adaptive behavior long-term, even when it is uncomfortable or less pleasurable. Participants learned to differentiate controllable (e.g., food kept at home) and uncontrollable (e.g., cravings) aspects of weight control, and to engage in change strategies for the former and psychologically acceptance for the latter. Participants clarified their values and how healthy eating and physical activity could move them toward those values and were taught mindful decision making, i.e., bringing values to mind during weight-related decision-making moments. Calorie intake and physical activity goals remained the same as SBT and several SBT strategies were integrated into ABT (e.g., self-monitoring, stimulus control).

Measures

In-person outcome assessments occurred at baseline, 6m and 18m with measurement staff blinded to participant treatment assignment.

Weight Change

The primary outcome was body weight change from baseline at 6m and 18m. Body weight and height were measured twice in light clothing without shoes using a digital scale and a portable, calibrated stadiometer (Seca 876 Flat Scale; Seca 217 Stable Stadiometer; SECA 437 Adapter for Flat Scale). Measurements differing by 0.2 kg or more for weight or 0.5 cm or more for height were repeated for a third time. Data for the multiple assessments were averaged. The following CDC-defined BMI categories were used in exploratory analyses: Class 1 (BMI 30 to < 35 kg/m^2); Class 2: (BMI 35 to < 40 kg/m^2; and Class 3 (BMI of 40 kg/m^2 or higher).

Binge Eating (BE)

BE was assessed with the Binge Eating Scale (BES) and a semi-structured interview adapted from the Eating Disorder Examination (EDE) [40, 41]. Participants were classified as follows: No BE (BES score 0–17 and no BE reported on the EDE); Subclinical Binge Eating Disorder (BED; BES score 18–26 and/or subclinical BED on EDE); or Probable BED (BES score >26 and/or met DSM-5 BED criteria on EDE).

Demographic characteristics

Demographic characteristics assessed included gender, age, race/ethnicity, marital status, education level, and employment status.

Intervention Process Evaluation.

Session length, completion, and PCM orders were tracked. Raters with experience in SBT, PCM and ABT randomly coded 5% of all sessions (n = 400) on a scale of 1 (skipped entirely) to 3 (thoroughly covered) adherence to each sub-section of the specific session manual. Avoidance of treatment contamination was rated by the presence or absence of specific SBT and ABT strategies in each treatment arm. Coding began before the intervention was complete so that adherence issues could be addressed in the ongoing supervision meetings. SAS was used to randomly select audios for coding equally distributed across the intervention period of the trial. Satisfaction and perceived helpfulness of the sessions were rated by participants.

Analysis

The analytic approaches for the primary, secondary, and exploratory aims were informed by the literature on SMART designs [4, 42–44]. Hypothesis 1 stated that suboptimal responders re-randomized to PCM would lose more weight at 6m than those re-randomized to ABT (H1a) but that ABT participants would lose more weight at 18m than PCM participants (H1b). This hypothesis was tested using a mixed linear model where weight changes between baseline and post-baseline among suboptimal responders were predicted from re-randomization (ABT, PCM) and measurement time (B, 6M, 18M) accounting for sex, baseline weight (grand mean-centered), TRA timing and percent of weight lost prior to re-randomization. A significant re-randomization by measurement time interaction was expected, with simple effects tests comparing PCM to ABT within measurement time testing H1a (6m) and H1b (18m). The contrast with the smaller *p*-value was tested at $\alpha_2 = 0.025$, and the second at $\alpha_2 = 0.05$ to ensure a family-wise Type I error rate of 0.05. The H1 and H2 mixed models treated all predictors as fixed parameters and included a random intercept for participant.

Hypothesis 2 stated that participants randomly assigned to Early TRA would lose more weight at 6m and 18m than those randomized to Late TRA and was tested using a mixed linear model where weight changes from all randomized participants were predicted from TRA timing accounting for sex, baseline weight and TRA result (PCM, ABT, responder, quit intervention before TRA). The main effect for Early versus Late TRA tested H2.

Sensitivity analyses applied the Hypothesis 1 and 2 analytic models to a multiply-imputed dataset and summarized the results of these analyses across $m = 20$ imputations [45]. The imputation model assumed missing at random conditional on covariates, which included all analysis covariates and the auxiliary variables education, income, coach and intervention completion [45]. A Markov chain Monte Carlo model imputed sporadically missing 6-month weight values ($n = 15$) from the auxiliary variables and all observed weight values. Fully conditional specification using the regression method, which readily accommodates binary auxiliary variables, imputed the monotonically missing 6 and then 18-month weight values from the auxiliary variables and prior weight values for participants who dropped out after baseline ($n = 38$) or 6 months ($n = 28$).

The exploratory aim was to compare 6m and 18m weight loss across the 4 AIs, overall (Early PCM, Early ABT, Late PCM, Late ABT) and by participant subgroups (sex, BMI category, binge eating disorder status). This aim was carried out using generalized estimating equations to fit a segmented linear regression model predicting imputed weight at baseline, 6m and 18m from indicators of first- and second-stage randomization results and controlling for baseline weight and sex [44]. The relative effectiveness of each AI is based on model-predicted weight change from baseline to 6m and 18m.

The power of the simple effects tests comparing 6m and 18m weights between participants re-randomized to PCM versus ABT was a function of the proportion of participants who were suboptimal responders and 6m and 18m retention rates. There were $N = 468$ randomized participants, a 55% suboptimal response rate ($n = 259$ re-randomized), and 89% and 85% retention at 6m and 18m. The minimum detectable standardized effect for the observed sample sizes ($n = 230$ at 6m, $n = 220$ at 18m) was Cohen's $d = 0.37$–0.38.

Results

Study Participants

The CONSORT diagram (Fig. 1) includes recruitment and retention information and Table 1 includes study sample descriptive characteristics. Of the 1540 participants who expressed interest, 363 did not complete a phone screening, 114 were not interested in participating after learning more about the study, 594 did not meet eligibility criteria over the phone or at the orientation or baseline session, and 469 completed baseline measures. One individual was excluded due to a randomization error and the remaining 468 were randomized (R1) to Early ($n = 233$) or Late ($n = 235$) treatment response assessment (TRA). Approximately 5% ($n = 26$) quit the intervention prior to their TRA session. At their TRA session, 55% of the participants ($n = 259$) were classified as suboptimal responders and re-randomized (R2) to ABT ($n = 127$, 27.1%) or PCM ($n = 132$, 28.2%). Responders ($n = 183$, 39.7%) continued SBT sessions.

Participants who quit the intervention prior to TRA were younger ($M = 43.5$ years, $SD = 10.6$), less educated (76.9% < college), and less likely to be married (46.2%) or employed full time (69.2%) than those who completed the TRA ($M = 49.0$ years, $SD = 10.3$; 37.8% < college; 70.0% married; 83.9% employed full time). The 38 participants who did not provide follow-up data were younger ($M = 42.8$ years, $SD = 10.2$), more likely to be female (84.2%), less educated (60.5% < college) and had higher baseline BMI (36.8% Class 1) than those who provided follow-up data ($M = 49.2$ years, $SD = 10.3$; 75.6% female; 38.1% < college; 46.1% Class 1).

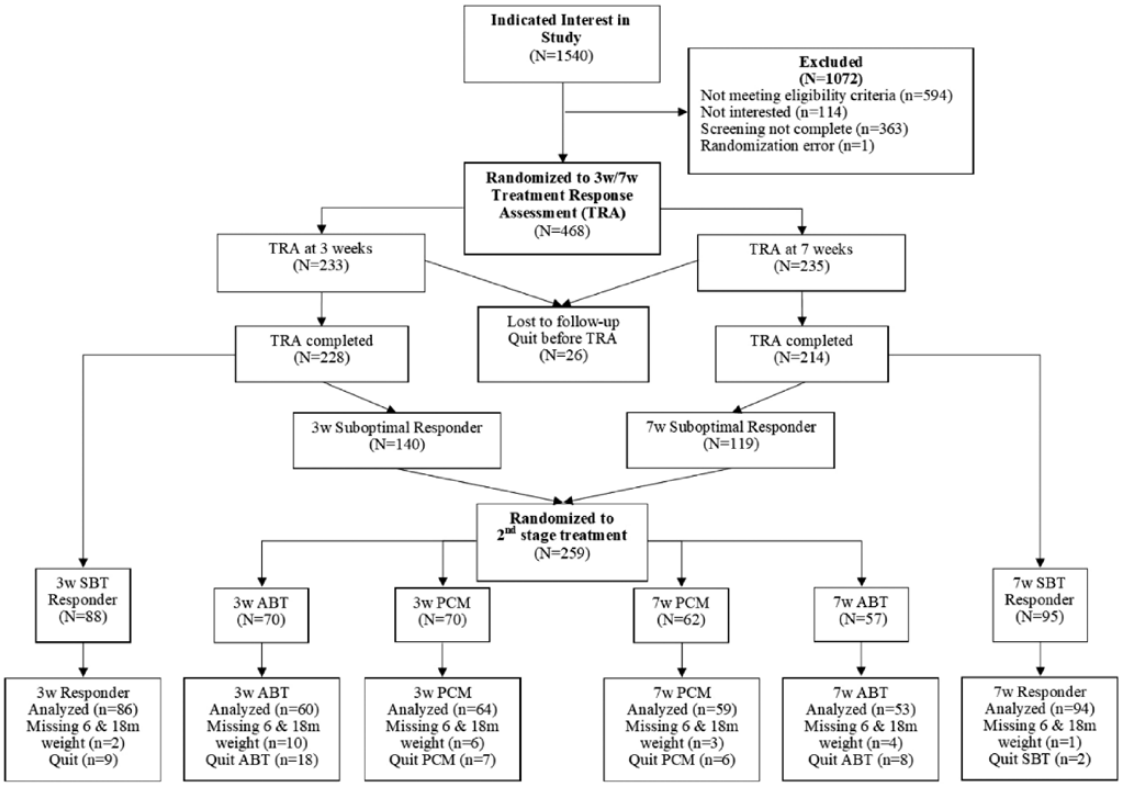

Fig. 1. BestFIT CONSORT diagram.

Primary Analyses

Table 2 summarizes mean weight measured at baseline and weight loss at 6m and 18m expressed as pounds lost, percent weight loss, and percent achieving 5% and 10% weight loss by TRA timing (Early, Late) and TRA result (responder, re-randomize to PCM, re-randomize to ABT). The primary hypothesis was that PCM would be more effective at 6m (H1a) while ABT would be more effective at 18m (H1b) among suboptimal responders. The re-randomization by measurement time interaction was not statistically significant (p = .25). The predicted baseline to 6m weight changes among PCM (−−18.4 lbs, 95% CI −20.5, −16.2) and ABT (−15.7 lbs, 95% CI: −18.0, −13.4) were in the expected direction but the difference of −2.7 lbs (95% CI: −5.8, 0.5) was not statistically significant (p = .09; Fig. 2). When the outcome was weight loss percent rather than pounds, the re-randomization by measurement time interaction was also not statistically significant (p = .26). The 6m mean percent weight loss among PCM (8.3% loss, 95% CI 7.3, 9.2) and ABT (7.2% loss, 95% CI: 6.2, 8.2) was in the expected direction, but the difference of 1.1% (95% CI: −0.2, 2.5) more loss in PCM was also not statistically significant (p = .11). For the H1 sensitivity analyses using imputed data, the baseline to 6m pattern in weight change was also consistent with H1a expectation in that suboptimal responders re-randomized to PCM (−17.6 lbs, 95% CI: −19.9, −15.3) lost more weight (−3.4 lbs, 95% CI: −6.8, 0.0, p = 05) than those re-randomized to ABT (−14.3 lbs, 95% CI: −16.9, −11.6); however, this difference was not significant using the $p < .025$ criterion. When weight loss percent was the outcome, the baseline to 6m pattern was consistent with H1a expectation in that suboptimal responders re-randomized to PCM (8.0% loss, 95% CI: 6.9, 9.0) lost a greater percentage of weight (1.5% more loss in PCM, 95% CI: −0.0, 3.0, p = .05) than those re-randomized to ABT (6.5% loss, 95% CI: 5.3, 7.4). The H1b-predicted baseline to 18m weight changes were not in the expected direction (PCM −8.5 lbs, 95% CI: −10.7, −6.3; ABT −7.4 lbs, 95% CI: −9.7, −5.2) nor was their difference statistically significant (−1.0 lbs, 95% CI: −4.2, 2.2, p = .53). A similar pattern was observed with 18m mean percent weight loss as the outcome (PCM 3.7% loss, 95% CI: 2.7, 4.6; ABT 3.3% loss, 95% CI: 2.7, 4.6); this difference was also not statistically significant (0.3% more loss in PCM, 95% CI: −1.0, 1.7, p = .63). The pattern of results for the H1b sensitivity analysis using imputed data were similar such that suboptimal responders re-randomized to PCM had more weight loss at 18m (−8.0 lbs, 95% CI: −10.3, −5.6; 3.5% loss, 95% CI: 2.4, 4.5) than those re-randomized to ABT (−6.5 lbs, 95% CI: −9.3, −3.7; 2.9% loss, 95% CI: 1.6, 4.1) but these differences were not statistically significant (−1.4 lbs, 95% CI: −5.0, 2.1, p = .43; 0.6% more loss in PCM, 95% CI: −1.0, 2.2). Comparable analyses treating weight change as a

Table 1. Baseline characteristics of the BestFIT study sample by Randomization 1 (Treatment Response Assessment Timing) and Randomization 2 (Second-Stage Treatment for Suboptimal Responders)

		Randomization #1		Randomization #2		
		Treatment Response Assessment Timing		Second-stage treatment for suboptimal responders		
	All (n = 468)	3 Weeks (n = 233)	7 Weeks (n = 235)	ABT (n = 127)	PCM (n = 132)	Responder (n = 183)
		Mean (sd)/%(n)	Mean (sd)/% (n)	Mean (sd)/% (n)	Mean (sd)/% (n)	Mean (sd)/% (n)
Age	48.65 (10.39)	48.58 (9.80)	48.71 (10.96)	47.73 (10.77)	49.80 (9.77)	49.19 (10.34)
Female	76.28 (357)	76.82 (179)	75.74 (178)	87.40 (111)	84.09 (111)	62.84 (115)
Race/ethnicity						
Non-Hispanic White	78.21 (366)	75.97 (177)	80.43 (189)	75.59 (96)	78.03 (103)	85.25 (156)
Non-Hispanic Black	11.54 (54)	14.59 (34)	8.51 (20)	11.81 (15)	13.64 (18)	6.56 (12)
Hispanic, Any Race	5.13 (24)	3.86 (9)	6.38 (15)	6.3 (8)	3.03 (4)	4.92 (9)
Other	5.13 (24)	5.58 (13)	4.68 (11)	6.3 (8)	5.3 (7)	3.28 (6)
Education						
< 4 year degree	39.96 (187)	38.63 (90)	41.28 (97)	37.80 (48)	45.45 (80)	32.24 (59)
4 year degree	38.46 (180)	39.48 (92)	37.45 (88)	40.16 (51)	37.88 (50)	42.08 (77)
>4 year degree	21.58 (101)	21.88 (51)	21.28 (50)	22.05 (28)	16.67 (22)	25.68 (47)
Married %	68.52 (320)	70.69 (164)	66.38 (156)	66.93 (85)	63.36 (83)	76.50 (140)
Employment status						
Full time	83.12 (389)	81.12 (189)	85.11 (200)	79.53 (101)	83.33 (110)	87.43 (160)
Part time	8.97 (42)	10.73 (25)	7.23 (17)	9.45 (12)	11.36 (15)	4.92 (9)
BMI	35.98 (3.85)	36.03 (3.96)	35.94 (3.75)	36.02 (3.72)	36.53 (3.85)	35.53 (3.96)
BMI category						
Class 1 (BMI 30 to < 35)	45.30 (212)	44.64 (104)	45.96 (108)	44.09 (56)	41.67 (55)	49.18 (90)
Class 2 (BMI 35 to < 40)	36.75 (172)	36.91 (86)	36.60 (86)	37.80 (48)	38.64 (51)	33.88 (62)
Class 3: BMI 40 or higher)	17.95 (84)	18.45 (43)	17.45 (41)	18.11 (23)	19.70 (26)	16.94 (31)

Table 2. Weight in pounds measured at baseline and weight loss from baseline to 6 and 18 months expressed as pounds, percent weight loss and percent who lost at least 5% and 10% of baseline weight

	6 Month Weight Loss expressed as					18 Month Weight Loss expressed as			
	Baseline Weight (lbs)	Pounds lost	Percent lost	Lost 5%	Lost 10%	Pounds lost	Percent lost	Lost 5%	Lost 10%
	M (SD)	M (SD)	M (SD)	% yes	% yes	M (SD)	M (SD)	% yes	% yes
All Participants									
ALL	224.6 (34.5)	22.1 (14.1)	9.8 (5.9)	78.3%	44.1%	11.8 (17.3)	5.2 (7.4)	45.3%	23.6%
Treatment Response Assessment Timing									
Early	225.1 (34.8)	21.7 (14.5)	9.7 (6.1)	75.0%	42.6%	12.0 (16.9)	5.3 (7.2)	46.8%	23.6%
Late	224.1 (34.2)	22.5 (13.8)	10.0 (5.7)	81.5%	45.5%	11.5 (7.8)	5.0 (7.6)	43.7%	23.6%
Treatment Response Assessment Result									
Responder	227.3 (35.2)	29.5 (14.1)	13.0 (5.6)	93.7%	65.1%	17.7 (18.4)	7.7 (7.8)	60.5%	37.1%
ABT	222.0 (33.4)	15.8 (9.8)	7.2 (4.3)	67.9%	27.5%	7.4 (14.3)	3.3 (6.3)	34.9%	16.0%
PCM	222.8 (34.5)	18.5 (12.4)	8.3 (5.4)	71.1%	32.2%	8.5 (15.4)	3.7 (6.6)	35.6%	12.2%
Treatment Response Assessment Timing & Results									
Early Responder	228.4 (36.0)	27.2 (15.2)	12.0 (6.3)	86.6%	54.9%	15.4 (17.0)	6.7 (7.3)	54.9%	32.9%
Early ABT	223.7 (32.3)	16.3 (10.2)	7.3 (4.4)	68.4%	29.8%	9.3 (12.7)	4.0 (5.3)	38.6%	15.8%
Early PCM	221.6 (36.1)	20.1 (14.4)	9.1 (6.1)	68.2%	39.7%	11.2 (18.2)	4.9 (7.8)	45.8%	18.6%
Late Responder	226.3 (34.7)	31.6 (12.8)	13.9 (4.9)	100%	74.2%	19.9 (19.5)	8.6 (8.1)	65.9%	41.2%
Late ABT	219.9 (34.8)	15.2 (9.5)	7.1 (4.1)	67.3%	25%	5.2 (15.9)	2.5 (7.3)	30.6%	16.3%
Late PCM	224.1 (32.9)	16.8 (9.8)	7.5 (4.3)	74.1%	24.1%	5.6 (11.2)	2.4 (4.8)	25.0%	5.4%

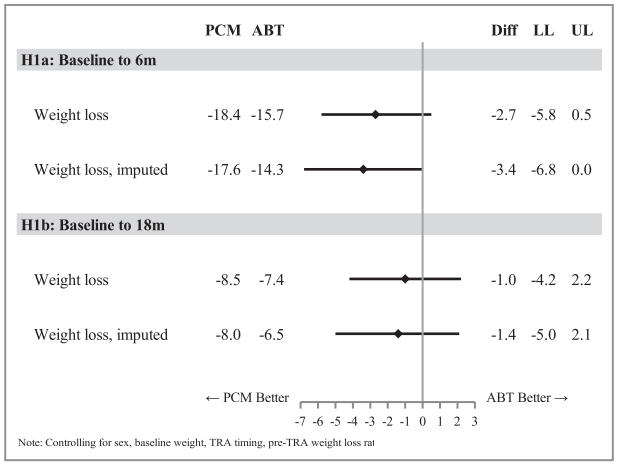

Fig. 2. Baseline to 6 and 18-month weight change in pounds.

percentage of baseline weight produced a virtually identical pattern of results.

Secondary Analyses

Hypothesis 2 predicted that Early TRA participants would lose more weight than Late TRA participants. The adjusted change from baseline to the average of the 6m and 18m post-baseline weights was −16.6 lbs (95% CI: −18.3, −14.9) among participants randomized to Early TRA and −16.7 lbs (95% CI: −18.4, −15.0) among those randomized to Late TRA. The difference between the TRA timing groups was not statistically significant (−0.1 lbs; 95% CI: −2.4, 2.3, $p = .96$). H2 sensitivity analyses using imputed data also showed no significant difference in baseline to post-baseline weight change (−0.1 lbs; 95% CI: −2.6, 2.4, $p = .93$) between Early (−15.5 lbs; 95% CI: −17.4, −13.7) and Late TRA (−15.6 lbs; 95% CI: −17.4, −13.8) participants.

Post Hoc Analyses

When checking the homogeneity of regression assumption for the re-randomization by measurement time interaction reported in the primary analysis, we found that the three-way re-randomization by measurement time by rate of weight loss prior interaction was statistically significant ($p < 0.04$). The weight loss rate covariate classified suboptimal responders as losing weight slowly if between treatment initiation and the TRA they had lost half or more of the weight required to be considered a responder; and very slowly if they had lost less than half of the necessary weight. In general, suboptimal responders who lost weight slowly prior to their TRA tended to have more weight loss at 6m (−4.5 lbs; 95% CI: −8.2, −0.9, $p < 0.02$) and 18m (−3.3 lbs; 95% CI: −7.0, 0.4, $p = .08$) if they had been re-randomized to PCM rather than ABT. The pattern was reversed among suboptimal responders who lost weight very slowly. They tended to have less weight loss at 6m (2.6 lbs; 95% CI: −3.1, 8.4) and 18m (5.0 lbs; 95% CI: −0.9, 10.9) if they had been re-randomized to PCM although neither of these changes relative to baseline was significant.

The weight change patterns observed in Table 2 inspired a post-hoc analysis to better quantify patterns of baseline to post-baseline weight change as a function of TRA timing (Early, Late) and TRA result (PCM, ABT, Responder). The role of TRA timing appeared to differ between responders and suboptimal responders. Adjusting for baseline weight and sex, the simple effect of TRA timing on post-baseline weight loss was significant among PCM (Late TRA vs. Early TRA weight change difference = 4.5 lbs, 95% CI: 0.3, 8.6, $p = .03$), but not among ABT participants (Late TRA vs. Early TRA weight change difference = 2.4 lbs, 95% CI: −1.9, 6.6, $p = .28$). Suboptimal responders re-randomized to PCM lost more weight if their TRA was Early than if it was Late. Among responders, the post-baseline weight loss pattern was also significantly related to TRA timing but in the other direction. Responders lost more weight if their TRA was Late than if it was Early (−4.3 lbs, 95% CI: −7.8, −0.9, $p = .01$).

Adaptive Interventions

Figs. 3 and 4 show the predicted 6m and 18m weight loss in each of the 4 embedded adaptive interventions (i.e., Early PCM, Early ABT, Late PCM, Late ABT). Overall, none of the AIs clearly resulted in more or less weight loss at 6 or 18 months. The 4 AIs resulted in similar 6m and 18m weight loss among men, but women in Early ABT lost 2–3 fewer pounds at 6m. Participants with Class 1 BMI had less 6m and 18m weight loss in Early ABT and Late PCM; those with Class 2 BMI had less 18m weight loss in Early PCM and Late ABT; and those with Class 3 BMI lost less weight in Early PCM and Early ABT, especially at 18m. Participants with subclinical BED lost more weight at 6m in Early PCM, and at 18m in Early PCM and Late ABT.

Intervention Adherence and Contamination

Suboptimal responders ($M = 16.8$, $SD = 4.5$) attended fewer sessions than responders ($M = 18.4$, $SD = 3.1$; $p < 0.001$). PCM participants attended more sessions ($M = 17.5$, $SD = 3.5$) than ABT participants ($M = 16.1$, $SD = 5.1$; $p < 0.01$). Session length was shorter among responders ($M = 39.6$ minutes, $SD = 6.0$) compared to suboptimal responders ($M = 41.1$ minutes, $SD = 5.5$, $p < .01$), but similar between suboptimal responder groups (PCM = 40.5 minutes, $SD = 5.8$; ABT=41.6

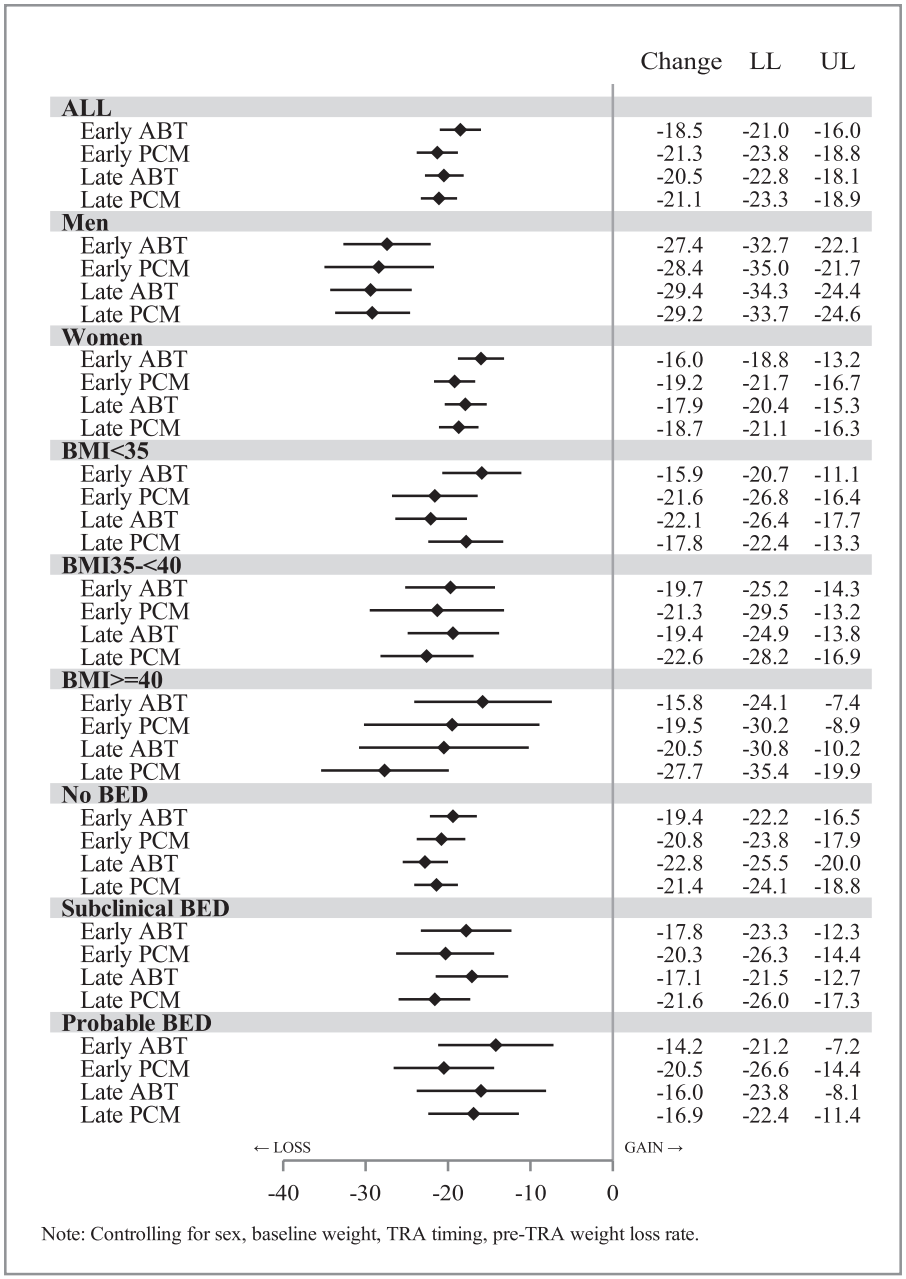

Fig. 3. Baseline to 6-month weight change in pounds by adaptive intervention.

minutes, SD = 5.2; p = .11). The average number of weeks PCMs were ordered was 14.6 and 11.4 for those re-randomized at 3 and 7 Weeks, respectively. Suboptimal responders were less satisfied with treatment (PCM M = 4.7, SD = 0.4; ABT M = 4.5, SD = 0.6) than responders (M = 4.7, SD = 0.5; p < .01). Suboptimal responders (PCM M = 4.5, SD = 0.4; ABT M = 4.3, SD = 0.6) did not perceive treatment to be more or less helpful than responders (M = 4.5, SD = 0.5; p < .07). Participants re-randomized to PCM were more satisfied with treatment, p < 0.02, and found it to be more helpful, p < .01, than those re-randomized to ABT. No treatment contamination was found (e.g., no ABT strategies in SBT or PCM sessions, SBT cognitive restructuring was not present in ABT sessions, PCMs were not discussed in ABT or SBT sessions).

Adverse Events

There were 64 adverse events (AEs) reported by 54 unique participants, six were classified as serious AEs. Three of the serious AEs required hospitalization; two were classified as possibly related to dietary intake and/or physical activity changes associated with

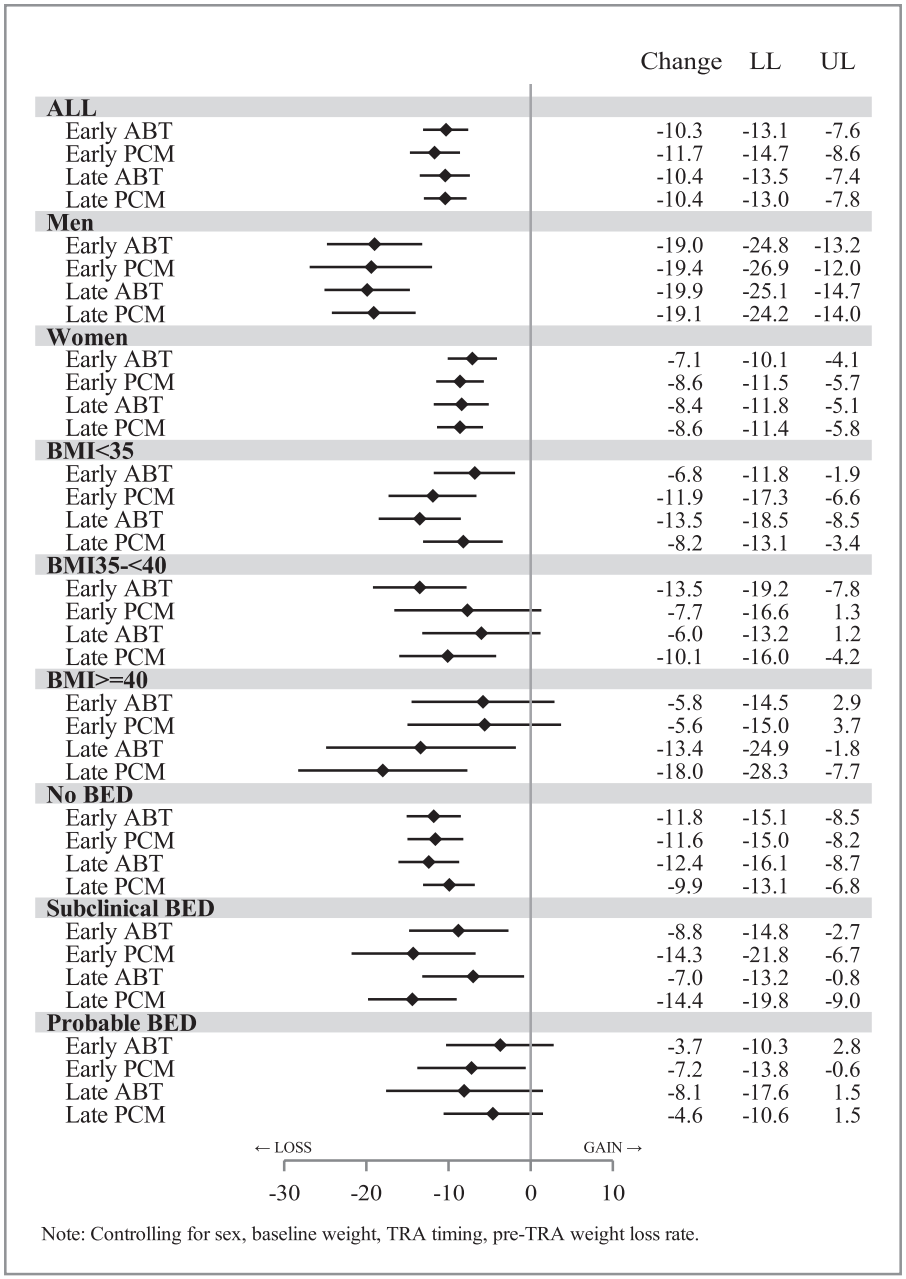

Fig. 4. Baseline to 18-month weight change in pounds by adaptive intervention.

study participation (i.e., kidney infection, depression). There were 31 non-serious AEs related to musculoskeletal and connective tissue disorders or injury; 12 were related to participation in physical activity and were classified as potentially related to study participation. There were two non-serious AEs (i.e., allergic reaction) reported by one person that were potentially related to dietary intake changes. The numbers of serious (SBT = 2, PCM = 1, ABT = 3) and non-serious AEs (SBT = 23, PCM = 22, ABT = 13) were similar across groups.

Discussion

BestFIT, a two-stage Sequential Multiple Assignment Randomized Trial (SMART) designed to inform the development of an adaptive behavioral weight loss intervention for adults, examined whether it was better to identify suboptimal responders to SBT at Session 3 (Early TRA) or Session 7 (Late TRA) and whether PCM or ABT was a more effective second-stage treatment. Results showed no significant weight loss difference between Early and Late TRA participants or between PCM

and ABT suboptimal responders at 6 or 18 months. However, sensitivity analyses using imputed data showed a non-significant trend that PCM participants lost more weight than ABT participants at 6 months. The weight loss difference at 6 months of 3.4 pounds was modest and equated to a difference of 1.5% more weight loss and an additional 5% of PCM individuals achieving a clinically significant weight loss (i.e., 10% loss) relative to ABT participants. Post hoc analyses prompted by descriptive data suggesting that the role of TRA timing differed among responders and suboptimal responders, showed that Early TRA suboptimal responders randomized to PCM lost 4.5 more pounds than Late TRA suboptimal responders randomized to PCM. At six months, nearly 40% of Early TRA participants re-randomized to PCM lost at least 10% of their body weight compared to 24% of Late TRA suboptimal responders randomized to PCM. Although there was some indication that PCM participants lost more weight than ABT participants, particularly those who started PCMs earlier, these differences were not maintained at 18-month follow-up. The weight loss pattern for treatment responders was in the opposite direction such that Late TRA responders lost more weight than Early TRA responders, an average difference of 4.3 pounds. Although identifying suboptimal responders and switching treatment early showed promise, these data suggest that not all participants identified as early responders were able to sustain their success over the course of treatment.

To aid future efforts to build a more deeply tailored adaptive treatment [4, 42], we also examined weight loss patterns for the four embedded adaptive interventions that began with SBT, transitioned suboptimal responders to PCM or ABT at the early or later time point, and continued SBT for suboptimal responders (i.e., Early PCM, Early ABT, Late PCM, Late ABT) and whether pre-specified characteristics predicted response to the different treatment sequences. Overall, none of the four AIs clearly resulted in more or less weight loss at 6 or 18 months, however, some interesting patterns were observed. Participants with Class 1 BMI lost more weight in Early PCM and Late ABT; those with Class 2 BMI lost more weight in Late PCM and Early ABT, and those with Class 3 BMI lost more weight in Late PCM and Late ABT. Finally, participants with subclinical BED lost more weight in Early and Late PCM, and participants with clinical BED appeared to lose more weight at 6m in Early PCM, and at 18m in Early PCM and Late ABT. Binge eating is a poor prognostic indicator for weight loss [46, 47]. These data suggest that PCMs may help people with moderate binge eating lose weight. Examination of whether initial weight loss rate influenced treatment response showed that suboptimal responders with a slow early weight loss rate were more successful at 6 months if re-randomized to PCM, whereas those with a very slow weight loss rate tended to lose more weight at 18 months if re-randomized to ABT. These results are consistent with the idea that ABT may facilitate longer term weight loss success [21].

Study strengths included high-quality SMART design implementation (e.g., re-randomization, treatment transitions), and high intervention participation and retention. Study limitations included that suboptimal responders were not re-randomized to continue SBT to assess whether PCM and/or ABT outperformed no treatment change. Participant diversity with respect to sex, education level, and race/ethnicity was limited. We also excluded individuals in the overweight category (BMI between 25 and 30 kg/m^2) who could benefit from weight loss treatment. An important direction for future research is to examine the efficacy of these and other interventions in minority populations at high risk for obesity-related comorbidities. Cost should also be considered in future research. PCMs were provided free of charge to participants which likely enhanced compliance; helping people identify low cost, nutritionally sound PCM options could increase the feasibility of this approach. Although group-based weight loss treatment can be more cost-effective, we chose to provide individual weight loss treatment because explicitly focusing on non-response and altering treatment course for participants who are not doing well can be a sensitive issue which could be exacerbated in the context of a group setting. Indeed, an interesting area for future work is to understand the acceptability and feasibility of adaptive interventions in the context of group-based therapies. Finally, BestFIT focused primarily on short-term weight loss and we know that long-term maintenance remains a challenge.

BestFIT was designed as a SMART with the goal of building an optimal adaptive intervention for weight loss that would substantively increase the number of adults that would benefit from treatment. Although the primary and secondary hypotheses were not supported, study results do point toward adaptive intervention sequences that warrant further research. Results suggest that a promising adaptive weight loss intervention would identify SBT suboptimal responders at Session 3 and potentially re-assess response at a subsequent session given that early response may not be sustained. Results suggest that PCMs may be a promising second stage strategy, particularly for suboptimal responders identified early in treatment. It should be noted, however, that the weight loss advantage of an early switch to PCMs was not maintained and that ABT and PCMs had similar long-term outcomes. Given evidence of the long-term effectiveness of ABT [21], exploring potential sequencing of a lower cost PCM option and ABT may enhance both short and long-term outcomes. Further exploration of more "deeply tailored" interventions based on binge eating status, BMI, and early weight loss rate is also needed. Utilizing the

SMART methodology to develop an adaptive weight loss intervention that would outperform gold standard SBT in a randomized controlled trial is an important next step, but may require additional optimization work.

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Compliance with Ethical Standards

Authors' Statement of Conflict of Interest and Adherence to Ethical Standards Authors Nancy E. Sherwood, A Lauren Crain, Elisabeth M. Seburg, Meghan L. Butryn, Evan M. Forman, Melissa M. Crane, Rona L. Levy, Alicia S. Kunin-Batson, Robert W. Jeffery declare that they have no conflict of interest. We purchased meals from Healthy for Life Meals™ at a discounted price for the trial. Healthy for Life Meals™ did not participate in the design, analysis, or interpretation of the study results. All procedures, including the informed consent process, were conducted in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000.

Authors' Contributions Nancy E. Sherwood, PhD made substantial contributions to the conception and design of the trial and the acquisition, analysis, and interpretation of data. She drafted and critically revised the article for important intellectual content, and has given final approval of the version to be published. A Lauren Crain, PhD made substantial contributions to the design of the trial and the acquisition, analysis, and interpretation of data. She drafted sections of the manuscript and critically revised the article for important intellectual content, and has given final approval of the version to be published. Elisabeth M. Seburg, MPH made substantial contributions to the acquisition, analysis, and interpretation of data. She drafted sections of the manuscript and critically revised the article for important intellectual content, and has given final approval of the version to be published. Meghan L. Butryn, PhD and Evan M. Forman, PhD made substantial contributions to the design of the trial and the acquisition, analysis, and interpretation of data. She critically revised the article for important intellectual content, and has given final approval of the version to be published. Melissa M. Crane, PhD made substantial contributions to the acquisition, analysis, and interpretation of data. She critically revised the article for important intellectual content, and has given final approval of the version to be published. Rona L. Levy, PhD made substantial contributions to the design of the trial and the interpretation of data. She critically revised the article for important intellectual content, and has given final approval of the version to be published. Alicia S. Kunin-Batson, PhD made substantial contributions to the acquisition and interpretation of data. She critically revised the article for important intellectual content, and has given final approval of the version to be published. Robert W. Jeffery, PhD made substantial contributions to the design of the trial and the interpretation of data. He critically revised the article for important intellectual content, and has given final approval of the version to be published.

Ethical Approval All procedures performed in this study were in accordance with the ethical standards of our institutional research ethics committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Slight deviation from this concerned informed consent, as explained below, but this was approved by our ethics committee.

Informed Consent Consent was obtained from all individual participants included in the study. However, given the nature of the research consent was not fully informed, although participants were aware that information was being withheld from them.

References

1. Alamuddin N, Wadden TA. Behavioral treatment of the patient with obesity. *Endocrinol Metab Clin North Am.* 2016;45:565–580.
2. Butryn ML, Webb V, Wadden TA. Behavioral treatment of obesity. *Psychiatr Clin North Am.* 2011;34:841–859.
3. LeBlanc ES, Patnode CD, Webber EM, Redmond N, Rushkin M, O'Connor EA. Behavioral and pharmacotherapy weight loss interventions to prevent obesity-related morbidity and mortality in adults: updated evidence report and systematic review for the US preventive services task force. *Jama.* 2018;320:1172–1191.
4. Almirall D, Nahum-Shani I, Sherwood NE, Murphy SA. Introduction to SMART designs for the development of adaptive interventions: with application to weight loss research. *Transl Behav Med.* 2014;4:260–274.
5. Collins LM, Nahum-Shani I, Almirall D. Optimization of behavioral dynamic treatment regimens based on the sequential, multiple assignment, randomized trial (SMART). *Clin Trials.* 2014;11:426–434.
6. Lavori PW, Dawson R, Rush AJ. Flexible treatment strategies in chronic disease: clinical and research implications. *Biol Psychiatry.* 2000;48:605–614.
7. Lavori PW, Dawson R. Dynamic treatment regimes: practical design considerations. *Clin Trials.* 2004;1:9–20.
8. Lei H, Nahum-Shani I, Lynch K, Oslin D, Murphy SA. A "SMART" design for building individualized treatment sequences. *Annu Rev Clin Psychol.* 2012;8:21–48.
9. Teixeira PJ, Mata J, Williams GC, Gorin AA, Lemieux S. Self-regulation, motivation, and psychosocial factors in weight management. *J Obes.* 2012;2012:582348.
10. Teixeira PJ, Palmeira AL, Branco TL, et al. Who will lose weight? A reexamination of predictors of weight loss in women. *Int J Behav Nutr Phys Act.* 2004;1:12.
11. Johnson F, Pratt M, Wardle J. Dietary restraint and self-regulation in eating behavior. *Int J Obes (Lond).* 2012;36:665–674.
12. Leahey TM, Xu X, Unick J, Wing RR. A preliminary investigation of the role of self-control in behavioral weight loss treatment. *Obesity Res Clin Practice*. 2014;8:e115–e200. doi:10.1016/j.orcp.2012.12.005. PMCID: PMC3992479.
13. Appelhans BM, French SA, Pagoto SL, Sherwood NE. Managing temptation in obesity treatment: a neurobehavioral model of intervention strategies. *Appetite.* 2016;96:268–279.
14. Wardle J, Carnell S. Appetite is a heritable phenotype associated with adiposity. *Ann Behav Med.* 2009;38 Suppl 1:S25–S30.
15. Stanek KM, Strain G, Devlin M, et al. Body mass index and neurocognitive functioning across the adult lifespan. *Neuropsychology.* 2013;27:141–151.
16. Fitzpatrick S, Gilbert S, Serpell L. Systematic review: are overweight and obese individuals impaired on behavioural tasks of executive functioning? *Neuropsychol Rev.* 2013;23:138–156.

17. Economos CD, Hatfield DP, King AC, Ayala GX, Pentz MA. Food and physical activity environments: an energy balance approach for research and practice. *Am J Prev Med.* 2015;48:620–629.
18. Townshend T, Lake A. Obesogenic environments: current evidence of the built and food environments. *Perspect Public Health.* 2017;137:38–44.
19. Astbury NM, Piernas C, Hartmann-Boyce J, Lapworth S, Aveyard P, Jebb SA. A systematic review and meta-analysis of the effectiveness of meal replacements for weight loss. *Obes Rev.* 2019;20:569–587.
20. Forman EM, Butryn ML. A new look at the science of weight control: How acceptance and commitment strategies can address the challenge of self-regulation. *Appetite.* 2015;84:171–180.
21. Forman EM, Manasse SM, Butryn ML, Crosby RD, Dallal DH, Crochiere RJ. Long-term follow-up of the mind your health project: acceptance-based versus standard behavioral treatment for obesity. *Obesity (Silver Spring).* 2019;27:565–571.
22. Forman EM, Butryn ML, Manasse SM, et al. Acceptance-based versus standard behavioral treatment for obesity: Results from the mind your health randomized controlled trial. *Obesity (Silver Spring).* 2016;24:2050–2056.
23. Forman EM, Butryn ML, Juarascio AS, et al. The mind your health project: a randomized controlled trial of an innovative behavioral treatment for obesity. *Obesity (Silver Spring).* 2013;21:1119–1126.
24. Rock CL, Flatt SW, Sherwood NE, Karanja N, Pakiz B, Thomson CA. Effect of a free prepared meal and incentivized weight loss program on weight loss and weight loss maintenance in obese and overweight women: a randomized controlled trial. *Jama.* 2010;304:1803–1810.
25. Miller CK, Nagaraja HN, Weinhold KR. Early weight-loss success identifies nonresponders after a lifestyle intervention in a worksite diabetes prevention trial. *J Acad Nutr Diet.* 2015;115:1464–1471.
26. Unick JL, Neiberg RH, Hogan PE, et al.; Look AHEAD Research Group. Weight change in the first 2 months of a lifestyle intervention predicts weight changes 8 years later. *Obesity (Silver Spring).* 2015;23:1353–1356.
27. Unick JL, Hogan PE, Neiberg RH, et al.; Look AHEAD Research Group. Evaluation of early weight loss thresholds for identifying nonresponders to an intensive lifestyle intervention. *Obesity (Silver Spring).* 2014;22:1608–1616.
28. Carels RA, Darby L, Cacciapaglia HM, et al. Applying a stepped-care approach to the treatment of obesity. *J Psychosom Res.* 2005;59:375–383.
29. Carels RA, Darby L, Cacciapaglia HM, et al. Using motivational interviewing as a supplement to obesity treatment: a stepped-ca0re approach. *Health Psychol.* 2007;26:369–374.
30. Jakicic JM, Tate DF, Lang W, et al. Effect of a stepped-care intervention approach on weight loss in adults: a randomized clinical trial. *Jama.* 2012;307:2617–2626.
31. Carels RA, Wott CB, Young KM, et al. Successful weight loss with self-help: a stepped-care approach. *J Behav Med.* 2009;32:503–509.
32. Jeffery RW, Wing RR, Thorson C, Burton LR. Use of personal trainers and financial incentives to increase exercise in a behavioral weight-loss program. *J Consult Clin Psychol.* 1998;66:777–783.
33. Wing RR, Jeffery RW. Food provision as a strategy to promote weight loss. *Obes Res.* 2001;9 Suppl 4:271S–275S.
34. Jeffery RW, Wing RR, Sherwood NE, Tate DF. Physical activity and weight loss: does prescribing higher physical activity goals improve outcome? *Am J Clin Nutr.* 2003;78:684–689.
35. Butryn ML, Forman EM, Lowe MR, Gorin AA, Zhang F, Schaumberg K. Efficacy of environmental and acceptance-based enhancements to behavioral weight loss treatment: The ENACT trial. *Obesity (Silver Spring).* 2017;25:866–872.
36. Sherwood NE, Butryn ML, Forman EM, et al. The BestFIT trial: A SMART approach to developing individualized weight loss treatments. *Contemp Clin Trials.* 2016;47:209–216.
37. Look AHEAD Research Group, Wadden TA, West DS, et al. The Look AHEAD study: a description of the lifestyle intervention and the evidence supporting it. *Obesity (Silver Spring).* 2006;14:737–752.
38. Forman EM, Butryn ML. *Effective Weight Loss: An Acceptance-Based Behavioral Approach: Clinician Guide*. New York, NY: Oxford University Press; 2016.
39. Forman EM, Butryn ML. Acceptance-based behavioral treatment for weight loss. In Haynos AF, Forman EM, Butryn ML, Lillis J. eds, *Mindfulness and acceptance for treating eating disorders and weight concerns: Evidence-based interventions*. Oakland, CA: Context Press/New Harbinger Publications; 2016:145–167.
40. Fairburn CG. *Cognitive Behavior Therapy and Eating Disorders*. New York, NY: Guilford Press; 2008.
41. Fairburn CG, Cooper Z, O'Connor M. *The Eating Disorder Examination (EDE) 17.0D*. 2018. https://www.credo-oxford.com/7.2.html.
42. Nahum-Shani I, Qian M, Almirall D, et al. Q-learning: a data analysis method for constructing adaptive interventions. *Psychol Methods.* 2012;17:478–494.
43. Nahum-Shani I, Qian M, Almirall D, et al. Experimental design and primary data analysis methods for comparing adaptive interventions. *Psychol Methods.* 2012;17:457–477.
44. Nahum-Shani I, Almirall D, Yap JRT, et al. SMART longitudinal analysis: A tutorial for using repeated outcome measures from SMART studies to compare adaptive interventions. *Psychol Methods.* 2020;25:1–29.
45. Hardt J, Herke M, Leonhart R. Auxiliary variables in multiple imputation in regression with missing X: a warning against including too many in small sample research. *BMC Med Res Methodol.* 2012;12:184.
46. Pacanowski CR, Senso MM, Oriogun K, Crain AL, Sherwood NE. Binge eating behavior and weight loss maintenance over a 2-year period. *J Obes.* 2014;2014:249315.
47. Gorin AA, Niemeier HM, Hogan P, et al.; Look AHEAD Research Group. Binge eating and weight loss outcomes in overweight and obese individuals with type 2 diabetes: results from the Look AHEAD trial. *Arch Gen Psychiatry.* 2008;65:1447–1455.