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#### ORIGINAL ARTICLE

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### Importance of early weight loss and other predictors of lower weight loss in a commercial program: A secondary data analysis

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### Abstract

Objective: There is substantial inter-individual variability in response to weight loss interventions and emerging evidence suggests that weight loss during the early weeks of an intervention may be predictive of longer-term weight loss. This secondary analysis of data from a commercial program therefore examined 1) the associations between early weight loss (i.e., week 4) with final visit weight loss and duration on the program, and 2) other predictors of lower weight loss at final visit. **Methods:** Client charts of adults with overweight or obesity (N = 748) were analyzed. Clients were stratified into categories of weight loss at the week 4 (< and  $\geq$ 2%, 3% and 4%) and final visits (< and  $\geq$ 5% and 10%). Multivariate logistic regression was used to assess predictors of <5% and <10% final visit weight loss. Results: The odds ratios for losing <5% or <10% of weight at the final visit were higher (49.0 (95% CI: 13.84, 173.63) and 20.1 (95% CI: 6.96, 58.06)) for clients who lost <2% or <3% compared to those who lost  $\geq$ 2% or  $\geq$ 3% at week 4. Other predictors of not losing a clinically relevant amount of weight included female sex, use of higher calorie meal plans and shorter time in the program, among others. Those who lost  $\geq$  2% at week 4 also had a significantly greater percent program completion  $(109.2 \pm 75.2\% \text{ vs. } 82.3 \pm 82.4, p < 0.01)$  compared with those who did not meet the 2% threshold.

**Conclusions:** Lower 4-week weight loss was identified as a strong predictor of not losing a clinically relevant amount of weight. These results may be useful for the early identification of individuals who can be targeted for additional counseling and support to aid in attaining weight loss goals.

#### KEYWORDS

meal replacements, non-responder, weight loss

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### 1 | INTRODUCTION

There is a large degree of inter-individual variability in response to weight loss interventions where some individuals experience a high level of weight loss while others lose very little weight or even gain weight.<sup>1</sup> Emerging evidence suggests that weight loss during the early weeks of an intervention may be predictive of greater longerterm weight loss.<sup>2–12</sup> For example, in the Look AHEAD study. Unick et al.<sup>9</sup> reported that participants who did not lose  $\geq 2\%$  of body weight after 4 weeks increased the likelihood of also not losing  $\geq$ 10% weight after 1 year by 5.6 times when compared to individuals who initially lost >2%. Preliminary findings suggest that a more intensive or stepped-care approach for early non-responders may improve outcomes.<sup>13</sup> However, weight loss thresholds to identify early non-responders are not well defined.<sup>12</sup> Some have suggested waiting for 6 weeks or even 3 months to provide additional support for those who do not meet program goals.<sup>12,14,15</sup> However. it is reasonable to hypothesize that earlier identification and support may prove more effective. Thus, further investigation into earlier weight loss (e.g., 4 weeks) as a predictor of longer-term weight loss is warranted.

Baseline characteristics have been evaluated but have not consistently predicted greater long-term weight loss.<sup>16</sup> There is also little evidence to suggest that the transtheoretical model of behavior change/readiness to change appropriately applies to weight loss management.<sup>17</sup> Further, results from other studies suggest that early non-responders have poorer adherence to intervention recommendations (e.g., lower session attendance, fewer days of self-monitoring) during the first 1–2 months of an intervention.<sup>14,15,20</sup> However, adherence metrics vary based on the intervention (i.e., number and type of sessions) and variability in early adherence is typically low.<sup>10,12,18</sup> Therefore, the identification of baseline characteristics and early behavioral predictors for a given intervention may be useful for identifying potential intervention targets, which could then be adapted and utilized across intervention types.

Results from a previous chart review of three Medifast Weight Control Centers (MWCC) indicated that, on average, clients lost a clinically relevant amount of weight ( $\geq$ 5%) within just 4 weeks of beginning the MWCC program.<sup>19</sup> Although these weight loss outcomes are notable, there was heterogeneity in response; therefore, identifying early non-responders and implementing additional interventions might further enhance client weight loss. Therefore, the aims of these secondary analyses were to (1) examine the relationship between 4-week weight loss and final visit weight loss and duration in the program among adults with overweight or obesity participating in Medifast programs, (2) examine the sensitivity and specificity of 4-week weight loss thresholds (i.e., 2%, 3%, 4%) for their ability to correctly classify individuals based upon whether they did not lose clinically relevant weight ( $\geq$ 5% and  $\geq$ 10%) at final visit, and (3) investigate predictors of suboptimal weight loss in the program, defined as not losing a clinically relevant weight of  $\geq$ 5% or  $\geq$ 10% at the final visit.<sup>20-22</sup>

#### 2 | MATERIALS AND METHODS

This is an analysis of data previously collected from two systematic retrospective chart review studies that included charts from 22 Medifast Weight Control Centers (MWCC) located in Maryland, Texas, Florida, and Pennsylvania. The study designs and data collection procedures have been published previously<sup>19,23,24</sup>: these studies were registered in ClinicalTrials.gov (#NCT01662830 and #NCT02150837). Briefly, charts from clients with overweight or obesity, and who were following one of three Medifast weight-loss meal plans [the 5&1 Plan® (800-1000 kcal per day), the 4&2&1 Plan<sup>®</sup> (1100-1300 kcal per day), or the 5&2&2 Plan<sup>®</sup> (1300-1500 kcal per day)], and who had signed a personal health information consent form (which included permission to use their data for research purposes) were included in these studies. Each meal plan utilized a combination of Medifast meal replacements (MR) (Medifast, Inc., Baltimore, MD, USA) and conventional foods. Each MR contained 90-110 calories, 11-15 g protein (primarily from soy and/ or dairy), 12-15 g carbohydrates, and 0-3.5 g fat. The meal plans provided between 800 and 1500 calories per day and incorporated 4-5 MRs, 1-2 self-prepared "lean and green meals" [each including 5-7 oz. of lean protein, 3 servings (~1½ cups) of non-starchy vegetables, and up to 2 healthy fat servings], and 0-2 healthy snacks (fruit, dairy or whole grains), depending on the plan. More details of each Medifast meal plan can be found in previous publications.<sup>19,23,24</sup> The specific weight-loss meal plan assigned to each client was determined based on several factors including weight status, personal preferences, lifestyle, exercise habits and medical history.

The weight-loss programs included weekly one-on-one in-person sessions with trained counselors who utilized motivational interviewing to promote long-term weight control. Clients' weight-loss goals were determined jointly by the counselor and client, which in turn determined the prescribed length of the client's active weightloss phase. Data were abstracted at baseline and up to 24 weeks, plus at the final visit (FV). The FV was defined as the client's last visit to the MWCC during active weight loss while following their original meal plan; the time of the FV varied by individual client and included clients who stopped their assigned meal plan early. Meal replacement adherence (i.e., number of meal replacements consumed during the week) was self-reported by clients and converted to a percentage (number of meal replacements consumed/meal replacements prescribed per meal plan) to determine adherence during the first 4 weeks. Visit adherence during the first 4 weeks was also converted into a percentage to determine adherence (number of visits through week 4/4). Abdominal circumference, body composition (measured by bioelectric impedance) and self-reported medical history including baseline use of prescription medication(s) were also extracted from the charts.

The original studies were approved by the Western Institutional Review Board (Puyallup, WA, USA), which concluded that the studies met the requirements for a waiver from the informed consent process per 45 CFR 66.116(d).<sup>19,23,24</sup>

### 2.1 | Statistics

Statistical analyses were conducted using SAS for Windows (version 9.4, Cary, NC, USA). All tests of significance were assessed at alpha = 0.05, 2-sided.

### 2.1.1 | Examination of the association between 4-week weight loss and final visit weight loss

Demographic and baseline characteristics were summarized for all clients and by meal plan. The percent change in body weight from baseline was calculated for the 4-week and FV and summarized by categories of weight loss. Clients were stratified into the following 4-week categories of weight loss (1) <2% and  $\geq$ 2% weight loss; (2) <3% and  $\geq$ 3% weight loss; and (3) <4% and  $\geq$ 4% weight loss. Additionally, the proportion of clients losing clinically relevant weight ( $\geq$ 5% and  $\geq$ 10%) at the FV was determined. The 4-week weight loss thresholds (i.e., 2%, 3%, and 4%) were chosen based on previous research evaluating early responders and non-responders.<sup>9-11</sup> The FV thresholds of  $\geq$ 5% and  $\geq$ 10% were based on previous research identifying these as thresholds for improvements in clinical outcomes such as blood pressure, blood glucose, etc.<sup>20-22</sup>

## 2.1.2 | Examination of the association between early weight loss and duration in the program

Analysis of variance was used to assess the difference in percent program completion (actual time in program/prescribed program length) between those who achieved the weight loss threshold at week 4 for each weight loss category versus those who did not (i.e., <2% vs.  $\geq$  2%, <3% vs.  $\geq$  3%, <4% vs.  $\geq$  4%). Correlation analysis was used to assess the association between percent change in weight from baseline to week 4 (treated as a continuous variable) and percentage of the program (prescribed program length) completed. Normality of model residuals was assessed using Shapiro-Wilk test with a significance level of 0.05. If normality was violated, values were ranked prior to running the ANOVA models and Spearman correlations were generated.

# 2.1.3 | Examination of the sensitivity and specificity of early weight loss thresholds for predicting clinically relevant weight loss

Sensitivity and specificity analyses were performed to examine the ability of the 4-week weight loss thresholds (i.e., 2%, 3%, and 4%) to correctly classify individuals based upon whether they did not lose clinically relevant weight ( $\geq$ 5% and  $\geq$ 10%) at FV.<sup>9</sup> See supplementary information for additional information regarding the methods for this analysis.

# 2.1.4 | Examination of predictors of lower weight loss in the program

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Logistic regression analyses were used to determine predictors of <5% and <10% weight loss at the final visit. Predictors evaluated were age, gender, meal plan, baseline anthropometrics (body weight, body mass index (BMI), lean body mass, body fat mass, body fat mass index (fat mass kg/m<sup>2</sup>), and percent body fat), prescribed program length, actual time in program (i.e., time to FV), number of MR consumed, MR adherence (percent adherence with meal plan MR), attendance (number of center visits attended and percent adherence), and 4-week weight loss. A predictor was included in the multivariate analysis if the *p*-value for its overall effect was less than 0.10 in the univariate analysis. Thresholds chosen for evaluation of early weight loss for the univariate analyses were based on the results of the 4-week categories of weight loss and the proportion of those clients losing clinically relevant weight loss ( $\geq5\%$  and  $\geq10\%$ ) at the FV.

Results from prior studies have suggested that a threshold of ~2% weight loss over 4 weeks has shown comparatively high specificity and low false positive frequency for the identification of weight loss intervention participants who do not lose a clinically relevant amount of weight during lifestyle interventions.<sup>9,25</sup> Larger thresholds (3% and 4%) were also evaluated for comparison to the 2% threshold. Since the 2% threshold had the highest specificity and lowest false positive frequency, this threshold was used for multivariate logistic regression analyses for models using <5% weight loss at the final visit as the dependent variable. However, since no subjects with <2% weight loss during the first 4 weeks lost  $\geq$ 10%, the 3% threshold was used for multivariate logistic regression models using <10% weight loss at the final visit as the dependent variable.

Body fat mass index was considered in the multivariate analysis instead of absolute or relative body fat mass since body fat mass index adjusts for height. Multivariate models were built using forward stepwise selection with entry and retention *p*-values of 0.20. Odds ratios and their corresponding 95% confidence intervals and *p*values are reported for the final multivariate logistic regression models. Logistic regression analyses were conducted for all clients and in clients who completed  $\geq$ 12 weeks of the program separately as sensitivity analyses. The assumption of linearity between the logit of the dependent variable and each predictor was assessed using the Box-Tidwell test.

### 3 | RESULTS

## 3.1 | Baseline characteristics & program information

All data from the previous MWCC chart review studies<sup>19,23,24</sup> that had baseline body composition measured (n = 748 of 818) were included in these analyses. On average, clients were 49.7  $\pm$  12.7 years of age and within the obesity class 2 BMI category (35.0–39.99 kg/m<sup>2</sup>). The average prescribed program

length was 23 weeks and the average time spent in one of the three Medifast programs was 20 weeks (Table 1).

## 3.2 | Examination of the relationship between early weight loss and final visit weight loss

Table 2 displays the proportion of clients who lost  $\geq$ 5% and  $\geq$ 10% of weight at the FV, stratified by their initial weight loss at 4 weeks. Most notably, 86.8% and 56.5% of clients who lost  $\geq$ 2% of weight at week 4, lost  $\geq$ 5% and  $\geq$ 10% of weight at the FV, respectively.

### 3.3 | Examination of the association between early weight loss and duration in the program

The percent program completion for each 4-week weight loss category is included in Table 2. For each category, those who met the

cut-off for weight loss (i.e.,  $\geq 2\%$ ,  $\geq 3\%$ , and  $\geq 4\%$ ) had a significantly greater percent program completion than those who did not meet the cut-off [*F*(1, 695) = 10.03, *F*(1, 695) = 22.97, *F*(1, 695) = 34.15 for  $\geq 2\%$ ,  $\geq 3\%$ ,  $\geq 4\%$  weight loss, respectively; all p < 0.01]. In the correlation analysis, there was a weak but significant correlation between percent change in weight from baseline to week 4 and percent program completion (r = -0.20; *p* = 0.003) indicating greater weight loss at week 4 was associated with higher percent program completion.

### 3.4 | Examination of the sensitivity and specificity of early weight loss thresholds for predicting clinically relevant weight loss

The ability of the 4-week weight loss thresholds to correctly classify individuals on the loss of <5% or <10% of weight at FV is shown in Table S1.

		Meal plan				
Characteristic	All (N = 748)	5&1 (N = 410)	4&2&1 (N = 282)	5&2&2 (N = 56)		
Age, years	49.7 (12.7)	47.3 (10.3)	53.9 (14.5)	46.4 (13.7)		
Males, n (%)	217 (29.0)	60 (14.6)	124 (44.0)	33 (58.9)		
Prescribed program length, weeks	23.2 (13.9)	18.3 (9.32)	25.9 (12.9)	45.0 (20.3)		
Actual time in program, weeks	20.1 (13.7)	20.7 (13.2)	19.3 (14.1)	20.2 (15.8)		
Weight, kg	104.3 (25.7)	95.3 (20.2)	108.4 (21.0)	149.2 (29.5)		
Body Mass index, kg/m <sup>2</sup>	36.6 (7.54)	34.3 (6.10)	37.4 (6.22)	48.8 (10.2)		
Lean body Mass, kg	57.2 (14.2)	52.2 (11.0)	61.7 (14.3)	77.6 (13.4)		
Body fat Mass, kg	45.4 (15.1)	42.4 (13.2)	46.7 (13.3)	69.4 (19.7)		
Body fat Mass index, kg/m <sup>2</sup>	16.2 (5.47)	15.4 (4.79)	16.4 (5.21)	23.1 (8.01)		
Body fat, %	43.9 (7.53)	44.2 (6.82)	42.9 (8.16)	46.7 (8.85)		

**TABLE 1** Baseline demographics and characteristics of participants were included in the analysis.

Note: Values are presented as mean (SD) or n (%).

TABLE 2 Final weight loss and percent program completion across initial 4-week loss categories.

4-week weight loss category	N (%) at week 4	Mean initial % change in weight (SD)	% Program completion (SD)	Mean final % change in weight (SD)	<u>≥</u> 5% weight loss at final visit, n (%)	<u>≥</u> 10% weight loss at final visit, n (%)
<2%	37 (5.3)	-0.88 (1.19)	82.3 (82.4)*	-1.98 (2.88)	4 (10.8%)	0 (0.0%)
≥2%	662 (94.7)	-5.78 (1.82)	109.2 (75.2)	-12.20 (7.00)	573 (86.8%)	373 (56.5%)
<3%	79 (11.3)	-1.82 (1.21)	78.1 (68.3)**	-4.28 (5.35)	24 (30.4%)	6 (7.6%)
≥3%	620 (88.7)	-6.00 (1.68)	111.5 (75.9)	-12.60 (6.88)	553 (89.5%)	367 (59.4%)
<4%	161 (23.0)	-2.70 (1.23)	85.2 (72.8)**	-5.55 (4.83)	74 (46.3%)	23 (14.4%)
≥4%	538 (77.0)	-6.37 (1.48)	114.5 (75.4)	-13.48 (6.81)	503 (93.7%)	350 (65.2%)

Note: Values are presented as mean (SD) or n (%). *p*-values for the comparison of percent program completion within each weight category were obtained from ranked, one-way ANOVA models. \* = p < 0.01 for comparison of percent program completion within each weight loss category. \*\* = p < 0.0001 for comparison of percent program completion within each weight loss category. Percent program completion values of >100% indicate the client stayed with the program longer than their prescribed program length.

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# 3.5 $\mid$ Examination of predictors of lower weight loss in the program

Tables showing select univariate logistic regression predictors of <5% and <10% weight loss at the FV are provided as supporting information (Tables S2 and S3). Briefly, the odds of not losing both 5% and 10% weight at the FV were significantly higher for those clients who did not attain the 4-week weight loss threshold, used higher calorie meal plans, had longer prescribed program lengths, less time in the program, higher baseline BMIs, higher body fat mass indexes, and lower percent rate of attendance adherence through week 4.

Table 3 presents the predictors of <5% and <10% of weight loss at the FV using a multivariate logistic regression model. For both the <5% and <10% weight loss models, 4-week weight loss thresholds demonstrated the greatest odds of losing <5% or <10% of weight at the FV. After adjusting for all other predictors in the model, the odds of losing <5% of weight at the FV were 49.0 (95% CI: 13.8, 174; p < 0.0001) times greater for clients who lost <2% compared to ≥2% of weight at week 4. After adjusting for all other predictors in the multivariate model, the odds of losing <10% of weight at the FV were 20.1 (95% CI: 6.96, 58.1; p < 0.0001) times greater for clients who lost <3% of weight compared to ≥3% weight at week 4. The odds of losing <5% and <10% of weight were higher for females versus males, for the 4&2&1 and 5&2&2 meal plans versus the 5&1 meal plan, for those with a shorter time in the program, and for those with a higher baseline body fat mass index (when all other variables were held constant).

Table 3 also presents predictors of <5% and <10% weight loss at the FV when meal plans were not included in the multivariate logistic regression models. The removal of meal plans from the multivariate analysis allows for evaluation of the MWCC program as a whole, irrespective of the meal plan used by the client. Both the <5% and <10% weight loss models, when analyzed with and without meal plans, were nearly identical, except for the prescribed program length, which arose as a significant predictor in the no meal plan

TABLE 3 Multivariate logistic regression of predictors of less than 5% and 10% weight loss at the final visit.

	Estimate (SEM)	Odds ratio (95% CI)	p-value	Estimate (SEM)	Odds ratio (95% CI)	p-value	
Predictor	Meal plans included   <5% weight loss at final visit			Meal plans removed			
				<5% weight loss at final visit			
Intercept	1.12 (1.12)		0.3173	2.97 (1.10)		0.0071	
Meal plan (4&2&1 vs. 5&1)	1.27 (0.30)	3.55 (1.96, 6.44)	< 0.0001	NA			
Meal plan (5&2&2 vs. 5&1)	1.36 (0.57)	3.90 (1.27, 11.98)	0.0176	NA			
Prescribed program length, weeks	0.01 (0.01)	1.01 (0.99, 1.03)	0.1898	0.03 (0.01)	1.03 (1.01, 1.05)	0.0002	
Attendance adherence through week 4, %	-0.03 (0.01)	0.97 (0.95, 0.99)	0.0070	-0.03 (0.01)	0.97 (0.95, 0.99)	0.0092	
Gender/Sex (male vs. Female)	-0.94 (0.31)	0.39 (0.21, 0.72)	0.0025	-0.28 (0.15)	0.57 (0.32, 1.00)	0.0513	
Actual time in program, weeks	-0.04 (0.01)	0.96 (0.94, 0.98)	0.0009	-0.05 (0.01)	0.95 (0.93, 0.98)	<0.0001	
Week 4 weight loss category (<2% vs. $\geq 2\%$ )	3.89 (0.65)	49.02 (13.84, 173.63)	< 0.0001	2.02 (0.32)	56.79 (16.15, 199.71)	<0.0001	
	<10% weight loss at final visit		<10% weight loss at final visit				
Intercept	2.63 (1.39)		0.0585	2.09 (0.38)		<0.0001	
Meal plan (4&2&1 vs. 5&1)	0.87 (0.22)	2.40 (1.54, 3.72)	< 0.0001	NA			
Meal plan (5&2&2 vs. 5&1)	1.10 (0.48)	2.99 (1.18, 7.59)	0.0211	NA			
Age, years	-0.01 (0.01)	0.99 (0.97, 1.01)	0.1654	NA			
Prescribed program length, weeks	NA			0.04 (0.01)	1.04 (1.02, 1.05)	<0.0001	
Attendance adherence through week 4, %	-0.02 (0.01)	0.98 (0.96, 1.01)	0.1505	NA			
Baseline body fat Mass index, kg/m <sup>2</sup>	0.05 (0.02)	1.05 (1.01, 1.10)	0.0130	NA			
Gender/Sex (male vs. Female)	-0.55 (0.23)	0.58 (0.37, 0.91)	0.0178	-0.25 (0.11)	0.60 (0.40, 0.91)	0.0156	
Actual time in program, weeks	-0.09 (0.01)	0.92 (0.90, 0.94)	< 0.0001	-0.09 (0.01)	0.91 (0.89, 0.93)	<0.0001	
Week 4 weight loss category (<3% vs. $\geq$ 3%)	3.00 (0.54)	20.11 (6.96, 58.06)	<0.0001	1.62 (0.27)	25.71 (8.89, 74.36)	<0.0001	

Note: Estimates and their standard errors (SEM), odds ratios and 95% confidence intervals, and *p*-values were obtained from multivariate logistic regression models. Weight loss at the final visit was categorized as <5% or <10% weight loss (coded as 1 in the models) versus  $\ge 5$  or  $\ge 10\%$  weight loss (coded as 0). Odds ratios greater than 1 indicate greater odds of not losing  $\ge 5$  or  $\ge 10\%$  weight at the final visit with increasing value of continuous predictors or for the category versus referent for discrete predictors. Models that did not include meal plan were run to allow for the evaluation of the MWCC program, irrespective of the meal plan used by the client.

models (i.e., those with longer prescribed program length had higher odds of losing <5% and <10%), but not in the meal plan models. Furthermore, body fat mass index was only a significant predictor in the <10% weight loss model, which included the meal plans, but was not significant in the model with meal plans removed.

### 4 | DISCUSSION

Emerging research<sup>13</sup> suggests that the provision of additional support to early non-responders in weight loss programs may improve weight loss outcomes; however, there are no uniform thresholds for identifying early non-responders and the strength of the relationship between early weight loss and longer-term weight loss has yet to be established for commercial weight loss programs. The current findings indicate, that similar to non-commercial behavioral weight loss programs,<sup>9-11</sup> 4-week weight loss in the MWCC was a strong predictor of weight loss at FV (average duration 20 weeks) and is modestly associated with percent program completion. Moreover, the use of a 2% weight loss threshold at 4 weeks yielded the greatest specificity in predicting not losing both 5% and 10% weight loss at the FV (see Supplemental Information).

Multivariate analyses were also conducted to examine predictors of suboptimal weight loss, defined as <5% and <10% weight loss at the FV. Use of a less energy restricted meal plan, lower attendance through week 4, female sex, a shorter time in the program, and <2% weight loss at week 4 were associated with greater likelihood of <5% weight loss at the FV. Losing <2% of body weight during the first 4 weeks emerged as the strongest predictor of <5% weight loss. This finding, using real-world data, is in agreement with results from other weight loss studies, which have also shown that not losing approximately 2% weight loss by week four is a strong predictor of lower final weight loss.<sup>9,25</sup>

Given that weight loss of  $\geq$ 10% of body weight has been shown to lead to larger improvements in cardiovascular risk factors,<sup>21</sup> multivariate analyses were repeated using a 10% FV weight loss threshold. Similar to the results from the 5% weight loss model, 4week weight loss, female sex, use of a less energy restricted meal plan, and a shorter time in the program were associated with a greater likelihood of <10% weight loss, with 4-week weight loss again being the strongest predictor. Dissimilar to the 5% weight loss model, a higher baseline body fat mass index was a significant predictor in the 10% model, but attendance through week 4 was not a significant predictor in the 10% model. While both thresholds have been used to define clinically relevant weight loss, given the differences in the proportion of the sample losing 10% versus 5% weight, differences between the two multivariate models are not surprising. Also not surprising, given results from prior research, was that those who did not meet an early weight loss threshold were at decidedly increased risk for not losing clinically relevant weight loss defined as either ≥5% or 10%.<sup>2,7,9,10,26</sup>

Individuals starting on higher calorie meal plans had greater odds of not losing 5% and 10% weight and also had higher baseline body weight and BMI. Previous analyses of Medifast programs which compared weight loss between those with and without type 2 diabetes/high blood sugar found no difference in percent weight loss or percentage losing 5% and 10% weight by FV, despite those with type 2 diabetes/high blood sugar having a higher baseline weight, longer prescribed program length and a greater proportion of individuals starting on higher calorie meal plans.<sup>27</sup> The group with type 2 diabetes/high blood sugar had a lower percent weight loss at 4 and 12 weeks, but also spent significantly more time in the program. This finding, coupled with the current finding which indicates that time in program was a significant predictor of losing both 5% and 10% weight, highlights the importance of staying with the program longer to lose clinically relevant weight.

The removal of meal plans from the multivariate analyses allowed for evaluation of the MWCC program as a whole, irrespective of the meal plan used. When this was done the odds of losing <5% or <10% of body weight increased for those who lost less than 2% or 3% of body weight during the first 4 weeks, respectively. Longer prescribed program lengths became a significant predictor of both thresholds. As observed in the baseline characteristics, the higher calorie meal plans had longer prescribed program lengths due to higher baseline BMI, which coincides with how the different meal plans were used. Additionally, this has been seen previously where, in a prospective examination of Medifast programs, individuals with baseline BMI  $\geq$ 30 kg/m<sup>2</sup> lost less weight over 16 weeks compared to individuals with a BMI in the overweight category.<sup>28</sup>

Another salient point with clinical relevance is how high the odds ratios were in the models predicting not losing clinically relevant weight at FV when the 4-week thresholds were not met. For example, in the multivariate analyses, when a <2% weight loss at week 4 was observed, the odds of losing <5% weight at FV were 49 times greater with meal plans included and 57 times greater with meal plans removed compared to when 4-week weight loss was  $\geq 2\%$ . Moreover, the odds of not losing 10% weight at FV were 20 (meal plans included) and 26 times greater (no meal plans) among those with 4-week weight loss <3%, compared to weight loss  $\geq3\%$ . Results from past research indicate that those who do not reach these early weight loss thresholds are between 3 and 11 times less likely to lose a clinically relevant amount of weight compared to individuals with greater weight loss initially.<sup>2,7,9,10,26</sup> The larger odds ratios observed in the current study could be related to the lower proportion of clients who were early non-responders: only 5% did not meet the 2% threshold at 4 weeks and only 11% did not meet the 3% threshold. Previous research reports indicate much higher proportions of early non-responders within weight loss programs; depending on the criteria used, approximately one-quarter to one-third of participants were classified as early non-responders.<sup>2,9,11</sup>

It is interesting that greater attendance during the first 4 weeks predicted  $\geq$ 5% weight loss but not  $\geq$ 10% weight loss. While an

explanation for this finding is unknown, it is important to note that attendance was high for all groups through week 4 (<5% = 89.2%,  $\geq$ 5% = 97.0%, <10% = 93.1%,  $\geq$ 10% = 97.9%). The other adherence variable assessed in this analysis was MR adherence through week 4. This variable, perhaps surprisingly, was not a significant predictor of weight loss of <5% or 10% in either the univariate or multivariate analyses. Again, adherence was relatively high across the threshold groups with limited variability. MR use was also self-reported by clients, which could have led to bias related to over-reporting. The fact that there was little variability in early adherence is not surprising and has been discussed previously.<sup>10,12</sup> Based upon current and prior findings, it is reasonable to hypothesize that long-term adherence for both attendance and MR may be more important than early adherence for overall weight loss, especially given that there tends to be little variability between individuals early during interventions.<sup>10,12</sup>

Sex differences in weight loss have been evaluated previously with mixed results: some studies showing either no relationship between sex and weight loss and others reporting that males exhibited greater weight loss in comparison to females.<sup>16,29-31</sup> In our analysis, we found that female sex was a predictor of lower weight loss. This is perhaps not unexpected given that the calorie content of the meal plans is standardized, likely creating a larger energy deficit for males who generally have higher energy needs compared to females.

A unique aspect of this study, not typically evaluable in clinical trials that have a defined study length or within research trials which incentivize participants for study completion, is the relationship between early weight loss and time spent in the program. The results here suggest that those who achieve the early weight loss thresholds stay in the program longer and that greater early weight loss is associated with a higher percent program completion (actual time in program/prescribed program length). This relationship is bolstered by the multivariate results that found a shorter time in the program was associated with greater likelihood of not losing a clinically relevant amount of weight. These results further emphasize the importance of early weight loss and, perhaps more so, the importance of early weight loss within a real-world setting.

While this analysis of real-world data corroborates existing clinical trial research related to early weight loss, additional research is needed to assess the effectiveness of different approaches for interventions aimed at increasing weight loss among those with low levels of early weight loss. Preliminary research has shown that adaptive interventions utilizing a stepped care model have improved overall weight loss for those with low early weight loss.<sup>13</sup> Unick et al., previously reviewed existing stepped care intervention studies.<sup>12</sup> The additional interventions focused primarily on additional coaching sessions, with other interventions including strategies such as adding meal replacements, goal setting, and customized meal plans. It is worth noting that all the interventions utilized differing criteria to identify low early weight loss.

There are several strengths of this study including the large sample size and the evaluation of several clinically relevant research questions which can be used to inform future trials. The study also has limitations: the data were from retrospective chart reviews and therefore the evaluable variables were limited to only the data routinely collected by the MWCC (e.g., race/ethnicity was not available). Other components of behavioral therapy such as baseline motivation, self-efficacy and self-regulation were not able to be assessed; however, a previous systematic review has shown that these did not consistently predict greater weight loss.<sup>16</sup> Additionally. this analysis only evaluates the weight loss phase for clients of the MWCC and not maintenance: however, based on previous research. early weight loss is also likely predictive of long-term weight maintenance.<sup>32</sup> Conversely, although retrospective in nature, the data from these chart reviews are of real-world clients enrolled in a commercial weight loss program and therefore may be expected to have good generalizability and pragmatic value, given that recent polling found 55% of US adults desired to lose weight with 26% actively trying to do so.<sup>33</sup> This real-world application also allowed for a unique assessment of the relationship between early weight loss and time spent in the program.

In conclusion, the current findings further corroborate the positive relationship between early weight loss and clinically relevant weight loss during participation in a commercial weight loss program. These results also suggest that early weight loss may impact how long an individual stays with a weight loss program. Therefore, reducing the likelihood of early discontinuation is another reason to assess early weight loss and intensify intervention in those with low early weight loss. Future studies can build off the current findings, and also examine the timing of early supplemental intervention as how supplemental interventions might be implemented in a costeffective manner.

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#### CONFLICT OF INTEREST STATEMENT

CDC, JRK, and SSJ are employees of Medifast, Inc. JLU is a member of the Medifast Scientific Advisory Board and receives consulting fees associated with that appointment. Within the prior 24 months, KCM has received consulting fees from entities that provide products or services related to weight management, including Medifast, Eli Lilly, Pharmavite, General Mills, and 89Bio; he also has current research grant funding from the National Dairy Council, Hass Avocado Board, Greenyn, the Indiana University Foundation, Naturmega, Cargill, and National Cattlemen's Beef Association. MLW and LLG are employees of and MB is a contractor for Midwest Biomedical Research, which has received consulting fees from entities that provide products or services related to weight management, including Medifast, Eli Lilly, Pharmavite, General Mills, and 89Bio.

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### SUPPORTING INFORMATION

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

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