Short-term weight trajectories and long-term weight outcomes from a lifestyle intervention in real-world clinical practice

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Abstract

Centers for Disease Control and Prevention aligned lifestyle change programs are effective in promoting weight loss among those with elevated cardiometabolic risk; yet, variability in weight outcomes among participants is high. Little is known about heterogeneity of short-term weight changes among participants in real-world clinical practice. We sought to identify short-term weight trajectory clusters among lifestyle change program participants in real-world clinical practice and to examine the relationship between cluster membership and long-term weight outcomes. We identified participants from the electronic health records (2010–2017) with weight measured ≤ 30 days prior to program initiation (baseline) and in four intervals (3-week segments) in the 12 weeks after baseline. Clustering analysis was performed to identify distinct trajectories in percent weight change over 12 weeks. Cluster-specific differences in weight change at 12 and 52 weeks were assessed. Among 1,148 participants, across 18 clinic sites, three clusters were identified: minimal-to-no weight loss (MWL), delayed-minimal weight loss (DWL), and steady-moderate weight loss (SWL), corresponding to mean weight changes of 0.4%, –2.3%, and –4.8% at 12 weeks follow-up, respectively. Mean weight changes were 0.4%, –1.8%, and –5.1% for MWL, DWL, and SWL clusters, respectively, at 52 weeks follow-up, which correlated in direction and magnitude with short-term weight changes. Clustering analysis reveals heterogeneous, short-term weight trajectories among lifestyle change program participants in real-world clinical practice. Given the relationship between the magnitudes of short- and long-term weight change, individual participant weight trajectories may be useful in identifying potential non-responders in need of adjunctive or alternative therapy.

Keywords

Behavioral lifestyle program, Weight loss, real world, Electronic health records

INTRODUCTION

Overweight and obesity affect nearly 70% of the U.S. adult population and are associated with an increased risk for cardiovascular disease and Type 2 diabetes [1, 2]. Weight loss is an effective and essential means for cardiometabolic risk reduction [3]. Multiple clinical guidelines recommend intensive, multicomponent behavioral lifestyle interventions as the foundational approach for promoting weight

Implications

Practice: Classifying participants' short-term weight loss trajectories may be a useful tool for identifying who is likely to attain weight loss goals and to intervene on potential non-responders who may need more intensive or alternative therapy to maximize weight loss and cardiometabolic risk reduction.

Policy: National efforts for overweight/obesity prevention should consider more individualized approaches to promote and sustain weight loss.

Research: Future research should focus on understanding the various patient factors that influence individual weight loss trajectories.

loss and treating the sequelae of overweight/obesity [3, 4].

Centers for Disease Control and Prevention (CDC)-aligned lifestyle change programs [5] are effective in promoting weight loss among overweight/obese adults with elevated cardiometabolic risk in a variety of settings [6–11]. Such CDC-aligned programs are typically 12 months in duration, yet the majority of weight loss occurs, on average, in the first 3–4 months, corresponding to the intensive, core phase of the curriculum [6, 12].

Variability in weight outcomes among lifestyle change program participants is high [13–15]. Prior studies have examined heterogeneity in weight outcomes among small numbers of clinical trial participants, and have mostly focused on long-term trends in weight loss [15–19]. These studies have generally identified distinct clusters of weight loss patterns that are associated with specific patient demographics and clinical characteristics. Yet heterogeneity of short-term weight changes among program participants in real-world clinical practice is relatively unexplored. An understanding of heterogeneity in short-term weight loss patterns is imperative to identify specific groups

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of patients who may differ in terms of their likelihood of achieving treatment goals, otherwise concealed by overall mean changes in weight, and to inform strategies to improve weight loss and cardiometabolic risk reduction. The early identification and assessment of those potentially in need of adjunctive or alternative treatment be it behavioral, pharmacological, or surgical, represents a crucial window of opportunity to improve treatment response.

In this study, our primary goal was to perform a clustering analysis to identify distinct short-term weight trajectories using an electronic health records (EHR) database among adults enrolled in a weight loss-focused lifestyle change program implemented in a large healthcare delivery system. Our secondary goals were to identify patient demographics and clinical characteristics that predict membership to specific short-term weight trajectory clusters and to examine the relationship between cluster membership and long-term weight outcomes.

METHODS

Study setting

This study was conducted at Sutter Health, a mixed-payer, fee-for-service, and multi-specialty healthcare delivery system (www.sutterhealth.org), in northern California. Sutter Health provides medical services across 130 ambulatory clinics and 24 acute-care hospitals, with approximately 11 million outpatient visits and 200,000 hospital discharges annually. In this study, we used an EHR research database that included healthcare information from more than 4 million patients between January 1, 2001 and December 31, 2017. Sutter Health's Institutional Review Board reviewed and approved this study.

Lifestyle change program

Sutter Health utilizes an adaptation of the Diabetes Prevention Program called the Group Lifestyle Balance (GLB). The GLB program is an in-person and group-based lifestyle change program aligned with CDC recommendations for diabetes prevention (see Box A1 for more information on the GLB program and curriculum) [20, 21]. GLB is designed for community settings, and has been shown to promote clinically significant weight loss [21–23]. At Sutter Health, the program is available at 18 clinic sites across the organization [5]. The program is a 12-month in-person curriculum, composed of three phases: (i) the *core phase* includes 12 weekly sessions; (ii) the *transition phase* includes sessions conducted weekly/biweekly, over an additional 12 weeks; and (iii) the *support phase* includes sessions conducted monthly/bimonthly over the remaining 6 months of the year.

The target population of the GLB program, and in general CDC-aligned lifestyle change programs, is individuals with clinical pre-diabetes or high-risk for diabetes. However, at Sutter Health the

program is open to patients with a wide range of cardiometabolic risk factors, including those with evidence of diabetes, given that the primary focus of the program is weight loss.

Subject eligibility criteria

We identified individuals in the EHR who participated in the lifestyle change program at Sutter Health between January 1, 2010 (time of first implementation at Sutter Health) and December 31, 2017 (end of study database). We required participants to have EHR activity in the 12–36 months prior to the date of their first program encounter (baseline) to capture medical history prior to program initiation. We excluded participants with International Classification of Disease (ICD) 9 or 10 diagnoses for conditions or procedures associated with substantial weight change, including metastatic cancer, pregnancy, gastric bypass surgery, or end-stage kidney disease in the 12 months prior to, or up to 24 months after, baseline. We required participants to have a weight measurement recorded in the EHR ≤ 30 days prior to program initiation. We used the weight value on or closest to baseline, if multiple values were available during this time. Clinicians record weight measurements in the EHR at routine clinical encounters and at each lifestyle change program session.

For the clustering analysis, we selected program participants with weight measurements in at least three of four time intervals (3-week segments) in the 12-week period post-baseline, corresponding to the core phase of the curriculum. We required participants to have weight measurements within these fixed intervals to achieve a uniform distribution of measurements across the observation window.

Data collection and management

We extracted demographic and clinical information from the EHR database in the 12 months prior to baseline. Demographics included date of birth, gender, race-ethnicity, preferred spoken language, and primary insurance type. We also extracted census tract median household income mapped to participants' zip codes, as a contextual measure of socioeconomic status. Clinical characteristics included body mass index (BMI), smoking status, and comorbidities (pre-diabetes, diabetes, hypertension, dyslipidemia, metabolic syndrome, atherosclerotic cardiovascular disease, and depression). Algorithms for the identification of comorbidities are in Table A1. We classified patients as having a high risk for diabetes if they had clinical evidence of pre-diabetes or were considered high risk based on an validated screening tool from the American Diabetes Association [24]. We calculated a Charlson comorbidity index (CCI) score for each patient as a measure of overall disease burden [25–27]. We also identified participants' medication orders in the EHR active at baseline.

Table 1 | Baseline participant characteristics by short-term weight trajectory clusters

	All program participants <i>n</i> = 1,148	Cluster 1: Minimal-to-no weight loss <i>n</i> = 170	Cluster 2: Delayed minimal weight loss <i>n</i> = 167	Cluster 3: Steady moderate weight loss <i>n</i> = 811	<i>p</i> -Value*
Demographics					
Mean age, years ± <i>SD</i>	53.86 ± 12.60	52.34± 12.74	52.41 ± 14.07	54.48 ± 12.22	0.04
Female, <i>n</i> (%)	900 (78.4)	141 (82.9)	129 (77.2)	630 (77.7)	0.29
Race/ethnicity, <i>n</i> (%)					
African American	48 (4.2)	8 (4.7)	11 (6.6)	29 (3.6)	0.04
Asian	75 (6.5)	11 (6.5)	18 (10.8)	46 (5.7)	
Hispanic	160 (13.9)	20 (11.8)	33 (19.8)	107 (13.2)	
Non-Hispanic white	748 (65.2)	115 (67.6)	91 (54.5)	542 (66.8)	
Other	13 (1.1)	3 (1.8)	1 (0.6)	9 (1.1)	
Unknown	104 (9.1)	13 (7.6)	13 (7.8)	78 (9.6)	0.15
English preferred, <i>n</i> (%)	1,118 (97.4)	163 (95.9)	165 (98.8)	790 (97.4)	
Established PCP, <i>n</i> (%)	1,093 (95.2)	157 (92.4)	161 (96.4)	775 (95.6)	
Clinical characteristics					
Mean systolic BP, mmHg ± <i>SD</i>	126.5 ± 15.1	126.0 ± 16.4	125.3 ± 13.7	126.9 ± 15.1	0.39
Mean diastolic BP, mmHg ± <i>SD</i>	76.8 ± 9.3	76.6 ± 10.6	76.7 ± 9.2	76.9 ± 9.0	0.86
Mean BMI, kg/m ² ± <i>SD</i>	36.1 ± 6.8	36.5 ± 7.4	36.2 ± 6.4	36.0 ± 6.8	0.66
BMI categories*, <i>n</i> (%)					
Healthy	16 (1.4)	3 (1.8)	0 (0)	13 (1.6)	0.55
Overweight	162 (14.1)	21 (12.4)	24 (14.4)	117 (14.4)	
Obese	681 (59.3)	97 (57.1)	98 (58.7)	486 (59.9)	
Severely obese	289 (25.2)	49 (28.8)	45 (26.9)	195 (24)	
Comorbidities					
High risk for diabetes, <i>n</i> (%)	632 (55.1)	89 (52.4)	83 (49.7)	460 (56.7)	0.19
Overweight/obese without other diabetes risk	273 (23.8)	37 (21.8)	44 (26.3)	192 (23.7)	0.61
Type 2 diabetes, <i>n</i> (%)	234 (20.4)	41 (24.1)	40 (24)	153 (18.9)	0.14
Hypertension, <i>n</i> (%)	522 (45.5)	76 (44.7)	87 (52.1)	359 (44.3)	0.18
Depression, <i>n</i> (%)	260 (22.7)	51 (30)	46 (27.5)	163 (20.1)	0.005
Dyslipidemia, <i>n</i> (%)	577 (50.3)	85 (50)	83 (49.7)	409 (50.4)	0.98

(Continued)

Table 1 | Continued

	All program participants <i>n</i> = 1,148	Cluster 1: Minimal-to-no weight loss <i>n</i> = 170	Cluster 2: Delayed minimal weight loss <i>n</i> = 167	Cluster 3: Steady moderate weight loss <i>n</i> = 811	<i>p</i> -Value*
Metabolic syndrome, <i>n</i> (%)	308 (26.8)	51 (30)	47 (28.1)	210 (25.9)	0.50
ASCVD, <i>n</i> (%)	91 (7.9)	16 (9.4)	15 (9)	60 (7.4)	0.58
CCI score, <i>n</i> (%)					
0	641 (55.8)	86 (50.6)	86 (51.5)	469 (57.8)	0.31
1–2	498 (43.4)	82 (48.2)	80 (47.9)	336 (41.4)	
3–4	9 (0.8)	2 (1.2)	1 (0.6)	6 (0.7)	
Medications					
Mean total Rx, count ± SD	4.5 ± 3.9	5.0 ± 4.3	4.9 ± 4.0	4.4 ± 3.7	0.0495
Weight loss/appetite suppressants, <i>n</i> (%)	82 (7.1)	18 (10.6)	9 (5.4)	55 (6.8)	0.14
Diabetes (weight loss drugs), <i>n</i> (%)	171 (14.9)	30 (17.6)	34 (20.4)	107 (13.2)	0.03
Other diabetes drugs, <i>n</i> (%)	84 (7.3)	15 (8.8)	15 (9)	54 (6.7)	0.41
Health resource utilization					
Outpatient visits, count ± SD	10.7 ± 11.1	11.7 ± 11.3	11.8 ± 10.9	10.3 ± 11.1	0.14
Tele/electronic visit count ± SD	16.2 ± 15.3	21.7 ± 23.0	16.7 ± 12.9	15.0 ± 13.4	<0.0001
Preventive visit, <i>n</i> (%)	518 (45.1)	63 (37.1)	64 (38.3)	391 (48.2)	0.005
Immunization, <i>n</i> (%)	376 (32.8)	47 (27.6)	49 (29.3)	280 (34.5)	0.13
Socioeconomic characteristics					
Smoking status					0.25
Current	48 (4.2)	12 (7.1)	7 (4.2)	29 (3.6)	
Ever	314 (27.4)	40 (23.5)	47 (28.1)	227 (28.0)	
Never	775 (67.5)	115 (67.6)	113 (67.7)	547 (67.4)	
Unknown	11 (1.0)	3 (1.8)	0 (0)	8 (1.0)	
Insurance payer, <i>n</i> (%)					0.66
Commercial FFS/PPO	598 (52.1)	93 (54.7)	85 (50.9)	420 (51.8)	
Commercial HMO	233 (20.3)	30 (17.6)	35 (21)	168 (20.7)	
Medicare FFS	175 (15.2)	20 (11.8)	29 (17.4)	126 (15.5)	
Medicare HMO	65 (5.7)	11 (6.5)	8 (4.8)	46 (5.7)	
Medicaid/Medi-Cal	20 (1.7)	3 (1.8)	5 (3)	12 (1.5)	

Table 1 | Continued

	All program participants n = 1,148	Cluster 1: Minimal-to-no weight loss n = 170	Cluster 2: Delayed minimal weight loss n = 167	Cluster 3: Steady moderate weight loss n = 811	p-Value*
Self	5 (0.4)	1 (0.6)	1 (0.6)	3 (0.4)	
Unknown	52 (4.5)	12 (7.1)	4 (2.4)	36 (4.4)	
Census median income, n (%)					0.002
<\$50,000	100 (8.7)	18 (10.6)	26 (15.6)	56 (6.9)	
≥\$50,000 to <\$75,000	462 (40.2)	66 (38.8)	71 (42.5)	325 (40.1)	
≥\$75,000 to <\$100,000	354 (30.8)	58 (34.1)	47 (28.1)	249 (30.7)	
≥\$100,000 to <\$200,000	232 (20.2)	28 (16.5)	23 (13.8)	181 (22.3)	
≥\$200,000	0 (0)	0 (0)	0 (0)	0 (0)	
Other program characteristics					
Year of initiation, n (%)					0.37
2010	11 (1.0)	4 (2.4)	1 (0.6)	6 (0.7)	
2011	102 (8.9)	10 (5.9)	13 (7.8)	79 (9.7)	
2012	127 (11.1)	21 (12.4)	25 (15)	81 (10)	
2013	263 (22.9)	38 (22.4)	32 (19.2)	193 (23.8)	
2014	203 (17.7)	34 (20)	31 (18.6)	138 (17)	
2015	216 (18.8)	26 (15.3)	31 (18.6)	159 (19.6)	
2016	156 (13.6)	26 (15.3)	21 (12.6)	109 (13.4)	
2017	70 (6.1)	11 (6.5)	13 (7.8)	46 (5.7)	
Season of initiation, n (%)					0.11
Spring	364 (31.7)	52 (30.6)	43 (25.7)	269 (33.2)	
Summer	288 (25.1)	46 (27.1)	51 (30.5)	191 (23.6)	
Fall	417 (36.3)	58 (34.1)	56 (33.5)	303 (37.4)	
Winter	79 (6.9)	14 (8.2)	17 (10.2)	48 (5.9)	

ASCVD atherosclerotic cardiovascular disease; BMI body mass index; BP blood pressure; CCI Charlson comorbidity index; DDP Diabetes Prevention Program; FFS fee for service; HMO health maintenance organization; PCP primary-care provider; PPO preferred provider organization; Rx prescription; SD standard deviation.

*p-Values derived from analysis of variance for continuous variables and chi-square tests for categorical variables.

We collected information on participants' resource utilization, as a proxy for health engagement and motivation, which may be related to weight loss. We identified whether or not participants had an established primary-care provider within the healthcare system and quantified the number of outpatient ambulatory encounters, telephonic/electronic encounters, and whether patients had a preventive visit or immunization in the 12 months prior to baseline. We also quantified the number of lifestyle change program sessions completed by each participant during the intensive, core phase of the curriculum as a measure of program participation (range: 1–12).

Statistical analysis

Clustering analysis

We performed a disjoint cluster analysis based on percent weight change during the 12 weeks post-baseline. When multiple weight measurements per person were available within an interval, we calculated the mean of those values. We imputed weight values when not measured for an individual in one of the four follow-up intervals. If a weight value was missing between two other values, it was imputed using linear interpolation. If a weight value was missing from the fourth (last) interval, it was imputed by last-observation carried forward (LOCF). We clustered participants using *k*-medoids with correlation-based distance, using a minimum of three and a maximum of six clusters [28]. The *k*-medoids approach allows for non-linear distance measures and is more robust to outliers than traditional methods, such as *k*-means. To determine the optimal number of clusters (*k*) in the final analysis, we assessed mean silhouette widths. The silhouette width measures the proximity of each data point to its assigned cluster compared with other clusters. The silhouette width ranges from -1 to $+1$. A more positive mean silhouette width represents better cohesion within clusters and separation from neighboring clusters [29]. Generally, a mean silhouette width of 0.50–0.70 is indicative of a reasonable clustering structure and a width of >0.70 is indicative of a strong clustering structure [30]. In addition to considering the mean silhouette width, we also visually inspected clustering using a bivariate cluster plot to examine potential cluster overlap [31].

We examined differences in patient demographics and clinical characteristics across clusters by analysis of variance for continuous variables and chi-square tests of independence for categorical variables. Using discriminant analysis, we then considered the extent to which membership to each cluster could be predicted from baseline demographic and clinical characteristics, among candidate variables that were associated with membership at a $p < 0.05$, as determined from bivariate analyses [32].

Short-term weight trajectories and long-term weight outcomes by cluster

For each cluster, we examined patterns in mean percent weight change each week from baseline to 12

weeks follow-up. We imputed missing weight values between 2 and 12 weeks follow-up using linear interpolation or LOCF, as described above.

Among participants with available weight measurements at 52 weeks from baseline, for each cluster we examined mean percent weight change from baseline and the percentage of individuals attaining at least 5% weight loss, which is considered clinically meaningful [33]. The weight measurement recorded in the EHR closest to 52 weeks from baseline (± 12 weeks) was used in the analysis, as this corresponds to the completion of the lifestyle change program curriculum. We did not impute missing weight at 52 weeks.

We used linear regression to examine differences in mean percent weight change and logistic regression to examine differences in odds of attaining clinically meaningful weight loss by short-term weight trajectory clusters. We calculated model point estimates and 95% CIs before and after statistical adjustment for patient demographics and clinical characteristics listed in Table 1. A p -value < 0.05 was considered statistically significant.

We performed sensitivity analysis to determine whether the following outcomes were robust to imputation of weight measurements: (1) cluster partitioning, (2) patterns in mean changes in weight, and (3) the selection of participants with a 52-week weight measurement. We also conducted sensitivity analyses to determine whether cluster partitioning and discrimination, as well as patterns in mean changes in weight, were robust to the exclusion of patients with Type 2 diabetes. We conducted clustering analysis in R version 3.4.5 (www.r-project.org) and all other analyses in SAS version 9.4 (SAS Institute; Cary, NC).

RESULTS

Cohort identification

From our EHR research database, we identified 4,463 patients with at least one lifestyle change program encounter during the study period across 18 clinic sites (Fig. 1); 3,062 patients (69%) met general eligibility criteria and 1,148 participants (37%) had at least three follow-up weight measurements during the 12-week post-baseline period for the clustering analysis. Some 384 eligible participants (33%) with a missing value in one of the four intervals had weight imputed. Participants who met follow-up weight measurement criteria for the clustering analysis ($n = 1,148$) were not systematically different from those who did not meet these criteria ($n = 1,914$) in terms of age (mean ~ 53 years), gender (78% female), baseline BMI (mean = 36 kg/m^2), or overall disease burden (44% with CCI score $>1-4$); however, those selected for the clustering analyses versus those who were excluded were more likely to have metabolic syndrome (27% vs. 23%; $p = 0.02$) and a high-risk for Type 2 diabetes (55.4% vs. 44.2%; $p < 0.001$), and were less likely to have existing Type 2 diabetes (20% vs. 25%; $p = 0.003$). Among participants with

Fig 1 | Eligibility criteria flow diagram. ESRD end-stage renal disease; EHR electronic health records.

available weight measurements, those selected for clustering analysis had similar trends in weight loss during the 12-week follow-up period compared with those not selected (data not shown).

Clustering analysis

Among 1,148 program participants, three clusters were optimal with a mean silhouette width of 0.59, corresponding to a reasonable clustering structure (Table A2). Visual inspection of the bivariate cluster plot revealed minimal cluster overlap (Fig. A1). Clusters represented distinct short-term weight trajectories (Fig. 2), qualitatively described as: minimal-to-no weight loss (MWL; $n = 170$; 14.8%), delayed-minimal weight loss (DWL; $n = 167$; 14.5%), and steady-moderate weight loss (SWL; $n = 811$; 70.6%). Imputation of weight did not alter observed clustering partitioning, nor did the exclusion of patients with Type 2 diabetes (data not shown).

Short-term weight loss by weight trajectory clusters

The overall mean weight loss trajectory was steady, with a mean weight change (95% CI) of -2.8% (-2.4% , -3.2%) and -3.7% (-3.9% , -3.5%) at 6 and 12 weeks from baseline, respectively (Fig. 2). In the MWL,

DWL, and SWL clusters, participants had mean changes in weight (95% CI) of 0.3% (0.02% , 0.6%), -2.3% (-2.6% , -2.0%), and -4.8% (-5.0% , -4.6%), respectively, at 12 weeks from baseline. Imputation of weight did not alter observed patterns in mean weight change over time (data not shown).

Demographics, clinical characteristics, and cluster membership

Based on bivariate analyses, participants in the SWL cluster were less likely to have depression compared with those in the DWL and MWL clusters (20% vs. 28% and 30%, respectively; $p = 0.005$), more likely to live in census tracts with a median household income of $>\$100,000$ (22% vs. 14% and 17%; $p = 0.002$), and more likely to have a preventive healthcare visit in the prior 12 months (48% vs. 38%, and 37%; $p = 0.005$) (Table 1). Participants in the SWL cluster attended, on average, more sessions during the first 12 weeks of the program than those in the DWL and MWL clusters (mean $\pm$ SD: 8.5 ± 2.9 vs. 6.9 ± 2.9 and 6.9 ± 2.5 sessions, respectively; $p < 0.0001$ each). Participants across the SWL, DWL, and MWL clusters were not statistically different in terms of cardiometabolic risk factors, including mean BMI

Fig 2 | Mean percent weight change from initiation of the lifestyle change program by short-term weight trajectory clusters. Error bars represent 95% confidence intervals. Cluster 1 (blue line): minimal-to-no weight loss ($N = 170$); Cluster 2 (red line): delayed-minimal weight loss ($N = 167$); Cluster 3 (green line): steady-moderate weight loss ($N = 811$); all clusters combined (gray line; $N = 1,148$).

Fig 3 | Mean change in weight through 52 weeks from initiation of the lifestyle change program by short-term weight trajectory clusters. Error bars represent 95% confidence intervals. Cluster 1 (blue line): minimal-to-no weight loss ($N = 132$); Cluster 2 (red line): delayed-minimal weight loss ($N = 141$); Cluster 3 (green line): steady-moderate weight loss ($N = 688$).

(36.0, 36.2, 36.5; $p = 0.66$), or the percentage of patients with a high risk for diabetes (56.7%, 49.7%, 52.4%; $p = 0.19$), metabolic syndrome (25.9%, 28.1%, 30.0%; $p = 0.50$), or Type 2 diabetes (18.9%, 24.0%, 24.1%; $p = 0.14$).

Baseline demographics and clinical characteristics were poor predictors of cluster membership. Based on these characteristics, the discriminant analysis assigned most individuals to the SWL cluster, the largest group, resulting in low correct classification rates for the other two clusters (DWL = 12% and MWL = 2.9%). The number of program sessions attended did not alter the results when this variable was included as a predictor in the discriminant analysis, nor did the exclusion of patients with Type 2 diabetes (data not shown).

Long-term weight outcomes by short-term weight trajectory clusters

Among, 961 program participants with a weight measurement at a mean of 52 weeks from baseline, mean weight changes (95% CI) were 0.4% (−0.5%,

1.4%), −1.8% (−2.7%, −0.9%), and −5.1% (−5.6%, −4.5%) among those in the MWL, DWL, and SWL clusters, respectively (Fig. 3), with 9.8%, 24.8%, and 40.4% attaining clinically meaningful ($\geq 5\%$) weight loss (Table 2). The magnitude of mean percent weight loss ($p < 0.01$ for each pairwise comparison) and the odds of attaining clinically meaningful weight loss ($p < 0.01$ for each pairwise comparison) were statistically significantly different across clusters, even after controlling for patient demographics and clinical characteristics (Table 2). The selection of participants with follow-up weight measurements at 52 weeks did not alter observed patterns in short-term weight change by cluster (data not shown).

DISCUSSION

In a cohort of participants from a lifestyle change program across 18 sites in real-world clinical practice, we identified heterogeneous, short-term weight trajectory clusters with reasonable partitioning structure (mean silhouette width = 0.59). The SWL cluster (the largest of three) differentiated from the

Table 2 | Weight outcomes at 52 weeks by short-term weight trajectory clusters

	Cluster 1: Minimal-to-no weight loss n = 132	Cluster 2: Delayed-minimal weight loss n = 141	Cluster 3: Steady-moderate weight loss n = 688	p-Value*
Mean percent weight change from baseline (95% CI)	0.4 (−0.5, 1.4)	−1.8 (−2.7, −0.9)	−5.1 (−5.6, −4.5)	<0.0001
Unadjusted mean difference	ref	−2.2 (−3.5, −0.9) p = 0.001	−5.5 (−6.8, −4.2) p < 0.0001	
Adjusted mean difference	ref	−2.2 (−3.8, −0.6) p = 0.007	−5.5 (−6.7, −4.2) p < 0.0001	
≥5% weight loss from baseline, n (%)	13 (9.8)	35 (24.8)	278 (40.4)	<0.0001
Unadjusted odds ratio	ref	3.0 (1.5, 6.0)	6.2 (3.4, 11.2)	
Adjusted odds ratio	ref	3.0 (1.5, 6.0) p = 0.002	6.2 (3.4, 11.2) p < 0.0001	

Unadjusted mean differences and unadjusted odds ratios with 95% confidence intervals (CIs) and p-values for cluster comparisons were derived from simple linear regression or logistic regression, respectively. Adjusted mean differences and odds ratios with 95% CI and p-values for cluster comparisons were derived from multivariable linear regression or logistic regression, respectively, adjusting for patient demographics and clinical characteristics. *p-Value derived from analysis of variance for bivariate comparisons of means by cluster and chi-square tests of independence for bivariate comparisons of categorical variables by cluster.

others at three weeks from baseline, and the DWL and MWL clusters differentiated from each other at 9 weeks from baseline. At the end of the 12-week follow-up period, these clusters had, on average, distinct treatment responses, which persisted at 52 weeks from baseline. Our study is one of the largest clustering analyses of weight outcomes from a behavioral lifestyle program conducted to date. The study is novel in its identification of short-term heterogeneity in treatment response among participants with a range of cardiometabolic risk factors in real-world clinical practice, and reveals specific patterns in early treatment response, otherwise concealed by overall trends in weight loss.

Our findings are consistent with other studies examining longitudinal patterns in weight change, which have also found distinct weight trajectories among behavioral lifestyle intervention participants [15–19]. Prior analyses were performed among patients from clinical trials, most of which focused on discerning long-term patterns in weight change [16–19]. Our study is unique in its focus on short-term trajectories. Similar to our study, Yank et al. identified three distinct short-term weight loss clusters at 12 weeks from baseline among 72 overweight/obese adults, who were randomized to receive a group-based lifestyle intervention like the one assessed in our current study [15]. Participants in these clusters lost, on average, 4.3%, 6.5%, and 6.9% of body weight, respectively at 12 weeks from baseline. As in our study, the magnitude of weight loss in the short term correlated with long-term trends.

Cluster membership in our study was associated with both participant baseline characteristics and the number of program sessions attended. Program participants in the cluster with the most pronounced weight loss (i.e., SWL cluster) were less likely to have a diagnosis of depression and were more likely to live in census tracts with a higher median household income, have a prior preventive healthcare visit, and attended more sessions during the intensive phase of the program than those in other clusters. These findings support existing literature that highlights the impact of program completion [34], as well as socioeconomic status and mental health on weight management [35–37]. Mounting epidemiologic evidence suggests that people with obesity are more likely to develop depression, and vice versa [38–42]. Depression may limit self-efficacy and program completion, resulting in poor weight outcomes. Furthermore, participants with a preventive visit in the 12 months prior to initiating the program may be indicative of health engagement and motivation.

Despite these associations, there was poor discrimination of clusters based on measured patient baseline demographics and characteristics, indicating that these factors cannot adequately differentiate cluster membership. These data suggest that other unmeasured factors may be at play. For example, in the aforementioned clustering analysis by Yank

et al. discriminant analysis revealed that high friend encouragement, high obesity-related problems, and low physical well-being, could differentiate cluster membership [15]. Still, there are likely additional unknown or unmeasured factors that require further investigation.

Individuals with clinical pre-diabetes or a high risk for diabetes are the primary target of the CDC-aligned program evaluated in this study; however, in this healthcare setting, the program was open to participants with a range of cardiometabolic risk factors, including those with evidence of Type 2 diabetes, who would benefit from the program's focus on weight loss. Notably, cardiometabolic risk factors were not associated with, nor could they accurately predict cluster membership, suggesting that patients may similarly benefit from the program regardless of underlying cardiometabolic risk. Indeed, the exclusion of patients with Type 2 diabetes from the clustering analysis did not alter cluster partitioning or discrimination. We note that patients with Type 2 diabetes were disproportionately excluded from our analysis, because many did not meet the minimum number of short-term weight follow-up requirements for the analysis. We hypothesize that this is due to poorer program compliance among patients with Type 2 diabetes. Future studies are needed in this area.

The association between short- and long-term weight loss is an important finding from this study. These results suggest that early weight loss may serve as a valuable predictor of long-term treatment success, or lack thereof. The early identification of participants who are unlikely to have a treatment response in the long-term (i.e., those identified within the MWL cluster) represents a crucial opportunity to assess the need for adjunctive or alternative treatment (behavioral, pharmacological, or surgical) to maximize weight loss and cardiometabolic risk reduction. Nevertheless, there is still much heterogeneity in individual treatment response. For example, the MWL cluster had, on average, no weight loss at 52 weeks follow-up; yet, nearly 10% of participants within this cluster achieved clinically meaningful weight loss. Thus, factors that influence individual weight trajectories need further investigation.

This study has several limitations. First, this was a retrospective, observational analysis and causal inferences are limited. Second, we restricted the sample to individuals that had at least three follow-up weight measurements in fixed intervals during the 12-week post-baseline. These criteria resulted in the exclusion of a large number of participants; however, this was necessary for the clustering analysis so that each individual had a sufficient number of uniformly distributed weight measurements across the observation period. Participants not selected for inclusion in the clustering analysis were similar to those selected in terms of demographics; however, the former group had, on average, fewer risk factors for Type 2 diabetes and was more likely to have diabetes. While trends in mean percent weight change during the 12-week follow-up period were similar, regardless

of inclusion in clustering analysis, we cannot know how our selection criteria affected cluster partitioning. We do not consider our cohort eligibility criteria to be overly strict, yet we recognize that our results are generalizable to individuals who fulfilled these requirements. Finally, as mentioned above, there are likely factors that determine cluster membership that we were unable to measure in our EHR research database, such as self-efficacy, friend-family support, and physical well-being. We cannot know if these factors would have improved our ability to predict cluster members.

Notwithstanding these limitations, the study has several strengths. We used a large EHR research database from real-world clinical practice, leveraging access to comprehensive information on patient demographics and clinical characteristics to examine weight trajectory clusters. To our knowledge, our study is the first to focus on short-term trajectories in weight change among patients participating in an evidence-based lifestyle program in the real world. It is one of the largest clustering studies to date and provides a better understanding of the heterogeneity of short-term treatment response to a behavioral lifestyle program in routine clinical practice. The results from this study, although derived from a single healthcare delivery system in northern California across 18 clinic sites, have high potential for generalizability to other mixed-payer, fee-for-service healthcare systems throughout the nation.

In summary, clustering analysis reveals heterogeneous, short-term weight trajectories among lifestyle change program participants in real-world clinical practice. Given the relationship between the direction and magnitude of short- and long-term weight change, individual participant weight trajectories may be useful in identifying potential non-responders in need of adjunctive or alternative therapy to maximize weight loss and cardiometabolic risk reduction.

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Compliance with Ethical Standards

Conflicts of Interest: DAG is a consultant for Mytonomy, Inc. All other authors report no conflicts of interest.

Human Rights: This study was conducted according to Health Insurance Portability and Accountability (HIPAA) act standards for the protection of human subjects.

Informed Consent: A HIPAA waiver of informed consent was obtained for this study.

Welfare of Animals: This study does involve animal subjects.

Box A1 Description of the Group Lifestyle Balance program

The Group Lifestyle Balance (GLB) program is an adaptation of the Diabetes Prevention Programs lifestyle intervention for community settings, developed by the Diabetes Prevention Support Center at the University of Pittsburgh [20, 21]. The GLB program is intended for non-diabetic, overweight/obese individuals, at least 18 years of age, with a diagnosis of pre-diabetes and/or metabolic syndrome. The GLB program is associated with improved weight management and a reduced incidence of Type 2 diabetes [21–23]. The GLB utilizes an in-person, group-based format that is facilitated by a trained lifestyle coach over a duration of 12 months. The underlying framework for the GLB curriculum is Social Cognitive Theory [43]. The program is designed to enhance self-efficacy through social support and gradual mastery of self-regulation skills (e.g., goal setting, self-monitoring). Participants are encouraged to track their weight, dietary intake, and physical activity daily. The primary behavioral goals of GLB are a 7% loss in body weight and an increase in physical activity to ≥ 150 min per week. The GLB program is composed of three phases:

- The *core phase (months 1–3)* promotes weight loss and behavioral goal setting through 12 weekly sessions;
- The *transition phase (months 4–6)* continues to promote weight loss and behavioral goals through four bimonthly/monthly sessions;
- The *support phase (months 7–12)*, through six monthly sessions, focuses on: (i) facilitating continued behavior change through an iterative guided mastery process; (ii) fostering participants' self-efficacy and independence; and (iii) reinforcing problem-solving and behavior maintenance skills.

Core phase	Transition phase	Support phase
1. Welcome to the GLB program	13. Long-Term Self-Management	17. Mindful Eating
2. Be a Fat and Calorie Detective	14. More Volume, Fewer Calories	18. Stress and Time Management
3. Healthy Eating	15. Balance Your Thoughts	19. Standing Up for Your Health
4. Move Those Muscles	16. Strengthen Your Exercise Program	20. Heart Health
5. Tip the Calorie Balance		21. Stretching: The Truth about Flexibility
6. Take Charge of What's Around You		22. Looking Back and Looking Forward
7. Problem Solving		
8. Four Keys to Healthy Eating Out		
9. Slippery Slope of Lifestyle Change		
10. Jump Start Your Activity Plan		
11. Make Social Cues Work for You		
12. Ways to Stay Motivated		

For further information, please visit <https://www.diabetesprevention.pitt.edu/>.

Table A1 | Criteria for comorbidities

Condition	ICD-9	ICD-10	Encounter, billing, or problem list	Medication GPI (2-digit)	Lab/Biometric/Other	Description (meet ≥1 criterion)	Exclusions
Metabolic syndrome	277.7	E88.81		N/A	See criteria below ^a	See criteria below ^a	
Pre-diabetes	790.29	R73.09 V77.1-1S		27	FBG: 100 to <126 mg/dL HbA1c: 5.7% to <6.5% OGTT: 140 to <200 mg/dL	(1) ≥2 abnormal labs 90–365 days apart; (2) ≥1 abnormal lab AND ≥1 medication order; (3) 1 problem list, encounter, or billing diagnosis AND ≥1 abnormal lab	Meet criteria for Type 2 diabetes (below) or has evidence of Type 1 diabetes, defined as a problem list, encounter, or billing diagnosis of 250.x1 or E10.x
Type 2 diabetes	250.x	E11.x		27	FBG: ≥126 mg/dL HbA1c: ≥6.5% OGTT: ≥200 mg/dL	(1) 1 problem list diagnosis AND ≥1 encounter or billing diagnoses; (2) ≥2 encounter or billing diagnoses ≥90 days apart; (3) ≥2 abnormal labs 90–365 days apart; (4) ≥1 abnormal lab AND ≥1 medication order; (5) 1 problem list, encounter, or billing diagnosis AND ≥1 medication order; (6) 1 problem list, encounter, or billing diagnosis AND ≥1 abnormal lab	Evidence of Type 1 diabetes, defined as a problem list, encounter, or billing diagnosis of 250.x1 or E10.x
Hypertension	401.x; 796.2	I10		37, 36, 34, 33	SBP: ≥140 (≥130 for T2D) DBP: ≥90 (≥80 for T2D)	(1) 1 problem list diagnosis AND ≥1 encounter or billing diagnoses; (2) ≥2 encounter or billing diagnoses ≥90 days apart; (3) ≥2 confirmatory SBP or DB ≥90–365 days apart; (4) ≥1 problem list, encounter, or billing diagnosis AND ≥1 medication order; (5) ≥1 problem list, encounter, or billing diagnosis AND ≥1 abnormal SBP or DBP	
Dyslipidemia	272.x	E78.x		39	TC: ≥200 mg/dL LDL: ≥160 mg/dL HDL: <40 mg/dL TG: ≥200 mg/dL	(1) 1 problem list diagnosis AND ≥1 encounter or billing diagnoses; (2) ≥2 encounter, or billing diagnoses ≥90 days apart (3) ≥2 abnormal labs 90–365 days apart; (4) ≥1 abnormal lab AND ≥1 medication order; (5) ≥1 problem list, encounter, or billing diagnosis AND ≥1 medication order; (6) 1 problem list, encounter, or billing diagnosis AND ≥1 abnormal lab	
Depression	311; 296.2x 296.3x 300.4	F32.x F33.x; F34.1		58	—	(1) 1 problem list diagnosis AND ≥1 encounter or billing diagnosis (2) ≥2 encounter or billing diagnoses; (3) ≥1 problem list, encounter, or billing diagnosis AND ≥1 medication order	

DBP diastolic blood pressure; FBG fasting blood glucose; GPI generic product identifier; HbA1c hemoglobin A1c; ICD International Classification of Disease; OGTT oral glucose tolerance test; SBP systolic blood pressure.

^aPatients must have at least three of the following:

1. Body mass index ≥30 kg/m² in non-Asian patients or ≥27 kg/m² in Asian patients.
2. Identified as having hypertension (described above).
3. Identified as having pre-diabetes or diabetes (described above).
4. Triglycerides ≥150 mg/dL (at least two values at least 90–365 days apart), or at least one value and evidence of a triglyceride lowering medication (fibrates [GPI = 3920]; omega-3 fatty acids [GPI = 3950]).
5. Low HDL <40 mg/dL in men or <50 mg/dL in women (at least two values at least 90–365 days apart), or at least one value and evidence of an HDL raising medication (fibrates [GPI = 3920], niacin [GPI = 3945]).

APPENDIX 1

Table A2 | Mean Silhouette widths based on partitioning around medoids by cluster number

k clusters	Mean Silhouette width
3	0.59
4	0.59
5	0.56
6	0.43

GLB session topics

APPENDIX 2

Fig A1 | Bivariate cluster plot of principal components.

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