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ORIGINAL ARTICLE

Association of changes in mental health with weight loss during intensive lifestyle intervention: does the timing matter?

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Summary

Objective

This study examined changes in mental health symptoms and weight during weight loss treatment. It was hypothesized that worsening mental health would negatively impact weight loss.

Methods

Data were analyzed from a trial of 92 Hispanic women with overweight/obesity and prediabetes, who were randomized to receive intensive lifestyle intervention (ILI), metformin 1,700 mg daily, or standard care. Depression, anxiety and perceived stress were assessed at 0, 6 and 12 months. Six- and 12-month weight change was compared among participants whose symptom scores worsened on any mental health measure (W) vs. improved or remained stable on all three (I/S).

Results

Among ILI participants, the 12-month difference in weight loss between I/S and W groups was statistically significant: −5.1 kg (P = 0.001). From baseline to 6 months, ILI participants in I/S and W groups experienced comparable weight loss. However, from 6 to 12 months, W participants regained weight, whereas I/S participants experienced continued weight loss. In the metformin and standard care arms, there was no weight difference between I/S and W groups.

Conclusions

In ILI, 12-month improvement or stability in mental health was significantly associated with weight loss. Weight trajectories between I/S and W groups diverged at 6 months.

Keywords: Anxiety, depression, perceived stress, weight loss.

Introduction

A large body of research has demonstrated the association of common mental health problems, such as depression, anxiety and stress, with excess body weight (1–7). These same psychological concerns can impair individuals' ability to successfully complete weight loss interventions (8,9). However, knowledge about the relationship between mental health and weight loss is limited for several reasons.

First, most weight loss trials have excluded those with comorbid mental health conditions (10). Second, mental health is most often operationalized as depressive symptoms or clinical depression, providing little information about other mental health concerns or multiple mental health comorbidities. Third, trials examining the relationship between mental health and weight loss have often only assessed baseline mental health status as a predictor, yielding inconsistent findings (10). Mental health symptoms likely change during weight loss treatments, necessitating evaluations that explore their trajectories over time (11). Such evaluations may promote understanding about how and when changes in mental health impact the success of weight loss efforts.

The landmark Diabetes Prevention Program (DPP) trial highlights challenges and opportunities for examining

the association of mental health with weight loss. This trial of 3,234 adults with overweight/obesity and prediabetes studied an intensive lifestyle intervention (ILI) that produced clinically significant weight loss (6.8 kg at 12 months) and a 58% reduction in the risk of developing type 2 diabetes relative to placebo (12). DPP participants randomized to receive metformin, a common antidiabetic medicine, experienced comparatively less weight loss and a lower reduction in diabetes risk. In this trial, elevated symptoms of depression and anxiety at baseline did not impact weight outcomes (13). However, participants in this study had low levels of mental health symptoms, limiting the ability to examine associations with weight loss (14). Many subsequent translational studies have used less stringent exclusion criteria and may provide unique data to investigate changes in mental health and weight loss during active treatment.

The primary objective of this analysis was to examine the association between 12-month changes in mental health symptoms and weight in a translational DPP trial of 92 Hispanic women (Latinas) with overweight/obesity and prediabetes. Trajectories of mental health symptoms and weight change during this trial were examined using data at 0, 6 and 12 months.

Methods

PREVENT-DM was a comparative effectiveness trial of group-based ILI (n = 33) vs. metformin 850 mg twice daily (n = 29) vs. standard care (n = 30) among 92 Latinas with prediabetes and overweight/obesity. The ILI delivered in this study was based on the Group Lifestyle Balance Program (copyright 2008, 2010, 2011, 2017; University of Pittsburgh), which is an evidence-supported adaptation of the original NIH/National Institute of Diabetes and Digestive and Kidney Diseases-funded DPP (15,16). In the current study, this intervention was delivered weekly for the first 14 weeks, followed by 10 biweekly or monthly sessions during the remainder of the trial. The metformin participants attended brief monthly study visits, during which they returned unused medication doses from the previous month and received the next month's medication supply. Participants in the standard care arm had two study visits during the 12-month intervention period when they received written educational materials about preventing type 2 diabetes. In the main effects from this trial, there was a significant difference in 12-month weight loss among ILI participants relative to metformin (−3.1 kg, P = 0.013) and standard care (−4.8 kg, $P < 0.001$) (17). The weight change observed in the metformin and standard care arms was not significantly different (17). The protocol for this study was approved by the Northwestern University IRB. Detailed descriptions of the study population, interventions and primary findings were previously published (17,18).

Eighty-five PREVENT-DM participants (92.4%) who completed data collection visits at 0, 6 and 12 months were included in the current analysis. The primary outcome of the current analysis was weight change from baseline to 12 months, and its association with changes in depression, anxiety and perceived stress was examined. The following widely used questionnaires were used to measure these mental health variables: Beck Depression Inventory II (BDI-II), Generalized Anxiety Disorder 7-item Scale (GAD-7) and the Perceived Stress Scale (PSS), which measures levels of general stress. For each mental health measure, we characterized participants as improved/stable (lower or equivalent scores at 12 months) or worsened (higher scores at 12 months). Participants whose symptom scores worsened on any of the three measures were considered to have worsened mental health (W), and those who improved or remained stable on all three measures were considered to have improved/stable mental health (I/S). Among the 85 participants included in this analysis, none were missing data for weight or mental health measures at 12 months.

The mean 12-month change in weight and mental health measures was assessed by treatment assignment and mental health status (Table 2). The significance of 12-month weight differences between I/S vs. W participants was assessed using independent-sample t-tests (Table 3). The difference in weight change was further stratified according to the number of mental health measures that worsened at 12 months (Table 3). To explore timing of these effects, 6-month changes in mental health symptoms and weight were explored in the same manner described previously (Figure 1). Key variables were assessed separately among participants in the ILI arm and in the combined metformin and standard care arms. These two study arms were combined in the analysis because: (1) neither metformin nor standard care is thought to impact mental health outcomes directly; and (2) the 12-month weight change did not differ between these groups (17). In a sensitivity analysis, the same analyses were repeated in the metformin and standard care groups individually. The mean 12-month weight change was also modeled using ANCOVA, adjusting for baseline weight and including an interaction term for treatment assignment x categorical change in mental health status (i.e. I/S and W). All analyses assumed a 5% level of significance and were conducted using SPSS, version 24.

RESULTS

Table 1 presents the baseline characteristics of the participants by treatment assignment. The overall mean BMI

Table 1 Baseline characteristics of study participants by treatment assignment

Characteristic[a]	Intensive lifestyle intervention (*n* = 33)	Metformin + standard care (*n* = 59)	*P*-value
Age, years	45.5 ± 12.3	44.9 ± 12.6	0.81
Education, years	10.2 ± 3.5	9.4 ± 3.7	0.32
Household income, $	14,905 ± 7,518	15,875 ± 11,088	0.62
Foreign born, *n* (%)	30 (90.9)	56 (94.9)	0.66
Weight, kg	85.4 ± 23.0	78.9 ± 13.9	0.15
BMI, kg/m^2	34.4 ± 7.9	32.7 ± 5.6	0.23
Depression score[b]	13.5 ± 9.9	11.2 ± 9.0	0.26
Anxiety score[c]	4.7 ± 4.6	4.3 ± 4.4	0.65
Perceived stress score[d]	23.9 ± 7.7	22.0 ± 7.3	0.22

[a]Data are presented as means ± SD except otherwise noted.
[b]Beck Depression Inventory II is scored from 0 to 63, with higher numbers indicating more depressive symptoms.
[c]GAD-7 is scored from 0 to 21, with higher numbers indicating more anxiety symptoms.
[d]Perceived Stress Scale is scored from 0 to 40, with higher numbers indicating higher levels of perceived stress.

was 33.3 kg/m^2 (data not shown) (18). Demographic and other cardiometabolic data have been presented in-depth elsewhere (17,18). In the ILI group, mean baseline scores for the BDI, GAD-7, and PSS were 13.5 ± 9.9, 4.7 ± 4.6, and 23.9 ± 7.7, respectively. The corresponding values in the combined metformin and standard care groups were 11.2 ± 9.0, 4.3 ± 4.4, and 22.0 ± 7.0. There were no meaningful differences in baseline characteristics between those whose mental health was improved or stable (I/S) vs. worsened (W), except for higher levels of perceived stress in the I/S group (24.4 ± 7.6) vs. 21.6 ± 6.8 in the W group (data not shown).

There was greater mean weight loss and larger mental health improvements among ILI participants than those who received metformin and standard care. (Table 2) Twelve-month mean changes in weight and mental health measures were also greater among those whose mental health status improved or remained stable vs. worsened. (Table 2).

Table 3 presents the mean 12-month weight change by treatment arm among participants who worsened on any

Table 2 12-month changes in weight and mental health measures by treatment assignment and mental health status

Characteristic	Treatment assignment		Mental health status	
	Intensive lifestyle intervention (n = 30) Mean ± SD[a]	Metformin + standard care (*n* = 55) Mean ± SD[a]	Improved or stable (*n* = 32) Mean ± SD[a]	Worsened (*n* = 53) Mean ± SD[a]
Change in weight, kg	−4.0 ± 4.4	−0.1 ± 3.8	−2.9 ± 4.7	−0.6 ± 4.0
Change in mental health measures				
Depression score[b]	−3.8 ± 9.1	−0.6 ± 6.6	−6.0 ± 5.6	0.9 ± 7.6
Anxiety score[c]	−1.0 ± 5.5	−0.2 ± 3.6	−2.7 ± 3.4	0.8 ± 4.4
Perceived stress score[d]	−0.9 ± 7.1	−0.6 ± 5.8	−5.3 ± 4.3	2.0 ± 5.7

[a]A negative sign before the observed mean change indicates weight loss and mental health improvement. No sign before the observed mean change indicates mental health worsening.
[b]Beck Depression Inventory II is scored from 0 to 63, with higher numbers indicating more depressive symptoms.
[c]GAD-7 is scored from 0 to 21, with higher numbers indicating more anxiety symptoms.
[d]Perceived Stress Scale is scored from 0 to 40, with higher numbers indicating higher levels of perceived stress.

Table 3 12-month weight change according to changes in mental health measures

	Intensive lifestyle intervention (*n* = 30)		Metformin + standard care (*n* = 55)	
Change in mental health measures	*n*	Weight change, kg (95% CI)[a]	*n*	Weight change, kg (95% CI)[a]
Improved or stable (I/S)	13	−6.9 (−9.4, −4.3)	19	−0.2 (−1.5, 1.2)
Worsened on any mental health measure (W)	17	−1.8 (−3.5, −0.1)	36	−0.1 (−1.5, 1.4)
Between group difference, *P*-value[b]	30	−5.1 (−2.3, −7.9), 0.001	57	0.1 (−2.1, 2.3), 0.919
Worsened on 1 mental health measure	10	−3.0 (−4.8, −1.2)	18	−0.1 (−1.5, 1.3)
Worsened on 2 mental health measures	2	−0.4 (−16.9, 16.1)	10	−0.8 (−3.8, 2.2)
Worsened on 3 mental health measures	5	0.3 (−5.1, 5.6)	8	1.0 (−4.7, 6.6)

[a]A negative sign before the observed mean weight change or 95% CI indicates weight loss, and no sign indicates weight gain.
[b]*P*-value for the difference in weight loss between I/S and W groups was generated using the independent samples t-test.

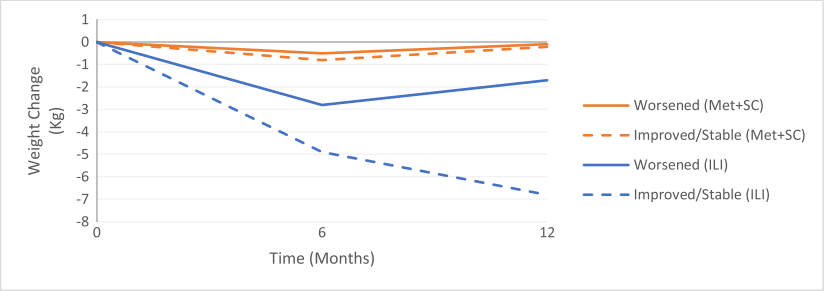

Figure 1 Change in weight at 6 and 12 months by changes in mental health (improved/stable vs. worsened) Legend: ILI = Intensive Lifestyle Intervention; Met = Metformin; SC = Standard Care.

of the mental health measures (W) vs. those who improved or remained stable on all three (I/S). Among the 30 ILI participants who completed follow-up, 17 experienced worsening in mental health status and 13 demonstrated stable or improved mental health status. A significant difference in weight loss was observed between the I/S and W groups of −5.1 kg (95% CI: −7.9, −2.3; $P = 0.001$). Among ILI participants in the W group, those who worsened on only one mental health measure still experienced significant, yet diminished weight loss (−3.0 kg, 95% CI: −4.8, −1.2). However, those who worsened on two or three measures experienced non-significant weight loss or weight gain. For metformin and standard care participants, there were no significant 12-month weight changes in any of the groups defined by mental health status. The same null findings were observed in a sensitivity analysis examining the metformin and standard care arms separately. When modeling 12-month weight change, the interaction term for treatment assignment × categorical mental health status was significant ($P = 0.01$).

Figure 1 displays the mean weight change at 6 and 12 months among improved/stable (I/S) and worsened (W) groups by treatment arm. Among ILI participants, the difference in weight loss between these groups was not significant at 6 months (data not shown). However, from 6 to 12 months, the W group regained weight, whereas the I/S group continued to lose weight.

Discussion

Among ILI participants in PREVENT-DM, those whose three mental health measures were either improved or stable (I/S) over 12 months experienced significantly greater weight loss than those who worsened on any mental health measure (W). Mean weight loss was comparable among both I/S and W groups from baseline to 6 months. Weight loss trajectories diverged between 6 and 12 months, with W participants regaining weight and I/S participants continuing to lose weight. None of these relationships were found in the metformin and standard care arms.

Strengths of this study include its unique population of socioeconomically disadvantaged Latinas with prediabetes and overweight/obesity. Clinical trials including such vulnerable populations are few, especially among those with mental health comorbidities (19). In addition, prior research examining the relationship between mental health status and weight loss has included few Latinas, leaving practitioners with limited insight into effective weight loss treatments in this group (20,21). Studying mental health in Latinas is especially important given differences in their presentation of mental health problems relative to other racial/ethnic and gender subgroups (22). In addition, self-reported data for three mental health indicators are presented here, expanding on similar weight loss trials that have focused primarily on depression. Furthermore, longitudinal changes were explored in the current study, whereas most trials have analyzed mental health measures only as baseline predictors of weight loss.

This analysis has several limitations. Most importantly, the observed association between mental health improvement and weight loss does not imply a direction of causality. Improvement or stability in mental health may cause weight loss, or weight loss may lead to improvement in mental health, or improvements in both indicators may be mutually reinforcing. Second, the infrequency of antidepressant medication use among ILI participants ($n = 3$, 9.1%) precluded examination of its association with weight change. This represents a lower rate of antidepressant medication use than that reported in similar studies (23), which may reflect limited healthcare access among mostly foreign born Latinas with low socioeconomic status in the current study. Third, generalizability of the findings may be limited in other racial/ethnic groups and among men. Fourth, the study used validated scales to measure symptoms of depression, anxiety and perceived stress, rather than using a clinician interview, which is considered the gold standard for diagnosing

mental health conditions. Finally, the small sample size and wide variation in mental health changes observed in this cohort limited statistical power and precluded drawing definitive conclusions about the relationships described here.

The significant association between mental health changes and weight loss observed in this analysis may be partly related to higher baseline levels of psychological distress relative to the original DPP trial (14,24). Specifically, only 10% of DPP participants had a BDI score $\geq$ 11, the threshold used to define mild depression in that trial, compared to 53.2% of participants in PREVENT-DM. The pragmatic consideration to not exclude participants with clinical levels of depression and anxiety in PREVENT-DM may better reflect the mental health status of adults participating in community-based ILI programs. On average, baseline depression and anxiety scores among participants in the current analysis were higher than the general population, but below clinical cutoffs used to define mild depression (14–19) and anxiety (5–10) on the same scales (25,26). However, the number of participants with baseline depression and anxiety scores above these clinical cutoffs was 35 and 37, respectively (data not shown). The current sample had substantially higher levels of baseline perceived stress than a national sample of Hispanics (27). Examining the association between reliable and clinically significant mental health changes with weight loss was not possible due to the small numbers of participants who met relevant clinical thresholds. This should be explored in future research including larger samples, where such analyses are feasible.

One other translational trial of ILI delivered by telephone reported similar baseline levels of depressive symptoms and stress to those observed here. In that study, high levels of depressive symptoms and perceived stress at baseline were associated with less subsequent weight loss (23). That trial, however, did not report longitudinal changes in mental health measures. Some evidence on successful maintenance of weight loss suggests that lower levels of depression may be associated with greater odds of success (28–30); however, a clear consensus remains elusive. Few data examining the impact of anxiety and perceived stress on weight loss or maintenance exist.

While the timing of changes in mental health status and weight loss cannot be definitively determined here, the current study provides preliminary evidence about when mental health changes may impact weight loss during behavioral treatment. Among ILI participants, 16 experienced worsening mental health status from baseline to 6 months (data not shown), and 17 met the same criteria at 12-month follow-up. These findings suggest that even with initial weight loss, participants whose mental health worsens may begin to regain weight after 6 months, while others continue to lose weight. A previous weight loss trial of women reported a similar pattern for changes in depressive symptoms and weight at 6 months (31). One explanation for these findings is the reduced frequency of contact between 6 and 12 months, which likely provides less psychosocial support for those with worsening symptoms.

The divergence of weight trajectories at 6 months among those with improved or stable vs. worsened mental health may partly explain why weight loss generally plateaus in behavioral treatment at this same time (32). To support ongoing weight loss or weight maintenance beyond 6 months, programs might consider monitoring mental health outcomes longitudinally and providing more intensive psychosocial support for participants whose mental health is worsening. Future research may consider the extent to which mental health improvements are related to the frequency of intervention contacts. In addition, future studies should replicate our findings in larger samples and develop psychosocial enhancements to existing lifestyle interventions that can be tested in diverse populations.

Clinical trial registration

The PREVENT-DM trial was recorded in the National Clinical Trials Registry (NCT02088034): www.clinicaltrials.gov. The current study represents a secondary analysis of data from this trial.

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Conflict of Interest Statement

The authors declared no conflict of interest.

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