Effect of a Behavioral Weight Loss Intervention in People With Serious Mental Illness and Diabetes

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OBJECTIVE

Given the high prevalence of obesity and diabetes in patients with serious mental illness (SMI) and the lack of evidence on the effects of weight loss programs in SMI patients with diabetes, we evaluated the effectiveness of a behavioral weight loss intervention among SMI participants with and without diabetes.

RESEARCH DESIGN AND METHODS

Using data from ACHIEVE, a randomized controlled trial to evaluate the effects of a behavioral weight loss intervention among overweight/obese people with SMI, we assessed and compared weight change from baseline to 18 months in participants with and without diabetes using a longitudinal mixed-effects model.

RESULTS

Of the 291 trial participants, 82 (28.2%) participants had diabetes (34 and 48 in intervention and control groups, respectively) at baseline. Participants with diabetes were more likely to be taking antipsychotics (31.7% vs. 18.7%, *P* = 0.02). At 18 months, participants in the control group with diabetes lost 1.2 lb (0.6%) of body weight compared with 0.8 lb (0.7%) among those without diabetes. In the intervention group, participants with diabetes lost 13.7 lb (6.6%) of their initial body weight compared with 5.4 lb (2.9%) for those without diabetes. Corresponding net effects (intervention minus control) were 4.6 lb (2.2%) and 12.5 lb (6.0%) net weight reduction over 18 months in the no diabetes and the diabetes subgroups, respectively. However, the between-group difference in intervention effects was statistically nonsignificant (absolute weight change: *P*-interaction = 0.08; % weight change: *P*-interaction = 0.10).

CONCLUSIONS

A behavioral weight loss intervention is effective among overweight and obese individuals with SMI regardless of their diabetes status.

People with serious mental illness (SMI) have an extremely high prevalence of obesity that is nearly double that of the general population (1). Furthermore, although the prevalence of diagnosed type 2 diabetes in this vulnerable population is ~12% (2), up to 70% of cases of diabetes in this population are undiagnosed (3,4). People with SMI who have diabetes have a higher rate of complications due to microvascular and macrovascular complications and deaths related to diabetes compared with people without SMI who have diabetes (4). Most antipsychotic medications are associated

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with weight gain, and some second-generation antipsychotics affect glucose metabolism, leading to glucose intolerance and diabetes (1). Moreover, people with SMI are more likely to be sedentary, smoke, and consume poor quality diets, which increase their risk of obesity and/or diabetes (5). Some evidence also indicates that metabolic abnormalities are present in people with SMI even before treatment (6,7).

Weight loss is recommended for people with diabetes who are overweight or obese because it can reduce medication therapy and improve glycemic control and quality of life (8). However, weight loss may be more difficult for people with diabetes because some diabetes medications cause weight gain. Additionally, initiating treatment and improved glycemic control can lead to a decline in energy expenditure due to decreased protein turnover and a decline in metabolic rate, both of which counteract weight loss (9). Studies examining whether people with diabetes are as successful in a behavioral weight loss intervention compared with people without diabetes have shown inconsistent results, with some studies showing that individuals with diabetes lose less weight in a behavioral weight loss intervention compared with individuals without diabetes (10,11), whereas other studies have shown that weight loss is similar among those with and without diabetes (12–15) or even greater among people with diabetes (16).

The Randomized Trial of Achieving Healthy Lifestyles in Psychiatric Rehabilitation (ACHIEVE) was the first long-term randomized controlled trial to evaluate the effects of a behavioral weight loss intervention among overweight/obese people with SMI. In the main findings, the intervention group lost significantly more weight (net difference in change of 7 lb) than the control group at 18 months follow-up (17). To our knowledge, no studies to date have examined the success of people with SMI who have diabetes in weight loss interventions.

Given the higher prevalence of diabetes and obesity and risk factors for these conditions among people with SMI and lack of evidence on the effect of behavioral weight loss interventions for people with SMI with and without diabetes, we used data from the ACHIEVE trial to *1*) evaluate the effectiveness of a behavioral weight loss intervention for people with SMI separately, in those with diabetes and without diabetes, and *2*) explore potential heterogeneity of treatment effect between these two subgroups.

RESEARCH DESIGN AND METHODS

ACHIEVE Trial Design

The ACHIEVE trial recruited overweight or obese adults between January 2009 and February 2011 who attended 1 of 10 community outpatient psychiatric rehabilitation programs in Maryland or their affiliated outpatient mental health clinics (17). Exclusion criteria included a medical contraindication to weight loss, cardiovascular event in prior 6 months, inability to walk, or an active alcohol use or substance use disorder (see previous publication for full details) (17,18). A total of 291 participants were randomly assigned to the control or intervention group. The intervention was a behavioral weight loss program that included three types of contact: group weight-management sessions, individual weight-management sessions, and group exercise sessions. The control group received standard nutrition and physical activity information at baseline and was offered health classes quarterly. The main outcome of the ACHIEVE trial was change in weight from randomization to 6 months and 18 months.

Primary Outcome: Weight Change Over 18 Months

The primary outcome for this secondary data analysis was absolute weight change from baseline to 18 months. Weight was measured at baseline and 6, 12, and 18 months using a calibrated, high-quality digital scale, with the participant wearing light indoor clothing without shoes. The intervention effect on body weight is defined as the net 18-month weight change, i.e., the difference in 18-month weight change between the intervention and control group.

Secondary Outcomes: Change in and Glucose Waist Circumference

We also examined change in fasting glucose and waist circumference from baseline to 18 months. Fasting glucose was measured at baseline and 6 and 18 months. Participants were required to be fasting at least 8 h prior to the laboratory measurement. Waist circumference was measured in centimeters by trained staff at baseline and 6 and 18 months. The intervention effect on these outcomes is defined as the net 18-month change of these outcomes, i.e., the difference in 18-month outcome changes between the intervention and control group.

Potential Effect Modifiers

We classified participants as having diabetes at baseline if they self-reported a diagnosis of diabetes, had a fasting glucose level $\geq$126 mg/dL, or reported use of any glucose-lowering medication (e.g., metformin or insulin). We classified participants as having prediabetes if they had a fasting glucose level of 100–125 mg/dL, did not self-report a diabetes diagnosis, and were not on a glucose-lowering medication. In the main analyses, we compared response to the intervention through examining the net 18-month weight changes by the presence or absence of diabetes. In further exploratory analyses, we also evaluated intervention effects by the status of no prediabetes or diabetes, prediabetes, and diabetes.

Statistical Analysis

We compared the weight at baseline and 18 months cross-sectionally by diabetes status using Student *t* tests, and percent achieving 5% weight loss at 18 months by diabetes status using a χ^2 test. Then we assessed the association between diabetes status and the intervention effect on weight change from baseline to 18 months using a longitudinal mixed-effects model. We used a repeated-measures model for visit-specific weight, including visit indicators (6, 12, and 18 months), randomization assignment indicator, and their cross-product interaction terms, adjusting for age, site, and sex. A 4 $\times$ 4 unstructured variance-covariance matrix was used in this likelihood-based base model to allow different outcome variances at different time points, and to address the correlations among outcome measures over time within participants. Missing weight data were included using the software-designated missing indicator. In this base model, the overall mean intervention effect on 18-month weight change was estimated through the regression coefficient of the cross-product interaction term of the 18-month visit and the intervention indicators.

To assess for heterogeneity in intervention effects by diabetes status, we

included a diabetes indicator and its relevant interaction terms to the base model. In this unified subgroup analysis model, the regression coefficient of the two-way interaction term of the 18-month visit by intervention group indicators estimates the mean intervention effect on 18-month weight change for people with SMI and without diabetes, whereas the three-way interaction term of diabetes by intervention by 18-month visit explored the mean difference in the net intervention effects between the with and without diabetes subgroups. Natural log-transformed weight outcomes were modeled similarly to produce percent weight change estimates over 18 months.

We also used a similar longitudinal mixed-effects model to assess the association between diabetes status and intervention effect on change in fasting glucose and change in waist circumference from baseline to 18 months. Time-dependent weight was further included to investigate potential intervention effects on fasting glucose and waist circumference not mediated through weight changes. We conducted sensitivity analyses to evaluate potential impacts of missing data using the model-based analyses with inverse weighting of propensity scores.

In addition to evaluating differences in response to the intervention by the presence or absence of diabetes, we also compared weight loss across the following categories: diabetes, prediabetes, and no prediabetes or diabetes. We additionally conducted a sensitivity analysis to evaluate the impact due to misclassification of participants as having diabetes. In this analysis, we removed individuals defined as having diabetes based on only self-report without meeting the other possible criteria (fasting glucose level $\geq$126 mg/dL or use of any diabetes medications). Finally, we examined in the intervention group the difference between those with and without diabetes in terms of participation in the total number of intervention sessions (individual and group) using Student *t* tests. Descriptive analyses were conducted using STATA 15.1, and longitudinal mixed-effects models were analyzed using SAS Studio.

RESULTS

Of the 291 participants, 82 (28.2%) individuals had diabetes (34 and 48 in the intervention and control groups, respectively), and 63 (21.7%) had prediabetes at baseline. There were no differences between those with and without diabetes for sex, race/ethnicity, health insurance, presence of care provider, and randomization group assignment (Table 1 and Supplementary Table 1). Those with diabetes tended to be older (48.4 vs. 44.1 years, P = 0.004), weigh more (239.3 vs. 220.4 lb, P = 0.001), and have less education (25.4% vs. 41.5% graduated from high school, P = 0.02). Participants with diabetes were more likely to have schizophrenia (43.9% vs. 23.4%, overall P = 0.002) and be on olanzapine or clozapine (31.7% vs. 18.7%, P = 0.02). There were no differences between the two groups in terms of psychiatric symptom measures (Behavioral and Symptom Identification Scale-24 [BASIS-24] and Center for Epidemiologic Studies-Depression [CES-D] scores).

At 18 months follow-up, participants in the control group with diabetes lost 1.2 lb (0.6%) of body weight compared with 0.8 lb (0.7%) among those without diabetes (Table 2). In the intervention group, participants with diabetes lost 13.7 lb (6.6%) of their initial body weight compared with 5.4 lb (2.9%) for those without diabetes. Overall, net weight reduction (active intervention minus control) over 18 months was 4.6 lb (2.2%) among those without diabetes and 12.5 lb (6.0%) among those with diabetes. However, the difference in intervention effects between the two subgroups was statistically nonsignificant (absolute weight change: P-interaction = 0.08; % weight change: P-interaction = 0.10).

For fasting glucose, we found that those with diabetes in the intervention group improved their glycemic control (reduction of mean fasting glucose by 14 mg/dL) compared with those with diabetes in the control group (increase of mean fasting glucose by 3 mg/dL), although the net intervention effect ($-$17 mg/dL, P = 0.30) was not statistically significant (Table 3). A smaller and nonstatistically significant net reduction estimate was observed in the no diabetes group. We also found a decrease in waist circumference among those with diabetes in the intervention group compared with the control group ($-$3.3 cm vs. +0.1 cm), but this difference was also not statistically different (Table 3). The differences in intervention effects on fasting glucose and waist circumference between the two subgroups were not statistically significant (Table 3).

The probability of missing data at 18 months for body weight and weight-related outcomes were not related to the values of the same outcome observed at earlier follow-up visits or at baseline (data not shown). Given the high within-person correlation among body weights and weight-related outcomes observed over time, this finding suggested missing at random as a reasonable assumption for missing data mechanism. Sensitivity analyses using inverse weighting of propensity scores were conducted and showed similar results (data not shown) for the intervention effects presented here.

In considering three categories of diabetes status (no prediabetes or diabetes, prediabetes, and diabetes), we found that participants with prediabetes had a similar response in weight loss compared with individuals without diabetes (data not shown). In our sensitivity analysis, 12 individuals were reclassified as not having diabetes because they only self-reported diabetes, i.e., they did not meet other criteria (elevated fasting glucose or treatment with a diabetes medication). Our results for the primary outcome of absolute and percent weight change were unchanged in the sensitivity analyses. Finally, we did not find differences between those with or without diabetes in terms of participation in the total number of intervention sessions (data not shown).

CONCLUSIONS

People with SMI are at a higher risk of developing diabetes and obesity compared with the general population (1,2). Some evidence suggests that people with diabetes may be less successful in a behavioral weight loss intervention compared with those without diabetes (10). In the ACHIEVE randomized clinical trial, we found clear evidence that overweight and obese individuals with SMI successfully lost weight in the behavioral weight loss intervention, regardless of whether they had diabetes. Although we did not find statistically significant evidence of effect modification by diabetes status, we observed a clinically significant amount of greater weight loss in the intervention group among people with SMI and diabetes.

Table 1—Baseline characteristics of participants in the ACHIEVE trial, stratified by diabetes status

Characteristic	Without diabetes (*n* = 209)	With diabetes (*n* = 82)	*P* value
Age, years	44.1 (11.7)	48.4 (9.6)	0.004
Male sex, *n* (%)	100 (47.9)	45 (54.9)	0.28
Weight, lb	220.4 (43.8)	239.9 (50.4)	0.001
BMI, km/m^2	35.4 (6.8)	38.4 (7.9)	0.002
Fasting glucose, mg/dL	95.8 (11.5)	128.8 (51.5)	<0.001
Race, *n* (%)			0.84
White	118 (56.5)	45 (54.9)	
Black	78 (37.3)	33 (40.2)	
Other	13 (6.2)	4 (4.9)	
Hispanic ethnic group, *n* (%)	10 (4.8)	3 (3.7)	0.68
Not a high school graduate, *n* (%)	53 (25.4)	34 (41.5)	0.02
Health insurance, *n* (%)			
Medicaid	176 (84.2)	64 (78.1)	0.21
Medicare	100 (47.9)	46 (56.1)	0.21
Unable to work/receiving disability, *n* (%)	164 (78.5)	65 (79.3)	0.88
Psychiatric diagnosis, *n* (%)			0.002
Schizophrenia	49 (23.4)	36 (43.9)	
Schizoaffective disorder	63 (30.1)	21 (25.6)	
Bipolar disorder	54 (25.8)	10 (12.2)	
Major depression	23 (11.0)	12 (14.6)	
Other	20 (9.6)	3 (3.7)	
Number of psychotropic medications	3.1 (1.3)	3.1 (1.7)	0.97
Any antipsychotic medication, *n* (%)	188 (90.0)	73 (89.0)	0.82
Atypical antipsychotic medication, *n* (%)	172 (82.3)	69 (84.2)	0.71
Clozapine or olanzapine, *n* (%)	39 (18.7)	26 (31.7)	0.02
Lithium or other mood stabilizer, *n* (%)	102 (48.8)	30 (36.6)	0.06
Antidepressant medication, *n* (%)	126 (60.3)	49 (59.8)	0.93
Current smoker, *n* (%)	83 (39.7)	35 (42.7)	0.64
Psychiatric measures			
BASIS-24 score	1.32 (0.85)	1.19 (0.72)	0.20
CES-D score	19.8 (10.6)	20.2 (12.8)	0.76
Have a care provider, *n* (%)	33 (25.0)	49 (30.8)	0.27
Randomization group, *n* (%)			
Intervention	110 (52.6)	34 (41.5)	0.09
Control	99 (47.4)	48 (58.5)	

Data are mean (SD) unless otherwise indicated.

Although there was no statistically significant interaction between diabetes status and randomized group, the effects in the diabetes subgroup appeared to be larger than corresponding effects in the subgroup without diabetes. The weight loss observed in SMI patients with diabetes was clinically important. Participants in the intervention group

Table 2—Change in weight at 18 months follow-up for participants with and without diabetes

	Without diabetes (*n* = 209)	With diabetes (*n* = 82)	*P* value, between group
Mean weight at baseline (SD), lb	220.4 (43.8)	239.9 (50.4)	0.001
Mean weight at 18 months (SD), lb	216.5 (47.1)	233.8 (50.4)	0.007
Mean weight change at 18 months (SE), lb*			
Control	−0.8 (2.2)	−1.2 (2.7)	0.90
Intervention	−5.4 (1.3)	−13.7 (3.7)	0.04
Net intervention effect, difference	−4.6 (2.6)	−12.5 (4.6)	0.08
P value, within group	0.07	0.01	
% weight change at 18 months (SE), lb*			
Control	−0.7 (0.9)	−0.6 (1.1)	0.91
Intervention	−2.9 (0.7)	−6.6 (2.0)	0.08
Net intervention effect, difference	−2.2 (1.1)	−6.0 (2.3)	0.10
P value, within group	0.06	0.008	
% achieving 5% weight loss at 18 months, *n* (%)	58 (28.9)	26 (33.3)	0.46

*Longitudinal mixed-effects model based estimates, adjusted for age, sex, and site.

Table 3—Change in glucose and waist circumference at 18 months follow-up for participants with and without diabetes

	Without diabetes (n = 209)	With diabetes (n = 82)	P value, between group
Glucose			
Mean fasting glucose at baseline (SD), mg/dL	95.8 (11.5)	128.8 (51.5)	<0.001
Mean fasting glucose at 18 months (SD), mg/dL	100.6 (21.2)	124.5 (51.0)	<0.001
Mean change in fasting glucose at 18 months (SE), mg/dL*			
Control	6.4 (2.8)	2.9 (11.6)	0.77
Intervention	3.6 (2.2)	−13.9 (11.3)	0.13
Net intervention effect, difference	−2.8 (3.5)	−16.8 (16.3)	0.68
P value, within group	0.43	0.30	
Waist circumference			
Mean waist circumference at baseline (SD), cm	114.2 (14.9)	124.2 (14.9)	<0.001
Mean waist circumference at 18 months (SD), cm	112.6 (17.0)	123.4 (18.2)	<0.001
Change in waist circumference (SE), cm*			
Control	−0.6 (0.9)	0.1 (1.5)	0.67
Intervention	−1.9 (0.8)	−3.3 (2.0)	0.52
Net intervention effect, difference	−1.3 (1.2)	−3.4 (2.5)	0.53
P value, within group	0.30	0.18	

*Longitudinal mixed-effects model–based estimates, adjusted for time-dependent weight, age, sex, site, psychiatric diagnosis, and baseline weight.

who had diabetes lost on average 6.6% of their initial body weight, which is similar to the 5–10% range seen in behavioral weight loss interventions in the general population (19). We speculate that the substantial weight loss success among those with diabetes in the intervention group may be because they were aware that they had diabetes and understood the importance of lifestyle change. In additional analyses examining attendance, we did not find differences between the two groups in terms of participation in the intervention sessions (individual and group).

Prior studies that included people with diabetes in the general population have demonstrated mixed results on the success of weight loss interventions. Many of these studies were nonrandomized and 1 year in duration or shorter. These study findings may have been mixed partly because diabetes medications have different effects on weight, with some promoting weight gain and others promoting weight loss. Only a few studies adjusted for diabetes medication use, and when they did, it was not by the specific type of diabetes medication. In a 26-week prospective cohort study, individuals with diabetes lost less weight in a standardized clinical meal replacement and lifestyle modification program compared with individuals with impaired fasting glucose or no diabetes (10). Similarly, in a 20-week behavioral weight-control program, 12 participants with diabetes lost significantly less weight than their spouses without diabetes, and this difference was not explained by use of oral diabetes medication (11). However, other studies showed that weight loss is similar among people with or without diabetes following low calorie diets with behavior therapy (12–14). In another prospective nonrandomized study, women with or without diabetes lost the same amount of weight in a 16-week behavioral weight loss program (15). Few randomized trials that include people with diabetes have reported intervention effects separately for the subgroup with diabetes. In the Heart Healthy Lenoir Project Phase III year-long randomized controlled trial, participants with diabetes lost significantly more weight than participants without diabetes, but these data were reported across all intervention groups and did not include a control group (16).

To our knowledge, no studies have examined the success of people with SMI who have diabetes in weight loss interventions. One study conducted a secondary analysis that investigated weight loss among veterans with prediabetes enrolled in a Diabetes Prevention Program demonstrating that veterans with SMI lost less weight over 6 months compared with veterans with affective disorder (included depression and anxiety disorders) or veterans without SMI or affective disorder (−1.5 kg in SMI group vs. −3.9 kg in affective disorder group and −3.7 kg in no SMI/no affective disorder group), although this trend was not significant at 12 months (20).

Our study supports prior evidence that antipsychotic use is associated with a higher prevalence of metabolic syndrome and diabetes (21). In our study population, a higher proportion of participants with diabetes were receiving the second-generation antipsychotics olanzapine or clozapine, which are well-known to contribute to weight gain and abnormalities in glucose metabolism (22). A large cohort study estimated that the diabetes prevalence in antipsychotic-treated patients with SMI was between 17.3% and 28.1%, which is nearly twice the prevalence in the general population (23). Despite the documented side effects of these medications, in ACHIEVE, participants with diabetes in the intervention group appeared to have a lower fasting glucose on average by 14 mg/dL and waist circumference by 3.3 cm in analyses adjusted for time-dependent weight to account for effects mediated through weight change, although these were not statistically significant.

The strengths of our study include enrollment of an important but understudied population that included substantial numbers of patients with SMI and diabetes. The trial was well conducted with 18 months of follow-up and few missing data. In contrast, prior studies examining weight loss interventions in people with SMI were short (≤6 months), uncontrolled, and with small samples (24,25). Furthermore, results were robust in a variety of sensitivity analyses that used advanced analytic methods.

Our study also has several limitations. First, the ACHIEVE trial was not powered for this subgroup analysis, so the study sample size was not sufficient to confirm the difference as observed between those with and without diabetes. Second,

our definition of diabetes included self-reported diabetes, a single fasting glucose level ≥126 mg/dL, or use of any diabetes medications. It is unclear if use of self-reported diabetes in the SMI population is reliable. However, in our sensitivity analysis, we found that results for the primary outcome of absolute weight loss were unchanged. Additionally, we did not have hemoglobin A_{1c} data available, and fasting glucose has high variability related to differences in fasting time before testing, medications, activity, and stress (26). Therefore, misclassification of diabetes status may have occurred.

In conclusion, overweight and obese individuals with SMI successfully lost weight in the ACHIEVE behavioral weight loss intervention regardless of whether they had diabetes. This finding is important because of the substantial burden of diabetes in patients with SMI and the dearth of information on the effectiveness of weight loss interventions in SMI patients with diabetes. Our results suggest that the behavioral weight loss intervention tested in the ACHIEVE trial could produce as large or greater weight loss in those with versus without diabetes in the population of people with SMI. However, larger studies are needed to confirm this hypothesis. Nonetheless, with effective behavioral weight loss interventions like the one developed and tested in the ACHIEVE trial, we may be able to substantially improve the health of this vulnerable and understudied population.

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