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Association Between Cardiovascular Risk and Depressive Symptoms Among People with Serious Mental Illness

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Abstract

Depressive symptoms have debilitating effects on the physical health and functioning of people with serious mental illness. We examined change in depressive symptoms among overweight and obese adults with serious mental illness (n=343) using data combined from two randomized trials comparing the 12-month In SHAPE program to a gym membership control condition. In SHAPE consists of a gym membership, weekly individual meetings with a fitness trainer, and instruction on healthy eating and nutrition. Depressive symptoms were measured at baseline, 3-, 6-, and 12-months. Change in depressive symptoms did not differ between groups, but depressive symptoms decreased over time across the entire sample (p=0.045). At 12-months, reduced depressive symptoms were associated with clinically significant improved cardiorespiratory fitness (p=0.030), ≥10% weight loss (p=0.044), and cardiovascular risk reduction (p=0.028) across both groups. Our findings suggest that participation in health promotion programs resulting in cardiovascular risk reduction may be associated with reduced depressive symptoms.

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Keywords

depression; lifestyle intervention; serious mental illness; mental health; fitness; weight loss; cardiovascular risk

Introduction

Obesity prevalence is nearly double among people with serious mental illness, including schizophrenia spectrum and mood disorders, compared to the general population (Dickerson et al., 2006). As a result, people with serious mental illness are at high risk for cardiometabolic disorders and experience dramatic reduction in life expectancy (Walker, McGee, & Druss, 2015). Numerous challenges interfere with treating obesity in this at-risk group, including metabolic effects of psychiatric medications, low motivation, poverty, and limited access to safe and affordable options for physical activity (Allison et al., 2009). Studies in the general population show a strong association between elevated obesity and more frequent and severe depressive symptoms (Onyike, Crum, Lee, Lyketsos, & Eaton, 2003; Strine et al., 2008). This is a potentially significant concern, because people with serious mental illness experience elevated depressive symptom severity across diagnostic groups (Mechanic, McAlpine, Rosenfield, & Davis, 1994).

Among people with serious mental illness, depressive symptoms are associated with greater disability (Meesters et al., 2014), poor physical health (Sajatovic et al., 2015), and elevated risk of substance use (Kerfoot et al., 2011). Depressive symptoms also contribute to poor life satisfaction (Fervaha, Agid, Takeuchi, Foussias, & Remington, 2013; Mechanic et al., 1994). Research highlights that low motivation and low satisfaction with life are predictors of unhealthy habits including poor diet and physical inactivity (Vancampfort et al., 2012). Therefore, the co-occurrence of elevated obesity and depressive symptoms among people with serious mental illness likely exacerbates cardiovascular risk factors and may present additional challenges to adopting healthy lifestyle behaviors.

Lifestyle interventions have emerged as effective for targeting obesity and poor health behaviors among people with serious mental illness and appear promising for addressing modifiable risk factors such as poor cardiorespiratory fitness that are linked to early mortality (McGinty, Baller, Azrin, Juliano-Bult, & Daumit, 2016; Vancampfort, Rosenbaum, Schuch, Ward, Richards, et al., 2016). Recent randomized trials of interventions focused on promoting exercise and healthy eating have achieved clinically significant weight loss in upwards of 47% of participants, or reduced cardiovascular risk through improved cardiorespiratory fitness and weight loss in as many as half of participants with serious mental illness (Bartels et al., 2013; Bartels et al., 2015; Daumit et al., 2013; Green et al., 2015). Little is known about whether participation in evidence-based lifestyle interventions implemented in real world community mental health settings can also contribute to reduction in depressive symptoms in this at-risk group.

Prior studies suggest that intensive lifestyle interventions aimed at achieving weight loss through healthy eating, caloric restriction, and increased exercise can lead to reduction in depressive symptoms among people with diabetes from the general population

(Faulconbridge et al., 2012; Look AHEAD Research Group, 2014) and obese individuals with clinical depression (Linde et al., 2011). Among people with serious mental illness, a pilot study of a behavioral weight loss intervention reported a reduction in depressive symptoms over a 6-month period (Daumit et al., 2011), though another pilot study found no change in depressive symptoms over a comparable duration (Van Citters et al., 2010). Lifestyle interventions for people with serious mental illness may offer promise for improving other health-related outcomes in addition to weight loss, including increased self-efficacy and more positive perceptions of body image (Yarborough et al., 2015), as well as improved self-perceived health status (Temmingh et al., 2013). Given the combined impact of depression and obesity on cardiovascular risk and early mortality, it is important to further investigate the impact of lifestyle interventions targeting fitness and weight loss on depressive symptoms among people with serious mental illness.

The purpose of this study was to examine the impact of lifestyle intervention participation on change in depressive symptoms among overweight and obese adults with serious mental illness. We combined data from two randomized controlled trials to explore the differential effect on change in depressive symptoms over time of participation in the 12-month In SHAPE lifestyle intervention compared to participation in a gym membership group. The In SHAPE program consists of a gym membership, weekly individual meetings with a fitness trainer, and instruction on healthy eating and nutrition. We hypothesized that the In SHAPE intervention group would show greater reduction in depressive symptoms compared to the gym membership comparison group, because of the additional support for engaging in physical activity provided by the fitness trainer. Additionally, given the established link between depressive symptoms and poor physical health, we also explored whether clinically significant improvement in cardiorespiratory fitness, weight loss, and cardiovascular risk were associated with change in depressive symptoms at 12-month follow-up across both groups.

Methods

Study Sample

The analyses in this study used pooled data from 343 participants with serious mental illness enrolled in two randomized trials comparing the 12-month In SHAPE lifestyle intervention to a gym membership comparison group. In the first randomized trial (N=133), conducted from April 2007 to November 2011 (registered at clinicaltrials.gov: NCT02334228), participants were randomly assigned to the In SHAPE lifestyle intervention or to gym membership at one community mental health center in Concord, New Hampshire (Bartels et al., 2013). In the second randomized trial (N=210), conducted from April 2008 to May 2013 (registered at clinicaltrials.gov: NCT02090335), participants were randomly assigned to the In SHAPE lifestyle intervention or to gym membership across three community mental health centers in Boston, Massachusetts (Bartels et al., 2015).

Participants in both trials were age 21 or older; had serious mental illness defined by an axis I diagnosis of major depressive disorder, bipolar disorder, schizoaffective disorder, or schizophrenia (based on the Structured Clinical Interview for *DSM–IV*), and persistent impairment in multiple areas of functioning (e.g., work, school, self-care) (First, Spitzer,

Gibbon, & Williams, 1995); had body mass index (BMI) greater than 25; and provided informed consent for participation. Participants were on stable pharmacological treatment, defined as receiving the same psychiatric medications over the 2 months prior to enrollment.

The design and methods, and detailed inclusion and exclusion criteria, are reported elsewhere (Bartels et al., 2013; Bartels et al., 2015). The randomized trials evaluated the effect of the In SHAPE lifestyle intervention compared to the gym membership comparison group on weight loss and improved fitness. Roughly half of participants receiving In SHAPE in each study, 49% (Bartels et al., 2013) and 51% (Bartels et al., 2015), achieved cardiovascular risk reduction defined as clinically significant weight loss or improved cardiorespiratory fitness. Committees for the Protection of Human Subjects at Dartmouth College and specific to each site approved all study procedures.

In SHAPE Program

In SHAPE is a 12-month lifestyle intervention consisting of a gym membership, weekly individual meetings with a certified fitness trainer, and instruction on healthy eating and nutrition. The fitness trainers completed a one-week In SHAPE training consisting of instruction in motivational interviewing, fitness goal setting, healthy nutrition, methods for tracking eating and exercise, and strategies for supporting health behavior change among people with serious mental illness, such as addressing mental health symptoms that interfere with exercise and healthy eating. Prior to enrollment, participants obtained medical clearance for exercise from their primary care provider. After conducting lifestyle and fitness evaluations, the fitness trainer developed personalized fitness plans for each participant using shared goal setting. Thereafter, they met with participants individually each week for 45–60 minutes at a local gym (YMCA) and provided fitness coaching, support, and reinforcement for exercise. The nutrition component consisted of individualized instruction during each session emphasizing healthy eating. Throughout the program the fitness trainers received ongoing supervision from a health psychologist, a personal fitness trainer, and a registered dietitian.

Gym Membership Comparison Group

The comparison condition consisted of a gym membership to the same local gym as the In SHAPE group (YMCAs) with an introduction in safe use of the exercise equipment.

Measures

Trained interviewers collected outcome measures at baseline, and at 3 months, 6 months, and 12 months. The interviewers were blind to group assignment. Depressive symptoms were measured using the Center for Epidemiological Studies Depression (CESD) scale. The CESD is a 20-item self-report depression symptom scale, with scores ranging from 0 to 60, where higher scores represent higher levels of depression (Radloff, 1977). The CESD has well-documented psychometric properties in psychiatric populations (Weissman, Sholomskas, Pottenger, Prusoff, & Locke, 1977).

Clinically significant improved cardiorespiratory fitness was calculated as the proportion of participants who achieved an increase in distance >50 meters (about 164 feet) on the 6-

Minute Walk Test (6-MWT) at 12-months. The 6-MWT measures the distance in meters that an individual can walk in six minutes and is a reliable and valid measure of cardiorespiratory fitness (Beriault et al., 2009). An increase of at least 50 meters is considered clinically significant, because it is associated with a reduction in cardiovascular risk (Rasekaba, Lee, Naughton, Williams, & Holland, 2009). Cardiorespiratory fitness is an important modifiable risk factor for cardiovascular disease, and a recent meta-analysis demonstrated that physical activity participation may contribute to improved cardiorespiratory fitness among people with schizophrenia (Vancampfort, Rosenbaum, et al., 2015).

Clinically significant weight loss was measured at 12-months using two different approaches. First, we calculated the proportion of participants who achieved ≥5% weight loss, because modest weight loss is associated with reduction in cardiovascular risk among overweight and obese individuals (Van Gaal, Wauters, & De Leeuw, 1997; Wing et al., 2011). We also calculated the proportion of participants who achieved ≥10% weight loss, because weight loss of this magnitude is associated with improvements in risk factors for heart disease and diabetes (Wing & Phelan, 2005).

We also collected data on participants' medication use, but not dosage. Different psychiatric medications can have an impact on mood and depressive symptoms (Siris, 2000), are associated with varying degrees of weight gain (Allison et al., 1999; Taylor & McAskill, 2000), and are known to affect ability to lose weight (Allison et al., 2009). We classified participants' medications as high weight gain propensity (e.g., olanzapine and clozapine), medium weight gain propensity (e.g., risperidone), or low weight gain propensity (e.g., ziprasidone). We also used a binary (Yes/No) variable to code participants' medications as antidepressants (e.g., duloxetine, fluoxetine, bupropion, or sertraline) or not according to the Food and Drug Administration's classification system.

Statistical Analysis

Participants in the In SHAPE lifestyle intervention were compared with participants in the gym membership condition at baseline on demographic characteristics, mental health diagnoses, obesity measures, fitness, use of antidepressant and psychiatric medications, and depressive symptoms using chi-square tests for categorical variables and t-tests for continuous variables. The impact of the In SHAPE intervention on depressive symptoms was examined using mixed-effects longitudinal regression models, controlling for study (RCT 1 or RCT 2), treatment group × time interaction, age, gender, mental health diagnosis, race, and use of antidepressant medications. Depressive symptoms were measured at four time points. Models included participant-level random intercept and random slope to allow for individual-level trajectories and account for repeated observations within individual. To determine whether depressive symptoms changed over time across both groups, the time effect was examined. To assess whether change in depressive symptoms differed between the In SHAPE and gym membership groups, according to our primary hypothesis, the treatment group × time interaction effect was examined. Analyses were intent-to-treat and included all randomized participants according to intervention assignment. We controlled for trial (RCT 1 or RCT 2) to account for the possibility that participants enrolled in one trial were more similar to each other than individuals recruited in the other trial. To explore

whether there was an association between clinically significant outcomes of improved fitness (>50 meter increase on the 6-MWT), weight loss (≥5% and ≥10%), and cardiovascular risk reduction (defined as ≥5% weight loss or >50 meter increase on the 6-MWT) and change in depressive symptoms at 12-months, we used linear regression models controlling for treatment group, study (RCT 1 or RCT 2), age, gender, mental health diagnosis, race, and use of antidepressant medications. All analyses were performed using Stata 14 software, and p-values less than 0.05 are considered statistically significant.

Results

Baseline characteristics for the 343 participants enrolled in both trials are listed in Table 1. Participants had a schizophrenia spectrum (46%) or mood disorder (54%), a mean age of 43.8±11.3 years, and were predominantly non-Hispanic white (62%). Baseline BMI was 37.1±8.2 kg/m^2. There were no differences between In SHAPE participants and gym membership participants on any characteristics except for marital status. More In SHAPE participants were never married, while more gym membership participants were previously married.

In total, 80% of participants completed 12-month assessments. The proportion of In SHAPE participants (81%) and gym membership participants (78%) who completed 12-month assessments was comparable. Participants lost to follow-up did not differ from participants who completed 12-month assessments on any baseline characteristics.

Table 2 shows the change in depressive symptoms over time between the In SHAPE and gym membership control groups. A decrease in depressive symptoms, measured using the CESD, was observed among both In SHAPE and gym membership participants over time as illustrated by the statistically significant time effect ($p = 0.045$). There were no between-group differences as reflected by the non-significant group × time interaction ($p = 0.475$).

Table 3 shows the association between clinically significant outcomes and change in depressive symptoms at 12-months across the entire study sample. Clinically significant improved fitness defined as >50 meter increase on the 6-MWT was associated with a reduction in depressive symptoms ($p = 0.030$). The relationship between ≥5% weight loss and change in depressive symptoms was not significant ($p = 0.107$), but ≥10% weight loss was associated with significant reduction in depressive symptoms ($p = 0.044$). Reduction in cardiovascular risk, defined as ≥5% weight loss or >50 meter increase on the 6-MWT, was significantly associated with a decrease in depressive symptoms ($p = 0.028$). Over the 12-month study duration, In SHAPE participants had an average of 27.0±13.2 visits with the fitness trainer, a value that was not associated with change in depressive symptoms ($p = 0.098$).

Discussion

We found that depressive symptoms decreased significantly over a 12-month period for our entire sample of overweight and obese adults with serious mental illness randomized to either the In SHAPE intervention or gym membership comparison group. Contrary to our initial hypothesis, the addition of weekly individual visits with a fitness trainer in the In

SHAPE program did not appear to result in further reduction in depressive symptoms beyond what was obtained from access to a gym membership. It is possible that providing free access to a community fitness facility contributed to the observed reduction in depressive symptoms. Prior studies have shown that participation in exercise programs of varying intensity can lead to fewer depressive symptoms among people with mental illness (Meyer, Koltyn, Stegner, Kim, & Cook, 2016; Stubbs, Rosenbaum, Vancampfort, Ward, & Schuch, 2016). However, a recent systematic review and meta-analysis of 41 randomized controlled trials of exercise interventions for adults with depression or major depressive disorder found that the control groups achieved significant improvement in depressive symptoms (Stubbs, Vancampfort, et al., 2016). Therefore, it is possible that we may have similarly observed a control group response in the form of reduction in depressive symptoms regardless of whether or not participants were provided access to a gym membership. As previously reported, the In SHAPE lifestyle intervention contributed to greater weight loss (Bartels et al., 2015) and improved cardiorespiratory fitness (Bartels et al., 2013) when compared to a gym membership only comparison group.

We also found that clinically significant improved cardiorespiratory fitness, ≥10% weight loss, and reduction in cardiovascular risk at 12-months were associated with significant reduction in depressive symptoms among participants in the In SHAPE program and gym membership comparison group. This suggests that health promotion efforts targeting weight loss and fitness may also contribute to reduced depressive symptoms. Our findings are consistent with prior studies that have demonstrated that depressive symptoms are inversely correlated with cardiorespiratory fitness among people with serious mental illness (Papasavvas, Bonow, Alhashemi, & Micklewright, 2016). The implications are important because people with serious mental illness experience an elevated burden of cardiovascular disease largely due to modifiable lifestyle behaviors such as physical inactivity and poor diet (McGinty et al., 2016). Epidemiologic studies have found associations between depressed mood and high rates of poor health behaviors, including physical inactivity, unhealthy eating, heavy drinking, inadequate sleep, and smoking (Allgöwer, Wardle, & Steptoe, 2001; Frederick, Frerichs, & Clark, 1988; Strine et al., 2008). Additionally, symptoms of depression have been identified as a significant predictor of cardiovascular events, with the relationship largely explained by associated behavioral factors such as physical inactivity (Whooley et al., 2008).

For people with serious mental illness, depressive symptoms are known to negatively impact participation in physical activity. Depressive symptoms were identified as a barrier to engaging in physical activity among people with schizophrenia (Stubbs, Firth, et al., 2016), and more frequent occurrence and longer duration of depressive symptoms were associated with sedentary behaviors among people with bipolar disorder (Sylvia et al., 2013). Another study found that worse performance on the 6-MWT was associated with more severe depressive symptoms among people with bipolar disorder (Vancampfort, Wyckaert, et al., 2015). In a mixed methods study, people with serious mental illness reported that mental health concerns such as depressive symptoms were the main reason for not participating in physical activity (Shor & Shalev, 2016).

Despite this observed relationship between depressive symptoms, poor health behaviors and increased cardiovascular risk, exercise interventions offer promise for addressing both mental and physical health concerns. A systematic review and meta-analysis of 90 randomized trials found that exercise training for people with chronic health conditions from general patient populations contributed to improvement in depressive symptoms, and this improvement was significantly associated with important functional and clinical outcomes such as improved fitness and reduced cardiovascular risk (Herring, Puetz, O'Connor, & Dishman, 2012). Our findings expand on these studies by demonstrating that if enrolling in interventions aiming to increase physical activity participation and cardiorespiratory fitness can achieve clinically significant reduction in cardiovascular risk among the high-risk group of people with serious mental illness, then it may also alleviate the depressive symptoms that can be associated with poor lifestyle habits. To our knowledge, this is the first study to demonstrate this finding among people with serious mental illness enrolled in a lifestyle intervention for weight loss. Importantly, our study also contributes to mounting evidence showing that efforts to promote exercise can contribute to improved cardiorespiratory fitness among people with serious mental illness (Vancampfort, Rosenbaum, Schuch, Ward, Richards, et al., 2016).

Important strengths of our study include the relatively large sample size and use of both rural and urban community mental health centers. We also observed high participant retention across both groups. When considering a recent review of participant dropout from physical activity interventions for people with serious mental illness (Vancampfort, Rosenbaum, Schuch, Ward, Probst, et al., 2016), it is possible that high participant retention in our study may have been due in part to the use of certified fitness trainers in the In SHAPE program and an active control condition consisting of access to a gym membership.

Several limitations should also be noted. First, our findings may not generalize to individuals with serious mental illness who are not enrolled in treatment or to those who are not interested in participating in lifestyle interventions involving physical activity. Second, it is important to note that while the observed reduction in depressive symptoms was statistically significant, this change was small and it is not clear whether it translates to other meaningful improvements in quality of life or functioning in participants' daily lives. Third, it is not possible to determine the direction of the relationship between reduced depressive symptoms and clinically significant improved cardiorespiratory fitness, weight loss, and cardiovascular risk reduction. Fourth, use of an active control group may have contributed to the observed reduction in depressive symptoms. However, we were unable to collect data on the frequency of visits to the gym, therefore we are unable to determine whether use of the gym was associated with reduction in depressive symptoms across both the intervention and control groups. Fifth, while we believe that the reduction in depressive symptoms is not reflective of regression to the mean, because this change was associated with objectively measured weight and fitness outcomes, it is not possible to rule out such temporal influences. Lastly, longer-term follow-up is necessary to determine whether reduction in depressive symptoms associated with clinically meaningful cardiovascular risk reduction is sustained over time.

Conclusion

People with serious mental illness experience elevated burden of depressive symptoms that have negative consequences on their physical health, functioning, and likelihood to adopt healthy behaviors. Our findings suggest that health promotion efforts that can achieve clinically significant reduction in cardiovascular risk through weight loss or improved cardiorespiratory fitness may also contribute to a reduction in depressive symptoms in this at-risk group. Future studies must determine whether these mental health benefits are sustained long term and whether these benefits contribute to other meaningful improvements in functioning, quality of life, and participation in daily activities. Research is also necessary to explore whether incorporating focused depression treatment into lifestyle programs such as In SHAPE could enhance the effectiveness of these programs for achieving clinically meaningful reduction in cardiovascular risk. The poor mental and physical health of people with serious mental illness and resulting early mortality represents a significant public health concern. Combined efforts spanning research, clinical practice, and policy must continue to work towards implementing evidence-based lifestyle interventions in community mental health settings aimed at addressing the health needs of this at-risk group. The results from our study provide additional compelling evidence necessary to support these efforts.

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Table 1

Baseline characteristics of participants in the In SHAPE intervention group and the gym membership comparison group

Characteristic	Total Sample	In SHAPE Program	Gym Membership	p-value[a]
n	343	171	172	
Age, years (M ± SD)	43.8 ± 11.3	43.8 ± 11.5	43.9 ± 11.2	0.984
Sex				0.177
Male	154 (45%)	83 (49%)	71 (41%)	
Female	189 (55%)	88 (51%)	101 (59%)	
Race				0.106
Black	72 (21%)	34 (20%)	38 (22%)	
Hispanic	31 (9%)	22 (13%)	9 (5%)	
Non-Hispanic white	212 (62%)	102 (60%)	110 (64%)	
Other	28 (8%)	13 (8%)	15 (9%)	
Education				0.619
Less than high school	51 (15%)	28 (16%)	23 (13%)	
High school	105 (31%)	49 (29%)	56 (33%)	
Greater than high school	187 (55%)	94 (55%)	93 (54%)	
Current Smoker	149 (43%)	72 (42%)	77 (45%)	0.619
Living Situation				0.421
Living Independent	229 (67%)	118 (69%)	111 (65%)	
Supervised/Supported Housing	113 (33%)	53 (31%)	60 (35%)	
Married				**0.007**
Never Married	209 (61%)	118 (69%)	91 (53%)	
Currently Married	25 (7%)	8 (5%)	17 (10%)	
Previously Married	109 (32%)	45 (26%)	64 (37%)	
Diagnosis				0.954
Schizophrenia Spectrum Disorder	159 (46%)	79 (46%)	80 (47%)	
Mood Disorder	184 (54%)	92 (54%)	92 (54%)	
BMI, kg/m^2 (M ± SD)[b]	37.1 ± 8.2	36.4 ± 7.6	37.8 ± 8.6	0.107
Weight, pounds (M ± SD)	234.0 ± 54.3)	230.0 ± 52.1	237.9 ± 56.4	0.179
Fitness (M ± SD)[c]				
CESD (M ± SD)[d]	22.6 ± 13.0	22.5 ± 12.6	22.8 ± 13.3	0.849
Medications				
Antidepressant medication use[e]	187 (58%)	92 (58%)	95 (59%)	0.784
Number of antipsychotic medications (M ± SD)	2.0 ± 1.1	2.1 ± 1.1	2.0 ± 1.0	0.573
Weight Gain Propensity				0.113

Characteristic	Total Sample	In SHAPE Program	Gym Membership	p-value[a]
High[f]	86 (27%)	49 (31%)	37 (23%)	
Medium[g]	137 (43%)	67 (42%)	70 (44%)	
Low[h]	77 (24%)	31 (40%)	46 (29%)	
None	19 (6%)	12 (8%)	7 (4%)	

[a] We compared means using t-tests and proportions using chi-square tests

[b] Body Mass Index (BMI) was measured as kg/m^2, with >25 kg/m^2 indicating overweight or obesity.

[c] Fitness was measured using the 6-Minute Walk Test (6-MWT), which measures the number of meters that an individual can walk in 6 minutes. Higher values indicate better fitness.

[d] The Center for Epidemiological Studies Depression (CESD) is a 20-item self-report depression symptom scale, with scores ranging from 0 to 60, where higher scores represent higher levels of depression.

[e] Antidepressant medications were classified according to the Food and Drug Administration classification system

[f] High weight gain propensity medications include: olanzapine, clozapine

[g] Medium weight gain propensity medications include: haloperidol, risperidone, quetiapine, thioridazine, chlorpromazine, paroxetine, amitriptyline, divalproex, valproate, doxepin, lithium, carbamazepine, imipramine, gabapentin

[h] Low weight gain propensity medications include: ziprasidone, perphenazine, fluphenazine, fluoxetine, buproprion, venlafaxine, molindone, lamotrigine, duloxetine, aripiprazole, fluvoxamine, trazodone, desipramine, loxapine, sertraline, escitalopram, clomipramine, nortriptyline, citalopram, paliperidone, topiramate, mirtazapine, lurasidone

Table 2

Change in outcomes over time between the In SHAPE and gym membership groups

	Assessment Period (M ± SD)[a]				p-Values[b]	
Outcome Measure and Group	**Baseline**	**3 Months**	**6 Months**	**12 Months**	**Time Effect**	**Group × Time Interaction**
Depressive symptoms						
CESD[c]					**0.045**	0.475
In SHAPE Program	29.29 ± 9.79	27.13 ± 12.15	25.66 ± 11.90	25.81 ± 12.51		
Gym Membership	30.29 ± 9.63	28.28 ± 11.33	26.54 ± 10.87	24.23 ± 11.16		

[a]The table shows the raw unadjusted means.

[b]The p values refer to the time effect as well as the group×time effect from the mixed effects linear regression models.

[c]The Center for Epidemiological Studies Depression (CESD) is a 20-item self-report depression symptom scale, with scores ranging from 0 to 60, where higher scores represent higher levels of depression.

Table 3

Association between change in depressive symptoms and clinically significant fitness and weight loss outcomes from baseline to 12-months

Clinically significant outcomes	β	95% CI	p[a]
Fitness (>50 meter increase on the 6-MWT)[b]	−4.39	−8.35 to −0.44	**0.030**
Weight loss (≥5%)	−2.58	−5.72 to 0.55	0.106
Weight loss (≥10%)	−4.38	−8.65 to −0.12	**0.044**
Cardiovascular risk reduction (≥5% or >50 meter increase on the 6-MWT)	−3.41	−6.45 to −0.37	**0.028**

[a] P-values from linear regression models controlling for treatment group, study (RCT 1 or RCT 2), age, gender, mental health diagnosis, race, and use of antidepressant.

[b] Fitness was measured using the 6-Minute Walk Test (6-MWT), which measures the number of meters that an individual can walk in 6 minutes. Higher values indicate better fitness.