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Effect of Integrated Behavioral Weight Loss Treatment and Problem-Solving Therapy on Body Mass Index and Depressive Symptoms Among Patients With Obesity and Depression
The RAINBOW Randomized Clinical Trial

Jun Ma, MD, PhD; Lisa Goldman Rosas, PhD, MPH; Nan Lv, PhD; Lan Xiao, PhD; Mark B. Snowden, MD, MPH; Elizabeth M. Venditti, PhD; Megan A. Lewis, PhD; Jeremy D. Goldhaber-Fiebert, PhD; Philip W. Lavori, PhD

IMPORTANCE Coexisting obesity and depression exacerbate morbidity and disability, but effective treatments remain elusive.

OBJECTIVE To test the hypothesis that an integrated collaborative care intervention would significantly improve both obesity and depression at 12 months compared with usual care.

DESIGN, SETTING, AND PARTICIPANTS The Research Aimed at Improving Both Mood and Weight (RAINBOW) randomized clinical trial enrolled 409 adults with body mass indices (BMIs) of 30 or greater (≥27 for Asian adults) and 9-item Patient Health Questionnaire (PHQ-9) scores of 10 or greater. Primary care patients at a health system in Northern California were recruited from September 30, 2014, to January 12, 2017; the date of final 12-month follow-up was January 17, 2018.

INTERVENTIONS All participants randomly assigned to the intervention (n = 204) or the usual care control group (n = 205) received medical care from their personal physicians as usual, received information on routine services for obesity and depression at their clinic, and received wireless physical activity trackers. Intervention participants also received a 12-month intervention that integrated a Diabetes Prevention Program–based behavioral weight loss treatment with problem-solving therapy for depression and, if indicated, antidepressant medications.

MAIN OUTCOMES AND MEASURES The co–primary outcome measures were BMI and 20-item Depression Symptom Checklist (SCL-20) scores (range, 0 [best] to 4 [worst]) at 12 months.

RESULTS Among 409 participants randomized (mean age of 51.0 years [SD, 12.1 years]; 70% were women; mean BMI of 36.7 [SD, 6.4]; mean PHQ-9 score of 13.8 [SD, 3.1]; and mean SCL-20 score of 1.5 [SD, 0.5]), 344 (84.1%) completed 12-month follow-up. At 12 months, mean BMI declined from 36.7 (SD, 6.9) to 35.9 (SD, 7.1) among intervention participants compared with a change in mean BMI from 36.6 (SD, 5.8) to 36.6 (SD, 6.0) among usual care participants (between-group mean difference, −0.7 [95% CI, −1.1 to −0.2]; P = .01). Mean SCL-20 score declined from 1.5 (SD, 0.5) to 1.1 (SD, 1.0) at 12 months among intervention participants compared with a change in mean SCL-20 score from 1.5 (SD, 0.6) to 1.4 (SD, 1.3) among usual care participants (between-group mean difference, −0.2 [95% CI, −0.4 to 0]; P = .01). There were 47 adverse events or serious adverse events that involved musculoskeletal injuries (27 in the intervention group and 20 in the usual care group).

CONCLUSIONS AND RELEVANCE Among adults with obesity and depression, a collaborative care intervention integrating behavioral weight loss treatment, problem-solving therapy, and as-needed antidepressant medications significantly improved weight loss and depressive symptoms at 12 months compared with usual care; however, the effect sizes were modest and of uncertain clinical importance.

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Author Affiliations: Department of Medicine and Institute of Health Research and Policy, University of Illinois, Chicago (Ma, Lv); Department of Health Research and Policy and Medicine, Stanford University, Palo Alto, California (Rosas); Department of Medicine, Stanford University, Palo Alto, California (Xiao, Goldhaber-Fiebert); Department of Psychiatry and Behavioral Sciences, University of Washington, Seattle (Snowden); Department of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania (Venditti); Center for Communications Science, RTI International, Seattle, Washington (Lewis); Department of Biomedical Data Science, Stanford University, Stanford, California (Lavori).

Corresponding Author: Jun Ma, MD, PhD, Institute of Health Research and Policy, University of Illinois, 1747 W Roosevelt Rd, Room 586 (MC 275), Chicago, IL 60608 (maj2015@uic.edu).

Obesity and depression commonly occur together in individual patients and their coexistence has major public health significance.[1-3] Adults with obesity are more likely to have depression than those with normal weight,[4] and 43% of adults with depression have obesity.[5] These conditions share common comorbidities (eg, type 2 diabetes, cardiovascular disease), and their coexistence is associated with poorer treatment adherence and response to therapy, leading to higher health care costs than either condition alone.[6,7]

Effective treatments independently targeting obesity[8,9] and depression[10-12] exist; however, integrated treatments are lacking. Few effective treatments simultaneously address both conditions. Two randomized clinical trials (RCTs)[13,14] have tested high-intensity behavioral interventions for coexisting obesity and depression. Both included women only. One of these studies found no treatment effect on depression or weight,[13] and the other reported improved depression but not weight loss.[14] Integrated treatment of obesity and depression is needed in the increasing population of individuals who have both obesity and depression.

The Research Aimed at Improving Both Mood and Weight (RAINBOW) RCT compared an integrated collaborative care intervention with usual care for improving weight loss and depressive symptoms among adult patients with obesity and depression in primary care.

Key Points

Question Does an integrated collaborative care intervention improve weight loss and depressive symptoms among patients with obesity and depression?

Findings In this randomized clinical trial that included 409 patients with obesity and depression, an intervention that integrated behavioral weight loss treatment and problem-solving therapy with as-needed antidepressant medications resulted in statistically significant reductions in body mass index compared with usual care (−0.7 vs −0.1, respectively) and depressive symptoms (−0.3 vs −0.1 on the 20-item Depression Symptom Checklist; score range, 0-4) at 12 months.

Meaning A collaborative care intervention integrating behavioral weight loss treatment and problem-solving therapy with as-needed antidepressant medication led to statistically significant reductions in body mass index and depressive symptoms compared with usual care; however, the effect sizes were modest and of uncertain clinical importance.

Methods

The institutional review board for Sutter Health, Northern California, approved the study. All participants provided written informed consent. The trial protocol appears in Supplement 1 and amendments to the trial protocol appear in Supplement 2. The baseline participant characteristics were published.[15]

Study Participants

Participants were recruited from September 30, 2014, to January 12, 2017, at family and internal medicine departments within 4 medical centers of Sutter Health's Palo Alto Medical Foundation. Adults of any sex and race/ethnicity were eligible if they (1) had a body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) of 30 or greater (≥27 for Asian adults), (2) had depressive symptoms defined by a 9-item Patient Health Questionnaire (PHQ-9) score of 10 or greater,[16,17] and (3) did not have any serious comorbidities or meet any other exclusion criteria (eg, pregnancy, inability to speak or read English, and plan to relocate). Detailed inclusion and exclusion criteria can be found in Supplement 1. Actual counts of patients excluded according to the criteria can be found in eAppendix 1 in Supplement 3. To comply with National Institutes of Health reporting requirements, participants were asked to self-identify their race and ethnicity from fixed categories.

Study Procedures

A patient with an elevated BMI that was documented in the electronic health record (EHR) received a recruitment invitation after his or her primary care physician gave approval to contact the patient. Study coordinators called the patients who had an EHR-documented depression diagnosis or treatment to complete the PHQ-9 screening. Patients without an EHR-documented depression diagnosis or treatment were offered raffle participation in exchange for completing the PHQ-9 screening on the study website, and study coordinators called those with a score of 10 or greater.

The height and weight measurements for BMI confirmation were collected at baseline visits and patients responded to questionnaires (eg, SCL-20). In addition, a study physician performed final EHR reviews to rule out any comorbidities that might have excluded the patient from participation.

Randomization and Blinding

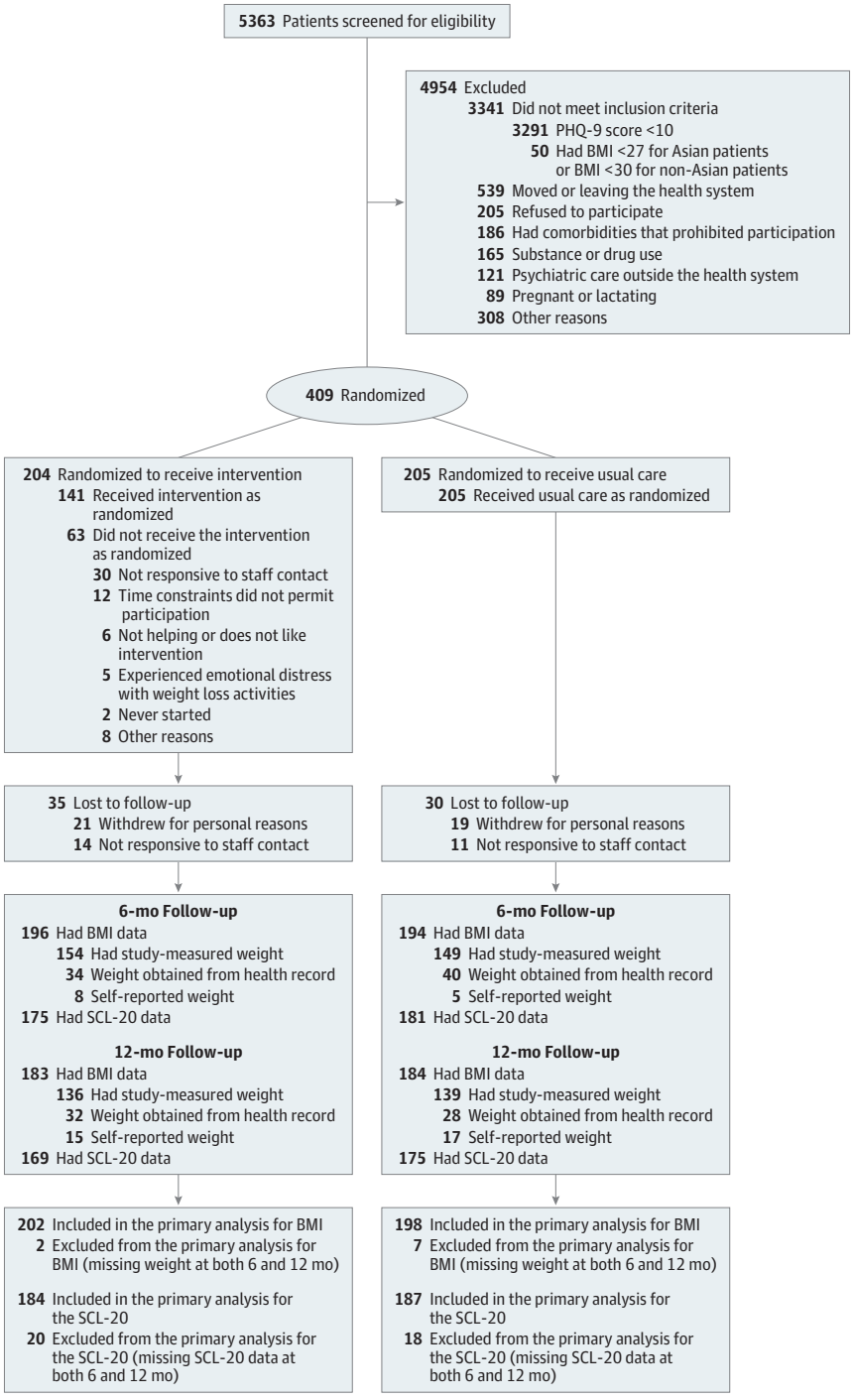
Participants were randomly assigned to receive usual care or the Integrated Coaching for Better Mood and Weight intervention using an online system[18] (**Figure 1**). The covariate-adaptive minimization method of Pocock and Simon[19] was used to achieve better-than-chance marginal balance across the baseline characteristics of clinic, age, sex, race/ethnicity, education level, BMI, SCL-20 score, use of antidepressant medications, and number of hospitalizations during the past year.

The minimization algorithm used the range distance measure[19] and equal weight for the 9 balancing factors to calculate imbalance scores. The randomization probabilities applied the biased-coin method (ie, 2/3 to 1/3) of Efron[20] to protect allocation concealment. Investigators, the data and safety monitoring board, outcome assessors, and the data analysts were blinded until after completion of the primary data review through 12 months.

Intervention

The 12-month intervention integrated core components of 2 effective interventions for patients with both obesity and depression. The Group Lifestyle Balance (GLB)[21] program was adapted from the Diabetes Prevention Program,[22] and consisted of videos for self-study, which were previously demonstrated to be effective for weight loss and cardiometabolic

Figure 1. Enrollment, Randomization, and Follow-up of the Study Patients



BMI indicates body mass index (calculated as weight in kilograms divided by height in meters squared); PHQ-9, 9-Item Patient Health Questionnaire; SCL-20, 20-item Depression Symptom Checklist.

risk reduction in primary care.[8] The GLB program was grounded in social cognitive theory[23] and used a goal-based approach to promote modest (5%-10%) weight loss through healthy dietary changes with reductions of 500 to 1000 kcal per day and at least 150 minutes of moderate-intensity physical activity (eg, brisk walking) per week. The Program to Encourage Active, Rewarding Lives for Seniors (PEARLS)[10,11] used problem-solving treatment with behavioral activation strategies as the first-line therapy and then supplemented with as-needed stepwise increases in doses and number of antidepressant medications. The study intervention integrated these 2 independent programs into 1 synergistic, 2-phased curriculum (eAppendix 2 in Supplement 3).

The intensive treatment phase included 9 individual face-to-face sessions lasting 60 minutes each (4 weekly, 2 biweekly, and then 3 monthly sessions) and 11 home-viewed GLB

videos lasting 20 to 30 minutes each watched over a 6-month period. The maintenance phase included monthly telephone sessions lasting 15 to 30 minutes each for 6 additional months. Participants received self-care materials, including intervention handouts, a DVD set or an online access code for the GLB videos, a wireless activity tracker with replacement batteries, and written instructions for creating a MyFitnessPal.com account to track weight and dietary intake.

A trained bachelor's-level health coach delivered the intervention, and a supervising master's-level registered dietitian oversaw fidelity assurance. The health coach and dietitian met every 1 to 2 weeks with a psychiatrist and a primary care physician to discuss the participants with poor progress and an overview of the clinical status of new participants. Based on these discussions, the psychiatrist might recommend initiating or adjusting antidepressant medications for a patient according to the medication protocol (eAppendix 3 in Supplement 3), and would communicate with the patient's primary care physician who was responsible for the management of any medication.

Usual Care

Participants in the intervention and usual care groups continued to receive medical care from their personal physicians. The physicians were notified if their patient was enrolled into the study but were not informed of the trial group assignment. All participants also received information on mental health services, weight management, and other wellness programs routinely available at their clinic. Usual care participants received a wireless activity tracker with batteries but not the other self-care materials (ie, no intervention handouts, DVD set, or online access code for the GLB videos).

Outcome Measures

Follow-up assessments occurred at 6, 12, 18, and 24 months and followed the same protocols as those used at baseline.[24] The co-primary outcome measures were BMI and SCL-20 score at 12 months; this study reports results up to 12 months. Height was mentioned in the protocol as an outcome, but was measured only at baseline for BMI calculation. The SCL-20 is a valid, reliable measure of depression severity and scores are the average of the 20 items and range from 0 (best) to 4 (worst).[25] Secondary outcome measures included weight, depression treatment response (ie, ≥50% decrease in SCL-20 score from baseline),[10,11,26] complete depression remission (ie, SCL-20 score <0.5),[10,11] and total score on the 7-item Generalized Anxiety Disorder scale. Patients with depression often experience anxiety symptoms. The 7-item Generalized Anxiety Disorder scale is valid and reliable for screening generalized anxiety disorder, is strongly associated with multiple domains of functional impairment, and scores range from 0 (best) to 21 (worst).[27] The mimimal clinically important differences for the SCL-20 and the 7-item Generalized Anxiety Disorder scale have not yet been defined.

Post hoc outcomes included a decrease of 5% or greater in weight from baseline,[28] health care use, and use of weight loss and wellness programs outside the trial. Outpatient and inpatient encounters and any prescriptions listed during the 12 months before and after randomization were abstracted from the EHR. A previously developed participant survey[8] assessed the use of weight loss, exercise, and wellness programs outside the trial. The prespecified secondary outcomes of waist circumference, resting blood pressure, obesity-related problems, disability, quality of life, and costs were collected but are not reported herein. Potential effect modifiers included age, sex, race/ethnicity, education level, and presence of posttraumatic stress disorder,[29] all of which were defined a priori, and binge eating disorder,[30] which was defined post hoc.

Statistical Analysis

The *t* test or the χ^2 test was used for the unadjusted bivariable analyses and Wald asymptotic 95% CIs were used for the unadjusted differences in proportions. The analyses of the between-group differences for the primary and secondary outcomes included all participants with follow-up data at 6 or 12 months. Participants were analyzed based on the group to which they were assigned.

Tests of group × time interactions in repeated-measures mixed-effects linear models (for continuous outcomes) or generalized linear mixed models (for categorical outcomes) were performed. The fixed effects of each model included baseline value of the outcome, randomization covariates, group (intervention or usual care), time point (6 or 12 months), and group × time interactions. The random effects accounted for repeated measures with an unstructured covariance matrix and clustering of patients within primary care physicians.

Adjusted differences in means with 95% CIs (continuous outcomes) or proportions (categorical outcomes) were obtained using model-based estimates and the 95% CIs for the differences in proportions were generated by bootstrapping.[31] The analyses used all available data for each outcome, and missing data were handled directly through maximum likelihood estimation via mixed modeling. Per the trial protocol, in the case of missing study-measured weight, the closest EHR weight within 3 months of the due date of a missed study visit or self-reported weight (if no EHR weight) was used.

Sensitivity analyses were conducted using study-measured weights only. The bootstrap resampling method[31] was used to verify that the results based on the mixed model were not sensitive to violations of modeling assumptions. Because of the potential for type I error due to multiple comparisons, findings for the analyses of the secondary outcomes should be interpreted as exploratory. The moderation analysis used marginal models with repeated measures that included the same covariates as mentioned above as well as the main effect of each potential effect modifier and its interaction with group; the latter, if significant, rejected the null hypothesis of no moderation.

As estimated, 202 participants would be needed per group to provide 90% power to detect a standardized between-group mean difference (Cohen *d* of 0.35) for BMI and SCL-20 scores at 12 months, assuming a 2-sided α level of 5% and 85% retention. Based on effect estimates and standard deviations reported in prior RCTs that separately tested the GLB video program for weight loss[8] and the PEARLS program for depression treatment,[10,11] a Cohen *d* of 0.35 was on the lower end of

the standardized effects that seemed plausible and that generated a feasible sample size. Specifically, a sample of 202 per group was planned to detect a mean difference in BMI of 0.76 (SD, 1.65) and a mean difference in SCL-20 score of 0.17 (SD, 0.5). Because treatment success would be judged on both the co-primary outcomes (not either), multiplicity adjustment was not performed.[32] The α level was not partitioned for the analysis of the 2 primary outcomes.

All analyses were conducted using SAS version 9.4 (SAS Institute Inc). Statistical significance was defined as a 2-sided *P* value < .05. The entire statistical analysis plan appears in Supplement 4.

Results

Study Participants

Of the 5363 patients who completed the screening, 205 refused to participate in the baseline visit and 4749 were ineligible (eAppendix 1 in Supplement 3). A total of 409 participants were randomized to the intervention group (n = 204) or the usual care group (n = 205). The primary outcome analyses included participants with follow-up data at either 6 or 12 months for BMI (202 in the intervention group and 198 in the usual care group) and for SCL-20 score (184 in the intervention group and 187 in the usual care group) (Figure 1).

The mean age of the participants was 51.0 years (SD, 12.1 years), 70% were women, 71% were non-Hispanic white adults, and 69% had at least a college education (**Table 1**). On average, participants had moderately severe obesity (mean BMI, 36.7 [SD, 6.4]), moderate depression (mean PHQ-9 score, 13.8 [SD, 3.1] and mean SCL-20 score, 1.5 [SD, 0.5]), and 59% reported not taking antidepressant medications at the time of enrollment. A total of 344 participants (84.1%) completed 12-month follow-up. The date of final 12-month follow-up was January 17, 2018.

Primary Outcomes

At 12 months, intervention participants had significantly greater improvements in BMI and SCL-20 score than usual care participants (**Table 2**). For BMI, the mean declined from 36.7 (SD, 6.9) to 35.9 (SD, 7.1) among participants in the intervention group compared with a change from 36.6 (SD, 5.8) to 36.6 (SD, 6.0) among usual care participants (between-group mean difference, −0.7 [95% CI, −1.1 to −0.2]; *P* = .01). For the SCL-20, the mean score declined from 1.5 (SD, 0.5) to 1.1 (SD, 1.0) among participants in the intervention group compared with a change from 1.5 (SD, 0.6) to 1.4 (SD, 1.3) among participants in the usual care group (between-group mean difference, −0.2 [95% CI, −0.4 to 0]; *P* = .01). The Cohen *d* effect was 0.28 (95% CI, 0.03 to 0.42) for BMI and 0.23 (95% CI, −0.03 to 0.34) for SCL-20 score. The sensitivity analyses using only study-measured weights produced consistent results (eAppendix 4 in Supplement 3).

Secondary Outcomes and Additional Analyses

At 6 months, the between-group mean differences for BMI (−0.6 [95% CI, −0.9 to −0.3]) and SCL-20 score (−0.3 [95% CI, −0.4 to −0.1) were statistically significant (Table 2). Among intervention participants, mean weight declined from 103.4 kg (SD, 22.3 kg) at baseline to 100.8 kg (SD, 22.8 kg) at 12 months compared with a change in mean weight from 103.2 kg (SD, 19.6 kg) among usual care participants at baseline to 103.4 kg (SD, 20.9 kg) at 12 months.

Significantly higher proportions of intervention than usual care participants had an improved SCL-20 score by at least 50% at 6 months (31% vs 16%, respectively) and attained full depression remission (SCL-20 score <0.50; 18% vs 6%); however, neither of these outcomes was significantly different between the 2 groups at 12-month follow-up. The between-group mean difference in GAD-7 scores was −1.2 (95% CI, −2.1 to −0.3) at 6 months and −1.5 (95% CI, −2.4 to −0.5) at 12 months.

Sex, race/ethnicity, education level, and binge eating disorder significantly modified the intervention effect on BMI at 12 months (**Figure 2**). Compared with usual care, the intervention resulted in significantly greater BMI reductions among men, non-Hispanic whites, participants with at least a college education, and participants reporting no binge eating disorder. However, the intervention did not result in greater BMI reductions among women, Hispanic or Asian adults, participants with less than a college education, and participants reporting binge eating disorder. Age, sex, and race/ethnicity significantly modified the intervention effect on SCL-20 score at 12 months. Compared with usual care, the intervention resulted in significantly greater reductions in SCL-20 score among participants aged 45 years or older, women, and non-Hispanic whites. However, the intervention did not result in greater reductions in SCL-20 score among participants aged 18 to 44 years, men, and Hispanic or Asian adults.

Post Hoc Outcomes

The post hoc outcome of weight loss of 5% or greater differed significantly by group (28% for the intervention group vs 15% for the usual care group). The proportion of participants who were prescribed antidepressant medications increased from 48.5% during the 12 months before randomization to 62.7% during the 12 months after randomization among intervention participants but decreased from 47.3% to 42.0% during the same periods among usual care participants (**Table 3**).

Bupropion, sertraline, and citalopram/escitalopram were the most commonly prescribed antidepressant medications (eAppendix 5 in Supplement 3). Frequencies of outpatient and inpatient visits, antiobesity medication prescriptions, and out-of-study weight loss or wellness program participation did not differ significantly by group (Table 3).

Intervention Adherence

Among 204 intervention participants, 73.5% completed at least 7 of the 9 intensive treatment sessions (median, 9 [interquartile range, 6-9]) and 64.7% completed at least 5 or all 6 maintenance telephone sessions (median, 6 [interquartile range, 0-6]).

Adverse Events

Of the 31 serious adverse events, 13 required hospitalization and 10 involved fractures or musculoskeletal injuries (eg, torn

Table 1. Baseline Characteristics by Treatment Group

Characteristics	Intervention (n = 204)	Usual Care (n = 205)
Clinic in Northern California, No. (%)[a]		
Los Altos	36 (18)	40 (20)
Sunnyvale	23 (11)	21 (10)
Palo Alto	82 (40)	84 (41)
Mountain View	63 (31)	60 (29)
Age, mean (SD), y[a]	50.9 (12.2)	51.0 (11.9)
Sex, No. (%)[a]		
Female	144 (71)	143 (70)
Male	60 (29)	62 (30)
Race/ethnicity, No. (%)[a]		
Non-Hispanic white	147 (72)	142 (69)
Black	3 (1)	3 (1)
Asian/Pacific Islander	20 (10)	20 (10)
Hispanic	26 (13)	30 (15)
Other[b]	8 (4)	10 (5)
Education level, No. (%)[a]		
≤High school graduate or GED	9 (4)	18 (9)
Some college	51 (25)	47 (23)
Undergraduate degree	79 (39)	72 (35)
Graduate-level work or degree	65 (32)	68 (33)
Body mass index, mean (SD)[a,c]		
Both sexes	36.7 (6.9)	36.6 (5.8)
Women	36.8 (6.6)	37.3 (5.9)
Men	36.4 (7.5)	35.1 (5.5)
Weight, mean (SD), kg		
Both sexes	103.4 (22.3)	103.2 (19.6)
Women	98.5 (20.0)	99.3 (17.9)
Men	115.4 (23.2)	112.2 (20.6)
Height, mean (SD), cm		
Both sexes	167.6 (9.6)	167.8 (10.2)
Women	163.3 (7.2)	163.0 (6.4)
Men	178.1 (6.2)	178.7 (8.8)
9-Item Patient Health Questionnaire score, mean (SD)[d]	14.1 (3.2)	13.5 (3.0)
20-Item Depression Symptom Checklist score, mean (SD)[a,e]	1.5 (0.5)	1.5 (0.6)
7-Item Generalized Anxiety Disorder scale score, mean (SD)[f]	8.2 (5.0)	8.5 (5.1)
Taking antidepressant medications, No. (%)[a,g]	85 (42)	84 (41)
Hospitalized during the last year, No. (%)[a,g]	17 (8)	18 (9)
Depression diagnosis or treatment, No. (%)	145 (71)	140 (68)
Employment status, No./total (%)		
Full-time	118/204 (58)	115/203 (57)
Part-time	30/204 (15)	29/203 (14)
Unemployed	56/204 (27)	59/203 (29)
Annual family income, No./total (%)		
<$75 000	46/176 (26)	47/189 (25)
$75 000-<$150 000	54/176 (31)	63/189 (33)
≥$150 000	76/176 (43)	79/189 (42)
Health insurance, No (%)		
Preferred provider organization	135 (66)	133 (65)
Health maintenance organization (HMO)	45 (22)	42 (20)
Medicare fee for service	17 (8)	20 (10)
Other (Medicare HMO, Medi-Cal, or self-insured)	7 (4)	10 (5)
Marital status, No./total (%)		
Married or living with a partner	124/203 (61)	123/203 (61)
Single, separated, divorced, or widowed	79/203 (39)	80/203 (39)
Household size, No./total (%)		
<2	40/203 (20)	36/197 (18)
2	74/203 (36)	70/197 (36)
≥3	89/203 (44)	91/197 (46)

[a] Indicates characteristic is a randomization balancing factor.

[b] In the intervention group, 6 reported mixed race and 2 reported other race (unspecified). In the usual care control group, 7 reported mixed race and 3 reported other race.

[c] Calculated as weight in kilograms divided by height in meters squared.

[d] Data are total scores for the 9 items. Score range: 0 (no symptoms) to 27 (most severe symptoms). The cutoff point of 10 corresponds to moderate depression; 15, moderately severe depression; and 20, severe depression.

[e] Data are average scores for the 20 items. Score range: 0 (not depressed at all) to 4 (extremely depressed). The cutoff point of 1.5 corresponds to moderate depression; and 2.0, severe depression.

[f] Data are total scores for the 7 items. Score range: 0 (no symptoms) to 21 (most severe symptoms). The cutoff point of 5 corresponds to mild anxiety; 10, moderate anxiety; and 15, severe anxiety.

[g] Based on self-report at baseline screening.

Table 2. Weight Loss, Depression, and Anxiety Outcomes

	Unadjusted Estimates		Treatment Difference	
	Intervention	Usual Care	Adjusted Between-Group Difference (95% CI)[a]	*P* Value
Primary Outcomes				
Body mass index				
No. of participants	202	198		
At 6 mo, mean (SD)	36.0 (6.9)	36.6 (6.2)	Mean, −0.6 (−0.9 to −0.3)	<.001
At 12 mo, mean (SD)	35.9 (7.1)	36.6 (6.0)	Mean, −0.7 (−1.1 to −0.2)	.01
20-Item Depression Symptom Checklist (SCL-20) score[b]				
No. of participants	184	187		
At 6 mo, mean (SD)	1.1 (0.7)	1.4 (0.8)	Mean, −0.3 (−0.4 to −0.1)	<.001
At 12 mo, mean (SD)	1.1 (1.0)	1.4 (1.3)	Mean, −0.2 (−0.4 to 0)	.01
Secondary Outcomes				
Weight, kg				
No. of participants	202	198		
At 6 mo, mean (SD)	101.5 (21.9)	103.2 (21.1)	Mean, −1.9 (−2.9 to −1.0)	<.001
At 12 mo, mean (SD)	100.8 (22.8)	103.4 (20.9)	Mean, −2.0 (−3.3 to −0.6)	.004
Depression treatment response (≥50% decrease in SCL-20 score from baseline)				
No. of participants	184	187		
At 6 mo, No. (%)	55 (31)	29 (16)	21.2 (9.8 to 33.3)[c]	<.001
At 12 mo, No. (%)	49 (29)	38 (22)	10.3 (−1.3 to 21.6)[c]	.09
Complete remission of depression symptoms (defined as SCL-20 score <0.50)				
No. of participants	184	187		
At 6 mo, No. (%)	31 (18)	10 (6)	14.4 (5.0 to 26.3)[c]	<.001
At 12 mo, No. (%)	30 (18)	23 (13)	4.7 (−3.8 to 16.0)[c]	.28
7-Item Generalized Anxiety Disorder scale total score[d]				
No. of participants	154	160		
At 6 mo, mean (SD)	5.1 (4.5)	6.4 (4.5)	Mean, −1.2 (−2.1 to −0.3)	.01
At 12 mo, mean (SD)	4.2 (3.8)	6.1 (4.6)	Mean, −1.5 (−2.4 to −0.5)	.003
Post Hoc Outcomes				
≥5% Weight loss from baseline				
No. of participants	202	198		
At 6 mo, No. (%)	48 (24)	17 (9)	11.4 (4.5 to 22.2)[c]	<.001
At 12 mo, No. (%)	51 (28)	27 (15)	9.8 (2.9 to 20.4)[c]	.003

[a] For the means, adjustment was made using a linear mixed model. For the proportions, adjustment was made using a generalized linear mixed model. The mean and the proportion data were calculated using model-based estimates. The 95% CIs were obtained using model-based intervals for differences in the means and using bootstrapping for the differences in the proportions. The mixed-effects models accounted for the random effects of the repeated measures and primary care physicians and were adjusted for the baseline value of the outcome of interest, clinic, age, sex, race/ethnicity, education level, use of any antidepressant medications at the time of enrollment, and the number of hospitalizations during the 12 months before randomization.

[b] Data are average scores for the 20 items. Score range: 0 (not depressed at all) to 4 (extremely depressed).

[c] Expressed as proportions.

[d] Data are total scores for the 7 items. Score range: 0 (no symptoms) to 21 (most severe symptoms).

meniscus) requiring outpatient repair procedures. Two of the serious adverse events were possibly related to the study (ie, fractures from falls while engaging in physical activity). There were 104 adverse events; of these, 37 involved minor musculoskeletal injuries and 13 were possibly related to the study. There were 47 adverse events or serious adverse events that involved musculoskeletal injuries (27 in the intervention group and 20 in the usual care group). The combined serious adverse events and adverse events were evenly distributed across both groups (serious adverse events: 16 in the intervention group vs 15 in the usual care group; adverse events: 51 vs 53, respectively). There were no deaths.

Discussion

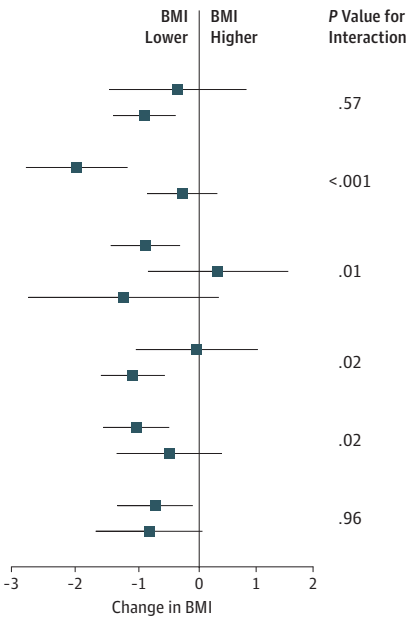
In this trial of 409 patients with obesity and depression treated by primary care physicians, an integrated collaborative care intervention resulted in improvements of modest effect size in weight loss and depressive symptoms at 12 months compared with usual care.

To our knowledge, this study was the first and largest RCT of integrated collaborative care for coexisting obesity and depression. The effects of the intervention on BMI and SCL-20 score reached statistical significance at 6 months and were

Figure 2. Effect Modification Analysis

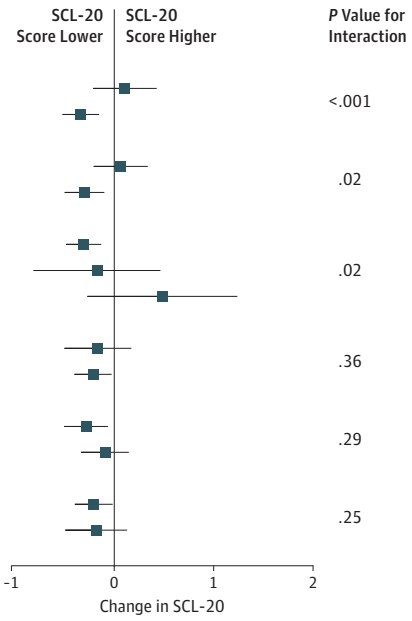
A Modifiers of the intervention effect on body mass index (BMI) at 12 mo

	No. of Patients	Mean (SD)		12-mo Adjusted Mean Difference (95% CI)	P Value for Interaction
		Intervention	Usual Care		
Age group, y					
18-44	115	37.6 (8.0)	36.5 (6.8)	-0.2 (-1.3 to 0.9)	.57
≥45	294	35.2 (6.6)	36.6 (5.8)	-0.8 (-1.3 to -0.3)	
Sex					
Male	122	35.1 (8.1)	35.6 (6.0)	-1.9 (-2.7 to -1.0)	<.001
Female	287	36.2 (6.7)	37.0 (6.0)	-0.1 (-0.7 to 0.4)	
Race/ethnicity					
White	289	36.3 (6.9)	36.9 (6.0)	-0.8 (-1.3 to -0.2)	.01
Hispanic	56	36.6 (6.6)	36.0 (5.1)	0.4 (-0.7 to 1.6)	
Asian	40	31.6 (9.1)	33.0 (5.9)	-1.1 (-2.7 to 0.5)	
Education					
<College	125	35.9 (5.7)	36.0 (5.7)	0.1 (-0.9 to 1.1)	.02
≥College	284	35.9 (7.7)	36.8 (6.2)	-1.0 (-1.5 to -0.4)	
Binge eating disorder					
No	242	34.8 (6.5)	36.5 (6.0)	-0.9 (-1.4 to -0.4)	.02
Yes	167	37.6 (7.8)	36.7 (6.2)	-0.4 (-1.2 to 0.5)	
Posttraumatic stress disorder					
No	257	36.4 (7.4)	36.7 (6.4)	-0.6 (-1.2 to 0)	.96
Yes	125	34.5 (5.5)	35.9 (5.2)	-0.7 (-1.6 to 0.2)	



B Modifiers of the intervention effect on 20-item Depression Symptom Checklist (SCL-20) at 12 mo

	No. of Patients	Mean (SD)		12-mo Adjusted Mean Difference (95% CI)	P Value for Interaction
		Intervention	Usual Care		
Age group, y					
18-44	115	1.3 (0.8)	1.3 (0.9)	0.1 (-0.2 to 0.4)	<.001
≥45	294	1.1 (0.7)	1.4 (0.8)	-0.3 (-0.5 to -0.2)	
Sex					
Male	122	1.1 (0.7)	1.1 (0.6)	0.1 (-0.2 to 0.3)	.02
Female	287	1.2 (0.7)	1.5 (0.9)	-0.3 (-0.5 to -0.1)	
Race/ethnicity					
White	289	1.1 (0.6)	1.4 (0.8)	-0.3 (-0.5 to -0.1)	.02
Hispanic	56	1.4 (0.8)	1.6 (1.1)	-0.2 (-0.8 to 0.4)	
Asian	40	1.4 (1.1)	1.0 (0.7)	0.5 (-0.3 to 1.2)	
Education					
<College	125	1.3 (0.8)	1.4 (0.8)	-0.2 (-0.5 to 0.2)	.36
≥College	284	1.1 (0.7)	1.4 (0.9)	-0.2 (-0.4 to 0)	
Binge eating disorder					
No	242	1.1 (0.8)	1.4 (0.9)	-0.3 (-0.5 to -0.1)	.29
Yes	167	1.2 (0.7)	1.3 (0.8)	-0.1 (-0.3 to 0.1)	
Posttraumatic stress disorder					
No	257	1.0 (0.7)	1.3 (0.9)	-0.2 (-0.4 to 0)	.25
Yes	125	1.3 (0.8)	1.5 (0.8)	-0.2 (-0.5 to 0.1)	



Body mass index was calculated as weight in kilograms divided by height in meters squared. The scores for the SCL-20 were calculated using the response categories: "not at all," "a little bit," "moderately," "quite a bit," and "extremely" that were assigned the scores of 0, 1, 2, 3, and 4, respectively. The average scores for the 20 items range from 0 (not depressed at all) to 4 (extremely depressed). The mean adjusted difference and 95% CIs were obtained from linear mixed-effects models accounting for the random effects of repeated measures and primary care physicians and adjusting for the baseline value of the outcome of interest and randomization covariates (clinic, age, sex, race/ethnicity, education level, use of any antidepressant medications at the time of enrollment, and number of hospitalizations during the 12 months prior to randomization). The *P* values for the interaction terms of the modifier and study group were obtained from general least-square models that accounted for repeated measures and were adjusted for the baseline value of the outcome of interest, randomization covariates as listed above, the main effect of the effect modifier (if not a randomization covariate), and the main effect of the study group.

Table 3. Outpatient and Inpatient Visits, Prescriptions for Antidepressant and Antiobesity Medications, and Weight Loss or Wellness Programs

Post Hoc Outcomes	No. (%)		Unadjusted Between-Group Difference (95% CI)
	Intervention (n = 204)	Usual Care (n = 205)	
Outpatient and Inpatient Visits[a]			
≥5 Non-mental health outpatient visits during prior 12 mo			
12 mo before randomization	97 (47.5)	96 (46.8)	0.7 (−9.0 to 10.4)
12 mo after randomization	88 (43.1)	94 (45.9)	−2.7 (−12.4 to 6.9)
Any mental health outpatient visits during prior 12 mo			
12 mo before randomization	11 (5.4)	8 (3.9)	1.5 (−2.6 to 5.6)
12 mo after randomization	13 (6.4)	11 (5.4)	1.0 (−3.6 to 5.6)
Any hospitalizations during prior 12 mo			
12 mo before randomization	14 (6.9)	16 (7.8)	−0.9 (−6.0 to 4.1)
12 mo after randomization	14 (6.9)	12 (5.9)	1.0 (−3.7 to 5.7)
Prescriptions for Antidepressant or Antiobesity Medications[a]			
Prescribed any antidepressant medications during prior 12 mo			
12 mo before randomization	99 (48.5)	97 (47.3)	1.2 (−8.5 to 10.9)
12 mo after randomization	128 (62.7)	86 (42.0)	20.8 (11.3 to 30.3)
Adjustments to antidepressant medication during 12 mo after randomization			
Start of a new medication among previously treated patients	41 (20.1)	23 (11.2)	8.9 (1.9 to 15.9)
Start of medication among previously untreated patients	40 (19.6)	9 (4.4)	15.2 (9.1 to 21.4)
Change in the daily dosage of an ongoing medication	28 (13.7)	8 (3.9)	9.8 (4.4 to 15.2)
Any antiobesity medications during prior 12 mo			
12 mo before randomization	3 (1.5)	3 (1.5)	0 (−2.3 to 2.3)
12 mo after randomization	1 (0.5)	3 (1.5)	−1.0 (−2.9 to 0.9)
Adjustments to antiobesity medication during 12 mo after randomization	2 (1.0)	2 (1.0)	0 (−1.9 to 1.9)
Weight Loss or Wellness Program Outside the Study[b]			
Any health club, gym memberships, and other exercise-related programs joined during 12-mo follow-up, No./total (%)	73/142 (51.4)	83/146 (56.8)	−5.4 (−16.9 to 6.1)
Any commercial weight loss or wellness programs joined during 12-mo follow-up, No./total (%)	41/133 (30.8)	40/138 (29.0)	1.8 (−9.1 to 12.8)

[a] Data abstracted from electronic health records.

[b] Based on self-report.

sustained at 12 months. The effects observed in this RCT were comparable with prior trials that targeted either condition using similar treatment approaches.

In this trial, the between-group mean difference in BMI was −0.7 (95% CI −1.1 to −0.2) at 12 months compared with −0.7 (95% CI, −1.3 to −0.1) at 15 months in the prior trial[8] that demonstrated the effectiveness of the GLB video program for weight loss in primary care and compared with −1.1 (95% CI, −1.4 to −0.8) at 12 months in a meta-analysis of 22 RCTs of behavioral weight loss interventions.[33]

In this trial, the between-group mean difference in SCL-20 score was −0.2 (95% CI, −0.4 to 0) at 12 months, which was the same as that reported in the PEARLS trial among older adults with minor depression or dysthymia.[10] Another PEARLS trial[11] among adults with epilepsy showed a mean reduction in SCL-20 score of −0.6 (SD, 0.7) in the intervention group vs −0.1 (SD, 0.5) in the usual care group at 12 months compared with a mean reduction in SCL-20 score in this trial of −0.3 (SD, 0.7) in the intervention group vs −0.1 (0.8) in the usual care group.

The significant intervention effects on depression response and remission at 6 months were not observed at 12-month follow-up and this effect was related to improvements among usual care participants between 6- and 12-month follow-up. Participants had similar amounts of health care encounters and participation in community weight loss and wellness programs in both groups. Increased prescription of antidepressant medications was an intended consequence of the intervention.

The effect sizes for both primary outcomes in this trial were modest and of uncertain clinical importance, and were limited to a duration of 12 months. Whether these outcomes will translate to important health outcomes or will be sustained over longer periods is unknown. Research on mechanisms underlying the intervention effect as well as facilitators and barriers to intervention adherence among subgroups is needed to optimize treatment efficiency and potency. For example, this study showed that the effects of the intervention were likely modified by sex with more favorable responses for BMI among men and more favorable responses for SCL-20 score among women, suggesting tailored strategies by sex may be warranted.

Katon et al[26] reported that a collaborative care intervention involving primarily pharmacotherapy and frequent nurse visits produced a net reduction in SCL-20 score of −0.4 (95% CI, −0.6 to −0.3) in patients with depression who also had diabetes or coronary heart disease (or both diabetes and coronary heart disease) in primary care. The current trial extends

that evidence. The demonstrated effectiveness of collaborative care with behavioral and medical treatments for patients with depression across a spectrum of cardiometabolic diseases is important for primary care practice because of the high prevalence and health care cost of these conditions.

Effective treatment models for primary care could support the Institute for Healthcare Improvement Triple Aim to improve patient experience of care, population health, and per-capita cost of health care.[34] The current intervention successfully integrated the Diabetes Prevention Program–based GLB program for weight loss and the PEARLS program for depression. Both of these programs are nationally recognized with established training and dissemination infrastructures and are conducive to delivery by primary care teams including nonmedical professionals and non-mental health professionals.[21,35] The intensity level of the intervention was less than or comparable with collaborative care for depression programs and behavioral weight loss programs that are currently reimbursed by Medicare,[36,37] holding promise for further dissemination and implementation.

Limitations

This study has several limitations. First, it was conducted at primary care clinics within a single health system in Northern California, and the study sample was relatively homogeneous and of high socioeconomic status, limiting generalizability to other settings and people of lower socioeconomic status.

Second, 9 of 409 participants (2%) were missing weight data and 38 (9%) were missing SCL-20 score data at both 6 and 12 months, and were thus excluded from the primary analyses. In addition, the primary analysis of BMI included values based on EHR weights or participant self-reported weights. Based on 2 behavioral weight loss trials,[8,38] Xiao et al[39] reported high agreement and statistical inference validity of EHR weights compared with study-measured weights using the same protocol as in this trial. Even so, not all randomized participants in this trial could be followed up to month 12. Because a strict intention-to-treat analysis was not possible, the outcomes for patients who dropped out of the study may not resemble those for patients who remained in the study, and this phenomenon may have resulted in an overestimate of the intervention effects.

Third, the health system where the trial was conducted is not a health maintenance organization and patients may have accessed care elsewhere, which would not be captured in the EHRs. However, 82% of the participants had at least 1 health care encounter within the study system during the 12 months after randomization, indicating ongoing care.

Conclusions

Among adults with obesity and depression, a collaborative care intervention integrating behavioral weight loss treatment, problem-solving therapy, and as-needed antidepressant medications significantly improved weight loss and depressive symptoms at 12 months compared with usual care; however, the effect sizes were modest and of uncertain clinical importance.

ARTICLE INFORMATION

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Concept and design: Ma, Lewis, Lavori.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Ma, Rosas, Lv, Xiao, Lewis.
Critical revision of the manuscript for important intellectual content: Ma, Rosas, Xiao, Snowden, Venditti, Lewis, Goldhaber-Fiebert, Lavori.
Statistical analysis: Xiao, Lavori.
Obtained funding: Ma, Lewis.
Administrative, technical, or material support: Rosas, Lv, Snowden, Venditti, Lewis.
Supervision: Ma, Rosas, Venditti.

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