Randomized controlled trial of behavioral treatment for comorbid obesity and depression in women: the Be Active Trial

Sherry Pagoto, PhD, Kristin L. Schneider, PhD, Matthew C. Whited, PhD, Jessica L. Oleski, MA, Phillip Merriam, MPH, Bradley Appelhans, PhD, Yunsheng Ma, PhD, Barbara Olendzki, RD, MPH, Molly E. Waring, PhD, Andrew M. Busch, PhD, Stephenie Lemon, PhD, Ira Ockene, MD, and Sybil Crawford, PhD

1University of Massachusetts Medical School, Worcester, MA, University of Massachusetts Medical School, Worcester, MA
2Rush University, Chicago, IL Rush University, Chicago, IL
3Alpert Medical School of Brown University and The Miriam Hospital

Abstract

Objective—Depression is associated with increased risk for obesity and worse weight loss treatment outcomes. The purpose of the present study was to test the hypothesis that delivering evidence-based behavior therapy for depression prior to a lifestyle weight loss intervention improves both weight loss and depression.

Design—In a randomized controlled trial, obese women with major depressive disorder (N=161, mean age=45.9 [SD: 10.8] years) were randomized to brief behavior therapy for depression treatment followed by a lifestyle intervention (BA) or a lifestyle intervention only (LI). Follow-up occurred at 6- and 12-months. Main outcome measures included weight loss and depression symptoms.

Results—Intention-to-treat analyses revealed both conditions lost significant weight, but no differences between conditions in weight change at 6-months (BA= −3.0%, SE= − 0.65%; LI= −3.7%, SE = 0.63%; p = 0.48) or 12-months (BA= −2.6%, SE= 0.77%; LI= −3.1%, SE=0.74%; p = 0.72). However, the BA condition evidenced significantly greater improvement in Beck Depression Inventory-II scores relative to the LI condition at both 6-months (BA mean change= −12.5, SD= 0.85; LI mean change= −9.2, SD=0.80, p= 0.005) and 12-months (BA mean change= −12.6, SD= 0.97; LI mean change= −9.9, SD= 0.93; p = 0.045). Participants who experienced
depression remission by 6-months (61.2%) lost greater weight (mean = −4.31%; SE=0.052) than those who did not (39.7%; mean= −2.47%, SE=0.53; p=.001).

**Conclusion**—Adding behavior therapy to a lifestyle intervention results in greater depression remission but does not improve weight loss within one year. Improvement in depression is associated with greater weight loss.

**Keywords**
Obesity; depression; lifestyle intervention; behavior therapy

**Introduction**

Obesity and depression are highly comorbid, particularly among women,[1] which is problematic because depression heightens risk for obesity-related morbidity and mortality. [1] About 37% of obese women who seek weight loss treatment have clinical depression [2] and depression is associated with worse weight loss outcomes.[2–4] Effective weight loss treatments for adults with depression are needed.

Four studies have tested weight loss interventions in individuals with clinical depression, but only one was a randomized controlled trial.[5] The first study compared weight loss outcomes in 131 patients with and without clinical depression following an outpatient hospital-based lifestyle intervention modeled after the Diabetes Prevention Program.[6] In this study, patients with depression lost significantly less weight than nondepressed patients (−4.0 kg versus −6.4 kg), suggesting that additional treatment is needed for patients with depression. A randomized trial then compared simultaneous delivery of cognitive behavioral therapy (CBT) for depression and a lifestyle intervention to a lifestyle intervention alone in 203 women. Findings revealed that the CBT condition did not improve weight or depression outcomes.[5] While depression and weight improved in both conditions, the weight loss in both conditions (mean = −1.8 kg and −2.8 kg) was still less than that observed in non-depressed samples. For example, the US Preventive Services Task Force review of lifestyle interventions reported average weight loss across trials ranging from 3–5 kg.[7] An uncontrolled trial evaluated simultaneous lifestyle intervention and CBT for depression reported much larger weight loss (i.e., mean weight loss of −10.4 kg) than typically observed in either depressed or nondepressed samples but only included 9 participants.[8] Another small uncontrolled trial tested the simultaneous delivery of a lifestyle intervention and brief behavior therapy for depression in 14 individuals [9] and found significant changes in weight and depression, however weight loss was also modest (i.e., mean = −2.5 kg) relative to nondepressed samples.[7] Given that the bulk of the evidence shows that people with depression lose less weight than their non-depressed counterparts, specialized interventions appear to be needed.

Administering weight loss and depression treatments simultaneously has not improved weight loss outcomes over a lifestyle intervention alone.[5] A sequential approach that involves treating depression first allows the lifestyle intervention to be introduced after depression symptoms have subsided. The present randomized clinical trial tests whether behavior therapy for depression administered prior to a lifestyle intervention facilitates
greater weight loss and improved depressive symptoms at 6 and 12 months than a lifestyle intervention alone in depressed obese women. We chose behavior therapy (also known as “behavioral activation”) which employs a structured approach to fostering behaviors that move the individual toward their value-driven life goals and reducing behaviors that are counterproductive to goals and generate negative affect [10, 11]. The focus on increasing healthy behaviors and eliminating avoidance behavior is very consistent with the goals of behavioral therapy for obesity. Behavior therapy for depression has well-established efficacy in a variety of populations and settings [12–15].

Materials and Methods

Sample—Detailed design and methods information has been published elsewhere.[16] Briefly, obese women (BMI 30–40 kg/m²) with major depressive disorder between ages 21–65 years were recruited (July 2007-March 2010) from the community and primary care population at the University of Massachusetts Medical School. The CONSORT diagram in Figure 1 shows participant flow through the study. The Institutional Review Board approved study protocol. Exclusion criteria included currently smoking, bipolar disorder, psychotic disorder, bulimia, post-traumatic stress disorder, type 1 or 2 diabetes, or medications that affect weight. The most common exclusion medications were tricyclic antidepressants and mood stabilizers.

Screening and Informed Consent—Participants were invited to an in-person screening appointment at the laboratory, which included written informed consent; depression assessment via the Structured Clinical Interview for DSM-IV (SCID-IV),[17] the Beck Depression Inventory- II (BDI-II)[18] and the Hamilton Rating Scale for Depression (HRSD);[19] physical measurements (weight and height); and medical history, medication, and physical activity. The SCID-IV and HRSD were administered by a licensed psychologist or a clinical psychology post-doctoral fellow under the supervision of a licensed psychologist. The clinical assessors also administered the BDI-II and HRSD at this visit. Eligible participants then attended a separate baseline visit with a phlebotomist for a fasting blood draw and weight and blood pressure measurements. BDI-II and HRSD were reassessed at the baseline visit to insure the participant was still eligible. The study was monitored by a Data and Safety Monitoring Review Board.

Randomization

Participants were randomized to the behavior therapy with lifestyle intervention (BA) or lifestyle intervention only (LI) conditions. Participants were stratified into 4 strata based on antidepressant medication status and depression severity (HRSD; 13–18, 19–24). Within each stratum, the biostatistician randomized participants at a 1:1 ratio to the conditions in randomly permuted blocks of size 3 and 6 using the ralloc program in Stata.[20]

Measures

All measures were administered at baseline and 6- and 12-months.
**Weight**—The primary outcome was percent change in weight from baseline to 6 months and from baseline to 12 months. Weight was measured without shoes using the digital Tronix scale.

**Depression**—Diagnosis of major depressive disorder was obtained via the SCID-IV using blind assessors.[17] The BDI-II,[21] a 21-item self-report questionnaire of depressive symptoms and the HRSD,[22] a 17-item clinician rating scale, were used to measure depression severity, treatment response, and remission. Treatment response is defined on both the HRSD and BDI-II as at least 50% reduction from baseline. Remission is defined as return to the normal range: HRSD <7 and BDI-II<10.[14]

**Dietary Intake**—Dietary intake was assessed with 3 computer-assisted telephone interview 24-hour recalls (24HRs) using the multipass method by blinded dietitians on randomly selected days (1 weekend and 2 weekdays) over a 3-week period, which has been deemed sufficient to characterize dietary intake.[23–25] Data were analyzed using the Nutrition Data System for Research (version 2010, Nutrition Coordinating Center, University of Minnesota, MN).[26]

**Physical Activity**—Physical activity was assessed in an interview-administered 24-hour physical activity recall survey which our group has validated against accelerometers.[27–29] Total minutes of moderate or greater intensity physical activity were summed.

**Blood Pressure**—Blood pressure was measured with a Dinamap XL automated BP monitor by study personnel blinded to treatment condition.

**Blood Lipids**—HDL-C was measured in the super natant after magnesium-phosphotungstate precipitation of apo B-containing lipoproteins. LDL-C was calculated by the Friedewald formula, i.e., LDL-C = total cholesterol – [triacylglycerol (TG)/5 + HDL-C].[30] When TG exceeded 400 mg/dl, the LDL-C was not calculated. All assays met the criteria of the CDC-NHLBI Lipid Standardization Program.[31, 32]

**Conditions**

Both conditions involved an Intensive Treatment phase and a Maintenance phase. The Intensive Treatment phase lasted 6-months and involved 26 sessions. Ten sessions were 60-minute individual sessions, and 16 sessions were 90-minute group behavioral weight loss sessions. The timing of the individual and group visits differed between the two conditions (Figure 2). In the BA condition, participants had 10 weekly individual visits of behavior therapy delivered by master- or doctoral-level counselors, with group behavioral weight loss visits starting on week 9. Participants in the LI condition began both the group behavioral weight loss sessions and individual health education sessions on week 1. Health education sessions were added to serve as an attention control for the nonspecific effects of behavior therapy.[33] The maintenance phase consisted of 6 monthly 90-minute group sessions and 6 monthly 20-minute counseling phone calls by their therapist or health education counselor, depending on their condition assignment.
BA Condition

**Lifestyle Intervention**—The Diabetes Prevention Program (DPP) Lifestyle Intervention protocol was delivered by a dietitian and exercise physiologist.[34] Participants received calorie goals estimated to produce a weight loss of 0.5-1 kgs per week and asked to work toward the goal of 30 minutes of moderate physical activity on 5 days/week.[35]

**Behavior Therapy**—Behavioral activation is an evidence-based treatment for depression.[36] The brief version developed by Lejuez and colleagues[11] was employed in 10 weekly sessions at the beginning of the Intensive phase and 10 telephone calls during the Maintenance phase. Behavior therapy involves structured attempts to engender increases in behaviors that are likely to bring the patient into contact with positive and productive experiences, thereby producing improvements in thoughts, mood, and overall quality of life.[10] The protocol includes activity monitoring and scheduling within an idiographic, values-driven framework.[11, 37, 38]

LI Condition

**Lifestyle Intervention**—Although the timing of the group visits differed between conditions, the content of the lifestyle intervention in the LI condition was identical to the BA condition as described above.

**Attention Control (Health Education)**—Health educators with no training in psychotherapy conducted the 10 individual health education sessions and the 10 phone calls during the Maintenance phase. Participants could select from 23 different women’s health topics including menopause, skin health, and breast self-exams.

Sample Size Considerations

This study randomized 161 participants into two conditions (78 were randomized to BA and 83 to LI). The original sample size estimation suggested 174 participants would be sufficient for approximately 80% power for detecting differences in weight between the conditions assuming a weight change difference of 3.1 kg at 1-year (standard deviation = 5.5 kg) and a 25% loss-to-follow-up rate. At the point at which 104 participants had reached their 1-year follow-up visit we had a 1-year drop-out rate of 13.5%, much lower than anticipated. The data and safety monitoring board approved an adjustment to the sample size to 161 based on the lower than drop-out rate. The final drop-out rate was at 1-year was 15.5%, resulting in 80% power for detecting the desired/anticipated effect size.

Statistical Analyses

The primary aims were to compare percent change in body weight between the two randomized groups at 6-months and 1-year follow-up using intent-to-treat analyses where all randomized cases were included in the analysis in their original condition. Data were censored due to pregnancy for 1 participant at 6-months and 3 participants at 12-months, and due to bariatric surgery for 1 participant at 12-months. An additional 16 participants were missing 6-month weight data, and 25 were missing 12-month weight data. Absolute change in depression symptoms was a secondary outcome. Daily energy intake, physical activity,
blood pressure, and lipids were tertiary outcomes. Linear mixed modeling, using SAS PROC MIXED [39] was employed to test time and condition interactions to assess whether within-subject changes in outcome variables differed by condition at 6 and 12 months. Antidepressant medication use was included as a time-varying covariate for depression analyses. Baseline outcome values also were included in the model as covariates to account for possible regression to the mean. [40] Binary versions of the outcomes (e.g., depression remission) were modeled using generalized estimating equations (GEE) logistic regression to account for within-subject correlation [41] including the same predictors as the corresponding linear mixed models. Exploratory analyses were conducted to understand the association between depression remission and weight change. Analyses were conducted in SAS (Version 9.2, SAS Institute, Cary, NC).

**Results**

**Descriptive Statistics**

Overall, mean age was 45.9 years old (SD=10.8), with a mean BMI of 35.4 (SD=3.3) kg/m$^2$, and mean BDI-II score of 21.1 (SD=5.8). At baseline, 29.5% of participants in the BA condition and 31.1% of participants in the ST condition were taking antidepressant medications (p=0.86). The BA condition had a higher mean BMI 36.0 (SD = 3.2) kg/m$^2$ than the LI condition 34.8 kg/m$^2$ (SD = 3.3; t(159) = −2.29, p = 0.02; d = 0.17; Table 1). Rates of anxiety disorders (24% and 30%), attention deficit/hyperactivity disorder (26%, 35%), and binge eating disorder (21%, 17%) were consistent with previous studies [42], but did not differ significantly by condition. No other characteristics differed by condition (Table 1). Seventeen women in the BA condition and 27 women in the LI condition experienced at least one depression-related adverse event during the course of the study (p=0.15), which was defined as suicidal ideation and/or severe depression (BDI ≥30 or HRSD ≥25).

**Weight Loss**

At 6-months, no differences in weight loss were observed between the BA condition (mean=−3.0%, SE = 0.65) and the LI condition (mean=−3.7%, SE = 0.63; t(143)=0.72, d=0.12, p =0.48). Participants in the BA condition were no more likely to achieve the 7% weight loss goal at 6-months (19.8%) than participants in the LI condition (23.0%; p = 0.65). Findings were similar at 12 months: no significant differences were found in mean percent weight loss between the BA (mean=−2.6%, SE = 0.77) and the LI conditions (mean = −3.1%; SE = 0.74, t(143)=0.48, d= 0.09.; p = 0.63), or for the proportion of participants achieving the 7% weight loss goal (BA: 22.5%, ST: 19.1%; p = 0.62).

**Depression**

At 6 months, the BA condition showed significantly greater declines in BDI-II scores (mean = −12.5, SE = 0.85) than the LI condition (mean = −9.2, SE = 0.80; t(144)= −2.87, d=0.48, p = 0.005). Similarly at 12 months, significantly greater improvements were observed in BA (mean = −12.6, SE = 0.97) relative to LI (mean = −9.9, SE = 0.93, t(144)= −2.02, d= −0.36; p = 0.045). At 6 months, BA (mean= −8.7, SE= 0.69) showed marginally significantly greater declines in mean HRSD scores than LI (mean= −6.9, SE=0.65; t(145)= −1.83, d=
At 12-months, BA declined by an average of −8.9 (SE=0.72), and LI declined by an average of −7.6 (SE=0.70) but the difference between conditions was not significant $t(145)=-1.22$, $d=-0.21$, $p=0.2233$). In terms of treatment response, using the BDI-II, 66.4% of BA participants and 44.4% of LI participants were considered responsive to treatment at 6 months ($p=0.01$; Table 3). The difference between conditions was also significant at 12 months ($p=0.01$). Using the HRSD, 69.7% of BA participants responded versus 56.1% of LI participants at 6 months ($p=0.09$). The difference between conditions (BA: 72.3%; LI: 65.9%) was not significant at 12 months ($p=0.44$). In terms of remission, using the BDI-II, 61.2% of BA participants and 39.7% of LI participants remitted at 6-months ($p=0.01$), and the difference was also significant at 12-months (BA: 66.8%; ST: 47.2%; $p=0.02$). Using the HRSD, 69.2% of BA participants remitted versus 50.5% of LI participants at 6 months ($p=0.0261$), but the difference were not significant at 12 months (BA: 68.3%; LI: 62.9%; $p=.52$).

**Depression Remission and Weight Loss**

Participants who were in remission from depression at 6 months per the BDI-II lost greater weight at 6 months (mean = −4.29%; SE=0.52%) than those who did not (mean= −2.48%, SE=0.53%; $t(144)=3.19$, $d=-0.41$, $p=0.0018$; Table 4), regardless of assigned treatment condition. Results were similar for the HRSD; at 6 months participants in remission lost greater weight (mean = −3.80%; SE=0.50%) than those who did not (mean = −2.72%; SE=0.55%; $t(144)=2.00$, $d=-0.24$, $p=0.048$).

**Diet and Physical Activity**

At 6-months, change in daily energy intake from baseline did not differ by treatment condition (mean = −502.2 kcal, SE = 51.4 for BA and −548.1 kcal, SE = 48.3 for LI, $t(146)=0.65$, $d=0.11$; $p = 0.52$). At 12 months, however, LI showed greater declines in their dietary intake from baseline (mean = −649.1 kcal, SE = 57.0) than BA (mean = −399.6 kcal, SE =58.3; $p = 0.0027$, $d=0.54$). Change in minutes of daily physical activity from baseline did not differ between the BA and IL conditions at 6-months ($t(138)=-0.44$, $d=-0.08$, $p=0.66$) or 12 months ($t(138)=1.06$, $d=0.22$, $p=0.23$; Table 2).

**Lipids and Blood Pressure**

Percent changes in lipid levels, adjusting for use of lipid-lowering medication, did not differ by condition at 6 months (for total cholesterol, $t(140)=0.70$, $d=0.12$, $p=0.49$; for HDL, $t(140)=0.15$, $d=0.03$, $p=0.88$; for LDL, $t(139)=0.92$, $d=0.16$, $p=0.36$; for total/HDL ratio, $t(139)=0.05$, $d=0.010$, $p=0.96$; Table 2). At 12 months, the two conditions did not differ significantly regarding change in total cholesterol ($t(140)=0.59$, $d=0.10$, $p=0.54$) or LDL ($t(139)=-0.01$, $d=-0.02$, $p=0.99$), but significant differences emerged for HDL and total/HDL ratio, such that BA had greater improvement in HDL levels (BA mean change= 6.80%, SE = 1.70%; LI mean change = −2.25%, SE=1.65; $t=2.97$, $d=0.53$, $p=0.004$) and a greater reduction in the total cholesterol/HDL ratio (BA mean change = −5.63%, SE = 2.11%; LI mean % change = 1.52%, SE=2.07; $t(139)=-2.42$, $d=-0.44$, $p = 0.017$). Neither systolic nor diastolic blood pressure change differed between the two conditions at 6 months (systolic blood pressure: $t(142)=-0.32$, $d=-0.05$, $p=0.75$; diastolic blood pressure: $t(142)=0.16$, $d=0.03$, $p=0.87$) or 12 months (for systolic blood pressure, $t(142)=0.73$, $d=0.13$, $p=0.47$).


**d=0.13, p=0.47; for diastolic blood pressure, t(142)=1.64, d=0.29, p=0.10; Table 2), adjusting for antihypertensive medication.**

**Attendance**—During the 6-month intensive intervention phase, attendance to individual visits (total possible = 10), group visits (total possible = 16), and total visits (total possible = 26) were analyzed separately. Participants in the BA condition (mean = 7.8, sd= 2.81) attended significantly more individual sessions compared to the LI condition (mean = 6.63, sd=3.21; F (1, 160) = 6.14, p= 0.014). However, participants in the LI condition (mean = 9.95, sd= 4.67) attended significantly more group sessions compared to the BA condition (mean = 8.29, sd=5.27; F (1, 160) = 4.46, p=.036), possibly due to condition differences in timing of visits. No differences emerged between the BA condition (mean= 17.79, sd=9.03) and the LI condition (mean= 17.95, sd=8.59) on total visits [F(1, 160)= 0.03, p= 0.91].

**Discussion**

A sequential approach to treating depression and obesity was found to be more effective than a lifestyle intervention alone on depression but not weight. The BA condition had a 35% and 29% higher depression remission rate at 6-months and 1-year, respectively. It is notable that the BA condition lost the same amount of weight in 6-months as the LI condition in two-thirds the time, given that the BA condition devoted the first 8 weeks to depression treatment. Weight loss in this study was comparable to weight loss reported in other lifestyle intervention studies in depressed samples,[2, 5, 9] but somewhat less than trials of non-depressed samples such as the DPP where 33% of women achieved 7% weight loss goal at 6 months (versus 21% of our participants).[42] In spite of no group differences in weight, physical activity, dietary intake, and LDL-C, the BA condition revealed an advantage at 1-year on HDL-C and the total-C/HDL-C ratio. Given the lack of effect on weight, physical activity, and diet, it is unclear why the BA condition showed an advantage on HDL-C.

Participants who remitted from depression achieved statistically and clinically greater weight loss than those who did not. These results suggest that depression may interfere with weight loss, and that depressed persons who remit are capable of clinically significant weight loss. Brief behavior therapy may not have been intensive enough for the individuals who did not experience remission. We originally selected a brief therapy given the evidence for its efficacy[11] and our concern for minimizing the number of visits of an already intensive lifestyle intervention (i.e., 22 visits). Further research is needed to understand the characteristics of non-responders since they appear to account for the suppressed weight loss outcomes in this population. When counseling depressed individuals for weight loss, clinicians should closely monitor changes in weight and depression symptoms in the first several weeks of a weight loss program to identify non-responders early in the process and intensify treatment as needed.

Although the BA condition was more effective in reducing depression, consistent with Linde and colleagues,[5] a lifestyle intervention also appears to be quite effective in reducing depressive symptoms with remission rates ranging from 39.7–50.5% at 6-months and 47.2–
62.9% at 12-months, depending on the measure. The LI condition also received attention control health education visits, although it is not clear why these would impact depression.

Overall, program attendance was not different between conditions, however, differences emerged between conditions for individual and group visits. Participants in the BA condition attended more individual visits than LI participants, an effect that could be due to time, since BA individual visits were clustered in the first 10 weeks of the program and LI visits were spread out across the program. The effect could also have been due to visit content, such that individuals could have found behavioral activation more interesting than health education, which was not directly relevant to weight loss. LI participants had greater group visit attendance than BA participants. Because content was identical, this finding might be due to time, since BA participants did not start group weight loss visits until week 9. Generally attendance declines over time in a trial, thus the pattern of differences suggests an effect of time. Declining attendance over time has implications for sequential interventions, such that lower attendance may be observed in the second intervention in the sequence. It is notable that weight loss outcomes were similar across conditions, even though BA participants attended fewer group weight loss visits on average.

The present study has some limitations. About 15% of participants were loss-to-follow up at 1-year. However, this is lower than the only other trial[5] of women with comorbid obesity and depression (i.e., 26% at 1 year). Also a possible limitation is that the failure to find weight loss differences could possibly be due to the fact that the BA condition spent less calendar time focused on weight loss (i.e., 16 weeks) during the intensive phase of treatment than the LI condition (i.e., 24 weeks; Figure 2). The lifestyle intervention included a goal of 1–2 pound weight loss per week, thus LI participants had more weeks to work on that goal. It was originally hypothesized that by improving depression symptoms, the BA condition would surpass the LI condition, but this did not occur. The finding of no differences in weight loss between conditions suggests that delaying weight loss intervention for the purpose of providing 8 weeks of behavior therapy does not compromise weight loss over a 6 month period. Physicians should advise patients with depression that the time invested in behavior therapy will not set their weight loss progress back, but it will increase their chance of recovering from depression. Another limitation is that group differences in depression were significant on the BDI-II at 6-and 12-months, but on the HRSD they only approached significance at 6-months and were not significantly different at 12-months. One reason for the discrepancy is that the HRSD has a larger number of items pertaining to somatic symptoms relative to cognitive and behavioral symptoms compared to the BDI.[43] Obesity and its comorbid physical conditions (e.g., obstructive sleep apnea, osteoarthritis) may generate somatic symptoms independent of depression, thus HRSD scores may show less change with depression intervention than BDI scores in an obese sample. Similar findings have been observed in multiple sclerosis patients.[44] The sample was also largely non-Hispanic white, limiting the generalization of results to minority populations. Further, exclusion criteria prevent generalization to people with type 2 diabetes or severe depression. However, psychiatric disorders that are frequently co-morbid with depression (i.e., anxiety disorders and binge eating disorder) were included.
In summary, brief behavior therapy for depression effectively reduces depression symptoms when administered directly prior to a lifestyle intervention in depressed women. Lifestyle interventions also appear to have a significant impact on depressive symptoms, however people achieving full remission from depression tend to have weight loss outcomes equivalent to studies of non-depressed patients. Future studies should explore individual characteristics that distinguish individuals with depression and obesity who are able to lose weight from those who are not. The impact of depression on the ability to lose weight may be a function of depression itself as well as the myriad co-morbidities that often complicate depression. Future studies should examine whether more intensive behavior therapy for depression prior to a lifestyle intervention would impact weight outcomes in this population.

Acknowledgments

The project described was supported by grant 1R01MH078012 to Dr. Pagoto from the National Institute of Mental Health. Partial salary support for Dr. Waring is provided by National Heart Lung Blood Institute grant 1U01HL105268.

References

1. Pagoto, SL.; Schneider, KL.; Appelhans, B.; Curtin, C.; Hajduk, A. Psychological Co-morbidities of Obesity. In: Pagoto, SL., editor. Psychological Co-Morbidities of Physical Illness: A Behavioral Medicine Perspective. 1. New York, NY: Springer; 2011.
2. Pagoto SL, Bodenlos JS, Kantor L, Gitkind M, Curtin C, Ma Y. Association of major depression and binge eating disorder with weight loss in a clinical setting. Obesity. 2007; 15(11):2557–59. [PubMed: 18070746]
3. Clark MM, Niaura R, King TK, Pera V. Depression, smoking, activity level, and health status: pretreatment predictors of attrition in obesity treatment. Addict Behav. 1996; 21(4):509–13. [PubMed: 8830908]
4. Pekarik G, Blodgett C, Evans RG, Wierzbicki M. Variables related to continuance in a behavioral weight loss program. Addict Behav. 1984; 9(4):413–6. [PubMed: 6532151]
5. Linde JA, Simon GE, Ludman EJ, Ichikawa LE, Operskalski BH, Arterburn D, et al. A randomized controlled trial of behavioral weight loss treatment versus combined weight loss/depression treatment among women with comorbid obesity and depression. Ann Behav Med. 2011 Sep 28.
6. Pagoto SL, Kantor L, Bodenlos JS, Gitkind M, Ma Y. Translating the Diabetes Prevention Program into a hospital-based weight loss program. Health Psychol. 2008; 27(1):S91–S8. [PubMed: 18248110]
7. U.S. Preventive Services Task Force. Screening and interventions for overweight and obesity in adults. Rockville, MD: Agency for Healthcare Research and Quality; 2003. Report No.: 00–4084
8. Faulconbridge L, Wadden T, Berkowitz RI, Pulcini M, Treadwell T. Treatment of comorbid obesity and major depressive disorder: A prospective pilot study for their combined treatment. Journal of Obesity. 2011; 2011
9. Pagoto SL, Bodenlos JS, Schneider KL, Olenzki B, Spates RC, Ma Y. Initial investigation of behavioral activation therapy for co-morbid major depressive disorder and obesity. Psychotherapy Theory, Research, Practice, Training. 2008; 45(3):410–15.
10. Hopko DR, Lejuez CW, Ruggiero KJ, Eifert GH. Contemporary behavioral activation treatments for depression: Procedures, principles, and progress. Clin Psychol Rev. 2003; 23(5):699–717. [PubMed: 12971906]
11. Lejuez CW, Hopko DR, Hopko SD. A brief behavioral activation treatment for depression. Treatment manual. Behav Modif. 2001; 25(2):255–86. [PubMed: 11317637]
12. Cullen JM, Spates RC, Pagoto SL, Doran N. Behavioral activation treatment for major depressive disorder: A pilot investigation. The Behavior Analyst Today. 2006; 7(1):151–66.
13. Porter JF, Spates RC, Smitham S. Behavioral activation group therapy in public mental health settings: A pilot investigation. Prof Psychol Res Pract. 2004 Jun; 35(3):297–301.
14. Dimidjian S, Hollon SD, Dobson KS, Schmaling KB, Kohlenberg RJ, Addis ME, et al. Randomized trial of behavioral activation, cognitive therapy, and antidepressant medication in the acute treatment of adults with major depression. J Consult Clin Psychol. 2006 Aug; 74(4):658–70. [PubMed: 16881773]
15. Jacobson NS, Dobson KS, Truax PA, Addis ME, Koerner K, Gollan JK, et al. A component analysis of cognitive-behavioral treatment for depression. J Consult Clin Psychol. 1996; 64(2):295–304. [PubMed: 8871414]
16. Schneider KL, Bodenlos JS, Ma Y, Olendzki B, Oleski J, Merriam P, et al. Design and methods for a randomized clinical trial treating co-morbid obesity and major depressive disorder. BMC Psychiatry. 2008 Sep 15;8(1):77. [PubMed: 18793398]
17. Spitzer RL, Williams JB, Gibbon M, First MB. The Structured Clinical Interview for DSM-III-R (SCID). I: History, rationale, and description. Arch Gen Psychiatry. 1992; 49(8):624–9. [PubMed: 1637252]
18. Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: Psychometric properties. J Consult Clin Psychol. 1988; 56(6):893–7. [PubMed: 3204199]
19. Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry. 1960; 23:56–62. [PubMed: 14399272]
20. Ryan P. sxd1.1: Update to random allocation of treatment to blocks. Stata Technical Bulletin. 1999:36–7.
21. Beck, AT.; Steer, RA.; Brown, GK. Manual for the Beck Depression Inventory-II. San Antonio, TX: The Psychological Corporation; 1996.
22. Williams J. A structured interview guide for the Hamilton Depression Rating Scale. Arch Gen Psychiatry. 1988; 45(8):742–7. [PubMed: 3395203]
23. Nelson M, Black AE, Morris JA, Cole TJ. Between- and within-subject variation in nutrient intake from infancy to old age: estimating the number of days required to rank dietary intakes with desired precision. Am J Clin Nutr. 1989; 50(1):155–67. [PubMed: 2750688]
24. Liu K, Stamler J, Dyer A, McKeever J, McKeever P. Statistical methods to assess and minimize the role of intra-individual variability in obscuring the relationship between dietary lipids and serum cholesterol. J Chronic Dis. 1978; 31(6–7):399–418. [PubMed: 711832]
25. el Lozy M. Dietary variability and its impact on nutritional epidemiology. J Chronic Dis. 1983; 36(3):237–49. [PubMed: 6826688]
26. Buzzard IM, Price KS, Warren RA. Considerations for selecting nutrient-calculation software: evaluation of the nutrient database. Am J Clin Nutr. 1991; 54(1):7–9. [PubMed: 2058591]
27. Matthews CE, Freedson P, Hebert J, Stanek E, Ockene I, Merriam P. Comparison of physical activity assessment methods in the Seasonal Variation of Blood Cholesterol Levels Study. Med Sci Sports Exerc. 2000; 32(5):976–84. [PubMed: 10795789]
28. Matthews CE, Hebert JR, Freedson PS, Stanek EJ 3rd, Merriam PA, Ebbeling CB, et al. Sources of variance in daily physical activity levels in the seasonal variation of blood cholesterol study. Am J Epidemiol. 2001 May 15; 153(10):987–95. [PubMed: 11384955]
29. Matthews CE, Freedson PS, Stanek EJ, Hebert JR, Merriam PA, Rosal MC, et al. Seasonal variation of household, occupational, and leisure-time physical activity: Longitudinal analyses from the Seasonal Variation of Cholesterol Study. Am J Epidemiol. 2001; 153(2):172–83. [PubMed: 11159163]
30. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem. 1972; 18(6):499–502. [PubMed: 4337382]
31. Myers GL, Kimberly MM, Waymack PP, Smith SJ, Cooper GR, Sampson EJ. A reference method laboratory network for cholesterol: a model for standardization and improvement of clinical laboratory measurements. Clin Chem. 2000; 46(11):1762–72. [PubMed: 11067811]
32. Myers GL, Cooper GR, Winn CL, Smith SJ. The Centers for Disease Control-National Heart, Lung and Blood Institute Lipid Standardization Program. An approach to accurate and precise lipid measurements. Clin Lab Med. 1989; 9(1):105–35. [PubMed: 2538292]
33. Turner JA, Deyo RA, Loeser JD, Von Korff M, Fordyce WE. The importance of placebo effects in pain treatment and research. JAMA. 1994 May 25; 271(20):1609–14. [PubMed: 7880221]
34. DPP Research Group. The Diabetes Prevention Program (DPP): Description of lifestyle intervention. Diabetes Care. 2002; 25(12):2165–71. [PubMed: 12453955]
35. Haskell WL, Lee IM, Pate RR, Powell KE, Blair SN, Franklin BA, et al. Physical activity and public health: Updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. Med Sci Sports Exerc. 2007 Aug; 39(8):1423–34. [PubMed: 17762377]
36. NICE. The treatment and management of depression in adults (Updated edition). The British Psychological Society and The Royal College of Psychiatrists; 2010.
37. Martell, CR.; Addis, ME.; Jacobson, NS., editors. Strategies for guided action. New York: W. W. Norton; 2001. Depression in context.
38. Lejuez CW, Hopko DR, Acierno R, Daughters SB, Pagoto SL. Ten year revision of the Brief Behavioral Activation Treatment for Depression (BATD): Revised treatment manual (BATD-R). Behav Modif. 2011; 35:111–61. [PubMed: 21324944]
39. Littell, R.; Milliken, G.; Stroup, W.; Wolfinger, R. SAS System for Mixed Models. Cary, NC: SAS Institute Inc; 1996.
40. Chuang-Stein C, Tong DM. The impact and implication of regression to the mean on design and analysis of medical investigations. Stat Methods Med Res. 1997; 6:115–28. [PubMed: 9261911]
41. Molenberghs, G.; Verbeke, G. Models for discrete longitudinal data. New York: Springer Science; 2005.
42. DPP Research Group. Achieving weight and activity goals among diabetes prevention program lifestyle participants. Obes Res. 2004; 12(9):1426–34. [PubMed: 15483207]
43. Shafer AB. Meta-analysis of factor structures of four depression questionnaires: Beck, CES-D, Hamilton, and Zung. J Clin Psychol. 2006; 62(1):124–46.
44. Moran PJ, Mohr DC. The validity of the Beck Depression Inventory and Hamilton Rating Scale for Depression items in the assessment of depression among patients with multiple sclerosis. J Behav Med. 2005; 28(1):36–41. [PubMed: 15878754]
45. Kessler RC, Adler L, Ames M, Demler O, Faraone S, Hiripi E, et al. The World Health Organization Adult ADHD Self-Report Scale (ASRS): A short screening scale for use in the general population. Psychol Med. 2005 Feb; 35(2):245–56. [PubMed: 15841682]
Figure 1.
Figure 2.
Intervention Conditions
|                                | BA Condition (n=78) | LI Condition (n=83) | p-value |
|--------------------------------|---------------------|---------------------|---------|
| Age (years old)                | 45.6 (11.0)         | 46.2 (10.8)         | 0.59    |
| Race                           |                     |                     |         |
| Hispanic/Latina                | 11.5%               | 8.4%                | 0.51    |
| Non-Hispanic White             | 82.1%               | 88.0%               | 0.29    |
| Non-Hispanic Black/African-American | 5.1%          | 3.6%                | 0.64    |
| Asian                          | 1.3%                | 1.2%                |         |
| American Indian Alaska Native  | 9.0%                | 3.6%                |         |
| Multi-ethnic                   | 2.6%                | 3.6%                |         |
| Education                      |                     |                     | 0.16    |
| Less than high school          | 0%                  | 0%                  |         |
| High School                    | 10.3%               | 6.0%                |         |
| Some college/technical school  | 51.3%               | 41.0%               |         |
| College degree                 | 20.5%               | 20.5%               |         |
| More than college              | 17.9%               | 17.9%               |         |
| BMI (kg/m$^2$)                 | 36.0 (3.2)          | 34.8 (3.3)          | 0.02    |
| Weight (kg)                    | 95.8 (11.9)         | 92.5 (10.1)         | 0.07    |
| Depression                     |                     |                     |         |
| HDRS                           | 17.9 (3.5)          | 17.9 (3.5)          | 0.68    |
| BDI-II                         | 21.1 (5.7)          | 21.0 (5.9)          | 0.58    |
| Psychiatric co-morbidities     |                     |                     |         |
| Anxiety disorder (any)         | 24%                 | 30%                 | 0.41    |
| Binge eating disorder          | 21%                 | 17%                 | 0.55    |
| Attention deficit hyperactivity disorder $^\dagger$ | 26% | 35% | 0.21 |
| Moderate intensity physical activity (mins/day) | 10.2 (17.9) | 8.9 (14.0) | 0.59 |
| Daily energy intake (kcal/day)  | 2213.8 (936)       | 2079.7 (580) (579.8) | 0.273 |
| Blood Pressure (mmHg)          |                     |                     |         |
| Systolic BP                    | 127.5 (11.7)        | 127.9 (13.3)        | 0.26    |
| Diastolic BP                   | 74.6 (9.3)          | 76.5 (8.6)          | 0.51    |
| Total cholesterol (mg/dL)      | 5.14 (.92)          | 5.28 (1.12)         | 0.30    |
| High density lipoprotein cholesterol (HDL-C) | 1.30 (.29) | 1.30 (.26) | 0.28 |
| Low density lipoprotein cholesterol (LDL-C) | 3.15 (.85) | 3.29 (.94) | 0.94 |
| Cholesterol/HDL ratio          | 4.3 (1.2)           | 4.2 (1.1)           | 0.67    |

$^\dagger$ As measured by the ADHD Self Report Scale[45]
Table 2

Effect of sequential addition of behavioral activation for depression to a lifestyle intervention on weight loss among women with comorbid obesity and major depressive disorder, M (SE)

|                      | BA Condition (N = 78) | LI Condition (N = 83) | p-value |
|----------------------|-----------------------|-----------------------|---------|
| **Primary outcome**  |                       |                       |         |
| Weight loss (%)      |                       |                       |         |
| 6 mos                | −3.0 (0.7)            | −3.7 (0.6)            | 0.48    |
| 12 mos               | −2.6 (0.8)            | −3.1 (0.7)            | 0.72    |
| **Secondary outcomes** |                     |                       |         |
| Depression severity (BDI-II) |               |                       |         |
| 6 mos                | −12.5 (0.8)           | −9.2 (0.8)            | 0.005   |
| 12 mos               | −12.6 (1.0)           | −9.9 (0.9)            | 0.045   |
| Depression severity (HRSD) |                   |                       |         |
| 6 mos                | −10.9 (0.8)           | −9.2 (0.8)            | 0.12    |
| 12 mos               | −11.5 (0.8)           | −9.7 (0.8)            | 0.12    |
| Dietary energy intake (kcal/day) |             |                       |         |
| 6 mos                | −502.2 (51.4)         | −548.1 (48.3)         | 0.52    |
| 12 mos               | −399.6 (58.3)         | −649.1 (57.0)         | 0.002   |
| Moderate intensity physical activity (mins/day) |         |                       |         |
| 6 mos                | 7.0 (2.7)             | 8.7 (2.5)             | 0.66    |
| 12 mos               | 10.6 (2.9)            | 5.6 (2.9)             | 0.23    |
| Systolic blood pressure (mmHg) |         |                       |         |
| 6 mos                | −3.1 (1.3)            | −2.5 (1.2)            | 0.75    |
| 12 mos               | −0.7 (1.2)            | −1.9 (1.2)            | 0.47    |
| Diastolic blood pressure |                   |                       |         |
| 6 mos                | −2.8 (0.8)            | −2.9 (0.8)            | 0.87    |
| 12 mos               | −0.3 (0.8)            | −2.1 (0.8)            | 0.10    |
| Cholesterol Total (%) |                       |                       |         |
| 6 mos                | −0.98 (1.40)          | −2.35 (1.34)          | 0.48    |
| 12 mos               | −0.02 (1.53)          | −1.17 (1.49)          | 0.59    |
| HDL-C (%)            |                       |                       |         |
| 6 mos                | 2.84 (1.60)           | 2.50 (1.53)           | 0.88    |
| 12 mos               | 6.80 (1.70)           | −0.25 (1.65)          | 0.0035  |
| LDL-C (%)            |                       |                       |         |
| 6 mos                | −1.45 (1.98)          | −3.99 (1.90)          | 0.36    |
| 12 mos               | 0.49 (2.68)           | 0.52 (2.61)           | 0.99    |
| Total Cholesterol/HDL-C ratio (%) |             |                       |         |
| 6 mos                | −3.08 (2.39)          | −3.25 (2.30)          | 0.96    |
| 12 mos               | −5.63 (2.11)          | 1.52 (2.07)           | 0.02    |
### Table 3
Response and Remission Rates on BDI-II and HRSD by Condition

| Outcome                  | BA  | LI  | p-value for difference<sup>(a)</sup> |
|--------------------------|-----|-----|-------------------------------------|
| **BDI-II response, raw %** |     |     |                                     |
| 6 mos                    | 65.7| 44.7| 0.02                                |
| 12 mos                   | 73.0| 50.0| 0.01                                |
| **BDI-II response, adjusted %<sup>†</sup>** |     |     |                                     |
| 6 mos                    | 66.4| 44.4| 0.01                                |
| 12 mos                   | 73.3| 49.3| 0.01                                |
| **BDI-II remission, raw %** |     |     |                                     |
| 6 mos                    | 59.7| 40.8| 0.03                                |
| 12 mos                   | 66.7| 48.5| 0.05                                |
| **BDI-II remission, adjusted %** |     |     |                                     |
| 6 mos                    | 61.2| 39.7| 0.01                                |
| 12 mos                   | 66.8| 47.2| 0.03                                |
| **HRSD response, raw %**  |     |     |                                     |
| 6 mos                    | 69.1| 56.6| 0.17                                |
| 12 mos                   | 71.4| 66.2| 0.57                                |
| **HRSD response, adjusted %** |     |     |                                     |
| 6 mos                    | 69.7| 56.1| 0.09                                |
| 12 mos                   | 72.3| 65.9| 0.44                                |
| **HRSD remission, raw %**  |     |     |                                     |
| 6 mos                    | 67.7| 51.3| 0.06                                |
| 12 mos                   | 66.7| 63.2| 0.71                                |
| **HRSD remission, adjusted %** |     |     |                                     |
| 6 mos                    | 69.2| 50.5| 0.03                                |
| 12 mos                   | 68.3| 62.9| 0.52                                |

<sup>(a)</sup>Fisher’s exact test for raw %’s, chi-square probability for adjusted %’s from GEE logistic regression

<sup>†</sup>Adjusted for antidepressant medication status
Table 4
Main effect analyses for depression treatment response and remission on percent weight change

|                  | Mean (SE) adjusted % weight change | p-value for between-group difference | p-value for group × visit interaction |
|------------------|------------------------------------|-------------------------------------|---------------------------------------|
| **BDI response:**|                                    |                                     |                                       |
|                  | Non-responder                      | Responder                           |                                       |
| 6 mos            | −2.33 (0.54)                       | −4.25 (0.51)                        | 0.0007                                |
| 12 mos           | −1.81 (0.66)                       | −3.54 (0.58)                        | 0.0101                                |
| **BDI remission:**|                                    |                                     |                                       |
|                  |                                    |                                     | 0.8758                                |
| 6 mos            | −2.48 (0.53)                       | −4.29 (0.52)                        | 0.0018                                |
| 12 mos           | −1.90 (0.65)                       | −3.61 (0.60)                        | 0.0129                                |
| **HRSD response:**|                                    |                                     |                                       |
|                  |                                    |                                     | 0.7506                                |
| 6 mos            | −2.61 (0.56)                       | −3.81 (0.49)                        | 0.0271                                |
| 12 mos           | −2.21 (0.70)                       | −3.17 (0.57)                        | 0.1562                                |
| **HRSD remission:**|                                    |                                     |                                       |
|                  |                                    |                                     | 0.4562                                |
| 6 mos            | −2.72 (0.55)                       | −3.80 (0.50)                        | 0.0479                                |
| 12 mos           | −2.52 (0.68)                       | −3.05 (0.58)                        | 0.4308                                |