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Intentional Weight Loss and Changes in Symptoms of Depression: A Systematic Review and Meta-Analysis

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Abstract

Objective—Obesity is related to increased risk of several health complications, including depression. Many studies have reported improvements in mood with weight loss, but results have been equivocal. The present meta-analysis examined changes in symptoms of depression that were reported in trials of weight loss interventions. Between-groups comparisons of different weight loss methods (e.g., lifestyle modification, diet alone, pharmacotherapy) were examined, as were within-group changes for each treatment type.

Method—MEDLINE was searched for articles published between 1950 and January 2009. Several obesity-related terms were intersected with terms related to depression. Results were filtered to return only studies of human subjects, published in English.

Of 5971 articles, 394 were randomized controlled trials. Articles were excluded if they did not report mean changes in weight or symptoms of depression, included children or persons with psychiatric disorders (other than depression), or provided insufficient data for analysis. Thirty-one studies ($n = 7937$) were included. Two authors independently extracted a description of each study treatment, sample characteristics, assessment methods, and changes in weight and symptoms of depression. Treatments were categorized as: lifestyle modification, non-dieting, dietary counseling, diet-alone, exercise-alone, pharmacotherapy, placebo, or control interventions.

Results—Random effects models found that lifestyle modification was superior to control and non-dieting interventions for reducing symptoms of depression, and marginally better than dietary counseling and exercise-alone programs. Exercise-alone programs were superior to controls. No differences were found for comparisons of pharmacologic agents and placebos. Within-group analyses found significant reductions in symptoms of depression for nearly all active

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Conflicts of Interest

Fabricatore has served as a consultant for Pfizer, Merck, and Ethicon-Endosurgery, and has received research support (including funding for this study) from Merck. Although he is now employed by Nutrisystem, Inc., Fabricatore was employed full-time at the University of Pennsylvania (where he retains an adjunct appointment) at the time the study was completed. Wadden serves on the Advisory Boards of Novo Nordisk and Orexigen and has received research support from Orexigen and Pfizer. Nguyen is employed by Merck and Heymsfield was employed by Merck at the time the work was completed. Faith has served as a consultant to, and has received research support from, Merck. The other authors have no potential conflicts to declare.

interventions. A meta-regression found no relationship between changes in weight and changes in symptoms of depression in lifestyle modification interventions.

Conclusions—On average, obese individuals in weight loss trials experienced reductions in symptoms of depression. Future studies should examine incidence and resolution of clinically significant depressive disorders with weight loss interventions.

Keywords

Depression; Meta-Analysis; Diet; Exercise; Lifestyle; Pharmacotherapy; Obesity

Introduction

Over the past two decades, obesity has emerged as a serious public health concern. Approximately one-third of American adults are now obese, defined by a body mass index (BMI) ≥ 30 kg/m² (1). Obesity is an independent risk factor for diabetes, cardiovascular disease, and several cancers (2), leading to significantly increased mortality rates (3).

Depression is another health complication that is commonly associated with obesity. Odds of ever having met criteria for major depressive disorder are 20–50% higher among obese individuals than normal weight persons (4–6). Extremely obese persons are at even greater risk (5). The relationship between obesity and depression appears to be bi-directional; some longitudinal studies have shown that depression is associated with subsequent weight gain and obesity (7–12), whereas others have found that obesity is associated with the development of depression (13–14). Obese women are particularly vulnerable to depression (15–17).

Behavioral interventions for obesity induce mean weight losses of 5% to 10% of initial weight (18). Despite patients' remaining obese, these modest reductions result in significant improvements in metabolic risk factors for cardiovascular disease (19–22). Patients also experience improvements in body image (23–24), physical functioning (25–26), and quality of life (27–28). Moreover, intentional weight loss is often accompanied by improvements in mood (29). These favorable psychological findings stand in sharp contrast to early reports that linked dieting and weight loss to depression (30–31).

Weight loss medications may present an exception to the generally favorable changes in mood associated with weight loss. Rimonabant, a cannabinoid-1 receptor (CB1R) inverse agonist, was removed from the market in Europe in 2008 after it was found to be associated with unexpectedly high rates of serious adverse psychiatric effects that included depression, anxiety, and suicidal ideation and behavior (32–33). The U.S. Food and Drug Administration now requires that all new weight loss medications be routinely evaluated for their risk of depression, suicidal ideation, and related complications (34).

The present meta-analysis sought to examine whether different types of weight loss interventions (including lifestyle modification, non-dieting, dietary counseling, exercise-alone, and pharmacotherapy) are associated with differential changes in symptoms of depression among obese individuals. We also assessed, through meta-regression, the relationship between weight loss and changes in symptoms of depression. We are careful not to use the term “depression” per se because most weight loss studies have excluded persons with major depressive disorder or failed to use a validated diagnostic interview to assess for the presence of clinically significant depression.

Method

Data Sources

We searched the Ovid MEDLINE database for studies published between 1950 and January 2009. The search strategy was to intersect several terms related to obesity and weight change (obese, obesity, body mass index, adipose, adiposity, overweight, weight loss, weight gain, weight change, weight reduction, weight increase) with terms related to depression (mood, depressed, depression, depressive, suicide, suicidal). Results were filtered to return only studies of human subjects, published in English. Additionally, we reviewed studies of intentional weight loss interventions that we knew reported changes in symptoms of depression, despite their not being identified by the search strategy.

Study Selection

The MEDLINE search returned 8799 publications, of which 5971 were published in English and included human subjects. Only randomized controlled trials ($n = 394$) were considered for inclusion. In addition, weight and symptoms of depression must have been assessed at baseline and post-treatment. Trials were excluded if they: included only persons with binge eating disorder; included children or adolescents; reported weight change with antidepressant or other psychotropic therapies; or manipulated individual macro- or micronutrients without weight loss as an intended outcome. These criteria yielded 39 studies for potential inclusion.

Data Extraction

Each included article was reviewed by two authors (ANF and AH) to extract the duration of treatment, the method of assessing symptoms of depression, and a description of each study intervention (see Table 1). An intervention was coded as lifestyle modification if its description included: mention of counseling related to diet and exercise; mention of diet and exercise prescriptions plus behavioral interventions; or use of a known lifestyle modification intervention (e.g., the LEARN manual) (35). We defined non-dieting interventions as those that were described as such, or that focused on health and self-acceptance rather than weight loss. We coded interventions that included counseling and instruction to achieve a reduction in calorie intake, without increasing energy expenditure, as dietary counseling. Interventions that manipulated energy level and content of participants' diets, but included no counseling, were coded as diet-alone interventions. Exercise-alone programs were defined as interventions in which increased physical activity was prescribed or supervised in the absence of instructions to reduce calorie intake. Pharmacologic interventions were those that included administration of orlistat, sibutramine, or rimonabant without an accompanying lifestyle modification program. Nearly all pharmacotherapy studies included a placebo group. Control groups included persons who were placed on a waiting list for one of the above active treatments, or who received only standard advice/printed materials, an attention-control intervention, or no treatment. (No studies of bariatric surgery met inclusion criteria.)

For each study group, the same two authors also extracted sample size and participants' mean ($\pm$ standard deviation or standard error) weights and depression scores at baseline and at post-treatment. BMI was extracted when weight was not reported. Data from intent-to-treat samples and analyses were used when available. When only change values were reported for weight or symptoms of depression, or when results were collapsed across multiple groups, we contacted the corresponding authors to request mean values (and a measure of variability) for each study group. Inability to ascertain the necessary data led to exclusion of eight studies. For the final 31 included studies (36–66) (total $n = 7937$), we requested the correlations between pre- and post-treatment values for weight and symptoms

of depression. When the correlations were not available, a conservative default value of 0.50 was used.

Two additional variables – presence/absence of supervised exercise sessions and intensity of counseling – were extracted for each treatment group. Interventions that included at least 16 counseling visits in the first 6 months (as in the Diabetes Prevention Program) (76) or before treatment ended (whichever occurred first) were coded as high-intensity-counseling. Those with fewer than 16 sessions in 6 months were coded as moderate-intensity-counseling. Interventions that included advice, provision of materials, or assessments with no mention of counseling were coded as low-intensity-counseling.

Statistical Analyses

The variety of interventions precluded a single meta-analysis. Thus, we computed separate between-groups effects for each of the following comparisons, which commonly occurred in the included studies: 1) lifestyle modification vs. control; 2) lifestyle modification vs. non-dieting; 3) lifestyle modification vs. dietary counseling; 4) lifestyle modification vs. exercise-alone; 5) exercise-alone vs. control; and 6) pharmacologic agent vs. placebo. In addition, we computed within-groups effects (i.e., changes from baseline) for each type of active treatment, as well as for diet-alone interventions.

A random effects model was computed for each of the six between-groups comparisons described above. For each analysis, we report the standardized mean difference (SMD) accompanied by its 95% confidence intervals (CI) and associated Z and *p* values. We assessed the statistical significance and magnitude of heterogeneity of effects using the Q test and I^2 statistic, respectively. (The latter measures the proportion of the observed variance that is accounted for by true differences in effect size.) Funnel plots were reviewed and a fail-safe N (the number of studies with null findings that would need to be included in the analysis to render a significant effect non-significant) was computed for each analysis to examine the possibility of publication bias. For the within-groups comparisons (of baseline vs. post-treatment symptoms of depression), a random effects model was computed for each active treatment type. When possible, meta-regressions also were conducted to determine the relationships of group-level covariates (e.g., mean weight change, treatment duration, counseling intensity, and the presence of supervised exercise sessions) to the effect size for changes in depressive symptoms. All analyses were conducted using Comprehensive Meta-Analysis software (77).

Results

Of the 31 included studies, 7 and 9 reported results from intent-to-treat and completers' analyses, respectively. Handling of missing data was not specified in the remaining 15 studies. Correlations between pre- and post-treatment values for weight and for depressive symptoms were unattainable for 65.8% of comparisons. The mean observed correlation was 0.54 (suggesting that the imputation of 0.50 for missing correlations was appropriate).

Between-Groups Comparisons of Active Treatments

The 31 included studies contributed a total of 34 comparisons to the six between-groups analyses. There were seven comparisons of lifestyle modification vs. control (total *n* = 1216), six of lifestyle modification vs. non-dieting (*n* = 364), three of lifestyle modification vs. dietary counseling (*n* = 95), four of lifestyle modification vs. exercise-alone (*n* = 281), and five of exercise-alone vs. control (*n* = 320). The nine comparisons of pharmacotherapy vs. placebo (*n* = 6075) included one group treated with orlistat, two with sibutramine, three with 5 mg of rimonabant, and three with 20 mg of rimonabant.

As shown in Figure 1, lifestyle modification programs were found to induce significantly greater reductions in symptoms of depression than control (Panel A) and non-dieting (Panel B) interventions. Fail-safe N analyses revealed that 26 and 6 comparisons with null findings would need to have been added to the 7 and 6 comparisons, respectively, of lifestyle modification vs. control and lifestyle modification vs. non-dieting interventions to render the meta-analytic results non-significant.

Reductions in symptoms of depression were marginally greater with lifestyle modification than with dietary counseling (Panel C, $p = 0.053$) and exercise-alone (Panel D, $p = 0.054$). The largest effect size was found for the comparison of exercise-alone with control (Figure 2), which significantly favored exercise for greater reductions in symptoms of depression. Eighteen comparisons, all with null findings, would need to have been added to the five comparisons of exercise-alone vs. control interventions in order to render the meta-analytic result non-significant. Pharmacologic interventions, as a whole, produced similar changes in symptoms of depression, compared with placebos (Figure 3).

Within-Groups Changes Observed in Each Treatment Type

Effect sizes for the within-groups changes in symptoms of depression (from baseline) could be computed for a total of 60 treatment groups. Among those, 27 groups received lifestyle modification, five received a non-dieting intervention, three received dietary counseling, eight received diet-alone, and seven received exercise-alone, for a total of 50 groups treated with non-pharmacologic interventions. Among 10 pharmacotherapy groups, one received orlistat, three received sibutramine, and three each received rimonabant at 5 mg and 20 mg.

As shown in Table 2, non-pharmacologic interventions, as a whole, were associated with significant reductions in symptoms of depression ($p < 0.001$). Examination of results from specific categories of non-pharmacologic interventions revealed significant changes in symptoms of depression in groups treated with lifestyle modification ($p < 0.001$), non-dieting interventions ($p = 0.002$), diet-alone ($p = 0.002$), and exercise-alone ($p = 0.006$), but not with dietary counseling ($p = 0.30$). The non-significant effect of dietary counseling may be due to the small number of studies included in that analysis or to an increase in symptoms of depression that was found in one group whose calorie intake was restricted by as much as 67%. Pharmacologic interventions, generally, induced a marginally significant reduction in symptoms of depression ($p = 0.07$). Separate analyses of rimonabant and non-rimonabant groups found no significant change in groups treated with rimonabant ($p = 0.53$), but a significant reduction in symptoms in groups treated with orlistat or sibutramine ($p = 0.007$). Further examination revealed that significant reductions were seen in the three groups treated with sibutramine ($p \leq 0.02$), but not in the group treated with orlistat ($p = 0.16$).

Effects of Covariates

Only the analysis of changes in depressive symptoms within groups treated with lifestyle modification was large enough to support post hoc meta-regression analyses. Weight change ($B = 0.16$), duration of treatment ($B = -0.01$), and counseling intensity ($B = 0.03$) were not significantly related to changes in symptoms of depression ($ps \geq 0.33$). The inclusion of supervised exercise sessions, however, was related to significantly greater reductions in symptoms of depression ($B = -0.28$, $p = 0.04$).

Discussion

This meta-analysis examined the effects of different weight loss interventions on symptoms of depression, and compared those effects across different types of treatment. In general, we found that nearly all non-pharmacologic weight loss approaches resulted in a significant

reduction in symptoms of depression, again contradicting early reports that dieting and weight loss precipitated mood disturbance. Comparisons of treatment types found that lifestyle modification induced significantly greater reductions in symptoms of depression than control and non-dieting interventions. Reductions in symptoms of depression were marginally greater with lifestyle modification than with alternative weight loss interventions, including dietary counseling and exercise-alone. Exercise-alone also was superior to control for reducing symptoms of depression. The significant between-groups effect sizes were in the small to medium range (78).

Two findings from the present analyses indicate that the reductions in symptoms of depression cannot be fully explained by weight loss. First, there were significant reductions in symptoms of depression with non-dieting programs, which were not intended to – and did not – induce weight loss. The beneficial effect of non-dieting on symptoms of depression may be due to the cognitive-behavioral strategies that encourage self-acceptance regardless of body weight. The same strategies may also reduce perceptions of stigma and of the severity of weight-related impairments, while fostering a sense of mastery and self-control that may have been previously limited in obese participants. Second, our meta-regression analysis of the lifestyle modification groups revealed that the within-groups effect for weight change was unrelated to the within-group effect for changes in symptoms of depression. That is, weight loss was not associated with increased or decreased symptoms of depression. Furthermore, neither the duration of treatment nor the intensity of the counseling intervention was related to the magnitude of change in depressive symptoms. Thus, other elements of treatment were likely responsible for the favorable effect on mood. Like those who received non-dieting interventions, obese individuals in lifestyle modification also may have achieved cognitive or behavioral changes that improved mood independently of the weight loss that resulted from those changes. They also may have benefited from the social support of their fellow group members and treatment providers. (Nearly all lifestyle modification programs studied here were delivered in group format.)

The meta-regression revealed that inclusion of a supervised exercise component was favorably related to changes in symptoms of depression among lifestyle modification participants. Several studies support a direct link between increased physical activity and improvements in mood (79–80). An alternative explanation for the added benefit of supervised physical activity sessions (which are typically done in groups) is that they carried many of the same benefits of the group counseling sessions, described above. Clinically, many obese patients report embarrassment about exercising at health clubs because they assume they will be unfavorably compared with others whom they perceive to be more fit, more attractive, more coordinated, or generally more competent to exercise. Exercising in the company of fellow participants in weight loss programs may have helped to normalize participants' perceptions of themselves in relation to others.

Our generally favorable findings contradict those of a previous meta-analysis that reported little improvement in quality of life (including depression) in randomized controlled weight loss trials (81). Maciejewski et al. analyzed results from eight studies that measured symptoms of depression with the BDI and found that the random-effects comparison of treatment and control interventions yielded a nonsignificant pooled effect size of 0.07 (95% CI = -0.32 to 0.46) (81). However, there are substantive differences between that analysis and ours, particularly with respect to the definitions of treatment and control arms. In only three of the eight studies included in the previous meta-analysis did the control participants receive no treatment (60,82–83), and in one of those, the active treatment was acupuncture (83). In three other studies, there were few differences between the interventions that were defined as treatment and control: group-based vs. individual lifestyle modification (84); cognitive-behavioral counseling plus nutrition education vs. cognitive-behavioral counseling

alone (85); and lifestyle modification vs. dietary counseling (86). In two other studies (which also were included in the present analysis), the comparisons appeared to be between lifestyle modification and non-dieting interventions. However, Maciejewski et al. classified the lifestyle modification program as the treatment in one study (38) and as the control in the other (54). By contrast, the present study provided operational definitions of treatment types and included separate analyses for each comparison that appeared frequently enough in our search results to support a meta-analysis.

Our findings directly contradict the notion that intentional weight loss interventions adversely affect psychological well-being. Keys' report in 1950 on the induction of neurotic – and even psychotic – symptoms with calorie restriction (30) remains of concern to some researchers and clinicians. We note, however, that the participants in Keys' classic starvation study were normal weight volunteers whose energy intake was restricted by 50%, and whose weight was reduced 26% (rendering participants clinically anorectic). Thus, the adverse effects observed should not be generalized to overweight and obese persons who are prescribed more modest reductions in calorie intake and lose approximately 10% of initial weight. In 1957, Stunkard described “dieting depression” as a constellation of negative affective and psychomotor symptoms that was found in some obese persons who engaged in weight loss therapy (31). Certainly, some people experience depression and other psychological distress while trying to lose weight. However, results of the Look AHEAD study, a large randomized controlled trial that is examining the effects of intentional weight loss in overweight and obese patients with type 2 diabetes, found that the incidence of significant symptoms of depression was significantly lower among those who received an intensive lifestyle intervention than among controls, who received usual care (29). These findings, as well as those from the present meta-analysis should allay any remaining concerns that attempting to lose weight with diet, exercise, and behavior therapy may be harmful to the psychosocial status of obese patients without pre-existing psychopathology.

Concerns, however, remain about the psychiatric side effects of pharmacologic agents. Christensen et al. reported that patients treated with rimonabant were significantly more likely to discontinue treatment due to mood disorders (odds ratio = 2.5) and anxiety disorders (odds ratio = 3.0) than those who received placebo (33). Our analysis, which found no difference in changes in symptoms of depression between pharmacologic interventions and placebo, must be interpreted cautiously for two reasons. First, our analyses only included mean changes on measures of depressive symptoms. The incidence of clinically significant distress and discontinuation rates were not included. Second, baseline and post-treatment depression scores were only reported for 79% to 82% of patients in the three studies of rimonabant that were included in the present meta-analysis. Thus, the analyzed data were incomplete. Separate examination of groups treated with sibutramine found significant improvements in symptoms of depression, suggesting that all pharmacologic weight loss interventions should not be assumed to have similar effects on mood.

Four additional limitations of the present meta-analysis must be noted. First, we were unable to include all relevant studies due to unavailability of necessary data. In particular, studies published before 2000 are underrepresented. Second, at least 9 of the included studies reported results of completers' analyses, rather than the more conservative intent-to-treat analyses. The type of analysis was not specified in nearly half of the studies. Third, the applicability of the present findings to the obese treatment-seeking population, as a whole, is questionable. Trials of weight loss interventions routinely exclude persons with significant psychological distress at screening. Given the elevated rates of psychopathology in obese individuals (4–6,15–17), the samples in the included studies must be considered highly selected. As a result, this analysis does not fully address the potential adverse effects of

dieting and weight loss on mood in obese individuals who suffer from depression, binge eating disorder, or other psychiatric disorders, prior to undertaking weight reduction.

Collectively, our findings suggest that the effects of most weight loss interventions – particularly non-pharmacologic therapies – on mood are favorable when weight loss is undertaken by obese individuals who are generally free of depression and other psychopathology. While exercise-alone interventions had the largest within-treatment pooled effect size, lifestyle modification programs, which incorporated exercise with dietary instruction and behavior therapy, were found to induce marginally or significantly greater reductions in symptoms of depression than other non-pharmacologic treatments. Future research on the effects of intentional weight loss on mood would benefit from including persons with higher levels of baseline distress, using diagnostic measures (based on the latest edition of the Diagnostic and Statistical Manual of Mental Disorders) rather than symptom inventories to assess depression, and expanding outcomes to include incidence and resolution of clinically significant distress among participants in weight loss trials.

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Figure 1.

Results of meta-analyses comparing reductions in symptoms of depression with lifestyle modification vs. control (Panel A), non-dieting (Panel B), dietary counseling (Panel C), and exercise-alone (Panel D) interventions. A positive standardized mean difference (SMD) indicates a greater reduction in symptoms of depression with lifestyle modification. The sizes of individual study markers are proportional to the weight of the corresponding study in the analyses. The midpoint of the diamond marker in each analysis represents the overall SMD, and the width of the diamond corresponds to the 95% CI. Note, Wadden (64) (Panel B) compared a non-dieting program to lifestyle modification programs with daily calorie targets of 1000 kcal/day (a) and 1200–1500 kcal/day (b). Williamson (65) (Panel C) compared a lifestyle modification program with dietary counseling interventions that induced a 25% energy deficit (a) and one that provided 890 kcal/day.

Figure 2.

Meta-analysis comparing exercise-alone with control interventions. A positive standardized mean difference (SMD) indicates a greater reduction in symptoms of depression with exercise. The size of individual study markers is proportional to the weight of that study in the analysis. Sarsan (55) compared aerobics (a) and resistance (b) training programs to controls. The midpoint of the diamond marker represents the overall SMD, and the width of the diamond corresponds to the 95% CI.

Figure 3.

Meta-analysis comparing pharmacologic interventions with placebo. The abbreviations “Sib,” “Orl,” and “Rim” refer to sibutramine, orlistat, and rimonabant, respectively. The dosage of rimonabant (mg/d) also is shown. A positive standardized mean difference (SMD) indicates a greater reduction in symptoms of depression with pharmacotherapy. The size of individual study markers is proportional to the weight of that study in the analysis. The midpoint of the diamond marker represents the overall SMD, and the width of the diamond corresponds to the 95% CI.

Table 1

Summary of studies and treatment groups included in analyses.

Study	Sample	Depression Measure	Post-treatment Assessment	Treatment Group	Description	Included in Between-Groups Analysis*	Included in Within-Groups Analysis
Andersen (36)	N = 40 100% F Age = 42.9 BMI = 32.9	BDI	16 weeks	LM + structured activity	Standard group-based LM with weekly sessions. Three supervised step aerobics classes per week.	--	LM
				LM + lifestyle activity	Same LM as above. Instructions to increase activity through the day in lieu of supervised exercise classes.	--	LM
Annesi (37)	N = 111 100% F Age = 43.9 BMI = 36.6	POMS subscale	6 months	LM	Set in community center. Six group nutrition sessions, six cognitive-behavioral treatment sessions with wellness professional, three 30-minute exercise sessions per week.	LM vs. C	LM
				Control	Wait-list.	LM vs. C	--
Bacon (38)	N = 78 100% F Age = 39.3 BMI = 36.3	BDI	1 year	LM	Standard group-based LM with 24 weekly sessions and six monthly aftercare visits.	LM vs. ND	LM
				Non-dieting	Same number and schedule of visits as above, but sessions focused on body acceptance, eating behavior, activity, nutrition, and social support. Participants were encouraged to improve diet quality and eat in response to hunger/satiety cues, rather than given specific goals for energy intake or diet composition.	LM vs. ND	ND
Cabloglu (39)	N = 165 100% F Age = 36.4 BMI = 33.2	SCL-90 subscale	20 days	Diet-alone	Diet was prescribed at 1450 kcal/day and patients were instructed to maintain normal physical activity.		DA
				Diet + electro-acupuncture	Same as above, plus three 30-minute sessions of electroacupuncture per week, with stimulation at sites related to weight loss.	--	--
				Diet + placebo electro-acupuncture	Same as above, however, needles were inserted superficially at sites unrelated to weight loss.	--	--
Carels (40)	N = 44 100% F Age = 54.7 BMI = 35.9	BDI	24 weeks	LM	Standard group-based LM with 24 weekly sessions lasting 60–75 minutes each.	--	LM
				LM + Self-control therapy	Standard group-based LM with 24 weekly sessions lasting 90–120 minutes each. Sessions also included cognitive and behavioral coping and self-control skills.	--	LM
Dennis (41)	N = 39 0% F Age = 31.2	CES-D	16 weeks	Exercise alone	Set aboard deployed U.S. Navy ship. Navy-mandated exercise program, including 1 hour of exercise 4 days per week.	LM vs. EX	EX

Study	Sample	Depression Measure	Post-treatment Assessment	Treatment Group	Description	Included in Between-Groups Analysis*	Included in Within-Groups Analysis
	BMI = 33.5			LM + exercise	Same as above plus standard group-based LM with weekly sessions.	LM vs. EX	LM
Evangelista (42)	N = 99 with advanced heart failure 25% F Age = 53.3 BMI = 30.6	MAACL subscale	12 weeks	Exercise	Home-based, graduated, low-level exercise protocol consisting of light aerobic exercise and resistive training. Participants instructed to complete protocol at least 4 times per week.	EX vs. C	EX
				No treatment	Participants were instructed to maintain their usual levels of activity.	EX vs. C	--
Faulconbridge (43)	N = 194 84% F Age = 43.3 BMI = 37.7	BDI	1 year	Sibutramine	5–15 mg/day of sibutramine and pamphlet on healthy eating and physical activity. Eight visits (10–15 minutes each) with physician.	--	RX
				LM	Standard group-based LM with weekly sessions through 18 weeks and every-other-week sessions thereafter through week 40.	--	LM
				Sibutramine + LM	Combined the two treatments described above.	--	--
				Sibutramine + Brief LM	Combined the sibutramine treatment described above plus brief individual LM sessions (10–15 minutes each), delivered by physician in 8 visits.	--	--
Fontaine (44)	N = 38 66% F Age = 36.5 BMI = 31.1	BDI	13 weeks	LM + structured activity	Standard group-based LM with weekly sessions. Participants instructed to complete an aerobic exercise of choice three to four times per week.	--	LM
				LM + lifestyle activity	Same LM as above. Participants instructed to increase lifestyle activity (rather than aerobic exercise).	--	LM
Gallerty (45)	N = 28 with polycystic ovarian syndrome 100% F Age = 32.5 BMI = 37.4	HADS	16 weeks	High-protein, low-carbohydrate LCD	Weekly group exercise sessions, instructions to exercise two additional times per week, dietary counseling every 2 weeks, and 3-day food records monthly. Instruction to consume 30% of calories from protein, 40% from carbohydrate, and 30% from fat at restricted level for 12 weeks and weight-maintaining level for 4 weeks.	--	LM
				Low-protein, high-carbohydrate LCD	Same as above, except prescribed diet provided 15% of calories from protein, 55% from carbohydrate, and 30% from fat.	--	LM
Hainer (46)	N = 80 100% F Age = 43.9 BMI = 36.9	BDI	4 months	LCD + placebo	LCD: Detailed instruction on self-monitoring, eating regularly (4–5 meals/day), restricting calorie intake (to 5–6 MJ/day), and increasing physical activity (150 minutes of walking per week). Monthly checkups that "encouraged	RX vs. PBO	--

Study	Sample	Depression Measure	Post-treatment Assessment	Treatment Group	Description	Included in Between-Groups Analysis*	Included in Within-Groups Analysis
					changes in lifestyle according to cognitive behavioral modification techniques."		
				LCD + sibutramine	Same LCD as above plus 10 mg/day of sibutramine.	RX vs. PBO	RX
Halyburton (47)	N = 93 with abdominal obesity + ≥ 1 additional metabolic risk factor 60% F Age = 50.2 BMI = 33.5	BDI	8 weeks	High-carbohydrate LCD	Prescribed LCD, providing 24% of calories from protein, 46% from carbohydrate, and 30% from fat. Key foods were supplied at every-other-week visits with a dietitian.	--	DA
				Low-carbohydrate LCD	Isocaloric dietary prescription and visits, but LCD provided 35% of calories from protein, 4% from carbohydrate, and 61% from fat.	--	DA
Kerr (48)	N = 401 100% F Age = 41.2 BMI = 32.3	CES-D	12 months	Internet-based LM	One face-to-face goal-setting session, completion of 12 internet-based educational modules with feedback monthly by email and quarterly by phone.	LM vs. C	LM
				Control	Standard advice and materials on weight from usual care provider.	LM vs. C	--
Kiortsis (49)	N = 60 100% F Age = 44.7 BMI = 34.4	HAM-D	3 months	LCD + placebo	LCD: "Low-calorie diet, promoting a 500-1000 kcal reduction in daily energy."	RX vs. PBO	--
				LCD + sibutramine	Same LCD as above plus 10 mg/day of sibutramine.	RX vs. PBO	RX
				LCD + orlistat	Same LCD as above plus 120 mg of orlistat three times daily.	RX vs. PBO	RX
Klem (50)	N = 535 100% F Age = 47 BMI = 25.1	BDI	20 weeks	LM	Standard group-based LM.	LM vs. C	LM
				Control	Assessment only.	LM vs. C	--
Melanson (51)	N = 90 86% F Age = 42.5 BMI = 31.2	POMS subscale	24 weeks	Diet and exercise counseling	Dietary counseling in weekly sessions, incorporating use of meal replacements to achieve 500 kcal/day deficit. "Simple, progressive walking program" delivered in weekly meetings with an exercise physiologist.	LM vs. EX	LM
				Exercise counseling	Same walking program as above with no dietary counseling.	LM vs. EX	EX
Neiman (52)	N = 91 100% F Age = 45.6 BMI = 33.1	GWBS subscale	12 weeks	Diet + Exercise	Weekly groups on nutrition and weight loss skills. Specific calorie goals set and meal plans provided. Four supervised aerobic activity (i.e., walking) sessions per week.	LM vs. C , LM vs. DC , LM vs. EX	LM

Study	Sample	Depression Measure	Post-treatment Assessment	Treatment Group	Description	Included in Between-Groups Analysis*	Included in Within-Groups Analysis
Pi-Sunyer (53)	N = 3045 with hypertension and/or dyslipidemia 80.7% F Age = 45.0 BMI = 37.6	HADS	1 year	Diet-alone	Same weekly groups as above. Four supervised sessions per week of mild stretching and range-of-motion exercises (vs. aerobic activity).	LM vs. DC	DC
				Exercise-alone	Four supervised aerobic activity (i.e., walking) sessions per week.	LM vs. EX , EX vs. C	EX
				Control	Four supervised sessions per week of mild stretching and range-of-motion exercises (vs. aerobic activity).	LM vs. C EX vs. C	--
Rapoport (54)	N = 75 100% F Age = 47.5 BMI = 35.7	BDI	10 weeks	LCD + placebo	LCD: Prescribed energy deficit of 600 kcal/day. At visits (every 14 days for 1 month and every 28 days thereafter), participants received dietary counseling and were encouraged to increase physical activity.	RX vs. PBO	--
				LCD + rimonabant, 5mg	Same LCD as above plus 5 mg/day of rimonabant.	RX vs. PBO	RX
				LCD + rimonabant, 20mg	Same LCD as above plus 20 mg/day of rimonabant.	RX vs. PBO	RX
Sarsan (55)	N = 76 100% F Age = 42.6 BMI = 34.9	BDI	12 weeks	LM	Standard group-based LM with weekly sessions. Specific goals set for energy intake and diet composition.	LM vs. ND	LM
				Non-dieting	Cognitive-behavioral intervention with weekly group sessions. Restrictive dieting was discouraged, but goals set for diet composition.	LM vs. ND	ND
				Aerobic exercise	Progressive program of walking and leg cycle exercise at 50–85% heart rate reserve, in three to four supervised sessions per week.	EX vs. C	EX
Shrocco(56)	N = 24 100% F Age = 41.3 BMI = 32.6	BDI	13 weeks	Resistance exercise	Supervised upper and lower body exercises with increasing resistance, three days per week.	EX vs. C	EX
				Control	No treatment.	EX vs. C	--
				LM	Standard group-based LM, based on Schlundt, with weekly sessions.	LM vs. ND	LM
Scheen (57)	N = 1045 with type 2 diabetes 51% F Age = 55.6	HADS	1 year	Non-dieting	Cognitive-behavioral intervention with weekly sessions. Restrictive dieting was discouraged and participants taught to view eating and exercise behavior "as a choice."	LM vs. ND	ND
				LCD + placebo	See Pi-Sunyer.	RX vs. PBO	--
				LCD + rimonabant, 5mg	See Pi-Sunyer.	RX vs. PBO	RX
				LCD + rimonabant, 20mg	See Pi-Sunyer.	RX vs. PBO	RX

Study	Sample	Depression Measure	Post-treatment Assessment	Treatment Group	Description	Included in Between-Groups Analysis*	Included in Within-Groups Analysis
BMI = 34.2							
Smith (58)	N = 133 with hypertension 56% F Age = 47.5 Weight = 94.2 kg	BDI	6 months	LM + exercise	Standard group-based LM with 26 sessions. Exercise goal of 35 minutes of activity at 70%–85% of maximal heart rate, with 10 minutes of warm-up and cool-down, four days per week.	LM vs. C, LM vs. EX	LM
Survit (59)	N = 42 100% F Age = 40.3 BMI = 35.4	BDI	6 weeks	Exercise-alone	Identical exercise goal. Participants instructed to maintain their usual diet.	LM vs. EX, EX vs. C	EX
				Control	Wait-list.	LM vs. C, EX vs. C	--
				Low-fat high-sucrose LCD	LCD providing 11% of energy as fat, 19% as protein, and 71% as carbohydrate, provided for 6 weeks. Sucrose accounted for 43% of daily energy intake.	--	DA
				Low-fat low-sucrose LCD	Same as above, except sucrose accounted for 4% of daily energy intake.	--	DA
Tanco (60)	N = 60 100% F BMI = 39.5	BDI	8 weeks	LM	Standard group-based LM with weekly sessions.	LM vs. ND, LM vs. C	LM
				Non-dieting	Cognitive intervention with weekly sessions, "aimed at fostering insight into maladaptive behaviors, enhancing emotional well-being, and promoting regular physical exercise and nondisordered eating in the absence of any attempt at weight reduction."	LM vs. ND	ND
				Control	Wait-list.	LM vs. C	--
Van Gaal (61)	N = 1057 with hypertension and/or dyslipidemia 79% F Age = 45.0 BMI = 36.6	HADS	2 years	LCD + placebo	See Pi-Sunyer.	RX vs. PBO	--
				LCD + rimonabant, 5mg	See Pi-Sunyer.	RX vs. PBO	RX
				LCD + rimonabant, 20mg	See Pi-Sunyer.	RX vs. PBO	RX
				Control	Wait-list.	LM vs. C	--
Vander Wal (62)	N = 166 73% F Age = 46.7	CES-D	4 weeks	Cereal substitution	Instruction to replace two meals per day with ready-to-eat cereal.	--	DA
				Cereal substitution + nutrient bar	Same as above, plus instruction to replace one snack per day with a nutrition bar.	--	DA
				Cereal and waffle substitution + nutrient bar	Instruction to replace one meal per day with ready-to-eat cereal, one meal per day with a waffle, and one snack per day with a nutrition bar.	--	DA
				Control	Wait-list with instruction to maintain normal dietary routines.	--	--

Study	Sample	Depression Measure	Post-treatment Assessment	Treatment Group	Description	Included in Between-Groups Analysis*	Included in Within-Groups Analysis
BMI = 37.0							
Wadden 1990 (63)	N = 15 100% F Age = 44.6 BMI = 42.5	BDI	18 weeks	LM with LCD	Standard group-based LM with weekly sessions. Calorie goal set at 1000–1200 kcal/day, with specific goals for diet composition and energy expenditure.	--	LM
Wadden 2004 (64)	N = 123 100% F Age = 44.2 BMI = 35.9	BDI	40 weeks	LM with VLCD	Same as above, except protein-sparing modified fast (500 kcal/day) was implemented from weeks 5–12.	--	LM
				LM with 1200–1500 kcal/day	Standard group-based LM with weekly then every-other-week sessions. Calorie intake goal set at 1200–1500/day, with specific goals for diet composition and energy expenditure.	LM vs. ND	LM
				LM with 1000 kcal/day	Same LM program described above. Liquid formula diet provided at 1000 kcal/day, with return to self-selected diet at 1200–1500 kcal/day beginning at week 14. Specific goals were set for diet composition and energy expenditure.	LM vs. ND	LM
Non-dieting							
Williamson (65)	N = 48 58% F Age = 37.5 BMI = 28.3	BDI	12 months	LM + Calorie restriction	Weekly group sessions with psychologist (emphasizing standard LM skills) and at least two individual sessions with a dietitian or exercise physiologist per month in the first 26 weeks. Provided diet and calorie intake goals set at 25% below weight-maintaining level. Participants were not encouraged to increase exercise.	LM vs. ND	ND
				LM + Calorie restriction and exercise	Same schedule of sessions as above. Provided diet and calorie intake goals set at 12.5% below weight-maintaining level, and energy expenditure goals set at 12.5% above weight-maintaining levels.	LM vs. DC	DC
				LM with VLCD	Same schedule of sessions as above. A liquid formula diet was provided at 890 kcal/day to achieve 15% reduction in initial weight, followed by provided and self-selected diets at (reduced) weight-maintaining levels. Participants were not encouraged to increase exercise.	LM vs. DC	DC

Study	Sample	Depression Measure	Post-treatment Assessment	Treatment Group	Description	Included in Between-Groups Analysis*	Included in Within-Groups Analysis
Wing (66)	N = 33 76% F Age = 51.3 Weight = 103.2 kg	BDI	20 weeks	Control	Provided diet and calorie intake goals were set at weight-maintaining level.	LM vs. C	--
				LM with LCD	Standard group-based LM with weekly sessions. Calorie goal set at 1000–1500 kcal/day, with specific goals for diet composition and energy expenditure.	--	LM
				LM with VLCD	Same as above, except calorie goal set at 400 kcal/day during months 2–3 and gradually increasing during month 4 to 1000–1500 kcal/day in month 5.	--	LM

* The group described in a given row represented the treatment printed in **boldface** in the between-group comparison(s) listed.

C = Control, DA = Diet-Alone, DC = Dietary Counseling, EX = Exercise-Alone, LM = Lifestyle Modification, ND = Non-Dieting, PBO = Placebo, RX = Pharmacotherapy.

% F = percentage of sample that was female; Age is expressed in mean years; BMI (body mass index) is expressed in mean kg/m²; Weight is expressed in kg if BMI was not reported.

BDI = Beck Depression Inventory (67) or Beck Depression Inventory-II (68); CES-D = Center for Epidemiologic Studies Depression scale (69); GWBS = General Well-Being Schedule (70); HADS = Hospital Anxiety and Depression Scale (71); HAM-D = Hamilton Rating Scale for Depression (72); MAACL = Multiple Affect Adjective Checklist (73); POMS = Profile of Mood States (74); SCL-90 = Symptom Checklist – 90 (75).

LCD = Low-calorie diet; VLCD = Very low-calorie diet; kcal = kilocalories.

Table 2

Summary of random effects meta-analyses examining within-group changes in symptoms of depression, by treatment type.

Treatment Type	Groups	Subjects	SMD	95% CI	Z, p	Q, p	I ²	Fail-Safe N
Non-Pharmacologic (All)	50	1789	0.50	0.40 to 0.59	10.33, < 0.001	179.9, < 0.001	72.8	4170
Lifestyle Modification	27	1103	0.60	0.47 to 0.72	9.30, < 0.001	96.9, < 0.001	73.2	1765
Non-Dieting	5	139	0.37	0.14 to 0.59	3.17, 0.002	6.3, 0.18	36.9	17
Dietary Counseling	3	45	0.40	-0.36 to 1.15	1.03, 0.30	6.8, 0.03	70.8	1
Diet-Alone	8	262	0.37	0.14 to 0.60	3.10, 0.002	10.2, 0.07	50.9	62
Exercise Program	7	240	0.50	0.14 to 0.85	2.75, 0.006	46.7, < 0.001	87.2	74
Pharmacologic (All)	10	3890	0.07	-0.01 to 0.15	1.83, 0.07	38.8, < 0.001	76.8	0
Rimonabant	6	3763	0.02	-0.03 to 0.06	0.62, 0.53	10.3, 0.07	51.3	0
Orlistat/Sibutramine	4	123	0.52	0.14 to 0.89	2.68, 0.007	11.1, 0.01	73.1	15