WEIGHT LOSS MEDICATION: A PRELIMINARY STUDY TO ASSESS IF IT WORKS

By
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Abstract

Background: Obesity is a rising global health problem (1,2). It is associated with increased incidence of chronic diseases such as Type 2 diabetes, heart disease, hypertension, cancer and mortality (3-6). Life style intervention including dietary modification and exercise are suggested as the first step to treat obesity (7). However, successful weight loss and maintenance of the results maybe hard to achieve. In these circumstances, pharmacotherapy is indicated (8).

Objective: This study represents an initial step in assessing comparative efficacy of weight loss medications. We hypothesized that weight loss medications would be differentially associated with observed weight loss over time in our study sample.

Methods: A retrospective study of 543 patients with obesity recruited from the Cleveland Clinic Bariatric and Metabolic Institute between January 2000 and December 2013 who received weight loss medications, which included five FDA approved medications.

Results: Of the 543 patients receiving weight loss medication, 67% of the study cohort showed weight loss of 2.5% at six months, and 62% showed weight loss of 2.6% at 12 months.
Conclusion: The study provided preliminary evidence that weight loss medications can be useful in patients who have not achieved weight loss with life style modifications alone.
**Background**

In 1998, the National Institutes of Health stated that "obesity is a chronic disease, and both patients and practitioners need to understand that successful treatment requires a life long effort" (9).

Body mass index (BMI) is a widely used method for estimating body fat mass and diagnosing obesity. BMI is defined as the weight in kilograms divided by the square of height in meters. Obesity is defined as BMI of 30 kg/m2 or more and overweight is defined as BMI of 25 kg/m2 to 29.9 kg/m2 (Table 1) (1). According to the Centers for Disease Control and Prevention (CDC), the U.S prevalence of obesity in 2015-2016 is 40% in adults and 19% in youth (10). The prevalence of obesity is higher in middle-aged adults (43%) and non-Hispanic black and Hispanic adults.

Obesity is considered a major risk factor for more than 30 diseases including cardiovascular diseases and certain cancers, which leads to increasing morbidity and mortality (4-6). The annual estimated health care cost of obesity-related illness is $190.2 billion, or nearly 21% of annual medical spending in the US (11). It is expected that by 2030, there will be additional 65 million obese patients in the US population, which will raise the cost of management of obesity and associated comorbidities by $48- $66 billion a year (1).

Obesity ranges from severe generalized obesity, which is lifelong and associated with clearly defined genetic abnormality, to predominantly visceral obesity in middle-aged and older individuals, and with a range of phenotypic variations between those extremes. The comorbidities associated with obesity are
variable, even between individuals with similar distribution of body fat and
duration of disease (12). Data on the benefits of intentional diet induced weight loss
are mixed (13). There is accumulating evidence highlighting the importance of diet
and exercise as the fundamental steps in management of obesity.

What causes obesity?

Obesity is generally considered a multifactorial disease resulting from
imbalance of over-consumption of high-energy food and lack of physical activity
resulting in increased fat deposition. However, in real life, it is a much more complex
process (12). Obesity the result of interaction between genetic and environmental
factors. In fact, some studies suggest that the predisposition to obesity lies in our
evolutionary past (12). Also there is clear evidence of ethnic susceptibility to
obesity and related morbidities (12). All these factors add to the complexity of
obesity and its management.

Management of obesity

Management of obesity starts with prevention by supporting healthy eating,
active living, reducing stress, and limiting screen time (14). However, when these
measures fail, treatment is indicated (15). Weight loss is universally difficult to
achieve or maintain. Current treatment options for obesity include lifestyle
modifications, pharmacotherapy, and bariatric surgery (16). Life-style modifications
include a reduced calorie diet, physical activity, and behavioral changes. These steps
represent the cornerstone of weight loss therapy and maintenance of the results (7).
Unfortunately, many patients do not respond to these interventions alone. In fact some studies showed that reduced calorie intake results in elevated appetite-stimulating hormones and decreased appetite-suppressing hormones (1). The net result of this hormonal imbalance was weight gain. Given the alteration in appetite regulating hormones, anti-obesity medications are likely to play an effective role in these circumstances because they suppress appetite-stimulating hormones.

There is growing evidence suggesting that bariatric surgery is currently the most effective treatment for obesity and consistently produces substantial weight loss (17). However, the long waiting periods, cost, potential risks and side effects of surgery limit the number of patients undergoing bariatric surgery. Also, despite the overall effectiveness of bariatric surgery, not all patients lose the same percentage of weight and weight regain has been reported (18). This indicates that obesity is a chronic disease and long-term management is needed.

There are still little data evaluating the role of medications preventing weight regain after bariatric surgery (19). However, it is a great area of scientific interest. Medical treatment of obesity with pharmacotherapies maybe an effective and less expensive approach to manage obesity.

**Development and use of weight loss medications**

The history of anti-obesity drugs goes back to 1890 when sheep thyroid extract was used to induce weight loss in euthyroid patients (Figure 1). Unfortunately, this drug resulted in cardiac arrhythmias and death (20). Further attempts to develop effective anti-obesity drugs have also encountered problems.
For example, the previously approved weight loss medications Fenfluramine and Dexfenfluramine were withdrawn from the market in 1997 due to concerns about development of valvular heart disease and pulmonary hypertension (21). Also, Sibutramine, a combined serotonin and noradrenaline reuptake inhibitor, was withdrawn from the market as patients with increased risk of cardiovascular disease showed higher incidence of cardiovascular events (22). Rimonabant, a cannabinoid receptor blocker, raised concerns about associated severe psychiatric side effects. Perhaps this is why anti obesity medications are still surrounded by controversy and not used often.

Despite this checkered history, growing efforts over the years have developed effective pharmacological therapy that causes weight loss. Currently available anti obesity medications work through a variety of mechanism targeting digestion and absorption, metabolic rate, and even by affecting certain parts of the brain that control appetite and satiety (Fig.2).

FDA-approved weight loss pharmacotherapies are divided into two main groups: short-term (usually used for 12 weeks or less) and long-term (used for more than 12 weeks) (23). An overview of FDA approved medications is shown in Table 2 and a description of commonly prescribed medications follows:

Phentermine is the most common and most effective short-term weight loss medication used. It is only approved for short-term use (24). It was FDA approved in 1959 and became available in 1970. Phentermine is an appetite suppressant that acts by inhibiting adrenaline reuptake. It is a controlled substance in the United States. It has a misuse potential and small risk of pulmonary hypertension. Thus, it is
approved for short-term use only but often prescribed off label for long-term use. A meta-analysis of 6 randomized controlled trials lasting up to 24 weeks reported an average weight loss of 3.6 kg (24). Phentermine is contraindicated in patients with cardiovascular diseases and hypertension (23).

Concerning long-term anti-obesity medications, Orlistat is an inhibitor of pancreatic and gastric lipases, which are the enzymes required for the digestion of dietary fats into free fatty acids and monoacylglycerols. This leads to excretion of about 30% of ingested fat (25). The FDA approved Orlistat for prescription sale in 1999. It has been available for over the counter sale since 2007. However, the prescription dose is different. Multiple studies have assessed the efficacy of Orlistat. In a meta-analysis of placebo-controlled trials, Orlistat showed 2.9% more weight loss than placebo (26).

Lorcaserin is a serotonin 2c receptor agonist approved in 2012 for weight loss. Numerous phase 3 clinical trials have demonstrated the efficacy of Lorcaserin in obese and overweight patients. In the “Behavioral Modification and Lorcaserin for Over-weight and Obesity Management “ (BLOOM study), Lorcaserin treated patients lost 5.8% of body weight from baseline compared to 2.2% in placebo (27).

A combination of Phentermine and Topiramate named Qsymia is approved for long-term weight loss. It is associated with greater mean weight loss than other available long-term medications. It was approved in 2012. This combination is contraindicated in hyperthyroidism, pregnancy and within 14 days of treatment with monoamine oxidase inhibitors. In the CONQUER trial, patients were treated with placebo, Phentermine 7.5 mg/Topiramate 46 mg, or phentermine 15
mg/Topiramate 92 mg for one year. Patients lost 1.2%, 7.8%, and 9.8% of baseline, respectively (p < 0.0001) (28).

Naltrexone/Bupropion is another combination therapy approved for chronic weight management. It is one of the newer agents in the market. Bupropion is a dopamine and norepinephrine reuptake inhibitor that has an anorexigenic effect. Naltrexone is an opioid receptor antagonist that causes weight loss. The combination was approved in 2014. In a one-year placebo controlled trial, patients receiving the combination lost 5% or more of body weight (29).

Liraglutide, marketed as Victoza, is used to treat type 2 diabetes. It is a GLP-1 agonist. It is now approved for treatment of obesity and is marketed as Saxenda. The Satiety and Clinical Adiposity – Liraglutide Evidence in non-diabetic and Diabetic Individuals (SCALE) study demonstrated statistically significant weight loss compared to placebo (6.2% vs. 0.2%, p < 0.0001) (30).

Venlafaxine is an antidepressant drug that inhibits norepinephrine and serotonin reuptake, as well as weak inhibition of dopamine reuptake. Weight loss is reported in up to 6% of patients. It is currently not an FDA approved weight loss medication. However, given the high prevalence of depression in obese patients, Venlafaxine is preferred over other anti depressant drugs that cause weight gain (31).

In 2015 the Endocrine Society appointed Task force of experts to formulate clinical practice guidelines for the pharmacological management of obesity (9). The Task Force followed the approach recommended by the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) group, an
international group with expertise in the development and implementation of
evidence-based guidelines (32). The task force made several recommendations.
Some medications used to treat diabetes; depression and other chronic condition
have their effect on weight by either promoting weight loss or weight gain. These
medications should be considered as an adjuvant to behavioral modifications to
suppress appetite and increased physical activity.

Moreover the advantages of using anti obesity medications that also target
associated comorbidities add to the overall benefit. Several factors should be taken
into consideration when prescribing anti-obesity medications. As with any
metabolic disease (such as diabetes, hypertension and hypercholesterolemia) for
which medications are used long term (9), obesity is a chronic disease, and weight
loss medications should be used as long-term rather than short-term treatment.

In general, anti-obesity medications have modest weight loss effects.
However, a modest effect is not to be underestimated. Weight loss of 3% - 5 % in
patients with obesity lead to improvement of their metabolic profile (7,8). This
weight loss could “jump-start” these patients, motivating them to make life style
changes. If we demonstrate success of these medications and their safe profile, more
practitioners will feel comfortable using them, which will improve management of
obesity.

Aims and Hypothesis

This study represents an initial step in assessing relative efficacy of weight
loss medications. Here, we retrospectively examined weight loss outcomes in
patients with BMI of 30 kg/m² or above who were seen at the Cleveland Clinic Bariatric and Metabolic Institute between January 2000 and December 2013. Patients received weight loss medications, which included five FDA approved medications. We hypothesized that weight loss medications would be differentially associated with observed weight loss over time in our study sample.

**Methods**

**Study population**

The study population consisted of 1214 patients with the diagnosis of obesity (BMI 30 kg/m² or above) seen at the Cleveland Clinic’s Bariatric and Metabolic Institute between January 2000 and December of 2013 and who were identified by a review of their Electronic Medical Records (EMR). Study inclusion criteria consisted of: age 18 years or older; BMI of 30 kg/m² or more with diagnosis of obesity received a prescription of one of seven following medications for weight loss: Phentermine, Topiramate, combination of Phentermine/Topiramate (Qysmia), Locaserin, combination of Naltrexone/Bupropion (Contrave), Liraglutide, and Venlafaxine. Five of these medications are FDA approved for weight loss (Phentermine, Qsymia, Locaserin, Contrave and Liraglutide). Topiramate and Venlafaxine are not FDA approved as anti-obesity medications but are known for their weight loss effect and used off-label to treat obesity. Exclusion criteria consisted of: patients who underwent bariatric surgery prior to receiving anti-obesity medication (n=671). The analytic sample consisted of 1214 patients. The
study was approved by The Cleveland Clinic institutional review board (IRB 15-344).

**Demographics and Chronic Medical Conditions**

Demographic variables such as age, gender, weight, height, BMI and comorbidities were collected from EMR. Diagnoses of diabetes mellitus, hypertension, coronary artery disease, depression, hyperlipidemia, binge eating disorder and chronic obstructive pulmonary disease were identified using EMR. The medications that were received and start and stop date for each drug were recorded from EMR.

**Outcome measures:**

The primary outcome of interest was percentage of weight loss among patients at 6 months and 12 months following the date of receiving medication.

**Statistical analysis:**

Data were summarized as the mean ± standard deviation or median and interquartile range for continuous variables and as counts and percentages for categorical variables. Patients were grouped by weight loss medication received (listed above) for weight loss mentioned above. Because of the relatively small sizes of some groups, for analytic purposes we created two groups: short term Phentermine versus all other medications (long term). Percent of weight loss in these two groups at 6 months and at 12 months were compared using Kruskal –
Wallis test and χ2 test. Statistical significance was inferred based on a 2-sided p value of < 5%.

**Results:**

*Sample characteristics:*

We initially identified a total of 1214 patients with obesity at the Bariatric and Metabolic Institute between January 2000 and December 2013. We excluded 671 patients who underwent bariatric surgery. The remaining analytic cohort contained 543 patients. Sample characteristics are reported in Table 3. The median age of the study population was 47 years, with 50% of the cohort falling between 38 and 56 years. The median weight was 110.6 kg, and the interquartile range (IQR) was 96.6 to 135.6. Height was missing from 24 patients (4%). This did not affect the end results since percent of weight loss rather than BMI was used. In the study population, 255 patients had type 2 diabetes (47%), 371 had hypertension (68%), 229 patients had obstructive sleep apnea (42%), 253 patients had hyperlipidemia (47%), 41 patients had coronary artery disease (8%), 359 had depression (66%), 63 patients had binge eating disorder and 18 patients had chronic obstructive pulmonary disease (COPD) (3%).

**Medications Used**

Phentermine was the most used medication in 221 patients from study population (40.7%) as shown in Table 4. It is the only medication used for 3 months only. Other medications were used for 12 months. Topiramate was the
second most used medication, prescribed for 135 patients (24.9%). Liraglutide was used in 53 patients (9.8%), Qysmia in 39 patients (7.2%), Venlafaxine in 31 patients (5.7%), Lorcaserin in 19 patients (3.5%), and Contrave in 10 patients (1.8%).

**Observed Weight Loss**

At six months, 483 patients had complete follow up records (89%). The median percentage of weight loss after 6 months was 2.5%, with 67% of the study population showing a successful weight loss.

Concerning weight loss by medication prescribed, phentermine, the most used drug, was associated with median weight loss of 3.3% (0.5,7.8) from baseline at six month. Liraglutide showed a median weight loss of 2.6 % (1.4,6.6) from baseline to six month. Qysmia as well as Venlafaxine showed median weight loss of 2.3% with IQR of (0.1,7.4) and (1.4,5.9), respectively. Lorcasein showed a median weight loss of 2 % (0.5,4.2). Topiramate showed a median weight loss of 1.4 % (2.3,5.6) from baseline at six month. Finally, the combination of Naltrexone/Bupropion showed a median weight loss of 1.1% (0.4,3) at six months (Table 5).

The percentage of weight loss of Phentermine versus all other medications was compared using Kruskal – Wallis test: 3.3% versus 1.8%. This difference between the two groups was statistically significant (*p* value 0.03).

We further looked at the 324 patients who lost 2.5% or more of their baseline weight at 6 months and compared their baseline characteristic with 159 patients who lost less than 2.5% of their baseline weight (Table 6). There was
statistically significant difference between number of patients who lost weight (lost 2.5% or more at 6 months) and patient who did not lose weight (p value 0.008). Also the first group had lower baseline mean weight. Patients who lost weight were on average older than patients who did not lose weight with median age of 48 and 45 respectively. There was no statistically significant difference in co-morbid diseases such as diabetes and hypertension between two groups (table 6).

At twelve months, 431 patients had complete follow up records. Fifty-two patients were lost to follow up between 6 month and 12 months. The median percentage of weight loss at 12 months was 2.6%.

**Discussion**

Obesity pharmacotherapy has seen the rise and fall of many drugs. We are in a desperate need to improve medical management of obesity. This study was a preliminary step in assessing the relative efficacy of weight loss drugs in a sample of persons with obesity (BMI 30 kg/m2 or above). We hypothesized that weight loss medications would be differentially associated with observed weight loss over time in our study sample. We observed a modest difference. Patients in Phentermine group lost 3.3% at 6 months and 2.3% at 12 months from their baseline weight compared to other medications group, a difference that was statistically significant difference.

Many studies suggested satisfactory weight loss as loss of 5 % of total body weight at 3 months in patients with obesity without diabetes; in patients with obesity and diabetes, loss of 3% of total body weight was suggested (33). Our
findings fell below average satisfactory weight loss, but this could be explained by the fact that we only looked at 6 months and 12 months but skipped the 3 months weight loss outcomes. It is well established that patients lose most weight in the first 3 months, when they are highly motivated and their metabolism changes fast.

*Study Limitations*

This preliminary study had notable limitations. First, characteristic of observational studies is a lack of knowledge about characteristics of the sample that might have influenced the results. For example, data about lifestyle changes and their dietary modification were unknown at time of study. A second limitation was the lack of statistical adjustment for potential confounders: e.g., age, baseline weight, diabetes and other variables. This statistical adjustment might have changed weight loss outcomes between groups.

Because patients were seen at a tertiary center, the generalizability of our finding to the general population is low. Perhaps our study participants were more complex cases, which is why that’s why weight loss was difficult.

It is important to note that no one medication is effective in every patient and medications should be changed if no successful weight loss is achieved after 3 month. Also effective lifestyle changes in terms of healthy diet and exercise should be provided with use of medication.

Many of the withdrawn drugs have very different mechanisms of action; we cannot generalize and think any potential anti-obesity drug is harmful or not effective.
Prior to 2012, Phentermine and Orlistat were the only weight loss medications approved in the United States. By 2015, four new drugs became available including Lorcaserin, phentermine/Topiramate, naltrexone/ bupropion and Liraglutide. This expands the treatment options for obesity. Although the percentage of weight loss in our study was less than 5 %, it is important to note that this can lead to improvement in metabolic profiles (33).

In light of study limitations, the following section describes future steps to research to provide a more definitive answer about the relative efficacy of the weight loss medications.

**Next Steps**

Ideally, conducting a randomized controlled trial of these medications would provide a definite answer to the comparative efficacy of weight loss medications. A prospective cohort study or a retrospective cohort with more detailed information about the sample would also be alternative designs. For these designs, the primary outcome would be 5% or more weight loss. The study could also include secondary outcome such as proportion of patients achieving at least 10% weight loss, change in blood pressure, change in fasting blood glucose, change in glycated hemoglobin, number of diabetic medications at baseline and at 12 months, number of anti hypertensive medications at baseline and at 12 months and change in BMI.
Conclusion

Our study provided preliminary evidence that weight loss medications may have different efficacy on weight loss. Although the observed weight loss was modest, such weight loss is important because it can lead to improvement in metabolic profile and can motivate patients. Further studies are needed to address the effect of chronic anti-obesity medications.
**Table 1. Classification of obesity**

<table>
<thead>
<tr>
<th>BMI</th>
<th>Classification</th>
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<tbody>
<tr>
<td>&lt;18.5</td>
<td>Underweight</td>
</tr>
<tr>
<td>18.5 – 24.9</td>
<td>Normal weight</td>
</tr>
<tr>
<td>25 – 29.9</td>
<td>Overweight</td>
</tr>
<tr>
<td>30 – 34.9</td>
<td>Class I obesity</td>
</tr>
<tr>
<td>35 – 39.9</td>
<td>Class II obesity</td>
</tr>
<tr>
<td>40 or more</td>
<td>Class III obesity</td>
</tr>
<tr>
<td>Generic name</td>
<td>Year of approval</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>------------------</td>
</tr>
<tr>
<td>Orlistat</td>
<td>1999</td>
</tr>
<tr>
<td>Lorcanerin</td>
<td>2012</td>
</tr>
<tr>
<td>Phentermine/topiramate (Qysima)</td>
<td>2012</td>
</tr>
<tr>
<td>Naltrexone/bupropion</td>
<td>2014</td>
</tr>
<tr>
<td>Liraglutide</td>
<td>2014</td>
</tr>
<tr>
<td>Phentermine</td>
<td>1959</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number (%) or Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>47 (38,56)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>110.6(96.6,135.6)</td>
</tr>
<tr>
<td>Heights (Meters)</td>
<td>1.65 (1.6,1.72)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>255 (47.1%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>371 (68.3%)</td>
</tr>
<tr>
<td>Obstructive sleep apnea</td>
<td>229 (42.2%)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>253 (46.6%)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>41 (7.6%)</td>
</tr>
<tr>
<td>Depression</td>
<td>359 (66.1%)</td>
</tr>
<tr>
<td>Binge eating disorder</td>
<td>63 (11.6%)</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>18 (3.3%)</td>
</tr>
<tr>
<td>Premenstrual syndrome/disorders</td>
<td>32 (6%)</td>
</tr>
</tbody>
</table>
Table 4. Different medications used and their distribution among study population (n=543)

<table>
<thead>
<tr>
<th>Medication</th>
<th>N  (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phentermine</td>
<td>221 (40.7%)</td>
</tr>
<tr>
<td>Topiramate</td>
<td>135 (24.9%)</td>
</tr>
<tr>
<td>Liraglutide</td>
<td>53 (9.8%)</td>
</tr>
<tr>
<td>Phentermine/Topiramate (Qysmia)</td>
<td>39 (7.2%)</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>31 (5.7%)</td>
</tr>
<tr>
<td>Lorcaserin</td>
<td>19 (3.5%)</td>
</tr>
<tr>
<td>Naltrexone/Bupropion (Contrave)</td>
<td>10 (1.8%)</td>
</tr>
</tbody>
</table>
Table 5. Weight loss by medication group at 6 months.

<table>
<thead>
<tr>
<th>Medication</th>
<th>N (%)</th>
<th>Percentage of weight loss at 6 month Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phentermine</td>
<td>221 (40.7%)</td>
<td>3.3 (0.5,7.8)</td>
</tr>
<tr>
<td>Liraglutide</td>
<td>53 (9.8%)</td>
<td>2.6 (1.4,6.6)</td>
</tr>
<tr>
<td>Phentermine/Topiramate (Qysmia)</td>
<td>39 (7.2%)</td>
<td>2.3 (0.1,7.4)</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>31 (5.7%)</td>
<td>2.3 (1.4,5.9)</td>
</tr>
<tr>
<td>Lorcanerin</td>
<td>19 (3.5%)</td>
<td>2.0 (0.5,4.2)</td>
</tr>
<tr>
<td>Topiramate</td>
<td>135 (24%)</td>
<td>1.4 (2.3,5.6)</td>
</tr>
<tr>
<td>Naltrexone/Bupropion</td>
<td>10 (1.8%)</td>
<td>1.1 (0.4, 3.0)</td>
</tr>
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</table>
Table 6. Baseline characteristics by weight loss group at 6 months

<table>
<thead>
<tr>
<th>Variable</th>
<th>Weight loss (&lt;2.5%) (N=159)</th>
<th>Weight loss 2.5% or more (N=324)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median (IQR) or Number (%)</td>
<td>Median (IQR) or Number (%)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>45(37.5,54)</td>
<td>48(38.75,56)</td>
<td>0.036</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>115.3(99.79,144.28)</td>
<td>109.34(94.5,131.13)</td>
<td>0.008</td>
</tr>
<tr>
<td>Height (meters)</td>
<td>1.65(1.6,1.71)</td>
<td>1.65(1.6,1.71)</td>
<td>0.601</td>
</tr>
<tr>
<td>Diabetes</td>
<td>81(50.9%)</td>
<td>150(46.3%)</td>
<td>0.388</td>
</tr>
<tr>
<td>Hypertension</td>
<td>118(74.2%)</td>
<td>215(66.4%)</td>
<td>0.099</td>
</tr>
<tr>
<td>OSA</td>
<td>67(42.1%)</td>
<td>143(44.1%)</td>
<td>0.75</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>78(49.1%)</td>
<td>158(48.8%)</td>
<td>1</td>
</tr>
<tr>
<td>CAD</td>
<td>14(8.8%)</td>
<td>20(6.2%)</td>
<td>0.382</td>
</tr>
<tr>
<td>Depression</td>
<td>111(69.8%)</td>
<td>210(64.8%)</td>
<td>0.322</td>
</tr>
<tr>
<td>BED</td>
<td>17(10.7%)</td>
<td>30(9.3%)</td>
<td>0.737</td>
</tr>
<tr>
<td>COPD</td>
<td>6(3.8%)</td>
<td>8(2.5%)</td>
<td>0.623</td>
</tr>
<tr>
<td>PMSD</td>
<td>11(6.9%)</td>
<td>20(6.2%)</td>
<td>0.907</td>
</tr>
</tbody>
</table>

Abbreviations: BEN = binge eating disorders, CAD = coronary artery disease, COPD = chronic obstructive pulmonary disease, OSA = obstructive sleep apnea, PMSD = premenstrual syndrome/disorders.
<table>
<thead>
<tr>
<th>Medication</th>
<th>Percentage of weight loss at 12 months (Median, IQ)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liraglutide</td>
<td>3.7 (0.7, 7.7)</td>
</tr>
<tr>
<td>Lorcaserin</td>
<td>3.6 (1.3, 10.4)</td>
</tr>
<tr>
<td>Phentermine/Topiramate</td>
<td>3.5 (2.1, 7.8)</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>3.3 (0.1, 6.0)</td>
</tr>
<tr>
<td>Phentermine</td>
<td>2.3 (2.4, 7.4)</td>
</tr>
<tr>
<td>Naltrexone/Bupropion</td>
<td>2.1 (0.4, 4.4)</td>
</tr>
<tr>
<td>Topiramate</td>
<td>1.5 (3.1, 7.7)</td>
</tr>
</tbody>
</table>
Figure 1. History of obesity medications


Figure 2. Interactions among hormonal and neural pathway

Adapted from J. Korner and R. L. Leibel: To eat or not to eat - how the gut talks to the brain. N Engl J Med. 2003;349:926–928
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