



**Review:**

**The Association of Antidepressant Medication and Body Weight Gain.**

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**Abstract: Objective:** To review the literature and discover which antidepressants are responsible for weight gain and then to discuss the areas with lack of adequate knowledge.

**Method:** An electronic search was conducted through Medline, Pubmed, Cochrane library, and ScienceDirect. Forty nine empirical researches were identified and reviewed.

**Results:** Amitriptyline, clomipramine, and mirtazapine have been associated with more weight gain induction in clinical studies, but not in animal-based studies. All TCAs have been reported to cause weight gain except protriptyline. MAOIs have been associated with weight gain. In SSRI group, citalopram and escitalopram induce weight, yet mixed results exist for paroxetine and fluoxetine. Researches unanimously reported weight loss effect for bupropion. Some studies suggest contributing factors in the relationship of antidepressants with body weight changes including age, gender, base-line weights and treatment duration. Various results of different treatment durations have been reported in some cases but there are not continuous time-dependent studies for the influences of antidepressants on body weight changes. **Conclusion:** More studies are required to discover underlying mechanisms and the time-dependent effects of antidepressants on body weight changes.

**Key Words:** Antidepressants; Body weight; Obesity

**Introduction:**

Psychotropic drugs have various side effects and body weight gain is one of the known side effects for a number of medications in this group. There is extensive empirical evidence displaying the relationship between antipsychotic therapy and body weight gain. More precisely second-generation antipsychotics (SGAs) are known for their potential to cause significant body weight gain.(1) Yet there exists a dearth of evidence regarding the effect of

antidepressants upon body weight changes, compared to antipsychotics and further controversies pertaining to the effect of antidepressant on weight changes remain.(1)

Depression and obesity are two common health problems in modern society.(2,3) There are studies suggesting a positive association between depression and obesity.(4-7) Some researchers have attempted to establish the underlying mechanisms for the positive association between obesity and depression.(4,6,8-11) Wild et al (4), McCarty et al (8), and Ball et al (9) suggested that women are more prone to become obese during depression compared to men. Heo et al (10) found gender, age, and race as contributing factors for the association of obesity and depression. Social and cultural factors may also contribute to the weight gain and obesity occurred in mood disorders.(6) Afari et al (11) investigated whether shared genetic influences are responsible for the association between these two conditions and they found a modest phenotypic association between depression and obesity. Antidepressant drugs have also been found to be the potential reasons for weight gain induction in depressed patients.(5,12,13)

Among antidepressants TCAs (Tricyclic antidepressants), MAOIs (Monoamine oxidase inhibitors), and mirtazapine are known to have more problems related to weight gain.(14) Some patients can also gain weight while taking SSRIs, particularly paroxetine.(15) The aim of this article is to undertake a comprehensive review of the literature regarding the effect of antidepressants upon body weight changes, to clarify if weight gain occurs frequently on antidepressant usage and which antidepressants are associated with weight gain. The available studies will be categorized according to each antidepressant in order to achieve a general perspective about the effect of each antidepressant on body weight

changes. Finally the areas with deficient knowledge in the field of antidepressant medication and the weight gain outcomes will be discussed.

#### **Methodology:**

An electronic search was conducted through Medline, Pubmed, Cochrane library, and Science Direct for the literature published between January 1973 and August 2012 with two groups of key words: antidepressants, the names of each particular antidepressant and antidepressant categories as the first group, and obesity and weight as the key words of the second group. The articles identified in the search procedure were reviewed and the reference lists of reviewed articles were manually searched. References identified as relevant were retrieved and reviewed. After reviewing all of the studies, those which did not have any contents about association between antidepressants and weight changes were excluded. The remaining articles all concluded the target content either as the main result or as the secondary result. Among these articles, forty nine empirical studies were identified among which some applied mixture of antidepressants without any discriminations and some used each particular antidepressant in separate groups. The latter group which contains more precise results for each specific antidepressant has been emphasized in the current review.

#### **Results:**

Forty nine empirical studies exist among literature regarding the effect of the antidepressants on body weight changes. Each antidepressant is discussed separately according to the relevant literature. Table 1 illustrates the summary of the results which have been achieved through the review.

#### **Amitriptyline**

Amitriptyline is the mostly reported antidepressant to cause weight gain.(12,13,16-22) In a clinical trial 51 depressed women being treated by amitriptyline were divided into two groups; one group maintained on amitriptyline for nine months and another group had the medication withdrawn after three months. Both groups gained weight during recovery. Yet the amitriptyline group continued to gain weight excessively, while the drug withdrawal after nine months treatment caused weight loss.(16) The result of another six-week randomized double-blind trial showed significantly higher body weight gains for taking amitriptyline than placebo and trazodone (the latter caused slight weight loss).(17) Pande et al (18) discovered that 100% of the patients receiving amitriptyline during their treatment gained weight. Amitriptyline induces remarkable weight gain in the patients, which is more than the weight gain due to clomipramine and imipramine administration.(12) Another study reported modest weight increases ( $1.7 \pm 4.1$  Kg) in 22% of patients being treated with amitriptyline in a double-blind placebo controlled trial.(20) Berilgen et al (22) found that amitriptyline causes weight gain and increase in serum leptin levels and they suggested amitriptyline may cause leptin resistance. Conversely Hinze-Selch et al (21) did not find TCAs including amitriptyline to affect plasma leptin levels while these agents induced weight gain.

Two animal-based experiments using Wistar rats (23) and OLETF rats (24) failed to mimic body weight gain due to amitriptyline medication and the study concluded that there was no linkage between weight gain and amitriptyline medication in rats.(23, 24) It shows that the available animal based studies for amitriptyline, could not model amitriptyline-induced weight gain observed in clinic.

#### **Clomipramine**

Clomipramine induces weight gain in human as supported by two clinical trials.(12, 25) On the contrary, clomipramine decreased weight gain and food intake in male Wistar rats maintained on a self-selection regime with separate sources of protein, fat and carbohydrate (macronutrient self-selection procedure).(26) During 27 days of this study clomipramine did not alter protein-rich or fat-rich diet consumption, yet it decreased energy intake as a result of a decrease in both carbohydrate-rich diet intake and body weight gain.(26)

#### **Imipramine**

Imipramine does not show the same potency to cause weight increase compared to amitriptyline and clomipramine. A non-significant weight gain was the result of the majority of the studies.(27- 29) Mean weights of  $2.1 \pm 1.5$  kg after 6 weeks, and  $4 \pm 1.4$  kg after 4-6 months were gained in patients taking imipramine in a controlled trial which both amounts were less than the weight gain for other TCAs.(12) In an animal based experimental study weight gain was achieved and even continued after stopping administering imipramine to the rats.(30)

#### **Desipramine**

Fifty one percent of the patients taking desipramine in a 10-year lasting clinical trial gained weight (18). Female Sabra mice also showed a gradual increase in their body weights while taking desipramine, compared to the placebo-controlled group of the rats.(31)

#### **Nortriptyline**

All of the five available clinical trials for nortriptyline reported various degrees of weight gain in the patients taking this medication.(18,21,32-34) A group of researchers explored the efficacy and tolerability of nortriptyline in 35 children and adolescents suffering from ADHD (Attention deficit hyperactivity disorder). One of their findings during their double-blind, placebo-controlled trial was that nortriptyline caused an average of 5.2 pounds weight gain through nine weeks of the study.(32) Hinze-Selch et al (21) found significant weight gains for amitriptyline/ nortriptyline in their controlled clinical trial, while they did not report any increase in plasma leptin levels. In geriatric patients nortriptyline was not a potent weight gainer as significant amounts of weight gain (>10 lb) occurred in only 17.2% of the patients over 30-week period of the study.(34) Twenty four percent of the patients in the same study showed weight loss below pre-morbid level and 20.7% showed no weight change.(34)

#### **Protriptyline**

An average weight loss of 1.75 lb per week was achieved for the patients being treated by protriptyline in a clinical trial investigating the influences of protriptyline on body weight changes of the patients who had low urinary level of 3-methoxy-4-hydroxy-phenylglycol.(35)

#### **Maprotyline (Tetracyclic Antidepressant)**

As a result of a controlled clinical trial which was investigating the effects of different antidepressants on body weight changes maprotyline and amitriptyline induced the more marked weight gain whereas imipramine and non-tricyclic antidepressants induced a smaller weight gain.(12) Maprotyline-treated patients gained a mean weight of  $3.2 \pm 2.6$  kg after 6 weeks and  $5.2 \pm 4.1$  kg after 4-6 months.(12)

#### **Phenelzine and Tranylcypromine**

In the only available clinical trial investigating the influence of phenelzine on body weight changes, weight gain was achieved for forty six percent of the patients taking this agent for ten years (18).In the same study tranylcypromine induced

the largest increase in the weight (an average of  $4.1 \pm 2.2$  Kg weight gain in the 73% of the patients) compared to other included antidepressants consisting of desipramine, nortriptyline, amitriptyline, and phenelzine.(18)

#### **Moclobemide**

The only available trial for the effect of moclobemide on body weight changes concluded just a non-significant weight gain as a result of taking this medication during both short-term (6 weeks), and long-term (18 weeks) treatment.(19)

#### **Fluoxetine**

Inconsistent results exist among literature regarding the effect of fluoxetine on body weight changes. Some researchers reported weight loss for applying fluoxetine (19, 35- 38), and some found this agent to inhibit food intake in rats (39). Conversely other researchers discovered that fluoxetine can provoke weight gain (30,40), or may not cause any changes in body weight.(24) Michelson et al (41) also searched for the effect of fluoxetine on body weight changes and detected both weight loss and weight gain during the acute and chronic phases of the treatment, respectively. During this one-year lasting clinical trial with 839 participants of depressed patients, modest weight loss happened after initial 4 weeks for patients taking fluoxetine.(41) In continuing phase and after remission of depressive symptoms all patients gained weight and these were similar in both fluoxetine and placebo consumed patients. Therefore this can be due to the remission and not necessarily the medication.(41) Another study which found counter results for fluoxetine was carried out according to the baseline weights of the depressed patients.(42) This study discovered weight loss for overweight patients as a result of fluoxetine treatment, and body weight gain for normal weight group.(42)

#### **Fluvoxamine**

In a double-blind study, Moon and Jesinger (43) compared side effects of fluvoxamine and mianserin in 59 depressed patients. As a result fluvoxamine did not cause any weight gain as a side effect while mianserin induced weight gain in the same study.(43) In another study with 40 participants of obese women, fluvoxamine caused mean weight loss of 3.1 kg during 12 weeks which was greater but not significantly different from placebo controlled group.(44) Correspondingly fluvoxamine does not induce weight gain and it can even cause weight loss in depressed obese women.(44)

#### **Paroxetine**

Paroxetine is another antidepressant which different results have been achieved for its influences on body weight changes. It can cause weight gain as supported by two randomized clinical trial.(37,45) Benkert et al (41) investigated the efficacy and tolerability of mirtazapine versus paroxetine and found that both drugs induced weight increases after 6 weeks in depressed patients and this effect was stronger for mirtazapine compared to paroxetine. Body weight changes of 284 patients with major depressive disorder who were randomly assigned to double-blind treatment with fluoxetine, sertraline, and paroxetine were analyzed in a clinical trial.(37) Significant weight increases only occurred in paroxetine group during a total of 26 to 32 weeks.(37) Contrarily paroxetine was not found to induce any statically significant weight increases in depressed patients during a comparative retrospective study which used clinical records of double-blind trials.(19) Another study which concluded paroxetine does not affect body weight is a clinical trial at which Hinze-Selch et al(21) investigated the effects of several antidepressants on body weight, plasma leptin levels, TNF- $\alpha$ , and soluble TNF receptors. The writers

reported that paroxetine did not make any changes in the mentioned factors including body weight which was similar to drug-free treatment effects, but opposite to TCAs treatment which caused increases in body weight and plasma leptin levels.(21) For animal based studies it is suggested that paroxetine significantly inhibits pelleted food intake in the rats.(39)

#### **Citalopram**

Wade et al conducted two 12-month trials: (i) a double-blind, randomized trial of placebo, citalopram, and clomipramine in 279 patients with panic disorder, and (ii) open trial of citalopram in 541 depressed patients. In the panic trial, citalopram-treated patients did not approach statistically significant weight gain and in the depression trial citalopram also caused no weight gain or a slight weight gain (<2.5 kg) in majority of patients.(25) Authors suggested that the minimal weight increases observed in the depressed patients may be a result of patients' appetites increasing as their condition improved.(25) Citalopram was also a cause of non-significant weight gain in another clinical trial.(46) Among 18 patients who were observed for carbohydrate craving due to treatment with citalopram (SSRI) in a mood disorder clinic, eight cases showed a significant increase in carbohydrate craving together with weight gain shortly after initiation of treatment.(47)

#### **Escitalopram**

During eight-months period of a double-blind clinical trial patients who were receiving escitalopram gained an average weight of 1.38 kg which was more than the weight gain in duloxetine-treated patients.(48) A non-significant weight gain of 0.14 kg over 6 months was the result of another part-randomized open trial.(33)

#### **Sertraline**

Sertraline can induce a modest weight gain in depressed patients.(37) Conversely obese patients can lose weight by taking sertraline particularly those who have low urinary MHPG (3-methoxy-4-hydroxyphenylglycol).(49) Meyerowitz and Jaramillo (1994) carried on a clinical trial to find out the effect of sertraline on the body weight of 23 depressed and overweight patients while measuring their urinary concentrations of 3-methoxy-4-hydroxyphenylglycol (MHPG). Results showed that sertraline can cause weight loss and with an average weight loss of 1.06 lb/week in patients with low urinary levels of MHPG which was found to be significantly greater than the average weight loss of 0.42 lb/week in patients with high urinary levels of MHPG.(49)

#### **Zimelidine**

The only available study reported that zimelidine caused no weight gain and, in many cases, weight loss was demonstrated with a mean weight change of  $0.2 \pm 1.8$  kg during one month of applying this antidepressant in a randomized clinical trial.(50)

#### **Duloxetine**

During a double blind controlled trial, duloxetine had significantly greater incidence of treatment-emergent abnormal weight gain (> 7% increase in weight from baseline) compared with placebo.(48) During 10 controlled clinical trials the effect of duloxetine on body weight of patients with major depressive disorder was analyzed.(51) The results of these trials indicated no consistent effect of Duloxetine on weight as the patients treated with this drug experienced modest weight loss in acute phase following by a modest weight gain on longer treatments.(51)

### **Mianserin**

In a double-blind, six-week study, Moon, and Jesinger (43) investigated the effectiveness of mianserin and fluvoxamine in patients suffering from major depressive episode, mianserin affected compliance due to weight gain over longer period.

### **Mirtazapine**

Mirtazapine has been reported in several studies to produce weight gain in humans.(20,45,46,52) During a double-blind placebo-controlled study in adult patients with major depressive disorder, the efficacy of mirtazapine was compared to amitriptyline. One of the findings of this study was that measured weight gain was more frequent with amitriptyline (22% of patients) compared with mirtazapine (13% of patients).(20) Another comparison was made between the efficacy and tolerability of mirtazapine versus paroxetine in 275 depressed outpatients. Patients were randomly assigned to 6 weeks of treatment with mirtazapine or paroxetine. The result regarding weight gain showed the more weight increase in the mirtazapine-treated group compared to paroxetine-treated group.(45) A multicenter randomized double-blind trial with the aim of comparing efficacy and tolerability of mirtazapine and citalopram in depressed patients yielded that mirtazapine-treated patients have significantly more increased appetite and body weight increase (8.8% and 15.3%) than citalopram-treated patients (1.5% and 4.5%).(46) Laimer et al investigated the influence of mirtazapine treatment on body weight, body fat mass, glucose metabolism, lipoprotein profile, and leptin in a group of seven depressed women compared to seven mentally and physically healthy female volunteers as a control group. Results confirmed that mirtazapine significantly increases the body weight (from a mean of 63.6 ± 13.1 kg to a mean body weight of 66.6 ± 11.9 kg), body fat mass, and leptin concentration of the patients.(52) In contrast with human based studies, there were no direct linkages between the development of obesity and mirtazapine according to the animal based controlled study carried on by Jeon, Joe, and Kee (24) who used OLETF (Otsuka Long-Evans Tokushima Fatty) rats for their study.

### **Bupropion**

Three randomized clinical trials have investigated the effects of bupropion on body weight changes. In all of these studies, researchers concluded that bupropion can induce weight loss in patients.(53-55) In a randomized double-blind trial, modest mean weight losses with long-term bupropion SR treatment was achieved in patients with depression which increased with increasing baseline body weight.(53) Another randomized, double-blind, placebo-controlled study evaluated the efficacy bupropion SR in reducing weight and depressive symptoms in 422 obese adults with depressive symptoms. After 26 weeks, the bupropion SR group lost a greater average amount of weight (4.4 kg: 4.6% of baseline weight) compared to the placebo (1.7 kg: 1.8% of baseline weight).(54) The third 48-week double-blind, placebo-controlled trial showed bupropion SR in conjunction with a lifestyle intervention program was associated with a dose-related reduction in body weight.(55)

### **Trazodone**

In a 6-week randomized double-blind research trazodone was found to cause a slight weight loss in the over-weight depressed patients. (17)

### **Discussion:**

Significant positive association has been reported between depression and obesity more markedly among women.(56) Body weight gain is a known side effect for number of

psychotropic drugs including antidepressants.(57) This review acknowledges the various and inconsistent effects of different antidepressants on body weight changes. TCAs and particularly amitriptyline are well known to cause weight gain among antidepressants.(18,58,59) Current review has also revealed that amitriptyline has been repeatedly reported as a weight gain inducer in clinical studies.(12,13,16- 22) All TCAs seems to cause weight gain in clinical studies except protriptyline which caused weight loss when administered to patients with major depression.(35) SSRI were thought to induce weight loss rather than weight gain in contrast to TCAs.(58) As seen among the results, the majority of studies reported weight loss for fluoxetine-treating patients, yet weight gain has been also found for fluoxetine in some researches. The same inconsistent results apply to paroxetine. Weight gain has been also achieved in the studies using other SSRIs including citalopram and escitalopram. Available researches for MAOIs reported weight gain for phenelzine and Tranylcypromine, but not any significant weight changes for moclobemide. Bupropion is the only antidepressant which all the studies confirm weight loss induction in depressed patients being treated with this agent.

Some studies suggested that weight gain can be at least in parts due to the remission from depression itself and not necessarily as a result of antidepressant medication.(25, 60) The fact that losing appetite is one of the important signs of depression supports this idea. However there are evidences that antidepressants cause weight gain in patients with other psychiatric disorders such as ADHD (32) and migraine.(22) The duration of the treatment is also an important factor that may affect the results. Number of studies found differences among short-term and long-term effects of antidepressants on body weight changes. Michelson *et al* (41) reported weight loss for patients taking fluoxetine during the acute phase (4 weeks), and weight gain for the same patients in continuing phase. Another study comprising of 10 clinical trials investigating duloxetine effects found also weight loss and weight gain in acute and chronic treatment phases respectively, but in non-significant and modest amounts. The categorization of acute-chronic and short-term, long-term phases is not the same among different studies considering the time-dependent effects of antidepressants and it adds more difficulties for interpreting the results as a general point of view.

Age is another factor that seems to affect the relationship between antidepressant medication and body weight gain. As seen in the study conducted by Corman *et al* (34) nortriptyline was not a potent weight gainer in geriatric patients and it caused even weight loss in some of the subjects. It is contrary to non-elder patients among whom nortriptyline shows more potency to induce weight gain.(18,21,32)

Base line weights of the patients can also impart in the final results of the weight changes due to antidepressant medication. This was confirmed in a clinical trial conducted by Orzack *et al* (42) who discovered weight gain among patients with normal weight, but weight loss in overweight patients when they were treated by fluoxetine.

The inconsistent results for the effects of antidepressants on body weight changes which have been identified from the current review can be related to the concurrent psychotropic medication which happens in co-morbid psychiatric patients. This phenomenon can also be due to different designs, sample sizes, and duration of the studies or as a result of other contributing factors such as genetic vulnerability in addition to the factors mentioned before.

Obesity and overweight condition may lead to serious health problems such as cardiovascular diseases. Moreover weight gain caused by antidepressant drugs is a major reason for patients' noncompliance with treatment and poor treatment

outcome and fighting weight gain once it has occurred can be very difficult.(57) Therefore understanding the underlying mechanisms that contribute to the effect of antidepressants on body weight changes is important.

The results of animal based studies are not always consistent with the clinical ones. For instance amitriptyline and mirtazapine failed to have any direct association with obesity in rats and in fact it was suggested by Jeon *et al* (24) that these two antidepressants may regulate circulating levels of adiponectin and adiponectin receptor. Amitriptyline has been also found to be unsuccessful in increasing daily food intake and body weight of the rats in series of experimental studies despite applying various dosages, route of administration, diet composition and palatability.(23) Clomipramine was chronically administered to male wistar rats exposing to macronutrient self-selection procedure and it decreased food consumption and body weight gain (26) while similar to amitriptyline and mirtazapine, clomipramine induces weight gain in clinical studies.(12,25) Interpreting the results of animal models for producing obesity after antidepressant medication is challenging when considering the real life situations for human. Mastronardi *et al* (30) tried to model the similar situation of patients experiencing stress/ depression and exposure to short-term antidepressant medication continuing by high-fat diet consumption in the rats. For achieving this kind of experiment, repeated restraint stress (RRS) and short-term antidepressant medication were applied to the rats following by exposure to high-fat diet for a long time.(30) Results showed weight gain effects even after discontinuing the antidepressants consisting of imipramine and fluoxetine in rats which supported the time-dependent sensitization phenomenon.(30) In another animal based experimental study desipramine first provoked weight loss in the rats following by weight gain in continuing phases of treatment lasting for more than 3 months.(31)

Many regulatory substances have been known to affect appetite behavior including neurotransmitters such as noradrenaline, 5HT, neuropeptides such as cholecystokinin, corticotropin releasing factor, neuropeptide Y, and opioids and other hormone-like peptides such as enterostatin, bombesin, amylin, and leptin (59). TCAs have been reported to associate with weight gain due to their antagonizing action on H1 receptors for many years.(61) It has been suggested that the weight gain induction of citalopram can also be due to its high affinity to H1 receptors.(61) Some researchers attempted to find the role of leptin in the association of antidepressants and obesity.(21, 22) Berilgen *et al* (22) discovered that amitriptyline may cause leptin resistance possibly by different mechanisms and thereby result in increases in serum leptin levels and BMI. Conversely in another study amitriptyline did not cause any increases in leptin levels while inducing weight gain.(21) The underlying mechanisms for weight gain results of antidepressant medication is not yet well understood and further studies are required for investigating the role of neurotransmitters and other possible contributing factors in the process of gaining weight due to antidepressant medication. The areas of controversies such as the opposite results reported in human versus animals based studies or the different time-dependent effects of antidepressants on body weight changes need to be addressed in future studies. More continuous and more precise time-dependent investigations of the influences of antidepressants such as what has been done for antipsychotics (61), can help to clear the role of the treatment duration in producing weight gain concurrent with antidepressant medication. Investigating the effects of other antidepressants which have not been included in previous studies such as doxepin, trimipramine, venlafaxine, nefazodone, and amoxapine is another issue which needs to be considered in the relevant future studies regarding the

association of antidepressant medication and body weight changes.

#### **Declaration of interest:**

None.

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Table 1: Effects of antidepressants on body weight				
Name of the Antidepressant	Design of the Study	Results	Reported Amounts in the Results	References and the Year of the Publications
Amitriptyline	Randomized double-blind - 6 weeks	Weight gain		17, 1986
	Randomized clinical trial - One month	Weight gain	>10 lb in 28%; 7-10 lb in 44%; 3-6 lb in 17%; No change in 11%	13, 1998
	Clinical trial	Weight gain	100% of patients (n=5)	18, 1989
	Controlled trial	Weight gain	After 6w: 3.2+3.1 kg; After 4-6m: 6.2+7.1 kg	12, 1994
	Retrospective study of double blind trials	Weight gain	In both 6week and continuing 18 weeks duration.	19, 1995
	Double-blind placebo controlled trial	Weight gain	22% of patients; Mean increase: 1.7 ± 4.1 Kg	20, 1998
	Controlled trial	Weight gain	3.5 ± 1.1 kg for amitriptyline/ nortriptyline	21, 2000
	Clinical trial	Weight gain and increased leptin level		22, 2005
	Animal based experimental study (Wistar rats)	No change in weight and food intake		23, 1987
Animal based experimental study (OLETF rats)	No direct linkage with obesity		24, 2008	
Clinical trial - 9 months	Weight gain and carbohydrate craving		63, 1973	
Imipramine	Clinical trial - 4months (16 weeks)	Weight gain but, not associated with rapid weight gain	Mean average of 5 lb weight gained in all subjects; 19%: 6-10 lb weight increase; 9%: 11-15 lb weight increase; 6%: gained > 15 lb; 6%: 6-10 lb weight loss	27, 1986
	Clinical trial - 33 weeks	Not significant changes	Weight changes of: 1.3 ± 5.3 lb for acute phase (9.5 weeks); 3.1 ± 7.8 lb for continuing phase (2.3 weeks)	28, 1990
	Randomized clinical trial - 8weeks	No significant increase in weight and appetite		29, 1993
	Controlled trial	Weight gain (less than other included TCAs)	After 6 w: 2.1 ± 1.5 kg; After 4-6 m: 4 ± 1.4 kg	12, 1994
	Animal based experimental study (Male Sprague-Dawley rats)	Weight gain even after discontinuing the medication		30, 2011
Nortriptyline	Clinical trial	Weight gain	62% of patients gained weight	18, 1989
	Double-blind, placebo-controlled trial	Weight gain	Average of 5.2 lb in 9 weeks	32, 2000
	Controlled clinical trial	Weight gain	3.5 ± 1.1 kg for amitriptyline/nortriptyline	21, 2000
	Part-randomized open-label study	Weight gain	1.82 kg after 6 months	33, 2011
	Clinical trial	Weight gain	Overall mean weight gain in 30 weeks: 3.92 ± 10.34	34, 1992
Desipramine	Clinical trial - ten years	Weight gain	51% of patients gained weight	18, 1989
	Animal based experimental (Female Sabra mice)	Weight gain, gradually increase in chronic treatment		31, 2006
Protriptyline	Clinical trial	Weight loss	Average weight loss: 1.75 lb/w	35, 1992
Clomipramine	Controlled trial - 4-6 months (6w- 6m)	Weight gain	After 6 w: 1.9 ± 3.4 kg; After 4-6m: 6.1 ± 6.3 kg	12, 1994
	a double-blind, randomised trial	Weight gain		25, 1999
	Animal based experimental, 27 days (Male Wistar rats)	Decrease food intake and weight		26, 2007
Maprotyline (TeCA)	Controlled trial	Weight gain	After 6 w: 3.2 ± 2.6 kg; After 4-6m: 5.2 ± 4.1kg	12, 1994
Fluoxetine	Clinical trial (6 patients, 9.8 months)	Weight gain	Average weight gain: 20 lb	40, 1991
	Clinical trial	Wight loss	Average weight loss of 1.20 lb/w	35, 1992
	Double-blind trials	Weight loss		19, 1995
	Double-blind parallel study	Weight loss		36, 1996
	Randomized clinical trial	Modest but non-significant weight loss		37, 2000
	Clinical trial	Weight loss	Mean weight losses: 4th week: 3.24 kg; 8th week: 6.67 kg	38, 2005
	Clinical trial	Weight loss Weight gain	At acute phase (4weeks): Mean absolute weight loss of 0.4 kg; At continuing phase, mean weight gain of: 26 w: 1.4+3.2 kg; 38 w: 3.1+3.8 kg; 50 w: 4.3+5.3 kg	41, 1999
	Clinical Trial	Weight loss; Weight gain	Weight loss in overweight patients; Weight gain in ideal weight patients	42
	Animal based experimental study (OLETF rats)	No linkage with weight gain		24, 2008
	Animal based experimental study (Male Sprague-Dawley rats)	Weight gain even after discontinuation		30, 2011
Animal based experimental study (Rats)	Inhibiting pelleted food intake		39, 1991	
Paroxetine	Randomized clinical trial	Weight gain		45, 2000
	Randomized clinical trial	Significant weight increase		37, 2000
	Double-blind trials	No change in weight		19, 1995
	Controlled clinical trial	No change in weight, and leptin level		21, 2000
	Animal based experimental study (Rats)	Inhibiting pelleted food intake		39, 1991
Sertraline	Clinical trial	Weight loss	Average weight loss of: 1.06 lb/week in those with low urinary MHPG; 0.42 lb/week in those with high urinary MHPG	49, 1994
	Randomized clinical trial	Non-significant (modest) weight increase.		37, 2000
Citalopram	Clinical trial with 8 patients	Significant weight gain and increasing carbohydrate craving		47, 1996
	Multicenter randomized double blind trial	Different adverse effects compared to mirtazapine	Weight gain only in 4.5% of patients	46, 1999
	1. Double blind, randomized; 2. Open trial	no weigh gain or slight weigh gain	Slight weight gain: <2.5 kg	25, 1999



Escitalopram	Double blind controlled trial	Weight gain	1.38kg in 8 months	48, 2007
	Part-randomized open-label study	Not significant weight change	Average of 0.14 kg weight increase in 6 months	33, 2011
Fluvoxamine	Double blind trial	No weight gain		43, 1991
	Double-blind placebo controlled	Weight loss	Overall mean weight loss of 3.1 kg in 12 weeks	44, 1986
Zimelidine	Randomized clinical trial	No weight gain	Mean weight change in one month: $0.2 \pm 1.8$ kg	50, 1988
Phenelzine	Clinical trial	Weight gain	In 46% of patients	18, 1989
Tranylcypromine	Clinical trial	Weight gain	In 73% of patients ( $4.1 \pm 2.2$ Kg)	18, 1989
Moclobemide	Double-blind trial	No changes in weight		19, 1995
Bupropion	Randomized double-blind trial	Modest weight loss in long-term		53, 2002
	Randomized, double-blind, placebo-controlled	Weight loss	Mean weight loss: 4.4 kg (4.6% of baseline weight) in 26 weeks	54, 2002
	Double blind placebo controlled trial	Dose-related reduction in weight	24-week weight loss (% of baseline body weight): 7.2% for SR 300; 10.1% for SR 400; 48-week weight loss: 7.5% for SR 300; 8.6% for SR 400	55, 2002
Trazodone	Randomized double-blind study	Slight weight loss in overweight patients		17, 1986
Duloxetine	Double blind controlled trial	Weight gain	0.6kg in 8 months	48, 2007
	10 controlled clinical trials	No consistent weight change	No significant differences from placebo groups	51, 2006
Mianserin	Double blind trial	Weight gain		43, 1991
Mirtazapine	Double-blind placebo controlled	Weight gain	Average of $1.4 \pm 3.1$ kg	20, 1998
	Multicenter randomized double blind trial	Different adverse effects compared to citalopram	15.3% of patients gained weight	46, 1999
	Randomized clinical trial	Weight gain		45, 2000
	Clinical trial	Weight gain	Weight increased from $63.6 \pm 13.1$ kg to $66.6 \pm 11.9$ kg	52, 2006
	Animal based experimental study (OLETF rats)	No linkage with weight gain		24, 2008