**RESEARCH PAPER**

# Selective Serotonin Reuptake Inhibitors and Serotonin Norepinephrine Reuptake Inhibitors and Body Mass Index in Patients on Long Term Treatment: A Cross-Sectional Comparative Study

Shreya Hegde[1], Padmaja Udaykumar[2*] and Aruna Yadiyal[3]

*[1]Assistant Professor, Department of Pharmacology, Kasturba Medical College, Manipal Academy of Higher Education, Manipal, India- 576104*

*[2*]Professor, Department of Pharmacology, Father Muller Medical College, Kankanady, Mangalore 575002, India*

*[3]Professor, Department of Psychiatry, Father Muller Medical College, Kankanady, Mangalore 575002, India*

*[1]shreya.arjun@manipal.edu, [2*]padmajaudaykumar@fathermuller.in and [3]aruna.g2779@gmail.com*

*Orcid: [1]0000-0002-9913-1427 and [2]0000-0002-5511-0982*

***Corresponding Author:** Dr Padmaja Udaykumar, MBBS, MD (Pharmacology), Professor, Department of Pharmacology, Father Muller Medical College, Kankanady, Mangalore 575002, India.*

*padmajaudaykumar@fathermuller.in*

*Orcid ID: 0000-0002-5511-0982*

***Received: 16th Dec, 2025; Revised: 8th Feb 2026; Accepted: 12th Feb, 2026; Available Online: 28th Feb, 2026***

**ABSTRACT**

**Background:** Selective Serotonin Reuptake Inhibitors (SSRIs) and Serotonin Norepinephrine Reuptake Inhibitors (SNRIs) are the most commonly prescribed antidepressants but changes in body weight (BW) is a concern with the chronic use of antidepressant. We observed the effect of SSRIs and SNRIs on BW and body mass index (BMI) in patients on long-term therapy while avoiding the other confounding factors.

**Objectives:** To assess and compare the changes in BW and BMI in patients on monotherapy with either SSRIs (escitalopram, sertraline or fluoxetine) or SNRIs (duloxetine, venlafaxine or desvenlafaxine).

**Methods:** In a cross-sectional, hospital-based, comparative study, the patients on monotherapy with- sertraline, fluoxetine, escitalopram, venlafaxine, desvenlafaxine or duloxetine for a period of ≥ 24 weeks were evaluated for the changes in their BW and BMI. In patients showing a change in weight, causality assessment was done by Naranjo's algorithm and severity assessment by modified Hartwig and Siegel scale.

**Results and Conclusion:** Fifty-eight patients were included (SSRIs = 30; SNRIs = 28). Escitalopram and sertraline were associated with increases in BW and BMI, whereas fluoxetine, duloxetine, venlafaxine, and desvenlafaxine showed reductions. Median weight gain with escitalopram and sertraline was 2.0 kg (IQR 1.5) and 2.0 kg (IQR 1.0), respectively. Fluoxetine showed mean reductions of 1.20 ± 1.32 kg in BW and 0.44 ± 0.50 kg/m² in BMI. Statistically significant changes were observed with SSRIs but not with SNRIs. Between-group analysis demonstrated significantly greater weight gain with SSRIs compared with weight reduction with SNRIs ($p < 0.001$). All changes were classified as probable and mild. As weight changes remained <5% of baseline BW over ≥24 weeks, they may not be considered clinically meaningful. These findings suggest that SSRIs and SNRIs have a relatively favourable weight profile in patients without significant comorbidities or concomitant medications.

**Keywords:** escitalopram; fluoxetine; sertraline; venlafaxine; duloxetine; antidepressants; body mass index.

**How to cite this article:** Hegde S, Udaykumar P, Yadiyal A. Selective Serotonin Reuptake Inhibitors and Serotonin Norepinephrine Reuptake Inhibitors and Body Mass Index in Patients on Long Term Treatment: A Cross-Sectional Comparative Study. Int J Drug Deliv Technol. 2026; 16(2): 355-363. DOI: 10.25258/ijddt.16.2.39

**Source of support:** Nil.

**Conflict of interest:** None

## INTRODUCTION

Antidepressants are employed in the treatment of a wide range of clinical conditions with major use in psychiatric disorders such as the management of depression, anxiety and mood disorders, personality disorders, eating disorders, substance use disorder and chronic pain syndromes,[(1)] and its prescription is showing an upward trend globally.[(2)] A positive association between antidepressants and weight gain is documented in clinical trials.[(3)] Depression and obesity are interrelated, though the underlying mechanisms are complex and poorly understood, particularly with long-term use.[(4)]The patients on antidepressants show a tendency towards weight gain, while the underlying cause for the same is still debated, as the changes in BMI could be owing to the disease, drugs or the global increase in obesity.

Presently, Selective Serotonin Reuptake Inhibitors (SSRIs) and Serotonin Norepinephrine Reuptake Inhibitors

**Author for Correspondence: padmajaudaykumar@fathermuller.in*

(SNRIs) are the preferred antidepressants globally for the advantages they offer over the earlier used agents due to their specific receptor selectivity. Some of the common adverse effects seen with these agents are sexual dysfunction, drowsiness, weight gain or loss, insomnia, anxiety, dizziness, headache and dry mouth. Among various adverse effects, the effect of SSRIs and SNRIs on body weight changes have shown unpredictable results in different scenarios, [3, 5, 6] with a few proving a positive association. [7] These agents may bring about weight gain, weight loss or some have been found to be weight neutral. [5]

In addition, changes in body weight can adversely affect the patient adherence to the therapy and most of the data on this regard is from the western population.[5, 8] In previous studies, the patients were on multiple medications, had associated co-morbid conditions, and were followed up for a short duration of time (< 3 months).

Hence, the present study aims to observe the effect of different SSRIs (escitalopram, fluoxetine, sertraline) and SNRIs (venlafaxine, desvenlafaxine, duloxetine) on body mass index in adult Indian patients on long term therapy (>24 weeks).

## MATERIALS & METHODS

This cross-sectional, hospital-based, prospective observational, comparative study was conducted by the departments of Pharmacology and Psychiatry of a tertiary care teaching hospital, after obtaining approval from the Institutional Ethics Committee, registered with the Department of Health Research, India. Prospective patients were screened after obtaining a written informed consent. The study aimed to assess and compare the changes in body mass index (BMI) in patients on long-term treatment with SSRI or SNRI.

Patients between 18-65 years of either sex, on monotherapy with either SSRIs (sertraline, fluoxetine or escitalopram) or SNRIs (venlafaxine, desvenlafaxine or duloxetine) irrespective of their diagnosis for a period of ≧24 weeks were included. Patients with comorbid medical conditions, on long term treatment with other medications that may affect body weight or history of with substance abuse were excluded.

Demographic data, diagnosis and treatment details were recorded. Baseline weight (kilograms) and height (metres) of the patient was obtained from the case records, current weight and height of the patient were noted when the patient visited the outpatient department. Body weight was measured with an analogue scale weighing machine and height with a wall mounted height measuring scale, BMI was calculated and recorded.[9] Based on the WHO BMI cut-offs, the patients were categorized into either normal, underweight, overweight or obese.[10] The changes in the weight and BMI in each patient were calculated. In patients showing a change in weight, causality assessment was done by Naranjo's algorithm and severity assessment by modified Hartwig and Siegel Scale. [11,12]

Patients were categorized into Group 1 – those who were on SSRIs and Group 2 - those who were on SNRIs.

## STATISTICAL ANALYSIS

Statistical analysis was performed using Microsoft Excel and Jamovi statistical software (The jamovi project (2025). jamovi (Version 2.6) [Computer Software]. Retrieved from https://www.jamovi.org). Descriptive statistics were applied to obtain the mean and frequency of the demographic and clinical data. The continuous variables were expressed either as mean ± SD or median (IQR) depending on its distribution. The Shapiro–Wilk test was used to assess normality of data. Within-group comparisons were performed using paired Student's t-test or Wilcoxon signed-rank test depending on normality. Between-group comparisons between SSRI and SNRI groups were performed using independent samples t-test. Effect sizes were estimated using Cohen's d for t-tests and rank-biserial correlation (r) for the Wilcoxon signed-rank test. A p-value <0.05 was considered statistically significant.

## RESULTS

We enrolled 58 patients (Group 1: 30; Group 2: 28), the mean±SD age of the patients was 37.29±7.54 years. Patients in the age group 31-40 years comprised 48.2% of the study population, while those aged >41 years were 32.8% and <30 years formed 19%.

There were 39 (67.24%) females.

In Group 1, patients were on escitalopram (n=11, 37%), fluoxetine (n=10, 33%) and sertraline (n=09, 30%). In Group 2, patients received duloxetine (n=10, 36%), venlafaxine (n=09, 32%) and desvenlafaxine (n=09, 32%). There was no statistically significant difference between the two groups in terms of age, gender distribution, body weight and duration of treatment.

**Tables 1 and 2** tabulate the demographic and baseline characteristics.

**Table 1**. Demographic characteristics

| Parameters | SSRIs | SNRIs | Total |
|---|---|---|---|
| Female | 20 (51.28%) | 19 (48.72%) | 39 (67.24%) |
| Male | 10 (52.63%) | 09 (47.37%) | 19 (32.76%) |
| Total | 30 (51.72%) | 28 (48.28%) | 58 (100%) |
| Physical exercise | 21 (47.73%) | 23 (52.27%) | 44 (75.85%) |
| Consumption of alcohol | 01 (25%) | 03 (75%) | 04 (6.9%) |
| Smoking | 01 | 01 | 02 (3.45%) |

Percentages expressed in the box represent values with respect to the total study population.

**Table 2:** Baseline characteristics of the study population

| Parameters | Mean± SD | Range | t value | p value |
|---|---|---|---|---|
| **Age (years)** | | | | |
| SSRIs | 35.73 ± 7.31 | 17-49 | 1.654 | 0.104 |
| SNRIs | 38.96 ± 7.57 | 21-53 | | |
| **Duration of treatment (in months)** | | | | |
| SSRIs | 7.43± 1.72 | 6-12 | 0.705 | 0.484 |
| SNRIs | 7.14± 1.63 | 6-14 | | |
| **Body weight at baseline (in kgs)** | | | | |
| | **Mean± SD** | **Median (IQR)** | **t value** | **p value** |
| SSRIs | 59.6± 8.69 | 58 (53-68.75) | 0.661 | 0.512 |
| SNRIs | 58.07± 7.76 | 60 (53.75-62.5) | | |

**Dose of each drug**

Escitalopram dose varied between 5 mg- 20 mg (5mg 30%,10 mg 50%, 15 mg and 20 mg, 10% each); fluoxetine at dose of 20 mg (70%) and 40 mg (30%), sertraline at 25 mg (44%) and 50 mg (56%) was given. Duloxetine at 30 mg (30%) and 40 mg (70%), venlafaxine at a dose of 37.5 mg (56%) and 75 mg (44%), desvenlafaxine at 50 mg (89%) and 150 mg (11%) were prescribed.

Diagnosis

The patients in the study were diagnosed with generalized anxiety disorder (GAD) (n=31, 53.45%), obsessive compulsive disorder (OCD) (n=14, 24.14%), depression (n=10, 17.24%) and panic disorders (n=03, 5.17%).

SSRIs were prescribed to 19 (32.76% of the study population) patients with GAD, nine (15.52%) patients with OCD and one patient each with depression and panic disorders. SNRIs were prescribed to 12 (20.69%) patients with GAD, nine (15.52%) with depression, three (5.17%) with OCD and two (3.45%) with panic disorder.

76% of the total patients exercised regularly; a greater proportion of the study population were non-alcoholics (alcohol consumers 7%) and non-smokers (3%).

**Changes in body weight and BMI**

On comparing the groups (Group 1 and 2), an independent samples t-test revealed a statistically significant difference in BMI change between patients receiving SSRIs and SNRIs ($t(56)=4.07$, $p<0.001$). Patients treated with SSRIs showed an overall increase in BMI, whereas those receiving SNRIs demonstrated a reduction in BMI.

**Weight Changes** (Table 3)

In Group 1, among patients receiving SSRIs, differential effects on body weight were observed. Patients treated with escitalopram demonstrated a statistically significant increase in median weight of 2.00 kg (IQR 1.5). As the data were non-normally distributed, Wilcoxon signed-rank test showed a significant difference ($W=66.0$, $p=0.003$), with a strong effect size (rank biserial correlation = 1), indicating a consistent weight gain trend.

Similarly, patients on sertraline experienced a significant median weight gain of 2.00 kg (IQR 1.00) ($W=45.0$, $p=0.008$), also demonstrating a strong effect size (rank biserial correlation = 1). In contrast, patients receiving fluoxetine showed a statistically significant reduction in weight (mean change −1.20 kg; $t(9)= -2.88$, $p<0.05$), with a large effect size (Cohen's $d = -0.91$).

In group 2, among serotonin-norepinephrine reuptake inhibitors (SNRIs), patients treated with duloxetine exhibited a small mean reduction in weight (−0.6 kg), which wasn't statistically significant. Patients on venlafaxine and desvenlafaxine showed modest mean weight reductions (−1.11 and −1.22 kg respectively); however, these changes were not statistically significant ($p>0.05$), despite moderate effect sizes.

**Table 3:** Within-Group Changes in Body Weight Following ≥24 Weeks of SSRI and SNRI monotherapy Within-group changes in weight after ≥24 weeks of SSRI and SNRI monotherapy

| Drug | Weight change (kg) | Normality test | Statistical test | Effect size |
|---|---|---|---|---|
| **SSRIs** | | | | |
| Escitalopram | 2.00 (1.50) | $p < 0.05$ | Wilcoxon signed-rank: $W = 66.0$, $p = 0.003$* | $r = 1$ |
| Fluoxetine | −1.20± 1.32 | $p > 0.05$ | Paired t-test: $t(9) = -2.88$, $p = 0.018$* | Cohen's $d = -0.91$ |
| Sertraline | 2.00 (1.00) | $p < 0.05$ | Wilcoxon signed-rank: $W = 45.0$, $p = 0.008$* | $r = 1$ |
| **SNRIs** | | | | |
| Duloxetine | −0.6±2.76 | $p > 0.05$ | Paired t-test: $t(9) = -0.69$, $p$ | Cohen's $d$ = |

| | | | | |
|---|---|---|---|---|
| | | | = 0.509 | −0.22 |
| Venlafaxine | −1.11± 1.62 | p > 0.05 | Paired t-test: t(8) = −2.06, p =0.073 | Cohen's d = −0.69 |
| Desvenlafaxine | −1.22±1.72 | p > 0.05 | Paired t-test: t(8) = −2.14, p =0.065 | Cohen's d = −0.71 |

Weight change values are expressed as mean ± SD or median (interquartile range) depending on distribution. Normality was assessed using the Shapiro–Wilk test. Paired t-test was used for normally distributed data and Wilcoxon signed-rank test for non-normal data. *p value<0.05 considered as significant.

**BMI Changes: (Table 4)**

Within-group changes in BMI were analyzed using paired Student's t-test for normally distributed variables and the Wilcoxon signed-rank test for non-normally distributed variables, after assessing normality with the Shapiro–Wilk test. Among patients receiving escitalopram, a statistically significant increase in BMI was observed t(10) = 9.13, p<0.05. Similarly, patients treated with sertraline demonstrated a significant increase in BMI (W = 45.0, p<0.05). In contrast, treatment with fluoxetine showed a statistically significant reduction in BMI with t (9) = −2.70, p<0.05. Among the SNRIs, patients receiving duloxetine showed a reduction in BMI though not statistically significant t(9) = −0.69, p>0.05. Similarly, treatment with venlafaxine and desvenlafaxine showed a decrease in BMI; however, these changes were also not statistically significant. For the between-group comparison, an independent samples t-test revealed a statistically significant difference in BMI change between patients receiving SSRIs and SNRIs (t(56) = 3.99, p < 0.001; Cohen's d = 1.05). Patients treated with SSRIs showed an overall increase in BMI, whereas those receiving SNRIs demonstrated a reduction in BMI.

**Table 4:** Within-Group Changes in BMI following ≥24 Weeks of SSRI and SNRI Monotherapy Within-group changes in BMI after ≥24 weeks of SSRI and SNRI monotherapy

| Drug | BMI change (kg/m²) | Normality test | Statistical test | Effect size |
|---|---|---|---|---|
| **SSRIs** | | | | |
| Escitalopram | 1.12 ± 0.4 | p > 0.05 | Paired t-test: t(10) = 9.13, p<0.001* | Cohen's d = 2.75 |
| Fluoxetine | −0.44± 0.51 | p > 0.05 | Paired t-test: t(9) = −2.70, p =0.024* | Cohen's d = −0.85 |
| Sertraline | 0.78 (0.35) | p < 0.05 | Wilcoxon signed-rank: W = 45.0, p =0.004* | r = 1 |
| **SNRIs** | | | | |
| Duloxetine | −0.25±1.15 | p > 0.05 | Paired t-test: t(9) = −0.69, p=0.510 | Cohen's d = −0.22 |
| Venlafaxine | −0.42±0.63 | p > 0.05 | Paired t-test: t(8) = −2.06, p=0.077 | Cohen's d = −0.68 |
| Desvenlafaxine | −0.48±0.67 | p > 0.05 | Paired t-test: t(8) = −2.14, p=0.065 | Cohen's d = −0.71 |

BMI change values are expressed as mean ± SD or median (interquartile range) depending on distribution. Normality was assessed using the Shapiro–Wilk test. Paired t-test was used for normally distributed data and Wilcoxon signed-rank test for non-normal data. *p value<0.05 considered as significant.

Among those who received SSRIs, three patients became overweight from normal weight and with SNRIs, two patients reduced weight and became normal weight (table 5).

**Table 5:** BMI category distribution among patients receiving SSRIs and SNRIs at baseline and 6 months

| BMI range | Nutrition status | Baseline | At month 6 |
|---|---|---|---|
| **SSRIs** | | | |
| 17-18.49 | Mild underweight | 0 | 0 |
| 18.5-24.9 | Normal | 20 (66.66%) | 17 (56.66%) |
| ≥25 | Overweight | 10 (33.33%) | 13 (43.33%) |
| 25-29.9 | Pre-obese | 0 | 0 |
| **SNRIs** | | | |
| 17-18.49 | Mild underweight | 1 (3.57%) | 1 (3.57%) |
| 18.5-24.9 | Normal | 19 (67.85%) | 21 (75%) |
| ≥25 | Over weight | 8 (28.57%) | 6 (21.42%) |
| 25-29.9 | Pre-obese | 0 | 0 |

Causality assessment was done as per Naranjo's algorithm which showed that all the observed body weight changes belonged to the probable category. No case could be labelled as certain or definite. Severity was assessed by modified Hartwig and Siegel scale. All the cases of weight change were graded as mild.

## DISCUSSION

There is a paucity of data on weight changes with antidepressants, particularly with long term (>24 weeks) therapy in Indian population. [5] Majority of these studies were conducted to see the body weight changes in the setting of short-term therapy (<12 weeks). There is a specific relevance of the duration of therapy in case of SSRIs and SNRIs due to their unique mechanism of action. These agents enhance serotonergic and noradrenergic neurotransmission by blocking serotonin transporter and norepinephrine transporter respectively. On repeated treatment with these drugs, there is a gradual downregulation and desensitization of these auto receptor mechanisms, requiring few weeks to exert their action. Moreover, SSRIs and SNRIs are used for long duration (> 24 weeks) in diseases such as depression, anxiety disorders and obsessive-compulsive disorders and chronic therapy is said to be one of the causes for weight gain. Frequently used SSRIs are escitalopram, fluoxetine, sertraline and SNRIs include venlafaxine, desvenlafaxine and duloxetine, and we compared these agents.

Weight changes associated with the use of antidepressants appear to be less pronounced in the elderly population (>65 years), while younger patients tend to experience greater weight gain, as observed in few studies.[14-17] Generally, weight remains either constant or reduces in the elderly due to reduced food intake and less physical activity, and antidepressants may have less impact on weight in this subset of patients. Our study population predominantly had younger patients and significant weight changes were observed, particularly among those receiving SSRIs. Weight gain associated with antidepressant therapy may be particularly concerning for young female patients. As our study population showed female predominance, monitoring weight changes during treatment becomes clinically relevant.

The effect of individual antidepressants on weight and BMI varies according to the duration of treatment. Various studies have analyzed the relationship between antidepressants and weight gain with short-term use of eight months to two years.[3] In our study, the mean duration of the treatment was 7.43±1.72 months in the SSRI group and 7.14±1.63 months in the SNRI group. A 10-year follow-up study involving the analysis of data of 2,94,719 patients has confirmed a strong temporal association between consumption of antidepressants and weight gain (≥5% from baseline). Duration of treatment is a determining factor as highest weight gain occurs during 2nd and 3rd year of treatment, with 46.3% higher in 2nd year and can be seen up to 5 years.[18] Lee et al., even hypothesized that increased consumption of antidepressants with rising psychiatric illness could be one of the contributing factor for increasing obesity, particularly in the high-income countries. [19] The current study observed patients receiving antidepressant therapy for up to 12 months; however, longer-duration studies are desirable to clarify the long-term effects of antidepressants on body weight. Studies have documented an increase in the range of 0.14 to 1.38 kgs over a period of 12 weeks to 8 months with escitalopram. [3, 20, 21] In the current study, an increase in weight between the range of 2-5 kg over a period of 6-12 months was recorded in patients on escitalopram. SSRIs and weight gain bear a positive association. Weight gain is reported with long-term use of escitalopram in elderly, however, in comparison with nortriptyline/tricyclic antidepressants, the weight gain is not significant. (0.14 Kg in 12 weeks). [21,22] Escitalopram does not bring significant weight gain and remained almost stable, hence, can be used in those who are overweight or obese, however, a mindful watch on eating and physical activity is required. [21]

The mean increase with sertraline is reported to be in the range of 1-1.5 kgs for sertraline over a period of 26-32 weeks treatment. [24, 25] We observed an increase in weight in the range of 1-2 kg in our study reflecting a similar trend as other studies. The weight and BMI increase with the drug were observed to be statistically significant.

Fluoxetine in our study population did show a reduction in weight and BMI. In our study, fluoxetine reduced weight on an average of 1.2 kg and an average BMI by 0.44 which was statistically significant. In the western population, fluoxetine long-term treatment induced minimal weight changes ranging from a loss of 0.2% of body weight at baseline to a gain of 0.9%.[25,26]A randomized trial showed a mean weight gain of 3.0 kg in patients on one year treatment.[27].A study reported that in those with normal weight, fluoxetine increased weight (4.4 lbs), while overweight patients recorded weight loss (3.3lbs); the trend was not consistent among those who were underweight.[28] Serralde-Zuñiga et al.,(2022) have observed weight loss (-2.7 kg; $p < 0.001$) and drop in BMI (-1.1 kg/m$^2$) with fluoxetine compared to placebo. [29] In a comparative study with placebo, fluoxetine though showed weight loss during treatment (fluoxetine: -8.2 kg; placebo: -4.5 kg; $P < 0.05$) but weight regained, whereas those in the placebo group did not.[30 ]Brunner et al., have noticed weight gain when fluoxetine is administered with olanzapine ( >7%, in 55.7% of patients). [31] In our study, SSRIs as a class did not demonstrate a uniform trend with respect to weight changes; escitalopram and sertraline were associated with weight gain, whereas fluoxetine was associated with weight loss.

Data on duloxetine, venlafaxine, and desvenlafaxine is limited. Analysis of pooled data showed a marginal weight

loss of 0.5 kg with duloxetine with short term treatment followed by modest weight gain on longer-term treatment. [32] However, these changes were statistically not significant. Weight changes induced by duloxetine were modest in our study and weren't statistically significant. Duloxetine induced weight reduction and corresponding decrease in BMI finds its clinical applications in conditions such as binge eating, which needs further exploration. [33, 34] No significant weight changes were seen with venlafaxine in treatment resistant major depression.[35] Similar observations were reported by Allard et al., boosting the support for a weight neutral agent.[36,37] A comprehensive review by Serretti & Mandelli., concluded that the venlafaxine causes a modest weight reduction of 0.5 kg and desvenlafaxine recorded a mean weight loss of 0.8 kg on 12-week treatment with the drugs. [3] In our study, venlafaxine and desvenlafaxine showed a negligible weight change which was not statistically significant.

Ranjbar et al., in a review article analysed the association between antidepressants and body weight and observed that SSRIs are associated with weight gain, though with inconclusive conclusion about individual agents.[8] A cross-sectional study has demonstrated a positive relationship between the antidepressants and body weight, with a prevalence of weight gain of 55%, and >7% weight gain in 40.6% with newer agents (citalopram, escitalopram, sertraline, paroxetine, venlafaxine, duloxetine, mirtrazepine.[38]

BMI, 28.57% patients were overweight and 3.57% were mildly underweight. However, for Asian population WHO has introduced an additional BMI cut-off point of 23 within the normal BMI range due to an increased predilection for type 2 diabetes mellitus and cardiovascular diseases seen in these patients. According to this cut-off, 63.33% subjects in SSRIs and 57.14% in SNRIs had a BMI >23. It implies that majority of the study participants belonged to the at- risk group and therefore an extreme caution must be taken in these patients while prescribing drugs which can induce weight. On the contrary, in patients who are overweight, an antidepressant causing weight loss can be prescribed if therapeutically indicated.

Choosing the antidepressant selectively according to the weight is therefore preferred. For example, for those who are overweight and obese, weight-neutral agents can be prescribed. In our study, although within-group analyses revealed significant weight gain with escitalopram and sertraline and weight reduction with fluoxetine, class-wise comparison between SSRIs and SNRIs did not demonstrate a clear uniform pattern. This suggests that antidepressant-associated weight changes may be drug-specific rather than purely class-dependent. Pooling medications within a class may obscure clinically meaningful differences at the individual drug level. Moreover, it has been documented that weight also influences the response to antidepressants with obesity decreasing the response.[39] Associated comorbidities with weight gain, and depression can result in unfavorable clinical outcomes. This makes it difficult to establish if the antidepressant alone has led to these changes. Hence, body weight is an important factor to be considered in evaluating the outcome(s) of therapy, and hence selecting a suitable antidepressant and customizing treatment options is highly recommended. [21, 40]

Small sample size and single-center study, however, stops us from arriving at a definite conclusion. A prospective study with a longer duration of follow-up, comparison with a control group would have guided us better and further towards more robust findings. Eliminating the confounding factors, considering diet and physical activities, socio-economic status, and correlation of the body weight and BMI changes with the dose of the drug would also have yielded more useful information. There is no guideline on the use of antidepressants based on BMI or measures to minimize weight gain when on these agents. We hope our results will be considered by the regulatory agencies while drafting guidelines in the future for antidepressant use.

**Conclusion:** Overall, these findings reinforce that antidepressant-associated weight changes are drug-specific rather than purely class-specific. From a clinical standpoint, SSRIs such as escitalopram and sertraline may warrant closer metabolic monitoring during long-term therapy, whereas fluoxetine and SNRIs may be preferable in patients where weight gain is a concern. However, the change in body weight observed in our patients remained <5% of baseline body weight over 24 weeks of therapy and may therefore not be considered clinically meaningful. In patients without significant comorbidities or concomitant medications, as represented in our study population, these antidepressants appear to have a relatively favourable weight profile.

**Funding:** None.

**Conflict of Interest:** None of the authors have any conflict of interest to declare.

**Author Contribution:** All authors have contributed significantly towards the conduct of the research and preparation of this manuscript. All authors have read the manuscript, agree and approve the content.

**CRediT author statement:** SH contributed to conceptualization, data curation, formal analysis, investigation, methodology, visualization, writing—original draft and editing. PK contributed to conceptualization, formal analysis, investigation, methodology, project administration, resources, supervision, and writing—review and editing. AY contributed to conceptualization, data curation, investigation, methodology, project administration and supervision, and writing—review and editing. Funding acquisition: not applicable.

**REFERENCES**


1. Avasthi A, Grover S, Aggarwal M. Research on antidepressants in India. Indian journal of psychiatry 2010;52(Suppl 1): S341–S354. https://doi.org/10.4103/0019-5545.69263
2. Lockhart P, Guthrie B. Trends in primary care antidepressant prescribing 1995-2007: a longitudinal population database analysis.The British journal of general practice:the journal of the Royal College of General Practitioners 2011; 61: e565–e572. https://doi.org/10.3399/bjgp11X593848
3. Serretti A, Mandelli L. Antidepressants and body weight: a comprehensive review and meta-analysis. The Journal of clinical psychiatry 2010; 71: 1259–1272. https://doi.org/10.4088/JCP.09r05346blu
4. Arterburn D, Sofer T, Boudreau DM, Bogart A, Westbrook EO, Theis MK, et al. Long-Term Weight Change after Initiating Second-Generation Antidepressants. Journal of clinical medicine 2016; 5: 48. https://doi.org/10.3390/jcm5040048
5. Dent R, Blackmore A, Peterson J, Habib R, Kay GP, Gervais A, et al. Changes in body weight and psychotropic drugs: a systematic synthesis of the literature. PloS one 2012; 7, e36889. https://doi.org/10.1371/journal.pone.0036889
6. Ferguson J M. SSRI Antidepressant Medications: Adverse Effects and Tolerability. Primary care companion to the Journal of clinical psychiatry 2001;3: 22–27. https://doi.org/10.4088/pcc.v03n0105
7. Mastronardi C, Paz-Filho GJ, Valdez E, Maestre-Mesa J, Licinio J, Wong ML. Long-term body weight outcomes of antidepressant-environment interactions. Molecular psychiatry 2011;16: 265–272. https://doi.org/10.1038/mp.2010.122
8. Ranjbar S, Pai NB, Deng C. The association of antidepressant medication and body weight gain. Online Journal of Health and Allied Sciences 2013;12:1-9.
9. Eknoyan G. Adolphe Quetelet (1796-1874)-the average man and indices of obesity. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 2008;23:47–51. https://doi.org/10.1093/ndt/gfm517
10. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet (London, England) 2004;363:157–163. https://doi.org/10.1016/S0140-6736(03)15268-3
11. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. Clinical pharmacology and therapeutics 1981;30: 239–245. https://doi.org/10.1038/clpt.1981.154
12. Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. American journal of hospital pharmacy 1992;49: 2229–2232.
13. Grover S, Avasthi A, Sinha V, Lakdawala B, Bathla M, Sethi S, et al. Indian Psychiatric Society multicentric study: Prescription patterns of psychotropics in India' Indian journal of psychiatry 2014;56: 253–264. https://doi.org/10.4103/0019-5545.140632
14. Hinze-Selch D, Schuld A, Kraus T, Kühn M, Uhr M, Haack M, et al. Effects of antidepressants on weight and on the plasma levels of leptin, TNF-alpha and soluble TNF receptors: A longitudinal study in patients treated with amitriptyline or paroxetine. Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology 2000;23:13–19. https://doi.org/10.1016/S0893-133X(00)00089-0
15. Paradis CF, Stack JA, George CJ, Miller MD, Pollock BG, Rifai AH, et al. Nortriptyline and weight change in depressed patients over 60. Journal of clinical psychopharmacology 1992; 12: 246–250.
16. Prince JB, Wilens TE, Biederman J, Spencer TJ, Millstein R, Polisner DA, et al. A controlled study of nortriptyline in children and adolescents with attention deficit hyperactivity disorder. Journal of child and adolescent psychopharmacology 2000;10: 193–204. https://doi.org/10.1089/10445460050167304
17. Patten SB, Williams JV, Lavorato DH, Khaled S, Bulloch AG. Weight gain in relation to major depression and antidepressant medication use. Journal of affective disorders 2011;134: 288–293. https://doi.org/10.1016/j.jad.2011.06.027
18. Gafoor R, Booth HP, Gulliford MC. Antidepressant utilisation and incidence of weight gain during 10 years' follow-up: population based cohort study. BMJ (Clinical research ed.) 2018; 361: k1951. https://doi.org/10.1136/bmj.k1951
19. Lee SH, Paz-Filho G, Mastronardi C, Licinio J, Wong ML.Is increased antidepressant exposure a contributory factor to the obesity pandemic? Translational psychiatry 2016;6:e759. https://doi.org/10.1038/tp.2016.25
20. Pigott TA, Prakash A, Arnold LM, Aaronson ST, Mallinckrodt C H, Wohlreich MM. Duloxetine versus escitalopram and placebo: an 8-month, double-blind trial in patients with major depressive disorder. Current medical research and opinion 2007;23:1303–1318. https://doi.org/10.1185/030079907X188107
21. Uher R, Mors O, Hauser J, Rietschel M, Maier W, Kozel D, et al. Body weight as a predictor of antidepressant efficacy in the GENDEP project.

Journal of affective disorders 2009;118:147–154. https://doi.org/10.1016/j.jad.2009.02.013

22. Seo HJ, Jung YE, Woo YS, Jun TY, Chae JH, Bahk WM. Effect of augmented atypical antipsychotics on weight change in patients with major depressive disorder in a naturalistic setting. Human psychopharmacology 2009;24:135–143. https://doi.org/10.1002/hup.1001
23. Kasper S, Lemming OM, de Swart H. Escitalopram in the long-term treatment of major depressive disorder in elderly patients. Neuropsychobiology 2006;54: 152–159. https://doi.org/10.1159/000098650
24. Maina G, Albert U, Salvi V, Bogetto F. Weight gain during long-term treatment of obsessive-compulsive disorder: a prospective comparison between serotonin reuptake inhibitors. The Journal of clinical psychiatry 2004;65:1365–1371. https://doi.org/10.4088/jcp.v65n1011
25. Fava M, Judge R, Hoog SL, Nilsson ME, Koke SC. Fluoxetine versus sertraline and paroxetine in major depressive disorder: changes in weight with long-term treatment. The Journal of clinical psychiatry 2000;61:863–867. https://doi.org/10.4088/jcp.v61n1109
26. Maina G, Albert U, Salvi V, Bogetto F. Weight gain during long-term treatment of obsessive-compulsive disorder: a prospective comparison between serotonin reuptake inhibitors. The Journal of clinical psychiatry 2004;65:1365–1371. https://doi.org/10.4088/jcp.v65n1011
27. Michelson D, Amsterdam JD, Quitkin FM, Reimherr FW, Rosenbaum JF, Zajecka J, et al. Changes in weight during a 1-year trial of fluoxetine. The American journal of psychiatry 1999;156: 1170–1176. https://doi.org/10.1176/ajp.156.8.1170
28. Orzack MH, Friedman LM, Marby DW. Weight changes on fluoxetine as a function of baseline weight in depressed outpatients. Psychopharmacology bulletin 1990;26: 327–330.
29. Serralde-Zuñiga AE, González-Garay AG, Rodríguez-Carmona Y, Meléndez-Mier G. Use of Fluoxetine to Reduce Weight in Adults with Overweight or Obesity: Abridged Republication of the Cochrane Systematic Review. Obesity facts 2022;15: 473–486. https://doi.org/10.1159/000524995
30. Darga LL, Carroll-Michals L, Botsford SJ, Lucas CP. Fluoxetine's effect on weight loss in obese subjects. The American journal of clinical nutrition 1991;54: 321–325. https://doi.org/10.1093/ajcn/54.2.321
31. Brunner E, Tohen M, Osuntokun O, Landry J, Thase ME. Efficacy and safety of olanzapine/fluoxetine combination vs fluoxetine monotherapy following successful combination therapy of treatment-resistant major depressive disorder. Neuropsychopharmacology: official publication of the American College of Neuropsychopharmacology 2014;39:2549–2559. https://doi.org/10.1038/npp.2014.101
32. Hudson JI, Wohlreich MM, Kajdasz DK, Mallinckrodt CH, Watkin JG, Martynov OV. Safety and tolerability of duloxetine in the treatment of major depressive disorder: analysis of pooled data from eight placebo-controlled clinical trials. Human psychopharmacology 2005;20: 327–341. https://doi.org/10.1002/hup.696
33. Leombruni P, Lavagnino L, Gastaldi F, Vasile A, Fassino S. Duloxetine in obese binge eater outpatients: preliminary results from a 12-week open trial. Human psychopharmacology 2009; 24: 483–488. https://doi.org/10.1002/hup.1040
34. Guerdjikova AI, McElroy SL Winstanley EL, Nelson EB, Mori N, McCoy J, et al. Duloxetine in the treatment of binge eating disorder with depressive disorders: a placebo-controlled trial. The International journal of eating disorders 2012;45:281–289. https://doi.org/10.1002/eat.20946
35. Mbaya P. Safety and efficacy of high dose of venlafaxine XL in treatment resistant major depression. Human psychopharmacology 2002;17:335–339. https://doi.org/10.1002/hup.419
36. Allard P, Gram L, Timdahl K, Behnke K, Hanson M, Søgaard J. Efficacy and tolerability of venlafaxine in geriatric outpatients with major depression: a double-blind, randomised 6-month comparative trial with citalopram. International journal of geriatric psychiatry 2004;19: 1123–1130. https://doi.org/10.1002/gps.1190
37. Nomikos, GG, Tomori D, Zhong W, Affinito J, Palo W. Efficacy, safety, and tolerability of vortioxetine for the treatment of major depressive disorder in patients aged 55 years or older. CNS spectrums 2017;22:348–362. https://doi.org/10.1017/S1092852916000626
38. Uguz F, Sahingoz M, Gungor B, Aksoy F, Askin R. Weight gain and associated factors in patients using newer antidepressant drugs. General hospital psychiatry 2015;37: 46–48. https://doi.org/10.1016/j.genhosppsych.2014.10.011
39. Oskooilar N, Wilcox CS, Tong ML, Grosz DE. Body mass index and response to antidepressants in depressed research subjects. The Journal of clinical psychiatry 2009;70: 1609–1610. https://doi.org/10.4088/JCP.09l05226blu

40. Jha MK, Wakhlu S, Dronamraju N, Minhajuddin A, Greer TL, Trivedi MH. Validating pre-treatment body mass index as moderator of antidepressant treatment outcomes: Findings from CO-MED trial. Journal of affective disorders 20;18234:34–7. https://doi.org/10.1016/j.jad.2018.02.089