Clinical assessment of liraglutide use in prediabetic and obese schizophrenic patients: A systematic literature review and meta-analysis

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Abstract

Background and Hypothesis

Schizophrenic patients are at a higher risk of developing prediabetes and obesity, which may increase their risk of cardiovascular and other diseases. Liraglutide, a glucagon-like peptide-1 receptor agonist, is effective in treating prediabetes and obesity in the general population. However, its efficacy and safety in schizophrenic patients remain unclear. This study aims to evaluate the effectiveness of liraglutide in managing prediabetes and obesity among schizophrenic patients.

Study Design

A systematic PRISMA-based literature search was conducted in three electronic databases to identify eligible studies. Different treatment outcomes were extracted from the study and analyzed using a random-effects model to calculate the pooled effect size at 95% confidence interval. Heterogeneity was assessed using the I^2 statistic. Publication bias was evaluated using funnel plots and Egger's test. Subgroup and sensitivity analyses have been performed to explore the potential sources of heterogeneity.

Study Results

Five studies were included in the meta-analysis after the screening process. The pooled mean difference in body weight between the liraglutide group and the placebo group was − 4.09 kg ($p = 0.0008$), indicating a significant reduction in body weight with liraglutide. Similarly, the overall mean difference in BMI was − 0.92 ($p < 0.00001$), and the overall mean difference in waist circumference was − 3.65 cm ($p = 0.02$), both indicating significant reductions of weight under liraglutide treatment. Liraglutide also significantly reduced fasting glucose (overall mean difference of -9.23; $p < 0.00001$) and total cholesterol (overall mean difference of -19.00; $p = 0.0003$).

Conclusions

Liraglutide is effective in reducing body weight, BMI, waist circumference, fasting glucose, HbA1c, total cholesterol, systolic blood pressure, and diastolic blood pressure. Since liraglutide might have a protective effect on the metabolic syndrome in schizophrenic patients, the add-on administration of liraglutide could improve the quality of life of these patients in the long term.

1. Introduction

Schizophrenia is a severe mental disorder that affects a person's perception, thoughts, affect, behavior, and ability to retain insight, with a 1% lifetime prevalence (1). Patients with schizophrenia are at twice the risk of developing metabolic syndrome compared with the general population (2–4). Metabolic syndrome refers to several cardio-metabolic disorders such as dyslipidemia, insulin resistance, hypertension, and obesity (5). The prevalence of obesity and related disorders has increased dramatically in the last 30 years. It seems that the same risk factors involved in these increases have also affected people with schizophrenia; in fact, the prevalence of obesity and overweight has grown at even faster rates among this cohort (6).

Several factors may be correlated with this increase. Patients with schizophrenia tend to consume more fatty and processed foods and fewer fibers, which could lead to obesity. Also, factors such as genetics, physical inactivity, and social and urban deprivation could be involved (7, 8); however, one of the main suspected reasons is the usage of antipsychotic medications (9). Although second-generation antipsychotics (SGAs) such as quetiapine and clozapine are effective for managing schizophrenia (10, 11), unfortunately, most SGAs increase appetite, leading to weight gain, reduce physical activity, and alter glucose metabolism, resulting in several cardiometabolic disorders (12). Thus, managing type 2 diabetes mellitus (DM2) and obesity is challenging for people with schizophrenia (13).

Glucagon-like peptide-1 receptor agonists (GLP-1RA) drugs have been generally recognized for their glycemic and body weight control in obese individuals with DM2, but their effectiveness among schizophrenia patients is not yet apparent (13). Liraglutide, a GLP-1RA, is an approved Food and Drug Administration (FDA) medication for the long-term management of obesity (14). Liraglutide seems to trigger weight reduction by stimulating GLP-1 receptors in brain areas that regulate satiety and appetite (15, 16). Liraglutide has been reported to improve cardio-metabolic parameters among prediabetic and overweight patients with schizophrenia treated with clozapine or olanzapine (17). Because it has not been adequately addressed in the literature, in this meta-analysis, we aimed to evaluate the effectiveness of liraglutide in managing prediabetes and obesity among schizophrenic patients.

2. Methods

This systematic review and meta-analysis adhere to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure a thorough and transparent methodology. The study aims to synthesize the available evidence for liraglutide as a treatment for prediabetes and obesity in schizophrenia patients by providing reliable and comprehensive conclusions for decision-makers and researchers. The methodology section outlines the steps to identify, assess, and synthesize the relevant literature.

2.1 Search Strategy

A comprehensive search strategy was conducted to identify relevant studies, targeting three electronic databases: PubMed, Scopus, and Web of Science. The search strategy utilized Medical Subject Headings (MeSH) terms, Emtree terms, and relevant keywords to capture all relevant literature. The search strategy was adapted for each database, ensuring the most accurate results. The following search strategy was used to identify relevant studies: ("Liraglutide" OR

"Victoza" OR "Saxenda" OR "NN2211" OR "GLP") AND ("Prediabet*" OR "glucose intoleran*" OR "impaired fasting glucose" OR "impaired glucose tolerance" OR "non-diabetic hyperglycemia" OR "borderline diabetes" OR "diabet*" OR "obes*" OR "weight" OR "hemoglobin A1c" OR "HbA1c" OR "body mass index" OR "BMI" OR "adiposity" OR "corpulence" OR "plumpness") AND ("Schizophreni*" OR "Schizo*" OR "psycho*" OR "delusional disorder" OR "split personality disorder").

2.2 Study Selection

Four independent authors (R.M.E, A.A.H, A.H.A.R, O.O.B) screened titles and abstracts for eligibility according to the predetermined inclusion and exclusion criteria.

Inclusion and exclusion criteria are illustrated in the Table 1. Any discrepancies between the reviewers during the selection process have been resolved through discussion or consultation with a fifth independent author, if necessary.

Table 1
Showing the inclusion and exclusion criteria

Item	Inclusion Criteria	Exclusion Criteria
Study design	Randomized controlled trials (RCTs), non-randomized controlled trials, cohort studies, and case-control studies	Case reports, case series, commentaries, letters to the editor, conference abstracts, and studies with insufficient data or unclear methodology
Population	Prediabetes and obese or overweight patients with schizophrenia	Other population
Intervention	Liraglutide	Other interventions
Comparator	Placebo, any other comparator, or without a comparator	-
Outcomes	Cardio-metabolic parameters such as body weight, body mass index (BMI), fasting blood glucose level, diastolic blood pressure (DBP), systolic blood pressure (SBP), waist circumference, and total cholesterol level	-

2.3 Data Extraction

Data extraction was done independently by two authors using a standardized data extraction form. The extracted data included study characteristics (e.g., authors, publication year, country), participant characteristics (e.g., sample size, age, gender), intervention and comparator details (e.g., diagnosis, duration, treatment), and outcome measures (e.g., effect size, mean, standard deviation, and number). Any discrepancies in data extraction had been resolved through discussion or consultation with a third author, if needed.

2.4 Quality Assessment

The methodological quality of the included studies has been assessed using the second version of Cochrane Risk of Bias (RoB 2.0) for RCTs, and the risk of observational studies has been conducted using the National Institutes of Health (NIH) tool. Two independent authors (R.M.E, A.A.H) evaluated the risk of bias, and any disagreements were resolved through discussion or consultation with a third author (A.A) if necessary.

2.5 Data Synthesis

A narrative synthesis has been conducted to summarize the findings of the included studies, detailing the study characteristics, population, intervention, comparator, and outcomes. Our meta-analysis has been performed on the latest version of RevMan software using random-effects models to account for potential heterogeneity across studies. Heterogeneity was assessed using the I^2 statistic, with values greater than 50% indicating substantial heterogeneity. One-out analysis has been done using OpenMetaAnalyst software if there has been heterogeneity to assess it. The effect size used was the mean difference between pre-intervention (liraglutide) and post-intervention, in addition to measuring the mean difference between the change from baseline in intervention and the change from baseline in placebo. Sensitivity analyses were performed to evaluate the robustness of the findings by excluding studies with a high risk of bias.

3. Results

3.1 Search strategy and screening

The databases we used to conduct our research yielded 782 research articles for us to review. About 603 studies were left after duplicates were eliminated for assessment. Five studies (17–21) that met our criteria and qualified for the systematic review and meta-analysis were included after looking at the remaining 15 full texts, as shown in (Fig. 1).

3.2 Baseline characteristics

The five studies included in our review had a total of 183 patients in the liraglutide group and 167 patients in the placebo group. There were different diagnoses for the patients and different treatments, as illustrated in the Table 2.

Table 2
Showing the baseline characteristics of the patients

Study ID	Study Design	Country	Intervention	Comparator	Doses	Sample Size	Age	Sex	Diagnosis	Treatment
Larsen 2017	RCT	Denmark	Liraglutide	Placebo	0.6 mg to 1.8 mg	Intervention: 52 Control: 51	Intervention: 42.1(10.7) Control: 43(10.5)	Male: 30 Female: 22	Schizophrenia, Psychosis	Olanzapine, Clozapine
Svensson 2018	RCT	Denmark	Liraglutide	Placebo	0.6 mg to 1.8 mg	Intervention: 52 Control: 51	-	-	-	-
Whicher 2021	pilot trial	England	Liraglutide	Placebo	0.3 mg	Intervention: 24 Control: 23	Intervention: 42.7(11.3) Control: 45.4(10.7)	Male: 15 Female: 9	Schizophrenia, Schizotypal disorder, Psychosis	Olanzapine, Clozapine, Aripiprazole, Flupentixol, Paliperidone Quetiapine, Risperidone, Zuclopenthi Decanoate, Amisulpiride
Lee2021	Retrospective cohort study	Korea	Liraglutide	-	0.6 mg to 3 mg	Intervention: 16	Intervention: 37.81(6.92)	Male: 7 Female: 9	Schizophrenia, Bipolar disease	Clozapine, Aripiprazole, Risperidone
Tomasik 2020	double-blinded clinical trial	Denmark	Liraglutide	Placebo	-	Intervention: 39 Control: 42	Intervention: 42.9(11.3) Control: 42.5(10.7)	Male: 25 Female: 14	-	Olanzapine, Clozapine

3.3 Quality assessment

Four studies were assessed by the RoB 2.0 tool; three have an overall score of "some concerns" and one has a "high" score (Table S1). One study was assessed by the NIH tool with "fair" overall (Table S2).

3.4 Statistical analysis

3.4.1 Overall mean difference in outcomes from baseline between liraglutide and placebo groups

We analyzed the changes from baseline for 8 outcomes in the double-arm studies (17–19) of participants who received liraglutide versus placebo (Fig. 2).

3.4.1.1 Overall mean difference in body weight

The mean difference in body weight was assessed across three studies (17–19), revealing an overall mean difference of -4.09 (95% CI: -6.48, -1.71, p = 0.0008) between the liraglutide group and the placebo group. This result indicates that individuals in the liraglutide group experienced an average body weight reduction of 4.09 units more than those in the placebo group, and this difference was statistically significant. Given the moderate to high level of heterogeneity among the studies, with an I^2 value of 81% and a p value of 0.005, we conducted a leave-one-out analysis to investigate the sources of heterogeneity (Fig. S1).

3.4.1.2 Overall mean difference in body mass index (BMI)

We analyzed three different studies that measured the mean difference in BMI between the liraglutide group and the placebo group (17–19). The results showed that the overall mean difference in BMI was − 0.92 (95% CI: -1.11, -0.73, p < 0.00001), indicating a statistically significant difference between the two groups. The I^2 value of 0% suggests low heterogeneity among the studies, indicating that the results are consistent across the studies. The p value of 0.41 further supports the finding of low heterogeneity. Our results demonstrate that the use of liraglutide is associated with a statistically significant reduction in BMI compared to the use of a placebo.

3.4.1.3 Overall mean difference in waist circumference

We analyzed three studies (17–19) and found that the overall mean difference in waist circumference was − 3.65 (95% CI: -6.75, -0.54, p = 0.02). The I^2 value of 90% and the p value of 0.0001 indicate a high level of heterogeneity among the studies. To address this heterogeneity, we conducted a leave-one-out analysis (Fig. S2). Our findings suggest that liraglutide may have a significant impact on reducing waist circumference compared to a placebo.

3.4.1.4 Overall mean difference of fasting glucose

We analyzed two studies (17, 19) and found that the overall mean difference in fasting glucose was − 9.23 (95% CI: -12.38, -6.07, p < 0.00001). The I^2 value of 0% and the p value of 0.75 indicate a low level of heterogeneity among the studies. Our findings suggest that liraglutide may have a significant impact on reducing fasting glucose compared to a placebo.

3.4.1.5 Overall standardized mean difference of HbA1c

Our analysis of three studies (17–19) revealed a standardized mean difference in HbA1c of -4.24 (95% CI: -7.27, -1.20, p = 0.006) overall. Our results indicate that liraglutide has a significant effect on reducing HbA1c levels compared to placebo. However, the I^2 value of 97% and the $p < 0.00001$ indicate a high degree of heterogeneity among the studies. Therefore, we conducted a leave-one-out analysis to investigate the impact of each study on the overall results (Fig. S3).

3.4.1.6 Overall mean difference of total cholesterol

We included two studies (17, 19) that measured the mean difference in total cholesterol. The overall analysis showed that the mean difference between the liraglutide group and the placebo group was − 19.00 (95% CI: -29.39, -8.61, p = 0.0003), with $I^2 = 44\%$ and p = 0.18. This indicates that the use of liraglutide is associated with a significant reduction in total cholesterol compared to a placebo.

3.4.1.7 Overall mean difference of systolic blood pressure (SBP)

We analyzed three studies (17–19). The findings revealed an overall mean difference in SBP of -3.68 (95% CI: -4.45, -2.91, p < 00001), little heterogeneity with an I^2 of 0%, and a p value of 0.41. This implies that liraglutide medication can dramatically lower SBP when compared to a placebo.

3.4.1.8 Overall mean difference of diastolic blood pressure (DBP)

Three studies (17–19) measured the mean difference in diastolic blood pressure (DBP) between the liraglutide group and the placebo group. The overall mean difference was found to be -1.93 (95% CI: -3.42, -0.45, p = 0.01), indicating that the liraglutide group had a significantly lower DBP compared to the placebo group. The heterogeneity among the studies was low, with an I^2 value of 19% and a p value of 0.29.

3.4.2 Overall mean difference in outcomes between pre-liraglutide and post-liraglutide

We analyzed 3 outcomes in a single group of participants who received liraglutide treatment in three studies (17, 19, 20). The measurements were taken at two time points: before the liraglutide treatment (pre-liraglutide) and after the liraglutide treatment (post-liraglutide), as shown in (Fig. 6).

3.4.2.1 Overall mean difference in body weight

The mean difference in body weight was determined by three studies (17, 19, 20). The study revealed that the pre-liraglutide and post-liraglutide groups' total mean difference was − 4.48 (95% CI: -8.09, -0.87, p = 0.01) with $I^2 = 0\%$ and p = 0.98. The analysis found that liraglutide is effective in reducing body weight, with a statistically significant reduction in body weight and an overall mean difference of -4.48 kg.

3.4.2.2 Overall mean difference of fasting glucose

We analyzed three studies (17, 19, 20) to measure the mean difference in fasting glucose levels. The results showed that the overall mean difference between the pre-liraglutide and post-liraglutide groups was − 8.99 (95% CI: -13.10, -4.88, $p < 0.0001$) with no heterogeneity ($I^2 = 0\%$) and a p-value of 0.43. This indicates a statistically significant reduction in fasting glucose levels in the post-liraglutide group compared to the pre-liraglutide group.

3.4.2.3 Overall mean difference of total cholesterol

Three studies measuring the mean difference in total cholesterol were analyzed (17, 19, 20). The analysis revealed that the overall mean difference between the pre-liraglutide and post-liraglutide groups was − 15.44 (95% CI: -30.31, -0.57, p = 0.04) with $I^2 = 0\%$ and p = 0.84. The results of the analysis suggest that the use of liraglutide leads to a significant reduction in total cholesterol levels when compared to pre-liraglutide.

Tomasik et al. (21) studied the effects of liraglutide on protein levels in prediabetic patients and found that serum levels of adiponectin increased with liraglutide treatment compared to placebo. This is in line with preclinical data and a clinical study where adiponectin was increased in Chinese patients with type 2 diabetes following treatment with liraglutide. However, it is important to note that this study focused on the effects of GLP-1RA treatment in prediabetic schizophrenia patients treated with clozapine or olanzapine and not specifically on the effects of liraglutide alone.

4. Discussion

Although it is crucial to address the issue of obesity in patients with serious mental illness (SMI) to improve their metabolic health and reduce risk factors for cardiovascular diseases, treating these patients with psychopharmacotherapeutics presents difficulties (22). Nevertheless, the primary contributor to weight gain in individuals with SMI is the use of antipsychotic medications, which can provoke, to a greater extent, a significant weight gain as an adverse effect and thus are considered as with obesogenic potential, affecting a substantial portion of patients with rates ranging from 15–72% (23). Additionally, other types of psychotropic medications, including antidepressants and mood-stabilizing drugs like lithium and sodium valproate, are commonly prescribed to individuals with schizophrenia or schizoaffective disorder. However, these medicaments may also contribute to significant weight gain, bearing an higher risk for a metabolic syndrome (24). Weight gain is often a reason for discontinuation of medication (non-adherence) and a potential factor for disease relapse. We suggest that implementing effective weight-management strategies could potentially improve adherence to antipsychotic medication and reduce relapse and hospitalization rates in individuals who discontinue their medication due to weight gain caused by antipsychotic use. However, despite some studies indicating that short-term lifestyle interventions may help with weight reduction in individuals with SMI, most studies did not find a significant effect of lifestyle interventions on body weight in patients with schizophrenia (25, 26). These findings indicate that weight management in individuals with schizophrenia may require a different approach compared to other SMIs. In this systematic review and meta-analysis, we aimed to assess the effectiveness of liraglutide for weight loss and glycemic control in obese and prediabetic patients with schizophrenia.

The results of our analysis showed that liraglutide has a statistically significant impact on body weight, BMI, waist circumference (WC), fasting glucose, HbA1c, and total cholesterol levels. Specifically, our analysis of three studies found a statistically significant reduction in body weight (-4.09 kg) and BMI (-0.92 kg/m^2) in the liraglutide group compared to the placebo group. The study's results were supported by a reduction in WC of -3.65 cm, adding further evidence to the effectiveness of weight loss with liraglutide. Several previous studies have established a significant association between WC and cardiovascular health risk factors (27). Multiple studies have demonstrated that individuals with a normal BMI but a higher WC are at an elevated risk for cardiovascular health issues (28). Furthermore, our meta-analysis revealed that liraglutide played a significant role in blood glucose control, as evidenced by statistically significant reductions in fasting glucose (-9.23), HbA1c levels (-4.24), and total cholesterol levels (-19.00) in the liraglutide group compared to the control group (29). Overall, the results of this meta-analysis suggest that liraglutide may be a viable treatment option for managing weight loss and glycemic control in overweight and prediabetic patients with schizophrenia.

Liraglutide is a GLP-1-receptor agonist with 97% homology to human GLP-1, and it is approved for the treatment of both obesity and diabetes (6, 30). Its main mechanism for reducing body weight is by decreasing calorie intake through reduced gastric motility and increased satiety rather than by increasing energy expenditure (31). When administered peripherally, it can pass through the blood-brain barrier in substantial quantities (32). Liraglutide directly stimulates neurons that suppress appetite which are proopiomelanocortin (POMC) and cocaine- and amphetamine-regulated transcript (CART) in the arcuate nucleus while inhibiting neurons that stimulate appetite such as neuropeptide Y/agouti-related protein (NPY/AgRP) (33). Liraglutide has also been found to promote neurogenesis and exhibit neuroprotective effects similar to those of second-generation antipsychotics, suggesting potential use in psychiatric disorders (32, 34–36). The exact mechanism of action of liraglutide is not fully understood. However, several proposed mechanisms could contribute to its effects in these areas. Firstly, liraglutide activates GLP-1 receptors in the brain, which play a role in appetite regulation and satiety. By targeting these receptors, liraglutide can potentially reduce food intake and promote weight loss in individuals with schizophrenia who are overweight or obese (37). Secondly, liraglutide has been shown to improve insulin secretion and enhance insulin sensitivity in peripheral tissues (38). This can lead to better glucose utilization and regulation, helping to manage prediabetes or impaired glucose tolerance in schizophrenic patients. It has been suggested that liraglutide affects dopamine and serotonin systems in the brain, which are implicated in both glucose regulation and the pathophysiology of schizophrenia (37). By influencing these neurotransmitter systems, liraglutide might have indirect effects on glucose metabolism and potentially improve metabolic parameters. Additionally, liraglutide has been associated with a reduction in inflammation and oxidative stress, which are factors that can contribute to insulin resistance and impaired glucose regulation (39, 40). By mitigating these processes, liraglutide could improve glucose homeostasis in schizophrenic patients.

There are other known pharmacological strategies that have been tried as add-on to adipogenic antipsychotics and are still used in clinical practice, e.g., Metformin, which is an anti-diabetic drug that has proven efficacy in wight loss among patients who take antipsychotics and suffer weight gain (41, 42). The use of metformin as adjunctive therapy to treat weight gain was implemented when non-pharmacological treatment failed. Metformin works by increasing insulin resistance and decreasing blood lipids. Greater effects are produced by metformin which are presented in decreased blood glucose levels (43). In the same direction, another GLP-1 agonist (semaglutide) was investigated by Prasad et al. in a case series to evaluate its efficacy in patients who gained weight due to antipsychotic drugs and failed to respond to metformin. A statistically and clinically significant weight improvement (i.e., > 5% body weight) was seen in the treated cohort. Despite the fact that a third of patients (4 of 12) initially reported mild GIT side-effects, semaglutide was generally well tolerated and correlated with the drug's known GIT adverse effects (44).

The variation in liraglutide dosage among the included studies in our study poses an important consideration in interpreting the findings. The use of different doses of liraglutide across the studies can introduce heterogeneity and potentially impact the overall conclusions. It is crucial to recognize that varying doses may yield different treatment outcomes, efficacy levels, and safety profiles. The observed variations in liraglutide dosing make it challenging to determine the optimal dose specifically for prediabetic and obese schizophrenic patients. The heterogeneity in dosage calls for a cautious interpretation of the pooled results and underscores the need for further research. Future investigations, such as well-designed randomized controlled trials, should be conducted to directly compare different doses of liraglutide in this specific population. Considering individual patient characteristics and tailoring the dose accordingly may also be beneficial. Addressing the dosage variation in liraglutide studies enhances the understanding of the limitations and highlights the importance of establishing an optimal dosing strategy for the targeted population.

The strengths of the study are present at several points. These include the comprehensiveness of our study, which included a variety of outcomes related to weight gain, pre-diabetes, and associated complications. It provides recent evidence of liraglutide use in prediabetic and obese schizophrenic patients. In addition, the methodological quality of the included studies was assessed using validated tools, ensuring a rigorous assessment of the risk of bias. Finally, the results of this systematic review and meta-analysis are reported following the PRISMA guidelines, ensuring transparency and replicability of the study. On the other hand, it has some limitations: The differences in patient characteristics and diagnosis across the analysed studies may impact the applicability of the findings to different patient populations, so we used the random effect model during the analysis to account for this difference, and the analysis was limited in its scope as it was based on a limited number of studies with small sample sizes. Additionally, the analysis was restricted to a sample population from only three countries, with three trials conducted in the same country. Further research is necessary to validate these findings. Moreover, while the overall quality of the included studies was moderate, one study had a high risk of bias, which could have impacted the overall results. As a result, it is important to approach these findings with caution, and more high-quality studies are needed to strengthen the evidence supporting the efficacy of liraglutide in this population.

Finally, to strengthen the evidence base on this topic, several recommendations can be made. Firstly, conducting randomized controlled trials (RCTs) with larger sample sizes and different countries' populations and ethnicities would provide more robust evidence of its effectiveness. Comparative studies that compare liraglutide with other weight management interventions, such as lifestyle modification, other medications, or combination therapies, in this population of overweight or prediabetic schizophrenic patients would enhance our understanding of its relative effectiveness and safety compared to other treatment options. Secondly, further research is needed to thoroughly evaluate the safety and tolerability of liraglutide in patients with schizophrenia, monitor for potential adverse effects, and assess its impact on psychiatric symptoms and medication adherence. Finally, investigating the underlying mechanisms of action of liraglutide in patients with schizophrenia, such as its effects on appetite regulation, neurogenesis, and neuroprotection, would provide a deeper

understanding of its potential therapeutic benefits and contribute to a better understanding of its effectiveness, safety, and utility as a potential treatment option for managing overweight in the studied population.

5. Conclusion

We found that the use of liraglutide is associated with significant improvements in various health outcomes compared to placebo. Our analysis showed that the use of liraglutide was associated with significant reductions in body weight, BMI, waist circumference, fasting glucose, HbA1c, and total cholesterol. Liraglutide might extent the pharmacologic repertoire of substances that may cause weight loss in antipsychotic induced obesity when used as add-on medication. However, further research is needed to confirm and expand on our findings on Liralutide, particularly in the context of long-term use and potential adverse effects.

Abbreviations

- Second-generation antipsychotics (SGAs)
- Glucagon-like peptide-1 receptor agonists (GLP-1RA)
- Type 2 diabetes mellitus (DM2)
- Food and Drug Administration (FDA)
- Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)
- Medical Subject Headings (MeSH)
- Randomized control trials (RCTs)
- Body mass index (BMI)
- Systolic blood pressure (SBP)
- Diastolic blood pressure (DBP)
- Cochrane Risk of Bias (RoB 2.0)
- National Institutes of Health (NIH)
- Glycated hemoglobin A1c (HbA1c)
- Serious mental illness (SMI)
- Pro-opiomelanocortin (POMC)
- Cocaine and Amphetamine-Regulated Transcript (CART)
- Neuropeptide Y (NPY)
- Agouti-related peptide (AgRP)
- Waist circumference (WC)

Declarations

Ethical Approval and consent to Participate: NA.

Consent to Publication: NA.

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Figures

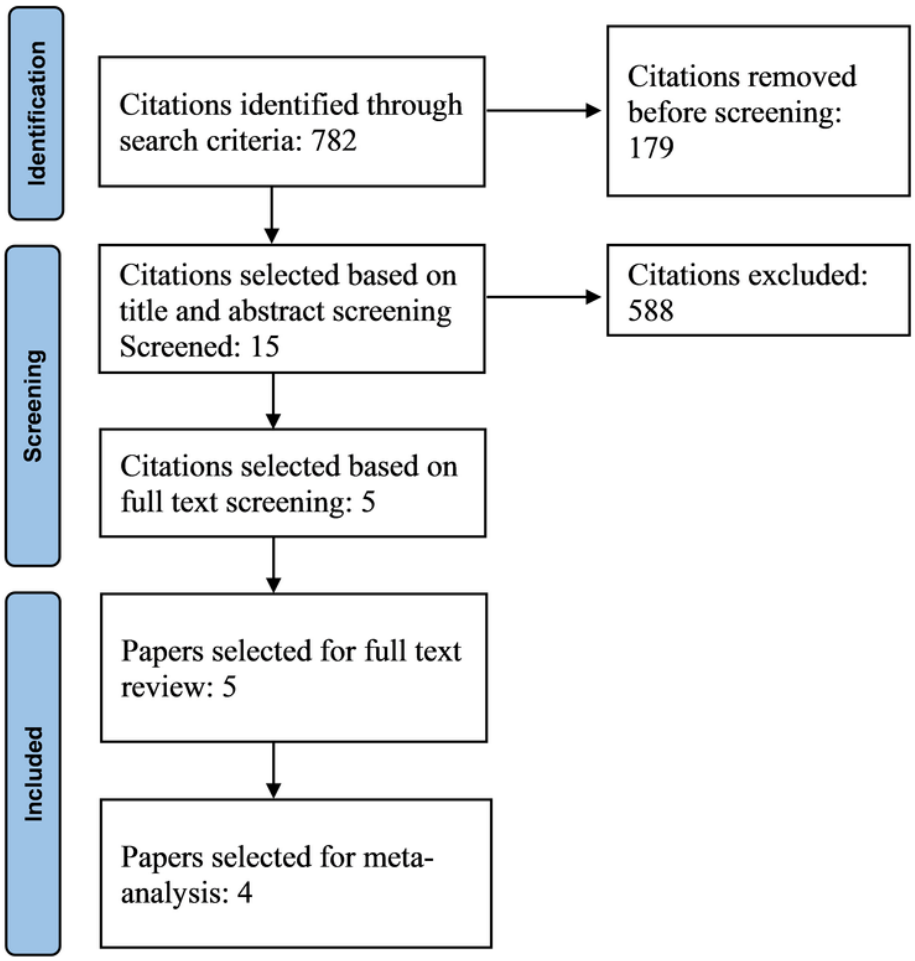

Figure 1

Showing the PRISMA flow diagram

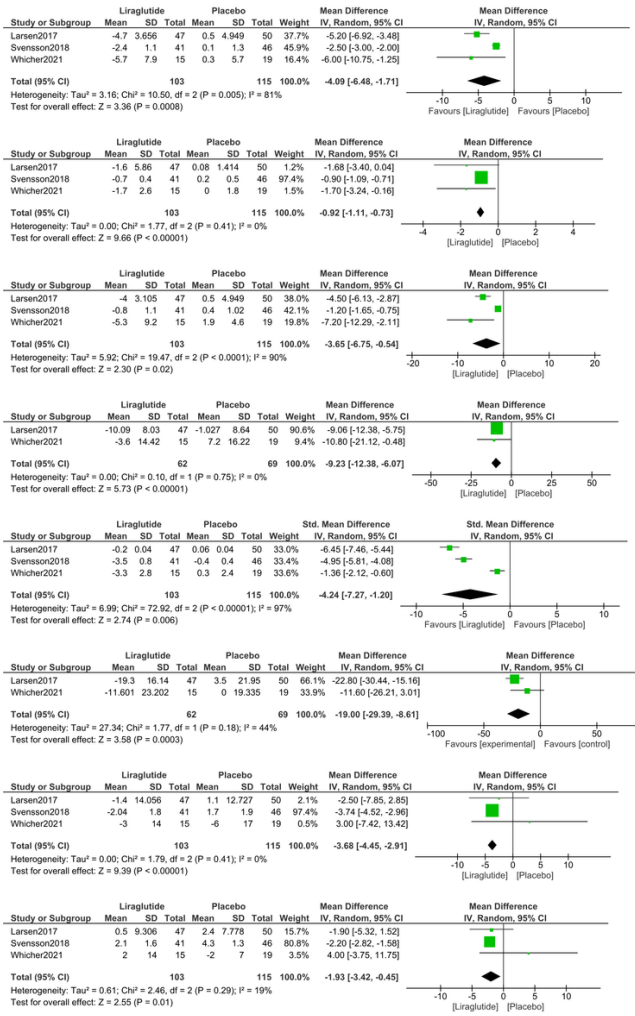

Figure 2

Showing the outcomes analyzed between the liraglutide and placebo groups

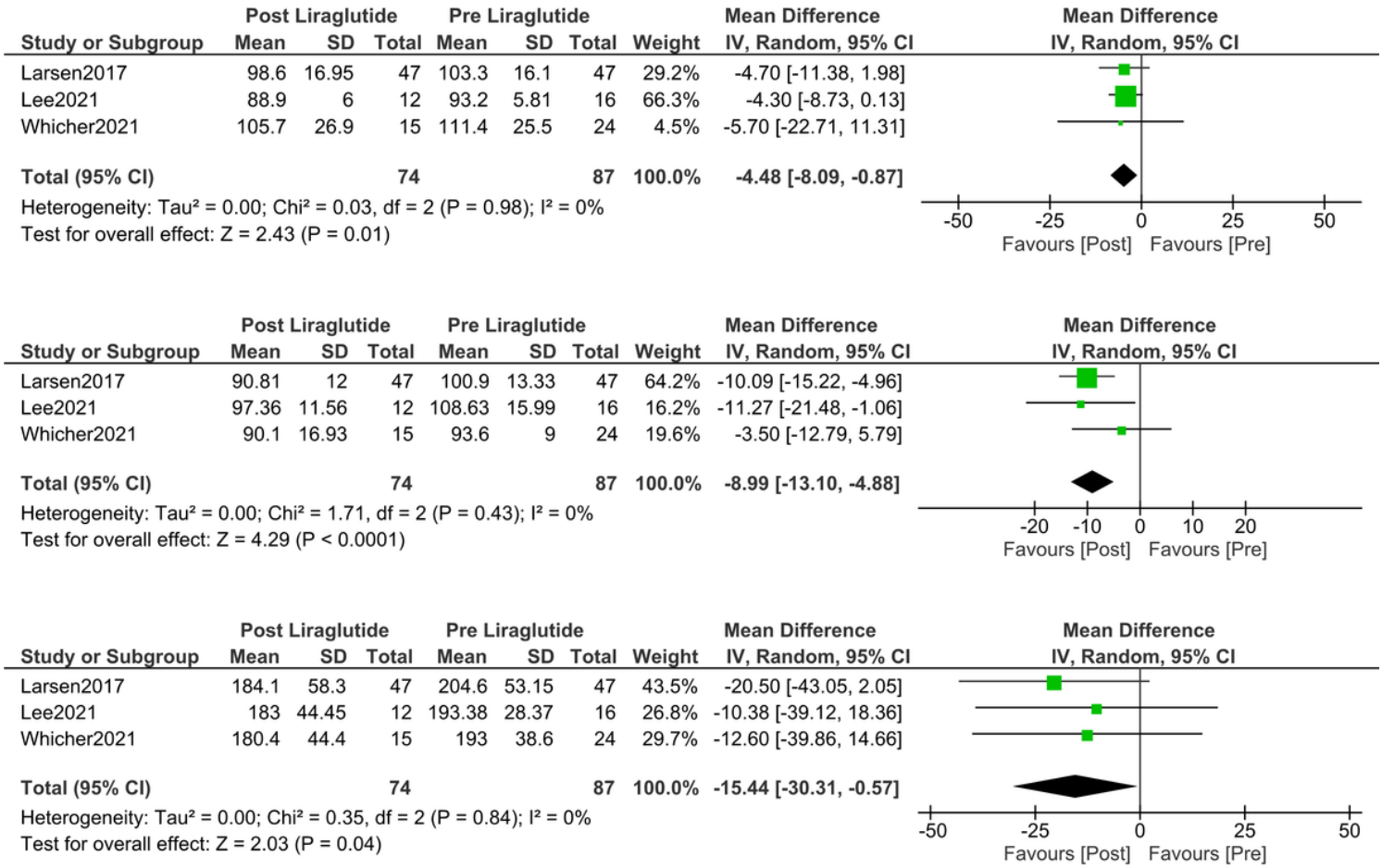

Figure 3

Fig. 6. Showing the outcomes analyzed between the pre-liraglutide and post-liraglutide groups

Supplementary Files

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