International Journal of Nursing and Health Care Research
OPEN ACCESS
Henderson L, et al. Int J Nurs Health Care Res 9: 1711
www.doi.org/10.29011/2688-9501.101711
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Research Article

Impacts of Adding GLP-1 Receptor Agonist on Weight Loss, Self-Esteem, and Depression Compared to Diet and Exercise Alone in Women Aged 30-45

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Citation: Henderson L, Patel B, Lee K, Batten LA (2026) Impacts of Adding GLP-1 Receptor Agonist on Weight Loss, Self-Esteem, and Depression Compared to Diet and Exercise Alone in Women Aged 30-45. Int J Nurs Health Care Res 9:1711. DOI: https://doi.org/10.29011/2688-9501.101711

Received Date: 27 May 2026; **Accepted Date:** 04 June 2026; **Published Date**: 08 June, 2026

Abstract

An amalgamated collaborative intervention was unbeaten for treating comorbid obesity, depression, and low self-esteem. Low self-esteem and depression are predicted to cause further weight gain in otherwise healthy women living with obesity. Generally, obesity is linked to many medical health problems. Failure of diet and exercise in the weight reduction process for obese women can decrease self-esteem and may even cause depression. Therefore, we investigated the effects of adding a glucagon-like peptide one receptor agonist (GLP1-RA) on reducing weight and how it affects women aged 30-45 self-esteem and depression compared to only diet and exercise. The current study was a randomized controlled trial. For this study, two groups of women aged 30-45 were selected: one willing to follow a diet and exercise only, and the other willing to take GLP-1 RA in addition to diet and exercise. During the three-month trial, 25 participants drank 8 glasses of water a day and engaged in moderate-intensity exercise for at least 5 days a week, for 30 min each day. A total of 25 participants started on GLP-1 RA in addition to dietary and exercise recommendations, as mentioned for the above group. We assessed obesity, self-esteem, and depression by using the BMI scale, the Rosenberg self-esteem scale, and the PHQ-9. This study resulted in the Augmentation of GLP-1 RA to diet and exercise, which will add more weight loss and decrease anxiety. Self-esteem improves in both groups, but it improves more with diet and exercise alone. Gathering, analyzing, and disseminating data results will guide healthcare providers in addressing obesity treatment.

Keywords: GLP1-RA, obesity, self-esteem, depression, diet, and exercise

Introduction

Obesity is one of the greatest threats to the future of human health, as it can reduce life span and cause chronic diseases such as heart disease, type 2 diabetes, breathing difficulties, cancer, arthritis, metabolic syndrome, and mental health problems. In addition, obesity significantly affects the economics of the healthcare system. Obesity-linked medical care costs in the United States were an estimated $147 billion annually in 2008. Obesity also influences military readiness [1]. Besides physical consequences, obesity has adverse mental impacts and brings down the quality of life. Critical psychological implications of this problem

incorporate sadness, weakened self-perception, low confidence, dietary issues, stress, and low quality of life, which are associated with age and orientation [2]. If the cause is not addressed, self-esteem can quickly deteriorate into depression.

In the past decade, obesity and related comorbidities have become critical public health problems and severe medical conditions worldwide. A state of positive energy balance occurs when energy intake exceeds energy expenditure, leading to the storage of excess calories in adipose tissue. The storage of excess calories in adipose tissue leads to a body phenotype of overweight (body mass index, BMI 25-30 kg/m^2). It then progresses to a weight disorder called obesity, defined as a BMI >= 30 kg/m^2 [3].

Weight stigma is often present on social media and can harm insecure females. Reaching the goal of an average weight improves not only physiological body variables but also psychological status and quality of life.

Generally, self-esteem correlates negatively with obesity and decreased physical activity [4], suggesting that obesity is associated with lower self-esteem. A 26-year Finnish follow-up study among a birth cohort echoed this by looking at Body Mass Index (BMI) and changes in self-esteem: 'Among females, higher and increasing BMI is associated with lower and more slowly developing self-esteem. This association is not restricted to adolescence but persists and strengthens into mid-adulthood. Among males, associations are weaker but indicate more age-related differences. A popular suggested causal mechanism is that self-esteem serves as a resource for resisting the temptations of unhealthy diets and poor exercise habits. When speculating why unhappy people were more obese, it is already argued that 'psychological distress has been rising over time' in modern Great Britain, and it is surmised that this has increased obesity rates [5].

Individuals with co-occurring obesity and depression report poorer health-related quality of life than those with only one of the conditions or neither condition. Despite the frequent co-occurrence of these conditions and their impact on quality of life, few interventions use an integrated approach to treat both conditions concurrently, and only one has been shown to be effective [6].

Depression and obesity are two conditions with a significant impact on global health. Their influence is mainly due to their high prevalence and associated morbidity and mortality. According to recent data from the World Health Organization (WHO), in 2016, it was estimated that more than 1.9 billion adults were overweight, and 650 million were obese. At least 2.8 million people die yearly due to being overweight or obese. The prevalence of obesity nearly tripled between 1975 and 2016 [7]. According to Global Health Data Exchange (GHDE), in 2021, it was estimated 3.8% of the population was affected by depression, including 5.0% among adults and 5.7% among adults older than 60. Approximately 280 million people in the world have depression. At its worst, depression can lead to suicide. Over 700 000 people die due to suicide every year [8].

The possible association between obesity and depression has been studied repeatedly in scientific literature, mainly because they both carry a high prevalence and an increased risk of cardiovascular disease. While many cross-sectional studies have documented this relationship, its significance remains unclear [9]. The main objectives of this study will be 1) to evaluate the relationship between weight loss and self-esteem or depression, and 2) to evaluate effective strategies for weight reduction with or without adding GLP1- RA to an individual's diet and exercise.

Weight Loss Strategies

Obesity is a complex subject to discuss with patients who have the issue of low self-esteem. Empathy and understanding are paramount when talking about obesity with a female patient. Several interventions can be advised for individuals who are overweight or suffer from obesity, such as behavioural change, dietary modifications, physical activity, pharmacological treatment, and bariatric surgery.

Lifestyle Modification Counselling

According to a 2021 critical appraisal by Kenneth and Dominique, exercise intervention is recommended, and some people with obesity even prefer exercise over dietary intervention as a single weight-loss strategy. However, evidence shows that the long-term loss of body weight and adipose tissue mass due to exercise interventions in these individuals needs to be greater. Although this may be due to various clinical factors, more recent evidence suggests that pathophysiological abnormalities are involved and cannot be remedied by exercise alone, especially in metabolically compromised patients. As a result, the role and importance of exercise intervention in treating obesity deserve significant reconsideration to avoid confusion and disappointment amongst clinicians, patients, and society. Hence, dietary intervention is much more effective than exercise intervention in reducing adipose tissue mass and body weight and is therefore crucial to this endeavour. However, dietary interventions must be supplemented by exercise training to induce clinically relevant changes in specific cardiovascular or metabolic risk factors, such as blood pressure, triglycerides, and high-density lipoprotein cholesterol concentrations, as well as visceral adipose tissue mass, physical fitness, muscle mass and strength, quality of life, and life expectancy.

Intermittent Fasting

When searching for alternative weight-loss methods, intermittent fasting is the most popular [10]. Limited research is available on this relatively new weight-loss method. Harmful research methods include low enrolment, short-term studies, and the absence of control groups [10]. This process comprises fasting for eight to sixteen hours and eating well-balanced foods during the remaining hours. The premise is that intermittent fasting may meet the body's metabolic needs while preserving greater fat and lean mass, thereby providing a greater ability to sustain weight loss [11]. This type of diet modification may be difficult due to the participant possibly working shift work, having a fixed income, or finding this dietary change time-consuming and tiresome.

Pharmacological Treatment

Pharmacotherapy of obesity has a long history of promising drugs being withdrawn due to safety concerns. In the last century, the pharmacological management of obesity has included amphetamines, thyroid hormones, dinitrophenol, and various drug combinations (rainbow pills) withdrawn shortly after regulatory approval due to serious adverse effects [12]. Several centrally acting sympathomimetics, such as phentermine, cathine, and diethylpropion, are still used in short-term therapy. Medicines investigated in obesity include agents as diverse as mitochondrial uncouplers, sympathomimetics, serotonergic agonists, lipase inhibitors, cannabinoid receptor antagonists, and a growing family of gastrointestinal-derived peptides chemically optimized for pharmaceutical use [12]. A sobering realization across most of these approaches is the inability to achieve placebo-adjusted mean weight loss greater than 10% of initial body weight when chronically administered at tolerable doses. As greater weight loss is achieved, it is typically accompanied by severe acute or chronic adverse effects [12]. A notable exception is the recently approved GLP1 RA Semaglutide (Wegovy) 2.4 mg, which, in phase III clinical trials, decreased body weight in individuals with obesity or overweight without diabetes after 68 weeks of treatment by −14.9%, compared with −2.4% in placebo-treated controls [12].

Surgical Intervention

The literature on weight-loss surgery suggests that most patients experience overwhelmingly positive changes following dramatic weight loss [13]. According to one study, increased self-esteem, quality of life, and decreased depression and anxiety were overwhelmingly positive in patients who underwent bariatric surgery. In another study comparing bariatric surgery and diet modifications in Type 2 diabetic patients, "the metabolic benefits of gastric bypass surgery and diet were similar and were related to weight loss itself, with no evident clinically important effects independent of weight loss" [14]. This type of medical intervention for weight loss to improve self-esteem is extreme, with possible complications including death. With this weight-loss option, there are also issues with insurance coverage, the cost of the procedure, and the length of the process from the request for surgery to the actual surgical date. The method includes psychiatric evaluations, monthly nutritional counselling, lab tests, and clearance from Gastroenterology, Cardiology, and Primary Care.

Evidence-Based Practice to Support GLP-1 Medication Use

For the chosen intervention, the proposal is to use GLP-1 in females aged 30-45 with a body mass index greater than 30 to improve weight loss and, in turn, self-esteem. The glucagon-like peptide (GLP)-1 hormone has been shown to have beneficial effects on the human body. These effects include nervous system regulation of satiety; increased cognitive function and cardio protection; decreased hypertension; suppression of acid secretion; delayed gastric emptying; and protection against inflammation [15]. Using GLP-1 can significantly reduce weight-related issues, including metabolic, cardiovascular, musculoskeletal, and mental health problems.

A study by Cacciottolo and Evans (2021) [16] evaluated the effectiveness of pharmacotherapy in managing obesity. Clinical trials of GLP-1 RA for managing type 2 diabetes found that weight loss was a critical side effect of the treatment. The Semaglutide treatment effect in people with Obesity 1 (STEP-1) trial was set up to investigate the safety and efficacy of the GLP-1 RA Semaglutide in managing obesity without diabetes. The review randomized 1,961 adults in a 2:1 ratio to 2.4 mg weekly Semaglutide or placebo for 68 weeks [16]. All participants received a lifestyle intervention comprising 4 weekly counselling sessions. There was a significant reduction in body weight. The group compared with placebo (-14.9% vs. 2.4%; $p \leq 0.001$), with 33% of participants losing at least 20% of their starting body weight [16]. Eighty-six percent of subjects in the treatment group met the primary endpoint of at least 5% weight loss [16]. In addition to weight benefits, the authors noted substantial reductions in cardiovascular and metabolic risk factors and a significant improvement in physical functioning. There was a greater incidence of side effects in the treatment group, namely diarrhoea, cholelithiasis, and nausea, as is typical for this drug class. In summary, this trial proved that once-weekly Semaglutide achieved a long-lasting, clinically applicable reduction in body weight in adults who are overweight or obese without type 2 diabetes [16].

A study by Elran-Barak (2019) [17] examined sex and ethnicity/race differences in the associations among self-esteem, weight status, and attempts to lose weight among young adults in the

United States. Self-esteem is a person's emotional assessment of their value. Reviews suggest that low self-esteem may promote weight gain and that obesity may lower self-esteem [17]. A randomly selected sample was drawn from the primary study sample. Of the 4,882 participants, 272 were excluded due to missing BMI measures at Wave III, and 16 were excluded because no answers were recorded for the self-esteem or trying to lose weight questions [17]. As a result, the total sample comprised 4,594 participants [17]. The study used a cross-sectional design to examine the associations among self-esteem, weight status, and weight-loss attempts. Chi-square tests and one-way analysis of variance were used to evaluate differences between sub-groups. Logistic regression models were conducted to assess the odds of trying to lose weight among participants with low vs. high self-esteem, stratified by weight status, sex (female/male), and race (Black/White). High self-esteem was defined using the median self-esteem score (>7) [17]. Females reported significantly (P<.001) higher rates of trying to lose weight (44.8%) than males (20.0%) and significantly (P=.029) higher rates of poor self-esteem (53.6%) than males (49.8%) [17]. Body mass index was higher (P<.001) among individuals who reported trying to lose weight (30.02 [6.34]) than among those who were not trying to lose weight (24.94 [5.2]) [17]. However, BMI did not differ between individuals with higher vs. lower self-esteem (P=.198). Data showed that attempts to lose weight were more common among females than among males [17]. The study is one of the first to suggest that obesity may be linked with poor self-esteem among Black and White females [17].

Owing to GLP-1 RA's effectiveness in reducing body weight, once-daily subcutaneous administration of liraglutide 3.0 mg has been granted, and once-weekly subcutaneous administration of Semaglutide 2.4 mg was given in June 2021 for obesity management [18]. Several clinical trials have reported the effects of a more significant reduction in body weight with GLP-1RA therapy compared with a placebo in participants with obesity. After five weeks of treatment with once-daily subcutaneous administration of liraglutide 1.8 mg and 3.0 mg, estimated reductions in body weight were −2.1 kg and −2.5 kg, respectively, vs. −0.3 kg with placebo [18].

In another liraglutide trial, 16-week median (interquartile range) body weight reductions were −5.8 kg (−6.9, −4.45) with liraglutide 3.0 mg and −1 kg (−3.5, 2.53) with placebo (p<0.003) [18]. For once-weekly subcutaneous administration of Semaglutide 1.0 mg, the change from baseline in mean body weight after 12 weeks was −5.0 kg vs. +1.0 kg with placebo [18]. A 20-week phase II trial investigated the effects of subcutaneous administration of Semaglutide 2.4 mg on gastric emptying, appetite, and energy intake in patients with obesity [18]. Patients receiving Semaglutide 2.4 mg in this trial lost 9.9% of their body weight, compared with 0.4% in those receiving a placebo [18]. Longer-term data with GLP-1RAs include results from a phase III, 56-week study of liraglutide 3.0 mg vs. placebo in patients with obesity and without diabetes. After 56 weeks of treatment with liraglutide 3.0 mg vs. placebo, patients had mean body weight reductions of −8.4 kg vs. −2.8 kg (ETD −5.6 kg; 95% confidence interval [CI] −6.0 to −5.1; p<0.001) [18].

According to the systematic review by Schmitz et al. (2021) [19] while the current evidence for combination therapies is limited, polypharmacotherapy is an area of active research, and emerging therapies are anticipated to be multi-target agents. Tirzepatide is a dual agonist of the glucose-dependent insulinotropic polypeptide (GIP) receptor and the GLP-1 receptor, approved for the treatment of type 2 diabetes under the brand name Mounjaro. It is a once-weekly subcutaneous injection. In phase 3 studies in people with type 2 diabetes, tirzepatide resulted in clinically significant weight loss superior to semaglutide 1.0 mg. Tirzepatide was studied for obesity in those without diabetes in the SURMOUNT-1 trial (n=2539). This 72-week phase 3 trial randomized individuals to tirzepatide 5 mg, 10 mg, 15 mg, or placebo. The mean percentage change in weight was−20.9% in the tirzepatide 15 mg weekly group versus−3.1% in the placebo group; 91% of patients in the tirzepatide 15 mg weekly group achieved weight loss of 5% or more, compared with 35% in the placebo group.

Pelluri et al. (2021) [21] studied to evaluate the link between depression, Body Mass Index (BMI), and the components of metabolic syndrome (MetS) in subjects with and without insulin resistance. Obesity was associated with a highly significant increase in the risk of depression (OR = 13.01, 95% CI 4.40–38.49) compared to overweight subjects. Female subjects with obesity had a greater risk for depression (β: 3.725, OR: 42.62, 95% CI: 5.74– 316.3, and p < 0.0001) than male subjects (β: 1.922, OR: 6.83, 95% CI: 1.8–26 and p = 0.005), and it was statistically significant.

GLP-1 receptor antagonists were selected as a pharmacological treatment for obesity due to their significant promise in prior studies and their rare, non-life-threatening side effects. It promotes weight loss and weight maintenance. Obesity is now considered a disease and not just a stage of an individual's lifespan. Obesity and depression are the leading causes of physical and mental disability, and the link between these disorders has not been explored well. The current study hypothesis is that GLP-1 receptor agonists will effectively manage weight and improve participants' self-esteem.

Methods

This research project was a randomized controlled trial using

the qualitative practice intervention method. For three months, participants will evenly be randomized to use GLP-1 RA therapy along with 8-10 glasses of water intake and a minimum of 30 minutes for at least five days a week of moderate-intensity aerobic physical activity and another group without GLP-1 RA. The tools for this project will include the BMI scale (to measure BMI/Obesity), the Patient Health Questionnaire appendix (PHQ-9) scale (to measure depression), the Rosenberg Self-Esteem (RSE) scale (to measure self-esteem), and dietary changes. BMI calculation requires only height and weight. BMI is an inexpensive and accessible tool for measuring obesity [1].

The PHQ-9 is a 9-item depression module from the full PHQ used to diagnose major depression and other depressive symptoms. The PHQ-9 score ranges from 0 to 27, with 0-4 indicating no depression to minimal; 5-9: mild; 10-14: moderate; 15-19: moderately severe; 20-27: severe depression. Kroenke, Spitzer, & Williams (2001) [21] examined the reliability and validity of the PHQ and PHQ-9 utilizing analyses of multiple and combined samples. According to the American Psychological Association (APA) [22], the diagnostic validity of the 9-item PHQ-9 was established in studies conducted across eight primary care and seven obstetrical clinics. PHQ-9 scores > 10 had a sensitivity of 88% and a specificity of 88% for Major Depressive Disorder (2022). The reliability and validity of the tool indicate that it has sound psychometric properties. The PHQ-9 has high internal consistency. A study involving two distinct patient populations yielded Cronbach's alpha coefficients of .86 and .89. Criterion validity was established through 580 structured interviews conducted by a mental health professional. These interviews showed that individuals who scored high (≥ 10) on the PHQ-9 were between 7 and 13.6 times more likely to be diagnosed with depression by a mental health professional. Individuals scoring low (≤ 4) on the PHQ-9 had less than a 1 in 25 chance of having depression. A free and publicly available copy of the PHQ-9 was obtained from the American Psychological Association website for use in this quality improvement project.

The Rosenberg Self-Esteem Scale was used to measure participants' self-esteem. Self-esteem predicts outcomes and is one of the social sciences most widely studied constructs. According to Monteiro et al. [23], the Rosenberg Self-Esteem Scale is the primary instrument for assessing self-esteem: it is used in almost half of the empirical studies published in major scientific journals that have assessed self-esteem. The Rosenberg Self-Esteem scale is a 10-item, global measure of self-esteem originally designed for high school students but now widely used across diverse populations, including adults. It can be scored as a Guttman-type scale using a combined-rating method or by summing the 4-point Likert responses after reverse-scoring negatively worded items, yielding a total score from 10 to 40 (higher scores indicate higher self-esteem). Reliability is strong, with a Guttman reproducibility of approximately 0.92 and test–retest correlations of approximately 0.85–0.88 over two weeks, and validity is supported by concurrent, predictive, and construct validity, as evidenced by meaningful associations with other self-esteem measures and with depression and anxiety [24].

Setting

The project took place at two different primary care offices located in southeast Georgia. Participants were women who had already established their care with the current practice. Height and weight measurements were taken for the patient's BMI with each visit. Participants completed the Rosenberg Self-Esteem Scale and the PHQ-9 at each visit. All participants received guidelines on diet and exercise. Instructions on the administration of GLP-1 RA injections were provided to the participants receiving GLP-1 RA as combination therapy. Participants either received a prescription for GLP-1 RA medication or received a sample medication if their insurance did not cover it. A convenience sampling design was used to select readily available participants willing to participate in the research. The selected participants were female, aged 30-45, with a BMI >30.

Data Collection

Data collection took place at the initial visit for baseline and again at 3 months. In addition to exercise and diet, demographic variables such as age, race, and height were assessed via self-report. Baseline weights were measured at the primary care clinics on their first office visit using the electronic scale. Patients' most recent heights were self-reported on their first visit. Each participant completed the PHQ-9 and the Rosenberg Self-Esteem Scale at their first clinic visit. All participants were given my weight-management plan tool from Appendix D, which focuses on drinking 8 glasses of water and being physically active for at least 30 minutes on at least 5 days a week. The participant's weight was checked again after 12 weeks, and height was self-reported; BMI was recalculated. Participants also completed the PHQ-9 and the Rosenberg Self-Esteem Scale at their 12-week follow-up appointment as part of the post-evaluation.

Results

A total of 58 participants initially enrolled; 8 dropped out due to non-compliance. A total of 25 participants used GLP1 RA along with a diet and exercise, and the other 25 participants followed only diet and exercise modification.

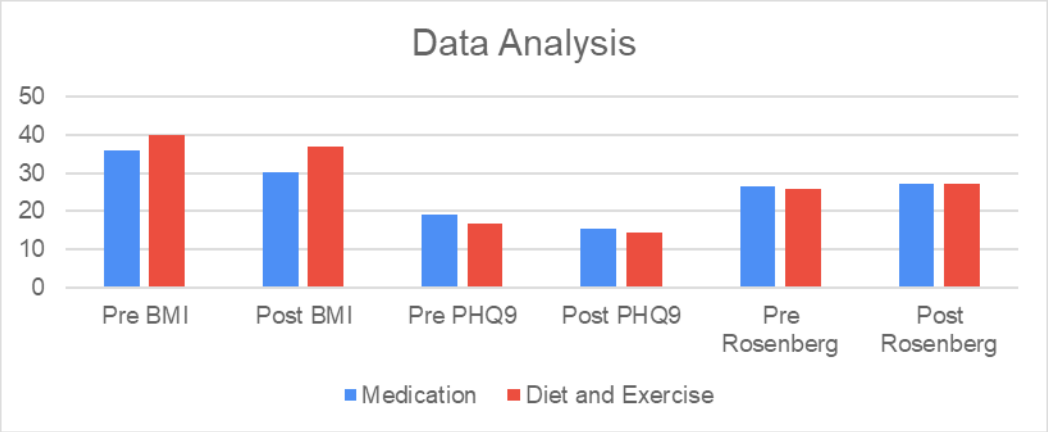
After completing the chosen treatment plan for 50 women in our study, GLP1-RA users exhibited a significant reduction in weight and depression, and a moderate increase in self-esteem, compared with non-users. The effectiveness increased with medication

duration, and a significant improvement was observed after 3 months. The average body mass index for the women who chose medicines in this study was 36. The average body mass index of the women who chose the diet and exercise plan was 40. The post-average BMI for the medication group was 30.33, a 5.67% decrease. The diet and exercise group's post-BMI was 37, with a 3% reduction. This was expected due to additional effects of GLP-1 RA on early satiety, slow gastric emptying, and calorie burning during exercise.

The PHQ-9 was used to measure depression pre- and post-study inclusion. The average PHQ-9 score for the medication group was 19.26, with a post-score of 15.43. This is a decrease of 3.83%. For the diet and exercise group, the pre-study PHQ9 score was 16.87, and the post-study score was 14.42. These numbers equate to a 2.45% decrease in the depression score.

The Rosenberg Self-Esteem questionnaire measured women's self-esteem pre- and post-study involvement. The average pre-study Rosenberg scale for the women who chose medication was 26.67, and the average post-study score was 27.23. This was a 0.56% increase in scoring. The diet and exercise group had an average pre-study Rosenberg score of 25.83 with a post-study score of 27.04. This was a 1.21% increase. Evaluating that exercisers' self-esteem does not rely solely on appearance may foster more autonomous engagement with exercise. Interventions that foster greater self-compassion have been shown to alleviate body image concerns and promote self-determination [25,26].

Medications Compared to Diet and Exercise	Pre BMI	Pre PHQ9	Pre Rosenberg	Post BMI	Post PHQ9	Post Rosenberg
Medications (25)	36	19.26	26.67	30.33	15.43	27.23
diet and exercise (25)	40	16.87	25.83	37	14.42	27.04



Conclusion

While everyone would love a magic pill for weight loss, the reality is that lifestyle changes remain the best option for long-term success. Many people have found that lifestyle changes and weight-loss medications have been very effective. GLP-1 RAs, recognized as calorie restriction mimetics or calorie restriction facilitators, are a newer class of injectable drugs in the pharmacological armamentarium for the management of T2DM as well as obesity. With benefits extending beyond glucose control, GLP-1 RAs are associated with extra-glycemic effects, including improvements in weight, BP, cholesterol levels, and β-cell function. As clinical factors largely influence the initiation of GLP-1 RA therapy, a pragmatic review of current evidence must be integrated and applied in an individualized, patient-centered approach. However, many questions remain about GLP-1 RA medications, including the durability of their weight-loss effects and their long-term safety. GLP1-RA users exhibited a significant reduction in weight and depression, and a moderate increase in self-esteem, compared with non-users. The effectiveness increased with treatment duration, and a significant improvement was observed after 3 months. It is anticipated that the ongoing evidence-based trials will continue to fill these gaps and bring new paradigm shifts in obesity management. Very little research has examined the correlation between obesity and self-esteem, an issue that remains for future studies.

Acknowledgements

Permission for access to the medical records of the healthcare facility where the project took place was requested and granted.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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