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Efficacy and Safety of Semaglutide in Glycemic Control, Body Weight Management, and Lipid Profile among Obese Type 2 Diabetes Patients: A Systematic Review

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Abstract

Background: Semaglutide showed an attractive weight loss effect in obese patients with T2D. Additionally, semaglutide significantly helped the to achieve glycemic control and improved lipid profiles. No adverse effects were documented in these studies secondary to semaglutide use. ***Objectives*:** To study the effects of semaglutide on body weight in obese individuals with type 2 diabetes (T2D), as well as effects and correlations between weight loss, glycemic control and lipid profile. ***Methods*:** We conducted a thorough search of PubMed, SCOPUS, Web of Science, and Science Direct to find pertinent literature. Rayyan QRCI was utilized during the entire process. ***Results*:** We included seven studies with a total of 480 T2D patients with obesity and 267 (55.6%) were males. Six of the seven included studies reported a significant decrease in HbA1C, body weight, and LDL among obese T2D patients. Regarding dosages, concurrent drugs, and the length of the intervention, there was a great deal of variation among studies. Several semaglutide dosage schedules were used in the trials that were found. Randomized and cohort studies substantiate semaglutide's better effectiveness over other GLP-1 RAs in helping T2D patients lose weight, achieve glycemic control, and improve lipid profiles. No adverse effects were documented in these studies secondary to semaglutide use. ***Conclusion*:** The current data of research was synthesized in this systematic review to investigate how semaglutide affects body weight, glycemic control, and lipid profiles in T2D patients. There is proof that semaglutide, a dual mechanism GLP-1/GIP RA, is superior to comparator GLP-1 RAs in terms of weight loss, glycemic control, and improving lipid profiles.

Keywords: Semaglutide, glucagon-like peptide-1 receptor agonists, Type 2 diabetes, Obesity, Systematic review.

INTRODUCTION

Globally, T2D is a leading cause of morbidity and death. T2D is characterized by insulin resistance, β-cell dysfunction, and overt hyperglycemia as a result of both hereditary and environmental factors [1]. The bulk of people with T2D are obese, which typically contributes to the development of insulin resistance and is linked to worse blood glucose management and longer-term clinical outcomes [2, 3].

Worldwide, individuals with T2D are advised to reduce their body weight and control their hyperglycemia by using glucagon-like peptide-1 (GLP-1) receptor agonists (RAs) [4]. Additionally, individuals with concurrent cardiovascular illness are advised to take certain GLP-1 RAs since they have positive effects on the cardiovascular system [5]. Because administering peptide-based medicines orally has inherent problems, GLP-1 RAs are generally delivered subcutaneously. An oral version of semaglutide has been created in order to provide patients with more therapy alternatives. Since peptides have a limited oral bioavailability, sodium N-(8-[2-hydroxybenzoyl] amino) caprylate, an absorption enhancer, is combined with oral semaglutide to make a tablet that both protects the drug from proteolytic destruction and facilitates absorption through the stomach mucosa [6].

There are currently a number of GLP-1 RAs available for the treatment of T2D, most of which are injected subcutaneously. Furthermore, the Food and Drug Administration recently approved tirzepatide, a

combination GLP-1/GIP agonist. In light of this, a systematic review was conducted to assess the effects of subcutaneous semaglutide in comparison to other GLP-1 RAs on body weight in individuals with T2D, as well as any negative effects and correlations between weight loss, glycemic control and lipid profile.

METHODOLOGY

Study Design and Duration

The conduct of this systematic review adhered to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [7]. This systematic review commenced in August 2024.

Search strategy

PubMed, SCOPUS, Web of Science, and Science Direct were the four main databases that were thoroughly searched to locate pertinent literature. We looked through exclusively English databases, taking into consideration each one's particular needs. We transformed the following keywords to PubMed Mesh terms to locate the pertinent studies; "Glucagon-like peptide-1," "Semaglutide," "Diabetes mellitus," "Type 2 diabetes," "Obesity," "Glycemic control," "HbA1C," "Weight," "BMI," and " Lipid profile." "OR," "AND," and "NOT," three Boolean operators, matched the necessary keywords. Full-text English publications, freely accessible articles, and human trials were among the search results.

Selection criteria

We considered the following criteria for inclusion in this review:

- Studies that summarized the effects of semaglutide on body weight in obese individuals with T2D, as well as effects and correlations between weight loss, glycemic control and lipid profile.
- Only human subjects.
- English language.
- Free accessible articles.

Data extraction

Rayyan (QCRI) was used for two output verifications of the search strategy [8]. Through application of inclusion/exclusion criteria, the researchers assessed the titles and abstracts' relevance to the aggregated search results. The reviewers gave careful consideration to each paper that satisfied the inclusion requirements. The writers discussed conflict resolution techniques. Utilizing a pre-made data extraction form, the authorized study was uploaded. The authors extracted data about the study titles, authors, study year, country, participants, gender, follow-up duration, glycemic control (HbA1C), weight control (BMI or body weight), lipid profile (mainly low density lipoprotein (LDL)) and main outcomes. A separate sheet was created for the risk of bias assessment.

Strategy for data synthesis

A qualitative evaluation of the components and conclusions of the research was provided by compiling summary tables containing data from pertinent studies. Following the collection of data for the systematic review, the most effective method for utilizing the data from the included study articles was selected.

Risk of bias assessment

The quality of the included studies was assessed using the ROBINS-I risk of bias assessment technique for non-randomized trials of treatments [9]. Confounding, research participant selection, intervention classification, deviance from planned treatments, insufficient data, outcome evaluation, and choice of reported result were among the seven themes that were addressed.

RESULTS

Search Results

The systematic search produced 811 study articles in total, of which 416 duplicates were eliminated. After 395 studies had their titles and abstracts screened, 301 were not included. After 94 reports were requested to be retrieved, 4 articles were found. After screening 90 studies for full-text assessment, 49 were rejected due to incorrect study results, 32 were rejected due to incorrect population type, and 2 articles were editor's letters. This systematic review included seven eligible study articles. A synopsis of the procedure for choosing studies is provided in **Figure 1.**

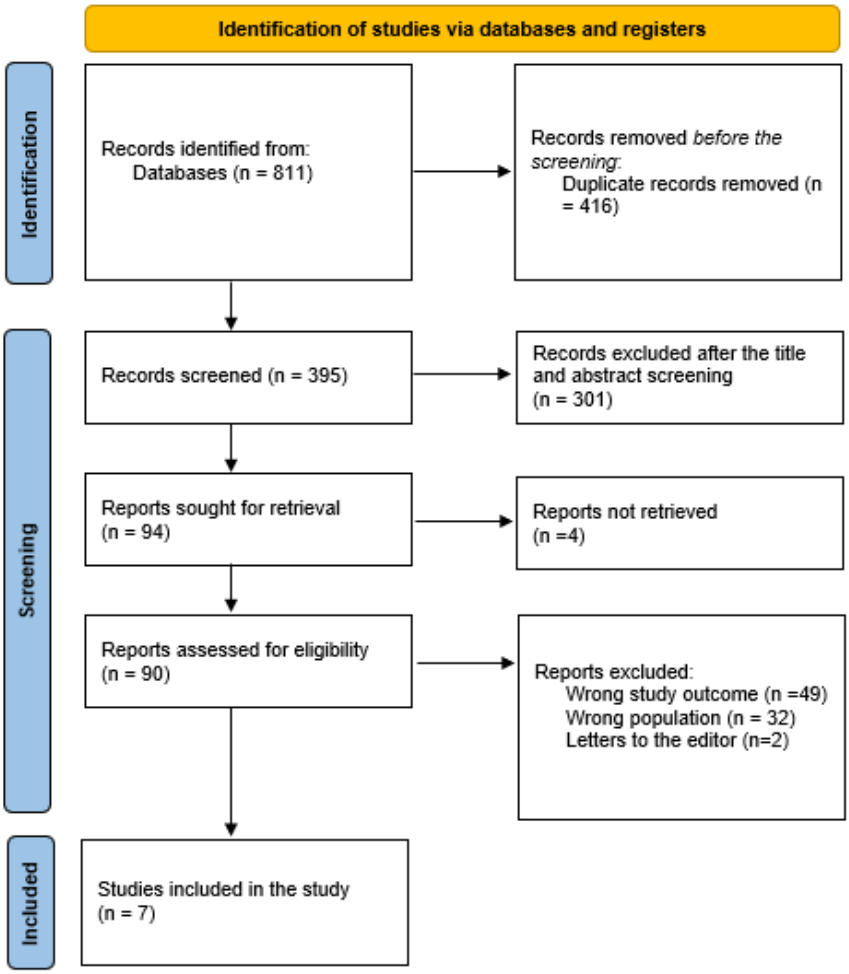

Figure 1: Study selection is summed up in a PRISMA flowchart

Characteristics of the included studies

Table (1) presents the sociodemographic characteristics of the included study articles. Our results included seven studies with a total of 480 T2D patients with obesity and 267 (55.6%) were males. Six studies were retrospective in nature [10, 11, 13-16] and one was a randomized control trial (RCT) [12]. Four studies were conducted in Japan [10, 14-16], one in Italy [11], one in the USA [12], and one in Denmark [13]. The earliest study was published in 2020 and the most recent one in 2022.

Table (2) presents the clinical characteristics. Six of the seven included studies reported a significant decrease in HbA1C, body weight, and LDL among obese T2D patients. Regarding dosages, concurrent drugs, and the length of the intervention, there was a great deal of variation among studies. Several semaglutide dosage schedules were used in the trials that were found. Randomized and cohort studies substantiate semaglutide's better effectiveness over other GLP-1 RAs in helping T2D patients lose weight, achieve glycemic control, and improve lipid profiles. No adverse effects were documented in these studies secondary to semaglutide use.

Table 1: Sociodemographic characteristics of the included participants

Study	Study design	Country	Participants	Mean age	Gender (Males)
Yanai *et al.*, 2022 [10]	Retrospective cohort	Japan	47	58.2 ± 13.5	25 (53.2%)
Di Loreto *et al.*, 2022 [11]	Retrospective cohort	Italy	135	64.1 ± 11.1	88 (65.2%)
Iacobellis *et al.*, 2020 [12]	RCT	USA	30	57 ± 10	21 (70%)
Pérez-Belmonte *et al.*, 2022 [13]	Retrospective cohort	Denmark	136	72.6 ± 11	74 (54.4%)
Okamoto *et al.*, 2021 [14]	Retrospective cohort	Japan	50	51.3 ± 11	21 (39.5%)
Masaki *et al.*, 2022 [15]	Retrospective cohort	Japan	34	52.8 ± 9.1	12 (35.3%)
Ozeki *et al.*, 2022 [16]	Retrospective cohort	Japan	48	52 ± 6.9	26 (54.2%)

*NM=Not-mentioned

Table 2: Clinical characteristics and outcomes of the included studies

Okamoto *et al.*, 2021 [14]	Pérez-Belmonte *et al.*, 2022 [13]	Iacobellis *et al.*, 2020 [12]	Di Loreto *et al.*, 2022 [11]	Yanai *et al.*, 2022 [10]	**Study**
6	12	12 w	12	6	**Follow-up (months)**
Patients were initially on a dose of 0.25 mg for four weeks then increased to 0.5 mg	Patients were initially on a dose of 0.25 mg for four weeks then increased to 0.5 mg	1 mg Semaglutide subcutaneous weekly	Mean semaglutide dose of 0.82 mg weekly	A daily dose of 7 mg of oral semaglutide with 31 patients, 14 mg with 7 patients and 3 mg with 9 patients.	**Intervention and dosage**
Mean HbA1C decreased from 7.19 ± 1.21 to 6.36 ± 0.5 in 6 months (p=0.04)	Mean HbA1C decreased from 8.1 ± 1.4 to 6.7 ± 1.0 in 12 months (p<0.01)	Mean HbA1C decreased from 7.3 ± 1.2 to 6.9 ± 1.2 in 12 weeks (ns)	Mean HbA1C decreased from 8.4 to 7.15 in 12 months (P<0.0001)	Mean HbA1C decreased from 8.1 ± 1.5 to 7.8 ± 1.5 in 6 months (P<0.05)	**Glycemic control**
Mean body weight decreased from 95.3 ± 8 kg to 91.5 ± 7.2 in 6 months (P=0.02)	Mean BMI decreased from 36.6 ± 7.2 to 29.5 ± 4.3 in 12 months (p<0.001)	Mean BMI decreased from 34.3 ± 5 to 33.8 ± 4 in 12 weeks (ns)	Mean body weight decreased from 95.25 kg to 90.03 in 12 months (P<0.0001)	Mean body weight decreased from 78.9 ± 17.7 to 77.3 ± 19.5 in 6 months (P<0.05)	**Body weight**
Mean LDL decreased from 93.9 to 88.4 mg/dl in 6 months (ns)	Mean LDL decreased from 78.4 ± 28.5 to 71.5 ± 21.2 mg/dl in 12 months (ns)	Mean LDL decreased from 99 ± 41 to 78 ± 30 mg/dl in 12 weeks (ns)	Mean LDL decreased from 90.02 to 80.37 mg/dl in 12 months (P<0.0001)	LDL decreased from 96.8 ± 28.5 to 91.3 ± 25.5 in 6 months (P<0.05)	**Prevalence of hypothyroidism (%)**
Even in individuals who were moved from other GLP-1 RAs, semaglutide had exceptional efficacy. Semaglutide may be a more effective T2D treatment than the GLP-1 RAs already on the market for controlling blood sugar and body weight in obese patients with T2D mellitus.	The use of once-weekly semaglutide was safe and clinically effective in enhancing health and functional status in obese patients with heart failure and T2D.	Semaglutide was found to significantly, quickly, and dose-dependently reduce the thickness of epicardial adipose tissue as evaluated by ultrasonography for the first time.	Real-world use of semaglutide in all stages of diabetic disease is supported by its strong glycemic and weight-loss advantages in persons with T2D.	In T2D obese patients, oral semaglutide decreased blood pressure, body weight, HbA1c, LDL-C, non-HDL-C, and UACR, particularly in patients who had never used GLP-1 analogues.	**Main outcomes**
Moderate	Moderate	High	Moderate	High	**ROBIN-I**

Masaki *et al.*, 2022 [15]	6	Patients were initially on a dose of 0.25 mg for four weeks then increased to 0.5 mg	Mean HbA1C decreased from 7.3 ± 1.1 to 6.4 ± 0.9 in 6 months (p<0.01)	Mean BMI decreased from 35.0 ± 6.2 to 33.2 ± 6.1 in 6 months (p<0.01)	Mean LDL decreased from 117.6 ± 30.4 to 113.3 ± 28.9 mg/dl in 6 months (p<0.01)	Eating habits are regulated by GLP1-RA semaglutide, and in obese T2D patients, eating habits are linked to improvements in HbA1c.	Moderate
Ozeki *et al.*, 2022 [16]	3	NM	Mean HbA1C decreased from 7.0 ± 1 to 6.4 ± 1 in 3 months (p<0.01)	Mean body weight decreased from 93.9 ± 14.6 kg to 90.8 ± 14.6 in 3 months (P<0.01)	Mean LDL decreased from 122.1 ± 24.2 to 109.1 ± 21.7 mg/dl in 3 months (p=0.05)	These findings imply that in obese T2D individuals, GLP1-RA semaglutide significantly lowers body adiposity while preserving skeletal muscle mass.	Moderate

*NM=Not-mentioned
*ns=not significant

DISCUSSION

Our systematic review of seven studies demonstrated that semaglutide showed an attractive weight loss effect in obese patients with T2D. Additionally, semaglutide significantly helped the to achieve glycemic control and improved lipid profiles. No adverse effects were documented in these studies secondary to semaglutide use. As the Introduction said, obesity has been a major problem for the healthcare system, which has been expanding quickly in recent years and is expected to continue to do so in the years to come [17, 18]. Therefore, the development of efficient and well-tolerated pharmaceuticals is essential to solving this problem. As of right now, the FDA has only approved five drugs for the long-term treatment of obesity or overweight in adults: semaglutide, liraglutide, phentermine-topiramate, naltrexone-bupropion, and orlistat [19]. Orlistat was found to cause a 3.16% weight reduction from the initial evaluation, phentermine-topiramate a 7.97% reduction, naltrexone-bupropion a 4.11% reduction, liraglutide a 4.68% reduction, and significantly, semaglutide a decrease of up to 11.41% in a recent network meta-analysis of RCTs comparing the efficacy of the aforementioned approved only five anti-obesity medications.

Stretton *et al.*, reported that semaglutide outperforms comparative GLP-1 RAs in terms of weight loss and glycemic management, but not in comparison to tirzepatide, which is a dual mechanism of GLP-1/GIP RA [20]. Since T2D is a chronic condition, medication must be taken continuously. Medication compliance is essential for maintaining glucose control and avoiding T2D comorbidities. Studies conducted in the real world have demonstrated that patients who take their diabetes drugs as prescribed had reduced medical care (nonpharmacy) expenses and a higher reduction in HbA1c after starting the prescription [21, 22]. The ADA/EASDs advocate a new class of AHAs called GLP-1 RAs [4]. However, a lot of patients are afraid about injectable medications, which makes them hesitant to use GLP-1 RAs. Oral semaglutide may present a different approach for those individuals in order to start GLP-1 RA medication early.

Weight loss may be mediated by semaglutide's effects on the GLP-1R, which are thought to affect the hypothalamus, hindbrain, and lateral parabrachial nucleus, among other brain locations. These areas regulate hunger, food intake, preference, reward, and meal termination, which ultimately results in consuming fewer calories [23]. Furthermore, studies have shown that neprilysin (NEP), an enzyme mostly found in the kidneys, catabolizes most semaglutide. Preclinical research indicates that NEP has lower activity in semaglutide therapy compared to liraglutide therapy. As a result, the blood's concentration of intact semaglutide increases. When weighed against liraglutide, this may have a greater impact on weight loss [24].

There are various restrictions on this study. First, our study, which comprised just seven studies, cannot definitively determine the relative benefits of semaglutide over other medications in the class due to the significant variability in dosage for specific GLP-1 RAs. This review also addressed the effects of both oral and subcutaneous semaglutide which may be a source of bias. Regarding dosages, concurrent drugs, and the length of the intervention, there was a great deal of variation among studies. Several semaglutide dosage schedules were used in the trials that were found. Randomized and cohort studies substantiate semaglutide's better effectiveness over other GLP-1 RAs

in helping T2D patients lose weight, achieve glycemic control, and improve lipid profiles.

CONCLUSION

The current data of research was synthesized in this systematic review to investigate how semaglutide affects body weight, glycemic control, and lipid profiles in T2D patients. There is proof that semaglutide, a dual mechanism GLP-1/GIP RA, is superior to comparator GLP-1 RAs in terms of weight loss, glycemic control, and improving lipid profiles. It is now appropriate to think about doing additional direct comparisons between GLP-1 RAs and a wider range of semaglutide dosages. Gaining a deeper mechanistic understanding of semaglutide's apparent superior efficacy above all current GLP-1RA comparators, including the role of GIP receptor agonism, will also be crucial.

REFERENCES

1. Reed J, Bain S, Kanamarlapudi V. A review of current trends with type 2 diabetes epidemiology, aetiology, pathogenesis, treatments and future perspectives. Diabetes Metab Syndr Obes 2021; 14: 3567–602.
2. Tobias DK, Pan A, Jackson CL, O'Reilly EJ, Ding EL, Willett WC et al. Body-mass index and mortality among adults with incident type 2 diabetes. N Engl J Med 2014; 370: 233–44.
3. Scheen AJ, Van Gaal LF. Combating the dual burden: therapeutic targeting of common pathways in obesity and type 2 diabetes. Lancet Diabetes Endocrinol 2014; 2: 911–22.
4. Davies MJ, D'Alessio DA, Fradkin J, Kernan WN, Mathieu C, Mingrone G, Rossing P, Tsapas A, Wexler DJ, Buse JB. Management of hyperglycemia in type 2 diabetes, 2018. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes care. 2018 Dec 1;41(12):2669-701.
5. Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, et al. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the american college of cardiology/American heart association task force on clinical practice guidelines. Circulation 2019;140 (11):e596–646.
6. Buckley ST, Bækdal TA, Vegge A, Maarbjerg SJ, Pyke C, Ahnfelt-Rønne J, et al. Transcellular stomach absorption of a derivatized glucagon-like peptide-1 receptor agonist. Sci Transl Med 2018; 10(467):eaar7047.
7. Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., ... & Moher, D. (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. International journal of surgery, 88, 105906.
8. Ouzzani, M., Hammady, H., Fedorowicz, Z., & Elmagarmid, A. (2016). Rayyan—a web and mobile app for systematic reviews. Systematic reviews, 5, 1-10.
9. Jüni, P., Loke, Y., Pigott, T., Ramsay, C., Regidor, D., Rothstein, H., ... & Shea, B. (2016). Risk of bias in non-randomized studies of interventions (ROBINS-I): detailed guidance. Br Med J.
10. Yanai H, Hakoshima M, Adachi H, Katsuyama H. A significant effect of oral semaglutide on cardiovascular risk factors in patients with type 2 diabetes. Cardiology Research. 2022 Oct;13(5):303.
11. Di Loreto C, Minarelli V, Nasini G, Norgiolini R, Del Sindaco P. Effectiveness in real world of once weekly semaglutide in people with type 2 diabetes: Glucagon-like peptide receptor agonist naïve or switchers from other glucagon-like peptide receptor agonists: Results from a retrospective observational study in Umbria. Diabetes Therapy. 2022 Mar;13(3):551-67.
12. Iacobellis G, Villasante Fricke AC. Effects of semaglutide versus dulaglutide on epicardial fat thickness in subjects with type 2 diabetes and obesity. Journal of the Endocrine Society. 2020 Apr;4(4):bvz042.
13. Pérez-Belmonte LM, Sanz-Cánovas J, García de Lucas MD, Ricci M, Cobos-Palacios L, López-Sampalo A, Bernal-López MR, Jansen-Chaparro S, Miramontes-González JP, Gómez-Huelgas R. Efficacy and safety of semaglutide for the management of obese patients with type 2 diabetes and chronic heart failure in real-world clinical practice. Frontiers in Endocrinology. 2022 Jun 24;13:851035.
14. Okamoto A, Yokokawa H, Nagamine T, Fukuda H, Hisaoka T, Naito T. Efficacy and safety of semaglutide in glycemic control, body weight management, lipid profiles and other biomarkers among obese type 2 diabetes patients initiated or switched to semaglutide from other GLP-1 receptor agonists. Journal of Diabetes & Metabolic Disorders. 2021 Dec;20:2121-8.
15. Masaki T, Ozeki Y, Yoshida Y, Okamoto M, Miyamoto S, Gotoh K, Shibata H. Glucagon-Like Peptide-1 Receptor Agonist Semaglutide Improves Eating Behavior and Glycemic Control in Japanese Obese Type 2 Diabetic Patients. Metabolites. 2022 Feb 4;12(2):147.
16. Ozeki Y, Masaki T, Kamata A, Miyamoto S, Yoshida Y, Okamoto M, Gotoh K, Shibata H. The effectiveness of GLP-1 receptor agonist semaglutide on body composition in elderly obese diabetic patients: a Pilot Study. Medicines. 2022 Sep 16;9(9):47.
17. Afshin A, Forouzanfar MH, Reitsma MB, et al. Health effects of overweight and obesity in 195 countries over 25 years. N Engl J Med. 2017; 377(1): 13-27.
18. Elagizi A, Kachur S, Carbone S, Lavie CJ, Blair SN. A review of obesity, physical activity, and cardiovascular disease. Curr Obes Rep. 2020; 9(4): 571-581.

19. Yanovski SZ, Yanovski JA. Progress in pharmacotherapy for obesity. JAMA. 2021; 326(2): 129-130.
20. Stretton B, Kovoor J, Bacchi S, Chang S, Ngoi B, Murray T, Bristow TC, Heng J, Gupta A, Ovenden C, Maddern G. Weight loss with subcutaneous semaglutide versus other glucagon-like peptide 1 receptor agonists in type 2 diabetes: a systematic review. Internal medicine journal. 2023 Aug;53(8):1311-20.
21. Buysman EK, Liu F, Hammer M, Langer J. Impact of medication adherence and persistence on clinical and economic outcomes in patients with type 2 diabetes treated with liraglutide: a retrospective cohort study. Advances in therapy. 2015 Apr;32:341-55.
22. Asche C, LaFleur J, Conner C. A review of diabetes treatment adherence and the association with clinical and economic outcomes. Clin Ther 2011;33(1):74–109.
23. Gabery S, Salinas CG, Paulsen SJ, et al. Semaglutide lowers body weight in rodents via distributed neural pathways. JCI Insight. 2020; 5(6): 18.
24. Christou GA, Katsiki N, Blundell J, Fruhbeck G, Kiortsis DN. Semaglutide as a promising antiobesity drug. Obes Rev. 2019; 20(6): 805-815.