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Long-Term Adverse Effects of Semaglutide Use: A Systematic Review / Efectos adversos por el uso de semaglutida a largo plazo: Revisión sistemática

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ABSTRACT

Introduction: semaglutide is a drug intended to treat type 2 diabetes. It works by mimicking a natural hormone in the body (GLP-1), helping to regulate blood glucose levels. Its use is part of a plan that includes a healthy diet and physical exercise, always under medical supervision. In recent years, it has gained significant notoriety due to one of its most prominent side effects: the considerable weight loss it causes. This effect has driven its increasing use not only in individuals with type 2 diabetes but also as a tool for short-term weight reduction, even among people who do not suffer from the disease. Semaglutide's ability to suppress appetite makes it a highly effective agent for weight management. However, it must be administered once a week via subcutaneous injection, and it requires strict medical supervision due to its potential effects on the endocrine, metabolic, gastrointestinal, cardiovascular, renal, and even psychological systems. This caution becomes especially important given the growing use of medication, particularly in populations for whom conclusive research is still pending. Current studies are focusing on assessing the clinical and social effects of semaglutide's application as a weight-loss strategy. Although initial findings highlight its short-term benefits, they also underscore the importance of further investigating its adverse effects, which appear to be increasing in frequency and severity. It is essential to study its long-term consequences, especially since many patients are using the drug beyond the official indications, with some even exceeding the recommended dosages.
Objective: evaluate the long-term adverse effects of semaglutide use in individuals with type 2 diabetes or obesity across different population groups.
Method: a systematic review of clinical studies that investigated the adverse effects associated with prolonged semaglutide administration.
Results: semaglutide has shown effectiveness in reducing body weight and improving blood glucose control. The most frequently reported adverse effects are gastrointestinal, including nausea, vomiting, diarrhea, and appetite suppression. These effects are generally mild to moderate and tend to subside over time. Most studies report a low incidence of serious side effects, suggesting a favorable safety profile during extended use.
Conclusions: while gastrointestinal adverse effects are common, the clinical benefits of semaglutide in weight loss and glycemic regulation justify its use under appropriate medical supervision. Semaglutide offers significant therapeutic advantages when used correctly. However, its long-term safety still requires ongoing monitoring, strict clinical oversight, and further scientific evidence to support its broader use beyond currently approved indications. Future projections indicate a growing demand for semaglutide, underscoring the need for continuous evaluation to ensure tolerability, adherence, and patient safety over time.

Keywords: Semaglutide; Long-Term; Adverse; Overuse; GLP-1.

RESUMEN

Introducción: la semaglutida es un fármaco indicado para la diabetes tipo 2 que actúa como agonista de los receptores GLP-1. Contribuye a regular los niveles de glucemia en sangre y su uso se enmarca en un plan que incluye una dieta saludable y ejercicio físico, siempre bajo supervisión médica. En años recientes, ha ganado gran notoriedad debido a uno de sus efectos adversos más sobresalientes: la notable disminución de peso que ocasiona. Este impacto ha impulsado su uso en aumento no solo en individuos con diabetes tipo 2, sino también para disminuir el peso a corto plazo, incluso en personas que no padecen esta enfermedad. Su capacidad para disminuir el apetito la convierte en una herramienta eficaz en el control del peso corporal. Sin embargo, su administración debe llevarse a cabo una vez a la semana por vía subcutánea, y necesita un estricto control médico debido a sus potenciales efectos en los sistemas endocrino, metabólico, gastrointestinal, cardiovascular, renal e incluso psicológico. Esta precaución adquiere una mayor importancia dado el uso creciente del medicamento, especialmente en grupos para los que todavía no se han realizado investigaciones definitivas. Los estudios actuales se enfocan en valorar el efecto clínico y social de la aplicación de la semaglutida como estrategia para la reducción de peso. Aunque los hallazgos iniciales resaltan sus ventajas a corto plazo, también enfatizan la importancia de profundizar en el estudio de los efectos adversos, que parecen incrementarse tanto en incidencia como en severidad. Es fundamental estudiar sus consecuencias a largo plazo, especialmente porque muchos pacientes prolongan su uso más allá de las recomendaciones, e incluso algunos exceden las dosis recomendadas.
Objetivo: evaluar los efectos adversos por el uso prolongado de semaglutida en individuos con diabetes tipo 2 u obesidad.
Método: revisión sistemática de estudios clínicos, que hayan investigado los efectos adversos de semaglutida en un contexto de administración prolongada.
Resultados: Las investigaciones examinadas demuestran que la semaglutida resulta efectiva para disminuir el peso corporal y mantener el control de la glucemia en pacientes con diabetes tipo 2 y obesidad. Los efectos secundarios más documentados fueron relacionados con el sistema gastrointestinal, tales como náuseas, diarrea, vómitos y reducción del apetito.
Conclusiones: aunque son comunes los efectos adversos gastrointestinales, su efecto clínico beneficioso en la pérdida de peso y la regulación de la glucemia justifica su empleo, siempre bajo supervisión médica. La semaglutida posee beneficios clínicos al ser utilizada correctamente; sin embargo, su seguridad a largo plazo todavía necesita supervisión constante, seguimiento médico adecuado y más pruebas científicas que respalden su uso ampliado más allá de las indicaciones aprobadas. El pronóstico futuro señala un uso creciente, requiriendo un seguimiento constante para garantizar tolerancia y adhesión.

Palabras clave: Semaglutide; Long-Term; Adverse; Overuse; GLP-1.

INTRODUCTION

Semaglutide is a glucagon-like peptide-1 (GLP-1) analog that selectively binds to and activates the GLP-1 receptor. GLP-1 is a physiological regulator of appetite and food intake, and the GLP-1 receptor is expressed in several brain regions involved in appetite regulation.

Semaglutide is a drug approved for the treatment of type 2 diabetes in adults and, more recently, as a treatment for weight reduction in people who are obese or overweight in the presence of at least one weight-related comorbidity, e.g., blood glucose disorders

(prediabetes or type 2 diabetes mellitus), hypertension, dyslipidemia, obstructive sleep apnea, or cardiovascular disease. It works by increasing feelings of fullness, reducing appetite, and controlling blood glucose levels.

Semaglutide has been shown in clinical trials to reduce blood glucose in a glucose-dependent manner by stimulating insulin secretion and reducing glucagon secretion when blood glucose is high. The mechanism of glucose reduction also involves a slight delay in gastric emptying in the early postprandial phase. During hypoglycemia, semaglutide decreases insulin secretion and does not affect glucagon secretion.[1]

GLP-1 receptors are also expressed in the heart, vasculature, immune system, and kidneys.

Both experimental and clinical research have shown that GLP-1 receptors (GLP-1R) are expressed in various components of the cardiovascular system, including cardiomyocytes, vascular endothelium, and blood vessel smooth muscle cells. This tissue distribution allows semaglutide, by activating these receptors, to exert direct effects on cardiac structure and function.

The activation of GLP-1R in these tissues modulates various intracellular signaling pathways, including cAMP-protein kinase A (PKA), phosphatidylinositol 3-kinase-Akt (PI3K-Akt), and mitogen-activated protein kinase (MAPK), thereby influencing hemodynamic, metabolic, and inflammatory regulatory processes at the cardiovascular level.

The protective effects of semaglutide on the cardiovascular system are manifested both indirectly, through improvements in risk factors, and directly, through its action on cardiac tissue.

Indirect effects

- Optimizes glycemic control.
- Contributes to weight loss.
- It lowers systolic blood pressure.
- Improves lipid profile by reducing cholesterol and triglycerides.

Direct effects

Through its action on GLP-1R in the heart, semaglutide can:

- Increase myocardial contractility, especially under functional compromise.
- Decrease oxidative stress and local inflammation, protecting the myocardium in ischemic contexts.
- Reduce hypoxia-induced cardiomyocyte apoptosis.
- Promote endothelium-dependent vasodilation to improve coronary blood flow.

Several relevant clinical trials, such as SUSTAIN-6 and LEADER, have shown that semaglutide significantly reduces the incidence of major adverse cardiovascular events (MACE) in patients with type 2 diabetes and high cardiovascular risk. In particular, a lower frequency of non-fatal acute myocardial infarction, non-fatal stroke, and cardiovascular mortality has been observed, consolidating its profile as an agent with cardioprotective potential.

Despite these benefits, a slight sustained increase in heart rate has been reported in some patients treated with GLP-1 receptor agonists, including semaglutide. Although this finding is

consistent, its clinical relevance remains to be further investigated.

Semaglutide also acts on receptors expressed in various renal structures, including proximal tubular cells, endothelial cells, and mesangial cells. Stimulation of GLP-1 receptors in the kidney regulates crucial functions, including glomerular filtration, tubular reabsorption, and maintenance of fluid and electrolyte Balance. In addition, semaglutide exerts a protective effect on the kidney, mainly by reducing oxidative stress,

inflammation, and the formation of renal fibrosis, key processes in the progression of diabetic nephropathy. In clinical practice, its use has been associated with a slowing of renal function decline and a significant reduction in albuminuria in patients with type 2 diabetes.

As for the immune system, semaglutide, by activating GLP-1 receptors on immune system cells such as macrophages and dendritic cells, plays a regulatory role in the immune response. Its action results in decreased synthesis of proinflammatory cytokines (such as TNF-α and IL-6) and increased production of mediators with anti-inflammatory effects. This modulation contributes to reducing both systemic and local inflammation, a central aspect in the development and progression of metabolic and cardiovascular diseases. Consequently, semaglutide promotes a less inflammatory immune environment, which can protect tissues and limit the progression of diabetes-related complications.

In the clinical trials evaluated, semaglutide has a beneficial effect on plasma lipids, lowers systolic blood pressure, and reduces inflammation. Likewise, animal studies have shown that semaglutide attenuated atherosclerosis development and exerted anti-inflammatory effects on the cardiovascular system.

The mechanism of action of semaglutide in reducing cardiovascular risk may involve multiple factors, partly driven by weight loss, effects on identified cardiovascular risk factors (lower blood pressure, improved lipid profile, and glucose metabolism), and anti-inflammatory effects, as evidenced by reduced high-sensitivity C-reactive protein levels. The exact mechanism for cardiovascular risk reduction has not been determined.[2]

Dosage and administration

Semaglutide is administered subcutaneously and has a long half-life, allowing for weekly dosing.

The maintenance dose of semaglutide 2,4 mg once weekly is achieved by starting at 0,25 mg. To minimize the risk of gastrointestinal symptoms, the dose should be escalated over 16 weeks to a maintenance dose of 2,4 mg once weekly. In cases of significant gastrointestinal symptoms, delaying dose escalation or reducing the dose to the previous dose until symptoms have improved should be considered. Weekly doses greater than 2,4 mg are not recommended.[3]

Known adverse effects

Short term: these effects often appear at the beginning of treatment, but their persistence or worsening may indicate a risk.

Gastrointestinal: nausea (in up to 40 % of patients at the start of treatment), vomiting, and diarrhea, which can lead to dehydration.

Endocrine: semaglutide has the potential to alter hormonal metabolic activity, such as increased prolactin or alterations in thyroid gland function. In preclinical research, an increased likelihood of developing thyroid C tumors was reported in rodents, although this has not been verified in humans.

Psychological: some users reported changes in mood and anxiety, possibly related to rapid weight loss. Some studies indicate that the use of weight loss drugs, such as semaglutide, may be linked to eating disorders, such as compulsive eating or alterations in body image. The effect of weight control on self-esteem, mental health, and social expectations increases the risk of eating disorders such as anorexia or bulimia.

Long term: risk of pancreatitis and biliary disease: A 2022 study (Diabetes Care) found that prolonged semaglutide administration increases the risk of cholelithiasis, particularly in patients with rapid weight loss (>10 % of initial weight).

Kidney dysfunction: dehydration caused by persistent vomiting and diarrhea can lead to acute kidney failure in vulnerable patients. Long-term use of semaglutide may affect kidney function, particularly in individuals with a history of kidney disease or with indiscriminate use of the medication.

Risk of cardiovascular disease in unauthorized situations: Although it has been shown to reduce cardiovascular risk in diabetics, there is insufficient evidence to support its cardiovascular safety in non-diabetics, raising concerns about its use in these groups.

Indiscriminate use and risks

The phenomenon of semaglutide use outside of medical indications has been stimulated by factors such as:

Social implications: dissemination on social media as a “miracle drug” for weight loss.

Improper access: purchase of the drug without a prescription, through pharmacies and online stores.

Unapproved doses: some users take doses exceeding the recommended amount, increasing the frequency of severe adverse effects.

Effects of unauthorized use: a 2023 study in the Journal of Obesity indicated that more than 20 % of semaglutide users did not follow medical recommendations, mostly young individuals with normal BMI seeking a quick Fix for weight loss.

Ethical and social implications

The use of semaglutide for cosmetic purposes raises ethical dilemmas, such as:

Diversion of medical resources: increased demand and shortages for individuals who have approved medical indications and require the drug.

Unnecessary risks: administration of a drug with potentially severe side effects in healthy individuals.

Social pressure: social media has played a crucial role in the spread of the drug, promoting an ideal model of a thin body that leads to large-scale use. A 2024 study of posts on Instagram and TikTok found that more than 70 % of content about semaglutide promoted its use for weight loss, without warnings about potential risks.

Fraudulent marketing: pharmaceutical companies do not adequately control product promotion, thereby facilitating its popularity as a "cosmetic medication."

Misinformation: many users are unaware of the side effects associated with prolonged use.

METHOD

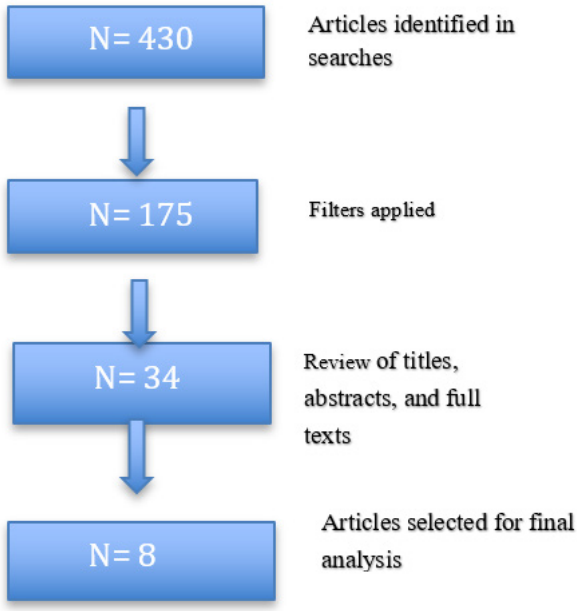

Figure 1. Process of identifying the included studies

The articles for this review were selected through a systematic search of several scientific databases, including PubMed, Embase, Cochrane Library, and Google Scholar. A combination of MeSH terms and keywords related to the review topic was used to identify relevant studies. The search was conducted between 2017 and 2024, and studies were filtered according to the previously established inclusion criteria.

The MeSH terms used in the search were: "Semaglutide" "long-term" "adverse" "overuse" "GLP-1"

These terms were combined using Boolean operators: AND to combine key terms and OR to include synonyms or related terms.

A detailed review of the selected articles followed initial searches of titles and abstracts. Studies that met the inclusion criteria were downloaded and analyzed in their entirety. Those that did not meet the established criteria or lacked the necessary information were discarded.

Study Design

This systematic review adopted quantitative Variables to examine and analyze the available articles. Studies of varied designs were included, such as randomized controlled trials (RCTs), meta-analyses, and systematic reviews. This work is based on a systematic review of research published between 2017 and 2024 on the long-term side effects of semaglutide, using databases such as PubMed and Google Scholar.

Study Population

The total number of articles selected is the sample size and constitutes the study population.

Inclusion criteria

Publications from:

- Studies published between 2017 and 2024 in Spanish, English, and Portuguese, including systematic reviews, meta-analyses, and randomized clinical trials, that examine the long-term adverse effects of semaglutide across various populations.
- Target populations: Adults aged 18 years and older who have received semaglutide for type 2 diabetes or obesity.
- Adverse effects analyzed: Assessments related to the digestive, cardiovascular, endocrine, renal, and psychological systems.

Exclusion criteria

- Research involving only animals or preclinical trials.
- Research that does not accurately detail the adverse effects associated with prolonged use of semaglutide.
- Opinion pieces, narrative analyses, or editorials.

Scope of the study

The study was conducted at the Inter-American Open University using bibliographic resources accessible in the academic environment.

RESULTS

Based on eight scientific studies published between 2017 and 2024, a decrease in body weight of between 7,9 % and 14,9 % was observed, with significant advances in glucose regulation and cardiovascular and renal safety.

Common adverse effects linked to the use of semaglutide, in its different methods of administration (subcutaneous or oral). Its therapeutic effect in patients with type 2 diabetes, obesity, or both conditions was detected. Mild to moderate gastrointestinal adverse effects were the most frequently reported, including nausea, vomiting, diarrhea, dyspepsia, constipation, and decreased appetite.

According to the studies, their frequency fluctuated, but in general, between 20 % and 40 % of participants experienced some digestive discomfort, especially at the beginning of treatment. Some studies reported more severe effects, such as pancreatitis, diabetic retinopathy, and cholelithiasis, especially in patients with comorbidities or under treatment control. The metabolic and cardiovascular benefits observed are favorable for the use of semaglutide under medical supervision.

Table 1. Presentation of results

Type of Study	Author's Name/Year of Publication	Patient Characteristics (N)	Intervention in the study	Dosage regimen (dose, duration of treatment)	Main adverse effects	Results
Phase III clinical trial	Wilding et al.[4]	Obese patients (N=1961)	Subcutaneous semaglutide versus placebo	2,4 mg/week for 68 weeks	Gastrointestinal effects increased mild cases of cholelithiasis and acute pancreatitis	Weight loss weight
Phase III clinical trial	Husain et al.[5]	Patients with type 2 diabetes and cardiovascular risk (N=3183)	Oral semaglutide versus placebo	14 mg/day for 16 months	Gastrointestinal effects intestinal, some mild cases of acute pancreatitis and renal complications	Reduction in cardiovascular events
Meta-analysis	Sattar et al.[6]	Patients with type 2 diabetes Multiple trials (N=8)	Oral and subcutaneous semaglutide versus placebo	Oral: 14 mg/day Subcutaneous: 0,5 mg and 1 mg/week	Gastrointestinal effects Intestinal, increase in mild cases of cholelithiasis and acute pancreatitis	Significant reduction significant in weight and cardiovascular events
Clinical phase III	Ahmann et al.[7]	Patients with type 2 diabetes, (N=813)	Semaglutide (subcutaneous) vs exenatide	Escalating 0,25 mg to 1 mg/ week, exenatide 2 mg/week for 56 weeks	Gastrointestinal effects Intestinal, some rare cases of diabetic retinopathy and hypoglycemia	Reduction in HbA1c and weight
Phase III clinical trial	Rubino et al.[8]	Obese without type 2 diabetes, (N=803)	Semaglutide subcutaneous versus placebo	2,4 mg/week for 20 weeks	Gastrointestinal effects	Maintains weight loss after 20 weeks
Phase III clinical trial	Aroda et al.[9]	Patients with type 2 diabetes, (N=703)	Semaglutide oral versus placebo	14 mg/day for 26 weeks	Gastrointestinal effects effects	Significant HbA1c HbA1c and weight
Clinical Phase II	Blundel l et al.[10]	Patients obese without type 2 diabetes, (N=30)	Subcutaneous semaglutide versus placebo	1 mg/week for 12 weeks	Gastrointestinal effects effects	Significant Significant appetite and weight loss
Review Systematic	Cornell et al.[11]	Patients with type 2 diabetes (N=10)	Semaglutide versus Dulaglutide versus exenatide (subcutaneous)	Semaglutide: 0,25–0,5 mg or 1 mg/week. Dulaglutide: 0,75–1,5 mg/ week. Exenatide: 2 mg/ week, for 26 to 104 weeks	Gastrointestinal effects Intestinal, mild hypoglycemia	Significant reduction HbA1c and weight, cardiovascular and renal benefits HbA1c and weight, cardiovascular and renal benefits

DISCUSSION

This systematic review examines semaglutide, a glucagon-like peptide-1 (GLP-1) receptor agonist widely used in the treatment of type 2 diabetes and, more recently, in the fight against obesity. However, its expanded use has raised concerns about possible adverse effects, especially in off-label use, such as weight loss in people without diabetes or clinical obesity.

The series of studies analyzed provides a comprehensive perspective on the effectiveness and safety of semaglutide, whether in subcutaneous or oral forms, in patients with type 2 diabetes, obesity, or overweight. The findings consistently corroborate that semaglutide is associated with notable reductions in body weight (5 %-17 %), improvements in glucose control (HbA1c reductions of up to 1,8 %), and cardiovascular benefits, particularly in high-risk patients.

However, when focusing on adverse effects and long-term tolerability, a clear trend is also apparent: semaglutide shows a favorable safety profile, although it is not free from adverse events, especially in the digestive tract. The most commonly reported effects include nausea, vomiting, diarrhea, and constipation, affecting between 20 % and 40 % of users in certain studies. Most of these symptoms appear at the beginning of treatment and decrease over time or with dose adjustment.

Another documented long-term adverse effect is cholelithiasis, especially in patients who experience rapid weight loss. A randomized review of clinical studies found that the use of GLP-1 agonists, including semaglutide, increased the likelihood of biliary disorders. This risk could be linked to alterations in vesicular motility caused by the treatment.

Regarding more serious effects, preclinical studies in rodents have shown a correlation between semaglutide and the development of thyroid C-cell tumors. Although this correlation has not been proven in humans, it remains a cause for concern, especially in patients with a family history of medullary thyroid carcinoma.[12]

Additionally, a recent study published in JAMA Ophthalmology showed a possible connection between semaglutide and non-arteritic anterior ischemic optic neuropathy (NAION), a serious but rare eye condition. In this observational study, a higher incidence of NAION was observed among semaglutide users compared with those receiving insulin therapy.[13]

Another growing concern is mental health. Although studies are inconclusive, cases of suicidal thoughts have been documented in patients treated with semaglutide and other GLP-1-like compounds. Science experts highlight the importance of conducting detailed studies on this relationship, especially in vulnerable groups such as adolescents or people with eating disorders, and the association with depression.[14]

Semaglutide is emerging as a safe and effective therapeutic method for controlling type 2 diabetes and obesity, with proven benefits in blood glucose control, weight reduction, and cardiovascular risk prevention. However, prolonged use requires thorough analysis, mainly due to common gastrointestinal side effects and possible rare but significant complications, such as pancreatitis and chronic digestive disorders.

Given its widespread and often indiscriminate use, especially for aesthetic purposes and without a prescription, it is essential to strengthen professional training and regulations governing access to this type of drug. More extensive research is recommended, with follow-

up exceeding 2–5 years, to establish the actual effects of semaglutide on organs such as the pancreas, gallbladder, and kidneys, as well as its impact on the quality of life of patients who use it regularly.

In conclusion, semaglutide offers significant clinical benefits when used appropriately; however, its long-term safety still requires ongoing monitoring, adequate medical follow-up, and additional scientific evidence to support its expanded use beyond approved indications.

BIBLIOGRAPHIC REFERENCES

1. Mahapatra MK, Karuppasamy M, Sahoo BM. Semaglutide, a GLP 1 receptor agonist with cardiovascular benefits for type 2 diabetes: mechanisms and pharmacology. Front Endocrinol. 2021;12. https://pmc.ncbi.nlm.nih.gov/articles/PMC8736331/

2. Marso SP, Bain SC, Consoli A, Eliaschewitz FG, Jódar E, Leiter LA, et al., LEADER Trial Investigators. Semaglutide and cardiovascular outcomes in patients with type 2 diabetes. N Engl J Med. 2017;376(7):637-49. https://doi.org/10.1056/NEJMoa1607141

3. StatPearls Publishing. Semaglutide. In: StatPearls [Internet]. 2023. https://www.ncbi.nlm.nih.gov/books/NBK603723/

4. Wilding JPH, Batterham RL, Calanna S, Davies M, Van Gaal LF, Lingvay I, et al., on behalf of the STEP 1 Study Group. Semaglutide once weekly for treatment of overweight and obesity in adults. N Engl J Med. 2021;384(11):989–1002. https://doi.org/10.1056/NEJMoa2032183

5. Husain M, Birkenfeld AL, Donsmark M, Dungan K, Eliaschewitz FG, Franco DR, et al. Oral semaglutide and cardiovascular outcomes in patients with type 2 diabetes. N Engl J Med. 2019;381(9):841–51. https://doi.org/10.1056/NEJMoa1901118

6. Sattar N, McLaren J, Kristensen SL, Preiss D, McMurray JJV. Cardiovascular, mortality, and kidney outcomes with GLP-1 receptor agonists in patients with type 2 diabetes: a systematic review and meta-analysis of randomized trials. Lancet Diabetes Endocrinol. 2021. https://eprints.gla.ac.uk/250144/8/250144.pdf

7. Ahmann AJ, Capehorn M, Charpentier G, Dotta F, Henkel E, Lingvay I, et al. Efficacy and safety of once-weekly semaglutide versus exenatide ER in subjects with type 2 diabetes (SUSTAIN 3): A 56-week, open-label, randomized clinical trial. Diabetes Care. 2018;41(2):258–66. https://doi.org/10.2337/dc17-0417

8. Rubino DM, Greenway FL, Khalid U, Bray GA, Klein S, Wilding JPH. Effect of continued weekly subcutaneous semaglutide vs placebo on weight loss maintenance in adults with overweight or obesity: The STEP 4 randomized clinical trial. JAMA. 2021;325(2):141–50. https://jamanetwork.com/journals/jama/fullarticle/2777886

9. Aroda VR, Ahmann A, Cariou B, Chaykin L, Fredrickson L, Garvey WT, et al. Efficacy, safety, and tolerability of oral semaglutide versus placebo added to insulin ± metformin in patients with type 2 diabetes: A randomized clinical trial. Diabetes Care. 2022. https://pmc.ncbi.nlm.nih.gov/articles/PMC7364672/

10. Blundell J, Finlayson G, Axelsen M, Flint A, Gibbons C, Kvist T, Hjerpsted JB. Effects of

once-weekly semaglutide on appetite, energy intake, control of eating, food preference and body weight in subjects with obesity: A randomized, double-blind, placebo-controlled, two-period crossover trial. Diabetes Obes Metab. 2017;19(9):1242–51. https://doi.org/10.1111/dom.12932

11. Cornell S. A review of GLP-1 receptor agonists in type 2 diabetes: A focus on the mechanism of action of once-weekly agents. J Clin Pharm Ther. 2020;45 Suppl 1:17–27. https://doi.org/10.1111/jcpt.13230

12. Feier CVI, Vonica RC, Faur AM, Streinu DR, Muntean C. Assessment of thyroid carcinogenic risk and safety profile of GLP1 RA semaglutide (Ozempic) therapy for diabetes mellitus and obesity: A systematic literature review. Int J Mol Sci. 2024;25(8):4346. https://doi.org/10.3390/ijms25084346

13. Hathaway JT, Shah MP, Hathaway DB, Zekavat SM, Krasniqi D, Gittinger JW, et al. Risk of nonarteritic anterior ischemic optic neuropathy in patients prescribed semaglutide. JAMA Ophthalmol. 2024;142(8):732–9. https://doi.org/10.1001/jamaophthalmol.2024.2296

14. Li J-R, Cao J, Wei J, Geng W. Semaglutide-associated depression: A report of two cases. Front Psychiatry. 2023;14:1238353. https://www.frontiersin.org/journals/psychiatry/articles/10.3389/fpsyt.2023.1238353/full

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CONFLICT OF INTEREST

None.

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