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The Risks of Taking Ozempic

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Abstract: This review examines the safety profile of semaglutide (Ozempic), a glucagon-like peptide-1 (GLP-1) receptor agonist originally developed for the treatment of type 2 diabetes and increasingly used for weight loss. While clinical trials have demonstrated its effectiveness in reducing body weight and improving glycemic control, the rapid rise of off-label use—particularly among non-diabetic individuals—has raised important safety concerns. The paper discusses the pharmacological mechanisms of semaglutide, including its effects on insulin secretion, appetite regulation, and gastric emptying. It also evaluates clinical evidence regarding weight loss outcomes and highlights commonly reported adverse effects such as gastrointestinal disturbances, fatigue, and injection site reactions. Furthermore, the review addresses emerging risks, including potential long-term metabolic consequences and rare but serious complications. Special attention is given to the influence of social media in promoting widespread, and sometimes unsupervised, use of the drug. Overall, this study emphasizes the need for careful monitoring and further research into the long-term safety of semaglutide, particularly when used outside approved medical indications.

Keywords: Semaglutide, Ozempic, GLP-1 receptor agonist, type 2 diabetes, weight loss, obesity, off-label use, pharmacological mechanism, adverse effects, gastrointestinal side effects, pancreatitis, gallbladder disease, cardiovascular outcomes, social media influence, patient experiences, long-term safety, metabolic control

Introduction

The global search for effective pharmacological weight-loss strategies has recently shifted toward glucagon-like peptide-1 (GLP-1) receptor agonists, particularly semaglutide. Originally developed for the treatment of type 2 diabetes, semaglutide improves glycemic control by enhancing insulin secretion, suppressing glucagon release, and slowing gastric emptying [1].

Following clinical observations of significant weight reduction, semaglutide gained widespread popularity as an off-label anti-obesity drug, especially through social media exposure. However, the rapid expansion of its use beyond approved indications has raised safety concerns, particularly among individuals without metabolic disorders. While randomized trials have demonstrated substantial weight loss, questions remain regarding long-term safety, dependency risk, and potential metabolic consequences after discontinuation [2].

Recent reports have highlighted a spectrum of adverse effects associated with semaglutide, including gastrointestinal disturbances, pancreatitis, gallbladder disease, and possible endocrine risks. Emerging

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case reports also suggest a potential association with severe complications such as gastroparesis and rare thyroid tumors, although causal relationships remain under investigation [3].

Given the rapid growth of non-diabetic use and the limited long-term real-world data, a critical evaluation of the safety profile of semaglutide is essential.

The aim of this review is to evaluate current evidence on the safety of semaglutide (Ozempic), with particular focus on adverse effects and potential long-term risks associated with its off-label use for weight loss [4].

Methodology

This study adopts a narrative review and analytical approach based on the examination of clinical trials, scientific literature, and regulatory reports related to semaglutide use. Relevant peer-reviewed articles, including randomized controlled trials and systematic reviews, were analyzed to evaluate both efficacy and safety outcomes.

Data sources include major medical journals such as *The New England Journal of Medicine*, *The Lancet*, and *Nature Reviews Endocrinology*, as well as regulatory documents from organizations such as the U.S. Food and Drug Administration (FDA). The analysis focuses on identifying patterns of adverse effects, therapeutic benefits, and long-term risks associated with semaglutide use [5].

Comparative analysis was used to evaluate differences between diabetic and non-diabetic populations, particularly in the context of off-label weight loss use. Additionally, qualitative synthesis methods were applied to interpret clinical findings and highlight emerging safety concerns [6].

Pharmacological mechanism of semaglutide

Semaglutide is a long-acting glucagon-like peptide-1 (GLP-1) receptor agonist that mimics the action of endogenous incretin hormones. By binding to GLP-1 receptors, it enhances glucose-dependent insulin secretion, suppresses glucagon release, and slows gastric emptying. These effects collectively improve glycemic control and promote satiety, making semaglutide effective not only in diabetes management but also in weight reduction [7].

At the central nervous system level, semaglutide influences appetite regulation through hypothalamic pathways. It modulates neuronal activity in appetite-controlling regions, leading to reduced caloric intake and improved energy balance. Functional imaging studies have demonstrated decreased reward-related responses to high-calorie foods in patients receiving GLP-1 receptor agonists [8].

In addition to metabolic effects, semaglutide alters gastrointestinal motility by delaying gastric emptying. While this contributes to prolonged satiety, it is also responsible for many of the drug's adverse effects, including nausea and bloating. Chronic stimulation of GLP-1 receptors may lead to adaptive changes in gut-brain signaling, which are still under investigation [8].

Emerging experimental data suggest that GLP-1 receptor agonists may exert pleiotropic effects beyond glucose regulation, including anti-inflammatory and cardioprotective actions. However, the extent to which these benefits apply to non-diabetic individuals remains unclear, particularly when the drug is used primarily for cosmetic weight loss rather than metabolic disease [9].

Thus, semaglutide exerts complex systemic effects involving endocrine, neurological, and gastrointestinal pathways. Understanding these mechanisms is essential for evaluating both therapeutic benefits and potential risks, especially in populations using the drug outside approved indications [10].

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Efficacy of Semaglutide in Treating Obesity

Obesity is a chronic metabolic condition associated with increased risk of Type 2 Diabetes and Cardiovascular Disease. While lifestyle interventions remain the cornerstone of treatment, they are often insufficient for sustained weight loss. In this context, Ozempic (semaglutide), a GLP-1 receptor agonist, has emerged as a promising pharmacological option. Originally developed for glycemic control, semaglutide has demonstrated significant weight reduction by suppressing appetite and delaying gastric emptying. However, its growing off-label use has raised important concerns regarding safety and long-term effects [11].

Obesity, a multifactorial disease, is a leading cause for increased incidence of cardiovascular risk factors, including dyslipidemia, type 2 diabetes (T2D), hypertension, and sleep disorders. The higher the body mass index (BMI), the greater is the risk of morbidity and mortality.

Reduction in BMI decreases the risk of development of type 2 diabetes mellitus, hypertension, acanthosis nigricans, and depression to name a few. Being a global epidemic, the prevalence of obesity in the United States has increased from 30.5% in 1999-2000 to 41.9% in 2017-2020, with an estimated annual burden of nearly $173 billion dollars in 2019. According to CDC, overweight and obesity are defined as BMI more than 25 and 30, respectively. Hence, obesity leads to a myriad of other diseases [12].

Lifestyle interventions and dietary modifications are the initial approaches to weight reduction. Currently, Food and Drug Administration (FDA) has approved five drugs for long-term use for obesity which includes orlistat, phentermine-topiramate, naltrexone-bupropion, liraglutide, and semaglutide of which phentermine is the commonly prescribed option [13].

Semaglutide 2.4 mg is to be administered subcutaneously, once a week for adults with overweight (body mass index >27 kg/m^2) with at least one weight-associated condition [for instance, high blood pressure, type 2 diabetes (T2DM), or high cholesterol], or adults with BMI of 30 kg/m^2 or greater, received FDA approval in 2021.

Secreted from the L-cells in the small intestine, glucagon-like peptide (GLP)-1, an incretin hormone lowers blood glucose levels by stimulating insulin and inhibiting glucagon secretions in a glucose level dependent way from the pancreatic islets. A decrease in appetite and craving for food, a relatively low proclivity for fatty, energy-rich foods, and better control of eating are the most likely mechanisms for semaglutide-induced weight loss. This systematic review has the primary objective to study the use of semaglutide for weight loss [14].

Adverse Effects of Ozempic (Semaglutide)

Semaglutide, marketed as Ozempic, is a glucagon-like peptide-1 (GLP-1) receptor agonist widely used for the management of Type 2 Diabetes and, more recently, for weight reduction. While it has demonstrated significant clinical benefits, its use is associated with a range of adverse effects that should be carefully considered [15].

The most commonly reported side effects are gastrointestinal in nature, including nausea, vomiting, diarrhea, constipation, and abdominal pain. These symptoms are typically mild to moderate in severity and tend to occur during the initial stages of treatment, often decreasing over time as the body adapts to the medication.

However, semaglutide may also cause more serious adverse events. One of the most concerning complications is acute pancreatitis, which presents with persistent and severe abdominal pain that may radiate to the back. In addition, gallbladder-related disorders, such as cholelithiasis, have been reported in some patients. Renal complications may occur secondary to dehydration caused by prolonged vomiting or diarrhea.

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Another important safety concern is hypoglycemia, particularly when semaglutide is used in combination with insulin or sulfonylureas. Patients may experience symptoms such as dizziness, confusion, sweating, and tachycardia.

Furthermore, there is evidence suggesting a potential risk of worsening diabetic retinopathy in individuals with pre-existing eye disease.
Although rare, serious allergic reactions, including angioedema and anaphylaxis, have also been documented. These require immediate medical attention [16].

Overall, current evidence suggests that the majority of adverse effects associated with semaglutide are manageable and transient. Nevertheless, careful patient selection, dose titration, and ongoing monitoring are essential to minimize risks. Further long-term studies are needed to fully evaluate the safety profile of semaglutide, especially in the context of its increasing off-label use for weight loss [17].

Results

The results indicate that semaglutide is highly effective in promoting weight loss and improving glycemic control. Clinical trials demonstrate significant reductions in body weight, with some studies reporting an average weight loss of up to 15% in obese individuals.

At the same time, the analysis identifies a range of adverse effects. The most common are gastrointestinal symptoms, including nausea, vomiting, diarrhea, and abdominal discomfort. These effects are generally mild and temporary but may lead to treatment discontinuation in some patients [18].

More serious complications were also identified, including pancreatitis, gallbladder disease, hypoglycemia (particularly in combination therapies), and potential renal issues. Emerging evidence suggests possible risks related to gastroparesis and endocrine abnormalities, although further research is required to establish causal relationships.

The findings also highlight that off-label use among non-diabetic individuals increases the likelihood of misuse and insufficient medical supervision, potentially amplifying health risks.

The science and potential of Ozempic in the future

In 2017, Ozempic was first approved for use in the USA to treat type II diabetes. In 2021, Wegovy was also approved for the US market but as a weight loss drug. According to Novo Nordisk, Ozempic is ‘an adjunct to diet and exercise to improve glycaemic control in adults with type 2 diabetes mellitus’.

Wegovy is ‘for adults with obesity (body mass index (BMI) ≥ 30) or overweight (excess weight) (BMI ≥ 27) who also have weight-related medical problems, to help them lose weight and keep it off’.Ozempic and Wegovy are taken via a single-dose weekly injection (0.5 mg to 2 mg and 2.4 mg per dose, respectively).

Semaglutide functions to treat type II diabetes in a number of ways. First, it assists in the control of blood glucose levels by mimicking the GLP-1 hormone which helps the production of insulin when blood glucose levels are elevated—insulin helps to move the glucose out of the bloodstream (extracellular) and into cells (intracellular), and when it does, so blood glucose levels decrease [19].

Semaglutide also slows gastric emptying and suppresses appetite by interacting with parts of the brain that signal hunger and satiation. This functions to treat diabetes as it encourages patients to consume fewer calories to be converted to glucose. Suppression of appetite also encourages weight loss. While the reasons people develop type II diabetes are not entirely clear, being overweight does play an important role in a person’s risk of developing type II diabetes and their ability to manage it.

This is because when people have a high BMI, their body sometimes requires ‘as much as two to three times more insulin’ than someone with a ‘healthy’ BMI.[8] These levels of insulin are typically more

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insulin than a person's pancreas is able to produce, and so having a high BMI can contribute to a person's ability to maintain healthy glucose levels.

As a drug to treat type II diabetes and weight loss, semaglutide has seen great success. With respect to type II diabetes, in one clinical trial (the Sustain 7 Study), patients with type II diabetes taking Ozempic showed a reduction in haemoglobin A1c—a measure of average blood sugar—of up to 1.8% over 40 weeks.[9] A person with 5.7% is in the normal range, 5.7%–6.4% is indicative of prediabetes, and 6.5% or higher indicates diabetes.

The haemoglobin A1c change seen in the Sustain 7 Study then can move someone from the range of having diabetes, to a normal 5.7%. In addition to these benefits, studies have shown evidence of a reduced risk of heart attack, stroke and kidney failure in patients with type II diabetes.

For people taking semaglutide for weight loss, the results so far have also been significant. In one 2-year randomised control trial (Semaglutide Treatment Effect in People 5 (STEP 5)) of 304 participants, participants were shown to have lost, on average, −15.2% of their body weight when taking Wegovy, compared with −2.6% taking the placebo. The participants were overweight adults (with BMI ≥ 27 kg m–2) or adults with obesity (with BMI ≥ 30 kg m–2), with at least one weight-related comorbidity, without diabetes. In addition to these outcomes, one time per week use of 2.4 mg of semaglutide has also been shown to be beneficial for the cardiovascular health of obese people without diabetes.

In one double-blind, randomised, placebo-controlled study (the SELECT trial), '17 604 adults aged 45 years or older with overweight or obesity and established cardiovascular disease (CVD) with no prior history of diabetes' were given 2.4 mg of semaglutide for up to 5 years. Results showed a 20% improvement in overall risks of major cardiac events including heart attack, stroke and cardiovascular death.

Participants also showed a reduced risk of 28% with respect to a reduction of non-fatal myocardial infarction, 15% of cardiovascular death and 7% of non-fatal stroke. According to Yale cardiologist Harlan Krumholz, the result of 'the SELECT trial is a major breakthrough' because it demonstrates that the use of semaglutide is an effective treatment for cardiovascular disease, independently of the presence of type II diabetes. Importantly, 'mechanisms of cardiovascular risk reduction with semaglutide may include those related to physiological benefits from the reduction of excess abnormal body fat and actions of semaglutide other than weight loss'.

The reductions in cardiovascular risks observed in other trials with similar weight-loss reductions, as Lincoff et al. explain, were consistent with the findings here. They also claim that 'more rapid treatment-induced physiological changes beyond the magnitude of body-weight loss may have mediated at least part of the cardiovascular benefit'. However, they acknowledge that this link is only speculative.

Discussion

The findings confirm that semaglutide represents a significant advancement in the pharmacological treatment of obesity and type 2 diabetes. Its mechanism of action, which combines appetite suppression, delayed gastric emptying, and improved insulin regulation, explains its high effectiveness in weight management.

However, the growing popularity of semaglutide beyond clinical indications raises important concerns. The influence of social media has contributed to increased demand, often without adequate medical oversight. This trend may lead to inappropriate use, incorrect dosing, and neglect of potential contraindications.

From a clinical perspective, while most adverse effects are manageable, the presence of serious complications highlights the need for careful patient selection and monitoring. The lack of long-term

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data further complicates risk assessment, particularly in individuals using the drug for non-medical purposes.

The study emphasizes that semaglutide should be viewed not only as a weight-loss solution but as a potent pharmacological agent requiring strict clinical control. Balancing its benefits with potential risks is essential to prevent misuse and ensure patient safety.

Conclusion

To conclude with, emaglutide represents a significant advancement in the pharmacological management of obesity and type 2 diabetes due to its demonstrated efficacy in promoting weight loss and improving metabolic control. However, the growing trend of its off-label use, particularly among non-diabetic individuals, raises important clinical and ethical concerns. Although most side effects are mild and manageable, the potential for more serious adverse events and the lack of comprehensive long-term safety data warrant caution. The influence of social media has further accelerated its widespread use, often without adequate medical supervision. Therefore, it is essential that semaglutide be used under proper clinical guidance, with careful patient selection and monitoring. Future research should focus on long-term outcomes, risk stratification, and the broader implications of its use beyond approved indications. Ultimately, balancing the benefits and risks of semaglutide is critical to ensuring its safe and effective application in clinical practice

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