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Exploring the Effects of GLP-1 Agonists on Weight Management in Non-Diabetic Individuals

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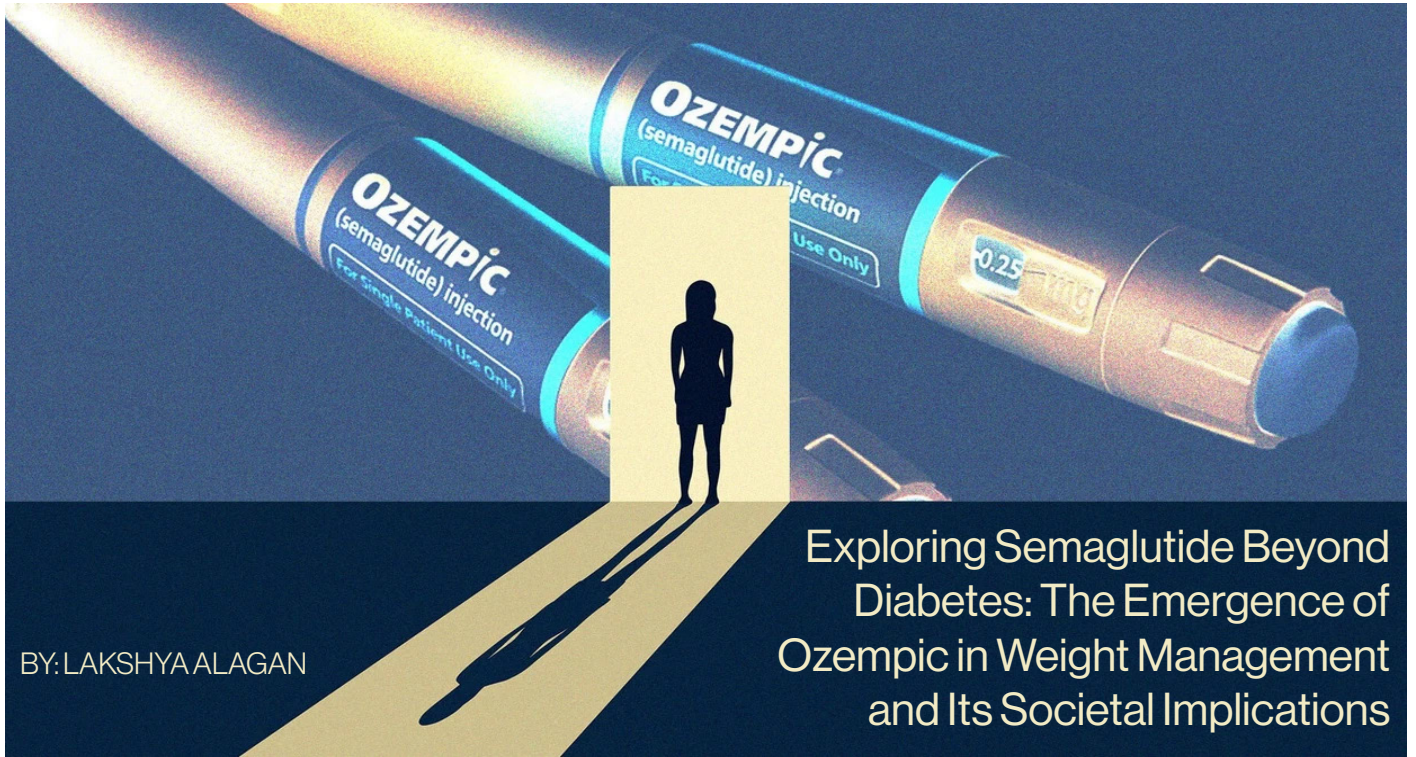
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Undergraduate



BY: LAKSHYA ALAGAN

Exploring Semaglutide Beyond Diabetes: The Emergence of Ozempic in Weight Management and Its Societal Implications

In just two years, from 2021 to 2023, the Google search volume for “Ozempic” skyrocketed by an astonishing 726.83%, signaling a surging interest in the drug.¹ Ozempic was developed as a medication to manage Type II Diabetes (T2D), and does so by stimulating insulin release and suppressing appetite. Although it is not the first T2D medication in its class, its once-a-week injections last longer than similar medications like liraglutide, which require once-a-day injections.^{2,3} This, however, is not the reason for the immense boom in Google searches. Rather, Ozempic has gained mass attention for its surprising role as a catalyst for weight loss. Although Ozempic is not FDA-approved or endorsed by the company for weight loss purposes, Wegovy, another medication with the same functional ingredient, is.^{4,5} The ability of both medications to induce speedy weight loss has triggered widespread attention, as media influencers undergo its use.⁴

One may wonder how a blood sugar medication can exert such impactful effects on weight, and what the potential consequences of glorifying its use as a weight loss treatment are?

The active ingredient in both Ozempic and Wegovy is medically referred to as semaglutide. Semaglutide is a type of Glucagon-like peptide 1 (GLP-1) receptor agonist.^{2,3,4} GLP-1 is a hormone secreted by the cells in the gut, which includes specialized

cells of the pancreas and intestine.⁵ Furthermore, it affects neurons located in regions of the brain that maintain the internal stability of physiological processes such as hunger.^{6,7,8} GLP-1 functions to signal the release of insulin into the bloodstream, allowing cells to take in consumed sugars and nutrients, thereby reducing blood sugar levels.^{3,8}

Agonist refers to a mimicking action; thus, as a GLP-1 receptor agonist, Ozempic mimics our own GLP-1, but is longer acting.⁷

Since Type II Diabetes is caused by the body’s inability to produce insulin, medicines like Ozempic can help reinstate healthy levels of insulin.

Weight-Loss Impact

Due to its popularity among celebrities and influencers, semaglutide has been gaining attention for its remarkable ability to induce weight loss. Studies have shown that semaglutide can cause significant weight loss in people with and without diabetes,⁷



Figure 1: Image of semaglutide injection: Ozempic.

FEATURES

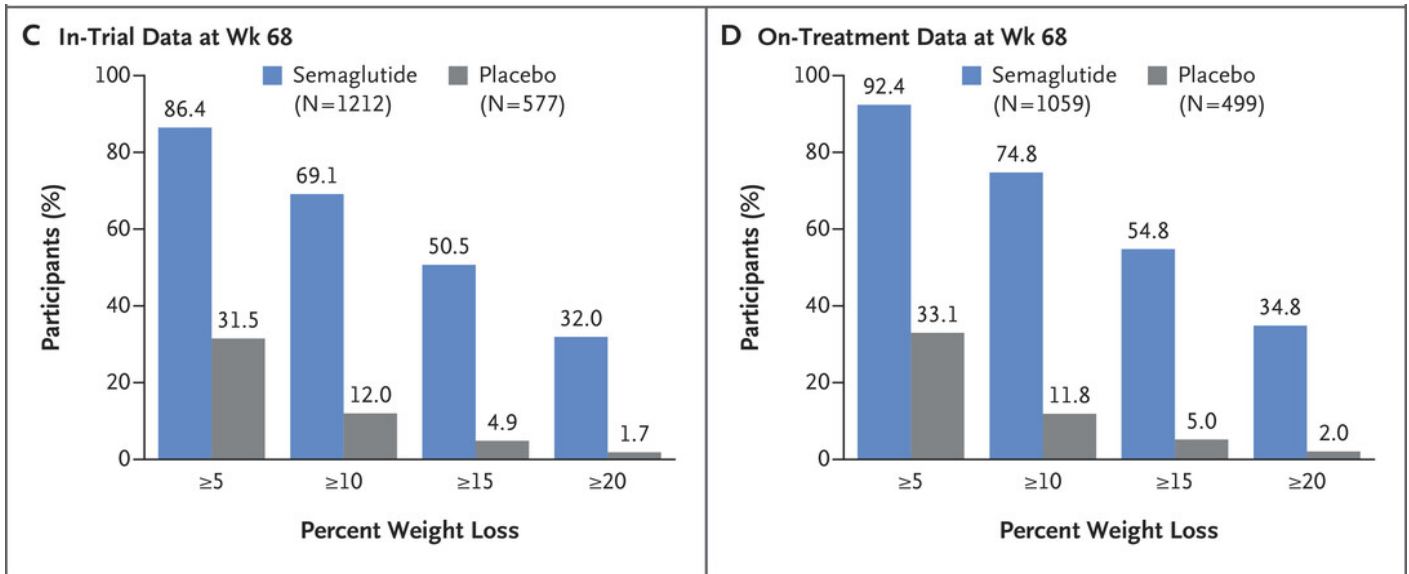


Figure 2: Graph of weight-loss data collected over 68 weeks in a New England Journal of Medicine study. The study found significant weight loss in the group receiving semaglutide injections (displayed by the blue bars on the graph) compared to the placebo group (displayed by the gray bars on the graph).

which can be especially helpful for obese individuals. The specific mechanism that causes such substantial effects is not entirely known, but certain studies are beginning to help us understand.

In a study consisting of individuals without diabetes, adults using semaglutide lost an average of 15% of their body weight over 68 weeks, while the placebo group lost only 2.5% (Figure 2).⁹ In another study with adolescent participants (ages 12-18), the agonist reduced body weight by an average of 14.7% in 68 weeks, while the placebo group gained about 2.7%.¹⁰ These results support a strong positive correlation between semaglutide use and the percentage of body

weight lost.

This weight loss is thought to be mainly caused by the ability of GLP-1 agonists to decrease patients' appetites and increase satiety, or the feeling of fullness, after a meal.^{5,6,11} Such hunger-altering effects can be attributed to the GLP-1 receptors located in regions of the brain such as the hypothalamus that work with homeostatic (regulatory) processes in the body like appetite.^{6,7} Researchers have since been investigating how exactly GLP-1 receptors in the brain and GLP-1 agonists interact with the body to drive significant weight loss effects.

Further investigation has turned researchers to studying the neuronal

properties of the brain. Satiety was found to be produced by gut receptors being activated after the stomach is swelled to accommodate food consumption. A bundle of nerves in the neck picks up on the activation, sending the signal to the brainstem.^{6,7} GLP-1 reduces the rate at which food exits the stomach, slowing the interpretation of stomach swelling after food is ingested. This in turn triggers feelings of fullness.^{8,11}

Implications of Supply Shortages

In June 2021, a new drug Wegovy, which also contains semaglutide, was FDA-approved specifically for weight loss.¹¹ However, due to the manufacturer's inability to keep up with growing demands, a Wegovy shortage was announced in December 2021.¹ During this shortage period, Google trends analysis saw a surge in searches for "Ozempic," suggesting that off-label Ozempic use increased during Wegovy shortages.¹ As a result, most GLP-1 Agonists including semaglutide, dulaglutide, and tirzepatide began facing global shortages in 2023.

As a result, clinicians were advised to cease GLP-1 agonists for off-label use and to refrain from prescribing newly diagnosed T2D patients these medications.^{12,13} The shortage has since pushed diabetic patients to alter doses or transition to insulin therapy until the supply of GLP-1 agonists stabilizes; projections, however, predict stabilization won't occur until the end of 2024.^{13,14} Thus, diabetic patients are hindered from accessing the medication essential for their health.

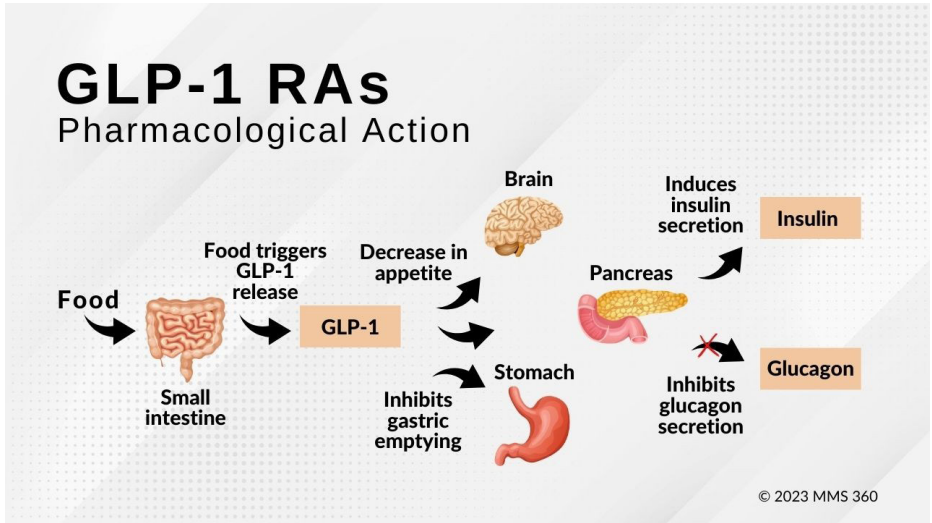


Figure 3: Pharmacological processes of the GLP-1 receptor agonist (GLP-1 RA), displaying the roles GLP-1 RAs play in the brain, stomach, and pancreas.

In response, many patients have turned to pharmacies that provide semaglutide mixed with other active ingredients.^{14,15} However, these compounded (mixed) medications are not from the approved manufacturer and their activity is unclear. In response, the manufacturer of Ozempic issued a statement emphasizing that their product is not intended for compounding purposes.¹⁴ The concern about compound-use stems from the lack of testing on the safety and efficacy of mixed semaglutide compounds.^{14,15} Thus, the use of altered semaglutide furthers the potential risks individuals may face as a result of these semaglutide shortages.

Health Risks and Potential Psychological Implications

Because semaglutide drugs have been controversially marketed through social media as an “easy fix” to unwanted weight, many seek out the drug without understanding its possible harmful effects on one’s health. The use of Ozempic, like any medication, comes with a long list of possible side effects, the most common ones affecting the gastrointestinal system; this includes bloating, discomfort to the stomach, and a change in bowel habits.^{11,16} Furthermore, without consistent lifestyle changes related to one’s diet and exercise, ceasing to take the drug will lead to a rapid regaining of lost weight. One study found that after the discontinuation of semaglutide, most consumers gained back two-thirds of their lost weight in one year (Figure 5).¹⁷

Due to the surge’s recency, the possible psychological risks associated with drug intake by adolescents remain unclear; however, social media platform analyses found that media containing keywords such as “Ozempic” and “Semaglutide” also contained keywords such as “Depression”, “Anxiety, and “Sleep Disorders.¹⁸ This suggests that semaglutide-use may garner adverse psychological effects, but also highlights the need for further research to yield more medically grounded conclusive findings.

Conclusion

The surge in Google searches for “Ozempic” from 2021 to 2023 highlights the dramatic impact media marketing has had on the societal perceptions of semaglutide. Originally developed to manage Type II Diabetes, semaglutide has emerged as a subject of intense interest, not for its original therapeutic purpose, but for its efficacy in weight loss management. This

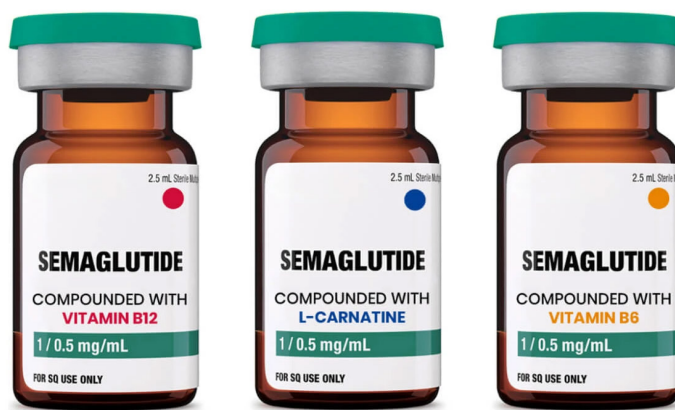
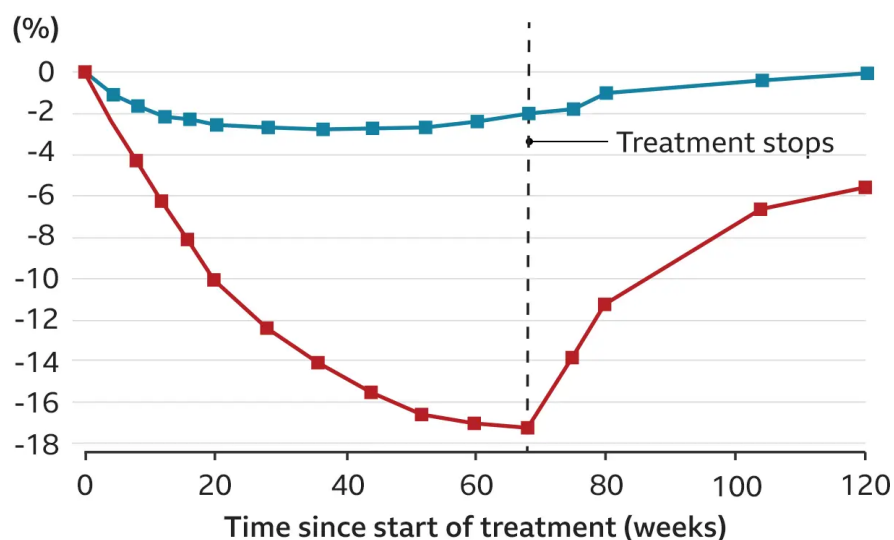


Figure 4: Examples of compounded semaglutide medications

Weight returns when treatment stops

Change in body weight (%)

■ Semaglutide 2.4mg ■ Placebo*



*Includes diet and exercise

Source: Diabetes, Obesity and Metabolism



Figure 5: Graph displaying the fluctuation of weight before and after stopping semaglutide treatment. While the placebo group maintained stable levels of weight throughout the trial, the semaglutide group showed a significant increase in weight after treatment stopped.

journey through the study of semaglutide and its mechanisms offers valuable insights into the intersection of medicine, societal perceptions, and public health, emphasizing the nuanced topic that is ripe for continued research. Moving forward, it is imperative to delve deeper into the implications of Ozempic’s weight-loss effects, while prioritizing its availability for individuals with T2D.

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