

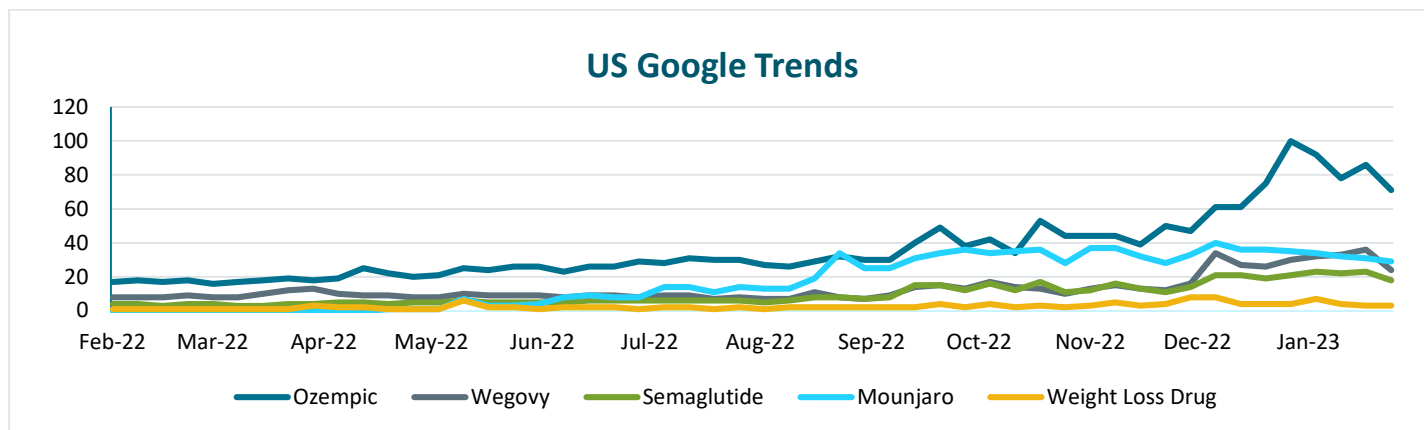
CLINICAL INSIGHTS

Diabetes Drugs and Weight Loss – What's the Skinny?

Weight loss is often at the top of mind for many at the start of a new year, but late 2022 and early 2023 are bringing increased attention to how people lose weight. Social and mainstream media are spotlighting newer medications that can help with significant weight loss. Public interest in using medications to help with weight loss is likely at an all-time high, but despite the attention, questions about these medications remain.

What medications are we talking about?

The "incretin mimetics", including GLP-1 (glucagon-like peptide 1 receptor agonist) and the new combined GIP/GLP-1 (glucose-dependent insulinotropic polypeptide receptor agonist) classes of medications, were originally approved for diabetes, but have also shown benefits with weight loss. The drugs getting the most attention are semaglutide (Ozempic, Wegovy) and to a lesser extent tirzepatide (Mounjaro), but there are even more in the class as well. As seen in the Google Search Trend chart from February 2023 below, public interest in these drugs has spiked over the last 6 months.



Data Source: Google Trends (<https://www.google.com/trends>). Accessed 2/23/23

Do they help with weight loss?

As a whole, yes. While not everyone responds to these medications for weight loss, in clinical trials of Wegovy (semaglutide) for weight loss, patients lost between 10% and 17.5% of their body weight, compared with either a weight gain or up to 5% weight loss without the treatment.¹ The other drugs in this class approved for diabetes also showed positive effects on weight, with Mounjaro being the most effective. Mounjaro is not approved for weight loss as of this writing but has clinical trial data showing average weight loss over 15%, with most patients losing over 20% of their body weight at the highest dose.² The manufacturer for Mounjaro received a "Fast Track" designation from the FDA for an approval to use Mounjaro to treat obesity and overweight with weight-related conditions.³ A decision from the FDA (likely an approval based on the data available) is expected sometime in 2023 or 2024.

What are the similarities and differences?

This is a tricky question, because some of these drugs have the same active ingredient – semaglutide (Ozempic, Wegovy) and liraglutide (Victoza, Saxenda), for example – and same mechanism of action, but are approved for different uses. Ozempic and Victoza are FDA-approved to treat type 2 diabetes, while Wegovy and Saxenda are FDA-approved for chronic weight management. They are the same drug but dosed and studied slightly differently, leading to different FDA approvals and insurance coverage.

Mounjaro differs from the other drugs in this general drug family as it is a dual-incretin (GIP/GLP-1) receptor agonist or "twincretin", meaning it targets two different hormones involved in the pathway. The exact mechanism of action to lower blood sugar and weight with the second hormone (GIP) is not entirely clear, but it is thought to help further enhance the body's insulin response and energy use.⁴

Injectable Incretin Mimetics		
Active Ingredient	Brand Name Product	FDA Approval
Semaglutide ^a	Ozempic	Diabetes
Semaglutide ^a	Wegovy	Weight management
Liraglutide ^a	Victoza	Diabetes
Liraglutide ^a	Saxenda	Weight management
Dulaglutide ^a	Trulicity	Diabetes
Exenatide ^a	Bydureon	Diabetes
Tirzepatide ^b	Mounjaro	Diabetes

a – GLP-1; **b** – GIP/GLP-1

The biggest differences are insurance coverage and the price to the patient. The drugs approved for diabetes have traditionally been covered by insurance at a branded copay tier for diabetes treatment. Wegovy and Saxenda are often excluded from coverage because weight management, overweight, and obesity medications are not frequently covered by insurance. Manufacturer savings cards are available to help with out-of-pocket costs, but without insurance coverage lowering copays, the \$225 to \$500 savings for a month supply of Wegovy is still largely unaffordable, due to list prices around \$1600 a month.⁵

What is the impact of the media hype?

Increased media attention has pros and cons. It highlighted that overweight and obesity are chronic health conditions that are treatable with effective drugs, which has been a challenging public and medical perception issue for many years.⁶ Also, many people will likely get treatment they did not otherwise realize was available to help them lose weight successfully.

However, increased off-label use of the drugs for diabetes (Ozempic, Mounjaro, Trulicity, etc.) to help lose weight has led to shortages of medication for those who need it to manage diabetes.⁷ This causes treatment delays, increases in blood sugar, and impairs adherence to the treatment. Supply issues may also require patients to go to other pharmacies where they do not have a relationship with their pharmacist and drug-drug interactions could be missed due to lack of a full medication profile to review. As these drugs also require gradual dose titration when starting treatment, patients may have to re-titrate their dose if they go without the medication for weeks at a time.

What are the pros and cons of using these medications for weight loss?

There are always two sides of the coin with using medications to treat disease, and weight management is no different.

Some benefits include:

- high effectiveness
- ease of use
- overall good safety and tolerability profile
- extra benefits for blood sugar and heart disease if someone is at risk

On the other hand, concerns include:

- high cost and limited insurance coverage
- prior authorization criteria for the drugs only approved for diabetes, which makes access more difficult and could cause people to lose access if they don't have diabetes
- not everyone responds to treatment
- side effects can happen, including GI symptoms, pancreatitis, and gallbladder issues
- need for ongoing treatment, as many patients will regain weight if treatment is stopped
- lack of evidence if someone does not have overweight or obesity
- may worsen body dysphoria or eating disorders for people who are already suffering from them

Bottom line

We are entering a new age of weight management as the established perception of overweight and obesity is shifting from a "moral failure" to a chronic health condition. Highly effective treatment options, namely the medications described above, help make it easier to think of overweight and obesity this way. However, there are still plenty of concerns and considerations before these drugs can be used for weight loss routinely. Cost, access, and the supply chain all play a role in patients getting successful treatment to help lower weight, improve quality of life, and decrease the burden of weight-related conditions such as diabetes, high blood pressure, high cholesterol, heart disease, arthritis, and others. Hopefully with time, data, and public support, these treatments will be more readily available to those who are appropriate to treat with them. Until then, it is important to understand the nuance involved in the different drugs available and who has access to them in different situations.

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