

The Increasing Availability and Risk of Injectable Skinniness

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STORY AT-A-GLANCE

- > Semaglutide, known by the brand names Ozempic, Wegovy, Rybelsus and others, is the latest weight-loss craze to hit Hollywood and beyond
- > The prescription drug, which is administered via a weekly injection, is intended to treat Type 2 diabetes, but it's widely used off-label for weight loss
- > Semaglutide is a glucagon-like peptide 1 (GLP-1) receptor agonist; along with affecting insulin, GLP-1 may influence the nervous system, leading to an appetite-reducing response
- > One year after stopping semaglutide, participants regained two-thirds of their prior weight loss
- > A pharmacovigilance study found an association between GLP-1RAs, including semaglutide, and pancreatic cancer

Semaglutide, known by the brand names Ozempic, Wegovy, Rybelsus and others, is the latest weight-loss craze to hit Hollywood and beyond. The prescription drug, which is administered via a weekly injection, is intended to treat Type 2 diabetes, but it's widely used off-label for weight loss.

For those who want to dive deeper into the science, the AMA video by Peter Attia does a nice job of providing the background of this very popular drug. You should be aware, however, that although Peter is a brilliant physician, he is stuck in the conventional paradigm and we disagree on many aspects of health and longevity.

A 2021 study funded by Novo Nordisk, the drug's maker, found using semaglutide once a week led to a 14.9% reduction in body weight among adults with obesity. There's been such a rush on the drugs that the U.S. Food and Drug Administration lists both Ozempic and Wegovy as "currently in shortage." This, despite the drug's hefty price tag of about \$1,400 a month.

But quick fixes are rarely the answer when it comes to better health, especially in the case of complex issues like maintaining a healthy weight, which has mental, emotional and physical elements.

A weight loss drug, even if it's seemingly effective, cannot address the underlying emotional drivers that may lead to overeating, for instance, and it won't save your health if you continue to eat an unhealthy diet — no matter how thin your outward appearance may be.

By relying on medication to get thin, you rob your body of the chance to balance its weight naturally, in the way biologically intended, and expose yourself to untold side effects in the process.

Semaglutide Mimics GLP-1 in Your Body, Reducing Appetite

Semaglutide is a glucagon-like peptide 1 receptor agonists (GLP-1RAs). As a peptide hormone, GLP-1 is, among other things, part of a group of incretin hormones, which are released when you eat to regulate insulin, along with many other functions.³

Along with affecting insulin, GLP-1 may influence the nervous system, leading to an appetite-reducing response. Many taking semaglutide report that the drug makes them feel full, faster, so they're satisfied eating smaller amounts. According to a scientist writing under the name Modern Discontent on Substack:⁴

"Although this effect of increasing insulin excretion may help aid diabetics, what's curious about Semaglutide is its strange association with weight loss, with many people reporting a lack of appetite when on GLP-1RAs. Given that incretin hormones are released when consuming food, it's possible that a

signaling pathway involving incretin hormones may also be utilized to signal fullness.

Indeed, it appears that the brain and CNS also contain GLP-1 receptors, which also respond to the GLP-1 released after eating. It also appears that some aspects of the nervous system may also produce GLP-1 themselves

... In this case, the feedback mechanism from GLP-1 produces an **anorectic** (appetite-reducing) response which can decrease food intake. Thus, there's an artificially induced effect of fullness produced by these GLP-1RAs."

In short, Dr. Robert Kushner of Northwestern University, who serves on Novo Nordisk's advisory board, told NPR, "This hormone is telling your brain, I'm full, I don't need to eat anymore ... What the pharmaceutical companies have done is taken this hormone that is naturally occurring and restructured it into a drug." 5

Weight Comes Right Back When Drug Is Stopped

Considering semaglutide does not address the underlying drivers of weight gain and obesity, it's not surprising that many people gain back the weight they lost as soon as they stop taking the drug. When one woman from South Holland, Illinois, who lost 60 pounds on Wegovy, could no longer access it due to an insurance change, she gained back 20 pounds within a few months.⁶

The so-called "Ozempic rebound" has been making headlines in the media, after a study found that one year after stopping semaglutide, participants regained two-thirds of their prior weight loss, and most of the changes in cardiometabolic variables also reverted back to pretreatment levels.

This, the researchers said, highlights "the importance of maintaining long-term pharmacological treatment for weight management in people with obesity," which, as Modern Discontent pointed out, is a "rather concerning remark to suggest that one solution to obesity is to continuously provide a pharmaceutical." ¹⁰

"Considering that GLP-1RAs appear to have actual neurological effects (i.e. blocking hunger and mimicking satiation), there's a serious mental component that's worth considering with respect to these medications and their influences on the relationship people have with food.

That is, the loss of a "off" button in eating means that weight gain is possibly an inevitable result if one did not get behavioral and lifestyle factors under full control (i.e. they return to the old habits that contributed to their weight gain).

This is a consequence of sacrificing long-term lifestyle changes that will lead to better health for quick fixes where the main goal is just to lose weight. It's also a growing sign of how out-of-touch many people are with what they put in their bodies- both food-wise and pharmaceutical-wise."¹¹

AAP Pushes Weight Loss Drugs for Children

Even children are falling victim to the mentality that medications are the answer for weight loss. The American Academy of Pediatrics (AAP) updated its guidance on childhood obesity, giving a wholehearted endorsement for weight loss drugs and surgery in children as young as 12 and 13, respectively.

The AAP guidance recommends "comprehensive treatment," which includes nutrition support, physical activity, behavioral therapy, medications and metabolic and bariatric surgery.

"There is no evidence to support either watchful waiting or unnecessary delay of appropriate treatment of children with obesity," the guidance explains, instead setting the tone that early and aggressive drug and surgical treatment is warranted.¹²

Coauthor Dr. Sandra Hassink, medical director for the AAP Institute for Healthy Childhood Weight, told The Associated Press that the guidelines are meant to change the view that obesity is "a personal problem, maybe a failure of the person's diligence. This is not different than you have asthma and now we have an inhaler for you."¹³ According to the guideline's executive summary:¹⁴

"Obesity has long been stigmatized as a reversible consequence of personal choices but has, in reality, complex genetic, physiologic, socioeconomic, and environmental contributors.

An increased understanding of the impact of social determinants of health (SDoHs) on the chronic disease of obesity — along with heightened appreciation of the impact of the chronicity and severity of obesity-related comorbidities — has enabled broader and deeper understanding of the complexity of both obesity risk and treatment."

Further, the guidelines specifically state:15

- Pediatricians and other primary health care providers should offer adolescents 12
 years and older with obesity (BMI ≥95th percentile) weight loss pharmacotherapy ...
 as an adjunct to health behavior and lifestyle treatment
- Pediatricians and other primary health care providers should offer referral for adolescents 13 years and older with severe obesity (BMI ≥120% of the 95th percentile for age and sex) for evaluation for metabolic and bariatric surgery

In December 2022, the FDA approved the use of semaglutide to treat obesity in children ages 12 and over.¹⁶ The approval came following a 68-week study of 12- to 18-year-olds, which found those taking the drug had a 16.1% decrease in BMI compared to 0.6% in the placebo group.¹⁷

Concern Over Cancer Risks, Long-Term Effects

The long-term risks of semaglutide are unknown. The most commonly reported side effects are gastrointestinal in nature, including nausea and vomiting, but concerns of pancreatitis, pancreatic cancer and retinopathy complications, including hemorrhage and blindness, have been reported.¹⁸

The cancer risks are a red flag, with one patient in the Sustain 5 trial developing metastatic pancreatic carcinoma about 65 days post-treatment.¹⁹ A pharmacovigilance

study using the FDA Adverse Events Reporting System also looked into "increasing data on the potential risk of pancreatic carcinoma associated" with GLP-1Ras, including semaglutide, finding a clear association.²⁰

"Based on this pharmacovigilance study, GLP-1RAs, except albiglutide, are associated with pancreatic carcinoma," the researchers noted, adding, "Based on the bibliometric investigation, cAMP/protein-kinase, Ca²⁺ channel, endoplasmic-reticulum stress, and oxidative stress are potential pathogenesis of pancreatic carcinoma resulting from GLP-1RAs."²¹

Already, the drug carries a black box warning because rodent studies found semaglutide causes thyroid C-cell tumors "at clinically relevant exposures."²²

Will Injectable Skinniness Ruin Exercise?

Another repercussion of quick weight loss via injection might be its influence on other healthy lifestyle parameters, like exercise. While exercise is about far more than weight loss — just one session leads to changes in a remarkable 9,815 molecules in your blood²³ — there are still many people who view it only as a tool to shed fat. "In the age of Ozempic, what's the point of working out?" posits one article in The Atlantic.²⁴

The writer, Xochitl Gonzalez, was initially among those who only worked up a sweat to see the numbers fall on her scale, but she eventually came to the conclusion that, even more importantly, exercise was critical to her mental health and happiness.

Will a new generation of people, content to shed pounds with a weekly injection, give up exercise and the countless beneficial "side effects" that go along with it? Gonzalez writes:²⁵

"[I]n the Age of Ozempic, the idea that we work out to get thin may be even more dangerous than ever, no matter your size. Ozempic now offers injectable skinniness to the same moneyed Alo- and Lululemon-wearing men and women who have been filling up fitness classes and gyms for years, all of them there to chase the elusive goal of "thinner," or, if they've caught it, to keep that slim frame in their clutches.

But at the same time, all of them have been benefiting from the side effects of endorphins and rising heart rates, the pleasure of experiencing the vitality of their own blood-pumping bodies.

If they can now stay skinny with just an injection and a few picked-over meals, will they abandon fitness? What is a life where you don't need to move your body and you don't need to eat, but you know you look good in designer clothes? What is real living if you are doing it for the 'gram?"

Keys to Maintain a Healthy Weight Naturally

Using medications to lose weight puts your health and risk and destines you to a lifetime of drug-taking, since you're likely to regain the weight once you stop taking the drugs. To lose weight naturally, dietary changes are essential. Collectively, consuming too much linoleic acid (LA) is the primary factor driving the overweight and obesity epidemics.

LA is the most common omega-6 fat found in seed oils like soybean, cottonseed, sunflower, rapeseed (canola), corn and safflower.²⁶ Reducing your intake of seed oils and all processed foods, while increasing your intake of healthy fats is a powerful way to support a healthy weight.

Ideally, consider cutting LA down to below 7 grams per day, which is close to what our ancestors used to get before chronic health conditions, including obesity, diabetes, heart disease and cancer, became widespread.

To do so, you'll need to avoid nearly all ultraprocessed foods, fast foods and restaurant foods, as virtually all of them contain seed oils. The easiest way to do this is to prepare the majority of your food at home so you know what you are eating.

Then there's the timing of your food, or time restricted eating (TRE) — another important factor in helping to optimize weight. Our ancient ancestors did not have access to food 24/7, so our genetics are optimized to having food at variable intervals, not every few hours. When you eat every few hours for months, years or decades, never missing a meal, your body forgets how to burn fat as a fuel.

In most cases, you can lose weight by eating real food — not ultraprocessed ones — and embracing TRE by limiting food intake to a certain number of hours per day.²⁷ Engaging in nonexercise movement throughout the day, and getting regular exercise, will provide further benefits, with no medications required and radically improving your entire health as a side effect.

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