

# **Popular Skinny Pills Linked to Digestive Problems**

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October 25, 2023

### **STORY AT-A-GLANCE**

- > A 2023 study in JAMA revealed glucagon-like peptide-1 (GLP-1) receptor agonist drugs prescribed for diabetes and weight loss increase your risk for pancreatitis, gastroparesis and bowel obstruction
- > These drugs include the two most popular GLP-1 receptor agonists semaglutide (Ozempic) and liraglutide (Saxenda and Victoza). They are part of the rising demand for prescription weight loss medication that skyrocketed by 2,082% from 2019 to 2022
- > GLP-1 receptor agonists mimic the body's natural hormone, trigger the slowing of the gastrointestinal tract and delay stomach emptying so the user feels full longer
- > Data show that while participants in the studies did lose weight, once the \$1,000 per month medication was withdrawn, most participants regained two-thirds of the weight lost
- > Using weight loss drugs could lead to permanent, debilitating health problems and it's likely you will regain the weight when you stop. Better solutions address the fundamental reason people gain weight — insulin resistance secondary to mitochondrial dysfunction from excess reductive stress

An October 2023 study<sup>1</sup> in JAMA revealed that glucagon-like peptide-1 (GLP-1) receptor agonists prescribed for diabetes and weight loss increase your risk for gastrointestinal disorders, including pancreatitis, gastroparesis and bowel obstruction. The demand for weight loss products is estimated to grow at a record compound annual growth rate (CAGR) of 9.7% from 2023 to 2032.<sup>2</sup> According to consulting firm Custom Market Insights, the value of the U.S. weight loss market in 2022 was \$135.7 billion and is forecasted to reach \$305.3 billion by 2030. Another estimate<sup>3</sup> projects the U.S. weight loss market will reach \$405.4 billion by 2030.

The demand for prescription weight loss medications has also skyrocketed, with prescriptions rising 2,082% from 2019 to 2022.<sup>4</sup> One of the popular GLP-1 receptor agonists is semaglutide, more commonly known as Ozempic. Semaglutide is sold under two names. As Ozempic, it is a diabetes drug and as Wegovy it is sold in higher doses as a weight loss drug.

The company boasts a weight loss of 14.9% in adults with obesity,<sup>5</sup> but this comes at a steep financial and physical cost. The drug costs more than \$1,000 each month,<sup>6</sup> and can lead to debilitating side effects, including stomach paralysis and pancreatitis. Before examining the results of the JAMA study, let's take a minute to learn how GLP-1 drugs work.

### **How GLP-1 Drugs Work**

GLP-1 agonists are a class of medication prescribed to manage blood sugar levels and more recently, to treat obesity.<sup>7</sup> Most are injectable medications and the first in this class was approved by the FDA in 2005. Your body naturally makes the GLP-1 hormone in the small intestines, which slows digestion, increases satiety, blocks the secretion of glucagon and triggers the pancreas to release insulin.

GLP-1 agonists mimic the hormone, so the medication binds to the receptor and triggers these same effects. Delayed gastric emptying is the hallmark of gastroparesis, in which there is a delay of food moving from the stomach to the small intestines without a blockage.<sup>8</sup> Symptoms include feeling full after starting a meal and feeling full long after eating a meal. The most common cause of gastroparesis is diabetes. In the Wegovy clinical trials,<sup>9</sup> 44% of the participants taking the drug experienced nausea, 24% vomited and 20% had abdominal pain. Mayo Clinic researchers also looked at the effects of liraglutide, another GLP-1 receptor agonist, in adults with obesity. They found the drug's weight loss effects were associated with "delay in gastric emptying of solids,"<sup>10</sup> and the longer food sat in the stomach, the greater the weight loss effects became.

In a placebo group, the stomach typically emptied within four minutes but after five weeks on the drug, the median gastric emptying time was 70 minutes, and up to 151 minutes in some participants. By 16 weeks, the gastric emptying time had decreased to 30.5 minutes, which was still longer than the placebo group. By dramatically slowing digestion, participants felt full longer and didn't eat as much. But that's not the only drug effect.

# Is Weight Loss Worth Pancreatitis, Gastroparesis and Ileus?

Injected GLP-1 agonists amplify the effect of the body's GLP-1 and slow digestion, which helps keep people feeling full longer.<sup>11</sup> In the featured study<sup>12</sup> researchers sought to evaluate the risk of gastrointestinal adverse events in GLP-1 agonists used in the treatment of diabetes and off label for weight loss.

The researchers acknowledged that past studies had found those with diabetes had an underlying increased risk for pancreatitis, bowel obstruction and gastroparesis. They took a random sample of patients from 2006 to 2020 using a health claims database that captures 93% of outpatient prescriptions and ICD-9 and ICD-10 diagnosis codes. They chose participants who were new users of one of the two GLP-1 agonists semaglutide or liraglutide.

They compared the results against bupropion-naltrexone. Within the cohort they had 4,144 participants taking liraglutide, 613 taking semaglutide and 654 taking bupropion-naltrexone. They found those taking GLP-1 agonists had an increased risk of pancreatitis, bowel obstruction and gastroparesis, but not biliary disease. When patients with hyperlipidemia were removed from the analysis it did not change the results.

Science Alert notes that while the increase in risk is relatively small, considering the rising number of people using the medications, it still represents a fourfold increase in the number of people who are at risk for developing these health conditions.

"When you have millions of people using these drugs, you know, a 1% risk still translates to many people who may experience these events," said lead study author Mahyar Etminan, Pharm.D, an epidemiologist at the University of British Columbia, speaking to CNN.<sup>13</sup>

As Forbes reported,<sup>14</sup> on September 22, 2023, just one month before the featured study was published, the FDA added "ileus" to the list of possible adverse events on the Ozempic label. Two other GLP-1 receptor agonists, Mounjaro and Wegovy, already had warnings about ileus, which is a health condition that can result in an intestinal blockage.

It's not surprising that if GLP-1 agonists slow gastric emptying speed, they would also slow the movement in the small intestines, thus increasing the risk of ileus and intestinal blockage.

# **GLP-1 Receptor Agonists Trigger Intestinal Changes**

In a 2023 letter to the editor of Acta Pharmaceutica,<sup>15</sup> the writers recount the results of a study in diabetic patients who used GLP-1 receptor agonists and found a 3.5-fold increase in the rate of intestinal obstruction in a study of 25,617 people. The drugs also increased the length and weight of the small intestines in animal studies.

In humans, they may increase intestinal length and villus height. The villi are the hair-like projections inside the small intestines that help absorb nutrients. Researchers explain this can seriously affect intestinal function, increasing the obstruction risk because "... the small intestine may become as inelastic and fibrotic as a loose spring, leading to long-term upper intestinal obstruction ..."

To date, these changes have not been measured in the human gut, likely because it's difficult to measure the length of the small intestines. The delay in stomach emptying

led the American Society of Anesthesiologists to release a warning for those taking GLP-1 drugs before elective surgery.<sup>16</sup> They suggest patients stop all GLP-1 receptor agonists to reduce the risk of complications associated with regurgitating food even if you fasted appropriately.

The ASA recommends not taking the medication for one day for those who take it daily to one week for those who take a weekly injection, and delaying the procedure if symptoms of delayed gastric emptying are present. The likelihood of having a full stomach and the associated risk with anesthesia is so high that the ASA suggests using ultrasound to evaluate the stomach contents before surgery if the patient did not withhold the drug.

# Long-Term Results Are Not What You Might Expect

It can take a few months to reach your personalized target dose while managing the side effects of the drug. In one New England Journal of Medicine study,<sup>17</sup> researchers administered 2.4 mg of semaglutide in a double-blind trial involving 1,961 adults with a body mass index of 30 or greater. The change in body weight from baseline at 68 weeks was a loss of 14.9% in the treatment group and 2.4% body weight loss in the placebo group.

In a second study<sup>18</sup> published in Nature Medicine, a cohort of adults with obesity or overweight and one related comorbidity, were administered 2.4 mg of semaglutide subcutaneously for 104 weeks. In that time, the intervention group lost 15.2% of their body weight versus 2.6% body weight loss in those taking a placebo.

While these results seem encouraging, it's important to note that the pharmaceutical company designed semaglutide as a chronic-use drug. In other words, it's meant to be used regularly over a long period. A study<sup>19</sup> funded by Novo Nordisk found that one year after withdrawing the drug, participants regained two-thirds of the weight lost and the researchers concluded that "ongoing treatment is required to maintain improvements in weight and health."

Most studies also recorded significant side effects with short-term treatment<sup>20</sup> that caused participants to withdraw from the studies.<sup>21</sup> Serious and common side effects of semaglutide<sup>22</sup> include anxiety, confusion, depression, trouble breathing, nightmares, seizures and slurred speech.

# Is There a Natural Option for 'Skinny Injections?'

In the Energy Balance Podcast above, independent health researchers Jay Feldman and Mike Fave explain why eating too much and exercising too little is not the reason for weight gain. Jay is one of the best teachers of the Bioenergetic view of health. I would strongly encourage you to listen to his YouTube channel, but watch the oldest ones first so you can get grounded in the basics.

It is my strong belief that we will never see the "miracle cure" drugs for weight loss in our lifetime. Using drugs to lose weight could lead to permanent, debilitating health problems and it's likely you'll regain the weight if you ever stop taking them, as was demonstrated by the pharmaceutical company selling Wegovy and Ozempic.

There are currently better solutions to address the fundamental reason people gain weight — insulin resistance secondary to mitochondrial dysfunction from excess reductive stress. Excess linoleic acid (LA) from seed oils is the primary cause of mitochondrial reductive stress. Some of the top strategies to lose weight and improve your health include:

 Reduce your intake of seed oils while increasing healthy fats — Consuming too much LA is the primary factor driving the overweight and obesity epidemics. LA is a type of omega-6 fat found in seed oils like soybean, cottonseed, sunflower, rapeseed (canola), corn and safflower.

Consider cutting LA down to below 5 grams per day, which is close to what our ancestors used to consume before chronic health conditions, including obesity, became widespread. The amount is better defined as a percentage of daily calories.

LA should be less than 2% of your daily calories. You can track this by carefully entering your food data into Cronometer.

- Avoid nearly all ultraprocessed foods, fast foods and restaurant foods Virtually all contain seed oils. The easiest way to do this is to prepare most of your food at home so you know what you are eating.
- Use time-restricted eating (TRE) Our 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, your body forgets how to burn fat as fuel. Most people who practice TRE limit the time they consume food to eight to 10 hours or less on most days of each week.
- Consider berberine to help regulate blood sugar and insulin sensitivity As I have reported before, berberine is called "nature's Ozempic" and is known to help prevent diarrhea, lower the risk of leaky gut, nourish beneficial microbes and improve symptoms of fatty liver disease.

Other beneficial effects outside the gastrointestinal tract include easing symptoms of anxiety and depression, improving symptoms of PTSD in an animal model and easing symptoms of opioid withdrawal.

### **Sources and References**

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