


# A New Concern About Weight Loss Drugs: What if They Work Too Well?

Some patients in a clinical trial of one new drug lost so much weight that they became concerned and dropped out.

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By Dani Blum

Feb. 18, 2026 Updated 9:18 a.m. ET

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Scientists raced to make drugs that help people lose as much weight as possible. Now, they're pumping the brakes.

Recent top-line results from a recent trial on retatrutide, a compound that Eli Lilly is developing, found that people with obesity and knee osteoarthritis lost an average of 28.7 percent of their body weight after 68 weeks on the highest dose. Currently available weight-loss drugs have helped people lose around 20 percent of their body weight over the same time period.

Between 12 and 18 percent of participants dropped out of the trial because of side effects, a higher percentage than is typical in trials of existing weight loss drugs. The company said that at least some of those people dropped out because they thought they were losing too much weight, alarming some outside researchers. Eli Lilly sponsored the trial, which included 445 participants. The full data has not been published yet, so it's difficult to make definitive conclusions about why patients dropped out.

"We're not trying to force a specific magnitude of weight loss in every patient," said Dr. David Hyman, the chief medical officer at Eli Lilly. He added that retatrutide will be aimed at patients who need to lose more weight than they could on other medications.

“We’re not of the belief that the most potent weight loss medicine is required for everybody, or that that’s even the goal,” he said.

It’s hard to know what, exactly, counts as too much weight loss. Some people on GLP-1s worry that they just don’t look right. Other patients and doctors are concerned that eating so little is unhealthy. In other cases, there’s a risk that these medications could fuel disordered eating, experts said.

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Researchers at the companies that develop these medications are paying close attention to those concerns.

“We have to use the dose that the patient needs,” said Dr. Ania Jastreboff, director of the Yale Obesity Research Center and a leading researcher who has studied retatrutide for Eli Lilly. The goal, she said, is to get patients on the lowest dose that works. “The underlying question is needing to approach and treat obesity as we would any other chronic disease,” Dr. Jastreboff said.

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Novo Nordisk, the company that makes Ozempic and Wegovy, has said it has changed its approach. In a late-stage trial of a new compound called CagriSema, which appears to be about as equally effective as some other injectable obesity drugs currently on the market, the company used a flexible dosing schedule. That means that if participants could not tolerate the side effects, or a lower dose of the drug was working well, they could stick with the lesser dose. The company asked the Food and Drug Administration to approve CagriSema in December and expects a greenlight later this year.

Maureen Chomko is a diabetes care and education specialist in Seattle who works with patients who have diabetes and take drugs like Ozempic. When people are losing too

much weight, she said, “we’re having a good hard look at what this person is eating, why they aren’t eating.” Patients can feel so nauseated on the drugs, she said, that when they do manage to eat, they’re not reaching for a kale salad with salmon — they’re trying to hold down a handful of crackers. She said she worries about people becoming malnourished and dehydrated on these medicines and urges patients to set alarms to remind themselves to eat.

Ms. Chomko is working with the biopharmaceutical company Amgen on clinical trials for MariTide, a new monthly weight loss compound that is in development. She is helping train the dietitians who are involved with the studies, working to ensure participants get enough vitamin D, calcium, fiber and protein, nutrients that she frequently sees people on these medications failing to get in sufficient amounts.

Ms. Chomko said excess weight loss was “a visible sign that these meds have pushed someone too far.”

“But I think what I’m more concerned about is the invisible,” she added.

Doctors are trying to figure out how to advise patients who seem to be losing too much weight. Dr. Janice Jin Hwang, the division chief of endocrinology and metabolism at the University of North Carolina School of Medicine, frequently sees patients who have hit what she called their “metabolic targets” on these medicines: Their blood sugar has fallen, their cardiovascular metrics have stabilized and they have reached their target weight. But then they want to lose even more.

“There are more nuanced discussions now about, how much weight does a person need to lose?” she said. And there is no clear pathway for doctors to ensure patients lose a Goldilocks amount of weight: not too much, not too little. She often ends up embarking on a kind of trial and error, seeing if patients can maintain their progress on a lower maintenance dose, with the understanding that they will almost certainly need to stay on the drugs for the rest of their lives to do so.

Dr. Sahib S. Khalsa, a psychiatrist at the University of California at Los Angeles Health, coauthored a paper in 2024 about these medications titled: “Highway to the Danger Zone?” In it, the authors warn that people who take these drugs need to be strictly monitored to ensure that they eat and hydrate sufficiently and do not lose too much weight. The paper also notes that the medications are particularly risky for people with histories of disordered eating.

Since that paper was published, Dr. Khalsa said he has only grown more concerned.

Dr. Andrew Kraftson, a clinical associate professor at the University of Michigan Medical

School, said that he had to stop a patient from continuing on the medications, because the person wanted to keep losing weight, even when there was no clear medical benefit to doing so.

“We have to recognize that society has brainwashed us all to certain beauty standards that are not always in alignment with health standards,” Dr. Kraftson said. “And so just because someone can starve themselves to get down to a lower weight doesn’t mean that we should make that easier by giving them an injection to promote anorexia.”

**Dani Blum** is a health reporter for The Times.