TuSalud

The New Weight-Loss Drugs and Cancer

What patients and doctors need to know when it comes to popular new medications like Wegovy and Zepbound.

April 4, 2024 By Fred Hutch News Service and Diane Mapes

Much has been written about the bumper crop of weight-loss drugs approved in the U.S. over the last several years.

Advocates of the new pills and injections say they'll help you attain your dream weight without even trying. Detractors warn there's a price: gastrointestinal issues, possible bowel obstructions and a hollowed, wrinkled "Ozempic face." And then there are all those YouTube videos claiming the stuff is made from lizard venom.

Where is the truth in all of this?

Obesity drives a number of different cancers, so it makes sense that both patients dealing with cancer — and the clinicians and researchers trying to kick it to the curb — are curious whether weight-loss drugs have a role in cancer prevention.

Shedding extra pounds could help patients cut back on their risk for not just cancer recurrence, but also diabetes, cardiovascular disease and other conditions driven by excess weight and the inflammation it causes. But there is much to consider when it comes to using the new semaglutide drugs — and that's not even factoring in the stiff price and daunting side effects.

What's the lowdown for those dealing with cancer? Are these new drugs a boon, a bust or just a big old can of worms? We talked to a host of stakeholders in the cancer community — patients, clinicians, psychologists, researchers, dietitians and more — to help you navigate the latest wave in the weight-loss world.

Cancer claims – good, bad and fuzzy

There are thyroid cancer concerns associated with semaglutides, and as a result, the FDA has boxed warnings on these products.

Ozempic, for instance, warns of "possible thyroid tumors, including cancer" and specifically

advises those at risk for medullary thyroid carcinoma or multiple endocrine neoplastic syndrome type 2 to avoid these drugs.

Animal studies have shown a connection found between semaglutides and thyroid cancer; people studies, not so much.

So if they're not causing cancers, are these new drugs preventing them? After all, obesity is linked to several different cancers. If people lose weight, will they cut their risk?

"The holy grail has always been getting a medication to treat obesity," said Fred Hutch Cancer Center obesity researcher Anne McTiernan, MD, PhD. "There are at least 13 types of cancer related to obesity including colorectal cancer, post-menopausal breast cancer, endometrial cancer, liver cancer, even some of the lymphomas and leukemias."

McTiernan said observational studies show a clear connection between weight loss and reduced cancer risk, but clinical trials, the gold standard for research, haven't yet. This is primarily because none have been large enough or gone on long enough to get reliable results.

"There have been trials focused on these medications' effects on diabetes and cardiovascular disease treatment, but no trials have tested their effects on cancer risk," she said, adding it's only a matter of time before someone studies GLP-1 medications and cancer prevention. "Usually many years' follow-up of large numbers of patients are needed to see cancer effects of a carcinogen or cancer-preventing intervention like a pill."

But there are intriguing data regarding semaglutides' role in prevention, including a large study in JAMA Oncology that found GLP-1 receptor agonists did reduce the risk of colorectal cancer. Tested on patients with and without extra weight, the drug was especially helpful in reducing colon cancer risk in those who were obese and overweight, "suggesting a potential protective effect against colorectal cancer partially mediated by weight loss and other mechanisms not related to weight loss."

A person's immune system also benefits, according to a very small study that found semaglutides helped increase the function of so-called NK, or natural killer cells, which squash cancer cells before they can grow into tumors.

Fred Hutch/UW Medicine gastroenterologist and clinical researcher Rachel Issaka, MD, MAS, said it's still early days, but the new drugs might be a boon for cancer prevention.

"Given the association between obesity and colorectal cancer, it is plausible that GLP-1 mediated weight loss could reduce an individual's risk of colorectal cancer," said Issaka, who holds the Kathryn Surace-Smith Endowed Chair in Health Equity Research. "The current data does not support using GLP-1 agents as a colorectal cancer prevention strategy, but future longer-term studies might change this."

"Everybody was happy — except my GI tract"

Vicki Webb Pouncey, a 58-year-old breast cancer patient from Melbourne, Florida, tried three of the drugs over the last few years, under the supervision of both her nurse practitioner (who discovered Pouncey was insulin resistant) and her oncologist, who worried her extra weight might drive a recurrence.

She first tried the low-dose pill Rybelsis, but after several weeks had zero results. So she tried Wegovy using a discount coupon for a six-month supply.

“On the Wegovy, I lost 40 pounds right away and my numbers all started to improve,” she said. “Cholesterol, blood sugar, insulin resistance — that all looked better. But then the coupon ran out and I couldn’t get any more so I went back on the Rybelsis.”

Again, her weight loss stalled. So her providers suggested she try Ozempic. Immediately, pounds started to come off again.

“I lost weight and my labs looked great,” she said. “Everybody was happy — except my GI tract.”

The drugs can have considerable side effects. Ozempic lists the most common as nausea, diarrhea, abdominal pain, vomiting and constipation. Zepbound lists the same plus indigestion, injection site reactions, fatigue, allergic reactions, belching, hair loss and heartburn. It also mentions the potential for kidney failure; gallbladder problems; pancreatitis; low blood sugar; changes in vision and depression.

At first, Pouncey only had nausea and diarrhea a few days after her weekly shot; then it started happening more often.

The drug “absolutely” diminished her food cravings and her sweet tooth, she said, and she felt healthier, at least for a while. But Ozempic may have been too effective.

“There were days when I had to make myself eat,” she said. “At one point, I think I became malnourished because of all the nausea and diarrhea. But my lab numbers were beautiful so I stayed on it.”

After several months, though, the GI issues became a daily ordeal and she started to have pain on her right side. Now, there were only “good hours, not good days,” she said.

She stopped the Ozempic and went to her doctor about the pain. He ordered a CT scan, thinking she’d developed pancreatitis, one of the noted side effects. Instead, the CT scan found metastatic breast cancer in her liver, which led to more scans and more tumors.

The scans also detected nodules on her thyroid, which have yet to be biopsied. The metastatic breast cancer treatment is her primary concern, she said.

She absolutely does not attribute her metastatic recurrence to the weight-loss drugs.

“I understand the difference between correlation and causation,” she said. “The thyroid nodules are the only thing I would associate with it. And it lists that in the risk factors on the label.”

“Even with the all the suffering,” Pouncey said the drugs were beneficial. All told, she lost 80 pounds; her cholesterol, insulin resistance and blood sugar improved dramatically and she was even free of the joint pain caused by her anti-hormone drugs.

“Once I got rid of processed sugar and carbs, my joint pain almost resolved itself,” she said. “And losing the weight took the pressure off my knees.”

Lifestyle change still necessary

But Pouncey did not like that she became malnourished and worries someone with body dysmorphia might “try and achieve perfection” and cause real self-harm.

Fred Hutch psychologist Jonathan Bricker, PhD, said behavior change is the real key to weight loss, not drugs. Without that, people will put the weight right back on when they stop using them, just as studies have shown.

“You shouldn’t take them alone, but in combination with a low-calorie, low-fat diet, non-processed food diet along with a program of exercise,” he said, citing a JAMA study that followed 175 semaglutide users for nearly a year and a half. “As an adjunct to that, it does enhance weight loss and improves the durability of weight loss and that’s very encouraging.”

He also expressed concerns about the drug’s infamous GI side effects, which per McTiernan, affected 30-50% of people randomized to the GLP-1 trials.

“Those are important concerns,” Bricker said. “And some of the side effects are very serious, like potential bowel obstruction. People should be monitored if they’re using these.”

Access, fake shots and other surprises

Bricker also pointed out the drugs were not made for people who just want to lose 10 or 15 pounds; shortages have already raised concerns that the popularity of semaglutides will increase health disparities, with the “health haves” getting them while the “have-nots” can’t. Even Lilly put out an ad stating the medications were to help people affected by obesity, not vanity.

“They’re very expensive,” Bricker said. “People without insurance or with minimum insurance can’t pay for it, and Medicare doesn’t pay for it although there’s a push to reduce that restriction. There’s an access issue that is serious.”

Without insurance, the drugs can cost up to $16,000 a year, and people may be on them for years. Currently, the Centers for Medicare & Medicaid Services doesn’t cover weight-loss drugs, but is considering changing that criteria. Meanwhile, drugmakers are going direct to consumers using online telehealth, which has also raised concerns about a lack of in-person monitoring, patient

safety and steep out-of-pocket costs.

Another safety concern: fake shots. In December, the FDA warned consumers that they had seized thousands of counterfeit Ozempic shots found within the supply chain and are currently testing them. And in an unexpected twist, a few women using the drugs have had "surprise babies," even while on birth control pills. Doctors believe the weight loss is helping to boost fertility but warn against taking the drugs specifically for that reason.

What do cancer patients need to know?

Fred Hutch registered dietitian Raymond Palko said there are definitely important considerations for anyone going through cancer treatment.

"You have to first determine the clinical appropriateness of weight loss for a cancer patient," he said. "To best tolerate therapy, we need you nourished."

Patients also need to be strong enough to withstand the side effects of treatment, he said. With the side effects of semaglutides so similar to those of chemo, it might be too much of a double whammy for patients to try both.

"My colleagues in weight management are seeing a lot of patients on GLP-1s with nausea and GI issues," he said. "Some patients are having to force themselves to eat. If it's emetogenic [i.e., it causes vomiting] and they're on a chemotherapy like ACT or R-CHOP, it would be challenging to tolerate both."

Drug-drug interactions can often be a concern for cancer clinicians, but Hannah Linden, MD, FACP, said there are no known contraindications with regard to the GLP-1 agonists.

"These drugs work by a very different pathway than chemotherapy or endocrine or other molecularly targeted agents, so we would not expect there to be an issue," said Linden, the clinical director of Fred Hutch's Breast Cancer Program and holder of the Athena Distinguished Professorship of Breast Cancer Research at UW Medicine. "But if chemo causes side effects and the GLP-1 agonist causes the same side effects, that may be challenging for the patient to endure."

If patients do decide to take weight-loss drugs — or any other drug or supplement during treatment — it's imperative they tell their oncology team. The slowing of digestion may affect the release and the effectiveness of some oral drugs and drug-drug interaction studies involving the new GLP-1 agonists are ongoing.

Patients should also be aware that the drugs need to be completely out of their body before undergoing any kind of surgery.

"People need to stop Ozempic or similar drugs sometimes two weeks prior to surgery," said Fred Hutch's Claire Buchanan, MD, who does breast cancer surgeries. "It can be very unsafe if they

haven't stopped it as they basically have a full stomach [due to slowed-down digestion] and can aspirate when intubated for surgery."

What about after cancer treatment? Some therapies can cause weight gain; ditto for simply being diagnosed with the disease. People eat more thanks to the stress, while exercising less due to diminished stamina.

"When men with prostate cancer go on Lupron [a synthetic hormone used in prostate cancer treatment], they can have massive weight challenges," Palko said. "The same for women after breast cancer treatment. These patients are often put on anti-hormone drugs that cause weight gain. We're doing a lot of work with those populations."

If patients do want to lose weight, Palko said they're usually referred to the UW Medicine Center for Weight Loss. But, he acknowledged, a GLP-1 agonist might be a "helpful little boost" to help survivors shed weight, which could then encourage them to get out and exercise more.

"Prior to diagnosis, many people have active lifestyles," he said. "But then, they lose the time to work out and maybe they get a taxane-based treatment regimen and start getting neuropathy in their feet. There is often a halting of normal baseline habits with cancer."

Traditionally, weight loss is not a top priority for those going through cancer, he said. If anything, patients lose weight during this time.

Pouncey, the patient with metastatic breast cancer, is there right now.

"Gaining weight is not my problem anymore," she said. "It's more important to get food into me now."

SIDEBAR:

Additional Health Effects of Semaglutides

In addition to reducing diabetes and promoting weight loss, the drugs have been associated with other benefits:

- Some taking the drugs have been able to curb other habits like smoking, drinking, compulsive shopping and more. Clinical trials are researching the effect of semaglutide on alcohol use, cocaine addiction, nicotine use, opioid cravings and mental health.

- Additionally, research has shown semaglutides help cut postoperative complications in

overweight patients undergoing hip replacement surgery.

- In a study conducted by Novo Nordisk, Ozempic also cut the risk of kidney disease progression.

- Another study published in the journal Gut found GLP-1 agonists were “promising agents to reduce risk of chronic liver disease progression in patients with diabetes.”

- The FDA approved the inclusion of cardiovascular benefits on the label of Wegovy, based on results of a five-year trial.

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