### In Defense of Diet Drugs

Judith Korner '92GSAS, '93VPS, an expert in the science of obesity at Columbia University Irving Medical Center, weighs the risks and benefits of Ozempic and other medications.

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**The sudden popularity** of weight loss medications has been one of the biggest health stories of the year, and also one of the most controversial. While experts say that drugs like Ozempic, Wegovy, and Zepbound represent a major advance in treating obesity, there are also growing concerns that people looking to lose a few

pounds may use them as a quick fix.

So, who are these medications designed for? And what are the potential health risks and benefits? *Columbia Magazine* recently spoke to endocrinologist Judith Korner '92GSAS, '93VPS, a professor of medicine at Columbia University Irving Medical Center and the director of its Metabolic and Weight Control Center, for answers.

#### First, can you explain how these new drugs work?

Ozempic, which came on the market in 2017, and Wegovy, which was released in 2021, contain a synthetic version of a hormone that is naturally produced in the intestines when you eat. This hormone, GLP-1, sends a signal to your brain indicating you've eaten enough. It announces: "You're full, now! Don't take another bite!" Ozempic was initially developed as a diabetes medication because GLP-1 also tells the pancreas when to make insulin and thus is instrumental in regulating blood sugar. Zepbound, which is the new kid on the block, received FDA approval as a weight-loss medication just this month. It also contains GLP-1, along with another hormone that modulates appetite. By boosting your levels of appetite-controlling hormones, all three drugs reduce your hunger and make you feel satiated after eating less food. They're injected once a week, using a device similar to an insulin pen.

# You've been treating people for obesity at Columbia's Metabolic and Weight Control Center for more than two decades. How has the availability of these drugs influenced your practice?

Having these medications in our toolbox is an absolute game-changer. Other weight loss drugs have been available in the past, but they were either less effective or caused dangerous side effects, including cardiovascular problems, so we'd prescribe them less frequently. The new drugs have an excellent safety profile and are incredibly effective. There are still some open questions, as with any new therapies. For example, we're not sure if their effectiveness may eventually decline after extended use. And there are safety concerns for certain demographics, including elderly people, some of whom may lose muscle mass. But so far, the drugs seem to be extremely successful, overall.

### Who do you recommend them for?

We consider body mass index, or BMI, which is a person's weight adjusted for height, and their overall health. If someone has a BMI of 30 or over, which is the clinical definition of obesity, and a history of unsuccessful attempts to lose weight through non-medical interventions, we consider them a good candidate for a medication. And if their weight already appears to be contributing other health problems, like diabetes, hypertension, high cholesterol, or sleep apnea, we may recommend a drug at a lower BMI of 27 or over. We'll offer the medication as part of a comprehensive package of clinical care that includes individualized dietary and lifestyle advice, counseling, and other supports.

#### What types of outcomes have you seen?

People who take these drugs often lose 15 percent of their body weight, and we have patients in our clinic who have lost 100 pounds or more. As you can imagine, that's a transformative experience, physically and mentally. Most of our patients have been struggling with their weight for years, and some for their whole lives. They've tried every diet imaginable and all sorts of exercise regimens. The majority have managed to lose significant amounts of weight, multiple times over the years, only to regain it and then some. By the time they come to us, many have lost their ability to exercise or even walk around. They feel defeated and hopeless. And then, after going on one of these drugs, the tide shifts. Patients will tell us things like, "For the first time ever, I'm not thinking about food constantly. I'm eating normally and feel like I'm in control of my life." Gradually, as chronic joint pain and fatigue goes away, they regain mobility.

On top of this, losing weight dramatically improves people's long-term health. When excess fat accumulates in the body, it seeps into the liver, pancreas, intestines, heart, and other organs, damaging them. It causes inflammation and increases our risk of cardiovascular disease and certain cancers. Studies show that people who take these drugs may reduce their risk of hearts attacks and strokes by 20 percent.

### What are the potential side effects of the drugs?

The main issues are gastrointestinal side effects, including nausea, vomiting, diarrhea, and constipation, which can be minor or quite severe. In rats, the drugs have been linked to two rare diseases, medullary thyroid carcinoma and multiple endocrine neoplasia, and so people with a family history of these conditions are advised to not take them.

## Some health experts have expressed concerns that people in a healthy weight range are using these drugs to lose that last 10 pounds.

This does seem to be a problem, although it's unclear how widespread. Clearly, people shouldn't be using the medications to drop a few pounds and look great in a bikini. While the drugs do appear to be very safe, it's certainly possible that decades from now we'll discover that these medications have negative long-term health consequences that we haven't anticipated.

I must say, though, that the amount of media attention that's been paid to the potential misuse of these drugs is frustrating to me, because I find that there's often an undercurrent to the public conversation that seems to call into question whether these drugs are truly necessary for *anyone*. Commentators often seem to be implying, "Can't overweight people just eat less? Can't they show more willpower and take better care of themselves?" This ignores the fact that obesity is a chronic disease that often requires medical treatment.

### Your own research has been instrumental in getting obesity recognized as a disease by the medical establishment in recent years.

I'm a molecular biologist by training, and I've always been fascinated by how the body controls appetite. For example, I'm interested in understanding why some people feel satisfied after eating a 400-calorie meal while others may need to consume 800 calories to experience the same feeling of satisfaction. Such differences may be based partly in genetics, which are thought to account for at least 40 percent of a person's risk of obesity. In addition, research by my group and others has shown that excess body fat alters our metabolism and appetite in ways that make losing weight extraordinarily difficult. The point of the new weight-loss drugs is to compensate for metabolic and hormonal irregularities that may be driving a person's obesity.

### If someone loses a lot of weight with the help of one of these drugs, and they subsequently stop taking it, will they keep the weight off?

That's rare, unfortunately. I don't want to categorically say that people can't do that because I think that if someone were to dramatically improve all aspects of their diet and lifestyle while taking the drug and then stick with those changes afterwards, it's possible. But studies have shown that people who stop taking these medications usually regain the weight, even if they're also taking better care of themselves.

## If obesity is a medical condition with genetic roots, why does its prevalence vary dramatically between demographic groups and cultures? Doesn't that suggest it is driven by our behavior?

Of course, our dietary and lifestyle choices, genes, and environment all contribute to obesity. But you're confusing the condition's cause with the fact that it results in a chronic disease state. A colleague once put it this way: "Smoking contributes to lung cancer. But nobody consequently suggests that lung cancer isn't a disease." In our society, people with obesity are stigmatized and blamed for having a disease. Even many physicians fail to appreciate how difficult it is for people lose weight. If they talk to these patients about the prospect of losing weight — and often they avoid the sensitive topic — they'll just say, "Try to lose fifty pounds" without offering much quidance.

### What advice would you give a person searching for a sympathetic provider to assist with weight loss?

Find a doctor who is credentialed by the American Board of Obesity Medicine. I'd also suggest regularly visiting a dietician or nutritionist. Their services are not typically covered by insurance, though, and they can be expensive. An affordable option is keeping a food diary, which promotes mindful eating and is one of the most effective ways to lose weight. There are also smart-phone apps that make monitoring your meals easier.

#### Do medical insurance plans cover weight-loss drugs?

In the past few years, private insurers have begun to cover the new class of weight loss drugs more frequently, but Medicaid and Medicare still do not. This is troubling because obesity rates are highest among disadvantaged populations who rely on those plans.

### What is your research focused on today?

My colleagues and I are studying how the effectiveness of different weight loss interventions, including drugs and bariatric surgery, vary depending on people's genetic profiles and medical histories. The goal is to bring more of a precision medicine approach to the care we provide. Currently, physicians in our field rely too much on trial and error when deciding which interventions are best for particular patients. In the next few years, many more weight loss drugs are going to be

released, targeting different molecular pathways, and we want to help doctors make more informed decisions when prescribing therapies.

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