

Weight loss drugs present more questions than answers, but they could be a key tool in reducing the obesity epidemic

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In the past five years, several new drugs have been brought to market that could lead to a profound, if not revolutionary, change in how health care providers—and the public—view weight loss.



Three drugs in particular—sold under the brand names <u>Wegovy</u>, <u>Ozempic</u> and <u>Mounjaro</u>—have <u>shown remarkable effects</u> on <u>weight</u> loss in clinical trials.

While Wegovy is approved by the Food and Drug Administration for weight loss, the other two medications are only approved as treatment for type 2 diabetes, though they do also contribute to significant weight loss. This has led to increased demand for these drugs, causing a shortage-of-Ozempic and Mounjaro in early 2023 that threatened the availability of these drugs for diabetes patients.

Globally, more than 650 million people are obese, and by 2030, an estimated 1 billion adults will be obese. This makes obesity the most prevalent chronic disease in the world.

As an exercise science scholar, I have spent more than 15 years studying the effects of diet and exercise on the <u>human body</u>, primarily focused on body composition changes such as gaining skeletal muscle or losing body fat, or both. In my lectures, I present data on the detrimental impacts on <u>personal health</u> of being overweight or obese. Then I show that, aside from <u>surgical intervention</u>, the best way to lower body fat is with starting an exercise program and improving dietary habits.

These new drugs have now altered what I teach in the classroom, and as a researcher I believe they raise many questions about the current approach to weight management and health. While these medications hold promise, they are not wonder drugs. In my view, they warrant much more research before they become the basis for a new weight management protocol.

How these drugs work

Ozempic and Mounjaro are FDA-approved for the treatment of type 2



diabetes, which affects more than <u>37 million people</u> in the U.S. On top of that, nearly 100 million people are considered prediabetic, meaning that together over 40% of the U.S. population suffers from an inability to properly manage blood sugar.

Obesity and type 2 diabetes are closely related conditions, so much so that some experts are now calling the <u>two conditions "diabesity."</u> These dire figures are what prompted <u>pharmaceutical companies</u> to search for new weight loss treatments.

Type 2 diabetes is a condition in which your body no longer responds to the <u>hormone insulin</u>, which in healthy people regulates glucose, or sugar, levels in the blood. Prolonged elevated blood sugar, if left untreated, can lead to <u>heart disease</u>, vision loss and even death.

We govy and Ozempic are a class of drug known as a semaglutide. Since people with type 2 diabetes are unable to properly manage blood sugar, injections with this class of drug help the body release the proper amount of insulin after eating by mimicking a naturally occurring hormone called GLP-1.

At the same time, semaglutides also reduce the release of the hormone glucagon, which works opposite of insulin to increase blood sugar. In non-diabetics, these two hormones work together to maintain normal blood sugar levels. But since this mechanism is not functioning properly in diabetics, which leads to high blood sugar, semaglutides help to control blood sugar and also reduce appetite.

For this reason, <u>Ozempic received approval</u> from the FDA in 2017 as a treatment for <u>type 2 diabetes</u>. But during the <u>clinical trials</u> for type 2 diabetes, pharmaceutical companies quickly recognized Ozempic's potential as a weight loss tool.



This led to the release of a new <u>drug</u>, Wegovy, which has a higher dose of semaglutide. A 2021 study showed that once-weekly injections of Wegovy over the course of 68 weeks resulted in about <u>a 15% loss of body weight in adult participants with obesity</u>.

The other novel <u>medication in the news lately</u>, Mounjaro, acts like a semaglutide, stimulating GLP-1, but it also mimics a second hormone called glucose-dependent insulinotropic polypeptide. This dual-hormone action works to not only lower <u>blood sugar</u> levels and increase insulin sensitivity, but also slows the digestive system and decreases appetite.

Staggering results

In early 2021, scientists began analyzing the data from a clinical trial program focused on using semaglutide treatments in people with obesity, which included more than 4,000 patients. Over 80% of participants lost more than 5% of their body weight, with the most common side effects being nausea, diarrhea, vomiting and constipation.

This data on effectiveness and efficacy led the FDA to officially approve Wegovy as a weight loss drug in the summer of 2021. The huge demand that ensued led to the <u>recent shortages of Wegovy</u>, forcing many physicians to look for other options. That's when Ozempic and Mounjaro entered the picture as off-label weight loss medications, even though they are only FDA-approved to treat type 2 diabetes.

In April 2023, the pharmaceutical company Eli Lilly released the results of the second <u>phase 3 clinical trial of Mounjaro</u>. The results were, quite frankly, amazing: Compared to a placebo, the 938 obese or <u>overweight</u> adults with type 2 diabetes lost more than 34 pounds, or roughly 15% of their body weight, with no required fitness and nutrition program.

This most recent study tracked with the first clinical trial of Mounjaro,



published in July 2022, that resulted in more than a 20% reduction in body weight in 2,539 adults. Similar to Wegovy and Ozempic, Mounjaro's most commonly reported side effects are general gastrointestinal distress such as nausea, vomiting and diarrhea.

Costs of obesity

The latest data from the National Institutes of Health estimates that more than 40% of U.S. adults are obese and another 30% are overweight, meaning that 7 in 10 adults need to lose weight. The World Health Organization estimates that, based on a 2017 global burden of disease study, more than 4 million people across the world are dying every year due to being overweight or obese, a trend that is also growing rapidly in children.

The WHO <u>defines obesity</u> as when an adult or child has a body mass index, or BMI, over 30; a BMI over 25 is considered overweight. In children, <u>doctors often rely on percentiles</u>, rather than an absolute number.

BMI is calculated by taking a person's <u>weight and dividing it by the</u> <u>square of their height</u>—a technique that <u>isn't the most accurate</u> for assessing body composition. But it is valuable for classifying millions of people where more accurate techniques such as <u>skinfold measurements</u> are not feasible.

Being overweight or obese greatly increases risks for <u>other significant</u> <u>health complications</u>, such as heart disease, type 2 diabetes, hypertension, osteoarthritis, stroke and asthma. In fact, obesity is responsible for <u>nearly half of the total cost of chronic disease</u> in the U.S. Studies show that obesity also leads to a <u>decrease in life expectancy</u>.

Recent data suggests that the direct medical costs of a person being



obese in the U.S. <u>is more than US\$2,500 annually</u>. And researchers estimate that the total cost of chronic diseases due to obesity in the U.S. <u>is more than \$1.7 trillion</u> annually, which is 9.3% of the country's gross domestic product. Predictions show the annual cost of obesity will be <u>more than \$4.3 trillion worldwide by 2030</u>.

Current <u>list prices for Mounjaro</u> and <u>Ozempic</u> top \$1,000 per month for off-label use, meaning for weight loss and not for type 2 diabetes. In this scenario, which is becoming more common, insurance companies are less likely to cover the medication.

Since most Americans can't afford these drugs, it's reasonable to ask whether more should be done to decrease costs and increase access.

The age-old benefits of exercise and a healthy diet

Still, these <u>new drugs</u> that can aid in weight loss present a dilemma for doctors and other <u>health care providers</u>: Where do they fit in with the decadeslong gospel of healthy eating and increasing physical activity?

Traditionally the most effective mechanism for weight loss <u>has been a twofold lifestyle intervention</u>: dietary modification resulting in an overall caloric deficit combined with 250 minutes or more of moderate-intensity exercise per week.

Research has long since established that <u>being physically active</u> improves mental health, including memory, depressive symptoms and mood, as well as immune function and bone health. Being active also reduces the risks of developing <u>conditions like heart disease</u>, type 2 diabetes and <u>some cancers</u>.

But given that more than two-thirds of the U.S. adult population is now overweight or obese, Americans are clearly not meeting these guidelines.



The most recent data shows that only a quarter of adults are getting the necessary <u>aerobic and muscle strengthening activity each week</u>.

For all these reasons, many clinical recommendations now suggest <u>the</u> <u>use of anti-obesity medications</u> as a <u>primary means of addressing</u> <u>overweight and obesity</u>.

The health care field now has a new strategy for meaningful weight loss, but there are still more questions than answers.

Will losing weight with only drugs still provide these same health benefits? What about the long-term efficacy of using these medications? Are there complications we don't know about yet because we simply haven't had these drugs available long enough to study? Researchers are also just beginning to understand what happens when you stop using these new weight loss medications.

Given the gravity of the obesity epidemic and the health costs that come with it, I believe the potential risks of using these drugs for <u>weight loss</u> may be worth the reward of lessening the burden on the health care system and improving the quality of life for hundreds of millions of people.

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