

Can a diabetes drug transform the treatment of obesity?

In studies, a weekly injection caused dramatic amounts of weight loss and improved other heart-related risk factors.

For treating most conditions closely linked to heart disease, a two-pronged approach works best: lifestyle changes plus medication. For obesity, however, the currently available drug options simply aren't very effective. But that may soon change if a high-dose version of semaglutide, a drug originally developed to treat type 2 diabetes, gains FDA approval for treating obesity.

Semaglutide works by mimicking a substance called GLP-1, which is made naturally by the gut and the brain. It prods the pancreas to release insulin when blood sugar rises too high; it also reduces appetite and helps you feel full following a meal.

A weekly injection of semaglutide, marketed under the brand name Ozempic, is approved for people with diabetes and causes modest weight loss. But a higher dose induced a weight loss of 15% of a person's body weight, on average, over a period of about 16 months, according to two large trials published earlier this year (see "A game-changing drug for obesity?").

"There's no question that semaglutide is more effective by far than any other anti-obesity medication we have now," says Dr. Lee Kaplan, who directs the Obesity, Metabolism, and Nutrition Institute at Harvard-affiliated Massachusetts General Hospital. Still, there's a lot of variability in how people respond to the drug, he cautions. Some people may lose no more than 5% of their weight. But in others, the drug may

be as effective as weight-loss surgery, which typically helps people shed at least 30% of their weight.

Obesity as a disease

A truly effective weight-loss drug could help change how people think about obesity, says Dr. Kaplan, which he stresses should be distinguished from the socially driven desire to lose weight. "People need to recognize that obesity—defined as excess weight that poses a risk to health—is a disease that has to be treated in the classic medical sense if we want to provide patients with the optimal benefit." It's a serious problem,

given that more than 40% of adults in this country have obesity. Like diabetes, obesity changes the body



Obesity puts your health at risk and should be treated like other chronic diseases.

so it doesn't function normally, and that underlying problem has to be corrected. And similar to how doctors treat high blood pressure and elevated cholesterol, treatment for obesity may require more than a single drug and last indefinitely.

Taking this new drug is generally easy and painless: you inject yourself in the abdomen or thigh using a pen-like device with a tiny needle the size of a human hair, says Dr. Kaplan. Side effects such as nausea and diarrhea are common soon after starting the medication, but they usually resolve within a month or two.

People with obesity frequently have other health problems, such as high blood pressure and elevated cholesterol, which are caused or made worse by the obesity, says Dr. Kaplan. Studies suggest that people who undergo weight-loss surgery may lower their risk of heart disease by as much as 60%. "Having a drug available that comes close to delivering a degree of weight loss similar to surgery is reason for great optimism," he says. ♥

A game-changing drug for obesity?

Currently available anti-obesity drugs help people lose an average of only about 5% to 8% of their body weight over a course of treatment. But results from two recent studies of the diabetes drug semaglutide look far more promising. Both included people with obesity (defined as a body mass index, or BMI, of 30 or higher) or who had a BMI of 27 or higher and at least one weight-related health problem, such as high blood pressure, high cholesterol, or sleep apnea. (BMI is a measure of weight in relation to height; to calculate yours, go to www.health.harvard.edu/bmi-calculator.)

The first study, published online Feb. 10, 2021, by *The New England Journal of Medicine*, included 1,961 adults. All participants received counseling focused on improving their diet and exercise habits, along with a weekly injection of 2.4 milligrams of semaglutide or a placebo for 68 weeks. Most (75%) of those taking semaglutide lost more than 10% of their initial weight, and nearly one-third lost more than 20%.

The second study, published online Feb. 24, 2021, by *JAMA*, tested the same dose of semaglutide in 611 adults who followed a moderately low-calorie diet for two months in addition to receiving intensive behavioral therapy (including 30 counseling sessions) during the 68-week-long study. Those taking semaglutide lost an average of 16% of their body weight, compared with 5.7% among those who got intensive behavioral therapy with a placebo.

Weight loss with semaglutide was also linked to improvements in blood pressure, cholesterol, and inflammation.

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