

Can Ozempic treat depression? Early signs point to yes

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Add depression to the growing list of chronic diseases that obesity medicines might alleviate. Signs of improved mental health are showing up in the health records of people who take the broader class of

medicines known as GLP-1s, which include Novo Nordisk's Wegovy and Eli Lilly & Co.'s Zepbound.

Formal studies are needed to confirm and understand the effect, but there's good reason to hope that it's real. If the data bear out, the potential for these drugs to address not just physical, but mental health must be part of the broader conversation around how and when to pay for them. Thus far, the biggest barrier to the drugs is their cost—employers and state governments have proven cautious about covering expensive drugs that patients may need indefinitely.

Epic Research said that an analysis of some 4 million patient health records showed that people prescribed a GLP-1 medicine for either diabetes or weight loss were less likely to experience anxiety and [depression](#). For the 3 million diabetic patients included in the study, the effect held up for nearly every GLP-1 drug on the market, and was most pronounced for those taking Lilly's diabetes drug Mounjaro (now also marketed as Zepbound for obesity).

It's an important counterpoint to alarming headlines that European regulatory bodies were probing reports of suicidal ideation in people taking obesity medicines. (Researchers at the National Institutes of Health later found that the people taking semaglutide—the ingredient in Wegovy and Ozempic—had a lower risk of suicidal thoughts compared to people taking other kinds of diabetes or weight loss medications, though the Food and Drug Administration continues to watch the issue closely).

Of course, health records aren't a replacement for actual clinical studies. But the results make sense to researchers who study obesity or mental health. The two diseases often go hand in hand—some 43% of adults with depression are also obese, and the risk of obesity rises alongside more severe depression, according to the Centers for Disease Control

and Prevention.

And a robust body of research has shown that symptoms of depression improve when people shed pounds, whether that's by diet and exercise, bariatric surgery, or other types of obesity medicines.

The pressing question, now, is whether the improvement goes beyond what is seen with other types of weight loss, if the substantial weight loss offered by Wegovy and Zepbound is responsible for the effect, or if there's something special about the way these drugs modulate hormones in the brain.

Or, more likely, all of the above.

"To me, the effect is not surprising," says Matthew Hayes, a neuroscientist at the University of Pennsylvania who studies the activity of GLP-1s in the brain. Researchers already know that weight loss can have ancillary mental health benefits—people feel better about how they look and might be exercising more, which has been shown to ease the symptoms of depression. But these drugs also appear to act on the reward centers in the brain, which could enhance that effect.

So far, studies of GLP-1s and mental health—in humans at least—are limited. Most recently, a team at the University of Toronto previously found that liraglutide, a GLP-1 drug that has long been on the market for diabetes, could improve cognitive function in people with depression or bipolar disorder. But the study was tiny and everyone enrolled got the drug; without a placebo arm, the findings are harder to generalize. The team is now conducting a small, placebo-controlled trial of an oral version of semaglutide in people with depression.

The goal is to understand whether the drug can ameliorate the cognitive symptoms associated with the disorder. Rodrigo Mansur, one of the

University of Toronto psychiatrists leading that study, points out that depression doesn't only affect someone's mood—it affects their motivation, short-term memory and ability to think and focus.

As scientists learn more about the connection between the gut and the brain, it's becoming increasingly clear that all of those issues could be closely connected to metabolism, he says. Results from his study could be available by as soon as the end of this year.

Another question that will very much matter for patients: If the mental health benefit of these drugs turns out to be real, is the effect the same for all the GLP-1 drugs on the market? "The devil may be in the details," Hayes says. Each [drug](#) stimulates hormones that control satiety in a different way. Each reaches different areas of the brain with varying concentrations and depths. And each offers a different magnitude of weight loss.

So far, most research connecting [weight loss](#) and mental health has centered on liraglutide, but Wegovy and Zepbound are expected to quickly dominate the market.

Designing a trial to carefully study the subtle mental health effects of the various obesity drugs is a daunting challenge, one companies seem unlikely to take on. Studies of depression treatments are notoriously fraught. With many other potential uses for the GLP-1s, drugmakers are focusing on conditions where the science—and the path to regulatory approval—is clearer.

As more people take these drugs for longer periods of time, extracting trends from [electronic health records](#) may be the best data we have in the near term.

That's a frustrating reality considering the twin epidemics of mental

health and obesity in the US. If the results from academic labs' small clinical trials prove promising, [government agencies](#) should consider how they can pitch in to fund or even run the kinds of larger studies needed to confirm them.

Even without more robust evidence, employers might eventually need to consider [mental health](#) as part of the suite of benefits that come with obesity medicines.

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