

Can a drug like Ozempic help treat addictions to alcohol, opioids or other substances?

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Credit: Markus Winkler from Pexels

Semaglutide (sold as Ozempic, Wegovy and Rybelsus) was initially developed to treat diabetes. It works by stimulating the production of



insulin to keep blood sugar levels in check.

This type of drug is increasingly being prescribed for weight loss, despite the fact it was initially approved for another purpose. Recently, there has been growing interest in another possible use: to treat addiction.

Anecdotal reports from patients taking semaglutide for <u>weight loss</u> suggest it reduces their appetite and craving for food, but surprisingly, it also may reduce their desire to drink alcohol, smoke cigarettes or take other drugs.

But does the research evidence back this up?

Animal studies show positive results

Semaglutide works on glucagon-like peptide-1 receptors and is known as a GLP-1 agonist.

Animal studies in rodents and monkeys have been overwhelmingly positive. Studies suggest GLP-1 agonists can reduce drug consumption and the rewarding value of drugs, including <u>alcohol</u>, <u>nicotine</u>, <u>cocaine</u> <u>and opioids</u>.

Out team has reviewed the evidence and found more than 30 different pre-clinical studies have been conducted. The majority show positive results in reducing drug and <u>alcohol consumption</u> or cravings. More than half of these studies focus specifically on alcohol use.

However, translating <u>research evidence</u> from animal models to people living with addiction is challenging. Although these results are promising, it's still too early to tell if it will be safe and effective in humans with alcohol use disorder, nicotine addiction or another drug dependence.



What about research in humans?

Research findings are mixed in human studies.

Only <u>one large randomized controlled trial</u> has been conducted so far on alcohol. This study of 127 people found no difference between exenatide (a GLP-1 agonist) and placebo (a sham treatment) in reducing alcohol use or heavy drinking over 26 weeks.

In fact, everyone in the study reduced their drinking, both people on active medication and in the placebo group.

However, the authors conducted further analyses to examine changes in drinking in relation to weight. They found there was a reduction in drinking for people who had both alcohol use problems and obesity.

For people who started at a normal weight (BMI less than 30), despite initial reductions in drinking, they observed a rebound increase in levels of heavy drinking after four weeks of medication, with an overall increase in heavy drinking days relative to those who took the placebo.

There were no differences between groups for other measures of drinking, such as cravings.

In another 12-week <u>trial</u>, researchers found the GLP-1 agonist dulaglutide did not help to reduce smoking.

However, people receiving GLP-1 agonist dulaglutide <u>drank 29% less</u> <u>alcohol</u> than those on the placebo. Over 90% of people in this study also had obesity.

Smaller studies have looked at GLP-1 agonists short-term for <u>cocaine</u> and <u>opioids</u>, with mixed results.



There are currently many other clinical studies of GLP-1 agonists and alcohol and other addictive disorders underway.

While we await findings from bigger studies, it's difficult to interpret the conflicting results. These differences in treatment response may come from individual differences that affect addiction, including physical and mental health problems.

Larger studies in broader populations of people will tell us more about whether GLP-1 agonists will work for addiction, and if so, for whom.

How might these drugs work for addiction?

The exact way GLP-1 agonists act are not yet well understood, however in addition to reducing consumption (of food or drugs), they also may reduce cravings.

Animal studies show GLP-1 agonists reduce craving for <u>cocaine</u> and <u>opioids</u>.

This may involve a key are of the brain reward circuit, the <u>ventral</u> <u>striatum</u>, with experimenters showing if they directly administer GLP-1 agonists into this region, rats show reduced "craving" for <u>oxycodone</u> or <u>cocaine</u>, possibly through reducing drug-induced dopamine release.

Using human brain imaging, experimenters can elicit craving by showing images (cues) associated with alcohol. The GLP-1 agonist exenatide reduced brain activity in response to an alcohol cue. Researchers saw reduced brain activity in the ventral striatum and septal areas of the brain, which connect to regions that regulate emotion, like the amygdala.

In studies in humans, it remains unclear whether GLP-1 agonists act directly to reduce cravings for alcohol or other drugs. This needs to be



directly assessed in future research, alongside any reductions in use.

Are these drugs safe to use for addiction?

Overall, GLP-1 agonists have been shown to be relatively safe in healthy adults, and in people with diabetes or obesity. However side effects do include nausea, digestive troubles and headaches.

And while some people are OK with losing weight as a side effect, others aren't. If someone is already underweight, for example, this drug might not be suitable for them.

In addition, very few studies have been conducted in people with addictive disorders. Yet some side effects may be more of an issue in people with addiction. Recent research, for instance, points to a <u>rare risk</u> <u>of pancreatitis</u> associated with GLP-1 agonists, and people with alcohol use problems already have a higher risk of this disorder.

Other drugs treatments are currently available

Although emerging research on GLP-1 agonists for addiction is an exciting development, much more research needs to be done to know the risks and benefits of these GLP-1 agonists for people living with addiction.

In the meantime, existing effective medications for addiction remain under-prescribed. Only <u>about 3%</u> of Australians with alcohol dependence, for example, are prescribed medication treatments such as like <u>naltrexone</u>, <u>acamprosate</u> or <u>disulfiram</u>. We need to ensure current medication treatments are accessible and health providers know how to prescribe them.



Continued innovation in addiction treatment is also essential. <u>Our team</u> is leading research towards other individualized and effective medications for alcohol dependence, while others are investigating treatments for nicotine <u>addiction</u> and other drug dependence.

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