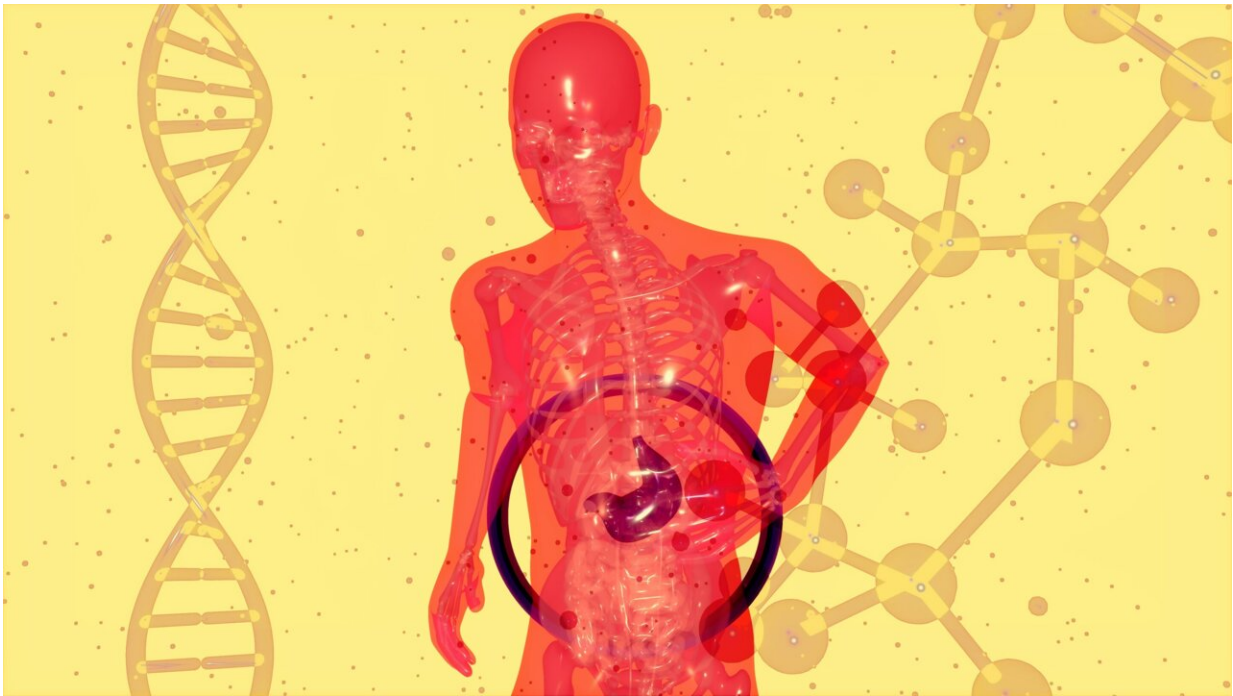


# Q&A: Researcher discusses how GLP-1 weight loss drugs affect the liver

August 20 2024

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Drugs such as Ozempic, Rybelsus and Wegovy have made news for their abilities to treat diabetes and encourage weight loss.

These drugs, called glucagon-like peptide-1 (GLP-1) receptor agonists, are now being investigated for their ability to help other patients, including those with liver disease. For example, GLP-1 agonists are

being studied for their use in treating [non-alcoholic fatty liver disease](#).

Researchers at the University of Michigan, however, recently published a [research letter](#) in *Clinical Gastroenterology and Hepatology* about the first known case of hepatitis and jaundice in a patient taking tirzepatide, an antidiabetic GLP-1 agonist.

To give a clearer understanding of the potential benefits and risks of GLP-1 agonists for patients with liver disease, Robert Fontana, M.D., a Michigan Medicine hepatologist, professor of medicine and the lead author on that research letter, answers the following questions on the topic.

## **As a hepatologist, why are you interested in GLP-1 agonist drugs like semaglutide or tirzepatide?**

My primary interest is in helping patients with [fatty liver disease](#).

Between 40 to 50% of the entire United States population is overweight or obese. And among them, a large proportion have underlying fat in their liver.

And many of these patients are at risk for progressive liver disease if left untreated, including adolescents and young adults.

I would like to catch these patients early and work with their [primary care physicians](#) to help them lose weight and improve their liver profile.

But that's not often the reality.

For me as a doctor, when I see patients in my clinic who have fatty liver, many are overweight and/or diabetic.

I want to do something to help them while they're asymptomatic.

As a liver doctor, I want to make sure they don't progress in front of me to cirrhosis over the course of the next few years.

I'm very interested in what's going on in the field of GLP-1 agonist drug development, as a means to help patients lose weight, treat their diabetes and potentially improve their liver health at the same time.

## **Are there any known uses for these drugs to help with liver disease beyond enhancing encouraging weight loss?**

Resmetirom, which is sold under the brand name Rezdiffra, was approved by the Food and Drug Administration in March 2024 for patients with noncirrhotic non-alcoholic steatohepatitis to treat liver scarring.

Although it isn't a GLP-1 agonist, it targets thyroid hormone receptors in the liver and is associated with improvements in the amount of liver fat, inflammation and scarring compared to placebo.

I, along with other gastroenterology and liver specialists, am starting to use orally administered resmetirom for patients with known metabolic associated steatohepatitis.

At the same time, newer drugs like the GLP-1 agonists, such as semaglutide and tirzepatide, which are already approved for diabetes and [weight loss](#), are being evaluated as treatments for this condition as well.

For patients I see in clinic, these GLP-1 agonists can be a two-in-one solution for diabetes and weight loss—maybe a three-in-one solution if

they prove to be safe and effective for metabolic associated steatohepatitis as well.

## **What about side effects of GLP-1 agonists—are there any specific to the liver?**

In general, these drugs are safe and well tolerated, but up to 10 to 20% of patients may need to reduce the dose of medication due to gastrointestinal side effects such as nausea, diarrhea and abdominal pain.

In addition, when you lose weight quickly, like over a six to 12 month span, you can precipitate the development of gallstones, which can affect the liver.

*Clinical Gastroenterology and Hepatology* recently published a paper on which I was the lead author about the first well-described case of drug hepatotoxicity caused by tirzepatide.

The paper shows you can get hepatitis, but we don't want to scare people.

Currently there are several hundred thousand people taking these agents on a daily basis and there are only a handful of individuals who developed direct drug toxicity from these agents.

These are low rate adverse events.

## **So you would still recommend GLP-1 agonists for your diabetic patients despite this specific case?**

Yes. It's all about risk versus benefit.

Patients need to know about potential side effects of any medication

they take, and your doctor needs to know as well.

Furthermore, emergency rooms need to know in light of how commonly these agents are being prescribed.

Although these drugs may show net benefit to the liver in ongoing studies of metabolic dysfunction-associated steatotic liver disease, patients and physicians need to remain vigilant.

### **Are there certain patients for whom you'd be more worried about serious liver-related side effects?**

Yes. The drug package inserts caution patients not to use the drugs if they have known advanced liver disease, cirrhosis or liver failure.

If you already have liver problems, we don't want to make it worse inadvertently.

### **Overall, are you optimistic about the future role of the GLP-1 agonist drugs in helping your patients with fatty liver disease?**

Yes. Studies have been completed.

Overall, the GLP-1 agonists look quite good, and they are already highly effective in reducing weight and improving diabetes.

We also, however, want to encourage lifestyle changes that will facilitate weight loss and healthier eating habits, including a low-carbohydrate Mediterranean diet.

All the medical societies agree that a high-quality, low-calorie diet and

physical activity are cornerstones of managing these common health problems.

It's important, first, to eat healthy foods and move around, which are tried and true therapies, but can be hard to sustain on an individual basis.

**More information:** Robert J. Fontana et al, First Report of Tirzepatide Hepatotoxicity with Jaundice, *Clinical Gastroenterology and Hepatology* (2024). [DOI: 10.1016/j.cgh.2024.06.025](https://doi.org/10.1016/j.cgh.2024.06.025)

Provided by University of Michigan

Citation: Q&A: Researcher discusses how GLP-1 weight loss drugs affect the liver (2024, August 20) retrieved 21 August 2024 from <https://medicalxpress.com/news/2024-08-qa-discusses-glp-weight-loss.html>

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