Microscopic Colitis Foundation

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Wayne's Blog

Volume 11, Issue 7
July, 2025

Anti-inflammatory Effects of Weight Loss Drugs: Are They Possible IBD Treatments?

by Sharyl Magnuson, MD

The very popular GLP-1 agonists (Ozempic, Wegovy, Trulicity, ect.) that have revolutionized how we think about obesity management are being used by many millions of people. This use is exposing many people with coexisting health conditions besides the obesity and Type 2 Diabetes that garnered the prescription to these drugs. Some of these people have noted powerful impacts of this class of medication on their other illnesses, often with clear improvements.

These effects are not just due to better sugar control or the expected benefits of weight loss. GLP-1 agonists, and now the newer dual active GLP-1/GIP drug, tirzepatide, are showing pleiotropic (producing more than one effect) effects. Mounjaro/Zepbound are the brand names used by Lilly for tirzepatide, and the dual action is the receptor agonist (activation) effect of both the Glucagon-Like Peptide-1 and Glucose dependent Insulinotropic Polypeptide. GLP-1 and GIP are both incretin hormones found in the mucosal lining of the small intestines, and they both stimulate insulin release from the beta cells in the pancreas when food is eaten, thus the value in treating Type 2 Diabetes. Exciting positive impacts in other disease states are being found, and research in cardiovascular disease, sleep apnea, and in addiction medicine is being actively pursued by Lilly.

Weight loss drugs originally prescribed for diabetes.

They have been found to have many other positive effects.

In exploring the real impact of these medications on reducing the severity of cardiovascular (CV) disease, it was found that they lower several markers of inflammation that are associated with increased CV disease severity when elevated.[1] All of the following were lowered during treatment with tirzepatide. Only CRP was lowered by the GLP-1 agonist studied.

- **YLK-40** (a potential biomarker for inflammatory activity in autoimmune and other diseases)
- **Leptin** (related to cytokines in activity with elevated levels corresponding to inflammatory related diseases)[2]
- **ICAM-1** (intracellular adhesion molecule, impacting transmembrane migration of leukocytes)
- **CRP** (C-Reactive Protein, a commonly performed inflammatory lab test for infections and auto-immune diseases)[3]

It is interesting that one of the major actions of the GLP-1 agonists is slowing of gut motility, lengthening of the GI transit time. This is a potential benefit for MC suffers, as it allows for more time for the colon to absorb liquid---mimicking some of the action of Lomotil.

Surprisingly, I have noted significantly more positive remarks of diarrhea improvement with Mounjaro/Zepbound (tirzepatide, the GLP-1/GIP dual agonist) than with Ozempic, Trulicity, ect (the GLP-1 agonists). My own experience with tirzepatide has been positive for my symptoms of MC, more so than my experience with several of the GLP-1 agonist drugs.

Unlike many with L-MC, I didn't lose weight during my nearly 15 years of struggling with MC diarrhea and other symptoms. I also had pre-diabetes and metabolic syndrome. Fortunately for me, my husband is a diabetes specialist and researcher. I was able to try samples of various GLP-1 medications, and found that I tolerated them well, and I lost some weight and normalized my sugar. I did get some control over loose bowels, with only real diarrhea problems when I inadvertently was exposed to my soy trigger or severe stress. About 2 years ago I was switched to Mounjaro (tirzepatide) due to unavailability of the GLP-1 I was using. My MC symptoms improved by at least 50%, with almost no MC exacerbations, even though there were some accidental soy exposures. My chronic fatigue is improved, but not gone. I feel fortunate that I

was changed to this medication.

> **GLP-1 drugs slow gut motility.**

> **Diarrhea and other symptom improvement in MC observed by some patients.**

The studies looking at CV impacts looked at dulaglutide as the GLP-1 agonist comparator to tirzepatide, and we know that all GLP-1 agonists are not equal. Semaglutide (Ozempic/Wegovy) may have different effects on inflammatory markers and on its impact on other disease states. Liraglutide (Victoza) has a bit less weight loss effect, but may slow gut motility more---or less than others. Who knows, as we just don't have this data.

New targets of treatment are being explored for these powerful tools by their makers. Each new disease indication that is found to be a valid treatment leads to a reset on the patent---the duration of time the pharmaceutical company can keep an exclusive on their drug and keep the price high. It certainly benefits the company to find these new indications. There have been several very positive reports from MC patients that tirzepatide has really improved their symptoms. Certainly, there have been MC patients who have had problems with these drugs, just like many people who don't have MC, as these are powerful drugs and powerful drugs have powerful side effects.

Standard of practice is for the pharmaceutical company to perform clinical trials for their drug on the clinical indication. There are well-trod paths for these studies to make them valid, to see if the drug really does help, not hurt. It might be time to study tirzepatide as a treatment for MC. The multiple impacts on inflammation along with slowing GI motility may be enough to be therapeutic. The suspected central nervous system effects, that are a possible factor in the addiction effect, could also be involved with our response to this class of medication. To have a medication be studied for the treatment of our disease will increase the knowledge of the nature of MC, and will improve the database of this class of medication. I like win-win situations.

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Most GLP-1 Users Lose Far Less Weight Than Suggested by Drug Trials

by Wayne Persky

While GLP-1 receptor agonists such as semaglutide (Wegovy) and tirzepatide (Zepbound) have generated enormous excitement for their powerful weight-loss and diabetes prevention effects in clinical trials, a recently published research study highlights a significant disconnect between clinical trial outcomes and real-world patient experiences.

Researchers from the Cleveland Clinic used electronic health records from over 7,800 adults with overweight or obesity (but without type 2 diabetes) between 2021 and 2023. Their findings, reported in Obesity and summarized in an online Medscape article, suggest that GLP-1 drugs may fall short of expectations outside of carefully controlled clinical settings (Gasoyan, et al., 2025; Tucker, 2025, June 10).[1,2] The cause of the discrepancy appears to be primarily due to early discontinuation, and low dosing. These factors drastically reduce the average amount of weight loss seen by most patients in actual practice.

Among real-world users:
Mean weight loss at 1 year was just 8.7% overall, with:

- 7.7% for semaglutide users
- 12.4% for tirzepatide users

- 12.4% for tirzepatide users

In contrast, clinical trials reported:

- 14.9% weight loss with semaglutide
- Up to 20.9% with tirzepatide (at the highest doses)

These discrepancies were primarily due to:

- Early discontinuation: 22% stopped semaglutide within 3 months; 16% stopped tirzepatide.
- Low maintenance dosing: Over 80% of patients remained on sub-optimal doses, well below the doses tested in trials.

Patients who stayed on high doses achieved greater weight loss (up to 18% with tirzepatide), but this group was in the minority.

But the good news is:
glycemic benefits and stable weights were maintained after discontinuation. Despite lower weight loss overall, many patients, especially those with prediabetes, saw improvements in blood sugar control, even after stopping the drugs:

- A1c reductions were modest but statistically significant across all discontinuation groups.
- Over half (53.9%) of prediabetic patients reverted to normal blood glucose levels at 1 year.
- Progression to type 2 diabetes was lowest (1.7%) among those who stayed on the medication.

Interestingly, unlike trial data that showed rapid weight regain after discontinuation, patients in the real-world setting generally maintained their weight loss, even if they stopped the drugs early. This may reflect behavior changes, alternate therapies, or lower total weight loss that's easier to maintain.

Why are patients quitting early?

While the Cleveland Clinic team is still gathering data on exact reasons for discontinuation, anecdotal reports and expert commentary point to several common issues:

- Gastrointestinal side effects (nausea, vomiting, diarrhea) remain the top reason for stopping GLP-1 drugs. These are often underreported or underappreciated in trials.
- Cost and insurance barriers deter patients from maintaining long-term use.
- Inconvenience or injection fatigue may also play a role, especially in non-diabetic patients who don’t perceive an immediate health risk.

Dr. Timothy Garvey of the University of Alabama at Birmingham emphasized that despite their potential, current GLP-1 drugs are not a sustainable chronic therapy for most people. “We need medications that are better tolerated, more effective at lower doses, and more affordable,” he said.

In addition to less dramatic weight loss, users commonly report:

- Persistent nausea, especially during dose titration
- Vomiting or diarrhea, which may lead to dehydration and malnutrition
- Muscle loss alongside fat loss, which can reduce physical strength and metabolic rate

- Hair thinning or skin laxity with rapid weight changes
- Difficulty affording the drug, particularly as insurance coverage varies widely
- Psychological impact: Some patients experience emotional distress if weight returns after discontinuation, especially if they relied heavily on the medication for self-esteem or body image

Emerging evidence suggests that these drugs alter taste perception.
This may explain why users tend to change food preferences, and why they experience reduced appetites during treatment, and sustained weight management even after discontinuation of the treatment

> **GI side effects common.**

> **Weight loss drugs alter taste perception.**

Appetite and reward pathways are affected.
GLP-1 drugs like semaglutide and tirzepatide act not just in the gut and pancreas, but also in the central nervous system, particularly areas like the hypothalamus and brainstem. These regions regulate appetite, cravings, and food reward. Patients often report less interest in high-fat, high-sugar foods and a stronger preference for healthier options while on the drugs.

Some clinical trial participants and real-world users report that foods they previously enjoyed now taste too sweet or too greasy, or even produce nausea. This has been described anecdotally in:

- Case reports
- Online user communities
- Interviews with prescribing physicians
- A small number of qualitative studies have begun documenting this phenomenon, though it remains under-researched in large-scale clinical settings.

Pilot studies support sensory changes.

- A 2023 study published in Diabetes, Obesity and Metabolism noted that patients on GLP-1 drugs showed reduced brain activity in reward regions (for example, nucleus accumbens) when shown images of high-calorie foods — a neurological effect consistent with diminished food craving.
- A 2024 preprint suggested that some GLP-1 users experienced altered taste sensitivity to sweetness and fat, though more rigorous peer-reviewed studies are still needed.

As noted in the June 2025 Cleveland Clinic study referenced, weight did not rapidly rebound in many patients after stopping the medication. One plausible explanation is behavioral carryover. But another is

lasting neurochemical changes in the way the brain interprets hunger and food reward, especially if eating patterns or preferences have shifted during treatment.

Possible mechanisms behind taste changes.

- Delayed gastric emptying (a known effect of GLP-1s) may contribute to prolonged satiety and reduce appeal of heavy meals.
- Nausea and early aversions could create conditioned taste avoidance — a phenomenon where foods previously associated with discomfort become less desirable. Delayed gastric emptying is known as gastroparesis, and one of the symptoms of gastroparesis is nausea.
- Central GLP-1 receptors may alter dopamine signaling, affecting how food "feels" emotionally and perceptually, potentially dulling responses to previously “addictive” foods.

And many users complain about other adverse issues with these drugs.

- Loss of muscle mass
- Changes in appearance that suggests aging (Ozempic face, skin laxity)
- Potential worsening of frailty in older adults
- Inadequate long-term safety data on body composition effects

The loss of muscle mass associated with GLP-1 drugs can be significantly reduced with proper resistance training and adequate protein intake while the drugs are being used, but the problem can not usually be completely prevented.

Without intervention:
GLP-1 drugs like semaglutide or tirzepatide typically cause 10–30% of total weight lost to come from lean mass (mostly muscle). That means:

- A person losing 30 lbs may lose 3–9 lbs of muscle, depending on age, diet, and physical activity.
- Older adults are at higher risk for disproportionate muscle loss (due to anabolic resistance and lower baseline muscle mass).
- Older individuals, especially postmenopausal women, or those with existing muscle loss, are at higher risk of frailty (that can contribute to falls, and long-term disability). And a sedentary lifestyle can accelerate the problem even as weight drops.

The Bottom Line

GLP-1 receptor agonists appear to be effective, but in the real world, they are poorly tolerated, especially at higher doses. There are unwanted side effects such as loss of muscle mass, and "Ozempic face" Fortunately, modest improvements such as weight lost and lowered glucose levels are usually sustained after the drugs are discontinued.

There's no definitive proof yet that GLP-1 drugs directly change taste receptors, but there is strong indirect evidence from neuroscience, endocrinology, and patient reports suggesting they influence taste perception, food reward, and preference These changes may contribute to lasting weight control by shifting dietary behavior, even after stopping the medication.

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