### **SUPER AGE**

# Microdosing GLP-1s: What the Science Actually Says (And What It Doesn't)

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GLP-1 drugs like Ozempic and Wegovy are reshaping weight loss and health. But does microdosing work and is it safe? Here's what the science says.

GLP-1 receptor agonists (like semaglutide, liraglutide, and dulaglutide) have moved from niche to mainstream, with celebrities and doctors touting their effects for improving weight loss and cognitive health, reducing substance use, and more. A new **RAND survey** of a nationally representative U.S. sample found that 1 in 8 Americans (nearly 12%) have used GLP-1 agonists. At the same time, a **2025 analysis** of real-world studies suggests 20–50% discontinue GLP-1s within a year, often due to cost, side effects, and comorbidities.

While GLP-1s are among the most effective, well-studied treatments for weight and metabolic health, they aren't risk-free. **Common side effects** like nausea and diarrhea, cost, and the need for lifestyle interventions to maintain muscle mass can be roadblocks for sustained use. Enter: GLP-1 microdosing.

Microdosing (fractional dosing) is an emerging tolerability and cost-driven practice, but it has limited outcomes data. We looked over recent peer-reviewed research to separate facts from hype and to help you have a grounded conversation with your clinician.

#### The Research on Full-Dose GLP-1s

Large, randomized controlled trials show substantial, durable weight loss and metabolic benefits with

approved dosing. The research is strongest for weight loss, but scientists are also uncovering potential benefits (and risks) across mood, brain health, heart health, and even addictive behaviors. Here's what we know so far:

- Weight loss: In the STEP-1 trial, people on weekly semaglutide 2.4 milligrams (mg) lost an average of 15% of their body weight, compared with just 2.4% on placebo. Gastrointestinal (GI) side effects like nausea and diarrhea were the most common complaints.
- Improved mood and depressive symptoms: A 2024 meta-analysis reported small but statistically significant improvements in depression scores among GLP-1 users.
- Reduced substance use and cravings: In a <u>2025 randomized trial</u>, adults with alcohol use disorder who took low-dose semaglutide significantly reduced drinking and cravings compared with placebo.
- **Brain health:** Early trials are exploring whether GLP-1s can **support cognitive resilience** in Alzheimer's disease and improve motor and mood symptoms in Parkinson's disease. Results are preliminary but promising.
- **Heart health:** Large <u>cardiovascular outcomes trials</u> show that GLP-1s can lower the risk of major heart events in people with type 2 diabetes and high cardiovascular risk, independent of weight loss.

It's clear that GLP-1s are powerful, not just for weight loss, but for how their effects may ripple across multiple systems in the body.

## What the Research Says About Microdosing GPL-1s

Microdosing isn't just a buzzword. It describes a growing practice of using fractions of standard GLP-1 doses (for example, holding semaglutide at 0.25–0.5 mg/week instead of titrating to a full dose). Clinicians and researchers note that patients sometimes do better on lower or slower doses, especially if side effects, costs, or supply shortages make the standard regimens hard to sustain.

A recent letter from experts published in *Diabetes Care* described how multi-dose pens can be used to deliver fractional "clicks" of semaglutide, allowing very small, personalized adjustments that improve tolerability and continuity of therapy. Similar flexibility exists with other GLP-1 medications as well.

There are early signals that low doses still deliver benefits. A **2024 observational study** in adults without diabetes found 6% mean weight loss over 12 weeks at 0.25–1.0 mg/week semaglutide, with mostly mild, transient GI symptoms. Still, the evidence is far from conclusive, as no randomized outcomes data exists yet.

Microdosing is a plausible harm-reduction and access strategy, but it remains off-label, individualized, and evidence-light. It requires health literacy, the ability to follow instructions, plus close physician guidance.

### Risks and Side Effects to Watch For (at Any Dose)

Like any medication, GLP-1s come with risks. Here's what to keep in mind if you're considering them:

- **Digestive upset is common.** Nausea, diarrhea, constipation, and stomach discomfort happen most often when **starting or increasing the dose**. For many people, these symptoms ease with time or slower titration.
- Gallbladder issues are possible. Studies show a slightly higher risk of gallstones or biliary problems, especially at higher doses over longer periods. A 2022 meta-analysis of 76 randomized controlled studies found GLP-1 users had a 37% higher risk of gallbladder or biliary disease, with the greatest risk at higher obesity doses. Know the warning signs: sudden upper-right abdominal pain, fever, or yellowing of the skin and get checked quickly if they appear.
- **Muscle loss can happen.** A 2024 review in *Diabetes, Obesity and Metabolism* found that GLP-1-based therapies can reduce lean mass, with some studies reporting 15–60% of weight lost coming from lean tissue. Protect yourself with protein-rich meals and regular strength training.

These risks don't mean you should avoid GLP-1s. They do mean you should go in informed, with a plan to monitor symptoms and support your body while you're on them. More than 70% of people reported no side effects at the Microdose GLP-1Rx dosage.\*\*

### What to Ask Your Doctor About GLP-1s: A Checklist

If you're considering a GLP-1, whether at a full dose or a microdose, it helps to have a roadmap for the conversation. Here's a guide, rooted in clinical research, to take with you to your next appointment:

- **1. Clarify your outcome goals:** The STEP-1 trial cited above shows an average 15% weight loss at full dose over 68 weeks. But not everyone needs or wants that level of change.
- **Ask:** Am I aiming for 5% in the first 3—4 months, or something closer to 10–15% over a year? Knowing this helps you and your doctor match the dose to your ambition.
- **2. Map out a titration plan:** Standard starts are 0.25 mg weekly with gradual increases, but tolerability varies.
- **Discuss:** What's our plan if I feel good at a lower dose? When should we hold, lower, or escalate? Research shows slower titration often improves GI side-effect tolerability.
- **3. Build your "health architecture" early:** Protect lean muscle and reduce gallstone risk with protein (1.2–1.6 g/kg/day), 2–3 resistance workouts per week, daily steps, fiber, hydration, and a smart alcohol plan.
- **Ask:** How do we align my nutrition and fitness plan with this medication so the weight loss supports long-term health?
- **4. Have a side-effect playbook:** Most people experience nausea, bloating, or constipation early on. Smaller meals, slower eating, and avoiding trigger foods can help.
- **Discuss:** What are safe anti-nausea options if I need them? What symptoms mean I should pause or seek urgent care? Know the red flags: sudden upper-right abdominal pain, jaundice, and persistent severe abdominal pain.
- **5. Commit to regular check-ins:** Track your progress. Monitor weight, waist circumference, get labs every 4–6 weeks (fasting glucose or A1c if relevant), track your digestive symptoms, and mood (given emerging evidence of small antidepressant effects).
- **Ask:** What labs or measures should we track to make sure this medication is working for me safely? And how often should we retest?

This checklist is about empowering you to have a structured, research-backed conversation. Your doctor should help tailor each step, from goals to dose adjustments, so the treatment plan fits your body, lifestyle, and long-term health.

#### From Our Sponsor:

**How Noom Can Support Your GLP-1 Journey** 

Noom Microdose GLP-1Rx combines the power of medication with the proven psychology of behavior change. The Noom team works with you to find the right dose and help you build sustainable habits that set you up for long-term success. If you clinically qualify for Noom Med, you'll get:

■ **Personalized care and ongoing support** from expert clinicians

■ Access to GLP-1 medications

**1:1 and group coaching** to keep you accountable

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