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Life with GLP-1s

It's Time to Reframe Obesity

Clinical and cultural conversations around obesity have long revolved around BMI (and its credibility), harmful stereotypes, issues of equity and the multi-million dollar weight loss industry. Now that GLP-1s have entered the picture as a quick-acting weight loss solution, there's an argument to be made that we're getting farther from the root of the problem: weight loss maintenance.

In the U.S., obesity rates have been steadily increasing since the 1980s, including a sharp increase in adult obesity starting around 2010, despite much attention and research. In 2023, chronic diseases, including diabetes and hypertension, were among the leading drivers of our nation's $4.1 trillion in **annual health care costs**.

When it comes to weight loss maintenance and long-term GLP-1 use, not all patients want to or need to de-prescribe, but many also will for a variety of reasons. For GLP-1 results to scale effectively, reframing the discourse around obesity is critical. Obesity is a complex chronic disease, as classified by the **AMA**, and it requires long-term––even lifelong––treatment that includes lifestyle interventions to sustain healthy weight loss during and long after GLP-1 use.

Regaining weight is the norm, not the exception

The widespread use of GLP-1s raises many questions about **price**, **access**, and **side effects**. But the leading question surrounding GLP-1s should be, how can patients achieve successful long-term outcomes? For many individuals hoping to control their weight, it's frequently a nonlinear, difficult journey.

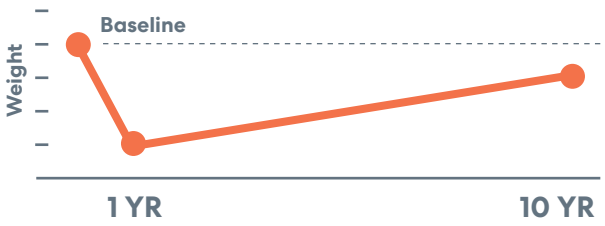
According to **NHANES data**, about 17% of people who've at any point dealt with having excess weight or obesity have maintained a 10% weight loss for at least a year. This isn't an indication that regaining weight is a self-fulfilling prophecy; rather, it illustrates how difficult weight loss and weight loss maintenance truly is. For example, **follow-up data** from the Diabetes Prevention Study (funded by the **National Institute of Diabetes and Digestive and Kidney Diseases)** showed that after losing an average of 15 lbs in one year, participants gained approximately 11 lbs of that back within 10 years.

In the age of GLP-1s, the same type of outcomes hold true. The **STEP 1 Extension study** examined body weight changes for individuals who completed an initial 68-week treatment period (which included semaglutide or placebo, along with lifestyle interventions). This trial determined that participants regained two-thirds of their initial weight loss during the 1-year off-treatment follow-up period after stopping semaglutide and lifestyle intervention support. The literature shows that weight regain is highly correlated with stopping the medication combined with the absence of active lifestyle intervention.

It's worth noting that even bariatric surgery, which shows better long-term weight loss effects than GLP-1s, still demonstrates how common weight regain is and how further research on the topic is necessary. In a 2016 systematic review of over 7,000 bariatric **studies**, only 29 (0.4%) of them had at least 80% retention and 2 years of follow-up. Only 4 studies had 5 or more years of follow-up. In those 4 studies, weight regain began 3 years after surgery for patients, implying that the long-term effects of these procedures might not be durable. Nearly 1 in 3 patients undergoing adjustable gastric banding regained almost all of their lost weight within 4 years of surgery, whereas 14.6% of patients undergoing sleeve gastrectomy experienced the same weight regain.

How Hard is Weight Loss?

DPP Study[1]



-15 lbs

+11 lbs

STEP 1 Extension Study (GLP-1s)[2]

Participants regained 2/3 of intial weight loss.

Bariatric Surgery Study[3]

1 in 2 patients undergoing banding regained all lost weight within 4 yrs of surgery.

1 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3135022/
2 https://pubmed.ncbi.nlm.nih.gov/35441470/
3 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5112115/

The physiology of weight loss—and regain

Taking the data on weight loss and weight regain at face value does a disservice to the millions of Americans living with obesity. Understanding the physiology at play is the only way to develop more empathy, and raise awareness for the need to develop comprehensive, long-term treatment plans.

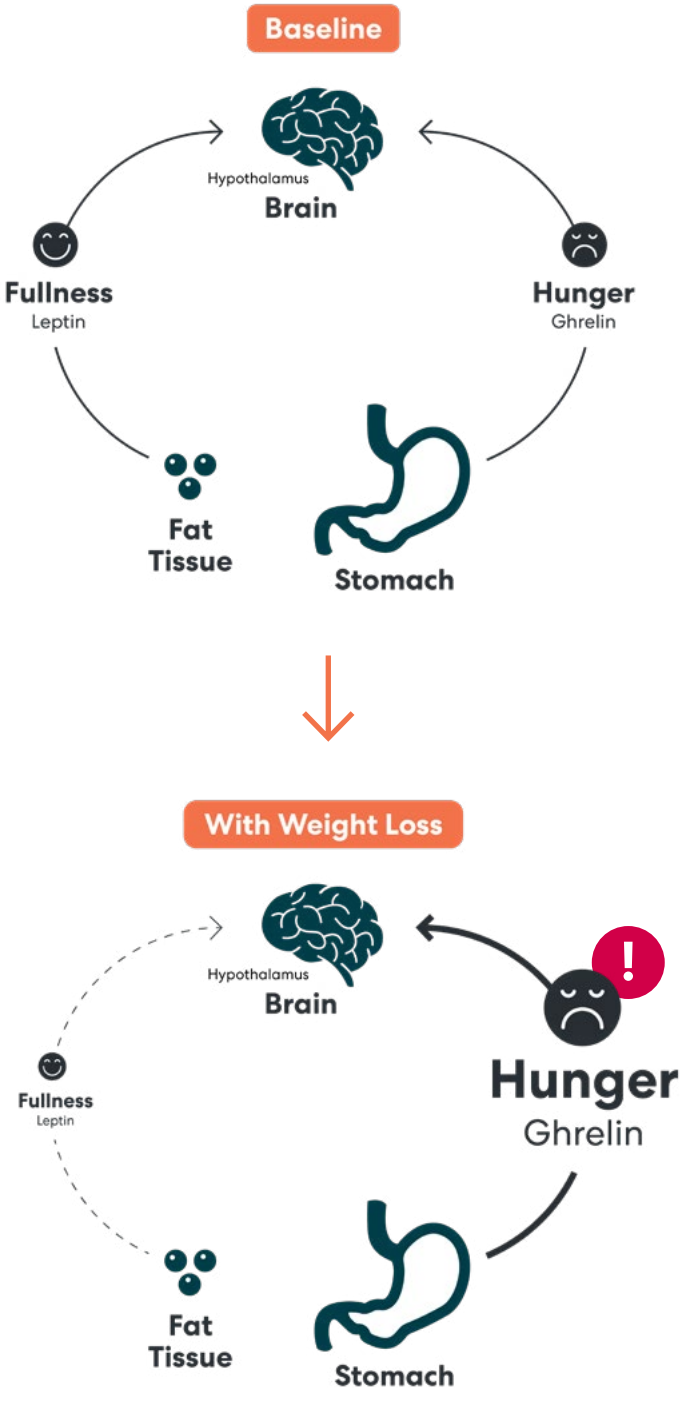
Unpacking the concept of energy balance, which refers to calories in and calories out, is a good starting point. If an individual is in a caloric deficit, they lose weight; and if an individual has a caloric surplus, they gain weight. However, many other complex factors—some modifiable and others not—impact the physiology of weight loss. For example, what are the primary drivers of appetite? And how does weight loss, and the brain on GLP-1s, affect them?

Hunger and satiety (feeling full) are managed by a complex interaction of hormones between the stomach and brain. The stomach produces **ghrelin**—the "hunger hormone"—which signals the hypothalamus to stimulate appetite. Fat tissue produces **leptin**—the "fullness" hormone—which signals stored energy to the hypothalamus; the signal relayed from both ghrelin and leptin helps the brain regulate how full or hungry we feel.

GLP-1s help decrease appetite, speed up satiety and slow down the process of stomach emptying by activating receptors that increase insulin release. Since these drugs lead to a reduction in fat mass, GLP-1 users typically see their metabolic rate—the number of calories burned when the body performs basic, life-sustaining functions—slow considerably. Based on genetics, age, and other factors, the body has a metabolic set point that responds accordingly to energy expenditure. The 24 hour **total energy expenditure** by the body is made up of three components:

- 60% Resting energy expenditure, i.e. watching TV
- 30% Non-resting energy expenditure, i.e. exercising
- 10% thermic effect of feeding, i.e. digesting, absorbing and metabolizing food

Since GLP-1s impact appetite, individuals can lose weight without exercise. This typically leads to lower metabolism. However, after finishing GLP-1 use, the appetite returns while lower metabolism can persist for years. Over time, if an individual starts eating more and their caloric intake exceeds the needs of their lower metabolism, it can lead to regaining lost weight. This underscores the importance of stepping up activity to maintain optimal weight health. Building up lean body mass can help with recovering their metabolism.



Weight loss isn't a cure for obesity

Obesity is a chronic, lifelong disease that requires long-term management even if they lose weight. The framework was established in 2013 by **AMA**, and the **Obesity Medicine Association** (OMA) has established it as "chronic, relapsing, multi-factorial, and neurobehavioral." The descriptor "complex" might be overused, but here it certainly applies. Obesity involves genetics, environment, and social factors, often beyond personal control—not willpower alone.

The story of relapsing, or losing weight only to gain it back, is all too familiar. This common cycle underscores why obesity is often a lifelong battle. In a **meta-analysis** of long-term weight loss studies, more than half of the weight lost was regained within two years, and by five years more than 80% of weight was regained. However, obesity can be successfully managed with the implementation of four key principles:

Reduced caloric intake

The need to reduce caloric intake cannot be escaped. After weight loss is achieved, an individuals' caloric needs are expected to be lower. Additional metabolic adaptations can also take place, further decreasing the caloric needs of an individual. This may come as a surprise to individuals, and can be very frustrating. What many don't realize is that significant fat loss is **associated** with a decrease in the production of body heat metabolic rate, which can facilitate a return to the initial weight.

Physical activity

In trials comparing exercise combined with GLP-1 use versus GLP-1 use alone, those with exercise **maintained more weight loss**. In terms of quantity, we always want to know how much. We know now that people who have lost over 5% of their body weight will need to **eat less and exercise more** than comparable never-obese peers to maintain results. But what type of exercise? A key tenet they need to adhere to is building lean body mass through strength training. **Evidence suggests** they do not need to spend long hours at the gym. Modest resistant training 3 times a week is important for all stages of GLP-1 care to maintain weight loss, as it increases muscle mass and, ultimately, metabolic rate.

However, 3 times per week may be hard to achieve for people who may not be exercising, especially if they were losing weight through their GLP-1 use without doing much exercise at all. When they're no longer on the medication, they are hungrier, their calorie burn is down, and now they need to exercise more. It can be daunting.

Weight monitoring

It's well documented that people who weigh themselves daily are more likely to maintain weight loss. In fact, a **meta-analysis from 2019** suggested that weighing in was one of the most predictive behavioral factors for long-term maintenance.

Lifestyle program support

Sustained behavior change, which is the most significant issue that underlies long-term weight loss after the drugs have been discontinued, is hard. While most people disengage after their initial weight loss, the ongoing support of a lifestyle program can help ensure lasting weight health. Omada follows four core principles for running a successful lifestyle program:

Develop self-efficacy: Helping individuals living with obesity build belief is crucial because behavior change isn't intended to be for the short-term. It takes care teams composed of **committed health coaches and clinicians** to help build self-efficacy. People are facing real barriers, both in and out of their control, but finding belief in themselves is something to aspire to.

Build a skillset: Providing the tools for committed behavior change is very important for individuals on GLP-1s and those who are going off the medications. There are many strategies that will help keep the weight off. Knowing them, honing them, and having a health coach available when slip-ups happen—as they do—removes pressure.

Provide social support: Social communities, specifically for prospective GLP-1 users, current users, or recent users, have quickly become popular. This provides the opportunity to build relationships with coaches and peers, and allows for multifaceted support during rough patches.

Support all stages of GLP-1 care: That's why Omada helps members do the hard work of maintaining weight health by starting the necessary behavior change while the member is taking the drug, as opposed to after. The goal is for members to develop healthy lifestyle changes while they are seeing quick results, then help turn those changes into habits.

As time goes on we will learn more about who needs obesity medication long-term and who is best-positioned to maintain weight loss after taking GLP-1s with lifestyle changes alone. It's becoming increasingly clear that traditional health care often has little to offer individuals living with obesity apart from continuing to take medication.

The takeaway is not that people should come off obesity medication. In fact, for many individuals these drugs are a very important tool to achieve long-term weight health. However, some data shows that many people stop taking the drugs **within a year**. This is partly due to challenging **side effects**, coverage limits, and preferences. However, for everyone considering GLP-1s, on GLP-1s, or just off GLP-1s, the most likely path to success is ongoing, comprehensive support.

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