MEDICAL STUDENTS FOR SIZE INCLUSIVITY

GLP-1 Agonist Medications: Informed Consent Resource

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I. Introduction

This resource was created by Medical Students for Size Inclusivity (MSSI), an international community of medical students dedicated to addressing weight bias in medicine. We have seen the huge increase in GLP-1 agonist prescriptions specifically aimed at promoting weight loss, and are concerned that patients may receive misleading or insufficient information from their healthcare providers before being started on them.

While MSSI does not believe weight & BMI are accurate measures of health, or that weight loss improves health outcomes, we also champion patient autonomy. Weight discrimination permeates so many aspects of society, and the physical and mental harm it directly causes fat people is immeasurable and far-reaching. Our goal is to give patients desiring to start medications to lose weight a more comprehensive understanding of the risks and benefits associated. Knowing what alternatives are available is part of full informed consent, so we also include evidence-based options for improving health that do not require weight loss.

II. An Overview of GLP-1 Agonists

Glucagon-like peptide 1 (GLP-1) receptor agonists are medications that cause a release of insulin from the pancreas, delaying stomach emptying and causing early satiety ("feeling full"), which reduces blood sugar and appetite. The medications are originally marketed for glycemic (blood sugar) control in adults with type 2 diabetes mellitus, in tandem with diet and exercise.

GLP-1 agonists have a side effect of weight loss, and recently made headlines as "miracle, game-changing, weight-loss drugs," increasing their desirability and overall use. As an unintended consequence, there has been decreased medication availability for those living with diabetes.

List of GLP-1 Agonists:

- Semaglutide is sold under the brand names OZEMPIC and WEGOVY*.
- Dulaglutide is sold under the brand name TRULICITY.
- Tirzepatide is sold under the brand name ZEPBOUND* and MOUNJARO.
- Liraglutide is sold under the brand name SAXENDA*.

All of the above medications are self-injected in the abdomen, thigh, or arm, once a week.

- RYBELSUS is a semaglutide formulation available orally.

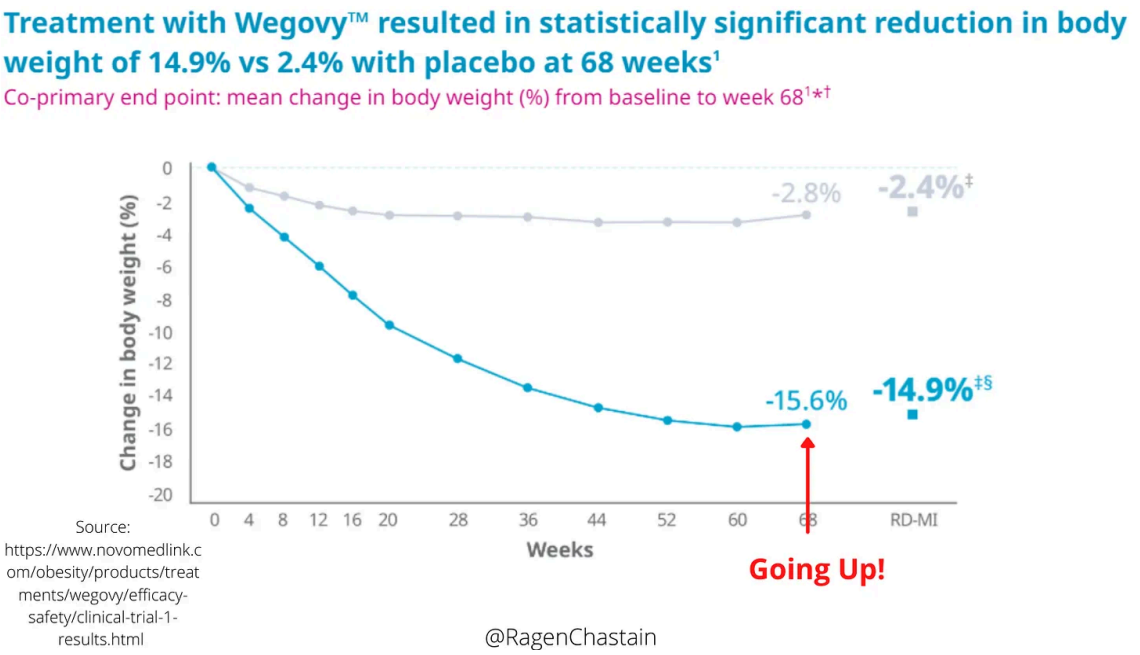
Those indicated by * have been granted FDA approval and specifically marketed for chronic weight management, with addition of a reduced calorie diet and exercise. Some limitations of FDA approval are discussed in Box #2 below.

III. Responses to 5 Common Claims

#1: GLP-1 agonists help patients lose weight rapidly.

A MORE COMPLETE VIEWPOINT:

- The Wegovy trial was only a year long, and by the end, weight loss had plateaued and was starting to increase, while patients were still on the medicine. (1)



- In addition to medication, the study's patients were on a **low calorie diet and exercising 180 min/wk**. The control group on the same regimen *also* lost large amounts of weight, without taking the medication.
- Weight was **regained** if the medication was stopped, along with loss of cardiometabolic benefits.

Currently, the longest study published on GLP-1 agonists for weight loss includes a follow-up period of only **2 years,** meaning that we do not know the safety or effectiveness of these medications past the 2-year mark. (2) In all interventions previously studied, weight from caloric restriction is regained, despite ongoing dieting, over a period of 2-10 years.

Read more here and here.

#2: These medications have limited side effect profile and are generally well tolerated, “safe” medications

A MORE COMPLETE VIEWPOINT:

In the Semaglutide trial, 74% participants experienced GI side effects, including nausea, vomiting, diarrhea, abdominal pain, and bloating. (3) Around 10% had more serious side effects including gastroparesis, kidney disease, and pancreatitis. The medication carries a black box warning for thyroid cancer, and has a possible association with pancreatic cancer.

In the United States, the FDA already acknowledges a risk of suicidal ideation with GLP-1 receptor agonists. Wegovy (semaglutide) and Saxenda (liraglutide) both carry warnings about suicidal behavior and ideation on their official FDA labels. (4, 5)

On September 28, 2023 the FDA added a warning for the life threatening side effect of ileus, a blockage of the intestines, which have been reported in 33 cases. (6)

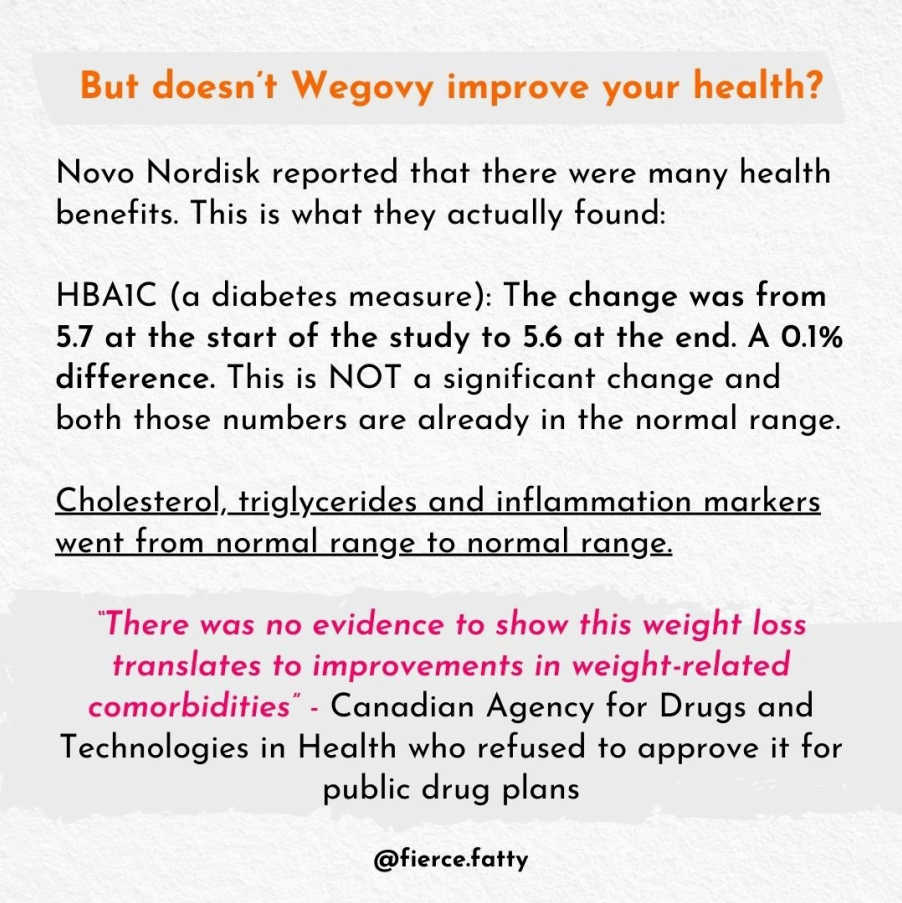
Other side effects that have not been tracked include the development of disordered eating and eating disorders, stigma associated with “cheating” for weight loss, and the psychological harms of weight regain.

Aside from stated adverse effects and lack of long-term evidence, it is also important to understand that **many previously FDA-approved weight loss medications were later removed from the market** due to safety concerns. For example, Fen-Phen (a combination drug of fenfluramine and phentermine) entered the market in the early 1990s, but was removed in 1997, after a third of patients in a safety clinical trial demonstrated heart valve abnormalities not noted previously. (7) Additionally, the weight loss drug Lorcaserin (Belviq), entered the market in 2012, but was removed in 2020 after being associated with an increased risk for cancer in safety trials. (8) These examples emphasize that medications can be approved by the FDA and made widely available to consumers, before long term effects and outcomes are known.

#3: Losing 5–10% of your body weight produces clinically meaningful health benefits.

A MORE COMPLETE VIEWPOINT:

Review of research has shown that the majority (95%) of people intentionally trying to lose weight regain that weight. (9) Studies also show that the cycle of losing weight then re-gaining weight (called "weight cycling") has negative impacts on health. (10)



The idea of other health issues being "obesity-associated" is scientifically questionable, since **weight cycling**, **weight stigma**, and **healthcare inequalities** are all correlated with the same health issues to which being higher weight is correlated. (11)

Weight loss as a profitable business:

GLP-1 agonists are the newest "kid on the block" as far as diet drugs go, but they are far from the first weight-loss drug we have seen approved and offered to patients. The weight loss/diet industry is a $76 billion dollar industry, with the best interest of profits in mind, not patients. Persistent and wide-spread direct to consumer advertising for GLP-1 agonists on social media has increased the demand for these drugs worldwide, encouraging folks to take part in the #ozempicchallenge (12). Keep this in mind when making the informed health decisions that are right for you.

#4: There are evidence based, promising research trials to support the use of these medications.

A MORE COMPLETE VIEWPOINT:

There are many limitations of the current research, including...

- The longest trials are only 2 years long, so long term safety and efficacy for health and weight loss have not been established.
- There is no evidence of long-term weight loss or health benefits after stopping the medication.
- Most GLP-1 agonists, including Ozempic and Trulicity, were approved to treat individuals with type 2 diabetes, not as weight loss medications. Weight loss was an *unintentional side effect* that became a profitable business venture.
- These medications have not been studied in patients with history of pancreatitis.
- The majority of data is on white women (13)
- Trials on these medications are funded, designed, overseen, and written by employees of the pharmaceutical companies and/or researchers with strong financial ties to these companies, ultimately increasing their profit in sales of these medications.

#5: GLP-1 agonists reduce "brain chatter/food noise," allowing those who overeat to stop thinking so much about food and eat less.

A MORE COMPLETE VIEWPOINT:

Brain chatter and obsessive thoughts about food and eating are a recognized phenomenon, and can occur whenever an individual under-fuels their body, regardless of body size or shape 14. In other words, food noise is an expression of hunger, and the body's natural response to inadequate fuel. (15, 16, 17)

Brain chatter can be improved by non pharmacological interventions.

GLP-1 agonist medications block these natural signals, thus quieting that voice, but also enable long term undernourishment, which can cause harmful health consequences, even in a larger bodied person. For those that can tolerate them, these medications do make it easier to "diet" in the short run. However, we see the same adaptations occur including weight loss plateaus, despite ongoing restriction. Some patients have reported the medications have led to a distressing loss of interest in food overall. In extreme cases, nutritional deficit associated illness can develop.

IV. Alternative Options to Weight Loss Medications

There are many reasons people want to lose weight. Given the limited evidence to suggest that weight loss is safe and sustainable, even with medication, we encourage patients who may be interested in improving their health, to consider alternatives. To start, if your doctor is recommending weight loss for a health condition, you could ask what they might recommend to treat the same condition in a patient of a smaller body size.

As simple as it might seem, an alternative to using weight loss medications is to make no changes. Weight alone does not determine health, and there are other markers of well-being that are more accurate and useful. As mentioned above, interventions to reduce weight, including dietary restriction, exercise, and medications, have not resulted in sustainable weight loss for most people in the long term. If your healthcare provider is not willing to move away from using weight as a metric of health, finding a more supportive environment may be your next step.

Suggestions for Finding Size Inclusive Providers:

- Use search terms "size-inclusive", "weight-neutral", "weight-inclusive", or "Health At Every Size (HAES)-aligned" when looking for a new physician. You can use size-inclusive provider directories to look for providers in your area:
  - Health at Every Size® Healthcare Provider Listing
  - Weight Neutral Provider Excel
  - https://www.fatfriendlydocs.com
- Ensure your provider's office promotes size inclusivity by offering inclusive seating in all patient care areas, access to appropriately sized blood pressure cuffs, and the option to decline being weighed and opt out of discussions about weight loss.

Below we present some other more sustainable ways to improve health, which do not focus on altering body weight, shape, or size:

Movement

Increasing movement by any amount can increase wellbeing, disease management and reduce mortality (18). This can look like exercise at a gym and can also include gardening, housework, dancing, playing with a dog or kids, and walking. Reducing uninterrupted time sitting with small amounts of movement also is helpful.

Nutritious Dietary Choices

Working on positive additions to your dietary intake can improve health outside of medication use. Here are a few ideas:

- Consuming a wide variety of foods, including servings of vegetables, fruits, legumes/beans, and whole grain products daily.
- Learning to recognize your body's natural hunger and fullness cues.
- Taking in enough calories every day for your body's needs.

- Working with a size-inclusive (and culturally safe) dietitian can help support health food choices, tune in to your body's requirements, and offer new ideas that are easy to integrate into your food prep.

Mental Health Care

Internalized weight stigma has significant negative implications on mental health, including increased depression, anxiety, body dissatisfaction, and eating disorder symptoms, and decreased self-esteem. This association held true even when the data was controlled for weight, suggesting that it is the experience of weight stigma, not an individual's weight, that contributes to poorer mental well-being. (19, 20)

- **Mental Health Services**
  - Individual counseling / virtual counseling services
  - Group therapy sessions
  - Support groups
- **Free/Low-Cost Mental Health Practices**
  - Journal prompts
  - Gratitude and Mindfulness practices
  - Guided meditations on apps like Insight Timer or on YouTube
  - Developing strong social ties
  - Recreation

Sleep Hygiene

Another proven way to positively impact health is to improve sleep quality & quantity. Strategies include:

- Having a consistent bedtime / wake time
- Ensuring a dark and slightly cool room
- Implementing "wind down time" when electronic exposure is limited 30 minutes prior to sleep
- Sticking to a consistent bedtime routine, which could include stretching, hot showers, reading, or journaling

MSSI would like to especially thank and credit Ragen Chastain, Marquisele Mercedes, and Vinny Welsby for the work they have put into reviewing and analyzing the clinical trials behind these medications.

V. In Summary...Questions to Ask Yourself Before Starting GLP-1's:

1	Do I have any health conditions that should be addressed more directly, rather than with a trial of weight loss? Are there screenings or preventative care measures that are being deferred for a trial of weight loss?
2	Do I feel that short term weight loss is worth the cost and potential side effects? What about if it results in weight cycling?
3	Do I have a history of disordered eating that might be triggered by beginning this medication, or by a loss of appetite?
4	If I were to set weight aside, what would make the biggest difference in my health? Am I pursuing that as well?
5	Do I need help caring for myself in the body I have now? What professionals or community could I access for help?

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www.sizeinclusivemedicine.org

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