

## Ozempic or Meal Replacement Shake? The Answer Might Surprise You!

**Nataniel Viuniski\***

*Department of Human Nutrition, School of Medicine, UNIDEAU - University Center, Caxias do Sul, Brazil*

**\*Corresponding Author:** Nataniel Viuniski, Department of Human Nutrition, School of Medicine, UNIDEAU - University Center, Caxias do Sul, Brazil.

**Received:** July 23, 2024; **Published:** August 22, 2024

### Abstract

Obesity, driven by high caloric intake, poor nutrition, sedentary lifestyles, and genetic factors, affects over 1 billion people globally and has severe health consequences.

Recent advancements have introduced effective medications like GLP-1 agonists, including semaglutide (Ozempic/Wegovy), which show promise in reducing obesity-related complications.

Meal replacement protein shakes, providing balanced nutrients and high-quality proteins, can complement GLP-1 agonists, mitigating side effects and preserving muscle mass. Studies comparing semaglutide and meal replacement protein shakes reveal that the latter might produce similar or better weight reduction while maintaining lean mass.

Combining these approaches with lifestyle changes, including diet, exercise, stress management, and sleep improvement, could optimize obesity treatment and outcomes. This review emphasizes the potential synergy of combining GLP-1 agonists and meal replacement shakes, advocating for further research to validate these strategies and improve obesity management.

**Keywords:** *GLP1 Agonists; Meal Replacement; Obesity*

### Introduction

People with high caloric intake and low nutritional quality food, a sedentary lifestyle, and genetic predisposition tend to develop obesity over time, resulting in various negative health impacts [1].

A study in collaboration with the WHO, published in *The Lancet*, revealed that more than 1 billion people worldwide live with obesity. Between 1990 and 2022, the incidence of the disease more than doubled among adults and quadrupled among children and adolescents aged 5 to 19 [2].

The good news is that, for the first time in the history of medicine, effective medications to treat excess weight have emerged which also produce a significant reduction in medical complications and mortality associated with obesity. Among these, GLP-1 agonists stand out, such as semaglutide, marketed as Ozempic or Wegovy.

### The rising of GLP-1 agonists

In the SELECT study [3], sponsored by Novo Nordisk and started in 2018 in 41 countries, 17,604 people with cardiovascular diseases were randomized into two groups. One group took 2.4 mg of semaglutide weekly, while the other received a placebo. After 24 months,

the average weight reduction was 9% in the semaglutide group, compared to only 1% in the placebo group. Participants who reduced approximately 9% of their weight in two years had, on average, 20% fewer occurrences of strokes, acute myocardial infarctions, and deaths from other causes.

In light of these findings, an important question to be answered is: did people live longer and have fewer diseases because they took the medication or because they reduced excess body fat, especially visceral fat? Would other effective weight reduction methods produce the same effects?

With the publication of these data, there has been little discussion on this issue. However, many medical colleagues have been celebrating “a historic date in obesity treatment,” and the manufacturer of semaglutide becoming the most valuable brand in Europe. We also observed that this rather expensive medication is in short supply in Brazilian pharmacies, where no medical prescription is needed to acquire it.

In the United States, more was spent on these medications than on cancer treatment by some health plans, and many plans have decided not to reimburse expenses for GLP-1 agonists for weight loss [4].

With decades of experience treating obesity scientifically and ethically, we have learned that many people do not want to lose weight; they want to be made to lose weight! If a health professional tells a patient that in order to treat obesity it is necessary to change diet and lifestyle, while another states that a weekly injection is enough, most people will opt for the second alternative.

The central point is that one choice does not exclude the other. The ideal scenario to prevent and treat global obesity crisis would be to correctly use effective existing drugs (and the new ones that will be launched soon), along with improvements in nutrition, physical activity, stress control, and sleep quality in the obese population [1].

People who use this type of medication without professional guidance and without improving their diet, especially without including high-quality proteins in all meals and without engaging in adequate physical exercise, lose less weight and have a higher number of medical complications. The most frequent complications are nausea, vomiting, constipation, hair loss, lack of energy, and loss of muscle mass with consequent reduction of metabolic rates which favors weight regain after discontinuation of the medication [5].

### The role of meal replacements

In preventing these undesirable effects and optimizing the expected results, protein shakes and partial meal replacements can play a central role, provided they are used along with a healthy and active lifestyle. A well-designed meal replacement shake, containing about 20 g of high biological value protein and a balance of macronutrients and micronutrients with about 200 kcal per serving, can be used to replace up to two of the three main meals of the day, with various flavors and preparation forms to avoid diet fatigue [6].

Patients using GLP-1 agonists report a lack of appetite and taste changes, making it difficult to consume many healthy foods [5]. This does not occur with protein shakes. Due to their practicality, palatability, and nutrient density, these foods can be considered great companions to drugs like semaglutide, which have been referred to as “Ozempic Friendly” foods in some scientific articles [7].

For individuals using these medications, meal replacement shakes can contribute to a higher protein intake, which can help preserve or promote muscle mass in people who exercise. Additionally, they provide the carbohydrates, healthy fats, vitamins, minerals, and calories necessary to build lean body mass [6].

**Protein shakes can be extremely useful at three distinct stages when using GLP-1 receptor agonists, as discussed below**  
**Initial decision-making on the use of protein shakes versus GLP-1 receptor agonists**

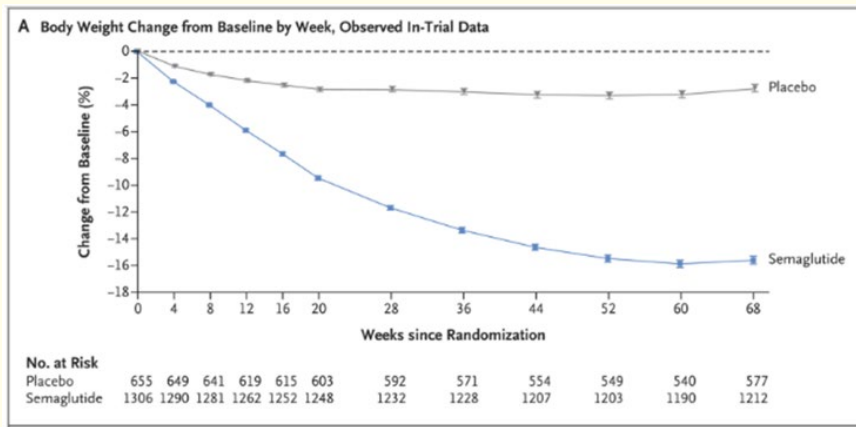
At this stage, it is crucial to compare the pros and cons of each approach: One option is to adopt a lifestyle that includes foods, nutritional supplements, stress management, and physical activity. The strategy of replacing one or two meals with a protein shake can be part of this healthy and active lifestyle.

Alternatively, one can opt for the use of hormonal receptor agonist medications, which require injections, have high costs, and may induce various side effects such as nausea, constipation, reduced energy levels, muscle mass loss, and even gastric paralysis.

For selected cases, the best approach would be to harmoniously and synergistically combine both strategies based on the best available scientific evidence.

A double-blind study published in the *New England Journal of Medicine* [8] included 1,960 obese adults randomly divided into two groups. The first group received weekly injections of 2.4 mg of semaglutide for 68 weeks, while the second group received a placebo. All participants received general lifestyle change guidance.

As shown in figure 1, at week 12 of the study, the average weight reduction in semaglutide users was approximately 6.5%, and after 68 weeks, the average weight reduction in the semaglutide group was 14.9%, compared to 2.4% in the placebo group.



**Figure 1:** Wilding., et al. [8].

In the supplementary appendix of the same publication [8], the authors presented body composition data from 95 individuals who received semaglutide and 45 individuals who received placebo. Using DEXA in this subpopulation, they evaluated the total weight loss and, of the weight lost, how much was represented by the reduction in total fat, visceral fat and muscle mass, as evidenced in figure 2.

Participants who used 2.4 mg semaglutide weekly lost an average of 17.89 kg body weight, of which 10.4 kg was fat mass, 0.47 kg visceral fat, and 6.92 kg muscle mass. This means that 38.68% of the weight lost was lean mass, which can be detrimental to health [8].

*Supportive secondary endpoints assessed in the DEXA subpopulation*

	N=95	N=45	
Body composition change from baseline to week 68 (DEXA)			
Total fat mass			
Kg change	-10.40	-1.17	ETD: -9.23 [-12.72; -5.74]
Percentage-points change in total fat mass proportion <sup>§</sup>	-4.19	-0.19	ETD: -4.00 [-6.27; -1.73]
Regional visceral fat mass <sup>¶</sup>			
Kg change	-0.47	-0.03	ETD: -0.45 [-0.60; -0.30]
Percentage-points change in regional visceral fat mass proportion <sup>  </sup>	-2.65	0.58	ETD: -3.23 [-5.35; -1.10]
Total lean body mass			
Kg change	-6.92	-1.48	ETD: -5.44 [-7.07; -3.81]
Percentage-points change in total lean body mass proportion <sup>¶</sup>	3.61	0.11	ETD: 3.50 [1.35; 5.64]

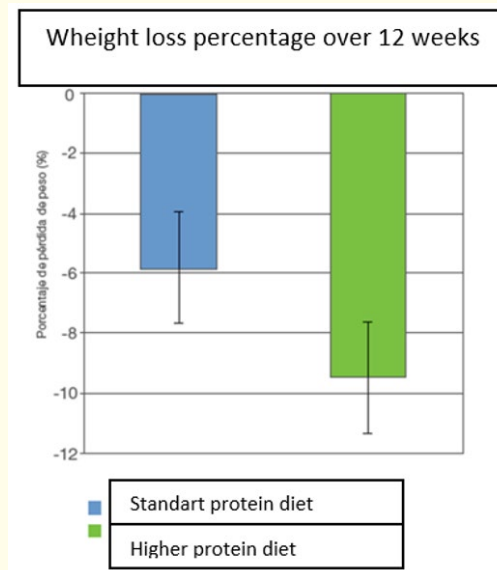
**Figure 2:** Wilding., et al. [8].

Ideally, a weight reduction program should produce fat loss without compromising muscle mass, with an acceptable muscle mass loss of up to 20% [9], well below the 38.68% observed in the study.

Regarding the use of protein shakes in the treatment of obesity, Campos-Nonato., et al. [10] conducted a study published in *Obesity Facts - European Journal of Obesity* to evaluate the effect of a high-protein diet compared to a standard diet. The study involved adults aged 20 to 60, divided into two groups over six months, both following a hypocaloric diet with protein shakes:

- Group A: Standard protein intake (0.8 g/kg).
- Group B: Higher protein intake (1.34 g/kg).

Subjects in both groups experienced weight loss and reduced abdominal circumference. However, those with high adherence to the plan (more than 75% of the time) in the higher protein intake group (Group B) had significantly greater weight loss compared to the standard protein intake group (Group A), as can be seen in figure 3 below.



**Figure 3:** Campos-Nonato., et al. [10].

When comparing the weight reduction results in this study using protein shakes with the results of the study using 2.4g semaglutide per week, as shown in figure 3, it can be seen that in the first 12 weeks of the clinical trial, the weight reduction in Group A - standard protein intake - was similar to the weight reduction in those receiving 2.4g semaglutide over the same 12 weeks; in both cases approximately 6% reduction from initial weight. In Group B - higher protein intake - weight reduction result at 12 weeks was significantly superior to the semaglutide group, with an approximate reduction of about 9% from of initial weight.

Despite the methodological differences between the studies, comparing the results is valid for the reasoning developed in this article. These data should be considered in choosing the therapeutic path, bearing in mind that changes in diet, physical exercise, and replacing two of the three main meals with protein shakes require more effort from the patient and the medical team than the simple recommendation of a weekly semaglutide injection [8,10].

In making any therapeutic decision, combining the two approaches may be the most appropriate solution for many cases. However, it is necessary to revisit the issue of body composition. As seen in figure 1, in the semaglutide group, there was a loss of lean body mass of about 38.6% [8]. What about the group that lost weight with meal replacement shakes? How did these individuals fare in this regard?

In a study published in *Nutrition Journal* [11], the authors compared two groups of patients:

- Group I - Protein diet group - using protein shakes.
- Group II - Traditional diet group.

The clinical trial was divided into two phases: weight loss and weight maintenance. In the weight loss phase, the protein diet group replaced two meals with protein shakes, and the traditional diet group used traditional foods, both producing the same caloric deficit. In the weight maintenance phase, all participants replaced one meal with a protein shake daily.

In the group that replaced two daily meals with protein shakes, there was an average reduction of 11 kg during the weight loss phase (12 weeks), of which approximately 9 kg was fat mass and 2 kg was muscle mass.

When comparing the two studies, it can be seen that while the semaglutide group had a lean body mass reduction of approximately 39%, the protein shake group had a loss of lean mass below 20%, as clearly shown in figure 4.

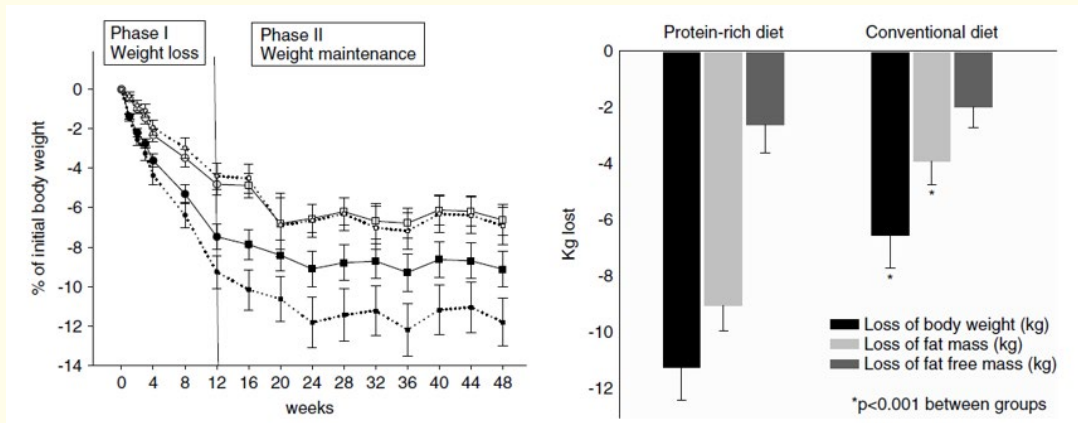


Figure 4: Treyzon., et al. [11].

In conclusion, it is evident that more studies using semaglutide in conjunction with protein shakes are necessary to compare both weight loss outcomes and preservation of lean mass, and especially to determine if the benefits of using both approaches together would be greater than the results obtained separately.

### The role of meal replacement shakes in optimizing GLP-1 agonist treatment and reducing side effects

GLP-1 agonists are often abandoned by patients due to their side effects, mainly those related to the digestive system, such as nausea, vomiting, constipation, taste changes, heartburn, and gastroesophageal reflux. In extreme cases, gastric paralysis may occur [7]. Additionally, muscle mass loss due to inadequate protein intake is a significant complication, commonly referred to in the lay press as “Ozempic face,” “Ozempic head,” or “Ozempic butt.” Hair loss, common in both sexes, is also a result of nutritional imbalances [5].

These side effects have led to a transformation in the food industry, with some multinational companies reformulating their products to meet the needs of Ozempic users, resulting in the creation of foods termed “Ozempic Companion” or “Ozempic Friendly” (<https://www.healthline.com/health-news/ozempic-best-and-worst-foods-to-eat-while-taking-weight-loss-drugs>).

Protein shakes emerge as an excellent “Ozempic Friendly” option, providing a balanced meal with essential micro and macronutrients, especially high biological value proteins, controlled calories, pleasant taste, and ease of digestion, reducing gastric side effects [12].

In clinical practice, replacing one or two main meals with protein shakes, combined with a healthy diet, regular physical exercise, and the use of GLP-1 agonists, not only decreases digestive side effects and protects against loss of lean mass but also improves health and weight loss outcomes, promoting better adherence to treatment.

### Use of protein shakes in weight maintenance after initial loss

Obesity is a chronic disease, and its long-term control represents one of the greatest challenges. It is often easier to lose weight than to maintain it long-term [12]. Most people manage to reduce body fat at some point in their lives, but maintaining a healthy weight is less common.

The success rate in weight maintenance varies according to several factors, including the intervention method, the initial severity of obesity, and post-treatment follow-up.

Studies indicate that after one year, only 20% to 30% of patients manage to maintain weight loss, and this rate decreases over time. After five years, it is estimated that only 5% to 10% of patients maintain reduced weight, with significant variations depending on the type of intervention and individual factors [13].

Recent studies published in the *Journal of the American Medical Association* (JAMA) have aimed to evaluate the effects of GLP-1 agonists, such as semaglutide and tirzepatide, in maintaining reduced weight after discontinuing their use. The results show that these medications are effective in reducing weight only during the period of continuous use.

In a study with 670 participants tirzepatide, when used at the maximum dose, once a week, reduced body weight by 20% after nine months. When the medication was replaced with a placebo, there was a 14% weight regain in three months, while the group that continued with the medication lost an additional 5% of the initial weight [14].

A similar study with semaglutide showed that after five months of treatment, participants lost 10% of the initial weight. In the subsequent 11 months, the group that continued with the medication lost an additional 8%, while the group that received a placebo regained 7% of body weight [8].

The strategy of using partial meal replacements along with the adoption of healthy habits has shown effectiveness both in maintaining lost weight and preventing weight regain. Studies indicate that protein shakes, soups, and nutritional bars, combined with a balanced diet and physical activity, can help control caloric balance and sustain weight loss [10,11,15].

These meal replacements offer a convenient and balanced alternative in terms of nutrients and calories, promoting good satiety and stability in glucose levels, contributing to metabolic health [11].

### Discussion

When comparing the effects of semaglutide versus the use of meal replacements, there is no question that the weight loss with GLP-1 drugs, on average, is greater than that seen with a meal replacement approach. In a multi-year study of meal replacements in a highly compliant population in Germany [16], subjects were randomly assigned to an energy-restricted diet or a diet with two meal and snack replacements for three months; for the remaining four years of the study, all subjects received one meal and one snack replacement daily. Those who received two meal replacements during the first three months experienced weight loss of approximately 10% from baseline and maintained this loss over the course of the first year, while the energy-restricted group lost less than 5% of their starting weight during the first three months of the study.

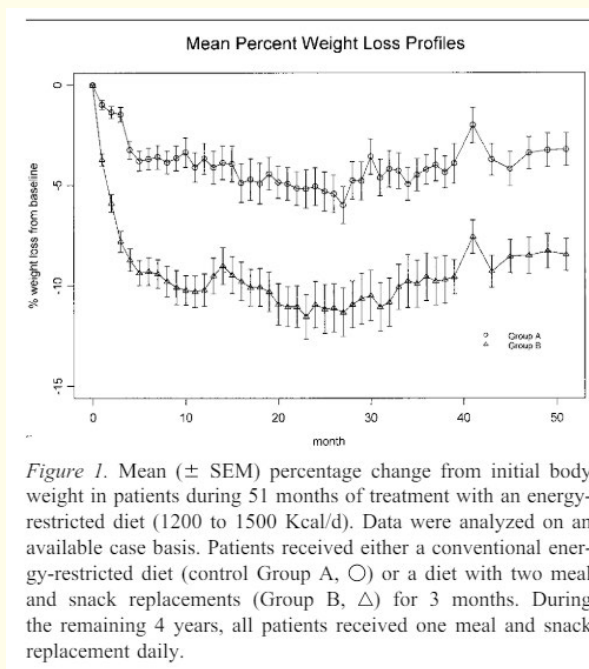


Figure 1. Mean ( $\pm$  SEM) percentage change from initial body weight in patients during 51 months of treatment with an energy-restricted diet (1200 to 1500 Kcal/d). Data were analyzed on an available case basis. Patients received either a conventional energy-restricted diet (control Group A,  $\circ$ ) or a diet with two meal and snack replacements (Group B,  $\triangle$ ) for 3 months. During the remaining 4 years, all patients received one meal and snack replacement daily.

Figure 5: Flechtner-Mors., et al. [16].

The comparison at 12 weeks is scientifically valid but longer-term studies of meal replacements have never shown an average of 20% weight loss, such as that seen with the use of semaglutide and other GLP1 agonists in the studies cited here.

These drugs reduce total calorie intake by affecting both taste and gastric motility. Although many healthcare professionals and the general population may choose to use a method based on supplements combined with diet and lifestyle changes, for severely obese individuals the most appropriate option might be the use of GLP-1 agonists or even a sleeve gastrectomy.

However, based on the best scientific evidence currently available, unless the side effects of sarcopenia and gastrointestinal disorders can be solved, GLP1 receptor agonists should not be used for cosmetic purposes but only in cases of obesity associated with clinical comorbidities and under strict medical supervision. And, due to cost and availability, these drugs are not the definitive solution for the global obesity epidemic.

### Conclusion

Maintaining a healthy weight long-term requires sustainable lifestyle changes, continuous support, and adequate follow-up by support networks. Success rates are influenced by treatment adherence, social support, underlying medical conditions, and other individual factors. For this, new drugs and advances in nutritional science are powerful allies that, when used together, will make a significant difference in solving one of today's greatest public health problems.

### Acknowledgment

I would like to express heartfelt gratitude to Susan Bowerman and David Heber for their inspiration, invaluable suggestions, and thorough revisions throughout the development of this manuscript. Their expertise and dedication significantly enhanced the quality of this work.

### Conflict of Interest

Dr. Nataniel Viuniski is a member of the Nutrition Advisory Board at Herbalife. This affiliation did not affect the data analysis, results, or conclusions presented in this manuscript.

### Bibliography

1. Caballero B. "Humans against obesity: who will win?" *Advances in Nutrition* 10.1 (2019): S4-S9.
2. Phelps NH., *et al.* "Worldwide trends in underweight and obesity from 1990 to 2022: a pooled analysis of 3663 population-representative studies with 222 million children, adolescents, and adults". *The Lancet* 403.10431 (2024): 1027-1050.
3. Ryan DH., *et al.* "Semaglutide effects on cardiovascular outcomes in people with overweight or obesity (SELECT) rationale and design". *American Heart Journal* 229 (2020): 61-69.
4. Young GM., *et al.* "Medicare coverage and patient out-of-pocket costs for cardiovascular-kidney-metabolic medications". *JAMA Network Open* 7.5 (2024): e2412437.
5. Garvey WT., *et al.* "Two-year effects of semaglutide in adults with overweight or obesity: the STEP 5 trial". *Nature Medicine* 28.10 (2022): 2083-2091.
6. Ministério da Saúde Secretária de Vigilância Sanitária, do Ministério da Saúde Portaria No 30, de 13 de janeiro de 1998 (\*). (n.d.).
7. Drucker DJ. "GLP-1 physiology informs the pharmacotherapy of obesity". *Molecular Metabolism* 57 (2022): 101351.
8. Wilding JPH., *et al.* "Weight regain and cardiometabolic effects after withdrawal of semaglutide: The STEP 1 trial extension". *Diabetes, Obesity and Metabolism* 24.8 (2022): 1553-1564.
9. Cava E., *et al.* "Preserving healthy muscle during weight loss". *Advances in Nutrition* 8.3 (2017): 511-519.
10. Campos-Nonato I., *et al.* "Effect of a high-protein diet versus standard-protein diet on weight loss and biomarkers of metabolic syndrome: a randomized clinical trial". *Obesity Facts* 10.3 (2017): 238-251.



11. Treyzon L., *et al.* "A controlled trial of protein enrichment of meal replacements for weight reduction with retention of lean body mass". *Nutrition Journal* 7.1 (2008): 23.
12. Busetto L., *et al.* "Mechanisms of weight regain". *European Journal of Internal Medicine* 93 (2021): 3-7.
13. Dulloo AG. "Physiology of weight regain: Lessons from the classic Minnesota Starvation Experiment on human body composition regulation". *Obesity Reviews* 22.S2 (2021): e13189.
14. Aronne LJ., *et al.* "Continued treatment with tirzepatide for maintenance of weight reduction in adults with obesity: The SURMOUNT-4 randomized clinical trial". *JAMA* 331.1 (2024): 38-48.
15. Sooriyaarachchi P., *et al.* "Meal replacement as a weight loss strategy for night shift workers with obesity: a protocol for a randomized controlled trial". *Trials* 23.1 (2022): 860.
16. Flechtner-Mors M., *et al.* "Metabolic and weight loss effects of long-term dietary intervention in obese patients: Four-year results". *Obesity Research* 8.5 (2000): 399-402.

**Volume 19 Issue 8 August 2024**

**©All rights reserved by Nataniel Viuniski.**