

## CLINICAL IMPORTANCE OF USING MEAL REPLACEMENTS WITH ANTI-OBESITY MEDICATIONS

Robard had six highly regarded medical professionals research the importance of supplying proper nutrition to people utilizing the current diabetes/weight loss medications. The following are the key findings of their research.

- **Meal replacements are an excellent option for those people using the GLP-1 receptor agonists** or other effective obesity medications to supplement the common lack of sufficient protein and certain essential nutrients. — *Dr. Sue Shapses, PhD, RD/RDN; Rutgers University*
- While GLP-1 agents reduce people’s appetite and food preoccupation, **it is also necessary to have behavioral support to navigate the food environment.** Including meal replacements in a person’s daily routine — along with appropriate food choices — is an important tool to support the nutrition needed to achieve and sustain healthy weight loss and maintenance. — *Dr. Kelly Alison, PhD, FAED, FTOS; University of Pennsylvania*
- To maintain vital Lean Body Mass (LBM), **use of high protein meal replacements with semaglutide and other GLP-1 medications will help reduce LBM loss**, which was observed to be 9.7% in DEXA evaluations of 140 patients in the Step 1 Study as reported in the literature.<sup>1</sup> — *Dr. Holly Lofton, MD; New York University*
- **Patients taking semaglutide should incorporate meal replacements** containing protein, prebiotic fiber, vitamins, and minerals to satisfy dietary requirements. — *Dr. Abby Gilman, PhD, RDN, LDN, and Stacey Weatherbee, RDN, LDN; Mainline Health Care*
- Meal replacements could be beneficial and **recommended for people using the GLP-1 Receptor Agents** or other effective obesity medications. Meal replacements could **supplement the anticipated adverse nutritional outcomes such as lack of sufficient protein and other essential nutrients.** Patients must have access to the tools they need to follow an appropriate diet that confers the maximum health benefit of their weight loss. — *Dr. Cheryl Anderson, PhD, MPH MS; University of California San Diego*

Maintenance of metabolic rate is directly related to lean body mass. During weight loss, due to calorie restriction or increased energy expenditure, meeting the body's demand for protein and essential micro nutrients is necessary to minimize the loss of lean body mass. This has been well documented in many placebo controlled weight loss studies utilizing a Very Low Calorie Diet (VLCD) and is the cornerstone of nutritional recommendations following bariatric surgery to maintain adequate protein and micronutrient intake needs.

- Adults with overweight or obesity without diabetes who took 2.4 mg of semaglutide weekly plus Low Calorie Diet (LCD) plus behavioral therapy over 68 weeks experienced a significantly higher change in mean body weight (-16.0%) compared to those who took a placebo + LCD + behavioral therapy (-5.7%).<sup>2</sup>
- Patients receiving 2.4mg of semaglutide via injection for 68 weeks lost significant amounts of weight, and a subset of participants had their body composition analyzed via DEXA. These participants lost an average of 10.4 kg of fat mass and 6.92 kg of lean mass, meaning approximately 40% of their weight loss came from lean mass.<sup>3</sup>

### **Physician Recommendations**

The following guidelines can provide a strong starting point to assist patients in maintaining diet quality while taking semaglutide or other weight loss medications.

- 1.** Focus on protein. A high protein diet of at least 1.2-1.6g / kg weight is advised to help reserve lean body mass throughout weight loss.<sup>8</sup>
- 2.** Distribution of protein intake throughout the day is important. Rather than one large high-protein meal, patients should aim to consume greater than 20 grams of protein at each eating episode to encourage appropriate muscle maintenance and enhance optimal muscle protein synthesis.<sup>9</sup>
- 3.** Patients taking semaglutide should incorporate meal replacements that contain protein, prebiotic fiber, vitamins and minerals to satisfy requirements while managing gastrointestinal side effects.<sup>10</sup>

For patients taking anti-obesity medications such as semaglutide or other GLP-1RAs, providers should consider recommending meal replacements to satisfy optimal nutritional intake and

assist with the management of transient adverse gastrointestinal effects of these medications.<sup>4,5</sup> Clinicians need to be aware of the high prevalence of micronutrient deficiencies, particularly in those individuals with obesity who are taking pharmaceutical products long-term to facilitate weight loss.<sup>6,7</sup>

The underlying goal of successful weight management is to guide patients to make lifestyle choices that construct a sustainable and nutritionally dense dietary pattern. In addition to behavior modification and nutrition education, meal replacements are helpful intervention for individualizing and supporting healthier eating over the long-term.

## Conclusions

While GLP-1 receptor agonists are a highly effective medication for weight loss, there are potential downsides to both the medications themselves and the type of weight loss in general. Many of these issues can be mitigated by proper nutrition and, in some cases, dietary supplementation.

In addition, a patient can lose a substantial amount of weight on these medications due to their anorexigenic effects; however, achieving a calorie deficit and losing weight does not guarantee that they are following a healthy diet. Weight loss medications must be paired with thorough nutritional counseling and patients must have access to the tools they need to follow an appropriate diet that confers the maximum health benefit of their weight loss.

## Contributors:

- Dr. Kelly Alison, PhD, FAED, FTOS, University of Pennsylvania, Penn Medicine
- Dr. Cheryl Anderson, PhD, MPH MS UC San Diego, Herbert Wertheim School of Public Health
- Dr. Abby Gilman, PhD, RDN, LDN; Bryn Mawr College
- Dr. Holly Lofton, MD, NYU Langone Weight Management Program
- Dr. Sue Shapses, PhD, RD/RDN; Rutgers University, NExT Center for Human Nutrition
- Stacey Weatherbee, RDN, LDN; Mainline Health Care

## References:

<sup>1</sup> Wilding, John P H, Rachel L Batterham, Salvatore Calanna, Luc F Van Gaal, Barbara M McGowan, Julio Rosenstock, Marie T D Tran, et al. 2021. "Impact of Semaglutide on Body Composition in Adults With Overweight or Obesity: Exploratory Analysis of the STEP 1 Study." *Journal of the Endocrine Society* 5 (Supplement\_1): A16–17. <https://doi.org/10.1210/jendso/bvab048.030>.

<sup>2</sup> Wadden, Thomas A., Timothy S. Bailey, Liana K. Billings, Melanie Davies, Juan P. Frias, Anna Koroleva, Ildiko Lingvay, et al. 2021. "Effect of Subcutaneous Semaglutide vs Placebo as an Adjunct to Intensive Behavioral

Therapy on Body Weight in Adults With Overweight or Obesity: The STEP 3 Randomized Clinical Trial.” *JAMA* 325 (14): 1403–13. <https://doi.org/10.1001/jama.2021.1831>.

<sup>3</sup> Wilding, John P.H., Rachel L. Batterham, Salvatore Calanna, Melanie Davies, Luc F. Van Gaal, Ildiko Lingvay, Barbara M. McGowan, et al. 2021. “Once-Weekly Semaglutide in Adults with Overweight or Obesity.” *New England Journal of Medicine* 384 (11): 989–1002. <https://doi.org/10.1056/NEJMoa2032183>.

<sup>4</sup> O’Neil, Patrick M., Andreas L. Birkenfeld, Barbara McGowan, Ofri Mosenzon, Sue D. Pedersen, Sean Wharton, Charlotte Giwercman Carson, Cecilie Heerdegen Jepsen, Maria Kabisch, and John P. H. Wilding. 2018. “Efficacy and Safety of Semaglutide Compared with Liraglutide and Placebo for Weight Loss in Patients with Obesity: A Randomised, Double-Blind, Placebo and Active Controlled, Dose-Ranging, Phase 2 Trial.” *Lancet (London, England)* 392 (10148): 637–49. [https://doi.org/10.1016/S0140-6736\(18\)31773-2](https://doi.org/10.1016/S0140-6736(18)31773-2).

<sup>5</sup> Rosenstock, Julio, Carol Wysham, Juan P. Frías, Shizuka Kaneko, Clare J. Lee, Laura Fernández Landó, Huzhang Mao, Xuewei Cui, Chrisanthi A. Karanikas, and Vivian T. Thieu. 2021. “Efficacy and Safety of a Novel Dual GIP and GLP-1 Receptor Agonist Tirzepatide in Patients with Type 2 Diabetes (SURPASS-1): A Double-Blind, Randomised, Phase 3 Trial.” *Lancet (London, England)* 398 (10295): 143–55. [https://doi.org/10.1016/S0140-6736\(21\)01324-6](https://doi.org/10.1016/S0140-6736(21)01324-6).

<sup>6</sup> Astrup, Arne, and Susanne Bügel. 2019. “Overfed but Undernourished: Recognizing Nutritional Inadequacies/Deficiencies in Patients with Overweight or Obesity.” *International Journal of Obesity (2005)* 43 (2): 219–32. <https://doi.org/10.1038/s41366-018-0143-9>.

<sup>7</sup> Morgan-Bathke, Maria, Suzanne Domel Baxter, Tanya M. Halliday, Amanda Lynch, Neal Malik, Hollie A. Raynor, Jessica L. Garay, and Mary Rozga. 2022. “Weight Management Interventions Provided by a Dietitian for Adults with Overweight or Obesity: An Evidence Analysis Center Systematic Review and Meta-Analysis.” *Journal of the Academy of Nutrition and Dietetics*, March, S2212-2672(22)00170-8. <https://doi.org/10.1016/j.jand.2022.03.014>.

<sup>8</sup> Leidy, Heather J., Peter M. Clifton, Arne Astrup, Thomas P. Wycherley, Margriet S. Westerterp-Plantenga, Natalie D. Luscombe-Marsh, Stephen C. Woods, and Richard D. Mattes. 2015. “The Role of Protein in Weight Loss and Maintenance.” *The American Journal of Clinical Nutrition* 101 (6): 1320S-1329S. <https://doi.org/10.3945/ajcn.114.084038>.

<sup>9</sup> Layman, Donald K, Tracy G Anthony, Blake B Rasmussen, Sean H Adams, Christopher J Lynch, Grant D Brinkworth, and Teresa A Davis. 2015. “Defining Meal Requirements for Protein to Optimize Metabolic Roles of Amino Acids.” *The American Journal of Clinical Nutrition* 101 (6): 1330S-1338S. <https://doi.org/10.3945/ajcn.114.084053>.

<sup>10</sup> Gorgojo-Martínez, Juan J., Pedro Mezquita-Raya, Juana Carretero-Gómez, Almudena Castro, Ana Cebrián-Cuenca, Alejandra de Torres-Sánchez, María Dolores García-de-Lucas, et al. 2022. “Clinical Recommendations to Manage Gastrointestinal Adverse Events in Patients Treated with Glp-1 Receptor Agonists: A Multidisciplinary Expert Consensus.” *Journal of Clinical Medicine* 12 (1): 145. <https://doi.org/10.3390/jcm12010145>.

---

## Nutritional Impact of Anti-Obesity Medications with Considerations for Meal Replacements

## Literature Citations

### **Loss of Lean Body Mass is a Concern with Appetite Suppressant Medications**

#### **Once-Weekly Semaglutide in Adults with Overweight or Obesity.** (Wilding et al. 2021)

Adults with obesity, with and without type 2 diabetes (T2D), who took 2.4 mg of semaglutide weekly over 68 weeks experienced a significantly higher change in mean body weight compared to those who took a placebo. These participants lost an average of 10.4 kg of fat mass and 6.92 kg of lean mass, meaning approximately 40% of their weight loss came from lean mass.

#### **Beyond Appetite Regulation: Targeting Energy Expenditure, Fat Oxidation, and Lean Mass Preservation for Sustainable Weight Loss.** (Christoffersen et al. 2022)

New appetite-regulating anti-obesity treatments such as semaglutide and agents under investigation such as tirzepatide show promise in achieving weight loss of 15% or more. Energy expenditure, fat oxidation, and lean mass preservation are important determinants of weight loss and weight-loss maintenance beyond appetite regulation. Regulatory guidelines should be revisited to focus more on the quality of weight loss and its maintenance rather than the absolute weight loss.

In large part, the reduction in energy expenditure induced by weight loss is attributable to the decline in lean mass, the metabolically active tissues. Moreover, besides reducing skeletal muscle mass, weight loss also decreases the mass of highly thermogenic organs such as liver, heart, and kidney. Furthermore, after weight loss, most of the weight regained is typically fat mass, leading to a progressive decline in lean mass over several weight cycles, thereby further exacerbating the reduction in energy expenditure.

### **Dietary Protein Supports Lean Body Mass During Weight Loss**

#### **High (Compared with Moderate) Protein Intake Reduces Adaptive Thermogenesis and Induces a Negative Energy Balance.** (Drummen et al. 2020)

These results indicate the relevance of compliance to an increased protein/carbohydrate ratio for long-term weight maintenance after weight loss. Long-term negative energy balance leads to weight loss. This underlines the impact of increasing the protein/carbohydrate ratio to prevent adipose tissue and combat overweight/obesity by supporting body weight maintenance. High protein diets are able

to affect energy balance via increased satiety and increased thermogenesis and have favorable effects on body composition. The lower energy balance in the high protein group compared to the moderate protein group can be explained by reduced adipose tissue in the high protein group.

**The Role of Protein in Weight Loss and Maintenance.** (Leidy et al. 2015)

The mechanism by which dietary protein preserves REE during energy restriction is likely due to the concomitant retention of lean mass observed with higher-protein. Data show a significant positive effect of increased protein consumption on energy metabolism. The higher-protein diets also preserved more lean mass during energy restriction than did the lower-protein diets

**Effects of Energy-Restricted High-Protein, Low-Fat Compared with Standard-Protein, Low-Fat Diets: A Meta-Analysis of Randomized Controlled Trials.** (Wycherley et al. 2012)

Reductions in fat-free mass (FFM) during diet-induced weight loss typically account for ~20% (1.2 of every 6 kg) of total weight loss. FFM, and specifically its skeletal muscle component, plays an important role in the regulation of resting energy expenditure (REE) and protein metabolism is the body's primary site of glucose uptake. A growing body of evidence suggests that compared with a conventional low-fat (<30% of total energy), standard-protein (SP) diet [12–18% of energy], a low-fat, high-protein (HP) diet [25–35% of energy] may increase body fat mass (FM) loss and attenuate reductions in FFM and REE.

## **Meal Replacements Utilized for Semaglutide Research Studies**

**Effect of Subcutaneous Semaglutide vs Placebo as an Adjunct to Intensive Behavioral Therapy on Body Weight in Adults with Overweight or Obesity.** (Wadden et al. 2021)

For the first eight weeks after randomization, participants received a low calorie diet (1000-1200 kcal/d) provided as meal replacements (e.g., liquid shakes, meal bars, portion-controlled meals). At week 68, the estimated mean weight change from baseline was –16.0% with semaglutide vs –5.7% with placebo, both combined with intensive behavioral therapy and meal replacements.

## **Nutritional Status Consideration — Considerations Relative Gastric Sleeve Caloric Restriction**

**The Effect of Protein Supplements on Weight Loss, Body Composition, Protein Status, and Micronutrients Post Laparoscopic Sleeve Gastrectomy (LSG): A Randomized Controlled Trial.** (Alshamari et al. 2022)

Low protein intake post-bariatric surgery can result in protein malnutrition, and muscle mass loss. Protein supplement helped in maintaining muscle mass and preventing muscle mass loss.

**The Relationship between Bariatric Surgery and Diet Quality: a Systematic Review.**

(Zarshenas et al. 2020)

The current evidence base suggests that despite being effective in reducing energy intake, bariatric surgery can result in unbalanced diets, inadequate micronutrient and protein intakes, and excessive intakes of fats. In combination with suboptimal adherence to multivitamin and mineral supplementation, this may contribute to nutritional deficiencies and weight regain.

**Nutritional Recommendations for Adult Bariatric Surgery Patients: Clinical Practice.**

(Sherf Dagan et al. 2017)

The long-term follow-up visits should include screening for micronutrient deficiencies, bone health, and control of nutrition-related non-communicable diseases. It is also recommended to reinforce healthy eating habits such as eating slowly, portion control, and meeting protein requirements.

## **Meeting Micronutrient Needs**

**Overfed but Undernourished: Recognizing Nutritional Inadequacies/Deficiencies in Patients with Overweight or Obesity.** (Astrup and Bügel 2019)

Studies have shown that many people with obesity have inadequate intake of iron, calcium, magnesium, zinc, copper, folate and vitamins A and B<sub>12</sub>, likely as a result of poor diet quality. Nutritional inadequacies or deficiencies may also occur due to altered pharmacokinetics in the individual with obesity and due to interactions in those with overweight or obesity with various pharmaceuticals. The adult population in the United States as a whole is deficient in certain micronutrients as a result of the availability and overconsumption of high-calorie, low-nutrient processed foods. Clinicians need to be aware of these gaps, particularly in those individuals with obesity who are undergoing bariatric surgery or taking pharmaceutical products long-term to facilitate weight loss.

**Diet Quality and Micronutrient Intake among Long-Term Weight Loss Maintainers.**

(Pascual et al. 2019)

Inadequate vitamin and mineral intake is documented among individuals with obesity. Behavioral weight loss trials that targeted healthy eating, activity, and behavioral strategies have also found significant increases in Healthy Eating Index-2015 scores in association with weight loss over four–six months. An 18-month study of weight loss and maintenance with portion controlled meals found that Healthy Eating Index-2010 scores increased initially by 20.3 points over six months, then moderated to an overall 11.3 increase.

## Addressing GI Side Effects of Medications

**Clinical Recommendations to Manage Gastrointestinal Adverse Events in Patients Treated with Glp-1 Receptor Agonists: A Multidisciplinary Expert Consensus.** (Gorgojo-Martínez et al. 2022; See Table 2 in Article)

The 2022 guidelines published in the *Journal of Clinical Medicine* promote patient education around practices that can help alleviate a variety of adverse gastrointestinal effects that are commonly experienced while utilizing GLP1 RA therapy to treat diabetes and obesity. [*Use of nutritionally balance meal replacements support eating in small portions and eating at frequent intervals, and ease in selecting options with bland flavors, while also supporting vital nutritional needs throughout the day for easily digested protein, healthful prebiotic fiber and 25-30% of the recommended daily intake for essential vitamins and minerals to optimize healthy metabolic support.*]

**Managing the Gastrointestinal Side Effects of GLP-1 Receptor Agonists in Obesity: Recommendations for Clinical Practice.** (Wharton et al. 2022)

If patients report upper GI side effects of short duration or mild severity, we suggest initial patient counseling on dietary modifications (e.g. decreasing the volume of food at each sitting [*as by intake of meal replacements*] and mindfulness to stop eating when full). Clinical and real-world studies indicate that constipation is common in patients with overweight/obesity treated with GLP-1RAs, and therefore strategies to manage constipation are also important — increasing fiber and water intake can be advised, and stool softeners considered. Patients should be advised to monitor these side effects, and clinicians should consider reducing the GLP-1RA dose if symptoms worsen.

## Bibliography

Alshamari, Sahar, Mohamed Aly Elsherif, Fahad Hanna, Leyan El Akhal, Hana Abid, and Wahiba Elhag. 2022. “The Effect of Protein Supplements on Weight Loss, Body Composition, Protein Status, and Micronutrients Post Laparoscopic Sleeve Gastrectomy (LSG): A Randomised Controlled Trial (RCT).” *Annals of Medicine and Surgery* (2012) 74 (February): 103220. <https://doi.org/10.1016/j.amsu.2021.103220>.

Astrup, Arne, Bügel, Susanne. 2019. "Overfed but Undernourished: Recognizing Nutritional Inadequacies/Deficiencies in Patients with Overweight or Obesity." *International Journal of Obesity (2005)* 43 (2): 219–32. <https://doi.org/10.1038/s41366-018-0143-9>.

Christoffersen, Berit Østergaard, Guillermo Sanchez-Delgado, Linu Mary John, Donna H. Ryan, Kirsten Raun, and Eric Ravussin. 2022. "Beyond Appetite Regulation: Targeting Energy Expenditure, Fat Oxidation, and Lean Mass Preservation for Sustainable Weight Loss." *Obesity (Silver Spring, Md.)* 30 (4): 841–57. <https://doi.org/10.1002/oby.23374>.

Drummen, Mathijs, Lea Tischmann, Blandine Gatta-Cherifi, Mikael Fogelholm, Anne Raben, Tanja C Adam, and Margriet S Westerterp-Plantenga. 2020. "High Compared with Moderate Protein Intake Reduces Adaptive Thermogenesis and Induces a Negative Energy Balance during Long-Term Weight-Loss Maintenance in Participants with Prediabetes in the Postobese State: A PREVIEW Study." *The Journal of Nutrition* 150 (3): 458–63. <https://doi.org/10.1093/jn/nxz281>.

Gorgojo-Martínez, Juan J., Pedro Mezquita-Raya, Juana Carretero-Gómez, Almudena Castro, Ana Cebrián-Cuenca, Alejandra de Torres-Sánchez, María Dolores García-de-Lucas, et al. 2022. "Clinical Recommendations to Manage Gastrointestinal Adverse Events in Patients Treated with Glp-1 Receptor Agonists: A Multidisciplinary Expert Consensus." *Journal of Clinical Medicine* 12 (1): 145. <https://doi.org/10.3390/jcm12010145>.

Leidy, Heather J., Peter M. Clifton, Arne Astrup, Thomas P. Wycherley, Margriet S. Westerterp-Plantenga, Natalie D. Luscombe-Marsh, Stephen C. Woods, and Richard D. Mattes. 2015. "The Role of Protein in Weight Loss and Maintenance." *The American Journal of Clinical Nutrition* 101 (6): 1320S-1329S. <https://doi.org/10.3945/ajcn.114.084038>.

Pascual, Rebecca W., Suzanne Phelan, Michael R. La Frano, Kari D. Pilolla, Zoe Griffiths, and Gary D. Foster. 2019. "Diet Quality and Micronutrient Intake among Long-Term Weight Loss Maintainers." *Nutrients* 11 (12). <https://doi.org/10.3390/nu11123046>.

Sherf Dagan, Shiri, Ariela Goldenshluger, Inbal Globus, Chaya Schweiger, Yafit Kessler, Galit Kowen Sandbank, Tair Ben-Porat, and Tali Sinai. 2017. "Nutritional Recommendations for Adult Bariatric Surgery Patients: Clinical Practice12." *Advances in Nutrition* 8 (2): 382–94. <https://doi.org/10.3945/an.116.014258>.

Wadden, Thomas A., Timothy S. Bailey, Liana K. Billings, Melanie Davies, Juan P. Frias, Anna Koroleva, Ildiko Lingvay, et al. 2021. "Effect of Subcutaneous Semaglutide vs Placebo as an Adjunct to Intensive Behavioral Therapy on Body Weight in Adults With Overweight or Obesity: The STEP 3 Randomized Clinical Trial." *JAMA* 325 (14): 1403–13. <https://doi.org/10.1001/jama.2021.1831>.

Wharton, Sean, Melanie Davies, Dror Dicker, Ildiko Lingvay, Ofri Mosenzon, Domenica M. Rubino, and Sue D. Pedersen. 2022. "Managing the Gastrointestinal Side Effects of GLP-1 Receptor Agonists in Obesity: Recommendations for Clinical Practice." *Postgraduate Medicine* 134 (1): 14–19. <https://doi.org/10.1080/00325481.2021.2002616>.

Wilding, John P.H., Rachel L. Batterham, Salvatore Calanna, Melanie Davies, Luc F. Van Gaal, Ildiko Lingvay, Barbara M. McGowan, et al. 2021. "Once-Weekly Semaglutide in Adults with Overweight or Obesity." *New England Journal of Medicine* 384 (11): 989–1002. <https://doi.org/10.1056/NEJMoa2032183>.

Zarshenas, Nazy, Linda Clare Tapsell, Elizabeth Phillipa Neale, Marijka Batterham, and Michael Leonard Talbot. 2020. "The Relationship Between Bariatric Surgery and Diet Quality: A Systematic Review." *Obesity Surgery* 30 (5): 1768–92. <https://doi.org/10.1007/s11695-020-04392-9>.