

GLP-1 RECEPTOR AGONISTS: TRANSFORMING WEIGHT LOSS AND LONG-TERM HEALTH

By James O. Hill, PhD and Holly R. Wyatt, MD

What you need to know:

- **GLP-1 receptor agonists (GLP-1 RAs)** have long treated type 2 diabetes but have recently become popular to support weight loss. GLP-1 RAs mimic the naturally occurring hormone GLP-1, which regulates appetite, blood sugar, and digestion.
- **GLP-1 RAs are revolutionizing weight loss** by leveraging the body's natural biology to promote significant weight reduction (often 15%-20% of body weight) while also improving metabolic health and reducing chronic disease risks.
- **Long-term success** depends on **medication, strength training, nutrition, and personalized lifestyle strategies** developed and provided by health professionals to their patients and clients for sustainable weight management.

For years, weight loss has felt like an uphill battle for so many. Despite their best efforts, even the most dedicated individuals have struggled to achieve and sustain meaningful weight loss. But today, we are witnessing a revolution. GLP-1 receptor agonists (GLP-1 RAs) are redefining obesity treatment, offering a breakthrough that helps millions achieve results once thought unattainable.

These medications are not just another diet trend or short-term fix. They represent a paradigm shift in how we approach obesity and metabolic health. By leveraging the body's own biology, GLP-1 RAs drive significant weight loss, improve metabolic markers, and reduce the risk of chronic diseases. The challenge now is not just achieving weight loss but maintaining it to ensure sustainable long-term health benefits beyond the scale.

How GLP-1 Receptor Agonists Work

GLP-1 RAs have been used to treat type 2 diabetes for years but have recently become popular to support weight loss. GLP-1 RAs mimic the naturally occurring hormone GLP-1, which regulates appetite, blood sugar, and digestion. By activating this pathway, they support weight loss through multiple mechanisms:¹

- **Enhanced Insulin Sensitivity:** These medications boost insulin secretion after meals, improving blood sugar control, particularly for those with type 2 diabetes.
- **Delayed Gastric Emptying:** Slowing the stomach's emptying process prolongs fullness, naturally leading to reduced calorie intake.
- **Increased Satiety:** Users feel satisfied with smaller portions, making it easier to adhere to a healthy eating plan.

- **Reduced Food Noise:** Many individuals report that GLP-1 medications significantly quiet the constant mental chatter about food, making weight management feel more natural and sustainable.²

GLP-1 Medications

- GLP-1 (Glucagon-Like Peptide-1) is an incretin, which is a hormone released by the gut that helps regulate appetite and body weight.³
- GLP-1 is primarily produced in the small intestine (L-cells) but is also secreted in smaller amounts from the colon, pancreas, and brain (hypothalamus).⁴
- GLP-1 receptors (GLP-1R) are found in multiple organs, including the pancreas, brain, heart, kidneys, gastrointestinal tract, and blood vessels.⁵
- GLP-1 helps regulate appetite and body weight by acting on the brain to promote satiety, reducing food intake, and slowing gastric emptying, leading to prolonged feelings of fullness.⁶

Achieving Unprecedented Weight Loss

For the first time in obesity medicine, medications consistently deliver double-digit weight loss percentages. On average, individuals taking Wegovy (semaglutide) lose around 15% of their body weight, while those on Zepbound (tirzepatide) often achieve losses greater than 20%.^{7,8} These results set a new benchmark in weight loss treatment.

The benefits extend far beyond weight loss. Research shows that GLP-1 RAs lower the risk of cardiovascular disease, kidney disease, liver disease, and sleep apnea.^{9,10} These medications are reshaping the perception of obesity, recognizing it as a complex medical condition with broad health implications rather than just a weight concern.

Understanding Side Effects

Like any medication, GLP-1 RAs may cause side effects. The most common include nausea, vomiting, diarrhea, constipation, and heartburn. While these can be uncomfortable, they typically improve as the body adjusts. More serious side effects, though rare, include bowel blockages, stomach paralysis, pancreatitis, kidney failure, and gallbladder disease.^{9,10}

Another emerging concern is the potential loss of lean muscle mass. Early research suggests that some users may lose more muscle than expected, which could impact metabolism and long-term weight maintenance. Further studies are needed, emphasizing the importance of strength training and adequate protein intake while using these medications.¹¹

The Future of Weight Loss Medications

The success of GLP-1 RAs has sparked a surge in research, with new and improved weight loss medications on the horizon. Innovations include:

- **Combination Therapies** that pair GLP-1 drugs with other weight-loss agents for even greater effects.
- **Oral Formulations** that eliminate the need for injections.
- **Personalized Treatment Plans** tailored to individual metabolic responses and lifestyle needs.

This area of innovation is just getting started. The next generation of obesity treatments will offer even more effective, targeted solutions.

The Biggest Challenge: Weight Loss Maintenance

While GLP-1 RAs are game-changers for weight loss, the real question is: What happens after the weight is lost? It has long been recognized that maintaining weight loss is harder than

losing it. For some, lifelong medication may be the answer, but not everyone can or wants to take these medications indefinitely.

A recent report found that of 125,474 patients initiating GLP-1 RAs, 46.5% of patients with and 64.8% without type 2 diabetes discontinued medication within 1 year. The most frequent reasons were side effects and cost.¹² Clinical trials of semaglutide found that patients who stopped the medication regained 2/3 of their weight over the following year.¹³ How do we help these individuals sustain their progress?

Weight loss maintenance strategies could include:

- **Long-Term Medication Use:** For some, staying on GLP-1 RAs indefinitely may be the best option. These drugs are designed for chronic use, and data suggests they remain safe and effective over time. However, adding lifestyle changes may improve health and quality of life beyond the scale.
- **Optimizing Lifestyle Interventions:** We need new lifestyle programs specifically designed for people who have lost weight on medication. Historically, weight loss and weight maintenance programs have been lumped together, but they require different strategies.
- **Combination Approaches:** Some individuals may benefit from a blended approach, using medication intermittently or at a lower dose while incorporating structured lifestyle interventions. Others might transition to non-GLP-1 medications like phentermine to help sustain their progress.

Much remains to be developed, but it is clear that weight maintenance must be an intentional, structured process. This is where dietitians, clinicians, and health professionals play a critical role. Innovative, evidence-based approaches to support people in keeping the weight off are needed.

The New Era of Obesity Treatment

GLP-1 RAs are not a silver bullet, but they are a powerful tool in the treatment of obesity. They have redefined what is possible, offering hope to millions who have struggled for years. But this is just the beginning. The real challenge is ensuring that weight loss is not only achieved but maintained. As we move forward, we must rethink our approach to obesity treatment. How do we create better weight maintenance strategies? How do we personalize treatments to fit individual needs? And how do we help people not just lose weight but transform their health for life?

Sustaining weight loss requires a shift in focus from short-term success to long-term health and quality of life. Healthcare providers must take the lead in developing better strategies, supporting patients beyond initial weight loss, and ensuring that treatment evolves with the science. The path forward is clear, and what we do next will define the future of obesity care.

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SOY FOODS WARRANT INCLUSION IN THE DIETS OF PATIENTS USING GLP-1 RECEPTOR AGONISTS

By Mark Messina, PhD, MS

What you need to know:

- **GLP-1 RAs are an exciting era in weight management, but maintaining muscle mass is crucial**, as users may lose 25%–40% of muscle during weight loss. Higher protein intake, especially from nutrient-dense sources like soy, can help counteract this effect.
- **Soy foods offer key advantages** for GLP-1 RA users, providing high quality protein, heart health benefits, and essential nutrients like calcium, with options suited for both constipation and diarrhea-related side effects.
- **Long-term weight maintenance remains a challenge**, with GLP-1 RA discontinuation rates in the range of 50% to 75% at 12 months. Encouraging soy food consumption during treatment can support sustained health benefits beyond medication use.

The advent of the new generation of anti-obesity medications such as glucagon-like peptide-1 receptor agonists (GLP-1 RAs) has ushered in an exciting era in weight management. While caloric restriction combined with exercise remains a widely preferred approach to weight loss, maintaining significant results over time can be challenging with traditional lifestyle measures alone. Nevertheless, patients using GLP-1 RAs still need dietary counseling because the nutrient density of the diet needs to be so much higher. The appetite suppression that occurs in patients using GLP-1 RAs means nutrient needs have to be met in far fewer calories.

The need for patients to consume protein in amounts exceeding the RDA to slow the loss of muscle mass that occurs with weight loss is a much discussed topic.¹ Estimates of the loss of muscle mass in response to GLP-1 RA use range from 25% to almost 40%, although it is not yet clear whether these drugs cause more loss than other approaches resulting in similar weight loss such as bariatric surgery.²

There are many options for increasing protein intake, but soy foods have advantages compared to most. For one, the quality of soy protein is greater than that of nearly all other plant proteins.³ It is on par with animal protein, but soy foods don't provide the amounts of saturated fat common to animal sources. For this reason, and because soy protein directly lowers blood cholesterol levels,^{4,5} soy foods may help boost the recently observed cardiovascular benefits of GLP-1 RAs.

In a multi-centered trial involving over 17,000 patients with preexisting cardiovascular disease, in comparison to the placebo, semaglutide reduced risk of a primary cardiovascular endpoint (a composite of death from cardiovascular causes, nonfatal myocardial infarction) by 20%.⁶ However, semaglutide reduced LDL-cholesterol by only about 2% relative to the placebo. Adding soy foods to the diet may improve upon that. Whether soy foods can enhance the hypotensive effects of semaglutide is an interesting question given recently published research.⁷

There are several side effects associated with GLP-1 RA use, especially during the dose escalation phase.⁸ One of these is constipation, at least in a subset of patients. Therefore,

higher fiber foods may be helpful. To get both protein and fiber, soy foods such as whole soybeans, edamame, and soy nuts come to mind. Conversely, some patients report having diarrhea, which suggests that high-fiber foods should be avoided. In this case, soy foods such as tofu and soymilk fit the bill. Tofu also has a neutral flavor, which is an attribute that many patients may find appealing given that their taste preferences may have been altered.

Furthermore, consuming tofu and soymilk that are calcium-fortified can help to meet the need for this mineral. Although many plant-based milk alternatives are fortified with calcium, relatively few provide the amount of protein soymilk does. And most importantly, calcium absorption from these soy foods is similar to the absorption of calcium from cow's milk.^{9,10} Little is known about the bioavailability of calcium from non-soy plant-based milk alternatives.

Concentrated forms of soy protein, such as soy protein isolate, are also a good choice. They provide protein without fiber and can be added to a range of products such as beverages, bars, and breakfast cereals, which makes it quite easy to incorporate them into the diet. An additional advantage is that patients can decide portion sizes for themselves as smaller meals are often preferred.

Finally, for a variety of reasons, many patients discontinue GLP-1 RA use. In fact, nearly 30% of individuals discontinued semaglutide in one large trial, with real-world estimates for GLP-1 RA discontinuation in the range of 50% to 75% at 12 months.¹¹ Relatively little research (at least compared to weight loss) has focused on maintaining weight loss, regardless of the method. By incorporating soy foods into the diet during weight loss, there is a greater chance these foods will be used upon discontinuation. Given the overall nutrient content, health benefits, and the variety available, there are ample reasons to encourage patients using GLP-1 RAs to try soy foods.

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PRACTICAL APPLICATIONS OF SOY IN WEIGHT MAINTENANCE

By Michelle Cardel, PhD, MS, RD, FTOS

What you need to know:

- **Sustainable lifestyle habits are key to weight maintenance**, including physical activity, nutrient-dense foods, hydration, sleep, and stress management.
- **Soy foods can support weight maintenance** by providing high quality protein, fiber, and essential nutrients while being lower in calories and saturated fat than some animal-based alternatives.
- **Soy products offer versatile options** such as fortified soymilk to support patients' calcium and protein needs, edamame for fiber and protein, and soybean oil for heart healthy unsaturated fats, making them easy to incorporate into daily meals.

Your patient has just reached their goal weight! “Now, how exactly do I keep the weight off?” they may ask. Time and time again, we’ve heard that the key to weight maintenance is to continue to engage in a sustainable and healthy lifestyle. The combination of physical activity, tracking food intake, restorative sleep, and stress management, as well as drinking plenty of water and incorporating foods that are nutrient dense, like soy foods, is one of the best ways to stay healthy.

The Role of Soy in Weight Maintenance

Soy foods can be incorporated into one’s weight maintenance diet in a variety of ways — whether in the form of a traditional soy food, concentrated source of protein, or a modern soy food such as meat and dairy substitutes.

- **Protein:** The quality of soy protein is greater than that of nearly all other plant proteins¹ and soybeans are higher in protein than other legumes, so it is not surprising that soy foods are excellent sources of this macronutrient. For example, 1 cup of tempeh contains 33 grams of protein,² making up two-thirds of one’s recommended daily intake.³ Similarly, 1 cup of edamame has 18 grams of protein,⁴ while 3 ounces of extra firm tofu has 9 grams.⁵ Eating protein-rich foods can help you feel full,⁶ which may lead to eating fewer calories and preventing weight regain.
- **Dairy:** Unsweetened, fortified soymilk is a great option to support patients in meeting their dairy recommendations,⁷ while promoting weight maintenance. Compared to a cup of whole milk, which is approximately 150 calories, one cup of unsweetened soymilk is only 80 calories.⁸ Unsweetened soymilk is low in saturated fat and has no added sugars, making it good for weight management. Fortified soymilk also provides vitamin D, calcium, and protein to support muscle and bone health. And importantly, soymilk is the only plant-based milk recommended by the [Dietary Guidelines for Americans](#).
- **Vegetables:** Soybeans and edamame are nutrient rich and low in calories. Half a cup of shelled edamame has fewer than 100 calories, 9 grams of protein, and 4 grams of fiber.⁴ High-fiber foods digest slowly, keeping you fuller for longer.⁹ This attribute, combined with their protein content, makes them a great choice for weight maintenance.
- **Dietary Fat:** Although some may be concerned about consuming too much fat during weight maintenance, unsaturated fat is a key nutrient to incorporate, as it helps the body absorb vitamins A, D, E, and K, and provides a source of essential fatty acids. Moreover, it adds to food enjoyment — an essential part of a sustainable diet. Soybean oil, often labeled as vegetable oil, has more unsaturated fat and less saturated fat than butter or coconut oil, making it ideal for weight maintenance and heart health. Soybean oil carries a Food and Drug Administration qualified health claim which suggests that it may reduce the risk of heart disease by lowering blood cholesterol levels.¹⁰ The claim states, “Supportive but not conclusive scientific evidence suggests that eating about 1½ tablespoons (20.5 grams) daily of soybean oil, which contains unsaturated fat, may reduce the risk of coronary heart disease.” It also has a neutral flavor, which works well in a variety of cooking applications like stir fries and pan-fried dishes.

Practical Applications for Patients and Clients

Soy foods can be incorporated into one’s weight maintenance diet in a variety of ways — whether in the form of a traditional soy food, concentrated source of protein, or a modern soy food such as meat and dairy substitutes.

- For breakfast, use unsweetened, fortified soymilk in oatmeal or smoothies to meet dairy needs while keeping saturated fat, added sugar, and calories low.
- If you’re looking for an afternoon snack, heat up a bag of frozen edamame for a protein- and fiber-packed option! Add “everything bagel” seasoning for an extra kick of flavor.

- When cooking, use soybean oil instead of butter or higher fat oils (like coconut oil or palm oil) to cut down on saturated fat.
- Need an appetizer for your party? Try air fried tofu for a crunchy, protein-rich treat that keeps everyone feeling full.

ABOUT THE AUTHOR

Michelle Cardel, PhD, MS, RD, FTOS, is a nutrition scientist, registered dietitian, and Chief Nutrition Officer at WeightWatchers. She also serves as a faculty member at the University of Florida, where she co-directs the Center for Integrative Cardiovascular and Metabolic Diseases.

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Beyond the Scale:

GLP-1 Medications and the Role of Soy in Weight Maintenance

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Consuming soy foods can support weight maintenance by providing high quality protein, fiber, and essential nutrients while being lower in calories and saturated fat than some animal-based alternatives.

Keys to Long-Term Weight Management Success

Nutrition

**Strength
Training**

Medication

**Lifestyle
Strategies**

Benefits of Soy Protein

- High quality plant protein that provides all the essential amino acids in amounts needed by the body.²
- Protein quality is greater than that of nearly all other plant proteins.²
- The only plant-based protein with an FDA-authorized health claim stating that “25 grams of soy protein a day, as part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease”.³
- A source of fiber, which can help with constipation-related side effects of GLP-1 RAs.⁴

Soy Foods to Try

 Protein

 Fiber



Edamame



Soy protein powder



Soy-based meat alternatives



Soymilk



Soynuts



Tempeh



Texturized vegetable/soy protein



Tofu

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Featured Dietitian-Endorsed Recipe:

Edamame Hummus

Total Time: 5 minutes

INGREDIENTS

- 2 cups edamame, shelled and cooked according to package directions
- 1/4 cup soybean oil
- 3 tablespoons lemon juice
- 2 teaspoons garlic, chopped
- 3/4 teaspoons cumin, ground
- 1/2 teaspoon salt

DIRECTIONS

1. Puree edamame, oil, lemon juice, garlic, cumin and salt in food processor for 30 seconds, scraping sides twice until almost smooth.
2. Cover and refrigerate until ready to serve.
3. Pair with crackers, cut vegetables, or pita bread.

**For more soy recipes and information
about soy, visit SoyConnection.com.**



Beyond the Scale: GLP-1 Medications & Weight Maintenance Nutrition Strategies
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