

## **For Appetite Control, Drugs vs. Diet for Weight Control**

Glucagon-like peptide-1 (GLP-1) agonists are among the newer tools in the obesity armamentarium. They reduce energy intake, leading to significant weight loss, with the added benefit of reducing blood glucose concentrations.

At the same time, they present issues regarding sustainability, cost, and adverse effects. In a study of 4,255 GLP-1 medication users conducted by the Blue Cross Blue Shield affiliate Prime Therapeutics, 68% of users discontinued treatment within the first year.

Discontinuation leads to weight regain. In a study of individuals initially treated with semaglutide 2.4 mg weekly, along with a 500-kcal per day calorie deficit and 150 minutes per week of physical exercise, the mean weight loss was 18.1 kg; drug discontinuation was followed by a mean regain of 11.5 kg within the first post-treatment year.

Semaglutide costs approximately \$15,600 annually in the U.S., and for every 1% of individuals beginning the treatment, insurance premiums for all insured group members increase approximately \$14.50 per month, according to Prime Therapeutics.

The adverse effects of GLP-1 receptor agonists include nausea, vomiting, diarrhea, gastroesophageal reflux, pancreatitis, bowel obstruction, and gastroparesis.

These findings raise the question, could nutrition present a safer and cheaper approach to weight loss for most patients? Evidence favoring a nutritional approach starts with the observation that carbohydrates, fiber, and unsaturated fatty acids increase intestinal GLP-1 secretion naturally.

In a randomized crossover study in 50 people with type 2 diabetes, the ingestion of a single plant-based sandwich increased GLP-1 secretion more than twofold, compared with an energy-matched meat sandwich.

The observed increase in GLP-1 secretion is comparable to that seen with sitagliptin. The foods that increase GLP-1 secretion also cause weight loss via other mechanisms. The low energy density of plant-derived foods means that satiety is achieved with relatively few calories. In a 16-week randomized trial of 244 participants testing a low-fat diet of unlimited fruits, vegetables, grains, and legumes, without exercise, reported energy intake fell by more than 350 kcal/d and body weight dropped by 5.9 kg, compared with an untreated control group.

Plant-based diets also cause weight loss by virtue of the slight “calorie-trapping” effect of high-fiber foods, such that unabsorbed energy is carried out with the wastes and a roughly 15% increase in postprandial energy expenditure (the thermic effect of food).

In the Adventist Health Study-2, including 60,903 adults, mean body mass index among those following vegan diets was 23.6 kg/m<sup>2</sup>, compared with 28.8 kg/m<sup>2</sup> for those following omnivorous diets, equating to a weight difference of about 16 kg.

In contrast to semaglutide's costs, a randomized trial found that a low-fat vegan diet reduces annual food costs by approximately \$500.

Despite these encouraging findings, most clinical trials of plant-based diets have been relatively brief; longer-term studies have typically been small and have focused on endpoints other than weight loss (e.g., cardiovascular health, control of diabetes). Moreover, nutritional treatment is not free. Support for any sort of treatment, nutritional or otherwise, often requires regular follow-

up with trained personnel. While drugs cannot provide a long-term solution for most patients, the long-term efficacy of dietary changes implemented on a wide scale remains to be seen. Large, long-term trials, including ongoing participant support, will provide important information on clinical effects and cost-effectiveness.

### **Conflict of Interest Disclosures**

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