

utilization [1]. In 2024, 6% of United States (US) adults report current GLP-1 use, and 12% report current or past use—rising to 22% among individuals told by a clinician that they have overweight or obesity [2].

Despite the efficacy and growing utilization of these medications, real-world challenges are increasingly evident [3]. These include gastrointestinal (GI) side effects; risk of inadequate nutrient intake from reduced food intake combined with insufficient nutritional counseling; potential loss of significant muscle mass and bone density [4]; high discontinuation rates (e.g., 50%–67% at 1 y and 85% at 2 years [5–8]) that may relate to side effects, costs, variable individual efficacy, or patient preferences [5, 9]; and limited public and clinician knowledge on the importance and implementation of complementary nutritional and lifestyle changes.

All these challenges may be partially mitigated by an evidence-based, structured lifestyle program, particularly around food, when prescribing GLP-1s for obesity. However, practical guidance for clinicians to implement such an approach is limited. This Advisory combines expertise across clinical and research societies focused on obesity, lifestyle, and nutrition to provide such guidance. It addresses current topics of interest among patients and clinicians, summarizes

uncertainties, and highlights future research directions. Although the general focus is on the US context, the recommendations have implications for use of GLP-1s for obesity management globally.

OVERVIEW OF EFFICACY, SIDE EFFECTS, AND KEY CHALLENGES

GLP-1 receptor agonists such as semaglutide and liraglutide, as well as combination agents like tirzepatide (which adds glucose-dependent insulinotropic polypeptide receptor agonism)—all hereafter referred to as GLP-1s for brevity—are effective new agents for obesity treatment which demonstrate weight reduction, weight maintenance, and reduced morbidity and mortality. These medications are approved by the Food and Drug Administration (FDA) for the treatment of obesity or overweight with weight-related comorbidities. Semaglutide and liraglutide are indicated for adults or youth aged ≥ 12 years and tirzepatide for adults aged ≥ 18 years [10–12]. GLP-1s for obesity have additional FDA-approved indications for cardiovascular disease risk

TABLE 1 Efficacy and outcomes at 52 weeks of GLP-1 therapy^a in the landmark industry-sponsored randomized controlled trials.

Medication	Mean intervention weight reduction	Mean placebo weight reduction	Mean placebo-adjusted GLP-1 effect	Metabolic risk and health outcomes improved	Key exclusion criteria
Liraglutide 3.0 mg/week ^b	7.9%	2.6%	5.3%	Glycemic control (glycated hemoglobin, fasting glucose, fasting insulin), systolic and diastolic blood pressure, cholesterol (total, LDL, HDL, VLDL, non-HDL), triglycerides, free fatty acids, health-related quality of life	Type 1 or 2 diabetes Use of medications that cause clinically significant weight gain or loss Previous bariatric surgery Personal history of pancreatitis; major depressive or other severe psychiatric disorders Personal or family history of multiple endocrine neoplasia type 2 or familial medullary thyroid carcinoma
Semaglutide 2.4 mg/week ^c	14.9%	2.4%	12.4%	Waist circumference, systolic blood pressure, physical functioning scores	History of type 1 or type 2 diabetes mellitus Glycated hemoglobin $\geq 6.5\%$ Personal history of chronic pancreatitis, acute pancreatitis within 180 days before enrollment Previous surgical treatment for obesity Treatment with a medication that promotes weight loss within 90 days before enrollment
Tirzepatide 5 mg/week ^d	15.0%	3.1%	11.9%	Waist circumference, systolic and diastolic blood pressure, physical functioning scores, triglycerides, cholesterol (total, LDL, VLDL, HDL, non-HDL), free fatty acids, fasting insulin	History of type 1 or type 2 diabetes mellitus Change in body weight >5 kg within 90 days before screening Previous or planned surgical treatment for obesity Treatment with a medication that promotes weight loss within 90 days before screening
Tirzepatide 10 mg/week ^d	19.5%	3.1%	16.4%	As above	As above
Tirzepatide 15 mg/week ^d	20.9%	3.1%	17.8%	As above	As above

^aIncludes tirzepatide, which combines GLP-1 agonism with glucose-dependent insulinotropic polypeptide receptor agonism.

^bData from reference [13], primary outcomes at 56 weeks.

^cData from reference [14], primary outcomes at 68 weeks.

^dData from reference [15], primary outcomes at 72 weeks.