muscle needs for repair or growth, can be converted to fat by the liver and increase visceral adiposity [167]. Structured strength (resistance) training or mixed training (resistance plus aerobic) programs are well established to help preserve lean mass during weight reduction [62, 168]. Aerobic activity alone has a smaller effect on preserving lean mass during rapid weight reduction [168]. Retrospective studies of GLP-1 therapy support the role of structured exercise programs, for example, 360 min/week with an emphasis on strength exercises to preserve fat-free mass [169]. In a recent randomized trial, 1 year of combined GLP-1 therapy with exercise training preserved bone mineral density, while GLP-1 therapy alone decreased bone mineral density [170]. In that trial, GLP-1 therapy plus exercise also produced larger reductions in abdominal fat and systematic inflammation than GLP-1 therapy alone [171]. Aerobic and resistance training exercises also improve insulin sensitivity, vascular function, and oxidative stress, critical for long-term cardiometabolic health [172].

Based on these findings, GLP-1s should be prescribed together with a structured exercise program, aiming for regular strength training at least three times weekly plus at least 150 min of moderate-intensity aerobic exercise weekly to preserve muscle and bone mass [62, 67, 158, 173–175]. These plans should be customized to match the individual's fitness level and physical capacity to ensure adherence and effectiveness [174, 175].

Several methods can monitor muscle mass for excessive reduction [176]. Bioelectrical impedance analysis (BIA) is pragmatic, easily implemented at point-of-care, and requires minimal staff training and clinic time. BIA allows for repeated measures at low cost, for instance, when weight reduction trajectories are high and muscle loss is more likely. Air displacement plethysmography can be used for individuals with pacemakers, implantable cardioverter defibrillators, or other electronic medical implants who cannot use a BIA machine—but require regular calibration, staff training, and use of close-fitting clothing, which may be uncomfortable for some individuals. Dual-energy X-ray absorptiometry (DXA) scanning with body composition programming is considered a gold standard, yet it is also more costly and less likely to be done frequently. For monitoring of individuals taking GLP-1s, DXA could be considered yearly or every 2 years, although such a timeline may impede the identification of early muscle loss and institution of appropriate interventions. Additionally, many imaging sites with DXA technology do not have or wish to use the additional body composition programming, given staff and time constraints. Newer technologies, such as visual-based capture using a smart phone, are being developed and validated and may be more widely used in the future [177].

All these technologies monitor muscle mass but not muscle health, quality, or function. Muscle strength can be monitored in several ways. Still, some are less sensitive to change (e.g., handgrip strength) or not feasible to conduct in a clinical setting (e.g., quadricep isometric strength). Sit-to-stand, stair climb, and timed-up-and-go measures can be helpful in older adults, but these measures may be less able to detect changes in younger individuals. While a one-repetition maximum is a classic measure of muscle strength, it is not recommended unless the individual is highly trained. Research is underway to examine how GLP-1 therapy affects muscle quality and physical function in younger populations, which should provide insights into appropriate imaging, functional testing, and lifestyle recommendations. Until then, consultation with an exercise physiologist or strength trainer may be beneficial for many individuals to establish general strength assessment, implement a resistance program (trainer, class, or self-directed), and monitor over time.

Maximization of weight reduction

A structured, comprehensive nutrition and lifestyle program could help augment the weight reduction efficacy of GLP-1s, although findings have been mixed. In the STEP 3 trial of semaglutide combined with intensive lifestyle intervention (30 counseling visits across 68 weeks, including nutrition, physical activity, and other behavioral strategies, plus 8 initial weeks of meal replacements with liquid shakes, meal bars, or portion-controlled meals), individuals experienced a 16% reduction from baseline in body weight (vs. 5.7% with intensive lifestyle intervention alone) [178]. In comparison, the STEP 1 trial that included semaglutide with general nutrition and physical activity instructions demonstrated a 14.9% weight reduction from baseline (vs. 2.4% with general nutrition and physical activity instructions alone) [14]. In the SURMOUNT 1 trial, tirzepatide 15 mg/week with general nutritional instructions produced a 20.9% reduction in body weight from baseline (vs. 3.1% with general nutrition instructions alone) [15], whereas in the SURMOUNT 3 trial, tirzepatide 10 or 15 mg/week started after 12 weeks of intensive lifestyle intervention produced a 25% reduction from baseline (vs. 4.8% with intensive lifestyle intervention alone) [178]. This 25% body weight reduction resulting from a staged approach with 12-week intensive lifestyle intervention followed by tirzepatide is the largest reduction seen in GLP-1 trials to-date. A challenge in interpreting the impact of the lifestyle strategies in these trials is lack of standardization on how "intensive" lifestyle intervention is defined or implemented. Such interventions can vary in many key components, including the frequencies of visits; individual or group settings; in-person, telehealth, or digital delivery; targets for food composition, calorie intake, physical activity, and other lifestyle habits; use of meal replacements; mechanisms for self-monitoring, feedback, and peer support; efforts to maximize adherence; and overall duration.

Effects of varying dietary patterns or specific food types on maximizing weight reduction with GLP-1s require further investigation. Based on the overall evidence around nutrition and obesity including potential impacts on metabolism, the microbiome, thermogenesis, and epigenetics, the authors of this Advisory recommend eating more minimally processed, nutrient-dense foods and fewer starch and sugar rich ultraprocessed foods for optimizing weight reduction while using GLP-1s (Table 6).

Other supportive lifestyle interventions

Other lifestyle interventions are essential to support individuals using GLP-1s as part of the recommended multicomponent lifestyle