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REVIEW

# To Reenvision and Redefine: Considering the Role of Lifestyle Interventions in the New Era of Second-Generation Obesity Management Medications

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## Abstract

**Purpose of Review** This narrative review examines lifestyle considerations before, during, and after second-generation obesity management medication (OMM) treatment.

**Recent Findings** Second-generation OMMs, including semaglutide and tirzepatide, have demonstrated unprecedented weight losses of around 15–20% in recent trials, leading to their swift uptake in clinical care. With increased pharmacotherapy effectiveness, attention has shifted to the accompanying role of lifestyle interventions in optimizing health and well-being. Emerging literature raises concerns regarding treatment sustainability, lean mass loss, nutritional risks, and weight regain following pharmacotherapy discontinuation, highlighting persistent gaps in the role of lifestyle strategies during OMM treatment.

**Summary** Lifestyle modification remains the cornerstone of obesity treatment, yet barriers to implementation and long-term success underscore the need for more sustainable strategies. As novel OMMs redefine obesity care, lifestyle programs may be able to shift focus from weight reduction to overall health promotion. However, the optimal timing, frequency, and content of such interventions alongside OMMs remain unclear. Because obesity is chronic and OMMs are costly, pre-treatment programs may precede pharmacotherapy, though this can limit access and reinforce stigma. During treatment, lifestyle approaches can mitigate medication-related effects and enhance health beyond weight loss, addressing concerns such as inadequate nutrition or muscle loss through protein intake and physical activity and reducing gastrointestinal side effects via dietary strategies. After discontinuation, behavioral programs may help prevent weight regain and sustain health improvements. Tailoring lifestyle interventions to modern pharmacotherapy offers an opportunity for health-centered, patient-focused obesity care.

**Keywords** Anti-obesity medications · Behavior change · Lifestyle modification · Randomized clinical trial

## Introduction

Comprehensive lifestyle modification programs have been the foundation of obesity treatment for decades [1]. Adults with overweight or obesity are recommended to receive 14 or more lifestyle counseling sessions led by a trained interventionist over six months with monthly sessions thereafter for maintenance [2]. Lifestyle counseling can be offered in individual or group sessions, and cover diet, physical activity, and behavioral strategies to promote weight loss and maintenance. For example, patients are typically advised to follow a reduced-calorie diet, engage in 200–300 min of physical activity per week, and participate in behavioral strategies that support weight loss, such as monitoring food intake and physical activity habits, problem-solving, and setting diet and physical activity goals [2]. Lifestyle modification programs typically yield 5–10% initial bodyweight losses, which can improve cardiometabolic health outcomes and health-related quality of life [3–5].

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Physical activity and dietary interventions can independently and jointly improve cardiometabolic risk factors central to atherosclerosis through both weight-dependent and weight-independent pathways. Structured aerobic and resistance exercise improves lipid profiles (increasing HDL-C and lowering triglycerides), reduces systolic and diastolic blood pressure, enhances insulin sensitivity via skeletal muscle adaptations, and decreases hepatic fat content [6–8]. In parallel, dietary interventions, particularly cardioprotective patterns such as the Mediterranean diet and Dietary Approaches to Stop Hypertension diet, improve lipid composition, lower blood pressure through reduced sodium and improved potassium intake, and enhance glycemic control and hepatic metabolism [9–12]. Importantly, many of these benefits occur even in the absence of significant weight loss, highlighting direct effects on vascular function, lipid handling, and insulin signaling [12–14]. However, when interventions lead to weight loss, especially reductions in visceral adiposity, there are amplified improvements in dyslipidemia, insulin resistance, and hepatic steatosis [14–17]. Collectively, both physical activity and dietary modification act through overlapping and distinct biological mechanisms to reduce atherogenic risk, with clinically meaningful benefits observed regardless of whether substantial weight loss is achieved.

While the health benefits of lifestyle modification programs are well-established, access to such programs is often limited by a lack of healthcare infrastructure necessary to support these services. In 2018, the United States Preventive Services Task Force recommended that primary care clinicians provide or refer all adults with obesity to an intensive, multi-component behavioral modification programs to reduce obesity [18] In the United States (US), the national ratio of primary care physicians to patients is just 83.8 per 100,000 people, with rural areas experiencing reduced access to primary care physicians as compared their urban counterparts [19]. Along with 280,000 primary care physicians, about 300,000 nurse practitioners and physician assistants are employed in the primary care setting, but this workforce is likely insufficient to meet the demands of the nearly 100 million adults affected by obesity in the US [19]. Additionally, weight stigma and bias [20], insufficient training in obesity treatment among healthcare providers [20–22], and lack of provider access to a multi-disciplinary team that supports lifestyle counseling efforts further hinder the capacity for primary care providers to deliver optimal obesity care [20].

Low patient access, uptake, and persistence with lifestyle modification programs remain significant barriers to long-term treatment success. In a nationally representative survey, only 3.6% of adults with obesity reported seeking weight loss help from a physician [23]. In addition to provider and system-level barriers, several patient-level factors contribute to suboptimal participation, including inaccurate weight perceptions [23], limited motivation or time to engage in a structured programs [24], cultural norms surrounding body weight [25], and a lack of recognition of obesity as a complex, chronic disease [23]. Even among those who enroll in a structured program, competing time demands are persistent challenges to adherence, which may be compounded by social, financial, and environmental barriers, such as limited social support, inability to afford healthy foods, and pervasively obesogenic environments [24, 26]. While lifestyle modification programs typically induce short-term weight losses of 5–10% alongside clinically meaningful health benefits, long-term weight maintenance remains difficult. Most patients regain one-third of their bodyweight within one year of stopping a lifestyle modification program, and roughly half return to their baseline weight within five years [27, 28]. These lifestyle modification program challenges underscore the need for more effective long-term therapies beyond lifestyle modification alone.

Novel, second-generation obesity management medications (OMMs) produce greater and more sustained reductions in body weight than previous pharmacotherapies [29, 30]. In clinical trials the second generation OMMs (i.e., semaglutide and tirzepatide), provided as an adjunct to lifestyle modification, have demonstrated 15–20% reductions in initial bodyweight, on average [29] — results that approach weight losses typically only achieved through bariatric surgery [31]. In addition, these medications have demonstrated cardiometabolic benefits, including improved glycemic control, lower blood pressure, and reduction in major adverse cardiovascular events [32, 33]. Semaglutide is an agonist of the glucagon-like peptide-1 (GLP-1) receptor, and tirzepatide is a dual agonist of both GLP-1 and glucose-dependent insulinotropic peptide (GIP). These medications regulate metabolism, satiety, and appetite [34]. Swift adoption of second-generation OMMs into clinical practice [35], along with multiple new medications moving through the pipeline [34], have prompted growing enthusiasm for this class of medications.

The increased use of highly effective OMMs is providing momentum for an already changing obesity treatment landscape. In recent years, obesity has been increasingly recognized as a multi-factorial, chronic, and relapsing disease, and leading health organizations are moving toward a health-centered, rather than weight-centric, treatment paradigm [36–38]. Beyond weight loss, health goals may include preventing or resolving obesity-related complications, improving quality of life, and enhancing longevity and physical fitness [36]. In this context, lifestyle interventions may be re-framed as strategies that promote overall health, rather than serving primarily as tools to achieve the

caloric deficit needed to produce weight loss. However, the optimal frequency, timing, and content of lifestyle interventions alongside second-generation OMMs is unclear. This narrative review will explore these important and timely considerations in the setting of second-generation OMMs.

## Lifestyle Counseling

The FDA has approved second-generation OMMs as an adjunct to a reduced-calorie diet and increased physical activity. While several recent reviews and papers with guidance on lifestyle interventions during second-generation OMM use have suggested practical dietary and physical activity targets (Table 1), the rapid adoption of second-generation OMMs into clinical practice has far outpaced scientific evidence. With second-generation OMMs now producing more weight loss than previous pharmacotherapies, there is a potential for these medications to transition the role of lifestyle counseling in obesity treatment from being predominantly focused on producing a caloric deficit to optimizing health.

## Frequency, Timing and Content

Models for the implementation of lifestyle counseling with OMMs may be considered as three approaches based on their timing with pharmacotherapy, including: before starting an OMM, in concurrence with an OMM (including for long-term maintenance), and when OMM discontinuation occurs. While these obesity treatment approaches are discussed separately throughout our review, they are not mutually exclusive strategies and may be considered as part of a continuum in a comprehensive, long-term treatment plan.

### Prior to Pharmacotherapy Initiation

Some insurance companies require documentation that a patient has participated in a lifestyle or behavioral modification program for a period (often around 6 months) before covering second-generation OMMs for obesity treatment. This requirement parallels bariatric surgery mandates; most insurance providers require documentation of participation in a structured lifestyle modification program, typically 3 to 6 months of medically supervised diet, exercise, and behavioral counseling, before approving bariatric surgery. The evidence supporting this practice in bariatric surgery is mixed [39].

Because GLP-1 RAs are high-cost medications and obesity is a chronic, multifactorial condition, insurers and payors may aim to ensure that pharmacotherapy is reserved for patients who have not achieved adequate weight loss through first-line, lower-cost interventions. Requiring a period of structured behavioral intervention may reinforce self-regulatory skills, and improve adherence to ongoing dietary and activity recommendations, factors that enhance the effectiveness and durability of GLP-1-RA induced outcomes, however this has not yet been demonstrated. Thus, these prerequisites may be intended not only to control utilization but also to promote comprehensive, sustainable obesity care.

However, requirements for lifestyle modification can create significant barriers to treatment access. Many patients face logistical, financial, and structural obstacles, such as limited availability of evidence-based behavioral programs, lack of insurance coverage for counseling visits, and competing work or caregiving demands, that make completion of programs difficult. These requirements can delay initiation of effective pharmacotherapy, exacerbating obesity-related comorbidities and increasing long-term healthcare costs. Moreover, the evidence that pre-treatment behavioral programs enhance outcomes with GLP-1 RA therapy is limited. For example, the SURMOUNT 3 study included a 12-week intensive lifestyle intervention lead-in that included a partial meal replacement program and weekly counseling. Those who attained at least 5% or greater initial weight loss were randomized to tirzepatide or placebo. From the start of the lead in, those on tirzepatide lost 24.3% of initial body weight over 84 weeks [40]. In the SURMOUNT 4 trial, there was a 36-week, open-label tirzepatide lead-in period. Participants who attained the maximum tolerated dose of tirzepatide (10 or 15 mg) were randomized to tirzepatide or placebo. From the start of the lead in, participants on tirzepatide lost 25.3% of initial body weight [41]. Thus, cautiously comparing outcomes from these two different studies, weight loss appears to be similar between approaches. Behavioral prerequisites can undermine the chronic disease model of obesity by implying that inadequate willpower or effort, rather than underlying biology, determines eligibility for advanced therapies. Thus, evidence supporting this requirement is sparse, and randomized controlled trials are needed to examine whether lifestyle modification prior to OMM use enhances outcomes.

### During Pharmacotherapy

Second-generation OMMs are recommended as an adjunct to a reduced-calorie diet and increased physical activity, and concurrent use of lifestyle interventions alongside medication was used in all Phase 3 OMM clinical trials [33, 42–50]. For example, the SURMOUNT 1 trial testing tirzepatide versus placebo for obesity treatment included counseling once every 4 weeks from weeks 0–12 and then extended

**Table 1** Select Lifestyle Intervention Guidelines, Reviews and Recommendations Related to Second-Generation Obesity Management Medications

| Author & year | Lifestyle intervention type | | | Concerns and considerations | | | | | Key dietary and physical activity recommendations | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Diet | Physical activity | Behavioral strategies | Reducing the risk for micronutrient deficiencies | Defining caloric and nutritional goals | Managing GI side effects | Lifestyle intervention benefits beyond weight loss | Mitigating muscle mass loss | Diet | Physical activity |
| Almandoz et al. (2024) | ✓ | | | ✓ | ✓ | ✓ | | ✓ | -Assess nutrient deficiency risk factors; evaluate nutrient intake; nutrition-focused history and physical<br>-Fluid: >2-3 L/day<br>-Energy: 1200-1500 kcal/day (women), 1500-1800 kcal/day (men)<br>-Macronutrient composition: 45-65% carbohydrates, 10-35% protein, and 20-35% fat<br>-Protein intake: >60-75 g/day and up to 1.5g/kg/day (or more depending on individual)<br>-Micronutrients: Treat preexisting deficiencies and counsel on adequate intake<br>-Dietary fiber intake: 21-25 g/day (women), 30-38 g/day (men)<br>-Management of OMM-associated adverse gastrointestinal events | |
| Dalle Grave (2024) | ✓ | ✓ | ✓ | | ✓ | ✓ | ✓ | ✓ | | -≥150 minutes/week moderate-intensity aerobic exercise<br>-≥2 sessions/week of muscle-strengthening activities |
| Dash (2024) | ✓ | ✓ | | ✓ | | ✓ | | ✓ | -Dietary strategies to mitigate gastrointestinal side effects<br>-Monitor for nutritional deficiencies with mineral and vitamin replacement as necessary<br>-Protein intake: up to 1.3 g/kg/day | |
| Grosicki et al. (2024) | ✓ | ✓ | | | ✓ | | | ✓ | -Protein intake: ≥1.2 g/kg/day or 80-120 g/day | -≥2 days of muscle-strengthening activities, performing 1-3 sets of 8-12 reps for each major muscle group |
| Jakicic and Rogers (2025) | ✓ | ✓ | ✓ | | | | ✓ | ✓ | | -Physical activity can provide benefits that extend beyond facilitating additional weight loss |

**Table 1** (continued)

| Author & year | Lifestyle intervention type | | | Concerns and considerations | | | | | Key dietary and physical activity recommendations | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Diet | Physical activity | Behavioral strategies | Reducing the risk for micronutrient deficiencies | Defining caloric and nutritional goals | Managing GI side effects | Lifestyle intervention benefits beyond weight loss | Mitigating muscle mass loss | Diet | Physical activity |
| Mozaffarian et al. (2025) | ✓ | ✓ | ✓ | ✓ | | ✓ | ✓ | ✓ | -Baseline nutritional assessment and screening<br>-Nutritional strategies to manage gastrointestinal side effects<br>-Protein intake: 1.5g/kg of lean body mass/day; 80-120 g/day; or 16-24% energy on a 2000 kcal/day diet<br>-Prevention and mitigation of nutrient deficiencies<br>-Maximization of weight reduction efficacy | -≥150 minutes/week of moderate-intensity aerobic exercise<br>-≥3 days of muscle-strengthening activities |
| Rogers et al. (2025) | ✓ | ✓ | ✓ | ✓ | ✓ | | ✓ | ✓ | -Focus on nutrition composition and eating behavior | -Exercise may enhance muscle health and function |
| Wadden et al. (2023) | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | -Assess dietary intake before and periodically during treatment<br>-Energy: 500 kcal/day deficit diet that promotes cardiometabolic health<br>-Fluid: 2.2-3 L/d<br>-Protein intake: at least 0.8 g/kg/day or more depending on BMI | -≥150 minutes/week during weight loss, with potential increase during weight maintenance<br>-≥2 days of muscle-strengthening activities |

counseling to every 12 weeks for the remainder of the trial [43]. In STEP 1, lifestyle counseling was conducted every four weeks by a dietitian or otherwise qualified healthcare professional (17 visits over 68 weeks) and produced weight losses of -14.9% of initial body weight [42]. The STEP 3 trial included an 8-week intensive lifestyle program with meal replacements and 30 individual intensive behavioral therapy visits over 68 weeks and resulted in a loss of 16.0% of initial body weight [44]. Thus, carefully extrapolating across the STEP trials, a key development with novel OMMs compared to lifestyle intervention alone is that these medications have provided clinically meaningful outcomes within the context of less frequent and lower intensity counseling sessions than traditionally used. However, in the new era of second-generation OMMs, pairing lifestyle counseling has the potential to amplify health benefits beyond weight loss alone.

While second-generation OMMs generally confer meaningful health benefits, there is substantial inter-individual variability in response to treatment. For example, in the STEP 1 trial, nearly one-third of participants did not achieve a ≥ 10% initial weight loss [42]. For individuals who experience suboptimal weight loss, lifestyle interventions may help augment treatment response. Because frequent contact is critical for producing clinically significant weight loss during lifestyle modification programs [51], clinicians may consider increasing the frequency of counseling sessions to potentially enhance outcomes. Counseling may also reinforce evidence-based strategies to support weight loss, including self-monitoring, maintaining a caloric deficit, consuming adequate protein and fiber to promote satiety, and increasing overall activity levels [2]. However, further research is needed to examine whether more intensive lifestyle interventions may help to enhance weight loss among those with suboptimal response to OMMs.

## Diet

The majority of Phase 3 trials of GLP-1 RAs have emphasized caloric reduction (e.g., 500 kcal/day deficit from total energy expenditure). In addition, some trials have included macronutrient intake guidance, typically recommending that participants consume up to 30% of energy intake comes from fat, 20% from protein, and 50% from carbohydrates (e.g., SURMOUNT 1, 2, 3 and SURMOUNT OSA) [40, 43, 50, 52]. Given concerns about loss of lean mass and potential nutrient concerns due to reductions in appetite [29, 53–59], several guidelines have provided recommendations for dietary intake with second-generation OMMs (Table 1). Many of these guidelines suggest high protein consumption (often > 60 g/day or at least 0.8 g/kg/day) [29, 53, 56, 57]. As practical approaches to macronutrient recommendations, a daily protein intake of 1.5 g per kilogram of fat-free mass or an absolute target of 80–120 g have been suggested, although this may be challenging for patients experiencing gastrointestinal side effects and reduced appetite [56, 57]. The incorporation of lean proteins (e.g. fish, eggs, Greek yogurt), and supplementation with high-protein meal replacement products may help meet protein needs [29, 53, 57]. Consumption of foods with lower fat and higher fiber may be helpful to reduce gastrointestinal side effects during OMM treatment [29, 57]. Additional recommendations include increased whole foods consumption (e.g. berries, leafy greens, nuts) and reduced processed foods intake (e.g. refined grains, sugar-sweetened beverages, fast foods) [29, 53, 57].While these strategies are generally recommended during OMM use, patients taking second-generation OMMs may experience unique challenges during treatment and benefit from lifestyle interventions tailored to address their needs. As previously mentioned, patients commonly report gastrointestinal side effects (e.g. nausea, vomiting, diarrhea) during clinical trials and in real-world settings [57]. Lifestyle counseling on dietary interventions may include advising patients to consume small, frequent meals every 3–4 h, avoid eating late at night, and drink adequate fluids, in addition to other supportive medical interventions [57].

Adults with obesity are at an increased risk for nutrient deficiencies [60]. Reduced appetite and energy intake experienced during GLP-1 RA use may alter dietary patterns and further increase the risk for deficiencies, though this effect has not been well studied. Some dietary concerns and subsequent recommendations have been based on bariatric surgery literature, which also tends to result in reduced dietary intake. Among people who have received bariatric surgery, caloric intake typically declines as patients consume smaller portion sizes and reduce intake of protein, carbohydrates, and fat [61]. Although improvements in dietary quality are observed, the risk of nutritional deficiencies is well established [62]. Nutritional deficiencies affect 30–70% of patients after bariatric surgery, and the most reported macro- and micronutrients deficiencies include protein, iron, calcium, and vitamins B1, B12, A, D, E, and K [63–65]. Unlike bariatric procedures such as Roux-en-Y Gastric Bypass, which directly impair nutrient absorption through anatomical alterations, GLP-1-based therapies do not inherently cause malabsorption; rather, deficiencies appear to arise primarily from reduced dietary intake and, in some cases, suboptimal diet quality. Current evidence suggests that these medications significantly reduce energy intake primarily through appetite suppression and potentially through delayed gastric emptying, which may contribute to inadequate consumption of protein, fiber, and essential micronutrients.

As part of a joint advisory from four professional organizations on nutritional priorities during GLP-1 treatment for obesity, Mozzafarian et al. recommended that dietary composition and quality should be emphasized during treatment to ensure optimal nutrient intake [57]. In this context, screening for micronutrient deficiencies may be warranted, especially in individuals with pre-existing nutritional concerns, low dietary intake, and those with a history of bariatric surgery. In addition, oral nutrition supplements may improve nutritional status [66, 67]. However, more research is needed to examine dietary quality during treatment, which will help better identify nutritional gaps within this patient population.

## Physical Activity

Lean mass comprises muscle, connective and organ tissues, and water, and is commonly used as a proxy for muscle mass [59]. While a reduction in lean mass is expected during weight loss, there is concern that treatment with semaglutide or tirzepatide may exacerbate this loss, potentially affecting muscle strength and function. Briefly, during the STEP 1 and SURMOUNT 1 clinical trials, participants lost approximately 10% of lean mass, although improvements in self-reported physical functioning were observed [67]. Sarcopenia, characterized by low muscle mass and reduced strength, is of particular concern due to its association with impaired functional status and increased risk of cardiovascular and all-cause mortality, especially among older adults [68, 69]. Indeed, greater muscle strength has been associated with lower mortality risk, although causal relationships remain to be established. In a meta-analysis of 1.9 million participants, higher handgrip strength was associated with a 31% reduction in mortality [70].

Although the musculoskeletal implications of second-generation OMMs are unclear, known ongoing studies (e.g. NCT06645470 and NCT06790160) may provide insight. Meanwhile, experts have suggested resistance training as potential strategies to mitigate this concern [29, 57, 67]. Previous recommendations for obesity management advise resistance training two to three times per week to attenuate the reduction in lean mass during weight loss [71], and recent evidence supports this exercise modality for adults undergoing dietary interventions [72]. However, other forms of exercise have also been shown to attenuate the loss of lean mass, and therefore this effect may not be limited to solely resistance exercise. Until findings from appropriately designed research trials become available, recommending physical activity that activates and places a resistance on skeletal muscle, which is not limited to traditional resistance exercise training (e.g., weightlifting) may be an appropriate strategy to potentially mitigate concerns related to muscle mass loss.

Given the demonstrated efficacy of second-generation OMMs for weight loss, there is an opportunity to re-frame physical activity as a behavior to support overall health beyond weight loss. Lifestyle counseling should highlight the benefits of physical activity that may not be fully realized with weight loss alone, such as a reduction in physiological markers associated with cardiovascular disease (e.g. triglycerides, arterial stiffness, liver fat), increased cardiorespiratory and muscle fitness, enhanced quality of life, and improvements in sleep, depressive symptoms and emotional health [13]. This position is supported by experts in the field [59] and a recent consensus statement from the American College of Sports Medicine, which highlights that physical activity should be considered in the context of holistic health and well-being [73].

## If Pharmacotherapy Discontinuation Occurs

As a chronic and relapsing disease, pharmacological treatment for obesity is recommended long-term, so long as it remains safe and effective [74]. However, real-world data shows that a large portion of patients discontinue GLP-1 RAs within the first year. In a patient cohort, 12-month discontinuation occurred in 47% of patients with type 2 diabetes and 65% without diabetes. Many of these patients restarted treatment following weight regain (reinitiation 36–47%). Common reasons cited were cost or coverage barriers, gastrointestinal side effects, changing insurance policies or supply shortages, and the perception that they no longer need the medication due to losing weight [75]. Qualitative data analyses of payer profiles also supported the prevalence of affordability and changes to coverage policies as reasons for pharmacotherapy discontinuation [75, 76].

Several randomized withdrawal and extension studies have demonstrated weight regain after medication discontinuation. In the STEP 4 trial, after the semaglutide lead-in those who continued on semaglutide lost an additional − 7.9% while those on placebo gained + 6.9% [77]. Participants had counseling every 4 weeks throughout the trial. In the SURMOUNT-4 trial, participants had a tirzepatide lead-in and those who continued on tirzepatide lost an additional − 5.5% while those on placebo gained + 14.0% [41]. Counseling was provided every 4 weeks until week 12 and then every 12 weeks. In the STEP-1 extension trial, participants who previously took semaglutide regained two-thirds of the weight lost within a year of medication discontinuation, with some results suggesting partial reversal of cardiometabolic improvements [78]. Real-world data support weight regain, though to a lesser extent and with substantial patient heterogeneity [41, 78–80].

Little is known about lifestyle modification programs that may mitigate weight regain after discontinuation. However, it may be necessary to intensify lifestyle counseling, specifically upon discontinuation, and incorporate lifestyle counseling content surrounding potential changes in appetite and eating after discontinuation. Behavioral weight loss treatments encourage an exercise maintenance goal of ≥ 200–300 min of physical activity per week; however, the specific amount of different forms of exercise is unclear. Therefore, it may be most appropriate for the specific exercise recommendations to be tailored to the physical abilities and health needs of the patient, and may blend different modes of exercise (e.g., aerobic activity, resistance exercise, balance training, etc.) to achieve these goals. At minimum, monthly contact with a counselor improves weight loss maintenance that prioritizes self-monitoring and problem-solving solutions surrounding hunger or cravings and schedule disruptions [2, 81–83]. Patients may experience increased appetite and return of food cravings and food noise following pharmacotherapy discontinuation. Cognitive-behavioral therapy strategies such as stimulus control, coping plans for high-risk situations, and relapse-prevention skills may be emphasized as a form of behavioral and psychosocial support. Transitioning patients to a structured caloric intake level with a focus on adequate protein levels and high-quality, fiber-rich foods may help control appetite. Meal replacements may be used for improved adherence. Trials testing the efficacy of such approaches post-discontinuation of GLP-1 RAs are needed.

## Conclusion

Recent advances in second-generation OMMs underscore the need to redefine the role of lifestyle interventions in obesity treatment. While more research and evidence-based recommendations are necessary to understand their role alongside second-generation OMMs, it is clear that there are potential opportunities for dietary, physical activity, and behavioral interventions to support comprehensive obesity treatment beyond weight loss. These opportunities may include tailoring lifestyle interventions to new treatment realities, such as adapting dietary interventions for patients experiencing gastrointestinal side effects, along with increasing protein, fiber, and nutrient intake and incorporation of resistance training along with other physical activity as part of a holistic approach to health. In recent years, increased recognition of obesity as a complex, chronic and relapsing disease has started to pave the way for a more holistic and health-centered obesity treatment paradigm. The demonstrated effectiveness of second-generation OMMs may provide further momentum for this shift by taking the pressure away from lifestyle interventions as the main source of weight loss, although numerous patient and provider-level barriers remain for access to both pharmacological and behavioral weight loss approaches to comprehensive obesity treatment. Moving forward, framing lifestyle interventions to support patient experiences and holistic health outcomes before, during and after second-generation OMM treatment will better place patients at the center of their care, which should always be the main priority during comprehensive obesity treatment.

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  Rationale: Provides potential mechanistic and clinical rationale for integrating dietary and physical activity strategies into second-generation OMM treatment, emphasizing the importance of muscle mass preservation and function.

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**Data Availability** No datasets were generated or analysed during the current study.

## Declarations

**Competing interests** AMC has served on advisory boards to Boehringer Ingelheim, Eli Lilly and Company, Novo Nordisk, and Roche, and received grant support, on behalf of Johns Hopkins University, from Eli Lilly and Company. JJ serves on the Scientific Advisory Board for Wondr Health. The other authors have nothing to disclose.

**Conflict of interest** AMC has served on advisory boards to Boehringer Ingelheim, Eli Lilly and Company, Novo Nordisk, and Roche, and received grant support, on behalf of Johns Hopkins University, from Eli Lilly and Company. The other authors have nothing to disclose.

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