

Contemporary Treatments for Obesity: Physical Activity in the Context of Antiobesity Medications

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Overweight and obesity and their associated negative health consequences are significant public health concerns. Lifestyle factors that include eating behavior and physical activity, in combination with behavior modification, provide the foundation for obesity treatment. However, body weight regulation is complex and may require the addition of medically focused approaches to be most effective for individuals with selective physiological and behavioral phenotypes.

There is excitement regarding the effectiveness of contemporary pharmacotherapy approaches to treat overweight/obesity, referred to as “game changers” for both patients and clinicians (1). These medications mimic the body’s naturally occurring nutrient-stimulated hormones (NuSH) that target the receptors of glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1. Semaglutide (Ozempic™) and tirzepatide (Zepbound™) are the most recently approved medications for overweight/obesity treatment. These medications have been shown to be highly effective for the treatment of overweight (body mass index (BMI) >27 kg·m⁻² with a concomitant health condition) and obesity (BMI over 30 kg·m⁻²), with the average weight loss exceeding what is typically achieved with lifestyle modification alone (2,3). In addition, NuSH-based therapies are effective for weight loss maintenance following lifestyle interventions (4,5). Chronic use of NuSH-based therapies may also have application to improve weight loss in patients who have not been optimally responsive or have experienced weight recurrence following metabolic/bariatric surgery (6). With additional targets in development, the use of pharmacotherapy is likely to expand as a treatment option.

Because of the effectiveness of NuSH-based therapies for obesity and other health outcomes (7), the role of lifestyle factors may need to be reconsidered and refocused. We posit that

there is a continued and expanded need to promote lifestyle factors, including physical activity, within the context of NuSH-based treatments. We propose a framework in Fig. 1 for how lifestyle factors fit into the care of individuals receiving medical treatments for obesity. As highlighted by Wadden et al. (8), there has been limited research to understand how lifestyle behaviors, such as physical activity, can influence the effectiveness of NuSH-based treatments. Despite the lack of published research in this area, there is ample evidence of the non-weight loss health benefits of physical activity to support health care providers continuing to promote it for NuSH-treated patients (9). However, this may require refocusing approaches to position physical activity as a foundational component of a patient’s care. In this context, a primary emphasis needs to be on enhancing favorable changes in body composition, which includes reducing adiposity and improving the retention and quality of lean body mass and particularly muscle mass.

Lifestyle-focused health care professionals, including exercise professionals, need to embrace NuSH-based treatments for obesity and excess body adiposity in a manner that is similar to the approach taken with other chronic health conditions; lifestyle behaviors, such as physical activity, should be considered within the context of comprehensive chronic care management rather than as an alternative to medical approaches for the treatment of chronic conditions. There are numerous examples of this approach, including 1) exercise-based cardiac rehabilitation to complement medical management of cardiovascular disease, 2) physical activity in combination with pharmacotherapy for hypertension and other cardiometabolic risk factors, 3) physical activity and healthful eating as an adjunct to medical treatment for type 2 diabetes, and 4) combined medical and physical activity rehabilitation paradigms for musculoskeletal injuries and conditions. With the introduction of effective medical treatments for overweight/obesity, which include pharmacotherapy and metabolic/bariatric surgery, a similar approach is warranted, adding lifestyle behaviors, such as physical activity, to medical treatments to enhance the care of patients.

Patients who received NuSH-based treatments for overweight/obesity may be most interested in maximizing their weight loss to achieve a desired body weight. Because, on average, these medications are highly effective for weight loss, the focus of physical activity should not be additional weight loss. Rather, we posit that physical activity is important for numerous health benefits beyond weight loss, which have been previously reported (10),

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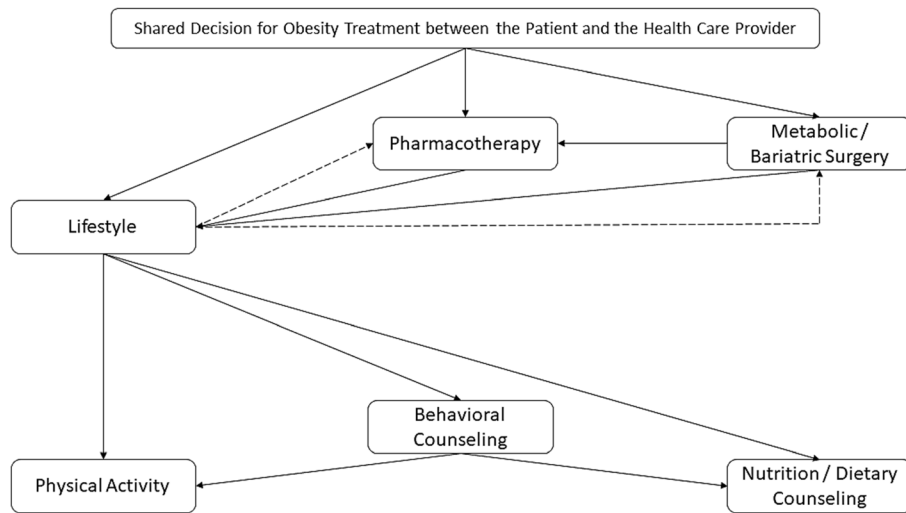


Figure 1: Framework for inclusion of lifestyle factors, including physical activity, in medical approaches for obesity treatment.

including favorable enhancements to body composition, cardiorespiratory fitness, muscular strength and endurance, physical function, and quality of life.

Despite the effectiveness of NuSH-based therapies for overweight/obesity and some other weight-related outcomes, the use of body weight or BMI to measure the effects of these therapies may not be sufficient. With NuSH-based treatments, there is a concomitant reduction in lean body mass, which seems to be in the range of 25%–40% of total weight loss (8). Thus, there are important considerations for exercise and other health care professionals. First, lean body mass is not solely constituted of muscle mass, so a reduction in lean body mass may not entirely reflect changes in muscle mass. Moreover, studies of NuSH-based treatments for overweight/obesity have not always included measures of body composition. Studies that have included measures of body composition have mostly used methodologies that measure lean body mass but not specifically muscle mass. Thus, studies of NuSH-based therapies need to include methods of measuring body composition that provide measures of muscle mass rather than solely a composite measure of lean body mass, such as dual-energy

x-ray absorptiometry or air displacement plethysmography, to fully understand the possible implications of these treatments.

Within the context of the loss of lean body mass, and possibly muscle mass, that accompanies NuSH-based therapies for overweight/obesity, it is important to consider if physical activity can counter this effect. Although there are few published studies of the effects of physical activity and structured exercise on body composition change when added to a NuSH-based therapy, evidence from other obesity treatment approaches suggests that physical activity does not fully protect against the reduction in lean body mass (11). However, studies that have examined muscle quality with muscle biopsies or other imaging techniques have demonstrated that physical activity and structured exercise can enhance muscle quality even in the presence of high amounts of weight loss, such as those induced by very-low energy diets or metabolic/bariatric surgery (12,13). This may support that the focus of physical activity and exercise should not be on preserving lean body mass and muscle mass volume, but rather on enhancing the function of these important body tissues with NuSH-based therapies.

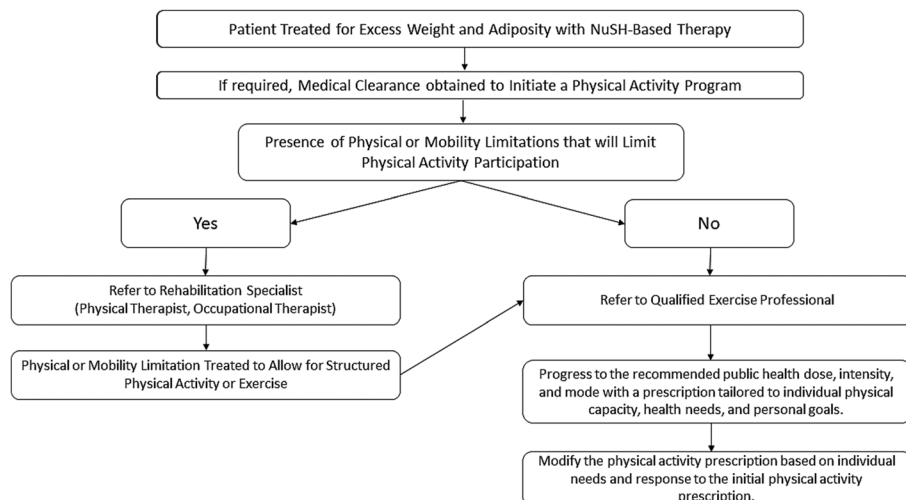


Figure 2: Framework for prescription and progression of physical activity for patients receiving NuSH-based therapies for weight loss.

There are currently no physical activity guidelines available that apply solely to the context of NuSH-based therapies for overweight/obesity. Whether there is a need for specific guidelines for this treatment context is unclear, and until that is determined, application of current physical activity guidelines should be considered for patients treated with NuSH-based therapies. The focus should be on progressively increasing physical activity to levels that are consistent with contemporary public health guidelines, 150 min·wk⁻¹ of moderate-to-vigorous physical activity and 2 d·wk⁻¹ of total body resistance exercises (14). Although there are guidelines for overweight/obesity that target higher levels of physical activity, approximately 200–300 min·wk⁻¹ (15), it is unclear if progressing to this higher physical activity level is required when combined with NuSH-based treatments for overweight/obesity. Progression to the higher level may only be needed if a patient is not responding adequately to a lower amount of physical activity. Moreover, it is possible that some patients may have mobility or other physical limitations that impair their participation in physical activity; in this situation, referral to appropriately trained rehabilitation professionals before progressing to a formalized physical activity program may be warranted. A framework for prescription and progression of physical activity for individuals receiving NuSH-based therapies is illustrated in Fig. 2.

Although not all individuals with overweight/obesity will seek treatment with NuSH-based therapies, it is important for exercise professionals to understand how physical activity can integrate into treatments for individuals who do receive these therapies. Moreover, it is pertinent for other health care providers to understand the importance of lifestyle factors, including physical activity, within these treatment options and to appropriately engage an exercise professional as an important member of the treatment team. The exercise professional may need to adapt their approach to physical activity prescription and progression to meet the clinical and relevant needs of the individual. Exercise professionals should be aware of the nutritional needs of individuals receiving NuSH-based therapies, which may require a higher level of protein to preserve lean body and muscle mass, and appropriately refer individuals for nutrition counseling.

To be most effective, access to exercise professionals and physical activity programming needs to be provided in an equitable manner by payers, including health insurance entities, health systems, and employers, with the goal of enhancing holistic health of individuals receiving these contemporary treatments for overweight/obesity. There is also a need for research support to better understand how physical activity can best enhance the health care of individuals and to refine the volume, intensity, and types of physical activity that are most effective within the context of NuSH-based therapies.

The results of the current study do not constitute endorsement by the American College of Sports Medicine.

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