International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Scholarly Publisher
RS Global Sp. z O.O.
ISNI: 0000 0004 8495 2390

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ARTICLE TITLE	OBESITY DISEASE - NON-SURGICAL TREATMENT METHODS - A LITERATURE REVIEW
ARTICLE INFO	Zuzanna Rabczak, Marcin Narloch, Jakub Kamiński, Jan Tomczyk, Aleksandra Żywicka, Oskar Sienkiel, Kamila Mozga, Mateusz Jasiński, Michał Szalach, Stanisław Kasprzak. (2025) Obesity Disease - Non-Surgical Treatment Methods - A Literature Review. *International Journal of Innovative Technologies in Social Science*. 3(47). doi: 10.31435/ijitss.3(47).2025.3566
DOI	https://doi.org/10.31435/ijitss.3(47).2025.3566
RECEIVED	11 July 2025
ACCEPTED	18 August 2025
PUBLISHED	20 August 2025
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OBESITY DISEASE - NON-SURGICAL TREATMENT METHODS - A LITERATURE REVIEW

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ABSTRACT

Introduction: Obesity, a global health crisis, is a leading risk factor for chronic diseases like diabetes and cardiovascular disease. Its prevalence has more than doubled since 1990, straining healthcare systems. Management involves primary prevention (lifestyle interventions), secondary prevention (early detection and treatment), and tertiary prevention (managing established obesity via lifestyle changes, pharmacotherapy, or bariatric surgery). This review focuses on non-invasive treatment methods for obesity.
Materials and methods: This review was conducted using PubMed and Google Scholar databases, focusing on recent systematic reviews, meta-analyses, and original research on non-surgical obesity treatments. Keywords included obesity, diet, exercise, pharmacotherapy, and education.
Results: Recent findings suggest that combining reduced calorie intake with limited carbohydrate consumption can lead to more effective weight loss. Diets high in protein, particularly those containing whey, are beneficial for maintaining muscle mass during weight reduction. Medications such as GLP-1 receptor agonists support weight loss and metabolic health. Regular physical activity enhances fat loss and cardiovascular performance. Additionally, patient-focused strategies are essential for improving adherence and ensuring long-term success in obesity treatment.
Conclusions: Effective obesity treatment requires combining personalized nutrition plan, physical activity, and medications. Prioritizing muscle preservation, protein intake, patient education, and stigma reduction enhances adherence and supports long-term weight and metabolic health outcomes.

KEYWORDS

Obesity, Non-Surgical Methods, Dietary Recommendations, Physical Activity, Pharmacotherapy

CITATION

Zuzanna Rabczak, Marcin Narloch, Jakub Kamiński, Jan Tomczyk, Aleksandra Żywicka, Oskar Sienkiel, Kamila Mozga, Mateusz Jasiński, Michał Szalach, Stanisław Kasprzak. (2025) Obesity Disease - Non-Surgical Treatment Methods - A Literature Review. *International Journal of Innovative Technologies in Social Science*. 3(47). doi: 10.31435/ijitss.3(47).2025.3566

Introduction.

Chronic diseases and conditions have become the leading health concerns of the past century.

While infectious diseases, previously the primary causes of death in 1900, have been largely controlled in the Western world [1], today, the leading causes for death and disability are chronic conditions such as diabetes, cardiovascular disease (CVD), and cancer [2], all of which are clinically associated with obesity. Obesity is closely linked to numerous complications and health conditions, including diabetes, CVD, obstructive sleep apnea, certain types of cancer, and increased risk of premature mortality [3]. Obesity is recognized as a chronic, complex disease energy intake imbalance and appetite dysregulation. Its development is influenced by genetic, environmental, and psychological factors [4], leading to excessive accumulation of adipose tissue that negatively impacts health. Globally, approximately 890 million people are living with obesity. According to the World Health Organization (WHO), the prevalence of adult obesity has more than doubled since 1990. As of 2022, approximately 43% of adults aged 18 and over were overweight, and 16% were living with obesity [5]. Due to its high prevalence in both developed and developing countries, obesity has become a major public health challenge, straining healthcare systems worldwide [6, 7]. Finding effective strategies for the treatment and prevention of obesity - particularly those that promote weight loss and long-term weight maintenance - is a significant global health challenge.

The management of obesity involves primary, secondary, and tertiary prevention:

Primary prevention measures are aimed at disease occurrence. It requires identifying individuals at high risk of developing diseases —those with established risk factors for chronic conditions—and addressing those risk factors and treating them early. This may include promoting certain lifestyle behaviors associated with lowered risk of obesity such as increased physical activity and dietary changes.

Secondary prevention is relying on detecting disease at an early stage through screening programs. It aims to identify individuals in the early stages of the disease and treating early in the hope of improved

outcomes through lifestyle modification and regular monitoring, especially in patients approaching obesity-level BMI thresholds.

Tertiary prevention addresses the treatment of established obesity, aiming to minimize complications and improve quality of life. Evidence-based treatment recommendations for obesity include lifestyle interventions, pharmacotherapy, and bariatric surgery [4]. Treating obesity with intensive measures may be conducted by a multidisciplinary team composed of physician, dietician, psychologist [8]. This study aims to review the non-invasive treatment methods of obesity.

Materials and methods.

This review was based on articles sourced from the PubMed and Google Scholar databases, with particular emphasis on the most recent systematic reviews and meta-analyses related to non-surgical treatments for obesity. Original articles, review articles, case reports and guidelines were used for this review. The literature review was conducted using the following keywords: obesity, calorie restriction, body weight, low-calorie diet, low-carbohydrate diets, body composition, fasting, amino acids, whey protein, pharmacotherapy, glucagon-like peptide-1 receptor agonists, naltrexone, bupropion, public health, physical activity, training, exercise, patient education.

Results.

a) Caloric deficit and low-sugar diet:

Lifestyle changes, including reduced calorie intake, increased physical activity, and behavioral therapy, form the foundation of clinical obesity treatment [9]. The key to weight loss is an energy deficit, meaning burning more calories than are consumed. This can be achieved through a low-calorie diet, typically involving meal plans that provide between 800 and 1800 kcal per day. Higher calorie intakes are recommended for individuals with greater body mass. Standard recommendations suggest consuming 1200–1500 kcal per day for individuals weighing less than 113.6 kg, while those weighing more than 113.6 kg are advised to consume 1500–1800 kcal per day. The diet's caloric value can be adjusted based on the estimated total energy expenditure of the patient, aiming for a daily caloric deficit of 500–750 kcal [10]. A diet may focus on limiting either fat or carbohydrates. In certain cases, under strict medical supervision, a very low-calorie diet (VLCD) providing fewer than 800 kcal per day may be necessary. However, VLCDs are not recommended for routine weight loss due to potential health risks. Alternatively, macronutrient-based diets, such as the ketogenic diet or high-protein diets, may be considered. It is important to note, however, that the long-term effectiveness and potential risks of these diets are not yet fully understood [11][12][13]. An essential element of most weight management strategies involves creating an energy deficit, typically achieved by adopting a nutritionally balanced eating pattern that limits fats and emphasizes complex carbohydrates. This, combined with increased physical activity, encourages the body to use stored energy, leading to fat loss. The term "diet" simply describes one's habitual food and beverage intake. Studies consistently support the effectiveness of substantial calorie reduction in treating obesity, particularly in promoting sustained weight loss over time [14][15]. Loss of muscle mass is a significant drawback of weight loss diets [13]. While reducing total body fat is a common objective, it's essential to recognize the distinction between fat types. Visceral fat, located around internal organs, poses a greater risk to metabolic health than subcutaneous fat, which lies under the skin. Effective weight management strategies should therefore prioritize maintaining or even increasing lean muscle mass. This not only supports metabolic efficiency and physical function but also contributes to long-term weight stability and improved overall health outcomes [16]. Traditionally, the commonly recommended diet has been low in calories, high in fiber, with over 50% of energy derived from carbohydrates and a limited amount of fat. Calorie restriction is known to improve metabolic health and help regulate blood sugar levels [17].

Traditionally, dieting approaches emphasized cutting overall calorie intake as the main method for improving health and reducing weight. However, newer findings highlight the potential benefits of adjusting macronutrient balance—particularly by lowering carbohydrate consumption. Notably, individuals following a low-carbohydrate diet often experience reductions in body fat, waist size, and weight even without strict calorie counting. When both calorie and carbohydrate intake are reduced together, the results tend to be more significant. Research consistently shows that such combined strategies outperform calorie restriction alone in promoting fat loss [18]. Consumption of sugar-sweetened beverages is significantly associated with higher body weight and weight gain. Replacing sugar-sweetened drinks with artificially sweetened beverages or unsweetened options such as water has been shown to result in a long-term reduction in body mass index (BMI) by an average of 0.31 kg/m². This corresponds to a weight loss of approximately 1 kg in adults with normal

body weight [19]. The type of beverage consumed has a significant impact on body weight. Studies have shown a correlation between the intake of sugar-sweetened beverages and weight gain, and long-term observations confirm this association. On the other hand, reducing calorie intake from liquids—especially sugar-sweetened drinks—leads to noticeable weight loss. Calorie reduction from beverages has a stronger effect on weight loss than reducing calories from solid foods. Several explanations have been proposed for the lack of a clear link between the consumption of other caloric beverages and weight loss. These differences may be due to their effects on satiety. For example, milk, which contains both protein and fat, may be more satiating. Additionally, nutrients such as calcium found in milk may promote weight loss by supporting lipolysis and thermogenesis [20]. Caloric restriction is a key component of lifestyle interventions and can be classified into four commonly used models [21]. The first model is continuous energy restriction, which involves reducing daily caloric intake by 20–30% relative to energy needs. The second model, short-term fasting, includes limiting intake to about 25% of daily energy requirements for 2–3 days per week. The third model, alternate-day fasting, consists of consuming 20–30% of energy needs on fasting days and 100% on non-fasting days. The final model is time-restricted eating, defined as consuming all meals within a daily window shorter than 12 hours. All four models have been shown to be effective in reducing body weight in adults. In particular, alternate-day fasting appears to be the most effective in lowering body weight, BMI, waist circumference, fat mass, and insulin resistance. Time-restricted eating may be more effective in reducing fasting glucose levels, while short-term fasting has been associated with greater loss of lean body mass [9][22][23][24].

b) Protein Intake in the Diet:

One of the key elements of weight loss is the reduction of fat mass while appropriately preserving lean body mass. This can be achieved, among other things, through the proper use of a high-protein diet and the appropriate selection of consumed amino acids [25]. There is a hypothesis suggesting that inadequate protein intake is compensated by increased hunger and overeating, leading to excessive calorie consumption and weight gain - this is known as the “Protein Leverage Hypothesis.” In practice, reduced protein intake results in increased consumption of fats and carbohydrates to compensate for the energy deficit. In fact, lowering the proportion of protein in the diet leads to excessive intake of non-protein nutrients (carbohydrates and fats) in an attempt to make up for the energy shortfall caused by reduced protein consumption [26]. A prospective study from Canada reported that lower protein intake in children aged 8–10 was associated with a greater tendency to develop an obesity phenotype at ages 10–12 [28]. Furthermore, studies show that increasing the amount of protein in meals not only promotes an increase in diet-induced thermogenesis — as widely reported in scientific research [28] – but also accelerates the onset of satiety, thereby leading to reduced food intake [29]. In a 2013 study, the authors compared a diet with moderate protein intake (0.8 g/kg body weight/day) and higher protein intake (1.2 g/kg body weight/day) among overweight individuals during a 6-month period of caloric restriction. It was concluded that the 0.8 g/kg diet led to a reduction in fat mass but also resulted in a loss of fat-free mass (FFM) and resting energy expenditure (REE). In contrast, the 1.2 g/kg diet helped preserve FFM [30]. A 2025 meta-analysis found a linear relationship between protein intake (g/kg body weight) and gains in fat-free mass (FFM). It was demonstrated that the more protein included in the diet, the better the preservation of muscle tissue. Recommendations stated that individuals undergoing significant caloric deficits should consume up to 2.4 g/kg of body weight, and those additionally engaging in resistance training as much as 3.2 g/kg of body weight [31]. In addition to the appropriate amount of protein intake, its quality is also important — that is, its digestibility and the content of individual amino acids [25]. An example is whey protein, which has been characterized as a “fast”-digesting protein enriched with leucine that activates postprandial protein synthesis and has a beneficial effect on the preservation of lean body mass, especially in older adults [32]. A meta-analysis of 37 randomized controlled trials involving 2,344 individuals concluded that whey protein supplementation in overweight and obese individuals contributes to a reduction in waist circumference, lowered blood pressure, and decreased plasma lipid or glucose levels [33]. Additional evidence of the beneficial effects of whey protein on the body was demonstrated in a study in which adult patients with obesity or overweight added either whey protein or maltodextrin, along with varying amounts of fiber, to their diets. Fasting and postprandial plasma lipid profiles improved in the group consuming whey protein with a low fiber content [34]. It is also worth noting that plant-based proteins, which are present in the diet, contain lower amounts of certain amino acids (leucine, isoleucine, and valine, as well as lysine and methionine) and are less digestible compared to animal proteins. Including legumes and grains in the diet can help prevent amino acid imbalances and compensate for these deficiencies. Additionally, plant-based diets are more effective in reducing body weight due to their lower calorie content, higher vitamin content, and greater meal volume [32].

c) Anti-obesity medications - selected drugs:

The American Association of Clinical Endocrinologists, Obesity Canada, and the Endocrine Society recommend initiating pharmacological treatment for obesity when BMI reaches ≥30 kg/m², or ≥27 kg/m² if obesity-related complications are already present — such as type 2 diabetes, cardiovascular disease, or metabolic syndrome [35]. The choice of medication should be personalized for each patient and take into account their individual characteristics, comorbid conditions, current medications, as well as their history of previous weight loss attempts, treatment methods, and their effectiveness. The patient's expectations regarding the outcomes they wish to achieve through treatment are also important [36].

GLP-1 receptor Agonists:

GLP-1 receptor agonists (GLP-1 RA) are an innovative and rapidly developing class of medications used not only in the treatment of obesity but also in the management of type 2 diabetes. Since their introduction to the market, they have gained considerable popularity due to their beneficial and multifaceted mechanisms of action. The mechanism of GLP-1 RA involves several key processes: they stimulate insulin secretion in response to hyperglycemia—that is, elevated blood glucose levels—thereby reducing the risk of hypoglycemia. At the same time, they inhibit the secretion of glucagon—a hormone that acts antagonistically to insulin—particularly under euglycemic and hyperglycemic conditions. Additionally, these medications slow gastric emptying, which reduces the rapid rise in blood glucose levels after meals. Their effect on the central nervous system—by decreasing appetite—contributes to reduced calorie intake and thus weight loss. Various forms of these drugs are available on the market, ranging from short-acting agents that require twice-daily injections (e.g., exenatide), to once-daily formulations (liraglutide, lixisenatide), and long-acting versions administered once a week (semaglutide, dulaglutide, albiglutide, extended-release exenatide). A major recent advancement is the development of an oral form of semaglutide, whose effectiveness in glycemic control has been found to be comparable to the once-weekly injectable form. This represents a breakthrough in the treatment of diabetes and obesity, offering greater convenience for patients who wish to avoid injections. The pharmacokinetic properties of each formulation directly affect their clinical performance. Short-acting agents like exenatide (twice daily) and lixisenatide are less effective in lowering fasting and nighttime glucose levels; however, their effect on gastric emptying remains stable even with long-term use. In contrast, long-acting agents such as liraglutide, dulaglutide, semaglutide, and albiglutide demonstrate stronger glucose-lowering effects overnight and at rest, and more effectively reduce HbA1c. Nevertheless, their impact on gastric motility may diminish over time—a phenomenon known as tachyphylaxis. Due to their favorable action profile—effective glycemic control, weight reduction, and low risk of hypoglycemia—GLP-1 RAs are recommended as the preferred injectable therapy before initiating insulin treatment in patients with type 2 diabetes. Moreover, they can be combined with basal insulin, either as separate injections or in fixed-dose combination formulations. There is also growing evidence of the cardioprotective effect of GLP-1 RAs. Numerous clinical trials have shown that these medications may reduce the risk of major cardiovascular events such as myocardial infarction, stroke, or cardiovascular death. As a result, current treatment guidelines support their use in individuals with obesity. An additional benefit of GLP-1 RA therapy in patients with type 2 diabetes is their positive effect on kidney function, making them a valuable option for those at risk of developing diabetic nephropathy. In the context of cardiovascular and renal complication prevention, the use of sodium-glucose cotransporter-2 inhibitors (SGLT-2 inhibitors) is also often considered. These agents have demonstrated protective effects as well, although their primary benefit lies in reducing the risk of heart failure [37].

Most patients taking weight loss medications consider them effective when they achieve a 5% reduction in body weight within the first 3 months after starting the maintenance dose [38]. Studies estimate that patients taking Liraglutide long-term lost 8% of their body weight over 56 weeks [39], while pharmacotherapy with Semaglutide resulted in a weight loss of 15–16% over 68 weeks [40][41]. The use of GLP-1 receptor agonists is also associated with the potential for various adverse effects. In a 2021 study involving 1,306 individuals taking semaglutide at a dose of 2.4 mg subcutaneously over a period of 68 weeks, 1,171 participants reported at least one adverse event. The most commonly reported side effects were nausea (44.2%), diarrhea (31.5%), vomiting (24.8%), constipation (23.4%), nasopharyngitis (21.5%), headache (15.2%), abdominal pain (10%), upper respiratory tract infections (8.78%), gallbladder-related issues (2.5%), and acute pancreatitis (0.2%). Injection site reactions were reported by approximately 5% of participants [41].

Naltrexone and Bupropion:

Naltrexone and bupropion (NB) is a combination drug used as a long-term therapeutic option for the treatment of overweight and obesity. Its use is intended to support the effects of a calorie-restricted diet and regular physical activity. Naltrexone works by autoinhibiting proopiomelanocortin (POMC) neurons in the hypothalamus, while bupropion is believed to enhance dopamine activity in specific areas of the brain [42].

A review published on January 9, 2020, compared the outcomes of four clinical trials in which participants received either the naltrexone-bupropion combination or a placebo. The treatment group was administered extended-release naltrexone at doses of 16 or 32 mg, along with extended-release bupropion at a dose of 360 mg. The composition of the placebo was not specified. A significantly higher proportion of individuals in the treatment group achieved a weight loss of at least 5% compared to the placebo group (RR = 2.1). Additionally, reductions in waist circumference, triglyceride levels, and LDL cholesterol were observed, along with an increase in HDL cholesterol.

The most commonly reported adverse effects included headache, nausea, drowsiness, insomnia, palpitations, elevated blood pressure, hot flashes, abdominal pain, dry mouth, constipation, paresthesia, and muscle tremors [43].

d) Physical activity:

In the treatment of obesity, pharmacological therapy alone has proven to be insufficient [44]. Physical activity plays a fundamental role in the process of fat reduction by enabling the achievement of an energy deficit [45]. The greatest decrease in BMI was observed in studies where the intervention was limited to aerobic exercise [46]. The American College of Sports Medicine defines aerobic exercise as activities that involve large muscle groups, performed in a continuous and rhythmic manner. Examples include cycling, dancing, hiking, jogging, long-distance running, swimming, and walking [47]. Aerobic training leads to a reduction in fat mass in overweight or obese adults — on average by 2–3 kg compared to a control group (without physical activity or dietary intervention), and approximately 1 kg more than with resistance training alone [48]. Observations have shown a correlation between changes in physical activity and changes in body weight: a decrease in activity led to weight gain, maintaining the current level had no effect on weight, and increasing activity resulted in weight loss [46]. Physical exercise, especially aerobic activity, has been associated with a reduction in visceral fat within the abdominal cavity, which translates into improved cardiometabolic health in individuals with obesity [44].

For adolescents struggling with obesity, exercise plans should be adapted to suit individual requirements. When the goal is to lower body weight and boost cardiovascular fitness, a mix of endurance, strength training, and high-intensity interval workouts proves most effective. If lipid imbalances increase cardiovascular risk, the focus should be placed primarily on aerobic activity. In contrast, for those with insulin resistance, combining aerobic and resistance exercises can be a valuable approach in reducing the risk of developing type 2 diabetes [49]. When recommending physical activity, it is important to establish a specific plan together with the patient. This plan should take into account the type of exercise, duration of activity, frequency, form, and intensity [44].

e) Patient Awareness and Motivation:

According to the Health Belief Model, the perception of obesity and awareness of its role as a risk factor for numerous diseases play a significant role in shaping and modifying health-related behaviors [50]. Individuals are often driven to lose weight due to health-related concerns, dissatisfaction with body image, encouragement from loved ones, and a desire to restore a sense of normal life. Key elements that facilitate this process include access to suitable exercise environments, commitment to a nutritious diet, and professional healthcare support. Psychological factors, such as confidence in self-regulation and awareness of health benefits, are strongly linked to successful outcomes. Moreover, guidance from healthcare providers can significantly aid those prepared to pursue weight management efforts [51][52]. Individuals affected by obesity can benefit significantly from personalized support provided by their general practitioners. This guidance should focus on building practical skills and fostering confidence in patients to manage their weight effectively. Clinician-led strategies may involve collaborative decision-making and the use of self-guided tools that encourage active participation and autonomy in the treatment process [53]. Enhancing patient education and raising public awareness remain essential in addressing the growing challenges of obesity. Many individuals lack a clear understanding of the factors contributing to their condition and often rely on misleading or inaccurate information. Weight-related stigma, including within medical environments, can negatively

influence patients' perceptions and willingness to seek care. Effective educational efforts are necessary to dispel misconceptions, empower informed decision-making, and encourage long-term commitment to treatment. Combating misinformation and reducing stigma are fundamental to improving health outcomes and fostering a more supportive care system [54][55].

Discussion.

The growing incidence of obesity and its related complications highlight the urgent need for holistic, scientifically supported methods that promote lasting weight reduction and better metabolic health. This work aligns with current research emphasizing the value of combining dietary changes, behavior modification, and medication in treating obesity. Discussion of the results is framed within modern clinical recommendations, focusing on the importance of individualized nutrition plans, lean mass preservation, and patient-centered support strategies involving education and interdisciplinary collaboration.

Behavioral changes remain at the core of effective obesity therapy. Most success is seen with moderate caloric deficits—typically between 500 and 750 kcal daily—achieved through a well-balanced, calorie-conscious diet (usually 1200–1800 kcal/day) and regular physical activity. Evidence shows that diets modifying macronutrient content, such as low-carb plans, may accelerate fat loss beyond what energy restriction alone can achieve.

Maintaining lean body mass during weight reduction is vital for sustained results. Research points to the benefits of higher protein consumption (over 1.2 g/kg of body weight) in supporting satiety, thermogenesis, and muscle retention. Whey protein, rich in leucine, is particularly effective due to its digestibility and metabolic advantages. Although plant proteins are often less complete, they can still fulfill amino acid needs when properly combined. Plant-based diets, low in calories and rich in fiber, also offer weight management benefits.

Pharmacological treatment is advised for patients with a BMI of 30 kg/m² or higher, or 27 kg/m² with coexisting conditions. Drugs like liraglutide and semaglutide—GLP-1 receptor agonists—have been shown to reduce appetite and slow gastric emptying, leading to notable weight loss (8–16% in trials) along with improved glucose control and cardiovascular outcomes. These medications are typically assessed after three months of use. Nausea, headache, and diarrhea are the most reported side effects.

Exercise is another critical element in obesity therapy, working synergistically with medications. Aerobic activity, in particular, reduces overall and visceral fat while improving heart and metabolic health. Among young people, blended programs involving endurance, strength, and interval training appear most effective. Outcomes improve when physical activity is tailored to individual preferences, capacity, and goals.

Recognizing obesity as a serious health issue increases motivation for behavior change. Successful interventions rely on accurate health information, consistent healthcare support, and building a sense of personal agency. Challenges such as social stigma, misinformation, and lack of self-awareness often hinder progress. Collaborative care and addressing patient misconceptions can greatly enhance adherence and long-term success in weight management.

Conclusions.

Effective obesity management requires a comprehensive, evidence-based approach integrating dietary, behavioral, and pharmacological strategies. Sustained weight loss is most successful when grounded in individualized caloric restriction, macronutrient balance, and regular physical activity. Preserving fat-free mass through adequate protein intake, particularly during energy deficit, is crucial for long-term success. Pharmacological options like GLP-1 receptor agonists further support weight reduction and metabolic health in eligible individuals. Patient education, stigma reduction, and multidisciplinary support enhance engagement, empower self-efficacy, and improve adherence, making long-term control of obesity more attainable.

Funding Statement: The article did not receive any funding.
Institutional Review and Board Statement: Not applicable.
Informed Consent Statement: Not applicable.
Data Availability Statement: Not applicable.
Conflict of Interest Statement: No conflicts of interest to declare.
Acknowledgements: None.

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