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COMPREHENSIVE APPROACHES TO OBESITY MANAGEMENT: INTEGRATING LIFESTYLE, BEHAVIORAL, AND PHARMACOLOGIC THERAPIES

Internal Medicine

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ABSTRACT

Obesity is a chronic, multifactorial disease associated with increased risk of diabetes, cardiovascular disease, and other metabolic complications. Its management requires an integrated approach combining lifestyle modification, pharmacologic therapy, and, in selected cases, surgical intervention. Nonpharmacologic interventions, including calorie-restricted diets, regular physical activity, and behavioral modification, remain the foundation of obesity treatment. Complementary and traditional approaches such as acupuncture, herbal supplements, and mind–body techniques may offer adjunctive benefits, although their efficacy and safety require further validation. Pharmacologic therapy is indicated for patients who fail to achieve adequate weight loss through lifestyle measures alone. Agents such as sibutramine and orlistat have demonstrated modest but clinically meaningful weight reduction and improvement in metabolic parameters. Investigational drugs like bupropion and topiramate show potential benefits but lack formal approval for obesity treatment. Over-the-counter preparations containing ephedrine and caffeine may produce short-term effects but raise significant cardiovascular safety concerns. Given obesity's chronic and relapsing nature, long-term follow-up and weight maintenance strategies are essential. Even modest weight loss of 5–10% significantly improves cardiovascular and metabolic health outcomes. Effective obesity management therefore requires a sustained, multidisciplinary, and patient-centered approach. This review focuses on current evidence-based strategies for the management of obesity, emphasizing nonpharmacologic, pharmacologic, and complementary approaches.

KEYWORDS

Obesity management, lifestyle modification, anti-obesity drugs, pharmacologic therapy.

INTRODUCTION

Obesity is linked to an increased risk of numerous medical conditions associated with significant morbidity and mortality, including type 2 diabetes, hypertension, and coronary heart disease (1). The risks related to many of these comorbidities can be mitigated through modest weight reduction. According to evidence-based guidelines from a National Institutes of Health (NIH) expert panel, treatment is recommended for individuals with obesity, defined as a body mass index (BMI) of 30 kg/m² or higher, as well as for overweight individuals with a BMI between 25 and 29.9 kg/m² (or elevated waist circumference) accompanied by two or more risk factors (1). The initial target is to achieve approximately 10% reduction in body weight, after which additional weight loss may be pursued if necessary. To sustain weight loss, the individualized management plan should be maintained indefinitely. This review focuses on the pharmacological and non-pharmacological approaches to the management of obesity [1].

The World Health Organization (WHO) defines obesity as an "abnormal or excessive fat accumulation that presents a health risk," typically classified using the body mass index (BMI; Table 1) (2). Although BMI is simple to calculate, it has certain limitations, as factors such as age, muscle mass, and ethnicity can affect its correlation with body fat. Therefore, additional anthropometric measures, including skinfold thickness, waist circumference, and waist-to-hip ratio, are increasingly employed to evaluate an individual's risk of obesity-related conditions such as type 2 diabetes mellitus (T2DM) and cardiovascular disease [2].

Table 1. WHO Adult Body Mass Index Classification [3]

Classification	Body mass index (kg/m^2)
Underweight	<18.5
Normal weight	18.5–24.9
Overweight	25.0–29.9
Obese class I	30.0–34.9
Obese class II	35.0–39.9
Obese class III	≥40

According to the WHO, obesity has reached epidemic proportions globally, affecting approximately 1.9 billion overweight and 650 million obese adults. In England, 26% of adults and 10% of children were classified as obese in 2016, with obesity-related illness estimated to cost the National Health Service (NHS) up to £6.1 billion annually-a figure projected to double by 2050. Recognizing the growing burden of obesity, Public Health England has allocated increasing resources and funding to address the condition and its broader societal impact.

Obesity is associated with a wide range of comorbid conditions that contribute to increased morbidity and mortality. These disorders affect multiple organ systems and significantly impact quality of life and healthcare costs. Hence, reducing obesity is crucial to lowering the risk and burden of these associated diseases. The major obesity-related comorbidities are summarized in Table 1.

Table 1. Obesity-related Comorbid Disorders [4]

Coronary heart disease or other atherosclerotic disease
Type 2 diabetes
Sleep apnea
Gynecologic abnormalities
Osteoarthritis
Gallbladder disease
Stress incontinence
Metabolic Syndrome (at least 3 of the following)
Waist circumference, >102 cm (men) or >88 cm (women)
Serum triglyceride, ≥150 mg/dL (106.9 mM)
Blood pressure, ≥130/85 mm Hg
Serum glucose, ≥110 mg/dL (6.1 mM)

In 2013, the Royal College of Physicians released a report titled *Action on Obesity: Comprehensive Care for All* to highlight this global issue, particularly among healthcare professionals. The report emphasized that education on obesity and nutrition is insufficiently covered in undergraduate medical curricula and that training for health professionals in obesity management remains inadequate. This review has been developed in consideration of these findings, aiming to provide a comprehensive overview of current pharmacological and non-pharmacological strategies for obesity management [2].

Goals Of Weight Loss And Management

The primary objective of weight loss therapy is to achieve an initial reduction of about 10% of baseline body weight. Once this goal is met, further weight reduction may be considered if clinically appropriate. A realistic timeframe for achieving this target is around six months. For individuals with a BMI between 27 and 35, a daily caloric deficit of 300–500 kcal typically results in a weight loss of 0.5–1 lb per week, leading to a 10% reduction over six months. In those with more severe obesity (BMI >35), a caloric deficit of 500–1,000 kcal per day usually produces a loss of 1–2 lb per week and a similar 10% reduction within six months.

Weight loss at this rate often continues for about six months before progress slows and plateaus due to reduced energy expenditure at a lower body weight. Evidence shows that weight regain is common unless long-term maintenance strategies—such as continued dietary control, physical activity, and behavioral therapy—are sustained.

Therefore, after six months of active weight loss, the focus should shift toward maintaining the achieved weight. If additional reduction is warranted, further adjustments to diet and exercise may be needed. For individuals unable to achieve significant loss, preventing further weight gain remains an important therapeutic goal, and participation in structured weight management programs is strongly recommended.[5].

Nonpharmacologic Treatment Options

First-line management of obesity should emphasize a combination of dietary modification and physical activity, tailored to the individual's lifestyle, preferences, and physical capabilities. Incorporating behavioral therapy alongside these interventions enhances adherence, supports long-term lifestyle changes, and improves overall treatment outcomes [4].

Various dietary approaches have been proposed for weight reduction, but successful weight loss depends primarily on reducing total energy intake and maintaining this reduction to prevent regain. Conventional low-calorie diets typically limit fat to about 30% of total calories while emphasizing complex carbohydrates and fiber from whole grains, vegetables, and fruits [6].

This dietary strategy supports a balanced energy intake that remains below total energy expenditure, which is essential for sustaining long-term weight loss. The use of prepackaged meals can aid calorie control by regulating portion sizes, promoting consistent eating habits, and improving dietary adherence. Such foods also help reduce unrecognized intake of fats and sugars often added during home meal preparation. Generally, a daily caloric deficit of 500–600 kcal results in a weight loss of about 0.5 kg per week, achieving roughly a 10% reduction in body weight over six months [7].

Several strategies can be employed to accomplish this, as summarized in **Table 2**.

Table 2. Summary Of Dietary Interventions For Weight Loss [2]

Diet	Principles	Mechanisms of action	Variants
Low-calorie diet	800–1600 kcal/day	Negative energy balance (net deficit of calories)	Cambridge diet Weight Watchers Nutrisystem diet Intermittent Fasting Biggest Loser Slim Fast Jenny Craig
Very low-calorie diet	200–800 kcal/day		
Low-calorie diet: meal replacement	Pre-cooked low-calorie meals		
Low-fat diet	Fat accounts for <30% of energy intake	Negative energy balance achieved by reduction of dietary fat, which is the most energy-dense macronutrient (9 kcal/g)	LEARN Ornish Rosemary Conley
Low-carbohydrate diet	Carbohydrate intake <130 g/day	Negative energy balance achieved by reduction of dietary carbohydrates (3.75 kcal/g) Mobilisation of glycogen stores and associated water loss Ketogenesis	Atkins South Beach Zone
Very-low-carbohydrate diet	Carbohydrate intake <60 g/day		
High protein diet	Protein accounts for >30% of energy intake	Increased satiety leading to reduced passive overconsumption of other macronutrients, thus achieving a lower energy balance	
Mediterranean-style diet	High intake of fruits, vegetables, grains; moderate intake of fat (mostly monounsaturated) and dairy (mostly cheese), reduced intake of meats (fish and poultry in preference to red meat)	Lipid reduction Lowering of oxidative stress and improved endothelial function Anti-inflammatory effects Gut microbiota changes	Regional variation

Macronutrient Composition

The three main dietary macronutrients, fat, carbohydrate, and protein, provide approximately 9, 3.75, and 4 kilocalories per gram, respectively. Fat is the most calorie-dense, least satiating, and most efficiently absorbed macronutrient, making it a key focus in weight reduction strategies. Studies have shown that low-fat diets lead to significant weight loss compared with baseline intake, though results are not consistently superior to those of other dietary approaches, including higher-fat regimens. Low-carbohydrate diets tend to produce more rapid initial weight loss—often greater than that achieved with low-fat diets, largely due to early depletion of glycogen stores and associated water loss, which can account for several kilograms lost within the first two weeks before the rate of weight reduction slows. Protein, being the most satiating macronutrient, forms the basis of high-protein diets aimed at reducing overconsumption of more energy-dense foods. However, evidence suggests that such diets have either minimal or no significant long-term effect on overall body weight [2].

Very Low-calorie Diets (VLCDs)

VLCDs providing fewer than 800 kcal per day, are designed to achieve more rapid weight loss than standard low-calorie diets. These regimens typically result in a weekly reduction of 1.5–2 kg in women and 2–2.5 kg in men, with an average total loss of around 20 kg after 12–16 weeks. While randomized controlled trials have shown greater short-term weight reduction with VLCDs compared to conventional diets, the difference tends to diminish over 6–12 months. Commercial VLCD formulations are available in various forms, including all-liquid protein meals, low-carbohydrate high-protein plans, and high-carbohydrate moderate-protein options. VLCDs are particularly useful for patients with severe obesity who are unable to undergo elective surgery due to excessive weight [8]. VLCDs generally produce greater short-term weight loss than LCDs, with more substantial reductions in total body fat over the first six months. However, their long-term advantages are less evident, as weight regain tends to be more pronounced with VLCDs, leading to comparable overall outcomes between the two approaches over time [9]. The main reasons for the weight re-gain are seen with these low-calorie diets range from metabolic adaptation to practicalities of calorie counting and resultant loss of diet adherence.

VLCDs are contraindicated in individuals with moderate to severe hepatic or renal disease and should be used cautiously in those with cardiac or gallbladder disorders. They may also worsen conditions such as osteoporosis, hyperuricemia, and gout, necessitate careful monitoring when prescribed [4].

High-protein Diet

High-protein diets typically contain greater amounts of total fat, saturated fat, and cholesterol due to the predominance of animal-based protein sources. By restricting carbohydrates, these diets often eliminate many nutrient-rich foods. The initial rapid weight loss seen with high-protein diets is largely due to fluid loss resulting from reduced carbohydrate intake. Prolonged adherence induces metabolic ketosis, which may suppress appetite and lower overall calorie consumption. Improvements in lipid profiles and insulin sensitivity observed with these diets are primarily attributed to weight loss rather than the high protein content itself. Excess dietary protein, however, is not efficiently utilized by the body and may increase strain on the kidneys and liver. Moreover, elevated protein intake can enhance urinary calcium excretion, potentially aggravating osteoporosis. The American Heart Association notes that while high-protein diets are

generally safe for healthy individuals in the short term, their long-term safety and efficacy have not been established [10].

Meal Replacement

Meal replacement, whether full or partial, uses nutritionally complete but low-calorie substitutes for regular meals, providing a practical and convenient way to limit calorie intake. Evidence indicates that meal replacement strategies can produce greater weight loss than conventional calorie-restricted diets. Partial meal replacement (PMR) programs have been shown to achieve more weight loss at both three months and one year, with better adherence among participants. Similar findings from later reviews confirmed that PMR results in greater weight reduction over one year compared with standard dietary interventions. Although some degree of weight regain may occur over time, the overall loss generally remains superior to that achieved with conventional diets.

Importantly, dietary-induced weight loss is often associated with improvement or even remission of obesity-related conditions such as type 2 diabetes mellitus (T2DM). In a major study, participants who lost more than 10 kg after 12 months of a low-calorie meal replacement program achieved diabetes remission in most cases. The proposed mechanisms for this include reduced hepatic glucose production, improved insulin sensitivity, and restoration of normal hepatic metabolism. Additional benefits observed included reductions in blood pressure and triglyceride levels [2].

Dietary Styles

The Mediterranean-style diet (MSD), originating from olive-growing regions around the Mediterranean, encompasses various regional adaptations but follows core nutritional principles. It emphasizes a high intake of fruits, vegetables, and whole grains; moderate consumption of fats predominantly from monounsaturated sources such as olive oil and dairy products, mainly cheese; and limited intake of meat, with a preference for fish and poultry over red meat. This dietary pattern has been shown to promote significant weight loss, typically ranging from 4.1 kg to 10.1 kg after 12 months, while also improving multiple cardiovascular risk factors. Moreover, it is generally less restrictive and more sustainable than many other dietary approaches [11].

Diet Choice

As no single dietary approach has proven superior, calorie restriction remains the fundamental principle for achieving weight loss, regardless of macronutrient composition. The effectiveness of any diet largely depends on adherence, as weight loss tends to plateau over time due to physiological adaptations that reduce energy expenditure.

According to current National Institute for Health and Care Excellence (NICE) guidelines, successful obesity management should include a dietary plan that ensures energy intake is lower than energy expenditure. A daily caloric deficit of approximately 600 kcal achieved through a low-calorie or low-fat diet is recommended for steady and sustainable weight loss, supported by professional guidance and regular follow-up. Low-calorie diets providing 800–1600 kcal per day may be used if nutritionally balanced, while very low-calorie diets of 200–800 kcal per day should be reserved for specific clinical situations requiring rapid weight reduction [12].

Physical Activity

Physical activity plays a critical role in obesity management and prevention. Obesity is strongly linked to a sedentary lifestyle, with body weight showing an inverse relationship to physical activity levels. Exercise acts as a potent physiological trigger for lipolysis, promoting the breakdown of triglycerides into free fatty acids for energy utilization by muscles. This process increases total energy expenditure, resulting in a negative caloric balance. Although exercise alone typically produces only a modest 2% to 3% reduction in BMI, it is significantly more effective when combined with dietary interventions.

For obese individuals, an initial exercise regimen of 30–45 minutes of moderate-intensity activity at least three times per week is recommended, gradually progressing to most days of the week. This level of activity expends approximately 150 kcal per day (500–1000 kcal per week), though 2000 kcal or more weekly may be necessary to maintain weight loss effectively.

Activities that elevate heart rate and energy expenditure are beneficial, with walking being the most practical and sustainable due to its safety and accessibility. The use of a pedometer can help monitor progress; patients may start with 10 minutes of walking three times weekly and gradually increase to the target level. The National Weight Control Registry suggests beginning with about 4,000 steps per day and progressively increasing to 12,000 steps over six months. Importantly, consistent physical activity remains essential during long-term weight maintenance, as it is one of the strongest predictors of sustained weight control [4].

Behavioral Modification

Behavioral modification is a cornerstone of comprehensive obesity management, focusing on reshaping eating and physical activity habits to promote long-term adherence to lifestyle changes. These strategies aim to address psychological and environmental barriers that often hinder sustained weight loss. Key behavioral approaches include self-monitoring of dietary intake and physical activity, stress management to prevent emotional overeating, and stimulus control to reduce exposure to food-related cues that trigger incidental eating. Additional techniques such as problem-solving help patients identify challenges and implement healthier responses, while cognitive restructuring corrects unrealistic weight loss expectations and distorted body image perceptions.

Social support from family, peers, and healthcare providers enhances motivation and accountability, while relapse prevention strategies prepare individuals to recover from episodes of overeating or weight regain. Behavioral modification programs are typically delivered in group settings, which provide peer support and reduce costs, though individualized sessions with a healthcare professional can be equally effective. Patients may also use self-help tools such as food and activity diaries or structured manuals to reinforce behavioral goals. Despite initial success, weight regain of approximately one-third of the lost weight within the first year after discontinuing therapy is common, underscoring the need for continuous behavioral reinforcement and long-term follow-up to sustain weight control [7].

Regular biweekly follow-up with a behavioral therapy provider can significantly improve long-term weight maintenance by reinforcing positive habits and accountability. Moreover, cognitive-behavioral decision-making interventions, which focus on enhancing self-regulation, goal setting, and adaptive coping strategies, have demonstrated greater effectiveness than traditional behavioral therapy in sustaining weight loss over 6 to 12 months, despite producing a slower initial rate of weight reduction [4].

Complementary And Traditional Healthcare Approaches

Complementary and alternative medical (CAM) approaches encompass a variety of practices and products that are used either in conjunction with or as substitutes for conventional Western medicine. The National Institutes of Health categorizes these interventions into five overlapping domains: biologically based practices, manipulative and body-based approaches, mind-body medicine, alternative medical systems, and energy medicine.

Biologically based practices involve the use of vitamins, minerals, and natural products derived from plants or animals. Examples include chondroitin sulfate from bovine or shark cartilage, and herbal preparations such as ginkgo biloba and echinacea. These agents are often used to improve metabolism, enhance well-being, or support weight management, although clinical evidence for their effectiveness varies.

Manipulative and body-based approaches focus on the physical manipulation of the body's structures to promote health and relieve discomfort. Massage therapy has been practiced for centuries, while chiropractic and osteopathic medicine formally emerged in the 19th century in the United States. These methods aim to improve musculoskeletal alignment, circulation, and overall physical function.

Mind-body medicine is based on the belief that the mind and body are interconnected and influence one another. Practices such as meditation, yoga, relaxation training, and spiritual healing aim to restore harmony between psychological and physical states. These approaches can help reduce stress-related eating behaviors and improve adherence to lifestyle modification programs.

Alternative medical systems are complete systems of theory and

practice that are developed independently of Western medicine. For example, traditional Chinese medicine and acupuncture are based on the concept of balancing vital energy (Qi) through specific body points. Acupuncture has been explored for obesity management, with some studies suggesting potential benefits in appetite control and metabolism regulation.

Energy medicine focuses on the use of energy fields, either biofield-based or bioelectromagnetic, to promote healing. Reiki therapy is one such approach, wherein practitioners channel healing energy through their hands to realign and strengthen the body's natural energy flow.

A systematic review and meta-analysis have suggested that acupuncture for obesity may offer modest benefits compared with placebo or lifestyle control. However, these findings are limited by clinical heterogeneity and poor methodological quality among the included trials, indicating the need for more rigorous research in this area [13].

Pharmacotherapy

Anti-obesity drug therapy serves as an important adjunct for patients who are unable to achieve adequate weight reduction through lifestyle modification and behavioral interventions alone. These medications are approved by the U.S. Food and Drug Administration (FDA) for individuals with a body mass index (BMI) of 30 kg/m² or higher, or for overweight individuals with a BMI between 27 and 29.9 kg/m² who also have at least one obesity-related comorbidity, such as type 2 diabetes mellitus, hypertension, or dyslipidemia. Pharmacologic treatment should always complement, not replace, dietary, physical activity, and behavioral interventions to maximize long-term weight management outcomes [4].

Most anti-obesity medications are approved only for short-term use, typically a few weeks to months. However, sibutramine and orlistat have received approval for long-term use in weight loss and weight maintenance (Table 2). In addition, several investigational agents such as bupropion and topiramate have shown promising effects on weight reduction, though they are currently approved by the FDA for other medical conditions rather than for obesity itself.

Anti-obesity drugs can be broadly classified according to their mechanism of action:
1. Appetite suppression – targeting central nervous system pathways to reduce hunger and caloric intake.
2. Altered nutrient absorption – reducing the absorption of dietary fats or other macronutrients in the gastrointestinal tract.
3. Increased energy expenditure – enhancing metabolic rate or thermogenesis to promote higher caloric burn [14].

Table 2. Agents Used In The Treatment Of Obesity [4]

Drug	Mechanism
FDA approved for short-term use	
Benzphetamine hydrochloride	Stimulates NE release
Phendimetrazine tartrate	Stimulates NE release
Phentermine hydrochloride or tartrate	Stimulates NE release
Diethylpropion hydrochloride	Stimulates NE release
Mazindol	Blocks NE reuptake
FDA approved for long-term use*	
Sibutramine hydrochloride	Blocks NE and 5-HT reuptake
Ortistat	Blocks gastric and pancreatic lipases
Investigational agents†	
Bupropion	Enhances NE activity
Topiramate†	Enhances GABA; blocks glutamate receptor subtypes

Appetite Suppressants

Appetite suppressants act mainly through central mechanisms that reduce food intake. Except for orlistat, most anti-obesity medications in this category work by stimulating norepinephrine release (such as phentermine, benzphetamine, phendimetrazine, and diethylpropion) or blocking its reuptake (as in the case of mazindol). The resulting increase in norepinephrine levels activates beta-adrenergic receptors in the hypothalamus, leading to appetite suppression [4].

Among these agents, phentermine is the most used in clinical practice due to its affordability and effectiveness. Although it is approved for short-term use of up to 12 weeks within 12 months, it is frequently used for longer durations under clinical supervision. In a long-term randomized controlled study involving 108 obese women, participants were treated with either a placebo or phentermine 30 mg daily, along with a low-calorie diet of 1000 kcal for 36 weeks. The results showed significantly greater weight loss with both continuous (12.2 kg) and intermittent (13.0 kg) phentermine use compared to placebo (4.8 kg). Phentermine is generally well tolerated, but some patients may experience stimulant-related symptoms such as agitation, insomnia, or restlessness [15].

The effectiveness of sibutramine in maintaining long-term weight loss has been demonstrated in several randomized controlled trials. In one study, obese participants who had lost at least 6 kg during a 4-week very low-calorie diet were randomly assigned to receive either sibutramine 10 mg or placebo for one year. Those treated with sibutramine achieved a mean additional weight loss of 5.2 kg, while those on placebo gained 0.5 kg. Moreover, 75% of patients in the sibutramine group maintained all their initial weight loss compared with only 42% in the placebo group.

In the Sibutramine Trial of Obesity Reduction and Maintenance (STORM), patients who had achieved more than 5% weight loss after six months of sibutramine therapy combined with a 600 kcal/day calorie deficit were randomly assigned to continue sibutramine or switch to placebo for an additional 18 months. The sibutramine dose was increased to 20 mg if weight regain occurred. Results showed that 43% of patients on sibutramine maintained at least 80% of their initial weight loss, compared with only 9% in the placebo group, indicating significant long-term efficacy [16].

Bupropion, an antidepressant that enhances norepinephrine activity and mildly inhibits dopamine reuptake, has shown weight-reducing effects in several studies. In trials involving depressed and obese patients, bupropion sustained release (SR) led to greater weight loss compared with placebo. In one 8-week study, patients receiving bupropion SR alongside a 1600-kcal diet lost an average of 5.0 kg versus 1.2 kg with placebo. Continued treatment over 24 weeks resulted in a mean total weight loss of 12.5 kg, primarily from fat reduction.

In a larger double-blind trial involving 327 obese nondepressed participants, bupropion SR at doses of 300 mg and 400 mg produced peak weight losses of 7.2% and 10.1%, respectively, compared with 5.15% in the placebo group. After 48 weeks, patients maintained 2.2% and 5.1% greater weight loss than placebo. Although bupropion is currently approved for depression and smoking cessation, it is not yet approved specifically for weight management [17].

Topiramate, an anticonvulsant approved in 1996 for epilepsy, has demonstrated beneficial effects on weight reduction. Its mechanism is thought to involve appetite suppression through blockade of kainate and AMPA glutamate receptor subtypes, along with modulation of voltage-gated sodium channels and γ-aminobutyric acid-A (GABA-A) activity. Experimental studies have shown that topiramate can reduce food intake, increase energy expenditure, and selectively decrease body fat while improving metabolic parameters such as leptin and insulin levels.

Clinical evidence supports its dose-dependent efficacy in weight loss. In a 6-month randomized, placebo-controlled trial, patients receiving 384 mg/day of topiramate achieved an average weight loss of 6.3% compared with 2.6% in the placebo group. Lower doses (64–192 mg/day) also produced significant weight reductions ranging from 4.8% to 6.3%. Among study completers, weight loss reached up to 8.5% at the highest dose.

Topiramate has also been studied in conditions associated with obesity, such as binge-eating disorder and medication-induced weight gain, with consistent findings of dose-related weight loss. Case reports describe benefits in patients with binge-eating disorder, psychiatric illness, and antipsychotic-associated weight gain. Despite these promising effects, topiramate remains approved only for seizure disorders and not specifically for obesity treatment [4].

Altered Nutrient Absorption

Orlistat is a potent, irreversible inhibitor of gastric and pancreatic

lipases that reduces the systemic absorption of dietary fat. By blocking these enzymes, it prevents the breakdown of triglycerides into absorbable free fatty acids and monoglycerols. In a randomized controlled trial involving 228 obese patients, orlistat 120 mg three times daily combined with a low-calorie diet resulted in an average weight loss of 8.5% after one year, compared to 5.4% in the placebo group. Similarly, in another study of 635 obese patients, both 60 mg and 120 mg doses of orlistat three times daily led to significantly greater weight loss than placebo during the first year (7.1 kg and 7.9 kg vs. 4.1 kg, respectively). Although some weight regain occurred in all groups during the second year, patients treated with orlistat maintained more of their weight loss, with an overall reduction of approximately 5% of initial body weight after two years.

The role of orlistat in weight maintenance was further evaluated in 729 obese subjects who had already achieved at least an 8% reduction in body weight through a low-calorie diet. These individuals were randomized to receive placebo or orlistat at 30, 60, or 120 mg three times daily, along with a maintenance diet. After one year, those on orlistat 120 mg regained significantly less weight than the placebo group (33% vs. 59%), while lower doses were less effective. The most common side effects were mild-to-moderate gastrointestinal symptoms such as loose stools and fecal urgency, which typically resolved without intervention [4].

Increased Energy Expenditure

Currently, no prescription medications are primarily designed to increase metabolic energy expenditure. Ephedrine is an example of a thermogenic agent that can stimulate heat production and calorie burning in humans and is often included in over the counter (OTC) weight-loss products. However, at doses of around 150 mg per day, ephedrine can cause adverse effects such as elevated blood pressure, tremors, and impaired glycemic control. Caffeine, which delays the breakdown of norepinephrine, has been found to act synergistically with ephedrine to enhance weight loss. In a study involving 180 obese patients, the combination of 200 mg caffeine and 20 mg ephedrine taken three times daily resulted in 3.4% greater weight loss than placebo, caffeine alone, or ephedrine alone.

These compounds, being available as OTC products and not regulated by the FDA, should be used with extreme caution due to their sympathomimetic effects. Patients are strongly advised to consult a physician before using such agents for weight reduction [4].

Beneficial Effects of Antiobesity Drugs on Other Risk Factors

Weight loss achieved through antiobesity drugs has additional benefits beyond reducing body weight, particularly in improving cardiovascular risk factors such as blood glucose, blood pressure, and lipid profiles. Both sibutramine and orlistat have been shown to produce significantly greater weight loss compared with placebo in obese patients with type 2 diabetes, accompanied by notable reductions in hemoglobin A1c and fasting blood glucose levels. A pooled analysis of three clinical trials found that orlistat 120 mg taken three times daily for two years not only improved glucose tolerance but also delayed the progression from impaired glucose tolerance to type 2 diabetes.

In clinical studies, orlistat produced modest reductions in blood pressure that correlated with the degree of weight loss. Sibutramine also lowered blood pressure, although the effect was smaller than expected, likely due to its enhancement of norepinephrine activity. However, some patients may experience a temporary increase in blood pressure during the early phase of sibutramine therapy. Because orlistat reduces dietary fat absorption, it can also produce additional improvements in lipid levels beyond those resulting from weight loss alone. Clinical trials have shown that orlistat can lower total cholesterol and LDL cholesterol by approximately 3% to 9% and 3% to 13%, respectively, compared with placebo, while its effects on HDL cholesterol and triglycerides remain variable [17].

Treatment Considerations

Clinical trials indicate that most antiobesity medications produce an average weight loss of 5–10%, offering meaningful health benefits even if ideal body weight is not reached. Since obesity is a chronic and relapsing condition, effective long-term management is essential. Among currently available drugs, only sibutramine and orlistat are FDA-approved for extended use and have demonstrated superior long-term outcomes compared with placebo in trials lasting one year or more. In contrast, investigational agents such as bupropion and topiramate show potential but lack sufficient long-term evidence.

Clinicians should closely monitor patients' progress and adjust therapy when needed. Those who fail to lose at least 4 pounds within 4–8 weeks are considered nonresponders and should be switched to an alternative medication. Once a significant weight loss is achieved, maintaining it becomes the central focus. Continuing pharmacotherapy, along with lifestyle and behavioral modifications, plays a crucial role in preventing weight regain and ensuring sustained improvements in overall health.[14].

Non-prescription Products For Weight Loss

Over the counter (OTC) weight-loss products are used more frequently than prescription medications. Data from the 1998 Behavioral Risk Factor Surveillance System involving over 14,000 adults revealed that 7% of respondents used nonprescription weight-loss agents, with phenylpropanolamine (2%) and ephedrine (1%) being the most common. Usage was especially high among young obese women (28.4%) and those already taking prescription antiobesity drugs (33.8%). Due to the risk of adverse cardiovascular and neurological effects, phenylpropanolamine was later withdrawn from the OTC market.

Several herbal and dietary supplements combining ephedrine and caffeine, such as Ma Huang–Guarana (72 mg ephedrine alkaloids + 240 mg caffeine daily) and Ma Huang–Kola nut (90 mg ephedrine alkaloids + 192 mg caffeine daily), have been evaluated in clinical trials. These formulations showed significantly greater reductions in body weight and fat compared with placebo, along with modest improvements in lipid profiles. However, they were consistently associated with increased blood pressure and heart rate, and some participants experienced side effects like palpitations, chest pain, and irritability. Although such ephedrine–caffeine combinations can enhance short-term weight loss, their cardiovascular risks restrict their safe long-term clinical application.[4].

Summary

Obesity reduction is crucial not only for improving appearance but also for preventing chronic diseases such as diabetes, hypertension, and cardiovascular disorders. Even modest weight loss can significantly improve metabolic health, quality of life, and functional capacity. Given its chronic and relapsing nature, obesity requires sustained lifestyle modification supported by medical interventions as needed to promote long-term individual and public health.

List Of Abbreviations

1. **BMI** – Body Mass Index
2. **FDA** – Food and Drug Administration
3. **OTC** – Over-the-Counter
4. **HDL** – High-Density Lipoprotein
5. **LDL** – Low-Density Lipoprotein
6. **HbA1c** – Hemoglobin A1c
7. **BP** – Blood Pressure
8. **RCT** – Randomized Controlled Trial

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