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Obesity as a Multidisciplinary Challenge

Aleksandra Mazur

ORCID: https://orcid.org/0009-0001-5037-0080

alekswisniewska98@gmail.com

University Clinical Hospital in Poznań

Przybyszewskiego 49, 60-355 Poznań, Poland

Krzysztof Sajewicz, MD

ORCID: https://orcid.org/0009-0007-2274-400X

k09022923@gmail.com

University Clinical Hospital in Poznań

Przybyszewskiego 49, 60-355 Poznań, Poland

Julia Dulęba

ORCID: https://orcid.org/0009-0009-1465-0809

jd5012773@gmail.com

University Clinical Hospital in Poznań

Przybyszewskiego 49, 60-355 Poznań, Poland

Paulina Strzałkowska
ORCID: https://orcid.org/0009-0000-7495-5561
strzalkowskapaulina@wp.pl
University Clinical Hospital in Poznań
Przybyszewskiego 49, 60-355 Poznań, Poland

Filip Kin
ORCID: https://orcid.org/0009-0008-9017-2901
filip.kin22@gmail.com
University Clinical Hospital in Poznań
Przybyszewskiego 49, 60-355 Poznań, Poland

Joanna Koszałko
ORCID: https://orcid.org/0009-0008-0790-0809
asia.koszalko@gmail.com
University Clinical Hospital in Poznań
Przybyszewskiego 49, 60-355 Poznań, Poland

Monika Kaźmierczak
ORCID: https://orcid.org/0009-0005-8868-8368
monikakazmierczak23@gmail.com
Independent Public Complex of Health Care Facilities of the Ministry of Interior and Administration in Poznań
Dojazd Str. 34, 60-631 Poznań, Poland

Maciej Hobot
ORCID: https://orcid.org/0009-0001-0087-6171
maciejhobot7@gmail.com
University Clinical Hospital in Poznań
Przybyszewskiego 49, 60-355 Poznań, Poland

Julia Kalisiak
ORCID: https://orcid.org/0009-0002-2432-0773;
julia.kalisiak2000@gmail.com
University of Zielona Góra
Licealna Str. 9; 65-417 Zielona Góra, Poland

Nel Geworkian
ORCID: https://orcid.org/0009-0008-2248-6052
nel.geworkian@gmail.com
University Clinical Hospital in Poznań
Przybyszewskiego 49, 60-355 Poznań, Poland

ABSTRACT

Purpose. Obesity is a chronic metabolic disease that has reached epidemic proportions worldwide, affecting individuals across all ages, genders, and socioeconomic backgrounds. Its growing prevalence presents a significant public health issue due to the various complications it leads to, such as metabolic disorders, cardiovascular diseases, and psychological or social problems. The aim of this article is to analyze the effectiveness of current therapeutic approaches to obesity, with particular focus on dietary interventions, pharmacotherapy, psychotherapy, and surgical treatment.

Materials and Methods. This article is based on a literature review of obesity treatment methods. Data from clinical trials, meta-analyses, and clinical guidelines were selected through searches in databases such as PubMed and Google Scholar. Keywords are "obesity", "diet", "anti-obesity drugs", "pharmacotherapy", "psychotherapy" and "bariatric surgery." Priority was given to studies published between 2020 and 2025.

Findings. This review provides an overview of current obesity treatment strategies. While dietary changes are the key element of treatment, combining them with pharmacotherapy and psychological support enhances effectiveness and leads to better long-term outcomes. Surgical intervention is reserved for severe cases after other methods have been explored. Each approach is assessed for its effectiveness, safety, and role within a comprehensive treatment plan.

Keywords: obesity, diet, anti-obesity drugs, psychotherapy, bariatric surgery

Introduction

Obesity is not only a multifactorial disease that affects an individual's quality of life, but also one of the most serious public health challenges of the 21st century. It can lead to a wide range of health problems and complications. The disease affects both children and adults, and its prevalence continues to grow worldwide.

Obesity is a significant modifiable risk factor for diseases such as cardiovascular conditions, type 2 diabetes, and cancer [1]. Due to its profound impact on the body's functioning, it is essential to discuss the available treatment options—dietary, psychological, pharmacological, and surgical.

In 2015, it was estimated that 603.7 million adults and 107.7 million children worldwide were living with obesity, and in nearly half of all countries, the prevalence of obesity had doubled since 1980 [1]. According to the most recent data from the World Health Organization (WHO) in 2022, 1 in 8 people globally were living with obesity, amounting to approximately 890 million adults [2]. Projections suggest that by 2030, the problem may affect every second adult in the United States [1].

According to the WHO definition, obesity is an excess of body fat that increases health risks. It is diagnosed based on the body mass index (BMI), which is the ratio of weight in kilograms to the square of height in meters. A BMI value exceeding 30 kg/m^2 is used to diagnose obesity [1].

A key factor in the development of obesity is a positive energy balance, resulting from increased energy intake relative to energy expenditure. However, it is important to recognize that obesity is a multifactorial disease. Its development may be influenced not only by environmental factors but also by genetic, psychosocial, and identifiable etiological causes such as medication use or immobility [2].

One of the main reasons increasing attention is being paid to obesity treatment is the wide range of diseases statistically associated with it. These include type 2 diabetes, non-alcoholic fatty liver disease (NAFLD), cardiovascular diseases, and stroke [3]. Obesity has also been linked to asthma, osteoarthritis, and chronic back pain [4]. Moreover, a correlation has been observed with thirteen types of cancer, including cancers of the breast, uterus, ovaries, esophagus, stomach, colon, liver, gallbladder, pancreas, kidneys, thyroid, meninges, and multiple myeloma. In terms of cardiovascular diseases, an increased risk has been documented for coronary artery disease, heart failure, atherosclerosis, and hypertension [3].

Diets

Due to the numerous health issues associated with obesity, various methods are employed to achieve weight reduction. One of the fundamental approaches is dietary modification. A study was conducted to assess the effectiveness of dietary interventions, based on the assumption that participants engaged in structured programs tend to achieve better outcomes than those outside such interventions. The study compared different diets and their effects [5].

In the case of a low-fat diet, the focus was on reducing fat intake rather than total calorie consumption. Due to the larger volume of food consumed and the high fiber content, this diet promoted a greater sense of satiety. In the Avanell study, which included 665 individuals who underwent dietary intervention and 688 in a control group, an average weight loss of 5.4 kg after 12 months and 3.6 kg after 3 years was observed [6].

In meal replacement diets, one or two full meals per day were substituted with low-calorie shakes or bars. Analysis showed that diets using meal replacements resulted in approximately 2.5 kg greater weight loss after 3 months compared to traditional calorie-restricted diets [5].

Low-carbohydrate diets, in which carbohydrates were replaced with protein or a combination of protein and fat (such as the ketogenic diet), were also studied. Meta-analyses demonstrated that these diets led to greater short-term weight loss (3–8 months) compared to control diets. However, after a longer period (18–30 months), the differences in weight loss between groups became minimal [7].

Due to the widespread popularity of the Mediterranean and ketogenic diets, these two dietary models were also directly compared. The time required to achieve a 5% weight reduction was analyzed. In the case of a very low-calorie ketogenic diet, this effect was achieved after just one month, while in the Mediterranean diet, it took about three months. However, it is believed that the very low-calorie ketogenic diet is not a long-term solution. Therefore, transitioning to the Mediterranean diet is recommended, especially considering the numerous health risks associated with obesity [7]. It is noted that the ketogenic diet may lead to a greater reduction in total cholesterol and serum triglycerides. However, it does not significantly improve glycemia, HbA1c, or LDL and HDL cholesterol levels—parameters that are often disrupted in individuals with obesity [7].

Despite the benefits associated with the ketogenic diet, its long-term use may carry the risk of nutritional deficiencies due to possible imbalances in micro- and macronutrient intake. An additional concern is its potentially negative impact on the gut microbiome [8].

Psychotherapy

Obesity is frequently associated with a range of psychological challenges, including low self-esteem, anxiety, disturbances in body image, and emotional eating. Psychological interventions can assist individuals in managing negative emotions and altering maladaptive behaviors. A deeper understanding of the psychological factors contributing to obesity may enhance the likelihood of achieving and sustaining long-term weight loss [9].

Among the available psychological approaches, behavioral therapy is supported by the strongest scientific evidence [9]. Other modalities—such as mindfulness-based interventions, psychodynamic therapy, acceptance and commitment therapy (ACT), dialectical behavior therapy (DBT), emotional freedom techniques (EFT), and compassion-focused therapy—have been studied, though empirical support for their effectiveness in the treatment of obesity remains limited [9].

Given the frequent occurrence of weight regain following initial treatment success, researchers have explored new strategies to support sustained weight loss. One such development is cognitive behavioral therapy for obesity (CBT-OB), a model designed to promote long-term weight maintenance by addressing key cognitive and behavioral factors involved in obesity [10].

Cognitive factors related to obesity treatment outcomes have been classified into three main categories:

1. Factors associated with treatment dropout, including:

    - Unrealistic expectations regarding body weight reduction within a year,
    - Excessive preoccupation with appearance,
    - Discrepancies between anticipated and actual weight loss,
    - Dissatisfaction with treatment progress.

2. Factors influencing the degree of weight loss, such as:

    - Increasing levels of dietary restriction,
    - High initial expectations for weight reduction.

3. Factors that facilitate weight maintenance, including:

    - Satisfaction with achieved outcomes,
    - Confidence in continuing weight management without professional support [10].

CBT-OB builds on the core components of traditional behavioral therapy for obesity (BT-OB), incorporating four foundational strategies: employing a theoretical model to explain the persistence of the problem, fostering active patient engagement in a collaborative therapeutic relationship, utilizing a present-focused problem-solving approach, and systematically evaluating treatment outcomes. Additionally, CBT-OB emphasizes cognitive restructuring alongside behavioral change to foster sustainable lifestyle modifications. A central feature is the development of a personalized cognitive formulation that identifies the psychological mechanisms most likely to hinder weight loss and its long-term maintenance [10].

A randomized controlled trial demonstrated that individuals on either high-protein or high-carbohydrate diets who also received CBT-OB showed lower dropout rates over a 51-week period and achieved greater weight loss compared to those who did not receive psychological support. These findings underscore the value of integrating cognitive behavioral therapy into comprehensive obesity management [10].

GLP-1 analogs

One of the groups of drugs used in the treatment of obesity are analogs of the human hormone GLP-1 (glucagon-like peptide-1). This hormone naturally regulates blood glucose levels and appetite – these properties are used therapeutically. In clinical practice, two analogs are mainly used: liraglutide and semaglutide. They work by delaying gastric emptying, reducing the feeling of hunger, and increasing the feeling of satiety. Additionally, semaglutide shows benefits not only in weight control but also reduces the risk of cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke in patients with type 2 diabetes and high

cardiovascular risk. In the case of liraglutide, its possible influence on reward and motivation responses related to food has also been observed, which may reduce the attractiveness of food. Both drugs show cardioprotective effects, which is an additional advantage since patients with obesity often have risk factors for cardiovascular diseases [11].

Liraglutide is dosed once daily and administered via subcutaneous injection. Treatment begins with a dose of 0.6 mg per day, gradually increasing by 0.6 mg/day every ≥1 week until the target dose of 3 mg per day is reached. If this dose is not tolerated, the highest dose tolerated by the patient is established as the target. Contraindications include hypersensitivity to the components of the preparation, pregnancy, and breastfeeding. Caution should be exercised in people with an increased risk of acute pancreatitis, gallstones, cholecystitis, and those at risk of dehydration. Very common side effects are nausea, vomiting, diarrhea, or constipation. Hypoglycemia may also occur frequently, which may require a reduction in the doses of hypoglycemic drugs in patients, mainly insulin or sulfonylurea derivatives [8].

Semaglutide used in obesity treatment is administered once weekly via subcutaneous injection. Treatment begins with a dose of 0.25 mg once a week. Over 16 weeks, the dose is gradually increased to the recommended target dose of 2.4 mg per week. In case of intolerance to the dose, manifested mainly by gastrointestinal symptoms, it is recommended to return to the previously tolerated dose until the symptoms subside. Contraindications to the use of semaglutide are hypersensitivity to the components of the preparation, pregnancy, and breastfeeding. Special caution should be exercised in cases of increased risk of acute pancreatitis, gallstones, cholecystitis, and increased susceptibility to dehydration in the patient [8].

In the SUSTAIN 10 study, one of the clinical trials evaluating the effectiveness and safety of subcutaneous semaglutide, it was shown that semaglutide surpassed liraglutide in terms of total body weight loss, as well as the percentage of participants who achieved a reduction in body weight of ≥5% and ≥10%.

An additional advantage of semaglutide is the less frequent dosing – once a week, in contrast to liraglutide, which requires daily injections. This may result in better adherence to treatment, and thus – higher effectiveness [11].

In the studies, the impact of semaglutide on the reduction of glycated hemoglobin (HbA1c) and body weight of participants was also compared with placebo and other antidiabetic drugs such as: insulin glargine, sitagliptin, extended-release exenatide, dulaglutide, canagliflozin, and liraglutide. The results indicated greater effectiveness of semaglutide.

Additionally, in the case of exenatide ER and dulaglutide, semaglutide proved more effective in achieving ≥5% weight loss [11].

TIRZEPATIDE – GIP and GLP-1

Tirzepatide is a dual agonist drugs that targets both the glucagon-like peptide-1 (GLP-1) receptor and the glucose-dependent insulinotropic polypeptide (GIP) receptor. Clinical trials have demonstrated that tirzepatide contributes to reduced energy intake and appetite, thereby enhancing satiety and diminishing hunger sensations in patients [8].

Tirzepatide therapy is initiated at a dose of 2.5 mg administered once weekly via subcutaneous injection. After four weeks, the dosage is increased to 5 mg weekly. If additional therapeutic benefit is required, further incremental increases of 2.5 mg may be made at four-week intervals, up to a maximum dose of 15 mg per week. The adverse event profile of tirzepatide is comparable to that of other GLP-1 receptor agonists, with gastrointestinal disturbances such as nausea, diarrhea, and constipation being the most frequently reported. The drug is contraindicated in individuals with known hypersensitivity to any of its components, and should be used with caution in patients with a history of pancreatitis [9].

The efficacy of tirzepatide has been evaluated in multiple randomized controlled trials, including the SURMOUNT-1, -3, and -4 studies.

In the SURMOUNT-1 trial, participants received tirzepatide at doses of 5 mg, 10 mg, or 15 mg, or placebo, over a 72-week period.

SURMOUNT-3 also evaluated treatment over 72 weeks, comparing participants receiving their maximum tolerated dose of tirzepatide (10 mg or 15 mg) with placebo [13].

In the SURMOUNT-4 trial, participants were assigned to receive 10 mg or 15 mg of tirzepatide or placebo for a duration ranging from 36 to 88 weeks. This study reported the greatest degree of weight reduction achieved to date in clinical obesity management [14].

Across all three studies, tirzepatide led to significantly greater weight reduction and metabolic improvement compared to placebo. On average, individuals treated with tirzepatide experienced a weight loss of 18.7% relative to baseline [13]. Improvements were also noted in waist circumference, systolic and diastolic blood pressure, and HbA1c levels [14].

A large cohort study compared the weight-reducing efficacy of tirzepatide and semaglutide in adults with overweight or obesity. The study analyzed data from 41,222 patients—32,029 using semaglutide and 9,193 using tirzepatide. After filtering, 18,386 individuals (average body weight of 110 kg) were included in the final analysis. Results

indicated that patients on tirzepatide were more likely to achieve ≥5%, ≥10%, and ≥15% weight loss compared to those receiving semaglutide. The incidence of side effects was similar in both groups [15].

Naltrexone and Bupropion

Both the naltrexone hydrochloride and bupropion hydrochloride used in this drug have central actions. Naltrexone is an opioid receptor antagonist, while bupropion is a non-selective inhibitor of dopamine and norepinephrine reuptake and an antagonist of nicotinic acetylcholine receptors [8].

Bupropion activates pro-opiomelanocortin (POMC), which reduces appetite by affecting hypothalamic function [16]. The combination of both substances exerts an anorectic effect, which involves the activation of anorexigenic neurons in the hypothalamus. An important mechanism of action of this therapy is also its effect on the reward system, which helps alleviate compulsive overeating [8,16].

The drug is available in the form of oral tablets. Treatment begins with the lowest dose of 8 mg of naltrexone and 90 mg of bupropion per day. The dose can be gradually increased – weekly – until the maximum dose of 32 mg of naltrexone and 360 mg of bupropion per day is reached, administered in two divided doses. In case of adverse effects that prevent dose escalation, the highest tolerable dose should be maintained [17].

The most common side effects include nausea, vomiting, diarrhea, and constipation. Less common: dizziness, concentration and attention disorders, hot flashes, palpitations. It is also possible to experience anxiety, insomnia, headaches, joint pain, depression, and increased blood pressure. Contraindications to starting treatment include uncontrolled hypertension, epilepsy, central nervous system tumors, bipolar disorder, pregnancy, history of bulimia or anorexia, dependence on benzodiazepines, opioids, and the period after sudden alcohol withdrawal [8].

In the randomized, double-blind phase 3 study COR-II (CONTRAVE Obesity Research – II), the effectiveness and safety of extended-release naltrexone and bupropion were evaluated in the treatment of obesity and overweight. The study included 1,496 participants who took 32 mg of naltrexone + 360 mg of bupropion (in two divided doses) or placebo for 56 weeks [18].

Participants taking bupropion with naltrexone lost an average of 6.5% of their body weight after 28 weeks, compared to 1.9% in the placebo group. After 56 weeks, weight loss was 6.4% in the treatment group and 1.2% in the placebo group. After both 28 weeks and 56

weeks, over 50% of participants in the treated group achieved a weight reduction of at least ≥5% [18].

Orlistat

Orlistat is a drug that acts as an inhibitor of lipase, an enzyme responsible for fat digestion in the gastrointestinal tract. Its action is based on reducing fat absorption in the intestines, which limits the number of calories absorbed [19]. Its effect on visceral fat tissue through the regulation of adipokines has also been demonstrated. Unlike other drugs used in the treatment of obesity, it does not act on the central nervous system [20].

The recommended dosage is 120 mg three times a day. The capsule should be taken before, during, or up to one hour after the main meal that contains fat. Treatment should not last longer than 6 months due to the risk of vitamin deficiencies, especially fat-soluble vitamins, and other nutrients [8].

Its main side effects include fatty stools, changes in bowel movements, abdominal pain, and anal fat spotting [20]. Contraindications to starting the drug include chronic malabsorption syndrome, gallstones, cholestasis, breastfeeding, and pregnancy [8].

In randomized controlled trials, greater weight loss, reduction in waist circumference, and BMI were demonstrated in patients using orlistat compared to placebo. Patients taking orlistat were more likely to achieve a weight loss of over 5% and 10% compared to those taking placebo [21].

Bariatric surgery

Various surgical procedures have been developed to support weight reduction in the management of obesity. The most widely performed bariatric operations include gastric bypass (conducted via either open or laparoscopic approaches), laparoscopic adjustable gastric banding (LAGB), and sleeve gastrectomy [22]. .

Gastric bypass surgery, introduced in the late 1970s, has undergone substantial refinement. The current standard involves a Roux-en-Y configuration, in which a small gastric pouch (approximately 20–30 ml in volume) is surgically connected to the small intestine, bypassing a portion of the gastrointestinal tract. A variation known as banded gastric bypass includes the placement of a prosthetic ring around the gastric pouch to help prevent long-term weight regain [22].

Laparoscopic Adjustable Gastric Banding (LAGB) is typically performed using minimally invasive techniques. An adjustable silicone band is placed around the upper portion of the stomach, just below the gastroesophageal junction, creating a small proximal pouch of roughly 30 mL. This pouch fills quickly during eating, promoting early satiety. The degree of restriction can be individualized by adjusting the volume of saline in the band's balloon component, allowing for tailored modifications of gastric outlet tightness [22].

Sleeve gastrectomy involves the surgical removal of approximately 80% of the stomach, resulting in a narrow, tubular-shaped gastric remnant. This approach restricts food intake and leads to a reduction in ghrelin production, a hormone that plays a central role in stimulating appetite [23].

Candidates for bariatric surgery typically include patients with a body mass index (BMI) greater than 40 kg/m², or greater than 35 kg/m² in the presence of obesity-related comorbidities such as cardiovascular disease, type 2 diabetes, dyslipidemia, or obstructive sleep apnea. Non-surgical interventions should typically be attempted before considering operative treatment [22].

Bariatric procedures promote weight loss primarily through restriction of gastric capacity and/or reduction of nutrient absorption. Long-term follow-up data indicate that these interventions produce durable results. Patients maintain, on average, a weight loss of approximately 23.4% from baseline five years after surgery, with a reduction of around 22.2% persisting at 15 years, emphasizing the sustained efficacy of bariatric treatment [23].

Conclusion

The treatment of obesity requires a comprehensive and individualized therapeutic approach. In addition to diet and physical activity modifications, which form the basis of therapy, psychotherapy can also be added to help identify and modify detrimental behavior patterns. Additionally, pharmacotherapy or bariatric surgery can provide support. Further research should focus on optimizing therapeutic strategies and enhancing the possibilities of multidisciplinary care.

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Author's contribution

Conceptualization: Aleksandra Mazur, Paulina Strzałkowska

Methodology: Julia Dulęba, Nel Geworkian

Software: Krzysztof Sajewicz

Check: Filip Kin, Joanna Koszałko, Monika Kaźmierczak

Formal analysis: Maciej Hobot

Investigation: Julia Kalisiak

Resources: Julia Dulęba, Maciej Hobot

Data curation: Nel Geworkian

Writing -rough preparation: Paulina Strzałkowska

Writing -review and editing: Filip Kin

Visualization: Krzysztof Sajewicz

Supervision: Monika Kaźmierczak

Project administration: Aleksandra Mazur

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