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The Growing Obesity Epidemic: Integrating Lifestyle, Pharmacological, and Surgical Interventions for Effective Management

Authors:

Jan Siwiec

Międzyleski Specialist Hospital in Warsaw, Bursztynowa 2, 04-749 Warsaw, Poland

jjsiwiec@gmail.com

ORCID: 0000-0002-7193-7074

Olga Śpiołek

LUX MED Sp. z o.o., Szturmowa 2, 02-678 Warsaw, Poland

olgaspiolek@gmail.com

ORCID: 0009-0008-6271-1242

Agnieszka Alicja Wąsowicz

National Medical Institute of the Ministry of the Interior and Administration, Wołoska 137, 02-507 Warsaw, Poland

agnieszkawasowicz99@gmail.com

ORCID: 0009-0008-3256-793X

Marcelina Paula Sztyler-Krąkowska

Dr Anna Gostynska Wolski Hospital, Independent Public Health Care Institution, Marcina Kasprzaka 17, 01-211 Warsaw, Poland

marcelina.sztyler@wp.pl

ORCID: 0009-0004-4817-9537

Mateusz Teofilak

Międzyleski Specialist Hospital in Warsaw, Bursztynowa 2, 04-749 Warsaw, Poland

teofilak.mateusz@gmail.com

ORCID: 0009-0007-3902-2484

Natalia Maria Smyl

John Paul II Western Hospital in Grodzisk Mazowiecki, Daleka 11, 05-825 Grodzisk Mazowiecki, Poland

nataliamaria.smyl@gmail.com

ORCID: 0009-0003-9571-3432

Aleksandra Słowikowska

National Medical Institute of the Ministry of the Interior and Administration, Wołoska 137, 02-507 Warsaw, Poland

aslowikowska0108@gmail.com

ORCID: 0009-0004-3705-822X

Julia Szatkowska

Hospital of Our Lady of Perpetual Help in Wołomin, Gdyńska 1/3, 05-200 Wołomin, Poland

julka.szatkowska32@gmail.com

ORCID: 0009-0007-5084-9378

Franciszek Kędziora

Medical University of Białystok, Jana Kilińskiego 1, 15-089 Białystok, Poland

fkedzior@gmail.com

ORCID: 0009-0003-7833-1985

Dariusz Paweł Fabian

Specialist Provincial Hospital in Ciechanów, Powstańców Wielkopolskich 2, 06-400 Ciechanów

Dfabianstudy@gmail.com

ORCID: 0009-0006-7241-7245

Abstract

Introduction: Obesity is a multifactorial disease with a growing global prevalence, significantly increasing the risk of numerous health conditions, including type 2 diabetes and cardiovascular diseases. Its management requires a multifaceted approach that includes lifestyle modifications, pharmacologic interventions and, in severe cases, surgical treatments.

Materials and methods: A literature review was conducted using PubMed and Google Scholar, using keywords: “obesity epidemiology”, “obesity consequences”, “obesity treatment”, “obesity pharmacology”

Conclusions: The prevalence of obesity is rising worldwide, with genetic, environmental, and lifestyle factors contributing to its development. Effective obesity management involves personalized interventions, including dietary and behavioural changes, alongside pharmacological options like GLP-1 receptor agonists and naltrexone-bupropion. Surgical interventions are considered for severe cases. Emerging treatments, such as tirzepatide, targeting both GLP-1 and GIP receptors, show promising results. A comprehensive, individualized approach remains crucial for improving patient outcomes and addressing the global obesity epidemic.

Keywords: obesity; epidemiology; risk factors; diagnosis; pharmacotherapy; behavioural; intervention; bariatric surgery.

1. INTRODUCTION

Obesity is a complex, multifactorial disease characterized by excessive body fat accumulation, defined by a body mass index (BMI) of 30 or greater. It significantly increases the risk of various non-communicable diseases, including type 2 diabetes, cardiovascular diseases, and certain cancers [1] . The global prevalence of obesity has nearly tripled since 1975, with significant increases observed across all demographics, particularly in urban areas of low- and middle-income countries [2,3] . Factors contributing to obesity include genetic predisposition, lifestyle choices, and environmental influences, such as the availability of high-calorie foods

and sedentary behaviors [1,4] . Effective management strategies are based on lifestyle modifications, including dietary changes and increased physical activity, alongside potential pharmacological and surgical interventions for severe cases [5,6] . This significant public health concern is associated with various health complications that can severely impact quality of life and longevity. Understanding these consequences is crucial for effective prevention and treatment strategies[5].

2. EPIDEMIOLOGY

The prevalence of obesity has significantly increased globally. It is estimated that approximately 42% of adults in the US are affected, and projections suggest this could rise to nearly 49% by 2030 [5] . In Europe, obesity has reached epidemic levels with nearly 60% of adults and one in three children living with overweight or obesity [7] . The number of people affected by this widespread condition varies significantly across countries, with higher rates observed in wealthier nations [7] . The highest incidence of both overweight and obesity are observed in Mediterranean and Eastern European nations. In the WHO European Region, the prevalence of obesity has continued to rise, and no member state is currently on track to meet the target of halting this upward trend by 2025 [7] . Obesity is also a significant public health issue in Poland, with a high prevalence observed among adults. A nationwide study indicated that 42.2% of adults were overweight, with 16.4% classified as obese, showing a higher prevalence in men (52.4% overweight and 16.5% obese) compared to women (32.0% overweight and 16.2% obese)[3].

3. Risk factors

Obesity is influenced by a complex interaction of various risk factors, including genetic predisposition, environmental influences, and lifestyle choices. The main factors that contribute to obesity include an energy imbalance characterized by increased caloric intake and decreased physical activity, which has been exacerbated by modern sedentary lifestyles and the availability of energy-dense foods [8] . Most forms of obesity are polygenic, involving multiple genetic variants associated with body mass index (BMI), while monogenic obesity due to single gene mutations is rare[1,5]. Specific genes, such as those in the leptin-melanocortin pathway, have been identified as critical in regulating appetite and weight [1] . In addition, epigenetic factors, which involve heritable changes in gene expression without altering the DNA sequence, also contribute to obesity risk[9,10]. Psychological factors, including depression and insufficient sleep may as well lead to the progression of the disease [5] . Additionally, socioeconomic aspects play an important role, as lower educational attainment is linked to higher obesity rates, particularly among children [7] . Family history significantly impacts

obesity risk, with children of obese parents being at a higher risk[1]. Overall, addressing these multifaceted risk factors is crucial for effective obesity prevention and management[9]

4. Consequences of obesity

Obesity has significant adverse effects on cardiovascular (CV) health, contributing to conditions such as hypertension, heart failure, and coronary heart disease. It increases total blood volume and cardiac output, leading to higher cardiac workload and a greater risk of left ventricular hypertrophy and dilation, which can result in heart failure and arrhythmias[11]. It is also associated with a higher incidence of atrial fibrillation and stroke, with each unit increase in body mass index (BMI) correlating with increased stroke risk [11,12]. In addition, obesity contributes to systemic inflammation and metabolic disorders, including type 2 diabetes and dyslipidemia, which further exacerbate CV risks [5,13]. The disease can also lead to psychological issues such as depression and anxiety, which complicate self-care and exacerbate health deterioration [14]. The stigma associated with obesity often results in social isolation and negative self-image, further influencing mental health[14]. Moreover, the impact of obesity on life expectancy has been quantified, revealing that obesity-related mortality could reduce life expectancy by up to 1.67 years among men and 1.54 years among women in various European countries[12].

5. Diagnosis

The World Health Organization classifies obesity into three classes: class I (BMI 30-34.9), class II (35-39.9), and class III (≥40)[1]. However, BMI alone does not account for individual differences in body fat distribution or associated health risks, prompting the use of additional measures like waist circumference to assess visceral fat[5,15]. Waist circumference is a critical measure in assessing obesity, particularly for individuals with a BMI between 25 kg/m² and 35 kg/m². A waist circumference of at least 102 cm in men and 88 cm in women indicates abdominal obesity, which is associated with increased risks for various adiposity-related diseases. Different thresholds may apply based on ethnicity, with lower measurements suggested for certain populations, such as South Asian and East Asian individuals [15]. The relationship between waist circumference and obesity underscores the importance of considering both BMI and waist measurements in clinical assessments to evaluate weight-related health risks effectively[1].

6. Treatment

Treatment approach for obesity should be multifaceted, including behavioural interventions, nutritional strategies, physical activity, pharmacotherapy, and surgical procedures. Evidence-

based obesity care plans should be individualized, addressing the root causes of obesity and supporting behavioural change through lifestyle modifications such as reduced caloric intake and increased physical activity [5,9]. Research highlights that non-individualized interventions can lead to feelings of objectification and alienation, which may hinder health progress [14]. A person-centered approach is essential for setting realistic goals, particularly for those with a sedentary lifestyle and a moderately high BMI, as subtle increases in daily activity can be beneficial [16]. Furthermore, various studies have explored the effectiveness of both individual and group interventions, indicating that personalized strategies can enhance engagement and outcomes in behavioural lifestyle interventions [17]. Pharmacological treatment for obesity is recommended as an adjunct to lifestyle modifications, particularly for individuals with a BMI of 30 kg/m² or higher, or 27 kg/m² with obesity-related complications, to support lifestyle interventions and prevent weight regain [7,9]. Commonly recommended treatments are orlistat, naltrexone-bupropion and various GLP-1 receptor agonists such as liraglutide and semaglutide, which enhance satiety and promote weight loss [9,16]. However, pharmacotherapy should be used chronically and tailored to individual patient needs, considering potential side effects and interactions [18] Additionally, comprehensive management may involve adjunctive therapies, including psychological support and, in some cases, bariatric surgery for those with severe obesity [7,15]. Overall, a multidisciplinary approach is essential for effective obesity management[7].

6.1. Dietary intervention

Dietary intervention plays an essential role in obesity management and mental health improvement. Studies indicate that non-pharmacological methods, particularly dietary changes, significantly enhance patients' quality of life, independent of weight loss, as evidenced by improvements in general health, physical functioning, and vitality among those following low-fat diets [19]. Strategies for managing obesity emphasize creating a negative energy balance through various approaches, including macronutrient composition and meal timing. Evidence suggests that the specific macronutrient distribution—whether low-fat, low-carbohydrate, or high-protein—does not significantly impact long-term weight loss, as all diets can lead to similar outcomes if they maintain a caloric deficit[8,20]. The Mediterranean diet, characterized by high consumption of fruits, vegetables, whole grains, and healthy fats, has shown effectiveness in promoting weight loss and improving metabolic health[21]. Additionally, increasing dietary fiber intake and reducing energy-dense foods are recommended to enhance

satiety and support weight management[19,22]. Ultimately, adherence to a chosen dietary pattern is crucial for long-term success in weight management[8].

6.2. Behavioural intervention

Behavioural interventions play an important role in treating obesity, particularly through structured lifestyle modification programs that combine dietary changes, physical activity, and behavioural strategies. High-intensity programs, which typically involve at least 14 sessions over six months, have been shown to produce significant weight loss, averaging 5-10% of initial body weight, and improve health outcomes such as glycemic control in individuals with type 2 diabetes [10,15] . These interventions often utilize techniques like self-monitoring, goal setting, and problem-solving to enhance adherence and facilitate behaviour change [10,23] . Self-monitoring is one of the most significant interventions in weight loss management, as evidenced by various studies. For instance, participants in a digital intervention that encouraged daily self-weighing lost significantly more weight (6.6%) compared to those who did not change their self-monitoring habits (0.4%)[10]. Additionally, a smartphone app that provided personalized feedback and encouraged self-monitoring of both weight and physical activity led to an average weight loss of 9.4 kg in participants, highlighting the effectiveness of structured self-monitoring combined with regular feedback[10]. Cognitive techniques can facilitate coping with hunger and cravings, enabling individuals to recover from dietary lapses[22]. Setting realistic goals in the management of obesity is crucial, as it is a chronic disease requiring long-term strategies. Health care providers should collaborate with patients to establish achievable expectations and personalized action plans that focus on sustainable behaviour changes and health outcomes, rather than solely on weight loss[9]. The role of personalized interventions was proven by Look AHEAD (Action for Health in Diabetes) study that investigated the effects of an intensive lifestyle intervention (ILI) on weight loss and diabetes management in individuals with obesity and type 2 diabetes. Enrolling 5,145 participants, the study aimed to achieve a minimum 7% weight loss and increase physical activity to at least 175 minutes per week. Initial results showed that ILI participants lost an average of 8.6% of their initial weight in the first year, significantly more than the 0.7% loss in the diabetes support and education (DSE) group (LOOK AHEAD). Additionally, understanding the psychological barriers that hinder access to treatment, such as feelings of shame or discrimination, is crucial for fostering a supportive environment that encourages engagement in weight management services[14]. A multidisciplinary approach that includes psychological support can enhance self-efficacy and resilience, ultimately leading to

more successful weight loss outcomes[14,19]. This approach involves acknowledging the various determinants of weight and mitigating anti-fat stigma by redefining success to include healthy behaviour changes, irrespective of body size[9]

6.3. Physical activity

Physical activity plays an inherent role in the management of obesity by increasing caloric expenditure and promoting maintaining a caloric deficit. Additionally, it improves physical fitness and reduce cardiometabolic risks [24] . Exercise training programs, including aerobic, resistance, and high-intensity interval training (HIIT), have been shown to enhance cardiorespiratory fitness (VO2max) and muscle strength in adults with overweight or obesity [24,25] . Recommendations suggest engaging in moderate to vigorous aerobic activity for 30-60 minutes most days to achieve various health benefits, including weight management and improved cardiorespiratory fitness [9] . While the effects on weight loss are modest, with expected reductions of about 2 to 3 kg, the benefits of increased physical activity extend beyond weight management to include improved quality of life and metabolic health[24,26]. Specifically, combining aerobic and resistance training is recommended for optimal outcomes in body composition and physical function[27].

6.4. Pharmacology

Pharmacological treatment for obesity is advised in addition to lifestyle changes for individuals with a BMI of 30 kg/m² or greater, or 27 kg/m² if they have obesity-related health issues. Approved medications include orlistat, liraglutide, semaglutide, tirzepatyd and the combination of naltrexone and bupropion, which can enhance weight loss beyond what lifestyle changes alone can achieve[8,9]. Pharmacological treatment for obesity is recommended to be used chronically, as obesity is a chronic disease, and short-term use (3-6 months) does not yield long-term health benefits [18] . In adults, if weight loss is less than 5% after three months of pharmacotherapy, its continuation is deemed unjustified, although earlier discussions about dietary and physical activity adjustments are encouraged [18] . Regular assessments of treatment efficacy and side effects are crucial to determine the appropriate duration and adjustments in pharmacotherapy [16] . It is also important to remember that

medications for other medical conditions may have significant impact on weight management and overall health outcomes. For instance, pharmacotherapy for mood disorders and other psychiatric conditions can lead to weight gain, necessitating a careful review of medication regimens to minimize this effect[16].

6.4.1. Orlistat

Orlistat is a pancreatic lipase inhibitor that reduces the intestinal absorption of dietary fat by approximately one-third[28]. This mechanism decreases the digestion of dietary fats, resulting in lower caloric intake and contributing to significant weight loss, with studies showing an average reduction of about 8% compared to placebo over 12 months[28]. The drug is effective in promoting weight loss and improving various cardiometabolic parameters, although it is associated with gastrointestinal side effects such as diarrhoea, faecal incontinence, oily spotting, and fatty stools, which affect over 10% of users during long-term treatment [29] . Additionally, it can lead to small decreases in fat-soluble vitamins, necessitating multivitamin supplementation for some patients[28]. Other potential side effects include increased oxalic acid in urine, which may contribute to renal stones [30] . While orlistat is generally considered safe, its side effects can lead to treatment discontinuation in some cases, with a reported rate of 8.8% in treated groups compared to 5.0% in placebo groups [30] . Despite its efficacy, newer anti-obesity medications may offer greater weight loss potential[30]

6.4.2. Naltrexone and bupropione

Naltrexone and bupropion are combined in a formulation used for the treatment of obesity, leveraging their complementary mechanisms to reduce food intake and cravings. Bupropion acts as a norepinephrine and dopamine reuptake inhibitor, stimulating pro-opiomelanocortin (POMC) neurons, which decreases appetite, while naltrexone, an opioid receptor antagonist, enhances this effect by blocking the auto-inhibition of POMC neurons, leading to a synergistic appetite-suppressing action [28,31] . Clinical studies have demonstrated that this combination significantly promotes weight loss, with participants achieving greater reductions in body weight compared to placebo [31,32] . Clinical trials, such as the COR-II study, demonstrated that participants receiving Naltrexone-Bupropione experienced significantly greater weight loss compared to those on placebo, with a mean weight loss of 6.5% at 28 weeks [31] . Furthermore, the combination therapy was linked to improvements in various cardiometabolic risk factors without worsening depressive symptoms [29] .While it does have

some side effects, mainly nausea, headache, and constipation, these are typically mild to moderate and tend to be temporary, especially during the initial dose adjustment phase[31,33].

6.4.3. Liraglutide

Liraglutide, a glucagon-like peptide-1 (GLP-1) analog, was primarily used for the treatment of type 2 diabetes (T2DM) and has shown significant efficacy in weight management among patients with obesity. It exerts its effects by activating GLP-1 receptors in the central nervous system, particularly in the hypothalamus, which leads to increased satiety and reduced appetite through the stimulation of anorexigenic neurons and inhibition of orexigenic neurons[18,28]. This mechanism is complemented by its ability to slow gastric emptying, further contributing to feelings of fullness [18] . Additionally, liraglutide enhances glucose-dependent insulin secretion from pancreatic beta-cells, thereby improving glycemic control[30]. The drug's efficacy in weight management is also linked to its impact on various cardiometabolic parameters, including reductions in blood pressure and improvements in lipid profiles[30,33]. In the SCALE Obesity and Prediabetes trial, participants receiving liraglutide 3.0 mg daily lost an average of 8.4 kg, while the placebo group lost only 2.8 kg, with 63.2% of liraglutide users achieving at least 5% weight loss [6,29] . Additionally, liraglutide has been associated with a lower incidence of developing T2DM in prediabetic patients, prolonging the time to diabetes onset significantly[28,30]. However, common side effects include gastrointestinal issues such as nausea and diarrhea[30]

6.4.5. Semaglutide

Semaglutide is a glucagon-like peptide-1 (GLP-1) receptor agonist approved for the treatment of type 2 diabetes and obesity, demonstrating significant weight loss and improvements in cardiometabolic risk factors. In clinical trials, semaglutide 2.4 mg administered weekly resulted in a mean weight loss of 14.9% over 68 weeks, compared to 2.4% with placebo, with 86% of participants achieving at least 5% weight loss [34,35] . Additionally, semaglutide was associated with improvements in cardiometabolic risk factors, including reductions in waist circumference, blood pressure, and lipid levels[28]. However, gastrointestinal disorders, such as nausea and diarrhoea, were the most common adverse effects, affecting a significant proportion of users[28,34].

6.4.6. Tirzepatide

Tirzepatide (TZP) functions as a dual agonist for the glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) receptors, which synergistically enhance its effects on body composition and glucose metabolism. This mechanism is thought to reduce fat synthesis and deposition by regulating adipose tissue processes such as lipolysis and fatty acid oxidation, leading to a significant decrease in visceral adipose tissue compared to other treatments [36]. The combined action of GLP-1 and GIP receptors may explain TZP's superior efficacy in weight reduction and metabolic improvements over other anti-obesity medications [37,38]. In the SURMOUNT-1 trial, participants without diabetes experienced a mean weight loss of up to 20.9% after 72 weeks of treatment with the highest dose of tirzepatide, compared to a mere 3.1% in the placebo group [39]. In clinical trials, participants receiving tirzepatide also showed a higher likelihood of achieving various weight loss targets, with 91% reaching a 5% reduction and 36% achieving a 25% reduction [38,40]. Additionally, tirzepatide was associated with substantial reductions in waist circumference and improvements in various cardiometabolic risk factors, including blood pressure and lipid levels[38,39]. However, gastrointestinal adverse events, such as nausea and diarrhoea, were more prevalent among those receiving tirzepatide compared to placebo, highlighting the need for careful monitoring during treatment[39,40].

6.5. Surgical treatment

Recent guidelines for bariatric surgery indicate that surgical treatment is now recommended for individuals with a body mass index (BMI) greater than 35 kg/m², regardless of the presence of co-morbidities. Additionally, surgery should be considered for those with metabolic diseases and a BMI between 30 and 34.9 kg/m² [41]. Common procedures include Roux-en-Y gastric bypass and sleeve gastrectomy, both of which have shown significant long-term weight loss and improvement in obesity-related comorbidities such as type 2 diabetes[33,42]. Studies indicate that these surgeries not only facilitate substantial weight loss but also enhance quality of life, with improvements in health-related quality of life (HRQoL) observed post-surgery[33]. The guidelines emphasize the importance of a multidisciplinary team in evaluating candidates for surgery, reflecting the complexity of obesity as a chronic disease [41,43]. The choice of surgical technique should be individualized based on patient characteristics and preferences, as both bypass and gastrectomy yield similar outcomes in weight loss and comorbidity resolution[42]

7. Conclusions

In conclusion, the treatment of obesity requires a comprehensive, multifaceted approach that includes lifestyle modifications, pharmacological treatments, and, in some cases, surgical interventions. Behavioural interventions and dietary changes remain the cornerstone of obesity management, with evidence supporting the importance of individualized, person-centered strategies to improve patient engagement and long-term adherence. Pharmacological options, such as GLP-1 receptor agonists (e.g., liraglutide and semaglutide), naltrexone-bupropion, and orlistat, provide valuable adjuncts to lifestyle changes, offering significant weight loss and metabolic improvements. As these medications continue to evolve, new agents like tirzepatide, which target both GLP-1 and GIP receptors, show promising results, potentially enhancing treatment outcomes.

Disclosure

Author's contribution

Conceptualization: Jan Siwiec, Olga Śpiołek; methodology: Agnieszka Wąsowicz, Marcelina Sztyler - Krąkowska, Mateusz Teofilak, Dariusz Fabian; formal analysis: Julia Szatkowska, Franciszek Kędziora, Aleksandra Słowikowska; check: Natalia Smyl, Mateusz Teofilak, Marcelina Sztyler - Krąkowska; investigation: Franciszek Kędziora; resources: Jan Siwiec, Natalia Smyl; writing - rough preparation: Jan Siwiec, Olga Śpiołek,, Aleksandra Słowikowska, Julia Szatkowska, Natalia Smyl; writing - review and editing: Franciszek Kędziora, Dariusz Fabian, Agnieszka Wąsowicz, Marcelina Sztyler - Krąkowska; visualization: Aleksandra Słowikowska; supervision: Jan Siwiec, Olga Śpiołek; project administration: Jan Siwiec.

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