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REVIEW ARTICLE

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Systematic review of clinical outcomes of anorexigenic treatment of obesity

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Abstract

Introduction: Obesity and its comorbidities are a public health burden that currently affects more than 2.0 billion people, affecting approximately 19% of women and 14% of men worldwide. Anti-obesity medications modify the biological processes that affect appetite and significantly improve outcomes such as type 2 diabetes, hypertension, and dyslipidemia. **Objective:** This was to develop a systematic review to present the main clinical results of using anorectic drugs to treat obesity and its comorbidities. **Methods:** The systematic review rules of the PRISMA Platform were followed. The search was conducted from March to April 2025 in the Scopus, Embase, PubMed, Science Direct, Scielo, and Google Scholar databases. The quality of the studies was based on the GRADE instrument and the risk of bias was analyzed according to the Cochrane instrument. **Results and Conclusion:** 107 articles were found. A total of 42 articles were fully evaluated and 30 were included and developed in the present systematic review study. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 06 studies with a high risk of bias and 29 studies that did not meet GRADE and AMSTAR-2. Most studies presented homogeneity in their results, with X^2=85.7%>50%. It was concluded, based on randomized clinical studies in recent years, that anorectic anti-obesity drugs associated with lifestyle change therapies are effective in weight loss and improvement of comorbidities. Furthermore, studies have shown that the combination of anti-obesity medicines and lifestyle intervention enables greater results in weight loss and maintenance of lost weight.

Keywords: Obesity. Drugs. Anorectic drugs. Efficacy. Complications.

Introduction

Obesity and its comorbidities are a public health burden that currently affects more than 2.0 billion people, affecting approximately 19% of women and

14% of men worldwide. Anti-obesity medications modify the biological processes that affect appetite and significantly improve outcomes such as type 2 diabetes, hypertension, and dyslipidemia. According to the 2021 National Health and Nutrition Examination Survey (NHANES), more than 40% of US adults and 20% of youth were obese, and 9% of adults and 7% of youth were severely obese. It is estimated that by 2030, almost 30% of the adult population will be obese in Brazil **[1]**.

Excess weight promotes an increase in mortality related to the development of cardiorespiratory and metabolic diseases **[3-8]**. Currently, different therapeutic measures can be offered to overweight or obese patients, such as nutritional reeducation, therapies, physical exercise and medications, and endoscopic and surgical procedures. They are selected according to the patient's clinical status, with a pre-screening, with the criteria based on BMI and associated comorbidities **[9]**.

The pharmacological treatment of obesity is constantly developing, but it has long been criticized due to the widespread prescription of medications, devaluation of physical activity and diet, and irrational use of available drugs, among other factors. One of the main objectives for treating an obese patient is to improve their quality of life and health, reducing the risk of death **[10-19]**.

Despite short-term weight loss with diet and exercise, weight regain remains a concern. The main anti-obesity drugs such as Sibutramine (SIB), Phentermine (PHEN), topiramate, Fenproporex (FEN), Mazindol (MAZ), Amfepramone (AMFE), Orlistat (ORL), semaglutide, tirzepatide, bupropion, and naltrexone may play a role in weight reduction in patients whose condition is refractory to non-pharmacological measures and in maintaining weight loss **[1,2,20-29]**.

These drugs have shown relatively favorable efficacy and safety in conjunction with lifestyle changes **[30-35]**. In this scenario, studies have shown that a 5.0% to 10.0% weight reduction also favors the reduction of cardiovascular risks and type 2 diabetes mellitus **[2,15,16]**. And, in this sense, anorectic drugs may establish an important therapeutic alternative for this purpose **[36-40]**.

Therefore, the present study developed a systematic review to present the main clinical results of the use of anorectic drugs in the treatment of obesity and its comorbidities.

Methods

Study Design

This study followed the international systematic review model, following the PRISMA (preferred reporting items for systematic reviews and meta-analysis) rules. Available at: http://www.prisma-statement.org/?AspxAutoDetectCookieSupport=1. Accessed on: 04/15/2025. The AMSTAR-2 (Assessing the methodological quality of systematic reviews) methodological quality standards were also followed. Available at: https://amstar.ca/. Accessed on: 04/15/2025.

Data Sources and Research Strategy

The literature search process was carried out from March to April 2025 and developed based on Scopus, Embase, PubMed, Lilacs, Ebsco, Scielo, and Google Scholar, covering scientific articles from various periods to the present day. The following descriptors (DeCS/MeSH Terms) were used "Obesity. Drugs. Anorectic drugs. Efficacy. Complications", and the Boolean "and" between MeSH terms and "or" between historical findings were used.

Study Quality and Risk of Bias

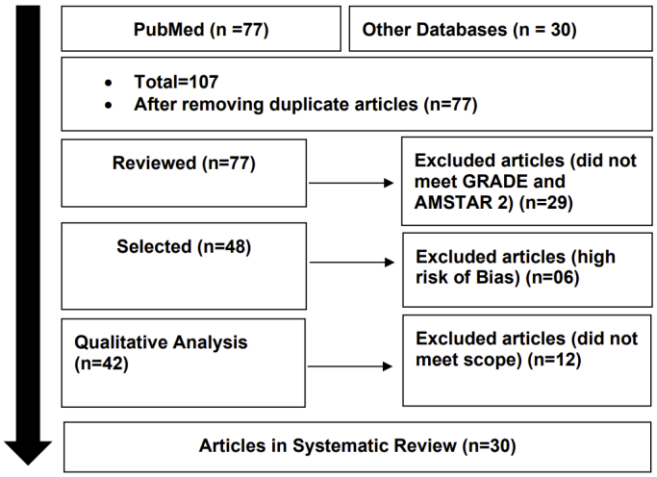
The quality was classified as high, moderate, low, or very low regarding the risk of bias, clarity of comparisons, precision, and consistency of analyses. The most evident emphasis was on systematic review articles or meta-analyses of randomized clinical trials, followed by randomized clinical trials. The low quality of evidence was attributed to case reports, editorials, and brief communications, according to the GRADE instrument. The risk of bias was analyzed according to the Cochrane instrument by analyzing the Funnel Plot graph (Sample size versus Effect size), using Cohen's d test.

Results and Discussion

Summary of Findings

A total of 107 articles were found and submitted to eligibility analysis, with 30 final studies selected to compose the results of this systematic review from a total of 42 references. The studies listed were of medium to high quality (Figure 1), considering the level of scientific evidence of studies such as meta-analysis, consensus, randomized clinical, prospective, and observational. Biases did not compromise the scientific basis of the studies. According to the GRADE instrument, most studies presented homogeneity in their results, with X^2=85.7%>50%. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 06 studies with a high risk of bias and 29 studies that did not meet GRADE and AMSTAR-2.

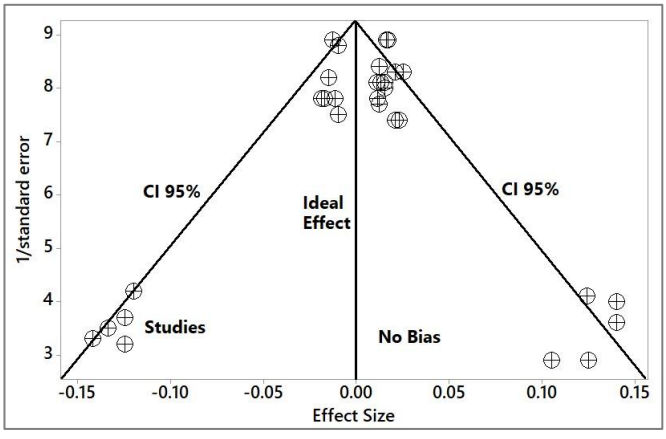
Figure 1. Selection and inclusion of the articles.



Source: Own authorship.

Figure 2 presents the results of the risk of bias of the studies using the Funnel Plot, showing the calculation of the Effect Size (Magnitude of the difference) using Cohen's Test (d). Precision (sample size) was determined indirectly by the inverse of the standard error (1/Standard Error). This graph had a symmetrical behavior, not suggesting a significant risk of bias, both among studies with small sample size (lower precision) that are shown at the bottom of the graph and in studies with large sample size that are shown at the top.

Figure 2. The symmetrical funnel plot does not suggest a risk of bias among the studies with small sample size that are shown at the bottom of the graph. Studies with high confidence and high recommendation are shown above the graph (n=30 studies).



Source: Own authorship.

Main Outcomes – Anorectic Drugs and Obesity

In the context of obesity treatment, anti-obesity drugs need to be prescribed together with lifestyle changes. Orlistat alters absorption in the digestive tract and causes gastrointestinal adverse effects, such as oily stools and gastrointestinal urgency, in more than 25% of patients. Centrally acting drugs, such as phentermine-topiramate and naltrexone-bupropion, regulate appetite in the brain and are associated with constipation in approximately 20% of patients, although the incidence of other adverse effects (e.g., paresthesia, nausea) varies by drug. Nutrient-stimulated hormone-based drugs, such as liraglutide, semaglutide, and tirzepatide, mimic the actions of enteropancreatic hormones that modify central appetite regulation and provide multiple cardiometabolic benefits for weight loss. Compared with placebo, orlistat was associated with 3.1% greater weight loss (52 randomized controlled trials (RCTs); 16,964 participants), phenterminetopiramate was associated with 8.0% greater weight loss (5 RCTs; 3,407 participants), naltrexone-bupropion was associated with 4.1% greater weight loss (6 RCTs; 9,949 participants), liraglutide was associated with 4.7% greater weight loss (18 RCTs; 6,321 participants), semaglutide was associated with 11.4% greater weight loss (5 RCTs; 4,421 participants), and tirzepatide 15 mg was associated with 12.4% greater weight loss (6 RCTs; 1,972 participants) **[2]**.

Authors Hong et al. (2025) **[15]** conducted a 56-week, randomized, double-blind, placebo-controlled, phase 4 study evaluating the efficacy and safety of a combination of phentermine and delayed-release topiramate (PHEN/TPM) versus placebo as an adjunct to standard lifestyle recommendations in 232 randomization participants. Adults aged 19 to 70 years with obesity (BMI ≥ 25 kg/m²) were included. After a 12-week lifestyle program, participants were randomly assigned in a 1:1 ratio to receive PHEN/TPM or placebo. PHEN/TPM was initiated at 3.75 mg/23 mg daily for 14 days and increased to 7.5 mg/46 mg daily, and 15 mg/92 mg if 3% weight loss was not achieved after 12 weeks. At 56 weeks, the percent change in body weight was -8.3% with hormone replacement therapy (RT) with PHEN/TPM and -2.3% with placebo (treatment difference: -6.1%; 95% confidence interval **[CI]**: -7.7 to -4.5, $p < 0.001$). Participants receiving hormone RT with PHEN/TPM were more likely to achieve ≥ 5% weight loss compared with those receiving placebo (68.5% vs. 25.0%, odds ratio [OR]: 6.4; 95% CI: 3.5 to 11.6; $p < 0.001$). Dizziness, paresthesia, and dry mouth were more common in the hormone RT with the PHEN/TPM group, although most adverse events were mild or moderate.

To corroborate this finding of the aforementioned clinical study, the authors Kurotschka, Serafini, and Barry (2024) **[16]** presented through a review study that all medications, when combined with lifestyle modifications, were more effective than lifestyle modifications alone in achieving weight loss. The phentermine-topiramate combination was most effective in inducing at least 5% weight loss (odds ratio [OR] 8.02; 95% CI 5.24-12.27; mean weight loss

7.98%), followed by GLP-1 receptor agonists (OR 6.33; 95% CI 5.00-8.00; mean weight loss 5.79%). Naltrexone-bupropion, phenterminetopiramate, GLP-1 receptor agonists, and orlistat were the most likely to be discontinued due to adverse effects (OR 2.69, 2.40, 2.22, and 1.71, respectively). After conducting additional post hoc analyses, the authors concluded that semaglutide, a GLP-1 agonist, was the most effective drug in achieving at least 5% weight loss (OR 9.82), with a similar rate of adverse events to the other drugs.

Thus, based on randomized clinical trials in recent years, no significant complications were found with the use of anorectic drugs, with only 6.0%. In addition, the overall success rate among these drugs was 85.7%, with an average overall weight loss of 7.5 (±2.8) kg in a mean time of 12 months, showing that they are effective for the treatment of obesity (Table 1).

Table 1. Summary of literary findings with the main information on the types of anorectic drugs used for weight reduction (kg), success rate (%), type of study, sample size (n), references and follow-up time in months.

References	Nº Patients	Drugs	Success (%)	Weight loss (kg)	Follow-up (months)
Hong et al. 2025	232	phentermine and topiramate	95%	≥ 5%	14
Kurotschka, Serafini and Barry (2024)	Mean: 2,000	- phentermine-topiramate; - GLP-1 receptor agonists - Naltrexone-bupropion - orlistat	95%	7.98%	10
Franco et al. 2014	73	Sibutramine	75.0	4.47	13
Biedermann et al. 2014	27	Sibutramine	94.0	6.1	6
Maggioni et al. 2017	4,018	Sibutramine	85.0	3.6	12
Kamil et al 2016	9,804	Sibutramine	77.5	4.3	36
Ham et al 2011	120	Sibutramine	90.0	4.5	12
Grilo et al 2015	104	Sibutramine	65.0	5.8	16
Jørgensen et al 2014	2,807	Sibutramine	87.0	5.0	12
Grilo et al 2014	104	Sibutramine	86.0	3.5	16
Seimon et al 2015	4,906	Sibutramine	78.0	3.0	12
Seimon et al. 2014	4,906	Sibutramine	60.0	2.5	1.5
Parks et al 2014	61	Sibutramine	90.3	2.23	6
Al-Tahami et al 2017	37	Sibutramine	50.0	3.84	9
Cambi et al 2015	30	Sibutramine	85	9.5	13
Smith et al. 2017	238	Phentermine	80.0	5.0	3
Hollander et al. 2017	335	Phentermine	90.0	5.0	6.5
Garvey et al. 2014	388	Phentermine	74.5	9.4	14
Moldovan et al 2016	77	Phentermine	85	13.4	3
Thomas et al 2016	27	Phentermine	61.1	5.4	2
Acosta et al. 2015	270	Phentermine	90.0	1.4	0.5
Garvey et al 2014	475	Phentermine	70.0	12.1	27
Suplicy et al. 2014	29	Mazindol	75.0	7.4	13
Suplicy et al. 2014	29	Fenproporex	80.0	7.8	13
Suplicy et al. 2014	28	Amfepramone	90.0	10.0	13
Soto-Molina et al. 2015	156	Amfepramone	80.0	4.9	6
Kargulewicz et al. 2016	114	Orlistat	92	10.0	3
Arzola-Paniagua et al 2015	84	Orlistat	70.0	6.0	0.5
Chukhin et al., 2015	71	Orlistat	80.0	2.56	4
Taghizadeh et al 2015	78	Orlistat	85.0	4.5	2
Moini et al 2014	86	Orlistat	87	5.25	24
McVay *et al* 2015	73	Orlistat	80.0	10.0	48
Panidis *et al* 2014	101	Orlistat	85.0	8.0	6

Source: Own authorship.

Authors Farah et al. (2019) **[17]** performed a meta-analysis to evaluate the safety and efficacy of four centrally acting drugs. Fifty-three studies were included, with a total of 16,903 patients with a median follow-up of 12 weeks (2-260 weeks). Appetite suppressants showed significant weight loss compared to placebo. There was an increase in the total number of adverse events, dry mouth, constipation, insomnia, dizziness, and tachycardia reported in the intervention group. Sibutramine showed a significant increase in heart rate and mean diastolic pressure compared to placebo. These drugs are effective in weight loss in overweight and obese patients but may increase the risk of adverse events.

Bou Khalil et al. (2017) **[18]** analyzed the effect of methylphenidate on weight loss and appetite. It has been observed that methylphenidate increases dopamine and noradrenaline in synapses due to the blockade of transporters of these monoamines in the frontal cortex and insular lobe. The intracerebral activity of methylphenidate is implicated in the dysregulation of appetite due to its probable effect, stimulating the sensation of disgust generated after the activation of the insular lobe by the drug. The anorectic effect of methylphenidate has been demonstrated in preclinical studies, although the dosage and administration routes are different in animals from those used in humans. In clinical studies, methylphenidate reduces the weight of children and adolescents during the first 3 to 6 months after its initiation due to the appetite reduction effect that it generates with a tendency for the weight curves to join the curves of individuals who did not receive treatment. The anorectic effect of methylphenidate does not persist in the long term in children and adolescents. A systematic review and meta-analysis study evaluated the efficacy and safety of AMFE, FEN, and MAZ as monotherapy in the treatment of obese or overweight patients. 25 studies were included in the meta-analysis. The Cochrane global assessment resulted in 19 studies with a high level of bias and six with unclear risk. Due to the lack of information, meta-analyses were performed only for AMFE and MAZ. Compared to placebo, AMFE resulted in greater short-term weight loss (180 days; mean difference of -1.281 kg) and long-term weight loss with a mean reduction of 6.518 kg. Treatment with mazindol showed greater short-term weight loss than with placebo (-1.721 kg).

However, metabolic results were poorly described, preventing a meta-analysis **[4]**. Other randomized clinical trials also showed desirable effects on weight reduction with the combined use of phentermine and topiramate **[19-21]**. A randomized, double-blind, placebo-controlled, and sibutramine versus placebo-controlled Cardiovascular Outcomes Trial of Sibutramine (SCOUT) provided the first evidence of the effect of weight loss on mortality in a high-risk obese population.

Eligibility for the study required men and women to be at least 55 years of age, with a BMI of at least 27 kg/m^2 and 45 kg/m2 or less. Study participants with type 2 diabetes mellitus (T2DM) were required to have at least one other risk factor defined as hypertension, dyslipidemia, smoking, or diabetic nephropathy, and/or had a history of cardiovascular disease. The study showed that mortality occurred equally in patients allocated to sibutramine and placebo. This ancillary analysis demonstrates that there is a general trend showing higher mortality in patients with greater weight loss (weight reduction >10 kg) and in those with weight gain (>1 kg). The impact of substantial weight loss on mortality is marked in those dying from noncardiovascular causes, specifically cancer **[9]**.

Another relevant randomized trial explored dietary habits pre-treatment with ENT. One pretreatment factor that may influence weight loss outcomes is macronutrient intake. Groups were divided into a low-carbohydrate diet (n = 71) and ENT drug therapy plus a low-fat diet (n = 73). Percentage intake of fat, carbohydrate, and protein before treatment was measured using 4-day food records. The mean participant age was 53 years, body mass index 39.3 kg m-2, and 72.0% were male. Higher pretreatment percent carbohydrate intake was associated with less rapid initial weight loss (p = 0.02) and less rapid weight regain (p = 0.03) in the low-carbohydrate diet condition, but was not associated with weight trajectories in the low-fat ENT condition. In both conditions, higher pre-treatment body fat intake was associated with faster weight regain (p < 0.01). None of the pre-treatment macronutrients were associated with weight loss at study completion in either condition. Selecting a weight loss approach based on pre-treatment macronutrient intake is unlikely to improve weight outcomes at the end of a 1-year treatment. However, pre-treatment macronutrient intake may have implications for tailoring interventions to delay weight gain after weight loss **[11]**.

A prospective, randomized, placebo-controlled study compared the efficacy and safety of AMFE, FEN, MAS, and SIB in promoting weight loss. A total of 174 obese premenopausal women were enrolled. Participants were randomly assigned to receive AMFE 75 mg (n = 28), FEN 25 mg (n = 29), MAZ 2 mg (n = 29), and SIB 15 mg (n = 30) daily for 52 weeks. Diet and physical activity were encouraged. The primary outcomes were changes in body weight with a mean reduction of 7.2 kg. There were also improvements in anthropometrics, safety, metabolic changes, and cardiovascular parameters, as well as significant improvements in depression and anxiety scores, binge eating episodes, and quality of life correlated with weight loss **[13]**.

Regarding AMFE, a double-blind, randomized, placebo-controlled clinical trial was designed in 156 volunteers with a body mass index (BMI) greater than 30 kg/m^2 and less than 45 kg/m^2 that demonstrated its efficacy and safety for periods longer than 3 months, as there are few studies on it. Thus, we evaluated the 6-month efficacy and safety of drug treatment in obese adult patients resistant to diet and exercise. The primary outcome was absolute body weight loss, while secondary outcomes were the percentage of patients achieving at least 5.0% or 10.0% weight loss, as well as improvement in anthropometric and metabolic parameters. Treatment with AMFE produced superior efficacy in decreasing body weight than placebo at 3 months (-4.9 ± 0.25 kg vs. -0.7 ± 0.32 kg) and 6 months (-7.7 ± 0.52 kg vs. -1.1 ± 0.7 kg). Furthermore, 64 and 34 patients achieved at least 5% or 10% weight loss, respectively, with AMFE at 6 months, compared with 8 and 0 patients with placebo. FEMA also significantly improved BMI and waist circumference but showed only a favorable trend in waist-to-hip ratio, glucose, total cholesterol, low-density lipoproteins (LDL), high-density lipoproteins (HDL), triglycerides, heart rate, systolic blood pressure, and diastolic blood pressure at 3 and 6 months. FEMA produced only mild adverse events **[14]**.

Another investigation showed the isolated use of SIB in weight loss in obese adolescents. The study followed a double-blind placebo-controlled crossover model lasting 13 months. The study included 73 obese adolescents of both sexes aged between 10 and 18 years. The anthropometric assessment was performed every 40 days on average. The percentage of patients who lost 10% of their initial weight in the placebo group was 46.0%, and in the SIB group, it was 75.0%. When using the placebo, the average weight increased by 1.61 kg, and the BMI reduced by an average of 0.24 kg/m^2, while with the use of SIB, the weight reduced by an average of 4.47 kg and the BMI reduced by an average of 2.38 kg/m^2 (p < 0.001) **[22]**.

Another placebo-controlled study analyzed the use of SIB in the side effects of patients undergoing treatment with antipsychotic drugs. The study investigated the effect of add-on treatment with SIB in schizophrenic outpatients who had gained more than 7.0% of their weight during the 24-week treatment course. Weight, waist-to-hip ratio, BMI, blood pressure/pulse, and ECG were monitored regularly. In addition, various laboratory tests were performed. Psychopathological symptoms and side effects were assessed frequently. Thus, fifteen patients were randomly assigned to add-on treatment with 10 mg sibutramine or placebo. The two groups did not differ in weight, sociodemographic, or clinical data. Eleven patients were considered for analysis. Significant weight

loss was observed in the SIB group (mean = -6.1 kg), while placebo patients experienced a mean weight gain of 1.9 kg. Furthermore, a reduction in HbA1c was apparent in the SIB but not in the placebo group. No significant differences between the groups were found in changes in psychopathology or drug safety **[23]**.

In this context, a controlled, randomized, double-blind, parallel clinical study with 161 patients (84 completed) evaluated the efficacy of a combination of OrlistatResveratrol (O-R) in individuals with obesity over a period of 6 months. Patients meeting the selection criteria (age between 20 and 60 years and body mass index (BMI) 30 and ≥ 39.9 kg/m2) consumed a low-energy diet with 500 calories less than their usual diet for two weeks. Then, participants were randomly assigned to four groups, placebo, Resveratrol (R), Orlistat (ORL), or O-R, and consumed the low-energy diet for 6 months. A significant weight loss of 26.82 kg was observed in the O-R group compared to 23.50 kg in the placebo group and compared to the ORL group with 26.64. Significant reductions in BMI, waist circumference, fat mass, triglycerides, leptin, and leptin/adiponectin ratio were observed with the combination of O-R and ORL **[35]**.

Regarding the use of Orlistat (ORL), an intestinal lipase inhibitor that promotes body weight reduction, a systematic review and meta-analysis study analyzed its efficacy in reducing body weight induced by lipid alterations. A systematic literature search was performed to identify randomized controlled clinical trials investigating the efficacy of ORL on total plasma levels, low-density lipoprotein and high-density lipoprotein, triglycerides, and lipoprotein-A. Thirty-three studies were included in the meta-analysis (5,522 and 4,210 participants in the therapy and control groups, respectively). Weight reduction by ENT was on average: -2.12, $p < 0.001$, average total cholesterol: -0.30 mmol/L, $p < 0.001$, average low-density lipoprotein (LDL): -0.27 mmol/g, $p < 0.001$, average high-density lipoprotein (HDL): -0.034 mmol/L, $p < 0.001$ and average triglyceride: -0.09 mmol/L, $p < 0.001$, concentrations, while no effect on lipoprotein (a) was observed. Reduction in total cholesterol and low-density lipoprotein cholesterol was negatively associated with the duration of ENT treatment and positively with changes in body weight. Treatment with orlistat slightly reduces cholesterol and triglyceride levels, but not lipoprotein (a) levels. Reductions in total cholesterol and low-density lipoprotein cholesterol levels are more pronounced in patients with greater body weight reduction and shorter duration of ENT treatment **[38]**.

Pharmacotherapy offers an option for overweight and obese adults to reduce their body weight if lifestyle modifications fail. A systematic review and meta-analysis included randomized controlled trials of weight-loss medications in overweight and obese adults. A total of 14,605 citations were identified by the search, of which 132 eligible studies enrolled 48,209 participants. All medications reduced body weight compared with lifestyle modification alone; all subsequent figures refer to comparisons with lifestyle modification. High- to moderate-quality evidence established phentermine-topiramate as most effective for weight reduction (odds ratio [OR] for weight reduction ≥5% 8.02, 95% CI 5.24 to 12.27; mean difference [MD] in percentage body weight change -7.98, 95% CI -9.27 to -6.69) followed by GLP-1 receptor agonists (OR 6.33, 95% CI 5.00 to 8.00; MD -5.79, 95% CI -6·34 to -5·25). Naltrexone-bupropion (OR 2.69, 95% CI 2.10 to 3.44), phentermine-topiramate (2.40, 1.68 to 3.44), GLP-1 receptor agonists (2.22, 1 74 to 2.84) and orlistat (1.71, 1.42 to 2.05) were associated with increased adverse events leading to drug discontinuation. In a post-hoc analysis, semaglutide, a GLP-1 receptor agonist, showed substantially greater benefits than other drugs with a similar risk of adverse events as other drugs for likelihood of weight loss of 5% or more (OR 9.82, 95% CI 7.09 to 13.61) and percentage change in body weight (MD -11.40, 95% CI -12.51 to -10.29). In overweight and obese adults, phentermine-topiramate and GLP-1 receptor agonists have proven to be the best weight-loss medications; of the GLP-1 agonists, semaglutide may be the most effective **[39]**.

A separate meta-analysis compared the benefits and harms of approved weight-control medications in overweight or obese adults. A total of 168 trials (97,938 patients) were included. No evidence approved weight-control medications had different associations with cardiovascular death (69 trials, 59,037 participants). The naltrexone/bupropion combination was associated with lower cardiovascular mortality than placebo (odds ratio [OR], 0.62 [95% CI: 0.39, 0.99]; low-quality evidence). All drugs were associated with greater weight loss at 12 months than placebo (33 trials, 37,616 participants), particularly semaglutide (mean difference [MD], -9.02 kg [95% CI: -10.42, -7.63]; moderate certainty) and phentermine/topiramate (MD, -8.10 kg [95% CI: -10.14, -6.05]; high certainty); and with a greater reduction in waist circumference at 12 months than placebo (24 trials, 35 733 participants), particularly semaglutide (MD, -7.84 cm [95% CI: -9.34, -6.34]; moderate certainty) and phentermine/topiramate (MD, -6.20 cm [95% CI: -7.46, -4.94]; moderate certainty). Semaglutide and phentermine/topiramate were associated with less or no difference in the odds of treatment discontinuation compared with all other drugs (87 trials, 70,860 participants) **[40]**.

Finally, pharmacologic management of obesity has

been found to improve outcomes and decrease the risk of obesity-related complications **[41]**. A guideline from the American Gastroenterological Association aimed to support practitioners in making decisions about pharmacologic interventions for overweight and obesity. A multidisciplinary panel of content experts and guideline methodologists used the Grading of Recommendations Assessment, Development, and Evaluation framework to prioritize clinical questions, identify patient-centered outcomes, and conduct an evidence synthesis for the following agents: semaglutide 2.4 mg, liraglutide 3.0 mg, phentermine-topiramate extended-release (ER), naltrexone-bupropion ER, orlistat, phentermine, diethylpropion, and Gelesis100 oral superabsorbent hydrogel. The guideline panel used the evidence-for-decision framework to develop recommendations for the pharmacologic management of obesity and provided implementation considerations for clinical practice. The guideline panel made 9 recommendations. The panel strongly recommended the use of pharmacotherapy in addition to lifestyle interventions in adults with overweight and obese (body mass index ≥30 kg/m^2, or ≥27 kg/m^2 with weight-related complications) who have an inadequate response to lifestyle interventions. The panel suggested the use of semaglutide 2.4 mg, liraglutide 3.0 mg, phentermine-topiramate ER, and naltrexonebupropion ER (based on moderate-quality evidence), and phentermine and diethylpropion (based on low-quality evidence) for long-term treatment of overweight and obesity. The guideline panel suggested against the use of orlistat. The panel identified the use of the oral superabsorbent hydrogel Gelesis100 as a knowledge gap **[42]**.

Conclusion

Based on randomized clinical trials conducted in recent years, it was concluded that anorectic anti-obesity medications associated with lifestyle change therapies are effective in weight loss and improving comorbidities. Furthermore, studies have shown that the combination of anti-obesity drugs and lifestyle intervention enables greater results in weight loss and weight maintenance.

CRediT

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