Received: 30 September 2022 | Revised: 25 September 2023 | Accepted: 30 October 2023

DOI: 10.1111/obr.13683

REVIEW

OBESITY Reviews WILEY

Consensus on pharmacological treatment of obesity in Latin America

Ana María Cappelletti[1,2] | Alex Valenzuela Montero[3] | Cintia Cercato[4] | John Jairo Duque Ossman[5] | Pablo Enrique Fletcher Vasquez[6] | Juan Eduardo García García[7] | Leonardo Guadalupe Mancillas-Adame[8] | Herald Andrés Manrique[9] | Flor de María Ranchos Monterroso[10] | Pablo Segarra[11,12] | Trina Navas[13]

[1]Favaloro University, Buenos Aires, Argentina

[2]Argentine Society of Nutrition, Buenos Aires, Argentina

[3]Chilean Society of Obesity, Santiago de Chile, Chile

[4]Endocrinology and Metabology Service, Clinics Hospital, University of São Paulo Medical School, São Paulo, Brazil

[5]Colombian Association of Endocrinology, Diabetes and Metabolism, Armenia, Colombia

[6]Latinamerican Federation of Endocrinology, Panama City, Panama

[7]Salvador Zubiran National Institute of Medical Sciences and Nutrition, Tlalpan, Mexico

[8]University Hospital and Medical School, Autonomous University of Nuevo León, Monterrey, Mexico

[9]Peruvian Society of Endocrinology, Lima, Peru

[10]Guatemalan Association of Endocrinology, Metabolism and Nutrition, Guatemala City, Guatemala

[11]Ecuadorian Society of Endocrinology, Quito, Ecuador

[12]Ecuadorian Society of Internal Medicine, Quito, Ecuador

[13]General Hospital "Dr. José Gregorio Hernandez", Los Magallanes, Caracas, Venezuela

Correspondence
Ana María Cappelletti, Favaloro University, Buenos Aires, Argentina.
Email: dra.anacappelletti@gmail.com

Summary

A panel of 10 experts in obesity from various Latin American countries held a Zoom meeting intending to reach a consensus on the use of anti-obesity medicines and make updated recommendations suitable for the Latin American population based on the available evidence. A questionnaire with 16 questions was developed using the Patient, Intervention, Comparison, Outcome (Result) methodology, which was iterated according to the modified Delphi methodology, and a consensus was reached with 80% or higher agreement. Failure to reach a consensus led to a second round of analysis with a rephrased question and the same rules for agreement. The recommendations were drafted based on the guidelines of the American College of Cardiology Foundation/American Heart Association Task Force on Practice. This panel of experts recommends drug therapy in patients with a body mass index of ≥30 or ≥27 kg/m^2 plus at least one comorbidity, when lifestyle changes are not enough to achieve the weight loss objective; alternatively, lifestyle changes could be maintained while considering individual parameters. Algorithms for the use of long-term medications are suggested based on drugs that increase or decrease body weight, results, contraindications, and medications that are not recommended. The authors concluded that anti-obesity treatments should be individualized and multidisciplinary.

KEYWORDS
Latin America, obesity, pharmacotherapy, weight management

Abbreviations: BMI, body mass index; CNCDs, chronic non-communicable diseases; EBM, evidence-based medicine; LE, level of evidence; PICO, Patient, Intervention, Comparison, Outcome (Result); R, grade of recommendation; SAN, Argentinian Society of Nutrition (Sociedad Argentina de Nutrición); WHO, World Health Organization.

Funding information
Adium Pharma

1 | INTRODUCTION

Chronic non-communicable diseases (CNCDs) are the primary cause of death worldwide, accounting for 60% of the overall mortality. The frequency of CNCDs continues to increase, particularly in low- and medium-income countries (most Latin American countries), and their economic burden for the current period (2011–2025) is estimated to generate losses of USD 7 billion. "These diseases drive inequity; contribute to poorer economic outcomes for individuals, communities, and societies; and create significant challenges to development. *The economic impact of CNCDs must be better understood, and their negative consequences for societies mitigated*."[1]

The global prevalence of obesity has almost tripled since 1975. Most of the population lives in countries where overweight and obesity are causing more deaths than underweight.[2] In 1997, the World Health Organization (WHO) acknowledged obesity as a global health problem, which was previously associated only with high-income countries; however, evidence shows that overweight and obesity in adults are much more frequent than underweight in Latin America and Northern Africa. Therefore, this CNCD is currently among the primary public health challenges, with México as the second highest combined prevalence of overweight and obesity in adults globally.[3] Diabetes, cardiovascular diseases, musculoskeletal system disorders, and certain types of cancers are attributable to overweight and obesity.[4]

In 2000, Peña and Bacallao published data from several countries in Central and South America, warning that poverty was a new public health challenge.[5] These data were considered by the Pan American Health Organization, because the global prevalence of overweight in the adult population was 36.6% and that of obesity was 11.5%; however, the prevalence was 59% and 24.6% in the Americas, respectively. This figure is more than double the world average, making our region the highest in obesity in the world; furthermore, there is a sex difference, because women are more likely to develop obesity than men.[6]

In 2008, a panel of experts from The Obesity Society of North America examined the evidence and argued the importance of classifying obesity as a disease. The panel unanimously and definitively stated that obesity is "a complex condition with several causal contributors, including many factors that, to a large extent, are beyond the control of the individual; this disease results in a lot of distress, is a cause of poor health, functional impairment, impaired quality of life, severe illnesses, and higher mortality. Successful treatment, though difficult to achieve, results in a significant number of benefits."[7]

The definition of overweight and obesity suggested by the WHO is "abnormal or excessive fat accumulation that presents a health risk"[3]; it is estimated using the body mass index (BMI) (body weight in kilograms divided by the square height in meters [kg/m^2]). The suggested values for obesity classification are presented in Table 1.[2]

This universal classification, which is useful for population studies, has some limitations in assessing individuals in clinical practice because of the presence of other factors that increase the risk of comorbidities beyond BMI, in particular, the amount and distribution of body fat. Sharma and Kushner suggested that the Edmonton Obesity Staging System, which considers clinical, psychological, and functional comorbidities, allows for the assessment of the effect of these comorbidities in individuals beyond body weight and optimizes treatment decision-making (Table 2).[8]

Cappelletti and Katz, in their manual *Obesity Crossroads and Approaches*, define obesity as a "Chronic, multifactorial disease with an impact on the neuro-immune-metabolic and psychosocial balance. Its inflammatory condition resulting from increased dysfunctional adipose tissue, accounts for the association with its comorbidities."[9]

The results of the Awareness, Care, and Treatment In Obesity maNagement International Observation trial[10] should be highlighted with regard to obesity treatment; its primary objective was to identify perceptions, attitudes, behaviors, and potential barriers to the effective care of patients with obesity and healthcare practitioners using a

TABLE 1 Classification based on body mass index (BMI).

Classification	BMI (kg/m^2)
Low weight	<18.5
Normal weight	18.5–24.9
Overweight	25–29.9
Obesity	≥30
Grade I	30.0–34.9
Grade II	35.0–39.9
Grade III	≥40

Source: Based on https://www.who.int/es/news-room/fact-sheets/detail/obesity-and-overweight.

TABLE 2 Edmonton Obesity Staging System (EOSS).

S0	No signs, physical or psychological symptoms No functional limitations
S1	Subclinical risk factors My psychological impairment
S2	Comorbidities requiring therapy Obesity-associated psychological disorders Moderate functional limitations affecting quality of life
S3	End-organ damage Significant obesity-related psychological symptoms Significant functional limitations affecting quality of life
S4	Severe clinical involvement Severe psychological involvement Severe functional limitations

Source: Based on Sharma and Kushner.[8]

survey in 11 countries on five continents, including 14,502 adults with obesity and 2785 healthcare practitioners. Half of the individuals with obesity said they did not talk to their physician about how to lose weight. When looking into the reasons, the primary reason was the lack of initiative from the practitioners. Healthcare providers said that they believe that patients have little interest or motivation to control their weight, which may be an obstacle for discussions on weight control. However, 68% of people with obesity said that they would like their physician to start a conversation on the topic, and only 3% felt insulted by such a conversation.[10]

The Argentinean Society of Nutrition (Sociedad Argentina de Nutrición [SAN]) published the "SAN Position: obesity is a chronic disease," with regard to the condition "… is a chronic disease with a very high and growing prevalence with a complex pathogenic etiology and results in multiple comorbidities exhibiting a high early mortality; therefore, obesity is an urgent public health imperative." Among its proposals, it highlights the need for universal coverage, including non-pharmacological and pharmacological strategies.[11]

In 2020, a joint international consensus statement was published in the *Nature Medicine* journal to put an end to weight stigmatization. The document involved the participation of a multidisciplinary team of international experts, including representatives of scientific organizations, who reviewed the available evidence on the causes and damage of obesity and developed recommendations to eliminate any obesity-associated biases. "The research indicates that the weight stigmatization may result in physical and psychological harm and that the individuals affected have a decreased probability of receiving adequate care; for these reasons, this stigmatization is detrimental to health, undermines human and social rights and is inacceptable in modern societies."[12]

The challenge raised in relation to containing the global obesity epidemic requires a multisectoral, multidisciplinary, and relevant approach based on the individual culture of each specific population.[13]

To date, political and public health measures have so far been insufficient to address this situation. Accordingly, continuous education of the treating or primary care physician is essential,[14] as they are the first contacts of the patient with the healthcare system; hence, they are the ones who may initiate the correct approach to the disease. According to the consensus of the authors of this document, the approach for people living with obesity should be based on five pillars:

1. healthy diet sustainable over time;
2. avoiding sedentarism;
3. reliable and safe medication;
4. long-term management and follow-up; and
5. acceptance of the frustration of "not always doing what is perfect" in the obesogenic environment we live in.

Key international guidelines[15–22] indicate that lifestyle changes to achieve a 5%–10% body weight reduction are the foundation for treatment, with a view to improve comorbidities. European guidelines state that achieving the maximum weight loss in the shortest possible time is not the key to successful treatment. "Reducing waist circumference should be considered even more important than weight loss per se, as it is linked to a decrease in visceral fat and associated cardiometabolic risks. Finally, preventing weight regain is the cornerstone of lifelong treatment, for any weight loss technique used: behavioural or pharmaceutical treatments or bariatric surgery."[20]

New obesity management guidelines from different countries highlight the importance of avoiding the stigmatization of people living with obesity, including the management of psychological issues, such as self-esteem, body image, and quality of life. These aspects should be considered together with optimizing eating patterns and physical activity to reduce the imbalance of calories consumed/expended typical of this disease.[20–23] This therapeutic approach should be complemented with adjuvant pharmacotherapy when considered appropriate.

According to the available literature, properly prescribed anti-obesity medications improve patient compliance and prevent long-term weight regain. However, some barriers prevent their adequate use by practitioners, probably related to the history of such drug therapy and poor knowledge of obesity as a chronic, complex, and relapsing disease.[24]

2 | DEVELOPING LATIN AMERICAN GUIDELINES ON PHARMACOLOGICAL MANAGEMENT OF OBESITY

The Latin American Federation of Endocrinology took the initiative to bring together Latin American experts who shared concerns about the need to develop guidelines for the pharmacological management of obesity in the region. All participants in this consensus had over 10 years of academic training and experience in the treatment of overweight and obese people living with obesity; they were members of institutions and scientific societies in their respective countries, although they did not act on behalf of these organizations. The objective of this study was to update and provide scientific evidence-based recommendations for the pharmacological treatment of adult patients living with obesity with access to all levels of care and suitable for inclusion in the multidisciplinary management of the disease.

2.1 | Methodology

To accomplish these goals, the 10 experts embraced the following methodology:

1. A questionnaire with 16 questions was developed using the Patient, Intervention, Comparison, Outcome (Result) (PICO) methodology. Once the questionnaire was completed, a pilot test was conducted with 10 specialists with the same characteristics as the selected group. The result was a complete understanding of the document, so the original design was maintained (Appendix A).

2. The modified Delphi methodology was used to reach a consensus on a particular topic through iteration of questions. Each question was subjected to iteration; then, a consensus answer was obtained with 80% agreement or higher. Failure to reach a consensus led to a second round of analysis with the reformulated question.
3. Literature review according to evidence-based medicine (EBM): the EBM scale was used to classify the information into levels of evidences A, B, and C (Table 3). The classes of recommendations were based on the American College of Cardiology Foundation/American Heart Association (ACCF/AHA) standards, determining Classes I, II (IIa and IIb), and III (Table 4).[25]

Consensus coordination was employed to develop the PICO questionnaire and submit it for validation. An initial literature search was conducted and continued during the consensus discussion; four expert meetings were held in October, November, and December 2021. The questions were iterated until the experts reached an agreement of 80% or higher (Figure 1).

2.2 | Anti-obesity drugs available in Latin America

Notwithstanding the fact that Latin America is a region with ethnic and cultural similarities among the 20 member countries, the availability of anti-obesity medications varied broadly, with very dissimilar regulatory frameworks in each country. In some countries, drugs and pharmacological compounds may be prescribed without any regulation and may even be purchased with non-medical prescriptions. In other countries, the rules are very strict, so approval, regulations, controls, and monitoring differ significantly from one country to another.

The experts participating in this consensus conducted a comprehensive search on the approval and current regulations for the prescription of anti-obesity medications in each country. However, access to information was difficult, limited, and confusing, which hindered the possibility of obtaining a list of approved drugs.

During discussions, concerns were expressed regarding the indiscriminate prescription of medications by physicians who were not specialists in obesity, as well as the sale of over-the-counter substances with no evidence of effectiveness or safety, contrary to medical ethics, which jeopardizes the health of patients living with the disease. Hence, general practitioners and specialists are advised to keep themselves updated on the comprehensive therapeutic management of this pathology, so that the patients receive the necessary benefits from the management of their condition.

This consensus focused on analyzing the available evidence on the efficacy and safety of approved medications or on the process of approval in most Latin American countries. Table 5 lists the mechanisms of action, indications, doses, adverse reactions, contraindications, and warnings.[26–78]

Obesity is associated with multiple comorbidities, which improve with a body weight reduction of 5%–10%. The clinical comorbidities are listed in Table 6.[16,79–82]

TABLE 3 Levels of evidence.

A level evidence	Data derived from multiple randomized clinical trials or meta-analyses
B level evidence	Data derived from a randomized clinical trial or numerous non-randomized trials
C level evidence	Consensus of expert opinions and/or small, retrospective trials and registries

Source: Based on Jacobs et al.[25]

TABLE 4 Classes of recommendations.

Recommendation	
Class I	Evidence or general agreement on the benefits, usefulness, and effectiveness of a particular treatment or intervention
Class II	Conflicting evidence and/or divergent opinions about the use/efficacy of a specific therapy or intervention
Class IIa	The weight of the evidence is in favor of its use and efficacy
Class IIb	The use or efficacy is milder according to the evidence or opinions
Class III	The general evidence agrees that a particular treatment or procedure is neither useful nor effective and, in some cases, may even be detrimental

Source: Based on Jacobs et al.[25]

3 | CONSENSUS STATEMENT

The experts participating in this consensus emphasized the importance of comprehensive therapy management for obesity, including the following:

1. healthy and enjoyable diet sustainable over time;
2. increased daily physical activity;
3. progression to practicing aerobic and anaerobic programmed exercise;
4. motivational and behavioral management of the patient and family environment;
5. increasing self-control and self-esteem; and
6. avoiding stigmatization of individuals with obesity.

The following recommendations are based on one of the key approaches for treating patients with obesity: pharmacological therapy. The level of evidence (LE) and grade of recommendation (R) are indicated at the end of each consensus recommendation.

Based on evidence and in accordance with the current treatment philosophy, pharmacological treatment plays a vital and complementary role in lifestyle changes and behavioral cognitive therapy for people with obesity.

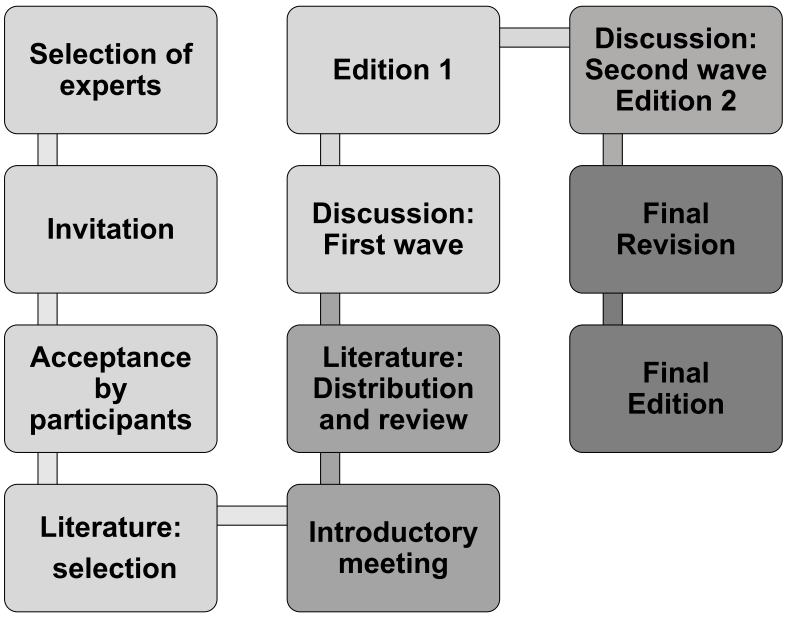

FIGURE 1 Sequence of experts' participation in the consensus.

3.1 | Indications

Pharmacological treatment is indicated in patients with a BMI of ≥30 or ≥27 kg/m^2 with at least one comorbidity when lifestyle changes are insufficient to achieve weight loss objectives or maintain those goals (LE: A; R: I).[15–22,83–91] The clinical and anthropometric parameters for prescribing pharmacological therapy are (LE: A; R: I)[83–95]

- age;
- BMI;
- waist circumference;
- body composition and adipose tissue distribution;
- cardiometabolic, functional, or mental comorbidities affecting quality of life; and
- previous attempts to lose weight.

Other individual parameters to consider include

- patient motivation level;
- patient willingness to undergo long-term treatment;
- availability of medicines in each country; and
- purchasing power of patients.

Evidence is insufficient to make a recommendation for the maximum age for pharmacological therapy. However, this group of experts considers that medication prescriptions should be specifically individualized after 65 years old.[16,85,93,96,97] BMI is strongly correlated with total body fat mass, but it is not an accurate indicator of cardiometabolic risk at the individual level.[98]

Waist circumference (measured at the end of normal expiration at the midpoint between the upper part of the iliac crest and the lower margin of the last palpable rib in the mid-axillary line)[17,21,92–95] is considered the best anthropometric parameter to define central obesity. It is a direct indicator of intra-abdominal fat and a good predictor of cardiometabolic diseases. It also provides independent and additional information to BMI to predict morbidity and mortality[93]; however, there are different suggestions regarding the measurement site and cutoff points. Specific values for waist circumference have recently been suggested depending on the patient's BMI category, which allows for better identification of a high risk of future coronary events (Table 7).[5,13,89–95]

Based on the above, this consensus group suggested the following pharmacological treatment algorithm for people living with obesity that is always associated with lifestyle modification strategies (Figure 2).

3.2 | Treatment duration

Pharmacological therapy may be prescribed indefinitely if the patient responds without any significant side effects (LE: B; R: IIa).[16,20,85,89,99–101] Treatment may be discontinued under the following circumstances:[16,20,85,90]

- lack of therapeutic response (<5% weight loss after 12 weeks with the optimal recommended dose);
- intolerance of active components;
- changes in clinical scenario; and
- women wanting to become pregnant or pregnant during therapy (R: I).

Short-term pharmacotherapy may be considered in special situations, for instance, bariatric surgery, to improve the patient's general condition prior to the intervention (LE: C; R: IIa).[102]

Once the therapeutic objective is achieved, patients should be followed up and monitored regularly. If the weight loss is regained

TABLE 5 Anti-obesity medications available in Latin America.

Drug Central action Short term	Mechanism of action	Indications	Dosing	Adverse reactions	Contraindications	Warnings
Phentermine[26–28]	Phentermine is a sympathomimetic phenylethylamine. Its anorexic effect is due to an increased release mostly of noradrenaline in the central nervous system and of dopamine and serotonin to a lesser extent.	≥16 years old (up to 12 weeks). Initial body mass index (BMI) ≥ 30 kg/m^2 (obesity) or BMI ≥ 27 kg/m^2 (overweight) in the presence of at least one weight-associated comorbidity.	*Prescription* 8 mg three times per day before meals—oral administration. 15–37.5 mg of extended release (ER) once a day, before breakfast/1–2 h after breakfast. 18.75 mg twice a day, before breakfast and before 18:00 h	- Frequent: Headache, increased blood pressure/heart rate, insomnia, mouth dryness, constipation, anxiety. - Cardiovascular: Palpitations, tachycardia, ischemic events. - Central nervous system: Overstimulation, restlessness, dizziness, euphoria, dysphoria, tremors, headache, psychosis. - Gastrointestinal: Unpleasant taste, diarrhea, constipation. - Allergies: Urticaria. - Endocrine: Erectile dysfunction, changes in libido.	- Pregnancy and lactation. - Uncontrolled high blood pressure. - History of cardiovascular disease. - For 14 days following the administration of monoaminoxidase inhibitors. - Hyperthyroidism. - Glaucoma. - Anxiety disorders. - History of drug abuse. - Known hypersensitivity or idiosyncrasy to sympathomimetic amines.	- Co-administration with other weight-lowering medications is not recommended. - Caution in activities requiring alertness. - May increase seizures in patients with epilepsy. - Discontinue the medication in case of intolerance. - In diabetic patients may lower the requirements for insulin or antidiabetic agents.
Amphepramone[29–31]	Amphepramone or diethylpropion is a sympathomimetic phenylethylamine. It stimulates the neurons to release and maintain high levels of catecholamines including dopamine and noradrenalin.	>16 years (for up to 12 weeks). Initial BMI ≥ 30 kg/m^2 (obesity) or BMI ≥ 27 kg/m^2 (overweight) in the presence of at least one weight-associated comorbidity.	- 25 mg capsules: One capsule three times a day before each meal. - ER 75 mg capsules: One capsule before breakfast.	- Cardiovascular: Palpitations, tachycardia, ECG changes, increased blood pressure, chest pain, arrythmias (including ventricular arrythmia). - Neurological: Dyskinesia, blurred vision, overstimulation, restlessness, euphoria, tremor, malaise, anxiety, insomnia, dizziness, depression, somnolence, mydriasis, headache. - Gastrointestinal: Mouth dryness, nausea, vomiting, diarrhea,	- Pregnancy and lactation. - Hypersensitivity to the drug. - Patients with idiosyncrasy to sympathomimetic amines. - Arousal, emotionally unstable individuals susceptible or with a history of drug or alcohol abuse. - Patients with glaucoma, hyperthyroidism, advanced atherosclerosis or severe hypertension, severe renal disease.	- Caution in cardiovascular disease (including arrythmias). - Do not administer together with or less than 14 days after using monoaminoxidase inhibitors (risk of hypertensive crisis). - May increase seizures in some epileptic patients. - Extended use may lead to dependency with withdrawal syndrome upon discontinuation of therapy.

TABLE 5 (Continued)

Drug Central action Short term	Mechanism of action	Indications	Dosing	Adverse reactions	Contraindications	Warnings
				constipation, dysgeusia, and other functional GI disorders. - Allergies: Urticaria, rash, ecchymosis, erythema. - Endocrinological: Impotence, changes in libido, gynecomastia, menstrual disorders. - Hematological: Bone marrow depression, agranulocytosis, leukopenia, dyspnea, hair loss, myalgia, dysuria, diaphoresis polyuria.		
DRUG **Central Action** **Long Term**	**Mechanism of action**	**Indications**	**Dosing**	**Adverse reactions**	**Contraindications**	**Warnings**
Phentermine–topiramate[26,32–37]	- Topiramate is a mood stabilizer and anticonvulsant drug. It indirectly inhibits the neurotransmission of orexigenic neurons NPY/AgRP in the arcuate nucleus of the hypothalamus, via independent gamma-aminobutyric acid (GABA) signaling. Its association with phentermine potentiates the anorexigenic effect, and lower doses of both drugs reduce the adverse effects.	≥18 years old for long-term use. Initial BMI ≥ 30 kg/m^2 (obesity) or BMI ≥ 27 kg/m^2 (overweight) in the presence of at least one weight-associated comorbidity. Adolescents: ≥12 years old for long-term use with a BMI of the 95th percentile or greater when standardized for age and sex.	Initial treatment dose: 3.75 mg of ER phentermine/23 mg of topiramate per day for 14 days; then, 14 days increased to the recommended dose of 7.5 mg/46 mg of phentermine–topiramate once a day in the morning with or without food intake. Then, the dose may be increased to 15/92 mg of phentermine–topiramate.	*Phentermine* - Allergies: Urticaria. - Cardiovascular: Increased blood pressure. - Central nervous system: Euphoria, psychosis, tremors. - Reproductive: Changes in libido, impotence. - Ophthalmological: Glaucoma. *Topiramate* - Dermatological: Bullous skin reactions (including erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, pemphigus).	- Pregnancy. - Glaucoma. - Hyperthyroidism. - During the 14 days following the administration of monoaminoxidase inhibitors. - Known hypersensitivity or idiosyncrasy to sympathomimetic amines. - Severe renal failure. - Psychosis. - Non-controlled cardiac arrythmias. - Renal lithiasis (calcium phosphate).	- Progressively titrate the dose. - Monitor heart rate and blood pressure. - Avoid high doses in patients with depression (doses of 15/92 mg/day). - In case of history of seizures, taper the dose progressively. - May reduce the effect of oral contraceptives. - Potentiates the effect of loop diuretics with risk of hypokalemia. - Potentiates the carbonic anhydrase inhibitors, increasing the risk of

(Continues)

TABLE 5 (Continued)

DRUG Central Action Long Term	Mechanism of action	Indications	Dosing	Adverse reactions	Contraindications	Warnings
				- Gastrointestinal: Pancreatitis. - Metabolic: Hyperammonemia, hypothermia. - Ophthalmic: Maculopathy glaucoma dose-dependently.		renal lithiasis and metabolic acidosis.
Naltrexone–bupropion[26,38–44]	Naltrexone is an opioid receptor antagonist; as a single drug, it is indicated for the treatment of addictions to opiates or alcohol. Bupropion is a noradrenalin and dopamine reuptake inhibitor, it has an antidepressant effect, and it is also indicated for smoking cessation. Bupropion stimulates the proopiomelanocortin (POMC)-producing neurons, precursor of anorexigenic peptides, such as alpha melanocyte-stimulating hormone, and of β endorphins that activate the μ receptor to opioids, limiting bupropion activity. The synergistic effect of bupropion and naltrexone, which antagonizes the μ receptors, results in an increased anorexigenic effect.	≥18 years of age for long-term use. Initial BMI ≥ 30 kg/m^2 (obesity) or BMI ≥ 27 kg/m^2 (overweight) in the presence of at least one weight-associated comorbidity.	16 mg of naltrexone and 180 mg of oral bupropion morning and afternoon (at least 8 h between each dose). The initial dose is 8 mg of ER naltrexone and 90 mg of ER bupropion (1 tablet) once per day for 1 week; the dose is progressively increased weekly up to two tablets am and 2 tablets pm.	- Frequent: Nausea, constipation, diarrhea, headache, dizziness, vomiting, insomnia, dry mouth. - Severe (require discontinuation of treatment): Seizures, suicidal ideation or injuring others, maniac episodes, increased BP or HR, visual problems, liver injury or hepatitis, severe allergic reaction, hypoglycemia in patients with diabetes mellitus type 2 treated with sulfonylureas or insulin.	- Pregnancy and lactation. - Uncontrolled hypertension. - Bulimia–anorexia. - Epilepsy or seizures or anticonvulsant therapy. - Treatment with other bupropion-containing medications. - Recent abrupt discontinuation of alcohol use. - Opiates treatments, methadone or opiate withdrawal syndrome. - Abrupt discontinuation of benzodiazepines or anticonvulsants. - MAO inhibitors treatment. - Allergy to naltrexone or bupropion. - Treatment with CYP2B6 inducers (ritonavir, lopinavir, carbamazepine, phenobarbital). - Treatment with levodopa or amantadine. - Narrow angle glaucoma.	- Should not be used in association with high-fat foods. - Watch for any behavioral changes or suicidal ideation.

TABLE 5 (Continued)

DRUG Central Action Long Term	Mechanism of action	Indications	Dosing	Adverse reactions	Contraindications	Warnings
Liraglutide[26,45–59]	Liraglutide is a glucagon-like peptide 1 (GLP-1) with 97% sequence alignment to the endogenous GLP-1, which causes weight loss via reduced food reduced. Liraglutide at a dose of 1.8 mg is indicated for the treatment of diabetes mellitus type 2. It increases satiety and reduces appetite due to its action on the arcuate nucleus of the hypothalamus. There, it directly stimulates the anorexigenic neurons POMC/CART and indirectly inhibits the neurotransmission of orexigenic neurons NPY/AgRP via GABA-dependent signaling.	≥18 years old with initial BMI ≥ 30 kg/m^2 (obesity) or BMI ≥ 27 kg/m^2 (overweight) in the presence of at least one weight-associated comorbidity, such as high blood sugar (pre-diabetes and type 2 diabetes mellitus), hypertension, dyslipidemia, or obstructive sleep apnea. - Adolescents > 12 years old with an initial BMI ≥ 30 kg/m^2 (obesity) and body weight over 60 kg.	3 mg once a day subcutaneous (pre-filled pen). The initial dose is 0.6 mg/day for 1 week; it is increased weekly by 0.6 mg until a dose of 3.0 mg/day for enhanced GI tolerability. Liraglutide therapy should be discontinued after 12 weeks at a dose of 3.0 mg/day if the patient has not lost at least 5% of the initial body weight.	- Very frequent: Nausea, vomiting, diarrhea, constipation. - Frequent: Other GI effects, cholelithiasis, insomnia, dizziness, injection site reactions, fatigue.	- Pregnancy and lactation. - Hypersensitivity to liraglutide or any of its excipients. - Personal or family history of bone marrow or thyroid cancer or type 2 multiple endocrine neoplasms.	- Its use is not recommended in association with another GLP-1 receptor agonist. - Pancreatitis: Suspicious pancreatitis leads to liraglutide of 3 mg treatment discontinuation; if acute pancreatitis is confirmed, treatment should not be reinitiated. Use with caution in patients with a history of pancreatitis. - Type 2 diabetes mellitus: Liraglutide of 3 mg should not be used to replace insulin. Patients with type 2 diabetes mellitus receiving liraglutide of 3 mg in combination with insulin and/or sulfonylurea may be at increased risk of hypoglycemia; the risk may be lowered by adjusting the insulin or sulfonylurea dose. - The efficacy and safety of liraglutide of 3 mg has not been established in - congestive heart failure class IV (NYHA) and - treatment with other weight control agents.

(Continues)

TABLE 5 (Continued)

DRUG Central Action Long Term	Mechanism of action	Indications	Dosing	Adverse reactions	Contraindications	Warnings
Semaglutide[26,60–67]	Semaglutide is a GLP-1 analogue with 94% sequence alignment with human GLP-1. It only differs in two amino acids. It has an 18-carbon fatty acid chain attached to amino acid 26 of the molecule, which provides a strong albumin bond and facilitates extended activity. Semaglutide at 0.5–2 mg/week is indicated for the treatment of type 2 diabetes mellitus.	(≥18 years old) with initial BMI ≥ 30 kg/m^2 (obesity) or BMI ≥ 27 kg/m^2 (overweight) in the presence of at least one weight-associated comorbidity.	Initial dose: 0.25 mg/week during the 1st month; 2nd month 0.50 mg/week; 3rd month 1 mg/week; 4th month 1.7 mg/week; 5th month 2.4 mg/week maintenance dose.	- Very frequent: Nausea, vomiting, diarrhea, constipation. - Frequent: Other GI effects, cholelithiasis, insomnia, dizziness, injection site reactions, fatigue.	- Hypersensitivity to semaglutide or to any of its excipients. - Personal or family history of bone marrow cancer, thyroid cancer, or multiple endocrine neoplasms (MEN2). - Pregnancy and lactation.	- Its use is not recommended in combination with another GLP-1 agonist or DDP4 blocker. - Pancreatitis: Suspicious pancreatitis should lead to discontinuation of semaglutide treatment; if acute pancreatitis is confirmed, treatment shall not be reinitiated. Use with caution in patients with a history of pancreatitis. - Diabetes mellitus type 2: Semaglutide should not be used to replace insulin. Patients with type 2 DM receiving semaglutide in combination with insulin and/or sulfonylurea may be at higher risk of hypoglycemia; the risk may be lowered by adjusting the insulin or sulfonylurea dose. - The efficacy and safety of semaglutide of 2 mg has not been established in - congestive heart failure class IV (NYHA) and - patients treated with other weight control products.

TABLE 5 (Continued)

DRUG Central Action Long Term	Mechanism of action	Indications	Dosing	Adverse reactions	Contraindications	Warnings
Sibutramine[68–73] This drug was officially removed from the market and is only approved for patients with obesity in Brazil. Therefore, it underwent a second iteration for inclusion in the Latin American therapy regimens.	Sibutramine promotes satiety blocking the reuptake of noradrenalin and serotonin, hence reducing food intake.	Age > 18 years old. BMI ≥ 30 kg/m^2 (in Brazil, it is only authorized for patients with obesity for 2 years maximum).	Recommended initial dose: 110 mg/day oral capsule in the morning, with or without food, swallowed with water. If the patient fails to lose at least 2 kg over the first 4 weeks, consider increasing the dose to 15 mg/day or discontinue sibutramine. Treatment should be discontinued in patients failing to respond to the 15 mg/day dose (at least 2 kg in 4 weeks).	- Dry mouth, insomnia, constipation, GI disorders, tremors, palpitations, anxiety, headache, dizziness, tachycardia, hypertension, nausea, abdominal pain.	- Pregnancy and lactation. - Patients with a history of coronary artery disease (angina, history of myocardial infarction), congestive heart failure, tachycardia, peripheral obstructive arterial disease, arrythmia, or cerebrovascular disease (stroke or TIA). - Patients with uncontrolled hypertension. - Patients with a history or existing eating disorders, such as bulimia and anorexia. - Patients receiving other central action weight loss medications or medications for psychiatric disorders. - Patients receiving monoaminoxidase receptor inhibitors.	- Caution should be used in patients with - glaucoma, - epilepsy, - predisposition to hemorrhage, - concomitant use of medications affecting hemostasis and platelet function, and - level of risk during pregnancy: C.
Drug **Peripheral action** **Short term**	**Mechanism of action**	**Indications**	**Dosing**	**Adverse reactions**	**Contraindications**	**Warnings**
Orlistat[26,71,74–78]	Orlistat is a reversible gastrointestinal lipase inhibitor that prevents the absorption of 30% of fat intake, which is excreted in the feces. Inhibiting fat digestion reduces the formation of mixed micelles and the absorption of long-chain fatty acids, cholesterol, and certain liposoluble vitamins.	>12 years old	One 120 mg capsule three times per day with each fat-containing meal (during or up to 1 h after eating). Patients should be advised to follow a nutritionally balanced diet and a reduced calorie intake,	- Frequent: Oily spots, flatulence with discharge. Fecal urgency, fatty feces, increased defecation, fecal incontinence. - Other frequent reactions: Abdominal pain/	- Pregnancy, chronic malabsorption syndrome or with cholestasis; known hypersensitivity to orlistat or any of its constituents; pregnancy or lactation.	- Drug interactions and reduced vitamin absorption: Orlistat may interact with concomitant medications, such as ciclosporin, levothyroxine, warfarin, amiodarone, anti-epileptic medications, and anti-retroviral medications. - Liver damage: Patients should be instructed to report any liver dysfunction symptoms (anorexia,

(Continues)

TABLE 5 (Continued)

Drug Peripheral action Short term	Mechanism of action	Indications	Dosing	Adverse reactions	Contraindications	Warnings
			with approximately 30% of the calories as fat. Distribute the daily intake of fats, carbohydrates, and proteins in the three main meals.	malaise, nausea, infectious diarrhea, rectal pain/malaise.		itching, jaundice, dark color urine, light-colored feces, or pain in the upper right quadrant) while taking orlistat. - Increased urinary oxalate. - Cholelithiasis.

Abbreviations: BP, blood pressure; CART, cocaine- and amphetamine-regulated transcript; DDP4, dipeptidyl peptidase 4; DM, diabetes mellitus; ECG, electrocardiogram; GI, gastrointestinal; HR, heart rate; MAO, monoamine oxidase; NYHA, New York Heart Association; TIA, transient ischemic attack.

TABLE 6 Obesity-associated comorbidities.

Cardiovascular	• Hypertension • Coronary artery disease • Heart failure • Venous insufficiency • Dyslipidemia
Endocrine	• Metabolic syndrome • Type 2 diabetes mellitus • Dyslipidemia • Polycystic ovary syndrome • Amenorrhea • Infertility • Menstrual disorders • Vitamin D deficiency • Thyroid cancer
Respiratory	• Dyspnea • Obstructive sleep apnea • Hypoventilation syndrome • Pickwick syndrome • Bronchial asthma
Gastrointestinal	• Gastroesophageal reflux disease • Metabolic dysfunction-associated fatty liver • Cholelithiasis • Hernias • Esophageal, gastric cardia, colon and rectum, pancreas, gallbladder, and liver cancers
Genitourinary	• Urinary incontinence • Glomerulopathies • Renal failure • Hypogonadism • Breast cancer (postmenopause), ovarian, endometrial, kidney, and prostate • Pregnancy complications
Neurological	• Cerebrovascular accident • Idiopathic intracranial hypertension • Alzheimer's disease • Meralgia paresthetica
Musculoskeletal	• Hyperuricemia and gout • Arthrosis—arthritis • Degenerative arthropathy of weight-bearing joints • Lumbar pain
Skin, adnexal structures, and soft parts	• Striae • Ochre dermatitis • Lymphedema • Intertrigo • Acanthosis nigricans and acrochordons • Suppurative hidradenitis
Psychological	• Depression • Body image disorders • Eating disorders • Poor quality of life

Source: Based on Garvey et al.,[16] Balcázar et al.,[78] Benziger et al.,[79] Catenacci et al.,[80] and Lauby-Secretan et al.[81]

consider discontinuation, change of medication or association with another drug in addition to reviewing, reinforcing, and maintaining lifestyle changes.[15,16,85,103–114]

3.3 | Treatment success

Treatment success should be defined as achievement of the following goals (LE: A; R: I):[16,83,85]

- sustained weight loss of 5%–10% over time;
- permanent lifestyle changes;
- improvement or prevention of comorbidities; and
- improved quality of life.

In responders, medications improve weight loss and enhance the management of concomitant metabolic diseases. A responder or rapid responder patient is defined as a patient that loses 5% or more of their initial weight after 12 weeks of treatment at optimal medication doses.[104]

Evidence is limited, and further clinical trials are required for pharmacological treatment for weight regain or insufficient weight loss after bariatric surgery. However, it may be useful to prevent and treat weight regain and increase weight loss when it becomes temporarily stagnant using a multidisciplinary approach (LE: C; R: IIa).[106–113]

The following parameters are suggested for follow-up purposes and to define treatment success:

- quality of life;
- BMI;
- metabolic comorbidities; and
- functional comorbidities.

TABLE 7 Cutoff points used for waist circumference in different guidelines or studies.

	Females	Males
European Group for the Study of Insulin Resistance (EGIR, 1999)	≥80 cm	≥94 cm
III National Cholesterol Study Program (NCEP/ATP III, 2001–2004)	≥88 cm	≥102 cm
International Diabetes Federation (IDF, 2005) based on ethnicity (Latin Americans)	≥80 cm	≥90 cm
Latin American Group for the Study of Metabolic Syndrome (GLESMO, 2011)	≥90 cm	≥94 cm

Source: Based on Ross et al.,[91] Batsis and Zagaria,[92] and Aschner et al.[93]

3.4 | Non-recommended therapies

To establish which medications should not be prescribed for the treatment of patients with obesity, experts state that the following medications are not considered anti-obesity and therefore should not be prescribed for weight loss purposes (LE: B; R: III):[18,83,88,90,115,116]

- thyroid hormones;
- human chorionic gonadotrophin;
- growth hormone;

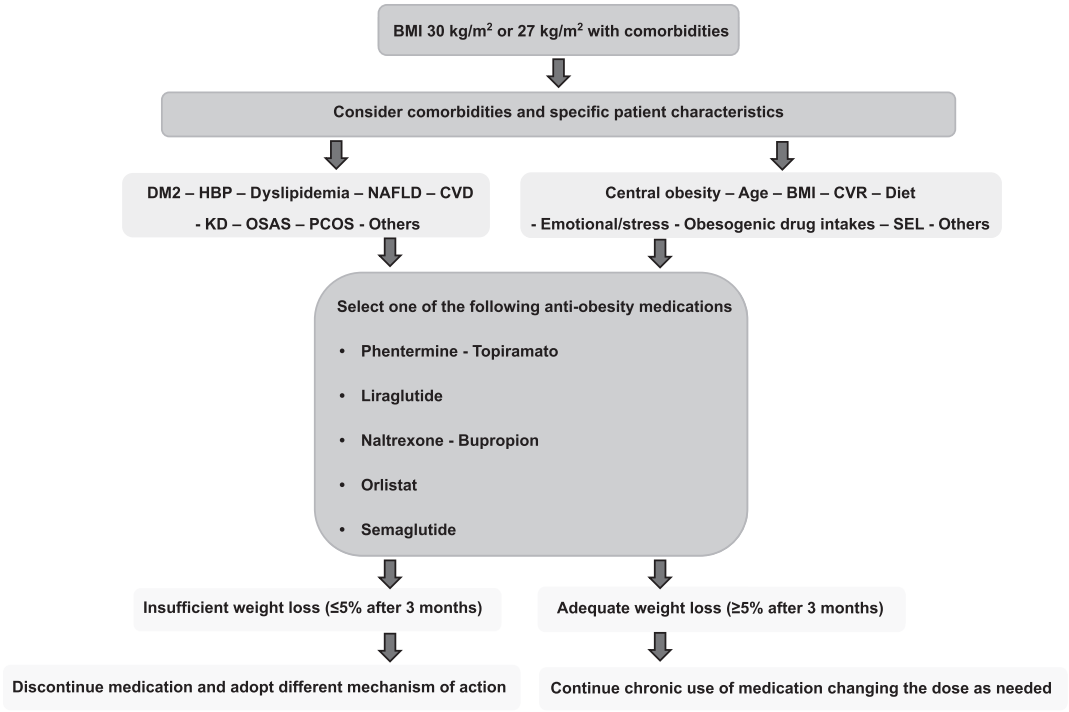

FIGURE 2 Algorithm for pharmacological therapy in obesity. BMI, body mass index; CVD, cardiovascular disease; CVR, cardiovascular risk; DM2, diabetes mellitus type 2; HBP, high blood pressure; KD, kidney disease; NAFLD, non-alcoholic fatty liver disease; OSAS, obstructive sleep apnea syndrome; PCOS, polycystic ovary syndrome; SEL, socioeconomic level.

- diuretics;
- laxatives; and
- drugs that have not been approved or that have been recalled.

Furthermore, some drugs may impact weight loss; however, the loss is not significant; hence, they are not approved as anti-obesity medications. These include (LE: B; R: III)[18,83,90,115,116]

- metformin;
- topiramate onotherapy;
- bupropion monotherapy;
- anxiolytics; and
- serotonin reuptake inhibitors.

Additionally, considering that obesity is a chronic disease, the panel of experts does not recommend the use of drugs that are exclusively approved for short-term use (LE: A; R: III).

3.5 | Contraindications

The general contraindications for anti-obesity drugs were as follows (LE: B; R: IIa):[16,20,85,114,117]

- renal failure with glomerular filtration rate < 30 mL/min;
- heart failure;
- liver failure;
- untreated psychosis;
- pregnancy and lactation; and
- alcohol abuse and other drug addictions.

Specific contraindications for each drug are listed in Table 5. Women of childbearing age are recommended to use contraceptives during anti-obesity drug therapy, and these medications should be discontinued for at least four to five half-lives before trying to become pregnant.

Encouraging the use of natural or nutritional supplements to support weight loss is a widespread practice in Latin American countries, either because the patient decides to use them or through medical or paramedical recommendations. The literature review conducted by the experts in this consensus led them to conclude that there is insufficient evidence to support the use of natural products to treat patients with obesity (LE: C; R: IIb).[118–129] These are some examples:

- chromium picolinate;
- Indian nut;
- Garcinia cambogia;
- Spirulina; and
- white kidney bean extract.

TABLE 8 Medications associated with weight gain and therapeutic options.

Associated disease or comorbidity	Drugs that increase body weight	Neutral medications or drugs that reduce body weight
Hypertension	Beta-adrenergic blockers (propranolol, metoprolol, and atenolol)	Inhibitors of the renin-angiotensin system Calcium blockers If beta-blockers are needed, carvedilol and nebivolol are less associated with weight gain
Diabetes mellitus type 2	Insulin Sulfonylureas Methylglycines Glitazones	GLP-1 receptor agonists SGLT2 inhibitors Pramlintide Metformin DDP4 inhibitors Alpha-glycosidase inhibitors
Depression	Monoaminoxidase inhibitors Tricyclic antidepressants Mirtazapine Paroxetine Doxepin Citalopram Escitalopram Fluoxetine and sertraline (long term)[a]	Bupropion Fluoxetine (short-term use) Sertraline (<1 year) Venlafaxine Desvenlafaxine Duloxetine
Epilepsy	Phenobarbital Valproic acid Carbamazepine Gabapentin Pregabalin	Topiramate Zonisamide Lamotrigine Levetiracetam
Chronic inflammatory disease	Corticosteroids	Non-steroidal anti-inflammatory drugs (NSAIDs) Disease-modifying antirheumatic drugs (DMARDs)
Psychosis	Olanzapine Clozapine Risperidone Quetiapine Thioridazine Haloperidol Lithium Mirtazapine	Aripiprazole Ziprasidone Trazodone

Abbreviations: DDP4, dipeptidyl peptidase 4; GLP-1, glucagon-like peptide 1; SGLT2, sodium–glucose cotransporter 2.
[a]Controversial evidence about the effect of these drugs on body weight.
Source: Based on Apovian et al.,[18] Li et al.,[82] Erlandson et al.,[83] Bray et al.,[129] Verhaegen and Van Gaal,[130] Gafoor et al.,[131] and Arterburn et al.[132]

3.6 | Medications associated with weight gain and therapeutic alternatives

Drugs prescribed to treat obesity comorbidities should be carefully managed to avoid those that may result in weight gain. There is a list of drugs used in the treatment of various chronic diseases that result in weight gain and optional pharmacological choices (Table 8).[18,83,84,130–132]

4 | CONCLUSIONS

Obesity is a chronic condition. Prescribing drugs with demonstrated efficacy and safety should be considered a Class I recommendation, which has appropriate levels of evidence, in the framework of long-term lifestyle changes intended to improve weight loss, comorbidities, and patient quality of life.

There are multiple barriers to the use of anti-obesity drugs, such as a limited number of specialized physicians, the belief that obesity is due to the lack of will of the patient, weight stigmatization, association with amphetamines, and a history of recalled drugs due to adverse effects. In contrast to other chronic diseases, medications approved for long-term treatment and access to these medications remain limited, which further hinders their adequate use. The objective of this process was to provide guidelines for the management of anti-obesity medications for physicians at all levels of care adapted for Latin American and Caribbean populations.

ACKNOWLEDGMENTS

The authors have no acknowledgments.

CONFLICT OF INTEREST STATEMENT

Ana María Cappelletti: Adium Pharma, Novo Nordisk, Raffo, and MEDICAMENTA ECUATORIANA. Alex Valenzuela Montero: Abbott, Adium Pharma, Chile-Teva, Eurofarma, Grunenthal, Tecnofarma, Sanitas, Saval, and Synthon. Cintia Cercato: Adium Pharma, Eurofarma, Lilly, Merck, and Novo Nordisk. John Jairo Duque Ossman: Adium Pharma. Pablo Enrique Fletcher Vasquez: Adium Pharma, Asofarma-Lilly, and Novo Nordisk. Juan Eduardo García García: Adium Pharma, Eli Lilly, and Novo Nordisk. Leonardo Guadalupe Mancillas-Adame: Adium Pharma, Eli Lilly, Merck, Novo Nordisk, and OPKO. Herald Andrés Manrique: Abbott, Adium Pharma, Asofarma, and Novo Nordisk. Flor de María Ranchos Monterroso: Adium Pharma, AstraZeneca, Merck, Novo Nordisk, and Sanofi. Pablo Segarra: Adium Pharma, AstraZeneca, Becton Dickinson, Boehringer Ingelheim, Eli Lilly, MEDICAMENTA ECUATORIANA, Merck, Novo Nordisk, Pfizer, Roche Diagnostics, and Sanofi Aventis. Trina Navas: Adium Pharma.

ORCID

Ana María Cappelletti https://orcid.org/0000-0002-9737-4193

REFERENCES

1. Legetic B, Medici A, Hernández-Avila M, Alleyne G, Hennis A (Eds). *Economic Dimensions of Non-communicable Disease in Latin America and the Caribbean. Disease Control Priorities. Companion Volume*. 3rd ed. PAHO; 2016.
2. *Obesidad y sobrepeso*. Who.int. [citado el 9 de octubre de 2021]. Disponible en: https://www.who.int/es/news-room/fact-sheets/detail/obesity-and-overweight
3. WHO Consultation on Obesity (1997: Geneva, Switzerland), World Health Organization, Division of Noncommunicable Diseases & World Health Organization. Programme of Nutrition, Family and Reproductive Health. *Obesity: Preventing and Managing the Global Epidemic: Report of a WHO Consultation on Obesity, Geneva, 3–5 June 1997*. World Health Organization; 1998.
4. Barquera S, Hernández-Barrera L, Trejo-Valdivia B, Shamah T, Campos-Nonato I, Rivera-Dommarco J. Obesidad en México, prevalencia y tendencias en adultos. Ensanut 2018–19 [Obesity in Mexico, prevalence and trends in adults. Ensanut 2018–19.]. *Salud Publica Mex*. 2020;62(6):682-692. doi:10.21149/11630
5. Peña M, Bacallao J (Eds). *Obesity and Poverty: A New Public Health Challenge*. PAHO; 2000. Scientific Pub:576. https://iris.paho.org/handle/10665.2/4007
6. Holub CK, Elder JP, Arredondo EM, et al. Obesity control in Latin American and U.S. Latinos: a systematic review. *Am J Prev Med*. 2013;44(5):529-537. doi:10.1016/j.amepre.2013.01.023 PMID: 23597819; PMCID: PMC4808744.
7. Allison DB, Downey M, Atkinson RL, et al. Obesity as a disease: a white paper on evidence and arguments commissioned by the Council of the Obesity Society. *Obesity (Silver Spring)*. 2008;16(6):1161-1177. doi:10.1038/oby.2008.231 Epub 2008 May 8. PMID: 18464753.
8. Sharma AM, Kushner RF. A proposed clinical staging system for obesity. *Int J Obes (Lond)*. 2009;33(3):289-295. doi:10.1038/ijo.2009.2 Epub 2009 Feb 3. PMID: 19188927.
9. Cappelletti AM. *El enigma de la obesidad. En Cappelletti, Katz y colaboradores. Obesidad Encrucijadas y abordajes*. Editorial Akadia; 2017.
10. Caterson ID, Alfadda AA, Auerbach P, et al. Gaps to bridge: misalignment between perception, reality, and actions in obesity. *Diabetes Obes Metab*. 2019;21(8):1914-1924. doi:10.1111/dom.13752 Epub 2019 May 3. PMID: 31032548; PMCID: PMC6767048.
11. Org.ar. Cited October 13, 2021. Available from: https://sanutricion.org.ar/wp-content/uploads/2022/01/Posicion-SAN-Obesidad-2020.pdf
12. Rubino F, Puhl RM, Cummings DE, et al. Joint international consensus statement for ending stigma of obesity. *Nat Med*. 2020;26(4):485-497. doi:10.1038/s41591-020-0803-x Epub 2020 Mar 4. PMID: 32127716; PMCID: PMC7154011.
13. *Obesity*. Who.int. [citado el 10 Oct 2021]. Disponible en: https://www.who.int/health-topics/obesity
14. Tsai AG. Integrating obesity treatment into routine primary care. *Ann Intern Med*. 2019;171(11):847-848. doi:10.7326/M19-2988 Epub 2019 Nov 12. PMID: 31711100.
15. Jensen MD, Ryan DH, Apovian CM, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. *Circulation*. 2014;129(25 Suppl 2):S102-S138. doi:10.1161/01.cir.0000437739.71477.ee
16. Garvey WT, Mechanick JI, Brett EM, et al. Reviewers of the AACE/ACE Obesity Clinical Practice Guidelines. American Association of Clinical Endocrinologists and American College of Endocrinology Comprehensive Clinical Practice Guidelines for Medical Care of Patients With Obesity. *Endocr Pract*. 2016;22(Suppl 3):1-203. doi: 10.4158/EP161365.GL Epub 2016 May 24. PMID: 27219496.

17. Yumuk V, Tsigos C, Fried M, et al. Obesity Management Task Force of the European Association for the Study of Obesity. European guidelines for obesity management in adults. *Obes Facts*. 2015;8(6):402-424. doi:10.1159/000442721 Epub 2015 Dec 5. Erratum in: Obes Facts. 2016;9(1):64. PMID: 26641646; PMCID: PMC5644856.
18. Apovian CM, Aronne LJ, Bessesen DH, et al. Endocrine Society. Pharmacological management of obesity: an endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2015;100(2):342-362. doi:10.1210/jc.2014-3415 Epub 2015 Jan 15. Erratum in: J Clin Endocrinol Metab 2015 May;100(5):2135–2136. PMID: 25590212.
19. Wharton S, Lau DCW, Vallis M, et al. Obesity in adults: a clinical practice guideline. *CMAJ*. 2020;192(31):E875-E891. doi:10.1503/cmaj.191707
20. Durrer Schutz D, Busetto L, Dicker D, et al. European practical and patient-centred guidelines for adult obesity management in primary care. *Obes Facts*. 2019;12(1):40-66. doi:10.1159/000496183 Epub 2019 Jan 23. PMID: 30673677; PMCID: PMC6465693.
21. Pedersen SD, Manjoo P, Wharton S. *Canadian Adult Obesity Clinical Practice Guidelines: Pharmacotherapy in Obesity Management*. Accessed October 24, 2021. Available from: https://obesitycanada.ca/guidelines/pharmacotherapy
22. Jastreboff AM, Kotz CM, Kahan S, Kelly AS, Heymsfield SB. Obesity as a disease: the Obesity Society 2018 Position Statement. *Obesity (Silver Spring)*. 2019;27(1):7-9. doi:10.1002/oby.22378 PMID: 30569641.
23. Rosero RJ, Polanco JP, Ciro V, Uribe A, Manrique H, Sánchez PE. Proposal for a multidisciplinary clinical approach to obesity. *J Med - Clin Res & Rev*. 2020;4(12):1-11. doi:10.33425/2639-944x.1185
24. Gossmann M, Butsch WS, Jastreboff AM. Treating the chronic disease of obesity. *Med Clin North am*. 2021;105(6):983-1016. doi:10.1016/j.mcna.2021.06.005 PMID: 34688422.
25. Jacobs AK, Kushner FG, Ettinger SM, et al. ACCF/AHA clinical practice guideline methodology summit report: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2013;61(2):213-265. doi:10.1016/j.jacc.2012.09.025 PMID: 31298150.
26. Hendricks EJ, Srisurapanont M, Schmidt SL, et al. Addiction potential of phentermine prescribed during long-term treatment of obesity. *Int J Obes (Lond)*. 2014;38(2):292-298. doi:10.1038/ijo.2013.74
27. Franke KB, Psaltis PJ. Coronary vasospasm induced by phentermine. *Mayo Clin Proc*. 2019 Jul;94(7):1138-1140. doi:10.1016/j.mayocp.2019.05.021 PMID: 31272562.
28. Lucchetta RC, Riveros BS, Pontarolo R, et al. Systematic review and meta-analysis of the efficacy and safety of amfepramone and mazindol as a monotherapy for the treatment of obese or overweight patients. *Clinics (Sao Paulo)*. 2017;72(5):317-324. doi:10.6061/clinics/2017(05)10 Erratum in: Clinics (Sao Paulo) 2018 Mar 15;73:e1err. PMID: 28591345; PMCID: PMC5439101.
29. Cercato C, Roizenblatt VA, Leança CC, et al. A randomized double-blind placebo-controlled study of the long-term efficacy and safety of diethylpropion in the treatment of obese subjects. *Int J Obes (Lond)*. 2009;33(8):857-865. doi:10.1038/ijo.2009.124
30. Soto-Molina H, Pizarro-Castellanos M, Rosado-Pérez J, et al. Six-month efficacy and safety of amfepramone in obese Mexican patients: a double-blinded, randomized, controlled trial. *Int J Clin Pharmacol Ther*. 2015;53(7):541-549. doi:10.5414/CP202135 PMID: 26073353.
31. Garvey WT, Ryan DH, Look M, et al. Two-year sustained weight loss and metabolic benefits with controlled-release phentermine/topiramate in obese and overweight adults (SEQUEL): a randomized, placebo-controlled, phase 3 extension study. *Am J Clin Nutr*. 2012;95(2):297-308. doi:10.3945/ajcn.111.024927 Epub 2011 Dec 7. PMID: 22158731; PMCID: PMC3260065.
32. Shank RP, Maryanoff BE. Molecular pharmacodynamics, clinical therapeutics, and pharmacokinetics of topiramate. *CNS Neurosci Ther*. 2008;14(2):120-142. doi:10.1111/j.1527-3458.2008.00041x. PMID: 18482025; PMCID: PMC6494007.
33. Hernández-Bastida A. Fentermina y topiramato contra fentermina más placebo en pacientes con sobrepeso u obesidad clase I o II. *Med Int Méx*. 2015;31:125-136.
34. Aronne LJ, Wadden TA, Peterson C, Winslow D, Odeh S, Gadde KM. Evaluation of phentermine and topiramate versus phentermine/topiramate extended release in obese adults. *Obesity (Silver Spring)*. 2013;21(11):2163-2171. doi:10.1002/oby.20584 Epub 2013 Oct 17. PMID: 24136928.
35. Gadde KM, Allison DB, Ryan DH, et al. Effects of low-dose, controlled-release, phentermine plus topiramate combination on weight and associated comorbidities in overweight and obese adults (CONQUER): a randomised, placebo-controlled, phase 3 trial. *Lancet*. 2011;377(9774):1341-1352. doi:10.1016/S0140-6736(11)60205-5 Epub 2011 Apr 8. Erratum in: Lancet. 2011 Apr 30;377(9776):1494. PMID: 21481449.
36. Allison DB, Gadde KM, Garvey WT, et al. Controlled-release phentermine/topiramate in severely obese adults: a randomized controlled trial (EQUIP). *Obesity (Silver Spring)*. 2012;20(2):330-342. doi:10.1038/oby.2011.330 Epub 2011 Nov 3. PMID: 22051941; PMCID: PMC3270297.
37. Greenway FL, Fujioka K, Plodkowski RA, et al. COR-I Study Group. Effect of naltrexone plus bupropion on weight loss in overweight and obese adults (COR-I): a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*. 2010;376(9741):595-605. doi:10.1016/S0140-6736(10)60888-4 Epub 2010 Jul 29. Erratum in: *Lancet*. 2010 Aug 21;376(9741):594. Erratum in: *Lancet*. 2010 Oct 23;376(9750):1392. PMID: 20673995.
38. Hollander P, Gupta AK, Plodkowski R, et al. Effects of naltrexone sustained-release/bupropion sustained-release combination therapy on body weight and glycemic parameters in overweight and obese patients with type 2 diabetes. *Diabetes Care*. 2013;36(12):4022-4029. doi:10.2337/dc13-0234
39. NICE. *Naltrexone–Bupropion for Managing Overweight and Obesity (TA494)*. 2017. Available from: www.nice.org.uk/guidance/ta494
40. Onakpoya IJ, Lee JJ, Mahtani KR, Aronson JK, Heneghan CJ. Naltrexone-bupropion (Mysimba) in management of obesity: a systematic review and meta-analysis of unpublished clinical study reports. *Br J Clin Pharmacol*. 2020;86(4):646-667. doi:10.1111/bcp.14210 Epub 2020 Feb 4. PMID: 31918448; PMCID: PMC7098870.
41. Hong K, Herrmann K, Dybala C, Halseth AE, Lam H, Foreyt JP. Naltrexone/bupropion extended release-induced weight loss is independent of nausea in subjects without diabetes. *Clin Obes*. 2016;6(5):305-312. doi:10.1111/cob.12157 Epub 2016 Aug 1. PMID: 27477337; PMCID: PMC5129540.
42. Apovian CM, Aronne L, Rubino D, et al. A randomized, phase 3 trial of naltrexone SR/bupropion SR on weight and obesity-related risk factors (COR-II). *Obesity (Silver Spring)*. 2013;21(5):935-943. doi:10.1002/oby.20309 PMID: 23408728; PMCID: PMC3739931.
43. Wadden TA, Foreyt JP, Foster GD, et al. Weight loss with naltrexone SR/bupropion SR combination therapy as an adjunct to behavior modification: the COR-BMOD trial. *Obesity (Silver Spring)*. 2011;19(1):110-120. doi:10.1038/oby.2010.147 Epub 2010 Jun 17. PMID: 20559296; PMCID: PMC4459776.
44. Wadden TA, Hollander P, Klein S, et al. Weight maintenance and additional weight loss with liraglutide after low-calorie-diet-induced weight loss: the SCALE Maintenance randomized study. *Int J Obes (Lond)*. 2013;37(11):1443-1451. doi:10.1038/ijo.2013.120 Epub 2013 Jul 1. Erratum in: Int J Obes (Lond). 2013 Nov;37(11):1514. Erratum in: Int J Obes (Lond). 2015 Jan;39(1):187. PMID: 23812094.
45. Lean ME, Carraro R, Finer N, et al. NN8022-1807 Investigators. Tolerability of nausea and vomiting and associations with weight loss in a randomized trial of liraglutide in obese, non-diabetic adults. *Int J*

Obes (Lond). 2014;38(5):689-697. doi:10.1038/ijo.2013.149 Epub 2013 Aug 14. PMID: 23942319; PMCID: PMC4010971.

46. Astrup A, Carraro R, Finer N, et al. Safety, tolerability and sustained weight loss over 2 years with the once-daily human GLP-1 analog, liraglutide. *Int J Obes (Lond)*. 2012;36(6):843-854. doi:10.1038/ijo.2011.158 Epub 2011 Aug 16. Erratum in: *Int J Obes* (Lond). 2012 Jun;36(6):890. Erratum in: Int J Obes (Lond). 2013 Feb;37(2):322. PMID: 21844879; PMCID: PMC3374073.
47. Ladenheim EE. Liraglutide and obesity: a review of the data so far. *Drug des Devel Ther*. 2015;30(9):1867-1875. doi:10.2147/DDDT.S58459 PMID: 25848222; PMCID: PMC4386791.
48. Wadden TA, Tronieri JS, Sugimoto D, et al. Liraglutide 3.0 mg and intensive behavioral therapy (IBT) for obesity in primary care: the SCALE IBT randomized controlled trial. *Obesity (Silver Spring)*. 2020;28(3):529-536. doi:10.1002/oby.22726 PMID: 32090517; PMCID: PMC7065111.
49. Kolotkin RL, Gabriel Smolarz B, Meincke HH, Fujioka K. Improvements in health-related quality of life over 3 years with liraglutide 3.0 mg compared with placebo in participants with overweight or obesity. *Clin Obes*. 2018;8(1):1-10. doi:10.1111/cob.12226 Epub 2017 Oct 16. PMID: 29045079; PMCID: PMC5813214.
50. van Bloemendaal L, IJzerman RG, Ten Kulve JS, et al. GLP-1 receptor activation modulates appetite- and reward-related brain areas in humans. *Diabetes*. 2014;63(12):4186-4196. doi:10.2337/db14-0849 Epub 2014 Jul 28. PMID: 25071023.
51. Wilding JP, Overgaard RV, Jacobsen LV, Jensen CB, le Roux CW. Exposure-response analyses of liraglutide 3.0 mg for weight management. *Diabetes Obes Metab*. 2016;18(5):491-499. doi:10.1111/dom.12639 Epub 2016 Mar 1. PMID: 26833744; PMCID: PMC5069568.
52. Hernández DC, Monroy DC, Porras A. Eficacia y seguridad de liraglutida para la disminución de peso en adultos: revisión sistemática. *Rev Col De Endocrinología, Diabetes Y Metabolismo*. 2020;7(4):250-257. doi:10.53853/encr.7.4.651
53. Davies MJ, Bergenstal R, Bode B, et al. Efficacy of liraglutide for weight loss among patients with type 2 diabetes: the SCALE diabetes randomized clinical trial. *Jama*. 2015;314(7):687-699. doi:10.1001/jama.2015.9676 Erratum in: JAMA. 2016 Jan 5;315(1):90. PMID: 26284720.
54. Garvey WT, Birkenfeld AL, Dicker D, et al. Efficacy and safety of liraglutide 3.0 mg in individuals with overweight or obesity and type 2 diabetes treated with basal insulin: the SCALE insulin randomized controlled trial. *Diabetes Care*. 2020;43(5):1085-1093. doi:10.2337/dc19-1745 Epub 2020 Mar 5. PMID: 32139381; PMCID: PMC7171937.
55. Blackman A, Foster GD, Zammit G, et al. Effect of liraglutide 3.0 mg in individuals with obesity and moderate or severe obstructive sleep apnea: the SCALE Sleep Apnea randomized clinical trial. *Int J Obes (Lond)*. 2016;40(8):1310-1319. doi:10.1038/ijo.2016.52 Epub 2016 Mar 23. PMID: 27005405; PMCID: PMC4973216.
56. Alruwaili H, Dehestani B, le Roux CW. Clinical impact of liraglutide as a treatment of obesity. *Clin Pharm*. 2021;13:53-60. doi:10.2147/CPAA.S276085 PMID: 33732030; PMCID: PMC7958997.
57. Pi-Sunyer X, Astrup A, Fujioka K, et al. SCALE Obesity and Prediabetes NN8022-1839 Study Group. A randomized, controlled trial of 3.0 mg of liraglutide in weight management. *N Engl J Med*. 2015;373(1):11-22. doi:10.1056/NEJMoa1411892 PMID: 26132939.
58. Kelly AS, Auerbach P, Barrientos-Perez M, et al. A randomized, controlled trial of liraglutide for adolescents with obesity. *N Engl J Med*. 2020;382(22):2117-2128. doi:10.1056/NEJMoa1916038 Epub 2020 Mar 31. PMID: 32233338.
59. Kushner RF, Calanna S, Davies M, et al. Semaglutide 2.4 mg for the treatment of obesity: key elements of the STEP trials 1 to 5. *Obesity (Silver Spring)*. 2020;28(6):1050-1061. doi:10.1002/oby.22794
60. Davies M, Færch L, Jeppesen OK, et al. Semaglutide 2·4 mg once a week in adults with overweight or obesity, and type 2 diabetes (STEP 2): a randomised, double-blind, double-dummy, placebo-controlled, phase 3 trial. *Lancet*. 2021;397(10278):971-984. doi:10.1016/S0140-6736(21)00213-0 Epub 2021 Mar 2. PMID: 33667417.
61. Wadden TA, Bailey TS, Billings LK, et al. Effect of subcutaneous semaglutide vs placebo as an adjunct to intensive behavioral therapy on body weight in adults with overweight or obesity: the STEP 3 randomized clinical trial. *Jama*. 2021;325(14):1403-1413. doi:10.1001/jama.2021.1831
62. Rubino D, Abrahamsson N, Davies M, et al. Effect of continued weekly subcutaneous semaglutide vs placebo on weight loss maintenance in adults with overweight or obesity: the STEP 4 randomized clinical trial. *Jama*. 2021;325(14):1414-1425. doi:10.1001/jama.2021.3224 PMID: 33755728; PMCID: PMC7988425.
63. Garvey WT, Batterham RL, Bhatta M, et al. Two-year effects of semaglutide in adults with overweight or obesity: the STEP 5 trial. *Nat Med*. 2022;28(10):2083-2091. doi:10.1038/s41591-022-02026-4
64. Blundell J, Finlayson G, Axelsen M, et al. Effects of once weekly semaglutide on appetite, energy intake, control of eating, food preference and body weight in subjects with obesity. *Diabetes Obes Metab*. 2017;19(9):1242-1251. doi:10.1111/dom.12932 Epub 2017 May 5. PMID: 28266779; PMCID: PMC5573908.
65. Smits MM, Van Raalte DH. Safety of semaglutide. *Front Endocrinol (Lausanne)*. 2021;12:645563. doi:10.3389/fendo.2021.645563
66. Wilding JPH, Batterham RL, Calanna S, et al. Once weekly semaglutide in adults with overweight or obesity. *N Engl J Med*. 2021;384(11):989-1002. doi:10.1056/NEJMoa2032183
67. Di Francesco V, Sacco T, Zamboni M, et al. Weight loss and quality of life improvement in obese subjects treated with sibutramine: a double-blind randomized multicenter study. *Ann Nutr Metab*. 2007;51(1):75-81. doi:10.1159/000100824
68. Wadden TA, Berkowitz RI, Womble LG, et al. Randomized trial of lifestyle modification and pharmacotherapy for obesity. *N Engl J Med*. 2005;353(20):2111-2120. doi:10.1056/NEJMoa050156
69. Caterson ID, Finer N, Coutinho W, et al. Maintained intentional weight loss reduces cardiovascular outcomes: results from the Sibutramine Cardiovascular OUTcomes (SCOUT) trial. *Diabetes Obes Metab*. 2012;14(6):523-530. doi:10.1111/j.1463-1326.2011.01554.x
70. Rucker D, Padwal R, Li SK, Curioni C, Lau DCW. Long term pharmacotherapy for obesity and overweight: updated meta-analysis. *BMJ*. 2007;335(7631):1194-1199. doi:10.1136/bmj.39385.413113.25
71. James WPT, Caterson ID, Coutinho W, et al. Effect of sibutramine on cardiovascular outcomes in overweight and obese subjects. *N Engl J Med*. 2010;363(10):905-917. doi:10.1056/NEJMoa1003114
72. Dedov II, Melnichenko GA, Troshina EA, Mazurina NV, Galieva MO. Body weight reduction associated with the sibutramine treatment: overall results of the PRIMAVERA primary health care trial. *Obes Facts*. 2018;11(4):335-343. doi:10.1159/000488880
73. Torgerson JS, Hauptman J, Boldrin MN, Sjöström L. XENical in the prevention of diabetes in obese subjects (XENDOS) study: a randomized study of orlistat as an adjunct to lifestyle changes for the prevention of type 2 diabetes in obese patients. *Diabetes Care*. 2004;27(1):155-161. doi:10.2337/diacare.27.1.155
74. Curran MP, Scott LJ. Orlistat: a review of its use in the management of patients with obesity. *Drugs*. 2004;64(24):2845-2864. doi:10.2165/00003495-200464240-00010
75. Kelley DE, Kuller LH, McKolanis TM, Harper P, Mancino J, Kalhan S. Effects of moderate weight loss and orlistat on insulin resistance, regional adiposity, and fatty acids in type 2 diabetes. *Diabetes Care*. 2004;27(1):33-40. doi:10.2337/diacare.27.1.33

76. Derosa G, Cicero AFG, D'Angelo A, Fogari E, Maffioli P. Effects of 1-year orlistat treatment compared to placebo on insulin resistance parameters in patients with type 2 diabetes: orlistat on insulin resistance. *J Clin Pharm Ther*. 2012;37(2):187-195. doi:10.1111/j.1365-2710.2011.01280.x
77. Gorgojo-Martínez JJ, Basagoiti-Carreño B, Sanz-Velasco A, Serrano-Moreno C, Almodóvar-Ruiz F. Effectiveness, and tolerability of orlistat and liraglutide in patients with obesity in a real-world setting: the XENSOR Study. *Int J Clin Pract*. 2019;73(11):e13399. doi:10.1111/ijcp.13399
78. Balcázar M, Cañizares S, Caicedo A, León Fierro A, Zambrano K. Protocolo de diagnóstico y manejo multidisciplinario de pacientes adultos con sobrepeso y obesidad en la consulta ambulatoria. *Bitácora académica USFQ*, 2021;9:1. Available from: https://revistas.usfq.edu.ec/index.php/bitacora/issue/view/182/134
79. Benziger CP, Bernabé-Ortiz A, Gilman RH, et al. Metabolic abnormalities are common among South American Hispanics subjects with normal weight or excess body weight: the CRONICAS cohort study. *PLoS ONE*. 2015;10(11):e0138968. doi:10.1371/journal.pone.0138968 PMID: 26599322; PMCID: PMC4658165.
80. Catenacci VA, Hill JO, Wyatt HR. The obesity epidemic. *Clin Chest Med*. 2009;30(3):415-444, vii. doi:10.1016/j.ccm.2009.05.001 PMID: 19700042.
81. Lauby-Secretan B, Scoccianti C, Loomis D, et al. Body fatness and cancer—viewpoint of the IARC Working Group. *N Engl J Med*. 2016;375(8):794-798. doi:10.1056/NEJMsr1606602 PMID: 27557308; PMCID: PMC6754861.
82. Li Z, Maglione M, Tu W, et al. Meta-analysis: pharmacologic treatment of obesity. *Ann Intern Med*. 2005;142(7):532-546. doi:10.7326/0003-4819-142-7-200504050-00012 PMID: 15809465.
83. Erlandson M, Ivey LC, Seikel K. Update on office-based strategies for the management of obesity. *Am Fam Physician*. 2016;94(5):361-368. PMID: 27583422.
84. Brauer P, Gorber SC, Shaw E, et al. Recommendations for prevention of weight gain and use of behavioural and pharmacologic interventions to manage overweight and obesity in adults in primary care. *CMAJ*. 2015;187(3):184-195. doi:10.1503/cmaj.140887 Epub 2015 Jan 26. PMID: 25623643; PMCID: PMC4330141.
85. Bersoux S, Byun TH, Chaliki SS, Poole KG. Pharmacotherapy for obesity: what you need to know. *Cleve Clin J Med*. 2017;84(12):951-958. doi:10.3949/ccjm.84a.16094 PMID: 29244650.
86. Alarcón-Sotelo A, Gómez-Romero P, De Regules-Silva S, et al. Up to date in the long-term pharmacological treatment of obesity. A therapeutic option? *Med Int Mex*. 2018;34(6):946-958.
87. Ferreira-Hermosillo A, Salame-Khouri L, Cuenca-Abruch D. Tratamiento farmacológico de la obesidad [Pharmacological treatment of obesity]. *Rev Med Inst Mex Seguro Soc*. 2018;56(4):395-409. Spanish. PMID: 30521744.
88. Alvarez V. Tratamiento farmacológico de la obesidad. *Rev médica Clín Las Condes*. 2012;23(2):173-179. doi:10.1016/s0716-8640(12)70295-x
89. Tassinari D, Giovanelli A, Asteria C. Obesity: medical and surgical treatment. In: Luzi L, ed. *Thyroid, Obesity and Metabolism*. Springer; 2021. Italy:131-175. doi:10.1007/978-3-030-80267-7
90. Tsai AG, Bessesen DH. Obesity. *Ann Intern Med*. 2019;170(5):ITC33-ITC48. doi:10.7326/AITC201903050
91. Ross R, Neeland IJ, Yamashita S, et al. Waist circumference as a vital sign in clinical practice: a consensus statement from the IAS and ICCR Working Group on Visceral Obesity. *Nat Rev Endocrinol*. 2020;16(3):177-189. doi:10.1038/s41574-019-0310-7
92. Batsis JA, Zagaria AB. Addressing obesity in aging patients. *Med Clin North am*. 2018;102(1):65-85. doi:10.1016/j.mcna.2017.08.007 Epub 2017 Oct 21. PMID: 29156188; PMCID: PMC5724972.
93. Aschner P, Buendía R, Brajkovich I, et al. Determination of the cutoff point for waist circumference that establishes the presence of abdominal obesity in Latin American men and women. *Diabetes Res Clin Pract*. 2011;93(2):243-247. doi:10.1016/j.diabres.2011.05.002 Epub 2011 May 31. PMID: 21632141.
94. Medina-Lezama J, Pastorius CA, Zea-Diaz H, et al. Optimal definitions for abdominal obesity and the metabolic syndrome in Andean Hispanics: the PREVENCION study. *Diabetes Care*. 2010;33(6):1385-1388. doi:10.2337/dc09-2353 Epub 2010 Mar 3. PMID: 20200303; PMCID: PMC2875461.
95. Batsis JA, Villareal DT. Sarcopenic obesity in older adults: aetiology, epidemiology, and treatment strategies. *Nat Rev Endocrinol*. 2018;14(9):513-537. doi:10.1038/s41574-018-0062-9 PMID: 30065268; PMCID: PMC6241236.
96. Wang M, Tan Y, Shi Y, Wang X, Liao Z, Wei P. Diabetes and sarcopenic obesity: pathogenesis, diagnosis, and treatments. *Front Endocrinol (Lausanne)*. 2020;11:568. doi:10.3389/fendo.2020.00568 PMID: 32982969; PMCID: PMC7477770.
97. Romero-Corral A, Somers VK, Sierra-Johnson J. Accuracy of body mass index in diagnosing obesity in the adult general population. *Int J Obes (Lond)*. 2008;32(6):959-966. doi:10.1038/ijo.2008.11
98. Bray GA, Kim KK, JPH W, World Obesity Federation. Obesity: a chronic relapsing progressive disease process. A position statement of the World Obesity Federation. *Obes Rev*. 2017;18(7):715-723. doi:10.1111/obr.12551 Epub 2017 May 10. PMID: 28489290.
99. Suissa K, Schneeweiss S, Kim DW, Patorno E. Prescribing trends and clinical characteristics of patients starting antiobesity drugs in the United States. *Diabetes Obes Metab*. 2021;23(7):1542-1551. doi:10.1111/dom.14367 Epub 2021 Mar 25. PMID: 33651454.
100. Hendricks EJ, Rothman RB, Greenway FL. How physician obesity specialists use drugs to treat obesity. *Obesity (Silver Spring)*. 2009;17(9):1730-1735. doi:10.1038/oby.2009.69 Epub 2009 Mar 19. PMID: 19300434.
101. Kadeli DK, Sczepaniak JP, Kumar K, Youssef C, Mahdavi A, Owens M. The effect of preoperative weight loss before gastric bypass: a systematic review. *J Obes*. 2012;2012:867540. doi:10.1155/2012/867540 Epub 2012 Jun 7. PMID: 22720139; PMCID: PMC3376766.
102. Middleton KM, Patidar SM, Perri MG. The impact of extended care on the long-term maintenance of weight loss: a systematic review and meta-analysis. *Obes Rev*. 2012;13(6):509-517. doi:10.1111/j.1467-789X.2011.00972.x Epub 2011 Dec 29. PMID: 22212682.
103. Hall KD, Kahan S. Maintenance of lost weight, and long-term management of obesity. *Med Clin North am*. 2018;102(1):183-197. doi:10.1016/j.mcna.2017.08.012 PMID: 29156185; PMCID: PMC5764193.
104. Thomas JG, Bond DS, Phelan S, Hill JO, Wing RR. Weight-loss maintenance for 10 years in the National Weight Control Registry. *Am J Prev Med*. 2014;46(1):17-23. doi:10.1016/j.amepre.2013.08.019 PMID: 24355667.
105. Redmond IP, Shukla AP, Aronne LJ. Use of weight loss medications in patients after bariatric surgery. *Curr Obes Rep*. 2021;10(2):81-89. doi:10.1007/s13679-021-00425-1 Epub 2021 Jan 25. PMID: 33492629.
106. Edgerton C, Mehta M, Mou D, Dey T, Khaodhiar L, Tavakkoli A. Patterns of weight loss medication utilization and outcomes following bariatric surgery. *J Gastrointest Surg*. 2021;25(2):369-377. doi:10.1007/s11605-020-04880-4 Epub 2021 Jan 8. PMID: 33420652.
107. Velapati SR, Shah M, Kuchkuntla AR, et al. Weight regain after bariatric surgery: prevalence, etiology, and treatment. *Curr Nutr Rep*. 2018;7(4):329-334. doi:10.1007/s13668-018-0243-0 PMID: 30168043.
108. Gazda CL, Clark JD, Lingvay I, Almandoz JP. Pharmacotherapies for post-bariatric weight regain: real-world comparative outcomes. *Obesity (Silver Spring)*. 2021;29(5):829-836. doi:10.1002/oby.23146 Epub 2021 Apr 4. Erratum in: *Obesity (Silver Spring)*. 2021 Sep;29(9):1567. PMID: 33818009.

109. Wharton S, Kamran E, Muqeem M, Khan A, Christensen RAG. The effectiveness and safety of pharmaceuticals to manage excess weight post-bariatric surgery: a systematic literature review. *J Drug Assess*. 2019;8(1):184-191. doi:10.1080/21556660.2019.1678478 PMID: 33110683; PMCID: PMC7567517.
110. Stanford FC. Controversial issues: a practical guide to the use of weight loss medications after bariatric surgery for weight regain or inadequate weight loss. *Surg Obes Relat Dis*. 2019;15(1):128-132. doi:10.1016/j.soard.2018.10.020 Epub 2018 Oct 30. PMID: 30527889; PMCID: PMC6441616.
111. Gutt S, Schraier S, González Bagnes MF, Yu M, González CD, Di Girolamo G. Long-term pharmacotherapy of obesity in patients that have undergone bariatric surgery: pharmacological prevention and management of body weight regain. *Expert Opin Pharmacother*. 2019;20(8):939-947. doi:10.1080/14656566.2019.1583746
112. Schiavon CA, Bhatt DL, Ikeoka D. Three-year outcomes of bariatric surgery in patients with obesity and hypertension. A randomized clinical trial. *Ann Intern Med*. 2020;173(9):685-693. doi:10.7326/M19-3781
113. Tak YJ, Lee SY. Long-term efficacy and safety of anti-obesity treatment: where do we stand? *Curr Obes Rep*. 2021;10(1):14-30. doi:10.1007/s13679-020-00422-w Epub 2021 Jan 6. PMID: 33410104; PMCID: PMC7787121.
114. Lee PC, Dixon J. Pharmacotherapy for obesity. *Aust Fam Physician*. 2017;46(7):472-477. PMID: 28697290.
115. Bray GA, Heisel WE, Afshin A, et al. The science of obesity management: an Endocrine Society scientific statement. *Endocr Rev*. 2018;39(2):79-132. doi:10.1210/er.2017-00253 PMID: 29518206; PMCID: PMC5888222.
116. Anekwe CV, Knight MG, Seetharaman S, Dutton WP, Chhabria SM, Stanford FC. Pharmacotherapeutic options for weight regain after bariatric surgery. *Curr Treat Options Gastroenterol*. 2021;19(3):524-541. doi:10.1007/s11938-021-00358-7 Epub 2021 Jul 16. PMID: 34511864; PMCID: PMC8425280.
117. Kato K, Matsushita A, Suzuki S, Sai H, Hirabayashi H, Hattori R. Drug-induced cystitis caused by herbal medicine (Bofutsushosan). *Urol Case Rep*. 2021;38:101644. doi:10.1016/j.eucr.2021.101644 PMID: 33850729; PMCID: PMC8024595.
118. Yeung KS, Hernandez M, Mao JJ, Haviland I, Gubili J. Herbal medicine for depression and anxiety: a systematic review with assessment of potential psycho-oncologic relevance. *Phytother Res*. 2018;32(5):865-891. doi:10.1002/ptr.6033 Epub 2018 Feb 21. PMID: 29464801; PMCID: PMC5938102.
119. Farzaei MH, Bayrami Z, Farzaei F, et al. Poisoning by medical plants. *Arch Iran Med*. 2020;23(2):117-127. PMID: 32061075.
120. Shaw D, Graeme L, Pierre D, Elizabeth W, Kelvin C. Pharmacovigilance of herbal medicine. *J Ethnopharmacol*. 2012;140(3):513-518. doi:10.1016/j.jep.2012.01.051 Epub 2012 Feb 9. PMID: 22342381.
121. Babos MB, Heinan M, Redmond L, et al. Herb-drug interactions: worlds intersect with the patient at the center. *Medicines (Basel)*. 2021;8(8):44. doi:10.3390/medicines8080044 PMID: 34436223; PMCID: PMC8401017.
122. Batsis JA, Apolzan JW, Bagley PJ, et al. A systematic review of dietary supplements and alternative therapies for weight loss. *Obesity (Silver Spring)*. 2021;29(7):1102-1113. doi:10.1002/oby.23110 PMID: 34159755; PMCID: PMC8231729.
123. Maunder A, Bessell E, Lauche R, Adams J, Sainsbury A, Fuller NR. Effectiveness of herbal medicines for weight loss: a systematic review and meta-analysis of randomized controlled trials. *Diabetes Obes Metab*. 2020;22(6):891-903. doi:10.1111/dom.13973
124. Kidambi S, Batsis JA, Donahoo WT, et al. Dietary supplements, and alternative therapies for obesity: a perspective from The Obesity Society's Clinical Committee. *Obesity (Silver Spring)*. 2021;29(7):1095-1098. doi:10.1002/oby.23189
125. Jairoun AA, Al-Hemyari SS, Shahwan M, Zyoud SH. Adulteration of weight loss supplements by the illegal addition of synthetic pharmaceuticals. *Molecules*. 2021;26(22):6903. doi:10.3390/molecules26226903
126. Wierzejska RE. Dietary supplements—for whom? The current state of knowledge about the health effects of selected supplement use. *Int J Environ Res Public Health*. 2021;18(17):8897. doi:10.3390/ijerph18178897
127. Lai S, Yu C, Dennehy CE, Tsourounis C, Lee KP. Online marketing of *ephedra* weight loss supplements: labeling and marketing compliance with the U.S. Food and Drug Administration ban on ephedra. *J Altern Complement Med*. 2021;27(9):796-802. doi:10.1089/acm.2021.0016
128. Lua PL, Roslim NA, Ahmad A, Mansor M, Aung MMT, Hamzah F. Complementary and alternative therapies for weight loss: a narrative review. *J Evid Based Integr Med*. 2021;26:2515690X211043738. doi:10.1177/2515690X211043738
129. Bray GA, Frühbeck G, Ryan DH, Wilding JPH. Management of obesity. *Lancet*. 2016;387(10031):1947-1956. doi:10.1016/S0140-6736(16)00271-3
130. Verhaegen AA, Van Gaal LF. Drug-induced obesity and its metabolic consequences: a review with a focus on mechanisms and possible therapeutic options. *J Endocrinol Invest*. 2017;40(11):1165-1174. doi:10.1007/s40618-017-0719-6
131. Gafoor R, Booth HP, Gulliford MC. Antidepressant utilisation and incidence of weight gain during 10 years' follow-up: population-based cohort study. *BMJ*. 2018;361:k1951. doi:10.1136/bmj.k1951
132. Arterburn D, Sofer T, Boudreau DM, et al. Long-term weight change after initiating second-generation antidepressants. *J Clin Med*. 2016;5(4):E48. doi:10.3390/jcm5040048

How to cite this article: Cappelletti AM, Valenzuela Montero A, Cercato C, et al. Consensus on pharmacological treatment of obesity in Latin America. *Obesity Reviews*. 2023; e13683. doi:10.1111/obr.13683

APPENDIX A: BASELINE QUESTIONS FOR CONSENSUS ON PHARMACOLOGICAL TREATMENT OF OBESITY IN LATIN AMERICA

Questions

P Patient problem description	I Intervention, exposure, risk factor, test, medication, treatment	C Comparison to another known agent	O Clinical outcome, what it is intended to accomplish, morbidity, mortality, complications
1. In whom is pharmacological weight loss treatment indicated?			
In what type of patient living with obesity	Pharmacological treatment	In contrast to non-pharmacological treatment	Improved outcomes
2. Which are the clinical parameters to consider when prescribing pharmacological treatment for obesity?			
In the patient living with obesity with pharmacological treatment	What clinical and paraclinical data	Are useful in the evolution of the therapeutic response	In follow-up and treatment success
3. What are the time periods (minimum and maximum) for the use of pharmacological therapy?			
In patient living with obesity	Duration of pharmacological treatment	Comparing to non-pharmacological prescriptions	Offer adequate results
4. Under what circumstances should treatment be discontinued?			
Patient living with obesity	With pharmacological treatment (monotherapy or combined therapy)	What adverse reactions may be experienced	That require treatment discontinuation
5. What is considered a therapeutic success of this treatment?			
The patient living with obesity undergoing pharmacological therapy	What measures for his/her comprehensive approach	Should be adopted in contrast to non-pharmacological treatment	When is it considered successful
6. What indications should be considered for the comprehensive approach of obesity?			
In the patient living with obesity	In pharmacological treatment	In contrast to a patient not receiving pharmacological treatment	To optimize the treatment goal
7. What is the maximum age to indicate pharmacological treatment?			
In adult patient living with obesity	Pharmacological treatment	In contrast with non-pharmacological therapy	May be used up to what age
8. What are the pharmacological alternatives that can be prescribed?			
In the adult patient living with obesity	What are the therapeutic options		Applicable to fulfill the goal
9. Which drugs should be prescribed or should not be considered as anti-obesity medications?			
In the patient living with obesity undergoing pharmacological treatment	What are the drugs that should NOT be prescribed	Versus those approved by the regulatory agencies	Contraindications
10. What are the contraindications of anti-obesity drugs?			
The patient living with obesity in pharmacological treatment	What are the drugs that should NOT be prescribed	In contrast with those approved by the regulatory agencies	At all times
11. What is the level of evidence for natural products in terms of prescription, ADR, and treatment success that justify their prescription, either alone or in combination?			
In the patient living with obesity	The use of nutritional adjuvants and/or natural products	Is there any evidence as compared to medications	For the treatment of obesity

P Patient problem description	I Intervention, exposure, risk factor, test, medication, treatment	C Comparison to another known agent	O Clinical outcome, what it is intended to accomplish, morbidity, mortality, complications
12. What treatment regimens are available for each drug?			
The treatment success of the patient living with obesity	Drug prescription, dose	In contrast with conventional treatment	Achieves an adequate weight and improves quality of life
13. Is there any special indication for the management of comorbidities while the patient is receiving pharmacological treatment for obesity?			
The patient with comorbidities	Treatment of these comorbidities	Is there any difference with regards to treatment considerations	To maintain adequate control
14. What is the role of drugs approved for short-term use in the treatment of obesity?			
Patient living with obesity	Treated with pharmacological options	Compared with conventional therapy	Long-term effect of the intervention
15. What is the long-term follow-up once the treatment objective is achieved?			
In the patient living with obesity	Treated with pharmacological options	Versus conventional therapy	Which are the control parameters in the long term
16. Is pharmacological treatment indicated in post-bariatric weight regain?			
In the patient living with obesity relapsing after bariatric surgery	Pharmacological therapy	In contrast to patients that do not relapse	Is indicated to achieve control of the disease