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GUIDELINES

iCARDIO Alliance Global Implementation Guidelines for the Management of Obesity 2025

Focus on Prevention and Treatment of Cardiometabolic Disease

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Abstract

There are a number of guidelines on how to manage obesity, but inconsistencies in healthcare access, varying infrastructure, resource constraints and diverse local practices restrict their global applicability. This underscores the need for universal recommendations that address the unique challenges faced by patients and healthcare providers worldwide. Our Global Guidelines emphasize the incorporation of novel therapies, while integrating standards of care with the most up-to-date evidence to enable clinicians to optimize obesity management. Context-specific recommendations tailored to individual patient needs are highlighted, providing a thorough evaluation of the risks, benefits, and overall value of each therapy, aiming to establish a standard of care that improves patient outcomes and reduces the burden of hospitalization in this susceptible population. These Global Guidelines provide evidence-based recommendations that represent a group consensus considering the many other published guidelines that have reviewed many of the issues discussed here, but they also make new recommendations where new evidence has recently emerged, and – most importantly – also provide recommendations on several issues where resource limitations may put constraints on the care provided to patients living with obesity. Such "economic adjustment" recommendations aim to guide situations when "Resources are somewhat limited" or when "Resources are severely limited". Hence, this document presents a comprehensive update to obesity management guidelines, thereby aiming to provide a unified strategy for the pharmacological, non-pharmacological, and invasive management of this significant global health challenge that is applicable to the needs of healthcare around the globe.

Key words: guidelines; obesity; cardiometabolic disease; CARDIO Alliance.

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Preamble

The International CARDIO Alliance to Improve Disease Outcomes (iCARDIO Alliance: https://icardioalliance.org) aims to gather leading cardiovascular societies around the globe as partner organizations to improve the quality of cardiovascular care, from prevention and diagnosis to treatment and follow-up. The goal of these global implementation guidelines is to achieve global representation in writing panels and to produce concise and practical guidelines applicable to all cardiovascular care worldwide. In addition to clinical practice guidelines developed by other medical associations, the recommendations by iCARDIO Alliance take into account resource availability on at least 3 economic levels (with no economic consideration; resources somewhat limited; resources severely limited). They are written by a team including world-renowned experts with a maximum of 50% of the writing task force representing Europe and North America and 50% or more from the rest of the world. The peer review team is also made up of global experts further enriching these documents and leading to a final phase of public review open to all. Furthermore, we implement a public review process for all our guideline documents. In this way, the viewpoints of many persons with lived experience are embedded within this global implementation guideline process. All guideline documents are published in several journals and open access. Through this innovative approach iCARDIO Alliance hopes to enhance guideline dissemination and implementation on a global scale.

Introduction

Obesity is a chronic, relapsing disease characterized by abnormal or excessive adipose tissue accumulation that impairs, amongst other consequences, physical, metabolic, and psychosocial health. It is defined by the World Health Organization (WHO) as a body mass index (BMI) ≥30 kg/m^2 or 27.5 kg/m^2 for Asian populations.[1] It emerged as an epidemic in the U.S. in the late 1970s,[2] before subsequently sweeping across the rest of the world.[3] Recently, there was a growing debate on the potential limitations of the role of BMI in classifying obesity, as it tends to over- and under-estimate adiposity, but more research is needed to define best pragmatic ways to find people at most risk. In the near-term, BMI will still be a very important – and in most cases – the leading parameter to assess presence of obesity fast and simple. The term 'clinical obesity' refers to the presence of excess adiposity that is associated with functional impairment or increased risk of cardiometabolic, physical, or psychological complications, regardless of BMI.[4,5] Recent data from the Global Burden of Disease Study 2023 estimate that over **1 billion individuals** globally are now living with obesity (504 million adult women, 374 million adult men, and 159 million children and adolescents), reflecting a dramatic rise over the past three decades.[6] This staggering figure underscores the growing public health challenge posed by obesity across age groups and geographic regions. Cawley *et al*.[7] concluded that in the U.S. alone, the obesity-related healthcare expenditure amounted to about $260 billion in 2016, constituting between 5% and 10% of overall healthcare-related spending.[8] The economic impact of overweight and obesity in 2019 is estimated be circa 2.2% of global gross domestic product, on average ranging from 20 USD per capita in Africa to 872 USD per capita in the Americas and from 6 USD in low-income countries to 1,110 USD in high-income countries.[9] This underscores the importance of adequate recognition of approaches for early detection, lifestyle modifications-based management, drug therapies, and surgical modalities quintessential to dealing with the perils of rapidly increasing prevalence of obesity.

The first comprehensive set of obesity-related guidelines was published in 1998 by the National Heart, Lung, and Blood Institute (NHLBI).[7] Since then, a diverse assortment of guidelines, principally from the developed world, has been published in the literature.[10-28] However, heterogeneity in the population pool used for devising these recommendations leading to poor generalizability, varying complexities in healthcare infrastructure across institutions, a perceived lack of knowledge amongst providers and a limited availability of resources especially prevalent in the developing world,[29] have been recognized as considerable impediments in their universal adoption and application for obesity diagnosis and management.

The last few decades have recorded a rapid evolution in obesity management, through a better understanding of the impact of lifestyle-based interventions, advancements in therapeutic options, and minimally invasive bariatric surgery options. The clinical practice guidelines (CPGs) have failed to

keep pace with this changing landscape of obesity management, underscoring the need for a new and up-to-date set of recommendations. In addition, a vast majority of the existing recommendations are derived from CPGs published in other disciplines that mention obesity only very briefly, underlining a paucity of comprehensive consensus statements on obesity management from international committees on obesity and cardio-metabolic health. Finally, the prevalence of obesity is increasing in both high and low-middle income countries,[30] highlighting the urgent need for successful adaptation of recommendations to be more relevant to and implementable in low-income countries as a step towards curtailing the growth in the obesity epidemic.

Interventional randomized controlled trials over the past two years have shown that targeting obesity as an independent risk factor in both people with and without diabetes mitigates the risk of cardiovascular adverse events, including atherosclerotic cardiovascular disease, heart failure hospitalizations, and chronic kidney disease, as well as MASH and obstructive sleep apnea.[31,32]

Hence, this statement aims to establish an up-to-date set of CPGs for diagnosing and treating obesity across a wide spectrum of healthcare settings, including both optimal treatment strategies, as well as alternative strategies in resource-limited settings (in both developed countries and developing countries). These guidelines were drafted in consultation with experts, independent reviewers, and members of the general public.

Methods

These consensus-based clinical practice guidelines for diagnosing and managing obesity were developed per the established methodology for best practices in guideline development. A systematic review of existing literature was conducted to establish a repository of published guideline documents and consensus statements, using the following search strategy: *(obesity OR overweight OR «body mass index» OR BMI) AND (guideline OR «clinical practice guideline» OR «practice guideline» OR «consensus» OR «consensus statement»).* After discussion amongst experts, the most relevant guidelines for each region were selected and their recommendations were compiled. Following this, redundant/similar recommendations were eliminated.

The remaining recommendations were reviewed by the committee, and over several iterations, outdated and non-pertinent recommendations were eliminated. New recommendations were added based on emerging data, that were not available when source guidelines were drafted. Based on the available evidence and consensus among the committee members regarding the risks and benefits of interventions, the recommendations were classified into four tiers: strongly recommended (SR), recommended (R), suggested (Su), and do not do (DND) (**Table 1**). Lastly, wherever relevant, alternative recommendations were added for low resource settings.

We acknowledge that there was uncertainty, whether to use the term “people with obesity” or “patients with obesity”. In this document, we will mostly use “patients with obesity”, as this is more commonly used globally. To make the document more readable and concise, we decided to not reference each recommendation when the evidence is widely known and already repeatedly referenced in other guidelines. When recommendations were made, also more recent published evidence was taken into account, for instance regarding GLP-1RA-based therapies.

Diagnosis

Body mass index (BMI) is the most widely used tool for diagnosing obesity. Due to its simplistic nature, it fails to provide a more granular estimate of total body composition, a key metric for calculating obesity-associated cardiometabolic risk. Moreover, the interracial phenotypic variations in stature and body fat distribution are not accounted for by BMI.[33] Alternative measure of adiposity have been proposed, including waist circumference. A comprehensive account of obesity-related diagnostic modalities is listed in **Table 1**.

Non-judgmental language

Individuals living with obesity experience discriminatory behaviors and scrutiny due to excess body weight, a phenomenon termed ‘weight stigma’.[34] Research has shown that the internalization of weight stigma is associated with significantly worse weight loss outcomes[35] secondary to a lack of confidence, anxiety, depression, and a reduced sense of self-esteem.[36] Healthcare workers should ascertain the extent of the patient’s willingness to discuss weight management, ask open-ended questions, and use non-judgmental language during patient encounters (e.g. replacing phrases such as, ‘obese individuals’ or ‘morbid obesity’ with ‘individuals with obesity’ results in better discussion outcomes).

The 5As framework (ask, assess, advise, agree, and assist) provides the foundation for initiating and conducting motivational interviewing for weight management in individuals living with obesity.[37]

Body mass index and anthropometric measures

Body mass index (BMI), calculated as weight /height^2 (reported in kg/m^2), is a useful first-line screening tool for identifying patients with obesity. The standard BMI cut-offs for overweight and obesity recommended by the World Health Organization (WHO) are 25-29.9 kg/m^2 and ≥30.0 kg/m^2, respectively. Despite its widespread adoption, BMI is limited in its ability to discern lean body mass from body fat, thus providing a poor estimation of the total body fat percentage- an important clinical marker for obesity-related cardiovascular disease (CVD) risk prognosis.[38] BMI fails to adjust for age, sex, and race-based differences in body fat composition, especially in adults. Wang *et al*. demonstrated that Asians recorded

higher total body fat percentages at lower BMI values than their Caucasian counterparts.[39]

Anthropometric measurements namely, higher waist circumference (males: ≥102 cm [40 inches]; females: ≥88 cm [35 inches] with lower cut-offs for Asian men [³90 cm] and women [³80 cm]) and higher waist-to-hip ratio (normal limits: <0.90 for males; <0.85 for females),[40] or higher waist-to-height ratio (≥0.50)[41,42] indicate increased cardiometabolic risk. DEXA and computed tomography (CT) scans provide more comprehensive measures of body fat distribution. Combining BMI with anthropometric measures of central obesity, which have demonstrated superior sensitivity and specificity in CVD risk prognostication, allows for a more robust evaluation of obesity-related complications. To date, however, BMI remains the primary obesity metric used in many countries, and more work is needed to determine if other measures can aid clinical practice and improve outcomes.

BMI evaluation for individuals of Asian descent

For a given level of body fat, age, and sex, individuals of Asian descent generally exhibit a lower BMI (by approximately 2-3 kg/m^2) compared to their White counterparts, likely attributable to variations in body composition and muscularity, mandating the need for using different BMI cut-offs for this cohort for severity and risk estimation.[43]

In 2004, a WHO Expert Consultation panel analyzed metabolic risk data from Asian countries and recommended lowering BMI thresholds for public health interventions in Asian populations. They proposed defining BMI ranges of 23.0-27.5 kg/m² as overweight and BMI ≥27.5 kg/m^2 as obese for this subset.[1] However, it is important to acknowledge that different Asian countries may have established their own BMI cut-offs for the diagnosis of overweight and obesity based on local epidemiological data. Where such country-specific thresholds exist, they should be used in place of the generalized WHO recommendations to ensure contextually appropriate risk stratification and intervention. Using the standard cut-offs in the United States, Asian Americans have low rates of overweight/obesity compared to the Non-Hispanic White (NH-White), African American, and Hispanic ethnic groups, yet they suffer from a disproportionately high burden of type 2 diabetes and associated metabolic abnormalities despite normal body weight profiles.[44]

Bioelectrical impedance analysis (BIA) for body fat estimation

BIA utilizes impedance to electric conduction as a surrogate for estimating total body fat percentage and fat-free mass.[45] The accuracy and precision of this approximation are affected by hydration status, body geometry, and body water distribution.[46] The most accurate methods for estimating total body fat percentage are densitometry-based modalities, namely, underwater plethysmography and DEXA scanning.[47] However, none of these more costly measures are ripe for widespread use.

Lifestyle modifications

Lifestyle-based interventions have until recently constituted the cornerstone of obesity management to improve health. It is an umbrella phrase encompassing a diverse array of non-pharmacological interventions that involve inducing a sustained change in habits pertaining mainly to diet and physical activity for risk factor modification and improved survival outcomes. They are recommended as the first-line treatment modality as a standalone therapy or in conjunction with pharmacological/surgical interventions.[48] Implementing high-frequency counseling (≥16 sessions in 6 months) focusing on nutritional changes, physical activity, and behavioral strategies can help achieve long-term energy deficit goals. Our group's recommendations for lifestyle modification-based interventions targeted at weight loss and maintenance are listed in **Table 2** and **Table 3**.

Dietary interventions

Calorie-restriction through dietary regulation can achieve a net-negative energy balance required for triggering weight loss but may also be associated with increases in hunger. Energy intake reduction of 500-750 Kcal per day can manifest in an initial weight loss of 0.5-1.0 kg (1.0-2.2 lbs) per week, or 2-3 kg (4.4-6.6 lbs) a month, not accounting for interpersonal variability.[49] Weight loss does not continue indefinitely despite continuous calorie restriction.

The Mediterranean Diet (MD) inspired by traditional eating habits in Mediterranean countries, emphasizes plant-based foods (fruits, vegetables, legumes, whole grains, nuts, and extra virgin olive oil), moderate intake of fish and dairy, and limited consumption of red meat. It is deemed as most effective at not only inducing weight loss,[50] but at maintaining 5-10% weight loss over prolonged periods, with or without physical activity.[51] Poulimeneas and colleagues recruited participants from the MedWeight study and adherence to MD was assessed among them. The study reported that the participants adherent to the MD were two-times more likely to maintain weight loss of 5-10% than their non-adherent counterparts.[51]

The dietary approaches to stop hypertension **(*DASH***) diet has demonstrated efficacy in inducing and maintaining weight loss as well, and is recommended as one of the first-line interventions for individuals with obesity suffering from hypertension. A meta-analysis underscored an additional -1.4 kg weight loss among the cohort consuming the DASH diet over other low-energy diets.[52]

Intermittent Fasting (IF) diets entail alternating between 12-20 hours long periods of fasting and unrestricted eating. The 16:8 method (fasting 16 hours a day followed by an 8-hour eating window) and fasting for 24 hours twice a week (the 5:2 method) are some of the most commonly adopted approaches for dieters practicing IF. In a meta-analysis conducted by Almabruk and colleagues,[53] the IF fasting group

experienced weight reductions ranging from 2 to 6 kg, and BMI decreased between 1 and 4 kg/m^2 over 1.5 and six months, respectively.

High-protein (HP) diets include consuming ≥1.6 g of protein per kg of body weight or obtaining ≥25% of calories from protein.[54]

Low-fat (LF) diets prescribe deriving less than 30% of daily calorie requirement from fats. Evidence on using LF-diets as a standalone therapy for weight loss is sparse. Astrup *et al*.[55] reported a mean weight loss of 3.2 kg (95% CI: 1.9-4.5 kg) in the LF-diet group compared to the control in their meta-analysis of 16 RCTs. On the contrary, the DIRECT trial[56] comparing low-carbohydrate, Mediterranean, and LF diets reported higher weight loss in the low-carbohydrate and Mediterranean groups (-4.7 kg and -4.4 kg, respectively). The PREDIMED trial[57] demonstrated better cardiovascular outcomes in the group on the Mediterranean diet supplemented with extra-virgin olive oil or nuts compared to the LF-diet group.

Low-carb diets (LCDs) and calorie-restricted diets (CRDs): Low-carb diets are further classified into very low, low, moderate, or high-carb diets based on per diem carbohydrate load (very low; 20-50 g/day, low; ≤130 g/day). Ketogenic diets are a type of very low-carb diet. They work by depleting the body's glycogen stores to use fat stores as the primary source for energy production through the generation of ketones. Although effective at inducing weight loss and improving glycemic control in diabetics, the LCDs have been linked to greater odds of cardiovascular morbidity and mortality.[58] Thus, warranting caution and careful patient selection when identifying candidates for LCD-based weight loss intervention. Calorie-restricted diets are an effective recourse for achieving 5-10% weight loss. Combined with increased proportions of protein and dairy intake, they may reduce body fat percentage, total cholesterol (TC), and low-density lipoprotein-cholesterol (LDL-c) levels. However, statins remain the mainstay of pharmacologic therapy for lowering LDL-c in patients with obesity due to their robust evidence in reducing atherosclerotic cardiovascular risk. Intermittent fasting has gained traction as a potent means for achieving calorie restriction. In a randomized controlled trial (RCT), Sun and colleagues uncovered the synergistic weight loss effect achieved by combining LCDs with CRDs. Compared to those in the calorie-restricted (CR) only group, participants in the LCD plus CR group lost 55% more body mass index (BMI).[59]

Wycherly *et al*.[60] performed a meta-analysis of 95 studies, wherein they established modest decreases in body weight (-0.79 kg; 95% CI, -1.50 to -0.08) and body fat mass (-0.87 kg; 95% CI, -1.26 to -0.48 kg) in the group consuming HP diets in comparison to the low-fat, low-carbohydrate, energy-restricted standard protein diet group.

In conclusion, this consensus statement recognizes that there is no universally superior dietary strategy for the management of obesity and that the average effects are modest. Rather, the optimal dietary approach is one that is tailored to the individual's preferences, cultural context, and lifestyle, and that supports long-term adherence. Notably, the limited long-term success of most diets is less often due to the specific macronutrient composition or structure of the diet itself, and more commonly attributable to challenges with sustained adherence over time.

Physical activity

Physical activity constitutes the second most important lifestyle intervention directed at inducing a weight loss of 5-10%. While, diet remains the primary driver of weight loss, as most individuals do not achieve substantial or sustained weight reduction through exercise alone, physical activity, in particular resistance training, has been shown to build and preserve lean muscle mass despite energy restriction.[61] Fat-free mass preservation has been shown to maintain a higher resting metabolic rate, improve strength and aerobic capacity, especially in older adults with obesity, and safeguard against sarcopenia.[62] The duration of exercise training and weight loss through visceral fat reduction exhibit a dose-response relationship.[63] Although there exists a great deal of heterogeneity in the literature, with regard to the duration of physical activity per week, the general consensus is that for patients with obesity, ≥150 minutes of exercise training a week is associated with weight loss induction[11] and maintenance, in addition to heralding an improvement in cardiovascular outcomes in the long run, although a reduction in cardiovascular mortality has not been shown. According to the American College of Sports Medicine, 150-225 min and 225-400 min of aerobic exercise per week were associated with 2 to 3 kg and 5 to 7.5 kg of weight loss, respectively, although long-term maintenance beyond 3 years remains a challenge.[64]

Willis *et al*.[65] concluded that aerobic training demonstrated a more significant decrease in total body fat content than resistance training. They also demonstrated that combining resistance training with aerobic exercise did not lead to incremental weight loss.

It may be helpful to consider the Metabolic Equivalent of Task (MET) values of common aerobic activities. For example, brisk walking typically ranges from 3.5 to 4.5 METs, cycling at a moderate pace yields 4 to 7 METs, and jogging or running ranges from 7 to 12 METs, depending on speed and incline. These estimates can help clinicians recommend activity levels that align with the patient's capacity and goals.

Physical activity is a strong predictor of long-term weight loss maintenance, independent of diet and caloric restriction. The National Weight Control Registry (NWCR) recommends 60 minutes of moderate-intensity exercise per day for long-term weight loss maintenance.[66]

In an RCT conducted by Jakicic and colleagues,[67] 275 min/week of physical activity when combined with restricted caloric intake was found to be associated with the highest odds of long-term weight loss maintenance of 5-10%.

Pharmacological treatment

Recommendations pertaining to optimal pharmacotherapeutic interventions for obesity management are listed in **Table 4** as well as in **Figure 1** and **Figure 2**.

Glucagon-like peptide (GLP)-1 receptor and dual agonists

In the last decade, incretin-based medications with high efficiency of weight loss have emerged. These include liraglutide, semaglutide, and tirzepatide. They act on GLP-1 receptors in the pancreatic β-cells, increasing intracellular cyclic AMP (cAMP) and triggering endogenous insulin release and appetite suppression. Tirzepatide is a dual GLP-1RA / Glucose-dependent insulinotropic polypeptide (GIP) agonist that works by modulating insulin release and increasing adiponectin levels.

Liraglutide

Liraglutide, a GLP-1 receptor agonist (RA) is approved for chronic weight management in adults with a BMI of 30 kg/m^2 or at least 27 kg/m^2, if at least one weight-related comorbid condition is present. Dosing begins at 0.6 mg daily for one week and is then titrated up weekly at 0.6 mg intervals until the recommended dose of 3 mg daily is reached. LEADER,[68] Satiety and Clinical Adiposity-Liraglutide Evidence in individuals with and without diabetes (SCALE),[69] SCALE Maintenance,[70] SCALE Diabetes,[71] and SCALE Sleep Apnea[72] were among the most prominent RCTs evaluating liraglutide's safety and efficacy profiles. A meta-analysis[73] revealed that liraglutide produced a mean 5.2 kg placebo-subtracted weight loss at 1 year, with 63% of participants achieving a ≥5% weight loss, inclusive of 34% of participants who lost ≥10% of initial weight. Weight loss of 7% was maintained for 3 years in the SCALE Prediabetes study.[74]

The recent expiration of liraglutide's patent protection in multiple countries opens the door for generic versions, which may become a cost-effective GLP-1 RA option in resource-limited settings. This could enable broader pharmacologic implementation, particularly in LMICs where newer agents like semaglutide and tirzepatide remain cost-prohibitive.

Semaglutide

Semaglutide, another GLP-1RA, works by up-regulating the downstream effects of GLP-1 receptor activation.[75] Once-weekly subcutaneous semaglutide 1.0 mg was approved by the FDA in 2017 and the European Medicines Association in 2018 for the treatment of type 2 diabetes.[76] In 2021, the FDA approved 2.4 mg once weekly semaglutide for treating obesity in adults. Ongoing trials of oral semaglutide may result in another option for the treatment of obesity, but at the time of publishing this guideline, oral semaglutide was not yet approved by any regulatory authorities, and hence it cannot be recommended. Higher dose (7.2 mg) once weekly semaglutide may also become available in the near future, but they are not yet approved for use.

Semaglutide Treatment Effect in People with obesity (STEP) was the first global program to evaluate semaglutide 2.4 mg once weekly for weight management.

STEP 1[77] The STEP 1 trial (Semaglutide Treatment Effect in People with obesity) was the first large-scale, double-blind, randomized controlled study to demonstrate that once-weekly subcutaneous semaglutide 2.4 mg led to significant weight loss in non-diabetic adults with overweight or obesity. Participants receiving semaglutide lost an average of 14.9% of body weight, compared to 2.4% in the placebo group over 68 weeks.

STEP 2[78] compared semaglutide 2.4 mg *vs* 1.0 mg with placebo. The 2.4 mg dose cohort had the highest 9.6% of baseline body weight loss compared to the 1.0 mg group that experienced 7% of baseline body weight loss.

STEP 3[79] showed that including intensive lifestyle therapy with semaglutide did not affect weight loss as the weight loss in the drug plus intensive lifestyle arm was 16%, the same as STEP 1, which did not have an intensive lifestyle component.

STEP 4[80] revealed that discontinuing semaglutide resulted in weight regain, while continuing semaglutide beyond 20 weeks resulted in 16-18% weight loss.

STEP 5[81] was the first long-term study that ran for 104 weeks and corroborated the findings of the previous studies, and showed how increased duration of treatment resulted in maintenance of the 16% weight loss achieved at 1 year. No weight regain was observed when the medication was continued.

STEP 8,[82] a phase 3 trial, compared once-weekly subcutaneous semaglutide (2.4 mg) with once-daily liraglutide (3.0mg) in adults with overweight or obesity without diabetes mellitus. Semaglutide resulted in significantly greater weight loss (-15.8%) compared to liraglutide (-6.4%). Semaglutide also showed higher odds of achieving ≥10%, ≥15%, and ≥20% weight loss. Both treatments had similar rates of gastrointestinal adverse events.

In the **STEP 9**[83] trial, semaglutide 2.4 mg administered once weekly resulted in significant improvements in knee pain, function, and stiffness, as well as weight loss, in individuals with obesity and symptomatic knee osteoarthritis. These findings suggest that semaglutide may have added musculoskeletal benefits, particularly in patients for whom joint pain limits mobility or exercise tolerance.

The recently concluded **STEP UP**[84] trial compared weekly 7.2 mg semaglutide to 2.4 mg semaglutide and placebo in adults with obesity without diabetes mellitus. People treated with semaglutide 7.2 mg achieved a superior weight loss of 20.7% after 72 weeks compared to a reduction of 17.5% with semaglutide 2.4 mg and 2.4% with placebo. In addition, 33.2% of those who received semaglutide 7.2 mg achieved

a weight loss of 25% or more after 72 weeks, compared to 16.7% with semaglutide 2.4 mg and 0.0% with placebo. In the **STEP UP T2D**[85] trial results were largely confirmed in adults with obesity with diabetes mellitus using the same treatment approach. People treated with semaglutide 7.2 mg achieved a superior weight loss of 13.2% after 72 weeks compared to a reduction of 3.9% with placebo (p<0.0001). In patients with semaglutide 2.4 mg, weight loss amounted to 10.4%.

In all these trials, weight losses were generally less in people with type 2 diabetes than without, though recent evidence suggests that weight losses are substantially greater in type 2 diabetes when HbA1c levels are lower.[86] The lower weight losses seen with weight loss therapies at higher HbA1c levels may be partly due to correction of unintentional weight losses due to glucosuria. In SURMOUNT-2, weight losses in in people with type 2 diabetes was similar to that in people without when HbA1c <7.0%.[87]

The **SELECT** study[88] showed weight maintenance for 4 years without any regain, provided the medication was continued. This is also the only RCT in patients with obesity without diabetes that has shown a reduction in major adverse cardiovascular events when an intentional weight loss strategy was used.[88]

Cardiovascular studies with semaglutide

The **SELECT**[88] trial was a large, randomized, placebo-controlled cardiovascular outcomes trial (CVOT) that enrolled 17,604 patients with established atherosclerotic cardiovascular disease (ASCVD) and either obesity or overweight (BMI ≥27 kg/m^2) but without diabetes. Over a mean follow-up of 39.8 months, subcutaneous semaglutide 2.4 mg once weekly significantly reduced the incidence of major adverse cardiovascular events (MACE), a composite of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke, by 20% compared to placebo (HR 0.80; 95% CI, 0.72-0.90; p<0.001). Although hazard ratios for cardiovascular death (HR 0.85; 95% CI, 0.71-1.01) and the composite of cardiovascular death or heart failure events (HR 0.82; 95% CI, 0.71-0.96) favored semaglutide, these endpoints did not meet the required significance thresholds in hierarchical testing.

STEP HFpEF[89] and **STEP HFpEF DM**[90] showed that treatment with semaglutide led to a reduction in heart failure events, NT-proBNP and CRP levels, as well as an improvement in 6-minute walking distance (6MWD) and Kansas City Cardiomyopathy (KCCQ) scores in patients with confirmed HFpEF and the obesity phenotype, over one year, compared to placebo.[91]

STRIDE,[92] a phase 3b randomized placebo-controlled trial, studying the role of semaglutide in peripheral artery disease (PAD) reported that in patients with concomitant diabetes and PAD with intermittent claudication, semaglutide (1.0 mg weekly) significantly improved maximum walking distance at 52 weeks by a mean of 39.9 meters versus placebo, a 13% greater median improvement from baseline (estimated treatment ratio: 1.13; 95% CI: 1.06-1.21; p= 0.0004). It also reduced the composite risk of rescue therapy or all-cause death by 54% (HR 0.46; 95% CI: 0.24-0.85), and improved quality of life.

The **ESSENCE** trial[93] enrolled adults with metabolic dysfunction-associated steatohepatitis (MASH) and moderate to advanced fibrosis (stage 2-3). Treatment with weekly semaglutide 2.4 mg for 72 weeks achieved resolution of steatohepatitis with no worsening of fibrosis in ~62.9% *vs* ~34.3% with placebo, and improvement in fibrosis with no worsening of steatohepatitis in ~36.8% *vs* ~22.4%. Patients also lost an average of ~10.5% of body weight *vs* ~2.0% with placebo, with a safety profile consistent with prior semaglutide obesity trials.

Tirzepatide

In the **SURPASS 1-5 trials**, which evaluated glycemic lowering efficiency as an primary endpoint, different dosages of tirzepatide (5 mg, 10 mg, and 15 mg once weekly) demonstrated significant weight reduction as a secondary endpoint in patients with type 2 diabetes mellitus (T2DM), especially when compared to placebo (**SURPASS 1**),[94] semaglutide 1 mg (**SURPASS 2**),[95] insulin degludec as an add-on to metformin with or without SGLT2 inhibitor (**SURPASS 3**),[96] insulinglargine (**SURPASS 4**),[97] and placebo +insulin glargine (**SURPASS 5**).[98] The overall weight loss ranged from 7.6 kg, 10.7 kg, to 12.9 kg with tirzepatide 5 mg, 10 mg, and 15 mg, respectively.

The **SURMOUNT 1-4 trials** were specifically designed to evaluate the weight-lowering effectiveness and safety of tirzepatide as an adjunct to lifestyle interventions compared to a placebo in patients with obesity, with or without T2DM.

SURMOUNT 1[99] compared tirzepatide 5 mg vs 10 mg *vs* 15 mg vs placebo in patients without diabetes. At the end of 72 weeks, 5 mg,10 mg, and 15 mg groups experienced a -15%, -19.5%, and -20.9% weight reduction *vs* -3.1% in those receiving placebo. In the 3-year extension of SURMOUNT-1 among participants with prediabetes, mean weight reductions at 176 weeks were -12.3% with tirzepatide 5 mg, -18.7% with 10 mg, and -19.7% with 15 mg, compared with -1.3% in the placebo group.[100]

SURMOUNT 2[87] included patients with concomitant obesity and type 2 diabetes mellitus. tirzepatide 10 mg, 15 mg, and placebo were compared for 72 weeks. The mean change in body weight at the end was -12.8%, -14.7%, and -3.2%, respectively.

SURMOUNT 3[101] patients were subjected to an intensive lifestyle intervention, and only those who lost ³5% weight on it were randomized to either tirzepatide (10 or 15 mg) or placebo. Mean weight change at the end of 72 weeks was -18.4% for tirzepatide, while the group treated with the intensive lifestyle intervention and placebo had a weight increase of 2.5%.

SURMOUNT 4[102] started as an open-label trial. Participants experienced a 20.9% weight loss. Then they were randomized. Those who switched to the placebo experienced a 14% weight gain, whereas those who continued with tirzepatide lost an additional 5.5% of their initial weight.

SURMOUNT 5[103] trial demonstrated that maximally tolerated tirzepatide (10 mg or 15 mg once weekly) achieved significantly greater weight loss than maximally tolerated semaglutide (1.7 mg or 2.4 mg) over 72 weeks in adults with obesity or overweight and at least one comorbidity. Specifically, tirzepatide led to a 20.2 % mean reduction in body weight *vs* 13.7% with semaglutide ($p<0.001$), along with a greater mean decline in waist circumference (-18.4 cm *vs* -13.0 cm).

For patients who plateau on GLP-1 receptor agonists, switching to an alternative GLP-1RA based drug could offer additional benefit in terms of weight loss. This statement reflects a consensus opinion based on available comparative trial data and clinical experience. However, it is important to note that no dedicated randomized «switch» study currently exists to formally evaluate this strategy. Until further studies are available, such an approach should be considered cautiously, considering safety, patient preference, and long-term goals. Drug accessibility, safety, and long-term adherence remain additional critical factors in therapy selection.

SURMOUNT-OSA[104] investigated the utility of tirzepatide in patients in two cohorts (Cohort 1 not using CPAP, Cohort 2 using CPAP) with obstructive sleep apnea (OSA). They found that among persons with moderate-to-severe obstructive sleep apnea and obesity, tirzepatide reduced the AHI, body weight, hypoxic burden, high-sensitivity C-reactive protein (hsCRP) concentration, and systolic blood pressure and improved sleep-related patient-reported outcomes.

SYNERGY-NASH[105] revealed that in patients with MASH and moderate or severe fibrosis, treatment with tirzepatide for 52 weeks was more effective than placebo with respect to the resolution of MASH without worsening of fibrosis.

Cardiovascular studies with tirzepatide

In the **SUMMIT** trial,[106] weekly subcutaneous tirzepatide (up to 15mg) was compared with placebo over 104 weeks in adults with obesity and heart failure with preserved ejection fraction (HFpEF; LVEF ≥50%). Tirzepatide reduced the risk of cardiovascular death or worsening heart failure events by 38% compared to placebo (HR 0.62; 95% CI, 0.41-0.95; $p=0.026$), and improved patient-reported symptom burden and quality of life. Mean Kansas City Cardiomyopathy Questionnaire Clinical Summary Scores increased by 19.5 points compared to 12.7 with placebo (mean difference 6.9; 95% CI, 3.3-10.6; $p<0.001$). These findings support tirzepatide's emerging role as a potential disease-modifying therapy for obesity-related cardiovascular comorbidities.

In the **SURPASS-CVOT** trial,[107] in more than 13,000 patients with T2DM, weekly subcutaneous tirzepatide (up to 15 mg) as compared to weekly dulaglutide (1.5 mg) was non-inferior for rate of major adverse cardiovascular events (MACE-3: hazard ratio 0.92, 95.3%CI: 0.83-1.01, $p=0.086$) and was found to nominally lower all-cause mortality by 16% ($p=0.002$). At the time of publication, the trial was not yet published.

Resource-limited settings

Consider using biosimilar liraglutide, which is expected to be less expensive than semaglutide or tirzepatide in resource-limited settings. Hopefully, in a few years, biosimilar semaglutide may become available, as well as multiple small-molecule non-peptide GLP-1RAs currently in development, which may be easier to produce in a more scalable fashion, making them more affordable. Unfortunately, compounded products of GLP-1RAs of unknown origin are being increasingly used as lower-cost alternatives in some countries, despite a lack of data on manufacturing quality control and the absence of randomized controlled trials to properly assess their safety and efficacy.

The authors of this guideline recognize the need to address access to obesity medications in lower- and middle-income countries. However, in many parts of the world, these incretin-related compounded medications are either disallowed or illegal, or are subject to litigation in courts, as they are associated with significant safety and efficacy concerns. We cannot recommend the use of these compounded obesity medications, but recognize the fact that they are a reflection of a serious call to the pharmaceutical industry to address the need to improve access and affordability to larger populations of the currently approved, properly tested obesity drugs.

Cost-effectiveness and access considerations in pharmacologic therapy

When selecting anti-obesity pharmacologic agents, both efficacy and cost-effectiveness must be considered. While GLP-1RAs demonstrate the greatest weight loss benefits, they are also among the most expensive options, with annual costs significantly higher than agents like orlistat or phentermine/topiramate. Economic analyses suggest that for populations with established cardiovascular disease or diabetes, semaglutide may be cost-effective due to associated reduction in adverse events. In contrast, orlistat and naltrexone/bupropion may offer more favorable cost-benefit profiles for primary obesity management in lower-income settings. However, for orlistat and naltrexone/bupropion as well as for phentermine/topiramate no cardiovascular outcome benefit has been documented.

Additionally, cold chain storage, injectable delivery routes,

and limited drug approvals in certain countries further constrain accessibility. Health systems should evaluate all these issues when selecting pharmacological interventions.

SGLT2 inhibitors

SGLT2 inhibitors are not approved to treat obesity *per se*, i.e. they are not drugs for treatment "of obesity". However, they are very effective medicines for patients "with obesity" and cardio-renal-metabolic disease. SGLT2 inhibitors work by blocking the re-uptake of sodium and glucose in the proximal convoluted tubule- a mechanism that is thought to underlie its weight loss effects. Although they cause minimal weight loss and are not considered weight loss agents per se, they are very effective in improving outcomes in chronic conditions that commonly co-exist with obesity, including heart failure and chronic kidney disease. Mazidi and colleagues,[81] in their meta-analysis of 43 RCTs evaluating the efficacy and safety profile of SGLT2 inhibitors in managing diabetes-related comorbidities, reported a weighted mean difference of -1.8 kg (95% CI: -2.1 to -1.6 kg) between the SGLT2 inhibitor group and those receiving placebo. In a meta-analysis of 15 randomized controlled trials, Usman and colleagues[108] demonstrated that SGLT2 inhibitors significantly reduced risks for HF-related hospitalization and cardiovascular mortality in patients with HF, type 2 diabetes, chronic kidney disease, and atherosclerotic cardiovascular disease.

Orlistat

Orlistat works by inhibiting the lipase mediated breakdown of fats, thus decreasing fatty uptake from the gut. One of the earliest investigations of Orlistat-mediated weight loss was conducted by Zavoral,[109] who performed a pooled analysis of data from five RCTs and reported that at the one year mark, patients taking orlistat 120 mg thrice daily, experienced significantly greater weight loss than those on a placebo, with an average reduction of 9.2% compared to 5.8% (p<0.001). Additionally, a higher percentage of orlistat-treated patients achieved weight loss of over 5% and over 10% of their initial body weight, compared to those on placebo (69.6% *vs* 51.9%; p<0.001 and 42.1% *vs* 22.7%; p<0.001, respectively). Since then, several RCTs[110-112] and prospective observational studies have detailed more comprehensive accounts of orlistat's efficacy in managing obesity and preventing the development of as well as treating its co-morbidities namely, dyslipidemias, MASLD and diabetes.

Phentermine / Topiramate

Phentermine, an adrenergic stimulant, induces weight loss by appetite suppression. Although the exact mechanisms underlying Topiramate's role in inducing weight loss have not been elucidated, it is hypothesized to reduce total body fat content.[113] The **EQUIP**-trial[114] showed a significant decrease in body weight (10.9% of baseline weight) in the group receiving Phentermine/Topiramate (15 mg/92 mg) when compared to matched controls receiving placebo (1.6% of baseline weight). Phentermine/ Topiramate is FDA approved for use as a weight loss regimen in the U.S. since 2012. It is also approved in more than 10 European countries; however a Europe-wide general approval of EMA has not been granted. This combination is contraindicated in patients with a with glaucoma, and in hyperthyroidism.

Naltrexone / Bupropion

Naltrexone / Bupropion induce weight loss by increasing signaling from the pro-opiomelanocortin (POMC) neurons in the hypothalamus. Consequently decreasing appetite by blunting the hyperphagia pathways in the mesolimbic system.[115] The recommended dose for obesity treatment is a total of 32 mg naltrexone and 360 mg bupropion. [116] The Contrave Obesity Research program encompasses a series of four RCTs (COR-I,[117] COR-II,[118] COR-DM[119] and COR-BMOD[120]) that form the central body of literature depicting the efficacy of the naltrexone/ bupropion combination drug in obesity management. These phase III trials demonstrated that over approximately 56 weeks, naltrexone 32 mg/bupropion 360 mg plus lifestyle intervention led to mean weight loss of 8.1-8.2% in COR-I and COR-II (*vs* 1.3-1.7% with placebo), 3.7% in COR-DM (*vs* 1.7%), and 9.3% in COR-BMOD with intensive behavioral modification (*vs* 5.1%). A history of hypertension, depression, breastfeeding or active substance abuse precludes the use of naltrexone/ bupropion.[121]

Lisdexamfetamine

A stimulant medication used very rarely for treating obesity in children and adolescents with underlying eating disorders. It is primarily approved for ADHS and binge eating. To avoid adverse effects (e.g., significant weight gain in a small subgroup of patients), close follow-up is needed when this treatment is applied.

The future of anti-obesity drug-based therapy

Several novel dual and triple agonists built on a GLP-1RA backbone are in various stages of clinical trials. In the phase III REDEFINE 1 trial,[122] weekly CagriSema (combination of amylin-based cagrilintide and incretin-based semaglutide) (2.4 mg each) produced a mean weight loss of 20.4 % *vs* 3.0 % with placebo at 68 weeks (difference -17.3 percentage points; p<0.001). In fully adherent participants, weight loss reached 22.7%, with over 40% achieving ≥25% reduction in body weight. Orforglipron, a once-daily oral nonpeptide GLP-1RA, demonstrated a placebo-adjusted weight

reduction of up to 5.9% and HbA1c reduction of up to 1.07% over 40 weeks in the phase 3 ACHIEVE-1 trial.[123] Novel drug therapies acting centrally (setmelanotide; melanocortin 4 [MC4] receptor activator, velneperit; neuropeptide Y antagonist, zonisamide-bupropion; combination drug comprised of sodium and T-type calcium channel blocker as well as norepinephrine-dopamine reuptake inhibitor, and cannabinoid type-1 receptor blockers), and peripherally including amylin mimetics (davalintide), pramlintide-metreleptin (amylin and leptin analogues working by slowing gastric emptying and inducing early satiety), beloranib (methionine aminopeptidase 2 inhibitors), and novel anti-obesity vaccines (ghrelin, somatostatin, adenovirus36) are currently under investigation as emerging adjuncts in obesity pharmacotherapy.[124]

Bariatric surgery

Since its inception, circa 70 years ago,[125] bariatric surgery has become an effective treatment option for patients with obesity, especially in the presence of complications such as diabetes mellitus, metabolic syndrome, and metabolic dysfunction-associated steatotic liver disease (MASLD). The BRAVE trial[126] randomized individuals with Metabolic Dysfunction-Associated Steatohepatitis (MASH) to lifestyle modifications plus best medical care group or a bariatric surgery group. The trial concluded that bariatric-metabolic surgery is more effective than lifestyle interventions and optimized medical therapy in the treatment of MASH.

Roux-en-Y gastric bypass, sleeve gastrectomy, endoscopic intragastric balloon, biliopancreatic diversion, and gastric banding are among the routinely offered options for patients considering undergoing bariatric surgery for achieving weight loss goals.[11] Recommendations pertaining to the use of bariatric surgery as a treatment modality for obesity are listed in **Table 4**.

Roux-en-Y gastric bypass

This is the most widely adopted technique for performing bariatric surgery owing to its superior safety and efficacy profile.[127] Mechanisms are complex - amongst other things it induces weight loss by increasing signaling from the gut to the brain, including hampering ghrelin release, increasing satiety hormones, bile acids and altering the gut microbiota.[128] It should especially be considered in patients with BMI ≥30 kg/m^2 (or higher) with diabetes mellitus, hypertension, hyperlipidemia or other CVD risk factors (**Table 5**).[129]

Sleeve gastrectomy

Sleeve gastrectomy is effective and comparable to slightly worse for weight loss, in comparison to the Roux-en-Y bypass,[130,131] but with a greater risk of developing gastroesophageal reflux disease (GERD) and Barrett's esophagus, and the irreversible nature of the procedure.[130]

Intragastric balloon (IGB) and banding

Abu Dayyeh *et al*.[132] conducted an RCT to demonstrate that; when used in conjunction with lifestyle interventions, adjustable IGB resulted in significant weight loss (15% in the aIGB group *vs* 3% in the control group; $p<0.0001$) which maintained for 6 months following balloon removal. Most other studies suggested weight regain when the balloon is removed.

Gastric banding utilizes laparoscopic approach to modulate gastric filling. The overall weight loss effect is achieved by invoking the early satiety mechanisms. There are a number of well conducted RCTs showing the safety and superior efficacy of gastric banding in comparison to lifestyle changes. The only long-term RCT comparing Roux-en-Y gastric bypass with gastric banding reported significantly superior weight loss outcomes for the former.[132]

Biliopancreatic Diversion with Duodenal Switch (BPD/DS)

The BPD/DS is another effective bariatric surgery procedure, characterized by a sleeve gastrectomy followed by gastroileal and ileoileal anastomoses.[134] In a longitudinal analysis of the weight loss effects of this procedure by Sorribas and colleagues reported 15%, 18% and 18% initial body weight loss at 2, 5 and 10 year intervals.[135] In a meta-analysis estimating the efficacy of bariatric surgery procedures, Buchwald *et al*., reported that the percentage of extra body weight lost (calculated as [preoperative BMI−current BMI)/(preoperative BMI−25] × 100) at 2-years of follow-up was the highest (73%) for the BPD/DS subgroup, followed by the gastric bypass (63%), gastroplasty (56%), and gastric banding (49%) subgroups.[136]

Considerations regarding special populations

Children and young adolescents

A forecasting study from the Global Burden of Disease Study 2021[6] examined the prevalence, trends, and future projections of overweight and obesity in children and adolescents across 180 countries from 1990 to 2021, with projections extending to 2050. The study reported that between 1990 and 2021, the global prevalence of overweight and obesity in youth doubled, while obesity alone tripled. In 2021, an estimated 93.1 million children (5-14 years) and 80.6 million adolescents (15-24 years) were living with obesity. The highest prevalence was noted in North Africa, the Middle East, and parts of Oceania, with the greatest increases observed in Southeast Asia, East

Asia, and Oceania. By 2050, obesity rates are expected to rise further, particularly in South Asia, surpassing historical trends globally. Routine screening for overweight and obesity should begin at age 6 years, using BMI-for-age percentiles based on WHO or CDC growth charts. Earlier screening may be warranted in children with risk factors such as a family history of obesity, rapid weight gain in infancy, or comorbid conditions such as sleep-disordered breathing or insulin resistance.[137] As with adults, effective weight management in children and adolescents requires more than dietary changes alone; it should include physical activity and psychosocial support, with dietary strategies tailored to the child's preferences, comorbidities, food restrictions, and personal context as part of a comprehensive care plan.[138]

School-based interventions such as healthier meal offerings, physical activity programs, and culturally relevant nutrition awareness talks can help foster healthier habits at a young age and prevent obesity, especially in resource-limited settings with limited healthcare access.

Recent evidence supports the use of GLP-1RAs in children and adolescents with obesity. In children aged 6 to <12 years, liraglutide 3.0 mg daily reduced BMI by 7.3% at 52 weeks (*vs* 1.5% with placebo).[139] Among adolescents, semaglutide 2.4 mg weekly achieved a 16.1% BMI reduction at 68 weeks (*vs* 0.6%),[140] and liraglutide 3.0 mg daily reduced BMI by 4.6% at 56 weeks (*vs* a 1.6% increase).[141] These trials support the adjunctive use of GLP-1RAs with lifestyle therapy in pediatric obesity (**Table 6**).

Pregnant females

The detrimental impact of gestational obesity on both maternal and fetal well-being has been well documented in the literature, making adequate weight control both in the antenatal period and during pregnancy of paramount importance. A holistic approach consisting of nutritional support, physical activity guidance, and supervision can optimize obesity management during pregnancy, improving health outcomes for both the fetus and the mother.[138]

The detrimental impact of gestational obesity on both maternal and fetal well-being has been well documented in the literature, making adequate weight control both in the antenatal period and during pregnancy of paramount importance. A holistic approach consisting of nutritional support, physical activity guidance, and supervision can optimize obesity management during pregnancy, improving health outcomes for both the fetus and the mother. Balanced dietary intake in line with gestational calorie requirements remains key. Restrictive or very-low-calorie diets are strongly discouraged.[142-145] Moderate-intensity physical activity, such as brisk walking or swimming, is generally safe and encouraged in the absence of contraindications and has been shown to be associated with better outcomes.[142,146,147] Early screening for gestational diabetes should be offered to all pregnant individuals with obesity, with repeat testing at 24 to 28 weeks where appropriate.[144,148] All obesity medications, including GLP-1 receptor agonists of any kind, orlistat and phentermine/topiramate etc., are contraindicated during pregnancy, and women of reproductive age on such therapies should receive counseling on contraception and medication discontinuation if pregnancy occurs[143,144,148,149] (**Table 7**).

Obesity and psychiatric illnesse

Recommendations pertaining to interventions for obesity in patients with psychiatric illnesses are listed in **Table 8**.

Emerging role of artificial intelligence in obesity

Artificial intelligence and machine learning tools are being increasingly utilized due to their growing utility in detecting early obesity-related comorbidity risks, creating individualized treatment plans, and monitoring.[150,151] The ability of machine-learning (ML) algorithms to analyze large deposits of multimodal data abstracted from electronic health records (EHRs) enables the identification of patients at high risk and can even anticipate treatment response.[150]

This can especially be useful in resource-limited settings where targeted intervention in at-risk patients can help alleviate the high obesity-related comorbidity and mortality burden.

Conclusions

This global consensus document provides an integrated, evidence-based framework for the diagnosis and management of obesity, for implementation across diverse healthcare systems. To ensure relevance across global contexts, the guidelines feature scalable interventions, including lifestyle and behavioral strategies, as well as flexible pathways for the incorporation of pharmacologic and surgical therapies where feasible. Recent therapeutic advances, such as GLP-1 receptor agonists and dual GIP/GLP-1 agents, hold substantial promise, but concerns around affordability, accessibility, and regulatory status represent a major hurdle in global adoption of these therapies.

The writing committee offers feasible alternatives after taking into account the individual level variability in comorbidities, health status, cultural beliefs, healthcare access and adherence barriers, and the social determinants of health.[152] Clinical judgment forms the cornerstone of adapting recommendations to the circumstances of each patient, especially in resource-constrained environments.

Ultimately, these guidelines aim not only to support evidence-based practice but also to advance equity, feasibility, and contextual sensitivity in obesity care across a wide range of health systems. Given the rapidly changing evidence base, we anticipate updating these guidelines within 2 years, with a focused update in between.

Table 1. Grading and recommendation.

No.	Definition	Level of Recommendation
1-01	Evidence or consensus that a specific diagnostic test or treatment is effective, beneficial and valuable.	**Strongly Recommended (SR)**
1-02	Majority of evidence or opinions support the benefits or effectiveness.	**Recommended (R)**
1-03	Usefulness or effectiveness is less clearly supported by evidence or opinion.	**Suggested (Su)**
1-04	Evidence or consensus suggests that it is ineffective and, in some cases, may even be harmful.	**Do not do (DND)**

Table 2. Recommendations for the approach to diagnosing obesity.

No.	Guideline Statement	Level of Recommendation
2-01	Use person-centered, non-judgmental language when working with individuals living with obesity.	**Su**
2-02	Measure BMI at least annually in individuals without a previous diagnosis of obesity.	**SR**
2-03	Use a lower cut-off for BMI (≥27.5 kg/m^2) and waist circumference (≥85 cm for men and ≥74 to 80 cm for women) in evaluating South Asian and Chinese adults for obesity.	**SR**
2-04	Use anthropometric measurements such as waist circumference as an additional tool to estimate and track adiposity.	**SR**
2-05	Use a waist circumference cut-off of ≥94 cm in men and ≥80 cm in women for diagnosing obesity. For the Asian populations, slightly lower cut-offs (≥90 cm men, ≥80 cm women) should be used. For populations in the USA, Canada, Europe, Australia and New Zealand, the cut-offs to use should be increased to ≥102 cm for men and ≥88 cm for women.	**SR**
2-06	Evaluate individuals with obesity for 'clinical obesity' by screening them for obesity-related comorbidities such as hypertension, diabetes, hypercholesterolemia, heart failure, and non-restorative sleep	**SR**
2-07	Screen individuals with overweight and obesity for eating disorders at their index clinical evaluation using questionnaires such as SCOFF, EDE-Q, or QEWP-R.	**R**

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2-08	Use primary care interventions, namely behavioral counseling, health education and awareness, and dietary modification alone or in conjunction with lifestyle and pharmacological therapies, to effectively manage obesity.	**R**
2-09	Use educational training programs for PCPs to address gaps in skills, knowledge, and attitudes necessary to effectively manage people living with obesity.	**R**

SR, strongly recommended; R, recommended; Su, suggested.

Table 3. Recommendations for lifestyle interventions for obesity management.

No.	Guideline Statement	Level of Recommendation
3-01	Use counseling, multicomponent psychological interventions, and comprehensive lifestyle interventions, including calorie restriction, physical activity, and individualized medical nutrition therapy for achieving and maintaining weight loss in adults with overweight and obesity.	**SR**
3-02	Recommend comprehensive lifestyle interventions for individuals with overweight or obesity by **a)** setting personalized weight loss goals, targeting a 5-10% reduction in body weight for most adults, including those living with hypertension, dyslipidemia, or MASLD, 5-7% for those with pre-diabetes, and 5-15% for individuals with diabetes or **b)** adopting evidence-based dietary patterns such as the Mediterranean, DASH, or intermittent energy restriction diets, higher-protein calorie-restricted diets, and specific programs, and **c)** engaging in regular physical activity with an initial goal of achieving 150 minutes per week of aerobic exercise or strength training two to three times weekly, eventually increasing to 300 minutes per week or ≥2,000 kcal/week expenditure for ≥5% weight loss.	**SR**
Resources somewhat or severely limited	*Use implementing strategies such as the WHO's Global School Health Initiative, governmental policy-based interventions (i.e., Mexico's sugar tax), the 'Eat More Color' initiative for promoting fruit and vegetable consumption in the Caribbean, and the Pan-American Health Organization's (PAHO) 'Get Moving' campaign for combating obesity with increased physical activity, for obesity management when resources are limited.*	
3-03	Recommend participation in long-term (>1-year) maintenance programs to increase the likelihood of weight loss maintenance.	**Su**
3-04	The short-term (3-5 months long) use of a low-calorie diet (LCD) followed by stepped food reintroduction is beneficial for long-term weight loss maintenance and glycemic control.	**R**

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3-05	Ensure long-term follow-up after weight loss, including face-to-face consultations or telephone calls, as a family centered approach has a positive impact on maintaining weight loss outcomes of 5%.	**R**
3-06	Use internet-based mobile apps as well as offline diet and nutritional education sessions to allow learning of nutrition knowledge and skills.	**R**
Resources somewhat limited	*Use SMS-based health promotion programs, toll-free services where users can dial-in and seek health promotion guidance, educational radio broadcasts, television programs with instructional videos and promote guideline documents when use of more costly approaches is not possible.*	
Resources severely limited	*When network connectivity and mobile phone coverage is limited, use educational pamphlets, door-to-door obesity awareness and management campaigns, and consider the establishment of community health centers with health agents trained in obesity counselling and treatment.*	
3-07	Adopt interventions that use technology (e.g., wearables) to increase reach to larger numbers of people asynchronously as a potentially viable lower-cost intervention in a community-based setting.	**R**
Resources somewhat or severely limited	*Consider using low-cost wearables (Xiaomi Mi Band, Fitbit Inspire etc.), which are readily available in low-to-middle-income regions, and have built-in step counters, energy expenditure calculations, heart rate, and sleep monitoring, as alternatives.*	

SR, strongly recommended; R, recommended; Su, suggested.

Table 4. Recommendations for pharmacological interventions for weight loss.

No.	Guideline Statement	Level of Recommendation
4-01	Use the GLP-1RA semaglutide, or the dual GLP-1 RA/GIP agonist tirzepatide for the treatment of obesity.	**SR**
Resources somewhat limited	*Consider lower-cost GLP-1RAs (such as liraglutide) and compounded GLP-1RAs as an alternative to semaglutide and tirzepatide. When aiming to do so, clinicians should engage in shared decision making with patients regarding risks and benefits. Local regulations, which may disallow the use of compounded drugs, need to be considered.*	
4-02	Consider orlistat and/or naltrexone/bupropion and/or phentermine / topiramate as alternative obesity medications.	**Su**

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4-03	The time for initiation of weight loss medication should be individualized based on obesity-related complications, patient preference, and cost. Note: Failure of lifestyle modification should not be a criterion for initiation of pharmacological therapy.	**Su**
4-04	Use semaglutide as the obesity medication of choice in patients with obesity who have established ASCVD to decrease cardiovascular events.	**SR**
4-05	In patients with obesity and heart failure with a preserved ejection fraction, use semaglutide or tirzepatide to achieve weight loss and improve heart failure symptoms and quality of life.	**SR**
4-06	In patients with obesity and moderate to severe obstructive sleep apnea, use tirzepatide to achieve weight loss and improve symptoms and quality of life.	**R**
4-07	In patients with obesity and moderate knee osteoarthritis with at least moderate pain, use semaglutide to achieve weight loss and improve symptoms and quality of life.	**R**
4-08	In patients with MASLD / MASH, use semaglutide or tirzepatide to achieve weight loss and improve liver function.	**Su**
4-09	Use SGLT2 inhibitors to improve cardiovascular disease outcomes and renal function in patients with obesity and HF, chronic kidney disease, and/or type-2 diabetes mellitus. Note: While SGLT2 inhibitors may induce modest weight loss in some patients, but they are not approved for the treatment of obesity.	**SR**
4-10	Re-evaluation and dose adjustment of obesity medications should be conducted to prevent therapeutic inertia.	**Su**
4-11	Consider switching to tirzepatide in individuals who experience a weight loss plateau with semaglutide. In individuals who experience a weight loss plateau with tirzepatide also switching to semaglutide may be an option.	**Su**

SR, strongly recommended; R, recommended; Su, suggested.

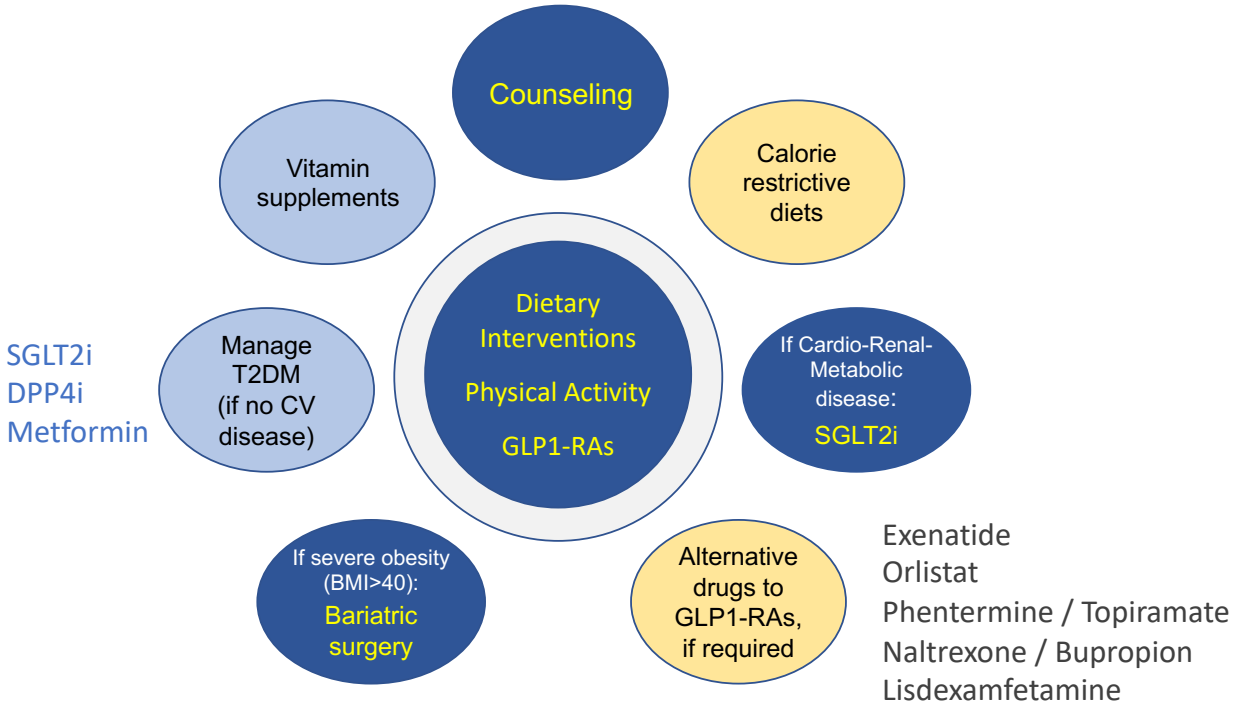

Figure 1. Treatment principles for obesity.

	Semaglutide 2.4 mg weekly	Tirzepatide 5/10/15 mg weekly	Liraglutide 3 mg daily	Naltrexone/Bupropion 32/360 mg	Orlistat 120 mg TID
Metabolic Indications					
General use for obesity	✓	✓	+	+	+
Type 2 Diabetes	✓	✓	✓	-	-
Prediabetes	✓	✓	✓	-	-
MASLD / MASH	+	+	+	-	-
Cardiovascular Indications					
ASCVD (with T2DM)	✓	✓ [1]	✓	-	-
ASCVD (without T2DM)	✓	-	-	-	-
HFpEF	✓	✓	-	-	-
Other Indications					
Obstructive Sleep Apnea	-	✓	-	-	-
Osteoarthritis	✓	-	-	-	-
Patient-Reported Outcomes					
Quality of life	✓	✓	+	-	-
Physical function	✓	✓	+	-	-
Cravings	-	-	-	✓	-
Average weight loss (%) (compared to placebo & rounded)	~12% / 15% [2]	~12% / 16% / 18%	~5-7%	~6-7% (up to 9% with intensive behaviour modification)	~3%

Strongly Recommended (✓)
Recommended (✓)
Suggested (+)
Do Not Do (DND) (Ø)
Insufficient Evidence (-)

[1] based on results of SURPASS-CVOT trial (EASD Congress 2025)
[2] based on results of STEP UP trial (reference 84)

Figure 2. Weight loss medication recommendation chart for obesity in adults.

Table 5. Recommendations for using bariatric surgery for weight loss in obese individuals.

No.	Guideline Statement	Level of Recommendation
5-01	Recommend bariatric surgery for: • BMI ≥30 kg/m^2 in select cases where the patient with severe comorbidities such as, poorly controlled type 2 diabetes mellitus despite maximal medical therapy, severe MASH/MASLD, or a very high cardiovascular risk, expresses a desire for surgery and has failed trial with novel weight loss therapies such as GLP-1RA-based drugs. • BMI ≥35 kg/m^2 and a history of diabetes, MASLD or metabolic-dysfunction associated steatohepatitis (MASH) or high cardiovascular event risk. • BMI ≥40 kg/m^2 regardless of comorbidities.	**SR**
5-02	Lower BMI cut-offs should be used for Asians (of ≥27.5 kg/m^2) and South Asians (BMI is >32.5 kg/m^2 with complications, and BMI is >37.5 kg/m^2 without comorbidity) populations when evaluating them for metabolic surgery eligibility.	**Su**
5-03	Consider bariatric surgery in children and adolescents BMI >120% of the 95th percentile and a major complication, or a BMI >140% of the 95th percentile.	**Su**
5-04	Consider long-term medical, behavioral and nutritional support in addition to screening for psychosocial and behavioral health changes for recipients of metabolic surgery.	**Su**
5-05	Monitor individuals who have undergone metabolic surgery for insufficient weight loss every 6-12 months.	**Su**
5-06	Use bariatric surgery for select patients with obesity and GERD, hiatal hernia, Barrett's esophagitis or concomitant PCOS.	**R**
5-07	Monitor for micro-nutrient deficiencies as part of nutritional evaluation in the post-operative follow-up visits. Consider Vitamin D supplementation of 800-1,000 IU/d in patients undergoing bariatric surgery.	**Su**

SR, strongly recommended; R, recommended; Su, suggested.

Table 6. Recommendations for managing obesity in children and young adolescents.

No.	Guideline Statement	Level of Recommendation
6-01	Do not use very-low-energy diets as a long-term strategy for managing obesity in children.	**R**
6-02	Combine a calorie-restricted diet (CRD) with at least 60 min of moderate-to-vigorous physical activity per day for children and adolescents with obesity.	**R**
6-03	Encourage children to engage in a minimum of 20 minutes (preferably 30) of moderate-to-vigorous physical activity daily with a target of achieving 60 minutes of such activity.	**R**
6-04	Ensure family involvement in dietary changes for children with obesity, particularly for younger children.	**SR**
6-05	Use GLP-1RA (liraglutide) in conjunction with lifestyle interventions for managing obesity in children under 12 years.	**R**
6-06	In children older than 12 years of age, liraglutide and semaglutide may be used for inducing weight loss.	**R**
6-07	In areas with limited availability of GLP-1RAs, orlistat may be used to manage obesity in children older than 12 years. If prescribed, it should be a 6- to 12-month trial, with regular monitoring for effectiveness, adherence, and side effects.	**R**
6-08	Discontinue weight-loss medications if there is no improvement after 12 months.	**R**
6-09	Consider bariatric surgery in children aged 13 years or older, and adolescents with a BMI >120% of the 95th percentile and a major complication, or a BMI >140% of the 95th percentile.	**Su**
6-10	Bariatric surgery should only be considered for adolescents who have achieved or nearly achieved physiological maturity.	**Su**
6-11	Bariatric surgery must be performed in specialist centers with pediatric expertise and include preoperative and postoperative psychological support.	**R**

SR, strongly recommended; R, recommended; Su, suggested.

Table 7. Recommendations for managing obesity in pregnant females.

No.	Guideline Statement	Level of Recommendation
7-01	Encourage pregnant women with obesity to consume a nutritionally balanced diet, avoiding restrictive or very-low-energy diets during pregnancy.	**Su**
7-02	Offer behavioral change interventions including both nutrition and physical activity to pregnant and post-partum women.	**SR**
7-03	Encourage and support pregnant women with obesity who do not have contraindications to exercise during pregnancy to engage in at least 150 minutes per week of moderate-intensity physical activity.	**Su**
7-04	Screen for gestational diabetes in all pregnant women with obesity at the first antenatal visit and again at 24–28 weeks.	**Su**
7-05	Provide individualized dietary advice to pregnant women with obesity, considering cultural and economic factors.	**Su**
7-06	Support weight management by integrating physical activity and dietary interventions into antenatal care.	**R**
7-07	Advise against very-low-energy diets (<800 kcal/day) for pregnant women due to risks to fetal development.	**R**
7-08	Use metformin or liraglutide for managing PCOS in women with obesity.	**SR**
7-09	Obesity medications should not be used during pregnancy.	**DND**
7-10	Women of childbearing potential using obesity medications should use contraception and discontinue medication if pregnancy occurs.	**Su**
7-11	Bariatric surgery is not recommended during pregnancy; women planning pregnancy should avoid conception for at least 12–18 months post-surgery.	**SR**
7-12	Pregnancy after bariatric surgery requires specialist antenatal care, including nutritional monitoring and supplementation.	**R**
7-13	Provide long-term follow-up care for women with prior bariatric surgery, including assessments for micronutrient deficiencies post-pregnancy	**Su**

SR, strongly recommended; R, recommended; Su, suggested; DND, do not do.

Table 8. Recommendations for managing obesity in individuals with depression and eating disorders.

No.	Guideline Statement	Level of Recommendation
8-01	Consider Orlistat, liraglutide, and phentermine/topiramate ER at initiation and low treatment doses or for managing obesity in patients receiving treatment for depression.	**Su**
8-02	Consider structured lifestyle therapy in combination with SSRIs for patients with obesity and concomitant eating disorders.	**Su**
8-03	In patients with binge-eating disorder, consider lisdexamfetamine or topiramate/bupropion containing drugs for treatment.	**Su**

Su, suggested.

Conflict of Interest

See Appendix.

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