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, these guidelines will take into account economic constraints that hamper the full implementation of typical evidence based guideline recommendations in many instances. Hence, the evidence-based recommendations by iCardio Alliance will take into account also resource availability on 3 economic levels: 1) "evidence-based" guideline recommendations with no economic consideration, 2) recommendations for when resources are 'somewhat limited', and 3) recommendations for when resources are 'severely limited'. 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 worldwide experts further enriching these documents and leading to a final phase of public review open to all (see below). The viewpoints of persons with lived experience are embedded within this global implementation guideline process. Through this innovative approach the iCardio Alliance hopes to enhance guideline dissemination and implementation on a global scale.

The public review phase the iCARDIO Global Implementation Guidelines on Obesity Management 2025 right now and will last until Monday 26 May, 2025. All comments must be submitted via the dedicated comment form which can be downloaded from the Global Cardiology website as well as from the iCARDIO Alliance website (Home - iCARDIO Alliance). Please use page, line, and/or table and recommendation numbers for reference in your commentaries as appropriate. Comments received will be taken into consideration, but will not be published. Anonymous comments will be disregarded.

The deadline for receiving comments is 26th of May, 2025.
To submit your comments please use the comment form and send it to: public.review@icardio.org

Draft Document for Public Consultation:

iCARDIO ALLIANCE GLOBAL IMPLEMENTATION GUIDELINES ON OBESITY MANAGEMENT 2025

Focus on Prevention and Treatment of Cardio-Metabolic Disease

ABSTRACT

Despite the availability of several guidelines, 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 standard of care with the most up-to-date evidence to enable clinicians to optimize heart failure (HF) 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 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 a number of issues where resource limitations may put constraints on the care provided to HF patients. Such "economic adjustment" recommendations aim to provide guidance for situations when "Resources are somewhat limited" or when "Resources are severely limited". Hence, this document presents a comprehensive update to HF 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.

INTRODUCTION

Obesity- a chronic disease affecting a multitude of organ systems is classified 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 Western world[3]. Recently, there has been a growing acknowledgment of the limitations of the role of BMI in classifying obesity, as it tends to over- and under-estimate adiposity and fails to adequately encompass its impact on health and well-being. Therefore, the concept of 'clinical obesity' as a chronic or systemic illness characterized by the detrimental interplay between adiposity and normal physiological operations has emerged as a new mode of describing obesity.[4] Current epidemiological surveys estimate the current global prevalence of obesity to be as high as 880 million people, which is predicted to increase to 1 billion people by 2025. This statistic is especially alarming when analyzed in the backdrop of the obesity-associated increase in healthcare costs. Cawley et al.[5] 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.[6] 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.[7-24] 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,[25] 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 medicinal therapeutics, 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 middle to low-income countries[26], 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 diabetics and non-diabetics mitigates the risk of cardiovascular adverse events, including atherosclerotic cardiovascular disease, heart failure hospitalizations, inflammation, and atrial fibrillation with a reduction in high-sensitivity C-reactive protein (CRP) levels,[27,28] underpinning a mechanistic relationship between obesity management and cardiovascular risk prevention.

This epidemiological and interventional evidence has also led to establishing a universal definition of Cardio-Kidney-Metabolic syndrome pathophysiologic staging with obesity as the initial trigger[29] and that the majority of patients with HFpEF and ASCVD have obesity and overweight as a major risk factor driving progression and CV risk.[30] Hence, this consensus statement aims to establish an up-to-date set of CPGs for diagnosing and treating obesity across a wide-spectrum of healthcare settings, considering the differences in attitudes and clinical practices across both the high and middle to low income countries, by integrating recommendations from the previously published literature with the latest evidence-based practices for optimal disease management. This document aims to serve as a comprehensive resource for healthcare providers by outlining the optimal strategies for diagnosing and treating obesity through the latest evidence-based recommendations in lifestyle modifications, drug therapies and surgical options.

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 three tiers: strongly recommend (SR), recommend (R), and suggest (Su). Lastly, wherever relevant, alternative recommendations were added for low resource settings.

Grading and Recommendation

DEFINITION	LEVEL OF RECOMMENDATION
Evidence or consensus that a specific diagnostic test or treatment is effective, beneficial and valuable.	**Strongly Recommend (SR)**
Majority of evidence or opinions support the benefits or effectiveness.	**Recommend (R)**
Usefulness or effectiveness is less clearly supported by evidence or opinion.	**Suggest (Su)**
Evidence or consensus suggests that it is ineffective and, in some cases, may even be harmful.	**Do not do (DND)**

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.[31] Alternative measure of adiposity have been proposed, including waist circumference, A comprehensive account of obesity-related diagnostic modalities is listed in **Table 1**.

(a) Non-judgmental language

Individuals living with obesity experience discriminatory behaviors and scrutiny due to excess body weight, a phenomenon termed 'weight stigma'.[32] Research has shown that the internalization of weight stigma is associated with significantly worse weight loss outcomes[33] secondary to a lack of confidence, anxiety, depression, and a reduced sense of self-esteem.[34] 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.[35]

(b) Body mass index and anthropometric measures

Body mass index (BMI), calculated as weight (kg)/height^2 (m), 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 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.[36] 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.[37]

Anthropometric measurements namely, waist circumference, waist: hip ratio, DEXA, and computed tomography (CT) scans are 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.

(c) 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/m²) 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.[38]

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 23–27.5 kg/m² as overweight and BMI ≥27.5 kg/m² 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.[39]

(d) 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.[40] The accuracy and precision of this approximation are affected by hydration status, body geometry, and body water distribution.[41]

The most accurate methods for estimating total body fat percentage are densitometry-based modalities, namely, underwater plethysmography and DEXA scanning.[42]

Table 1. Recommendations for the approach to diagnosing obesity.

No.	Guideline Statement	Level of Recommendation
1-01	Use person-centered, non-judgmental language when working with individuals living with obesity.	**Su**
1-02	Measure BMI at least annually in individuals without a previous diagnosis of obesity.	**SR**
1-03	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, Southeast Asian, and East Asian adults for obesity.	**SR**
1-04	Use anthropometric measurements such as waist circumference as an additional tool to estimate and track adiposity.	**SR**
1-05	Use a waist circumference cut-off point of ≥94 cm in men and ≥80 cm in women for diagnosing obesity; for the U.S. and the Canadian populations, the cutoff points should be increased to ≥102 cm for men and ≥88 cm for women.	**SR**
1-06	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**
1-07	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**
1-08	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**
1-09	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 recommend; R, Recommend; Su, Suggest; and DND, Do not do.

LIFESTYLE MODIFICATIONS

Lifestyle-based interventions constitute 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.[43] 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**.

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. An 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. 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[44] but at maintaining 5-10% weight loss it over prolonged periods, with or without physical activity.[45] Poulimeneas D and colleagues recruited participants from the MedWeight study and adherence to MD was assessed among them. The study reported that the subjects adherent to the MD were two-times more likely to maintain weight loss of 5-10% than their non-adherent counterparts.[45]

The dietary approaches to stop hypertension **(*DASH***) diet has demonstrated efficacy in inducing and maintain 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 DASH diet over other low-energy diets[46].

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,[47] 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.

Low-fat (LF) diets prescribe deriving less than 30% of daily calorie requirement from fats. While seldom used as a standalone therapy, LF diets are often combined with calorie restriction for optimal effect. The Diabetes Prevention Program (DPP)[48] and Look AHEAD trial[49] provide a robust evidence base for the efficacy of LF-diets in reducing BMI, body fat mass, and comorbidities associated with obesity, including diabetes. Astrup et al.[50] reported a mean weight loss of 3.2 kg (CI: 1.9-4.5 kg) in the LF-diet group compared to the control in their meta-analysis of 16 RCTs.

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.[51] 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. Intermittent fasting has gained traction as a potent means for achieving calorie restriction. In a randomized controlled trial (RCT), Sun J. 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).[52]

Wycherly et al.[53] 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 summary, this consensus statement

In conclusion, this consensus statement recognizes that there is no universally superior dietary strategy for the management of obesity. 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

Exercise constitutes the second most important piece of the lifestyle interventions puzzle directed at inducing a weight loss of 5-10%. The duration of exercise training and weight loss through visceral fat reduction exhibit a dose-response relationship.[54] 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[8] 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. [55]

Willis et al.[56] 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.

LONG-TERM WEIGHT LOSS MAINTENANCE STRATEGIES:

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.[57]

In an RCT conducted by Jakicic and colleagues,[58] 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%.

Table 2. Recommendations for lifestyle interventions for obesity management.

No.	Guideline Statement	Level of Recommendation
2-01	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**
2-02	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 Metabolic dysfunction-associated steatotic liver disease (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 programs like the Diabetes Prevention Program and Look AHEAD for managing obesity in individuals with diabetes, 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.*	**Su**

2-03	Use Vitamin D supplementation of 800-1,000 IU/d in patients with obesity undergoing weight loss.	**Su**
2-04	Recommend participation in long-term (> 1 year) maintenance programs to increase the likelihood of weight loss maintenance.	**Su**
2-05	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**
2-06	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**
2-07	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.*	**Su**
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.*	**Su**
2-08	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.*	**Su**

SR, Strongly recommend; R, Recommend; Su, Suggest; and DND, Do not do.

PHARMACOLOGICAL TREATMENT

Recommendations pertaining to optimal pharmacotherapeutic interventions for obesity management are listed in **Table 3**. Appropriate doses for relevant drugs are listed in the **Supplementary Table 1**.

GLP-1RA–BASED THERAPIES

In the last decade, a new class of highly efficacious medications called nutrient-stimulating hormone (NuSH) therapies has emerged. FDA-approved NuSH-based therapies include liraglutide, semaglutide, and tirzepatide.

a) 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. It binds to GLP-1 receptors in the pancreatic β-cells, increasing intracellular cyclic AMP (cAMP) and triggering endogenous

insulin release and appetite suppression. 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[59], Satiety and Clinical Adiposity- Liraglutide Evidence in individuals with and without diabetes (SCALE)[60]; SCALE Maintenance[61]; SCALE Diabetes[62]; and SCALE Sleep Apnea[63] were among the most prominent RCTs evaluating liraglutide's safety and efficacy profiles. A meta-analysis[64] 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.[65]

Following the expiry of patents for liraglutide in 2024, third-party manufacturers are producing generic variants of standalone and compounded liraglutide-containing drugs. This development is expected to increase accessibility to liraglutide by decreasing the total cost incurred in addition to bolstering availability, especially in the Western hemisphere.

b) Semaglutide

Semaglutide, another GLP-1RA, works by up-regulating the downstream effects of GLP-1 receptor activation.[66] Once-weekly subcutaneous semaglutide 1.0mg was approved by the FDA in 2017 and the European Medicines Association in 2018 for the treatment of type 2 diabetes.[67] In 2021, the FDA approved 2.4 mg once weekly semaglutide for treating obesity in adults. **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**[68] was the first trial to show the weight loss benefit associated with semaglutide. It ran for 68 weeks; results were a significant body weight reduction of 16% compared to placebo. **STEP 2**[69] compared semaglutide 2.4mg vs 1.0mg with placebo. The 2.4mg dose cohort had the highest 9.6% of baseline body weight loss compared to the 1.0mg group that experienced 7% of baseline body weight loss. **STEP 3**[70] 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**[71] revealed that discontinuing semaglutide resulted in weight regain, while continuing semaglutide beyond 20 weeks resulted in 16-18% weight loss. **STEP 5**[72] 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**[73], 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. The recently concluded **STEP UP**[74] trial compared weekly 7.2mg semaglutide to 2.4mg semaglutide and placebo. People treated with semaglutide 7.2mg achieved a superior weight loss of 20.7% after 72 weeks compared to a reduction of 17.5% with semaglutide 2.4mg and 2.4% with placebo. In addition, 33.2% of those who received semaglutide 7.2mg achieved a weight loss of 25% or more after 72 weeks, compared to 16.7% with semaglutide 2.4mg and 0.0% with placebo. The **SELECT** study[75] 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.[75]

Cardiovascular studies with semaglutide:

The SELECT[75] 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, weekly subcutaneous semaglutide 2.4 mg 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 to 0.90; P<0.001). Although hazard ratios for cardiovascular death (HR 0.85; 95% CI: 0.71 to 1.01) and the composite of cardiovascular death or heart failure events (HR 0.82; 95% CI: 0.71 to 0.96) favored semaglutide, these endpoints did not meet the required significance thresholds in hierarchical testing.

STEP-HFpEF[76] & STEP-HFpEF DM[77] 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.[78]

c) Tirzepatide

Tirzepatide is a dual GLP-1 RA/Glucose-dependent insulinotropic polypeptide (GIP) agonist that works by modulating insulin release and increasing adiponectin levels. In the **SURPASS 1-5 trials**, different dosages of tirzepatide (5 mg, 10 mg, and 15 mg) demonstrated significant weight reduction in patients with obesity and type 2 diabetes mellitus (T2DM), especially when compared to placebo (**SURPASS 1**), semaglutide 1 mg (**SURPASS 2**), insulin degludec (**SURPASS 3**), insulin glargine (**SURPASS 4**), and placebo+ insulin glargine (**SURPASS 5**). 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 designed to evaluate the 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: Compared tirzepatide 5mg vs 10mg vs 15mg vs placebo in patients without diabetes. At the end of 72 weeks, 5mg, 10mg, 15mg groups experienced a -15%, -19.5%, -20.9% weight reduction. Placebo had -3.1%. The SURMOUNT 1 extension study in patients with prediabetes showed that weight loss of more than 20% was maintained for 3 years with tirzepatide.
SURMOUNT 2: Patients with diabetes were included. Tirzepatide 10mg, 15mg and placebo were compared for 72 weeks. Mean change in body weights at the end were -12.8%, -14.7%, -3.2%, respectively.
SURMOUNT 3: Patients were subjected to an intensive lifestyle intervention and only those that lose >_5% weight on it were randomized to either tirzepatide (10 or 15mg) and placebo. Mean weight change at the 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: Started as an open-label trial. Participants experienced a 20.9% weight loss. Then they were randomized. Those who switched to placebo experienced a 14% weight gain, whereas those who continued with tirzepatide lost another 5.5% of their initial weight.

SURMOUNT-OSA[79] investigated the utility of tirzepatide in patients 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.

The **SYNERGY-NASH**[80] trial 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 resolution of MASH without worsening of fibrosis.

GLP-1RA based therapies in resource-limited settings:

Compounded products of GLP-1RA based therapies are increasingly being used as cost-effective alternatives in resource-limited settings. However, data on their long-term safety and efficacy are limited. Moreover, a lack of standardization in manufacturing processes leads to differences in safety and efficacy outcomes.

SGLT2 INHIBITORS

SGLT2-inhibitors are not drugs for treatment “of obesity”, but they are 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[72], 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) between the SGLT2i group and those receiving placebo. In a meta-analysis of 15 randomized controlled trials, Usman and colleagues[81] demonstrated 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[82], 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%. 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%; and 42.1% vs. 22.7%, respectively). Since then, several RCTs[83-85] 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, MAFLD and diabetes.

PHENTERMINE / TOPIRAMATE

Phentermine, an adrenergic stimulant, induces weight loss by appetite suppression. The application is oral once daily. 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.[86] The EQUIP-trial[87] showed a significant decrease in body weight within 12 months (10.9% of baseline weight) in the group receiving phentermine / topiramate (15mg/92mg) when compared to matched controls receiving placebo (1.6% of baseline weight). Licensed for use as a weight loss regimen in the U.S since 2012, it initially failed to receive centralized authorization in Europe due to concerns over the cardiovascular effects of protracted phentermine use. Today it is approved in Europe in more than 15 countries through the decentralized approval pathway. This combination is contraindicated in patients with a history of significant cardiovascular disease and pregnant women.

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.[88] The recommended dose for obesity treatment is a total of 32 mg naltrexone and 360 mg bupropion.[89] The Contrave Obesity Research program encompasses a series of four RCTs (COR-I[90], COR-II[91], COR-DM[92] and COR-BMOD[93]) that form the major body of literature depicting the efficacy of naltrexone/ bupropion combination drug in reducing body fat percentage and improving lipid chemistry in the recipients of this therapy. A history of hypertension, depression, breastfeeding or active substance abuse precludes the use of naltrexone/ bupropion.[94]

LISDEXAMFETAMINE

A stimulant medication used very rarely for treating obesity in children and adolescents with underlying eating disorders.

THE FUTURE OF ANTI-OBESITY DRUG-BASED THERAPY

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), dual action GLP-1/glucagon receptor agonists (oxyntomodulin), 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 going to shape the future of anti-obesity pharmacotherapies.[95]

Table 3. Recommendations for pharmacological interventions for weight loss.

No.	Guideline Statement	Level of Recommendation
3-01	Use the GLP-1 RA-based therapies semaglutide or tirzepatide for weight loss in patients with diabetes or in individuals with obesity.	**SR**
3-02	The time for initiation of semaglutide or tirzepatide may be individualized, based on obesity-related complications, patient preference, and cost. Failure of lifestyle modification should not be a criterion for initiation of pharmacological therapy.	**Su**
3-03	Use semaglutide as the weight-loss agent of choice in patients with obesity who have established ASCVD.	**SR**
3-04	In patients with heart failure and preserved ejection fraction, use semaglutide or tirzepatide to achieve weight loss and improvement in heart failure symptoms and quality of life.	**SR**
3-05	When semaglutide or tirzepatide cannot be used, consider using one of the other weight loss agents: liraglutide, phentermine / topiramate, orlistat, naltrexone / bupropion, exenatide or lisdexamfetamine	**Su**
Resources somewhat limited	Consider orlistat and/or naltrexone/bupropion as alternative weight loss agents.	**Su**
Resources somewhat limited	Consider lower-cost GLP-1 RAs (such as liraglutide) and compounded GLP-1 RAs as an alternative to semaglutide and tirzepatide.	**Su**
3-06	Avoid phentermine / topiramate due to questionable cardiovascular risk, especially in patients with established cardiovascular disease.	**DND**
3-07	Use SGLT2 inhibitors to improve cardiovascular disease outcomes in patients with obesity and HF, chronic kidney disease, and/or type-2 diabetes mellitus.	**SR**
3-08	Re-evaluation and dose adjustment of weight loss therapies should be conducted to prevent therapeutic inertia.	**Su**

SR, Strongly recommend; R, Recommend; Su, Suggest; and DND, Do not do.

BARIATRIC SURGERY

Since its inception, 50 years ago, 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[96] 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[8]. Recommendations pertaining to the use of bariatric surgery as a treatment modality for obesity are listed in **Table 4**.

a) Roux-en-Y gastric bypass

This is the most widely adopted technique for performing bariatric surgery owing to its superior safety and efficacy profile.[97] 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.[98]It should especially be considered in patients with BMI ≥ 30 kg/m^2 and diabetes mellitus, hypertension, hyperlipidemia or other CVD risk factors.[99]

b) Sleeve gastrectomy

Sleeve gastrectomy is effective and comparable to slightly worse for weight loss, in comparison to the Roux-en-Y bypass,[100,101] but with a greater risk of developing gastroesophageal reflux disease (GERD) and Barrett's esophagus, and the irreversible nature of the procedure.[100]

c) Intragastric balloon (IGB) and banding

Abu Dayyeh et al.[102] 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.[103]

d) 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.[104] 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.[105] 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.[106]

Table 4. Recommendations for using bariatric surgery for weight loss in obese individuals.

No.	Guideline Statement	Level of Recommendation
4-01	Recommend bariatric surgery for: • BMI ≥30 kg/m^2 in select cases where the patient expresses a desire for surgery and has failed trial with novel weight loss therapies such as GLP-1 RA-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**
4-02	Use lower BMI cut-offs should be used for Asians (of ≥27.5 kg/m^2) and Asian Indians (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**
4-03	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**
4-04	Consider long-term medical, behavioral and nutritional support in addition to screening for psychosocial and behavioral health changes for recipients of metabolic surgery.	**Su**
4-05	Monitor individuals who have undergone metabolic surgery for insufficient weight loss every 6-12 months.	**Su**
4-06	Use bariatric surgery for select patients with obesity and GERD, hiatal hernia, Barrett's esophagitis or concomitant PCOS.	**R**

SR, Strongly recommend; R, Recommend; Su, Suggest; and DND, Do not do.

CONSIDERATIONS REGARDING SPECIAL POPULATIONS

a) Children and young adolescents

A forecasting study from the Global Burden of Disease Study 2021[107] 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 findings revealed 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. 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..[108]

Table 5. Recommendations for managing obesity in children and young adolescents.

No.	Guideline Statement	Level of Recommendation
5-01	Do not use very-low-energy diets as a long-term strategy for managing obesity in children.	**R**

5-02	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**
5-03	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**
5-04	Ensure family involvement in dietary changes for children with obesity, particularly for younger children.	**SR**
5-05	Use GLP-1 RA (liraglutide) in conjunction with lifestyle interventions for managing obesity in children under 12 years.	**R**
5-06	In children older than 12 years of age, liraglutide and semaglutide may be used for inducing weight loss.	**R**
5-07	In areas with limited availability of GLP-1 RAs, 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**
5-08	Discontinue weight-loss medications if there is no improvement after 12 months.	**R**
5-09	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**
5-10	Bariatric surgery should only be considered for adolescents who have achieved or nearly achieved physiological maturity.	**Su**
5-11	Bariatric surgery must be performed in specialist centers with pediatric expertise and include preoperative and postoperative psychological support.	**R**

SR, Strongly recommend; R, Recommend; Su, Suggest; and DND, Do not do.

b) 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.[108]

Table 6. Recommendations for managing obesity in pregnant females.

No.	Guideline Statement	Level of Recommendation
6-01	Encourage pregnant women with obesity to consume a nutritionally balanced diet, avoiding restrictive or very-low-energy diets during pregnancy.	**Su**
6-02	Offer behavioral change interventions including both nutrition and physical activity to pregnant and post-partum women.	**SR**
6-03	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**
6-04	Screen for gestational diabetes in all pregnant women with obesity at the first antenatal visit and again at 24–28 weeks.	**Su**
6-05	Provide individualized dietary advice to pregnant women with obesity, considering cultural and economic factors.	**Su**

6-06	Support weight management by integrating physical activity and dietary interventions into antenatal care.	**R**
6-07	Advise against very-low-energy diets (<800 kcal/day) for pregnant women due to risks to fetal development.	**R**
6-08	Use metformin or liraglutide for managing PCOS in women with obesity.	**SR**
6-09	Weight-loss medications such as orlistat and GLP-1RA-based drugs liraglutide should not be used during pregnancy.	**DND**
6-10	Women of childbearing potential using weight-loss medications should use contraception and discontinue medication if pregnancy occurs.	**Su**
6-11	Bariatric surgery is not recommended during pregnancy; women planning pregnancy should avoid conception for at least 12–18 months post-surgery.	**SR**
6-12	Pregnancy after bariatric surgery requires specialist antenatal care, including nutritional monitoring and supplementation.	**R**
6-13	Provide long-term follow-up care for women with prior bariatric surgery, including assessments for micronutrient deficiencies post-pregnancy	**Su**

SR, Strongly recommend; R, Recommend; Su, Suggest; and DND, Do not do.

c) Obesity and psychiatric illnesses

Table 7. Recommendations for managing obesity in individuals with depression and eating disorders.

No.	Guideline Statement	Level of Recommendation
7-01	Consider Orlistat, liraglutide, and phentermine/ topiramate ER at initiation and low treatment doses or for managing obesity in patients receiving treatment for depression.	**Su**
7-02	Consider structured lifestyle therapy in combination with SSRIs for patients with obesity and concomitant eating disorders .	**Su**
7-03	Consider lisdexamfetamine or topiramate/bupropion containing drugs for treating obesity in patients with binge-eating disorder.	**Su**

SR, Strongly recommend; R, Recommend; Su, Suggest; and DND, Do not do.

CONCLUSION:

This consensus statement by the writing committee provides a comprehensive, consolidated summary of evidence-based recommendations pertinent to diagnosing and managing obesity across a diverse array of healthcare settings. While these guidelines serve as a framework for guiding disease management, it is imperative that clinicians utilize clinical reasoning to analyze implementation in the context of patient-specific factors, namely, race, comorbidities, genetic factors, as well as their symptoms, complications, adherence to recommendations, socio-cultural differences, financial limitations and access to treatment modalities, that might hamper individual-level adoption of the recommendations.

REFERENCES

1. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet* **363**, 157-163 (2004).
2. Rodgers, A., Woodward, A., Swinburn, B. & Dietz, W.H. Prevalence trends tell us what did not precipitate the US obesity epidemic. *The Lancet Public Health* **3**, e162-e163 (2018).
3. Temple, N.J. The Origins of the Obesity Epidemic in the USA-Lessons for Today. *Nutrients* **14**(2022).
4. Rubino, F*., et al.* Definition and diagnostic criteria of clinical obesity. *The Lancet Diabetes & Endocrinology*.
5. Cawley, J*., et al.* Direct medical costs of obesity in the United States and the most populous states. *J Manag Care Spec Pharm* **27**, 354-366 (2021).
6. Tsai, A.G., Williamson, D.F. & Glick, H.A. Direct medical cost of overweight and obesity in the USA: a quantitative systematic review. *Obes Rev* **12**, 50-61 (2011).
7. Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults--The Evidence Report. National Institutes of Health. *Obes Res* **6 Suppl 2**, 51s-209s (1998).
8. Garvey, W.T*., et al.* AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND AMERICAN COLLEGE OF ENDOCRINOLOGY COMPREHENSIVE CLINICAL PRACTICE GUIDELINES FOR MEDICAL CARE OF PATIENTS WITH OBESITY. *Endocr Pract* **22 Suppl 3**, 1-203 (2016).
9. Marx, N*., et al.* 2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes: Developed by the task force on the management of cardiovascular disease in patients with diabetes of the European Society of Cardiology (ESC). *European Heart Journal* **44**, 4043-4140 (2023).
10. Grunvald, E*., et al.* AGA Clinical Practice Guideline on Pharmacological Interventions for Adults With Obesity. *Gastroenterology* **163**, 1198-1225 (2022).
11. Guidelines for medical nutrition treatment of overweight/obesity in China (2021). *Asia Pac J Clin Nutr* **31**, 450-482 (2022).
12. 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes-2024. *Diabetes Care* **47**, S158-s178 (2024).
13. Visseren, F.L.J*., et al.* 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. *Eur Heart J* **42**, 3227-3337 (2021).
14. Arnett, D.K*., et al.* 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation* **140**, e596-e646 (2019).
15. Jain, R*., et al.* Canadian Cardiovascular Harmonized National Guideline Endeavour (C-CHANGE) guideline for the prevention and management of cardiovascular disease in primary care: 2022 update. *Cmaj* **194**, E1460-e1480 (2022).
16. Nelson, M.R*., et al.* 2023 Australian guideline for assessing and managing cardiovascular disease risk. *Med J Aust* **220**, 482-490 (2024).
17. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int* **105**, S117-s314 (2024).
18. Whelton, P.K*., et al.* 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension* **71**, e13-e115 (2018).
19. Mancia, G*., et al.* 2023 ESH Guidelines for the management of arterial hypertension The Task Force for the management of arterial hypertension of the European Society of Hypertension: Endorsed by the International Society of Hypertension (ISH) and the European Renal Association (ERA). *J Hypertens* **41**, 1874-2071 (2023).
20. Cusi, K*., et al.* American Association of Clinical Endocrinology Clinical Practice Guideline for the Diagnosis and Management of Nonalcoholic Fatty Liver Disease in Primary Care and Endocrinology Clinical Settings: Co-Sponsored by the American Association for the Study of Liver Diseases (AASLD). *Endocrine Practice* **28**, 528-562 (2022).
21. Handelsman, Y*., et al.* DCRM Multispecialty Practice Recommendations for the management of diabetes, cardiorenal, and metabolic diseases. *J Diabetes Complications* **36**, 108101 (2022).
22. McDonagh, T.A*., et al.* 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC. *European Heart Journal* **42**, 3599-3726 (2021).

23. Atherton, J.J., *et al.* National Heart Foundation of Australia and Cardiac Society of Australia and New Zealand: Guidelines for the Prevention, Detection, and Management of Heart Failure in Australia 2018. *Heart, Lung and Circulation* **27**, 1123-1208 (2018).
24. Wharton, S., *et al.* Obesity in adults: a clinical practice guideline. *Canadian Medical Association Journal* **192**, E875 (2020).
25. Wang, T., Tan, J.-Y., Liu, X.-L. & Zhao, I. Barriers and enablers to implementing clinical practice guidelines in primary care: an overview of systematic reviews. *BMJ Open* **13**, e062158 (2023).
26. Żukiewicz-Sobczak, W., *et al.* Obesity and poverty paradox in developed countries. *Annals of Agricultural and Environmental Medicine* **21**, 590-594 (2014).
27. Zhang, H.-D., *et al.* Semaglutide for the prevention of atrial fibrillation: A systematic review and meta-analysis. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews* **18**, 103067 (2024).
28. Verma, S., *et al.* Inflammation in Obesity-Related HFpEF: The STEP-HFpEF Program. *J Am Coll Cardiol* **84**, 1646-1662 (2024).
29. Ndumele, C.E., *et al.* A Synopsis of the Evidence for the Science and Clinical Management of Cardiovascular-Kidney-Metabolic (CKM) Syndrome: A Scientific Statement From the American Heart Association. *Circulation* **148**, 1636-1664 (2023).
30. Administration, U.S.F.D. FDA Approves First Treatment to Reduce Risk of Serious Heart Problems Specifically in Adults with Obesity or Overweight. (2024).
31. Caleyachetty, R., *et al.* Ethnicity-specific BMI cutoffs for obesity based on type 2 diabetes risk in England: a population-based cohort study. *Lancet Diabetes Endocrinol* **9**, 419-426 (2021).
32. Rubino, F., *et al.* Joint international consensus statement for ending stigma of obesity. *Nat Med* **26**, 485-497 (2020).
33. O'Brien, K.S., *et al.* The relationship between weight stigma and eating behavior is explained by weight bias internalization and psychological distress. *Appetite* **102**, 70-76 (2016).
34. Vartanian, L.R. & Porter, A.M. Weight stigma and eating behavior: A review of the literature. *Appetite* **102**, 3-14 (2016).
35. Vallis, M., Piccinini-Vallis, H., Sharma, A.M. & Freedhoff, Y. Clinical review: modified 5 As: minimal intervention for obesity counseling in primary care. *Can Fam Physician* **59**, 27-31 (2013).
36. Romero-Corral, A., *et al.* Accuracy of body mass index in diagnosing obesity in the adult general population. *International Journal of Obesity* **32**, 959-966 (2008).
37. Wang, J., *et al.* Asians have lower body mass index (BMI) but higher percent body fat than do whites: comparisons of anthropometric measurements. *The American Journal of Clinical Nutrition* **60**, 23-28 (1994).
38. Deurenberg, P., Deurenberg-Yap, M. & Guricci, S. Asians are different from Caucasians and from each other in their body mass index/body fat per cent relationship. *Obes Rev* **3**, 141-146 (2002).
39. Karter, A.J., *et al.* Elevated rates of diabetes in Pacific Islanders and Asian subgroups: The Diabetes Study of Northern California (DISTANCE). *Diabetes Care* **36**, 574-579 (2013).
40. Samouda, H. & Langlet, J. Body fat assessment in youth with overweight or obesity by an automated bioelectrical impedance analysis device, in comparison with the dual-energy x-ray absorptiometry: a cross sectional study. *BMC Endocrine Disorders* **22**, 195 (2022).
41. Deurenberg, P. Limitations of the bioelectrical impedance method for the assessment of body fat in severe obesity. *The American Journal of Clinical Nutrition* **64**, 449S-452S (1996).
42. Ginde, S.R., *et al.* Air displacement plethysmography: validation in overweight and obese subjects. *Obes Res* **13**, 1232-1237 (2005).
43. Wilson, K. Obesity: Lifestyle Modification and Behavior Interventions. *FP Essent* **492**, 19-24 (2020).
44. Esposito, K., Kastorini, C.M., Panagiotakos, D.B. & Giugliano, D. Mediterranean diet and weight loss: meta-analysis of randomized controlled trials. *Metab Syndr Relat Disord* **9**, 1-12 (2011).
45. Poulimeneas, D., *et al.* Exploring the relationship between the Mediterranean diet and weight loss maintenance: the MedWeight study. *Br J Nutr* **124**, 874-880 (2020).
46. Soltani, S., Shirani, F., Chitsazi, M.J. & Salehi-Abargouei, A. The effect of dietary approaches to stop hypertension (DASH) diet on weight and body composition in adults: a systematic review and meta-analysis of randomized controlled clinical trials. *Obes Rev* **17**, 442-454 (2016).
47. Almabruk, B.A., *et al.* The Role of Intermittent Fasting on Metabolic Syndrome: A Systematic Review and Meta-Analysis. *Cureus* **16**, e71623 (2024).
48. The Diabetes Prevention Program (DPP): description of lifestyle intervention. *Diabetes Care* **25**, 2165-2171 (2002).

49. Salvia, M.G. The Look AHEAD Trial: Translating Lessons Learned Into Clinical Practice and Further Study. *Diabetes Spectr* **30**, 166-170 (2017).
50. Astrup, A., Grunwald, G.K., Melanson, E.L., Saris, W.H. & Hill, J.O. The role of low-fat diets in body weight control: a meta-analysis of ad libitum dietary intervention studies. *Int J Obes Relat Metab Disord* **24**, 1545-1552 (2000).
51. Noto, H., Goto, A., Tsujimoto, T. & Noda, M. Low-carbohydrate diets and all-cause mortality: a systematic review and meta-analysis of observational studies. *PLoS One* **8**, e55030 (2013).
52. Sun, J.*, et al.* The effect of dietary carbohydrate and calorie restriction on weight and metabolic health in overweight/obese individuals: a multi-center randomized controlled trial. *BMC Medicine* **21**, 192 (2023).
53. Wycherley, T.P., Moran, L.J., Clifton, P.M., Noakes, M. & Brinkworth, G.D. Effects of energy-restricted high-protein, low-fat compared with standard-protein, low-fat diets: a meta-analysis of randomized controlled trials. *Am J Clin Nutr* **96**, 1281-1298 (2012).
54. Ohkawara, K., Tanaka, S., Miyachi, M., Ishikawa-Takata, K. & Tabata, I. A dose–response relation between aerobic exercise and visceral fat reduction: systematic review of clinical trials. *International Journal of Obesity* **31**, 1786-1797 (2007).
55. Swift, D.L.*, et al.* The Effects of Exercise and Physical Activity on Weight Loss and Maintenance. *Progress in Cardiovascular Diseases* **61**, 206-213 (2018).
56. Willis, L.H.*, et al.* Effects of aerobic and/or resistance training on body mass and fat mass in overweight or obese adults. *J Appl Physiol (1985)* **113**, 1831-1837 (2012).
57. Catenacci, V.A.*, et al.* Physical activity patterns in the National Weight Control Registry. *Obesity (Silver Spring)* **16**, 153-161 (2008).
58. Jakicic, J.M., Marcus, B.H., Lang, W. & Janney, C. Effect of Exercise on 24-Month Weight Loss Maintenance in Overweight Women. *Archives of Internal Medicine* **168**, 1550-1559 (2008).
59. Marso, S.P.*, et al.* Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes. *New England Journal of Medicine* **375**, 311-322 (2016).
60. Pi-Sunyer, X.*, et al.* A Randomized, Controlled Trial of 3.0 mg of Liraglutide in Weight Management. *New England Journal of Medicine* **373**, 11-22.
61. Wadden, T.A.*, 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)* **37**, 1443-1451 (2013).
62. Davies, M.J.*, et al.* Efficacy of Liraglutide for Weight Loss Among Patients With Type 2 Diabetes: The SCALE Diabetes Randomized Clinical Trial. *Jama* **314**, 687-699 (2015).
63. Blackman, A.*, 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)* **40**, 1310-1319 (2016).
64. Khera, R.*, et al.* Association of Pharmacological Treatments for Obesity With Weight Loss and Adverse Events: A Systematic Review and Meta-analysis. *Jama* **315**, 2424-2434 (2016).
65. le Roux, C.W.*, et al.* 3 years of liraglutide versus placebo for type 2 diabetes risk reduction and weight management in individuals with prediabetes: a randomised, double-blind trial. *Lancet* **389**, 1399-1409 (2017).
66. Hinnen, D. Glucagon-Like Peptide 1 Receptor Agonists for Type 2 Diabetes. *Diabetes Spectr* **30**, 202-210 (2017).
67. Chao, A.M., Tronieri, J.S., Amaro, A. & Wadden, T.A. Semaglutide for the treatment of obesity. *Trends Cardiovasc Med* **33**, 159-166 (2023).
68. Wilding, J.P.H.*, et al.* Once-Weekly Semaglutide in Adults with Overweight or Obesity. *N Engl J Med* **384**, 989-1002 (2021).
69. Davies, M.*, 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* **397**, 971-984 (2021).
70. Wadden, T.A.*, 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* **325**, 1403-1413 (2021).
71. Rubino, D.*, 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* **325**, 1414-1425 (2021).
72. Garvey, W.T.*, et al.* Two-year effects of semaglutide in adults with overweight or obesity: the STEP 5 trial. *Nat Med* **28**, 2083-2091 (2022).

73. Rubino, D.M.*, et al.* Effect of Weekly Subcutaneous Semaglutide vs Daily Liraglutide on Body Weight in Adults With Overweight or Obesity Without Diabetes: The STEP 8 Randomized Clinical Trial. *JAMA* **327**, 138-150 (2022).
74. Nordisk, N. Novo Nordisk A/S: Semaglutide 7.2 mg s.c. achieved 20.7% weight loss in the STEP UP obesity trial, and 18.7% regardless of treatment adherence. Vol. 2025 (Novo Nordisk, 2025).
75. Lincoff, A.M.*, et al.* Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes. *New England Journal of Medicine* **389**, 2221-2232 (2023).
76. Kosiborod, M.N.*, et al.* Semaglutide in Patients with Heart Failure with Preserved Ejection Fraction and Obesity. *New England Journal of Medicine* **389**, 1069-1084 (2023).
77. Kosiborod, M.N.*, et al.* Semaglutide in Patients with Obesity-Related Heart Failure and Type 2 Diabetes. *New England Journal of Medicine* **390**, 1394-1407 (2024).
78. Haykowsky, M.J.*, et al.* Determinants of exercise intolerance in elderly heart failure patients with preserved ejection fraction. *J Am Coll Cardiol* **58**, 265-274 (2011).
79. Malhotra, A.*, et al.* Tirzepatide for the Treatment of Obstructive Sleep Apnea and Obesity. *New England Journal of Medicine* **391**, 1193-1205 (2024).
80. Loomba, R.*, et al.* Tirzepatide for Metabolic Dysfunction-Associated Steatohepatitis with Liver Fibrosis. *N Engl J Med* **391**, 299-310 (2024).
81. Usman, M.S.*, et al.* Effect of SGLT2 inhibitors on heart failure outcomes and cardiovascular death across the cardiometabolic disease spectrum: a systematic review and meta-analysis. *Lancet Diabetes Endocrinol* **12**, 447-461 (2024).
82. Zavoral, J.H. Treatment with orlistat reduces cardiovascular risk in obese patients. *J Hypertens* **16**, 2013-2017 (1998).
83. Sjöström, L.*, et al.* Randomised placebo-controlled trial of orlistat for weight loss and prevention of weight regain in obese patients. European Multicentre Orlistat Study Group. *Lancet* **352**, 167-172 (1998).
84. Zahmatkesh, A., Sohouli, M.H., Shojaie, S. & Rohani, P. The effect of orlistat in the treatment of non-alcoholic fatty liver in adolescents with overweight and obese. *Eur J Pediatr* **183**, 1173-1182 (2024).
85. Alanazi, J.*, et al.* Significance of Orlistat in management of dyslipidemia, systolic blood pressure and body mass index. *Eur Rev Med Pharmacol Sci* **26**, 8326-8332 (2022).
86. Cignarella, A., Busetto, L. & Vettor, R. Pharmacotherapy of obesity: An update. *Pharmacological Research* **169**, 105649 (2021).
87. Allison, D.B.*, et al.* Controlled-release phentermine/topiramate in severely obese adults: a randomized controlled trial (EQUIP). *Obesity (Silver Spring)* **20**, 330-342 (2012).
88. Billes, S.K., Sinnayah, P. & Cowley, M.A. Naltrexone/bupropion for obesity: An investigational combination pharmacotherapy for weight loss. *Pharmacological Research* **84**, 1-11 (2014).
89. Tek, C. Naltrexone HCl/bupropion HCl for chronic weight management in obese adults: patient selection and perspectives. *Patient Prefer Adherence* **10**, 751-759 (2016).
90. Greenway, F.L.*, et al.* 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* **376**, 595-605 (2010).
91. Apovian, C.M.*, et al.* A randomized, phase 3 trial of naltrexone SR/bupropion SR on weight and obesity-related risk factors (COR-II). *Obesity (Silver Spring)* **21**, 935-943 (2013).
92. Hollander, P.*, 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* **36**, 4022-4029 (2013).
93. Wadden, T.A.*, et al.* Weight loss with naltrexone SR/bupropion SR combination therapy as an adjunct to behavior modification: the COR-BMOD trial. *Obesity (Silver Spring)* **19**, 110-120 (2011).
94. Gazewood, J.D.B.K. Phentermine/Topiramate (Qsymia) for Chronic Weight Management. Vol. 2024 (AAFP, 2014).
95. Srivastava, G. & Apovian, C.M. Current pharmacotherapy for obesity. *Nat Rev Endocrinol* **14**, 12-24 (2018).
96. Verrastro, O.*, et al.* Bariatric–metabolic surgery versus lifestyle intervention plus best medical care in non-alcoholic steatohepatitis (BRAVES): a multicentre, open-label, randomised trial. *The Lancet* **401**, 1786-1797 (2023).
97. Adams Ted, D.*, et al.* Weight and Metabolic Outcomes 12 Years after Gastric Bypass. *New England Journal of Medicine* **377**, 1143-1155.
98. le Roux, C.W. & Bloom, S.R. Why Do Patients Lose Weight after Roux-en-Y Gastric Bypass? *The Journal of Clinical Endocrinology & Metabolism* **90**, 591-592 (2005).

99. Abdeen, G. & le Roux, C.W. Mechanism Underlying the Weight Loss and Complications of Roux-en-Y Gastric Bypass. Review. *Obes Surg* **26**, 410-421 (2016).
100. Biter, L.U*., et al.* Long-term effect of sleeve gastrectomy vs Roux-en-Y gastric bypass in people living with severe obesity: a phase III multicentre randomised controlled trial (SleeveBypass). *The Lancet Regional Health – Europe* **38**(2024).
101. Hedberg, S*., et al.* Comparison of Sleeve Gastrectomy vs Roux-en-Y Gastric Bypass: A Randomized Clinical Trial. *JAMA Network Open* **7**, e2353141-e2353141 (2024).
102. Abu Dayyeh, B.K*., et al.* Adjustable intragastric balloon for treatment of obesity: a multicentre, open-label, randomised clinical trial. *Lancet* **398**, 1965-1973 (2021).
103. Angrisani, L., Cutolo, P.P., Formisano, G., Nosso, G. & Vitolo, G. Laparoscopic adjustable gastric banding versus Roux-en-Y gastric bypass: 10-year results of a prospective, randomized trial. *Surg Obes Relat Dis* **9**, 405-413 (2013).
104. Scopinaro, N*., et al.* Biliopancreatic diversion. *World J Surg* **22**, 936-946 (1998).
105. Sorribas, M*., et al.* Experience in biliopancreatic diversion with duodenal switch: Results at 2, 5 and 10 years. *Cirugía Española (English Edition)* **100**, 202-208 (2022).
106. Buchwald, H*., et al.* Bariatric surgery: a systematic review and meta-analysis. *Jama* **292**, 1724-1737 (2004).
107. Ng, M*., et al.* Global, regional, and national prevalence of adult overweight and obesity, 1990–2021, with forecasts to 2050: a forecasting study for the Global Burden of Disease Study 2021. *The Lancet* **405**, 813-838 (2025).
108. NICE. Overweight and obesity management. (2025).

This document has been authored by the "Writing Task Force of the iCARDIO-Alliance Global Implementation Guideline on Obesity Management". The members of this task force will remain confidential until final publication of the document.

The document was already reviewed by the "Peer Reviewer Group for the iCARDIO-Alliance Global Implementation Guideline on Obesity Management". The members of this task force will remain confidential until final publication of the document.

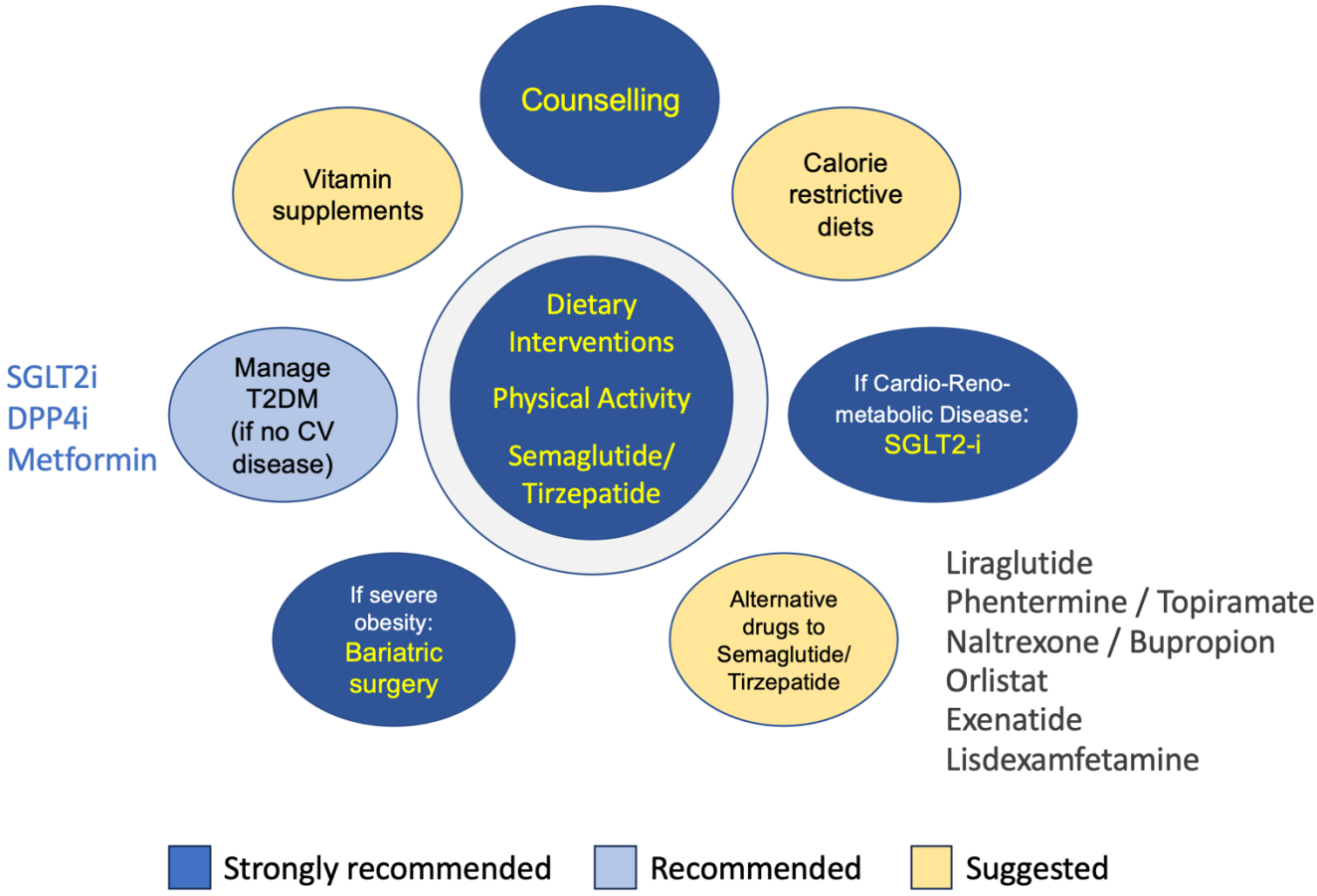
This document is now published as a draft document intended for public consultation & review.
Comments and suggestions for revision can be send together with supporting information to: public.review@icardio.org

The deadline for receiving comments is the 26th of May, 2025.

All comments must be submitted via the dedicated comment form which can be downloaded from the Global Cardiology website as well as from the iCARDIO Alliance website (Home - iCARDIO Alliance). Please use page, line, and/or table and recommendation numbers for reference in your commentaries as appropriate. Comments received will be taken into consideration but will not be published. Anonymous comments will be disregarded.

FIGURE 1

Treatment Principles for Obesity



Supplementary Table

FDA & EMA Approved Dosages for Weight Loss Medications and SGLT2 Inhibitors

Drug Name	Approved Dosages
Weight Loss Medications	
Liraglutide	Initiate at 0.6 mg subcutaneously daily; increase by 0.6 mg weekly to a maintenance dose of 3.0 mg daily (for weight loss)
https://www.novonordisk.ca/content/dam/nncorp/ca/en/products/saxenda-product-monograph-24-april-2024.pdf	
Semaglutide	2.4 mg subcutaneously once weekly (for weight loss)
https://www.novonordisk.ca/content/dam/nncorp/ca/en/products/Wegovy-product-monograph.pdf	
Tirzepatide	5 mg, 10 mg, or 15 mg subcutaneously once weekly (for weight loss and diabetes)
https://pi.lilly.com/ca/mounjaro-ca-pm.pdf	
Orlistat	120 mg orally three times daily with fat containing meals (for weight loss)
https://www.medsafe.govt.nz/profs/datasheet/x/Xenicalcap.pdf	
Phentermine/Topiramate ER	Start at 3.75 mg/23 mg orally once daily; titrate to 7.5 mg/46 mg or up to 15 mg/92 mg once daily (for weight loss)
https://qsymia.com/patient/include/media/pdf/prescribing-information.pdf	
Naltrexone/Bupropion	32 mg naltrexone / 360 mg bupropion orally daily, divided into two doses (for weight loss)
https://bauschhealth.ca/wp-content/uploads/2023/08/Contrave-PM-E-2023-08-21.pdf	
Lisdexamfetamine	30-70 mg orally once daily (FDA-approved for binge eating disorder, not specifically for obesity)
https://www.medicines.org.uk/emc/product/14089/smpc	
SGLT2 inhibitors	
Empagliflozin	10 mg orally once daily; may increase to 25 mg once daily (for type 2 diabetes, heart failure, chronic kidney disease)
https://www.medsafe.govt.nz/profs/datasheet/j/jardiancetab.pdf	
Dapagliflozin	10 mg orally once daily (for type 2 diabetes, heart failure, chronic kidney disease)
https://www.medsafe.govt.nz/profs/datasheet/f/forxigatab.pdf	
Canagliflozin	100 mg orally once daily before the first meal; may increase to 300 mg daily (for type 2 diabetes)
https://www.medsafe.govt.nz/profs/datasheet/i/Invokanatab.pdf	
Ertugliflozin	5 mg orally once daily; may increase to 15 mg daily (for type 2 diabetes)
https://www.merck.com/product/usa/pi_circulars/s/steglatro/steglatro_pi.pdf	