

# Tailored weight-management recommendations for obesity patients with cardiovascular-metabolic diseases

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## INTRODUCTION

Obesity represents a global health issue that profoundly impacts health and associated consequences.<sup>1</sup> The global population inflicted with obesity alone or alongside cardiovascular-metabolic diseases (CVMD) presents an expanding global health challenge. The recent clinical consensus statement emphasizes the epidemiology and etiology of obesity and CVMD, as well as its clinical management.<sup>1</sup> There is hope, as the tools available to manage this epidemic continue to expand, encompassing a variety of options that include lifestyle modifications, pharmacological therapies, and surgical interventions. Furthermore, the advent of cutting-edge technologies (AI, LLMs, wearable devices, etc.) is seen to pave the way for innovative approaches to early intervention.

Obesity is recognized as a chronic relapsing disease that compromises the quality of life and shortens lifespan, with most of the mortality attributable to CVMD. The intricate relationship between obesity and CVMD needs a comprehensive approach to weight management. Obesity remains an under-recognized and poorly addressed problem.<sup>1</sup> This multifaceted challenge requires not only an understanding of the mechanisms underlying the relationship between obesity and CVMD, but also the implementation of interventions tailored to the unique needs. This guideline discusses tailored weight-management recommendations for obesity patients with CVMD, emphasizing lifestyle modifications, pharmacological therapies, surgical interventions, and ongoing research and references for clinical treatment.

## METHODS

This guideline was developed by a multidisciplinary panel (endocrinologists, cardiologists, bariatric surgeons, etc.). We systematically reviewed evidence from 2014 to 2024, prioritizing randomized controlled trials (RCTs) and systematic review and meta-analyses. Cohort studies and real-world evidence were also considered, case reports and case series were excluded. We used body mass index (BMI) as the criterion for differentiating interventions. The formula is: BMI = weight (kg)/(height [m]).<sup>2</sup> The recommendations are summarized in Figure 1.

## Lifestyle modifications

All patients with BMI  $\geq 27.5$  kg/m<sup>2</sup> and obesity should be advised on lifestyle modifications as a basis for weight management. This patient population encompasses dietary adjustments, increased physical activity, psychological intervention, and behavioral therapy to address the multifaceted condition. In the realm of primary CVMD prevention, both Mediterranean and low-fat diets exhibit efficacy.<sup>2</sup> However, when considering secondary prevention, the Mediterranean diet demonstrates superior efficacy in preventing major cardiovascular events compared with the low-fat diet, crude rate per 1,000 person-years: 28.1 (95% confidence interval [CI] 27.9–28.3) in the Mediterranean diet group vs. 37.7 (95% CI: 37.5–37.9) in the low-fat diet group.<sup>2</sup> These interventions are designed not only to facilitate weight loss but also to mitigate associated cardiovascular risk factors. Psychological interventions, such as mindfulness and stress management techniques, when integrated into comprehensive lifestyle modification, merit consideration as they are hopeful of fostering

sustainable weight management. This emphasizes the critical role of behavioral therapies in the overall management of these intricate health conditions. Additionally, the integration of digital health tools and personalized nutrition plans could be considered in the future. The implementation of these strategies needs collaborative and multidisciplinary management to ensure comprehensive and sustained patient care.

## Pharmacological therapies

The past few years have heralded a new era in the treatment of obesity, marked by the introduction of innovative pharmacological therapies, such as glucagon-like peptide-1 receptor agonists (GLP-1 RAs), which offer multiple benefits in addition to weight loss, including cardiovascular improvements. In clinical practice, pharmacological therapies, in conjunction with lifestyle modifications, are employed to facilitate weight reduction in adult individuals with a BMI of  $\geq 30$  or  $\geq 27.5$  kg/m<sup>2</sup>, with at least one obesity-related disease. This population typically includes individuals who have not responded adequately to lifestyle modifications alone or who exhibit obesity with significant cardiovascular risk factors. These patients often require a more intensive therapeutic approach. The U.S. Food and Drug Administration has approved a variety of weight loss drugs, including (1) gastrointestinal medications (orlistat), (2) central nervous system-acting medications (phentermine, phentermine-topiramate, naltrexone-bupropion), and (3) nutrient-stimulated hormone-based medications (semaglutide, tirzepatide, liraglutide). Among the available medications, phentermine-topiramate and GLP-1 RAs have demonstrated superior efficacy in promoting weight loss. Semaglutide currently emerges as the most potential agent within the GLP-1 RA class. The usage of semaglutide presently stands as a pivotal subject of international research. In an RCT comparing weekly subcutaneous semaglutide 2.4 mg with daily subcutaneous liraglutide 3.0 mg in adults with overweight or obesity without diabetes, participants had significantly higher odds of achieving weight loss of 10% or more, 15% or more, and 20% or more with semaglutide compared with liraglutide, resulted in significant weight loss at 68 weeks.<sup>3</sup> Among patients with pre-existing CVMD, integrating overweight or obesity without diabetes, a weekly subcutaneous injection of 2.4 mg of semaglutide demonstrated superiority over placebo in decreasing the occurrence of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke over a mean follow-up period of 39.8 months.<sup>4</sup> Tirzepatide is also a dual glucose-dependent insulinotropic polypeptide and GLP-1 RA. At the same time, the combination therapy of GLP-1 RAs with other drugs is currently under investigation and demonstrates promising effects. Large-scale clinical trials will be essential to evaluate the efficacy and safety of various drugs. Adopting a patient-centered approach is critical to ensure optimal treatment. Integrating pharmacological therapies into a comprehensive management plan, can effectively address the intricate needs and mitigate the progression of cardiovascular complications. The incorporation of lifestyle modifications alongside pharmacological therapies shows significant potential for enhancing therapeutic efficacy. Therefore, it is essential to conduct a thorough validation of this approach through clinical research.

## Surgical interventions

Patients undergoing surgical interventions typically exhibit severe obesity, defined by a BMI  $\geq 35$  or  $\geq 30$  kg/m<sup>2</sup> with significant obesity-related diseases (BMI thresholds should be reduced by 2.5 in Asian population). Surgical interventions for weight management in

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## Indications

### Lifestyle Modifications

1. BMI  $\geq 27.5$  kg/m<sup>2</sup>
2. ALL patients with obesity



### Pharmacological Therapies

1. BMI  $\geq 30$  kg/m<sup>2</sup>
2. BMI  $\geq 27.5$  kg/m<sup>2</sup> with at least one obesity related diseases



### Surgical Interventions

1. BMI  $\geq 35$  kg/m<sup>2</sup>
2. BMI  $\geq 30$  kg/m<sup>2</sup> with significant obesity related diseases

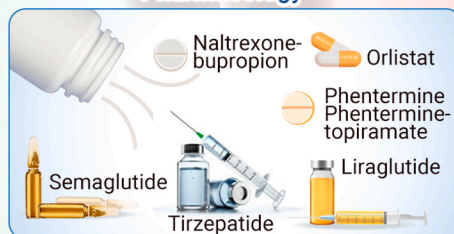


## LPS Management

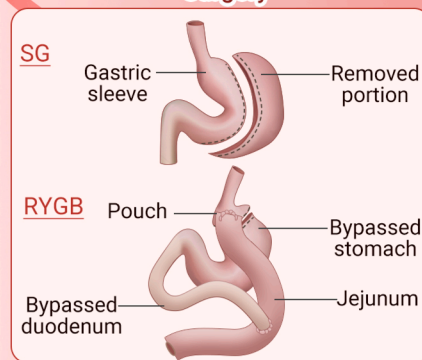
### Lifestyle



### Pharmacology



### Surgery



## Recommendations

**Figure 1. Tailored weight-management recommendations for obesity patients with cardiovascular-metabolic diseases** Further efforts include lifestyle modifications, pharmacological therapies, and surgical interventions. BMI thresholds should be reduced by 2.5 in the Asian population.

Individuals with obesity and CVMD are designated for patients who have not achieved sustained weight loss through conventional approaches, including lifestyle modifications and pharmacological therapies. CVMD represents a major contributor to mortality among patients with severe obesity, and medical interventions inclusive of lifestyle modifications and pharmacological therapies may inadequately mitigate the risk. The decision to pursue surgical intervention is based on a rigorous assessment of the patient's overall health status, the severity of obesity-related complications, and the potential for surgical benefit. Along with being safe, metabolic and bariatric surgery (MBS) is the most elective durable modality for weight loss. MBS can reduce all-cause mortality (pooled hazard ratio [HR] of 0.55; 95% CI: 0.49–0.62) and cardiovascular mortality (HR 0.59, 95% CI: 0.47–0.73) in patients with obesity and reduces the incidence of CVMD.<sup>5</sup> Candidates for MBS must undergo comprehensive evaluations to ensure they are medically fit for the procedure and have realistic expectations for postoperative outcomes. MBS reduces cardiovascular-metabolic risk and mortality, with follow-up care essential for micronutrient deficiencies. The chosen surgical approach, whether laparoscopic Roux-en-Y gastric bypass, laparoscopic sleeve gastrectomy, or one anastomosis gastric bypass, is tailored to the individual patient's needs and situation, taking into account factors such as the class of obesity and comorbid conditions. Minimally invasive surgical modalities present superior therapeutic alternatives for individuals afflicted with obesity as well as cardiovascular-metabolic disorders. By significantly reducing postoperative discomfort, expediting the recovery process, and decreasing the risk of adverse effects, these advanced surgical techniques have greatly enhanced their accessibility and applicability. At present, there is a significant lack of quantitative comparisons to ascertain the most efficacious surgical procedure, needing further investigation to establish definitive conclusions. By offering a durable solution to weight management and metabolic dysregulation, surgical interventions can significantly improve the quality of life and long-term prognosis.

## CONCLUSION

Research in the field of weight management for obesity patients with CVMD must emphasize innovative and multidisciplinary strategies. We should evaluate the long-term efficacy and safety of existing and emerging weight-management strategies, including lifestyle modifications, pharmacological therapies, and surgical interventions, in diverse patient populations. It is crucial to investigate the potential synergistic effects of combining these modalities, as well as to explore personalized medicine in treatment. Large-scale clinical studies should be conducted on multidisciplinary management protocols to obtain quantitative data and ascertain feasibility. Furthermore, future research should focus on the psychosocial and behavioral factors that impact weight-management outcomes. It is essential to integrate behavioral interventions and mental health support into comprehensive treatment. By fostering collaboration across multidisciplinary management, we can drive forward the development of more effective and sustainable weight-management strategies.

## DECLARATION OF INTERESTS

The authors declare no competing interests.

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