

CONCISE CLINICAL GUIDANCE

2025 Concise Clinical Guidance: An ACC Expert Consensus Statement on Medical Weight Management for Optimization of Cardiovascular Health



A Report of the American College of Cardiology Solution Set Oversight Committee

**Writing
Committee
Members**

Olivia Gilbert, MD, MSc, FACC, *Chair*
Martha Gulati, MD, MS, FACC, *Vice Chair*
Ty J. Gluckman, MD, MHA, FACC

Michelle M. Kittleson, MD, PhD, FACC
Rishi Rikhi, MD, MS
Joseph J. Saseen, PHARM D
Beverly G. Tchang, MD

**Solution Set
Oversight
Committee**

Gurusher S. Panjra, MBBS, FACC, *Chair*
Nicole M. Bhav, MD, FACC, *Immediate Past Chair*
Niti R. Aggarwal, MD, FACC*
Katie Bates, ARNP, DNP
Eugene Chung, MD, MPH, FACC
David M. Dudzinski, MD, JD, FACC
John P. Erwin, III, MD, FACC*
Martha Gulati, MD, MS, FACC

Robert Hendel, MD, MACC
Chayakrit Krittanawong, MD, FACC
Dharam J. Kumbhani, MD, SM, FACC*
Barbara Wiggins, PHARM D, FACC
Megan Coylewright, MD, MPH, FACC, Ex Officio

*Former Committee members who also provided oversight for this document

TABLE OF CONTENTS

PREFACE	537	2.3. Etiology and Pathophysiology of Obesity	538
1. INTRODUCTION	537	Figure 1 Causes of Obesity and Its Association With Increased Cardiovascular Risk Factors	539
2. ASSUMPTIONS AND DEFINITIONS	538	2.4. Risks Associated With Obesity	539
2.1. Assumptions and Definitions	538	3. SUMMARY GRAPHIC	540
2.2. Diagnosis	538	Figure 2. Obesity Management for Optimization of Cardiovascular Health	540

This document was approved by the American College of Cardiology Clinical Policy Approval Committee in May 2025.

The American College of Cardiology requests that this document be cited as follows: Gilbert O, Gulati M, Gluckman TJ, Kittleson MM, Rikhi R, Saseen JJ, Tchang BG. 2025 concise clinical guidance: an ACC expert consensus statement on medical weight management for optimization of cardiovascular health: a report of the American College of Cardiology Solution Set Oversight Committee. *J Am Coll Cardiol*. 2025;86(7):536-555.

Copies: This document is available on the website of the American College of Cardiology (www.acc.org). For copies of this document, please contact Elsevier Inc Reprint Department via fax (1-212-633-3820) or e-mail (reprints@elsevier.com).

Permissions: Multiple copies, modification, alteration, enhancement, and/or distribution of this document are not permitted without the express permission of the American College of Cardiology. Requests may be completed online via the Elsevier site (<https://www.elsevier.com/about/policies/copyright/permissions>).

4. DESCRIPTION, RATIONALE, AND IMPLICATIONS FOR MEDICAL THERAPIES	540
4.1. Rationale and Eligibility for NuSH Therapies	540
Figure 3A. Weight Loss Thresholds Associated With Comorbidity Improvements	541
Figure 3B. Achieving Clinically Significant Weight Reduction	542
4.2. Evolution and Current Landscape of Obesity Medications	541
4.3. Pharmacological Options	542
4.4. Implications on Comorbidities	545
4.5. General Treatment Considerations	546
4.5.1. General Principles That Apply to the Medical Management of Obesity	546
4.5.2. The Patient Experience	546
Figure 4. Examples of Ways to Reduce Weight Stigma and More Optimally Deliver Care in Clinic and Hospital Settings	546
Figure 5. General Overview of Patient's Weight Management Journey With NuSH Therapies	547
4.6. Multidisciplinary Care Approaches	547
Figure 6. Multidisciplinary Team Approach for Weight Management	548
4.7. Access Considerations	548
4.8. Conclusions/Future Directions	549
REFERENCES	549
APPENDIX 1	
Author Relationships with Industry and Other Entities (Relevant)	553
APPENDIX 2	
Peer Reviewer Relationships with Industry and Other Entities (Comprehensive)	554
APPENDIX 3	
Abbreviations	555

PREFACE

The American College of Cardiology (ACC) has a long history of developing documents (eg, decision pathways, appropriate use criteria) to provide clinicians with guidance on both clinical and nonclinical topics relevant to cardiovascular care. In most circumstances, these documents have been created to complement clinical practice guidelines and to inform clinicians about areas where evidence is new and evolving or where sufficient

data is more limited. Despite this, numerous gaps persist, highlighting the need for more streamlined and efficient processes to implement best practices in patient care.

Central to the ACC's strategic plan is the generation of actionable knowledge—a concept that places emphasis on making clinical information easier to consume, share, integrate, and update. To this end, the ACC has shifted from developing isolated documents to creating integrated “solution sets.” These are groups of closely related activities, policy, mobile applications, decision-support tools, and other resources necessary to transform care and/or improve heart health. Solution sets address key questions facing care teams and offer practical guidance to be applied at the point of care. They use both established and emerging methods to disseminate information for cardiovascular conditions and their related management. The success of solution sets rests firmly on their ability to have a measurable impact on the delivery of care. Because solution sets reflect current evidence and ongoing gaps in care, the associated tools will be refined over time to match changing evidence and member needs.

Concise Clinical Guidance (CCG) documents are a key component of solution sets. Highly focused and limited in scope, CCGs provide recommendations where none currently exist and/or outline actions required for evidence to be implemented in practice for specific patient populations. Concise Clinical Guidance aim to illustrate clinical decision-making processes using tools (ie, figures, tables, and checklists) and are limited in scope, focusing on patient populations which share certain characteristics, such as conditions, subtypes, or lines of therapy. In some cases, covered topics will be addressed in subsequent expert consensus decision pathways, appropriate use criteria, clinical practice guidelines, and other related ACC clinical policy as the evidence base evolves. In other cases, these will serve as stand-alone policy and represent best standards.

*Gurusher S. Panjra, MBBS, FACC
Chair, ACC Solution Set Oversight Committee*

1. INTRODUCTION

Affecting >1 billion adults worldwide, obesity is a debilitating, chronic disease with cardiovascular implications, including increased risk of heart failure, coronary artery disease, and stroke.^{1,2} Across 3 decades, obesity rates in adults have doubled, and in children and adolescents, they have quadrupled internationally.¹ Within the United States, 40.3% of adults have obesity (body mass index [BMI] ≥ 30 kg/m²), and 9.4% have severe obesity (BMI ≥ 40 kg/m²).³

As severe obesity is associated with significant reduction in life expectancy of 9.1 years in men and 7.7 years in women, treatment is critical.⁴ Whereas specific BMI cut points are recommended for different races, controversy still exists as to which diagnostic criteria for obesity are most accurate.

Obesity therapeutics vary in effectiveness regarding weight loss and cardiovascular disease (CVD) mitigation. In general, weight loss thresholds for risk reduction are 10% to 15% for CVD and >15% for cardiovascular mortality and adverse outcomes in heart failure with preserved ejection fraction (HFpEF).^{5,6} Disappointingly, weight loss achieved with lifestyle interventions has not been associated with a reduction in adverse cardiovascular outcomes.⁷ Although bariatric surgery is able to achieve substantial weight loss and reduced CVD events, it may be less desirable for some patients.⁸

More effective than lifestyle interventions and with less risk than procedure-based interventions, modern obesity medications are increasingly relevant to cardiologists for CVD modification. The intent of the current document is to provide the foundation for cardiologists to medically manage obesity using agents with proven CVD benefit.

In accordance with ACC’s Relationships With Industry and Other Entities policy, relevant disclosures for the writing committee and comprehensive disclosures for external peer reviewers can be found in [Appendices 1 and 2](#). A list of abbreviations relevant to this Concise Clinical Guidance can be found in [Appendix 3](#). To ensure transparency, a comprehensive table of the writing committee’s relationships with industry, including those not pertinent to this document, has been created. This can be found in the online [Supplemental Appendix](#).

2. ASSUMPTIONS AND DEFINITIONS

2.1. Assumptions and Definitions

As the newest generation of obesity medications, nutrient-stimulated hormone (NuSH) therapies represent a broad treatment category that acts on metabolic pathways, while helping to control appetite. Current targets of U.S. Food and Drug Administration (FDA)-approved NuSH therapies include glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) ([Section 4.3](#)).⁹ For the purposes of the current document, we utilize the term *NuSH therapies* to encompass the GLP-1 receptor agonists liraglutide and semaglutide, as well as the GLP-1/GIP receptor agonist tirzepatide.

2.2. Diagnosis

Overweight and obesity are defined as “abnormal or excessive fat accumulation that presents a risk to

TABLE 1 Obesity Threshold Classification

	Europoid	Asian
BMI category, kg/m ²		
Healthy weight	18.5 to <25	
Overweight	25 to <30	23 to <25
Obesity	≥30	≥25
Class 1	30 to <35	25 to <30
Class 2	35 to <40	≥30
Class 3 (severe obesity)	≥40	
Additional anthropometric measures		
Waist circumference (in)	Women: ≥35 in Men: ≥40 in	Women: ≥31.5 in* Men: ≥35.5 in* Japanese women: ≥35.4 in Japanese men: ≥33.5 in
Waist-to-height ratio	≥0.50	

*South Asian, Chinese.
BMI = body mass index.

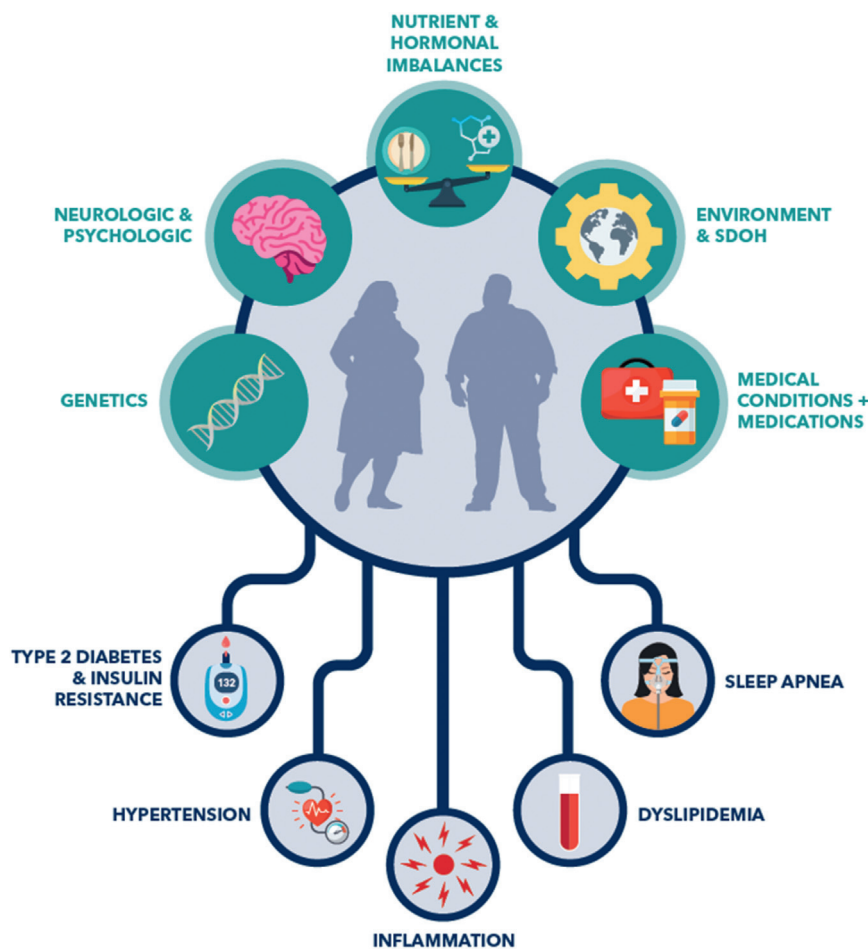
health.”^{10,11} Obesity is often diagnosed using BMI, which is calculated using an individual’s weight and height. As classified by the Centers for Disease Control and Prevention, weight thresholds based on BMI are summarized in [Table 1](#).¹²⁻¹⁵

At a population level, BMI is a useful measure to assess excess weight; among individuals, however, BMI does not always correlate with adiposity. BMI cannot fully account for fat distribution or muscle mass in an individual. Additionally, it cannot account for sex or racial differences in adiposity distribution and health risks. Classifications may be inaccurate, particularly for South Asian and Chinese populations, where BMI cutoffs for overweight and obesity have been proposed to be ≥23 kg/m² and ≥25 kg/m², respectively.¹⁶⁻²¹ Whereas other anthropometric measurements, such as waist circumference and waist-to-height ratio, may also be used to identify central adiposity and may better predict association with cardiovascular events, they require broader acceptance and definition of optimal thresholds across weight categories.²² Combining these concepts, obesity is defined by excess adiposity in association with impaired organ and/or functional status where adiposity can be obtained by direct measurements of body fat (eg, dual-energy x-ray absorptiometry scan) or anthropometric measurements ([Table 1](#)) in addition to BMI.^{11,23}

2.3. Etiology and Pathophysiology of Obesity

The etiology of obesity is complex.^{24,25} Genetics,²⁶⁻²⁹ neurological/psychological disorders,^{30,31} nutrient and hormonal imbalances,³² social determinants of health, the environment in which people live,^{33,34} medications³⁵⁻³⁸ and medical conditions³³ can all contribute to obesity ([Figure 1](#)). Its pathophysiology is defined by the

FIGURE 1 Causes of Obesity and its Association With Increased Cardiovascular Risk Factors



The causes of obesity are multiple and include genetics, neurological, psychological, nutrient and hormonal imbalances, and environmental, in addition to medical conditions and medications. The physiological consequences are multiple, with direct effects on cardiovascular risk factors. SDOH = social determinants of health.

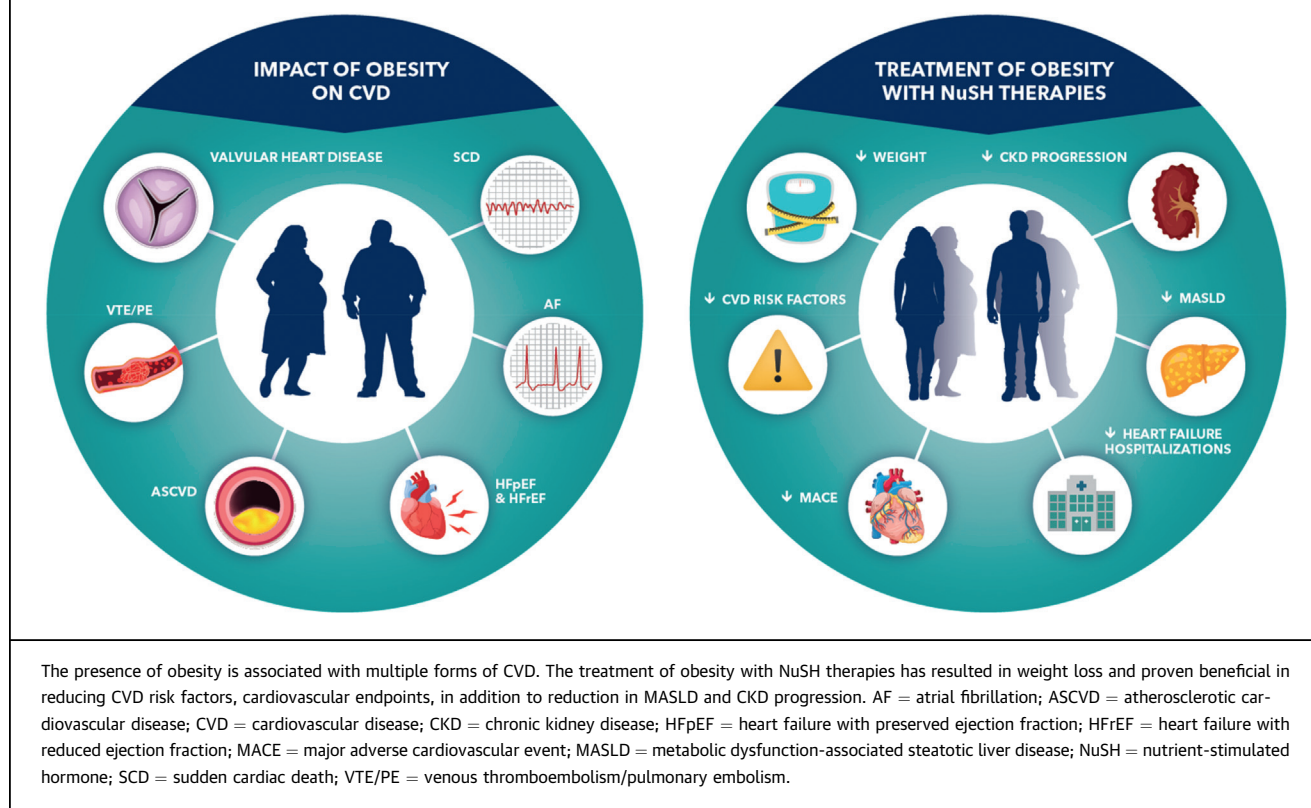
development and defense of an elevated lipostat that is accompanied by dysregulated appetitive hormone signaling and abnormal adipose tissue, which promotes inflammation characteristic of weight-related cardiometabolic and mechanical diseases.³⁹ Obesity has a strong impact on cardiovascular risk factors, including an increased risk of type 2 diabetes mellitus (T2DM), hypertension, hyperlipidemia, and obstructive sleep apnea,⁴⁰⁻⁴² along with other disabilities that can contribute to physical inactivity (Figure 1).^{30,43} Obesity by itself is an independent risk factor for CVD.

2.4. Risks Associated With Obesity

Obesity is associated with many different forms of CVD, including atherosclerotic CVD, heart failure (more commonly with HFpEF than reduced ejection fraction via inflammatory mechanisms), atrial fibrillation, sudden cardiac death, venous thromboembolism, and valvular heart disease (Figure 2).^{28,43-45} Obesity-related mechanisms result in hemodynamic, functional, and structural changes to the cardiovascular system, which contribute to the development of these disparate forms of CVD.^{41,43}

3. SUMMARY GRAPHIC

FIGURE 2 Obesity Management for Optimization of Cardiovascular Health



4. DESCRIPTION, RATIONALE, AND IMPLICATIONS FOR MEDICAL THERAPIES

4.1. Rationale and Eligibility for NuSH Therapies

NuSH therapies are a crucial component of comprehensive obesity care for three reasons:

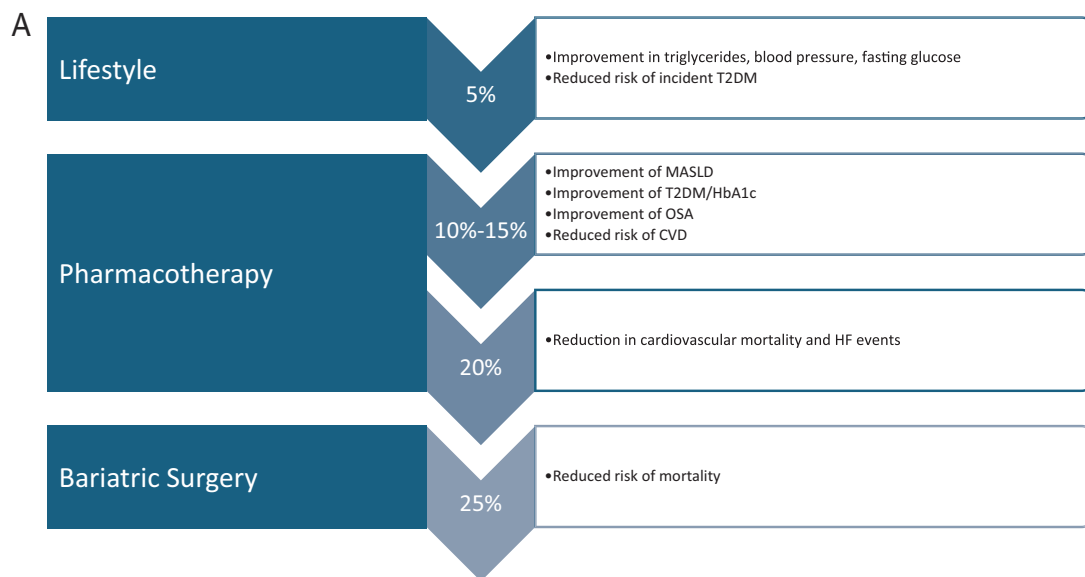
1. NuSH therapies fill the treatment gap between lifestyle therapy and bariatric surgery (Figures 3A, 3B). Unfortunately, lifestyle therapy achieves insufficient long-term weight loss to resolve complications and comorbidities for a majority of patients.⁴⁶ By contrast, bariatric surgery, while highly effective, is often undesired by patients. Pharmacotherapy strikes the balance between effectiveness and invasiveness.
2. NuSH therapies help to address the disease mechanisms of obesity by targeting the hormonal pathways that control appetite (eg, hunger, satiety, satiation, and cravings).

3. Because NuSH therapies are titratable, they allow dosing to minimize side effects and maximize weight loss, making them well suited to individualize care and address the obesity epidemic.

Eligibility for NuSH therapies may be determined by BMI thresholds, which other anthropometric data (Table 1) or direct measurement of excess adiposity, in combination with weight-related consequences. The BMI used to establish eligibility may be the patient's nonpregnant lifetime high, reflecting current understanding around the "weight set point"⁴⁹ and in concordance with managing obesity as a chronic disease.²³

Whereas prior guidelines suggested a trial of lifestyle intervention prior to pharmacotherapy,⁵⁰ data from phase 3 trials evaluating semaglutide and tirzepatide show minimal additional weight loss when combined with intensive behavioral therapy/lifestyle intervention.^{51,52} Patients should not be required to "try and fail" lifestyle

FIGURE 3A Weight Loss Thresholds Associated With Comorbidity Improvements



Sources for this figure: Rinella ME, et al.⁴⁷, Ryan DH, Yockey SR, et al.⁵, and Younossi ZM, et al.⁴⁸ Weight loss with lifestyle changes results in approximately 5% weight reduction and is associated with a reduction in blood pressure, triglycerides, fasting glucose, and a reduction in incident T2DM. Current pharmacotherapy can result in 10% to 20% weight loss with a reduction in MASLD, T2DM, OSA, and cardiovascular events. Bariatric surgery can achieve approximately 25% weight loss with a demonstrated reduction in all-cause mortality, in addition to the reduction in other cardiovascular consequences of obesity. CVD = cardiovascular disease; HbA_{1c} = hemoglobin A1c; HF = heart failure; MASLD = metabolic dysfunction-associated steatotic liver disease; OSA = obstructive sleep apnea; T2DM = type 2 diabetes mellitus.

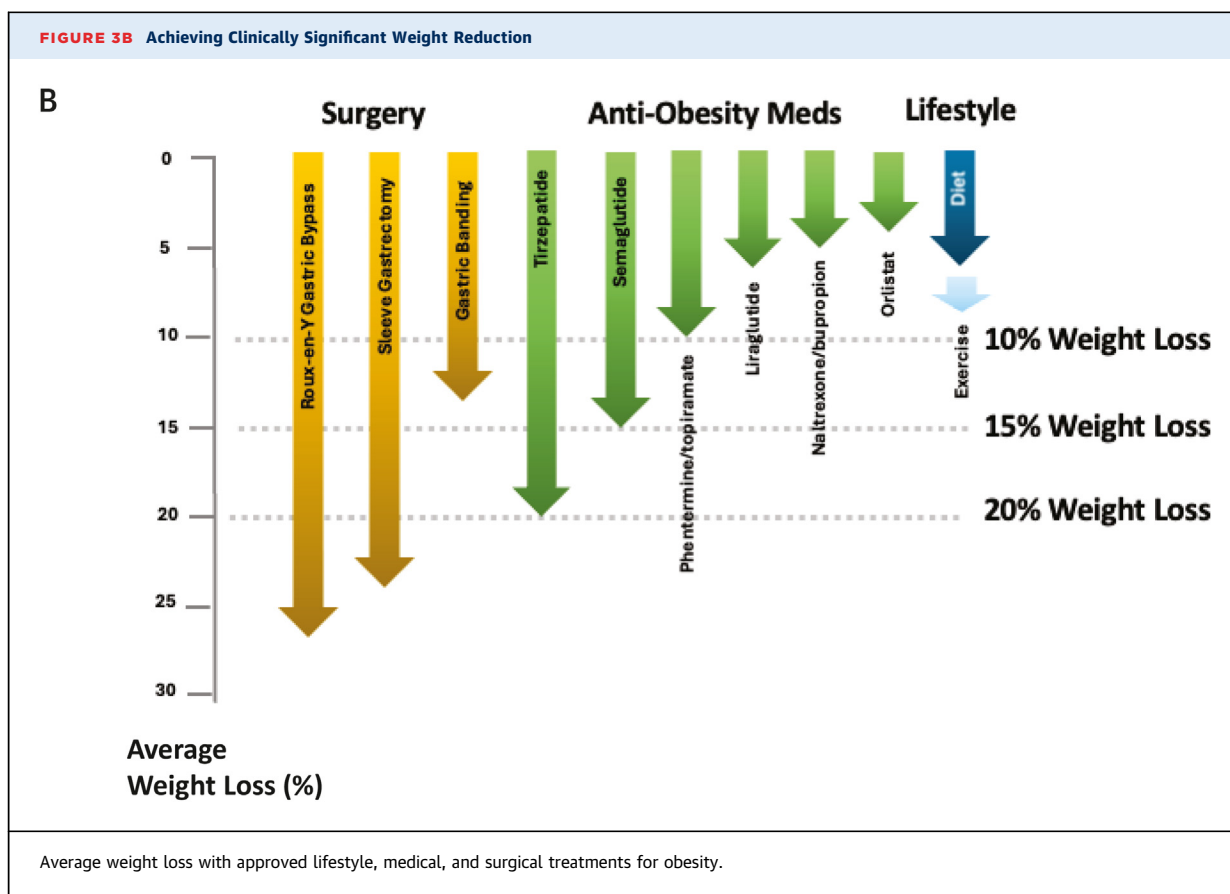
changes prior to initiating pharmacotherapy; nonetheless, lifestyle interventions should always be offered in conjunction with NuSH therapies.

4.2. Evolution and Current Landscape of Obesity Medications

Obesity medications have a long history dating back to the early 1900s.^{53,54} First-generation medications included thyroid hormone, dinitrophenol, and amphetamines. Thyroid hormone stimulated metabolic rate but was accompanied by harmful cardiovascular side effects. Dinitrophenol, a mitochondrial uncoupler that increased metabolic rate, resulted in weight loss but increased hyperthermia, tachycardia, diaphoresis, tachypnea, nausea, and vomiting.⁵⁴ Ultimately, the FDA suspended use of dinitrophenol in 1938 due to the development of cataracts. Amphetamines, that are still available today and

FDA-approved for short-term weight management (eg, phentermine, phendimetrazine, diethylpropion, benzphetamine), are effective appetite suppressants but lack data to support their long-term efficacy and safety with respect to cardiovascular and psychological effects.⁵³

Second-generation medications were developed in accordance with the FDA clinical trial requirements seeking to prove long-term clinical efficacy and safety, and include oral therapies with novel mechanisms of action.^{53,54} Some medications (ie, fenfluramine, dexfenfluramine, sibutramine, and lorcaserin) have been withdrawn from the market due to safety concerns.⁵³ Currently available second-generation agents approved for long-term weight management include orlistat,⁵⁵ phentermine/topiramate,⁵⁶ and naltrexone/bupropion.⁵⁷ Each of these is limited by modest weight loss



(5.9%–9.8%),^{55–57} side effects, and a lack of outcome data related to CVD.

Third-generation weight loss medications that target NuSH have changed the landscape of obesity management with robust long-term (up to 4 years) efficacy and safety data for the management of obesity in those with and without CVD.⁵⁸ While all currently available medications (liraglutide, semaglutide, and tirzepatide) were initially approved by the FDA to treat T2DM, they are also approved for obesity. They share a similar side effect profile that includes primarily gastrointestinal side effects (eg, nausea, diarrhea, vomiting, abdominal pain, constipation) that can be mitigated with dose reductions or

behavioral modifications (eg, hydration). Liraglutide, semaglutide, and tirzepatide have been shown to reduce body weight by an average of 8.0%, 14.9%, and 20.9% on maximal doses, respectively (Figures 3A and 3B).^{59–61}

4.3. Pharmacological Options

Among FDA-approved obesity medications, NuSH therapies are most effective (Table 2). Liraglutide and semaglutide are GLP-1 receptor agonists. GLP-1 regulates blood glucose by stimulating glucose-dependent insulin secretion, slowing gastric emptying, and increasing satiety, collectively promoting weight loss. Tirzepatide is a dual-acting agent that is both a GLP-1 receptor and a GIP

TABLE 2 FDA-Approved NuSH Obesity Medications

Medication (Brand Name)	FDA-Approved Indication for Weight Management	Dosage/Titration/Storage	Clinical Efficacy for Weight Loss	Contraindications/Cautions	Most Common Side Effects
GLP-1 receptor agonists					
Liraglutide (Victoza,* Saxenda†) ⁶⁵	Adults with an initial BMI ≥30 kg/m ² or ≥27 kg/m ² with a weight-related comorbidity	- Start 0.6 mg subcutaneously daily - Increase weekly up to a dose of 3 mg for adults - Can be stored for 30 days at controlled room temperature and longer with refrigeration‡	SCALE Obesity and Prediabetes ⁵⁹ 56-week double-blind trial (n=3,731): ↓ weight: 8.0% liraglutide, 2.6% placebo ↓ weight ≥5%: 63.2% liraglutide, 27.1% placebo	Contraindicated if: - Personal/family history of medullary thyroid carcinoma, personal/family history of multiple endocrine neoplasia syndrome type 2 - Hypersensitivity to the medication or any excipients Cautions: Acute pancreatitis, acute gallbladder disease, hypoglycemia, renal impairment/acute kidney injury, hypersensitivity reaction, suicidal behavior/ideation	Nausea, diarrhea, constipation, vomiting, injection-site reactions
Semaglutide (Ozempic,* Wegovy†) ⁶⁶	Adults with obesity or overweight and a weight-related comorbidity	- Start 0.25 mg subcutaneously weekly - Increase every 4 weeks up to a maintenance dose of 1.7 or 2.4 mg for adults - Ozempic can be stored for 56 days and Wegovy for 28 days at controlled room temperature and longer with refrigeration‡	STEP-1 ⁶⁰ 68-week double-blind trial (n=1,961): ↓ weight: 14.9% semaglutide, 2.4% placebo ↓ weight ≥5%: 86.4% semaglutide, 31.5% placebo		
Dual GLP-1 and GIP receptor agonist					
Tirzepatide (Mounjaro, ⁶⁷ Zepbound†) ⁶⁸	Adults with obesity or adults with overweight with a weight-related comorbidity	- Start 2.5 mg subcutaneously once weekly - Increase the dose every 4 weeks up to a maintenance dose of 5, 10, or 15 mg - Can be stored for 21 days at controlled room temperature and longer with refrigeration‡	SURMOUNT-1 ⁶¹ 72-week double-blind trial (n=2,539): ↓ weight: 15.0% with tirzepatide 5 mg, 19.5% with tirzepatide 10 mg, 20.9% with tirzepatide 15 mg, 3.1% with placebo ↓ weight ≥5%: 85% with tirzepatide 5 mg, 89% with tirzepatide 10 mg, 91% with tirzepatide 15 mg, 35% with placebo		

*Victoza, Ozempic, and Mounjaro are FDA-approved for T2DM regardless of weight status.

†Saxenda, Wegovy, and Zepbound are FDA-approved for weight loss with or without T2DM.

‡Refrigerator storage: 36 °F to 46 °F (2 °C to 8 °C), controlled room temperature: 59 °F to 86 °F (15 °C to 30 °C).

BMI = body mass index; FDA = U.S. Food and Drug Administration; GIP = glucose-dependent insulinotropic polypeptide; GLP-1 = glucagon-like peptide-1; NuSH = nutrient-stimulated hormone; SCALE = Satiety and Clinical Adiposity—Liraglutide Evidence; STEP-1 = Semaglutide Treatment Effect in People with Obesity-1; SURMOUNT-1 = Study of Tirzepatide in Participants With Obesity or Overweight-1; T2DM = type 2 diabetes mellitus.

receptor agonist. GIP is a potent gut-derived NuSH that stimulates glucose-dependent insulin secretion in response to food, contributing to endogenous postprandial insulin release. GIP regulates energy balance through cell-surface receptor signaling in the brain to suppress appetite and in adipose tissue to modify lipid metabolism.⁶² This dual mechanism likely explains the greater weight loss achieved with tirzepatide compared with that of GLP-1 receptor agonists. Several novel agents with dual and triple mechanisms of action that target other NuSH therapies (eg, glucagon, amylin) are in development.

Among the NuSH therapies, semaglutide and tirzepatide have the highest efficacy and are the obesity medications of choice. Clinical trial and real-world observational data support slightly greater weight loss with tirzepatide.^{58,63} Insurance coverage, availability, and affordability are likely to dictate agent selection.

Both GLP-1 and GIP receptor agonists are contraindicated in patients who have a personal or family history of medullary thyroid carcinoma, multiple endocrine neoplasia syndrome type 2, or known hypersensitivity to an individual product or any excipients (Table 2). In contrast with liraglutide, which is dosed

TABLE 3 Cardiovascular Outcomes of FDA-Approved NuSH Obesity Medications

Trial	Medication	Population	Size/Duration (Participants)/ (Years)	Average Baseline BMI and Weight Change in Treatment Group	Effect on Primary Outcome (Composite of Cardiovascular Death, AMI, or CVA Unless Specified)	Effect on HF Hospitalization
Obesity with diabetes and high cardiovascular risk or CVD						
LEADER ⁶⁹	Liraglutide 1.8 mg	T2DM and high cardiovascular risk or disease (81.3% with CVD)	9,340 participants/ 3.8 years	32.5 kg/m ² –2.3 kg	Reduction HR: 0.87; 95% CI, 0.78–0.97	No difference HR: 0.87; 95% CI, 0.73–1.05
SUSTAIN-6 ⁷⁷	Semaglutide 1.0 mg	T2DM and high cardiovascular risk (83.0% with CVD)	3,297 participants/ 2.1 years	33.0 kg/m ² –4.3 kg	Reduction HR: 0.74; 95% CI, 0.58–0.95	No difference HR: 1.11; 95% CI, 0.77–1.61
SURPASS-CVOT ⁸⁶ (NCT04255433)	Tirzepatide up to 15 mg vs dulaglutide 1.5 mg	CVD, T2DM, BMI ≥25 kg/m ²	13,299 participants enrolled	Trial fully recruited and ongoing	Estimated completion date 2025	Not available
Obesity without diabetes						
SELECT ⁷⁹	Semaglutide 2.4 mg	CVD and BMI >27 kg/m ²	17,604 participants/ 3.3 years	33.4 kg/m ² –9.1 kg	Reduction HR: 0.80; 95% CI: 0.72–0.90	No difference HR: 0.79; 95% CI: 0.60–1.03
STEP-HFpEF ⁸²	Semaglutide 2.4 mg	HF with EF ≥45% and BMI ≥30 kg/m ²	529 participants/ 12 months	37.0 kg/m ² –13.9 kg	Improvement in KCCQ	No difference (exploratory endpoint)
SUMMIT ⁸⁵	Tirzepatide 15 mg	HF with EF ≥50% and BMI ≥30 kg/m ²	731 participants/ 2.3 years	38.2 kg/m ² weight change of –13.9%	Reduction in cardiovascular death, worsening HF HR: 0.62; 95% CI: 0.41–0.95	Reduction HR: 0.44; 95% CI: 0.22–0.87
SURMOUNT-MMO (NCT05556512)	Tirzepatide 15 mg	CVD or risk, BMI ≥27 kg/m ²	15,374 participants enrolled	Trial fully recruited and ongoing	Estimated completion date 2027	Not available

Weight changes represent placebo-subtracted outcomes from intention-to-treat analyses. Shaded cells indicate that the trials are ongoing.

AMI = acute myocardial infarction; BMI = body mass index; CVA = cerebrovascular accident; CVD = cardiovascular disease; EF = ejection fraction; FDA = U.S. Food and Drug Administration; HF = heart failure; HR = hazard ratio; KCCQ = Kansas City Cardiomyopathy Questionnaire; LEADER = Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results; NuSH = nutrient-stimulated hormone; SELECT = Semaglutide Effects on Cardiovascular Outcomes in People With Overweight or Obesity; STEP-HFpEF = Semaglutide Treatment Effect in People with Obesity and Heart Failure with Preserved Ejection Fraction; SUMMIT = Study Comparing the Efficacy and Safety of Tirzepatide Versus Placebo in Patients With Heart Failure With Preserved Ejection Fraction and Obesity; SURMOUNT-MMO (NCT05556512) = Study of Tirzepatide in Participants With Obesity or Overweight Metabolic and Mobility Outcomes; SURPASS-CVOT = Effect of Tirzepatide Versus Dulaglutide on Major Adverse Cardiovascular Events in Patients With Type 2 Diabetes; SUSTAIN-6 = Semaglutide Unabated Sustainability in Treatment of Type 2 Diabetes-6; T2DM = type 2 diabetes mellitus.

daily, both semaglutide and tirzepatide are dosed once weekly. All agents require dose titration to minimize adverse effects, which are largely gastrointestinal. Slow titration (Table 2) mitigates intolerance. For patients with adverse effects, decreasing the dose to a previously tolerated dose is recommended.⁶⁴ In clinical trials, 4.3% to 7.1% of participants discontinued therapy due to adverse events.^{59–61}

Among published clinical trials, the longest duration of treatment with a NuSH (liraglutide) was 3.8 years.⁶⁹ Observational data across 5 years, however, suggest that GLP-1 receptor agonists are safe and effective.⁷⁰ This is an important issue, given that obesity is a chronic disease,

and weight regain after discontinuation of therapy is expected.⁷¹ Nonetheless, this highlights the importance of long-term medication persistence and maintaining lifestyle modifications if pharmacotherapy is discontinued.

In addition to tolerance, major challenges with contemporary obesity medications, especially semaglutide and tirzepatide, include limited access (related to payer denial and supply shortages) and affordability. Should a patient miss dosages due to lack of access, published strategies to address this exist and also guide therapeutic interchanges.⁷² For example, if ≥3 missed dosages of once-weekly semaglutide or tirzepatide occur, a dose reduction may be considered. Semaglutide and

TABLE 4 Multidisciplinary Considerations for Patients on NuSH Therapies

Specialty Topic	Obesity-Related Condition	Medication	Procedure
Cardiology	■ ASCVD ■ Atrial fibrillation ■ Heart failure ■ Hypertension ■ Hypertriglyceridemia/dyslipidemia	■ De-escalate antihypertensives to avoid low blood pressure ■ De-escalate diuretics in heart failure to avoid intravascular depletion	
Endocrinology	■ T2DM	■ Consider repeat TSH at 10% weight loss as levothyroxine dose may be weight-based⁹⁵ ■ Reduce medications for T2DM to avoid hypoglycemia⁹⁶⁻⁹⁹	■ Screening thyroid ultrasound is not required prior to NuSH therapy initiation
Nephrology	■ Chronic kidney disease	■ AKI may occur in the setting of gastrointestinal side effects⁶⁸	■ Adjust hemodialysis protocol for weight or body surface area¹⁰⁰ ■ Adjust dry weight in hemodialysis in patients undergoing active obesity treatment¹⁰¹
Gastroenterology/hepatology	■ MASLD ■ GERD ■ Gallbladder disorders	■ Because NuSH therapies are associated with a higher risk of gallbladder disorders, there could be a low threshold to consider ursodiol in patients with cholelithiasis^{64,102} ■ Adjust antireflux medications, given known improvement with weight loss¹⁰³ but common side effects of NuSH therapies^{66,68}	■ There are no data to support stopping a GLP-1 receptor agonist prior to elective upper endoscopy^{104,105} ■ Consider adjusting bowel preparation regimen for patients on NuSH therapy¹⁰⁶
Obstetrics/gynecology	■ PCOS ■ Infertility	■ Tirzepatide may reduce the efficacy of some contraceptive agents⁶⁸ ■ Weekly NuSH therapies should be discontinued ≥ 2 months prior to conception¹⁰⁷	
Psychiatry	■ Eating disorders ■ Depression ■ Anxiety ■ Severe mental illness	■ Consider re-evaluating medication dosages after significant weight loss, as the therapeutic window of some psychotropic medications may depend on body weight¹⁰⁸	
Hematology/oncology	■ Some cancers ■ Venous thromboembolism	■ Consider re-evaluating medication dosages after significant weight loss, as chemotherapy or anticoagulant dosing may be weight-based¹⁰⁹	
Surgery/anesthesiology			■ GLP-1 receptor agonist therapy may be preoperatively continued in patients without elevated risk of delayed gastric emptying and aspiration. If the decision to hold semaglutide or tirzepatide is made, there is a lack of evidence to inform duration, but 1 week may be considered^{110,111}
Pulmonary/critical care	■ OSA		■ Adjust CPAP settings or repeat OSA assessment after significant weight loss ($\geq 7\%$)⁸⁸
Geriatrics		■ Caution with excess weight loss and higher risk of sarcopenia and frailty in this age group ■ Re-evaluate medications and dosages after significant weight loss to reduce the risk of polypharmacy¹¹²	

AKI = acute kidney injury; ASCVD = atherosclerotic cardiovascular disease; CPAP = continuous positive airway pressure; GERD = gastroesophageal reflux disease; GLP-1 = glucagon-like peptide-1; MASLD = metabolic dysfunction-associated steatotic liver disease; NuSH = nutrient-stimulated hormone therapy; OSA = obstructive sleep apnea; PCOS = polycystic ovarian syndrome; T2DM = type 2 diabetes mellitus; TSH = thyroid-stimulating hormone.

tirzepatide can also be interchanged based on clinical judgment. Use of compounded NuSH therapies is discouraged due to the potential for dosing errors and concern regarding counterfeit agents, which may contain impurities.⁷³⁻⁷⁵

4.4. Implications on Comorbidities

A summary of the effects of NuSH therapies on cardiovascular outcomes is shown in [Table 3](#). NuSH therapies have been shown to reduce weight along with the risk of

cardiovascular death, myocardial infarction, or stroke in patients with T2DM⁷⁶ at increased cardiovascular risk or with established CVD.^{69,77,78}

The benefits of NuSH therapies extend beyond T2DM. In patients without T2DM but with atherosclerotic CVD and a BMI >27 kg/m², semaglutide resulted in significant weight loss as well as a reduction in a composite of cardiovascular death, myocardial infarction, and stroke.⁷⁹ Whether this benefit is also observed with tirzepatide is being tested in a similar population (NCT05556512)⁸⁰ as

FIGURE 4 Examples of Ways to Reduce Weight Stigma and More Optimally Deliver Care in Clinic and Hospital Settings

Space and equipment	Medical devices	Procedures
☐ Armless chairs or wide chairs with arms	☐ Large or extra-large blood pressure cuffs	☐ Ultrasound enhancing agents in echocardiograms
☐ High-capacity exam tables	☐ High-capacity weight scales (>400 lb)	☐ High-capacity procedure tables
☐ Extra-large patient gowns		☐ High-capacity CT or MRI (weight and girth)
		☐ Extra long intravenous catheters

Sources for this figure: Beavers and Bagal¹¹⁵; Bianchetti et al¹¹⁶; Gerstein et al¹¹⁷; Madder et al¹¹⁸; Plourde et al¹¹⁹; Powell-Wiley et al⁴³; Refahiyat et al¹²⁰; Singh et al.¹²¹ Reducing weight stigma should be built into clinics and hospitals, improving the care of patients with excess weight. Some examples are listed in this figure. CT = computed tomography; MRI = magnetic resonance imaging.

well as in patients with CVD and T2DM with a lower BMI threshold of 25 kg/m² (NCT04255433).⁸¹

In patients with HFpEF, semaglutide resulted in improvement in symptoms, physical limitation, and exercise function.⁸² Whereas the magnitude of benefit was directly related to the extent of weight loss,⁸³ there may be weight-independent mechanisms of benefit.⁸⁴ In a separate study that evaluated tirzepatide in patients with obesity and HFpEF, a significant reduction in the composite outcome of cardiovascular death and worsening heart failure was observed,⁸⁵ which may further extend the role of these agents to patients with HFpEF.⁸⁵

4.5. General Treatment Considerations

4.5.1. General Principles That Apply to the Medical Management of Obesity

Comprehensive treatment of obesity is multimodal. Lifestyle interventions support overall weight management,^{50,60,61} and their utility alongside highly effective obesity medications is evolving.^{51,52,87}

Obesity treatment is multidisciplinary. The use of NuSH therapies may necessitate adjustments in the management of obesity-related comorbidities; as such, these patients benefit from coordination of care (Table 4).^{5,88-90} Patients should be guided toward evidence-based interventions whenever possible and be

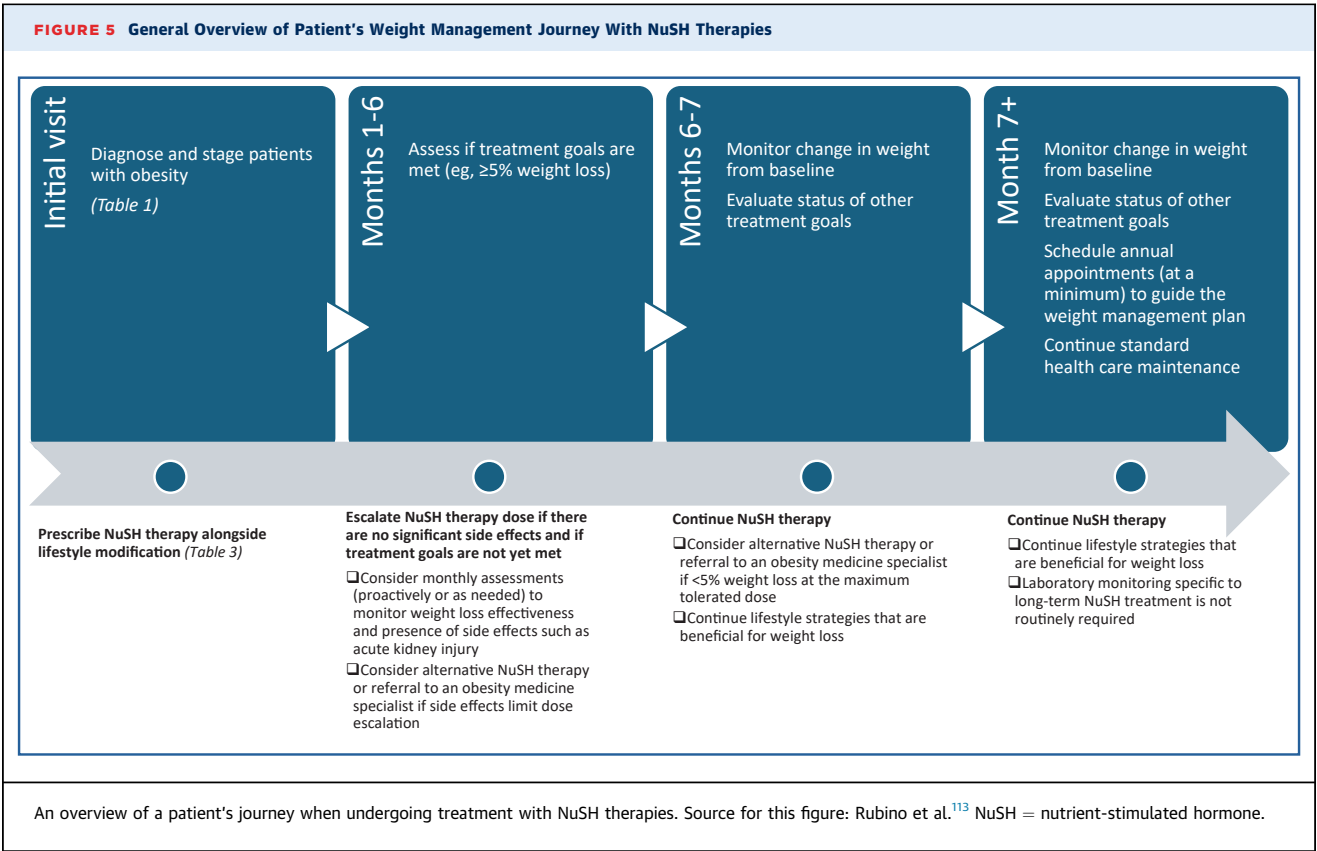
educated regarding nonevidence-based options (eg, compounded peptides, over-the-counter supplements) that may pose potential harm.^{91,92}

Clinicians should incorporate shared decision-making into their treatment approach to best balance risks and benefits. Off-label, but evidence-based, strategies may be considered to mitigate potential harms and optimize health outcomes (eg, lowest therapeutic dose for weight loss maintenance,⁹³ combination therapies).^{88,94}

4.5.2. The Patient Experience

Obesity care should include attention to reducing weight bias and stigma. Person-first language should be used. In addition, the clinical space should be designed to appropriately welcome and treat patients (Figure 4).^{113,114} Clinicians should make every effort to validate the lifelong journey that patients experience with this chronic disease.

The initial encounter should elicit potential contributors to and consequences of obesity, identify contraindications to obesity medications, and obtain anthropometric and clinical data to aid in the diagnosis and staging of obesity.²³ Blood work is unlikely to change the decision to pursue NuSH therapies, given that these medications' contraindications cannot be detected by laboratory results, but may be helpful for insurance coverage, however, if T2DM is diagnosed.¹²² Published resources



may guide clinicians in establishing an obesity care practice.^{50,114,123}

Frequency of follow-up depends on the stage of the patient's journey and the practice's capabilities (Figure 5). More frequent interactions with a weight management team have been associated with greater weight loss and weight loss maintenance success.^{7,71,124} Given a paucity of data, practitioners should use their clinical judgment to best manage situations that might be concerning for unintentional or rapid weight loss, signs or symptoms of vitamin/mineral deficiencies, signs or symptoms of disordered eating behaviors, or excess weight loss associated with frailty.⁷¹

The goals of obesity treatment should be tailored to the individual. A reasonable initial goal is achievement of clinically significant weight loss, defined as $\geq 5\%$ from baseline, which is associated with improvement in triglycerides, fasting blood glucose, and systolic blood pressure as well as the prevention of incident disease.^{50,125} Individuals who seek to resolve weight-related comorbidities (eg, CVD, sleep apnea, metabolic dysfunction-associated steatotic liver disease) should aim

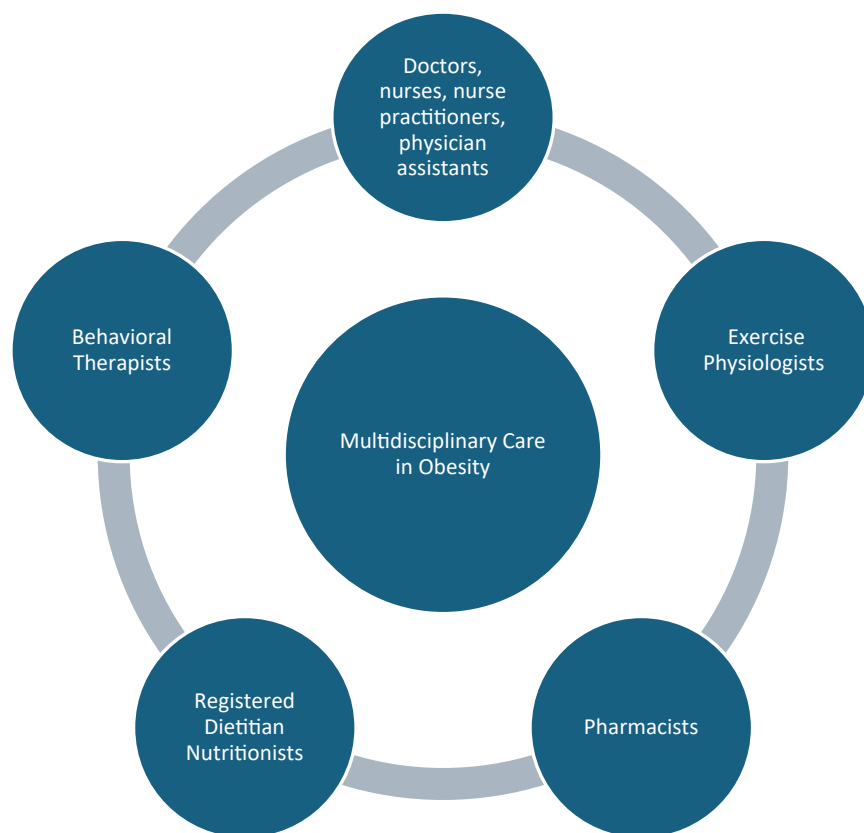
for $\geq 10\%$ weight loss.⁵ Patient quality of life, functional status, and psychosocial health should also be considered as part of one's treatment goals, supporting a holistic approach to obesity care.

Therapies for weight-related comorbidities and weight-based medications should be de-escalated as needed (Table 4). As a patient achieves their weight management goals, actively reduce or discontinue interventions to avoid harm from overtreatment, mitigate polypharmacy, and reinforce progress.^{96-99,126,127}

Long-term treatment should be the default plan. As such, obesity medications should not be discontinued unless determined by the patient and/or treating clinician, as this commonly results in weight regain.^{71,124}

4.6. Multidisciplinary Care Approaches

Weight management is best optimized using a team-based approach to create personalized health assessments and identify contributing factors, modifiable risk factors, and comorbid conditions (Figure 6).¹²⁸ Early involvement with behavioral therapists can be beneficial to recognize individual stressors, encourage social support systems,

FIGURE 6 Multidisciplinary Team Approach for Weight Management

A multidisciplinary team-based approach to weight management is recommended, creating a personalized approach for individual patients. This integrated model will allow for comprehensive and tailored weight management.

identify long-term patient goals, and set reasonable expectations.¹²⁹ Additionally, health coaching with registered dietitians and exercise physiologists has been shown to improve weight loss, physical activity, and metabolic markers.^{130,131} Finally, a team of clinicians with pharmacy support is integral for monitoring medication side effects, therapeutic goals, and improving access to care.¹³² Thus, a multidisciplinary team approach allows for comprehensive and tailored weight management.¹²⁸

4.7. Access Considerations

Despite profound cardiovascular and weight loss benefits with NuSH therapies, medication coverage serves as a major barrier for patients.¹³³ Whereas the average yearly cost for semaglutide, liraglutide, and tirzepatide in the United States is \$14,080, \$15,738, and \$8,126,

respectively, cost is significantly lower in other countries (eg, \$2,066 for liraglutide, Switzerland).¹³³ NuSH therapies are covered by Medicare Part D for patients with obesity and other comorbid conditions, including T2DM and specific CVD diagnoses; however, these medications are not covered for obesity alone.¹³⁴ Initial strategies to improve access to NuSH therapies include identifying individuals most likely to benefit, close monitoring of treatment outcomes, and price negotiations.¹³³ There is ongoing need to improve access to NuSH therapies in the United States, acknowledging that this may be delayed by current price points limiting its cost-effectiveness.¹³³ It should also be noted that until prices are further adjusted, individuals may seek unregulated routes to access, such as compounding, which can be associated with increased risk of complications.^{135,136} Advocacy efforts on behalf of

patients and health care professionals are ongoing with a focus on increasing access to comprehensive obesity care.¹³⁷

4.8. Conclusions/Future Directions

In this new era of obesity management, there exists an ever-expanding set of tools to assist patients in diagnosis, weight reduction, and CVD risk mitigation. With more precise ways of identifying adipose tissue on the horizon, care will be further personalized. Beyond improvement of CVD risk factors, third-generation obesity medications (NuSH therapies) have been shown to reduce adverse cardiovascular events among those with obesity and established atherosclerotic CVD and/or HFpEF. In addition, a growing number of therapies are in development. Obesity management by the cardiovascular community needs to be embraced, given both the prevalence of obesity and the impact it has on many forms of CVD.

Several questions remain that will need to be resolved to effectively assist our patients with initiation and continuation of these therapies in the treatment of this chronic disease.

PRESIDENT AND STAFF

Christopher M. Kramer, MD, FACC
Cathleen C. Gates, Chief Executive Officer
Richard J. Kovacs, MD, MACC, Chief Medical Officer
Brendan Mullen, Executive Vice President
Joseph M. Allen, MA, Team Leader, Science & Quality
Amy Dearborn, Team Leader, Decision Science
Ashleigh M. Covington, MA, Team Leader, Decision Science Delivery
Severa Chavez, Associate, Decision Science Delivery
Grace D. Ronan, Senior Production and Operations Manager, Clinical Policy Publication

REFERENCES

1. NCD Risk Factor Collaboration (NCD-RisC). World-wide trends in underweight and obesity from 1990 to 2022: a pooled analysis of 3663 population-representative studies with 222 million children, adolescents, and adults. *Lancet*. 2024;403:1027-1050.
2. Ndumele CE, Matsushita K, Lazo M, et al. Obesity and subtypes of incident cardiovascular disease. *J Am Heart Assoc*. 2016;5(8):e003921. <https://doi.org/10.1161/JAHA.116.003921>
3. Centers for Disease Control and Prevention. Obesity and severe obesity prevalence in adults: United States, August 2021–August 2023. Accessed December 2024. <https://www.cdc.gov/nchs/products/databriefs/db508.htm>
4. Bhaskaran K, Dos-Santos-Silva I, Leon DA, et al. Association of BMI with overall and cause-specific mortality: a population-based cohort study of 3.6 million adults in the UK. *Lancet Diabetes Endocrinol*. 2018;6:944–953.
5. Ryan DH, Yockey SR. Weight loss and improvement in comorbidity: differences at 5%, 10%, 15%, and over. *Curr Obes Rep*. 2017;6:187–194.
6. Usman MS, Davies M, Hall ME, et al. The cardiovascular effects of novel weight loss therapies. *Eur Heart J*. 2023;44:5036–5048.
7. Wing RR, Bolin P, Brancati FL, et al. Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes. *N Engl J Med*. 2013;369:145–154.
8. Chang SH, Stoll CR, Song J, et al. The effectiveness and risks of bariatric surgery: an updated systematic review and meta-analysis, 2003–2012. *JAMA Surg*. 2014;149:275–287.
9. Gudzone KA, Kushner RF. Medications for obesity: a review. *JAMA*. 2024;332:571–584.
10. World Health Organization. Obesity. Accessed October 2024. https://www.who.int/health-topics/obesity#tab=tab_1
11. Rubino F, Cummings DE, Eckel RH, et al. Definition and diagnostic criteria of clinical obesity. *Lancet Diabetes Endocrinol*. 2025;13:221–262.
12. Centers for Disease Control and Prevention. Adult BMI categories. Accessed October 2024. <https://www.cdc.gov/bmi/adult-calculator/bmi-categories.html>
13. Gupta RD, Parry AA, Kothadia RJ, et al. The association between body mass index and abdominal obesity with hypertension among South Asian population: findings from nationally representative surveys. *Clin Hypertens*. 2024;30:3.
14. Ogawa W, Hirota Y, Miyazaki S, et al. Definition, criteria, and core concepts of guidelines for the management of obesity disease in Japan. *Endocr J*. 2024;71:223–231.
15. Zhang C, Rexrode KM, van Dam RM, et al. Abdominal obesity and the risk of all-cause, cardiovascular, and cancer mortality: sixteen years of follow-up in US women. *Circulation*. 2008;117:1658–1667.
16. Razak F, Anand SS, Shannon H, et al. Defining obesity cut points in a multiethnic population. *Circulation*. 2007;115:2111–2118.
17. Caleyachetty R, Barber TM, Mohammed NI, et al. Ethnicity-specific BMI cutoffs for obesity based on type 2 diabetes risk in England: a population-based cohort study. *Lancet Diabetes Endocrinol*. 2021;9:419–426.
18. Rao G, Powell-Wiley TM, Ancheta I, et al. Identification of obesity and cardiovascular risk in ethnically and racially diverse populations: a scientific statement from the American Heart Association. *Circulation*. 2015;132:457–472.
19. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet*. 2004;363:157–163.
20. Misra A, Chowbey P, Makkar BM, et al. Consensus statement for diagnosis of obesity, abdominal obesity and the metabolic syndrome for Asian Indians and recommendations for physical activity, medical and surgical management. *J Assoc Physicians India*. 2009;57:163–170.
21. Seo MH, Lee WY, Kim SS, et al. 2018 Korean Society for the Study of Obesity guideline for the management of obesity in Korea. *J Obes Metab Syndr*. 2019;28:40–45.
22. World Health Organization. Regional Office for the Western Pacific. The Asia-Pacific perspective: redefining obesity and its treatment. *Health Communications Australia*. 2000. Accessed October 2024. <https://iris.who.int/handle/10665/206936>
23. Busetto L, Dicker D, Frühbeck G, et al. A new framework for the diagnosis, staging and management of obesity in adults. *Nature Medicine*. 2024;30:2395–2399.
24. Bluher M. Obesity: global epidemiology and pathogenesis. *Nat Rev Endocrinol*. 2019;15:288–298.
25. Lopez-Jimenez F, Almahmeed W, Bays H, et al. Obesity and cardiovascular disease: mechanistic insights and management strategies. A joint position paper by the World Heart Federation and World Obesity Federation. *Eur J Prev Cardiol*. 2022;29:2218–2237.
26. Dubern B, Mosbah H, Pigeyre M, et al. Rare genetic causes of obesity: diagnosis and management in clinical care. *Ann Endocrinol (Paris)*. 2022;83:63–72.
27. Hinney A, Nguyen TT, Scherag A, et al. Genome wide association (GWA) study for early onset extreme obesity supports the role of fat mass and obesity associated gene (FTO) variants. *PLoS One*. 2007;2:e1361.
28. Larsson SC, Back M, Rees JMB, et al. Body mass index and body composition in relation to 14 cardiovascular conditions in UK Biobank: a Mendelian randomization study. *Eur Heart J*. 2020;41:221–226.

29. Sun YQ, Burgess S, Staley JR, et al. Body mass index and all cause mortality in HUNT and UK Biobank studies: linear and non-linear mendelian randomisation analyses. *BMJ*. 2019;364:l1042.
30. Hall KD, Farooqi IS, Friedman JM, et al. The energy balance model of obesity: beyond calories in, calories out. *Am J Clin Nutr*. 2022;115:1243-1254.
31. Fernandez-Aranda F, Granero R, Jimenez-Murcia S. Editorial: neurological, psychological and endocrine markers of eating disorders and obesity. *Front Nutr*. 2023;10:1289370.
32. Ludwig DS, Ebbeling CB. The carbohydrate-insulin model of obesity: beyond "calories in, calories out". *JAMA Intern Med*. 2018;178:1098-1103.
33. Masood B, Moorthy M. Causes of obesity: a review. *Clin Med (Lond)*. 2023;23:284-291.
34. Javed Z, Valero-Elizondo J, Maqsood MH, et al. Social determinants of health and obesity: Findings from a national study of US adults. *Obesity (Silver Spring)*. 2022;30:491-502.
35. Bryson C, Psaty B. A review of the adverse effects of peripheral alpha-1 antagonists in hypertension therapy. *Curr Control Trials Cardiovasc Med*. 2002;3:7.
36. Gammon MA, Efthymakis K, D'Orazio N. Effect of third-generation beta blockers on weight loss in a population of overweight-obese subjects in a controlled dietary regimen. *J Nutr Metab*. 2021;2021:5767306.
37. Dayabandara M, Hanwella R, Ratnatunga S, et al. Antipsychotic-associated weight gain: management strategies and impact on treatment adherence. *Neuropsychiatr Dis Treat*. 2017;13:2231-2241.
38. Verhaegen AA, Van Gaal LF. *Drugs that affect body weight, body fat distribution, and metabolism*. In: Feingold KR, Ahmed SF, Anawalt B, et al, eds. *Endotext* [Internet]. MDTextcom; 2000.
39. Jastreboff AM, Kushner RF. New frontiers in obesity treatment: GLP-1 and nascent nutrient-stimulated hormone-based therapeutics. *Annu Rev Med*. 2023;74:125-139.
40. Lyall DM, Celis-Morales C, Ward J, et al. Association of body mass index with cardiometabolic disease in the UK Biobank: a Mendelian randomization study. *JAMA Cardiol*. 2017;2:882-889.
41. Csige I, Ujvarosy D, Szabo Z, et al. The impact of obesity on the cardiovascular system. *J Diabetes Res*. 2018;2018:3407306.
42. Burke GL, Bertoni AG, Shea S, et al. The impact of obesity on cardiovascular disease risk factors and subclinical vascular disease: the Multi-Ethnic Study of Atherosclerosis. *Arch Intern Med*. 2008;168:928-935.
43. Powell-Wiley TM, Poirier P, Burke LE, et al. Obesity and cardiovascular disease: a scientific statement from the American Heart Association. *Circulation*. 2021;143:e984-e1010.
44. Global BMI Mortality Collaboration, Di Angelantonio E, Bhupathiraju SN, Wormser D, et al. Body-mass index and all-cause mortality: individual-participant-data meta-analysis of 239 prospective studies in four continents. *Lancet*. 2016;388:776-786.
45. Savji N, Meijers WC, Bartz TM, et al. The association of obesity and cardiometabolic traits with incident HFpEF and HFrEF. *JACC Heart Fail*. 2018;6:701-709.
46. Hall KD, Kahan S. Maintenance of lost weight and long-term management of obesity. *Medical Clinics of North America*. 2018;102:183-197.
47. Rinella ME, Neuschwander-Tetri BA, Siddiqui MS, et al. AASLD practice guidance on the clinical assessment and management of nonalcoholic fatty liver disease. *Hepatology*. 2023;77:1797-1835.
48. Younossi ZM, Corey KE, Lim JK. AGA clinical practice update on lifestyle modification using diet and exercise to achieve weight loss in the management of nonalcoholic fatty liver disease: expert review. *Gastroenterology*. 2021;160:912-918.
49. Garvey WT. Is obesity or adiposity-based chronic disease curable: the set point theory, the environment, and second-generation medications. *Endocr Pract*. 2022;28:214-222.
50. Jensen MD, Ryan DH, Apovian CM, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. *J Am Coll Cardiol*. 2014;63:2985-3023.
51. Wadden TA, Bailey TS, Billings LK, et al. Effect of subcutaneous semaglutide vs placebo as an adjunct to intensive behavioral therapy on body weight in adults with overweight or obesity (STEP 3). *JAMA*. 2021;325:1403.
52. Wadden TA, Chao AM, Machineni S, et al. Tirzepatide after intensive lifestyle intervention in adults with overweight or obesity: the SURMOUNT-3 phase 3 trial. *Nat Med*. 2023;29:2909-2918.
53. Muller TD, Bluher M, Tschop MH, et al. Anti-obesity drug discovery: advances and challenges. *Nat Rev Drug Discov*. 2022;21:201-223.
54. Muller TD, Clemmensen C, Finan B, et al. Anti-obesity therapy: from rainbow pills to polyagonists. *Pharmacol Rev*. 2018;70:712-746.
55. Davidson MH, Hauptman J, DiGirolamo M, et al. Weight control and risk factor reduction in obese subjects treated for 2 years with orlistat: a randomized controlled trial. *JAMA*. 1999;281:235-242.
56. Gadde KM, Allison DB, Ryan DH, et al. Effects of low-dose, controlled-release, phentermine plus topiramate combination on weight and associated comorbidities in overweight and obese adults (CONQUER): a randomised, placebo-controlled, phase 3 trial. *Lancet*. 2011;377:1341-1352.
57. Greenway FL, Fujioka K, Plodkowski RA, et al. Effect of naltrexone plus bupropion on weight loss in overweight and obese adults (COR-1): a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*. 2010;376:595-605.
58. Maki KC, Kirkpatrick CF, Allison DB, et al. Pharmacotherapy for obesity: recent evolution and implications for cardiovascular risk reduction. *Expert Rev Endocrinol Metab*. 2023;18:307-319.
59. Pi-Sunyer X, Astrup A, Fujioka K, et al. A randomized, controlled trial of 3.0 mg of liraglutide in weight management. *N Engl J Med*. 2015;373:11-22.
60. Wilding JPH, Batterham RL, Calanna S, et al. Once-weekly semaglutide in adults with overweight or obesity. *N Engl J Med*. 2021;384:989-1002.
61. Jastreboff AM, Aronne LJ, Ahmad NN, et al. Tirzepatide once weekly for the treatment of obesity. *N Engl J Med*. 2022;387:205-216.
62. Samms RJ, Coghlan MP, Sloop KW. How may GIP enhance the therapeutic efficacy of GLP-1? *Trends Endocrinol Metab*. 2020;31:410-421.
63. Rodriguez PJ, Goodwin Cartwright BM, Gratzl S, et al. Semaglutide vs tirzepatide for weight loss in adults with overweight or obesity. *JAMA Intern Med*. 2024;184:1056-1064.
64. Gorgojo-Martinez JJ, Mezquita-Raya P, Carretero-Gomez J, et al. Clinical recommendations to manage gastrointestinal adverse events in patients treated with GLP-1 receptor agonists: a multidisciplinary expert consensus. *J Clin Med*. 2022;12.
65. Novo Nordisk. Saxenda (liraglutide) [package insert]. Accessed December 2024. <https://www.novo-pi.com/saxenda.pdf>
66. Novo Nordisk. Wegovy (semaglutide) [package insert]. Accessed December 2024. <https://www.novo-pi.com/wegovy.pdf>
67. Lilly USA, LLC. Mounjaro (tirzepatide) [package insert]. Accessed December 2024. <https://uspl.lilly.com/mounjaro/mounjaro.html#pi>
68. Lilly USA, LLC. Zepbound (tirzepatide) [package insert]. Accessed December 2024. <https://pi.lilly.com/us/zepbound-uspi.pdf>
69. Marso SP, Daniels GH, Brown-Frandsen K, et al. Liraglutide and cardiovascular outcomes in type 2 diabetes. *N Engl J Med*. 2016;375:311-322.
70. Huang YN, Liao WL, Huang JY, et al. Long-term safety and efficacy of glucagon-like peptide-1 receptor agonists in individuals with obesity and without type 2 diabetes: a global retrospective cohort study. *Diabetes Obes Metab*. 2024;26:5222-5232.
71. Aronne LJ, Sattar N, Horn DB, et al. Continued treatment with tirzepatide for maintenance of weight reduction in adults with obesity: the SURMOUNT-4 randomized clinical trial. *JAMA*. 2024;331:38-48.
72. Whitley HP, Trujillo JM, Neumiller JJ. Special report: potential strategies for addressing GLP-1 and dual GLP-1/GIP receptor agonist shortages. *Clin Diabetes*. 2023;41:467-473.
73. U.S. Food and Drug Administration. FDA drug safety and availability. Accessed October 2024. <https://www.fda.gov/drugs/drug-safety-and-availability/fda-warns-consumers-not-use-counterfeit-ozempic-semaglutide-found-us-drug-supply-chain>
74. Hach M, Engelund DK, Mysling S, et al. Impact of manufacturing process and compounding on properties and quality of follow-on GLP-1 polypeptide drugs. *Pharm Res*. 2024;41:1991-2014.
75. U.S. Food and Drug Administration. FDA's concerns with unapproved GLP-1 drugs used for weight loss. Accessed January 2025. <https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/fdas-concerns-unapproved-glp-1-drugs-used-weight-loss>
76. Gerstein HC, Colhoun HM, Dagenais GR, et al. Dulaglutide and cardiovascular outcomes in type 2 diabetes (REWIND): a double-blind, randomised placebo-controlled trial. *Lancet*. 2019;394:121-130.
77. Marso SP, Bain SC, Consoli A, et al. Semaglutide and cardiovascular outcomes in patients with type 2 diabetes. *N Engl J Med*. 2016;375:1834-1844.

78. Gerstein HC, Sattar N, Rosenstock J, et al. Cardiovascular and renal outcomes with efglenatide in type 2 diabetes. *N Engl J Med*. 2021;385:896-907.
79. Lincoff AM, Brown-Frandsen K, Colhoun HM, et al. Semaglutide and cardiovascular outcomes in obesity without diabetes. *N Engl J Med*. 2023;389:2221-2232.
80. A Study of Tirzepatide (LY3298176) on the Reduction of Morbidity and Mortality in Adults With Obesity (SURMOUNT-MMO). Accessed March 2025. <https://clinicaltrials.gov/study/NCT05556512>
81. A Study of Tirzepatide (LY3298176) Compared With Dulaglutide on Major Cardiovascular Events in Participants With Type 2 Diabetes (SURPASS-CVOT). Accessed March 2025. <https://clinicaltrials.gov/study/NCT04255433>
82. Kosiborod MN, Abildstrøm SZ, Borlaug BA, et al. Semaglutide in patients with heart failure with preserved ejection fraction and obesity. *N Engl J Med*. 2023;389:1069-1084.
83. Borlaug BA, Kitzman DW, Davies MJ, et al. Semaglutide in HFpEF across obesity class and by body weight reduction: a prespecified analysis of the STEP-HFpEF trial. *Nat Med*. 2023;29:2358-2365.
84. Petrie MC, Borlaug BA, Butler J, et al. Semaglutide and NT-proBNP in obesity-related HFpEF: insights from the STEP-HFpEF program. *J Am Coll Cardiol*. 2024;84:27-40.
85. Packer M, Zile MR, Kramer CM, et al. Tirzepatide for heart failure with preserved ejection fraction and obesity. *N Engl J Med*. 2025;392:427-437.
86. Nicholls SJ, Bhatt DL, Buse JB, et al. Comparison of tirzepatide and dulaglutide on major adverse cardiovascular events in participants with type 2 diabetes and atherosclerotic cardiovascular disease: SURPASS-CVOT design and baseline characteristics. *Am Heart J*. 2024;267:1-11.
87. Wadden TA, Chao AM, Moore M, et al. The role of lifestyle modification with second-generation anti-obesity medications: comparisons, questions, and clinical opportunities. *Curr Obes Rep*. 2023;12:453-473.
88. Garvey WT, Mechanick JL, Brett EM, et al. American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology (ACE) comprehensive clinical practice guidelines for medical care of patients with obesity. *Endocr Pract*. 2016;22(suppl 3):1-203.
89. Centers for Disease Control. Obesity and cancer. Accessed October 2024. <https://www.cdc.gov/cancer/risk-factors/obesity.html>
90. Leutner M, Dervic E, Bellach L, et al. Obesity as pleiotropic risk state for metabolic and mental health throughout life. *Transl Psychiatry*. 2023;13(1):175.
91. Batsis JA, Apolzan JW, Bagley PJ, et al. A systematic review of dietary supplements and alternative therapies for weight loss. *Obesity*. 2021;29:1102-1113.
92. U.S. Food and Drug Administration. Tainted weight loss products. Accessed October 2024. <https://www.fda.gov/drugs/medication-health-fraud/tainted-weight-loss-products>
93. O'Neil PM, Birkenfeld AL, McGowan B, et al. Efficacy and safety of semaglutide compared with liraglutide and placebo for weight loss in patients with obesity: a randomised, double-blind, placebo and active controlled, dose-ranging, phase 2 trial. *Lancet*. 2018;392:637-649.
94. Weintraub MA, D'Angelo D, Tchang BG, et al. Five-year weight loss maintenance with obesity pharmacotherapy. *J Clin Endocrinol Metab*. 2023;108:e832-e841.
95. Jonklaas J, Bianco AC, Bauer AJ, et al. Guidelines for the treatment of hypothyroidism: prepared by the American Thyroid Association Task Force on thyroid hormone replacement. *Thyroid*. 2014;24:1670-1751.
96. Dahl D, Onishi Y, Norwood P, et al. Effect of subcutaneous tirzepatide vs placebo added to titrated insulin glargine on glycemic control in patients with type 2 diabetes: the SURPASS-5 randomized clinical trial. *JAMA*. 2022;327:534-545.
97. Lind M, Hirsch IB, Tuomilehto J, et al. Liraglutide in people treated for type 2 diabetes with multiple daily insulin injections: randomised clinical trial (MDI Liraglutide trial). *BMJ*. 2015;351:h5364.
98. Rodbard HW, Lingvay I, Reed J, et al. Semaglutide added to basal insulin in type 2 diabetes (SUSTAIN 5): a randomized, controlled trial. *J Clin Endocrinol Metab*. 2018;103:2291-2301.
99. Rosenstock J, Nino A, Soffer J, et al. Impact of a weekly glucagon-like peptide 1 receptor agonist, albiglutide, on glycemic control and on reducing prandial insulin use in type 2 diabetes inadequately controlled on multiple insulin therapy: a randomized trial. *Diabetes Care*. 2020;43:2509-2518.
100. Daugirdas JT, Schneditz D. Hemodialysis ultrafiltration rate targets should be scaled to body surface area rather than to body weight. *Semin Dial*. 2017;30:15-19.
101. National Kidney Foundation, Daugirdas JT, Depner TA, Inrig J, et al. Kidney disease outcomes quality initiative: clinical practice guideline for hemodialysis adequacy: 2015 update. *Am J Kidney Dis*. 2015;66:884-930.
102. He L, Wang J, Ping F, et al. Association of glucagon-like peptide-1 receptor agonist use with risk of gallbladder and biliary diseases: a systematic review and meta-analysis of randomized clinical trials. *JAMA Intern Med*. 2022;182:513-519.
103. Katz PO, Dunbar KB, Schnoll-Sussman FH, et al. ACG clinical guideline for the diagnosis and management of gastroesophageal reflux disease. *Am J Gastroenterol*. 2022;117:27-56.
104. Hashash JG, Thompson CC, Wang AY. AGA rapid clinical practice update on the management of patients taking GLP-1 receptor agonists prior to endoscopy: communication. *Clin Gastroenterol Hepatol*. 2024;22:705-707.
105. American Gastroenterological Association. No data to support stopping GLP-1 agonists prior to elective endoscopy. Accessed December 2024. <https://gastro.org/news/gi-multi-society-statement-regarding-glp-1-agonists-and-endoscopy/>
106. Abu-Freha N, Yitzhak A, Shirin H, et al. Glucagon-like peptide-1 receptor agonists significantly affect the quality of bowel preparation for colonoscopy. *Endoscopy*. 2025;57:126-133.
107. Novo Nordisk. Ozempic (semaglutide) [package insert]. Accessed December 2024. <https://www.novo-pi.com/ozempic.pdf>
108. Apovian CM, Bruno CD, Kyle TK, et al. Incomplete data and potential risks of drugs in people with obesity. *Curr Obes Rep*. 2023;12:429-438.
109. Sanofi. Lovenox (enoxaparin sodium) [package insert]. Accessed December 2024. <https://products.sanofi.us/lovenox/lovenox.pdf>
110. Kindel TL, Wang AY, Wadhwa A, et al. Multisociety clinical practice guidance for the safe use of glucagon-like peptide-1 receptor agonists in the perioperative period. *Surg Obes Relat Dis*. 2024;20:1183-1186.
111. Mizubuti GB, Ho AM, Silva LMD, et al. Perioperative management of patients on glucagon-like peptide-1 receptor agonists. *Curr Opin Anaesthesiol*. 2024;37:323-333.
112. Prado CM, Phillips SM, Gonzalez MC, et al. Muscle matters: the effects of medically induced weight loss on skeletal muscle. *Lancet Diabetes Endocrinol*. 2024;12:785-787.
113. Rubino F, Puhl RM, Cummings DE, et al. Joint international consensus statement for ending stigma of obesity. *Nat Med*. 2020;26:485-497.
114. Fitch AK, Bays HE. Obesity definition, diagnosis, bias, standard operating procedures (SOPs), and telehealth: An Obesity Medicine Association (OMA) Clinical Practice Statement (CPS) 2022. *Obes Pillars*. 2022;1:100004.
115. Beavers CJ, Bagai J. Moderate sedation practices for adult patients in the cardiac catheterization laboratory (CCL). Accessed December 2024. <https://scai.org/moderate-sedation-practices-adult-patients-cardiac-catheterization-laboratoryccl>
116. Bianchetti RG, Lavie CJ, Lopez-Jimenez F. Challenges in cardiovascular evaluation and management of obese patients: JACC State-of-the-Art Review. *J Am Coll Cardiol*. 2023;81:490-504.
117. Gerstein NS, Young A, Schulman PM, Stecker EC, Jessel PM. Sedation in the electrophysiology laboratory: a multidisciplinary review. *J Am Heart Assoc*. 2016;5(6):e003629. <https://doi.org/10.1161/JAHA.116.003629>
118. Madder RD, VanOosterhout S, Mulder A, et al. Patient body mass index and physician radiation dose during coronary angiography. *Circ Cardiovasc Interv*. 2019;12:e006823.
119. Plourde G, Pancholy SB, Nolan J, et al. Radiation exposure in relation to the arterial access site used for diagnostic coronary angiography and percutaneous coronary intervention: a systematic review and meta-analysis. *Lancet*. 2015;386:2192-2203.
120. Refahiyat L, VanOosterhout S, Pageau S, et al. Patient body mass index and occupational radiation doses to circulating nurses during coronary angiography. *Cardiovasc Revasc Med*. 2021;26:48-52.
121. Singh M, Sethi A, Mishra AK, et al. Echocardiographic imaging challenges in obesity: guideline recommendations and limitations of adjusting to body size. *J Am Heart Assoc*. 2020;9:e014609.
122. American Diabetes Association Professional Practice Committee, Elsayed NA, Aleppo G, Bannuru RR, et al. Diagnosis and classification of diabetes: standards of care in diabetes-2024. *Diabetes Care*. 2024;47(suppl 1):S20-S42.
123. Tchang BG, Saunders KH, Igel LI. Best practices in the management of overweight and obesity. *Medical Clinics of North America*. 2021;105:149-174.
124. Rubino D, Abrahamsson N, Davies M, et al. Effect of continued weekly subcutaneous semaglutide vs placebo on weight loss maintenance in adults with overweight or obesity (STEP 4). *JAMA*. 2021;325:1414.

125. Apolzan JW, Venditti EM, Edelstein SL, et al. Long-term weight loss with metformin or lifestyle intervention in the Diabetes Prevention Program (DPP) Outcomes Study (DPPOS). *Ann Intern Med.* 2019;170:682–690.
126. Karakus KE, Shah VN, Akturk HK. Tirzepatide-induced rapid weight loss-related thyrotoxicosis. *JAMA Intern Med.* 2024;184:1246–1247.
127. Malhotra A, Bednarik J, Chakladar S, et al. Tirzepatide for the treatment of obstructive sleep apnea: Rationale, design, and sample baseline characteristics of the SURMOUNT -OSA phase 3 trial. *Contemp Clin Trials.* 2024;141:107516.
128. Yurista SR, Eder RA, Feeley M, et al. A closer look at ACC/AHA and ESC guidelines for managing obesity and overweight in adults. *JACC Adv.* 2023;2:100570.
129. Olateju IV, Ogwu D, Owolabi MO, et al. Role of behavioral interventions in the management of obesity. *Cureus.* 2021;13:e18080.
130. Alencar M, Johnson K, Gray V, et al. Telehealth-based health coaching increases m-health device adherence and rate of weight loss in obese participants. *Telemed J E Health.* 2020;26:365–368.
131. Johnson KE, Alencar MK, Coakley KE, et al. Telemedicine-based health coaching is effective for inducing weight loss and improving metabolic markers. *Telemed J E Health.* 2019;25:85–92.
132. Francis BR, Challen LM. The impact of a clinical pharmacist in an interdisciplinary weight loss service: a follow-up study. *Innov Pharm.* 2021;12(4). <https://doi.org/10.24926/iip.v12i4.4356>
133. Vokinger KN, Nussli E, Dusetzina SB. Access to GLP-1 weight loss drugs in the US, Canada, Switzerland, and Germany. *JAMA Intern Med.* 2024;184:1002–1004.
134. Congressional Research Service. Medicare coverage of GLP-1 drugs. Accessed December 2024. <https://crsreports.congress.gov/product/pdf/IF/IF12758>
135. Gomez Lumbreras A, Tan MS, Villa-Zapata L, et al. Cost-effectiveness analysis of five anti-obesity medications from a US payer's perspective. *Nutr Metab Cardiovasc Dis.* 2023;33:1268–1276.
136. Neumiller JJ, Bajaj M, Bannuru RR, et al. Compounded GLP-1 and dual GIP/GLP-1 receptor agonists: a statement from the American Diabetes Association. *Diabetes Care.* 2025;48:177–181.
137. Obesity Action Coalition. Advocacy, what we fight for. Accessed February 2025. <https://www.obesityaction.org/advocacy/what-we-fight-for/>

KEY WORDS GIP, GLP-1, NuSH, obesity, weight management

APPENDIX 1. AUTHOR RELATIONSHIPS WITH INDUSTRY AND OTHER ENTITIES (RELEVANT)—2025 CONCISE CLINICAL GUIDANCE: AN ACC EXPERT CONSENSUS STATEMENT ON MEDICAL WEIGHT MANAGEMENT FOR OPTIMIZATION OF CARDIOVASCULAR HEALTH

Committee Member	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Olivia Gilbert (Chair)	Wake Forest University School of Medicine—Associate Professor	None	None	None	None	None	None
Martha Gulati (Vice Chair)	Smidt Heart Institute, Cedars-Sinai Medical Center—Director of Prevention & Associate Director of the Barbra Streisand Women's Heart Center	■ Esperion Therapeutics ■ NewAmsterdam Pharma ■ Medtronic* ■ Boehringer Ingelheim Pharmaceuticals ■ Eli Lilly	None	None	■ Merck & Co. (DSMB)	None	None
Ty J. Gluckman	Providence Heart Institute—Medical Director, Center for Cardiovascular Analytics, Research, and Data Science	None	None	None	None	None	None
Michelle M. Kittleson	Smidt Heart Institute, Cedars-Sinai Medical Center—Professor of Medicine	None	None	None	None	None	None
Rishi Rikhi	Wake Forest University School of Medicine—Cardiology Fellow	None	None	None	None	None	None
Joseph J. Saseen	University of Colorado Anschutz—Professor and Associate Dean	None	None	None	■ Amgen (DSMB)	None	None
Beverly G. Tchang	Weill Cornell Medical College, Cornell University—Assistant Professor of Clinical Medicine	■ Novo Nordisk* ■ Roman Health Ventures*	None	None	■ KVK TECH (DSMB)	None	None

This table represents the relationships of committee members with industry and other entities that were determined to be relevant to this document. These relationships were reviewed and updated in conjunction with all meetings and/or conference calls of the writing committee during the document development process. The table does not necessarily reflect relationships with industry at the time of publication. A person is deemed to have a significant interest in a business if the interest represents ownership of $\geq 5\%$ of the voting stock or share of the business entity or ownership of $\geq \$5,000$ of the fair market value of the business entity; or if funds received by the person from the business entity exceed 5% of the person's gross income for the previous year. Relationships that exist with no financial benefit are also included for the purpose of transparency. Relationships in this table are modest unless otherwise noted. According to the ACC, a person has a relevant relationship IF: a) the relationship or interest relates to the same or similar subject matter, intellectual property or asset, topic, or issue addressed in the document; b) the company/ entity (with whom the relationship exists) makes a drug, drug class, or device addressed in the document or makes a competing drug or device addressed in the document; or c) the person or a member of the person's household, has a reasonable potential for financial, professional or other personal gain or loss as a result of the issues/content addressed in the document.

*Significant relationship.

ACC = American College of Cardiology; DSMB = Data Safety Monitoring Board.

APPENDIX 2. PEER REVIEWER RELATIONSHIPS WITH INDUSTRY AND OTHER ENTITIES (COMPREHENSIVE)—2025 CONCISE CLINICAL GUIDANCE: AN ACC EXPERT CONSENSUS STATEMENT ON WEIGHT MANAGEMENT FOR OPTIMIZATION OF CARDIOVASCULAR HEALTH

Peer Reviewer	Representation	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Craig Beavers	Content Reviewer—ACC Expert	University of Kentucky—Assistant Adjunct Professor	None	None	None	None	None	None
Nicole Bhavé	Content Reviewer—ACC Expert	University of Michigan—Clinical Professor	None	None	■ Doximity ■ Rednvia	None	None	None
Robert Kushner	Content Reviewer—ACC Expert	Northwestern University—Medical Director, Wellness Institute	■ Antag ■ AstraZeneca Pharmaceuticals ■ Boehringer Ingelheim Pharmaceuticals* ■ Currax* ■ Eli Lilly and Company* ■ Novo Nordisk* ■ Regeneron ■ Structure ■ Weight Watchers*	None	None	None	None	None
Michael Shapiro	Content Reviewer—ACC Expert	Wake Forest University School of Medicine—Professor of Cardiology and Molecular Medicine	■ Aidoc ■ Novartis Corporation* ■ Amgen ■ Arrowhead ■ Merck & Co. ■ NewAmsterdam ■ Ionis ■ Regeneron*	None	None	None	■ American Society of Pre-ventive Cardiology† ■ ACCLAIM, Eli Lilly and Company† ■ BROOKLYN, New Amsterdam† ■ CLEAR-PATH, Esperion† ■ CORE Study, Ionis† ■ MK-0616-015 and-017 Studies, Merck & Co† ■ MUIR-3, Arrowhead† ■ OCEAN(a), Amgen† ■ ORION-16, Novartis Corporation† ■ PREVAIL, New Amsterdam† ■ PREVENTABLE, National Institutes of Health† ■ TRANSFORM, Cleerly† ■ Victorion 1-PREVENT, Novartis Corporation† ■ Victorion 2-PREVENT, Novartis Corporation†	None
Barbara Wiggins	Official Reviewer—Solution Set Oversight Committee	scPharmaceuticals—Regional Medical Lead	None	None	None	None	None	None

This table represents all relationships of reviewers with industry and other entities that were reported by reviewers, including those not deemed to be relevant to this document, at the time this document was under development. The table does not necessarily reflect relationships with industry at the time of publication. A person is deemed to have a significant interest in a business if the interest represents ownership of $\geq 5\%$ of the voting stock or share of the business entity, or ownership of $\geq \$5,000$ of the fair market value of the business entity; or if funds received by the person from the business entity exceed 5% of the person's gross income for the previous year. Relationships that exist with no financial benefit are also included for the purpose of transparency. Relationships in this table are modest unless otherwise noted. Please refer to <https://www.acc.org/Guidelines/About-Guidelines-and-Clinical-Documents/Relationships-with-Industry-Policy> for definitions of disclosure categories or additional information about the ACC Disclosure Policy for Writing Committees.

*Significant relationship.

†No financial benefit.

‡Relationship with this company is limited to enrolling patients in clinical trials. This disclosure was entered under the Clinical Trial Enroller category in the ACC's disclosure system. To appear in this category, the author acknowledges that there is no direct or institutional relationship with the trial sponsor as defined in the ACC Disclosure Policy for Writing Committees.

ACC = American College of Cardiology.

APPENDIX 3. ABBREVIATIONS

ACC = American College of Cardiology

BMI = body mass index

CVD = cardiovascular disease

FDA = U.S. Food and Drug Administration

GIP = glucose-dependent insulintropic polypeptide

GLP-1 = glucagon-like peptide-1

HFpEF = heart failure with preserved ejection fraction

NuSH = nutrient-stimulated hormone

T2DM = type 2 diabetes mellitus