VA/DOD CLINICAL PRACTICE GUIDELINE FOR THE MANAGEMENT OF ADULT OVERWEIGHT AND OBESITY

Department of Veterans Affairs

Department of Defense

QUALIFYING STATEMENTS

The Department of Veterans Affairs (VA) and the Department of Defense (DOD) guidelines are based on the best information available at the time of publication. The guidelines are designed to provide information and assist decision making. They are not intended to define a standard of care and should not be construed as one. Neither should they be interpreted as prescribing an exclusive course of management.

This clinical practice guideline (CPG) is based on a systematic review of both clinical and epidemiological evidence. Developed by a panel of multidisciplinary experts, it provides a clear explanation of the logical relationships between various care options and health outcomes while rating both the quality of the evidence and the strength of the recommendation.

Variations in practice will inevitably and appropriately occur when providers consider the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Therefore, every health care professional using these guidelines is responsible for evaluating the appropriateness of applying them in the setting of any clinical situation with a patient-centered approach.

These guidelines are not intended to represent VA or DOD policies. Further, the inclusion of recommendations for specific testing, therapeutic interventions, or both within these guidelines does not guarantee coverage of civilian sector care.

Version 4.0 – 2025

Prepared by

The Management of Overweight and Obesity in Adults Work Group

With support from

Office of Quality and Patient Safety, Veterans Health Administration

And

Clinical Quality Improvement Program, Defense Health Agency

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[1] VA/DOD Clinical Practice Guideline. (2025). Management of Overweight and Obesity in Adults Work Group. Washington, DC: U.S. Government Printing Office.

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I. Introduction

The Department of Veterans Affairs (VA) and Department of Defense (DOD) Evidence Based Practice Work Group (EBPWG) was established and first chartered in 2004. Its mission is to advise the "…Health Executive Council on the use of clinical and epidemiological evidence to improve the health of the population across the Veterans Health Administration and Military Health System," by facilitating the development of clinical practice guidelines (CPGs) for the VA and DOD populations.(4) The development and update of VA/DOD CPGs is funded by VA Evidence Based Practice, Office of Quality and Patient Safety. The system-wide goal of evidence-based CPGs is to improve patient health and well-being.

In 2020, the VA and DOD updated the 2014 CPG for the Management of Adult Overweight and Obesity (2020 OBE CPG), based on evidence reviewed from February 1, 2013, to April 8, 2019. Since the release of the 2020 OBE CPG, the evidence base has expanded. Consequently, an update was recommended in 2024. This updated CPG uses the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach, reflecting a rigorous application of the methodology.(5) Therefore, the strength of some recommendations may have been modified based on the confidence in the quality of the supporting evidence (see Evidence Quality and Recommendation Strength).

The updated 2025 VA/DOD CPG for the Management of Overweight and Obesity in Adults includes objective, evidence-based information on managing overweight and obesity. Successful implementation of this CPG will assist providers in:

- Assessing the patient's condition and, in collaboration with the patient, determining the most appropriate therapeutic plan;
- Optimizing each patient's functional independence, health outcomes, and quality of life.
- Minimizing preventable complications and morbidity; and
- Emphasizing the use of patient-centered care.

II. Background

A. Epidemiology, Physiology, and Impact in the General Population

Overweight and obesity affect approximately 75% of U.S. adults.(6) Obesity alone affects 40% of U.S. adults and is projected to rise to 50% by 2030.(7) Obesity is a chronic, relapsing, multifactorial, neurobehavioral disease. It is characterized by an excessive increase and storage of body fat, which leads to adverse metabolic, biomechanical, and psychosocial health consequences.(8,9) Obesity is also characterized by brain and hormonal dysfunctions that impair metabolism and increase appetite, leading to abnormal weight gain and regain after weight loss, often despite efforts to apply and maintain lifestyle modifications.(10) Effective treatment requires an individualized and comprehensive approach, including lifestyle interventions, obesity medications, and/or endoscopic and surgical bariatric procedures. Recognizing obesity as a disease is crucial for de-stigmatization and effective management, as it is associated with serious

health consequences, including cardiovascular diseases, diabetes, musculoskeletal disorders, and cancer, among others.(11)

The Physiology and Diagnosis of Obesity

Obesity is defined as a chronic, relapsing, multifactorial disease characterized by abnormal or excessive adipose tissue accumulation that impairs health and increases the risk of comorbidities and premature mortality. The causes of obesity are multifactorial and include genetic susceptibility, environmental and social determinants, behavioral patterns, and physiological dysregulation of multiple systems, including neuroendocrine signaling, metabolism, and inflammation. The imbalance between energy intake and energy expenditure leads to the accumulation of excessive adiposity.(12-15)

Weight regulation is governed by complex neuroendocrine mechanisms and adaptive physiological responses. While caloric restriction and increased energy expenditure can initially produce weight loss, these efforts trigger compensatory hormonal changes: levels of the hunger-promoting hormone ghrelin rise, while satiety hormones such as leptin, peptide YY (PYY), cholecystokinin (CCK), and glucagon-like peptide-1 (GLP-1) decrease.(16) These hormonal shifts increase appetite and reduce feelings of fullness. At the same time, resting and total energy expenditure may decline disproportionately relative to the loss of body mass, a phenomenon known as adaptive thermogenesis or metabolic adaptation, but whether this disproportionate reduction in metabolism occurs or even hinders weight loss is controversial.(17) This altered physiological state promotes weight regain, making long-term weight loss maintenance particularly difficult. Together, these processes underscore the biological challenges in managing obesity. However, evidence shows that comprehensive lifestyle interventions (CLI) plus obesity pharmacotherapy and metabolic/bariatric surgery when indicated, can counteract these adaptive responses and support sustained weight reduction.(8) Individualized, comprehensive treatment not only improves the durability of weight loss but also yields meaningful improvements in cardiometabolic health, physical function, and quality of life.(18)

The most used screening tool for overweight and obesity is the Body Mass Index (BMI), calculated as weight in kilograms divided by height in meters squared (kg/m^2), because it is low-cost, easy to use, scalable, and convenient.(19)

From a public health and epidemiological standpoint, BMI is linked to many health outcomes, including health costs, morbidity, and mortality. At the population level, BMI correlates with the risk of developing adiposity-related health conditions. However, despite BMI being the primary method for diagnosis and staging, it has limitations in differentiating between body fat, lean muscle mass, and body fat distribution, making it less accurate at the individual level for predicting health risk.(20) Therefore, BMI should be used as a screening tool, but not alone to diagnose obesity.

Anthropometric measurements such as waist circumference (WC) and waist-to-hip ratio are commonly used surrogate markers of abdominal or visceral fat. Epidemiological evidence links these indices to increased cardiometabolic risk and higher body fat percentage. However, their performance can vary across different populations and sexes. Additionally, they cannot reliably distinguish visceral fat from subcutaneous fat on an individual level. Despite these limitations, these measurements are more accurate than BMI in identifying increased adiposity and

individuals at higher risk of obesity-related complications, especially when combined with BMI, making them useful tools for early intervention.(11,21)

Other advanced body composition imaging modalities (e.g., bioelectrical impedance analysis [BIA], dual-energy x-ray absorptiometry scan [DXA], and magnetic resonance imaging [MRI]) are more specific in identifying visceral adiposity and cardiometabolic risk. However, while imaging technologies offer enhanced precision, they can increase cost, be more time-consuming, and be impractical in routine clinical settings or on the scale required for population health management.(22)

Consequently, from a clinical standpoint, the integration of BMI and anthropometric measurements can help identify phenotypes that may have a higher risk of developing obesity or obesity-related complications.

Obesity-Related Complications

Obesity is linked to more than 200 chronic health conditions and is associated with reduced quality of life (QoL) and decreased lifespan and health span, particularly in Class 2 and Class 3 obesity (see Table O-1).(23-26) The relationship between BMI and mortality follows a J-shaped or U-shaped curve, suggesting that mortality is highest at both extremes of BMI, with the lowest risk observed at a BMI between 22 – 24 kg/m^2.(26,27) Earlier studies that suggested overweight conferred a survival advantage were confounded by factors such as smoking, preexisting illness, and limited follow-up duration.(24,26)

Overweight and obesity are major risk factors for numerous conditions, including type 2 diabetes mellitus (T2DM), hypertension (HTN), dyslipidemia, metabolic syndrome, osteoarthritis, obstructive sleep apnea (OSA), depression, metabolic dysfunction-associated steatotic liver disease (MASLD), Alzheimer's disease, and various cancers.(2,28-32) The pathophysiology of obesity-related diseases includes two primary mechanisms: adiposopathy (dysfunctional fat tissue) and fat mass effects (mechanical burden). Adipose tissue is now recognized as a complex, highly active metabolic and endocrine organ, rather than just an energy storage site. It consists of adipocytes, connective tissue matrix, nerve tissue, stromovascular cells, and immune cells, all functioning as an integrated unit. Adipose tissue responds to signals from traditional hormone systems and the central nervous system while also secreting key endocrine factors such as leptin, adiponectin, TNF-α, IL-6, MCP-1, plasminogen activator inhibitor-1, and resistin, which regulate metabolism, inflammation, and cardiovascular function.

Adiposopathy occurs when excess adipose tissue becomes dysfunctional, driving a chronic inflammatory state that promotes insulin resistance, dyslipidemia, and cardiovascular disease, especially via excess visceral fat. In parallel, the mechanical effects of increased fat mass further contribute to disease by exerting mechanical stress on organs and joints, leading to conditions such as osteoarthritis, lymphedema, obstructive sleep apnea, and gastroesophageal reflux disease. Together, these mechanisms highlight how obesity is not just a matter of excess weight but a complex, disease-promoting condition affecting multiple organ systems.(33,34)

There are strong connections between excess weight and the development of many chronic medical conditions and cardiovascular risk factors. The Framingham Heart Study indicated a strong link between obesity and essential hypertension, attributing 78% of cases in men and 65%

in women to obesity.(35) The duration of obesity also plays a significant role in blood pressure. A study in Mauritius, a country in the Indian Ocean,(36) found that a one standard deviation (SD) increase in BMI over five years was associated with a 30% higher risk of hypertension compared to individuals with stable weight. Long-term impact is also evident, as young adults with obesity in the Johns Hopkins Precursors Study had a threefold higher risk of hypertension 46 years later, regardless of later lifestyle changes.(37) Large epidemiologic studies in the United States demonstrate that the prevalence of type 2 diabetes increases with increasing obesity class: among adults with class 1 obesity (BMI 30.0–34.9 kg/m²), prevalence is approximately 18–20%, rising to about 43% in those with class 3 obesity (BMI ≥40 kg/m²).(38) Adults with obesity were four times as likely to have T2DM, and the Centers for Disease Control and Prevention (CDC) estimates that 9 out of 10 people with diagnosed T2DM have overweight or obesity.(39) Cardiovascular disease (CVD) accounts for 67.5% of deaths globally, with more than one-third of these deaths in persons with overweight.(40) Dyslipidemia affects 60-70% of adults with obesity (41) and is a major contributor to mortality and disability-adjusted life years (DALY)(41). The development or worsening of T2DM, HTN, and dyslipidemia is particularly hazardous due to their independent effects on risk for coronary artery disease and stroke. CVD is the leading cause of death among individuals with a high BMI and a major contributor to mortality and DALY.(13,41-43)

Obesity is also a leading contributor to MASLD, the most common cause of chronic liver disease, and a growing indication for liver transplantation. Prevalence is projected to reach 41.4% by 2050, accompanied by dramatic increases in cirrhosis, liver cancer, and transplant need. (44,45) A recent study analyzing trends in the United States found MASLD-related age-standardized mortality rates (ASMRs) increased from 0.25 to 1.27 per 100,000 persons between 2006 and 2023, and ASMRs will continue to rise, reaching 2.24 per 100,000 by 2040, disproportionately impacting older adults, non-Hispanic Whites, and Hispanic individuals.(46)

Obesity is the second most preventable cause of cancer in smokers and the leading cause of cancer in nonsmokers.(3) The National Cancer Institute reports that overweight and obesity are associated with at least 13 types of cancer, accounting for 4.7% of new cases in men and 9.6% of new cases in women.(2) Obesity can negatively impact cancer survivorship, including quality of life, risk of recurrence, disease progression, overall prognosis, and the likelihood of developing second primary cancers. A meta-analysis of over 6.3 million participants found that obesity is associated with increased overall and cancer-specific mortality, particularly in breast, colon, and uterine cancers. However, patients with obesity and renal cell carcinoma, lung cancer, or melanoma had better survival rates, possibly due to factors like the poor health status of individuals with very low BMI or the association of weight loss with frailty and smoking. These findings suggest that obesity generally worsens cancer prognosis, though certain cancers may show improved survival in patients with obesity.(47) Observational studies suggest that intentional weight loss is linked to a reduced risk of breast, endometrial, colon, and prostate cancers, likely due to decreases in hormone levels such as insulin, estrogens, and androgens, which are known to contribute to cancer risk.(48) Bariatric surgery, in particular, is associated with reduced cancer incidence and improved survival in individuals with obesity.(49)

Individuals with obesity consistently report lower health-related quality of life (HRQoL) scores, particularly in physical domains such as mobility, pain, and ability to perform usual activities, compared to those with normal weight. Obesity is also associated with increased prevalence of chronic pain, fatigue, insomnia, and reduced physical and psychological working ability,

independent of comorbidities. The adverse effects on quality of life persist even after adjusting for obesity-related comorbidities such as diabetes, hypertension, and osteoarthritis, indicating that high BMI itself is an independent risk factor for reduced well-being.(50,51) Individuals with overweight and obesity perceive or experience stigma and discrimination across multiple domains, including employment, healthcare, and media representation.(52) Beyond personal suffering, obesity imposes substantial financial burdens. From 2001 to 2015, expenditures related to obesity rose by nearly 30% and continue to rise.(53) In 2019, adults with obesity and overweight incurred $1,861 and $600 more in annual medical expenses, respectively, than those with a healthy weight. This figure rose to $3,097 for adults with severe obesity defined by a BMI greater than or equal to 35.(54) Obesity was estimated to cost $260 billion in annual health care spending and is projected to grow to more than $385 billion in 2024.(55) Indirect costs from increased absenteeism from work, reduced productivity while at work (presenteeism), and higher rates of disability have been estimated at over $250 billion per year.(56)

B. Overweight and Obesity in the Department of Defense and the Department of Veterans Affairs Populations and its Impact

Overweight and obesity may be a threat to national security. A recent report indicated that as of 2020, approximately 77% of young adults ages 17-24 were disqualified from military service. 36% were disqualified due to their weight, and of those, 11% were disqualified based on weight alone, and 25% were disqualified due to weight and another factor.(57) This problem will only get worse as 50% of U.S. adults are predicted to have obesity by 2030.(58)

The active-duty military and Veteran population have been similarly affected by increases in obesity. In 2002, less than 8% of active-duty Service members had a BMI within the obesity range.(57) In 2022, this number increased to 21.6% with 68% classified as having overweight or obesity according to the DOD's Health of the Force 2022 Report, which provides an evidence-based portrait of the health and well-being of U.S. Service Members.(59) This represents an increase from 2018, when the prevalence of obesity was 17%. Rates of obesity vary across branches of the Armed Services, including 11% (Marines), 21% (Army), 23% (Air Force), and 27% (Navy). Prevalence of obesity was highest in males and the age category of 35–44 years (32.5%). Obesity in the U.S. military is driven by a combination of biological, environmental, and systemic factors. While the military generally screens BMI and physical readiness at accession, waivers may be granted, particularly when applicants meet performance benchmarks despite elevated BMI. Additionally, some services offer preparatory courses to help interested recruits meet weight standards. For example, the Army's Future Soldier Preparatory Course permits prospective recruits who exceed the standard body fat percentage by up to 6%, based on age, sex, and height, to enroll in a structured 90-day program emphasizing physical training and nutritional guidance. Upon achieving a reduction to 2% above the Army's body fat standards, participants are eligible to advance to basic training, with the expectation of continued weight loss during basic training.(60) This has resulted in a higher number of Service members who start their careers already at risk for obesity-related conditions. Furthermore, the risk for weight regain following basic training is high due to high-stress environments, inconsistent sleep, poor dietary options, and decreased time for exercise. Obesity is complicated by genetic predispositions and neurobehavioral mechanisms that make sustained weight loss difficult. Despite these

complexities, military policies often frame obesity as a matter of discipline rather than health. Evidence dictates that obesity is a chronic disease requiring medical treatment and support.(61)

Millennium Cohort Study data from 2001-2008 found a doubling of obesity rates per BMI in Service members (10-20%) with statistically significant increased rates of hypertension, type 2 diabetes, obstructive sleep apnea, depression, and post-traumatic stress disorder.(62) Several analyses reported that Service members with obesity were 33-47% more likely to suffer musculoskeletal injuries(63,64), contributing to more than 3.6 million injuries that occurred among Service members between 2008 and 2017.(65) The consequences of obesity in active-duty Service members may negatively influence a range of operations related to recruitment, retention, resilience, readiness, and retirement.(66)

A growing prevalence imposes a substantial financial strain on the Department of Defense (DOD). A 2007 study estimated that TRICARE Prime spends $1.1 billion annually on obesity-related health care among active-duty and their dependents, along with an additional $61 million due to early separation from service and $103 million in lost workdays.(67) More recent data show that the cost burden has continued to rise, with obesity among active-duty Service members now estimated to exceed $1.65 billion annually, $1.25 billion in direct care costs, and $99 million in lost productivity from hospitalizations alone in 2023.(61)

Veterans

There is an increased prevalence of overweight or obesity among Veterans compared to the general U.S. population. In 2017, obesity prevalence ranged from 28% to 49% across 140 VHA facilities.(68) Veterans are 12% more likely to have overweight or obesity per data from 2003-2019.(69) In a retrospective study evaluating the BMI of Veterans enrolled within 90 days of military discharge and followed for 10 years, it was found that one-third of Veterans had a BMI in the overweight or obesity range upon enrollment, and after 10 years, more than 98% of the population had a weight gain of 22% to 40%.(70) The Veteran population also faces a heightened risk of obesity-related chronic diseases, including arthritis, diabetes mellitus, cancers, chronic heart disease, and kidney disease. Obesity has a profound impact on Veterans' physical health, increasing risk for chronic disease, while also negatively impacting mental health and quality of life.(71,72)

C. Impact of Weight Loss on Obesity-associated Conditions

Clinically meaningful weight loss has long been defined as 5% from baseline, as this threshold has been shown to improve glycemic control, triglyceride levels, blood pressure, and high-density lipoprotein cholesterol (HDL-c) levels. However, increasing evidence demonstrates that greater weight loss leads to progressively more substantial health benefits.(11,73-75) Weight loss of at least 10% is often required for meaningful improvements in obstructive sleep apnea and MASLD, while metabolic dysfunction-associated steatohepatitis (MASH) requires 10-40% weight loss to show improvements in liver inflammation and fibrosis.(75,76) For patients with type 2 diabetes, weight loss exceeding 15% is frequently associated with remission of diabetes.(11) Additionally, cardiovascular benefits, including reductions in hypertension, dyslipidemia, and cardiovascular events, are more pronounced with weight loss exceeding 10-15%.(11,73) In the realm of

reproductive health, at least 10% weight loss is often necessary to improve female infertility, whereas male hypogonadism shows improvements with 5-10% weight loss. Osteoarthritis benefits from at least 5-10% weight loss, while gastroesophageal reflux disease (GERD) typically requires 10% or more to see symptom relief.(11,73) While modest weight loss can improve metabolic markers and lower healthcare costs, greater weight loss leads to superior outcomes across multiple obesity-related conditions, reinforcing the importance of individualized weight loss goals beyond the traditional 5% benchmark.(77,78)

In this guideline, we selected weight loss as a critical outcome for evaluating weight management interventions for overweight and obesity, largely because most studies on lifestyle modifications, pharmacotherapy, and bariatric surgery use the magnitude of weight loss as a primary measure. However, as our understanding of obesity as a complex disease evolves, it is clear that the percentage of weight loss alone does not provide the full picture. Weight loss metrics fail to capture crucial changes in body composition, specifically, whether individuals are losing fat mass, muscle mass, or both. More importantly, the distribution of fat loss matters. The reduction of visceral fat, which is strongly linked to adiposopathy or dysfunctional fat tissue, is particularly important, as it drives chronic inflammation, insulin resistance, dyslipidemia, and cardiovascular disease. Future research should place greater emphasis on body composition and fat distribution to better assess the metabolic benefits of weight management interventions.

Additional information on assessment, clinical workflows, operational considerations in active-duty Service members, team-based roles, and suggested follow-up appears in Appendix O.

III. Scope of This Guideline

This CPG is based on clinical evidence and related information published from April 1, 2019, to January 6, 2025. It is intended to provide general guidance on evidence-based best practices (see Appendix A for additional information on the evidence review methodology). Although the CPG is intended to improve the quality of care and clinical outcomes (see Introduction), it is not intended to define a standard of care (i.e., mandated or strictly required care).

A. Guideline Audience

This CPG is designed to assist providers in managing or co-managing patients with overweight and/or obesity.

B. Guideline Population

This CPG is for adults with overweight and obesity.

IV. Highlighted Features of This Guideline

A. Highlights in This Guideline Update

The current document is an update to the 2020 VA/DOD OBE CPG. The major strength of this CPG is the coordination and collaboration of the multidisciplinary team, ensuring a broad

representation of providers engaged in overweight and obesity management. The following significant updates make it important that providers review this version of the CPG:

- Updated Algorithm;
- Updated Pharmacotherapy section;
- Recommendations: added 8 new, reviewed and replaced 4, reviewed and amended 7, and carried over 4 unchanged.

The methodology used in developing this CPG has been updated since the prior versions and reflects a more rigorous application of the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology. The result is a refined CPG that includes methodologically rigorous, evidence-based recommendations for the management of adults with overweight and/or obesity.

This CPG also provides expanded recommendations on research needed to strengthen future guidelines.

B. Components of This Guideline

This CPG provides clinical practice recommendations for the care of patients with overweight and obesity (see Recommendations). In addition, the Algorithm incorporates the recommendations in the context of the flow of patient care. This CPG also includes Research Priorities, which list areas the Work Group identified as needing additional research. To accompany this CPG, the Work Group also developed toolkit materials for providers and patients, including a provider summary, a patient summary, and a quick reference guide, which can be found at: https://www.healthquality.va.gov/index.asp.

C. Demographic and Other Terminology in This Guideline

The demographic terms in this guideline are based on the published literature sources included in the systematic review (SR) and evidence base. The Work Group used terms like Black rather than African American and White rather than Caucasian to avoid presumptions about ancestry and enhance clarity and consistency. In order to accurately present the research evidence on which this CPG is based, the Work Group made every effort to use the same terminology as reported in the published literature base of SRs, clinical trials, and other studies. Consequently, usage of demographic terms in this CPG may vary and appear inconsistent. For the purposes of this document, we have deliberately and consistently used the term “Obesity Medications” for medical clarity. This reflects the use of these medications in healthcare settings to address the disease of obesity. “Weight Management Medications,” however, is the preferred terminology for patient-centered communication and public health messaging to avoid stigmatizing language.

V. Guideline Development Team

The VA Evidence Based Practice, Office of Quality and Patient Safety, in collaboration with the Clinical Quality Improvement Program, Defense Health Agency, identified the following four providers to serve as Champions (i.e., leaders) of this CPG’s Work Group: Stéphanie B. Mayer,

MD, MHSc, Dipl. ABCL, Dipl. ABOM and Susan Raffa, PhD, FSBM from VA; and Elizabeth M. Bauer, MD, FACP, FACE Dipl. ABOM and Richele Corrado, DO, MPH, FACP, Dipl. ABOM from DOD. The Work Group comprised individuals with the following areas of expertise: bariatric surgery, behavioral medicine, dietetics, endocrinology, gastroenterology, medical nutrition therapy, mental health, nursing, obesity medicine, pharmacy, physical therapy, population health, preventive medicine, and primary care. Table 1 lists the Work Group and Guideline Development Team members.

This CPG Work Group, led by the Champions, was tasked with:

- Determining the scope of the CPG;
- Crafting clinically relevant key questions (KQ) to guide the systematic evidence review;
- Identifying discussion topics for the patient focus group and considering the patient perspective;
- Providing direction on inclusion and exclusion criteria for the systematic evidence review and the assessment of the level and quality of evidence; and
- Developing evidence-based clinical practice recommendations, including determining the strength and category of each recommendation.

The Sigma Team (Sigma Health Consulting and Duty First Consulting) was contracted by VA to help develop this CPG.

Table 1. Guideline Work Group and Guideline Development Team

Organization	Names*
Department of Veteran Affairs	**Stéphanie B. Mayer, MD, MHSc, Dipl. ABCL, Dipl. ABOM (Champion)**
	Susan Raffa, PhD, FSBM (Champion)
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	Erin J. Arra, MS, RDN, CSOWM, LD
	Dan Eisenberg, MD, MS
	Denise Gratias, MSN, ACNP
	Andrew Harris, MD
	Jenna Klimovich, MD
	Robin Masheb, PhD
	Natalia Weare-Regales, MD
Department of Defense	**Elizabeth M. Bauer, MD, FACP, FACE, Dipl. ABOM (Champion)**
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Clinical Quality Improvement Program Defense Health Agency	Jenifer Meno, DNP, FNP-BC, AMB-BC, NEA-BC, FAANP
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*Additional contributor contact information is available in Appendix D

VI. Summary of Guideline Development Methodology

The methodology used in developing this CPG follows the Guideline for Guidelines, an internal document of the VA/DOD EBPWG updated in January 2019 that outlines procedures for developing and submitting VA/DOD CPGs.(79) The Guideline for Guidelines is available at http://www.healthquality.va.gov/policy/index.asp. This CPG also aligns with the National Academy of Medicine's (NAM) principles of trustworthy CPGs (e.g., explanation of evidence quality and strength, management of potential conflicts of interest [COI], interdisciplinary stakeholder involvement, use of SR and external review).(80) Appendix A provides a detailed description of the CPG development methodology.

A. Evidence Quality and Recommendation Strength

The Work Group used the GRADE approach to craft each recommendation and determine its strength. Per the GRADE approach, recommendations must be evidence based and cannot be made based on expert opinion alone. The GRADE approach uses the following four domains to inform the strength of each recommendation (see Determining Recommendation Strength and Direction).(81)

1. Balance of desirable and undesirable outcomes
2. Confidence in the quality of the evidence
3. Patient or provider values and preferences

4. Other implications, as appropriate (e.g., resource use, equity, acceptability, feasibility, subgroup considerations)

Using these four domains, the Work Group determined the relative strength of each recommendation (*Strong or Weak*). The strength of a recommendation is defined as the extent to which one can be confident that the desirable effects of an intervention outweigh its undesirable effects and is based on the framework above, which incorporates the four domains.(82) A Strong recommendation generally indicates High or Moderate confidence in the quality of the available evidence, a clear difference in magnitude between the benefits and harms of an intervention, little variability in patient values and preferences, and limited concerns about the influence of other implications (e.g., resource use, feasibility).

In some instances, insufficient evidence exists on which to base a recommendation for or against a particular therapy, preventive measure, or other intervention. For example, the systematic evidence review might have found little or no relevant evidence, inconclusive evidence, or conflicting evidence for the intervention. The way this finding is expressed in the CPG might vary. In such instances, the Work Group might include among its set of recommendations a statement of insufficient evidence for an intervention that might be in common practice, although it is unsupported by clinical evidence, and particularly if other risks of continuing its use might exist (e.g., high opportunity cost, misallocation of resources). In other cases, the Work Group might decide to exclude this type of statement about an intervention. For example, the Work Group might remain silent where an absence of evidence occurs for a rarely used intervention. In other cases, an intervention might have a favorable balance of benefits and harms but might be a standard of care for which no recent evidence has been generated.

Using these elements, the Work Group determines the strength and direction of each recommendation and formulates the recommendation with the general corresponding text as shown in Table 2.

Table 2. Strength and Direction of Recommendations and General Corresponding Text

Recommendation Strength and Direction	General Corresponding Text
Strong for	We recommend…
Weak for	We suggest…
Neither for nor against	There is insufficient evidence to recommend for or against…
Weak against	We suggest against…
Strong against	We recommend against...

It is important to note that a recommendation's strength (i.e., Strong versus Weak) is distinct from its clinical importance (e.g., a Weak recommendation is evidence based and still important to clinical care). The strength of each recommendation is shown in Recommendations.

This CPG's use of GRADE reflects a more rigorous application of the methodology than previous iterations; the determination of the strength of the recommendation is more directly linked to the confidence in the quality of the evidence on outcomes that are critical to clinical decision making.

The confidence in the quality of the evidence is assessed using an objective, systematic approach independent of the clinical topic of interest. Therefore, recommendations on topics for which designing and conducting rigorous studies might be inherently more difficult (e.g., randomized controlled trials [RCT]) are typically supported by lower quality evidence and, in turn, Weak recommendations. Recommendations on topics for which rigorous studies can be designed and conducted might more often be Strong recommendations. Per GRADE, if the quality of evidence differs across the relevant critical outcomes, the lowest quality of evidence for any of the critical outcomes determines the overall quality of the evidence for a recommendation.(5,83) This stricter standard provides a consistent approach to determining recommendation strengths. For additional information on GRADE or CPG methodology, see Appendix A.

B. Categorization of Clinical Practice Guideline Recommendations

Evidence-based CPGs should be current. Except for an original version of a new CPG, staying current typically requires revision of a CPG's previous versions based on new evidence or as scheduled subject to time-based expirations.(84) For example, the U.S. Preventive Services Task Force (USPSTF) has a process for monitoring the emergence of new evidence that could prompt an update of its recommendations, and it aims to review each topic at least every five years for either an update or reaffirmation.(85)

Recommendation categories were used to track how the previous CPG's recommendations could be reconciled. These categories and their corresponding definitions are similar to those used by the National Institute for Health and Care Excellence (NICE, England).(86,87) Table 3 lists these categories, which are based on whether the evidence supporting a recommendation was systematically reviewed, the degree to which the previous CPG's recommendation was modified, and whether a previous CPG's recommendation is relevant in the updated CPG.

Additional information regarding these categories and their definitions can be found in Recommendation Categorization. The 2025 CPG recommendation categories can be found in Recommendations. Appendix C outlines the 2020 VA/DOD Overweight and Obesity CPG's recommendation categories.

Table 3. Recommendation Categories and Definitions*

Evidence Reviewed*	Recommendation Category*	Definition*
Reviewed	New-added	New recommendation following review of the evidence
	New-replaced	Recommendation from previous CPG that has been carried over to the updated CPG that has been changed following review of the evidence
	Not changed	Recommendation from previous CPG that has been carried forward to the updated CPG where the evidence has been reviewed but the recommendation is not changed
	Amended	Recommendation from the previous CPG that has been carried forward to the updated CPG where the evidence has been reviewed and a minor amendment has been made
	Deleted	Recommendation from the previous CPG that has been removed based on review of the evidence

Evidence Reviewed*	Recommendation Category*	Definition*
Not reviewed	Not changed	Recommendation from previous CPG that has been carried forward to the updated CPG, but for which the evidence has not been reviewed
	Amended	Recommendation from the previous CPG that has been carried forward to the updated CPG where the evidence has not been reviewed and a minor amendment has been made
	Deleted	Recommendation from the previous CPG that has been removed because it was deemed out of scope for the updated CPG

*Adapted from the NICE guideline manual (2012) (86) and Garcia, et al. (2014)(87)
Abbreviation: CPG: clinical practice guideline

C. Management of Potential or Actual Conflicts of Interest

Management of COIs for the CPGs is conducted as described in the Guideline for Guidelines.(79) Further, the Guideline for Guidelines refers to details in the VHA Handbook 1004.07 Financial Relationships between VHA Health Care Professionals and Industry (November 2014, issued by the VHA National Center for Ethics in Health Care)(88) as well as to disclosure statements (i.e., standard disclosure form completed at least twice by CPG Work Group members and the guideline development team).(79) The disclosure form inquiries regarding relevant financial and intellectual interests or other relationships with, for example, manufacturers of commercial products, providers of commercial services, or other commercial interests. The disclosure form also inquires regarding any other relationships or activities that could be perceived to have influenced, or that give the appearance of potentially influencing, a respondent's contributions to the CPG. In addition, instances of potential or actual COIs among the CPG Work Group and the guideline development team were subject to random web-based identification via standard electronic means (e.g., Centers for Medicare & Medicaid Services Open Payments, ProPublica).

D. Patient Perspective

When developing a CPG, consideration should be given to patient perspectives and experiences, which often vary from those of providers.(83) Focus groups can be used to help collect qualitative data on patient perspectives and experiences. VA and DOD Leadership arranged a virtual patient focus group on November 21, 2024. The focus group aimed to gain insights into patient perspectives of adult patients with overweight and/or obesity who have received care in the VA and DOD healthcare systems and incorporate these insights into the CPG, as appropriate. Topics discussed included screening and management of overweight and obesity in the VA and DOD healthcare systems, including patients' weight loss treatment history, preferences for care delivery setting and transitions, priorities and treatment challenges, as well as the impact their weight and treatment have had on their lives.

The Patient Focus Group, which may include up to nine patients (i.e., subject to the Paperwork Reduction Act), was comprised of a convenience sample of five participants, which included four women and one man. Participants were mixed in terms of receiving care from VA or DOD, with one participant also receiving care from Kaiser Permanente. The participants were also mixed in terms of being active-duty Service members and Veterans. Three participants reported receiving

treatments in the form of obesity medications, starting within the last two years. For more information on the patient focus group methods and findings, see Appendix E. The patient focus group participants were provided with the opportunity to review the final draft of this CPG and provide additional feedback.

E. External Peer Review

The Work Group drafted, reviewed, and edited this CPG using an iterative process. For more information, see Drafting and Finalizing the Guideline. Once the Work Group members completed a near-final draft, they identified experts from VA and DOD health care systems and outside organizations generally viewed as experts in the respective field to review it. The draft was sent to those experts for a 14-business-day review and comment period. The Work Group considered all feedback from the peer reviewers and modified the CPG where justified, in accordance with the evidence. Detailed information on the external peer review can be provided by the VA Office of Quality and Patient Safety.

F. Implementation

This CPG is intended for adaptation by individual healthcare providers, considering local services, resources, and capacity (professional, administrative, and logistical). The algorithm serves to inform providers of key decision points throughout the complex long-term management of overweight and obesity; both of these chronic medical conditions require long-term management with similar resource allocation to other chronic illnesses, such as diabetes and HTN.

The Work Group aims to widely disseminate these evidence-based weight management recommendations to improve the health and well-being of Veterans and Service members. To this end, the Work Group has produced supplemental educational materials: a provider summary and pocket card for practitioners, and a patient summary for patients.

The VA and DOD have specific plans for the dissemination and implementation of CPGs. This CPG is sent to several focused email groups within the VA and DOD systems for dissemination. Newly released CPGs are presented on quarterly calls to chief medical officers nationally within the VA system. VA/DOD CPGs are presented at various national professional society conferences and published in respected peer-reviewed medical journals. CPGs are posted to national/international guideline clearinghouses, available free of charge, and submitted to frequently consulted online medical resources, including epocrates® and UpToDate®, to broaden dissemination.

The CPG aims to inform the VA and DOD about the efficacy of combined weight loss tools, specifically comprehensive lifestyle intervention programs (e.g., VA's MOVE!® Weight Management Program for Veterans [MOVE!], pharmacologic treatments, and metabolic/bariatric surgical interventions. Nationwide harmonization of these weight loss interventions across VA and DOD healthcare facilities will improve quality of life and reduce obesity-related conditions for Veterans and Service Members.

Operationalization of these recommendations to achieve efficient coordinated management of overweight and obesity across the system nationally and across service lines is of great

importance. We must first establish that the management of overweight and obesity is an organization-wide priority and allocate adequate resources to effectively treat Service members and Veterans with overweight/obesity, particularly as therapeutic interventions continue to evolve. Next is the need to track patient, program, and population-level achievement of clinically meaningful outcomes. System-wide integration will ensure access to overweight and obesity care across VA and the DOD. This integration will promote effective care coordination, stratification by level of patient risk, and patient engagement strategies. System-wide integration is clearly needed to implement an evidence-based, multicomponent approach to weight management.(89)

Although this CPG represents the recommended practices on the date of its publication, medical practice is evolving and requires ongoing awareness by providers and policymakers alike of newly published information. New technology and additional research will improve patient care in the future. This CPG can assist in identifying priority areas for research and informing the optimal allocation of resources. Future studies examining the results of CPG implementation may lead to the development of new evidence, particularly relevant to clinical practice and resource allocation.

VII. Approach to Care in the Department of Veterans Affairs and the Department of Defense

A. Patient-Centered Care

Intended to consider patient needs and preferences, guideline recommendations represent a whole/holistic health approach to care that is patient-centered, culturally appropriate, and available to people with varied literacy skills and physical, sensory, or learning abilities. VA/DOD CPGs encourage providers to use a patient-centered, whole/holistic health approach (i.e., individualized treatment based on patient needs, characteristics, values, and preferences). This approach aims to treat the condition while optimizing the individual's overall health and well-being.

Regardless of the care setting, all patients should have access to individualized, evidence-based care. Patient-centered care can decrease patient anxiety, increase trust in providers, and improve treatment adherence.(90,91) A whole/holistic health approach (https:/www.va.gov/wholehealth/) empowers and equips individuals to meet their personal health and wellbeing goals. Good communication is essential and should be supported by evidence-based information tailored to each patient's needs. An empathetic and non-judgmental approach facilitates discussions sensitive to sex, culture, ethnicity, and other differences. The 5 As of obesity management (see Table 4) is a structured, patient-centered framework for effective communication about obesity care adapted from behavioral counseling models. This approach helps clinicians engage patients in respectful, nonjudgmental conversations about weight, assess health risks and contributing factors, provide clear and personalized treatment recommendations, set collaborative goals, and ensure appropriate support and follow-up. Using the 5 As aligns obesity care with chronic disease management principles, promotes shared decision-making, and supports individualized, evidence-based treatment plans to improve health outcomes.

Table 4. The 5 As Framework of Obesity Management (92)

Action	Step	Description / Clinical Focus	Example Clinical Prompts
ASK	Ask permission to discuss weight	Respectfully initiate the conversation in a nonjudgmental, patient-centered way.	"Would it be okay if we talked about how your weight may be affecting your health and what options you might consider?"
ASSESS	Assess BMI, waist circumference and obesity stage Evaluate health status, drivers, and barriers	Evaluate weight history, adiposity measures, obesity stage, comorbidities, lifestyle habits, medications, psychosocial factors, and readiness to change.	"Can you tell me about changes in your weight over time?" "Let's look at how your sleep, stress, and medications might be contributing."

ADVISE	Advise on health risks and treatment options	Provide clear, evidence-based information about the health impact of obesity and available treatment options tailored to disease severity.	"A 5–10% weight reduction could help improve your blood pressure and sleep apnea. Here are some treatment approaches we could consider."
AGREE	Agree on goals, behavioral changes, and a care plan	Collaboratively set realistic goals and develop a personalized care plan based on the patient's values, preferences, and readiness.	"What's a health goal that feels most important to you right now?" "Would it feel manageable to start with meal planning or walking after work?"
ASSIST/ARRANGE	Assist in identifying and navigating barriers; Assist with resources and arrange follow-up	Provide tools, referrals, medications, and support. Help patients navigate barriers and ensure regular follow-up to monitor progress and adapt the plan.	"Let's refer you to the weight management program, and I'll follow up in a couple of months to check in. We can try switching out this medication that causes weight GAIN, for one that promotes weight loss instead."

Abbreviations: BMI: body mass index

B. Shared Decision Making

This CPG encourages providers to practice shared decision making, a process in which providers, patients, and family/friend/caregiver consider clinical evidence of benefits and risks as well as patient values and preferences to make decisions regarding the patient's treatment.(93) Shared decision making is emphasized in *Crossing the Quality Chasm*, an Institute of Medicine report from 2001(94), and is a core component of a holistic health approach. Providers must be adept at presenting information to their patients regarding individual treatments, expected risks, expected outcomes, and levels or settings of care, or both, especially where patient heterogeneity in weighing risks and benefits might exist. The Veterans Health Administration and the Military Health System have embraced shared decision-making. Providers are encouraged to use shared decision-making to individualize treatment goals and plans based on patient capabilities, needs, and preferences.

C. Patients with Co-occurring Conditions

Co-occurring health conditions are important to recognize because they can contribute to the risk of developing overweight and obesity, impact the management of overweight and obesity, influence patient or provider treatment priorities and clinical decisions, and affect the overall provider approach to the management of overweight or obesity. Providers should expect that many Veterans, Service members, and their families will have one or more co-occurring health conditions. Because overweight and obesity management often takes place in parallel with

ongoing care for co-occurring conditions and can be affected by the treatment of other conditions, especially pharmacologic choices, it is generally best to manage overweight and obesity collaboratively with other care providers. When caring for patients with overweight or obesity, a careful review of their medication list may reveal medications that promote weight gain and are counterproductive to patient weight loss efforts (see Sidebar 2). Some co-occurring conditions may require early specialist consultation to coordinate necessary changes in treatment and/or to establish a common understanding of how care will be coordinated and delivered. VA/DOD CPGs exist for Chronic Insomnia Disorder/OSA[1], Chronic Kidney Disease (CKD)[2], Diabetes Mellitus[3], Hypertension[4], and Major Depressive Disorder (MDD)[5]. See Appendix O, Sidebar 4, and Sidebar 3 for guidance regarding the medical assessment of patients with overweight and obesity.

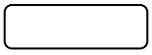
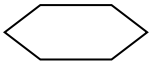
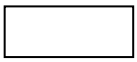
[1] See the VA/DOD Clinical Practice Guideline for the Management of Chronic Insomnia Disorder and Obstructive Sleep Apnea. Available at: https://www.healthquality.va.gov/guidelines/CD/insomnia/index.asp
[2] See the VA/DOD Clinical Practice Guideline for the Management of Chronic Kidney Disease. Available at: https://www.healthquality.va.gov/guidelines/CD/CKD/
[3] See the VA/DOD Clinical Practice Guideline for the Management of Type 2 Diabetes Mellitus in Primary Care. Available at: https://www.healthquality.va.gov/guidelines/CD/diabetes/
[4] See the VA/DOD Clinical Practice Guideline for the Diagnosis and Management of Hypertension in the Primary Care Setting. Available at: https://www.healthquality.va.gov/guidelines/CD/HTN/
[5] See the VA/DOD Clinical Practice Guideline for the Management of Major Depressive Disorder. Available at: https://www.healthquality.va.gov/guidelines/MH/mdd/

VIII. Algorithm

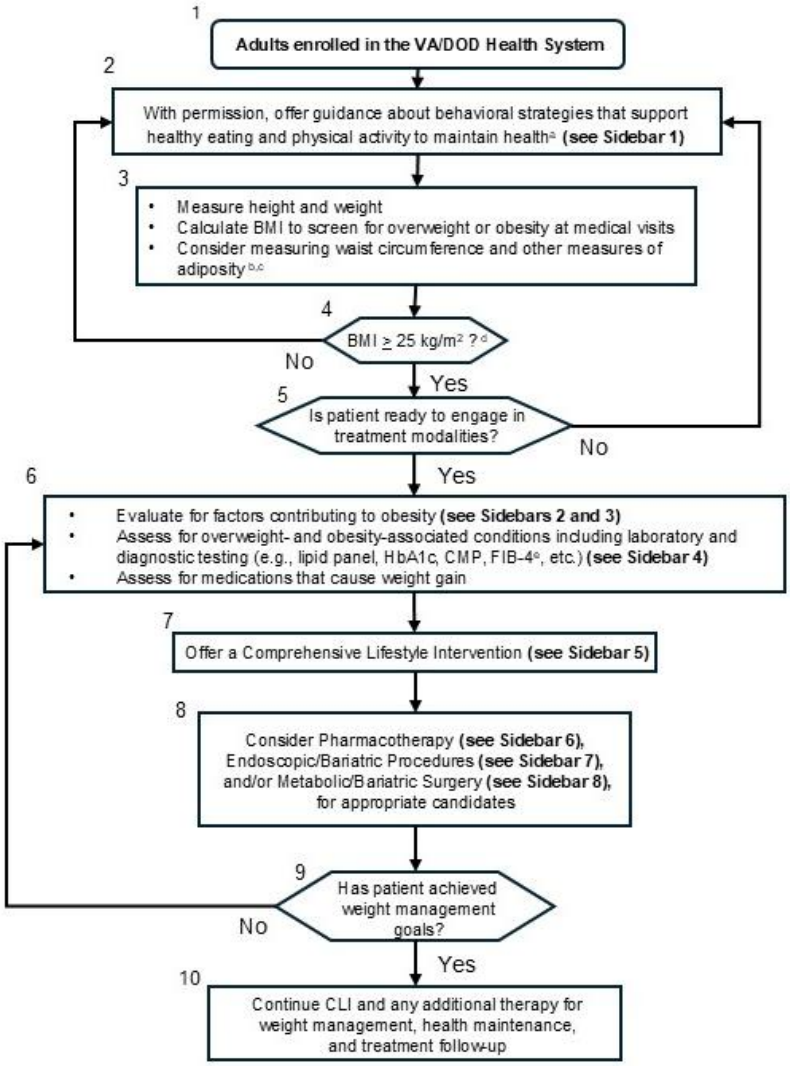
This CPG includes an algorithm that is designed to facilitate understanding of the clinical pathways and decision-making processes used in managing patients with overweight or obesity. The use of the algorithm format as a way to represent patient management was chosen based on the understanding that such a format may promote more efficient diagnostic and therapeutic decision making; it also has the potential to change patterns of resource use. Although the Work Group recognizes that not all clinical practices are linear, the simplified linear approach depicted through the algorithm and its format allows the provider to assess the critical information needed at the major decision points in the clinical process. It includes:

- An ordered sequence of steps of care
- Recommended observations and examinations
- Decisions to be considered
- Actions to be taken

The algorithm is a step-by-step decision tree. Standardized symbols are used to display each step, and arrows connect the numbered boxes, indicating the order in which the steps should be followed.(95) Sidebars provide more detailed information to assist in defining and interpreting elements in the boxes.

Shape	Description
	Rounded rectangles represent a clinical state or condition.
	Hexagons represent a decision point in the guideline, formulated as a question that can be answered “Yes” or “No”.
	Rectangles represent an action in the process of care.
	Ovals represent a link to another section within the algorithm

Algorithm Module



[a] See, for example, *2020-2025 Dietary Guidelines for Americans, 9th edition,* available at: Dietary Guidelines for Americans and *Physical Guidelines for Americans, 2nd Edition*, available at: Physical Activity Guidelines for Americans | odphp.health.gov

[b] Waist circumference: ≥102 cm (40 in) for men and ≥88 cm (35 in) for women, for those of Asian descent: ≥90 cm (35.4 in) for men and ≥80 cm (31.5 in) for women or waist-to-hip ratio (WHR) >0.90 for men and >0.80 for women. , or waist-to-height ratio (WtHR)(96) ≥ 0.50 for all

[c] The waist circumference measurement should be made with a tape measure placed around the bare abdomen just above the iliac crest. The tape should be snug, but should not compress the skin, and the measurement should be obtained while the patient is standing at the end of normal exhalation(97)

[d] For patients of Asian descent: is BMI ≥23 kg/m^2?;(98) for patients >65 years old: consider individualized assessment(99)

[e] The Fibrosis-4 (FIB-4) index(100) is a non-invasive scoring system used to estimate liver fibrosis based on several laboratory tests

Abbreviations: BMI: body mass index; CLI: comprehensive lifestyle intervention; CMP: comprehensive metabolic panel; DOD: Department of Defense; VA: Department of Veterans Affairs; WHR: waist-to-hip ratio; WtHR: waist-to-height ratio

Sidebar 1: Principles and Core Strategies of Motivational Interviewing and Behavioral Counseling

- Respect autonomy and resist directing
- Understand the patient's motivations
- Listen with empathy
- Empower the patient by building confidence
- Ask **O**pen-ended questions to evoke change talk and provide **A**ffirmations, **R**eflections, and **S**ummaries (OARS)
- Use the 5 A's: Ask, Assess, Advise, Agree, Assist[a]

[a] See information for Behavioral Counseling Interventions, available at: Behavioral Counseling Interventions: An Evidence-based Approach | United States Preventive Services Taskforce

Sidebar 2: Select Medications and their Potential Effects on Weight[a]

Providers will need to individualize recommendations to their patient

Medication Classes	Medications with Potential for Weight GAIN	Medications that are Weight Neutral or have Potential for Weight LOSS
Antipsychotics[d]	• Chlorpromazine • Clozapine • Iloperidone • Olanzapine • Paliperidone • Quetiapine • Risperidone • Thioridazine	Consider an antipsychotic with minimal to no effect on weight gain if possible. NOTE: No antipsychotic medication is associated with weight loss. • Aripiprazole • Asenapine • Brexpiprazole • Cariprazine • Fluphenazine • Haloperidol • Loxapine • Lumateperone • Lurasidone • Molindone • Perphenazine • Pimavanserin • Xanomeline-trospium • Ziprasidone

Medication Classes	Medications with Potential for Weight GAIN	Medications that are Weight Neutral or have Potential for Weight LOSS
Antidepressants[e]	• Mirtazapine • Some selective serotonin reuptake inhibitors (SSRI) (e.g., paroxetine, sertraline, citalopram[b], and escitalopram[b]) • MAOIs (e.g., phenelzine) • Tricyclic anti-depressants (e.g., amitriptyline, clomipramine, doxepin, imipramine, nortriptyline, protriptyline[b])	Consider an antidepressant with minimal to no effect on weight gain if possible. • Bupropion (associated with weight loss) • Some SSRIs (e.g., fluoxetine) • SNRIs (e.g., desvenlafaxine, venlafaxine, duloxetine) • Trazodone, Nefazodone • Vortioxetine
Antiseizure drugs or mood stabilizing agents	• Divalproex • Gabapentin • Lithium • Perampanel • Pregabalin • Valproic acid • Vigabatrin	Associated with weight loss: • Topiramate • Zonisamide • Cannabidiol • Stiripentol Associated with minimal weight loss, conflicting or no evidence for weight gain or loss: • Brivaracetam, levetiracetam • Carbamazepine, Eslicarbazepine, Oxcarbazepine • Cenobamate • Clobazam • Ethosuximide • Felbamate • Lacosamide • Lamotrigine • Phenobarbital • Phenytoin • Primidone • Rufinamide • Tiagabine NOTE: Prioritize seizure control

Medication Classes	Medications with Potential for Weight GAIN	Medications that are Weight Neutral or have Potential for Weight LOSS
Antihyperglycemic agents	• Insulin[c] • Sulfonylureas (e.g., chlorpropamide, glimepiride, glipizide, glyburide) • Meglitinides (e.g., nateglinide, repaglinide) • Thiazolidinediones (e.g., pioglitazone, rosiglitazone)	Associated with weight loss: • GLP-1/GIP tirzepatide • GLP-1 containing agonists (e.g., semaglutide, liraglutide, exenatide, dulaglutide, lixisenatide) • SGLT2 inhibitors (e.g., empagliflozin, canagliflozin, dapagliflozin, ertugliflozin) • Metformin • Alpha-glucosidase inhibitors (e.g., acarbose, miglitol) • Pramlintide Weight neutral: • Dipeptidyl-peptidase-4 inhibitors (e.g., alogliptin, linagliptin, saxagliptin, sitagliptin)
Beta-blockers	• Metoprolol • Atenolol • Propranolol Less weight gain than above: • Carvedilol[b] • Nebivolol[b]	Consider calcium channel blockers, angiotensin receptor blockers, angiotensin-converting enzyme inhibitors, and thiazide or loop diuretics, as indicated. NOTE: Other alternative classes of antihypertensive medications may be an option depending on the indication (e.g., angina, heart failure, HTN, migraine).
Alpha-blockers	• Terazosin • Doxazosin • Prazosin	• Alfuzosin • Tamsulosin
Glucocorticoids	• Systemic Steroids (e.g., Prednisone, Dexamethasone, Methylprednisolone, Hydrocortisone)	Consider weight-neutral steroid-sparing alternatives based on indication. Some examples include: • Biologics/disease-modifying antirheumatic drugs • Nontraditional therapies • NSAIDs

Medication Classes	Medications with Potential for Weight GAIN	Medications that are Weight Neutral or have Potential for Weight LOSS
Hormonal agents	Oral or Depot Progestin-only therapy (e.g., medroxyprogesterone, megestrol acetate)[f] Less weight gain than above: Combination contraceptives (e.g., oral, patch)[f]	Consider alternative methods based on indication (e.g., contraception; menopause). Some examples include: • Copper intrauterine device • Barrier Method
Antihistamines(101,102)	• H1 antihistamines (e.g., hydroxyzine, diphenhydramine, fexofenadine), cetirizine, and desloratadine	Depending on symptoms, consider alternatives such as: ipratropium nasal spray, decongestants, inhalers, and/or nonpharmacologic measures (e.g., nasal irrigation)
Antiretrovirals	• Protease Inhibitors (e.g., atazanavir, darunavir) • Integrase Inhibitors (e.g., bictegravir, dolutegravir, raltegravir)	Other ARVs are typically weight-neutral. Prioritize viremia control.

[a] The information provided in the table is not to be considered all-inclusive and is a compilation of information from the medical literature (systematic reviews, meta-analyses, subgroup analysis of clinical trials, cohort studies, reviews), some of which may have included differing comparators with variable results based on length of follow-up, baseline weight, patient comorbidities, etc.; medical and pharmacy resources; and select product information (adverse events, post-marketing and case reports).

[b] Weight gain and weight loss have been reported. *should there be more description of initial vs. long-term effects on weight* for beta blockers: Bakris GL, Fonseca V, Katholi RE, et al. Metabolic Effects of Carvedilol vs Metoprolol in Patients With Type 2 Diabetes Mellitus and Hypertension: A Randomized Controlled Trial. JAMA. 2004;292(18):2227–2236. doi:10.1001/jama.292.18.2227(103)

[c] High basal insulin (≥ 0.5units/kg) can cause sub-clinical hypoglycemia that can increase appetite (see Clinical Care Note in Introduction to the 2025 OBE CPG Pharmacotherapy Recommendations)

[d] See Table D-3: Antipsychotic Adverse Event Profiles in the April 2023 VA/DOD Clinical Practice Guideline for Management of First-Episode Psychosis and Schizophrenia. Available at: https://www.healthquality.va.gov/guidelines/MH/scz/

[e] See Table J-2: Antidepressant Adverse Event Profiles in the February 2022 VA/DOD Clinical Practice Guideline for the Management of Major Depressive Disorder. Available at: https://www.healthquality.va.gov/guidelines/MH/mdd/

[f] Lopez LM, Ramesh S, Chen M, et al. Progestin-only contraceptives: effects on weight. Cochrane Database Syst Rev. 2016(8):CD008815.(104); Gallo MF, Lopez LM, Grimes DA, Carayon F, Schulz KF, Helmerhorst FM. Combination contraceptives: effects on weight. Cochrane Database Syst Rev. 2014(1):CD003987.(105)

Abbreviations: ARB: angiotensin receptor blocker; ARV: antiretroviral; GLP-1: glucagon-like peptide-1 receptor; HTN: hypertension; MAOI: monoamine oxidase inhibitor; NSAID: nonsteroidal anti-inflammatory drug; SGLT2: sodium-glucose cotransporter 2

Sidebar 3: Assessment of Factors Associated with Obesity

- Assess for presence of obesogenic medications (see Sidebar 2 on pharmacotherapy)
- Assess for factors associated with overweight or obesity if physical exam and personal family history warrant, including but not limited to: depression, eating disorders or disordered eating, food insecurity and nutritional insufficiency, menopause, endocrine disorders (e.g., hypothyroidism, acromegaly, hypogonadism, hypercortisolism), neurologic conditions (e.g., hypothalamic obesity, traumatic brain injury, brain tumor, cranial irradiation, spinal cord injury), sleep apnea

Sidebar 4: Common Overweight- & Obesity-Associated Conditions By System[a]

- Endocrine conditions (e.g., Prediabetes and Diabetes Mellitus, Metabolic Syndrome[b])
- Cardiovascular conditions (e.g., ASCVD, HTN, Dyslipidemia, Atrial Fibrillation, CHF, Stroke)
- Gastrointestinal conditions (e.g., MASLD, GERD)
- Musculoskeletal (e.g., OA/degenerative joint disease)
- Mental health conditions (e.g., depression, PTSD, anxiety, disordered eating)
- Respiratory conditions (e.g., OSA, asthma, hypoventilation syndrome)
- Genitourinary conditions (e.g., PCOS, female infertility, male hypogonadism, stress incontinence)
- Renal (e.g., microalbuminuria, CKD)
- Cancer(1-3)
- Neurological (e.g., IIH)

[a] This list of conditions is not a comprehensive list of overweight and obesity associated conditions.

[b] See National Cholesterol Education Program definition of metabolic syndrome, available at: https://www.nhlbi.nih.gov/files/docs/guidelines/atglance.pdf

Abbreviations: ASCVD: atherosclerotic cardiovascular disease; CHF: congestive heart failure; CKD: chronic kidney disease; GERD: gastroesophageal reflux disease; HTN: hypertension; IIH: idiopathic intracranial hypertension; MASLD: metabolic dysfunction-associated steatotic liver disease; OA: osteoarthritis; OSA: obstructive sleep apnea; PCOS: polycystic ovarian syndrome; PTSD: post-traumatic stress disorder

Sidebar 5: Comprehensive Lifestyle Intervention

- Defined as an intervention that combines behavioral, nutritional, and physical activity components together (see Recommendation 2, Recommendation 6, Recommendation 8, Recommendation 9, and Appendix O)
- The intervention can be delivered in an individual or group setting, in person, by telephone, or through synchronous video (see Recommendation 2, Recommendation 4, Recommendation 5, and Appendix O)
- Though there is insufficient evidence to recommend a specific number of sessions of comprehensive lifestyle intervention, most CLIs offer at least 12 intervention sessions in the first 12 months of intervention (see Recommendation 2)

Abbreviations: CLI: comprehensive lifestyle intervention

Sidebar 6: Assessment for Pharmacotherapy

The thresholds listed below are for the initiation of therapy. These medications may be continued for maintenance of BMI target goals.

Consider for long-term pharmacotherapy (see Appendix J):

- Patients with a BMI ≥30 kg/m^2
- Patients with a BMI ≥27 kg/m^2 and an obesity-related comorbidity (see Table J-1)
- Individualize choice of medication to patient-specific comorbidities, dosing, administration, and potential for side effects

NOTE: Patients with BMI≥25-27 kg/m2 with additional adiposity measures require special considerations. See Recommendations for further information.

Abbreviations: BMI: body mass index; kg: kilograms; m: meters

*Use Asian population cutoffs per Table O-2

Sidebar 7: Assessment for Endoscopic and/or Bariatric Therapies

Consider for endoscopic and/or bariatric therapies (see Recommendation 11, Recommendation 13, and Appendix K:

- For intragastric balloons, patients with a BMI of 30-40 kg/m^2
- For endoscopic sleeve gastrectomy, patients with a BMI of 30-50 kg/m^2

Abbreviations: BMI: body mass index; kg: kilograms; m: meters

Sidebar 8: Assessment for Metabolic and/or Bariatric Surgery

Consider for metabolic/bariatric surgery (see Recommendation 12 and Appendix K):

- Patients with a BMI ≥30 kg/m^2 and T2DM
- Patients with a BMI ≥35 kg/m^2

Abbreviations: BMI: body mass index; kg: kilograms; m: meters; T2DM: type 2 diabetes mellitus

IX. Recommendations

The evidence-based clinical practice recommendations listed in the table below were developed using a systematic approach considering four domains as per the GRADE approach (see Summary of Guideline Development Methodology). These domains include confidence in the quality of the evidence, balance of desirable and undesirable outcomes (i.e., benefits and harms), patient values and preferences, and other implications (e.g., resource use, equity, acceptability).

Table 5. Evidence-Based Clinical Practice Recommendations with Strength and Category

Topic	Sub-topic	#	Recommendation	Strength[a]	Category[b]
Measures of Adiposity		1.	There is insufficient evidence to recommend either for or against a particular measure of adiposity to manage clinical outcomes in patients with overweight or obesity.	Neither for nor against	Reviewed, New-added
Management of Overweight and Obesity	*Lifestyle Interventions (LI)*	2.	We recommend offering an in-person group or individual comprehensive lifestyle intervention that always includes behavioral, dietary, and physical activity components for patients with overweight or obesity.	Strong for	Not Reviewed, Not-changed
		3.	We suggest offering a comprehensive lifestyle intervention for weight maintenance to patients who have completed a comprehensive lifestyle intervention for weight loss.	Weak for	Not Reviewed, Not-changed
		4.	We suggest offering an individual or group telephone-delivered comprehensive lifestyle intervention for weight loss, either as an alternative to or in conjunction with an in-person intervention.	Weak for	Not Reviewed, Not-changed
		5.	There is insufficient evidence to recommend either for or against a specific number of sessions, or a specific technology (except for telephone, see Recommendation 4), as the primary mode of delivery of a comprehensive lifestyle intervention.	Neither for nor against	Reviewed New-replaced
	Dietary Component of a CLI	6.	We recommend offering patients a dietary approach that contributes to a negative energy balance to achieve weight loss as the dietary component of a comprehensive lifestyle intervention.	Strong for	Reviewed, Not-changed
		7.	For weight loss and weight maintenance, there is insufficient evidence to recommend either for or against a particular dietary approach and/or strategy over another.	Neither for not against	Reviewed, New-replaced
	Physical Activity Component of a CLI	8.	We suggest physical activity of any type for weight management and other health outcomes, and as the physical activity component of a comprehensive lifestyle intervention.	Weak for	Reviewed, New-replaced

Topic	Sub-topic	#	Recommendation	Strength[a]	Category[b]
		9.	To optimize health outcomes, we suggest moderate to vigorous intensity aerobic exercise combined with resistance training.	Weak for	Reviewed, New-replaced
Management of Overweight and Obesity (continued)	*Weight Bias and Stigma*	10.	We suggest offering cognitive behavioral interventions to individuals experiencing internalized weight bias and stigma.	Weak for	Reviewed, New-added
	Metabolic/Bariatric Procedures – Short-term	11.	For temporary weight loss, we suggest intragastric balloons, in conjunction with a comprehensive lifestyle intervention, in patients with a body mass index ≥30 kg/m^2, adherent to FDA guidelines*(read narrative).	Weak for	Reviewed, Amended
	Metabolic/Bariatric Procedures – Long-Term	12.	We suggest metabolic and bariatric surgery, in conjunction with a comprehensive lifestyle intervention, for durable weight loss in patients with a body mass index ≥30 kg/m² with type 2 diabetes mellitus or with a body mass index ≥35 kg/m².	Weak for	Reviewed, Amended
		13.	We suggest endoscopic sleeve gastroplasty (ESG) for weight loss, in conjunction with a comprehensive lifestyle intervention, in patients with a body mass index ≥30 kg/m².	Weak for	Reviewed, New-added
	Pharmacotherapy – Initiation and Discontinuing/Tapering	14.	There is insufficient evidence to recommend either for or against delaying the start of pharmacotherapy, in relationship to CLI, to improve outcomes in patients with overweight or obesity.	Neither for nor against	Reviewed, New-added
		15.	We suggest against discontinuing obesity medications, taking into account patient characteristics and preferences, as it results in weight regain.	Weak against	Reviewed, New-added
		16.	There is insufficient evidence to recommend either for or against reduction of the dose or frequency of pharmacotherapy to maintain achieved weight loss and avoid weight regain.	Neither for not against	Reviewed, New-added
	Pharmacotherapy – Medication	17.	We recommend semaglutide or tirzepatide for both weight loss and to maintain weight loss, in conjunction with a comprehensive lifestyle intervention, in patients with a body mass index ≥27 kg/m^2 who also have an obesity-associated condition; and those who have a body mass index ≥30 kg/m^2.	Strong for	Reviewed, New-added

Topic	Sub-topic	#	Recommendation	Strength[a]	Category[b]
Management of Overweight and Obesity (continued)	*Pharmacotherapy – Medication (cont.)*	18.	We suggest phentermine/topiramate extended release(ER) or liraglutide for both weight loss and to maintain weight loss, in conjunction with a comprehensive lifestyle intervention, in patients with a body mass index ≥27 kg/m^2 who also have an obesity-associated condition; and, those who have a body mass index ≥30 kg/m2.	Weak for	Reviewed, Amended
		19.	We suggest naltrexone/bupropion extended release (ER) for weight loss, in conjunction with a comprehensive lifestyle intervention, in patients with a body mass index ≥27 kg/m^2 who also have an obesity-associated condition; and those who have a body mass index ≥30 kg/m^2.	Weak for	Reviewed, Amended
		20.	We suggest the use of glucagon-like peptide type 1 agonist-containing agents, in conjunction with CLI, for the treatment of patients with overweight and obesity, with either co-occurring prediabetes or type 2 diabetes mellitus.	Weak for	Reviewed, New-Added
		21.	There is insufficient evidence to recommend either for or against orlistat, metformin, sodium glucose co-transporter type 2 inhibitors, or pramlintide for weight loss.	Neither for nor against	Reviewed, Amended
		22.	There is insufficient evidence to recommend either for or against phentermine monotherapy, benzphetamine, diethylpropion, or phendimetrazine, for weight maintenance.	Neither for nor against	Reviewed, Amended
	Dietary Supplements and Nutraceuticals	23.	We suggest against using dietary supplements or nutraceuticals for clinically meaningful weight management.	Weak against	Not reviewed, Amended

[a] For additional information, please refer to Determining Recommendation Strength and Direction
[b] For additional information, please refer to Recommendation Categorization

Recommendation

1. There is insufficient evidence to recommend either for or against a particular measure of adiposity to manage clinical outcomes in patients with overweight or obesity.
   (Neither for nor against | Reviewed, New-added)

Discussion

A summary of the various methods for measuring body composition is presented in Appendix M. Data comparing the accuracy of one modality to another exists, however, there is minimal data on the clinical utility of using these various modalities to define excess adiposity and improve clinical outcomes. One cross-sectional study of 3,675 participants compared dual-energy x-ray absorptiometry visceral adipose tissue (DXA-VAT) to standard anthropometric measurements (body mass index (BMI), waist circumference (WC), waist-to-hip ratio (WHR), waist-to-height ratio [WHtR]) found that DXA-VAT was not superior for predicting diabetes.(106) In the same study, as well as an additional cross-sectional observational study, the DXA-VAT was found to be superior to BMI, WC, WHR, and WHtR for the prediction of cardiometabolic risk factors, specifically low HDL-C, raised BP, triglycerides, HbA1c, and metabolic syndrome, compared to BMI, with some variances between DXA-VAT and DXA-VAT/total fat ratio. WC was also superior to BMI.(106,107) One study showed that for each standard deviation (SD) increase in DXA-VAT, there was an associated fourfold increase in odds for females and a fivefold increase in odds for males of having metabolic syndrome (MetS). After adjusting for BMI, WC, or WHR, the DXA-VAT remained independently predictive, with adjusted odds ratios (ORs) of 2.5-3.5 per standard deviation (SD) change. The prediction cut-point for MetS was approximately 900g in females and 1600g in males.(107) While these cross-sectional observational studies provide some evidence, the lack of higher-quality studies, poor study quality of the retrieved studies, higher costs, lower feasibility, and higher resource usage are reasons why the Work Group found insufficient evidence to recommend for or against using specific measures of adiposity.

Although a specific modality of measurement cannot be recommended, body composition can aid in the evaluation of excess adiposity, specifically visceral adiposity, help risk-stratify individuals with an elevated BMI, and identify those with a lower BMI who have low lean muscle mass. Additionally, special groups such as military personnel and athletes who have prolonged physical training and higher physical requirements are more likely to have higher muscle mass, which can lead to overdiagnosis of overweight and obesity. This was demonstrated in a study of female Marines, where comparing BMI and body adiposity index to DXA scans revealed significant individual variability, and on average, the BMI predicted body fat can be off by nearly 5%.(108) A study of varsity male and female athletes found that a BMI of 25 or greater over diagnosed excess adiposity, with a specificity of 27% and 66% in diagnosing excess adiposity, but it had 100% sensitivity in both groups. The optimal BMI cut point in this group was calculated to be closer to 28 kg/m² in both groups and 34.1 kg/m² in male linemen.(109) Conversely, there is also substantial evidence that BMI can underdiagnose excess adiposity in both the general and special populations. A meta-analysis of 32 research studies from 12 countries found a pooled sensitivity of only 50% in diagnosing excess adiposity with a specificity of 90%. Although high, this specificity indicates that using only BMI can lead to a misdiagnosis of excess adiposity in 10% of people, while this low sensitivity will miss the diagnosis of excess

adiposity in 50% of people.(110) In a study of over 3,800 Brazilian military firefighters, BMI underestimated the prevalence of obesity, with a sensitivity of ≤ 67%, indicating BMI missed over one-third of true cases. Specificity, the ability of BMI to correctly rule out non-obese individuals, was ≥81.2%.(111) Body composition can provide a more accurate measure of adiposity, thereby avoiding misdiagnosis and treatment strategies that are directed at weight reduction when it is not needed.

Another area where body composition analysis would be beneficial is in monitoring the decrease in fat-free mass (FFM) (lean mass) and fat mass during weight loss. With weight loss, average FFM loss typically ranges between 5% and 35% of the total weight lost. The degree of loss depends on several factors, including age, sex, the amount of body fat present before weight loss, and whether caloric restriction and/or exercise were part of the weight loss regimen, among others. Still, it is unclear if physical function, such as muscle strength, is affected.(112) Additional studies are needed to examine the use of body composition modalities in helping to decrease skeletal muscle mass (SMM) loss associated with large amounts of weight loss and to determine if physical function is affected.

As this is a Reviewed, New-added recommendation, the Work Group systematically reviewed evidence related to this recommendation.(106,107) Overall, the evidence investigating the comparative clinical utility of various modalities and measures of body composition in defining and managing excess adiposity and improving clinical outcomes is minimal, with only cross-sectional observational studies retrieved in the data review. Additionally, none of the studies reviewed directly reported the outcomes of interest. The body of evidence had several limitations and confounders, including the poor methodological quality of cross-sectional studies, unclear inclusion criteria, homogeneity of the population, and unclear variations in exposures, which collectively led to the overall low Strength of Evidence (SOE) for the outcomes assessed.

The Work Group concluded that the evidence was insufficient to favor a particular measure of adiposity for managing clinical outcomes in individuals with overweight and obesity. However, the evidence reviewed suggested that DXA-derived VAT may be associated with a better identification of cardiometabolic diseases, such as metabolic syndrome (primarily characterized by elevated triglycerides, low high-density lipoprotein) and diabetes (elevated fasting blood glucose, HbA1c), in comparison to anthropometric measures like body mass index, waist circumference, and waist-to-hip ratio. Consequently, using body composition methods to assess visceral adiposity may provide better identification of those at increased metabolic risk and could be more beneficial than relying solely on standard anthropometric measures or BMI for risk stratification and treatment evaluation. Thus, the Work Group decided upon a *Neither for nor against* recommendation.

Recommendation

2. We recommend offering an in-person group or individual comprehensive lifestyle intervention that always includes behavioral, dietary, and physical activity components for patients with overweight or obesity.
   (Strong for | Not reviewed, Not-changed)

3. We suggest offering a comprehensive lifestyle intervention for weight maintenance to patients who have completed a comprehensive lifestyle intervention for weight loss.
   (Weak for | Not reviewed, Not-changed)

4. We suggest offering an individual or group telephone-delivered comprehensive lifestyle intervention for weight loss, either as an alternative to or in conjunction with an in-person intervention.
   (Weak for | Not reviewed, Not-changed)

5. There is insufficient evidence to recommend either for or against a specific number of sessions, or a specific technology (except for telephone, see Recommendation 4), as the primary mode of delivery of a comprehensive lifestyle intervention.
   (Neither for not against | Reviewed, New-replaced)

Discussion

In-person Group or Individual Comprehensive Lifestyle Intervention

We define comprehensive lifestyle interventions (CLI) for weight loss and weight maintenance as interventions that combine three critical lifestyle components (i.e., behavioral, dietary, and physical activity) in a structured curriculum or protocol(113) and aim to produce a negative energy balance. CLI is the term used in the 2014 and 2020 VA/DOD Obesity CPGs, other recent CPGs, and evidence reviews of weight management interventions.(9,114) In this guideline, we define "in-person" as an intervention that necessitates the patient's and provider's physical presence rather than telephone or synchronous interactive video, or synchronous online chat or text.

The 2014 VA/DOD Obesity CPG found that CLIs produced clinically significant weight loss among patients with overweight or obesity. CLIs were recommended as "central to successful and sustained weight loss" and, more specifically, as a primary intervention to achieve weight loss and improve obesity-associated conditions in adults with overweight or obesity. For the 2020 VA/DOD Obesity CPG, a 2018 systematic review of CLIs commissioned by the U.S. Preventive Services Task Force (USPSTF) identified 80 good or fair quality randomized controlled trials (RCTs) of CLIs for weight loss (n=30,394 adults with overweight or obesity).(115) Findings were also published in a 2018 article from the Journal of the American Medical Association.(116) Results from 67 of the RCTs (n=22,065) indicated greater weight loss from CLIs compared to minimal intervention or usual care control conditions at 12 – 18 months (mean difference [MD] in weight change: -2.39 kg; 95% confidence interval [CI]: -2.86 to -1.93).(115) Moreover, intervention participants had a 1.94 times greater probability of losing 5% of their initial weight over 12 – 18 months compared with the control group, which translated into a number needed to treat of eight.(115) Additionally, at 24 months, the pooled risk ratio (RR) of achieving a 5% weight loss

was 1.51 (95% CI: 1.25 to 1.81), and the pooled RR of a 10% weight loss at 12 – 18 months was 3.06 (95% CI: 2.41 to 3.88). For all weight loss outcomes, there is moderate confidence in the quality of evidence.(115) Weight outcomes beyond 24 months are rarely studied or reported. A 2011 systematic review(117) found that patients, on average, regain a third of lost weight within 1 year of treatment ending, thus the importance of offering maintenance interventions (see evidence discussed in CLI for Weight Maintenance section below).

The 2018 USPSTF systematic review also examined the impact of CLIs versus control conditions on a variety of health outcomes, although studies that focused on a specific chronic disease for which weight loss/maintenance is part of disease management (e.g., cardiovascular disease (CVD), HTN, DM) were excluded.(115) Across nine trials (n=3,140) that evaluated the impact of CLIs compared to control conditions among individuals with overweight and obesity selected for baseline impaired fasting glucose, the pooled RR of developing incident DM was 0.67 (95% CI: 0.51 to 0.89).(115) Within these, the two largest, good quality studies (n=1,817 combined) that focused on the prevention of DM (the Finnish Diabetes Prevention Study [n=522])(118,119) and the Diabetes Prevention Program Outcomes Study [n=1,295])(120) showed an absolute risk reduction of developing type 2 diabetes mellitus (T2DM) of approximately 14.5% over 3 – 9 years, as described in the 2018 USPSTF systematic review.(115)

Evidence on the long-term impact of CLIs versus control conditions on the prevalence of HTN, metabolic syndrome, use of cardiovascular disease (CVD) medications, and 10-year risk of CVD was limited to a small number of trials or was inconclusive and limited or inconsistent on the long-term impact of CLIs on all-cause mortality, cardiovascular (CV) events, and quality of life (QoL).(115) CLIs delivered in studies evaluating long-term health outcomes generally lasted for only 1 – 2 years, limiting the ability to assess an effect on these outcomes. Moreover, both observational studies and controlled trials in populations with specific chronic conditions have demonstrated that a 5% weight loss produces clinically significant improvements in these conditions.(9)

We recommend both group and individual in-person modalities for delivering CLIs. Subgroup analyses performed for the 2018 USPSTF systematic review found no pattern of effects on the main outcome of weight change at 12 – 18 months follow-up according to the main mode of intervention delivery (i.e., group versus individual versus technology-based versus mixed)(115), though, as discussed below, there were limitations to the evidence for the technology-based interventions included in the systematic review.

Other intervention characteristics (e.g., intervention duration, the number of sessions in the first year) did not modify the effect of the intervention on change in weight(115) (See discussion of evidence for the number of intervention sessions below). Additional subgroup analyses found that the mean baseline weight category (i.e., overweight, Class 1 obesity, Class 2 obesity) was not associated with differences in effects on weight change,(115) supporting the Work Group's recommendation of CLI for weight loss for patients with overweight as well as obesity. However, the heterogeneity of the interventions and differences in the populations, settings, and trial quality made it difficult to identify which variables may be associated with larger effects.(115)

As noted above, CLIs combine behavioral, dietary, and physical activity components that aim to produce a negative energy balance. Although the evidence reviewed does not allow us to recommend any specific constellation of behavioral strategies for achieving clinically significant weight loss, the behavioral component of the CLIs included in the 2018(115) and the 2011 USPSTF systematic reviews(121) usually included the following elements: setting weight loss, physical activity, and dietary goals; self-monitoring (e.g., weighing, physical activity, and calorie/food tracking); stimulus control; cognitive strategies; identifying barriers to change; problem solving; relapse prevention; peer support; and in-treatment support.(115,121) These elements are also emphasized in other reviews of CLIs for weight loss. Most interventions provided tools to assist with weight loss (e.g., pedometers, food scales, exercise videos), and 12 of the CLIs included an explicit motivational interviewing component to promote participant follow-through with CLI sessions and use of behavioral strategies.(122) For more information about specific approaches and behavioral strategies commonly included in CLI, see Appendix L and Appendix O. See also recommendations and discussions on physical activity (Recommendation 8 and Recommendation 9) and dietary components (Recommendation 6 and Recommendation 7).

Despite the high heterogeneity found across the 80 CLIs in the 2018 USPSTF systematic review, the consistency in effects seen across specific interventions and various adult subgroups emphasizes a broad range of benefits from CLIs. The heterogeneity found across studies is likely related to unmeasured individual, social, and environmental factors influencing an individual's weight loss, rather than specific intervention characteristics.(115)

CLI for Weight Maintenance

The 2014 VA/DOD Obesity CPG Work Group found that offering a maintenance CLI that includes behavioral, dietary, and physical activity components with ongoing support reduces the likelihood of weight regain.(114,121,123) The 2018 USPSTF systematic review (n=2,704) compared CLIs for weight maintenance after weight loss to no interventions (four trials), minimal intervention (three trials), or usual care (two trials). The systematic review included RCTs of participants with pre-intervention body mass index (BMI) ≥25 kg/m^2 who reported weight or adiposity change at least 12 months following the start of the weight maintenance intervention. Interventions included group or individual counseling sessions delivered by phone, in-person, or through technology. The interventions were designed to help study participants maintain weight loss by continuing a healthy diet, physical activity, and use of behavioral strategies (see Appendix K and Appendix O). The frequency and intensity of interventions were variable. In most studies, the duration of the maintenance intervention was 12 – 18 months and included 12 – 26 sessions in the first year.

The SR found a significant difference favoring the intervention versus controls (eight studies, n=1,408) in maintenance of previous weight loss.(115) Results of one included trial (n=1,029) also favored the intervention group regarding continued maintenance of ≥5% weight loss at 30 months post-intervention and 60 months post-intervention. Although there are relatively few maintenance trials and the net benefit is small, three of the maintenance trials included some participants who were not successful in meeting initial weight loss goals, limiting the likelihood of finding a significant difference in maintained weight loss between maintenance intervention conditions versus control conditions. The 2018 USPSTF systematic review also determined there is insufficient evidence to favor group or individual treatment.

Telephone-Delivered CLI

As noted in Recommendation 2, the Work Group recommends offering an in-person group or individual CLI to patients with overweight or obesity for weight loss to prevent or improve obesity-associated conditions. Based on the evidence reviewed in the 2014 and 2020 VA/DOD Obesity CPGs, the Work Group suggests offering telephone-based CLI for weight loss to support long-term weight management, either as an alternative to or in conjunction with a face-to-face intervention. “In conjunction with” is defined as in addition to another intervention, while “an alternative” is defined as in place of an intervention.

As detailed in Recommendation 2, a 2018 USPSTF systematic review of 80 RCTs of CLIs for weight loss demonstrated greater weight loss from CLIs compared to minimal intervention or usual care control conditions.(115) Fifteen of these RCTs tested CLIs that included a telephone-delivered component. Investigators examined the effects of intervention modality on weight loss outcomes produced by CLI and found no significant difference in the magnitude of effects between in-person versus telephone modalities. Two fair-quality RCTs, not included in the 2018 USPSTF systematic review, directly compared the impact of telephone-delivered versus face-to-face CLIs on weight loss outcomes and found no significant differences between the intervention conditions.(124,125) Based on this evidence, the Work Group concluded that telephone-delivered CLI is effective as an alternative to face-to-face CLI and in conjunction with face-to-face CLI (i.e., when used to increase the total number of sessions attended.(114,115,124,125)

Number of Sessions

As described in Recommendation 2, we recommend offering an in-person group or individual CLI to patients with overweight or obesity for weight loss to support long-term weight management and to prevent or improve obesity-associated conditions. The Evidence Synthesis Report generated for this update of the VA/DOD CPG found that, overall, the evidence assessing the comparative effectiveness of CLIs for overweight or obesity, including CLIs of different intensities, is sparse and based exclusively on single trials, each comparing different types of CLIs, except for a single trial comparing varying exercise intensities in the same CLI (see Recommendation 8 and Recommendation 9).

While the 2014 VA/DOD Obesity CPG recommended offering at least 12 sessions of a CLI within 12 months, based on the evidence reviewed at that time, review of additional studies for the 2020 VA/DOD CPG led to the conclusion that there is insufficient evidence to recommend offering a specific number of sessions to produce significant weight loss. However, the evidence also suggests that CLIs that offer at least 12 sessions in the first 12 months of intervention produce a larger and more consistent effect on weight loss at 12 – 18 months of follow-up than CLIs that offer fewer than 12 sessions in the first 12 months.

As detailed in Recommendation 2, a 2018 USPSTF systematic review of 80 RCTs of CLIs for weight loss demonstrated greater weight loss from CLIs compared to minimal intervention or usual care control conditions.(115) To examine the effect of intervention intensity on weight loss outcomes, investigators who conducted the 2018 USPSTF systematic review abstracted the total number of sessions conducted in the first 12 months for each intervention arm.(115) Sessions

were defined as any group or individual counseling session conducted face-to-face or by telephone, or any web- or computer-based module or session.(115) When the number of sessions was examined as a continuous measure, a higher number of intervention sessions in the first 12 months was associated with significantly more weight loss (coefficient: -0.03; p=0.023).(115) However, the number of sessions in the first year was not associated with greater weight loss after controlling for the presence of group sessions (coefficient: -0.015; p=0.212). Moreover, when intervention intensity was examined in a subgroup analysis according to the number of intervention sessions in the first year (>26 sessions, 12 – 26 sessions, and <12 sessions), results showed significantly greater effects versus controls for all three subgroups. Although there were larger effect estimates among interventions with more sessions in the first 12 months of intervention, the CIs across all three of the subgroups overlapped, so these differences were not statistically significant.

Although there was no significant difference found for the number of sessions in the first 12 months of intervention, almost two-thirds (n=44) of the 67 interventions included in the analysis of weight loss at 12 – 18 months offered at least 12 sessions within the first year of the intervention.(115) Also, the absence of a significant difference for number of sessions in the first year was likely influenced by the inclusion of eight technology-based trials in the 0 – 11 session subgroup that offered a high volume of additional contacts (through mobile phone text messages, emails, or interactions with other web-based or social media platforms) to supplement the sessions. Moreover, the quality of the evidence for a differential impact based on the number of CLI sessions was rated as low due to the large clinical and statistical heterogeneity of the CLIs included in the SR and the lack of studies directly evaluating the impact of the number of sessions on weight loss outcomes while controlling for other intervention characteristics.(115)

Although the Work Group concluded that there is insufficient evidence to recommend a specific number of CLI sessions in the first 12 months of a CLI, the larger effect sizes found for CLIs that offer 12 – 26 sessions (MD: -2.48 kg), or >26 sessions (MD: -3.06 kg), when compared to <12 sessions (MD: -1.73 kg), are meaningful differences and suggest CLI intensity matters. Moreover, the American Heart Association/American College of Cardiology/The Obesity Society Guideline for the Management of Overweight and Obesity in Adults, published in 2013, strongly recommended providing a high-intensity CLI (≥14 sessions in the first six months).(9)

Mode of Delivery

The Evidence Synthesis Report generated for this update of the VA/DOD CPG found that, overall, the evidence assessing the comparative effectiveness of CLIs for overweight or obesity is sparse and based exclusively on single trials, each comparing different types of CLIs. There was no evidence identified comparing the efficacy of different delivery modes for the administration of CLIs. No relevant systematic reviews were identified due to most systematic reviews on this topic failing to include CLIs that met our requirements of including behavioral, dietary, and physical activity components, inclusion of participants with additional disorders above the ≤15% threshold used in this review, or assigning heterogeneous CLIs to the same comparator condition.

As noted in Recommendation 2, we recommend offering an in-person group or individual CLI to patients with overweight or obesity for weight loss to support chronic weight management and to

prevent or improve obesity-associated conditions. However, there was insufficient evidence to recommend for or against offering a technology-delivered CLI either as an adjunct or alternative to CLI delivered in-person or by telephone. Support for this recommendation is based on the evidence review conducted for the 2020 VA/DOD Obesity CPG.

As detailed in above, a large 2018 USPSTF systematic review included RCTs of studies that used technology as the main mode of intervention for CLI, along with trials that featured other CLI delivery modalities (i.e., individual, group, mixed).(115) Subgroup analyses found no consistent pattern of effects on weight loss outcomes according to the main mode of intervention delivery on change in weight, suggesting technology-delivered interventions were effective.(115) However, the MD in weight loss outcomes favoring the 12 technology-delivered interventions versus control was small (MD: -1.14 kg; 95% CI: -1.59 to -1.09), especially considering the MD between CLI versus control for all 67 trials included in the primary analysis (-2.39 kg; 95% CI: -2.86 to -1.93). Moreover, the 12 studies of technology-delivered CLIs(126-137) included in the 2018 USPSTF systematic review identified a wide range of technologies employed across the trials. Seven(126,128,131,132,135-137) of the 12 individual trials did not find a significant difference between intervention and minimal intervention or usual care control groups on weight loss at 12 – 18 months. One of the five positive trials focused on post-partum weight loss(133) another was found to be effective in men but not women(134) and two explicitly described face-to-face, interactive components.(126,131) Most of the other trials included some form of human interaction, making it difficult to determine the degree to which the technology component of the intervention contributed to outcomes.

Though the systematic evidence review conducted as part of this guideline update did not identify any studies that specifically evaluated the impact of synchronous video-delivered CLI, this intervention modality is likely to be as efficacious as telephone-delivered CLI. The visual cues offered by synchronous video-delivered CLI may enhance provider-patient communication and thereby enhance patient engagement in the intervention.

Evidence indicates the risk of harm from CLI is low. Rates of adverse events were reported in 27 trials (n=12,235) among the 80 behavior-based weight loss trials included in the 2018 USPSTF systematic review.(115) There were no serious harms related to the interventions, and most trials noted no differences between groups in the rates of adverse events, including CV events.(115) Musculoskeletal events were most commonly related to the intervention groups, although only one trial found a statistically significant difference in events across intervention and control groups. In the Diabetes Prevention Program trial (n=2,161), a statistically significant increased rate of musculoskeletal symptoms (e.g., myalgia, arthritis, arthralgia) was seen among those in the lifestyle intervention group (24.1 events per 100 person-years) compared with those in the control group (21.1 events per 100 person-years) ($p<0.0167$) over four years of follow-up.(120) Although there is some burden to patients when participating in a CLI that includes multiple clinical contacts over many months or weeks, the benefits are significant, and there are many options for participating in effective interventions, including telephone-delivered counseling and video-telehealth programming that may attenuate the burden.

The Patient Focus Group that was convened for this CPG update highlighted the value of non-pharmacological therapies and lifestyle changes when managing overweight and obesity. Moreover, the focus group participants emphasized the importance of goal setting, having an individualized treatment plan, and having a coach or provider to provide support and accountability. These patient preferences and values are aligned with the elements and approach inherent in the delivery of CLIs and the findings that a variety of modalities, including group, individual, and mixed modalities, are effective for weight loss.

The Work Group also notes that there are limitations in offering a weight management intervention that features many sessions, including the large variability in the way patients wish to receive their sessions. Some may prefer a CLI that includes fewer sessions, while others may prefer one that includes a greater number of sessions. Additionally, some subgroups of patients may be unable to participate in CLIs that require many sessions (e.g., a patient who is limited by transportation, telephone availability, or lack of a computer). CLI session number and frequency may also be limited by healthcare facility constraints, such as a lack of staff and space, and an inability to provide the interventions in accordance with all patient preferences. Lastly, there are differences in the ability of VA and DOD programs to provide CLIs of greater intensity. In the VA, the MOVE! program, which meets the criteria for a CLI, has already been integrated into clinical practice, increasing resources devoted to CLIs. No comparable agency-wide standardized voluntary weight management program has been consistently adopted across the DOD, which may present a challenge for many DOD locations. It may also be less feasible for some groups of patients (e.g., rural Veterans, soldiers who are deployed or on temporary field training) to access a maintenance CLI.

Despite general consistency in the evidence supporting telephone-based CLI, there is some variability in patient preferences regarding this modality. CLI can be burdensome to patients, as CLI requires frequent contacts. For certain populations, telephone-delivered intervention may be less feasible (e.g., patients with hearing impairment or unreliable phone service). Furthermore, there may be limited access to telephone-based CLI, as there are relatively few providers who have been trained in CLI or have dedicated time for telephone-delivered interventions. While telephone-delivered CLI may increase access to care, and patients may feel more comfortable and less self-conscious, it can be difficult to obtain clinical measurements over the phone.

Although the Work Group found insufficient evidence to recommend for or against the use of technology as a primary means to deliver CLIs, it is important to consider variation in patient values and preferences, efficiency of resource utilization, and potential reach of interventions. Patients vary in their desire or preference for technology-delivered interventions; for some patients, a technology-delivered intervention may increase their access to lifestyle interventions. While these interventions may reduce the burden and travel time related to in-person intervention, the use of technology may introduce burdens as well, which vary depending on the type of technology. In terms of equity, while most Service members and Veterans have access to smartphones, data plans vary, and not all individuals have access to all types of technology. Also, individuals in rural or remote locations may not have the same opportunity to benefit from technology-based interventions when infrastructure lags in these areas.

The Work Group did not systematically review evidence related to Recommendation 2, but did consider evidence from the prior VA/DOD CPG.(115) Therefore, it is categorized as Not Reviewed, Not Changed. The Work Group's confidence in the quality of the evidence was moderate. The body of evidence had some limitations, including heterogeneity of interventions, few trials reporting differences in weight change at longer follow-up, and few trials reporting the baseline CV risk status of participants.(115) The benefits of CLI (e.g., clinically important weight loss), outweighed the potential harm of minor musculoskeletal events, which were small. Patient values and preferences varied somewhat because patients vary in their ability to access CLI and attend numerous sessions. Thus, the Work Group decided upon a *Strong for* recommendation.

The Work Group did not systematically review evidence related to Recommendation 3, but did consider evidence from the prior VA/DOD CPG.(115,124,138) Therefore, it is categorized as Not Reviewed, Not Changed. The Work Group's confidence in the quality of the evidence was moderate. The body of evidence had some limitations, including a small number of trials reporting 5% weight loss and one trial with wide confidence intervals(115); however, all nine trials reviewed in the 2018 USPSTF systematic review were rated fair or good quality. The benefits of maintenance CLIs for maintenance of weight loss outweighed the potential harm of minor adverse events, e.g., musculoskeletal symptoms. Patient values and preferences somewhat varied as discussed in the preceding paragraph. Thus, the Work Group decided upon a *Weak for* recommendation.

The Work Group did not systematically review evidence related to Recommendation 4, but did consider evidence from the prior VA/DOD CPG(115,124,125) Therefore, it is categorized as a Not Reviewed, Not Changed. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations, including the fact that no good-quality RCTs were identified that directly compared telephone to face-to-face modalities while controlling for other characteristics of the CLI. The benefits of weight loss outweighed any potential harm, which is minimal for CLIs as discussed above. Patient values and preferences were varied because some patients prefer in-person interventions, and telephone participation may be less feasible for some (e.g., patients with hearing impairment or unreliable phone service). Thus, the Work Group decided upon a *Weak for* recommendation.

The Work Group systematically reviewed evidence related to Recommendation 5(139-141) and considered the evidence put forth in the 2020 VA/DOD CPG.(115) Therefore, it is categorized as Reviewed, New-replaced. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had significant limitations, including poorly defined and heterogeneous interventions, minimal intervention or no treatment controls, weight loss outcomes at less than 12 months of follow-up, high attrition, lack of blinding of patients and providers, and small sample sizes(115,139-141) The benefits of having options for how (i.e., modality) and how intensely (i.e., number of sessions) an individual participates in CLI outweigh the potential harm associated with participation in CLI described above. Patient values and preferences were similar because patients want flexibility in how they participate in CLI. Thus, the Work Group decided upon a *Neither for nor against* recommendation.

Recommendation

6. We recommend offering patients a dietary approach that contributes to a negative energy balance to achieve weight loss as the dietary component of a comprehensive lifestyle intervention.
   (Strong for | Reviewed, Not-changed)

Discussion

A negative energy balance occurs when energy expenditure exceeds energy intake, resulting in the body utilizing stored energy and leading to weight loss. A dietary approach that achieves a negative energy balance and promotes weight loss in patients with overweight and obesity remains a core component of comprehensive lifestyle interventions (CLI) (see Appendix H for specific dietary approaches and guidance).(115,142-153) A 2018 USPSTF systematic review of 80 RCTs of CLIs for weight loss demonstrated greater weight loss from CLIs that included a dietary component compared to minimal intervention or usual care control conditions.(115) A negative energy balance to support weight loss can be achieved through a variety of dietary approaches.(142-164)

The importance of providing a caloric deficit was first explored in the Overweight/Obesity CPG from the VA/DOD in 2014[1] and was carried forward by the 2020 CPG Work Group. In order to maintain a *Strong for* recommendation, we looked back at the data from the 2014 CPG.(165-175) The 2014 studies compared dietary approaches to usual care, while the evidence pulled for the 2025 CPG consisted of studies comparing dietary approaches to each other. The quality of the 2025 evidence ranged from very low to moderate. The 2025 evidence reinforced the weight loss effect provided by a calorie deficit, as all the dietary approaches reviewed achieved weight loss via a negative energy balance. Even though the studies were comparative, there was a weight loss trend in all the dietary approaches reviewed in the 2025 evidence, which we felt reinforced conclusions made from the 2014 evidence.(154-164)

The concept of negative energy balance, essential to the success of a comprehensive lifestyle intervention, has been extensively explored with varying levels of evidence regarding its role in weight loss and health. The evidence from the 2014 review, rated as moderate, highlights the effectiveness of dietary interventions in achieving weight loss, supported by studies that investigated the impact of caloric restriction and macronutrient composition on energy balance.(165-175) The 2014 CPG supports the use of calorie restriction for weight loss, recommending a daily caloric deficit of 500-750 kcal for effective weight management. The 2020 evidence further contributed to the field, while recent comparative effectiveness studies from 2025 continue to explore the different impacts of negative energy balance through various dietary and lifestyle interventions.(154-164) These studies reinforce the importance of individually tailoring strategies to effectively achieve energy balance and improve health.

[1] Request the 2014 VA/DOD Clinical Practice Guideline for the Management of Obesity and Overweight. Available at: https://www.healthquality.va.gov/CPGArchives.asp

Though not required, access to a registered dietitian nutritionist can help with navigating a desired dietary approach and ensuring that a negative energy balance is achieved, while limiting micronutrient deficiency. Limitations in access to the services of a registered dietitian nutritionist by Active-duty military personnel and Veterans could affect their ability to implement and sustain effective dietary strategies. Addressing access barriers to these services is important to support the health and well-being of these individuals. Ultimately, the best dietary approach is one to which the patient can adhere.

The benefits of a dietary approach with a negative energy balance outweigh potential harms. Overall, there is no evidence of harm to patients in achieving a modest negative energy balance.(142-153,165-176) Ketogenic diets can lead to increases in low-density lipoprotein (LDL) but also high-density lipoprotein (HDL) and more significant reductions in triglycerides (TG).(158) Patients following a ketogenic diet will benefit from additional monitoring and support. Elevations in LDL-C may be clinically significant in some patients and should be balanced against other options for calorie-restricted diets, especially in patients at risk for atherosclerotic cardiovascular disease. Patient harm is possible if a very low-calorie diet (≤800 kcal) is used for a prolonged period of time due to effects from sarcopenia and decreased bone density, particularly in postmenopausal women.(148,163,177)

The Work Group systematically reviewed evidence related to this recommendation.(154-175) Therefore, it is categorized as Reviewed, Not changed. The Work Group's confidence in the quality of the evidence was moderate. The body of evidence had some limitations, including that the 2025 study pull included studies with very low-quality evidence, but since this was based on comparisons of one dietary approach to another rather than comparison to a placebo, we looked back to the data from 2014 to carry forward this recommendation. The benefits of offering patients a dietary approach that contributes to a negative energy balance through comprehensive lifestyle intervention outweigh the potential harm and adverse effects from specific dietary choices. Patient values and preferences were similar because patients prefer guidance and choice on effective diets that will help them with weight loss. Thus, the Work Group decided upon a *Strong for* recommendation.

Recommendation

7. For weight loss and weight maintenance, there is insufficient evidence to recommend either for or against a particular dietary approach and/or strategy over another. **(Neither for not against | Reviewed, New-replaced)**

Discussion

When considering dietary interventions for weight loss and weight maintenance, current evidence suggests that no single dietary approach is superior to others. However, dietary approaches may have differing impacts on other health outcomes. All diets reviewed can effectively contribute to weight loss through a caloric deficit.(154-164) However, their effectiveness is a product of patient adherence and, when adhered to, actual influence on total caloric intake. However, their effectiveness is a product of patient adherence and, when adhere to, actual influence on total caloric intake, which may both be driven by patient preference. The

approaches in the current review included calorie tracking, meal replacements, low-fat, low glycemic, low carbohydrate, ketogenic, vegetarian dietary patterns, and several methods of intermittent fasting.

Offering a variety of dietary approaches for those seeking weight loss is important to ensure individualized patient care. The importance of access to various dietary choices that are considered personal preferences was highlighted by participants in the patient focus group. These concerns can affect both active military Service members and Veterans, who may have limited choices due to deployment locations or socioeconomic factors. Dietary approaches such as a ketogenic diet may be more expensive or less readily available. A dietary approach such as intermittent fasting can offer flexibility, providing relief from the rigidity of traditional calorie counting, but for some can lead to overconsumption or excess hunger.

To effectively implement a chosen diet, it is desirable to have the guidance of a registered dietitian nutritionist. Registered dietitian nutritionists can provide education, support skill building, evaluate nutritional adequacy, and ensure that dietary changes are both safe and effective. Certain dietary approaches may not be suitable for all populations. For instance, severe energy restriction in post-menopausal women has been associated with greater loss of total hip bone mineral density compared to moderate energy restriction.(163) Some dietary approaches, particularly ketogenic and vegetarian diets, may lead to nutritional deficiencies and therefore require individualized guidance.

Some dietary approaches offer a negative energy balance without the need for strict calorie counting, such as a ketogenic diet and intermittent fasting (IF). The Workgroup found evidence on the effectiveness of these approaches since the 2020 CPG; therefore wanted to highlight this information. A ketogenic or low-carbohydrate diet leads to a calorie deficit primarily through mechanisms of appetite suppression and reduced energy intake. A state of ketosis has been shown to suppress the secretion of ghrelin, the hunger hormone, and increase the release of satiety peptides like glucagon-like peptide-1 (GLP-1) and cholecystokinin (CCK).(178-180) Reduced feelings of hunger and increased feelings of fullness contribute to a lower overall caloric intake.(180,181) With IF, a negative energy balance is achieved primarily through the reduction of overall caloric intake and the metabolic adaptations that occur during fasting periods. IF regimens (see Appendix H), such as alternate-day fasting (ADF; defined as one fasting day or 25% of usual energy intake, alternative with one ad libitum feeding day), the 5:2 diet (defined as fasting 2 days per week on nonconsecutive days with 5 feeding days per week), and time-restricted eating (TRE; defined as a shortened daily eating window which inherently limits the time available for eating), often lead to a reduction in total caloric intake.(154,155) Studies have shown that these regimens can reduce energy intake by 10-30% from baseline, contributing to weight loss.(182,183) During fasting periods, the body depletes its glycogen stores and shifts to mobilizing fatty acids, which are then converted to ketones. This metabolic switch from glucose to fatty acid-derived ketones enhances fat oxidation and preserves muscle mass, further promoting a negative energy balance.(184)

If the patient wishes to prioritize Hemoglobin A1c (HbA1c) improvement, a ketogenic diet showed more significant HbA1c reductions than other dietary patterns. The meta-analysis by

Choi et al. (2020) showed that in 14 RCTs, 7 of which only included subjects with diabetes, all achieved improvements in their average HbA1c reduction.(158) A ketogenic diet may be a desired option for rapid improvements in HbA1c for those seeking improved glycemic control before an elective procedure. The potential barriers of this dietary approach are that it requires special instruction as well as should be utilized with caution due to an increased risk for hypoglycemia, especially when a patient is taking a hypoglycemic agent (e.g., insulin, sulfonylureas, meglitinides, etc.). The meta-analysis by Choi et al. (2020) also showed a slight increase in low-density lipoprotein (LDL) cholesterol, but also an increase in high-density lipoprotein (HDL) and a reduction in triglyceride levels (TG).(158) On a ketogenic diet, patients with diabetes experienced a significant drop in triglycerides (−35.1 mg/dL) and an increase in HDL cholesterol (+3.5 mg/dL); across all patients, triglycerides fell by −20.7 mg/dL and HDL rose by +1.9 mg/dL. However, total cholesterol and LDL increased overall (+6.8 mg/dL and +5.9 mg/dL, respectively), with greater increases seen in patients without diabetes (total cholesterol: +10.1 mg/dL, LDL: +9.2 mg/dL).(158) Adequate dietary instruction and assessment may be necessary to ensure this diet yields the desired weight loss and health benefits.

Based on a systematic review (SR) of 23 randomized control trials (RCTs), meal replacements, either partial or total, continue to be an effective option for those seeking weight loss as they are a convenient way to achieve a caloric deficit.(142,159) The 2014 and 2020 CPGs included a recommendation with low-quality evidence designating a standalone recommendation for meal replacements. One study of 66 matched participants included in the 2014 VA/DOD CPG revealed equal weight loss between participants using meal replacements and participants using a structured weight-reduction diet.(185) Evidence indicates that meal replacements are not harmful to patients.(142) The use of meal replacements as a dietary approach is not superior to other approaches when reviewing comparative effectiveness; therefore, it was the Work Group's decision not to carry this forward as a standalone recommendation. The current recommendation has broadened the ability to offer a variety of dietary approaches.(185)

The Work Group systematically reviewed evidence related to this recommendation(154-164) including the evidence put forth from the 2014(165-175) and the 2020 iterations of this CPG.(115,142-153,176) Therefore, it is categorized as reviewed, new replaced. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations, including several very low-quality studies.(158,159,161) The benefits of not limiting dietary choices for those seeking weight loss improve access, preference, nutritional value, individualization, and equity, which outweigh the potential harm of adverse events, which was small. Patient values and preferences were similar because this provides choices. Thus, the Work Group decided upon a *Neither for nor against* recommendation.

Recommendation

8. We suggest physical activity of any type for weight management and other health outcomes, and as the physical activity component of a comprehensive lifestyle intervention.
   (Weak for | Reviewed, New-replaced)

Discussion

The 2025 Work Group reaffirmed and expanded upon its 2020 CPG suggestion for the inclusion of physical activity in weight loss, weight maintenance, prevention of further weight gain, and promotion of health outcomes as a component of a comprehensive lifestyle intervention.(186-197) Specific to weight loss, the effects of physical activity in isolation were generally modest and below the minimally clinically important difference of 5%. (188) However, physical activity is a necessary component of all comprehensive lifestyle interventions recommended for patients with overweight and/or obesity. Even within control groups with increased physical activity, there were notable improvements in weight management and other health outcomes regardless of intensity, supervision, or mode of activity.(188-191) In an RCT by Letnes et al. (2022)(197), health outcomes for seniors engaged in supervised activity and a control group given recommendations to follow Norwegian guidelines for activity, both had notable improvements. This should be encouraging for patients who are hesitant to initiate. See Recommendation 2, regarding a comprehensive lifestyle intervention.

Type of Physical Activity

When choosing types of physical activity, sustainability is the most important consideration. As discussed throughout this guideline, patient preferences are key in reducing sedentary time and generally increasing physical activity. However, as discussed in Recommendation 9, there are ways to optimize physical activity for weight loss, weight maintenance, prevention of further weight gain, and health outcomes. While changes in body composition differed between types of exercise(190) and intensity(191), there were mixed results in superiority for total weight loss(191,197), but health benefits resulted from all types of exercise.(186) Duration of exercise (length of intervention in weeks)(188,191) had a large impact on fat loss and body composition. Adherence and attrition were significant influences in outcomes and highlight the role of patient preference in choosing a favorable activity. In the Letnes et al. (2022) study(197), for example, participant adherence to assigned groups was around half, with the other half self-selecting preferred workout styles during the study. Authors noted across many studies that patients tended to prefer the shorter high-intensity interval training (HIIT)(188), and hybrid(190) style training vs. moderate-intensity continuous training (MICT) and combined training, respectively. Many also favored Zumba, which has a higher adherence rate.(195)

Physical activity is also well-known to have positive effects on mental health and quality of life, which were emphasized in a meta-analysis by Carraça et al. (2021).(194) Any type of exercise had large positive effects on quality of life with smaller positive effects on function, pain, vitality, and mental health. Some types of group exercise may have positive social effects, including increasing a patient's sense of community; in other cases, some forms like Zumba may be a more enjoyable entry-level exercise. As described above and in Recommendation 9, there are increased benefits to health outcomes and weight loss the longer an exercise intervention is undertaken. This emphasizes patient preference for adherence. Regarding all health benefits and potential harms or burdens from exercise, see Recommendation 9.

The Work Group also considered how patient values and preferences regarding physical activity interventions might impact the recommendation. See the same category in Recommendation 9 and Appendix I.

The Work Group systematically reviewed evidence related to this recommendation.(115,120,186-205) Therefore, it is categorized as Reviewed, New-replaced recommendation. The Work Group's confidence in the quality of the evidence is very low. The body of evidence had some limitations, including limited studies of long duration, heterogeneity of definitions of exercise types, and differing measures of adiposity. The benefits of exercise on weight status, body composition, and general health outcomes outweighed the potential of musculoskeletal events, which were relatively minor. Patient values and preferences varied widely. Patients prefer different modalities of training, have differing access to equipment, and have differing time available for the intervention. Thus, the Work Group decided upon a *Weak for* recommendation.

Recommendation

9. To optimize health outcomes, we suggest moderate to vigorous intensity aerobic exercise combined with resistance training.
   (Weak for | Reviewed, New-replaced)

Discussion

While the importance of any type of physical activity outweighs any one type, the Work Group did find ways in which patients can optimize outcomes.(186-197,206) While the general health benefits of physical activity are well-established, reviewed evidence shows a dose-dependent impact on both health and weight-related outcomes. It is important for clinicians to educate patients that these dose-response effects are nonlinear, with diminishing returns at very high levels of exercise and physical activity. Further, while physical activity is a required component of a CLI, diet should still be regarded as the primary component of a CLI for weight loss.(207-209) (See Recommendation 2, regarding a comprehensive lifestyle intervention. This was unchanged from the 2020 CPG which may be referenced for the full narrative).

Of note, our Work Group selected weight status as our primary outcome of interest due to the breadth of evidence utilizing this outcome measure. However, there are some limitations in using weight status for outcomes comparing exercise due to gains in fat-free mass (e.g., bone, muscle). Hence, measurements of body composition are also of considerable importance. Combined exercise performed at higher intensities, for example, more consistently resulted in changes in body composition than weight status.

Type of Physical Activity

The included studies sought to compare different types of exercise in isolation; however, there was significant heterogeneity in the way they were conducted. These studies grouped exercise into distinct categories: Resistance Training (RT) using machines, free weights, and bodyweight to increase strength and muscle mass, and aerobic training such as walking, cycling, and jogging, to increase cardiovascular function. These were further subdivided into intensity which may be based on perceived rate of exertion, or heart rate; interval training, a form of aerobic training including High Intensity Interval Training which is punctuated with recovery periods and higher intensities; continuous endurance training which is aerobic training at a constant pace, or heart rate; combined training which includes both resistance training and aerobic training

performed in separate workouts or in blocks within a workout session; and hybrid training which intermixes strength and aerobic training. However, these are loose categories, and RCTs within each review differed in protocols.

For body composition, the evidence supports combined interventions that include aerobic and resistance training over either component alone. As an example of the discussion above, the systematic review by Hao et al compared aerobic exercise of different intensities to resistance training and combined exercise, with included RCT interventions from 4 weeks to greater than 12 weeks. Outcomes for reducing total weight were best with vigorous intensity (AE-V) at 4.33kg vs control. However, body composition measured through body fat (BF)% was most improved with high-intensity combined exercise (4.7% vs. control). Even still, included studies measuring only body mass index (BMI)(189) found optimized outcomes (-1.34 decrease in BMI vs. control) with high-intensity combined exercise, suggesting it is at least equal, if not better, for total bodyweight reduction. Low-moderate intensity combined training was best for reducing waist circumference (-7.14cm vs. control), but only because there was no study with high intensity as a comparator for this outcome. Hao et al. (2023) noted "a conservative attitude towards the result that *c*ombined low-moderate*,* moderate intensity aerobic/low-to-moderate load resistance (COM-LM) is the best type of exercise to improve waist circumference*,*" instead of high intensity.

In the Batrakoulis et al. (2022) systematic review(190), the findings "support previous recommendations concerning the importance of combined training in reducing body mass and body fat in individuals with excess adiposity." The authors compared combined training (separating resistance training sessions from aerobic sessions) and hybrid training (combining them within the session) and found hybrid had better outcomes for reducing waist circumference (-3.98cm vs. -8.3cm vs. control respectively); whereas combined training had the best outcomes for body mass (-2.57kg vs. control), body fat %(-2.76 vs. control), and fat-free mass (1.62kg vs. control). Much of this is dependent on the outcomes measured from particular studies. Given large known differences in patient preferences when performing types of exercise, providers may recommend hybrid methods (e.g., CrossFit, Orangetheory), which may provide similar outcomes with less training time. In the Chavarrias et al. (2021) study of Zumba(195), of note, the highest reduction in total fat mass% among Zumba participants was observed when combining Zumba workouts plus bodyweight exercises, with a 3.37% decrease. The authors stated, "to be more effective, the Zumba training should be combined with other training modalities such as strength training."

Combined training was also favored for psychological impacts.(194) Patients with overweight/obesity reported better outcomes for self-esteem, life satisfaction, quality of life, and social function with combined training over other forms of exercise.

Dose-Dependent Impacts

Several exercise program variables influence the magnitude of outcome effect size, especially when compounded. These were exercise intensity, frequency of sessions per week, duration (weeks) of physical activity undertaken, modality of aerobic exercise, and duration of program.

Beginning with training intensity, increased vigor led to improvements in body composition, with larger impacts when undertaken for a longer period of time. For example, Guo et al. (2023) showed improvements in percent fat mass to be greater in high-intensity interval training (HIIT) vs moderate-intensity continuous training (MICT), but this was for durations longer than 6 weeks and at a frequency of >3 days per week. In smaller doses, the changes in body composition may have been too small to detect. Regarding the amount of exercise, duration of intervention, and weekly frequency were consistently shown to be dose dependent. When comparing the volume of activity, Guo et al. (2023) found significant effects of greater than 3 times per week (-0.94cm in waist circumference) and a duration of longer than 6 weeks (-0.62% fat mass) for any intensity of aerobic exercise. Poon demonstrated significantly decreased body fat percentage (BF%) with any type of interval training over MICT; however, there was no difference in BMI. Interval trainees gained approximately 1.4kg of fat-free mass, which reduced outcomes in BMI. These were prominent in durations greater than 12 weeks (-1.10% vs MICT) but not significant in durations of less than 12 weeks. Outcomes were also better in patients with higher BMI and in those who cycled as the preferred modality.(191) They outperformed non-exercise controls as well as MICT. This again explains the weak findings for weight status outcomes. Further, patients who prefer shorter times within workouts may be more amenable to HIIT-style exercise. Conversely, martial arts exercise of lower intensity, such as Tai Chi, was not superior to inactive controls for weight loss, which the authors noted still received non-activity interventions in most.(196)

Additionally, age may impact the utility of intensity in aerobic exercise. In the Guo et al. (2023) systematic review(188), HIIT had better outcomes in young and middle-aged adults than MICT. This was the finding in Letnes et al. (2022)(197), where seniors had no difference between high intensity vs. moderate activity or against active controls for weight status outcomes. However, as described in Recommendation 8 only about half of the participants strictly adhered to the assigned groups. All physical activity, however, had beneficial health outcomes, which exhibited a dose-dependent relationship.(186)

Some types of training (i.e., HIIT) are shorter per session than others (i.e., MICT), this was not directly compared. However, interventions in the Batrakoulis et al. (2022) study(190) generally found the following parameters for intervention types:

- Interval Training (85-95% HRmax, 2-3 days per week, 91 min/week)
- Hybrid Training (75-85% HRmax, 2-3 days per week, 128 min/week)
- Continuous Endurance Training (60-70% HRmax, 3-5 days per week, 176min/week)
- Combined Training (3-4 days per week, 187 min/week)
- Resistance Training (70-80% 1 Rep Max, 2-3 days per week, 126 min/week)

These are comparable to the ACSM guidelines(210) of:

- Moderate-intensity aerobic activity for a minimum of 30 minutes, five times per week, or vigorous-intensity aerobic activity for a minimum of 20 minutes, three times per week
- Resistance exercises for the major muscle groups, a minimum of 2 times per week

- Flexibility exercises for the major muscle groups, a minimum of 2 times per week

Health Outcomes

Regarding all health benefits from exercise, they are numerous and beyond the scope of this guideline. However, in reviewing specific health outcomes from compared exercise, there were differing impacts, with a dose-dependent response generally demonstrated. Vigorous aerobic exercise (AE) had better outcomes than moderate AE for leptin, adiponectin, C-reactive protein (CRP), IL-6, TNF-alpha(186), and VO2 max(189,190), with HIIT being more effective than MICT.(188,190,192,197) There was no difference in outcomes between HIIT and MICT for HDL, LDL, TC, A1c, and glucose. Data conflicted on impacts on triglycerides, with HIIT showing superiority over MICT(190) but not for older populations(197). Hybrid-type training (HYB), combined training (COM), and resistance training (RT) were most effective for elevating HDL; COM was highly effective for reducing LDL.(190) Combined training, whether traditional or in a hybrid format, was most effective for fasting glucose and fasting insulin.(190) In patients with metabolic syndrome, combined training was beneficial for the largest amount of laboratory markers (TNF-A, CRP, IL-6, IL-10)(193), with aerobic exercise being nearly equal.

The benefits of including physical activity were judged to outweigh the relatively minor potential harms. The full benefits are large and far-reaching, but are beyond the scope of this guideline. For the background on these benefits, please see the 2018 Physical Activity Guidelines for Americans 2nd Edition (PAGA).(211) In addition to the general health benefits of physical activity, there is evidence that patients with overweight and obesity are likely to benefit from increasing physical activity regardless of its impact on weight status. This includes the positive effects of increased physical activity on comorbid conditions associated with overweight and obesity(199,204,211,212) and related benefits/effects such as health-related QoL and self-efficacy/physical function.(205) For example, osteoarthritis, chronic pain syndromes, and hypertension (HTN) (among others) are responsive to the doses and types of physical activity included in CLIs for weight loss. The harms of physical activity are musculoskeletal events, although only one trial found a statistically significant difference in events across intervention and control groups.(120) Other potential harms include the burden of time and effort expended to follow a physical activity program.

The Work Group also considered how patient values and preferences regarding physical activity interventions might impact the recommendation. Patients often want specific information on practical steps for increasing physical activity to support weight loss and maintenance (see Appendix E). The Work Group judged that both patients and providers might have large variations in preferences for different kinds of physical activity. In addition, there are variations in constraints faced by different subgroups of patients, such as access to a gym or exercise spaces/equipment, preexisting musculoskeletal or other health-related conditions that limit activity ability, and proximity to safe outdoor activity options. In the evidence(191), cycling tended to have superior outcomes, which was noted by authors as an option that may have lower risk for injury and less pain as a non-impact modality. Given that osteoarthritis is an associated comorbidity of obesity, a low-impact exercise may be a preferable option. Further, some patients mentioned a preference for exercise setups that saved time. For aerobic training, patients performing high-intensity interval training instead of moderate continuous interval

training had improved outcomes and time savings.(189) When combining aerobic training with resistance training, some patients may prefer hybrid training for time savings. Unlike conventional combined training, which separates resistance and aerobic exercises either within the same session or into different sessions, hybrid training integrates resistance and aerobic training together. This includes methods like mixed resistance training and aerobic training performed simultaneously or in a blended format.(190) The Physical Activity Guidelines for Americans (PAGA) recommends choosing physical activity types that align with the patient's values, abilities, and preferences, as well as consideration of activities that are accessible and more easily incorporated into the patient's daily life (e.g., walking).(211) See Appendix I for further details on approaches to physical activity.

The Work Group systematically reviewed evidence related to this recommendation.(115,120,186-205) Therefore, it is categorized as Reviewed, New-replaced recommendation. The Work Group's confidence in the quality of the evidence is very low. The body of evidence had some limitations, including limited studies of long duration, heterogeneity of definitions of exercise types, and differing measures of adiposity. The benefits of exercise on weight status, body composition, and general health outcomes outweighed the potential of musculoskeletal events, which were relatively minor. Patient values and preferences varied widely; patients prefer different modalities of training, have differing access to equipment, and have differing time available for the intervention. Thus, the Work Group decided upon a *Weak for* recommendation.

Recommendation

10. We suggest offering cognitive behavioral interventions to individuals experiencing internalized weight bias and stigma.
    (Weak for | Reviewed, New-added)

Discussion

Internalized weight bias and stigma are defined as holding negative beliefs about oneself due to weight or size. These beliefs are associated with negative health outcomes, including obesity. Our recommendation is to offer interventions to reduce internalized weight bias and stigma in affected individuals. Here, cognitive behavioral interventions are used to describe a category of interventions that target maladaptive thoughts (e.g., I would be able to lose weight if I were stronger) and or behaviors that reinforce maladaptive thoughts (e.g., avoidance of social situations due to internalized weight stigma). It is critical to note that healthcare providers and systems can be sources of weight bias and discrimination(213) and thus, potential targets for intervention. However, the systematic literature review did not identify provider-level interventions with outcomes at the patient level, a requirement for the Clinical Practice Guideline (CPG).

One systematic review(214), two randomized clinical trials (RCTs) (215,216), and one pilot RCT (217) provided the evidence for the internalized weight bias and stigma recommendation. Chew et al. (2023) was a systematic review and meta-analysis of studies examining the effectiveness of Acceptance and Commitment Therapy (ACT) on weight, eating behaviors, and psychological outcomes, including weight-related stigma. ACT is a third-wave cognitive behavioral therapy

that has been shown to improve mental and physical health conditions. Four studies were included in this systematic review(218-221) with sample sizes ranging from 17 to 79, samples being solely or predominantly female, and treatments lasting 8-11 weeks/sessions. Two were pilots(220,221), two had waitlist conditions (219,221), one had a treatment-as-usual (TAU) condition(218), one had an active treatment comparison condition (standard behavioral weight loss [BWL])(220), and one had three treatment arms(221). Evidence from these four trials (considered 5 studies due to the three-treatment arm trial) favored ACT for reducing internalized weight stigma compared to waitlist, TAU, and standard BWL therapy at immediate post-treatment (SOE: Very low). Evidence from two additional RCTs (215,216) (N=72-105; with predominantly female samples) comparing 6-month BWL interventions plus a stigma-reduction intervention to BWL alone to reduce internalized weight stigma favored BWL plus the stigma-reduction intervention at 26-46 weeks but found no difference between treatment groups at 72 weeks. (SOE: Very low). A final pilot study(217) compared a virtual lifestyle modification intervention followed by a mindful self-compassion intervention or dietary education intervention for 6 months in 28 women, in which both treatment conditions had reductions in internalized weight stigma at post-treatment (SOE: Very low).

It was determined that the benefits of this recommendation (e.g., potential to reduce internalized weight bias and stigma within patients, and to reduce weight bias and discrimination in providers through greater awareness of having interventions offered) outweighed the potential harms/burden (none noted).

Data from the Patient Focus Group was factored into this recommendation. Participants reported feeling stigmatized and singled out for their weight, as well as having negative feelings about how weight affects one's military career and promotion. Participants made connections between unrealistic weight standards and eating disorders and body dysmorphia. They reported that provider suggestions of weight loss interventions (e.g., obesity medication) led to embarrassment and shame. Participants additionally reported a lack of supportive guidance from providers, with most reporting that providers simply instruct them to lose weight as if the patient had not recognized or tried to lose weight. This approach made participants feel stigmatized and misunderstood, leading to diminished motivation to pursue weight loss. Both past experiences with judgment and present negative tone or stigmatizing language from providers worsened internalized weight stigma. This, in turn, resulted in a lack of confidence in and motivation for seeking weight management care. Being weighed was met with reluctance. Although waist circumference measurement may be important as another metric of adiposity beyond BMI, the intrusiveness of this method and potential harm as it relates to stigma, especially in light of the harms associated with mandatory military weigh-ins, may need to be considered. Focus group participants discussed the value of providers expressing empathy and patience when working with patients on weight loss and weight maintenance, and this was perceived as a motivator for weight management efforts.

Resource use for this recommendation was deemed low. Implications for providing these interventions involve the potentially large need for intervention, provider training and resources, education and awareness about internalized weight stigma and its interventions, and space for

the interventions. The recommendation was deemed feasible and acceptable, and at this time, there are no known subgroup considerations.

As this is a Reviewed, New-Added recommendation, the Work Group systematically reviewed evidence related to this recommendation from the systematic evidence review(214-217), as well as four studies found in the Chew et al. (2023) systematic review and meta-analysis.(218-221) The Work Group's confidence in the quality of evidence was very low. The body of evidence had some limitations in that it was a small number of randomized trials (N=7), of which three were pilot studies. It was determined that the benefits of this recommendation (e.g., potential to reduce internalized weight bias and stigma within patients, and to reduce weight bias and discrimination in providers through greater awareness of having interventions offered) outweighed the potential harms/burden (none noted). Patient values and preferences varied somewhat (e.g., experiences of weight bias and stigma among participants, and support/lack of support from providers). Thus, the Work Group decided upon a *Weak for* recommendation.

Recommendation

11. For temporary weight loss, we suggest intragastric balloons, in conjunction with a comprehensive lifestyle intervention, in patients with a body mass index ≥30 kg/m2, adherent to FDA guidelines*(see narrative).
    (Weak for | Reviewed, Amended)

Discussion

Endoscopic bariatric therapies (EBT) are minimally invasive, endoscopic weight loss procedures performed with an endoscope in patients with obesity. Currently, there are two FDA-approved modalities that are commercially available. These modalities are intragastric balloons (IGB) and endoscopic sleeve gastroplasty (ESG).

IGBs are placed into the stomach endoscopically and infused with saline to occupy space in the stomach and lead to weight loss in combination with comprehensive lifestyle interventions. There are two FDA-approved and commercially available IGBs in the US: Orbera(222) and Spatz3(223). There are other similar FDA-approved devices that are not commercially available due to the manufacturer's decisions. Orbera and Spatz3 are endoscopically placed and removed after the duration of the intervention is completed. Both devices are options for temporary weight loss who have a BMI of 30-40 kg/m^2.

A systematic review and meta-analysis were completed in 2022, looking at the effectiveness of endoscopic bariatric interventions(224) at 6 months. 10 studies reviewed IGB compared to lifestyle intervention. The pooled estimate was 6.37% total body weight loss (TBWL) at 6 months (95% CI [3.94, 8.80]). A technical review completed on IGBs by the American Gastroenterology Association (AGA) showed similar findings to the group's initial data review, with a mean weight loss of 15.62–37.60 lb. (MD, 15.46 lb.; 95% CI, 10.42–20.51 lb.) at six months and a mean weight loss of 16.2–20.68 lb. (MD, 9.76 lb.; 95% CI, 6.38– 13.14 lb.) at 12 months.(225) In this technical review safety of IGB was also evaluated. The overall rate of serious adverse events was 5.6% (58 of 1028) in a pooled analysis including esophageal

mucosal injury, gastric ulcer/bleeding, severe dehydration, bowel obstruction, and aspiration pneumonia.

The Orbera device is a non-adjustable IGB that is approved for 6 months of insertion in the US. The Spatz3 device is an adjustable IGB that is approved for 8 months of insertion in the US. Following FDA approval, the safety of both devices has been demonstrated for 12 months.(226,227) The Work Group felt that the benefits of having a reversible, minimally invasive procedure would be desirable to most patients. The weight loss with the IGB was consistent, and the procedure could be completed in the outpatient setting. The rates of adverse events prompting early removal were of concern.

Consistency and evidence support short-term use of IGB with a CLI for weight loss in patients with obesity, and IGBs should be offered as part of a comprehensive program to respect provider and patient preferences. Access to IGB is limited to areas that have endoscopists with training and supplies to complete the procedure. Compared to other metabolic and bariatric procedures, IGB is technically the least challenging. IGB may provide a short-term, non-permanent option for active-duty Service members, as the IGB does not permanently alter the gastrointestinal organs and can be removed to meet operational demands. There was a higher approval amongst active-duty Service members than the VA, as IGB is the only therapy approved for use for active-duty Service members.(228-230) In the VA population, other endoscopic therapies or surgeries are approved and demonstrate more durability.

While IGBs are effective therapies for short-term weight loss, there is a concern for weight regain following removal. A recent database review in the VA showed that IGB resulted in more rapid weight loss than semaglutide (12.7 vs 9.4 kg) in 6 months following initiation of therapy. However, despite ongoing participation in CLI, the average weight regain was 3kg at 1 year (23.6% of weight lost).(231) Another study looked at intragastric balloons as an option for short-term weight management as a bridge to non-bariatric elective surgery in patients with a BMI >35. The IGB was effective at reaching goal weight loss of 14.0 kg ± 7.4 kg prior to surgery. However, at 3 months following removal, an average of 5.8kg was regained.(232)

The Work Group systematically reviewed evidence related to this recommendation.(224,225) Therefore, it is categorized as Reviewed, Amended. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations, including a small sample size and no long-term follow-up in US patients.(224,225) The benefits of the intragastric balloon on weight loss slightly outweigh the potential harm of adverse events, including symptoms prompting early removal. Patient values and preferences were similar because patients preferred the minimally invasive, reversible, and outpatient nature of the procedure. Thus, the Work Group decided upon a *Weak For* recommendation.

Recommendation

12. We suggest metabolic and bariatric surgery, in conjunction with a comprehensive lifestyle intervention, for durable weight loss in patients with a body mass index ≥30 kg/m² with type 2 diabetes mellitus or with a body mass index ≥35 kg/m².

(Weak for | Reviewed, Amended)

Discussion

Metabolic/bariatric surgery (MBS), in conjunction with comprehensive lifestyle intervention, is shown to result in significant and durable weight loss. Advances in minimally invasive surgical techniques, surgical instrumentation, and quality improvement and accreditation programs have led to significant reductions in morbidity and mortality and increased public acceptance of these procedures. Despite the invasiveness of surgery and the small but real risk of significant adverse events, including those associated with gastrointestinal surgery in general, and those associated with metabolic surgery specifically, such as dumping syndrome, mineral/vitamin deficiency, decreased bone density, and postprandial hypoglycemia syndrome (NIPHS [noninsulinoma pancreatogenous hypoglycemia syndrome]).(233-235) Nonetheless, the benefits of MBS, which include a large amount of sustained weight loss, improvement in significant metabolic comorbidities, and increased long-term survival, outweigh the potential harms.

The CPG reviewed an evidence base that included a meta-analysis of randomized clinical trials comparing MBS versus lifestyle intervention (LI), medical therapy (MT), or both.(236) A systematic review of 47 studies comparing different metabolic/bariatric operations (237), and a systematic review of 15 studies comparing MBS with non-operative weight management for the presence of fractures after weight loss (238) were also reviewed. In the meta-analysis of 21 randomized clinical trials comparing MBS and LI/MT, surgery was associated with a significantly greater reduction of BMI and percent weight loss (by 6.01 kg/m^2 and by 17.7%, respectively).(236)

Multiple randomized studies confirm the superiority of surgical intervention over medical management without pharmacotherapy in the treatment of type 2 diabetes mellitus in individuals with Class 1 obesity (BMI 30-34.9 kg/m^2). In a 2016 study of individuals with BMI $\geq$30 kg/m^2, Cummings et al. (2016) showed that more than half of patients who underwent MBS had diabetes remission after 1 year, exceeding the rate of remission in the group undergoing intensive lifestyle and medical intervention, and concurrently showed superior weight loss outcomes. (239) Others demonstrated similar weight loss and diabetes control benefit, 2 and 3 years after surgery in patients with a BMI $\geq$30 kg/m^2.(240,241) In the 2018 study by Simonson et al. (241) that included patients with BMI $\geq$30 kg/m^2 (32% of whom had BMI 30-34.9 kg/m^2), 42% of the surgical cohort had diabetes remission, while 0% of the intensive lifestyle management cohort achieved this glycemic control after 3 years. Randomized trials with 5-year outcomes, published 2017-2020, demonstrated superior partial or complete remission of type 2 diabetes mellitus after MBS compared with CLI, along with superior weight loss.(242-244)

A subgroup analysis of patients with BMI <35 kg/m^2 by Schauer et al. (2017) showed consistent, durable weight loss and glycemic control following surgery that was superior to intensive medical therapy in this BMI range, and similar to the subgroup of BMI $\geq$35 kg/m^2.(244) Furthermore, they subsequently identified unique metabolomic profiles in the surgical group.(245) Similarly, in a 2-year randomized clinical trial of 100 patients with type 2 diabetes

and BMI 30-35 kg/m^2, Cohen et al. (2020) demonstrated a rate of remission of diabetes of 24.4% after best medical treatment, compared with 44.5% after MBS.(246) Randomized trials in Asian populations with Class 1 obesity and type 2 diabetes mellitus similarly demonstrated superior weight loss and improvement in diabetes parameters in cohorts undergoing MBS compared with usual care, after 1 and 5 years.(247,248) In the study by Cheng et al. (2022)(247), complete diabetes remission was achieved in 50% of the cohort undergoing surgery, compared with 0% in the medical group after 12 months. After 5 years, 42% of the surgical patients remained in diabetes remission. Liang et al. (2013) found that 90% of the surgical group experienced diabetes remission after 1 year, compared with none in the non-surgical group.(248)

Multiple randomized clinical trials included the population with a BMI ≥35 kg/m^2. However, there have been no prospective trials comparing MBS vs. CLI in the population with BMI ≥35 kg/m^2 with no other morbidity. Nonetheless, analysis of this group in available evidence suggests a clear weight loss benefit to MBS. Superior weight loss outcomes after surgery were demonstrated in the cohort with BMI ≥35 kg/m^2 and sleep apnea after 2 and 10 years.(249,250) Similar results were also found in the population without specific obesity-related metabolic disease. In a randomized clinical trial of 80 patients with BMI ≥35 kg/m^2 in need of total knee arthroplasty, Dowsey et al. (2022) showed that BMI reduction was significantly greater in the surgical group compared with the group receiving non-surgical treatment as usual after 12 months.(251) In a randomized trial of 20 patients with end-stage renal disease undergoing kidney transplant, with or without MBS, the patient with a BMI ≥35 kg/m^2 who underwent surgery had significantly greater weight loss after 1 year compared with those patients who did not have MBS.(252) In a prospective randomized trial comparing MBS with a no-surgery program in a population with Class 1 obesity that included patients with a BMI of 35 kg/m^2, O'Brien et al. (2013) showed significantly better weight reduction after 10-year follow-up in the surgical group.(253) And in a randomized clinical trial of 66 participants with BMI ≥35 kg/m^2, who also had idiopathic intracranial hypertension, MBS produced weight reduction that was significantly better than community weight management with meal replacement, throughout the 2 years of the study.(254)

MBS has been performed for decades and is recognized as an effective modality to produce significant and durable weight loss in individuals with severe obesity.(255) More recently, it has also been shown to produce lasting improvement in obesity-related comorbidity. Thus, although it involves abdominal surgery with the potential for morbidity, the risk for significant adverse events is low and deemed acceptable.(256) Patients generally seek surgical management reflecting their values that incorporate these findings, anticipating that the desired endpoints will be achieved, and understanding that MBS is associated with improved quality of life.(237) Nonetheless, surgery is generally associated with a higher potential for morbidity than other treatment modalities and is likely a significant patient consideration when deciding whether to undergo MBS. In addition, patients experience stigma related to undergoing bariatric surgery(257,258), which may impact their decision-making.

Subgroup considerations are largely influenced by the large number of resources necessary to maintain a bariatric surgical program; among these are specialty surgeons with training in MBS who are not available at every VA or DOD medical center. In addition, providers with expertise in early recognition and knowledge of intervention for the potential of early weight plateau or weight regain after surgery are an important adjunct to optimal long-term outcomes. Long term, however, the durable improvement of obesity comorbidities such as diabetes leads to overall cost savings after surgery.(259) In patients who are treated with pharmacotherapy alone, studies demonstrate that significant weight regain occurs with discontinuation of these agents, so that pharmacotherapy alone would require long-term medication adherence and associated incurred costs (see Recommendation 15). Similar recommendations have been endorsed by a joint statement of the largest national and international organizations representing metabolic/bariatric surgeons.(260) Reports comparing long-term outcomes of surgery and pharmacotherapy with GLP-1 RAs are needed. The references cited in this section are outside the scope of the review and, therefore, did not influence the strength of the recommendation. Yet, here they provide context in support of the accumulated body of knowledge that is associated with obesity, obesity stigma, and metabolic/bariatric surgery.

The Work Group systematically reviewed evidence related to this recommendation.(236-238) Therefore, it is categorized as Reviewed, Amended. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations, including small sample sizes, comparator (non-operative) groups whose components were not fully defined, different kinds of operations included in the surgical groups, and a lack of blinding of participants. The benefits of weight loss after MBS, and improved glycemic control in patients with type 2 diabetes, outweigh the potential harm of gastrointestinal surgery. Patient values and preferences varied largely because some patients prefer non-invasive treatments, and stigma persists around surgery for weight loss among patients and referring providers. Thus, the Work Group decided upon a *Weak For* recommendation.

Recommendation

13. We suggest endoscopic sleeve gastroplasty (ESG) for weight loss, in conjunction with a comprehensive lifestyle intervention, to patients with a body mass index ≥30 kg/m². **(Weak for | Reviewed, New-added)**

Discussion

Endoscopic sleeve gastroplasty (ESG) is a minimally invasive, organ-sparing endoscopic procedure where the anterior and posterior walls of the stomach are sutured together and the length of the stomach is shortened. The overall size of the stomach is reduced by 70-80%. Currently, the FDA has approved an endoscopic suturing system specifically for ESG, the Apollo ESS System.(261) The procedure can be used as a primary modality for EBT or as a revision procedure. ESG is FDA-approved for a BMI of 30-50 kg/m^2.

A systematic review and meta-analysis were completed in 2022, looking at the effectiveness of endoscopic bariatric interventions(224) at 6 months. 2 studies reviewed ESG compared to

lifestyle intervention and showed superior weight loss at 6 months. 12-month studies showed similar effects. An additional randomized control trial with ESG and CLI was identified with 71 patients showing TBWL of 11% for ESG + CLI: 11(95% CI = 8.86 to 13.15) vs 2.7% with CLI alone(95% CI 0.14 to 5.44).(262) In this study, there were no device-related SAEs observed. The ESG group reported that 80% (41/51) of patients had improvement in one or more metabolic comorbidities. This data is similar to other studies, which demonstrate efficacy and safety compared to comprehensive lifestyle interventions.(262)

Additional studies were available that were outside the scope of the evidence review. In the endoscopic sleeve gastroplasty for treatment of Class 1 and 2 obesity (MERIT) trial, ESG was reviewed in a prospective multicenter fashion.(263) The trial looked at 209 patients (ESG=85, control=124) over the course of 52 weeks.

ESG has been demonstrated to be a safe modality with pooled adverse events ranging from 1.5-2.5% in several meta-analyses and is generally regarded as having lower SAEs compared to laparoscopic sleeve gastrectomy.(264-267) SAEs associated with the procedure include nausea requiring hospitalization, bleeding, and perigastric leaks.

Despite the efficacy and safety of ESG, access to the therapy is limited. The procedure is technically more challenging compared to IGB and requires an endoscopist trained in endoscopic suturing. There is limited insurance coverage of the procedure at this time, which decreases access to care for some patient populations. When compared to semaglutide, the cost-effectiveness of ESG over 5 years is favorable ($3591 vs 13,618).(268) The procedure is not allowed in active-duty Service members as it has gastrointestinal-altering effects similar to bariatric surgeries.

The Work Group systematically reviewed evidence related to this recommendation.(224,262) Therefore, it is categorized as Reviewed, New-added. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations, including small sample sizes and a lack of study data longer than 2 years. The benefits of ESG were having a minimally invasive, organ-sparing procedure with no difference in SAEs compared to CLI and improved QoL outcomes. These benefits outweighed the potential harm of device failure or preclusion of other bariatric procedures. Patient values and preferences were similar because of the minimally invasive nature of the procedure. Thus, the Work Group decided upon a *Weak for* recommendation.

Introduction to the 2025 OBE CPG Pharmacotherapy Recommendations:
Pharmacotherapy should be used in conjunction with CLI for weight loss for individuals with a BMI ≥30 kg/m^2 or BMI ≥27 kg/m^2 with an obesity-associated condition, as this was the patient population represented in the evidence base. All clinical trials of pharmacotherapy were conducted in conjunction with a CLI, and study medication was generally administered concurrently. Therefore, the Work Group specified the importance of initiating pharmacotherapy in conjunction with a CLI in the recommendation. However, the Work Group did not identify evidence to guide decisions for when to initiate pharmacotherapy in conjunction with CLI.

Providers should acknowledge and respect patients' decisions regarding pharmacotherapy. This involves ensuring that patients are well-informed about their treatment options, including the risks, benefits, and potential alternatives, and that their decisions are made voluntarily and without coercion.

For the purposes of this document, we have deliberately and consistently used the term "Obesity Medications" for medical clarity. This reflects the use of these medications in healthcare settings to address the disease of obesity. "Weight Management Medications," however, is the preferred terminology for patient-centered communication and public health messaging to avoid stigmatizing language.

Clinical Care Notes: When managing patients with diabetes mellitus who are taking anti-glycemic medications (most notably sulfonylureas, meglitinides, or insulin therapy), patient education and close glucose monitoring are appropriate at the start of any weight loss intervention, including diet and exercise, to decrease the risk of hypoglycemia. When adding pharmacotherapy agents, such as NuSH /GLP-1 RA agonist-containing agents, dose reduction of other diabetes medications that cause hypoglycemia, such as insulin therapy, may be warranted. Avoiding hypoglycemia events is important. Excess basal insulin dosing (e.g, glargine insulin) can also hinder weight loss efforts as hypoglycemia, especially nocturnal hypoglycemia, will trigger the release of counterregulatory hormones that will stimulate appetite and insulin resistance. It is not recommended to combine Dipeptidyl peptidase 4 inhibitors (DPP4i) therapy with NuSH /GLP-1 RA agonist-containing agents, as this combination does not provide additive glucose-lowering effects.

Recommendation

14. There is insufficient evidence to recommend either for or against delaying the start of pharmacotherapy, in relationship to CLI, to improve outcomes in patients with overweight or obesity.
    (Neither for nor against | Reviewed, New-added)

Discussion

Many clinical guidelines(9,269) recommend a 6-month course of comprehensive lifestyle intervention (CLI) before initiating pharmacotherapy for overweight and obesity. Landmark trials such as the Diabetes Prevention Program and Look AHEAD report average weight losses of 5–10% at one year with CLI, versus 1–2% in control groups.(270,271) While 55–65% of participants achieve ≥5% weight loss, and 10–15% lose ≥15%, 35–50% do not reach the clinically meaningful 5% threshold.(9,272,273) Weight loss often plateaus by 6–9 months, and most individuals regain about one-third of their lost weight within a year, with further regain over time.(117,274) Maintenance strategies like monthly counseling can slow regain, though some regain occurs in the majority of individuals. CLI is the pillar of any weight management strategy, but often metabolic adaptations that favor weight regain will cause individuals to regain weight despite their best efforts.(16,17)

A stepped-care model, in which patients initiate treatment with CLI and escalate to pharmacotherapy or surgery based on response, may pose several limitations. Patients face

practical barriers, logistical, financial, and social, that impede participation in intensive programs, and access to intensive CLI often remains limited, especially in primary care, with most programs concentrated in academic or commercial settings.(275) While the VA MOVE! program is available to all Veterans receiving care in VHA, the Military Health System (MHS) often lacks the staff and infrastructure to provide comparable services. Feedback from Veterans, dependents, and active-duty personnel from the Patient Focus Group highlights inconsistent content and specificity of CLI messaging, reducing its effectiveness. Requiring CLI as a prerequisite to pharmacologic therapy may inadvertently reinforce weight stigma by attributing treatment failure to personal shortcomings rather than recognizing the complex neurobiological and physiological mechanisms underlying obesity. The Patient Focus Group conducted for this CPG expressed frustration with being required to participate in specific CLI programs before accessing obesity medications, particularly after experiencing repeated difficulty achieving sustainable weight loss through prior individual or structured lifestyle interventions.

Phase 3 trial data evaluating semaglutide and tirzepatide demonstrate that adding intensive behavioral therapy or lifestyle intervention provides minimal additional weight loss beyond what is achieved with pharmacotherapy alone.(276-279) Both agents also led to significant improvements in hypertension, lipid profiles, and other metabolic parameters compared to placebo, highlighting their potential to deliver substantial health benefits beyond weight reduction. While these findings stem from indirect comparisons, the results support a potential shift toward earlier, individualized pharmacologic treatment, particularly for patients with obesity-related comorbidities.

Given the above information, the Work Group aimed to evaluate the optimal timing for the initiation of pharmacotherapy for obesity medications, whether that was alongside CLI or after a period of CLI. However, our systematic search identified no studies that directly addressed this question.

To date, no randomized controlled trials have directly compared outcomes of initiating pharmacotherapy after a period of CLI versus starting pharmacotherapy concurrently with CLI, particularly in patients with obesity-related comorbidities. For individuals with more severe obesity-related comorbidities (i.e., Stage 3-4), early initiation of obesity medications may lead to better outcomes. Requiring a course of CLI before prescribing pharmacotherapy may delay weight loss, contribute to patient frustration, and reduce engagement in care. Alternatively, initiating a course of CLI prior to pharmacotherapy may offer benefits, particularly for individuals without severe obesity-related comorbidities, those not yet prepared to initiate pharmacologic treatment, or in whom pharmacotherapy is contraindicated. Given the challenges of maintaining weight loss with CLI alone and the high risk of weight regain due to physiological adaptations(16,17), it is critical to identify optimal time points for intensifying treatment with pharmacotherapy and bariatric surgery. Proactive discussions about pharmacologic or surgical options, even when patients are making progress with lifestyle efforts, can support shared decision-making and improve long-term weight loss and weight maintenance success. While a network meta-analysis would be needed to determine the ideal timing of medication initiation relative to other weight loss interventions, adopting a more flexible, individualized approach that prioritizes timely access to effective therapies is both reasonable and supported by emerging evidence.

With the advent of newer and more effective obesity medications, there is growing support for earlier use of obesity medications, particularly in patients with more severe obesity and/or obesity-related comorbidities. Rather than serving as a prerequisite, clinical practice experts (275,280-285) are starting to discuss the importance of CLI as a necessary complement to pharmacologic therapy to ensure nutritional adequacy, preserve lean mass and physical function, and reduce the risk of sarcopenia and micronutrient deficiencies during weight loss.

The Work Group systematically reviewed the evidence on the optimal timing of pharmacotherapy in relation to CLI; however, no studies meeting the inclusion criteria were identified. Therefore, it is categorized as Reviewed, New-added. The Work Group's confidence in the quality of the evidence was not applicable, as there was no evidence pulled. Thus, the Work Group decided upon a *Neither for nor against* recommendation.

Recommendation

15. We suggest against discontinuing obesity medications, taking into account patient characteristics and preferences, as it results in weight regain.
    (Weak against | Reviewed, New-added)

Discussion

Substantial weight regain occurs after discontinuation of weight loss pharmacotherapy. Two RCTs [SURMOUNT 4, Aronne et al. (2024) (279), and STEP 4 Rubino et al. (2021) (286)] compared continuation of tirzepatide or semaglutide to discontinuation of these medications with a placebo control, after 36 or 20 weeks of initial therapy, respectively. In both studies, on nearly all measures, including body weight, waist circumference, laboratory markers of glucose and lipid metabolism, as well as mental health and quality of life outcomes, continuation of the medication was superior to discontinuation. In STEP 4(286) after 20 weeks, switching to placebo resulted in +6.9% mean body weight gain compared to -7.9% mean body weight loss with continuing semaglutide from 20-68 weeks (difference, -14.8 [95% CI, -16.0 to -13.5] percentage points; P < .001). In SURMOUNT 4, the mean percent weight change from week 36 to week 88 was −5.5% with continued tirzepatide vs +14.0% with switch to placebo (difference, −19.4% [95% CI, −21.2% to −17.7%]; *P* < .001)There was no difference in the frequency of serious adverse events between the continuation arm vs. the placebo arm. The evidence in both studies is of high quality, with double blinding, randomization, and allocation concealment procedures clearly defined. Each had over 200 patients per arm, allowing for sufficient power. A noteworthy limitation is that both SURMOUNT 4 Aronne et al. (2024). (279) and STEP 4 Rubino et al. (2021) (286), selected to compare only those patients who had tolerated up-titration to maximally tolerated doses of the agent, which may lead to an overestimation of benefit when applied to a more general population.

Though not specifically designed to compare the effect of discontinuation after weight loss, in SURMOUNT 1 Jastreboff et al. (2024) (287) RCT comparing tirzepatide vs. placebo, after the initial 176-week study period, participants were followed for an additional 17 weeks off-treatment period. Weight regain occurred during the 17-week off-treatment period after tirzepatide discontinuation.

There is some variation in patient preference, with some patients preferring to continue with an agent that has created effective weight loss, and others who would discontinue due to polypharmacy or concern for potentially unknown long-term risks of use, or intolerance. Some patients may potentially choose to continue on medications for secondary benefits on other comorbidities (e.g., OSA, CKD, CVD, heart failure), though data remains unclear whether these additional benefits are still achieved in the absence of weight loss. Resource use for long-term therapy is also an important consideration that requires further evaluation in the context of both resource scarcity as well as QALY (quality adjusted life year) gained, and morbidity avoided, from maintained weight loss.

Note that data is lacking for the weight effects of gradual de-escalation prior to discontinuation of pharmacotherapy for weight loss. Please see Recommendation 16 below.

An additional study that was not in the evidence base, STEP 1 Wilding et al. (2022)(288), also found that one year after the withdrawal of once-weekly subcutaneous semaglutide 2.4 mg and lifestyle intervention, participants regained two-thirds of their prior weight loss.

The Work Group systematically reviewed evidence related to this recommendation (279,286,287). Therefore, it is categorized as Reviewed, New-added. The Work Group's confidence in the quality of the evidence was high. The harms and burdens of weight regain that ensue from discontinuing obesity medications outweigh the benefits of discontinuing obesity medications. However, patient values and preferences varied because some patients prefer not to be on a long-term medication for weight loss, and resource use remains a concern. Longer-term studies >4 years are needed to determine whether weight regain also results when obesity medications are discontinued after a longer period of use. Thus, the Work Group decided upon a *Weak against* recommendation.

Recommendation

16. There is insufficient evidence to recommend either for or against reduction of the dose or frequency of pharmacotherapy to maintain achieved weight loss and avoid weight regain. **(Neither for nor against | Reviewed, New-added)**

Discussion

Patients and providers are eager to know, once weight targets are met with an obesity medication, does reducing the dose or the frequency of the medication permit maintenance over time? What happens to additional measures of health after dose or frequency reduction of obesity medications? The Work Group dedicated a Key Question to attempt to answer this specific question. However, in reviewing the literature published on or after April 1, 2019, to January 6, 2025, the only data available compared continuation at the highest dose tolerated vs. complete discontinuation of the obesity medication. The data suggest that substantial weight regain occurs after complete discontinuation of weight loss pharmacotherapy (see Recommendation 15 for a more thorough discussion in this regard. Briefly, the Work Group suggests against discontinuing obesity medications as it results in weight regain. No studies were found that evaluated reducing the dose or frequency of a medication initiated for weight loss and using a lower maintenance dose or frequency of dosing to maintain weight loss. Therefore, given the lack of data, we are

unable to make a recommendation in this regard. This highlights the need for future research regarding weight management pharmacotherapy dosing and frequency options.

The Work Group recognizes that there is a large variation in patient perspectives regarding long-term obesity medication use. Some patients do not want to be on any medications, while others prioritize maintaining the weight loss achieved, so they would prefer to continue at a reduced dose or frequency if able to maintain the weight loss achieved. The potential harms from dose or frequency reduction of obesity medications include the risk of weight regain and subsequent complications of obesity. There is an ongoing cost associated with ongoing medical management, as well as risks of side effects. In the absence of data, individualization of therapy is necessary for each patient based on their preferences, values, and goals. Patients who are actively losing weight will benefit from clinical monitoring to assess whether other medications, such as antihypertensives and anti-glycemic agents, require de-escalation or discontinuation. Close monitoring and continued engagement in lifestyle and behavioral weight management resources may be beneficial to support weight maintenance if pharmacotherapy is de-escalated.(289) Patients who do not respond to weight loss medications should be engaged in discussion to identify possible factors such as adherence, negative emotions with weight loss leading to anxiety and depression.

The Work Group systematically reviewed evidence related to this recommendation, and no studies from April 1, 2019, to January 6, 2025, were found to meet the inclusion criteria to determine whether reducing the dose or frequency of pharmacotherapy maintains achieved weight loss and avoids weight regain. Therefore, it is categorized as Reviewed, New-Added. With no studies to assess, the Work Group is unable to make any statement on confidence in the quality of the evidence. Patient values and preferences vary largely because some patients prefer to discontinue pharmacologic agents, while others would prioritize maintaining the weight loss achieved and remaining on an obesity medication that is effective for them long-term. Thus, the Work Group decided upon a *Neither for nor against* recommendation.

Recommendation

17. We recommend semaglutide or tirzepatide for both weight loss and to maintain weight loss, in conjunction with a comprehensive lifestyle intervention, in patients with a body mass index ≥27 kg/m^2 who also have an obesity-associated condition; and those who have a body mass index ≥30 kg/m^2.
    (Strong for | Reviewed, New-added)

Discussion

Pharmacotherapy should be used in conjunction with CLI for weight loss for individuals with a BMI ≥27 kg/m^2 with an obesity-associated condition or BMI ≥30 kg/m^2, as this was the patient population represented in the evidence base. All included clinical trials of pharmacotherapy were conducted in conjunction with a CLI, and study medication was generally administered concurrently. Therefore, the Work Group specified the importance of initiating pharmacotherapy in conjunction with a CLI in the recommendation.

The overall confidence in the quality of the evidence was determined to be moderate. Semaglutide and tirzepatide had a clinically and statistically significant benefit over placebo in the critical outcome of percent change in relative body weight. For semaglutide, a network meta-analysis (NMA) by Dorneles et al. (2024) (290) included studies with follow-up ranging from 24 to 104 weeks. The average percent change in relative body weight was -11.8% compared to placebo, demonstrating semaglutide's efficacy in both weight loss and maintaining weight loss. For tirzepatide, an NMA by Liu et al. (2024)(291) included studies with follow-up ranging from 72 to 88 weeks. The average percent change in relative body weight from the included studies ranged from -15% to -21.2%, depending on the maintenance dose of tirzepatide used. A higher percent change in relative body weight appeared to be associated with higher doses. FDA-approved maintenance doses for tirzepatide are 5mg, 10mg, and 15mg weekly. A longer, 176-week, follow-up is reported in an article by Jastreboff et al. (2024)(287) in patients with obesity and prediabetes, with an average percent change in relative body weight of -11.1%, -17.5%, and -18.4% for tirzepatide 5mg, 10mg, and 15mg weekly, respectively, versus placebo. This demonstrates tirzepatide's efficacy in maintaining weight loss.

A study by Knop et al. (2023)(292) demonstrated significant weight loss (average -12.7% relative body weight change) at 68 weeks with oral semaglutide 50mg daily versus placebo. It should be noted that semaglutide is not currently commercially available in 50mg tablets, nor is a 50mg dose achievable in the currently commercially available oral tablets of semaglutide (RYBELSUS®). The FDA is currently evaluating the application for oral semaglutide 25mg daily for the treatment of overweight and obesity based on results from the OASIS 4 trial (article not published at the time of CPG publication, NCT05564117). Oral semaglutide has also not had evidence to support the other health benefits that subcutaneous semaglutide has for people with overweight and obesity (discussed later in this narrative). The Knop et al. (2023) study supports the efficacy potential for oral semaglutide in weight loss.

The Work Group determined that the benefits for weight loss and maintenance of weight loss slightly outweighed the harms and burdens. For all the included evidence(287,290,291), there was no significant increase in serious adverse events for semaglutide or tirzepatide versus placebo. The most common (≥ 10% reported incidence) side effects of both semaglutide and tirzepatide are GI intolerances, including nausea, vomiting, diarrhea, constipation, and abdominal pain.(293,294) The provision of CLI in conjunction with these medications may help improve GI tolerance as well as prevent nutritional deficiencies (e.g., muscle and bone loss).(295) Both medications have boxed warnings contraindicating use in people with a personal or family history of medullary thyroid cancer or Multiple Endocrine Neoplasia Syndrome Type 2. Other warnings include risk of acute pancreatitis, gallbladder disease, acute kidney injury, hypoglycemia, and, in people with type 2 diabetes, diabetic retinopathy. Because of the potential for fetal harm, it is recommended that semaglutide be discontinued in females and males at least 2 months before they plan pregnancy. Tirzepatide is also not recommended for use during pregnancy, and in addition, there are cautions that oral hormonal contraceptive efficacy may be decreased by tirzepatide. It is recommended that patients using oral hormonal contraceptives switch to a non-oral contraceptive method or add a barrier method of contraception for four weeks after initiation and any dose increases of tirzepatide. There have been rare post-marketing reports of pulmonary aspiration in patients taking GLP-1 agonists who are undergoing general anesthesia or deep

sedation. Suicide behavior and ideation continue to be warnings on the prescribing information of both tirzepatide and semaglutide, though recent evidence suggests that there may not be an associated risk with this class of medications.(296)

There are many subgroups of patients with overweight and obesity that may have the potential for additional health benefits from semaglutide or tirzepatide. Some of these studies were outside the evidence review but noted here as potential reasons a provider may choose semaglutide or tirzepatide as an opportunity to treat overweight/obesity and another condition. Both semaglutide and tirzepatide have evidence to improve HbA1c in people who have diabetes(297,298), reduce the new onset of type 2 diabetes(287), and improve symptoms with heart failure with preserved ejection fraction(299,300). The SELECT trial(301) demonstrated that people with overweight or obesity and cardiovascular disease (defined as prior myocardial infarction; prior ischemic or hemorrhagic stroke; or symptomatic peripheral arterial disease with an ankle-brachial index < 0.85, peripheral arterial revascularization procedure, or amputation due to atherosclerotic disease) had a 20% decreased risk of secondary cardiovascular events with semaglutide versus placebo. The SURMOUNT-OSA(302) trial demonstrated an improved apnea-hypopnea index with tirzepatide versus placebo in people with obesity and moderate to severe obstructive sleep apnea.

As once-weekly injected medications, some patients may prefer semaglutide or tirzepatide because of their less frequent administration than a daily medication. On the other hand, some patients may prefer oral medications over injected ones. Both semaglutide and tirzepatide should be stored in refrigeration, which may present a challenge for some subgroups who do not have access to refrigeration for their medications. Both semaglutide and tirzepatide are only available as branded medication (i.e., no generic is currently available), which may make them cost-prohibitive to some patients and/or healthcare systems. Obesity medications are also something that needs to be taken long-term, if not lifelong, as current evidence supports that weight regain occurs when the medication is discontinued (see Recommendation 15).

A cohort study by Rodriguez et al. (2025)(303) found that most patients with type 2 diabetes had higher rates of discontinuation and lower rates of reinitiation of GLP-1 therapy, compared to patients with overweight and obesity without type 2 diabetes in a one-year time frame. It is important to consider patient-specific factors and monitor for adverse effects in the titration of these agents for optimal tolerance and weight management success.

The Work Group systematically reviewed evidence related to this recommendation.(287,290,291) Therefore, it is categorized as Reviewed, New-added. The Work Group's confidence in the quality of the evidence was moderate. The body of evidence had some limitations, including inconsistency of results, which may have been a function of NMAs that included a variety of studies with different inclusion and exclusion criteria for their participants. The benefits of weight loss and maintenance of weight loss slightly outweigh the potential harms of adverse event risk. Patient values and preferences varied somewhat because of the route of administration, dosing frequency, and duration of treatment to maintain weight loss. Thus, the Work Group decided upon a *Strong for* recommendation.

Recommendation

18. We suggest phentermine/topiramate extended release (ER) or liraglutide for both weight loss and to maintain weight loss, in conjunction with a comprehensive lifestyle intervention, in patients with a body mass index ≥27 kg/m^2 who also have an obesity-associated condition; and, those who have a body mass index ≥30 kg/m^2.
    (Weak for | Reviewed, New-added)

Discussion

The critical outcomes of a decrease in body weight and an increased number of participants with ≥5%, ≥10% and >15% body weight reduction compared to lifestyle intervention were evaluated in several studies.

For liraglutide, two studies were found in the literature search. There was evidence from 4 RCTs in 1 SR(304) that liraglutide + CLI reduced both body weight and proportion of participants achieving >5% and >10% weight loss compared to placebo + CLI during a follow-up duration of 52 to 160 weeks with a moderate quality of evidence. In Wadden et al. (2019), liraglutide plus intensive behavioral therapy (IBT) reduced body weight, BMI, and proportion of participants achieving > 5%, > 10% and > 15% weight loss compared to placebo + CLI during a follow-up duration of 24 to 52 weeks. The quality of evidence was found to be low due to a small sample size.

For phentermine/topiramate ER, one study was found in the literature search. Evidence from 5 RCTs in 1 SR,(305) phentermine/topiramate ER reduced body weight and found a higher proportion of participants achieving >5% and >10% weight loss compared to lifestyle intervention during a follow-up duration of 24 to 52 weeks with moderate to high quality of evidence.

Additionally, the critical outcome of weight loss was evaluated with respect to liraglutide and phentermine-topiramate ER, which were reviewed in the 2020 VA/DOD Obesity CPG. The critical outcome of weight loss was evaluated in a large, comprehensive SR and meta-analysis (306) that included 28 RCTs. The combination of a CLI and either liraglutide or fixed-combination phentermine-topiramate ER resulted in greater weight reduction than a CLI alone, with moderate confidence in the quality of the evidence. The meta-analysis reported that after a minimum follow-up of 12 months, both medications were associated with a greater reduction in total body weight compared to placebo. Further, a greater proportion of patients in the medication group achieved at least 5% or 10% weight loss from baseline compared to placebo, which is considered to be clinically significant. Another study reviewed in the 2020 CPG, in le Roux et al. (2017),(307) liraglutide + CLI led to greater weight loss than CLI alone at 160 weeks.

Although liraglutide has been found to be effective for clinically significant weight loss, and no head-to-head clinical trials are included in the data analyzed, the average weight loss with liraglutide is consistently less than that seen with tirzepatide and semaglutide. In the Shi et al 2024 meta-analysis, the average weight loss with liraglutide was 4.67%, whereas with semaglutide, 11.4% weight loss was seen. In the Khera et al. (2016) (306) systematic review and meta-analysis, which did not include semaglutide or tirzepatide, patients who received fixed-combination phentermine/topiramate ER had the highest probability of achieving a 5% or 10%

weight loss, followed by liraglutide. Although liraglutide is recommended for weight loss and to maintain weight loss, one might consider a more efficacious medication if given a choice. Patients who do not achieve their weight loss goal with liraglutide should be transitioned to other weight loss pharmacotherapy with proven benefit to provide 7-10% weight loss (for example, in patients with MASH).

Importantly, for both liraglutide and phentermine/topiramate ER in multiple studies, there were no significant differences in adverse effects reported with liraglutide or phentermine-topiramate ER compared with CLI alone.(304,305,308)

We suggest both liraglutide and phentermine-topiramate ER for weight maintenance after initial weight loss. Evidence from 4 RCTs in 1 SR(304), Liraglutide + CLI reduced both body weight and proportion of participants achieving >5% and >10% weight loss compared to placebo + CLI during a follow-up duration of 160 weeks, with moderate quality of evidence. As the weight loss was maintained for 160 weeks, we recommend liraglutide for weight maintenance in addition to weight loss. The quality of this data was low, thus we could only assign a *Weak for* recommendation. One systematic review (115) and one RCT (307) reviewed in the 2020 VA/DOD Obesity CPG also demonstrated a benefit on maintenance of weight loss with liraglutide. LeBlanc et al. (2018) (115) demonstrated a maintenance of 5% or 10% weight loss during 13 months of follow-up (after an initial weight loss of at least 5%), favored treatment with liraglutide compared to placebo. In le Roux et al. (2017),(307) liraglutide induced greater weight loss than placebo at week 160.

The 2014 VA/DOD Obesity CPG included high certainty evidence in support of the role of fixed-combination phentermine/topiramate ER in maintenance of weight loss. Garvey et al. (2012) (309) found that significantly more patients in the fixed-combination phentermine/topiramate ER treatment groups experienced a ≥5% weight loss (79.3% with fixed-combination phentermine/topiramate 15 mg/92 mg versus 30% with placebo) or ≥10% weight loss (53.9% with fixed-combination phentermine/topiramate 15 mg/92 mg versus 11.5% with placebo) after 108 weeks. This leads us to continue to recommend phentermine-topiramate ER to maintain weight loss.

Unlike newer NuSHes/GLP-1 RA containing agents, liraglutide is a once-daily injection compared to once weekly. Some patients may prefer the routine of using an injection daily, whereas this medication may be less desirable to patients who prefer a weekly injection. Given the shorter half-life of liraglutide, it will metabolize more rapidly should significant side effects develop, and dose titration is more rapid. Like all NuSHes/GLP-1 RA-containing agents, the most common reported side effects are GI distress, including nausea, vomiting, and diarrhea. All GLP-1 receptor agonists are recommended to remain refrigerated before use. As of this writing, liraglutide is currently the only GLP-1 agonist available as a generic medication, which may make it more affordable in the future. Liraglutide was noted to reduce the risk of major adverse cardiovascular events, including MI, stroke, and CV death, in adults with type 2 diabetes in the LEADER trial.(310) Liraglutide was also shown to reduce the AHI in patients with obesity.(311)

As a once daily oral pill, phentermine-topiramate ER may be preferred by those who either want to avoid agents that require injection, or to minimize pill burden or frequency of medication administration per day. It comes in multiple different doses, so the dosing can be titrated to the

individual patient based on effectiveness and tolerability. The topiramate component may be helpful in patients who have alternative uses for topiramate, such as migraine headaches or restless leg syndrome.

The Work Group systematically reviewed evidence related to this recommendation(304,305) identified through the systematic evidence review and considered evidence put forth in the 2014 VA/DOD Obesity CPG(309) and 2020 VA/DOD Obesity CPG.(115,306,307) Therefore, it is categorized as Reviewed, Amended. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations, including a small sample size and confounders in the analysis. The benefits of both greater weight loss and maintenance of weight loss with pharmacotherapy in conjunction with CLI, compared to CLI alone, outweighed the potential harms of adverse events. Patient values and preferences varied somewhat because some patients prefer daily oral medications, whereas others may prefer less frequent dosing or opt for no medications. Thus, the Work Group decided upon a *Weak for* recommendation.

Recommendation

19. We suggest naltrexone/bupropion extended release (ER) for weight loss, in conjunction with a comprehensive lifestyle intervention, in patients with a body mass index ≥27 kg/m^2 who also have an obesity-associated condition; and those who have a body mass index ≥30 kg/m^2.
    (Weak for | Reviewed, New-added)

Discussion

Evidence from 1 SR and 6 RCTs(305) suggests that naltrexone/bupropion ER did not lead to a clinically important difference in percent bodyweight change compared to lifestyle intervention at 24 to 52 weeks follow-up. (SOE: Moderate). However, naltrexone/bupropion did lead to a clinically important increase in the percentage of participants with body weight reduction ≥5% or ≥10% compared to lifestyle intervention at 24 to 52 weeks follow-up (SOE: High).(305)

As the maintenance dose of naltrexone/bupropion (ER) is 2 tablets twice daily, pill burden and adherence can be a concern for patients. Additionally, adjustments are needed in patients with renal and hepatic impairment; the medication must be held before sedation, and patients on chronic opiates should not use it concurrently. However, naltrexone/bupropion ER can be beneficial in the concurrent treatment of smoking cessation, alcohol use disorder, and depression. Oral formulation of the medication (as opposed to an injection) allows for ease of use and storage.

Naltrexone/bupropion ER's common adverse side effects include headache, sleep disorder, nausea, constipation, diarrhea, vomiting, dizziness, and xerostomia. Use of the medication is contraindicated with concurrent opioid use, pregnancy, uncontrolled hypertension, seizure disorder, bulimia or anorexia nervosa, abrupt discontinuation of alcohol, acute opioid withdrawal, and concurrent use of MAOI, linezolid, or IV methylene blue. Significant warnings to consider include suicidal thinking/behavior (black box warning). Neuropsychiatric symptoms may precipitate acute opioid withdrawal in patients receiving opioids, increased blood pressure

and heart rate, hepatotoxicity, and hypoglycemia requiring adjustments to antihyperglycemic medications (See Appendix J).

The critical outcomes of weight loss and safety were evaluated in one large, comprehensive SR and meta-analysis that included 28 RCTs (n=29,018).(306) This contributed to moderate confidence in the quality of the evidence that the combination of a CLI and an obesity medication, approved by the FDA for long-term use, including naltrexone/bupropion ER, results in greater weight reduction than a CLI alone. The meta-analysis reported that after a minimum follow-up of 12 months, naltrexone/bupropion ER was associated with a greater reduction in total body weight compared to placebo. Further, a greater proportion of patients in the medication group achieved at least 5% or 10% weight loss from baseline compared to placebo, which is considered to be clinically significant.(306) The longest duration of therapy for naltrexone/bupropion ER for weight loss is currently 52 weeks. As the workgroup considered a minimum duration of therapy of 2 years required to make a statement regarding medication use for maintenance therapy, no statement could be made regarding the use of naltrexone/bupropion ER for weight maintenance.

A meta-analysis by Shi et al. (2024)(305), found naltrexone/bupropion and phentermine had the highest risks of adverse effects leading to discontinuation. Naltrexone/bupropion ER had less weight loss overall when compared to phentermine-topiramate; however, more participants taking naltrexone-bupropion ER achieved >5% and >10% bodyweight reduction when compared with liraglutide.(305,306)

Pharmacotherapy may produce significant weight loss in conjunction with CLI; however, treatment individualization is critically important due to the potential for adverse effects. As reported in the SR by Khera et al. (2016), all of the obesity medications evaluated were associated with a statistically significant risk of medication discontinuation due to adverse events when compared to placebo.(306). Naltrexone/bupropion ER had the second-highest odds of treatment discontinuation when compared with liraglutide, phentermine/topiramate, and orlistat. (see Table J-2)(305,306) As noted in the 2018 USPSTF systematic review(115), trials of obesity medications often had very selective inclusion and exclusion criteria. Patients who volunteer for participation in research may have higher levels of adherence than community-dwelling patients. Patients may be excluded from participation due to medical conditions that are often present in the patient populations intended for management by this CPG. The Work Group considered the applicability of these results to the general patient population as well as the potential harms from the obesity medications. Naltrexone/bupropion ER may be specifically inappropriate for patients with conditions such as HTN, seizure disorder, drug misuse disorder potential, pregnancy, or who are breastfeeding. Patients should be informed of the risks and adverse effects of each medication to properly incorporate patient preference in the medication selection (see Appendix J for additional information on pharmacotherapy considerations).

Most studies, including the SR (312), documented the serious limitation of attrition above 30%. The benefits of naltrexone/bupropion (ER) outweigh potential patient harms when the medication regimen selected is customized to individual patients and considers comorbidities, potential contraindications, and adverse effects of the medication. Additional data should help

determine the long-term outcome benefit of specific pharmacotherapy as well as any potential harms with long-term maintenance. Obesity medications also have the potential for high cost and resource use with long-term therapy. In addition, as noted above, the high attrition rates in clinical trials and the SRs suggest low feasibility for long-term use. Participants in the patient focus group were interested in pharmacologic therapy for weight loss and in obtaining additional information on the efficacy as well as potential side effects of these medications (see Appendix J on pharmacotherapy and Sidebar 2 on select medications and their potential effects on weight).

The Work Group systematically reviewed evidence related to this recommendation(115,306,307,309,312-318) and considered the evidence extracted in the 2020 and the current 2025 CPGs.(309,319,320) The Work Group's confidence in the quality of evidence was moderate. The body of evidence had high attrition, which was considered a serious limitation. The benefit of greater weight loss with pharmacotherapy in conjunction with CLI compared to CLI alone outweighed the potential harms of adverse events, which may be reduced if medication selection is individualized for the patient. The lack of outcome data for long-term benefits and harms, limited feasibility due to high attrition, and higher cost and resource use compared to CLI alone were also noted. Patient values and preferences were somewhat varied. Thus, the Work Group decided upon a *Weak for* recommendation. Research is needed to address the numerous knowledge gaps in pharmacotherapy for weight loss and weight maintenance (see Knowledge Gaps and Recommended Research for more information).

Recommendation

20. We suggest the use of glucagon-like peptide type 1 agonist-containing agents, in conjunction with CLI, for the treatment of patients with overweight and obesity, with either co-occurring prediabetes or type 2 diabetes mellitus.
    (Weak for | Reviewed, New-added)

Discussion

Our Work Group reviewed the available evidence to determine how co-occurring obesity-related medical conditions impact the safety and effectiveness of treatments for overweight and obesity. Evidence to answer this question was limited and primarily focused on the use of glucagon-like peptide type 1 agonists and polyagonists (including a combination of Glucose-Dependent Insulinotropic Polypeptide (GIP), glucagon, and others) for weight loss in patients with and without diabetes. A network meta-analysis of 27 RCTs demonstrated significantly greater weight loss in patients with diabetes treated with NuSHes/GLP-1RA containing agents (tirzepatide, retatrutide*, semaglutide, liraglutide) versus placebo; however, retatrutide, semaglutide, and tirzepatide all showed significantly greater weight loss among patients without T2DM compared to patients with T2DM.(321) The confidence in the quality of the evidence was low due to indirect cross-trial comparisons between subgroups. GLP-1RAs also led to improvements in

* Not FDA-approved at time of publication

waist circumference with a similar pattern of significantly greater reductions in waist circumference among patients without T2DM compared to patients with T2DM for retatrutide, semaglutide, and tirzepatide. There were no differences in severe adverse outcomes (cardiovascular events, severe gastrointestinal reactions, or infections) in those with and without diabetes. A meta-analysis of 46 RCTs comparing GLP-1 agonist containing agents (semaglutide, dulaglutide, danuglipron*, efpeglenatide*, exenatide, liraglutide, orforglipron*) showed greater reductions in Hemoglobin A1c and fasting plasma glucose for patients with diabetes (-0.90%, -1.32 mmol/L) and pre-diabetes (-0.44%, -0.71 mmol/L) compared to those without diabetes (-0.23%, -0.35 mmol/L).(322) One post-hoc RCT analysis of semaglutide use in patients with Metabolic Dysfunction-Associated Steatotic Liver Disease/Metabolic Dysfunction-Associated Steatohepatitis (MASLD/MASH) also showed significant weight loss in patients with pre-T2DM and T2DM compared to placebo.(323)

Our evidence review also returned a post hoc analysis of an RCT investigating the use of Intensive Lifestyle Intervention (ILI) in patients with T2DM, but the study did not include a comparison group without diabetes.(324) A meta-analysis of 14 RCTs examining the effectiveness of ketogenic diets in those with and without T2DM did not include the critical outcome of weight loss and thus did not contribute to our recommendation.(158) We did not retrieve any studies that compared treatments in patients with and without ASCVD, heart failure, or MASLD/MASH. Additional studies were retrieved from other key questions in our evidence review that support the use of GLP-1RAs in a variety of co-occurring obesity related conditions; however, they lack direct comparisons of patients with and without the conditions. This limits our ability to answer how a given condition impacts the safety and effectiveness of the intervention. For example, the SURMOUNT-4 trial showed sustained weight loss at 88 weeks with tirzepatide in a variety of obesity-related conditions, such as ASCVD and MASLD, but outcomes were not compared among subgroups.(279) In addition, RCTs such as SUSTAIN-6, PIONEER-6, and SOUL have demonstrated the cardiovascular benefits of semaglutide (in both injection and oral formulations) for T2DM; however, these studies were not included in our evidence review because they were not limited to patients with overweight and obesity, which is the focus of this guideline. As such, we are not able to make specific recommendations on how co-occurring ASCVD impacts the safety and effectiveness of treatments for overweight and obesity.(325-327) The evidence review highlights the difficulty of assessing the complex interplay of multiple comorbidities typically seen in clinical practice.

Our review of the evidence demonstrated multiple benefits of NuSHes/GLP-1 RA-containing agents for patients with obesity/overweight and T2DM, including weight loss, decreased abdominal circumference, and improved glycemic control. Improved glycemic control also extended to patients with prediabetes. In clinical practice, we have also observed the benefit of being able to wean other obesogenic medications, such as insulin and sulfonylureas, by using GLP-1 RAs. Notably, there was no significant difference in serious adverse events compared to placebo. However, we acknowledge that side effects are common and can lead to discontinuation of therapy in clinical practice. Overall, we find that the potential benefits of GLP-1 RA therapy outweigh the risk of harms in diabetes mellitus and prediabetes. GLP-1 RA therapy is also consistent with patient values and preferences. Patients from our focus group

valued effective therapy and highlighted their struggles with prior attempts at weight loss using less effective treatments. While we feel many patients want to avoid pharmacological therapy, there is generally a more positive perception of GLP-1RA therapy due to commercials, social media, and interactions with friends and family who have experienced weight loss with the medication. They also value the multiple benefits of GLP-1RAs and the potential to reduce the use of other, less effective medications. While we find some patients hesitant to use injections, oral GLP-1 RA medications are currently being evaluated in clinical trials and, if available, may mitigate this concern. We acknowledge that many patients are concerned about being on GLP-1RA long term; however, in patients with diabetes, this is less of a concern, as they are more accustomed to long-term therapy for their chronic condition. Overall, we feel patient values and preferences are similar across those with diabetes and prediabetes.

We also considered resource use, acceptability, and feasibility as part of our recommendation. Resource use negatively impacted our recommendation. GLP-1 RA medications are currently very expensive for individuals and for health systems. We hope that generic medications and increasing market competition may mitigate this cost in the future. Similarly, supply availability has been highly variable, thus limiting the number of patients with access to therapy. We considered GLP-1 RA medication to be highly acceptable to providers because of its evidence of weight loss in T2DM and prediabetes, as well as providers being aware of multiple benefits, such as A1c reduction and potential cardiovascular benefits. We also considered these therapies to be feasible for the majority of patients. GLP-1 RA injectable pens are easy to use and can be administered in all outpatient settings with minimal teaching for most patients. Feasibility will only increase over time as more oral medications become available.

The Work Group systematically reviewed evidence related to this recommendation.(279,321-324) Therefore, it is categorized as Reviewed, New-Added. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations including lack of direct comparisons between patients with and without diabetes,(321,322) lack of primary weight loss outcome,(321) and a post hoc study design.(323) The benefits of GLP-1 RAs in obesity/overweight and co-occurring T2DM and prediabetes for weight loss, decreased abdominal circumference, and improved glycemic control outweighed the potential harm of adverse events. Patient values and preferences were similar because of the desire for more effective medications for weight loss and the multiple benefits of therapy. Thus, the Work Group decided upon a *Weak for* recommendation.

Recommendation

21. There is insufficient evidence to recommend either for or against orlistat, metformin, sodium glucose co-transporter type 2 inhibitors, or pramlintide for weight loss. **(Neither for nor against | Reviewed, Amended)**

Discussion

Evidence reviewed from SRs or RCTs published on or after April 1, 2019, to January 6, 2025, included Shi et al. (2024)(305). This systematic review network meta-analysis included 132 trials enrolling 48,209 participants in total. The strength of the evidence was overall moderate.

Limitations include significant variability and heterogeneity in comparator interventions, given that lifestyle interventions were different even among studies looking at similar ages. Most studies included were funded by the pharmaceutical industry. Most were multicenter, and most included centers within the United States.

Compared to lifestyle intervention at 24-52 weeks, across 52 randomized control trials, Shi et al. (2024) (305) found that orlistat did not lead to a clinically significant difference in percent bodyweight change (at least 5% weight loss). Similarly, in 13 RCTs,(305) metformin did not lead to a clinically important difference in percent bodyweight change at 24 to 52 weeks of follow-up. In 2 RCTs,(305) pramlintide also did not lead to a clinically important difference in percent bodyweight change at 24 to 52 weeks of follow-up when compared to lifestyle intervention. Finally, in 10 RCTs,(305) pramlintide also did not lead to a clinically important difference in percent bodyweight change at 24 to 52 weeks of follow-up.

The Work Group felt that there are benefits to having agents available that may assist with preventing weight gain associated with antipsychotic drug use, such as metformin, and agents that do not have significant central nervous system effects due to little systemic absorption, such as orlistat, and agents that treat comorbid conditions such as diabetes mellitus without causing weight gain, such as metformin, pramlintide and sodium glucose co-transport inhibitor therapies. These agents are largely oral (with the exception of pramlintide, which is a subcutaneous injection administered pre-meals), cost-effective, and promote equity since they can be prescribed by most providers. These benefits are however balanced with the potential harms of non-clinically significant weight loss seen with these agents, falling below the minimal important difference (MID) most often cited by the FDA of 5% body weight loss, as well as side effects associated with each, including gastrointestinal side effects of orlistat, metformin and pramlintide, as well as risk of genitourinary tract infections and euglycemic diabetic ketoacidosis risk from sodium glucose cotransport inhibitors if used in patients without sufficient endogenous insulin production remaining. (Note: when considering SGLT2i therapy, and it is unclear what endogenous insulin production remains, consider checking a postprandial glucose and C-peptide level to assess.)

The Work Group systematically reviewed evidence related to this recommendation.(305) Therefore, it is categorized as Reviewed, Amended. The Work Group's confidence in the quality of the evidence was moderate. The body of evidence had some limitations in that some agents had few studies evaluating their effects.(305) The benefits of orlistat, metformin, sodium glucose co-transporter type 2 inhibitors, or pramlintide for weight loss were balanced with the potential harm, given the lack of overall efficacy for weight loss of these agents, less than the minimal important difference of 5% body weight change, while still causing adverse events, most often gastrointestinal. Patient values and preferences varied significantly because some patients prefer oral agents and do not prefer invasive treatments. Thus, the Work Group decided upon a *Neither for nor against* recommendation.

Recommendation

22. There is insufficient evidence to recommend either for or against phentermine monotherapy, benzphetamine, diethylpropion, or phendimetrazine, for weight maintenance.
(Neither for nor against | Reviewed, Amended)

Discussion

There are several medications approved by the FDA for short-term (i.e., "few weeks") weight reduction (e.g., phentermine, benzphetamine, diethylpropion, and phendimetrazine). However, these approvals were based on studies conducted before 1975. The systematic evidence review carried out as part of this guideline update did not identify any current SRs or individual studies, from April 1, 2019 to January 6, 2025, that evaluated any of these agents that met the inclusion criteria. The prior 2020 VA/DOD Obesity CPG update found one small RCT compared diethylpropion (n=28) as one of five different medications (two not available in the U.S. [fenproporex, mazindol], one removed from the market [sibutramine], one off-label [fluoxetine]) to placebo (n=29) for weight loss in premenopausal women with obesity.(313) After 52 weeks, treatment with diethylpropion resulted in a significant weight reduction (-10.0 kg) compared to a placebo (-3.1 kg). In addition, 71.4% of patients treated with diethylpropion versus 33.3% of patients in the placebo group experienced a ≥5% reduction in body weight. Adverse events with diethylpropion included constipation, anxiety, and irritability, which were reported more frequently with treatment versus placebo. These sympathomimetic drugs are classified by the U.S. Drug Enforcement Administration as Schedule III or IV controlled substances, as they have potential for abuse, and prescribing information suggests they should not be used in individuals with a history of cardiovascular disease (CVD).

The LEAP trial (Project Number5UH3HL155801-04), actively underway, should provide data on safety measures with longer-term use of phentermine. However, at the time of this writing, given the lack of additional data on long-term treatment in a large patient population, as well as the unknown long-term benefits and harms of intermittent short-term weight loss with this class of agents, the Work Group determined there was insufficient evidence to make a recommendation regarding the use of these medications for long-term use.

It is important to recognize that these agents are oral medications that have been prescribed for decades. They are available in a generic formulation, which positively affects resource use, and are available at the VA, in military treatment facilities, and covered under Tricare. In addition, lower dose phentermine 15mg combined with extended release topiramate (phentermine/topiramate extended release [ER]) is FDA approved for long-term use (See Recommendation 18).

The Work Group systematically reviewed evidence related to this recommendation, and no new studies were found to meet the inclusion criteria. The 2020 VA/DOD CPG update review found a single study, Suplicy et al. (2014), which provided low-quality evidence due to the small sample size. Therefore, it is categorized as Reviewed, Amended. The Work Group's confidence in the quality of the evidence was low. The body of evidence had significant limitations, including small sample size, single-blind, and moderate to high attrition in a single study since 1975. Results from

an ongoing longer-term phentermine monotherapy study (LEAP, Long-Term Effectiveness of the Anti-obesity medication Phentermine, NCT05176626) remain pending as of this writing. The benefits of phentermine monotherapy, benzphetamine, diethylpropion, or phendimetrazine for weight maintenance were balanced with the potential harm. Patient values and preferences varied largely because some patients prefer a pharmacologic agent over no agent if no other agent is accessible financially. Thus, the Work Group decided upon a *Neither for nor against* recommendation.

Recommendation

23. We suggest against using dietary supplements or nutraceuticals for clinically meaningful weight management.
    (Weak against | Not reviewed, Amended)

Discussion

There is insufficient evidence demonstrating clinically significant short-term weight loss or supporting long-term weight management or maintenance through nutraceutical or dietary supplements. A nutraceutical can be defined as "a food or dietary supplement that is believed to provide health benefits".(328) A combination of eight SRs and RCTs, which studied various nutraceuticals, was identified and reviewed for this recommendation.(329-336) Overall, the confidence in the quality of evidence was rated low to very low due to a lack of adequate randomization, blinding, allocation concealment, and high risk of bias. Inconsistent dosing of specific nutraceuticals and lack of generalizability of findings were noted across multiple studies.

An SR of 15 RCTs (n=1,130) by Huang et al. (2018) showed a small but statistically significant weight loss of 0.89 kg (p=0.0006) with chitosan versus placebo for short-term weight loss (<24 weeks).(329) No serious adverse events were reported. The most commonly reported adverse events were GI complaints (e.g., abdominal pain, bloating, constipation, indigestion, non-infectious diarrhea). The studies included in this large SR utilized multiple dosing regimens and used varying products and formulations of nutraceuticals, making dosing recommendations impossible.

Mousavi et al. (2018) conducted an SR of 12 trials on the effects of cinnamon supplementation on obesity, finding statistically significant differences in short-term weight loss (-1.02 kg; p=0.002) and BMI (-0.39 kg/m^2; p<0.001).(330) The generalizability of outcomes to the VA/DOD population is limited. Specifically, of the 14 studies included in the systematic review, only three were conducted in Western cultures – two in the United States and one in the United Kingdom (U.K.); the remainder were conducted in the Middle East. Furthermore, at least half of the included studies included only female subjects. Additionally, inconsistent heterogeneous dosing of cinnamon was also noted.

In reference to Garcinia Cambogia, a small randomized controlled trial conducted by Tripathy et al. (2013) demonstrated statistically significant (p<0.0001) short-term weight loss, as measured by Body Mass Index (BMI), following the consumption of Garcinia Cambogia for four months.(331) Limitations included a small study population (n=100) and non-stratified results between men and women. An online search of FDA warnings lists garcinia cambogia as a nutraceutical dietary

supplement that is sold as a combination supplement. When taken in that form, it is associated with risk for coronary disease events, stroke, and liver damage. Harms and burdens of Garcinia Cambogia outweigh the benefits. In addition, the FDA previously recalled a product being used for weight loss for being associated with reports of liver damage related to the ingredient hydroxycitric acid, an ingredient in Garcinia Cambogia products or dietary supplements. Considering the potential risks, harms, and burdens associated with Garcinia Cambogia, its limited benefits were deemed insufficient to justify its use.

No statistically significant weight loss was observed when green tea was used in comparison to a placebo across the two studies reviewed.(332,333) Limitations included that comparators were not the same between subject groups. Green tea was used in conjunction with other supplements, making it unclear whether green tea had a specific effect.

Statistically significant weight loss was seen in one small RCT (n=60) looking at Phaseolus vulgaris over 12 weeks, with an MD in weight loss of 1.7 kg between Phaseolus vulgaris and control.(334) Phaseolus vulgaris is also known as the common bean, green bean, and French bean. Adverse events were not severe, not serious, and not related to the supplement. Pill burden was a concern, with subjects taking six tablets per day.

An SR of 15 studies using probiotics showed no statistically significant difference in weight loss outcomes versus placebo.(335) Limitations included the heterogeneity of supplements studied.

A small RCT using raspberry ketones did not show a statistically significant outcome for weight loss for up to 12 weeks.(336) The study participants were all female.

Furthermore, dietary supplements and nutraceuticals have not been extensively studied in conjunction with CLIs, resulting in insufficient evidence to determine whether the active dietary supplement or nutraceutical product is superior to a placebo when combined with CLI. Although there may be isolated supplements that are safe, these are rarely sold as individual ingredients and may be combined with other supplements that are not safe. Specifically, liver toxicity has been documented as a side effect of some weight loss supplements.(337,338) The Work Group considered this aspect to be a fundamental component of any long-term weight management intervention. Additionally, marketing may be misleading when companies claim to treat or cure a disease without evidence to prove effectiveness.(339) The perceived advantages of dietary supplements and nutraceuticals, often promoted through marketing and anecdotal reports, may create unrealistic expectations that hinder patient and clinician interest and investment in the evidence-based interventions recommended in this CPG.

In the review of dietary supplements for weight loss, additional consideration was given to potential issues such as increased cost, safety, effectiveness, pill burden, and diverting patient interest away from evidence-based interventions. Concerns exist that supplements are frequently marketed to present inaccurate or exaggerated benefits at an excessive cost.(339) The FDA regulatory guidelines treat items listed as dietary supplements as a food, as defined by the Dietary Supplement Health and Education Act (DSHEA) of 1994.(340) Dietary supplements and nutraceuticals do not require investigation as a new drug.(340) The overall safety concerns, cost,

and pill burden using dietary supplements often complicate medical treatment and have the potential to delay treatment with effective therapeutics.

The Work Group did not systematically review evidence related to this recommendation. The studies were obtained from the 2020 CPG. (329-336) Therefore, it is categorized as Not reviewed, Amended. The Work Group's confidence in the quality of the evidence was low. The body of evidence had many limitations including small sample sizes,(331) heterogeneity of supplement dosing and concentration,(330) use of a highly selective study population,(334) and risk for bias.(334). The supplements also have a risk of potential harm due to a lack of regulations and monitoring, and drug interactions with prescribed medications; thus, the harms/burden slightly outweigh the benefits. Patient values and preferences varied significantly because of high costs, false advertising, and pill burden. Thus, the Work Group decided upon a *Weak against* recommendation.

X. Research Priorities

Obesity is a chronic, relapsing neurohormonal disease that is associated with over 200 other diseases. There are several areas that require more focused research to provide stronger evidence for further recommendation development across the spectrum of career recommendations and aid in refining interventions. In summary, the Work Group recommends research on comprehensive lifestyle interventions, dietary approaches, metabolic and bariatric surgery, pharmacotherapy, weight bias and stigma, and cost-effective strategies. Research on how to best implement CPG recommendations would be helpful in both the VA and DOD.

A. Comprehensive Lifestyle Interventions

Comprehensive lifestyle intervention (CLI) programs can be resource-intensive, particularly regarding training and retaining clinical staff and maintaining evidence-based program support tools (educational materials, technology-assisted programming). Therefore, more research is needed to identify accessible, scalable, and practical ways to deliver the three core elements of these programs (behavior change, nutrition, and physical activity) in ways that align with patients' abilities, values, and preferences. For example, comparative effectiveness studies to compare modes of CLI delivery as well as different intensities of CLI would inform refinements to recommendations and potentially more efficient resource utilization. In addition, trials evaluating how to optimally combine CLI with other interventions, particularly in light of newer, more effective pharmacotherapy, are needed. Research is also needed on the use of artificial intelligence (AI) tools to support CLI, particularly the use of data to provide individualized feedback and treatment tailoring, as well as trials evaluating AI-assisted delivery of behavioral weight management interventions. Additionally, research should examine how different types of exercise, especially when combined with obesity medications, impact body composition and health outcomes, while also evaluating adherence and attrition rates related to these interventions.

B. Dietary Approaches

Further research is needed to identify dietary approaches that are particularly effective in addressing appetite regulation and increasing satiety, which could play a key role in supporting long-term weight management. Well-designed studies should also focus on evaluating the effectiveness of various diets in promoting sustained weight loss over time. In addition, expanding research on the comparative health benefits of different dietary patterns could provide valuable insights for developing more personalized and outcome-driven dietary recommendations. Future research should prioritize investigating the nuanced role of micronutrient and macronutrient deficiencies, particularly protein and vitamins, in patients on obesity medications, to better understand their impact on treatment efficacy, safety, and long-term nutritional status.

C. Metabolic and Bariatric Procedures and Surgery

There is a growing need for research to evaluate the outcomes of metabolic and bariatric surgery (MBS) in individuals with Class 1 and 2 obesity who do not present with obesity-related comorbid conditions. Additionally, investigations should examine the interaction between MBS and emerging pharmacotherapies for obesity, as these medications may influence surgical outcomes or serve as alternatives in certain populations. Evidence for combination medications and

procedures is lacking. Comparative studies are also essential to determine the effectiveness and safety of surgery compared to pharmacotherapy. There is emerging evidence to support some obesity medications in the prevention of weight regain after metabolic and bariatric procedures and surgery.(341-343) Additional literature to assess the potential role of pharmacologic agents as adjuvant or neoadjuvant treatments in the context of bariatric surgery is essential to better understand optimal timing/sequencing of these interventions.

The left gastric artery embolization (LGAE) procedure for obesity does not have full FDA approval for general use, but has been studied under experimental device exemptions and for pilot clinical trials by the FDA, such as the GET LEAN and BEAT Obesity studies. LGAE aims to reduce the hunger hormone ghrelin by decreasing blood flow to the stomach's fundus, potentially leading to weight loss. It is an experimental, minimally invasive procedure with promising early results but also potential complications, and requires further research to establish its safety and efficacy for treating obesity.

D. Pharmacotherapy

The individualization of pharmacotherapy plans is essential to ensure that patients receive the most effective and appropriate treatments tailored to their unique needs. This personalized approach is particularly crucial when considering insurance coverage and tapering obesity medications.

As pharmacologic options for obesity expand, future research must prioritize a more individualized, equitable, biologically informed, and practical approach to treatment. Although long-term safety data for most established obesity medications exist, critical evidence gaps remain that limit optimal care delivery. Pharmacotherapy requires a highly individualized approach, informed by factors such as comorbidities, risk of sarcopenia in older adults, and psychiatric history. Yet most existing studies compare full-dose continuation to abrupt discontinuation, with limited data on stepwise dose reduction strategies that could optimize both tolerability and adherence. Comparative effectiveness studies in real-world populations are needed to guide decision-making between drug classes and in relation to other interventions. Additionally, cost-effectiveness analyses are crucial to inform policy, promote equitable access, and shape clinical guidelines.

Underrepresented populations, including racial and ethnic minorities, individuals with specific genetic profiles, and those with coexisting medical and psychiatric conditions, remain largely excluded from clinical trials. Research must also explore the optimal duration of use, management of plateaus, management of treatment discontinuation, as well as long-term metabolic, cardiovascular, and psychological effects of treatment discontinuation to inform strategies for weight maintenance. Ongoing evaluation of long-term safety, especially in vulnerable populations such as peripartum and lactating women, is critical to ensure that expanding access to pharmacologic obesity care does not compromise long-term health.

Future studies should investigate how genetic, metabolic, and behavioral phenotyping can enable precision medicine approaches, tailoring treatment to individual biology. Additionally, future research would explore when the optimal time is to start pharmacotherapy for individuals with overweight and obesity. To improve efficacy and durability, research must further elucidate the neurohormonal biology of obesity. Exploring biological targets beyond the GLP-1 axis may lead to

drugs with greater potency and fewer side effects, while combination therapies that address multiple mechanisms of appetite and energy regulation offer another promising direction.

E. Weight Bias and Stigma

Future research on weight bias and stigma should include fully powered randomized clinical trials that are inclusive and representative of active-duty Service members and Veterans. Studies should explore whether reducing weight stigma leads to improved engagement in weight loss treatments. Interventions targeting weight bias and discrimination among providers, particularly within the VA and DOD systems, are essential, with outcomes assessed for both providers and patients. Addressing obesity could lead to improved health outcomes and reduced healthcare expenditures.

F. Cost-Effective Strategies

Research should also examine the potential cost savings of treating obesity and preventing other consequential conditions such as hypertension, diabetes, obstructive sleep apnea, cardiovascular disease, and certain cancers. Obesity is a significant risk factor for these chronic diseases, which impose substantial economic burdens on healthcare systems. Effectively treating obesity could lead to improved health outcomes and reduced healthcare expenditures.

Appendix A: Guideline Development Methodology

A. Developing Key Questions to Guide the Systematic Evidence Review

To guide this CPG's systematic evidence review, the Work Group drafted 12 KQs on clinical topics of the highest priority for the VA and DOD populations. The KQs followed the population, intervention, comparison, outcome, timing, and setting (PICOTS) framework, as established by the Agency for Healthcare Research and Quality (AHRQ) (see **Table A-1**).

Table A-1. PICOTS (344)

P	Patients, Population, or Problem	Patients of interest. It includes the condition(s), populations or sub-populations, disease severity or stage, co-occurring conditions, and other patient characteristics or demographics.
I	Intervention or Exposure	Treatment (e.g., drug, surgery, lifestyle changes), approach (e.g., doses, frequency, methods of administering treatments), or diagnostic/screening test used with the patient or population.
C	Comparison	Treatment(s) (e.g., placebo, different drugs) or approach(es) (e.g., different dose, different frequency, standard of care) that are being compared with the intervention or exposure of interest described above.
O	Outcome	Results of interest (e.g., mortality, morbidity, quality of life, complications). Outcomes can include short, intermediate, and long-term outcomes.
(T)	Timing, if applicable	Duration or follow-up of interest for the particular patient intervention and outcome to occur (or not occur).
(S)	Setting, if applicable	Setting or context of interest. Setting can be a location (e.g., primary, specialty, inpatient care) or type of practice.

Abbreviation: PICOTS: population, intervention, comparison, outcome, timing, and setting

The Champions, Work Group, and evidence review team carried out several iterations of this process, each time narrowing the scope of the CPG and the literature review by prioritizing the topics of interest. Due to resource constraints, all developed KQs were not able to be included in the systematic evidence review. Thus, the Champions and Work Group determined which questions were of highest priority, and those were included in the review. **Table A-4** contains the final set of KQs used to guide the systematic evidence review for this CPG.

a. Population(s)

- The clinical population considered in this systematic review are adults (aged 18 years or older) with overweight or obesity.
- For KQ 12, the population of interest is the standard clinical population with one of the following co-occurring conditions:
  - Type 2 diabetes,
  - atherosclerotic cardiovascular disease (ASCVD) (including Congestive Heart Failure), or
  - metabolic dysfunction-associated steatotic liver disease (MASLD) (aka non-alcoholic fatty-liver disease (NAFLD), MASH, etc.).

b. Interventions and Comparators

KQ	Intervention(s)	Comparator(s)
1	CLI (must include diet, physical activity, behavior change components)	▪ Different CLI ▪ Same CLI delivered at a different intensity (e.g., once per week vs. once per month; 6 sessions vs. 12 sessions) ▪ Same CLI delivered in a different mode (in-person behavioral counseling vs. telehealth [Including telephone, clinical video telehealth, virtual, synchronous, asynchronous, automated])
2	▪ Cardio (aerobic) ▪ HIIT (High Intensity Interval Training) ▪ Non-structured physical activity (including step count) ▪ Qigong ▪ Recreational sports ▪ Resistance/strength training ▪ Tai Chi ▪ Yoga	Any intervention compared with a different one
3	See pharmacotherapy list	▪ CLI ▪ Same medication plus CLI
4	▪ Atkins ▪ Alkaline diet ▪ Anti-inflammatory diet ▪ Blood Type diet ▪ Calorie Restrictive ▪ Counting Macros ▪ DASH (Dietary Approaches to Stop Hypertension) ▪ Detox and Cleanse Diets ▪ Dukan diet ▪ Eat Stop Eat ▪ Flexitarian diet ▪ Intermittent Fasting (e.g. ▪ 16:8 method, 5:2 diet, Alternate-Day Fasting) ▪ Juice Cleanses ▪ Ketogenic diet ▪ Low-carb diet ▪ Low-fat diet ▪ Master Cleanses ▪ Meal replacements	▪ Any intervention compared with another one

KQ	Intervention(s)	Comparator(s)
	▪ Mediterranean Diet ▪ Noom diet (low density foods) ▪ Nutrisystem ▪ Ornish diet ▪ Paleo diet ▪ Plant-based diet ▪ Raw Food diet ▪ Renaissance Periodization ▪ South Beach diet ▪ Time Restricted Eating ▪ Traditional low-fat diet ▪ Vegetarian diet ▪ Vegan diet ▪ Vertical Diet ▪ Weight Watchers (use of point system) ▪ Whole 30 diet ▪ Zone diet	
5	▪ Biliopancreatic diversion ▪ Gastric bypass ▪ Gastroplasty ▪ Partial gastrectomy ▪ Sleeve gastrectomy ▪ Single anastomosis duodenoileostomy	CLI
6	▪ Air displacement plethysmography ▪ Bioelectrical Impedance Analysis (BIA) ▪ Body Mass Index (BMI) ▪ Body Mass Index (BMI) + waist circumference ▪ body round index ▪ Dual-energy X-ray absorptiometry (DXA) ▪ Hydrostatic weighing ▪ Magnetic resonance imaging (MRI) or magnetic resonance spectroscopy (MRS) ▪ Nuclear magnetic resonance (NMR) spectroscopy ▪ plethysmography BodPod ▪ Quantitative magnetic resonance	Compared to each other

KQ	Intervention(s)	Comparator(s)
	▪ Quantitative computed tomography (QCT) scan	
7	Continue weight loss medication at current dose	▪ Reduce dose ▪ Discontinue medication
8	▪ Endoscopic gastric plication ▪ Endoscopic sleeve gastroplasty ▪ Intragastric balloon	CLI
9	CLI plus medication started at the same time	CLI plus medication started at different points in time
10	▪ Acceptance and Commitment Therapy for weight stigma ▪ Cognitive behavioral therapy for weight stigma ▪ Mindfulness for weight stigma ▪ Photovoice for weight stigma ▪ Psychoeducation for weight stigma ▪ Self-Compassion Therapy for weight stigma	▪ CLI ▪ Intervention plus CLI
11	▪ Calorie tracking ▪ CBT for weight loss ▪ Serial weigh in ▪ Sleep hygiene ▪ Stress reduction ▪ Tracking apps	CLI alone
12	▪ Exercise regimens ▪ Personalized dietary plans ▪ Pharmacological treatments that are adjusted to safely and effectively manage both weight and the associated conditions ▪ See pharmacotherapy list	▪ CLI ▪ A standard weight-management strategy that does not specifically consider the presence of co-occurring conditions

c. Standard Pharmacotherapy List

Drug Class	Example Drugs: Generic (BRAND)
Alpha-glucosidase inhibitors	▪ Acarbose (PRECOSE)
Anorexiants	▪ Phentermine-topiramate (QSYMIA), Bupropion-naltrexone (CONTRAVE)
Antihyperglycemic - Amylin Analog-Type	▪ Pramlintide (SYMLIN)
Attention Deficit-Hyperactivity (ADHD) Therapy, Stimulant-Type	▪ Lisdexamfetamine (VYVANSE)
Biguanides	▪ Metformin (GLUCOPHAGE)

Drug Class	Example Drugs: Generic (BRAND)
Carbonic anhydrase inhibitors	▪ Topiramate (TOPAMAX) ▪ Zonisamide (ZONEGRAN)
Central nervous system stimulants	▪ Dextroamphetamine-Amphetamine (ADDERALL) ▪ Methylphenidate (RITALIN) ▪ Phedimetrazine tartrate (FENDIQUE)
Dual Agonist Therapy GIP (Glucose-dependent Insulinotropic Polypeptide) + GLP1 agonist	▪ Dulaglutide: (TRULICITY) ▪ Exenatide: (BYETTA and BYDUREON) ▪ Liraglutide: (VICTOZA for T2DM and SAXENDA for obesity) ▪ Retatrutide ▪ Semaglutide: (OZEMPIC and RYBELSUS for T2DM and WEGOVY for obesity) ▪ Tirzepatide: (MOUNJARO for T2DM and ZEPBOUND for obesity)
Activin Receptor Antagonists	▪ Bimagrumab
Lipase Inhibitor	▪ Xenical (ORLISTAT)
Melanocortin receptor agonists	▪ Setmelanotide (IMCIVREE)
Opiate agonists	▪ Naltrexone (VIVITROL)
Sodium-glucose transport protein 1 inhibitors (SGLT1i)	▪ Sotagliflozin (INPEFA)
Sodium-glucose transport protein 2 inhibitors (SGLT2i)	▪ Bexaglifloxin: (BRENZAVVY) ▪ Canagliflozin: (INVOKANA) ▪ Dapagliflozin: (FORGIXA) ▪ Empagliflozin: (JARDIANCE) ▪ Ertugliflozin: (STEGLATRO)
Stimulants	▪ Diethylproprion (TENUATE, TEPANIL), ▪ Phentermine (ADIPEX-P, LOMAIRA)
Other	▪ Buproprion (WELLBUTRIN, ZYBAN)

d. Outcomes

KQ	Critical Outcome(s)	Important Outcome(s)
1	▪ Body Composition - Changes or maintenance (e.g., waist circumference), fat-free body mass, fat distribution ▪ Weight Status - Changes or maintenance (in lbs, kg, BMI, weight change, % of weight loss 5, 10, 15, 20, ≥25%)	▪ Adherence to Therapy ▪ Functional status/Quality of Life (QOL) ▪ Laboratory markers (e.g., CBC, BMP/CMP; Lipid panel including non-HDL cholesterol; Apo B; high-sensitivity C-reactive protein (hs-CRP); Hemoglobin A1c) ▪ Mental Health (e.g., Anxiety; Depression; PHQ9, GAD7, Disordered eating/Eating disorder symptoms) ▪ Serious adverse events (SAEs) as reported by study

KQ	Critical Outcome(s)	Important Outcome(s)
2	▪ Weight Status - Changes or maintenance (in lbs, kg, BMI, weight change, % of weight loss 5, 10, 15, 20, ≥25%)	▪ Adherence to Therapy ▪ Body Composition - Changes or maintenance (e.g., waist circumference), fat-free body mass, fat distribution ▪ Functional status/Quality of Life (QOL) ▪ Laboratory markers (e.g., CBC, BMP/CMP; Lipid panel including non-HDL cholesterol; Apo B; high-sensitivity C-reactive protein (hs-CRP); Hemoglobin A1c) ▪ Mental Health (e.g., Anxiety; Depression; PHQ9, GAD7, Disordered eating/Eating disorder symptoms) ▪ Serious adverse events (SAEs) as reported by study
3	▪ Major Adverse Cardiovascular Events (MACE) not included under SAEs ▪ Serious adverse events (SAEs) as reported by study ▪ Weight Status - Changes or maintenance (in lbs, kg, BMI, weight change, % of weight loss 5, 10, 15, 20, ≥25%)	▪ Apnea-Hypopnea Index (AHI) ▪ Hepatic steatosis (MASLD/NAFLD/MASH, FIB-4, elastography) ▪ Laboratory markers (e.g., CBC, BMP/CMP; Lipid panel including non-HDL cholesterol; Apo B; high-sensitivity C-reactive protein (hs-CRP); Hemoglobin A1c) ▪ Progression to/of Atherosclerotic cardiovascular disease (ASCVD) (including Heart Failure)
4	▪ Adherence to therapy ▪ Weight Status - Changes or maintenance (in lbs, kg, BMI, weight change, % of weight loss 5, 10, 15, 20, ≥25%)	▪ Body Composition - Changes or maintenance (e.g., waist circumference), fat-free body mass, fat distribution ▪ Functional status/Quality of Life (QOL) ▪ Laboratory markers (e.g., CBC, BMP/CMP; Lipid panel including non-HDL cholesterol; Apo B; high-sensitivity C-reactive protein (hs-CRP); Hemoglobin A1c) ▪ Mental Health (e.g., Anxiety; Depression; PHQ9, GAD7, Disordered eating/eating disorder symptoms) ▪ Serious adverse events (SAEs) as reported by study
5	▪ Body Composition - Changes or maintenance (e.g., waist circumference), fat-free body mass, fat distribution ▪ Serious adverse events (SAEs) as reported by study ▪ Weight Status - Changes or maintenance (in lbs, kg, BMI, weight change, % of weight loss 5, 10, 15, 20, ≥25%)	▪ Adherence to therapy ▪ Functional status/Quality of Life (QOL) ▪ Laboratory markers (e.g., CBC, BMP/CMP; Lipid panel including non-HDL cholesterol; Apo B; high-sensitivity C-reactive protein (hs-CRP); Hemoglobin A1c) ▪ Mental Health (e.g., Anxiety; Depression; PHQ9, GAD7, Disordered eating/eating disorder symptoms)

KQ	Critical Outcome(s)	Important Outcome(s)
6	▪ Body Composition - Changes or maintenance (e.g., waist circumference), fat-free body mass, fat distribution ▪ Weight Status - Changes or maintenance (in lbs, kg, BMI, weight change, % of weight loss 5, 10, 15, 20, ≥25%)	▪ Functional status/Quality of Life (QOL) ▪ Laboratory markers (e.g., CBC, BMP/CMP; Lipid panel including non-HDL cholesterol; Apo B; high-sensitivity C-reactive protein (hs-CRP); Hemoglobin A1c) ▪ Mental Health (e.g., Anxiety; Depression; PHQ9, GAD7, Disordered eating/eating disorder symptoms) ▪ Progression to/of Atherosclerotic cardiovascular disease (ASCVD) (including Heart Failure) ▪ Progression to/of Diabetes Mellitus
7	▪ Body Composition - Changes or maintenance (e.g., waist circumference), fat-free body mass, fat distribution ▪ Serious adverse events (SAEs) as reported by study ▪ Weight Status - Changes or maintenance (in lbs, kg, BMI, weight change, % of weight loss 5, 10, 15, 20, ≥25%)	▪ Adherence to therapy ▪ Functional status/Quality of Life (QOL) ▪ Laboratory markers (e.g., CBC, BMP/CMP; Lipid panel including non-HDL cholesterol; Apo B; high-sensitivity C-reactive protein (hs-CRP); Hemoglobin A1c) ▪ Mental Health (e.g., Anxiety; Depression; PHQ9, GAD7, Disordered eating/eating disorder symptoms)
8	▪ Serious adverse events (SAEs) as reported by study ▪ Weight Status - Changes or maintenance (in lbs, kg, BMI, weight change, % of weight loss 5, 10, 15, 20, ≥25%)	▪ Adherence to therapy ▪ Body Composition - Changes or maintenance (e.g., waist circumference), fat-free body mass, fat distribution ▪ Functional status/Quality of Life (QOL) ▪ Laboratory markers (e.g., CBC, BMP/CMP; Lipid panel including non-HDL cholesterol; Apo B; high-sensitivity C-reactive protein (hs-CRP); Hemoglobin A1c) ▪ Mental Health (e.g., Anxiety; Depression; PHQ9, GAD7, Disordered eating/eating disorder symptoms)
9	▪ Adherence to therapy ▪ Weight Status - Changes or maintenance (in lbs, kg, BMI, weight change, % of weight loss 5, 10, 15, 20, ≥25%)	▪ Body Composition - Changes or maintenance (e.g., waist circumference), fat-free body mass, fat distribution ▪ Functional status/Quality of Life (QOL) ▪ Laboratory markers (e.g., CBC, BMP/CMP; Lipid panel including non-HDL cholesterol; Apo B; high-sensitivity C-reactive protein (hs-CRP); Hemoglobin A1c) ▪ Mental Health (e.g., Anxiety; Depression; PHQ9, GAD7, Disordered eating/eating disorder symptoms) ▪ Serious adverse events (SAEs) as reported by study

KQ	Critical Outcome(s)	Important Outcome(s)
10	▪ Functional status/Quality of Life (QOL) ▪ Mental Health (e.g., Anxiety; Depression; PHQ9, GAD7, Disordered eating/eating disorder symptoms, internalized weight stigma)	▪ Adherence to therapy ▪ Body Composition - Changes or maintenance (e.g., waist circumference), fat-free body mass, fat distribution ▪ Laboratory markers (e.g., CBC, BMP/CMP; Lipid panel including non-HDL cholesterol; Apo B; high-sensitivity C-reactive protein (hs-CRP); Hemoglobin A1c) ▪ Serious adverse events (SAEs) as reported by study ▪ Weight Status - Changes or maintenance (in lbs, kg, BMI, weight change, % of weight loss 5, 10, 15, 20, ≥25%)
11	▪ Adherence to therapy ▪ Weight Status - Changes or maintenance (in lbs, kg, BMI, weight change, % of weight loss 5, 10, 15, 20, ≥25%)	▪ Body Composition - Changes or maintenance (e.g., waist circumference), fat-free body mass, fat distribution ▪ Functional status/Quality of Life (QOL) ▪ Laboratory markers (e.g., CBC, BMP/CMP; Lipid panel including non-HDL cholesterol; Apo B; high-sensitivity C-reactive protein (hs-CRP); Hemoglobin A1c) ▪ Mental Health (e.g., Anxiety; Depression; PHQ9, GAD7, Disordered eating/eating disorder symptoms) ▪ Serious adverse events (SAEs) as reported by study
12	▪ Weight Status - Changes or maintenance (in lbs, kg, BMI, weight change, % of weight loss 5, 10, 15, 20, ≥25%)	▪ Adherence to therapy ▪ Body Composition - Changes or maintenance (e.g., waist circumference), fat-free body mass, fat distribution ▪ Functional status/Quality of Life (QOL) ▪ Laboratory markers (e.g., CBC, BMP/CMP; Lipid panel including non-HDL cholesterol; Apo B; high-sensitivity C-reactive protein (hs-CRP); Hemoglobin A1c) ▪ Mental Health (e.g., Anxiety; Depression; PHQ9, GAD7, Disordered eating/eating disorder symptoms) ▪ Serious adverse events (SAEs) as reported by study

e. Timing

Standard timing: “weight loss” is weight at a minimum of 6 months of a program or intervention, and “weight maintenance” is 24 months and beyond.

f. Setting(s)

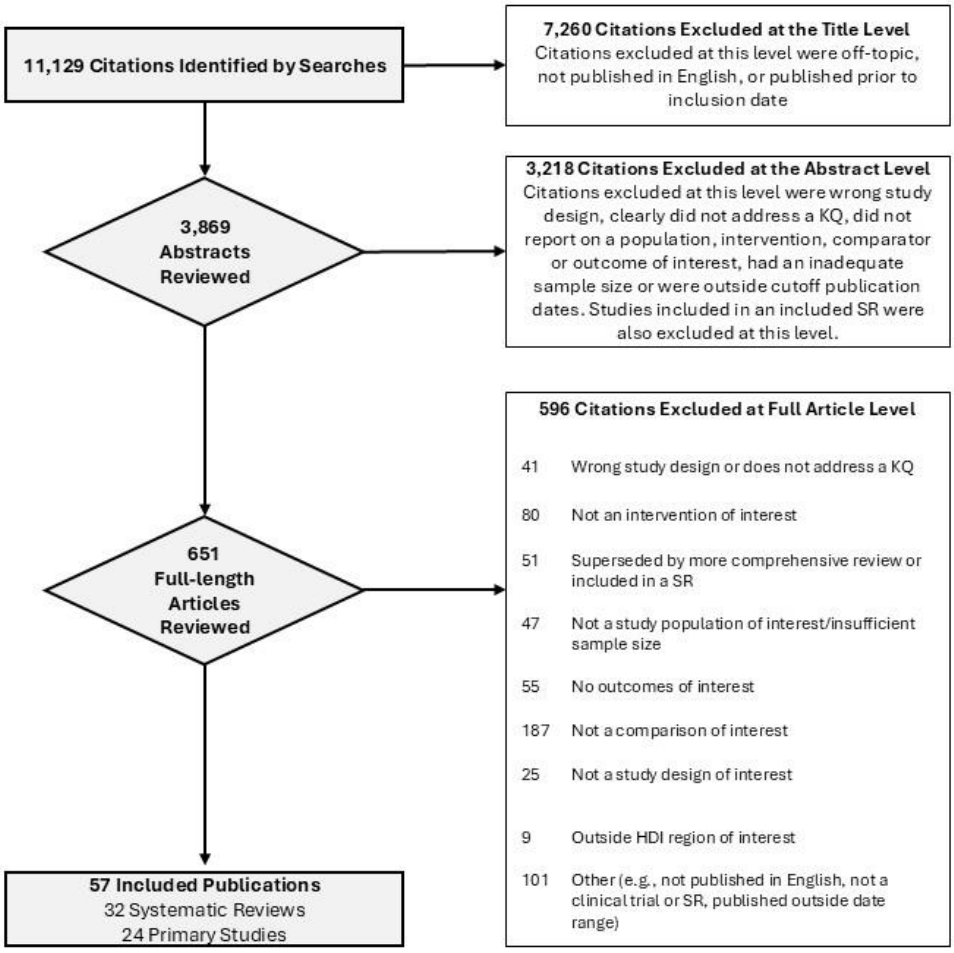
Outpatient delivery of care (with the exception that some types of bariatric surgery may require inpatient care).

B. Conducting the Systematic Review

Extensive literature searches identified 11,129 citations potentially addressing the KQs of interest to this evidence review. Of those, 7,260 were excluded upon title review for clearly not meeting inclusion criteria (e.g., not pertinent to the topic, not published in English, published prior to study inclusion publication date, or not a full-length article). Overall, 3,869 abstracts were reviewed, with 3,218 of those being excluded for the following reasons: wrong study design, clearly did not address a KQ, did not report a population, intervention, comparator, or outcome of interest, had an inadequate sample size, were outside cutoff publication dates, or were included in an included SR. A total of 651 full-length articles thought to address one or more KQs were reviewed. Of those, 596 were excluded for the following reasons: wrong study design, clearly did not address a KQ, did not report a population, intervention, comparator, or outcome of interest, had an inadequate sample size, were outside cutoff publication dates, outside HDI region of interest, or were superseded by a more comprehensive SR or included in an included SR, these are presented in **Figure A-1** below.

Overall, 57 publications addressed one or more of the Key Questions and were considered as evidence in this review. **Table A-2** indicates the number of studies that addressed each of the KQs.

Figure A-1. Study Flow Diagram



Abbreviations: CS: comparative study; HDI: Human Development Index; KQ: key question; SR: systematic review

Alternative Text Description of Study Flow Diagram

Figure A-1. Study Flow Diagram is a flow chart with nine labeled boxes linked by arrows that describe the literature review inclusion-exclusion process. Arrows point down to boxes that describe the next literature review step, and arrows point right to boxes that describe the excluded citations at each step (including the reasons for exclusion and the numbers of excluded citations).

1. Box 1: 11,129 citations identified by searches.
    a. Right to Box 2: 7,260 excluded at the title level. Excluded citations were off topic, not published in English, or published prior to inclusion date.
    b. Down to box 3.
2. Box 3: 3,869 abstracts reviewed.
    a. Right to Box 4: 3,218 citations excluded at the abstract level. Citations excluded were wrong study design, clearly did not address a KQ, did not report on a population, intervention, comparator or outcome of interest, had an inadequate sample size or were outside cutoff publication dates. Studies included in an included SR were also excluded at this level.
    b. Down to Box 5.
3. Box 5: 651 full-length articles reviewed.
    a. Right to Box 6: 596 citations excluded at 1st pass full-article level.
        i. 41 wrong study design or doesn't address a KQ.
        ii. 80 not an intervention of interest.
        iii. 51 superseded by more comprehensive review or included in a SR.
        iv. 47 not a study population of interest/insufficient sample size.
        v. 55 no outcomes of interest.
        vi. 187 not a comparison of interest.
        vii. 25 not a study design of interest.
        viii. 9 outside HDI region of interest.
        ix. 101 other.
    b. Down to Box 7.
4. Box 7: 57 included publications.
    a. 32 systematic reviews.
    b. 24 primary studies.

Table A-2. Evidence Base for KQs

KQ Number	KQ	Number and Study Type
1	What is the comparative effectiveness of various intensities and modalities of comprehensive lifestyle interventions (CLIs) on weight loss, weight maintenance, and other health outcomes?	3 RCTs
2	What is the comparative effectiveness of different types of physical activity on weight loss, weight maintenance, and other health outcomes?	1 umbrella review, 4 network meta-analyses, 6 SRs, and 1 RCT
3	What is the safety and effectiveness of pharmacotherapy on weight loss, weight maintenance and other health outcomes?	4 SRs and 7 RCTs
4	What is the comparative effectiveness of various dietary approaches/strategies on weight loss, weight maintenance, and other health outcomes?	1 network meta-analysis, 7 SRs, and 3 RCTs
5	What is the safety and effectiveness of bariatric surgery on weight loss, weight maintenance, and other health outcomes?	3 SRs
6	What is the clinical utility of various modalities and measures of adiposity and body composition to define and manage excess adiposity and improve clinical outcomes?	1 SR and 2 cross-sectional observational studies
7	Once weight targets are met, what is the comparative effectiveness of continuing weight loss medication vs. reducing vs. discontinuing medications on weight loss, weight maintenance, and other health outcomes?	2 RCTs
8	What is the safety and effectiveness of endoscopic procedures for weight management?	2 SRs and 1 RCT
9	What is the optimal timing to initiate pharmacotherapy for weight management (e.g., at the start of comprehensive lifestyle intervention or at a later time)?	No evidence
10	What is the safety and effectiveness of interventions to reduce weight bias and stigma?	1 SR and 3 RCTs
11	What is the safety and effectiveness of a specific behavioral intervention compared to comprehensive lifestyle interventions (CLI) on weight loss, weight maintenance, and other health outcomes?	1 RCT
12	How do co-occurring obesity-related conditions affect the safety and effectiveness of interventions and strategies for weight management?	3 SRs and 2 post-hoc analyses
Total Evidence Base		**57 papers***

*Some papers address more than one KQ, and some studies are reported in more than one paper, therefore the total number for the evidence base is greater than the total number of includes in the study flow diagram and description.
Abbreviations: KQ: key question; RCT: randomized controlled trial; SR: systematic review

a. General Criteria for Inclusion in Systematic Evidence Review

- Randomized control trials (RCTs) or systematic reviews of RCTs published on or after April 1, 2019, through January 6, 2025. If multiple systematic reviews addressed a key question, we selected the most recent and/or comprehensive review.
- Studies had to be published in English.
- Publication had to be a full clinical study or systematic review; abstracts alone were not included. Similarly, letters, editorials, research protocols, and other publications that were not full-length clinical studies were not accepted as evidence.
- Systematic reviews must have searched MEDLINE or EMBASE for eligible publications, performed a risk of bias assessment of included studies, and assessed the quality of evidence using a recognizable rating system, such as Grading of Recommendations Assessment, Development and Evaluation (GRADE) or something compatible (e.g., the tool used by the AHRQ Evidence-based Practice Centers [AHRQ-EPCs]). If an existing review did not assess the overall quality of the evidence, evidence from the review must have been reported in a manner that allowed us to judge the overall risk of bias, consistency, directness, and precision of evidence. We did not use an existing review as evidence if we were not able to assess the overall quality of the evidence in the review.
- Randomized control trials must have had an independent control group. Randomized crossover trials were only included if data from the first period (prior to treatment crossover) was reported separately and an adequate washout period was used.
- Study must have enrolled at least 20 patients (10 per study group for RCTs and 20 for prospective non-randomized studies) unless otherwise noted (see Key Question Specific Criteria below).
- Study must have enrolled at least 85% of patients who met this SR's population criteria: adults aged 18 years or older with overweight or obesity. If the patient population fell below this threshold but the relevant population were reported separately, then that study was included.
- To ensure applicability to the VA/DOD healthcare systems, and ensure consistency across the CPG program, inclusion of individual studies was limited to very high Human Development Index (HDI), countries with an index ≥0.8 where standards of healthcare are comparable (e.g., United States, Canada, United Kingdom, Western Europe, Israel, Japan, Hong Kong, Australia, and New Zealand). Inclusion of systematic reviews was limited to those including more than half of the studies from eligible regions.
- These regions of interest are listed in Table 1 of the Statistical Annex of the 2023/24 Human Development Report produced by the United Nations Development Programme.
- Study must have reported on at least one outcome of interest.

b. Key Question Specific Criteria for Inclusion in Systematic Evidence Review

- If no RCTs are available to address KQ 6, prospective, non-randomized comparative studies were included. In the event there is no data identified for this KQ, we then looked at longitudinal cohort studies. Similarly, if no systematic reviews of RCTs are available for KQ 6, SRs of eligible non-RCT designs were used.
- For KQ 12, RCTs and SRs of RCTs that performed subgroup analyses of the specified co-occurring conditions were included. We also considered SRs of observational studies that compare treatment effects in patients with and without the specified co-occurring conditions.

c. Literature Search Strategy

Information regarding the bibliographic databases, date limits, and platform/provider can be found in **Table A-3**, below. Additional information on the search strategies, including topic-specific search terms and search strategies can be found in Appendix F.

Table A-3. Bibliographic Database Information

Name		Date Limits	Platform/ Provider
Bibliographic Database	Embase/Medline	April 1, 2019, through January 6, 2025	Elsevier
	PsycINFO	April 1, 2019, through January 6, 2025	EBSCO
	PubMed in process	April 1, 2019, through January 6, 2025	PubMed
Grey Literature Resources	AHRG Evidence-based Practice Center (EPC) Reports	April 1, 2019, through January 6, 2025	AHRQ
	VA Evidence Synthesis Program Reports	April 1, 2019, through January 6, 2025	VA ESP

d. Rating the Quality of Individual Studies and the Body of Evidence

The Sigma Team assessed the methodological risk of bias of individual diagnostic, observational, and interventional studies using the USPSTF method. Each study is assigned a rating of *Good*, *Fair*, or *Poor* based on a set of criteria that vary depending on study design. Detailed lists of criteria and definitions appear in Appendix VI of the USPSTF procedure manual.(345)

Next, the Sigma team assessed the overall quality of the body of evidence for each critical and important outcome using the GRADE approach. This approach considers the following factors: overall study quality (or overall risk of bias or study limitations), consistency of evidence, directness of evidence, and precision of evidence. The overall quality of the body of evidence is rated as *High*, *Moderate*, *Low*, and *Very Low*.

C. Developing Evidence-Based Recommendations

In consultation with the VA Office of Quality and Patient Safety and the Clinical Quality Improvement Program, Defense Health Agency, and the Sigma Team convened a 3.5-day in-person recommendation development meeting from April 8-11, 2025, to develop this CPG's evidence-based recommendations. Two weeks before the meeting, the Sigma Team finalized the systematic evidence review and distributed the report to the Work Group; findings were also presented during the recommendation development meeting (see Determining Recommendation Strength and Direction).

Led by the Champions, the Work Group interpreted the systematic evidence review's findings and developed this CPG's recommendations. The strength and direction of each recommendation were determined by assessing the quality of the overall evidence base, the associated benefits and harms, patient values and preferences, and other implications.

Determining Recommendation Strength and Direction

Per GRADE methodology, to assess the quality of the evidence base and assign a grade for the strength of each recommendation. The GRADE system uses the following four domains to assess the strength of each recommendation:(81)

1. Confidence in the Quality of the Evidence

Confidence in the quality of the evidence reflects the quality of the evidence base and the certainty in that evidence. This second domain reflects the methodological quality of the studies for each outcome variable. In general, the strength of recommendation follows the level of evidence, but not always, as other domains may increase or decrease their strength. The evidence review used for the development of recommendations for overweight and obesity, conducted by the Sigma Team, assessed the confidence in the quality of the evidence base and assigned a rate of "High," "Moderate," "Low," or "Very Low."

The elements that go into the confidence in the quality of the evidence include:

- Is there high or moderate quality evidence that answers this question?
- What is the overall certainty of this evidence?

2. Balance of Desirable and Undesirable Outcomes

Balance of desirable and undesirable outcomes refers to the size of anticipated benefits (e.g., increased longevity, reduction in morbid events, resolution of symptoms, improved quality of life, decreased resource use) and harms (e.g., decreased longevity, immediate serious complications, adverse events, impaired quality of life, increased resource use, inconvenience/hassle) relative to each other. This domain is based on the understanding that most providers will offer patients therapeutic or preventive measures if the advantages of the intervention exceed the risks and adverse effects. The certainty or uncertainty of the provider about the risk-benefit balance will greatly influence the strength of the recommendation.

Some of the discussion questions that fall under this domain include:

- Given the best estimate of typical values and preferences, are you confident that the benefits outweigh the harms and burden or vice versa?
- Are the desirable anticipated effects large?
- Are the undesirable anticipated effects small?
- Are the desirable effects large relative to undesirable effects?

3. Patient Values and Preferences

Patient values and preferences is an overarching term that includes patients' perspectives, beliefs, expectations, and goals for health and life. More precisely, it refers to the processes that individuals use in considering the potential benefits, harms, costs, limitations, and inconvenience of the therapeutic or preventive measures in relation to one another. For some, the term "values" has the closest connotation to these processes. For others, the connotation of "preferences" best captures the notion of choice. In general, values and preferences increase the strength of the recommendation when there is high concordance and decrease it when there is great variability. In a situation in which the balance of benefits and risks are uncertain, eliciting the values and preferences of patients and empowering them and their surrogates to make decisions consistent with their goals of care becomes even more important. A recommendation can be described as having "similar values," "some variation," or "large variation" in typical values and preferences between patients and the larger populations of interest.

Some of the discussion questions that fall under the purview of values and preferences include:

- Are you confident about the typical values and preferences and are they similar across the target population?
- What are the patient's values and preferences?
- Are the assumed or identified relative values similar across the target population?

4. Other Implications

Other implications consider the practicality of the recommendation, including resources use, equity, acceptability, feasibility and subgroup considerations. Resource use is related to the uncertainty around the cost-effectiveness of a therapeutic or preventive measure. For example, statin use in the frail elderly and others with multiple co-occurring conditions may not be effective and depending on the societal benchmark for willingness to pay, may not be a good use of resources. Equity, acceptability, feasibility, and subgroup considerations require similar judgments around the practicality of the recommendation.

The framework below (Table A-4) was used by the Work Group to guide discussions on each domain.

Table A-4. GRADE Evidence to Recommendation Framework

Decision Domain	Questions to Consider	Judgement
Balance of desirable and undesirable outcomes	▪ What is the magnitude of the anticipated desirable outcomes? ▪ What is the magnitude of the anticipated undesirable outcomes? ▪ Given the best estimate of typical values and preferences, are you confident that benefits outweigh harms/burdens or vice versa?	▪ Benefits outweigh harms/burdens ▪ Benefits slightly outweigh harms/burdens ▪ Benefits and harms/burden are balanced ▪ Harms/burden slightly outweigh benefits ▪ Harms/burden outweigh benefits
Confidence in the quality of evidence	▪ Among the designated critical outcomes, what is the lowest quality of relevant evidence? ▪ How unlikely is further research to change the confidence in the estimate of effect?	▪ High ▪ Moderate ▪ Low ▪ Very low
Patient values and preferences	▪ Are you confident about the typical values and preferences and are they similar across the target population? ▪ What are the patient's values and preferences? ▪ Are the assumed or identified relative values similar across the target population?	▪ Similar values ▪ Some variation ▪ Large variation
Other implications (e.g. resource use, equity, acceptability, feasibility, subgroup considerations)	▪ Are the resources worth the expected net benefit from the recommendation? ▪ What are the costs per resource unit? ▪ Is this intervention generally available? ▪ Is this intervention and its effects worth withdrawing or not allocating resources from other interventions? ▪ Is there lots of variability in resource requirements across settings?	Various considerations

D. Recommendation Categorization

5. Recommendation Categories and Definitions

For use in the 2025 OBE CPG, a set of recommendation categories was adapted from those used by the United Kingdom National Institute for Health and Clinical Excellence (NICE).(86,87) These categories, along with their corresponding definitions, were used to account for the various ways in which recommendations could have been updated from the 2020 OBE CPG. The categories and definitions can be found in Table 3.

6. Categorizing Recommendations with an Updated Review of the Evidence

Recommendations were first categorized by whether they were based on an updated review of the evidence. If evidence had been reviewed, recommendations were categorized as "New-added," "New-replaced," "Not changed," "Amended," or "Deleted."

"Reviewed, New-added" recommendations were original, new recommendations that were not in the 2020 OBE CPG. "Reviewed, New-replaced" recommendations were in the previous version of the guideline but were modified to align with the updated review of the evidence. These recommendations could have also included clinically significant changes to the previous version. Recommendations categorized as "Reviewed, Not changed" were carried forward from the previous version of the CPG unchanged.

Recommendations could have also been designated "Reviewed, Deleted." These were recommendations from the previous version of the CPG that were not brought forward to the updated guideline after review of the evidence. This occurred if the evidence supporting the recommendations was out of date, to the extent that there was no longer any basis to recommend a particular course of care and/or new evidence suggests a shift in care, rendering recommendations in the previous version of the guideline obsolete.

7. Categorizing Recommendations without an Updated Review of the Evidence

There were also cases in which it was necessary to carry forward recommendations from the previous version of the CPG without an SR of the evidence. Due to time and budget constraints, the update of the OBE CPG could not review all available evidence on management of overweight and obesity, but instead focused its KQs on areas of new or updated scientific research or areas that were not previously covered in the CPG.

For areas of research that have not changed, and for which recommendations made in the previous version of the guideline were still relevant, recommendations could have been carried forward to the updated guideline without an updated SR of the evidence. The support for these recommendations in the updated CPG was thus also carried forward from the previous version of the CPG. These recommendations were categorized as "Not reviewed." If evidence had not been reviewed, recommendations could have been categorized as "Not changed," Amended," or "Deleted."

"Not reviewed, Not changed" recommendations refer to recommendations from the previous version of the OBE CPG that were carried forward unchanged to the updated version. The category of "Not reviewed, Amended" was used to designate recommendations that were modified from the 2020 CPG with the updated GRADE language, as explained above.

Recommendations could also have been categorized as "Not reviewed, Deleted" if they were determined to be out of scope. A recommendation was out of scope if it pertained to a topic (e.g., population, care setting, treatment, condition) outside of the scope for the updated CPG as defined by the Work Group.

The categories for the recommendations included in the 2020 version of the guideline are noted in the Recommendations. Recommendations 2, 3, 4, 22, and 23 were carried forward from the 2020 OBE CPG using this method. The categories for the recommendations from the 2020 OBE CPG are noted in Appendix C.

E. Drafting and Finalizing the Guideline

Following the face-to-face meeting, the Champions and Work Group members were given writing assignments to craft discussion sections to support each of the new recommendations and/or to update discussion sections from the 2020 OBE CPG to support the amended "carried forward" recommendations. The Work Group also considered tables, appendices, and other sections from the 2020 OBE CPG for inclusion in the update. During this time, the Champions and Work Group also made additional revisions to the algorithms, as necessary.

After developing the initial draft of the updated CPG, an iterative review process was used to solicit feedback on and revise the CPG. Once they were developed, the first two drafts of the CPG were posted on the OBE Wiki Website for a period of 10-20 business days for internal review and comment by the Work Group. Draft 3 was made available for a 14-day peer review and comment period (see External Peer Review). All feedback submitted during each review period was reviewed and discussed by the Work Group, and appropriate revisions were made to the CPG. Following the Draft 3 review and comment period, the Work Group reviewed external feedback and created a final draft of the CPG. The Champions then presented the CPG to the VA/DOD EBPWG for approval, and the final CPG was approved in October 2025. To accompany the CPG, the Work Group produced toolkit products, including a provider summary, quick reference guide, and patient summary.

Appendix B: Evidence Table

Table B-1. 2025 Overweight/Obesity Evidence Table [1, 2, 3, 4]

#	Recommendation	2020 Strength of Recommendation[1]	Evidence[2]	2025 Strength of Recommendation[3]	2025 Recommendation Category[4]
1.	There is insufficient evidence to recommend either for or against a particular measure of adiposity to manage clinical outcomes in patients with overweight or obesity.	Not applicable	**Additional References** (20,21,106-112,346-349)	Neither for nor against	Reviewed, New-added
2.	We recommend offering an in-person group or individual comprehensive lifestyle intervention that always includes behavioral, dietary, and physical activity components for patients with overweight or obesity.	Strong for	**Additional References** (9)	Strong for	Not reviewed, Not-changed
3.	We suggest offering a comprehensive lifestyle intervention for weight maintenance to patients who have completed a comprehensive lifestyle intervention for weight loss.	Weak for	**Additional References** (115,124,138)	Weak for	Not reviewed, Not-changed
4.	We suggest offering an individual or group telephone-delivered comprehensive	Weak for	**Additional References**	Weak for	Not reviewed, Not-changed

[1] 2020 Strength of Recommendation column: "Not applicable" indicates that the 2025 VA/DOD OBE CPG recommendation was a new recommendation, and therefore does not have an associated 2020 strength of recommendation.
[2] Evidence column: The first set of references listed in each row in the evidence column constitutes the evidence base for the recommendation. To be included in the evidence base for a recommendation, a reference needed to be identified through a systematic evidence review carried out as part of the initial development or update of this CPG. The second set of references in the evidence column (called "Additional References") includes references that provide additional information related to the recommendation, but which were not identified through a systematic evidence review. These references were, therefore, not included in the evidence base for the recommendation and did not influence the strength and direction of the recommendation.
[3] 2025 Strength of Recommendation column: The 2025 VA/DOD OBE CPG was developed using the GRADE approach to determine the strength of each recommendation. Refer to the Grading Recommendations section for more information.
[4] Recommendation Category column: Refer to the Recommendation Categorization section for more information on the description of the categorization process and the definition of each category

#	Recommendation	2020 Strength of Recommendation[1]	Evidence[2]	2025 Strength of Recommendation[3]	2025 Recommendation Category[4]
	lifestyle intervention for weight loss, either as an alternative to or in conjunction with an in-person intervention.		(115,124,125)		
5.	There is insufficient evidence to recommend either for or against a specific number of sessions, or a specific technology (except for telephone, see Recommendation 4), as the primary mode of delivery of a comprehensive lifestyle intervention.	Neither for nor against	(139-141) **Additional References** (113,115)	Neither for nor against	Reviewed, New-replaced
6.	We recommend offering patients a dietary approach that contributes to a negative energy balance to achieve weight loss as the dietary component of a comprehensive lifestyle intervention.	Strong for	(154-175) **Additional References** (142-153,176-184)	Strong for	Reviewed, Not-changed
7.	For weight loss and weight maintenance, there is insufficient evidence to recommend either for or against a particular dietary approach and/or strategy over another.	Weak for	(154-164) **Additional References** (115,142-153,165-176)	Neither for nor against	Reviewed, New-replaced
8.	We suggest physical activity of any type for weight management and other health outcomes, and as the physical activity component of a comprehensive lifestyle intervention.	Weak for	(115,120,186-205)	Weak for	Reviewed, New-replaced
9.	To optimize health outcomes, we suggest moderate to vigorous intensity aerobic exercise combined with resistance training.	Weak for	(115,120,186-205) **Additional References** (206-212)	Weak for	Reviewed, New-replaced

#	Recommendation	2020 Strength of Recommendation[1]	Evidence[2]	2025 Strength of Recommendation[3]	2025 Recommendation Category[4]
10.	We suggest offering cognitive behavioral interventions to individuals experiencing internalized weight bias and stigma.	Not applicable	(214-217) **Additional References** (218-221)	Weak for	Reviewed, New-added
11.	For temporary weight loss, we suggest intragastric balloons, in conjunction with a comprehensive lifestyle intervention, in patients with a body mass index ≥30 kg/m^2, adherent to FDA guidelines*(read narrative).	Weak for	(224,225) **Additional References** (222,223,226-232)	Weak for	Reviewed, Amended
12.	We suggest metabolic and bariatric surgery, in conjunction with a comprehensive lifestyle intervention, for durable weight loss in patients with a body mass index ≥30 kg/m² with type 2 diabetes mellitus or with a body mass index ≥35 kg/m².	Weak for	(236-238) **Additional References** (233-235,239-260)	Weak for	Reviewed, Amended
13.	We suggest endoscopic sleeve gastroplasty (ESG) for weight loss, in conjunction with a comprehensive lifestyle intervention, in patients with a body mass index ≥30 kg/m².	Neither for nor against	(224,262) **Additional References** (263-268)	Weak for	Reviewed, New-added
14.	There is insufficient evidence to recommend either for or against delaying the start of pharmacotherapy, in relationship to CLI, to improve outcomes in patients with overweight or obesity.	Not applicable	**Additional References** (9,16,17,117,269-279,281-284,350,351)	Neither for not against	Reviewed, New-added
15.	We suggest against discontinuing obesity medications, taking into account patient characteristics and preferences, as it results in weight regain.	Not applicable	(279,286,287) **Additional References** (288)	Weak against	Reviewed, New-added
16.	There is insufficient evidence to recommend either for or against reduction of the dose or frequency of	Not applicable	**Additional References** (289)	Neither for nor against	Reviewed, New-added

#	Recommendation	2020 Strength of Recommendation[1]	Evidence[2]	2025 Strength of Recommendation[3]	2025 Recommendation Category[4]
	pharmacotherapy to maintain achieved weight loss and avoid weight regain.				
17.	We recommend semaglutide or tirzepatide for both weight loss and to maintain weight loss, in conjunction with a comprehensive lifestyle intervention, in patients with a body mass index ≥27 kg/m^2 who also have an obesity-associated condition; and those who have a body mass index ≥30 kg/m^2.	Not applicable	(287,290,291) **Additional References** (292-298,300-303,352)	Strong for	Reviewed, New-added
18.	We suggest phentermine/topiramate extended release(ER) or liraglutide for both weight loss and to maintain weight loss, in conjunction with a comprehensive lifestyle intervention, in patients with a body mass index ≥27 kg/m^2 who also have an obesity-associated condition; and, those who have a body mass index ≥30 kg/m^2.	Weak for	(304,305) **Additional References** (115,306,307,309)	Weak for	Reviewed, Amended
19.	We suggest naltrexone/bupropion extended release (ER) for weight loss, in conjunction with a comprehensive lifestyle intervention, in patients with a body mass index ≥27 kg/m^2 who also have an obesity-associated condition; and those who have a body mass index ≥30 kg/m^2.	Weak for	(115,306,307,309,312-318) **Additional References** (309,319,320)	Weak for	Reviewed, Amended
20.	We suggest the use of glucagon-like peptide type 1 agonist-containing agents, in conjunction with CLI, for the treatment of patients with overweight and obesity, with either co-occurring prediabetes or type 2 diabetes mellitus.	Not applicable	(279,321-324) **Additional References** (325-327)	Weak for	Reviewed, New-added

#	Recommendation	2020 Strength of Recommendation[1]	Evidence[2]	2025 Strength of Recommendation[3]	2025 Recommendation Category[4]
21.	There is insufficient evidence to recommend either for or against orlistat, metformin, sodium glucose co-transporter type 2 inhibitors or pramlintide for weight loss.	Neither for nor against	(305)	Neither for nor against	Reviewed, Amended
22.	There is insufficient evidence to recommend either for or against phentermine monotherapy, benzphetamine, diethylpropion, or phendimetrazine, for weight maintenance.	Neither for nor against	**Additional References** (313)	Neither for nor against	Reviewed, Amended
23.	We suggest against using dietary supplements or nutraceuticals for clinically meaningful weight management.	Weak against	(329-336) **Additional References** (337-340)	Weak against	Not reviewed, Amended

Appendix C: 2020 Recommendation Categorization

Table C-1. 2020 Overweight and Obesity CPG Recommendation Categorization Table [1, 2, 3]

2020 CPG Recommendation #	2020 Recommendation Text[1]	2020 CPG Strength of Recommendation	2020 CPG Recommendation Category[2]	2025 CPG Recommendation Category[3]	2025 CPG Recommendation #
1	We recommend offering an in-person group or individual comprehensive lifestyle intervention that always includes behavioral, dietary, and physical activity components for patients with overweight or obesity.	Strong for	Reviewed, New-replaced	Not reviewed, Not-changed	2
2	There is insufficient evidence to recommend a specific number of sessions of a comprehensive lifestyle intervention for patients with overweight or obesity.	Neither for nor against	Reviewed, New-replaced	Reviewed, New-replaced	5
3	We suggest offering a comprehensive lifestyle intervention for weight maintenance to patients who have completed a comprehensive lifestyle intervention for weight loss.	Weak for	Reviewed, New-replaced	Not reviewed-Not-changed	3
4	We suggest offering an individual or group telephone-delivered comprehensive lifestyle intervention for weight loss, either as an alternative to or in conjunction with an in-person intervention.	Weak for	Reviewed, Amended	Not reviewed, Not-changed	4
5	There is insufficient evidence for or against offering a comprehensive lifestyle intervention for weight loss that uses technology as its primary mode of delivery.	Neither for nor against	Reviewed, New-Replaced	Reviewed, New-replaced	5
6	We suggest choosing one or more of the following as the physical activity component of a comprehensive lifestyle intervention: aerobic, resistance, and/or lifestyle physical activity.	Weak for	Reviewed, New-replaced	Reviewed, New-replaced	8, 9

[1] The 2020 Recommendation Text column contains the wording of each recommendation from the 2020 OBE CPG.
[2] The Recommendation Category column indicates the way in which each 2020 OBE CPG recommendation was updated.
[3] For recommendations that were carried forward to the 2025 OBE CPG, this column indicates the new recommendation(s) to which they correspond.

2020 CPG Recommendation #	2020 Recommendation Text[1]	2020 CPG Strength of Recommendation	2020 CPG Recommendation Category[2]	2025 CPG Recommendation Category[3]	2025 CPG Recommendation #
7	We recommend offering patients a dietary approach that contributes to a negative energy balance to achieve weight loss as the dietary component of a comprehensive lifestyle intervention.	Strong for	Reviewed, Amended	Reviewed, Not-changed	6
8	We suggest meal replacement (for example portion-controlled shake, protein bar, or meal) as an option to achieve negative energy balance as a component of a comprehensive lifestyle intervention.	Weak for	Reviewed, New-replaced	Reviewed, New-replaced	7
9	We suggest offering prescribed pharmacotherapy (specifically liraglutide, naltrexone/bupropion, orlistat, or phentermine/topiramate) for long-term weight loss in patients with a body mass index ≥30 kg/m^2 and for those with a body mass index ≥27 kg/m^2 who also have obesity-associated conditions, in conjunction with a comprehensive lifestyle intervention.	Weak for	Reviewed, New-replaced	Reviewed, Amended	18, 19
10	There is insufficient evidence to recommend for or against offering phentermine monotherapy, benzphetamine, diethylpropion, or phendimetrazine, for short-term, long-term, or intermittent weight loss in patients with overweight or obesity.	Neither for nor against	Reviewed, New-added	Not Reviewed, Amended; Reviewed, Amended	21, 22
11	We suggest against using dietary supplements or nutraceuticals for clinically meaningful short-term weight loss or long-term weight management.	Weak against	Reviewed, New-added	Not reviewed, Amended	23
12	We suggest offering the option of metabolic/bariatric surgery, in conjunction with a comprehensive lifestyle intervention, to patients with a body mass index of ≥30 kg/m^2 and type 2 diabetes mellitus.	Weak for	Reviewed, New-added	Reviewed, Amended	12
13	We suggest offering the option of metabolic/bariatric surgery, in conjunction with a comprehensive lifestyle intervention, for long-term weight loss/maintenance and/or to improve obesity-associated condition(s) in adult patients with a body mass index ≥40 kg/m^2 or those with body mass index ≥35 kg/m^2 with obesity-associated condition(s).	Weak for	Reviewed, New-replaced	Reviewed, Amended	12
14	There is insufficient evidence to recommend for or against metabolic/bariatric surgery to patients over age 65.	Neither for nor against	Reviewed, Amended	Not reviewed, Deleted	NA
15	There is insufficient evidence to recommend for or against percutaneous gastrostomy devices for weight loss in patients with obesity.	Neither for nor against	Reviewed, New-added	Not reviewed, Deleted	NA

2020 CPG Recommendation #	2020 Recommendation Text[1]	2020 CPG Strength of Recommendation	2020 CPG Recommendation Category[2]	2025 CPG Recommendation Category[3]	2025 CPG Recommendation #
16	We suggest offering intragastric balloons in conjunction with a comprehensive lifestyle intervention to patients with obesity (body mass index ≥30 kg/m^2) who prioritize short-term (up to six months) weight loss.	Weak for	Reviewed, New-added	Reviewed, Amended	11
17	There is insufficient evidence to recommend for or against intragastric balloons for long-term weight loss to support chronic weight management or maintenance.	Neither for nor against	Reviewed, New-added	Reviewed, Amended	11
18	We suggest offering a low-carbohydrate diet over a low-fat diet as the dietary component of a comprehensive lifestyle intervention for patients who prioritize short-term (up to six months) weight loss.	Weak for	Reviewed, New-added	Reviewed, New-replaced	7

Appendix D: Participant List

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Appendix E: Patient Focus Group Methods and Findings

A. Methods

VA and DOD Leadership recruited five participants for the focus group, with support from the Champions and other Work Group members as needed. A convenience sample was utilized in the selection of participants, and therefore, the sample of patients used is not generalized for the entirety of VA and DOD patients who have experience with overweight and obesity. The goal of recruitment for this Patient Focus Group was to have a group of engaging, diverse patients receiving VA or DOD healthcare services, who could cogently explain their experience with overweight and/or obesity. Participants were not incentivized for their participation or reimbursed for travel expenses.

The Work Group, with support from the Sigma Team, identified topics on which patient input was important to consider in developing the CPG. The Sigma Team developed, and the Work Group approved, and patient focus group guide covering these topics. The focus group facilitator led the discussion and used the guide to elicit the patients' perspectives about their treatment and overall care. Given the limited time and the range of interests of the focus group participants, not all questions were addressed.

B. Patient Focus Group Findings

a. Participants value communication and shared decision making with providers in accessing obesity medications and treatment.

- Participants value advocacy for the patient when seeking a provider.
- Participants discussed the complexities in obtaining and maintaining weight management treatments.

b. Participants highlighted the challenges of weight management due to age, medical conditions, and personal circumstances, emphasizing the importance of individualized treatment plans in weight loss and weight management.

- Participants shared the challenges they and their colleagues have faced related to their weight.
- Participants emphasized the importance of goal setting and individualized treatment plans in weight loss and weight maintenance.

c. Participants discussed the impact that their weight treatment has had on their mental health and career aspirations, emphasizing the need for effective weight management to maintain career standards and personal well-being.

- Participants raised stigma as an issue while dealing with their weight.
- Participants shared their experience with depression and body dysmorphia.
- Participants shared strategies to maintain their personal well-being during weight loss and weight maintenance.

d. Participants emphasized the value of non-pharmacological therapies and lifestyle changes when managing weight.

- Participants engaged in various physical activities, including mind and body groups, yoga, swimming, aquatic therapy, and extra high-intensity, short-duration workouts.
- Participants utilized mindfulness-based stress reduction techniques.
- Participants substituted healthier food options for processed foods.

e. In order to reduce the stigma of overweight and obesity, participants discussed the value of providers expressing empathy and patience when working with patients on weight loss and weight maintenance.

- Participants feel discouraged when providers tell them to lose weight as if it is a given, rather than offering supportive guidance.
- Participants felt belittled when providers used a negative tone/stigmatizing language about weight loss instead of engaging in goal-setting discussions.

f. Participants emphasized the need for better communication and support from healthcare providers.

- Participants experienced delays in care and medication refills when their current provider was deployed, highlighting the need for continuity of care.
- Participants preferred to receive information from their weight management specialist, emphasizing the importance of specialized care.

Appendix F: Literature Review Search Terms and Strategy

The search strategies employed combinations of free-text keywords as well as controlled vocabulary terms including (but not limited to) the following concepts. Strategies for each bibliographic database follow this table.

Table F-1. Embase/Medline Search Strategy (Embase.com syntax)

Set #	Search Statement
#1	'obesity'/exp
#2	'adiposity-based chronic disease':ti,ab OR corpulen*:ti,ab OR (((excess* OR hyperplasia) NEAR/3 (adipos* OR 'body weight')):ti,ab) OR obes*:ab,ti OR overweight:ab,ti OR 'over weight':ab,ti
#3	(('body mass index' OR bmi*) NEAR/1 (25* OR 26* OR 27* OR 28* OR 29* OR 3* OR 4*)):ab,ti
#4	#1 OR #2 OR #3
#5	'attitude to change'/exp OR 'behavior change'/exp OR 'behavior modification'/exp OR 'behavioral economics'/exp OR 'counseling'/exp OR 'goal attainment'/exp OR 'habit'/exp OR 'health behavior'/exp OR 'health program'/exp OR 'healthy lifestyle'/exp OR 'lifestyle modification'/exp OR 'motivational interviewing'/exp OR 'patient education'/exp OR 'problem solving'/exp OR 'psychotherapy'/exp OR 'social learning'/exp OR 'stress management'/exp
#6	(((adjust* OR adapt* OR adopt* OR alter* OR chang* OR improv* OR modif* OR new*) NEAR/2 (attitude* OR behav* OR environment* OR habit* OR lifestyle*)):ab,ti) OR ((behav* NEAR/2 (coach* OR counsel* OR economic* OR health* OR intervention* OR 'life style*' OR lifestyle* OR manag* OR support* OR theor* OR therap* OR train* OR treat*)):ab,ti) OR (((cognitive* OR dialectical OR emotion* OR 'mental health*' OR mindful* OR psychotherapy OR 'stress reduction') NEAR/2 (coach* OR counsel* OR intervention* OR manag* OR support* OR therap* OR treat* OR train*)):ab,ti) OR 'goal setting':ab,ti OR ((motivat* NEAR/2 interview*):ab,ti) OR psychotherap*:ab,ti OR ((self NEAR/2 (monitor* OR report*)):ab,ti) OR ((social* NEAR/2 learn*):ab,ti)
#7	#5 OR #6
#8	'exercise'/exp OR 'physical activity'/exp OR 'sport'/exp OR 'training'/exp
#9	(((aerobic* OR cardio* OR interval* OR 'non structured' OR resistance OR strength* OR unstructured) NEAR/2 (activit* OR exercis* OR train* OR workout* OR 'work out*')):ab,ti) OR exercis*:ab,ti OR hiit:ab,ti OR 'physical activit*':ab,ti OR 'qi gong':ti,ab OR qigong:ab,ti OR run*:ab,ti OR sport*:ab,ti OR 'tai chi':ab,ti OR walk*:ab,ti OR workout*:ab,ti OR 'work out*':ab,ti OR yoga:ab,ti OR ((weight* NEAR/2 (lift* OR train*)):ab,ti)
#10	#8 OR #9
#11	'alkaline diet'/exp OR 'atkins diet'/exp OR 'diet therapy'/exp OR 'eating habit'/exp OR 'fasting'/exp OR 'paleolithic diet'/exp OR 'plant-based diet'/exp OR 'raw food diet'/exp

Set #	Search Statement
#12	(((alkaline OR 'anti inflammatory' OR antiinflammatory OR atkins OR 'blood type' OR cleanse OR dash OR detox* OR dukan OR fast* OR flexitarian* OR keto* OR 'low density' OR macro* OR mediterranean* OR mind OR noom OR ornish OR paleo* OR 'plant based' OR 'raw food*' OR 'south beach' OR southbeach OR vegan* OR vegetarian* OR vertical OR zone) NEAR/2 (ate OR consum* OR diet* OR eat* OR fed OR feed* OR food* OR nutrition* OR plan* OR program* OR regimen*)):ab,ti) OR 'dietary approaches to stop hypertension':ab,ti OR 'eat stop eat':ab,ti OR 'jenny craig':ab,ti OR 'meal replace*':ab,ti OR 'mediterranean-dash intervention for neurodegenerative delay':ab,ti OR nutrisystem:ab,ti OR 'protein powder*':ab,ti OR 'renaissance periodization':ab,ti OR 'weight watchers':ab,ti OR 'whole 30':ab,ti OR ((('16:8' OR '5:2') NEAR/2 (diet* OR fast* OR method* OR plan* OR program*)):ab,ti) OR ((('alternate day' OR 'every other day' OR intermittent) NEAR/2 fast*):ab,ti) OR ((juice* NEAR/2 (cleanse OR fast)):ab,ti) OR (((cut OR decrease OR limit OR low* OR minim* OR reduc* OR restrict*) NEAR/2 (calorie* OR carb* OR fat*)):ab,ti) OR ((time* NEAR/2 restrict* NEAR/2 (diet* OR eat* OR feed*)):ab,ti)
#13	#11 OR #12
#14	(((combin* OR comprehensive OR intensive) NEAR/3 lifestyle* NEAR/3 (intervention* OR program*)):ab,ti) OR ((('multi component' OR multicomponent OR 'multi disciplinary' OR multidisciplinary) NEAR/3 (intervention* OR program*)):ab,ti)
#15	#7 AND #10 AND #13
#16	#4 AND (#14 OR #15)
#17	'exercise'/exp/mj OR 'physical activity'/exp/mj OR 'sport'/exp/mj OR 'training'/exp/mj
#18	((aerobic* OR cardio* OR interval OR 'non structured' OR recreational* OR resistance OR strength* OR unstructured) NEAR/2 (activit* OR exercis* OR train* OR workout* OR 'work out*')):ti
#19	exercis*:ti OR hiit:ti OR 'physical activit*':ti OR 'qi gong':ti OR qigong:ti OR run*:ti OR sport*:ti OR 'tai chi':ti OR walk*:ti OR workout*:ti OR 'work out*':ti OR yoga:ti
#20	(weight* NEAR/3 (lift* OR train*)):ti
#21	#4 AND (#17 OR #18 OR #19 OR #20)
#22	'alpha glucosidase inhibitor'/exp/mj OR 'amfebutamone'/exp/mj OR 'amfebutamone plus naltrexone'/exp/mj OR 'amylin derivative'/exp/mj OR 'anorexigenic agent'/exp/mj OR 'antiobesity agent'/exp/mj OR 'biguanide derivative'/exp/mj OR 'carbonate dehydratase inhibitor'/exp/mj OR 'glucagon like peptide 1 receptor agonist'/exp/mj OR 'human monoclonal antibody'/exp/mj OR 'lorcaserin'/exp/mj OR 'melanocortin receptor agonist'/exp/mj OR 'naltrexone'/exp/mj OR 'opiate agonist'/exp/mj OR 'orlistat'/exp/mj OR 'phendimetrazine'/exp/mj OR 'phentermine'/exp/mj OR 'psychostimulant agent'/exp/mj OR 'sibutramine'/exp/mj OR 'sodium glucose cotransporter inhibitor'/exp/mj OR 'tetrahydrolipstatin'/exp/mj OR 'topiramate'/exp/mj
#23	(('alpha glucosidase' OR 'carbonate dehydratase' OR 'carbonic anhydrase' OR lipase OR 'sodium-glucose transport*') NEAR/1 inhibit*):ti
#24	((anorexigenic OR antihyperglycemic OR 'anti-obes*' OR antiobes* OR 'appetite suppressant*' OR psychostimulant* OR obes* OR 'weight loss') NEAR/2 (agent* OR drug* OR medicat* OR pharm*)):ti

Set #	Search Statement
#25	acarbose*:ti OR adderall*:ti OR 'adipex-p':ti OR alli:ti OR amfebutamone*:ti OR amphetamine*:ti OR belviq*:ti OR benzphetamine*:ti OR bexagliflozin:ti OR biguanide*:ti OR bimagrumab*:ti OR brenzavvy*:ti OR bupropion*:ti OR bydureon*:ti OR byetta*:ti OR canagliflozin*:ti OR contrave*:ti OR dapagliflozin*:ti OR diethylpropion*:ti OR dulaglutide*:ti OR empagliflozin*:ti OR ertugliflozin*:ti OR exenatide*:ti OR fendique*:ti OR forxiga*:ti OR glp1*:ti OR 'glp 1*':ti OR 'glucagon like peptide*':ti OR glucophage*:ti OR imcivree*:ti OR inpefa*:ti OR invokana*:ti OR jardiance*:ti OR liraglutide*:ti OR lisdexamfetamine*:ti OR lomaira*:ti OR lorcaserin*:ti OR metformin*:ti OR methylphenidate*:ti OR 'monoclonal antibod*':ti OR mounjaro*:ti OR naltrexone*:ti OR orlistat*:ti OR ozempic*:ti OR phendimetrazine*:ti OR phentermine*:ti OR pramlintide*:ti OR precose*:ti OR qsymia*:ti OR retatrutide*:ti OR ritalin*:ti OR rybelsus*:ti OR saxenda*:ti OR semaglutide*:ti OR setmelanotide*:ti OR sglt1i:ti OR sglt2i:ti OR sibutramine*:ti OR sotagliflozin*:ti OR steglatro*:ti OR symlin*:ti OR tenuate*:ti OR tepanil*:ti OR tetrahydrolipstatin*:ti OR tirzepatide*:ti OR topamax*:ti OR topiramate*:ti OR trulicity*:ti OR victoza:ti OR vivitrol*:ti OR vyvanse*:ti OR wegovy*:ti OR wellbutrin*:ti OR xenical*:ti OR zepbound*:ti OR zonegran*:ti OR zonisamide*:ti OR zyban*:ti
#26	#4 AND (#22 OR #23 OR #24 OR #25)
#27	'alkaline diet'/exp/mj OR 'atkins diet'/exp/mj OR 'diet therapy'/exp/mj OR 'eating habit'/exp/mj OR 'fasting'/exp/mj OR 'paleolithic diet'/exp/mj OR 'plant-based diet'/exp/mj OR 'raw food diet'/exp/mj
#28	((alkaline OR 'anti inflammatory' OR antiinflammatory OR atkins OR 'blood type' OR cleanse OR dash OR detox* OR dukan OR fast* OR flexitarian* OR keto* OR 'low density' OR macro* OR mediterranean* OR mind OR noom OR ornish OR paleo* OR 'plant based' OR 'raw food*' OR 'south beach' OR southbeach OR vegan* OR vegetarian* OR vertical OR zone) NEAR/2 (ate OR consum* OR diet* OR eat* OR fed OR feed* OR food* OR nutrition* OR plan* OR program* OR regimen*)):ab,ti
#29	'dietary approaches to stop hypertension':ab,ti OR 'eat stop eat':ab,ti OR 'jenny craig':ab,ti OR 'meal replace*':ab,ti OR 'mediterranean-dash intervention for neurodegenerative delay':ab,ti OR nutrisystem:ab,ti OR 'protein powder*':ab,ti OR 'renaissance periodization':ab,ti OR 'weight watchers':ab,ti OR 'whole 30':ab,ti
#30	(('16:8' OR '5:2') NEAR/2 (diet* OR fast* OR method* OR plan* OR program*)):ab,ti
#31	(('alternate day' OR 'every other day' OR intermittent) NEAR/2 fast*):ab,ti
#32	(juice* NEAR/2 (cleanse OR fast)):ab,ti
#33	((cut OR decrease OR limit OR low* OR minim* OR reduc* OR restrict*) NEAR/2 (calorie* OR carb* OR fat*)):ti
#34	(time* NEAR/2 restrict* NEAR/2 (diet* OR eat* OR feed*)):ab,ti
#35	#4 AND (#27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34)
#36	'bariatric surgery'/exp/mj OR 'gastroplasty'/exp/mj OR 'partial gastrectomy'/exp/mj
#37	((bariatric* OR metabolic OR obes* OR 'weight loss' OR 'weight reduct*') NEAR/3 (operation* OR procedure* OR surg*)):ti

Set #	Search Statement
#38	'biliopancreatic bypass':ti OR 'biliopancreatic by-pass':ti OR 'biliopancreatic diversion':ti OR 'duodenal switch':ti OR 'enteric bypass':ti OR gastrectomy:ti OR 'gastric band*':ti OR 'gastric bypass':ti OR 'gastric by-pass':ti OR 'gastric restrictive':ti OR gastroplast*:ti OR 'jejunoileal bypass':ti OR 'one anastomosis gastric bypass':ti OR 'roux-en-y gastric bypass':ti OR 'sadi':ti OR 'sadi-s':ti OR 'single anastomosis duodeno-ileostomy':ti OR 'single anastomosis duodenoileostomy':ti OR 'single anastomosis gastric bypass':ti OR 'sleeve gastrectomy' OR 'surgical weight procedures':ti OR 'vertical gastrectomy':ti
#39	(#4 OR ((weight NEAR/2 (los* OR reduc*)):ab,ti)) AND (#36 OR #37 OR #38)
#40	((adipos* OR anthropomet* OR 'body composition' OR fat*) NEAR/3 (assess* OR defin* OR evaluat* OR measur* OR metric* OR modal* OR reliability OR utility OR validity OR value*)):ti
#41	'air displace*':ab,ti OR bia:ab,ti OR 'bioelectrical impedance analysis':ab,ti OR bmi:ab,ti OR bodpod:ab,ti OR 'body mass index':ab,ti OR 'body round index':ab,ti OR 'dual-energy x-ray absorptiometry':ab,ti OR dexa:ab,ti OR dxa:ab,ti OR 'hydrostatic weigh*':ab,ti OR 'magnetic resonance':ab,ti OR mri:ab,ti OR plethysmograph*:ab,ti OR 'qct scan*':ab,ti OR 'quantitative comput* tomograph*':ab,ti OR spectroscop*:ab,ti OR 'waist circumference*':ab,ti
#42	#4 AND #40 AND #41
#43	'endoscopic surgery'/exp/mj
#44	'aspiration therap*':ab,ti OR endobariatric*:ab,ti OR endoscop*:ti OR (((gastric* OR intragastric*) NEAR/2 balloon*):ab,ti)
#45	#4 AND (#43 OR #44)
#46	'weight bias'/exp
#47	((obes* OR 'over weight' OR overweight OR weight) NEAR/2 (bias* OR discriminat* OR prejudice* OR stigma*)):ab,ti
#48	(('anti-fat*' OR antifat* OR 'anti-obes*' OR antiobes*) NEAR/2 (attitude* OR bias* OR discriminat* OR prejudice* OR stigma*)):ab,ti
#49	'body sham*':ab,ti OR 'fat sham*':ab,ti OR ((negativ* NEAR/3 'body image*'):ab,ti)
#50	'cognitive therapy'/exp OR 'mindfulness'/exp OR 'psychoeducation'/exp OR 'self compassion'/exp OR 'acceptance and commitment':ab,ti OR cbt:ab,ti OR 'cognitive behav*':ab,ti OR educat*:ab,ti OR eliminat*:ab,ti OR intervention*:ab,ti OR lessen:ab,ti OR mindful*:ab,ti OR photovoice:ab,ti OR policy:ab,ti OR policies:ab,ti OR program*:ab,ti OR psychoeducat*:ab,ti OR reduc*:ab,ti OR remov*:ab,ti OR 'self compassion':ab,ti
#51	#4 AND (#46 OR #47 OR #48 OR #49) AND #50
#52	'sleep hygiene'/exp OR 'stress reduction'/exp
#53	(calori* NEAR/2 (track* OR log)):ab,ti
#54	(cbt:ab,ti OR 'cognitive behavioral':ab,ti OR 'cognitive behavioural':ab,ti) AND ((weight NEAR/2 (los* OR reduc*)):ab,ti)
#55	'sleep hygiene':ab,ti
#56	(stress* NEAR/2 (manag* OR reduc*)):ab,ti
#57	((log* OR track*) NEAR/4 (app OR apps OR application* OR calori* OR weight)):ab,ti
#58	((weigh OR weighed OR weighing) NEAR/2 (frequen* OR regular* OR serial*)):ab,ti
#59	#4 AND (#52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58)

Set #	Search Statement
#60	'non insulin dependent diabetes mellitus'/exp/mj OR (((2 OR ii OR two) NEAR/3 diabet*):ab,ti) OR t2dm:ab,ti OR tiidm:ab,ti OR 'type 2':ab,ti OR 'type ii':ab,ti
#61	'congestive heart failure'/exp/mj OR 'coronary atherosclerosis'/exp/mj OR 'atherosclerotic cardiovascular disease*':ti OR ((congestive NEAR/2 (cardiac OR heart) NEAR/2 fail*):ti) OR (((coronary OR heart) NEAR/2 (arteriosclero* OR atherosclero* OR sclero*)):ti) OR ascvd:ab,ti OR chf:ab,ti
#62	'metabolic dysfunction associated steatotic liver disease'/exp/mj OR 'nonalcoholic fatty liver'/exp/mj OR 'metabolic dysfunction-associated steatotic liver disease':ab,ti OR 'non-alcoholic fatty liver disease':ab,ti OR masld:ab,ti OR nafld:ab,ti
#63	((diet* OR nutrition*) NEAR/2 (personal* OR plan OR plans OR tailored)):ti
#64	#4 AND (#60 OR #61 OR #62) AND (#21 OR #26 OR #63)
#65	#16 OR #21 OR #26 OR #35 OR #39 OR #42 OR #45 OR #51 OR #59 OR #64
#66	#65 AND [1-04-2019]/sd NOT [07-01-2025]/sd AND [2019-2025]/py
#67	#66 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab)
#68	#66 AND ('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR cochrane*:ti,ab OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR (search*:ti,ab AND (cinahl*:ti,ab OR databases:ti,ab OR ebsco*:ti,ab OR embase*:ti,ab OR psychinfo*:ti,ab OR psycinfo*:ti,ab OR 'science direct*':ti,ab OR sciencedirect*:ti,ab OR scopus*:ti,ab OR systematic*:ti,ab OR 'web of knowledge*':ti,ab OR 'web of science':ti,ab)) OR ((systematic* NEAR/3 review*):ti,ab))
#69	#42 AND ('case control study'/exp OR 'cohort analysis'/de OR 'comparative study'/exp OR 'control group'/de OR 'controlled clinical trial'/de OR 'controlled study'/de OR 'crossover procedure'/de OR 'double blind procedure'/de OR 'major clinical study'/de OR 'observational study'/de OR 'prospective study'/de OR 'single blind procedure'/de OR 'triple blind procedure'/de OR '2 arm*':ti,ab OR '3 arm*':ti,ab OR 'case control':ti,ab OR cohort*:ti,ab OR compar*:ti,ab OR (((controlled OR experimental OR 'non random*' OR nonrandom* OR observational OR prospective) NEXT/3 (design OR study OR trial)):ti,ab) OR 'cross over':ti,ab OR crossover:ti,ab OR 'double arm*':ti,ab OR 'double blind*':ti,ab OR 'matched controls':ti,ab OR group:ti,ab OR groups:ti,ab OR 'multiple arm*':ti,ab OR 'non inferiority':ti,ab OR noninferiority:ti,ab OR placebo*:ti,ab OR 'quasi experiment*':ti,ab OR quasiexperiment*:ti,ab OR registries:ti,ab OR registry:ti,ab OR sham:ti,ab OR 'three arm*':ti,ab OR 'triple arm*':ti,ab OR 'triple blind*':ti,ab OR 'two arm*':ti,ab OR versus:ti OR vs:ti)
#70	#67 OR #68 OR #69
#71	#70 NOT (abstract:nc OR annual:nc OR 'book'/de OR book:it OR book:pt OR 'case report'/de OR 'case report':ti OR 'chapter'/it OR comment:ti OR conference:nc OR [conference abstract]/lim OR 'conference paper'/exp OR [conference paper]/lim OR 'conference proceeding':ab,ti OR 'conference proceeding':pt OR [conference review]/lim OR 'conferences and congresses'/exp OR congress:nc OR [editorial]/lim OR editorial:ti OR 'letter'/de OR letter:it OR [letter]/lim OR letter:ti OR meeting:nc OR proceedings:nc OR sessions:nc OR 'symposium'/exp OR symposium:nc)

Set #	Search Statement
#72	#71 NOT ((adolescen*:ti OR babies:ti OR baby:ti OR boys:ti OR child*:ti OR girls:ti OR infancy:ti OR infant*:ti OR juvenile*:ti OR neonat*:ti OR newborn*:ti OR nurser*:ti OR paediatric*:ti OR pediatric*:ti OR preschool*:ti OR 'school age*':ti OR schoolchildren*:ti OR teen*:ti OR toddler*:ti OR youth*:ti) NOT (adult*:ti OR men:ti OR women:ti))
#73	#72 NOT ([animals]/lim NOT [humans]/lim OR ((animal:ti OR animals:ti OR canine*:ti OR dog:ti OR dogs:ti OR feline:ti OR hamster*:ti OR lamb:ti OR lambs:ti OR mice:ti OR monkey:ti OR monkeys:ti OR mouse:ti OR murine:ti OR pig:ti OR piglet*:ti OR pigs:ti OR porcine:ti OR primate*:ti OR rabbit*:ti OR rat:ti OR rats:ti OR rodent*:ti OR sheep*:ti OR swine:ti OR veterinar*:ti OR (vitro:ti NOT vivo:ti)) NOT (human*:ti OR patient*:ti)))
#74	#72 NOT ([animals]/lim NOT [humans]/lim OR ((animal:ti OR animals:ti OR canine*:ti OR dog:ti OR dogs:ti OR feline:ti OR hamster*:ti OR lamb:ti OR lambs:ti OR mice:ti OR monkey:ti OR monkeys:ti OR mouse:ti OR murine:ti OR pig:ti OR piglet*:ti OR pigs:ti OR porcine:ti OR primate*:ti OR rabbit*:ti OR rat:ti OR rats:ti OR rodent*:ti OR sheep*:ti OR swine:ti OR veterinar*:ti OR (vitro:ti NOT vivo:ti)) NOT (human*:ti OR patient*:ti))) AND [english]/lim
#75	#74 AND [1-04-2019]/sd NOT [07-01-2025]/sd AND [2019-2025]/py

Table F-2. PsycInfo Search Strategy (EBSCO syntax)

Set #	Search Statement
#1	DE "Obesity" OR DE "Overweight"
#2	(AB (obes* OR overweight OR “overweight”)) OR (TI (obes* OR overweight OR “overweight”))
#3	(AB ((“body mass index” OR bmi*) N1 (25* OR 26* OR 27* OR 28* OR 29* OR 3* OR 4*))) OR (TI ((“body mass index” OR bmi*) N1 (25* OR 26* OR 27* OR 28* OR 29* OR 3* OR 4*)))
#4	S1 OR S2 OR S3
#5	DE "Attitude Change" OR DE "Behavior Change" OR DE "Behavior Contracting" OR DE "Behavior Modification" OR DE "Behavior Therapy" OR DE "Behavioral Economics" OR DE "Client Education" OR DE "Cognitive Behavior Therapy" OR DE "Counseling" OR DE "Dialectical Behavior Therapy" OR DE "Goal Setting" OR DE "Habits" OR DE "Health Behavior" OR DE "Lifestyle Changes" OR DE "Motivational Interviewing" OR DE "Positive Behavior Support" OR DE "Problem Solving" OR DE "Psychotherapy" OR DE "Readiness to Change OR DE "Social Learning" OR DE "Stress Management"
#6	(AB ((adjust* OR adapt* OR adopt* OR alter* OR chang* OR improv* OR modif* OR new*) N2 (attitude* OR behav* OR environment* OR habit* OR lifestyle*))) OR (TI ((adjust* OR adapt* OR adopt* OR alter* OR chang* OR improv* OR modif* OR new*) N2 (attitude* OR behav* OR environment* OR habit* OR lifestyle*))) OR (AB (behav* N2 (coach* OR counsel* OR economic* OR health* OR intervention* OR “life style*” OR lifestyle* OR manag* OR support* OR theor* OR therap* OR train* OR treat*))) OR (TI (behav* N2 (coach* OR counsel* OR economic* OR health* OR intervention* OR “lifestyle*” OR lifestyle* OR manag* OR support* OR theor* OR therap* OR train* OR treat*))) OR (AB ((cognitive* OR dialectical OR emotion* OR “mental health*” OR mindful* OR psych*) N2 (coach* OR counsel* OR intervention* OR manag* OR support* OR therap* OR treat* OR train*))) OR (TI ((cognitive* OR dialectical OR emotion* OR “mental health*” OR mindful* OR psych*) N2 (coach* OR counsel* OR intervention* OR manag* OR support* OR therap* OR treat* OR train*))) OR (AB “goal setting”) OR (TI “goal setting”) OR (AB (motivat* N2 interview*)) OR (TI (motivat* N2 interview*)) OR AB psychotherap* OR TI psychotherap OR (AB (self N2 (monitor* OR report*))) OR (TI (self N2 (monitor* OR report*))) OR (AB (social* N2 learn*)) OR (TI (social* N2 learn*))

Set #	Search Statement
#7	S5 OR S6
#8	DE "Aerobic Exercise" OR DE "Exercise" OR DE "Exercise Therapy" OR DE "Movement Therapy" OR DE "Physical Activity" OR DE "Physical Fitness" OR DE "Sports" OR DE "Walking" OR DE "Weightlifting" OR DE "Yoga"
#9	(AB ((aerobic* OR cardio* OR interval* OR “non structured” OR resistance OR strength* OR unstructured) N2 (activit* OR exercis* OR train* OR workout* OR “work out*”))) OR (TI ((aerobic* OR cardio* OR interval* OR “non structured” OR resistance OR strength* OR unstructured) N2 (activit* OR exercis* OR train* OR workout* OR “work out*”))) OR (AB (exercis* OR hiit OR “physical activit*” OR qigong OR run* OR sport* OR “tai chi” OR walk* OR workout* OR “work out*” OR yoga)) OR (TI (exercis* OR hiit OR “physical activit*” OR qigong OR run* OR sport* OR “tai chi” OR walk* OR workout* OR “work out*” OR yoga)) OR (AB (weight* N2 (lift* OR train*))) OR (TI (weight* N2 (lift* OR train*)))
#10	S8 OR S9
#11	DE "Diets" OR DE "Dietary Treatment" OR DE "Eating Behavior" OR DE "Healthy Eating" OR DE "Nutrition" OR DE"Vegan Diet" OR DE "Vegetarian Diet"
#12	(AB ((alkaline OR “anti inflammatory” OR antiinflammatory OR atkins* OR “blood type” OR cleanse OR dash OR detox* OR dukan OR fast*OR flexitarian* OR keto* OR “meal replace*” OR mediterranean* OR mind OR ornish OR paleo* OR “plant based” OR “rawfood*” OR “south beach” OR southbeach OR vegan* OR vegetarian*)N2 (ate OR consum* OR diet* OR eat* OR fed OR feed* OR food* OR nutrition* OR plan* OR program* OR regimen* OR style*))) OR (TI ((alkaline OR “anti inflammatory” OR antiinflammatory OR atkins* OR “blood type” OR cleanse OR dash OR detox* OR dukan OR fast* OR flexitarian* OR keto* OR “meal replace*” OR mediterranean* OR mind OR ornish OR paleo* OR “plant based” OR “raw food*” OR “south beach” OR southbeach OR vegan* OR vegetarian*) N2 (ate OR consum* OR diet* OR eat* OR fed OR feed* OR food* OR nutrition* OR plan* OR program* OR regimen* OR style*))) OR (AB ((low* OR minim* OR reduc* OR restrict*) N2 (calorie* OR carb* OR fat*))) OR (TI ((low* OR minim* OR reduc* OR restrict*) N2 (calorie* OR carb* OR fat*))) OR (AB (“dietary approaches to stop hypertension” OR “eat stop eat” OR “jenny craig” OR “mediterranean-dash intervention for neurodegenerative delay” OR nutrisystem OR “protein powder*” OR “weight watchers” OR “whole 30”)) OR (TI (“dietary approaches to stop hypertension” OR “eat stop eat” OR “jenny craig” OR “mediterranean-dash intervention for neurodegenerative delay” OR nutrisystem OR “protein powder*” OR “weight watchers” OR “whole 30”)) OR (AB ((juice* OR master) N2 (cleans* OR diet*))) OR (TI ((juice* OR master) N2 (cleans* OR diet*))) OR (AB ((“16:8” OR “5:2”) N2 (diet* OR fast* OR method* OR plan* OR program*))) OR (TI ((“16:8” OR “5:2”) N2 (diet* OR fast* OR method* OR plan* OR program*))) OR (AB ((“alternate day” OR intermittent) N2 fast*)) OR (TI ((“alternate day” OR intermittent) N2 fast*)) OR (AB (time* N2 restrict* N2 (diet* OR eating OR feed*))) OR (TI (time* N2 restrict* N2 (diet* OR eating OR feed*)))
#13	S11 OR S12
#14	(AB ((combin* OR comprehensive OR intensive) N3 lifestyle* N3 (intervention* OR program*))) OR (TI ((combin* OR comprehensive OR intensive) N3 lifestyle* N3 (intervention* OR program*))) OR (AB ((“multi component” OR multicomponent OR “multi disciplinary” OR multidisciplinary) N3 (intervention* OR program*))) OR (TI ((“multi component” OR multicomponent OR “multi disciplinary” OR multidisciplinary) N3 (intervention* OR program*)))
#15	S7 AND S10 AND S13
#16	S4 AND (S14 OR S15)
#17	DE "Weight-Based Discrimination"
#18	(AB ((obes* OR “overweight” OR overweight OR weight) N2 (bias* OR discriminat* OR prejudice* OR stigma*))) OR (TI ((obes* OR “over weight” OR overweight OR weight) N2 (bias* OR discriminat* OR prejudice* OR stigma*)))

Set #	Search Statement
#19	(AB ((“anti-fat*” OR antifat* OR “anti-obes*” OR antiobes*) N2 (attitude* OR bias* OR discriminat* OR prejudice* OR stigma*))) OR (TI ((“anti-fat*” OR antifat* OR “anti-obes*” OR antiobes*) N2 (attitude* OR bias* OR discriminat* OR prejudice* OR stigma*)))
#20	(AB “fat sham*”) OR (TI “fat sham*”)
#21	(AB (eliminat* OR intervention* OR lessen OR reduc* OR remov*)) OR (TI (eliminat* OR intervention* OR lessen OR reduc* OR remov*))
#22	S4 AND (S17 OR S18 OR S19 OR S20) AND S21
#23	DE "Sleep" OR DE "Stress Management"
#24	(AB (calori* N2 track*)) OR (TI (calori* N2 track*))
#25	(AB ((cbt OR “cognitive behavioral” OR “cognitive behavioural”) AND ((weight N2 loss))) OR (TI ((cbt OR “cognitive behavioral” OR “cognitive behavioural”) AND ((weight N2 loss)))
#26	(AB “sleep hygiene”) OR (TI “sleep hygiene”)
#27	(AB (stress* N2 reduc*)) OR (TI (stress* N2 reduc*))
#28	(AB (track* N4 (app OR apps OR application OR calori* OR weight))) OR (TI (track* N4 (app OR apps OR application OR calori* OR weight)))
#29	(AB ((weigh OR weighed OR weighing) N2 (frequen* OR regular* OR serial*))) OR (TI ((weigh OR weighed OR weighing) N2 (frequen* OR regular* OR serial*)))
#30	S4 AND (S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29)
#31	S16 OR S22 OR S30
#32	S31 AND ((AB (“phase 3” OR “phase iii” OR random* OR rct)) OR (TI (“phase 3” OR “phase iii” OR random* OR rct)))
#33	((AB (cochrane* OR metaanaly* OR “metaanaly*” OR (search* AND (cinahl* OR databases OR ebsco* OR embase* OR psychinfo* OR psycinfo* OR “science direct*” OR sciencedirect* OR scopus* OR systematic* OR “web of knowledge*” OR “web of science”)) OR (systematic* N3 review*)) OR (TI (cochrane* OR metaanaly* OR “metaanaly*” OR systematic*OR (search* AND (cinahl* OR databases OR ebsco* OR embase* OR psychinfo* OR psycinfo* OR “science direct*” OR sciencedirect* OR scopus* OR systematic* OR “web of knowledge*” OR “web of science”)) OR (systematic* N3 review*)))
#34	S31 AND S33
#35	S32 OR S34

Table F-3. PubMed in process Search Strategy (PubMed syntax)

Set #	Search Statement
1	obese OR obesity [TIAB] OR "over weight"[TIAB] OR overweight[TIAB]
2	#1 AND (inprocess[sb] OR publisher[sb] OR pubmednotmedline[sb])
3	#2 AND ("phase 3"[TIAB] OR "phase iii"[TIAB] OR random*[TIAB] OR rct[TIAB])
4	#2 AND (systematic*[TI] OR cochrane*[TIAB] OR metaanaly*[TIAB] OR "meta analy*"[TIAB] OR (search*[TIAB] AND (cinahl*[TIAB] OR databases[TIAB] OR ebsco*[TIAB] OR embase*[TIAB] OR psychinfo*[TIAB] OR psycinfo*[TIAB] OR "science direct*"[TIAB] OR sciencedirect*[TIAB] OR scopus*[TIAB] OR systematic*[TIAB] OR "web of knowledge*"[TIAB] OR "web of science"[TIAB])))
5	#3 OR #4
6	#3 OR #4
7	#6 NOT ("case report"[TI] OR comment[TI] OR "conference proceeding"[TIAB] OR editorial[TI] OR letter[TI])

Set #	Search Statement
8	#7 NOT ((adolescen*[TI] OR babies[TI] OR baby[TI] OR boys[TI] OR child*[TI] OR girls[TI] OR infancy[TI] OR infant*[TI] OR juvenile*[TI] OR neonat*[TI] OR newborn*[TI] OR nurser*[TI] OR paediatric*[TI] OR pediatric*[TI] OR preschool*[TI] OR "school age*"[TI] OR schoolchildren*[TI] OR teen*[TI] OR toddler*[TI] OR youth*[TI]) NOT (adult*[TI] OR men[TI] OR women[TI]))
9	#8 NOT (((animal[TI] OR animals[TI] OR canine*[TI] OR dog[TI] OR dogs[TI] OR feline[TI] OR hamster*[TI] OR lamb[TI] OR lambs[TI] OR mice[TI] OR monkey[TI] OR monkeys[TI] OR mouse[TI] OR murine[TI] OR pig[TI] OR piglet*[TI] OR pigs[TI] OR porcine[TI] OR primate*[TI] OR rabbit*[TI] OR rat[TI] OR rats[TI] OR rodent*[TI] OR sheep*[TI] OR swine[TI] OR veterinar*[TI] OR (vitro[TI] NOT vivo[TI])) NOT (human*[TI] OR patient*[TI]))
10	(((adjust* OR adapt* OR adopt* OR alter* OR chang* OR improv* OR modif* OR new) NEAR/2 (attitude* OR behav* OR environment* OR habit* OR lifestyle*)):ab,ti) OR ((behav* NEAR/2 (coach* OR counsel* OR economic* OR health* OR intervention* OR "life style*" OR lifestyle* OR manag* OR support* OR theor* OR therap* OR train* OR treat*)):ab,ti) OR (((cognitive* OR dialectical OR emotion* OR "mental health*" OR mindful* OR psych*) NEAR/2 (coach* OR counsel* OR intervention* OR manag* OR support* OR therap* OR treat* OR train*)):ab,ti) OR "goal setting"[TIAB] OR "motivational interview"[TIAB] OR psychotherapy[TIAB] OR "self monitor"[TIAB] OR "self monitoring"[TIAB] OR "self report"[TIAB] OR "social learning"[TIAB]
11	(behavior[TIAB] OR behavioral OR behaviour[TIAB]) AND (coach*[TIAB] OR counsel*[TIAB] OR economic*[TIAB] OR health*[TIAB] OR intervention*[TIAB] OR "life style*"[TIAB] OR lifestyle*[TIAB] OR manag*[TIAB] OR support*[TIAB] OR theor*[TIAB] OR therap*[TIAB] OR train*[TIAB] OR treat*[TIAB])
12	(cognitive*[TIAB] OR dialectical[TIAB] OR emotion*[TIAB] OR "mental health*"[TIAB] OR mindful*[TIAB] OR psych*) AND (coach*[TIAB] OR counsel*[TIAB] OR intervention*[TIAB] OR manag*[TIAB] OR support*[TIAB] OR therap*[TIAB] OR treat*[TIAB] OR train*[TIAB])
13	"goal setting"[TIAB] OR "motivational interview"[TIAB] OR "motivational interviewing"[TIAB] OR psychotherapy[TIAB] OR "self monitor*"[TIAB] OR "self report*"[TIAB] OR "social learn*"[TIAB]
14	#10 OR #11 OR #12 OR #13
15	(aerobic*[TIAB] OR cardio*[TIAB] OR interval*[TIAB] OR "non structured"[TIAB] OR resistance[TIAB] OR strength*[TIAB] OR unstructured) AND (activit*[TIAB] OR exercis*[TIAB] OR train*[TIAB] OR workout*[TIAB] OR "work out*"[TIAB])
16	exercis*[TIAB] OR hiit[TIAB] OR "physical activit*"[TIAB] OR qigong[TIAB] OR run[TIAB] OR running[TIAB] OR sport*[TIAB] OR "tai chi"[TIAB] OR walk*[TIAB] OR workout*[TIAB] OR "work out*"[TIAB] OR yoga[TIAB] OR "weight lift*"[TIAB] OR "weight train*"[TIAB]
17	#15 OR #16
18	(alkaline[TIAB] OR "anti inflammatory"[TIAB] OR antiinflammatory[TIAB] OR atkins*[TIAB] OR "blood type"[TIAB] OR cleanse[TIAB] OR dash[TIAB] OR detox*[TIAB] OR dukan[TIAB] OR fast*[TIAB] OR flexitarian*[TIAB] OR keto*[TIAB] OR "meal replace*"[TIAB] OR mediterranean*[TIAB] OR mind[TIAB] OR ornish[TIAB] OR paleo*[TIAB] OR "plant based"[TIAB] OR "raw food*"[TIAB] OR "south beach"[TIAB] OR southbeach[TIAB] OR vegan*[TIAB] OR vegetarian*) AND (ate[TIAB] OR consum*[TIAB] OR diet*[TIAB] OR eat[TIAB] OR eating[TIAB] OR fed[TIAB] OR feed*[TIAB] OR food*[TIAB] OR nutrition*[TIAB] OR plan*[TIAB] OR program*[TIAB] OR regimen*[TIAB] OR style*[TIAB])

Set #	Search Statement
19	(low[TIAB] OR minim*[TIAB] OR reduc*[TIAB] OR restrict*[TIAB]) AND (calorie*[TIAB] OR carb*[TIAB] OR fat[TIAB] OR fats[TIAB])
20	"dietary approaches to stop hypertension"[TIAB] OR "eat stop eat"[TIAB] OR "jenny craig"[TIAB] OR "mediterranean-dash intervention for neurodegenerative delay"[TIAB] OR nutrisystem[TIAB] OR "protein powder*"[TIAB] OR "weight watchers"[TIAB] OR "whole 30"[TIAB]
21	((juice[TIAB] OR juices[TIAB] OR juicing[TIAB]) OR master[TIAB]) AND (cleans*[TIAB] OR diet*[TIAB])
22	("16:8"[TIAB] OR "5:2"[TIAB]) AND (diet[TIAB] OR fast[TIAB] OR fasted[TIAB] OR fasting[TIAB] OR method[TIAB] OR plan[TIAB] OR program[TIAB])
23	(("alternate day"[TIAB] OR intermittent[TIAB]) AND fast*[TIAB]) OR (time*[TIAB] AND restrict*[TIAB] AND (diet*[TIAB] OR eating[TIAB] OR feed*[TIAB]))
24	#18 OR #19 OR #20 OR #21 OR #22 OR #23
25	((combin*[TIAB] OR comprehensive[TIAB] OR intensive[TIAB]) AND lifestyle*[TIAB] AND (intervention*[TIAB] OR program*[TIAB])) OR (("multi component"[TIAB] OR multicomponent[TIAB] OR "multi disciplinary"[TIAB] OR multidisciplinary[TIAB]) AND (intervention*[TIAB] OR program*[TIAB]))
26	#9 AND ((#14 AND #17 AND #24) OR #25)
27	(aerobic*[TI] OR cardio*[TI] OR interval*[TI] OR "non structured"[TI] OR recreational*[TI] OR resistance[TI] OR strength*[TI] OR unstructured) AND (activit*[TI] OR exercis*[TI] OR train*[TI] OR workout*[TI] OR "work out*"[TI])
28	exercis*[TI] OR hiit:ab,ti OR "physical activit*"[TI] OR qigong[TI] OR run[TI] OR running[TI] OR sport*[TI] OR "tai chi"[TI] OR walk*[TI] OR "weight lift*"[TI] OR "weight train*"[TI] OR workout*[TI] OR "work out*"[TI] OR yoga[TI]
29	#9 AND (#28 OR #27)
30	("alpha glucosidase"[TI] OR "carbonate dehydratase"[TI] OR "carbonic anhydrase"[TI] OR lipase[TI] OR "sodium-glucose transport*"[TI]) AND inhibit*[TI]
31	(anorexigenic[TI] OR antihyperglycemic[TI] OR "anti-obes*"[TI] OR antiobes*[TI] OR "appetite suppressant*"[TI] OR psychostimulant*[TI] OR obes*[TI] OR "weight loss"[TI]) AND (agent*[TI] OR drug*[TI] OR medicat*[TI] OR pharm*[TI])

Set #	Search Statement
32	acarbose[TI] OR adderall[TI] OR "adipex-p"[TI] OR alli[TI] OR amfebutamone[TI] OR amphetamine[TI] OR belviq[TI] OR benzphetamine[TI] OR bexagliflozin[TI] OR biguanide[TI] OR bimagrumab[TI] OR brenzavvy[TI] OR bupropion[TI] OR bydureon[TI] OR byetta[TI] OR canagliflozin[TI] OR contrave[TI] OR dapagliflozin[TI] OR diethylpropion[TI] OR dulaglutide[TI] OR empagliflozin[TI] OR ertugliflozin[TI] OR exenatide[TI] OR fendique[TI] OR forxiga[TI] OR glp1[TI] OR "glp 1"[TI] OR "glucagon like peptide"[TI] OR glucophage[TI] OR imcivree[TI] OR inpefa[TI] OR invokana[TI] OR jardiance[TI] OR liraglutide[TI] OR lisdexamfetamine[TI] OR lomaira[TI] OR lorcaserin[TI] OR metformin[TI] OR methylphenidate[TI] OR "monoclonal antibody"[TI] OR mounjaro[TI] OR naltrexone[TI] OR orlistat[TI] OR ozempic[TI] OR phendimetrazine[TI] OR phentermine[TI] OR pramlintide[TI] OR precose[TI] OR qsymia[TI] OR retatrutide[TI] OR ritalin[TI] OR rybelsus[TI] OR saxenda[TI] OR semaglutide[TI] OR setmelanotide[TI] OR sglt1i[TI] OR sglt2i[TI] OR sibutramine[TI] OR sotagliflozin[TI] OR steglatro[TI] OR symlin[TI] OR tenuate[TI] OR tepanil[TI] OR tetrahydrolipstatin[TI] OR tirzepatide[TI] OR topamax[TI] OR topiramate[TI] OR trulicity[TI] OR victoza[TI] OR vivitrol[TI] OR vyvanse[TI] OR wegovy[TI] OR wellbutrin[TI] OR xenical[TI] OR zepbound[TI] OR zonegran[TI] OR zonisamide[TI] OR zyban[TI]
33	#9 AND (#30 OR #31 OR #32)
34	(alkaline[TI] OR "anti inflammatory"[TI] OR atkins*[TI] OR "blood type"[TI] OR cleanse[TI] OR dash[TI] OR detox*[TI] OR dukan[TI] OR fast*[TI] OR flexitarian*[TI] OR keto*[TI] OR mediterranean*[TI] OR mind[TI] OR ornish[TI] OR paleo*[TI] OR "plant based"[TI] OR "raw food*"[TI] OR "south beach"[TI] OR southbeach[TI] OR vegan*[TI] OR vegetarian*[TI]) AND (ate[TI] OR consum*[TI] OR diet*[TI] OR eat[TI] OR eating[TI] OR eats[TI] OR fed[TI] OR feed*[TI] OR food*[TI] OR nutrition*[TI] OR plan*[TI] OR program*[TI] OR regimen*[TI] OR style*[TI])
35	"dietary approaches to stop hypertension"[TI] OR "eat stop eat"[TI] OR "jenny craig"[TI] OR "meal replace*"[TI] OR "mediterranean-dash intervention for neurodegenerative delay"[TI] OR nutrisystem[TI] OR "protein powder*"[TI] OR "weight watchers"[TI] OR "whole 30"[TI]
36	("16:8" OR "5:2") AND (diet*[TI] OR fast*[TI] OR method*[TI] OR plan*[TI] OR program*[TI])
37	(("alternate day"[TI] OR intermittent[TI]) AND fast*[TI])
38	((juice[TI] OR juices[TI] OR juicing[TI]) OR master[TI]) AND (cleanse[TI] OR diet*[TI])
39	(low[TI] OR minim*[TI] OR reduc*[TI] OR restrict*[TI]) AND (calori*[TI] OR carb*[TI] OR fat[TI] OR fats[TI])
40	time*[TI] AND restrict*[TI] AND (diet*[TI] OR eat[TI] OR eating[TI] OR feed*[TI])
41	#9 AND (#34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40)
42	(bariatric[TI] OR metabolic[TI] OR obes*[TI] OR "weight loss"[TI] OR "weight reduct*"[TI]) AND (operation*[TI] OR procedure*[TI] OR surg*[TI])
43	"biliopancreatic bypass"[TI] OR "biliopancreatic by-pass"[TI] OR "biliopancreatic diversion"[TI] OR gastrectomy[TI] OR "gastric band*"[TI] OR "gastric bypass"[TI] OR "gastric by-pass"[TI] OR gastroplast*[TI] OR "jejunoileal bypass"[TI] OR "sadi"[TI] OR "sadi-s"[TI] OR "single anastomosis duodeno-ileostomy"[TI] OR "single anastomosis duodenoileostomy"[TI] OR "sleeve gastrectomy"[TI]
44	#9 AND (#42 OR #43)

Set #	Search Statement
45	(adiposity[TI] OR anthropometric[TI] OR "body composition"[TI] OR fat[TI] OR fatness[TI]) AND (assess[TI] OR assessment[TI] OR define[TI] OR evaluate[TI] OR measure[TI] OR measured[TI] OR metric[TI] OR metrics[TI] OR modality[TI] OR modalities[TI] OR utility[TI] OR validity[TI] OR value[TI] OR values[TI])
46	"air displace*"[TI] OR bia[TI] OR "bioelectrical impedance analysis"[TI] OR bmi[TI] OR bodpod[TI] OR "body mass index"[TI] OR "body round index"[TI] OR "dual-energy x-ray absorptiometry"[TI] OR "hydrostatic weigh*"[TI] OR dxa[TI] OR "magnetic resonance"[TI] OR mri[TI] OR plethysmograph*[TI] OR "qct scan*"[TI] OR "quantitative comput* tomograph*"[TI] OR spectroscop*[TI] OR "waist circumference*"[TI]
49	#2 AND (#45 AND #46) AND ("2 arm*"[TIAB] OR "3 arm*"[TIAB] OR "case control"[TIAB] OR cohort*[TIAB] OR compar*[TIAB] OR ((controlled[TIAB] OR experimental[TIAB] OR "non random*"[TIAB] OR nonrandom*[TIAB] OR observational[TIAB] OR prospective[TIAB]) AND (design[TIAB] OR study[TIAB] OR trial[TIAB])) OR "cross over"[TIAB] OR crossover[TIAB] OR "double arm*"[TIAB] OR "double blind*"[TIAB] OR "matched controls"[TIAB] OR group[TIAB] OR groups[TIAB] OR "multiple arm*"[TIAB] OR "non inferiority"[TIAB] OR noninferiority[TIAB] OR placebo*[TIAB] OR "quasi experiment*"[TIAB] OR quasiexperiment*[TIAB] OR registries[TIAB] OR registry[TIAB] OR sham[TIAB] OR "three arm*"[TIAB] OR "triple arm*"[TIAB] OR "triple blind*"[TIAB] OR "two arm*"[TIAB] OR versus[TI] OR vs[TI])
51	#9 AND (#45 OR #46)
52	#51 OR #49
55	#9 AND ("aspiration therap*"[TIAB] OR endobariatric*[TIAB] OR endoscop*[TIAB] OR "gastric balloon"[TIAB] OR "intragastric balloon*"[TIAB])
56	(obes*[TIAB] OR "over weight"[TIAB] OR overweight[TIAB] OR weight[TIAB]) AND (bias*[TIAB] OR discriminat*[TIAB] OR prejudice*[TIAB] OR stigma*[TIAB])
57	("anti-fat*"[TIAB] OR antifat*[TIAB] OR "anti-obes*"[TIAB] OR antiobes*[TIAB]) AND (attitude*[TIAB] OR bias*[TIAB] OR prejudice*[TIAB])
58	"body sham*"[TIAB] OR "fat sham*"[TIAB]
59	educat*[TIAB] OR eliminat*[TIAB] OR intervention*[TIAB] OR lessen[TIAB] OR policy[TIAB] OR policies[TIAB] OR reduc*[TIAB] OR remov*[TIAB]
60	#9 AND (#56 OR #57 OR #58) AND #59
61	calori*[TIAB] AND track*[TIAB]
62	(cbt[TIAB] OR "cognitive behavioral"[TIAB] OR "cognitive behavioural"[TIAB]) AND "weight loss"[TIAB]
63	"sleep hygiene"[TIAB]
64	"stress reduc*"[TIAB] OR "reduc* stress*"[TIAB]
65	track*[TIAB] AND (app[TIAB] OR apps[TIAB] OR application[TIAB] OR calori*[TIAB] OR weight[TIAB])
66	(weigh[TIAB] OR weighed[TIAB] OR weighing[TIAB]) AND (frequen*[TIAB] OR regular*[TIAB] OR serial*[TIAB)
67	#9 AND (#61 OR #62 OR #63 OR #64 OR #65 OR #66)
68	(t2dm[TIAB] OR tiidm[TIAB] OR "type 2"[TIAB] OR "type ii"[TIAB]) AND diabet*[TIAB]

Set #	Search Statement
69	"atherosclerotic cardiovascular disease*"[TIAB] OR (congestive[TIAB] AND (cardiac[TIAB] OR heart[TIAB) AND fail*[TIAB]) OR ((coronary[TIAB] OR heart[TIAB]) AND (arteriosclero*[TIAB] OR atherosclero*[TIAB] OR sclero*[TIAB])) OR ascvd[TIAB] OR chf[TIAB]
70	"metabolic dysfunction-associated steatotic liver disease"[TIAB] OR "non-alcoholic fatty liver disease"[TIAB] OR masld[TIAB] OR nafld[TIAB]
71	(diet*[TIAB] OR nutrition*[TIAB]) AND (personal*[TIAB] OR plan[TIAB] OR plans[TIAB] OR tailored[TIAB])
72	#9 AND (#68 OR #69 OR #70) AND (#27 OR #28 OR #30 OR #31 OR #32 OR #71)

Table F-4. AHRQ Evidence-based Practice Center Reports Search Strategy

Set #	Search Statement
#1	Obesity [Search by keyword]
#2	Overweight [Search by keyword]

Table F-5. VA Evidence Synthesis Program Reports Search Strategy

Set #	Search Statement
#1	Obesity [Search ALL ESP Reports]
#2	Overweight [Search ALL ESP Reports]
#3	Scanned list of PubBriefs for title words: obesity, overweight, weight

Appendix G: Alternative Text Descriptions of Algorithm

The following outline narratively describes the Management of Overweight and Obesity in Adults OBE Algorithm. An explanation of the purpose of the algorithm and description of the various shapes used within the algorithm can be found in the Algorithm section. The sidebars referenced within this outline can also be found in the Algorithm section.

Algorithm Module

1. The Algorithm Module begins with Box 1, in the shape of a rounded rectangle: "Adults enrolled in the VA/DOD Health System"
2. Box 1 connects to Box 2, in the shape of a rectangle: "With permission, offer guidance about behavioral strategies that support healthy eating and physical activity to maintain health (see **Sidebar 1**)"
3. Box 2 connects to Box 3, in the shape of a rectangle:
    a. "Measure height and weight
    b. Calculate BMI to screen for overweight or obesity at medical visits
    c. Consider measuring waist circumference and other measures of adiposity".
4. Box 3 connects Box 4, in the shape of a hexagon, asks the question: "BMI ≥ 25 kg/m^2?
    a. If the answer is "Yes" to Box 4, then Box 5.
    b. If the answer is "No" to Box 3, then Box 2, in the shape of a rectangle: "With permission, offer guidance about behavioral strategies that support healthy eating and physical activity to maintain health (see **Sidebar 1**)"
5. Box 5, in the shape of a hexagon, asks the question: "Is patient ready to engage in treatment modalities?"
    a. If the answer is "Yes", then Box 6, in the shape of a rectangle:
        i. "Evaluate for factors contributing to obesity (see **Sidebars 2 and 3**)
        ii. Assess for overweight- and obesity-associated conditions including laboratory and diagnostic testing (e.g., lipid panel, HbA1c, CMP, FIB-4, etc.) (see **Sidebar 4**)
        iii. Assess for medications that cause weight gain"
    b. If the answer is "No", then Box 2, in the shape of a rectangle: "With permission, offer guidance about behavioral strategies that support healthy eating and physical activity to maintain health (see **Sidebar 1**)"
6. Box 6 connects to Box 7, in the shape of a rectangle: "Offer a Comprehensive Lifestyle Intervention (see **Sidebar 5**)"
7. Box 7 connects to Box 8, in the shape of a rectangle: "Consider Pharmacotherapy (see **Sidebar 6**), Endoscopic/Bariatric Procedures (see **Sidebar 7**), and/or Metabolic/Bariatric Surgery (see **Sidebar 8**), for appropriate candidates"
8. Box 8 connects to Box 9, in the shape of a hexagon, asks the question: "Has patient achieved weight management goals?"
    a. If the answer is "Yes", then Box 10, in the shape of a rectangle: "Continue CLI and any additional therapy for weight management, health maintenance, and treatment follow-up"
    b. If the answer is "No", then Box 6, in the shape of a rectangle:
        i. "Evaluate for factors contributing to obesity (see **Sidebars 2 and 3**)

ii. Assess for overweight- and obesity-associated conditions including laboratory and diagnostic testing (e.g., lipid panel, HbA1c, CMP, FIB-4, etc.) (see **Sidebar 4**)
iii. Assess for medications that cause weight gain”

Appendix H: Dietary Approaches

For all the diets listed below, formal consultation with a registered nutritional dietitian is advised.

The Academy of Nutrition and Dietetics (Academy) Evidence Analysis Library (EAL) Adult Weight Management Guideline (2014)(353,354) found strong evidence that weight loss, weight maintenance, and a nutritionally adequate diet with adjusted calories should be part of a comprehensive weight management program that also includes appropriate physical activity and behavioral strategies. This is supported by the 2024 Academy Position Statement for treating overweight and obesity.(355) The Academy EAL guideline further states that, "the registered dietitian (or international equivalents) should prescribe client-centered interventions based on each client's needs, circumstances, and goals.". Calorie reduction can be achieved by one of the following:

A. Caloric and Nutritional Recommendations

- When in the healthcare setting in which direct or indirect calorimetry is not available, and estimating resting energy expenditure (REE), the Mifflin St. Jeor equation and actual body weight have the most accuracy for estimating calorie needs for those with overweight or obesity.(356)
  - A 500 to 750 energy deficit/day that contributes to a negative energy balance.
  - A 30% energy deficit may be used for estimating caloric reduction to achieve negative energy balance.(357)
- A reduction to 1,200 to 1,500 kcal per day for women and 1,500 to 1,800 kcal per day for men, adjusted based on the individual's body weight, may be used when there is limited information about an individual.
- Individuals should focus on consuming nutrient-dense foods that are satiating, like protein and fibrous foods, while limiting foods that are energy-dense and not satiating.
- Individuals should focus on consuming nutrient-dense, minimally processed foods over ultra-processed energy-dense foods.
- Individuals should select eating plans that are easy to adhere to while trying to consider the above recommendations.
- The Dietary Reference Intake (DRI) Calculator for Healthcare Professionals(358) is a tool that can be utilized by healthcare professionals to estimate daily caloric needs, BMI, and recommended intakes of macronutrients, water, vitamins, and minerals based on DRI data.

Many dietary approaches can be used to achieve a negative energy balance/calorie reduction. The systematic evidence review conducted for this CPG update did not yield any exhaustive review of the various dietary approaches that may be considered for weight loss and weight maintenance; therefore, the dietary approaches described in this appendix do not encompass the totality of evidence-based approaches that a patient and healthcare provider may consider. The Academy Position Statement recommends "interventions based on shared decision making and

clinical judgement" and adjusted for "clients' value specific, tailored and usable diet and exercise plans."

Table H-1 provides a summary of dietary approaches for which evidence exists to support weight loss when accompanied by an energy deficit/negative energy balance. For all the diets listed below, formal consultation with a registered dietitian is advised for at least five interactive sessions when feasible.(354)

Table H-1. Dietary Approaches to Support Weight Management

Dietary Approaches	Description
American Heart Association (AHA) Dietary Guidance	Dietary patterns rather than isolated nutrients, recommending a flexible, food-based approach that prioritizes high intake of fruits, vegetables, whole grains, healthy protein sources (mostly plants, fish/seafood, low-fat dairy, lean unprocessed meats if chosen), use of liquid plant oils, minimal added sugars and salt, and avoidance of ultra-processed foods. The AHA guidance is designed to be adaptable to personal, cultural, and economic preferences, and is intended for lifelong adherence to support cardiometabolic health and weight management.
Dietary Approaches to Stop Hypertension (DASH) diet[b] (355)	Dietary pattern that is moderate in fat (25–30% of energy, low in saturated fat), high in fruits, vegetables, and low-fat dairy, and has the strongest evidence for blood pressure reduction and cardiometabolic benefit.
High Protein Diet	Dietary pattern in which protein provides more than 20% of total daily energy intake, or typically 1.2–1.6 g/kg body weight per day, with some studies using up to 30–45% of energy from protein. These diets often reduce carbohydrate and/or fat intake to maintain energy balance.
Ketogenic diet	Dietary pattern that is very high in fat (>70% of energy), very low in carbohydrates (<10% of energy). Short-term weight loss is similar to low-fat diets, but ketogenic diets may increase LDL cholesterol and have less favorable long-term cardiovascular profiles.
Intermittent Fasting	• **Intermittent fasting**: a general term for dietary regimens that alternate periods of voluntary fasting (no or minimal caloric intake) with periods of normal eating • **Alternate day fasting**: a form of intermittent fasting in which individuals alternate between days of significant caloric restriction (typically 0–600 kcal, or about 25% of energy needs) and days of ad libitum (unrestricted) food intake. This regimen induces repeated cycles of fasting and feeding, leading to metabolic adaptations such as increased fatty acid oxidation, ketone body production, and improved insulin sensitivity. • **5:2 diet**: a form of intermittent fasting in which individuals consume a very low-calorie diet (typically 500–600 kcal) on two non-consecutive days per week and eat ad libitum (without restriction) on the remaining five days. This regimen is designed to create an overall weekly caloric deficit while allowing flexibility and fewer days of restriction compared to alternate-day fasting (ADF) • **Time-restricted eating (TRE)**: a form of intermittent fasting in which all caloric intake is confined to a consistent daily window, typically 4–10 hours, with fasting (zero-calorie beverages allowed) for the remaining hours of the day. TRE does not prescribe specific foods or calorie targets but instead focuses on the timing of food intake, often aligning eating with circadian rhythms to optimize metabolic health.
Lacto-ovo vegetarian diet	Dietary pattern that excludes all meat, poultry, and fish but includes dairy products and eggs, along with plant-based foods.

Dietary Approaches	Description
Low-carbohydrate diet	Dietary pattern in which carbohydrates provide less than 40–45% of total daily energy intake, or, in some protocols, less than 130 g/day. These diets typically increase fat and/or protein intake to compensate for the reduction in carbohydrates.
Low-fat diet	Dietary pattern in which less than 30% of total daily energy intake is derived from fat, with saturated fat typically limited to less than 10% of energy. Carbohydrates generally comprise 55–60% or more of total energy, and protein intake is moderate. This pattern emphasizes fruits, vegetables, whole grains, and lean proteins, while minimizing added fats and high-fat animal products.
Low-glycemic index (GI) diet	Dietary pattern that emphasizes carbohydrate-containing foods with a GI less than 55, resulting in smaller and slower postprandial glucose excursions. Such diets are rich in nonstarchy vegetables, legumes, whole grains, and certain fruits, and are designed to flatten postprandial glycemia and insulin response, which may promote satiety and improve glycemic control.
Mediterranean diet (359)	Dietary pattern that is higher in total fat (35–40% of energy, mostly unsaturated from olive oil and nuts), moderate in carbohydrates, and associated with the most consistent and robust improvements in weight, glycemia, and cardiovascular outcomes.
Meal Replacement	Dietary pattern that includes commercially prepared products such as shakes, bars, or portion-controlled packaged meals – formulated to provide a defined amount of calories and essential nutrients designed to substitute one or more conventional meals per day.
MyPlate	Dietary guideline developed by the United States Department of Agriculture that divides the plate into four sections: fruits, vegetables, grains (with an emphasis on whole grains), and protein, with a side of dairy. It emphasizes variety, nutrient density, and portion control, and limits added sugars, saturated fat, and sodium. MyPlate is designed to be flexible and adaptable to individual preferences and cultural traditions, and aligns with the Healthy US-Style dietary pattern referenced in the American Heart Association dietary guidance.
Vegan diet	Dietary pattern that excludes all foods and beverages derived wholly or partly from animals, including meat, poultry, fish, dairy, eggs, and often honey, relying exclusively on plant-based foods such as vegetables, fruits, grains, legumes, nuts, and seeds.

More Dietary Approaches can be found in Medical Nutrition Therapy Interventions provided by Dietitians for Adult Overweight and Obesity Management: An Academy of Nutrition and Dietetics Evidence-Based Practice Guideline**.** *J Acad Nut Diet 2023:23(3):520-545.* doi: https://doi.org/10.1016/j.jand.2022.11.014(354)

[a] For further information about the Mediterranean eating pattern see the 2020-2025 Dietary Guidelines for Americans, available at: https://www.dietaryguidelines.gov/sites/default/files/2021-03/Dietary_Guidelines_for_Americans-2020-2025.pdf

[b] For further information on the DASH dietary pattern visit: https://www.nhlbi.nih.gov/health-topics/dash-eating-plan and https://www.dietaryguidelines.gov/sites/default/files/2021-03/Dietary_Guidelines_for_Americans-2020-2025.pdf

Abbreviations: ACC: American College of Cardiology; ADF: alternate-day fasting; AHA: American Heart Association; DASH: Dietary Approaches to Stop Hypertension; g: grams; kg: kilograms; LDL: low-density lipoprotein; mg: milligrams; RDA: recommended dietary allowance; SR: systematic review; TOS: The Obesity Society; TRE: Time-restricted eating; USDA: United States Department of Agriculture

Appendix I: Physical Activity Approaches

For all the strategies listed below, the Work Group **recommends emphasizing the benefits of any amount of physical activity over none.** While many may have difficulties in following specific recommendations, patients should be encouraged that any increase in activity will have benefits for weight management and health outcomes.

Physical activity plans should be structured, individualized, and align with patient-centered goals, medical status, and preferences. Regular physical activity is a key component of a comprehensive lifestyle intervention and has additional benefits for general health, cardiometabolic health, mental well-being, and functional capacity.(212,360)

Patients may increase their activity from planned exercise or non-exercise physical activities.

A. Non-Exercise Activity

- Accounts for the majority of variation in a patient's total daily caloric expenditure.
- Includes conscious activity (walking upstairs instead of taking an elevator) or spontaneous/subconscious activity (fidgeting while sitting at a desk or posture).
- Step counts are a useful way to monitor this. Higher daily step counts are associated with weight loss, cardiovascular health (CV), decreased all-cause and CV mortality, and improved cardiometabolic risk factors.
  - 2,600-4,000 steps/day→initial benefits
  - Progressive risk reduction up to approximately 8,000–10,000 steps/day.(201,212,360-363)
- **Increasing daily step count is an evidence-based, accessible intervention for managing obesity and improving cardiovascular health, with benefits seen well below the traditional 10,000 steps/day target**.(212,360,364,365)

There is a dose-dependent response to the amount of physical activity and intensity:

- For moderate intensity, <150 minutes per week → minimal weight loss; prevention of weight gain
- 150-225 minutes per week → small weight loss; prevention of weight gain
- 225-420 minutes per week → moderate weight loss (<3 kg)
- For vigorous activity, approximately half of this time for each category is needed
- Modest caloric restriction added to aerobic physical activity amounts per above will enhance weight loss

Patients who have lost weight may also benefit from balance training to improve potential deficits in kinesthetic awareness that may accompany weight loss.(212)

B. Patient Preference

- Patient adherence must be of primary focus given the critical impact of exercise on health, prevention of weight gain, and modest impacts on weight loss. Thus, Table I-1 below highlights common types of physical activities for patient experimentation.
- Common themes for higher adherence are:

- Group classes for social aspects and accountability
- Sports/recreational activities for enjoyment or the motivation of competition
- Low-impact activities that are less pain-provoking or therapeutic
- Ease of implementation into daily schedule
- Choosing a competition/race/event involving a chosen mode of exercise
- Of note, patients should be encouraged to add any of these themes to their favorite modalities of exercise. For example, someone who enjoys walking/jogging may enjoy joining a running club or signing up for a race.
- Impacts on hunger
- Different modalities of exercise can have differing impacts on hunger for different patients. They may increase or decrease hunger in different types of patients. Hence, patients should be encouraged to experiment.(360)

Table I-1. Common Types of Physical Activities with Higher Patient Adherence

Physical Activity Category	Examples
Cardiovascular (Aerobic) Activities	• Cycling (outdoor or indoor) • Hiking • Jogging/Running • Jumping rope • Kayaking/Canoeing • Rowing • Swimming • Brisk walking
Group classes	• Cardio kickboxing • Cross Training • Cycling • Dance/Zumba • HIIT • Step aerobics • Strengthening
High-Intensity Interval Training (HIIT)	• HIIT circuits • HIIT/SIIT Sprint intervals • Tabata workouts
Low-Impact, Therapeutic Movement, and Balance	• Pilates • Tai Chi or Qigong • Walking with poles (Nordic walking) • Yoga (power or vinyasa styles) • Balance specific training
Resistance Training	• Bodyweight exercises • Circuit training • Resistance band training • Weightlifting (machine, free-weight, competitive)
Sports and Recreational Activities	• Dance classes (hip hop, ballroom, etc.) • Martial arts (Brazilian jiu-jitsu, boxing, etc.) • Pick-up sports (basketball, soccer, tennis) • Pickleball • Tennis

Appendix J: Pharmacotherapy

A. Medications FDA-Approved for Weight Maintenance

The following tables summarize pharmacotherapy options for the long-term treatment of weight loss and maintenance. Refer to each drug's prescribing information for full details.

Included in Table J-1 are dose escalation titrations for each medication per manufacturer labeling. However, titrations should be individualized based on patient tolerance and response. Many patients do not need higher dosages of obesity medications to reach desired goals, and patients tolerate best if titrated slowly. A weight loss goal of about 0.5-2lbs per week with optimal nutrition, physical activity, sleep, stress management, and the appropriate individualized dose for the patient should be practiced. Rapid and large amounts of weight loss may be associated with increased loss of skeletal muscle, vitamin deficiencies, and gallstone formation.

Table J-1. Pharmacologic Information for Obesity Medications[a]

Medication	Dosing	Monitoring	Common Side Effects	Contraindications	Warnings
Semaglutide (Wegovy®) Two Additional FDA-approved indications for: (1) secondary prevention of MACE in adults with overweight or obesity; and (2) metabolic dysfunction-associated steatohepatitis (MASH)	▪ Initial dose-escalation: ▪ Week 1-4: 0.25 mg subQ weekly ▪ Week 5-8: 0.5 mg subQ weekly ▪ Week 9-12: 1 mg subQ weekly ▪ Week 13-16: 1.7mg subQ weekly ▪ Week ≥17: 2.4mg subQ weekly ▪ Maintenance doses are 2.4 mg weekly (preferred) or 1.7 mg weekly (if 2.4 mg is not tolerated)	Common to all NuSHes/GLP-1 RA containing agents listed except where agent-specific information is listed: ▪ Weight ▪ Blood pressure: hypotension risk may warrant de-escalation of antihypertensives ▪ Heart rate ▪ Glucose and/or signs/symptoms of hypoglycemia. Use additional caution if the patient is prescribed another glucose-lowering agent ▪ Mood (symptoms of depression) and sleep disorders ▪ Delayed gastric emptying may impact absorption of some oral medications. Tirzepatide PI recommends women using oral hormonal contraceptives to switch to a non-oral contraceptive method or add a barrier method of contraception for 4 weeks after initiation and for 4 weeks after each dose escalation. Common to all NuSHes/GLP-1 RA containing agents listed except where agent-specific information is listed: ▪ Increased heart rate ▪ Headache ▪ Nausea ▪ Diarrhea ▪ Constipation			

<table>
<tr><th>Medication</th><th>Dosing</th><th>Monitoring</th><th>Common Side Effects</th><th>Contraindications</th><th>Warnings</th></tr>
<tr><td>irrespective of BMI</td><td></td><td colspan="4" rowspan="3">Vomiting
Dyspepsia
Abdominal pain
Fatigue
Injection site reactions
<u>Common to all NuSHes/GLP-1 RA containing agents listed except where agent-specific information is listed:</u>
Personal or family history of medullary thyroid carcinoma or MEN2 [U.S. Boxed Warning]
Pregnancy: Liraglutide PI recommends discontinuation if a woman wishes to become pregnant or pregnancy occurs. Semaglutide PI recommends discontinuation at least 2 months prior to planning pregnancy. Tirzepatide PI recommends women using oral hormonal contraceptives to switch to a non-oral contraceptive method or add a barrier method of contraception for 4 weeks after initiation and for 4 weeks after each dose escalation.
<u>Common to all NuSHes/GLP-1 RA containing agents listed except where agent-specific information is listed:</u>
Thyroid C-cell tumors [U.S. Boxed Warning]
Injection site reactions
Hypersensitivity reactions (caution if previous reactions to GLP-1 agonist)
Gallbladder disease
Pancreatitis
Renal impairment
Acute/chronic renal failure exacerbation
Suicidal behavior and ideation
Hypoglycemia
Pulmonary aspiration risk during general anesthesia or deep sedation
Tachycardia (not a warning in tirzepatide PI, but is increased heart rate was experienced in clinical trials)
Severe GI effects and not recommended in patients with severe gastroparesis (not a warning in liraglutide PI, but listed in post-marketing experience)
Diabetic retinopathy (in semaglutide and tirzepatide PIs only)</td></tr>
<tr><td>Tirzepatide (Zepbound®)

Additional FDA-approved indication for treatment of moderate to severe OSA in adults with obesity</td><td>Initial dose-escalation: 2.5 mg subQ weekly for 4 weeks. Increase by 2.5mg/week every 4 weeks
Maintenance doses are 5 mg, 10 mg, and 15 mg weekly (for OSA, recommended doses are 10 mg or 15 mg weekly)</td></tr>
<tr><td>Liraglutide (Saxenda®)</td><td>Initiate dose titration with 0.6 mg daily, subcutaneously for 1 week; increase daily dose by 0.6 mg per week until reaching a target dose of 3 mg; slow titration to every other week if the patient cannot tolerate weekly titration
Per the product information, discontinue if 4% weight loss is not achieved by week 16 as it is unlikely that a meaningful weight loss will be achieved and sustained with continued treatment
<u>Patients on secretagogues (such as sulfonylureas) or insulin:</u> Consider reducing the dose of the secretagogue (e.g., by 50%) or insulin to avoid hypoglycemia</td></tr>
</table>

Medication	Dosing	Monitoring	Common Side Effects	Contraindications	Warnings
Phentermine / topiramate ER (Qsymia®) Controlled Substance: CIV	▪ Phentermine 3.75 mg/topiramate 23 mg capsule each morning for 14 days; then 7.5 mg/46 mg each morning for additional 12 weeks ▪ If a 3% loss of baseline body weight is not achieved after 12 weeks, increase dose to 11.25 mg/69 mg each morning for 14 days; then increase to 15 mg/92 mg daily ▪ If a 5% loss of baseline body weight is not achieved after 12 weeks, it is unlikely that the patient will achieve a clinically meaningful weight loss with further treatment; discontinue by tapering (one dose every other day for ≥1 week) ▪ Moderate/Severe Renal Impairment (CrCl <50 mL/min): Maximum dose: 7.5 mg/46 mg daily ▪ Moderate Hepatic Impairment (Child-Pugh score 7 - 9): Maximum dose: 7.5 mg/46 mg daily	▪ Weight ▪ Blood pressure ▪ Resting heart rate ▪ Serum bicarbonate, especially if taking another carbonic anhydrase inhibitor ▪ Serum potassium, especially if taking another carbonic anhydrase inhibitor ▪ Glucose and/or signs/symptoms of hypoglycemia in patients with diabetes ▪ Mood (depression) and sleep disorders ▪ Pregnancy tests in women of reproductive potential ▪ Baseline and periodic monitoring of serum creatinine / estimated glomerular filtration rate	▪ Increased heart rate ▪ Paresthesia ▪ Dizziness ▪ Dysgeusia ▪ Headache ▪ Insomnia ▪ Decreased serum bicarbonate ▪ Xerostomia ▪ Constipation ▪ Upper respiratory tract infection ▪ Nasopharyngitis	▪ Pregnancy (REMS program exists to inform prescribers and patients of risks) ▪ Glaucoma ▪ Hyperthyroidism ▪ MAOI use during or within 14 days ▪ Allergy to Yellow dye No 5	▪ Metabolic acidosis ▪ Cognitive impairment ▪ Elevated heart rate ▪ Nephrolithiasis ▪ Hypokalemia ▪ Mood and sleep disorders ▪ Depression or suicidal ideation ▪ Increased creatinine ▪ Oligohidrosis/hyperthermia ▪ Serious skin reactions ▪ Hypoglycemia: May require adjustment of hypoglycemic medications ▪ Abuse potential: Phentermine is pharmacologically related to amphetamines, which have a high abuse potential; prolonged use may lead to dependency ▪ Avoid abrupt discontinuation to minimize the risk of seizure; taper recommended (see Dosing) ▪ Avoid concomitant consumption of alcohol due to increased CNS depressant effect
Naltrexone / bupropion ER (Contrave®)	Naltrexone 8mg/bupropion 90 mg dose-escalation schedule (Morning Dose/Afternoon Dose): ▪ Week 1: 1 tablet / None ▪ Week 2: 1 tablet / 1 tablet	▪ Weight ▪ Pregnancy ▪ Glucose and/or signs / symptoms of	▪ Headache ▪ Sleep disorder ▪ Nausea ▪ Constipation ▪ Diarrhea	▪ Opioid use (agonists or partial agonists) ▪ Uncontrolled hypertension	▪ Suicidal thinking/ behavior **[U.S. Boxed Warning]** ▪ Neuropsychiatric symptoms

Medication	Dosing	Monitoring	Common Side Effects	Contraindications	Warnings
	▪ Week 3: 2 tablets / 1 tablet ▪ Week ≥4 (Maintenance dose): 2 tablets / 2 tablets ▪ If a 5% loss of baseline body weight is not achieved after 12 weeks, it is unlikely that the patient will achieve a clinically meaningful weight loss with further treatment; consider discontinuation ▪ Moderate to Severe Renal Impairment (CrCl <50mL/min): Maximum dose 1 tablet twice a day. Not recommended in patients with end-stage renal disease. ▪ Moderate Hepatic Impairment (Child-Pugh score 7-9): Maximum dose: 1 tablet twice daily. Not recommended in patients with severe hepatic impairment.	hypoglycemia in patients with diabetes ▪ Blood pressure ▪ Heart rate ▪ Signs and symptoms of depression, suicidal thought or behavior, cognitive impairment, or changes in mood ▪ Baseline and periodic monitoring of renal and hepatic function	▪ Vomiting ▪ Dizziness ▪ Xerostomia	▪ Seizure disorder ▪ Increased seizure risk in concurrent (bulimia, anorexia nervosa, other eating disorders, abrupt discontinuation of alcohol, opioid, or benzodiazepine ▪ Concomitant MAOI use or initiation in patients receiving linezolid or IV methylene blue	▪ May precipitate acute opioid withdrawal in patients receiving opioids ▪ Seizures ▪ Increase blood pressure, heart rate ▪ Hepatotoxicity ▪ Adjust hypoglycemic medications to avoid hypoglycemia ▪ Angle-closure glaucoma
Orlistat (Xenical®, Alli®)	▪ Xenical®: 120 mg 3 times daily with each main meal containing fat (during or up to one hour after the meal); omit dose if meal is occasionally missed or contains no fat. ▪ Alli®: OTC labeling: 60 mg 3 times daily with each main meal containing fat There are no dosage adjustments provided in the manufacturer's labeling for either renal or hepatic impairment	▪ Weight ▪ Blood pressure ▪ Glucose and/or signs/symptoms of hypoglycemia in patients with diabetes ▪ Liver function tests if signs or symptoms of hepatic dysfunction ▪ Renal function in patients at risk of renal impairment	▪ GI effects (e.g., oily rectal leakage, abdominal distress/pain, flatulence with discharge, bowel urgency, steatorrhea). Frequency may decline over time and low-fat diet. ▪ Headache	▪ Pregnancy ▪ Chronic malabsorption syndrome ▪ Cholestasis	▪ Increased urinary oxalate, nephrolithiasis, and nephropathy ▪ Hepatotoxicity ▪ Cholelithiasis

Medication	Dosing	Monitoring	Common Side Effects	Contraindications	Warnings
		▪ Interference with absorption of fat-soluble vitamins, cyclosporine, thyroid hormone, and anticonvulsants	▪ Menstrual irregularity ▪ Back and lower extremity pain ▪ URTI / Influenza		
Setmelanotide (Imcivree®)	▪ **For use only in patients with obesity due to Bardet-Biedl syndrome (BBS), or due to pro-opiomelanocortin (*POMC*), proprotein convertase subtilisin/kexin type 1 (*PCSK1*), or leptin receptor (*LEPR*) deficiency confirmed by genetic testing demonstrating variants in *POMC*, *PCSK1*, or *LEPR* genes** ▪ Initial dose: 2 mg subQ daily for 2 weeks ▪ Maintenance dose if initial dose tolerated: 3 mg subQ daily ▪ Maintenance dose of initial dose not tolerated: 1 mg subQ daily	▪ Monitor sexual adverse reactions (e.g., spontaneous penile erection, priapism, labial hypersensitivity) ▪ New or worsened depression (including suicidal ideation) ▪ GI adverse reactions during dose initiation and titration	▪ Skin hyperpigmentation ▪ Injection site reactions ▪ GI effects (e.g., vomiting, constipation, diarrhea) ▪ Nasophyaryngitis / URTI ▪ Headache ▪ Dry mouth / dry skin ▪ Insomnia ▪ Vertigo ▪ Back pain	▪ Not listed as a contraindication, however prescribing information recommends discontinuation when pregnancy is known	▪ Disturbance in sexual arousal for men and women ▪ Development or worsening of depression ▪ Suicidal ideation/behavior ▪ Hypersensitivity ▪ Skin hyperpigmentation/development or darkening of melanocytic nevi

[a] If applicable, refer to VA (https://www.va.gov/formularyadvisor/) or DOD (http://www.health.mil/PandT) guidance/criteria for further recommendations on use of these agents

Abbreviations: CIV: Schedule IV controlled substance; CNS: central nervous system; CrCl: creatinine clearance; ER: extended-release; FDA: U.S. Food and Drug Administration; GI: gastrointestinal; GLP-1: glucagon-like peptide-1; IV: intravenous; MACE: major adverse cardiovascular events (for semaglutide this includes cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke); MAOI: monoamine oxidase inhibitor; MEN2: multiple endocrine neoplasia type 2; NuSH: nutrient-stimulated hormonal therapies; OSA: obstructive sleep apnea; PI: prescribing information; REMS: Risk Evaluation and Mitigation Strategy; subQ: subcutaneously; URTI: upper respiratory tract infection; XR: extended-release

Table J-2. Pooled Placebo-Controlled Efficacy and Discontinuation Due to Adverse Event Rates from Meta-Analyses

Medication for Weight Loss	Average % Weight Loss vs. Baseline	≥5% Weight Loss (OR)	≥10% Weight Loss (OR)	Discontinuation Due to Adverse Events (OR)
Tirzepatide (291)	-18.73	19.28	18.99	3.27
Semaglutide (305)	-11.4	9.82	13.32	1.98
Phentermine/topiramate (305)	-7.98	8.02	9.74	2.4
Liraglutide (305)	-4.67	4.91	4.8	2.45
Naltrexone/bupropion (305)	-4.11	5.04	5.19	2.69
Orlistat (305)	-3.06	2.73	2.43	1.71

Abbreviations: OR: odds ratio

B. Medications and Potential Weight Gain

In the overall management of patients with obesity or overweight, it is critical to consider the impact of prescribed medications on the potential for weight gain and whether alternate medications may be a more appropriate option for patients who have overweight, obesity, or at risk. Providers should review the patient's current medications for any medications that may be contributing to increased weight. The side effect of weight gain, and potentially additive effect when more than one obesogenic medication is prescribed, should be considered when prescribing a medication for a patient in whom weight gain may be of concern. If an alternate medication is not an option, participation in a weight management program and weight monitoring may benefit the patient whose only option is a medication associated with weight gain. The information in Sidebar 2 is provided as only one aspect of medication selection for a patient with overweight or obesity (or at risk for transition to overweight or obesity). Optimal medication management should take into account the potential effect on weight, as well as other patient factors, efficacy, safety, and available long-term outcome data.

C. Off-Label Pharmacotherapy

Several drugs have been used off-label as a long-term treatment for weight loss.(366-368) Below is a list and brief discussion of some of these medications.

a. Topiramate (Monotherapy)

Weight loss was noted as a side effect when topiramate was used to treat epilepsy. A mean of 3.9 kg is lost at three months and 5.9 kg at one year, although the amount of weight loss tends to be greater in those with a higher BMI. Studies that have identified greater weight loss with higher doses have reported a ceiling effect at a dose of 192 mg/day.(369)

A meta-analysis that included 3,320 patients with obesity from 10 studies (19 treatment arms) comparing topiramate (64 mg – 400 mg/day as a weight loss agent) to placebo over periods of 16 to 60 weeks found that the mean weight loss experienced by patients taking topiramate was 5.34 kg greater than with placebo. The amount of weight loss was a function of both dosage and duration of exposure. Safety data were available for 6,620 patients. The risk of study withdrawal due to an adverse event was greater for topiramate-treated patients (OR: 1.95) and was associated with a higher dosage. This same dose-related pattern was observed with the other common adverse events, including paresthesia, taste change or dysgeusia, psychomotor impairment, hypoesthesia, difficulty concentrating, anorexia, memory impairment, and nervousness.(370) In a meta-analysis of patients with obesity and T2DM, topiramate reduced weight and HbA1c; however, serious and total number of adverse events occurred more frequently with treatment.(371)

Topiramate has also been used for binge eating disorder. In a meta-analysis including three RCT studies of 528 patients with binge eating disorder, Nourredine et al. (2021) found that topiramate reduced the number of binge eating episodes per week (MD = -1.31; 95% CI = -2.58 to –0.03), the number of binge days per week (MD = -0.98; 95% CI –1.80 to –0.16), as well as weight (MD = -4.91 kg;95% CI = -6.42 to –3.41).(372) However, patients in the topiramate arms also discontinued study drug more frequently due to safety concerns (RR = 1.90; 95% CI = 1.13-3.18)

b. Zonisamide

Weight loss and anorexia were noted as side effects when zonisamide was used to treat epilepsy in participants with binge eating disorder and obesity. A randomized, double-blind, placebo-controlled trial concluded a mean weight loss of 4.8kg from baseline to study endpoint in the intent-to-treat group, with weight loss of 8.9kg in participants completing the 16 weeks of treatment, and a significant reduction in binge frequency. Patients started at zonisamide 100mg/day for 7 days, then increased as tolerated to a max dose of 600mg/day. The mean daily dose at the last evaluation was 436mg. Adverse effects were more common in the zonisamide treatment group (leading to discontinuation of therapy) compared to placebo, although not statistically significant.(373)

A 1-year randomized, double-blind, placebo-controlled trial showed zonisamide 400mg/day moderately enhanced weight loss with diet and lifestyle counseling, with an increase in gastrointestinal, nervous system, and psychiatric adverse events compared to placebo.(374) A mean weight loss of 7.3kg was found in patients taking zonisamide 400mg/day, and a mean weight loss of 4kg for zonisamide 200mg/day. Zonisamide 400mg/day resulted in 3.3kg of greater weight loss than diet and lifestyle intervention alone, while the 200mg/day dose was found to not be effective. Although zonisamide 400mg/day showed moderate efficacy in a similar magnitude of weight loss seen with orlistat and lorcaserin, mood changes and memory problems occurred at a higher frequency than with placebo.

c. Metformin

Modest weight loss has been well-documented with the use of metformin when used to treat patients with DM, pre-diabetes, metabolic syndrome, and polycystic ovary syndrome (PCOS).(120,375-379) It has also been shown to cause weight loss in patients without DM with antipsychotic-induced weight gain.(380) In patients with T2DM, reductions have persisted for ten years or more, and the most important influence on both weight loss and maintenance is adherence to metformin therapy.(381) Additional data are needed for the use of metformin for weight loss in patients without the aforementioned conditions.(382) Metformin is generally safe, though the risk of lactic acidosis (boxed warning) must be considered, particularly in patients with dehydration, renal insufficiency, or those receiving acute loads of intravenous contrast media for radiologic procedures. According to the product information, GI side effects are one of the most commonly reported adverse events in patients treated with metformin; measures may be taken to minimize these side effects (e.g., take the dose with a meal; use of the extended-release formulation).

d. Glucagon-Like Peptide-1 Receptor Containing Agonists indicated for Type-2 Diabetes Mellitus management (dulaglutide, exenatide, liraglutide, lixisenatide, semaglutide, tirzepatide)

A Cochrane review of 17 RCTs involving 6,899 participants and typically lasting 26 weeks showed weight loss of 2.87 kg and 3.24 kg for exenatide and liraglutide (3 mg dose FDA-approved for weight loss), respectively, in patients with T2DM.(383) Additional data on weight loss are available in an open-label trial designed to evaluate the effect of treatment on HbA1c in patients with T2DM; the mean baseline BMI of patients in this trial was approximately 34 kg/m^2, with a weight loss of 5.6 kg with semaglutide and 1.9 kg with exenatide.(384) A Phase 2 trial with semaglutide in patients with obesity (without DM) compared to liraglutide 3.0 mg daily and placebo has also been

published with positive results. Weight loss was significantly higher in all semaglutide groups versus placebo, and significantly higher compared to 3.0 mg liraglutide at doses of semaglutide of 0.2 mg per day or more.(385) Nausea is common with these agents and tends to subside with continuation of therapy. Clinically, it is feasible to dose escalate more slowly to an eventual goal dose if a patient reports GI intolerance, given multi-click pen formulations. The risk of inducing pancreatitis is a concern, though in the Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results (LEADER) trial including a total of 9,340 patients with T2DM, there was a higher absolute number of patients in the placebo arm with acute pancreatitis (23, 0.5%, 1.7 events/1000 patient-years of observation [PYO]) than in the treatment arm with liraglutide (18, 0.4%, 1.1 events/1000 PYO).(386) Due to rat and mouse data with increased C-cell tumors in those animals, there is a boxed warning of thyroid C-cell (medullary) tumor risk, and GLP-1 agonists are contraindicated in patients with a personal or family history of medullary thyroid cancer (MTC) or multiple endocrine neoplasia type 2 (MEN2).

e. Sodium-Glucose Cotransporter 2 Inhibitors (empagliflozin, dapagliflozin, canagliflozin, ertugliflozin)

As a class, sodium-glucose cotransporter 2 inhibitors cause glucosuria by inhibiting the reabsorption of the filtered glucose load in the proximal tubule. In this fashion, calories are lost through the urine. This can result in some weight loss in patients with T2DM in whom this class of agents has current FDA approval for use. In trials of 12 – 52 weeks duration, with two of these agents (dapagliflozin, canagliflozin), weight loss of 2 – 3 kg was seen.(387) In a meta-analysis of trials of one to two years duration, SGLT2 inhibitors (canagliflozin, dapagliflozin, and empagliflozin) showed an MD at two years compared to placebo of –2.99 kg, 95% CI: –3.64 to –2.34. Warnings and precautions for the SGLT2 inhibitors include ketoacidosis, genital mycotic infections, and rare cases of necrotizing fasciitis.(388,389) There remains a boxed warning for the use of canagliflozin in the setting of foot ulcers or amputations. Renal function should be monitored with use.

f. Bupropion

Bupropion, as monotherapy, has been noted to cause weight loss when used in patients with depression or those seeking to abstain from tobacco.(390) In studies of patients taking daily bupropion combined with naltrexone, there was a weight loss of approximately 5 kg more with treatment compared to those receiving a placebo.(391-393) The combination of naltrexone sustained-release/bupropion sustained-release is now FDA-approved for long-term weight management. Bupropion has a boxed warning for suicidality and is contraindicated in patients with a seizure disorder, bulimia, or anorexia. (390)

g. Naltrexone Monotherapy

As a μ-opioid receptor antagonist, naltrexone is commonly used for the treatment of opioid and alcohol use disorders.(394) It is conjectured that naltrexone reduces food consumption through the blockage of β-endorphin action at the μ-opioid receptor as well as preventing autoinhibition of pro-opiomelanocortin neurons, thus influencing the neurological reward pathways in the brain. In a small proof-of-concept study, N=11, Tek et al. (2014)(395) found that compared to placebo patients, patients in the naltrexone 25mg daily arm had significant weight loss (-3.4 kg) compared with weight gain (+1.37 kg) in the placebo group. Indications for naltrexone use include moderate to severe alcohol use disorder and moderate to severe opioid use disorder. It is recommended to

avoid use in patients with acute hepatitis, liver enzymes greater than 3 times the upper limit of normal, or liver failure.

h. Acarbose

Acarbose is a competitive inhibitor of pancreatic alpha-amylase and intestinal brush border alpha-glucosidases. It inhibits the metabolism of sucrose to glucose and fructose. It has an FDA indication for the treatment of type 2 diabetes mellitus, initiated at 25 mg 3 times daily with the first bite of each main meal (or starting with 1 meal with gradual up titration), maximum dose for less than 60 kg is 50 mg 3 times per day, and a greater than 60 kg is 100 mg 3 times a day. Consider liver function testing at full dosing. Contraindicated in patients with cirrhosis. Off-label use for the treatment of postprandial hyperinsulinemic hypoglycemia after gastric bypass. Zhang et al. (2020)(396) performed a systematic review network meta-analysis of randomized control trials comparing acarbose with dipeptidyl peptidase-4 inhibitors, found comparable glucose lowering but superior weight loss with acarbose use (MD −1.23 kg, −2.08 to −0.33). More adverse events were seen with acarbose use initially, with similar event numbers with longer treatment. More frequent dosing requirements with each meal could be a hindrance to use, however.

i. Pramlintide

Pramlintide is a synthetic analog of the human peptide hormone amylin that is co-secreted by pancreatic beta cells in response to eating food. Amylin in the body reduces postprandial hyperglycemia by causing some delay in gastric emptying, lowering glucagon release, and causing appetite suppression at central appetite centers. In a 4-month RCT of N=411(397), patients who had obesity (with an 8 month single blind extension) were randomized to different doses of pramlintide vs. placebo. At the end of the randomized 4-month portion, weight loss from baseline in the pramlintide arms ranged from 3.8 ± 0.7 to 6.1 ± 0.8 kg vs. 2.8 ± 0.8 kg with placebo. At 12 months, weight regain occurred in the placebo group but was maintained in patients on the higher doses of pramlintide of 120 µg t.i.d. and 360 µg b.i.d. Weight loss was not maintained in the lower 120-µg b.i.d. group. While not approved for the indication of weight management, pramlintide is FDA-approved for the treatment of both type 1 and type 2 diabetes mellitus. Per package insert, dosing recommendations are to start SUBQ: 15 mcg immediately prior to major meals and to reduce mealtime insulin (including premixed insulin) dose by 50% when starting pramlintide. Side effects include nausea and hypoglycemia when combined with insulin therapy.

j. Amphetamines/Stimulants (e.g., mixed amphetamine salts, lisdexamfetamine, methylphenidate)

Weight loss in children prescribed stimulants is considered a treatment-limiting adverse event. No studies have been published with weight loss as a desired outcome in adults with obesity. All of these medications have concerns and/or boxed warnings for abuse/dependence and CV/central nervous system side effects. Vyvanse has FDA approval for binge eating disorder.(398)

k. Cyanocobalamin (Vitamin B-12)

Vitamin B-12 has a very limited role in promoting weight loss. Based on theoretical extrapolation of the actions of vitamin B-12 at the cellular level, it is sometimes used to promote weight loss. There are no studies evaluating weight loss with Vitamin B-12 injections, tablets, sublingual pills, or drinks. Conversely, B-12 deficiency has been associated with weight loss, particularly after

bariatric surgical procedures, and can lead to permanent nerve damage if left untreated.(399) No weight loss should be anticipated as a result of the use of exogenous vitamin B-12. Risks of injection site reaction might be anticipated if that route is chosen. In patients with normal renal function, a hypervitaminosis state is unlikely.

l. Testosterone Replacement Therapy

Testosterone replacement therapy has been advocated to achieve weight loss in hypogonadal men with obesity.(400) However, two SRs showed that adipose tissue decreased by only 1.6 kg while lean body mass increased by 1.6 kg, with no overall difference in body weight versus placebo.(401,402) Similarly, testosterone supplementation in eugonadal men (total testosterone 350-400 ng/dL or higher) leads to no improvement in weight loss. There also remains significant controversy and mixed results regarding the cardiovascular effects of testosterone therapy in general.(403-405) This is an area requiring further review.(406)

m. Estradiol Replacement Therapy

On average, women gain about 1.5 lbs. per year during midlife (between the ages of 40 and 59), independent of initial body size or race/ethnicity, though roughly 20% may gain 10 pounds or more.(407,408) Controversy remains regarding the contributions of aging, with loss of lean muscle mass resulting in a decrease in resting metabolic rate and subtle decreases in physical activity with age, vs. the estrogen deprivation of menopause. Because aging results in a decrease in both basal and total energy expenditure, basal metabolic rate calculators are age dependent.(409,410) Midlife women are exposed to several unique and interrelated influences that promote weight gain: estrogen deprivation, mood disorders, and sleep disturbances.(411) With the loss of estrogen, there is preferential deposition in visceral fat due to estrogen receptors on adipocytes.(412) Estrogen is weight-neutral but improves body fat redistribution.(413) However, despite its favorable influence on body fat distribution menopausal hormone therapy cannot be specifically recommended as a treatment for the sole indication of central obesity in midlife women as it is not FDA-approved for that specific purpose and may carry a non-zero thromboembolic risk, risk for breast cancer, hypertriglyceridemia, and must be combined with progesterone, an anabolic hormone associated with weight gain, in the presence of a uterus to avoid uterine dysplasia. Current indications for the use of estradiol include, but are not limited to, genitourinary and vasomotor symptoms associated with menopause for patients under the age of 60 or within 10 years of menopause. Contraindications to use include breast cancer. Caution is encouraged in patients with hypertriglyceridemia, risk factors for venous thromboembolic disease, active gallbladder disease, and/or migraine headache with aura.

While the ovaries stop producing estradiol, they continue to produce androgens, and levels of sex hormone-binding globulin (SHBG) fall, leading to higher levels of circulating free androgens. These changes are linked to a higher risk of metabolic diseases, type 2 diabetes, and cardiovascular disease, as cholesterol levels shift unfavorably with rising low-density lipoprotein (LDL) and falling high-density lipoprotein (HDL) levels. Effective treatment strategies should combine culturally sensitive lifestyle and behavioral interventions with consideration of pharmacologic and surgical options when appropriate. Menopause hormone therapy (MHT), while not a weight-loss treatment, can improve symptoms like hot flashes, sleep disturbances, and quality of life.

n. Thyroid Hormones

Several small studies have evaluated the association between weight loss and the use of levothyroxine and liothyronine replacement in hypothyroid patients.(414) Normalization of the hypothyroid state is associated with small losses of weight (typically less than 1 kg), which are not durable beyond 12 – 24 months. Normalization of the hyperthyroid state is associated with a weight gain of approximately 7 kg. Treatment of euthyroid patients to hyperthyroid levels has not been reported outside of control groups in early-phase clinical trials. The risks associated with hyperthyroidism, particularly cardiac, ocular, bone, and neuropsychiatric, make intentional creation of a hyperthyroid state highly inadvisable for weight loss. Hyperthyroidism (e.g., Graves' disease) is a condition that requires treatment to avoid negative health consequences. Iatrogenic hyperthyroidism accrues significant harm.

o. Human Chorionic Gonadotropin

Human chorionic gonadotropin (HCG) has no role in weight loss therapy, is ineffective, and has serious safety concerns. A meta-analysis published in 1995 reviewed the use of intramuscular HCG in 24 studies to include 14 RCTs.(415) The authors concluded that HCG was no more effective than a placebo or diet alone for weight loss, fat redistribution, or a sense of well-being. Since 1995, there have been no further trials evaluating intramuscular HCG. To date, there are no studies demonstrating the efficacy of HCG drops, pellets, lozenges, or HCG injections (in the absence of severe calorie restriction) over placebo or alternate therapy. Serious adverse events, including deep vein thrombosis and pulmonary embolism (PE), have been reported.(416)

Appendix K: Metabolic/Bariatric Surgery

A. Background

Metabolic/bariatric surgery (MBS) is one of the most common abdominal operations performed, paralleling the persistent prevalence of obesity in the U.S. and globally. It has been shown to be the most effective and durable treatment for severe obesity. Advances in minimally invasive surgical techniques, surgical instrumentation, and quality improvement and accreditation programs (e.g., American College of Surgeons and American Society of Metabolic and Bariatric Surgery) have led to significant reductions in morbidity and mortality and increased public acceptance of these procedures.

Since the National Institutes of Health (NIH) consensus statement on gastrointestinal surgery for severe obesity in 1991, the accepted indications for MBS included: patients with a BMI ≥40 kg/m^2 who have failed to achieve significant weight loss by non-surgical means and are fit for surgery, or those with an obesity-related comorbidity and BMI ≥35 kg/m^2.(417) Recently, however, the American Society for Metabolic and Bariatric Surgery (ASMBS) and the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) updated the indications for MBS in a joint statement to better reflect accumulated knowledge of obesity and MBS and reflect modern practice.(418) This included the recommendation for MBS for individuals with a BMI≥35 kg/m^2 regardless of comorbidity status, and evidence to support the option of MBS in conjunction with a comprehensive lifestyle intervention, for patients with DM or other metabolic disease and a BMI ≥30 kg/m^2.

B. Outcomes

Significant and durable weight loss has been shown in multiple studies. Evidence from observational and experimental studies consistently shows significant absolute and excess weight loss among adults with obesity, persisting 5, 10, and >10 years after surgical intervention.(255,419-425) Evidence from several randomized clinical trials demonstrates that MBS significantly improves systolic blood pressure, HbA1c, fasting blood glucose, HDL cholesterol, and triglycerides, and reduces medication requirements, compared with non-surgical interventions, variably at 1 – 12 years follow-up.(244,426-430) Furthermore, multiple studies demonstrated a survival benefit in different populations with obesity undergoing MBS.(431-434) Overall cancer risk is also reduced in the population with Class 2 or Class 3 obesity after MBS compared with the population with Class 2 or Class 3 obesity that does not undergo MBS.(49,435) In addition, evidence from observational studies suggests that MBS significantly reduces the incidence of hirsutism, menstrual irregularity, and infertility in women with PCOS and obesity at one year and longer follow-up.(436) Surgery in older patients is associated with increased morbidity, especially in the presence of frailty. Nonetheless, MBS has been shown to be safe and effective in carefully selected septuagenarians.(437-439). Weight regain can occur after MBS, as with any weight loss modality, highlighting the chronicity of the disease of obesity. A median weight regain of 9.5% of the maximum weight lost has been reported after 1 year.(440)

C. Preoperative Optimization

Irrespective of surgical approach, MBS represents a major abdominal surgical procedure with a target population that often has multiple comorbid conditions. Yet, perioperative mortality and overall major morbidity rates are low (<0.1% and <4%, respectively).(427,441-444) Nonetheless, all patients considering surgical intervention should undergo a multidisciplinary preoperative evaluation, with particular attention to cardiopulmonary risk factors, psychosocial barriers, and prehabilitation.(445)

As with all surgical procedures, a complete history and physical is required, and the preoperative evaluation should include a review of the screening and assessment elements noted in Appendix O. This includes identification of problematic maladaptive eating patterns that may require further assessment or management. Screening for sleep apnea should be considered in all patients with Class 3 obesity, and severe shortness of breath requires a formal assessment for sleep apnea and cardiopulmonary function to identify any potential contraindications to surgery or correctable health issues that could be optimized before surgery.(445,446) Any biliary symptoms should be evaluated with ultrasonography.(447) Patients who smoke should be encouraged to quit and abstain from smoking due to its deleterious effects on pulmonary function and wound healing, especially those undergoing surgery with a gastrointestinal anastomosis. Patients who have active, untreated addictions to drugs or alcohol should not be referred for MBS.(448)

Patients considering MBS should be concomitantly enrolled in an integrated comprehensive lifestyle intervention program, both prior to and after the surgical procedure, to provide ongoing guidance and support. The support includes counseling concerning dietary regimen, appropriate physical activity, behavioral treatment, and social support. Adherence to lifestyle changes is essential to long-term and sustained metabolic improvement. Patients should receive preoperative nutritional counseling to ensure they understand postoperative dietary requirements and the need for lifestyle alteration. MBS support groups often facilitate this education both pre-operatively as well as postoperatively. In addition, lifelong medical surveillance after MBS should include monitoring for changes in the status of chronic health conditions and procedure-specific complications such as nutritional deficiencies.(449)

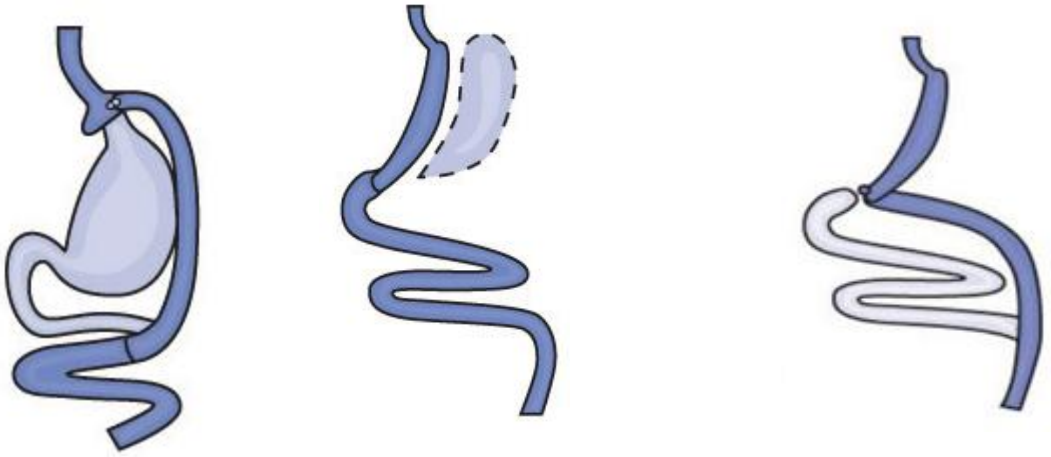
Numerous insurance companies mandate enrollment in a structured weight-loss program for a prescribed period of time before patients can be considered for these procedures. There is conflicting evidence as to the benefit of such an approach, and it has been condemned by the American Society of Metabolic and Bariatric Surgery as a barrier to receiving effective health care.(419) The majority of third-party payers and >80% of bariatric programs in the U.S. require pre-surgical psycho-social evaluations for patients seeking MBS. Psychosocial factors have significant potential to affect long-term outcomes of bariatric procedures, including emotional adjustment, adherence to recommended postoperative lifestyle regimens, weight-loss outcomes, and comorbidity improvement and/or resolution. The evaluating provider plays several important roles in the multidisciplinary treatment of the bariatric patient. Central among these is the role of identifying factors that may pose challenges to optimal surgical outcome and providing recommendations to the patient and bariatric team on how to address these issues.(450) ASMBS and IFSO acknowledge that individuals seeking MBS may benefit from consultation with a multidisciplinary team to help identify and potentially treat modifiable risk factors.(418)

D. Potential Contraindications

There are few absolute contraindications to MBS, and consultation with the bariatric surgeon should be performed to thoroughly review past medical and surgical history. Relative contraindications that are supported by expert consensus include severe heart failure, unstable coronary artery disease, severe coagulopathies, severe chronic obstructive pulmonary disease (COPD)/end-stage lung disease, active peptic ulcer disease, active cancer treatment, portal hypertension/advanced liver disease, active alcohol/substance abuse, and impaired intellectual capacity/inability to follow pre- and postoperative instructions.(451,452) Expert consensus also states that pregnancy is not recommended during the rapid weight-loss phase after MBS; therefore, counseling and follow-up regarding contraception and delay of pregnancy during this period are important.(453,454)

E. Operations

Figure K-1: Most Common Types of Metabolic/Bariatric Procedures Performed in the U.S. (455)



Roux-en-Y Gastric (RYGB)

Sleeve Gastrectomy (SG)

Biliopancreatic Diversion with a Duodenal Switch (BPD-DS)

MBS is increasingly recognized as having significant beneficial neurohormonal effects on the regulation of energy balance and hunger control.(456) These effects contribute to weight loss and positive metabolic changes. All operations are preferentially performed using minimally invasive techniques (laparoscopic or robotic).

a. Roux-en-Y Gastric Bypass

Roux-en-Y gastric bypass involves creating a small gastric pouch and a Roux-en-Y reconstruction of the small intestine. An approximately 30 mL gastric pouch is constructed and empties into a Roux limb of jejunum through a gastrojejunostomy. A variable distance downstream from this anastomosis (~100-150 cm), another anastomosis (jejunojejunostomy) is created with the

biliopancreatic limb to form a “common channel” that then proceeds normally to the ileum and empties into the cecum.(457-459)

b. Sleeve Gastrectomy

The sleeve gastrectomy is the most commonly performed MBS procedure in the U.S. and globally.(460) Its origins began as a component of Scopinaro’s biliopancreatic diversion (BPD) with a duodenal switch (DS).(457,461-463)

The procedure involves creating a ‘sleeve’ of the stomach by removing 75 – 80% of the volume of the stomach by excising the greater curvature of the stomach, re-shaping the stomach into a banana or “sleeve” shaped organ. Resection starts approximately 4 – 6 cm proximal to the pylorus and progresses close to the gastric cardia to preserve the lesser curvature. It is usually fashioned over a 36-40 French bougie.

Studies suggest that medium- and long-term weight loss and metabolic improvement after sleeve gastrectomy are similar to gastric bypass.(244,427,430,461,464,465) Worsening or de novo gastroesophageal reflux disease (GERD) is a risk of sleeve gastrectomy, although some patients with GERD report improvement or remission.(466)

c. Biliopancreatic Diversion with Duodenal Switch

BPD with DS entails an SG and duodenal bypass affected by a proximal Roux-en-Y duodenojejunostomy. This operation has the greatest malabsorptive effect and produces the greatest weight loss and rates of T2DM resolution, but also has a higher risk of significant surgical and metabolic morbidity.(424,467) Technical complexity and long-term nutritional deficiencies have limited its acceptance and popularity in the U.S. ASMBS estimates from 2022 are that BPD comprised only 2.2% of bariatric procedures performed.(468)

d. Other Operations

Single anastomosis duodenoileostomy with sleeve (SADI-S) is performed by creating a sleeve gastrectomy, an end-to-side duodenoileostomy to a loop of ileum, leaving a blind end of the hepatobiliary limb. This, like BPD-DS, is a highly malabsorptive procedure that produces significant weight loss and excellent metabolic improvement. This can be performed following a sleeve gastrectomy. Like BPD, the SADI-S is associated with greater early postoperative morbidity compared with RYGB and SG. The risk of nutritional deficiency is similar to BPD.(469)

One anastomosis gastric bypass (OAGB) is a common operation outside the United States. It consists of creating a vertically oriented gastric pouch based on the lesser curvature, and a gastrojejunostomy to a loop of jejunum 150-250 cm from the ligament of Treitz. Durable weight loss outcomes and improvement of comorbidities have been demonstrated. Malnutrition and bile reflux remain a concern.(470,471)

F. Mortality Risk

Mortality risk after primary MBS is low, compares favorably with other abdominal surgeries, and varies by surgical procedure. A systematic review and meta-analysis including more than 3,650,000 patients showed an overall perioperative mortality risk of 0.08%.(444) By operation

type, the mortality risk after SG is 0.05%, after RYGB 0.09%, and 0.41% after BPD-DS. Risk factors for one-year mortality included older age, male sex, higher BMI, presence of 30-day leak, 30-day PE, and 30-day hemorrhage.(442,472-474) Revisional MBS carries a higher risk of mortality and morbidity.

G. Morbidity Risk

Overall complication rates are low and have decreased over time from 4.6% (2006) to 3.0% (2013).(467) The type of procedure performed and surgical approach are associated with the risk of morbidity. A one-year analysis of 4,756 patients from the American College of Surgeons' National Surgical Quality Improvement Program (ACS NSQIP) database showed that laparoscopic adjustable gastric banding (LAGB) carried a lower 30-day rate of major complications compared with laparoscopic RYGB (1.0% versus 3.3%), return visits to the operating room (0.9% versus 3.6%), and shorter postoperative stay (median one versus two days).(475) Similarly, from the same database, open RYGB had a higher morbidity (7.4%) than the laparoscopic approach (3.4%). BPD with DS had the highest rate of morbidity and mortality, paralleling its increased technical difficulty.(476)

H. Suicide/Self-harm Risk

A review of observational studies suggested an increased risk of suicide after bariatric surgery. Compared with age, sex, and BMI-matched controls, individuals who underwent bariatric surgery had an odds ratio for suicide of 3.8 (95% CI, 2.19-6.59), based on 5 case-control studies.(477) However, the findings by others suggest that the rate of suicide after bariatric surgery may be lower than the global rate in the general population.(478) Lifetime suicide attempt rates may not be significantly different between the population with and without bariatric surgery.(479). A study specific to the VA population demonstrated an increased risk of suicidal ideation (adjusted hazard ratio (aHR) = 1.21, 95% CI:1.03-1.41), and an increased risk of suicide attempt (aHR=1.62, 95% CI:1.22-2.15).(480)

At the same time, studies of short- and medium-term outcomes of MBS demonstrated lower rates of depression after bariatric surgery; but it is unclear whether these are sustained long-term or may worsen after 4-9 years.(481) Nonetheless, findings underscore the importance of a pre-operative psychosocial evaluation of individuals considering MBS, as well as post-operative follow-up.(445,450)

Table K-1. Potential Complications Associated with Surgical Procedures

Complication	Operation	Prevalence[a]
Gastrointestinal Leak(482,483)	RYGB, SG, BPD-DS	<3%
Bleeding(484,485)	RYGB, SG, BPD-DS	0.4-4.4%
Marginal Ulcer(486)	RYGB, BPD-DS	0.5-16%
Stricture/Stenosis(487)	RYGB, SG, BPD-DS	<3.9%
Bowel Obstruction(488)	RYGB, BPD-DS	<1%
Pulmonary Embolism(484,489)	RYGB, SG, BPD-DS	<1%

Complication	Operation	Prevalence[a]
Portomesenteric Vein Thrombosis(490)	RYGB, SG, BPD-DS	<0.5%
Nutritional Deficiency[b](449,491)	RYGB, BPD-DS	<1-49%

[a] Varies, based on operation performed

[b] Vitamins B1, B12, A, D, E, K, Folate, Iron, Calcium, Zinc, Copper

Abbreviations: BPD-DS: Biliopancreatic Diversion with Duodenal Switch; RYGB: Roux-en-Y Gastric Bypass; SG: Sleeve Gastrectomy

I. Nutritional Concerns

It is recommended that all patients receive daily [bariatric] multivitamin and be monitored routinely by an experienced team to detect nutritional deficiencies (see Table K-2). The American Association of Clinical Endocrinologists, American College of Endocrinology, The Obesity Society, American Society for Metabolic and Bariatric Surgery, the Obesity Medicine Association, and the American Society of Anesthesiologists jointly published clinical practice guidelines for the nutritional and metabolic support of patients undergoing MBS.(449) Susceptibility to nutritional deficiencies varies between the different bariatric procedures. Individuals undergoing RYGB or BPD-DS are at greater risk for micronutrient and macronutrient deficiency. A low-carbohydrate diet can avoid dumping syndrome.

Non-metabolic surgeries can also result in nutritional deficiencies since the volume of food intake is markedly reduced. Bariatric-specific multivitamins are recommended long-term. Furthermore, it is recommended that postoperative patients receive an average of 60 – 120 g of protein daily to avoid protein malnutrition.(449,492)

Several nutritional deficiencies are common, and supplementation at higher than the usual recommended daily dose may be required.

Table K-2. Example of Post-Surgical Schedule for Clinical/Biochemical Monitoring(449)

	Pre-operative	1 month	3 months	6 months	12 months	24 months	Continue Annually
Complete Blood Count	X	X	X	X	X		X
Complete Metabolic Panel	X	X	X	X	X		X
Liver Function Tests	X	X	X	X	X		X
Lipid Panel**	X			X	X		X
Iron	X		X	X	X		X
Folate	X	X	X	X	X		X
Vitamin B1	X	+/-	+/-	+/-	+/-		+/-

	Pre-operative	1 month	3 months	6 months	12 months	24 months	Continue Annually
Vitamin B12	X		X	X	X		X
Vitamin 25(OH)D/Calcium/PTH	X		X	X	X		X*
Vitamin A	X			X			+/-
Vitamin E**	X						
Vitamin K**	X						
Zinc	X				X		X
Copper	X				X		X
Bone mineral density and body composition						X	X***

X: Indicates the suggested schedule for laboratory monitoring after metabolic/bariatric surgery
+/-: Recommended for high-risk patients, including those with excessive weight loss
*24-h urinary calcium excretion measurement at 6 months and annually for BPD-DS
**Selectively for symptomatic patients or patients at increased risk for deficiency
***Continue annually for patients with ongoing weight loss or increased risk

a. Recommended Post-metabolic/Bariatric Surgery Nutritional Supplementation and Medications (493)

1. Daily (lifelong) multivitamin (bariatric/pre-natal) with the following requirements:
    - Thiamine (B1) 50 – 100 mg
    - Cobalamin (B12) 350 – 1,000 ug (if duodenum bypassed then recommend 1,000 ug sublingual or parenteral (IM/SQ) administration to maintain normal levels
    - Folate 400 – 800 ug (800 – 1,000 ug in women of child-bearing age)
    - Iron 18 mg males/45 – 60 mg elemental iron in menstruating females or with duodenal bypass
    - Calcium 1,200 – 1,500 mg/d
    - Vitamin D (D3) 3,000 IU/d
    - Vitamin A 5,000 – 10,000 IU/d
    - Vitamin E 15 mg/d
    - Vitamin K 90 – 120 ug/d
    - Zinc 100 – 200% RDA (8 – 22 mg/d)
    - Copper 100 – 200% RDA

2. Ursodiol 300 mg twice a day for six months (if gallbladder present without stones) for gallstone prophylaxis during acute weight loss
3. Chemical venous thromboembolism prophylaxis – no clear consensus on dosage or postoperative length of treatment
4. Proton Pump Inhibitors for RYGB/BPD with DS to prevent marginal ulceration. Not indicated for SG unless the development of symptomatic reflux.
5. Avoidance of ALL potential ulcerogenic medications (i.e., NSAIDs/acetylsalicylic acid)
6. Diabetes medications will likely stop or at least substantially reduce after surgery
7. Weight-based medication doses will likely decrease over time

All bariatric procedures can lead to deficiencies in iron, vitamin B12, folate, and calcium during subsequent pregnancies. These deficiencies can result in maternal complications, such as severe anemia, and in fetal complications, including neural tube defects, intrauterine growth restriction, and failure to thrive. Nutrient supplementation following metabolic/bariatric surgery and close supervision before, during, and after pregnancy can help prevent nutrition-related complications and improve maternal and fetal health. Therefore, women who have undergone weight loss surgery and subsequently become pregnant need to receive intensive nutritional follow-up from providers with expertise in clinical nutrition.

Appendix L: Specific Behavioral Strategies Featured in Comprehensive Lifestyle Interventions

A. Goal Setting

Goal setting involves setting realistic, specific goals for behavior change. The goal includes the specific action to be taken and when, where, how, how long, and how often the individual will engage in that behavior. Writing down or electronically recording the goal and keeping a record of progress with self-monitoring helps to monitor progress toward goals that might be modified as goals are attained. Attaining goals motivates and reinforces continued adherence to changing behaviors. An example of a behavioral goal for increased physical activity is, “I will walk around the block for 20 minutes at a brisk pace every day at 11:30 A.M. If it rains, I will do 20 minutes of low-impact aerobics in the living room.” An example of a behavioral goal for making healthier food choices is, “I will eat at least three servings of non-starchy vegetables per day.”

B. Self-monitoring

Self-monitoring is perhaps the most often employed and the most important behavioral strategy. This involves recording all instances of the target behaviors. For weight management purposes, individuals record all details of food intake, physical activity, and body weight daily. Recording often includes information about times of day and associated thoughts, feelings, places, and events that might affect food intake and physical activity. This record-keeping allows individuals to identify eating and physical activity patterns, cues, measurement of actual food intake, and physical activity. Awareness of these factors promotes the development of specific actions to address unhealthy behaviors.

C. Stimulus Control or Cue Reduction

Stimulus control or cue reduction strategies refer to efforts to change the environmental signals or cues for any specific behavior. It includes both techniques to reduce cues, for example, related to caloric intake and physical inactivity; and to strengthen cues for desired behaviors, for example, healthy eating and physical activity. Examples include removing unhealthy food from sight, eating only at the table rather than in the living room, not watching TV when eating, avoiding fast-food restaurants, having healthy snacks immediately available, placing walking shoes in a convenient spot where they will be noticed, and so on. The overall idea is to eliminate signals for unhealthy eating and substitute cues for helpful weight management behaviors in their place.

D. Positive Reinforcement

Positive reinforcement involves providing rewards for desirable behavior. In the context of weight management, this means offering positive consequences for engaging in health behaviors that are consistent with an individual’s weight and health goals. Clinically, reviewing food and activity monitoring logs offers a consistent opportunity to give positive feedback and reinforcement. Individuals may also identify their own rewards for engaging in desired behaviors, e.g., self-praise, buying a new pair of running shoes, starting a garden, or getting a new book from the library.

E. Stress Management

Stress management is used in the treatment of numerous conditions to reduce felt stress because excess stress can stimulate unhelpful thoughts and behaviors. In weight management, excessive stress may frequently lead to changes to eating patterns to physical activity routines. Stress management includes a wide variety of techniques such as relaxation training, biofeedback training, stimulus control, cognitive restructuring, social support, assertiveness training, problem-solving, and mindfulness and meditation. Taken together, the individual becomes more resistant to becoming overly stressed and more capable of coping with and reducing felt stress when it is noticed.

F. Problem-solving

Problem-solving involves teaching an individual to effectively analyze problems, which might otherwise lead to unhelpful behaviors such as eating past the point of fullness. Once contributing factors are accurately analyzed, possible solutions are considered and evaluated for the pros, cons, and probable outcome of each solution, and a workable solution is agreed upon.

G. Skill Training

Skill training refers to training an individual in those skills that are likely to enhance success. For example, participants in weight management are taught skills in evaluating the caloric content of various foods and in planning to attenuate situations where they may be more likely to make choices that are inconsistent with their health goals. They may be taught skills in eating more slowly, cooking more healthfully, or practicing assertiveness to combat weight bias and stigma.

H. Social Support

Social support is widely acknowledged to improve coping in challenging situations. People receive encouragement, positive reinforcement, emotional empathy and support, and guidance from others. A comforting (and stress-reducing) feeling of “not being alone” comes from being in the presence of others who are in the same difficult situation, as occurs in weight management groups, cancer support groups, and many others.

I. Cognitive Restructuring

Cognitive restructuring is a process whereby individuals are taught to become fully aware of automatic negative thoughts, to evaluate those thoughts, and to then replace them with more realistic, adaptive thoughts. Those thoughts then stimulate more desirable behaviors. Negatively oriented, discouraging, over-reactive, and unrealistic thoughts mediate maladaptive behavior. People are frequently not aware of underlying automatic thoughts such as “I MUST clean my plate!” or “I will NEVER be able to do this!” These thoughts often lead to engaging in undesirable behavior. Cognitive restructuring can be used to identify and modify unhelpful thoughts and attitudes about weight management. Cognitive restructuring may be particularly useful for internalized weight stigma, e.g., “It’s my fault that I have a weight problem” or “People will think I don’t have self-control because of my weight.”

J. Relapse Prevention Training

Relapse-prevention training helps individuals respond productively to lapses in their efforts to adopt new behaviors or reduce and avoid maladaptive behaviors. Lapses are inevitable during efforts to change any health behavior. However, many people respond negatively to lapses and experience feelings of guilt or shame, as well as negative thoughts such as “I am a failure!” or “I’ll never be successful at managing my weight!”. Relapse prevention approaches help people to reframe lapses as learning opportunities rather than failures and help them to use cognitive restructuring to address negative thinking and problem-solving strategies to both proactively and reactively plan ways of managing situations that lead to lapses. Role-playing and even “planned lapses” are used to help people practice adaptive responses to lapses.

Appendix M: Assessing Body Composition

Table M-1: Modalities of Assessing Body Composition

Modality	Considerations	Strengths	Limitations
MRI ("Gold Standard")	Accuracy ⭐⭐⭐⭐⭐ Cost 💰💰💰💰💰 Practicality 🧰🧰	• High qualitative and quantitative accuracy • Good spatial resolution • No radiation exposure • Can measure regional and total adiposity	• Costly • Limited accessibility • Requires expertise in measurement • Size constraint of scanner • Debate about optimal anatomical site for measurement
CT ("Gold Standard")	Accuracy ⭐⭐⭐⭐½ Cost 💰💰💰💰 Practicality 🧰🧰	• High qualitative and quantitative accuracy • Good spatial resolution • Validated cutoff values • Can measure regional and total adiposity	• Costly • Radiation Exposure • Requires expertise in measurement • Size constraint of scanner • Debate about optimal anatomical site for measurement
DXA ("Gold Standard")	Accuracy ⭐⭐⭐⭐ Cost 💰💰💰 Practicality 🧰🧰🧰	• Quick • High reliability and accuracy • Minimal effort from participant • More clinical utility than just PBF (i.e., bone density) • Can measure regional and total adiposity	• Intermediate cost • Operator training required • Low-level radiation exposure • Inability to distinguish between visceral and subcutaneous fat • May underestimate fat at lower adiposity and overestimate at higher adiposity • Individual's hydration status may affect output
ADP (e.g., BodPod)	Accuracy ⭐⭐⭐⭐ Cost 💰💰💰 Practicality 🧰🧰🧰	• Quick • Similar accuracy to DXA • Minimal technical expertise needed • Minimal effort from participant • No physical discomfort or radiation	• Expensive • Results influenced by clothing, hair, and lung volume estimation • Estimates whole-body fat but cannot assess fat distribution • Overestimates FFM and underestimates fat mass compared to DXA in normal weight and higher BMI's. • Less accurate at the extremes of BMI

Modality	Considerations	Strengths	Limitations
BIA (Multi-frequency) (e.g., INBODY, SECA)	Accuracy ⭐⭐⭐ Cost 💰💰 Practicality 🧰🧰🧰🧰	• Quick, Simple & noninvasive • Reproducible (<2% variability) • Low cost • Acceptable accuracy in controlled conditions (within 3-5% compared to DXA) • Some models can estimate body water and regional body composition • Moderate to high correlations to DXA	• Reduced accuracy in hydration-altered states • Less reliable in severe obesity • Results are population and device-specific • Cannot accurately assess fat distribution (location/ subcutaneous/ visceral) • Tends to underestimate body fat percentage in higher adiposity and overestimate in lean individuals compared to DXA
BIA (Basic, Single-freq)	Accuracy ⭐⭐ Cost 💰 Practicality 🧰🧰🧰🧰🧰	• Quick, Simple & noninvasive • Low cost	• Significant error margins • Reduced accuracy in hydration-altered states • Similar limitations as multi-frequency BIA
Skinfold Calipers	Accuracy ⭐⭐ Cost 💰 Practicality 🧰🧰🧰🧰	• Inexpensive • Portable • Accurate when performed by a skilled assessor	• Operator dependent • Caliper accuracy varies • Primarily measures subcutaneous fat → may underestimate total body fat • Poor predictor of visceral fat • Poor accuracy in individuals with high adiposity or loose connective tissue • Uncomfortable
Consumer Smart Scales with BIA	Accuracy ⭐ Cost 💰 Practicality 🧰🧰🧰🧰🧰	• Quick, Simple & noninvasive • Low cost • Portable	• Least accurate • Similar limitations to other BIA

Legend:

- **Accuracy: ⭐ = Very Low → ⭐⭐⭐⭐⭐ = Very High**
- **Cost: 💰 = Low → 💰💰💰💰💰 = Very High**
- **Practicality: 🧰 = Low → 🧰🧰🧰🧰🧰 = Very High**

Note: Sex, age, and ethnicity-specific thresholds for body fat percentage in defining obesity have been proposed for several body composition measurement methods, but there is no universally established or consensus set of cutoffs that have been established for these methods.(494-496)

Abbreviations: ADP: air displacement plethysmography; BIA: bioelectrical impedance analysis; CT: computed tomography; DXA: dual-energy X-ray absorptiometry; FFM: free fat mass; MRI: magnetic resonance imaging; PBF: percent body fat

Appendix N: Staging and the Classification of Excess Adiposity

Clinical staging is commonly used to assess and communicate an individual's health status and disease progression. It provides a streamlined, standardized framework to describe disease severity in a clear and concise manner. Similarly, in obesity management, staging enables providers to assess not only the degree of excess adiposity but also the severity of associated comorbidities, functional impairments, and overall health risk and align treatment intensity with disease severity. While BMI has traditionally been used to classify obesity, it does not account for individual differences in fat distribution, metabolic health, or the physical and psychological impact of obesity. In addition to anthropometric measurements, providers should consider the following clinical criteria when determining an individual's stage of obesity: 1) Medical signs and symptoms of abnormal tissue or organ function; 2) Biomechanical/functional signs or symptoms of age-adjusted limitations of daily activities; 3) Behavioral signs or symptoms, including mood disorders, eating disorders, and reduced quality of life.(497,498)

Staging systems such as the Edmonton Obesity Staging System (EOSS)(498) and the complications-centric model endorsed by The Obesity Society and the American Association of Clinical Endocrinologists (AACE)(499) offer a more nuanced approach to risk stratification and management than BMI measurement alone.

Higher obesity stages are independently associated with increased risk of complications and all-cause mortality, regardless of BMI category. For example, EOSS incorporates comorbid conditions and functional status and has been shown to predict adverse health outcomes and all-cause mortality more accurately than BMI or waist circumference (WC) alone.(500,501) These staging tools help providers identify patients who may benefit from more intensive or early interventions.

Obesity staging enhances clinical decision-making, allows for more tailored treatment plans, and facilitates shared decision-making with patients. Ultimately, staging supports a more individualized, risk-based approach to care, aligning treatment intensity with disease severity to improve health outcomes, especially in healthcare systems where rising costs and resource allocation become important. Given the importance of diagnosing and staging, the CPG Workgroup recommends that busy providers use the table below to assist in quickly assessing disease severity and identifying when to initiate or escalate treatment earlier in the care continuum.

Table N-1: Edmonton Obesity Staging System (EOSS)(502)

	Stage 0	Stage 1	Stage 2	Stage 3	Stage 4
	No Sign of Obesity-Related Complications	Mild Obesity-Related Disease	Obesity-Related Chronic Disease	Severe End-Organ Damage	Severe/Disabling & Dysfunctional Chronic Disease
Physical/ Medical	None	Pre-clinical/Mild • PreHTN • PreDM • Dyspnea on exertion	Established/Moderate • HTN • T2DM • Mild- moderate OSA • MASLD • GERD	Severe organ damage • CAD/CVA • MASH • HF • T2DM, severe OSA, and HTN with complications	End-stage • CVA with disability • End-stage heart, liver, lung, and renal disease • Obesity-related cancer • T2DM with severe complications
Mental Health	None	Mild impairment • Occasional symptom fluctuations	Moderate impairment • Symptoms impacting quality of life	Severe impairment • Symptoms significantly impacting quality of life	Psychologically Disabling Symptoms
Functional	None	Mildly restrictive • Occasional joint pain	Moderately restrictive • OA impacting quality of life	Severely limited • Severe OA with significant mobility limitations	• Immobile • Ability to work

Abbreviations: CAD: coronary artery disease; GERD: gastrointestinal reflux disease; HF: heart failure; HTN: hypertension; MASH: metabolic dysfunction-associated steatohepatitis; MASLD: metabolic dysfunction-associated steatotic liver disease; OA: osteoarthritis; OSA: obstructive sleep apnea; preDM: prediabetes; preHTN: pre-hypertension; T2DM: type 2 diabetes mellitus

Appendix O: Additional Information for Managing Patients with Overweight and Obesity

Caring for patients with overweight and obesity is clinically important. While ongoing research continues to strengthen the empirical foundation for obesity management, the following accepted practices are meant to guide clinical judgment and support consistent, patient-centered care.

A. Screening and Clinical Assessment for Overweight and Obesity

a. Screening

Assessment of weight and health-related risk involves the consideration of three key measurements: body mass index (BMI), measurement of adiposity, and evaluation of risk factors for diseases and conditions associated with obesity. The BMI calculation is the most commonly used screening tool in adult populations to determine an individual's risk of having overweight and obesity. The BMI calculation, despite its limitations, is considered a quick, easy, reliable, reproducible, and scalable population measurement that can be followed over time. It is defined as a person's weight in kilograms divided by the square of the person's height in meters (kg/m^2). The optimal frequency of BMI measurements has not been evaluated, but it is generally recommended that they occur at least annually.(8,11) Classifications by BMI are listed in Table O-1.

Because BMI is an indirect measure of adiposity, it can be influenced by factors like edema and muscular composition. Hence, although BMI measurements remain a useful tool for assessing adiposity at a population level, it has limitations in determining an individual patient's risk of adiposity-associated complications. Patients with increased muscle mass leading to a higher weight and consequently a higher BMI may be classified as having overweight or obesity; alternatively, among individuals with decreased lean muscle mass, the low BMI may lead to decreased recognition of their true adiposity and elevated cardiometabolic risk. Additionally, patients of different ages and ethnic backgrounds have different target BMI ranges, making it more difficult for a provider to determine if a patient is at a healthy weight for their height. Clinical obesity requires confirmation of excess adipose tissue. Due to these limitations, additional anthropometric measures are recommended to better assess adiposity. In the context of insufficient evidence to recommend for or against a particular measure of adiposity to manage clinical outcomes in patients with overweight or obesity (see Recommendation 1), our Work Group recognizes the importance of individualization when choosing a screening modality that respects patient dignity and promotes a supportive, non-stigmatizing environment.

Visceral fat, also known as intra-abdominal fat, is a significant indicator of risk for obesity-related conditions. Measurements of visceral adiposity can vary between anthropometric measurements and body composition imaging modalities.(503) Among these, waist circumference (WC) is the most practical and cost-effective anthropometric measurement for assessing a patient's level of abdominal fat and is an indicator of increased disease risk.(504) This is particularly useful for those who have a BMI between 25 kg/m^2 and 30 kg/m^2, as WC can help identify those with central adiposity who may be at increased risk for cardiometabolic

disorders. For individuals with a BMI ≥35 kg/m², virtually all individuals will already exceed established waist circumference thresholds, and measuring a WC is unlikely to add further risk stratification.(449,504) A WC of ≥ 88 cm [≥ 35 in] (>88 cm [>35 in] for women and ≥ 102 cm [≥ 40 in] for men (see Table O-2), indicates increased risk of visceral adiposity and developing cardiometabolic complications. For individuals identified under the broad social category of "Asian," lower thresholds (≥ 80 cm for women and ≥ 90 cm for men; see Table O-2) are often applied based on epidemiological studies that reported higher cardiometabolic risk at lower levels of adiposity. Clinicians should therefore apply these cutoffs with recognition of their limitations, engage patients in shared discussion about their relevance, and consider complementary, race-neutral approaches such as waist-to-hip ratio or waist-to-height ratio, which may provide more equitable risk assessment across populations.(9,98,494) To ensure accurate measurement, WC should be assessed with a tape measure placed around the bare abdomen just above the iliac crest. The tape should be snug, but should not compress the skin, and the measurement should be obtained while the patient is standing at the end of normal exhalation. The measurement should be repeated twice.(505)

Two variations of the WC assessment are the waist-to-height ratio (WHtR) and the waist-to-hip ratio (WHR). The WHtR is calculated by dividing waist circumference by height. Compared to BMI or WC alone, WHtR has been shown to be a superior screening tool for cardiometabolic risk factors.(494,506,507) Having a WHtR of ≥ 0.5 has significantly greater discriminatory power for detecting hypertension, type-2 diabetes, dyslipidemia, metabolic syndrome, and cardiovascular outcomes. The other metric, the WHR, is a useful tool in identifying increased cardiometabolic risk associated with central obesity, especially among those with smaller body frames.(508) Unhealthy values for WHR are defined as ≥0.90 for men and ≥0.85 for women.(43)

The introduction of scales that feature bioelectrical impedance analysis (BIA) technology to measure percent body fat in clinical settings may enhance the assessment of overweight and obesity, for both Service members and Veterans. Recent research indicates that bioelectrical impedance analysis (BIA) technology is a reliable method for measuring percent body fat in clinical settings. Clinicians should remain aware of its limitations, particularly regarding hydration status, and ensure standardized protocols are followed to optimize accuracy and clinical utility.(509) Studies have shown that high-frequency direct segmental multifrequency BIA (DSM-BIA) at 500 kHz and 1000 kHz strongly correlates with dual-energy X-ray absorptiometry (DXA), the reference standard for body composition assessment, with no significant increase in accuracy at higher frequencies. Additionally, BIA devices, particularly octopolar and select foot-to-foot models, have demonstrated high reliability and potential utility for tracking body composition over time. While taking into account its limitations, these findings suggest the use of BIA as a practical tool for body composition assessment in military populations, with acceptable accuracy relative to reference standards. (510,511)

Techniques such as dual-energy X-ray absorptiometry (DXA) and magnetic resonance imaging (MRI) offer more precise assessments of body composition, including visceral adiposity and lean muscle mass. This may be a consideration in the evaluation, as low lean muscle mass is independently associated with higher cardiovascular and all-cause mortality, and the prevalence of sarcopenia increases with age and comorbidities (348). Despite their growing availability,

these methods are still rarely utilized in routine clinical practice due to factors such as cost, time constraints, and the need for specialized equipment, dedicated space, and trained personnel (see Appendix M). As the healthcare landscape evolves, integrating these advanced techniques of adiposity assessment could enhance our understanding of patient health by providing a more comprehensive picture of body fat distribution and its implications for disease risk.

In the context of insufficient evidence to recommend for or against a particular measure of adiposity to manage clinical outcomes in patients with overweight or obesity (see Recommendation 1), our Work Group recognizes the importance of individualization when choosing a screening modality that respects patient dignity and promotes a supportive, non-stigmatizing environment.

Table O-1: Body Mass Index (BMI) classifications according to the World Health Organization (WHO) standards

BMI Category	BMI Range (kg/m²)	BMI Range for Asian Populations (kg/m²)
Underweight	Less than 18.5	Less than 18.5
Normal weight	18.5 – 24.9	18.5–22.9
Overweight	25.0 – 29.9	23.0–24.9
Obesity Class 1	30.0 – 34.9	25.0–29.9
Obesity Class 2	35.0 – 39.9	30.0-34.99
Obesity Class 3	40.0 and above	35.0 and above

Abbreviations: BMI: body mass index

Table O-2: Common Methods and Diagnostic Cutoffs for Diagnosing Obesity (512,513)

Measurement	Standard Cutoff for Obesity	Asian Population Cutoff	Notes
Body Mass Index (BMI) (weight (kg) /height (m²)	≥30 kg/m²	≥27.5 kg/m²	BMI is widely used, but does not capture adiposity distribution or lean mass differences
Waist Circumference	≥102 cm (40 in) for men ≥88 cm (35 in) for women	≥90 cm (35.4 in) for men ≥80 cm (31.5 in) for women	Reflects central (visceral) adiposity and is a stronger predictor of cardiometabolic risk

Measurement	Standard Cutoff for Obesity	Asian Population Cutoff	Notes
Waist-to-Height Ratio	≥0.5	≥0.5	Reflects fat distribution and is strongly associated with increased cardiometabolic risk.
Percent Body Fat (PBF) (%) (Total body fat/Total body weight)	Age 20-39		Measured using multiple modalities with varying levels of accuracy, ranging from calipers to MRI. Useful in those with suspected elevated or low lean muscle mass. Limited availability in a clinical setting. Variations in cutoffs based on study, age, sex, and ethnicity. These cutoffs obtained from NHANES data. Note that modality measuring PBF can have limitations (e.g., BIA often underestimates PBF in normal to elevated BMI levels)
	>25% for men >39% for women	>28% for men >40% for women	
	Age 40-59		
	>28% for men >40% for women	>29% for men >41% for women	
	Age 60-79		
	>30% for men >42% for women	>29% for men >41% for women	

Abbreviations: BIA: bioelectrical impedance analysis; BMI: body mass index; MRI: magnetic resonance imaging; NHANES: National Health and Nutritional Examination Survey; PBF: percent body fat

b. Obesity-associated Conditions

Obesity is linked to numerous chronic health conditions and an increased risk of morbidity. These include various types of cancer, as well as pulmonary, cardiovascular, cerebrovascular, endocrinologic, rheumatologic, gynecologic, urologic, gastrointestinal, neurologic, and psychiatric complications(514-516) Essentially, all organ systems can be affected in some way (see Sidebar

4). The presence of obesity-related comorbidities should increase the urgency and intensity of treatment strategies aimed at addressing obesity.

c. Active-Duty Specific Challenges and Operational Readiness

Nearly 70% of U.S. Service members have overweight or obesity, and rates have more than doubled over the last decade.(61) This rise threatens military readiness by increasing the risk of obesity-related conditions and injuries, reducing deployment capability, driving up healthcare costs, and creating challenges in recruitment and retention.(59,66)

Occupational factors play a significant role in the rising rates of obesity, particularly among military personnel. Sedentary work, high levels of physical and mental occupational stress, short or irregular sleep patterns, and adverse lifestyle conditions contribute to excess weight gain. Service members are especially vulnerable due to the intense stress of military duties, deployments, and frequent relocations, which are also linked to mental health issues like depression, PTSD, and disinhibited eating. Environmental challenges, such as limited access to healthy food options at home stations, and even more so during deployments or aboard ships, further compound the problem. Environmental challenges, such as limited access to healthy food options during deployments, aboard ships, or on installations with limited health retail or dining options. Food insecurity among some military families, coupled with limited family health literacy and education on nutrition, may further influence dietary behaviors. Addressing these multifactorial influences is essential to implementing effective, evidence-based standards and interventions.(517-519) Obesity in Service members is also associated with reduced physical performance, increased risk of heat stress, sleep apnea, musculoskeletal injuries, and psychological conditions, including anxiety, depression, and substance use disorders.(520-522)

Significant challenges, including earlier existing body composition standards, underdiagnosis, lack of access to qualified obesity care, and inconsistent or ineffective weight management programs, may undermine efforts to address obesity. Social stigma can discourage Service members from seeking care, while military appearance regulations may allow commanders to subjectively apply or bypass interventions.(523,524) Lack of transparent data on obesity prevalence and related discharges may hinder implementation of effective, evidence-based solutions.(61)

Weight loss strategies aimed at operational readiness in the military must focus on achieving and maintaining optimal body composition and physical fitness. DOD Instruction 1308.03, updated 25 June 2025, titled DOD Physical Fitness/Body Composition Program mandates that all Service members maintain readiness through a holistic approach to physical fitness comprising cardiorespiratory endurance, muscular strength and endurance, and healthy body composition tailored to the occupational demands of their specific military specialties.(525) Each branch is allowed to choose from approved body composition assessment methods, including height-weight screening, BMI, waist-to-height ratio, abdominal circumference, or body-fat calculations, provided standards adhere to DOD's minimum health thresholds. The instruction also requires science-based physical testing and training programs that enhance general health, prevent injury, and ensure members can meet "mission-critical operational physical tasks," with flexibility for evolving training methodologies.

Lifestyle and behavioral modifications remain the foundation of obesity treatment in the DOD. A 2024 meta-analysis of 10 randomized controlled trials in military populations found a statistically significant mean weight loss of −1.84 kg (-4.0 lbs.) with behavioral interventions, though most studies lasted only 3–6 months and had limited follow-up beyond 12 months.(522) These modest results do not meet clinically significant weight loss, which is generally defined as greater than or equal to 5% reduction in baseline body weight.(9,11,526)

Overall, there are rising obesity rates among active-duty Service members (ADSM). Despite TRICARE coverage since 2018, weight management medications are underutilized. A 2024 study of the Military Health System revealed that only 0.44% of eligible ADSM had received a prescription for an obesity medication.(527) Currently, no overarching DOD or DHA instruction on obesity treatment exists. Service-specific policies vary: the Air Force limits prescription duration for obesity medications; the Army prohibits medications used for “anorexic activity” but does not address obesity treatment; and the Navy and Marine Corps have no formal restrictions.(528,529)

As with other chronic medical conditions, the evaluation and treatment of overweight and obesity, and consideration of obesity medications, should follow standard clinical care while also taking into account the ADSM military-specific factors. These include, but are not limited to, the Service member’s rate or military occupational specialty (MOS), deployment status, medication safety and storage requirements, potential side effects, duty restrictions, and overall medical readiness. Additionally, the Service member’s readiness for change and ability to adhere to therapy should be assessed to ensure safe and effective treatment. ADSMs who have experienced weight regain, have not achieved sufficient results with intensive lifestyle interventions, or have obesity-related complications may be appropriate candidates for obesity medication therapy.

d. Clinical Assessment of Patients with Overweight or Obesity

An assessment of a patient’s history (see Sidebar 3) identifies the medical, genetic, social, and behavioral factors that may affect his or her weight and energy balance. Using person-centered, nonjudgmental language, patients should be assessed for factors contributing to obesity, including obesogenic medications that may be being prescribed (see Sidebar 2), comorbid medical and psychiatric conditions (e.g., depression, anxiety, eating disorders, substance abuse), a family history of diabetes and heart disease, dietary patterns and physical activity behaviors (and the potential need for additional education), previous experience with weight management (including clinical interventions as well as self-management), and the patient’s motivation and readiness to commit to a weight management intervention.(514,515) It is helpful to assess a patient’s current level of physical activity (including activity type, frequency, duration, and intensity) and the presence of sedentary behaviors (e.g., prolonged periods of inactivity). A nutritional evaluation and history may include an assessment of eating behaviors (e.g., frequency of snacking, intake of high-caloric foods and sugar-sweetened beverages, nocturnal eating, and other behaviors that may suggest disordered eating or an eating disorder). A comprehensive nutritional assessment also goes beyond food intake, incorporating environmental and lifestyle factors such as family preferences, social and occupational demands, scheduling challenges, and access to healthy food and cooking resources. Recognizing these influences is essential, as they directly shape the feasibility and sustainability of individualized treatment strategies for obesity. Weight and weight

management history may include the number and types of methods and attempts at weight loss, possible triggers of weight gains and losses, and the range of weight fluctuations. Assessment may identify strengths and resources as well as factors that may impact patient participation in weight management programs.

A physical exam, including vital signs, height, weight, calculation of BMI, and incorporating measurements of body fat distribution, such as waist circumference, waist-to-hip ratio, and waist-to-height ratio, should be performed. If readily available and necessary for clinical evaluation, providers can consider the use of additional adiposity measurement tools such as bioimpedance analysis (BIA), air displacement plethysmography (BodPod), etc. Laboratory evaluation plays an important role in the clinical assessment of individuals with overweight or obesity. It can help identify obesity-related comorbidities, screen for secondary causes, guide treatment decisions, and establish a baseline for monitoring progress or treatment effects. Blood tests that evaluate metabolic biomarkers provide critical insight into health status beyond BMI and anthropometric measures. Identifying abnormalities in glucose regulation, lipid profiles, liver function, and inflammatory markers can reveal underlying dysfunction and guide more precise, targeted interventions in obesity treatment and metabolic healing. The specific tests ordered should be tailored to individual risk factors, but commonly include a comprehensive metabolic panel (CMP), hemoglobin A1c, Complete Blood Count (CBC), Thyroid Stimulating Hormone (TSH), and a lipid panel including non-HDL or apo B (note that a post-prandial lipid panel after food intake assesses cardiovascular risk better than a fasting panel).(530,531) FIB-4 scores should be used to evaluate for MASLD/MASH risk, especially in individuals with prediabetes, diabetes, and any cardiovascular risk factor.(532) Information obtained from this assessment may identify opportunities to eliminate or reduce obesogenic factors or mitigate the contribution of associated medical or psychiatric conditions to the patient's overweight or obesity.

A careful review of patients' medication lists should also be done, as they may reveal medications that cause weight gain that can undermine efforts at maintaining a healthy weight (see Sidebar 2). Reaching out to providers who are prescribing medications that cause weight gain, asking them regarding alternative options that are weight-neutral or possibly promote weight loss, and encouraging patient/provider dialogue is key (Medications that May Affect Weight). The knowledge gathered will be useful when promoting healthy behaviors and engaging in shared decision-making on weight management options.

B. Counseling Patients Without Overweight and Obesity

As noted in the Algorithm, the CPG Work Group encourages providers to offer guidance on dietary intake and physical activity to patients who have a normal range BMI. This is supported by a USPSTF recommendation that emphasizes that in adults without known cardiovascular disease (CVD) risk factors, behavioral counseling interventions to promote a healthy diet and physical activity are associated with small but statistically significant benefits across various intermediate health outcomes.(533) These outcomes include reductions in blood pressure, low-density lipoprotein cholesterol levels, and body mass index, as well as improvements in dietary and physical activity behaviors.(534)

The CPG Work Group encourages providers to: 1) encourage patients without overweight and obesity to implement or maintain, as applicable, a healthy weight; 2) discuss strategies for healthy eating, recommended levels of physical activity, consistent and sufficient sleep, and stress management; 3) conduct nutritional counseling focused on prioritizing minimally processed, nutrient-dense whole foods such as vegetables, fruit, lean protein, whole grains, nuts, and dairy products (avoiding those with significant added sugars including high fructose corn syrup);(535) and 4) encourage patients to move more and sit less throughout the day, emphasizing that some physical activity is better than none. For substantial health benefits, adults should do at least 150 minutes per week of moderate-intensity aerobic activity and 2 or more days per week of muscle-strengthening activities of moderate or greater intensity that involve all major muscle groups.(212,536) Brief physical activity counseling by healthcare providers can have a small to moderate positive effect on increasing physical activity levels and reducing sedentary time.(537) A careful review of patients' medication lists should also be done, as they may reveal medications that cause weight gain that can undermine efforts at maintaining a healthy weight (see Sidebar 2). Also, screening for sleep disturbances and stress, and considering referral for sleep medicine or cognitive-behavioral therapy when indicated.(295)

C. Shared Decision Making to Choose Among Weight Management Options

In individuals with overweight or obesity, the clinical team should engage the patient in a shared decision-making process regarding weight management options. Shared decision making (538) is derived from evidence-based principles of health education (539) and health behavior counseling.(540,541) It is important to use a person-centered communication style that includes active listening and nonjudgmental language to elicit individual preferences and beliefs, which is essential for optimizing health outcomes and quality of life.(531,542,543)

Strategies for effectively reaching shared understanding are:

- To support patient autonomy, ask permission to discuss weight-related health risks and the potential benefits and concerns of weight loss and/or weight management(543)
- Explore the patient’s understanding, beliefs, experience, and values regarding the health risks associated with their weight and the potential impact of weight management on their health and well-being
- If a patient declines to discuss their weight, honor that decision and ask permission to discuss at a future visit
- Share information about potential health risks that are tailored to the patient’s understanding, his or her weight, his or her current health status, and the presence of weight-associated conditions
- Emphasize obesity as a chronic disease that requires ongoing attention as well as individualized and comprehensive management
- Provide appropriate amounts of information in a manner that is easy to understand
- Use a “teach-back” method to confirm shared understanding(539,541-544)

- Review patients' prior experience with weight management interventions, their perceptions about the benefits of weight loss management, and their values
- Explore what matters to patients about their health and function to align recommendations with their values (e.g., "preventing complications of diabetes will help you to be available to your family, which you said is very important to you")

Ultimately, the process of reaching a shared understanding goes beyond simply educating patients about their conditions and the benefits of weight loss. It is a dialogue that begins with exploring the patients' perceptions, beliefs, and experiences, and allows for the creation of a plan that is tailored to them. Exploring, accepting (without judgment), and affirming patients' values and preferences supports their autonomy, builds trust, and fosters provider-patient partnerships. This, in turn, is associated with increased patient follow-through with health behavior change and participation in recommended treatment.(543,545)

a. Weight Stigma

Applying a patient-centered approach also requires that providers address the impact that weight stigma and bias have on patients' physical and psychological health, well-being, their willingness to participate in weight management, and their progress with weight management efforts.(546) We suggest offering cognitive behavioral interventions to reduce internalized weight bias and stigma in affected individuals (see Recommendation 10). Many healthcare providers hold strong, negative attitudes about people with overweight and obesity, and there is evidence that such attitudes may impact the care they provide, further exacerbating negative effects on patient well-being.(546,547) A patient-centered approach that emphasizes provider awareness of their contributions to stigma and bias, use of person-first language (e.g., using the word obesity as a noun, rather than as an adjective, "people with obesity" instead of "obese patients"), and increased use of empathy and patient-centered communication skills can enhance the quality of clinical interactions.(546-548)

b. Motivational Interviewing

If an initial assessment of the patient's motivation indicates they are not ready to commit to a recommended treatment, motivational interviewing techniques can be applied to build motivation and patient engagement. Motivational interviewing is a patient-centered counseling style that involves four key tasks: engaging, focusing, evoking, and planning.(549-551) Engaging strategies, including open-ended questions, active listening, reflections, and empathetic response, builds trust and deepens both patient and clinician understanding of patients' motivations. Focusing identifies and clarifies the patient's goals and values, respecting their autonomy and negotiating a collaborative agenda. Evoking strategies that elicit "change talk" (e.g., desire, ability, reasons, and need) using targeted questions, requests for elaboration, and reflections, while also softening "sustain talk" can build motivation. Planning involves developing a concrete action plan that aligns with the patient's readiness and resources and, if the patient is willing, setting SMART goals (**S**pecific, **M**easurable, **A**ction-oriented, **R**ealistic, and **T**ime-based) (see Table O-3), and ensuring follow-up.

Although there is considerable evidence that using motivational interviewing increases the likelihood that a patient will follow through with treatment recommendations across a wide range of health behaviors, there is only limited evidence for the impact of motivational interviewing on follow-through with weight management treatment.(543,552-560) Principles and core strategies of motivational interviewing are listed in Sidebar 1.(561) A comprehensive lifestyle intervention, as defined in this CPG, that incorporates the principles of motivational interviewing has the potential to enhance patient engagement and weight management outcomes.

Table O-3: SMART Goals for Healthy Weight

Letter	Meaning	Description	Obesity-Related Examples
S	Specific	The goal should be clear and detailed, stating exactly what is to be achieved.	"I will walk after dinner for 15 minutes." "I will add an extra serving of vegetables for dinner."
M	Measurable	The goal should include a way to track progress or success.	"I will walk 5 days a week and record it on my smart watch." "I will add an extra serving of vegetables at dinner Monday through Friday and take a picture on my phone."
A	Action-Oriented	The goal should feature a specific behavioral action that the person will take	"I will drink water with dinner instead of soda." "I will go for a 10-minute walk after lunch every day."
R	Realistic	The goal should be realistic and achievable, given the individual's resources and abilities.	"I will buy frozen vegetables that I can microwave, in case I run out of fresh options." "I can walk after dinner because I have time and safe sidewalks nearby."
T	Time-based	The goal should have a specific timeframe or deadline.	"I will do this for the next 4 weeks and reassess my progress."

✅ SMART Goal Examples	**"I will walk after dinner for 15 minutes, five days a week, for the next four weeks and record it using my smart watch."** **"I will add an extra serving of vegetables for dinner, five days a week, for the next four weeks and record it by taking pictures on my phone."**

c. Eliciting a Commitment to Participate in Weight Management and Choosing Among Treatment Options

After reaching a shared understanding, the next step is to elicit a commitment from the patient to engage in a recommended evidence-based weight management intervention. This critical step is accomplished by asking an open-ended question. For example, a provider might say, "Given what we discussed about the potential benefits of participation in a weight management program, how ready are you to commit to treatment?" If the patient expresses a willingness to commit, share the available options for engaging in treatment. Guide the patient to choose a treatment that is aligned with their needs and preferences. This step in the process can be initiated by referring the patient to an established comprehensive lifestyle intervention (CLI) (e.g., VHA's MOVE! Weight Management Program for Veterans) (562) or a member of the healthcare team (e.g., a dietitian, a clinical pharmacist) who can guide the patient to decide among available treatment options. Referring to a clinician with expertise in obesity may be particularly important for those with complex medical histories and/or concurrent pharmacotherapies that may impact the potential benefits and harms of specific weight management treatment components.

Emphasizing the role of CLI in weight management is a key element of the shared decision-making process (see Sidebar 5). It is critical for patients and providers to understand that pharmacotherapy and metabolic/bariatric surgery should always be offered in conjunction with or concurrent to CLI, with these interventions viewed as components of a broader treatment strategy.

The process of choosing among specific evidence-based weight management interventions includes: a review of previous experience with weight loss and response to treatments; identification of conditions or factors that increase risk of untoward reactions to elements of treatments (e.g., previous adverse effects from weight loss pharmacotherapy or surgical risks); and further exploration of patient preferences for CLI modality (e.g., group versus individual; telephone versus in-person or video) and preferences regarding concurrent pharmacotherapy or metabolic/bariatric surgery.

Dietary approaches should promote a negative energy balance to facilitate weight loss, choosing a diet that the patient feels they can maintain (see Recommendation 6 and Recommendation 7). In addition to creating a negative energy balance, dietary approaches should account for the hormonal and metabolic effects of food, recognizing that nutrient composition influences insulin, satiety hormones, and other regulators of weight and appetite. Aligning both caloric and hormonal balance supports more effective and sustainable obesity treatment. In terms of physical activity,

encouraging any form of physical activity is beneficial for weight management and overall health outcomes (see Recommendation 8 and Recommendation 9).

Consider referral for procedural or surgical intervention evaluation for patients interested in considering those options in combination with CLI. (see Recommendation 11, Recommendation 12, and Recommendation 13). We recommend combining pharmacotherapy with CLI. There is no evidence for or against delaying the initiation of FDA-approved pharmacotherapy when combined with CLI (See Recommendation 14). Once a medication is found to be safe and effective for a patient, continuation of the medication is encouraged due to the risk of weight regain after discontinuation and the chronicity of obesity as a disease. Slow tapering of medication, with monitoring of impact, is recommended if the patient prefers to discontinue treatment (see Appendix J and Recommendations 14-20).

d. Management of the Patient Not Ready to Engage

If the patient is not able to commit to a recommended weight management intervention, the provider might offer educational materials and ask permission to revisit options for weight management in future encounters. Motivational interviewing strategies can be applied at these and subsequent encounters. Providers might also assist the patient to select more limited health behavior goals (e.g., reducing sugar-containing beverages and alcohol, OR adding an extra serving of veggies at dinner, OR increasing physical activity as a first step) that may contribute to future weight management efforts. Using SMART goals is applicable in this scenario (see Table O-3).

D. Emphasizing the Role of Comprehensive Lifestyle Intervention

Comprehensive lifestyle interventions (CLI) for weight loss and weight maintenance are defined as standardized interventions that combine three critical “lifestyle” components (i.e., behavioral, dietary, and physical activity components) that aim to produce a negative energy balance. Whenever a patient expresses an interest in participating in a CLI, it is important to emphasize several key concepts that apply to all CLIs:

- An “energy deficit” should be reached with a combination of reduced caloric intake and increased physical activity
- A nutritionally adequate diet with adjusted calories should be part of a comprehensive weight management program
- Incremental changes in both dietary changes and physical activity can be supported by using specific behavioral strategies (e.g., goal setting, monitoring, problem solving) to support diet, physical, sleep, and mood management (see Appendix L)
- Creating SMART goals for changes in dietary patterns and physical activity will support weight loss and weight maintenance (see Table O-3)
- A short-term initial weight loss goal of 0.5 – 2.0 pounds per week may be achievable with a net caloric deficit of 500-1,000 kcal/day
- Weight management is a lifelong commitment, not a brief episode of treatment

- Obesity is a chronic disease, and CLI alone may not be sufficient for sustainable weight loss for many adults with overweight and obesity. However, CLI remains important for metabolic, biomechanical, and psycho-social health as part of a comprehensive weight management treatment plan
- Weight management strategies that are sustainable over the long term are highly preferred over those that produce short-term weight loss but are unsustainable.

E. Assessment of Progress Toward Weight Management Goals

CLI is foundational to obesity care, not only for promoting weight loss but also for preserving metabolic health, physical function, balance, nutrition, and muscle mass. While change in weight is one measure of progress, providers should help individuals focus on broader markers of success, including improvements in glucose control, blood pressure, lipid profiles, endurance, mobility, mood, energy levels, and quality of life. From the outset, providers should assist patients with identifying realistic expectations and work with them to establish goals that extend beyond weight change. Celebrating non-weight change victories, such as improved sleep, reduced joint pain, improved mood, or lower HbA1c, builds motivation and reinforces long-term engagement.

Importantly, individuals must be counseled that weight loss may be easier than maintenance of weight loss, due to adaptive neurohormonal responses that promote weight regain. These biological defenses, such as increased hunger and reduced energy expenditure, make sustained weight loss difficult to maintain with CLI alone (563,564). Observational and retrospective analyses consistently associate higher volumes of physical activity (often >250–300 minutes per week of moderate-intensity exercise) with better long-term weight loss maintenance.(201,565). Thus, it is critical for providers to explain that obesity is a chronic disease requiring long-term, often lifelong management. For many individuals, with moderate to severe obesity or significant complications, pharmacotherapy and/or bariatric procedures or surgery will be important components of an effective treatment plan, concomitant with CLI. We encourage continuation of obesity medication that are impactful and well-tolerated in an effort to reduce the likelihood of weight regain that is often associated with discontinuation. (See Recommendation 16). Ongoing pharmacotherapy may be necessary to counterbalance the physiological mechanisms that drive weight regain.(566) Pharmacotherapy and bariatric procedural and surgical interventions support and enhance the benefits of lifestyle changes and do not replace them.

When progress stalls or barriers persist, providers should adjust the treatment plan. This may include intensifying the lifestyle approach, initiating or adjusting obesity medications, or referring for a bariatric procedure or surgery evaluation. Additionally, individuals should be cautioned regarding discontinuing medications in the absence of significant adverse events, as ongoing pharmacotherapy helps counter the physiologic drive to regain weight. Sustained success in obesity care and weight management depends on personalized, progressive, and proactive treatment strategies that integrate lifestyle, medication, and procedural tools to support long-term health and weight stability.

To mitigate potential patient frustration, talk with patients and their family members about realistic expectations for weight loss and maintenance, including the importance of long-term follow-

through with lifestyle change, particularly the adoption of a healthy diet, regular physical activity, and other weight management behaviors.

a. Supporting Long-Term Weight Maintenance

Once long-term weight management goals have been achieved, the focus of weight management shifts to the prevention of weight regain. As noted, this goal requires maintenance of dietary and physical activity behaviors and many of the other self-management behaviors that contributed to successful weight loss. Thus, all patients reaching their long-term goals should be offered a maintenance program, ongoing support, and periodic reassessment that may include the need to continue pharmacotherapy or support of post-bariatric procedural or surgical nutritional needs (see Recommendation 3).

Appendix P: Abbreviation List

Abbreviation	Definition
Academy	The Academy of Nutrition and Dietetics
ACT	Acceptance and Commitment Therapy
ADF	alternate-day fasting
ADP	air displacement plethysmography
AE	Aerobic exercise
AE-V	Aerobic exercise; vigorous intensity
AGA	American Gastroenterology Association
AGB	adjustable gastric band
aHR	adjusted hazard ratio
AHRQ	Agency for Healthcare Research and Quality
AI	artificial intelligence
ASCVD	atherosclerotic cardiovascular disease
ASMRs	age-standardized mortality rates
ASMBS	American Society for Metabolic and Bariatric Surgery
BEI	bioelectrical impedance
BF	body fat
BIA	Bioelectrical Impedance Analysis

Abbreviation	Definition
BMI	body mass index
BP	blood pressure
BPD	biliopancreatic diversion
BWL	behavioral weight loss
CBC	Complete Blood Count
CCK	cholecystokinin
CDC	Centers for Disease Control and Prevention
CI	confidence interval
CIV	Schedule IV controlled substance
CKD	chronic kidney disease
CLI	comprehensive lifestyle intervention
CMP	comprehensive metabolic panel
CNS	central nervous system
COI	conflict of interest
COM-LM	Combined low-moderate; moderate intensity aerobic/low-to-moderate load resistance
CPGs	clinical practice guidelines
CrCl	creatinine clearance
CRP	C-reactive protein
CT	computed tomography
CV	cardiovascular
CVD	cardiovascular disease
DALY	disability-adjusted life years
DASH	Dietary Approaches to Stop Hypertension
DBP	diastolic blood pressure
DM	diabetes mellitus
DOD	Department of Defense

Abbreviation	Definition
DS	duodenal switch
DSM-BIA	direct segmental multifrequency BIA
DXA	dual-energy X-ray absorptiometry
DXA-VAT	dual-energy x-ray absorptiometry visceral adipose tissue
EAL	evidence analysis library
EOSS	Edmonton Obesity Staging System
ESG	endoscopic sleeve gastrectomy
FDA	U.S. Food and Drug Administration
FFM	fat-free mass
FIB-4	Fibrosis-4 Index for Liver Fibrosis
FPG	fasting plasma glucose
g	grams
GERD	gastroesophageal reflux disease
GI	gastrointestinal
GLP-1	glucagon-like peptide 1
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
HbA1c	hemoglobin a1c
HCG	human chorionic gonadotropin
HDL	high-density lipoprotein
HDL-c	high-density lipoprotein cholesterol
hg	hectograms
HIIT	high-intensity interval training
HRQoL	health-related quality of life
HTN	hypertension
HYB	hybrid-type training
IBT	Intensive Behavioral Therapy
IF	intermittent fasting

Abbreviation	Definition
IFSO	International Federation for the Surgery of Obesity and Metabolic Disorders
IGB	intragastric balloon
ILI	Intensive Lifestyle Intervention
IV	intravenous
KQs	key questions
LAGB	laparoscopic adjustable gastric banding
LDL-c	low-density lipoprotein cholesterol
LGAE	left gastric artery embolization
LEADER	Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results
LI	lifestyle intervention
LSG	laparoscopic sleeve gastrectomy
MACE	major adverse cardiovascular events
MAOI	monoamine oxidase inhibitor
MASH	Metabolic Dysfunction-Associated Steatohepatitis
MASLD	Metabolic Dysfunction-Associated Steatotic Liver Disease
MBS	Metabolic/Bariatric surgery
MD	mean difference
MEN2	multiple endocrine neoplasia type 2
mg	milligrams
MHS	Military Health System
MHT	Menopause Hormone Therapy
MI	motivational interviewing
MI	myocardial infarction
MICT	moderate-intensity continuous training
MID	minimal important difference
MOS	military occupational specialty

Abbreviation	Definition
MRI	magnetic resonance imaging
MT	medical therapy
MTC	medullary thyroid cancer
NAFLD	non-alcoholic fatty liver disease (see MASLD)
NAM	National Academy of Medicine
NMA	network meta-analysis
ng	nanogram
NICE	National Institute for Health and Care Excellence
NIH	National Institutes of Health
NSAID	non-steroidal anti-inflammatory drug
NIPHS	non-insulinoma pancreatogenous hypoglycemia syndrome
OAGB	one anastomosis gastric bypass
OSA	obstructive sleep apnea
OTC	over-the-counter
PAGA	Physical Activity Guidelines for Americans
PBF	percent body fat
PCOS	polycystic ovary syndrome
PI	prescribing information
PICOTS	population, intervention, comparison, outcome, timing, and setting
PE	pulmonary embolism
PEG	percutaneous endoscopic gastrostomy
PYO	patient years of observation
QoL	quality of life
RCT	randomized controlled trial
RD	registered dietitian
REE	resting energy expenditure
REMS	Risk Evaluation and Mitigation Strategy

Abbreviation	Definition
RR	risk ratio
RT	resistance training
RYGB	roux-en-Y gastric bypass
SADI-S	Single anastomosis duodenoileostomy with sleeve
SBP	systolic blood pressure
SCr	serum creatinine
SHBG	sex hormone-binding globulin
SG	sleeve gastrectomy
SMM	skeletal muscle-mass
SR	systematic review
subQ	subcutaneously
T2DM	type 2 diabetes mellitus
TAU	treatment-as-usual
TBWL	total body weight-loss
TG	triglycerides
TRE	time-restricted eating
TSH	Thyroid Stimulating Hormone
URTI	upper respiratory tract infection
U.S.	United States
USPSTF	U.S. Preventive Services Task Force
WC	waist circumference
WHR	waist-to-hip ratio
WHtR	waist-to-height ratio
XR	extended-release

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