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 and the Department of Defense guidelines are based upon the best information available at the time of publication. They 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 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 clinicians take into account the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Every healthcare professional making use of these guidelines is responsible for evaluating the appropriateness of applying them in the setting of any particular clinical situation.

These guidelines are not intended to represent Department of Veterans Affairs or TRICARE policy. Further, inclusion of recommendations for specific testing and/or therapeutic interventions within these guidelines does not guarantee coverage of civilian sector care. Additional information on current TRICARE benefits may be found at www.tricare.mil or by contacting your regional TRICARE Managed Care Support Contractor.

Version 3.0 – 2020

Prepared by:

The Management of Adult Overweight and Obesity Work Group

With support from:

The Office of Quality and Patient Safety, VA, Washington, DC

&

Office of Evidence Based Practice, U.S. Army Medical Command

Version 3.0 – 2020

Based on evidence reviewed through April 2019

Table of Contents

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, with a mission to advise the Health Executive Committee (HEC) "…on the use of clinical and epidemiological evidence to improve the health of the population…" across the Veterans Health Administration (VHA) and Military Health System (MHS), by facilitating the development of clinical practice guidelines (CPGs) for the VA and DoD populations.[1] This clinical practice guideline (CPG) is intended to provide healthcare providers with a framework by which to evaluate, treat, and manage the individual needs and preferences of patients with overweight or obesity, thereby leading to improved clinical outcomes.

In 2014, the VA and DoD published a CPG for the Screening and Management of Overweight and Obesity (2014 VA/DoD Obesity CPG), which was based on evidence reviewed through February 2013. Since the release of that guideline, a growing body of research has expanded the general knowledge and understanding of overweight and obesity. Consequently, a recommendation to update the 2014 Obesity CPG was initiated in 2018. The updated, 2020 VA/DoD CPG Clinical Practice Guideline for the Management of Adult Overweight and Obesity (2020 VA/DoD Obesity CPG) includes objective, evidence-based information on the management of overweight and obesity. It is intended to assist healthcare providers in all aspects of patient care. The system-wide goal of evidence-based guidelines is to improve the patient's health and well-being by guiding health providers who are caring for patients with overweight and obesity along management pathways that are supported by evidence. The expected outcome of successful implementation of this guideline is to:

- Assess the individual's condition and determine, in collaboration with the patient, the best treatment method
- Optimize health outcomes and improve quality of life (QoL)
- Minimize preventable complications and morbidity
- Emphasize the use of patient-centered care

II. Background

A. Epidemiology and Impact in the General Population

The epidemic of overweight and obesity is one of the most significant problems facing the United States (U.S.) healthcare system today. The Centers for Disease Control and Prevention (CDC) defines overweight and obesity using body mass index (BMI), which is the most widely used and practical way to evaluate the degree of overweight. Body mass index is calculated as weight in kilograms divided by height in meters squared (kg/m^2).[2]

For adults, having a BMI of 25 – 29.9 kg/m^2 is considered "overweight," while a BMI of 30 kg/m^2 or higher is considered "obese". The category of "obese" is further divided into subcategories of Class I obesity (BMI 30.0 – 34.9 kg/m^2), Class II obesity (BMI 35.0 – 39.9 kg/m^2), and Class III obesity (BMI ≥40 kg/m^2).[3] For individuals of Asian descent, the World Health Organization suggests a lower threshold for overweight (BMI >23.0 kg/m^2) and obesity (BMI >27.5 kg/m^2). Based on data reported for 2015 – 2016 from the National Health and Nutrition Examination Survey, the prevalence of obesity in the U.S. is 39.8% among

adults,[4] and the prevalence of overweight in the U.S. is 31.8% among adults.[5] Moreover, approximately 1 in 13 Americans have a BMI of >40 kg/m^2 (i.e., more severe, Class III obesity).[5]

The evidence links overweight and obesity with an increased risk of chronic health conditions and reduced QoL, as well as earlier mortality, particularly among those with Class II and Class III obesity.[6-8] Overweight and obesity increase the risk of all-cause mortality with a J-shaped dose-response association.[8] The nadir of the dose-response curve is the BMI range of 23 – 24 kg/m^2 among never smokers and 22 – 23 kg/m^2 among healthy never smokers.[8] Though earlier epidemiologic analyses suggested that overweight was associated with a reduced risk of mortality compared to normal weight,[6] these findings were confounded by smoking and existing illness and also reflect shorter durations of follow-up.[8]

Overweight and obesity are associated with increased prevalence and worsening of several obesity-associated conditions, including type 2 diabetes mellitus (T2DM), hypertension (HTN), dyslipidemia, metabolic syndrome, osteoarthritis, and obstructive sleep apnea (OSA).[9] High BMI is also associated with elevated risk for at least 17 different cancers.[10] Based on data from 2010 through 2015, nearly 50% of adults with obesity had HTN compared with 20% of adults with normal weight, and adults with obesity were four times as likely to have T2DM.[11] The CDC estimates that 9 out of 10 people with diagnosed T2DM have overweight or obesity.[12] Furthermore, as a result of the obesity epidemic, the lifetime risk of diagnosed T2DM from age 20 is 40.2% for men and 39.6% for women, representing an increase of 20% and 13%, respectively, from 1985 – 1989.[13] The development or worsening of T2DM, HTN, and dyslipidemia are particularly hazardous due to their independent effects on risk for coronary artery disease and stroke.

In addition to the aforementioned obesity-associated conditions, obesity and insulin resistance are among the most common risk factors for the development of non-alcoholic fatty liver disease (NAFLD),[14] which is the leading cause of chronic liver disease in the U.S.[15] Overall, NAFLD prevalence among adults (≥15 years old) is projected to be 33.5% in 2030.[16] Non-alcoholic fatty liver disease has surpassed alcohol as a top reason for liver transplants in the U.S. and will likely become the leading condition necessitating liver transplants (ahead of hepatitis C) by the year 2030.[17,18]

Overweight and obesity have important impacts on many aspects of QoL and well-being, including physical and psychosocial functioning, pain experience, and perceptions of health.[19] Individuals with overweight and obesity perceive or experience stigma and discrimination across multiple domains from work to healthcare to mass media.[20] In addition to morbidity and mortality associated with excess body weight, there are significant healthcare expenditures that result from costly associated medical conditions.[a] From 2001 through 2015, increases in medical expenditures were greater for adults with obesity than for adults with normal weight. From 2010 through 2015, adults with Class III obesity incurred $7,800 in annual medical expenditures on average, which was 75% more than adults without overweight or obesity.[11] Moreover, based on data from the Medical Expenditure Panel Survey, the share of total healthcare spending for treating obesity-related illnesses in non-institutionalized adults has risen from 20.6% in 2005 to 27.5% in 2010 and 28.2% in 2013.[21] Importantly, expenditures appear to have a J-shaped curve over the full range of BMI. Specifically, expenditures decrease with BMI through the categories of underweight

[a] See the infographic on *Medical Care Use and Expenditures Associated With Adult Obesity in the United States*, available at: https://jamanetwork.com/journals/jama/fullarticle/2669713

and normal weight, are constant when BMI is in the overweight range, rise slowly through Class I obesity, and then rise more rapidly with increasing BMI.[21]

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

The active duty military and Veteran populations have been similarly affected by the obesity epidemic. According to the DoD's *Health of the Force* 2018 Report, which provides an evidence-based portrait of the health and well-being of U.S. Service Members, the overall prevalence of obesity was 17.4% in 2018.[22] This represents an increase from 2014 when the prevalence of obesity was 15.8%. Rates of obesity varied across branches of the Armed Services, ranging from 8.3% to 22.0%. It was noted, however, that Service Members with higher lean body mass may be misclassified as overweight or obese based on their BMI which would require further assessment (see Standards of Care). The consequences of obesity in active duty Service Members may negatively influence a range of operations related to recruitment, retention, resilience, readiness, and retirement.[23] Moreover, in a study of adult non-active duty beneficiaries and retirees, 63% of beneficiaries and 86% of retirees have overweight or obesity.[24] Compared with the general U.S. population, the combined prevalence of overweight (37%) and obesity (41%) is higher in Veterans receiving care in the VA.[4,5,24] This current combined prevalence in Veterans of 78% reflects a steady increase over the past two decades, up from 64% in 1996.[25]

C. Impact of Weight Loss on Obesity-associated Conditions

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.[26] Thus, in this guideline we chose weight loss as a critical outcome for evaluating the effects of weight management interventions for overweight and obesity.

III. About this Clinical Practice Guideline

This guideline represents a significant effort toward improving the management of patients with overweight or obesity who are eligible to receive care in VA and/or DoD. As with other CPGs, however, challenges remain. These include evidence gaps, as well as ongoing needs to develop effective strategies for guideline implementation and to evaluate the effect of guideline adherence on clinical outcomes. This guideline is intended for VA and DoD healthcare practitioners including physicians, nurse practitioners, physician assistants, social workers, psychologists, dietitians, nurses, pharmacists, physical therapists, kinesiotherapists, and others involved in caring for Service Members or Veterans with overweight or obesity. Additionally, this guideline is intended for those in community practice involved in the care of Service Members or Veterans with overweight or obesity.

As elaborated upon in the qualifying statement on page one, this CPG is not intended to serve as a standard of care. Standards of care are determined based on all clinical data available for an individual patient and are subject to change as scientific knowledge and technology advance and clinical practice patterns evolve. This CPG is based on information available through April 8, 2019, and is intended to provide a general guide to best practices. The guideline can assist care providers, but the use of a CPG must always be considered as a recommendation within the context of a variety of factors such as

providers' clinical judgment, scope of practice, patient values and preferences, state and federal legal statutes, ethical guidelines, professional standards, and healthcare system policies.

A. Methods

The current document is an update to the 2014 VA/DoD Obesity CPG. The methodology used in developing the 2020 VA/DoD Obesity CPG follows the *Guideline for Guidelines*, an internal document of the VA and DoD EBPWG that was updated in January 2019.[1] The *Guideline for Guidelines* can be downloaded from http://www.healthquality.va.gov/policy/index.asp. This document provides information regarding the process of developing guidelines, including the identification and assembly of the Guideline Champions (Champions) and other subject matter experts from within the VA and DoD (known as the Work Group) and the development and submission of an updated Obesity CPG.

The Champions and Work Group for this CPG were charged with developing evidence-based clinical practice recommendations and writing and publishing a guideline document to be used by providers within the VA/DoD healthcare systems as well as those within the community who treat individuals within the VA and DoD. Specifically, the Champions and Work Group members for this guideline were responsible for identifying the key questions (KQs) of the most clinical relevance, importance, and interest for the diagnosis and management of patients with overweight or obesity. The Champions and the Work Group also provided direction on inclusion and exclusion criteria for the evidence review and assessed the level and quality of the evidence. The amount of new scientific evidence that had accumulated since the previous version of the CPG was also taken into consideration in the identification of the KQs. In addition, the Champions assisted in:

- Identifying appropriate disciplines of individuals to be included as part of the Work Group
- Directing and coordinating the Work Group
- Participating throughout the guideline development and review processes

The VA Office of Quality and Patient Safety, in collaboration with the Office of Evidence Based Practice, U.S. Army Medical Command, the proponent for CPGs for the DoD, identified four clinical leaders to serve as Champions: LTC Sky D. Graybill, MD; Michael Goldstein, MD; Stéphanie B. Mayer, MD, MHSc; and LTC Christopher Tracy, MD.

The Lewin Team, including The Lewin Group, Duty First Consulting, ECRI, Sigma Health Consulting, and Anjali Jain Research & Consulting, was contracted by the VA to support the development of this CPG and conduct the evidence review. The first conference call was held in December 2018, with participation from the contracting officer's representative (COR), leaders from the VA Office of Quality and Patient Safety and the DoD Office of Evidence Based Practice, and the Champions. During this call, participants discussed the scope of the guideline initiative, the roles and responsibilities of the Champions, the project timeline, and the approach for developing and prioritizing specific research questions on which to base a systematic review (SR) about the management of overweight or obesity. The group also identified a list of clinical specialties and areas of expertise that are important and relevant to the management of overweight and obesity, from which Work Group members were recruited. The specialties and clinical areas of interest included: metabolic/bariatric surgery, endocrinology, internal medicine, family medicine, nutrition, nursing, pharmacology, physical therapy, psychiatry, psychology, rheumatology, general surgery, and primary care.

The guideline development process for the 2020 VA/DoD Obesity CPG consisted of the following steps:

1. Formulating and prioritizing KQs and defining critical outcomes
2. Convening a patient focus group
3. Conducting the systematic evidence review
4. Convening a face-to-face meeting with the CPG Champions and Work Group members to develop recommendations
5. Drafting and submitting a final CPG on the management of overweight and obesity to the VA/DoD EBPWG

Appendix A provides a detailed description of each of these tasks.

a. Grading Recommendations

The Champions and Work Group used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system to assess the quality of the evidence base and assign a strength for each recommendation. The GRADE system uses the following four domains to assess the strength of each recommendation:[27]

- Balance of desirable and undesirable outcomes
- Confidence in the quality of the evidence
- Patient or provider values and preferences
- Other implications, as appropriate, e.g.:
    - Resource use
    - Equity
    - Acceptability
    - Feasibility
    - Subgroup considerations

Additional information regarding these domains can be found in Appendix A.

Using these four domains, the Work Group determined the relative strength of each recommendation ("Strong" or "Weak"). Generally, a "Strong" recommendation indicates a high confidence in the quality of the available scientific evidence, a clear difference in magnitude between the benefits and harms of an intervention, similar patient or provider values and preferences, and understood influence of other implications (e.g., resource use, feasibility). Generally, if the Work Group has less confidence after the assessment across these domains and believes that additional evidence may change the recommendation, it assigns a "Weak" recommendation. It is important to note that the GRADE terminology used to indicate the assessment across the four domains (i.e., "Strong" versus "Weak") should not be confused with the clinical importance of the recommendation. A "Weak" recommendation may still be important to the clinical care of a patient with overweight or obesity.

Occasionally, instances may occur when the Work Group feels there is insufficient evidence to make a recommendation for or against a particular therapy or preventive measure. This can occur when there is an absence of studies on a particular topic that met evidence review inclusion criteria, studies included in the evidence review report conflicting results, or studies included in the evidence review report inconclusive results regarding the desirable and undesirable outcomes.

Using these elements, the grade of each recommendation is presented as part of a continuum:

- Strong for (or "We recommend offering this option …")
- Weak for (or "We suggest offering this option …")
- No recommendation for or against (or "There is insufficient evidence …")
- Weak against (or "We suggest not offering this option …")
- Strong against (or "We recommend against offering this option …")

The grade of each recommendation made in the 2020 VA/DoD Obesity CPG can be found in the section on Recommendations. Additional information regarding the use of the GRADE system can be found in the section on Grading Recommendations.

b. Reconciling 2014 Clinical Practice Guideline Recommendations

Evidence-based CPGs should be current, which typically requires revisions of previous guidelines based on new evidence or as scheduled and subject to time-based expirations.[28] For example, the U.S. Preventive Services Task Force (USPSTF) has a process for refining or otherwise updating its recommendations pertaining to preventive services.[29]

The Obesity CPG Work Group largely focused on developing new and updated recommendations based on the evidence review conducted for the priority areas addressed by the KQs. In addition to developing new and updated recommendations, the Work Group considered the current applicability of other recommendations included in the 2014 VA/DoD Obesity CPG, categorizing them as appropriate based on current clinical practice. The 2020 VA/DoD Obesity CPG was developed using the GRADE methodology, which does not allow for recommendations to be made based on expert opinion alone; therefore, some recommendations from the 2014 VA/DoD Obesity CPG that were based on expert opinion alone and not covered in the systematic evidence review carried out as part of this guideline update, or otherwise determined to not be included in the scope of the 2020 VA/DoD Obesity CPG, were removed in the 2020 VA/DoD Obesity CPG. For additional information, see Grading Recommendations, Recommendation Categorization, and Appendix D.

A set of recommendation categories was adapted from those used by the National Institute for Health and Care Excellence (NICE).[30,31] These categories, along with their corresponding definitions, were used to account for the various ways in which older recommendations could have been updated. In brief, the categories considered whether the evidence that related to a recommendation was systematically reviewed, the degree to which the recommendation was modified, and the degree to which a recommendation is relevant in the current care environment and within the scope of the CPG. Additional information regarding these categories and their definitions can be found in Recommendation Categorization. The categories for the recommendations included in the 2020 version of the guideline can

be found in the section on Recommendations. The categories for the recommendations carried forward from the 2014 VA/DoD Obesity CPG are noted in Appendix D.

c. Peer Review Process

The CPG was developed through an iterative process in which the Work Group produced multiple drafts of the CPG. The process for developing the initial draft is described in more detail in Drafting and Submitting the Final Clinical Practice Guideline.

Once a near-final draft of the guideline was agreed upon by the Champions and Work Group members, the draft was sent out for peer review and comment. The draft was posted on a wiki website for 14 business days. The peer reviewers comprised individuals working within the VA and DoD healthcare systems as well as experts from relevant outside organizations designated by the Work Group members. Organizations designated by the Work Group to participate in the peer review and that provided feedback included:

- American Society for Metabolic and Bariatric Surgery
- Endocrine Society
- National Institute of Diabetes and Digestive and Kidney Diseases
- The Obesity Society
- VA National Metabolic Work Group

The VA and DoD Leadership reached out to both the internal and external peer reviewers to solicit their feedback on the CPG. Reviewers were provided a hyperlink to the wiki website where the draft CPG was posted. All feedback from the peer reviewers was discussed and considered by the Work Group. Modifications made throughout the CPG development process were in accordance with the evidence.

B. Summary of Patient Focus Group Methods and Findings

When forming guideline recommendations, consideration should be given to the values of those most affected by the recommendations: patients. Patients bring perspectives, values, and preferences into their healthcare experience that can vary from those of clinicians. These differences can affect decision making in various situations and should be highlighted and made explicit due to their potential to influence a recommendation's implementation.[32,33] Focus groups can be used as an efficient method to explore ideas and perspectives of a group of individuals and collect qualitative data on a thoughtfully predetermined set of questions.

Therefore, as part of the effort to update this CPG, VA and DoD Leadership held a patient focus group. The patient focus group was held on March 7, 2019, at Womack Army Medical Center in Fort Bragg, NC. The focus group aimed to further understand and incorporate the perspective of patients with overweight or obesity and who are covered and/or receiving their care through the VA and/or DoD healthcare systems, as these patients are most affected by the recommendations put forth in the CPG. The focus groups delved into the patients' perspectives on a set of topics related to their overweight or obesity management, including their priorities, challenges they have experienced, the information they received regarding their care, as well as the impacts of their care on their lives.

The focus group comprised a convenience sample and the Work Group recognizes the lack of generalizability and other limitations inherent in the small sample size. The patient focus group consisted of seven participants, five men and two women, being treated for overweight/obesity. Fewer than 10 people in total were included in the focus group to be consistent with the requirements of the Federal Paperwork Reduction Act, 1980. Five participants were receiving care from the DoD, one from the VA, and one from both the VA and the DoD. Participants' ages ranged from early-20s to mid-70s, with the majority of the group being in their 20s or 30s. The majority of the participants were active duty Service Members in the Army. One participant was a Veteran and the spouse of an active duty Service Member and another was a Veteran in his/her 70s. Four of the male participants were medics in the Army. One of the women, an active duty Service Member in her 40s or 50s joined midway through the focus group. The Work Group acknowledges that the sample included in this focus group is not representative of all patients within the VA and DoD healthcare systems. Further, time limitations for the focus group prevented exhaustive exploration of all topics related to overweight and obesity management in the VA and DoD and the patients' broader experiences with their care. Thus, the Work Group made decisions regarding the priority of topics to discuss at the focus groups. These limitations, as well as others, were considered during guideline development as the information collected from the discussion was being used. Recruitment for participation in the focus groups was managed by the Champions and VA and DoD Leadership, with assistance from coordinators at the facility at which the focus groups took place.

Additional details regarding the patient focus group methods and findings can be found in Appendix B.

C. Conflicts of Interest

At the start of this guideline development process and at other key points throughout, the project team was required to submit disclosure statements to reveal any areas of potential conflict of interest (COI) in the past 24 months. Verbal affirmations of no COI were used as necessary during meetings throughout the guideline development process. The project team was also subject to random web-based surveillance (e.g., Centers for Medicare & Medicaid Services [CMS] open payments or ProPublica).

If a project team member reported a COI (actual or potential), then it was reported to the VA and DoD program offices. It was also discussed with the Obesity CPG Champions in tandem with their review of the evidence and development of recommendations. The VA and DoD program offices and the Obesity CPG Champions determined whether action, such as restricting participation or voting on sections related to the conflict or removal from the Work Group, was necessary due to authorship of the literature included in the SR. If it was deemed necessary, action to mitigate the COI was taken by the Champions and VA and DoD program offices, based on the level and extent of involvement. No COIs were identified for the Obesity CPG Work Group members or Champions. Disclosure forms are on file with the VA Office of Quality and Patient Safety and available upon request.

D. Scope of this Clinical Practice Guideline

Regardless of setting, any patient in the VA and DoD healthcare system should ideally have access to the interventions that are recommended in this guideline after taking into consideration the patient's specific circumstances.

Guideline recommendations are intended to support the delivery of evidence-based, patient-centered healthcare which occurs at the intersection of the best available evidence, patient preference, and

practitioner expertise and experience. Effective, open communication between healthcare professionals and the patient is essential and should be supported by evidence-based information tailored to the patient's needs. Use of an empathetic and non-judgmental approach facilitates discussions sensitive to gender, culture, ethnicity, and other considerations. The information that patients are given about treatment and care should be culturally appropriate and available to people with limited literacy skills. Treatment information should also be accessible to people with additional needs such as physical, sensory, or learning disabilities. Family and caregiver involvement should be considered, if appropriate.

This CPG is designed to assist providers in managing or co-managing patients with overweight or obesity. Moreover, the patient population of interest for this CPG is adult patients with overweight or obesity who are eligible for care in the VA and DoD healthcare delivery systems including those who are in the community receiving care from community-based clinicians. It includes Veterans as well as deployed and non-deployed active duty Service, Guard, and Reserve Members and their adult dependents.

E. Highlighted Features of this Clinical Practice Guideline

The 2020 VA/DoD Obesity CPG is the second update to the original CPG. It provides practice recommendations for the care of individuals with overweight or obesity as well as guidance for treatment. A particular strength of this CPG is the multidisciplinary stakeholder involvement from its inception, ensuring representation from the broad spectrum of clinicians and providers engaged in the diagnosis and management of overweight and obesity.

The framework for recommendations in this CPG considered factors beyond the strength of the evidence, including balancing desired outcomes with potential harms of the intervention, the potential for variation in patient values and preferences, and other considerations (e.g., resource use, subgroup considerations) as appropriate. Applicability of the evidence to VA/DoD populations was also taken into consideration. An algorithm accompanies the guideline to provide an overview of the recommendations in the context of the flow of patient care and to assist with training providers (see Algorithm section). The algorithm may be used to help facilitate translation of guideline recommendations into practice.

F. Patient-centered Care

VA/DoD CPGs encourage providers to use a patient-centered care approach that is individualized based on patient needs, characteristics, and preferences. Regardless of setting, all patients in the healthcare system should be able to access evidence-based care appropriate to their specific needs or condition. When properly executed, patient-centered care engages, activates and empowers patients to take a more active role in their health and health care. Patient-centered approaches may decrease patient anxiety, increase trust in clinicians, and improve treatment adherence.[34-36] A patient-centered approach improves patient-clinician communication and supports disclosure of current and future concerns.

As part of the patient-centered approach, providers should ask each patient about any concerns he or she has and barriers to high-quality care he or she has experienced.

G. Shared Decision Making

Throughout this VA/DoD CPG, the authors encourage clinicians to focus on shared decision making, a key component of patient-centered care. A shared decision making model was featured in *Crossing the Quality Chasm*, an Institute of Medicine (IOM) (now called the National Academy of Medicine [NAM]) report, in

2001.[37] Patients, together with their clinicians, make decisions regarding their plan of care and management options. Patients with overweight or obesity require sufficient information and time to be able to make informed decisions. Clinicians must be adept at presenting information to their patients regarding risks of overweight and obesity, benefits and potential harms of treatments, expected outcomes, and levels and/or locations of care. Clinicians are encouraged to use shared decision making to individualize treatment goals and plans based on patient capabilities, needs, values, goals, and preferences. See Standards of Care for additional guidance about the use of shared decision making in the care of the patient with overweight or obesity.

H. 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 Kidney Disease (CKD),[b] Diabetes Mellitus,[c] Hypertension,[d] and Chronic Insomnia Disorder/OSA.[e] See Standards of Care, Sidebar 1, and Sidebar 3 for guidance regarding the medical assessment of patients with overweight and obesity.

I. Implementation

This CPG is designed to be adapted by individual healthcare providers with consideration of 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 or obesity; both of these chronic medical conditions require long-term management with similar resource allocation to diabetes and HTN treatments.

The Work Group's goal is to disseminate these evidence-based recommendations for weight management as widely as possible throughout the medical field, with the aim of improving Veteran and Service Members' health and well-being. To this end, the Work Group has also produced supplemental

[b] See the VA/DoD Clinical Practice Guideline for the Management of Chronic Kidney Disease. Available at: https://www.healthquality.va.gov/guidelines/CD/CKD/

[c] 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/

[d] 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/

[e] 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

educational materials to convey this information as effectively as possible: to practitioners as a provider summary and pocket card and to patients in the form of a patient summary.[f]

The VA and DoD have respective plans for 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 is also meant to inform the VA and DoD about the efficacy of combined tools for weight loss; specifically, comprehensive lifestyle intervention programs (e.g., the MOVE! program at the VA), with both pharmacologic and metabolic/bariatric surgical interventions. Nationwide harmonization of these three weight loss interventions, across VA and DoD healthcare facilities, will improve quality of life and reduce progression of obesity-related conditions for our nation's 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. Next is the need to track patient, program, and population level achievement of clinically meaningful outcomes. System-wide integration will assure 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.

Although this CPG represents the recommended practices on the date of its publication, medical practice is evolving and requires ongoing awareness by providers and policy makers 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.

[f] See https://www.healthquality.va.gov/guidelines/CD/obesity/ for links to the Obesity CPG's Provider Summary, Pocket Card, and Patient Summary

IV. Guideline Work Group

Organization	Names[a]
Department of Veterans Affairs	**Michael G. Goldstein, MD (Champion)**
	Stéphanie B. Mayer, MD MHSc (Champion)
	Erin J. Arra, MS, RD, CSOWM, LD
	Elaine Furmaga, PharmD
	Earl Gaar, MD, FACS
	Navjit (Nicky) Goraya, MD
	Gwen Hampton, PMHCNS-BC
	Susan D. Raffa, PhD
	Carol Volante, DNP, APRN-C
Department of Defense	**LTC Sky Graybill, MD (Champion)**
	LTC Christopher Tracy, MD, FACP, FACR (Champion)
	Charolotte Baldridge, FNP
	Maj Zachary M. Leftwich, PharmD
	COL Stephanie A. Meyer, SP, DrPH, MS, RD, LD, CHES
	CPT Scott J. Santos, PsyD
	Col Jason L. Silvernail, DPT, DSc
	CPT Bryan A. Stepanenko, MD, MPH
	CAPT Gordon G. Wisbach, MD, MBA, FACS, FAMBS, MC, USN
Office of Quality and Patient Safety Veterans Health Administration	M. Eric Rodgers, PhD, FNP-BC
	James Sall, PhD, FNP-BC
	Rene Sutton, BS, HCA
Office of Evidence Based Practice U.S. Army Medical Command	Corinne K. B. Devlin, MSN, RN, FNP-BC
	Patrick Brian Polk, RN, BSN, MHSM, CIC, NEA-BC
The Lewin Group	Clifford Goodman, PhD
	Erika Beam, MS
	Charlie Zachariades, MSc
	Nicolas Stettler-Davis, MD, MSCE
ECRI	Kristen D'Anci, PhD
	Stacey Uhl, MS
	Amber Moran, MA
	Gina Giradi, MS
	Laura Koepfler, MLS
Anjali Jain Research & Consulting	Anjali Jain, MD
Sigma Health Consulting	Frances Murphy, MD, MPH
Duty First Consulting	Rachel Piccolino, BA
	Megan McGovern, BA

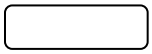
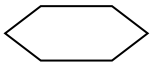
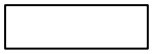
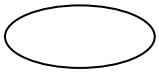
[a] Additional contributor contact information is available in Appendix E.

V. 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:

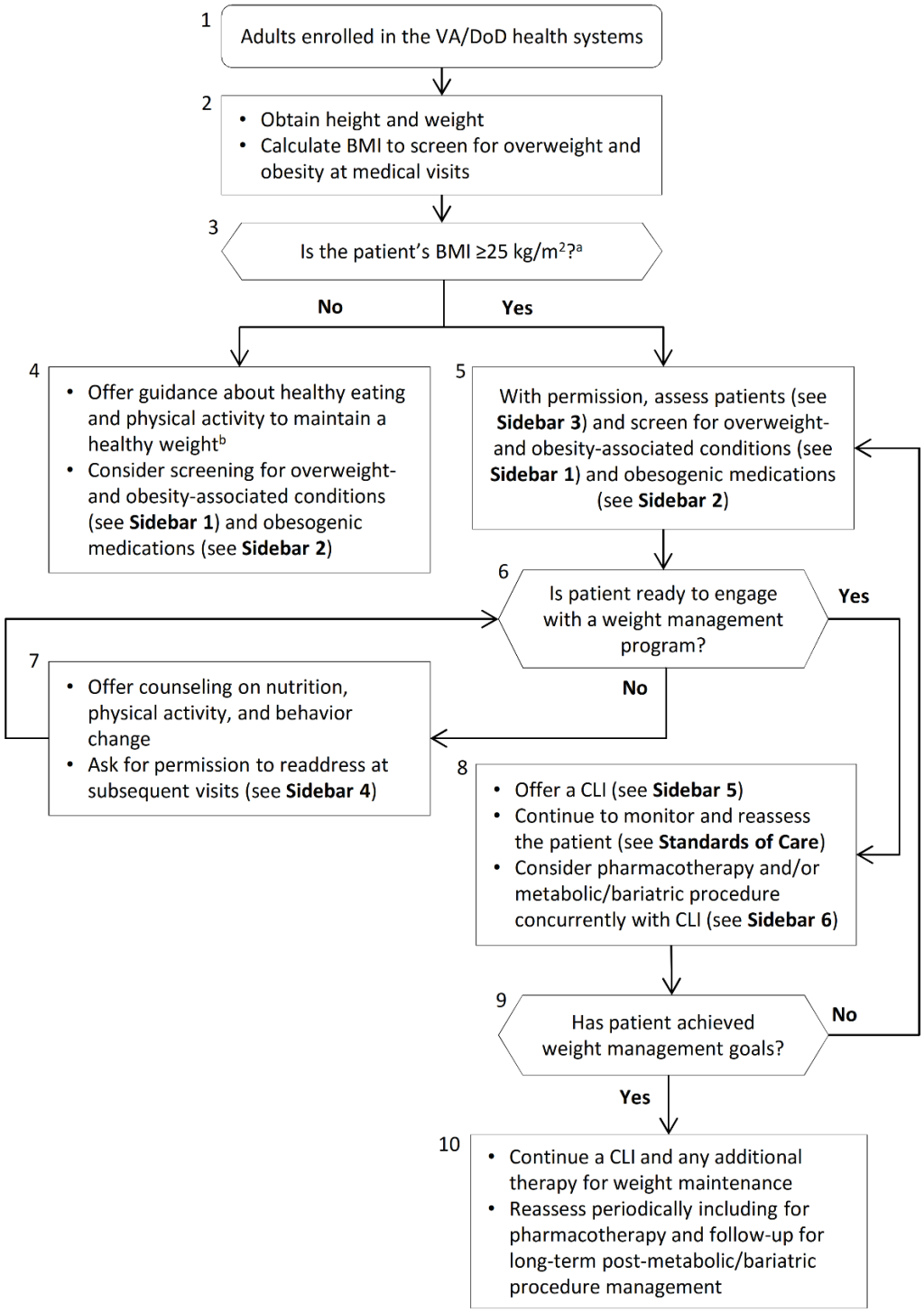
- An ordered sequence of steps of care
- Recommended observations and examinations
- Decisions to be considered
- Actions to be taken

For each VA/DoD CPG, there is a corresponding clinical algorithm that is depicted by a step-by-step decision tree. Standardized symbols are used to display each step in the algorithm, and arrows connect the numbered boxes indicating the order in which the steps should be followed.[38]

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 guideline

Appendix K contains alternative text descriptions of the Algorithm.

Algorithm Module



[a] For patients of Asian descent: is BMI ≥23 kg/m^2?; [39] for patients >65 years old: consider individualized assessment [40]

[b] See, for example, *2015-2020 Dietary Guidelines for Americans, 8th edition*, available at: https://health.gov/dietaryguidelines/2015/ and *Physical Guidelines for American, 2nd Edition*, available at: https://health.gov/paguidelines/second-edition/

Abbreviations: BMI: body mass index; CLI: comprehensive lifestyle intervention; DoD: Department of Defense; kg: kilograms; m: meters; VA: Department of Veterans Affairs

Sidebar 1: Common Overweight- and Obesity-Associated Conditions
• HTN • T2DM and prediabetes • Dyslipidemia • Metabolic syndrome[a] • OSA • OA/degenerative joint disease • NAFLD • GERD • Cancer [10]

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

Abbreviations: GERD: gastroesophageal reflux disease; HTN: hypertension; NAFLD: non-alcoholic fatty liver disease; OA: osteoarthritis; OSA: obstructive sleep apnea; T2DM: type 2 diabetes mellitus

Sidebar 2: Select Medications and their Potential Effects on Weight[a]		
Medication Classes	**Medications with Potential for Weight Gain**	**Medications that may be Weight Neutral or have Potential for Weight Loss**
Antipsychotics	• Quetiapine • Clozapine • Olanzapine • Risperidone • Thioridazine	• Aripiprazole • Haloperidol • Ziprasidone
Antidepressants	• Mirtazapine • Selective serotonin reuptake inhibitor (e.g., paroxetine, sertraline, citalopram[b], escitalopram[b], fluoxetine[b]) • MAOIs (e.g., phenelzine) • Tricyclic anti-depressants (e.g., amitriptyline, clomipramine, doxepin, imipramine, nortriptyline, protriptyline[b])	• Bupropion • Desvenlafaxine • Venlafaxine
Antiepileptic drugs or mood stabilizing agents	• Gabapentin • Pregabalin • Carbamazepine • Divalproex • Lithium • Valproic acid • Vigabatrin	• Topiramate • Lamotrigine • Zonisamide

Sidebar 2: Select Medications and their Potential Effects on Weight[a]		
Medication Classes	**Medications with Potential for Weight Gain**	**Medications that may be Weight Neutral or have Potential for Weight Loss**
Antihyperglycemic agents	• Insulin • Sulfonylureas (e.g., chlorpropamide, glimepiride, glipizide, glyburide) • Meglitinides (e.g., nateglinide, repaglinide) • Thiazolidinediones (e.g., pioglitazone, rosiglitazone)	• GLP-1 agonists (e.g., semaglutide, liraglutide, exenatide, dulaglutide, lixisenatide) • SGLT2 inhibitors (e.g., empagliflozin, canagliflozin, dapagliflozin, ertugliflozin) • Metformin • Pramlintide • Alpha-glucosidase inhibitors (e.g., acarbose, miglitol) • Dipeptidyl-peptidase-4 inhibitors (e.g., alogliptin, linagliptin, saxagliptin, sitagliptin)
Beta-blockers	• Metoprolol • Atenolol • Propranolol	• Carvedilol • Nebivolol *Note:* Other alternative classes of antihypertensive medications may be an option depending on the indication (e.g., angina, heart failure, HTN, migraine). Consider calcium channel blockers, angiotensin-converting enzyme inhibitor, ARBs, and thiazide or loop diuretics, as indicated.
Alpha-blockers	Terazosin	For benign prostatic hyperplasia (e.g., doxazosin; alfuzosin, tamsulosin)
Glucocorticoids	• Prednisone • Methylprednisolone • Hydrocortisone	Alternatives for rheumatologic disorders: • NSAIDs • Biologics/disease-modifying antirheumatic drugs • Nontraditional therapies
Hormonal agents	Progestins (e.g., medroxyprogesterone, megestrol acetate)	For contraception, consider alternative methods (e.g., copper intrauterine device)
Antihistamines	• Cetirizine • Cyproheptadine	Depending on symptoms, consider ipratropium nasal spray, decongestants, inhalers, and/or nonpharmacologic measures (e.g., nasal irrigation)

[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.

Abbreviations: ARB: angiotensin receptor blocker; 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 Patients with Overweight or Obesity

- Assess for presence of obesogenic medications (see Sidebar 2 on pharmacotherapy)
- Consider assessing waist circumference for patients with a BMI of 25 – 29.9 kg/m^2 (see Standards of Care)
- Assess for common overweight and obesity-associated conditions (see Sidebar 1)
- Assess for secondary causes of overweight or obesity if physical exam and history warrant, including but not limited to: depression, binge eating disorder, hypothyroidism, hypercortisolism (Cushing's disease or syndrome), traumatic brain injury, brain tumor, cranial irradiation, hypogonadism, menopause, acromegaly
- Assess the potential benefit of starting pharmacotherapy and/or bariatric procedure
- Assess conditions for which weight loss may not be beneficial (e.g., sarcopenia, active carcinoma, some eating disorders)

Abbreviations: BMI: body mass index; CPG: Clinical Practice Guideline; kg: kilograms; m: meters

Sidebar 4: Principles and Core Strategies of Motivational Interviewing

- 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)
- For more information refer to the guide, "Moving Veterans To MOVE!"[a]

[a] Available at: https://www.move.va.gov/

Sidebar 5: Comprehensive Lifestyle Intervention

- Defined as an intervention that combines behavioral, dietary, and physical activity components together (see Recommendation 1, Recommendation 6, Recommendation 7, and Standards of Care)
- The intervention can be delivered in an individual or group setting, in person, by telephone, or through synchronous video (see Recommendation 1 and Recommendation 4)
- 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; CPG: Clinical Practice Guideline

Sidebar 6: Assessment for Pharmacotherapy and/or Bariatric Procedures

In addition to CLIs, consider pharmacotherapy and/or bariatric procedures in the following scenarios:

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

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

Consider for bariatric procedures (see Appendix I):

- Patients with a BMI ≥30 kg/m^2 and T2DM
- Patients with a BMI ≥35 kg/m^2 and an obesity-related comorbidity
- Any patient with a BMI ≥40 kg/m^2

Abbreviations: BMI: body mass index; CLI: comprehensive lifestyle intervention; CPG: Clinical Practice Guideline; kg: kilograms; m: meters; T2DM: type 2 diabetes mellitus

VI. Standards of Care for the Patient with Overweight and Obesity

Some aspects of care of patients with overweight and obesity, although clinically important and part of the generally accepted standard of care, do not have sufficient high-quality evidence to support stand-alone recommendations. In some cases, clinical studies assessing the efficacy of these standards of care do not exist because they are determined to be routine actions (e.g., measurement of weight and calculation of BMI). In other cases, the standards are based on expert opinion, as was the case for several of the recommendations found in the previous version of this CPG.

A. Screening and Assessment for Overweight and Obesity

a. Screening

Calculating BMI is a practical screening tool to determine overweight and obesity in adult populations. The BMI is easily calculated, reliable, and is the basis for mortality risk estimates.[41] BMI is defined as a person's weight in kilograms divided by the square of the person's height in meters (kg/m^2). When weight is measured in pounds and inches, the BMI is calculated as (weight [in pounds]/height [in inches]^2)x 703. The optimal frequency for calculating BMI in the clinical setting has not been evaluated and is a matter of clinical discretion.[42] Screening at least annually provides an opportunity for patients and providers not only to identify overweight and obesity, but also to engage in productive discussions about the benefits of maintaining a healthy weight.

Although BMI is the most common way to identify overweight and obesity, there are questions regarding its accuracy in distinguishing between some individuals with and without obesity. For example, the optimal BMI for those over 65 may be slightly higher than for younger people.[40,43] Moreover, the use of BMI alone may lead to misclassification of highly fit individuals who have increased lean body mass, impacting assessments of fitness for duty. Measurement of body fat has been suggested as an alternative to BMI for screening for obesity, as truncal obesity may be an important indicator of risk for obesity-associated conditions, especially in people with a BMI below 30 kg/m^2.[44] Waist circumference (WC) is the most practical and reproducible anthropometric measurement for assessing a patient's level of abdominal fat and is an indicator of increased disease risk for patients with overweight.[45] Measurement of WC is less relevant in individuals with BMI ≥35 kg/m^2 because the WC will likely be elevated and will add no additional risk information.[26] We recommend cutpoints (>88 cm [>35 in] for women and >102 cm [>40 in] for men) as indicative of increased cardiometabolic risk.[26] The WC 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.[46] Measuring an individual's waist-to-hip ratio may be useful in identifying increased cardiometabolic risk associated with central obesity, especially among those with smaller body frames.[47] Though there are several other ways to estimate body fat (e.g., skin-fold caliper measurement, hydrodensitometry, dual-energy X-ray absorptiometry, magnetic resonance imaging [MRI], and bioelectrical impedance [BEI]), most of these methods are not readily available or convenient in clinical settings. The introduction of scales that feature BEI technology to measure percent body fat in clinical settings may enhance the assessment of overweight and obesity, particularly among Service Members.

b. Obesity-associated Conditions

Obesity is associated with a large and varied number of chronic health conditions, including several common conditions listed in Sidebar 1. In addition to these conditions, obesity contributes to increased risk and/or morbidity for many other conditions, including many cancers, as well as pulmonary, cardiovascular (CV), cerebrovascular, endocrinologic, rheumatologic, gynecologic, urologic, gastrointestinal (GI), and psychiatric conditions, including anxiety, depression, and eating disorders.[48,49]

c. Medical Assessment of Patients with Overweight or Obesity

An assessment of a patient's health history (see Sidebar 3) identifies the clinical, social, and behavioral factors that may affect his or her weight. In addition to the basic medical history and physical examination, patients should be assessed for factors contributing to obesity, including obesogenic medications, comorbid medical and psychiatric conditions (e.g., depression, anxiety, eating disorders, substance abuse), dietary and physical activity behaviors, 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.[48,49] Information obtained from the assessment may identify opportunities to eliminate or reduce obesogenic medications or mitigate the contribution of comorbid medical or psychiatric conditions to the patient's overweight or obesity.

The assessment can be useful when counseling the patient regarding healthy behaviors and engaging in shared decision making regarding weight management options.

B. Counseling Normal Weight Patients

As noted in the Algorithm, the CPG Work Group encourages providers to offer guidance on diet and physical activity to patients who are assessed to have a healthy weight. This is supported by a USPSTF recommendation to consider offering or referring adults without obesity and without other risks for cardiovascular disease (CVD) to behavioral counseling to promote a healthful diet and physical activity.[50] This recommendation is based on a USPSTF review of existing evidence that indicates a small benefit of behavioral counseling for the prevention of CVD in this population.[51]

Normal weight patients may be praised for maintaining a healthy weight and encouraged to implement or maintain, as applicable, healthy eating, and physical activity behaviors. They may also be educated about the health benefits of maintaining a healthy weight, eating in accordance with the Dietary Guidelines for Americans, staying physically active, and encouraged to balance caloric intake and energy expenditure. Patient education may also include recommending a diet balanced in fruits, vegetables, lean protein, whole grains, and low-fat dairy products.[g] In addition, moderate-intensity daily physical activity (≥30 min/day, five or more days/week) should be encouraged.[h] A careful review of medication lists for all

[g] See *MyPlate*, available at: http://www.choosemyplate.gov, *2015-2020 Dietary Guidelines for Americans,* available at*:* https://health.gov/dietaryguidelines/2015/, or *VHA's Eat Wisely Healthy Living Message*, available at: https://www.prevention.va.gov/Healthy_Living/Eat_Wisely.asp

[h] See *Physical Activity Guidelines for American, Second Edition*, available at: https://health.gov/paguidelines/second-edition/, or VHA's *Be Physically Active Healthy Living Message*, available at: https://www.prevention.va.gov/Healthy_Living/Be_Physically_Active.asp

patients may reveal medications that promote weight gain and may undermine efforts at maintaining a normal weight over time (see Sidebar 2).

C. Shared Decision Making to Choose Among Weight Management Options

Once an assessment has been conducted, and factors contributing to overweight and obesity have been addressed, the clinical team should engage the patient in a shared decision making process regarding weight management options. Shared decision making [52] is derived from evidence-based principles of health education [53] and health behavior counseling [54,55] and is also informed by motivational interviewing.[56,57] The first step in the shared decision making process is achieving a shared understanding of the risks related to the individual's weight and health status and the potential benefits of participating in a weight management intervention. It is useful to begin by asking permission to discuss weight to ensure that patients are receptive. Asking permission supports patient autonomy and is consistent with the principles of motivational interviewing, an evidence-based clinical method for building motivation for behavior change.[57] Specific strategies for effectively reaching shared understanding are:

- Ask permission to discuss weight-related health risks and the potential benefits and risks of weight loss and weight management
- 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
- Share information about potential health risks that are tailored to the patient's understanding, his or her BMI, his or her current health status, and the presence of weight-associated conditions
- Emphasize, if needed, the value of viewing obesity as a chronic disease condition that requires ongoing attention and weight management
- Provide small amounts of information in a manner that is easy to understand
- Use a "teach-back" method to confirm shared understanding [53,55-58]

The process of reaching a shared understanding goes beyond simply educating patients about their conditions and the benefits of weight loss. Instead, it is a dialogue that begins with exploring the patients' understanding, beliefs, and experiences, and then providing information that is tailored to them. It is particularly useful to review patients' prior experience with weight management, their perceptions about the benefits of weight loss, and their values. Exploring what matters to patients about their health and function allows the healthcare team to respond empathically and tailor information and advice and align recommendations with values (e.g., "preventing complications of DM will help you to be available to your family, which you said is very important to you"). 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.[57,59]

Applying a patient-centered approach also requires that clinicians address the impact that weight stigma and bias have on patients' physical and psychological health and well-being, willingness to participate in weight management, and success in weight management efforts.[60] 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 patient well-being.[60,61] A patient-centered approach that emphasizes clinician awareness of his or her contributions to stigma and bias, use of person-first language (e.g., "people with obesity" instead of "obese patients"), and increased use of empathy and patient-centered communication skills can enhance the quality of clinical interactions.[60,61]

a. Motivational Interviewing

If an initial assessment of the patient's motivation indicates that the patient is not ready to commit to recommended treatment, an intervention based on motivational interviewing may be considered. 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.[57,62-70] Principles and core strategies of motivational interviewing are listed in Sidebar 4.

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

After achieving shared understanding, and after utilizing motivational interviewing if needed to build motivation to participate in evidence-based weight management interventions, the next step in the process of shared decision making is to elicit a commitment to engage in a recommended 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 to a weight management intervention, the next step is to share the available options for engaging in treatment and guiding 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 [MOVE!];[i] see Emphasizing the Central Role of Comprehensive Lifestyle Intervention and Recommendation 1 for more information about CLIs) or to a member of the healthcare team (e.g., a dietitian, a health coach, a clinical pharmacist), who can guide the patient through the process of deciding among available treatment options. If the patient is not willing to commit to a recommended weight management intervention, the provider might offer educational materials and inform the patient that they will have an opportunity to revisit options for weight management in future encounters. A novel technology app, funded by the DoD, called Army H.E.A.L.T.H. (Healthy Eating Activity Lifestyle Training Headquarters)[j] has been developed for active duty, reserves, and national guard service men and women. This app offers content and resources to encourage healthy eating, physical activity, fitness, and other healthy behaviors; however, as we noted in our recommendations, there is insufficient evidence for or against offering a CLI for weight loss that uses technology as its primary mode of delivery (see Recommendation 5).

Motivational Interviewing strategies may also be applied at these and subsequent encounters. (See the discussion of Motivational Interviewing above). Providers might also assist the patient to select a more

[i] Available at: https://www.move.va.gov/
[j] Available at: https://myarmyhealth.org/

limited health behavior goal (e.g., increased physical activity, OR eliminating sugar-containing beverages as a first step) that may contribute to future weight management efforts.

D. Emphasizing the Central Role of Comprehensive Lifestyle Intervention

In this CPG, the Work Group strongly recommends offering a CLI that combines behavioral, dietary, and physical activity components as a foundational element of any weight management intervention (see Recommendation 1 and 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 a CLI. Emphasizing the central role of CLI in weight management is a key element of the shared decision making process, as is reviewing the relative benefits and risks of specific pharmacotherapies, surgical procedures, and devices when these interventions are under consideration. 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, of course, further exploration of patient preferences for CLI modality (e.g., for group versus individual and telephone versus in-person) and preferences regarding concurrent pharmacotherapy or metabolic/bariatric surgery, if the patient is a candidate. Consultation with a dietitian, a clinical pharmacist, or a bariatric surgeon may help with decision making about the choice of specific weight management interventions, especially for patients with complex medical histories and/or concurrent pharmacotherapies that may impact the potential benefits and harms of specific weight management treatment components.

Whenever patients express an interest in participating in a CLI, it is useful to share and emphasize several key concepts that apply to all CLIs:

- Understand weight management is a lifelong commitment rather than a brief episode of treatment
- Emphasize applying weight management practices that are maintainable, rather than those that might produce short-term weight loss but are not sustainable
- Create an “energy deficit” through a combination of reduced caloric intake and increased physical activity
- Apply specific behavioral strategies (e.g., goal setting, monitoring, problem solving) to support incremental changes in both diet and physical activity (see Appendix J)
- Set specific, measurable, and realistic goals for changes in diet and physical activity, as well as realistic goals for weight loss and maintenance

We suggest that providers prepare patients to address the challenges of maintaining weight loss in the setting of metabolic, hormonal, and neuroendocrine adaptations to significant weight loss that make it challenging for individuals to maintain reduced weight.[71,72] Such preparations may include the expectation that they will need to increase their participation in moderate or vigorous physical activity to maintain significant weight loss.[73]

Once a patient has engaged in a CLI, it is useful to assess current levels of physical activity (including activity type, frequency, duration, and intensity) and the presence of sedentary behaviors (e.g., prolonged television watching). A dietary evaluation may include an assessment of problem eating behaviors (e.g., excessive snacking, frequent high caloric fast foods or liquid sugars). Weight and dieting history may include the number and types of diets 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 barriers that may impact patient participation in weight loss programs.

As noted above, setting specific and realistic weight loss goals is a key component of CLIs. Achieving 5 – 10% weight loss after six months is a reasonable initial treatment goal that can produce clinically significant benefits, especially for patients with obesity-associated conditions. A short-term initial weight loss goal of 0.5 – 2.0 pounds per week is achievable with a net caloric deficit of 500 – 1,000 kcal/day. This short-term weight loss goal, along with specific dietary, physical activity, and self-monitoring goals can serve as benchmarks for assessing progress during initial treatment.[2,74,75]

E. Assessment of Progress Toward Weight Loss Goals

When patients participate in a CLI, the multiple encounters that characterize all CLIs provide opportunities for patients and providers to assess progress toward weight loss goals (through regular weighing and monitoring of dietary and physical activity behaviors), and to make adjustments to address barriers that may arise, particularly in meeting short- and intermediate-term dietary and physical activity goals. Patients who are meeting short- and intermediate-term goals should continue current treatment until long-term weight loss goals are achieved. When patients are not meeting short- and intermediate-term goals, the treatment plan should be modified to address identified barriers to health behavior change. If, despite increased attention to these barriers, the patient continues to struggle, consideration should be given to increasing the intensity of treatment. This can be achieved by increasing the intensity or frequency of the CLI, adding a recommended pharmacotherapeutic agent for weight loss, and consultation with, or referral to, a bariatric surgical team. As noted in Emphasizing the Central Role of Comprehensive Lifestyle Intervention above, consultation with a dietitian or clinical pharmacist may help with decision making about the selection or modification of dietary elements of the CLI or consideration of a specific weight management medications (see the Algorithm and Sidebar 6).

Once long-term weight loss goals have been achieved, the focus of weight management shifts to preventing weight regain, a goal that 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 (see the Algorithm and Recommendation 3).

VII. Recommendations

Topic	Sub-topic	#	Recommendation	Strength[a]	Category[b]
Management of Overweight or Obesity	*a. Comprehensive Lifestyle Interventions (CLIs)*	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
		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
		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
		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
		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
	b. Physical Activity Component of a CLI	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
	c. Dietary Component of a CLI	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
		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
	d. Long-term Pharmacotherapy	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

Topic	Sub-topic	#	Recommendation	Strength[a]	Category[b]
Management of Overweight or Obesity (cont.)	*d. Long-term Pharmacotherapy (cont.)*	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
	e. Dietary Supplements and Nutraceuticals	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
	f. Metabolic/Bariatric Procedures and Devices	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
		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
		14.	There is insufficient evidence to recommend for or against metabolic/bariatric surgery to patients over age 65.	Neither for nor against	Reviewed, Amended
		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
Short-term Weight Loss (Up to Six Months)		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
		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
		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

[a] For additional information, please refer to Grading Recommendations.

[b] For additional information, please refer to Recommendation Categorization and Appendix A.

A. Management of Overweight or Obesity

a. Comprehensive Lifestyle Interventions

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)

Discussion

We define CLIs for weight loss and weight maintenance as interventions that combine three critical "lifestyle" components (i.e., behavioral, dietary, and physical activity components) that aim to produce a negative energy balance. CLI is the term used in the 2014 VA/DoD Obesity CPG, other recent CPGs, and evidence reviews of weight management interventions.[26,75] In this guideline, we define "in-person" as an intervention that necessitates the patient's and clinician'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. Comprehensive lifestyle interventions 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. Since the 2014 VA/DoD Obesity CPG, a 2018 SR of CLIs commissioned by the USPSTF identified 80 good or fair quality randomized controlled trials (RCTs) of CLIs for weight loss (n=30,394 adults with overweight or obesity).[2] Findings were also published in a 2018 article from the Journal of the American Medical Association.[76] 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).[2] 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 (risk ratio [RR]: 1.94; 95% CI: 1.70 to 2.22), which translated into a number needed to treat of eight.[2] Additionally, at 24 months, the pooled 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.[2]

When considering the impact of weight loss on health outcomes, the 2014 VA/DoD Obesity CPG Work Group found evidence that weight loss, including weight loss associated with participation in CLIs, produced clinically significant benefits for patients with DM and HTN.[77-86] 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., CVD, HTN, DM) were excluded.[2] 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).[2] Within these, the two largest, good quality studies (n=1,817 combined) that focused on the prevention of DM (the Finnish Diabetes Prevention Study [87,88] [n=522] and the Diabetes Prevention

Program Outcomes Study [89] [n=1,295]) showed an absolute risk reduction of developing T2DM of approximately 14.5% over 3 – 9 years, as described in the 2018 USPSTF systematic review.[2]

However, data from the 2018 USPSTF systematic review on the long-term impact of CLIs versus control conditions on the prevalence of HTN, metabolic syndrome, use of CVD medications, and 10-year risk of CVD was limited to a small number of trials or was inconclusive.[2] Data were also limited or inconsistent on the long-term impact of CLIs on all-cause mortality, CV events, and QoL.[2] However, 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.[26]

We recommend both group and individual in-person modalities for delivering CLIs, as subgroup analyses performed for the 2018 USPSTF systematic review found no pattern of effects on the main outcome of change in weight at 12 – 18 months follow-up according to the main mode of intervention delivery (i.e., group versus individual versus technology-based versus mixed).[2] Technology-based modalities included computer- or web-based intervention modules, web-based self-monitoring, mobile phone-based text messages, smartphone applications, social networking platforms or DVD learning.[2]

However, there was evidence of a greater effect among CLIs that included any group sessions versus those that did not (coefficient: -1.19; p=0.004).[2] 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.[2] Additional subgroup analyses found that mean baseline weight category (i.e., overweight, Class I obesity, Class II obesity) was not associated with differences in effects on weight change,[2] 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, confounded with differences in the populations, settings, and trial quality, made it difficult to identify which variables may be driving larger effects.[2] (See Recommendation 2 regarding the number of intervention sessions, Recommendation 4 regarding telephone-delivered CLI sessions, and Recommendation 5 regarding technology-delivered CLI for additional information that supports these recommendations.)

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 [2] and 2011 USPSTF systematic reviews [74] 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.[2,74] These elements are also emphasized in other reviews of CLIs for weight loss not included in the systematic evidence review carried out for this CPG update.[75,90] 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.[91] For more information about specific approaches and behavioral strategies commonly included in CLI, see Standards of Care. See also recommendations and discussions on physical activity (Recommendation 6) and dietary components (Recommendation 7 and Recommendation 8).

Additional SRs and individual studies testing CLIs for weight loss that were identified in the evidence review conducted for this CPG update either did not compare a CLI with an appropriate control (i.e., usual care or minimal intervention) or were rated as low or very low quality. Therefore, these studies did not contribute to the VA/DoD CPG Work Group's recommendation.

Data from the 2018 USPSTF systematic review showed that larger differences in weight change were seen in trials that specifically enrolled adults with increased CV risk, subclinical risk of CVD or cancer (e.g., prehypertension, prediabetes, gestational diabetes), and elevated cancer risk compared to trials that enrolled adults who were unselected or generally at low risk (coefficient: -1.15; p=0.004). Sample retention at 12 months was also associated with greater weight loss (coefficient: -0.05; p=0.011).[2] These data suggest that CLIs have a greater impact among individuals at increased risk for CVD and cancer and that interventions that effectively engage subjects produce larger effects.

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 benefit from CLIs that is likely related to unmeasured individual, social, and environmental factors influencing an individual's weight loss, rather than on specific intervention characteristics.[2]

Evidence indicates the risk of harms 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.[2] 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.[2] Musculoskeletal events were most commonly found to be 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.[89] 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 importance of developing a patient-centered lifestyle modification treatment plan that includes dietary and exercise components as well as education on how to make changes that will lead to sustained weight loss. Moreover, the focus group participants emphasized the importance of having a treatment plan that is individualized, offers treatments in a variety of formats, and includes access to tools and resources that leverage technology (see Patient Focus Group Methods and Findings). 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.

Summary

As this is a *Reviewed, New-replaced* recommendation, the Work Group systematically reviewed evidence related to this recommendation[2] and considered the evidence put forth in the 2014 CPG.[77-86] The primary source of evidence was a large 2018 USPSTF-sponsored SR that included 80 good and fair quality

RCTs that randomized 30,394 adults with overweight and obesity to CLIs for weight loss versus minimal treatment or usual care control interventions.[2] Results included greater weight loss from CLIs versus control at 12 – 18 months follow-up (MD: -2.39 kg) and a 1.94 times greater probability of losing 5% of participants' initial weight over 12 – 18 months compared with control groups, which translated into a number needed to treat of eight.[2] Across nine trials (n=3,140) that compared the impact of CLIs compared to control conditions among individuals selected for baseline impaired fasting glucose, the pooled RR of developing incident DM was 0.67; however, the impact on other intermediate outcomes and health outcomes was mixed.[2] Evidence indicates the risk of harms from CLIs is low. The Work Group recommends both group and individual in-person modalities for delivering CLI, as subgroup analyses performed for the 2018 USPSTF systematic review found no pattern of effects on weight change at 12 – 18 months follow-up based on whether the main mode of intervention delivery was group or individual.[2] The Work Group's confidence in the quality of evidence was moderate. Patient focus group participants highlighted the value of CLIs, particularly when they are available in a variety of modalities. Thus, the Work Group decided upon a "Strong for" recommendation.

Recommendation

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)

Discussion

As noted in Recommendation 1, 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 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. However, the Work Group's review of additional studies conducted since the 2014 VA/DoD Obesity CPG was published led them to conclude that there is insufficient evidence to recommend offering a specific number of CLI 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 less than 12 sessions in the first 12 months.

As detailed in Recommendation 1, 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.[2] 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.[2] 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.[2] When 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).[2] 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 (>26 sessions, MD: -3.06 kg, 95% CI: -3.85 to -2.28; 12 – 26 sessions, MD: -2.48 kg, 95% CI: -3.35 to -1.61; 0 – 11 sessions, MD: -1.73, 95% CI: -2.32 to -1.13), the CIs across all three of the subgroups overlapped, so these differences were not statistically significant.

Although there was no significant difference found for 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.[2] 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, more than half (n=12) of the 23 trials in this subgroup offered at least five sessions in the first year, and several trials in the 0 – 11 session subgroup offered sessions beyond the first 12 months of the intervention. 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 number of sessions on weight loss outcomes while controlling for other intervention characteristics.[2] Also, the systematic evidence review carried out as part of this CPG update did not identify individual studies that specifically tested the differential impact of number of sessions while controlling for other characteristics of the CLI.

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. As noted previously, although there was a significant effect of CLI over controls conditions for CLIs that offered 0 – 11 sessions, the majority of the studies that were in this subgroup provided at least five sessions in the first 12 months, and most of the others were technology-based and included other forms of contact with participants. 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) CLI.[26]

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 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.

Summary

As this is a *Reviewed, New-replaced* recommendation, the Work Group systematically reviewed the evidence related to this recommendation.[2] The Work Group concluded that there is insufficient evidence to recommend a specific number of sessions of a CLI for patients with overweight or obesity, although as noted, there may be a dose-response effect for number of sessions in the first 12 months of a CLI, as almost two-thirds of RCTs of CLI offered at least 12 sessions during the first 12 months. Confidence in the quality of the evidence is low due to heterogeneity of CLIs and the lack of studies that directly tested high versus low number of sessions. There is likely variation in patient preferences regarding participating in CLIs with many sessions. Thus, the Work Group decided upon a "Neither for nor against" recommendation.

Recommendation

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)

Discussion

The 2014 VA/DoD Obesity CPG Work Group found that offering a maintenance CLI that includes dietary, physical activity, and behavioral components plus ongoing support reduces the likelihood of weight regain.[74,75,92] Since the publication of the 2014 VA/DoD Obesity CPG, a 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).[2] The SR included RCTs of participants with pre-intervention 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 such as goal setting, problem solving, relapse prevention, and self-monitoring (see Standards of Care for more information about the components of a CLI). 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 reported as kilograms or pounds lost at 12 – 18 months post-intervention (MD: -1.59 kg; 95% CI: -2.38 to -0.79).[2] 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 (intervention: 42%, control: 34%; RR: 1.24; 95% CI: 1.02 to 1.51) and 60 months post-intervention (intervention: 37%, control: 27%; RR: 1.37; 95% CI: 1.03 to 1.82). 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. An additional RCT by Mai et al. (2018) was identified but the study quality was rated as poor.[93] The 2018 USPSTF systematic review also determined there is insufficient evidence to favor group or individual treatment.[2]

Comprehensive lifestyle interventions for weight maintenance have a very low risk of harms. This was reflected in the results of the 2018 USPSTF systematic review, which found no serious harms and similar rates of adverse events between participants in behavior-based interventions and controls (see Recommendation 1 for discussion of potential harms for CLI).[2] Therefore, the benefit of participation in CLI for weight maintenance was determined to outweigh potential harms.

Despite general consistency in supporting CLI for weight maintenance, there is some variability in patient preferences for this treatment. Significant time is required for participation, and patients vary in their willingness and ability to travel to receive an intervention. Patients also vary in their willingness to devote resources to weight maintenance. To benefit, patients must engage with the intervention and practice skills. There are also limitations related to intervention resource availability, as clinicians who deliver maintenance CLI also usually deliver CLI for weight loss. It may 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.

Summary

As this is a *Reviewed*, *New-replaced* recommendation, the Work Group systematically reviewed evidence related to this recommendation [2,93] and considered the evidence put forth in the 2014 CPG.[74,75,92] Maintenance CLIs were found to significantly impact maintenance of weight loss at 12 – 18 months and maintenance of ≥5% weight loss at 30 and 60 months post-maintenance intervention compared to controls. Though the net benefit was small, these benefits outweighed the potential harm from adverse events, which was minimal. The body of the evidence had some limitations including a small number of trials reporting >5% weight loss and one trial with wide confidence intervals;[2] however, all nine trials reviewed in the 2018 USPSTF systematic review were rated fair or good quality, and overall, the Work Group's confidence in the quality of evidence was moderate. Patient values and preferences were somewhat varied. Thus, the Work Group decided upon a "Weak for" recommendation.

Recommendation

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)

Discussion

The 2014 VA/DoD Obesity Work Group recommended offering telephone-based CLI either as an alternative to, or in conjunction with, an in-person intervention. As noted in Recommendation 1, 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 VA/DoD Obesity CPG and evidence published since then, the Work Group suggests offering an individual or group 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 1, 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.[2] Fifteen of these RCTs tested CLIs that included a telephone-delivered component.[2] 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.[94,95] 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 emerging intervention modality is likely to be efficacious compared to 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. 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).[2,75,94,95]

Despite general consistency in the evidence supporting telephone-based CLI, there is some variability in patient preferences regarding this modality. The patient focus group revealed that any CLI can be burdensome to patients, as CLI requires frequent contacts (see Appendix B). 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.

Summary

As this is a *Reviewed*, *Amended* recommendation, the Work Group systematically reviewed evidence related to this recommendation.[2,94,95] and considered the evidence put forth in the 2014 CPG.[75,92] The Work Group's confidence in the quality of evidence was low. No good quality RCTs were identified that directly compared telephone to face-to-face modalities of intervention while controlling for other characteristics of the CLI. The benefit of weight loss outweighed any potential harm, which is minimal for CLIs (see the discussion for Recommendation 1). Patient values and preferences were somewhat varied. Thus, the Work Group decided upon a "Weak for" recommendation.

Recommendation

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)

Discussion

For this recommendation, the Work Group considered interventions that use technology as a primary mode of intervention delivery. These include computer- or web-based intervention modules, web-based self-monitoring, mobile phone-based text messages, smartphone applications, social networking platforms, DVD learning, and print-based tailored materials.

As noted in Recommendation 1, 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.

As detailed in Recommendation 1, 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).[2] 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.[2] 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 [96-107] included in the 2018 USPSTF systematic review identified a wide range of technologies employed across the trials. Seven [96,98,101,102,105-107] 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.[103] Another was found to be effective in men but not women.[104] In addition, two trials explicitly described face-to-face, interactive components.[96,101] 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.

Additionally, a 2019 SR evaluated the effectiveness of web-based digital health interventions compared to no active intervention.[108] The authors conducted a meta-analysis of five RCTs and found a significant effect favoring active interventions on weight loss, though the quality rating of the SR was poor. None of the trials reported outcomes beyond nine months, and three of the five trials reported outcomes at four months or less. Another recent SR by Park et al. (2019) evaluated the effectiveness of mobile phone-delivered CLI for weight loss versus no treatment or educational materials.[109] Twenty RCTs in adults with overweight or obesity were included in this SR. However, weight loss outcomes at 12 or 24 months were reported for only four mobile phone intervention conditions in three trials,[106,110,111] and none of these produced significant effects versus controls. Moreover, the meta-analysis conducted in the Park et al. (2019) SR [109] was flawed, as the investigators included 12- and 24-month outcomes from a single trial [110] as two separate trials in the meta-analysis. Several additional individual studies testing technology-delivered CLIs for weight loss that were identified in the evidence review conducted for this CPG update had poor or very poor quality ratings due to methodological deficiencies.

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 intervention. While these interventions may reduce burden and travel time related to in-person intervention, 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.

Summary

As this is a *Reviewed, New-replaced* recommendation, the Work Group systematically reviewed evidence related to this recommendation.[2,106,108-111] The Work Group's confidence in the quality of evidence was very low. The body of the evidence had significant limitations including poorly defined and heterogeneous interventions, small MDs between interventions, and minimal intervention or no treatment controls and/or reported weight loss outcomes at less than 12 months of follow-up. Thus, the Work Group decided upon a "Neither for nor against" recommendation regarding technology-delivered CLIs for weight loss. However, technology-inspired tools and resources can play a valuable role in supporting self-monitoring and tracking of diet, physical activity, and weight loss outcomes when patients are engaged in an in-person or telephone-delivered CLI, especially for those Veterans and Service Members who value technology-supported approaches. Internet, text-based, mobile apps, or other technology-supported approaches also have great potential for extending or increasing interaction with CLI staff.

b. Physical Activity Component of a Comprehensive Lifestyle Intervention

Recommendation

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)**

Discussion

The primary evidence in support of physical activity interventions for weight loss is nested in studies of CLIs for weight loss to support long-term weight management that combines physical activity, dietary, and behavioral interventions.[2,112-114] As detailed in the discussion accompanying Recommendation 1, 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.[2] A physical activity component is also a core element of CLIs recommended for weight maintenance.[2] The CLIs included in the 2018 USPSTF systematic review all featured similar messages related to energy balance (i.e., gradual increases in moderate-to-vigorous intensity physical activity and healthful dietary patterns following national guidelines).[2] The physical activity component generally promoted at least 150 minutes of moderate-intensity activity per week (see also the discussion for Recommendation 1). There was additional evidence from two fair quality SRs showing an improvement in weight loss with the addition of physical activity to a dietary-only component and the addition of physical activity to a comparator that combined dietary and behavioral interventions.[112,113] The Work Group did not review research that evaluated exercise-alone weight-loss interventions, as a large body of previous research concluded that exercise alone produces small impacts on weight, especially when compared to studies that included both dietary and physical activity elements.[112,113,115-117]

The evidence reviewed compared different types of physical activity utilized in a CLI for weight loss including aerobic training (e.g., cycling, supervised walking programs), resistance training (e.g., weight

training), and "lifestyle physical activity" (generally increasing activity during the day such as climbing extra stairs, unstructured walking activity, or getting more steps using a pedometer). Studies comparing the kind of physical activity used as part of a CLI, or as part of a multimodal (physical activity and diet) approach, did not reveal important differences by the kind of physical activity for weight loss or other important variables;[114,118,119] however, some evidence indicated higher intensity of physical activity has better effects on weight variables than lower intensity activity programs.[118] There was no specific weight loss benefit associated with a specific kind of physical activity (aerobic, resistance, or lifestyle) in the evidence reviewed. While not reviewed in this guideline, higher volumes of physical activity (e.g., over 300 minutes of moderate activity per week) were associated with improved weight maintenance after weight loss.[115]

The benefits of having physical activity as part of a CLI were judged to outweigh the relatively minor potential harms. The 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 (PAGA).[120] 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 [113,118,120,121] and related benefits/effects such as health-related QoL and self-efficacy/physical function.[119] For example, osteoarthritis, chronic pain syndromes, and HTN (among others) are responsive to the doses and types of physical activity included in CLIs for weight loss. As noted in the discussion for Recommendation 1, musculoskeletal events were commonly related to CLI groups, although only one trial found a statistically significant difference in events across intervention and control groups.[89] 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 B). 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. Since the systematic evidence review carried out as part of this guideline update did not find significant differential effects of specific activity types, patients and providers have a wide scope of options when considering specific physical activity modalities. The 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).[120][k,l]

Summary

As this is a *Reviewed, New-replaced* recommendation, the Work Group systematically reviewed evidence related to this recommendation,[2,112-114,118,119] and considered the evidence put forth in the 2014 CPG.[89,115-117] The overall confidence in the quality of evidence comparing types of physical activity for weight loss is low. The benefits of having physical activity as part of a CLI outweighed the relatively minor

[k] These options are discussed in the PAGA at https://health.gov/paguidelines/second-edition/.

[l] Physical activity options are reviewed in detail at https://health.gov/moveyourway/.

potential harms. Thus, the Work Group decided upon a "Weak for" recommendation. However, beyond the impact of physical activity on weight, there are large benefits of increasing physical activity levels in this population for general health and to reduce the impact of common comorbid conditions.[113,118,120,121] The Work Group recommends future research to compare different kinds of physical activity (aerobic, resistance, lifestyle) in CLI programs for weight loss to discover any differential effects and reveal any differences in adherence, acceptability, or feasibility.

c. Dietary Component of a Comprehensive Lifestyle Intervention

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)**

Discussion

Using a dietary approach that enables patients to achieve a negative energy balance is a core component of CLIs and has been found to promote weight loss in patients with overweight and obesity.[2,122-134] As detailed in the discussion accompanying Recommendation 1, 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.[2] A dietary component is also a core element of CLIs recommended for weight maintenance.[2] The CLIs included in the SR all featured similar messages related to energy balance (i.e., gradual increases in moderate-to-vigorous intensity physical activity and healthful dietary patterns following national guidelines).[2] See also the discussions for Recommendation 1 and Recommendation 3**.** Based on these studies, a negative energy balance to support weight loss can be achieved through a variety of dietary approaches.[122-134] Findings from multiple other studies, conducted in a variety of patient populations, have been consistent with this finding.[135-144] There is no evidence of harm to patients in achieving a modest negative energy balance.[122-145] However, patient harm is possible if a very low-calorie diet (≤800 kcal) is followed; that harm may include "cholecystitis, asthenia, fatigue, headache, constipation, and nausea."[129,146]

Patients seeking to lose weight recognize the need to achieve negative energy balance, but determining how to do that can be difficult. Providers can discuss a patient's medical condition(s) and dietary preferences to help guide patients to the dietary approach best suited to those preferences to promote adherence during weight loss as well as maintenance once weight loss is achieved. Ideally, patients are referred to a CLI that is delivered by an inter-professional team, including a registered dietitian, who can work with the patient to best meet nutrient needs for health and management of the medical condition(s) while promoting weight loss. See Appendix G on dietary approaches for additional guidance on selecting the dietary component of a comprehensive lifestyle intervention.

Summary

As this is a *Reviewed, Amended* recommendation, the Work Group systematically reviewed evidence related to this recommendation,[2,122-126,128-134,142] and considered the evidence put forth in the 2014 CPG.[127,135-141,143-145] The Work Group's confidence in the quality of evidence was moderate. The body of evidence had some limitations including heterogeneity in dietary approaches, heterogeneity

in how specific diets were defined, variable lengths in the intervention duration across studies, small sample size in some individual studies, and insufficient control for confounding variables in the analyses limiting interpretation of study results.[122,123,130,135,140] The benefits of weight loss on comorbid conditions outweighed the potential harm of adverse events, which was small. Patient values and preferences were aligned with achieving a negative energy balance. Thus, the Work Group decided upon a "Strong for" recommendation. Providers should refer patients to a registered dietitian to aid in determining the approach for achieving a negative energy balance that best supports the patients' overall medical history and dietary practices.

Recommendation

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)

Discussion

Meal replacement has been found to support weight loss in patients with overweight and obesity when provided in conjunction with a CLI to support long-term weight management (for all CLIs see Recommendation 1).[122] Based on an SR of 23 RCTs, meal replacement provided significantly more weight loss than other dietary approaches (MD: -1.44 kg at one year; MD: -2.71 kg at more than one year; and MD: -4.20 kg at four years). Greater weight losses were achieved when meal replacement was coupled with weight loss support.[122] Meal replacement also resulted in improvements in systolic and diastolic blood pressure (BP), total cholesterol, and fasting serum insulin levels.[122] Findings from multiple other studies, conducted in a variety of patient populations, have been consistent with this finding.[147-149] One study of 66 matched participants included in the 2014 VA/DoD Obesity CPG revealed equal weight loss between participants using meal replacements and participants using a structured weight-reduction diet.[150] Evidence indicates that meal replacement does not pose harm to patients.[122]

Meal replacement can be used to achieve a negative energy balance as part of a CLI. While the evidence review only identified one SR on this topic, it included 23 studies and 7,884 study participants.[122] The findings of the SR and meta-analysis [122] align with evidence from the 2014 VA/DoD Obesity CPG [150] that meal replacements are convenient to use and provide manageable dining out options.

There is general consistency in the evidence supporting meal replacement.[151] There may be some variability in provider and patient preferences regarding this treatment based on the acceptability and cost of meal replacement products. Service Members receiving Subsistence in Kind (SIK) are provided meals in DoD dining facilities – an entitlement that cannot be used to purchase meal replacement products. Veterans with limited financial resources or those on a fixed income may also find purchasing meal replacement products burdensome. Patients may get weary of eating the same meal replacement product every day; however, providing a variety of meal replacement options may promote adherence.

Meal replacements address patients' desire to know how to achieve negative energy balance, aligning with the focus group members' preference for specific guidance. Meal replacement products enable patients to know what to eat for the meal(s) being replaced. Meal replacement, when offered in conjunction with a

CLI, can help patients develop the knowledge, skills, and confidence needed to manage their weight and address both short- and long-term weight management needs.

Summary

As this is a *Reviewed, New-replaced* recommendation, the Work Group systematically reviewed evidence related to this recommendation [122] and considered the evidence put forth in the 2014 CPG.[147-150]The Work Group's confidence in the quality of evidence was moderate. The body of evidence had some limitations including variability in the level of bias, with five out of the 23 studies deemed to be at high risk for bias in at least one domain. Biases included unclear allocation and concealment of intervention and heterogeneity of meal replacement products used; additionally, several studies were industry funded.[122] Most studies (19 out of 23) included in the Astbury et al. (2019) SR and meta-analysis were included predominantly of female participants.[122] Other considerations regarding this recommendation included the benefits (including weight loss as well as improvements in systolic and diastolic BP, total cholesterol, and fasting insulin) outweighing the potential harm of adverse events, which was small (reported adverse events were not likely associated with the meal replacement). Patient values and preferences were somewhat varied. Thus, the Work Group decided upon a "Weak for" recommendation.

d. Long-term Pharmacotherapy

Recommendation

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)

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)

Discussion

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.

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).[152] This contributed to moderate confidence in the quality of the evidence that the combination of a CLI and a weight loss medication, approved by the U.S. Food and Drug Administration (FDA) for long-term use (specifically liraglutide, fixed-combination

naltrexone/bupropion, orlistat, and fixed-combination phentermine/topiramate) results in greater weight reduction than a CLI alone. This SR and meta-analysis also included data on the weight-loss medication lorcaserin. However, in February 2020, the FDA requested the withdrawal of the weight-loss drug lorcaserin (Belviq, Belviq XR) from the U.S. market citing potential risk of cancer outweighing the benefits of use.[153] The meta-analysis reported that after a minimum follow-up of 12 months, each of the four medications 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.[152]

Based on the meta-analysis, patients who received fixed-combination phentermine/topiramate had the highest probability of achieving a 5% or 10% weight loss, followed by liraglutide, fixed-combination naltrexone/bupropion, and orlistat.[152] The mean weight loss of these agents compared to placebo followed the same pattern and is also shown in Table 1 below.

Table 1. Weight Loss and Adverse Event Outcomes with Medications for Long-term Weight Loss* [152]

Medication for weight loss	Mean weight loss versus placebo	≥5% weight loss (OR)	≥10% weight loss (OR)	Discontinuation due to an adverse event (OR)
Phentermine/topiramate	-8.80 kg	9.22	11.40	2.29
Liraglutide	-5.24 kg	5.54	4.99	2.95
Naltrexone/bupropion	-4.95 kg	3.96	4.19	2.64
Orlistat	-2.63 kg	2.70	2.42	1.84

* lorcaserin is not included in this table as it was requested to be removed from the U.S. market in February 2020.[153] Data for lorcaserin: MD -3.25 kg; OR ≥5%: 3.10; OR ≥10%: 3.20; OR discontinuation due to adverse event: 1.34.

Abbreviations: OR: odds ratio

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 weight loss medications evaluated were associated with a statistically significant risk of medication discontinuation due to adverse events when compared to placebo.[152] Liraglutide had the highest odds of treatment discontinuation, followed by fixed-combination naltrexone/bupropion, fixed-combination phentermine/topiramate, then orlistat (see Table 1).[152] As noted in the 2018 USPSTF systematic review,[2] trials of weight loss medications often had very selective inclusion and exclusion criteria. Included 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 weight loss medications. In addition, certain pharmacotherapies may be inappropriate for patients with conditions such as HTN, hyperthyroidism, valvular heart disease, nephrolithiasis, glaucoma, cholestasis, seizure disorder, drug misuse disorder potential, pregnancy, or 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 H for additional information on pharmacotherapy considerations). It is also appropriate to carefully evaluate medication lists to eliminate or reduce agents that cause weight gain as a side effect (see Sidebar 2).

There are also several medications approved by the FDA for short-term (i.e., "few weeks") weight reduction (e.g., benzphetamine, diethylpropion, phendimetrazine, phentermine). 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 that evaluated benzphetamine, diethylpropion, phendimetrazine, or phentermine for short-term use (i.e., less than or equal to six months). Therefore, the Work Group was unable to comment on the safety or efficacy of these medications for short-term weight loss.

This CPG update also evaluated the long-term health benefits (e.g., impact on morbidity and mortality) following long-term (defined as greater than six months) or intermittent use of these medications. 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.[154] 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. 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 or intermittent use. Moreover, 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 not be used in individuals with a history of CVD. As treatment options for short-term weight loss were noted as a topic of interest by participants in the patient focus group, additional data on the safety, efficacy, benefits, and durability to achieve and maintain weight loss goals using this practice are needed.

Weight Maintenance

The Work Group also reviewed evidence on continued use of weight-loss medications for weight maintenance. One SR comprised the evidence base; it demonstrated a benefit on maintenance of weight loss with liraglutide or orlistat.[2] 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 addition, patients receiving higher dose orlistat had significantly less weight regain (2.6 kg) than patients receiving a placebo (4.4 kg). However, when evaluating results from both the higher and lower doses of orlistat, there was no difference in the proportion of patients who maintained a 5% or 10% weight loss compared to placebo.[2] It was also noted that orlistat was more likely to cause adverse reactions resulting in treatment discontinuation compared to placebo. A larger percentage of patients experienced GI adverse events with orlistat (up to 95%) versus placebo (up to 68%). Patients treated with liraglutide also experienced more GI adverse events compared to placebo (74% versus 45%, respectively), and withdrawal due to GI adverse events was higher with liraglutide versus placebo.[2] The 2014 VA/DoD Obesity CPG also included evidence in support of the role of fixed-combination phentermine/topiramate in maintenance of weight loss.[155] This study found that significantly more patients in the fixed-combination phentermine/topiramate 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.[155] As reported in the SR by Khera et al. (2016), there is a lack of data on maintenance therapy (i.e., after the initial 13 months of use) with fixed-combination naltrexone/bupropion.[152] Due to the lack of studies on this medication in the evidence base, it is not addressed in the recommendation. Data are available on the benefits of weight loss maintenance following two years of continued lorcaserin use after initial weight loss of ≥5%.[156] However, the FDA requested this agent be removed from the U.S. market on February 13, 2020, over the potential increased risk of cancer outweighing the benefits of use.[153]

Although the evidence on weight maintenance was not included as supporting evidence for the current recommendation on pharmacotherapy, the Work Group included this topic in the discussion given the recognition in 2013 of obesity as a chronic disease requiring intervention by the American Medical Association.[157] Further, it is important to emphasize that long-term weight management includes both initial weight loss as well as maintenance of weight reduction. As patients regain weight when weight loss medications are discontinued, many patients may require long-term therapy (see also Recommendation 3 regarding offering a CLI for weight maintenance). Long-term use of medication for weight maintenance may be challenging, especially given the potential for adverse events and subsequent high discontinuation of medications.[2,152]

Comorbidities and Cardiometabolic Parameters

As patients with overweight or obesity may also have related comorbid conditions, the Work Group sought evidence on the impact of weight-loss pharmacotherapy on the critical outcomes of weight loss and adverse events in patients with select comorbidities. In addition, the effects of treatment on cardiometabolic parameters were considered important outcomes in patients with overweight or obesity who may or may not have a weight-related comorbidity. In general, the impact on cardiometabolic parameters was inconsistent and varied across medications.[152] According to one SR that included studies with orlistat and phentermine/topiramate, in addition to weight reduction, weight-loss pharmacotherapy had a beneficial effect on BP reduction in patients with HTN.[158] Additionally, pharmacotherapy improved glycemic parameters and reduced progression to and increased remission of T2DM.[159-161] The benefit of weight-loss pharmacotherapy in patients with T2DM or prediabetes is also supported in the literature noted in the 2014 VA/DoD Obesity CPG,[162-164] as well as in an individual RCT from an SR included in systematic evidence review carried out as part of this guideline update.[165]

Overall, treatment with weight-loss pharmacotherapy appeared to be well tolerated; however, treatment-related side effects were also noted in several of the studies.[158,159,166] Data were limited on the long-term outcome benefit of weight-loss pharmacotherapy on reduction in CV events or mortality in patients with overweight or obesity. Evidence from one RCT with 3.3 years follow-up designed to assess the CV safety of lorcaserin found no difference compared to placebo in the primary safety outcome of major CV events. However, this agent has been removed from the U.S. market.[153] Additional evaluation of the efficacy outcome of extended major CV events reported no difference with treatment compared to placebo.[16] Regarding the effect on cardiometabolic parameters, one SR and meta-analysis noted that, overall, pharmacotherapy for obesity had a modest reduction in fasting blood glucose and hemoglobin A1c (HbA1c) compared to placebo, a small-to-moderate decrease in WC, and minimal changes in BP and lipid parameters.[167] The Work Group acknowledged the variable effects on cardiometabolic parameters of the different weight-loss medications and the need for individualized treatment based on these as well as

other factors, including the potential for adverse effects and patient tolerability (see Appendix H on pharmacotherapy). Also, the scope of the systematic evidence review carried out as part of this guideline update included only FDA-approved medications with the specific indication for weight loss at the time of the inquiry. Additional agents may gain FDA-approval for an indication of weight loss in the future.

The evidence to support the recommendation was moderate for the outcomes of weight loss and achievement of 5% and 10% weight loss in comparative studies of treatment versus placebo. Most studies, including the SR,[167] documented the serious limitation of attrition above 30%. For the weight-loss medications considered in the evidence review (specifically liraglutide, fixed-combination naltrexone/bupropion, orlistat, and fixed-combination phentermine/topiramate, lorcaserin having been removed from the U.S. market) [153] the benefits 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. Weight-loss 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 H on pharmacotherapy and Sidebar 2 on select medications and their potential effects on weight).

Summary

As Recommendation 9 is a *Reviewed, New-replaced* recommendation, the Work Group systematically reviewed evidence related to this recommendation [2,152,154-156,158-160,164,166,167] and considered the evidence put forth in the 2014 CPG.[155,162,163] 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).

As Recommendation 10 is a *Reviewed, New-added* recommendation, the Work Group systematically reviewed evidence related to this recommendation.[154] The Work Group's confidence in the quality of evidence was low. The body of evidence had serious study limitations including a single-blind evaluation and moderate-to-high attrition. The benefits and harms were unknown due to the small sample size in the only trial evaluating long-term treatment and no evidence that met the search parameters for short-term or intermittent use. The potential for harm with long-term use of these sympathomimetic agents is unknown, especially in an older patient population with potential for CVD, or in patients at risk for or with a history of substance use disorder. Patient values and preferences were somewhat varied. Thus, the Work Group decided upon a "Neither for nor against" recommendation. Given that most research with these

medications was conducted decades ago, and primarily for short-term use, additional research is needed to determine the safety and efficacy of these medications when prescribed long term or for intermittent use. In addition, as treatment options for short-term weight loss were noted by participants as a topic of interest in the patient focus group, additional data on the safety, efficacy, benefits, and durability to achieve and maintain weight loss goals using this practice are needed.

e. Dietary Supplements and Nutraceuticals

Recommendation

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)

Discussion

There is a lack of evidence demonstrating clinically meaningful short-term weight loss or to support long-term weight management or weight maintenance using nutraceutical or dietary supplements. A nutraceutical can be defined as "a food or dietary supplement that is believed to provide health benefits".[168] A combination of eight SRs and RCTs, which studied various nutraceuticals, were identified and reviewed for this recommendation.[169-176] Overall, the confidence in the quality of evidence was rated low to very low due to lack of adequate randomization, blinding, allocation concealment, and high risk of bias. Inconsistent dosing of specific nutraceuticals and lack of generalizability of findings was noted across multiple studies.

An SR of 15 RCTs (n=1,130) by Huang et al. (2019) 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).[169] 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. (2019) 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).[170] The generalizability of outcomes to the VA/DoD population is limited. Specifically, of the 14 studies included in the SR, only three were conducted in western cultures – two in the U.S. and one in the United Kingdom (U.K.); the remainder were conducted in the Middle East. Additionally, at least half of the included studies included only female subjects. Inconsistent heterogeneous dosing of cinnamon was also noted.

With regard to garcinia cambogia, a small RCT conducted by Tripathy et al. (2013) found statistically significant (p<0.0001) short-term weight loss, measured by BMI, following four months of garcinia cambogia use.[171] 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 benefit. 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. Given these risks, harms and burdens of garcinia cambogia were judged to outweigh the limited potential benefit.

No statistically significant weight loss was found with the use of green tea versus placebo across the two studies reviewed.[172,173] 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 specifically had any 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.[174] Phaseoulus 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.[175] 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.[176] The study participants were all female.

Responses obtained from the patient focus group reflected some interest in dietary supplements, nutraceuticals, and over-the-counter (OTC) products for short-term weight loss, particularly in the active duty cohort who noted the negative effects of overweight and obesity on their military careers (see Appendix B). However, the Work Group found insufficient evidence of benefit to support an evidence-based, positive recommendation for the use of any nutraceutical for clinically meaningful short-term weight loss or long-term weight management. Since dietary supplements and nutraceuticals are not evaluated for safety and effectiveness before sale to consumers in the U.S., products sold to consumers may vary in purity, consistency, ingredient content, and dosing.[177]

Moreover, dietary supplements and nutraceuticals have generally not been studied in conjunction with CLIs, so there is insufficient evidence on whether the active dietary supplement or nutraceutical product outperforms placebo in conjunction with CLI, which the Work Group considered being a core component of any long-term weight management intervention. Moreover, the perceived benefits of dietary supplements and nutraceuticals, fueled by marketing and anecdotal reports, may create unrealistic expectations that limit patient and clinician interest and investment in the specific evidence-based interventions recommended in this CPG.

Summary

As this is a *Reviewed, New-added* recommendation, the Work Group systematically reviewed evidence related to this recommendation.[169-176] The Work Group's confidence in the quality of evidence was low. The body of evidence had many limitations and confounders of the evidence, including small sample sizes,[171] heterogeneity of supplement dosing and concentration,[170] use of highly selective study population,[174] and risk for bias.[174] Additional considerations were cost to the patient, pill burden, and the potential to divert patient interest and investment away from evidence-based interventions. There is

also concern that dietary supplements and nutraceuticals are not tested by the FDA for safety and effectiveness before being sold, allowing for product contamination and inconsistent formulation of product contents. The limited evidence for benefit was weighed against potential harms, including toxicity and other adverse health effects. Thus, the Work Group decided upon a "Weak against" recommendation.

e. Metabolic/Bariatric Procedures and Devices

Recommendation

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)

Discussion

Surgeries for weight loss – also known as metabolic/bariatric surgeries – are procedures that involve stapling part of the GI system. There is growing recognition that these procedures contribute to neurohormonal effects on the regulation of energy balance and hunger control. Metabolic/bariatric surgeries, in conjunction with CLIs, are the most durable modality to affect long-term weight loss and offer a potential remission of T2DM without the use of diabetic medications. Multiple studies confirm the superiority of surgical intervention to medical management of T2DM for achieving remission of T2DM among Class I obesity.[178,179]

One RCT of participants with a BMI of 30 to <35 kg/m^2 (Class I obesity) demonstrated that 65% of those who had metabolic/bariatric surgery experienced remission of T2DM compared to 0% with medical management; HbA1c decreased from 7.7% to 6.2% with surgery and from 7.9% to 7.4% with medical management.[178]

An SR of 13 controlled trials of metabolic/bariatric surgery versus medical management (which included lifestyle modification and weight management) in patients with T2DM and a mean BMI <40 g/m^2 included two RCTs and six observational clinical studies that only included subjects with a BMI <35 g/m^2.[179] Among the eight studies in the SR that included only patients with BMI <35 kg/m^2 (n=331), the odds ratio (OR) for achieving remission of T2DM was 21.8 favoring surgery (95% CI: 7.7 to 61.6), and the OR for achieving an HbA1c less than 7% with or without DM medication was 11.4 (95% CI: 3.8 to 34.7), favoring surgery.[179]

Of the two RCTs [180,181] from the Muller-Stich et al. (2014) SR [179] that only included subjects with a BMI <35 g/m^2, one included participants with a BMI over 28 kg/m^2 and a mean BMI of 30.48±0.94 kg/m^2.[180] Type 2 diabetes mellitus remission (HbA1c from 10.47% to 5.98%) was achieved in 90% of patients who underwent surgery, in contrast to no remission (HbA1c from 10.88% to 8.14%) with medical management. In the second RCT [181], which included participants with a BMI of 25–30 kg/m^2, T2DM remission was achieved in 52% of patients who underwent surgery (mean HbA1c from 6.9% to 6.1% after surgery), in contrast to only 8% of participants with medical management (HbA1c from 7.2% to 7.3%).

Randomized controlled trials that included only participants with a BMI of 30 – 40 kg/m^2 showed similar results. For example, another RCT [182] from the Muller-Stich et al. (2014) SR [179] in which the mean BMI

was 37±2.7 kg/m^2 showed T2DM remission in 73% of patients following surgery (HbA1c from 7.8% to 6%) and 13% of patients with medical management (HbA1c from 7.6% to 7.21%). Similarly, in another RCT [183] from the Muller-Stich et al. (2014) SR [179] in which the mean BMI was 34.9 kg/m^2, T2DM remission was achieved in 49% of patients following surgery (HbA1c from 9.6% to 6.3%). This contrasted with T2DM remission in 19% of patients with medical management (HbA1c from 9.6% to 7.8%). Likewise, in another RCT [184] from the Muller-Stich et al. (2014) SR [179] in which mean BMI was 35.5±3, T2DM kg/m^2, T2DM remission was seen in 50% of patients with Roux-en-Y Gastric Bypass (RYGB) (HbA1c from 8.7% to 6.4%), in 27% of patients with sleeve surgery (HbA1c: 7.9% to 6.85%), and in no patients with medical management (HbA1c from 7.0% to 6.94%).

Additionally, an RCT [185] from the Muller-Stich et al. (2014) SR [179] of participants with a BMI of 27 – 43 kg/m^2 (mean BMI: 37 kg/m^2 ±3.3 kg/m^2) showed superior remission of T2DM with metabolic/bariatric surgery compared to medical management. T2DM remission was achieved in 42% of patients following surgery (HbA1c from 9.4% to 6.5%) and 12% with medical management (HbA1c from 8.9 to 7.5%).

Type 2 diabetes mellitus and obesity are both chronic diseases, with an expectation of progressive deterioration over time in glucose control (secondary to progressive loss of beta-cell function). The opportunity to intervene in this disease earlier in its course is appealing. The potential benefits (improved QoL with remission of T2DM) of metabolic/bariatric surgery outweighed potential harms (surgical complications). Patients with Class I obesity have been observed to not lose "excessive weight" (i.e., they do not reach an unhealthy weight loss resulting in malnutrition) as a result of surgical intervention.

Surgical intervention is a major decision and an individual patient may not accept potential surgical inconveniences or risks, or be a suitable surgical candidate. Moreover, active duty military personnel are not authorized to receive metabolic/bariatric surgery.[186]

Similar recommendations have stemmed from the Diabetes Surgery Summit II and have been endorsed by numerous medical and scientific organizations worldwide.[187] These society endorsements, however, did not contribute to the process we utilized to generate this recommendation.

Summary

This is a *Reviewed, New-added* recommendation, the Work Group systematically reviewed evidence related to this recommendation.[178,179,187-189] The Work Group's confidence in the quality of evidence for most outcomes assessed in the reviews comparing metabolic/bariatric surgery to non-surgical interventions was rated as low to very low. These ratings are primarily due to limitations in the methodological quality of both the randomized and non-randomized trials and to evidence of substantial heterogeneity in the effect estimates between trials. Most of the reviews involved small study populations and long-term data is lacking. Thus, the Work Group decided upon a "Weak for" recommendation.

Recommendation

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)

Discussion

The 2014 VA/DoD Obesity CPG recommended offering metabolic/bariatric surgery in addition to a CLI for weight loss and to improve most obesity-associated conditions in adult patients with BMI >40 kg/m^2 or those with BMI 35.0 – 39.9 kg/m^2 with one or more obesity-associated conditions. Evidence published since 2014 further supports that metabolic/bariatric surgery, in conjunction with a CLI, results in significant weight loss and sustained weight management in patients with a BMI ≥40 kg/m^2 or those with BMI >35.0 – 39.9 kg/m^2 with one or more obesity-associated conditions.

Based on research conducted by Cheng et al. (2016) and O'Brien et al. (2019), treatment with metabolic/bariatric surgery was associated with improvements in excess weight loss and long-term (>10 years) excess weight loss.[187,189] Yang et al. (2018) also found a significant improvement in BMI.[190] The evidence for the effect of metabolic/bariatric surgery on weight loss included a large, fair quality SR of 16 RCTs (n=1,194) comparing metabolic/bariatric surgery to lifestyle and/or medication interventions in patients with obesity. Follow-up ranged from 1 – 3 years.[187] The investigators reported an MD of -20.96 kg (CI: -24.51 to -17.41) in weight loss at least one year post-surgery across all metabolic/bariatric surgery techniques (sleeve gastrectomy, RYGB, laparoscopic adjustable gastric banding [LAGB], biliopancreatic diversion [BPD]).[187] Across the eight studies (n=478) that calculated percent excess weight loss, the MD was 63.74% (95% CI: 58.73 to 68.76).

Metabolic/bariatric procedures are associated with T2DM remission.[191,192] as well as improvements in WC,[187,193] fasting glucose and HbA1c,[187,191] triglycerides, BP, total cholesterol,[187,191,193] QoL,[194] and physical functioning.[195]

Evidence from an SR of 19 non-randomized studies (n=28,528 patients who received surgery, n=169,704 patients who received non-surgical interventions) suggests that metabolic/bariatric surgery reduced all-cause mortality (OR: 0.55; 95% CI: 0.46 to 0.65) as well as mortality from myocardial infarction (MI), stroke, angina, ischemic heart disease, any type of cancer, and obesity-related cancer compared to non-surgical interventions at an average of 10 years follow-up.[196] However, evidence from seven RCTs reported in the same SR did not demonstrate a significant difference between metabolic/bariatric surgery and non-surgical interventions for these outcomes at 1 – 2 years follow-up. Six RCTs from another SR had no treatment-related deaths among patients with T2DM who underwent RYGB, nor were there deaths among patients who received non-surgical lifestyle or medication therapy at 1 – 5 years follow-up.[193] However, there were more nutritional deficiencies, anastomotic ulcers and leaks, and intestinal obstructions in the surgical group.[193] In addition, there is evidence from an SR of 32 non-RCTs (n=148,643) that suggests patients who undergo metabolic/bariatric surgery are at elevated risk for death by suicide and suicide attempt/self-harm compared to control populations with similar demographic characteristics.[188] This

may be related to a range of contributing factors including possible psychiatric, medical, psychosocial, and physiologic changes.

Despite general consistency in the evidence supporting bariatric procedures for weight loss and improvement in obesity-associated medical conditions, there is variability in provider and patient preferences regarding this treatment. Furthermore, active duty Service Members are not authorized to receive this permanent weight loss surgery.[186] Therefore, by denying this effective obesity treatment, an active duty career may be affected by decreased promotion and retention. Other considerations include access to trained surgical personnel, high cost for the procedure, insurance coverage, availability of post-surgical monitoring, and requirements for managing comorbid medical and psychiatric conditions.

Summary

As this is a *Reviewed, New-replaced* recommendation, the Work Group systematically reviewed evidence related to this recommendation.[187-196] The Work Group's confidence in the quality of evidence was very low because it included observational data. The marked benefits, such as including improved mean weight loss, improvement in percent excess weight loss, improved weight maintenance for a large proportion of surgical patients, T2DM remission, and remission of other obesity-related conditions, outweighed the potential harm of adverse events. Patient values and preferences were somewhat varied. Thus, while the Work Group considered metabolic/bariatric surgery standard of care, the data limitations restricted the Work Group to a "Weak for" recommendation.

Recommendation

14. There is insufficient evidence to recommend for or against metabolic/bariatric surgery to patients over age 65.
    (Neither for nor against | Reviewed, Amended)

Discussion

There are data comparing people older or younger than age 65 who underwent metabolic/bariatric surgery. One observational study showed that the benefits of weight loss, remission of T2DM, and incidence of HTN and OSA after metabolic/bariatric surgery were similar for both age groups.[197]

However, three observational studies showed that people ≥65 years who received metabolic/bariatric surgery experienced a higher prevalence of early post-surgical complications and mortality than younger people.[198-200] One of these studies included 24,014 people between the ages of 40 and 49 and 739 people over age 70. It showed the prevalence of minor complications was 4.6% in the younger cohort and 9.1% in the older cohort; major complications were 2.2% in the younger and 6.3% in the older cohort; and 30-day mortality was 0.1% in the younger and 0.5% in the older cohort.[198] Another of these studies included 5,395 people age 65 or younger and 5,395 people over the age of 65. This study found that mortality was 0.14% higher and nonfatal complications were 1.01% higher after sleeve gastrectomy in people 65 years or older than in those who were younger than 65 years. The complication rates were higher overall for patients undergoing RYGB than sleeve gastrectomy, but there was no significant difference in complication rates for older versus younger patients who received an RYGB in this study.[199] The final study included 39,465 people who received an RYGB and 42,495 people who received a laparoscopic sleeve gastrectomy whose average age was 43.7±10.8 years. It also included 2,010 people

who received an RYGB and 2,055 people who received a laparoscopic sleeve gastrectomy whose age was 67.5±2.48 years. The study showed that serious morbidity with RYGB was 3.4% in younger and 5.7% in older people. It also showed that serious morbidity with laparoscopic sleeve gastrectomy was 2.2% in younger and 4% in older people. Furthermore, it showed that 30-day mortality with laparoscopic sleeve gastrectomy was 0.07% in younger and 0.29% in older people.[200]

Additionally, there is data comparing people older or younger than age 60 who underwent metabolic/bariatric surgery. An SR of nine observational studies that included 4,025 people under the age of 60 and 366 people age 60 or older who had metabolic/bariatric surgery showed that people age 60 or older who underwent RYGB experience significantly higher rates of early post-surgical complications (OR: 1.89; 95% CI: 1.07 to 3.3).[201] Similarly, older people had higher mortality at 1.6% than younger people at 0.3% (OR: 4.38; 95% CI: 1.25 to 15.31). Interestingly, three of the studies included in this SR, including 793 younger people and 148 older people, suggest people 60 years and older did not lose as much weight compared to younger people (MD: -5.86; 95% CI: -9.15 to -2.56). This contrasts with the data comparing people who are older or younger than 65 years where weight loss benefits were similar.

The decision to offer metabolic/bariatric surgery is a clinical judgment based on individual patient risk factors and preferences. The benefits of weight loss and remission of obesity-related comorbidities appear similar for people ≥65 years compared to those who are younger. However, part of the surgical benefit is the length of improved QoL, and older people have, on average, a shorter lifespan after surgery than those who are younger.

Summary

As this is a R*eviewed, Amended* recommendation, the Work Group systematically reviewed evidence related to this recommendation.[197-201] The Work Group's confidence in the quality of evidence was very low. Concerns about the quality of studies comparing older and younger patients contribute to the uncertainty about the relationship between older age and benefits and harms from surgery. Limitations of the evidence including retrospective observational study designs, limited information about patient selection, and cofounder analyses. Patient values and preferences have large variations regarding surgery. Thus, the Work Group decided upon a "Neither for nor against" recommendation.

Recommendation

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)

Discussion

Percutaneous gastrostomy is a device used for weight loss and is similar in structure to percutaneous endoscopic gastrostomy (PEG) tubes. However, patients remove gastric contents after meals with the percutaneous gastrostomy device instead of using it for feeding. The use of a percutaneous gastrostomy as a weight-loss device has been found to offer a modest improvement in short-term weight loss for patients with a BMI of 40 – 45 kg/m^2 or a BMI of 35 – 39.9 kg/m^2 with comorbid conditions.

A 2017 RCT by Thompson et al. (n=207) compared the percutaneous gastrostomy device plus a CLI versus CLI alone.[202] At 52 weeks, subjects in the device group achieved a mean excess weight loss of 35.1% and total weight loss of 12.1% compared to a mean excess weight loss of 9.8% and total weight loss of 3.5% in the CLI-only group.[202] This study was limited to one year and does not provide long-term safety or efficacy data. The most frequent adverse events reported were abdominal pain and discomfort, peristomal granulation tissue, and peristomal irritation.

The overall findings of the limited evidence available assessing the efficacy of the FDA-approved gastrostomy device suggest there was a reduction in weight loss as compared to a control that included a CLI. The evidence from these trials also suggests the device may improve obesity-related comorbid conditions including T2DM, hyperlipidemia, and HTN. It may also improve CV and metabolic biomarkers including fasting blood glucose, HbA1c, and BP. Ikramuddin et al. (2014) notes the limitations of low representation of patients with T2DM, hyperlipidemia, and HTN within their study group population.[203]

Summary

As this is a *Reviewed, New-added* recommendation, the Work Group systematically reviewed evidence related to this recommendation.[202-205] The Work Group's confidence in the quality of evidence was moderate. The benefits of weight loss and improved QoL outweighed the potential harms, which include pain and gastroesophageal reflux disease (GERD). However, there is concern that the use of percutaneous gastrostomy devices could promote continued poor lifestyle habits. Overall, because the evidence for efficacy of each device is limited to one RCT, the Work Group determined there is insufficient evidence to recommend for or against the use of percutaneous gastrostomy devices for weight loss. Further research is required to compare the effectiveness of weight-loss devices to other obesity treatments and to assess long-term durability of weight loss and safety.

B. Short-term Weight Loss (Up to Six Months)

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)

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)

Discussion

Intragastric balloon (IGB) devices are placed into the stomach either endoscopically or by swallowing the deflated device while being medically supervised. The device is then inflated with gas or fluid and resides in the stomach for up to six months. These non-permanent devices are deflated and subsequently removed after a treatment period.

The use of any non-permanent bariatric device for the treatment of obesity (BMI ≥30 kg/m^2) or obesity-related conditions should be discussed with a bariatric surgeon or gastroenterologist as they can manage the placement, monitoring, and removal of the device.

IGB devices are currently FDA approved for a treatment duration of up to six months for patients with a BMI of 30 – 40 kg/m^2. No studies that examined longer term use of IGBs met criteria for inclusion in the evidence review carried out as part of this guideline update. Additionally, there were no long-term studies (>12 months) evaluating the impact of short-term use of IGBs in combination with CLI on long-term weight loss to support chronic weight management or weight maintenance.

Short-term use (up to six months) of IGBs reduces weight, BMI, waist circumference, and percent body fat to a greater degree than lifestyle interventions or sham therapy alone.[206-209] In a 2015 SR of four RCTs, Zheng et al. found that when the IGB treatment duration was less than six months, the MD in weight loss was -1.54 kg (95% CI: -2.02 to -1.06; n=171) and the MD in BMI was -1.19 kg/m^2 (95% CI: -2.10 to -0.281; n=82).[209] When the duration of treatment with IGB was six months, the MD in weight loss was -8.87 kg (95% CI: -10.28 to -7.46; n=262); the MD in BMI was -3.10 kg/m^2 (95% CI: -3.91 to -2.30; n=244); and the MD in percent excess weight loss was -21.0 kg (95% CI: -27.4 to -14.6; n=256). Treatment with an IGB was also associated with higher remission of comorbid T2DM when compared to CLI alone.

A fair quality SR by Popov et al. (2017) found an OR of 1.4 (95% CI: 1.3 to 1.6; n=4,232) for the remission of T2DM with IGB compared to conservative control in nine observational studies. It also found that the MD in fasting blood glucose was -12.7 mg/dL (95% CI: -21.5 to -4.0; n=555), and the MD in HbA1c was -1.1% (95% CI: -1.6 to -0.6; n=63) in the IGB group compared to the control group in eight RCTs.[206] There was conflicting evidence, however, regarding improvements in comorbid conditions including HTN, dyslipidemia, and NAFLD.[206,207] Evidence also indicates some level of harm associated with IGB. A 2015 SR of four RCTs, Zheng et al. identified the following adverse events: nausea (72%), vomiting (39%), abdominal pain (50%), and gastric erosion (32%).[209] In a 2018 SR of 10 studies (five RCTs and five prospective non-randomized trials), Trang et al. identified the following adverse events: nausea (63%), vomiting (55%), abdominal pain (59%), and gastroesophageal reflux (21%).[210] It is unclear if and how frequently these adverse events led to attrition before the FDA-approved six month treatment period.

Despite general consistency in the evidence supporting short-term use of an IGB in conjunction with a CLI for weight loss in patients with obesity, there is a high amount of variability in provider and patient preferences regarding this treatment. The patient focus group revealed that patients want education and counseling on more weight-loss options. They specifically want more options to achieve short-term weight loss, which can affect them medically (e.g., weight loss prior to surgery, weight loss to get pregnant, weight loss to control T2DM) and professionally (e.g., retention in the military, promotion candidacy). There is little, if any, evidence that there is a medical benefit to achieving short-term weight loss. Access to this treatment is limited, as the procedure usually requires a surgeon or endoscopist with adequate training as well as a facility meeting safety and quality standards to support the procedure. Active duty Service Members have additional constraints, as they are not permitted to undergo permanent metabolic/bariatric surgery procedures.[186] Temporary and removable bariatric devices like the IGB may provide an effective short-term, non-permanent alternative for active duty Service Members. Financial constraints may additionally burden the patient, as the cost of treatment is not always covered by insurance companies. A certain level of subjectivity in candidacy for this bariatric procedure is present

based on the professional experience of the surgeon or endoscopist in identifying the true and total risks and benefits unique to each patient.

Summary

As these are *Reviewed, New-added* recommendations, the Work Group systematically reviewed evidence related to them.[206-210] The Work Group's confidence in the quality of evidence was moderate. The main limitation regarding the body of evidence is the short-term use of the intervention (up to six months) with short-term follow-up (up to 12 months). Other considerations regarding these recommendations included the benefits of comorbid T2DM control or even remission outweighing the potential harm of adverse events as they were mild in severity, despite being common. Thus, regarding IGBs, the Work Group decided upon a "Weak for" recommendation for short-term weight loss and a "Neither for nor against" recommendation for chronic weight management or weight maintenance.

Recommendation

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)

Discussion

A low-carbohydrate diet (the specific definition of which varies substantially from study to study) of ≤40% of calories from carbohydrate or ≤120 grams of carbohydrate a day has been found to promote weight loss (MD weight loss ranged from -2.04 kg to -3.6 kg) in the short-term (≤6 months) in patients with overweight and obesity compared to low-fat diets.[130,134,137,139,141,144,211]

An SR of 17 trials (n=1,797) by Sackner-Bernstein et al. (2015) found that, compared to a low-fat diet, a low-carbohydrate diet was associated with statistically significant improvements in BMI (MD: -0.7 kg/m^2), triglycerides (MD: -28.8 mg/dL), and systolic BP (MD: 1.7 mmHg). There was, however, a statistically significant worsening of total cholesterol (MD: 9.1 mg/dL) and low-density lipoprotein cholesterol (LDL-c) (MD: 8.6 mg/dL) but a statistically significant increase in high-density lipoproteins cholesterol (HDL-c) (MD: 5.1 mg/dl) in those on a low-carbohydrate diet compared to a low-fat diet.[130] A meta-analysis of five trials (n=447) by Nordman et al. (2006) which was not included in the evidence review also found that, compared to participants on a low-fat diet, participants on a low-carbohydrate diet lost more weight than those on a low-fat diet at six months (weighted MD: -3.3 kg); however, at 12 months the difference was no longer significant. Those randomized to a low-carbohydrate diet had significant improvements in triglycerides (weighted MD: -22.1 mg/dL) and HDL-c (weighted MD: 4.6 mg/dL) but worsening of total cholesterol and LDL-c on a low-carbohydrate diet (weighted MD: 5.4 mg/dL) at six months.[139]

Another meta-analysis of 23 RCTs (n=2,788) by Hu et al. (2012) found that, compared to participants on a low-fat diet, participants on a low-carbohydrate diet had less reduction in total and LDL-c (2.7 mg/dL and 3.7 mg/dL, respectively), but the low carbohydrate arm had more triglycerides lowering (-14.0 mg/dL), and a 3.3 mg/dL improvement in HDL-c.[138] Finally, a fourth SR by Hession et al. (2009), not included in the evidence review, which included 13 RCTs of low-carbohydrate diets compared with low-fat/low-calorie diets of at least six months duration, also found that there were significant differences between the groups

for weight at six months, HDL-c, triglycerides, and systolic BP in favor of the low-carbohydrate diet. There was similar weight loss between arms at 12 months. They found lower attrition for the low-carbohydrate arms, suggesting there may be a patient preference for low-carbohydrate diets.[211]

Other smaller studies, some of which were not included in the evidence review, yielded similar results of more weight loss at six months on a low-carbohydrate diet compared to a low-fat diet, with similar weight loss on both diets at 12 months and more improvement in HDL-c and triglycerides in the low-carbohydrate arms.[134,137,141,211] In a 2004 study by Yancy et al., not included in the evidence review, 120 participants (BMI 30 – 60 kg/m^2 with total cholesterol >200 mg/dL and LDL-c >200 mg/dl or triglycerides >200 mg/dL) were randomized to either a low-carbohydrate ketogenic diet (initially, <20 g of carbohydrate daily), or a low-fat diet. Participants on the low-carbohydrate ketogenic diet reported a statistically significant increase in adverse events compared to participants in the low-fat arm: constipation (68% versus 35%), headache (60% versus 40%), halitosis (38% versus 8%), muscle cramps (35% versus 7%), diarrhea (23% versus 7%), general weakness (25% versus 8%), and rash (13% versus 0%), deemed 'mild' by the authors. The authors reported greater weight loss in the low-carbohydrate diet group at six months (MD: -12.9% versus -6.7%; p<0.001), and more patients randomized to the low-carbohydrate diet completed the study (76% in the low-carbohydrate arm versus 57% in the low-fat arm).[144]

Despite general consistency in the evidence supporting a weight loss advantage to low-carbohydrate diets over low-fat diets for short-term weight loss (up to six months), there is some variability in provider and patient preferences regarding this treatment. As discussed in Recommendation 7, the dietary approach most appropriate for each patient is determined by what the patient can adhere to and sustain for weight loss and maintenance. The patient focus group revealed that patients want specific information about effective dietary approaches, but some patients may find that following a low-carbohydrate diet does not meet their food preferences.

Summary

As this is a *Reviewed, New-added* recommendation, the Work Group systematically reviewed the evidence related to this recommendation.[130,134,138] The Work Group's confidence in the quality of evidence was very low. The body of evidence had some limitations including short duration, loss to follow-up, high dropout, and heterogeneity in study interventions.[130] The benefits of improved body weight and lipid values outweighed the potential harm of adverse events, which was small. Patient values and preferences were somewhat varied. The Work Group also considered the resources requirements of training providers to provide diet plans and the challenges patients may face in adhering to diets. Therefore, the Work Group decided upon a "Weak for" recommendation.

VIII. Knowledge Gaps and Recommended Research

During the development of the 2020 VA/DoD Obesity CPG, the Work Group identified many topics for future research. Given the continued rise in national rates of obesity, as tracked in the Behavioral Risk Factor Surveillance System monitored by the CDC,[212] more effective interventions and implementation of current options are needed. Projects to address these topics will lead to stronger evidence to support current recommendations, as well as new evidence to guide future CPGs.

Despite the progress that has been made since the publication of the 2014 VA/DoD Obesity CPG in identifying effective interventions to assess and treat overweight and obese adults, many important gaps remain, particularly regarding the impact of weight management interventions on long-term outcomes, including long-term maintenance of weight loss, QoL, NAFLD, CV morbidity (e.g., MI and ischemic stroke), and all-cause mortality. Because BMI may not be the best predictor of future disease and mortality, future trials should include more recently developed classification systems to characterize obesity severity, including use of body composition measures that are relevant to military service and readiness.[213,214] There is an imperative to develop an actionable diagnosis and staging system relevant to the current needs of the U.S. military. Future research should also focus on the benefits of weight-loss interventions in lower risk and specific subgroups (e.g., those who are overweight, older, from lower risk racial/ethnic groups, after spinal cord injury/disorder, or "metabolically healthy") to determine if weight loss has lasting benefits in these populations.[2]

Comprehensive lifestyle intervention programs can be expensive and difficult to deliver and maintain. 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 physical activity, more research is needed comparing the effectiveness of offering interventions that feature generalized "lifestyle physical activity" with more intense and structured exercise programs on multiple key outcomes, including weight loss, weight maintenance, obesity-related comorbid conditions, and other health-related outcomes. Within the sphere of nutrition, ongoing confusion remains, and there is a need for clarity regarding the standard definitions of specific dietary patterns. This is most evident when attempting to compare the efficacy of dietary interventions between and among studies, as the actual dietary interventions vary, limiting true comparisons. Specifically coming to a consensus within the research community as to what constitutes various dietary interventions (e.g., a low-fat diet, a low-carbohydrate diet, a low glycemic index diet, a Mediterranean diet, duration and timing of fasts within intermittent fasting) would be of critical importance to move this field forward from hypotheses to a more solid evidence base. Clarity and consistency in definitions of diets would then allow for more head-to-head comparisons between diets. For example, when considering the dietary component of CLI, consensus is needed on definitions of "low-carbohydrate" and "low-fat" nutrition. Research comparing calorie restriction and carbohydrate restriction to assess effectiveness and feasibility in the long term is also needed. Research must also consider how individual preferences, whole diets (diets characterized by types of foods and meals, rather than on micro or macronutrient content), and eating patterns impact long-term adherence to diets that support weight loss and weight maintenance. Such research would improve our ability to offer treatments that more closely align with sustainable behavior change for individual patients.

As with all other chronic disease states (e.g., HTN), obesity pharmacotherapy management likely requires long-term use. Research is needed to determine the underlying causes of variability in weight-loss response to medications among individuals. Research is needed to quantify the degree of weight regain after cessation of each of the pharmacologic agents to better inform patients and providers before initiation. Longer study durations are therefore needed. Further, patients struggling with obesity may benefit from multi-modal pharmacotherapy for weight loss, which may be synergistic when agents with different mechanisms of action are used in tandem. Research is needed to determine benefits and harms and head-to-head comparisons of various multi-agent regimens. Certain pharmacologic therapy

combinations may be more effective for initial weight loss and other combinations may be more effective for long-term weight maintenance. It is unknown whether the approach to maintenance of weight loss requires a different approach or different medications to maintain weight that has been lost than interventions and medications to produce initial weight loss. This raises the concern of whether short-term pharmacologic interventions are of true benefit if overshadowed by weight regain after cessation. Further research is needed on the safety (e.g., cardiac, abuse potential) of long-term use of sympathomimetic agents currently approved only for short-term weight loss (e.g., phentermine, diethylpropion). Phentermine, when combined with topiramate (Qsymia), is approved for long-term use, noting that dosages of phentermine used in combination with topiramate (ranging from 3.75 mg to 15 mg maximum dose phentermine + 92 mg topiramate) are lower than typically prescribed phentermine dosing in short-term monotherapy (15 to 37.5 mg daily phentermine, or 8 mg 3x daily for Lomaira). Finally, further research into the underlying biology of food intake and body weight regulation is needed to provide new pharmacotherapeutic targets.

While network meta-analysis provides some moderate-quality evidence supporting the use of different weight-loss medications, more direct comparison trials are needed to provide information for selection of optimal drug therapy for distinct patient populations to provide an appropriately tailored management approach. In addition, long-term outcome data on the safety and efficacy of maintenance pharmacotherapy for all the chronic weight management medications are needed, as well as direct comparison trials for maintenance pharmacotherapy. More research is also required to appropriately assess the safety and efficacy of pharmacotherapy for long-term weight management, including chronic or intermittent use of medications traditionally prescribed for short-term use. In addition, data are not currently available on the safety and efficacy of the combination of two or more weight management medications in conjunction with CLI for patients with obesity, so more research is needed.

The currently available research on dietary supplements and nutraceutical agents is lacking in methodological rigor and clear protocol implementation. For these products to be viable, consistent, and trusted therapeutic options that can be measured and evaluated, clarity is needed in product content and dosage, and assurance is needed in purity and quality. Nationally, more rigorous regulation of dietary supplements and nutraceuticals would be required for these products to be of therapeutic value in the U.S.

When considering research needs in bariatric procedures, developing a validated screening tool to assess patient suitability and potential benefit versus risk would be beneficial. There is a particular need for subgroup population evaluation for weight loss procedures in those over age 65 and active duty personnel for whom immediate fitness for deployment is of critical importance. Potential alternative procedures such as the mini-gastric bypass and endoscopic plication will need to be further explored and matched to the population most suitable to benefit. Research is needed to evaluate the long-term effects of weight-loss devices, specifically, the rate of weight regain after removal of short-term weight-loss devices. The replacement, implementation, and practice of weight-loss devices, and their efficacy comparison one to the other, requires further investigation.

Moreover, the vast majority of reviewed research studies were conducted in academic settings, among non-active duty and non-Veteran populations that also included individuals who were predominantly women, white, young or middle aged, and motivated to participate in a weight management trial. There is

a need for more research evaluating screening and weight management intervention effectiveness in Veterans and Service Members, particularly active duty service men and women, among older adults, and in those with mental illness. Gaps also remain regarding the efficacy of alternative modalities of lifestyle interventions (e.g., internet, phone apps, secure messaging), the efficacy and comparative effectiveness of various interventions for maintaining weight loss, and the efficacy and comparative effectiveness of low- and intermediate-intensity lifestyle interventions (e.g., number and frequency of CLI sessions over what span of time), particularly when integrated within primary care settings and/or paired with pharmacotherapy. Finally, there is also a need for research that evaluates comparative cost-effectiveness among weight management interventions. A recurring concern among providers is how to best implement recommendations within healthcare systems, including the VHA and DoD. Research specifically evaluating implementation and effectiveness in real-world clinical settings is needed to best inform policies and resource allocation.

The Work Group also recommends research that addresses the following specific questions:

- What is the best method for screening for overweight and obesity and risk stratification (e.g., WC, waist-hip ratio, BMI, fitness, metabolic status) in active duty Service Members to meet the needs of the U.S. military? In Veterans?
- Are there individual differences (e.g., racial/ethnic, genetic, socioeconomic, geographic, psychological, presence of specific comorbidities such as spinal cord injury/disorder, polycystic ovarian syndrome (PCOS), and transgender persons) that predict response to a specific CLI, a specific pharmacotherapy, or a specific bariatric procedure?
- How should a provider prioritize choice of intervention based on the presence of specific obesity-associated conditions?
- What is the comparative effectiveness of varying modalities for delivering comprehensive lifestyle interventions: for example, comparing individual sessions, telephone sessions, internet modalities, mobile apps, video conferencing, to group sessions?
- What is the comparative effectiveness of varying types and combinations of physical activity (e.g., “lifestyle activity” versus more structured fitness approaches versus both)?
- What are the essential intervention components of CLI (including specific behavioral strategies, intervention modality, number of contacts, duration, and intensity)?
- Is there an optimal number of sessions of a CLI that should be provided to patients with overweight or obesity?
- What are the benefits and harms of weight loss or weight management in patients who are overweight with or without obesity-associated conditions?
- What tailoring of the risk profile is required for different ethnic groups? What BMI cutoffs confer additional risk for various ethnic groups?
- What is the degree of weight regain after cessation of weight loss pharmacotherapy? Is pharmacotherapy for the treatment of obesity by necessity long-term therapy, similar to the treatment of other chronic disease states?
- What are the benefits and harms of long-term use of weight-loss medications that are currently only approved for short-term use, such as phentermine and diethylpropion?

- Is there any advantage to specific weight-loss pharmacotherapy choice for initial weight loss versus maintenance of weight that has been lost?
- Is multi-modality pharmacotherapy (using dual, triple, or more therapy), each with different mechanisms of action for weight loss, synergistic? Would multi-agent therapy confer a weight-loss advantage over a single agent? Which medication combinations are most effective for weight loss? For weight maintenance long term?
- How do we more rigorously regulate supplements and nutraceuticals to assure clarity in product content, dosage, and assurance of purity and quality?
- What are the benefits and harms of bariatric procedures for patients with a BMI of 30–35 and how do benefits and harms vary based on the presence or absence of obesity-associated conditions?
- What are the effects of bariatric procedures on active duty personnel and benefits and harms to deployment readiness?
- What are the best screening measures for bariatric procedure candidates to optimize outcomes and minimize adverse events from the surgical intervention?
- What role should ethnic background play in recommendations for bariatric procedures?
- What is the degree of weight regain after removal and long-term effects of devices currently only approved for short-term use?
- When directly compared, which weight-loss device is most effective both in the short term and long term? Are there patient characteristics that favor use of one device over another?
- What is the appropriate role of the primary care clinical team in addressing the stigma associated with overweight and obesity; communicating with patients about weight and weight management, engaging in shared decision making about intervention options; motivating patients to actively participate in treatment and self-management; and delivering weight management interventions?
- What organizational and health system interventions are needed to: address equity and ensure all patients have equal access to treatment options; increase access to interventions, especially among rural populations; implement an integrated and coordinated approach for overweight and obesity care that enhances care coordination and health outcomes; and promotes efficient use of resources across the entire population of patients served?
- What kind of clinical decision support should be considered to provide healthcare teams with tailored options that are based on the individual patient's care needs?

Appendix A: Evidence Review Methodology

A. Developing the Scope and Key Questions

The CPG Champions, along with the Work Group, were tasked with identifying KQs to guide the SR of the literature on overweight and obesity. These questions, which were developed in consultation with the Lewin team, addressed clinical topics of the highest priority for the VA and DoD populations. The KQs follow the population, intervention, comparison, outcome, timing, and setting (PICOTS) framework for evidence questions, as established by the Agency for Healthcare Research and Quality (AHRQ). Table A-1 provides a brief overview of the PICOTS typology.

Table A-1. PICOTS [215]

PICOTS Element	Description
Population, Patients, or Problem	Describes the 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.
Intervention or Exposure	Refers to the specific treatments or approaches used with the patient or population. It includes doses, frequency, methods of administering treatments, etc.
Comparison	Describes the interventions or care that is being compared with the intervention(s) of interest described above. It includes alternatives such as placebo, drugs, surgery, lifestyle changes, standard of care, etc.
Outcome	Describes the specific results of interest. Outcomes can include short, intermediate, and long-term outcomes, or specific results such as quality of life, complications, mortality, morbidity, etc.
Timing, if applicable	Describes the duration of time that is of interest for the particular patient intervention and outcome, benefit, or harm to occur (or not occur).
Setting, if applicable	Describes the setting or context of interest. Setting can be a location (such as primary, specialty, or inpatient care).

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 highest priority, and those were included in the review. Table A-2 contains the final set of KQs used to guide the SR for this CPG.

Once the KQs were finalized, the Work Group prioritized the outcomes they had defined for each KQ based on how important the Work Group judged each outcome to be. Rating outcomes by their relative importance can help focus attention on those outcomes that are considered most important for clinical decision making when making judgments regarding the overall quality of the evidence to support a recommendation.[216]

Using GRADE methodology, the Work Group rated each outcome on a 1 – 9 scale (7 – 9, critical for decision making; 4 – 6, important, but not critical, for decision making; and 1 – 3, of limited importance for decision making). Critical and important outcomes were included in the evidence review (see Outcomes); however, only outcomes judged to be critical were used to determine the overall quality of evidence (see Grading Recommendations).

a. Population(s)

- Adults age 18 years or older who are candidates for weight loss/maintenance interventions based on an above-normal BMI (e.g., ≥25 kg/m^2)
- Adults with secondary causes of obesity (e.g., due to certain medications)
- Including pregnant women, women of childbearing age, women with a history of preeclampsia, deployed Service Members, and patients with comorbidities (e.g., DM, CKD)

b. Interventions

- Key Questions 1 and 2
    - CLIs need to incorporate the following 3 components:
        - Diet
        - Physical activity
        - Behavioral change components (e.g., monitoring, goal setting, problem-solving, stress management, cognitive strategies, stimulus control, etc.)
- Key Question 3
    - Modes of delivery include technology-assisted; individual; group; face-to-face; telephone; virtual, video, or clinical video telehealth (CVT); automated; or self-delivered
- Key Question 4
    - Dietary approaches of interest include different macronutrient (low carb, Atkins, South Beach, ketogenic, Ornish, Zone, LEARN, low-fat, or balanced low calories); eating plans (DASH, Mediterranean, paleo); meal replacement; intermittent fasting or time-restricted; very low calorie (<800 kcal/day) (includes interventions that are primarily diet but may also include a behavioral component)
- Key Question 5
    - Aerobic, strength training, moderate or high-intensity physical activity, or other structured or prescribed physical activity; exercise interventions should be added to a weight loss intervention
- Key Questions 6 and 7
    - FDA-approved medications for short-term use, or studied for intermittent use (benzphetamine, diethylpropion, phendimetrazine, phentermine) and FDA-approved medications for chronic weight management (liraglutide [3 mg], lorcaserin, combination naltrexone/bupropion, orlistat, combination phentermine/topiramate)
- Key Question 8
    - Bitter orange (Citrus aurantium L.)
    - Caffeine (as added caffeine or from guarana, kola nut, yerba maté, or other herbs)
    - Chitosan

- Cinnamon
- Cissus quadrangularis
- Fenugreek (Trigonella foenum-graecum L)
- Garcinia cambogia (hydroxycitric acid)
- Germander (teucrium)
- Ginseng
- Glucomannan (konjac root fiber)
- Green coffee bean extract (Coffea arabica, Coffea canephora, Coffea robusta)
- Green tea (Camellia sinensis) and green tea extract
- Guar gum
- Hoodia (Hoodia gordonii)
- Raspberry ketone
- White kidney bean (Phaseolus vulgaris)
- Forskolin
- Dandelion
- Oregano
- Gymnema sylvestre
- Rosemary
- Cuminum cyminum L
- Probiotics

- Key Questions 9 and 10
  - Lap adjustable gastric band
  - Sleeve Gastrectomy
  - Roux-n-Y Gastric Bypass
  - Duodenal Switch
  - Endoscopic gastric plication
- Key Questions 11 and 12
  - Electrical Stimulation Systems - Maestro Rechargeable System
  - Intragastric balloons: Orbera, ReShape, Obalon, Spatz, Elipse
  - Gastric Emptying Systems – AspireAssist equivalence (versus inconclusive), using defined clinical significance thresholds

c. Comparators

- Key Questions 1 and 2
  - No treatment
  - Waitlist
  - Inactive control
  - Standard of care or treatment as usual
  - Active comparator with diet or lifestyle alone
- Key Question 3
  - Other modalities of delivery of the same or an equivalent CLI
- Key Question 4
  - Different dietary approaches (study must have controlled for other elements of lifestyle interventions, such as physical activity and behavioral strategies)
- Key Question 5
  - Diet and/or behavioral intervention without exercise or different exercise approaches (e.g., aerobic versus strength or weight training; high versus low intensity). Participants should be enrolled in behavioral/diet intervention w/o exercise.
- Key Questions 6 and 7
  - Placebo, other FDA-approved weight loss medication, or other non-pharmacologic weight loss intervention, such as comprehensive lifestyle, weight loss device or bariatric surgery
- Key Question 8
  - Placebo, no treatment, different dietary supplement, or FDA-approved weight loss medication
- Key Question 9
  - Non-operative management
  - Reversible FDA-approved weight-loss devices
  - Sham procedure
- Key Question 10
  - Different type of surgical procedure (does not compare variations in how a single surgical procedure is performed or the materials/techniques used to perform that surgery)
- Key Question 11
  - Non-operative weight-loss intervention
  - Sham device
- Key Question 12
  - Other FDA-approved weight-loss medical device

d. Outcomes

- Critical outcomes
    - Changes in or maintenance of weight status (as defined by the publication of interest and at different time points), including:
        - Absolute weight loss (kg/lb), relative weight loss as percentage of baseline weight, relative weight loss as percentage of excess weight, changes in percent ideal body weight
        - Changes in absolute BMI (kg/m^2), relative BMI as percentage of baseline BMI
        - Percentage achieving clinically significant weight loss, defined as >5%, >10% reduction
    - Safety/adverse events (for Key Questions 6-12), including:
        - Any treatment-related adverse events
        - Discontinuations due to adverse events
        - Hypotension related intervention
        - Syncope
        - HTN, change in systolic BP/diastolic BP
        - Dyslipidemia
        - Falls, injuries
        - Cardiac valve injury
        - Eating disorders, binging
        - Surgical complications, infection
        - Death: all-cause, death from surgical complications, suicide
        - Malabsorption, malnutrition, micro-nutrient deficits
        - Gallstones
        - Kidney stones
        - Tachycardia, arrhythmias
        - Anxiety, or any changes in behavioral/mental health status
        - Depression or depressive episodes
        - Suicide behavior (ideation or attempt)
        - Substance use disorders, risky alcohol use

- Important outcomes
  - Changes in or maintenance of body composition, fat mass, fat distribution (as defined and measured by the publication of interest and at different time points), including:
    - Changes in absolute body fat (kg/lb), percent body fat (%), fat mass index (kg/m^2)
    - Changes in skinfold thickness
    - Changes in waist, hip, neck, arm, or thigh circumferences
    - Changes in circumferences ratios
  - Prevention and risk of an event, progression or reversal of comorbid conditions; conditions of interest include:
    - Diabetes, prediabetes (as defined by the Americans with Disabilities Act), metabolic syndrome
    - Hypertension, change in systolic BP/diastolic BP
    - CVD: congestive heart failure, major adverse cardiac events, MI, coronary artery disease, aortic events (e.g., aneurysm rupturing)
    - Dyslipidemia
    - Stroke
    - Transient ischemic attack (TIA)
    - CKD
    - Osteoarthritis
    - OSA
    - GERD
    - Cancer
    - Non-alcoholic fatty liver disease
    - Non-alcoholic steatohepatitis (NASH)
    - PCOS
  - Changes in biomarkers of comorbid conditions, including:
    - Lipids: total cholesterol, non-HDL cholesterol (total cholesterol minus HDL cholesterol), triglyceride, LDL-c level, HDL-c level,
    - Aspartate transaminase (AST), alanine transaminase (ALT), albumin, platelet count
    - NAFLD fibrosis score
    - Total testosterone level in males
    - Glycemic control: blood glucose (fasting, postprandial), insulin level fasting and post-prandial, HbA1c, insulin resistance (homeostatic model assessment [HOMA], homeostatic model assessment of insulin resistance [HOMA IR], homeostatic model assessment of β-cell function [HOMA-β])

- Functional status/QoL
  - As measured in included publication
- Safety/adverse events (for Key Questions 1-5), including:
  - Any treatment-related adverse events
  - Discontinuations due to adverse events
  - Hypotension related intervention
  - Syncope
  - Hypertension, change in SBP/DBP
  - Dyslipidemia
  - Falls, injuries
  - Cardiac valve injury
  - Eating disorders, binging
  - Surgical complications, infection
  - Death: all-cause, death from surgical complications, suicide
  - Malabsorption, malnutrition, micro-nutrient deficits
  - Gallstones
  - Kidney stones
  - Tachycardia, arrhythmias
  - Anxiety, or any changes in behavioral/mental health status
  - Depression or depressive episodes
  - Suicide behavior (ideation or attempt)
  - Substance use disorders, risky alcohol use
- Adherence to therapy
  - As measured in included publication

B. Conducting the Systematic Review

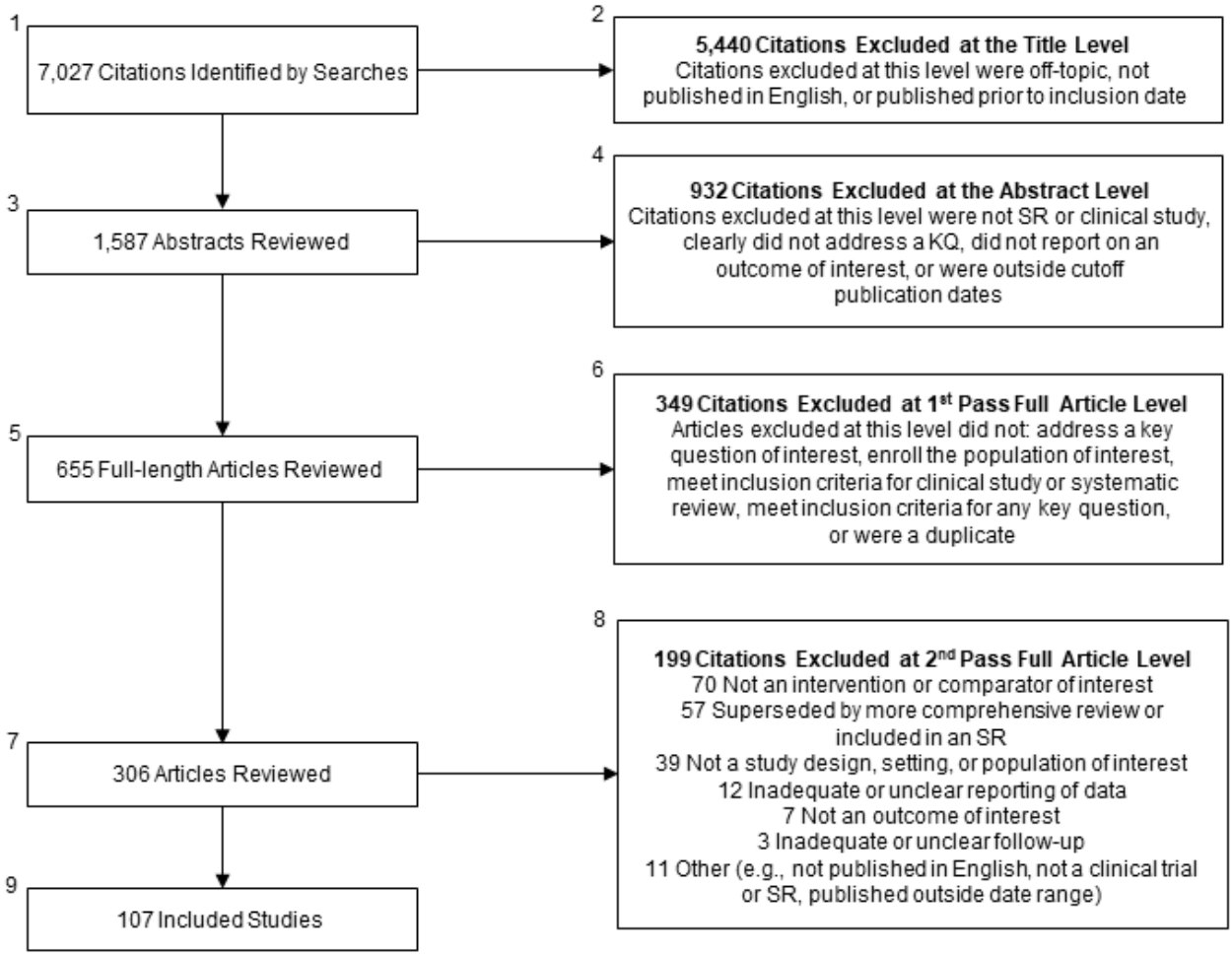
Based on the decisions made by the Champions and Work Group members regarding the scope, the KQs, and the PICOTS statements, the Lewin Team produced an SR protocol prior to conducting the review. The protocol was reviewed and approved by the Champions and Work Group members. It described in detail the final set of KQs, the methodology to be used during the SR process, and the inclusion/exclusion criteria to be applied to each potential study, including, but not limited to, study type, sample size, and PICOTS criteria.

Extensive literature searches identified 7,027 citations potentially addressing the key questions of interest to this evidence review. Of those, 5,440 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, 1,587 abstracts were reviewed with 932 of those being excluded for the following reasons: not an SR or clinical study (see the General Criteria for Inclusion in Systematic Review), did not address a key question of interest to this review, did not enroll a population of interest, or published prior to February 1, 2013. A total of 655 full-length articles were reviewed. Of those, 349 were excluded at a first pass review for the following: not addressing a key question of interest, not enrolling the population of interest, not meeting inclusion criteria for clinical study or SR, not meeting inclusion criteria for any key question, or being a duplicate. A total of 306 full-length articles were thought to address one or more key questions and were further reviewed. Of these, 199 were ultimately excluded and reasons for their exclusion are presented in Figure A-1 below.

Overall, 107 studies 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 questions.

Figure A-1. Study Flow Diagram



Abbreviations: CS: clinical study; 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: 7,027 citations identified by searches
    a. Right to Box 2: 5,440 citations excluded at the title level
        i. Citations excluded at this level were off-topic, not published in English, or published prior to inclusion date
    b. Down to Box 3: 1,587 abstracts reviewed
2. Box 3: 1,587 abstracts reviewed
    a. Right to Box 4: 932 citations excluded at the abstract level
        i. Citations excluded at this level were not an SR or clinical study, clearly did not address a KQ, did not report on an outcome of interest, or were outside cutoff publication dates
    b. Down to Box 5: 655 full-length articles reviewed
3. Box 5: 349 full-length articles reviewed
    a. Right to Box 6: 349 citations excluded at 1st pass full article level
        i. Articles excluded at this level did not: address a key question of interest, enroll the population of interest, meet inclusion criteria for clinical study or systematic review, meet inclusion criteria for any key question, or were a duplicate
    b. Down to Box 7: 306 articles reviewed
4. Box 7: 306 articles reviewed
    a. Right to Box 8: 199 citations excluded at 2nd pass full article level
        i. 36 Wrong study design or doesn't address a KQ
        ii. 70 Not an intervention or comparator of interest
        iii. 7 No outcome of interest
        iv. 3 Not a study population of interest
        v. 3 Unclear or inadequate follow-up
        vi. 12 Inadequate reporting of data/no data extract
        vii. 11 Other (e.g., duplicate, published outside date range)
    b. Down to Box 9: 107 included studies
5. Box 9: 105 included studies

Table A-2. Evidence Base for KQs

Question Number	Question	Number of Studies and Type of Studies
1	What are the benefits and harms of comprehensive lifestyle interventions on weight loss and health outcomes?	5 SRs 9 RCTs
2	Among adults who have achieved initial weight loss, what are the benefits and harms of comprehensive lifestyle interventions on weight maintenance and health outcomes?	1 SR 1 RCT
3	What is the comparative effectiveness of different modes of delivering comprehensive lifestyle interventions on weight loss or weight maintenance and health outcomes?	5 SRs 12 RCTs
4	What is the comparative effectiveness and harms of various dietary approaches on short and long-term weight loss and health outcomes?	4 SRs 9 RCTs
5	What are the benefits and harms of physical activity on short- and long-term weight loss and health outcomes?	2 SRs 8 RCTs
6	What are the benefits and harms of FDA approved medications for short-term use (<6 months) or chronic use (>6 months) on weight loss and health outcomes?	3 SRs 3 RCTs in 5 publications
7	What are the benefits and harms of FDA approved medications on weight maintenance and health outcomes?	1 SR 1 RCT
8	What are the benefits and harms of dietary supplements or nutraceuticals on initial weight loss and long-term weight loss?	5 SRs 7 RCTs
9	What are the benefits and harms of bariatric surgery on short- and long-term weight loss, health outcomes, and comorbid health conditions?	14 SRs
10	What is the comparative effectiveness of different forms of bariatric surgery on short- and long-term weight loss, health outcomes, and comorbid health conditions?	6 SRs 1 RCT
11	What are the benefits and harms of FDA-approved weight loss devices on short- and long-term weight loss, health outcomes, and comorbid health conditions?	4 SRs 3 RCTs
12	What is the comparative effectiveness and harms of FDA-approved weight loss devices on short- and long-term weight loss status, health outcomes, and comorbid health conditions?	1 SR
	Total Evidence Base	**107 studies**

Abbreviations: FDA: Food and Drug Administration; RCT: randomized controlled trial; SR: systematic review

a. General Criteria for Inclusion in Systematic Review

- RCTs or SRs published on or after February 1, 2013, to April 8, 2019. If multiple SRs addressed a KQ, the most recent and/or comprehensive review was selected. SRs are supplemented with RCTs published subsequent to the SR.
- Studies must have been published in English.
- Publication must be a full clinical study or SR; abstracts alone were not included. Similarly, letters, editorials, and other publications that are not full-length clinical studies were not accepted as evidence.

- SRs 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 GRADE or something compatible (e.g., the Strength of Evidence grading used by the Evidence-based Practice Centers of the Agency for Healthcare Research and Quality). 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 allows us to judge the overall risk of bias, consistency, directness, and precision of evidence. SRs were not used as evidence if the overall quality of the evidence in the review was unable to be assessed.
- Intervention studies assessed CLIs, various dietary approaches, physical activity, FDA-approved weight loss medications, select dietary supplements or nutraceuticals, FDA-approved medical devices for weight loss, and bariatric surgical procedures and must have been a prospective, RCT with an independent control group. Crossover trials will not be included unless they report data for the first phase of the study separately.
- Study must have enrolled at least 20 patients (10 per study group).
- Study must have enrolled at least 85% of patients who meet the study population criteria: adults aged 18 years or older with overweight or obesity.
- Study must have reported on at least one critical or important outcome of interest.

b. Literature Search Strategy

Information regarding the bibliographic databases, date limits, and platform/provider can be found in the table 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
Cochrane Database of Systematic Reviews (Cochrane Reviews)	February 1, 2013, to April 8, 2019	Wiley
Cochrane Central Register of Controlled Trials	February 1, 2013, to April 8, 2019	Wiley
Database of Abstracts of Reviews of Effects	February 1, 2013, to April 8, 2019	Wiley
EMBASE (Excerpta Medica)	February 1, 2013, to April 8, 2019	Elsevier
Health Technology Assessment Database (HTA)	February 1, 2013, to April 8, 2019	Wiley
MEDLINE/PreMEDLINE	February 1, 2013, to April 8, 2019	Elsevier
PsycINFO	February 1, 2013, to April 8, 2019	OvidSP
PubMed (In-process and Publisher records)	February 1, 2013, to April 8, 2019	National Library of Medicine

C. Convening the Face-to-face Meeting

In consultation with the COR, the Champions, and the Work Group, the Lewin Team convened a three and one half-day face-to-face meeting of the CPG Champions and Work Group members on July 16 – 19, 2019. These experts were gathered to develop and draft the clinical recommendations for an update to the 2014 VA/DoD Obesity CPG. The Lewin Team presented findings from the evidence review in order to facilitate and inform the process.

Under the direction of the Champions, the Work Group members were charged with interpreting the results of the evidence review and were asked to categorize and carry forward recommendations from the 2014 VA/DoD Obesity CPG, modifying the recommendations as necessary. The members also developed new clinical practice recommendations not presented in the 2014 VA/DoD Obesity CPG based on the 2019 evidence review. The subject matter experts were divided into three smaller subgroups at this meeting.

As the Work Group members drafted clinical practice recommendations, they also assigned a grade for each recommendation based on a modified GRADE and USPSTF methodology. Each recommendation was graded by assessing the quality of the overall evidence base, the associated benefits and harms, the variation in values and preferences, and other implications of the recommendation.

In addition to developing recommendations during the face-to-face meeting, the Work Group members also began to revise the 2014 VA/DoD Obesity CPG algorithms to reflect the new and amended recommendations. They discussed the available evidence as well as changes in clinical practice since 2014, as necessary, to update the algorithms.

D. Grading Recommendations

This CPG uses the GRADE methodology to assess the quality of the evidence base and assign a strength for each recommendation. The GRADE system uses the following four domains to assess the strength of each recommendation:[27]

- Balance of desirable and undesirable outcomes
- Confidence in the quality of the evidence
- Values and preferences
- Other implications, as appropriate,
    - Resource use
    - Equity
    - Acceptability
    - Feasibility
    - Subgroup considerations

The following sections further describe each domain.

Balance of desirable and undesirable outcomes refers to the size of anticipated benefits (e.g., increased longevity, reduction in morbid event, resolution of symptoms, improved quality of life, decreased resource use) and harms (e.g., decreased longevity, immediate serious complications, adverse event, impaired quality of life, increased resource use, inconvenience/hassle) relative to each other. This domain is based on the understanding that the majority of providers will offer patients therapeutic or preventive measures as long as 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?

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 the strength. The evidence review used for the development of recommendations, conducted by ECRI, assessed the confidence in the quality of the evidence base using GRADE methodology and assigned a rating of "High," "Moderate," "Low," or "Very Low." The outcomes judged to be critical were used to determine the overall quality of evidence. Per GRADE, if the quality of evidence differs across the critical outcomes, the lowest quality of evidence for any of the relevant critical outcomes determines the overall quality of the evidence for a recommendation; the overall confidence cannot be higher than the lowest confidence in effect estimates for any outcome that is determined to be critical for clinical decision making.[33,216]

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?

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?

Other implications consider the practicality of the recommendation, including resource 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	Judgment
Balance of desirable and undesirable outcomes	• 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?	• Benefits outweigh harms/ burden • Benefits slightly outweigh harms/burden • Benefits and harms/burden are balanced • Harms/burden slightly outweigh benefits • Harms/burden outweigh benefits
Confidence in the quality of the evidence	• Is there high or moderate-quality evidence that answers this question? • What is the overall certainty of this evidence?	• High • Moderate • Low • Very low
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

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 combines the four domains.[217] GRADE methodology does not allow for recommendations to be made based on expert opinion alone. While strong recommendations are usually based on high or moderate confidence in the estimates of effect (quality of the evidence) there may be instances in which strong recommendations are warranted even when the quality of evidence is low.[27] In these instances, the balance of desirable and undesirable outcomes and values and preferences played large roles in

determining the strength of a recommendation. This is explained in the discussion section for the recommendation.

The GRADE of a recommendation is based on the following elements:

- Four decision domains used to determine the strength and direction (described above)
- Relative strength (Strong or Weak)
- Direction (For or Against)

The relative strength of the recommendation is based on a binary scale, "Strong" or "Weak." A strong recommendation indicates that the Work Group is highly confident that desirable outcomes outweigh undesirable outcomes. If the Work Group is less confident of the balance between desirable and undesirable outcomes, they present a weak recommendation.

Similarly, a recommendation for a therapy or preventive measure indicates that the desirable consequences outweigh the undesirable consequences. A recommendation against a therapy or preventive measure indicates that the undesirable consequences outweigh the desirable consequences.

Occasionally, instances may occur when the Work Group feels there is insufficient evidence to make a recommendation for or against a specific therapy or preventive measure. This can occur when there is an absence of studies on a particular topic that met evidence review inclusion criteria, studies included in the evidence review report conflicting results, or studies included in the evidence review report inconclusive results regarding the desirable and undesirable outcomes.

Using these elements, the grade of each recommendation is presented as part of a continuum:

- Strong For (or "We recommend offering this option …")
- Weak For (or "We suggest offering this option …")
- No recommendation for or against (or "There is insufficient evidence …")
- Weak Against (or "We suggest not offering this option …")
- Strong Against (or "We recommend against offering this option …")

Note that Weak (For or Against) recommendations may also be termed "Conditional," "Discretionary," or "Qualified." Recommendations may be conditional based upon patient values and preferences, the resources available, or the setting in which the intervention will be implemented. Recommendations may be at the discretion of the patient and provider or they may be qualified with an explanation about the issues that would lead decisions to vary.

E. Recommendation Categorization

a. Recommendation Categories and Definitions

A set of recommendation categories was adapted from those used by NICE.[30,31] These categories, along with their corresponding definitions, were used to account for the various ways in which recommendations could have been updated from the 2014 VA/DoD Obesity CPG. The categories and definitions can be found in Table A-5.

Table A-5. 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 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 previous CPG that has been removed based on review of the evidence
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 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 previous CPG that has been removed because it was deemed out of scope for the updated CPG

*Adapted from the NICE guideline manual (2012) [30] and Garcia et al. (2014) [31]

Abbreviation: CPG: clinical practice guideline

b. Categorizing Recommendations with an Updated Review of the Evidence

Recommendations were first categorized by whether or not 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 2014 VA/DoD Obesity 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.

The "Reviewed, Not Changed" category was used for recommendations carried forward to the updated CPG with review of the evidence and where no changes were deemed necessary to the recommendation language. For recommendations carried forward to the updated CPG with review of the evidence and slightly modified wording, the "Reviewed, Amended" recommendation category was used. This allowed for the wording of the recommendation to reflect GRADE methodology as well as for any other non-substantive (i.e., not clinically meaningful) language changes deemed necessary. The evidence used to support these recommendations was carried forward from the previous version of the CPG and/or was identified in the evidence review for the update.

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.

c. 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 updated SR of the evidence. Due to time and budget constraints, the update of the Obesity CPG could not review all available evidence on the 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 Obesity CPG that were carried forward unchanged to the updated version. The category of "Not reviewed, Amended" was used to designate recommendations which were modified from the 2014 VA/DoD Obesity 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, and 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. The categories for the recommendations from the 2014 Obesity CPG are noted in Appendix D.

F. Drafting and Submitting the Final Clinical Practice 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 2014 VA/DoD Obesity CPG to support the amended "carried forward" recommendations. The Work Group also considered tables, appendices, and other sections from the 2014 VA/DoD Obesity 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 make revisions to the CPG. Once they were developed, the first two drafts of the CPG were posted on a wiki website for a period of 14 – 20 business days for internal review and comment by the Work Group. All feedback submitted during each review period was reviewed and discussed by the Work Group and appropriate revisions were made to the CPG.

Draft 3 of the CPG was made available for peer review and comment. This process is described in the section titled Peer Review Process. After revisions were made based on the feedback received during the peer review and comment period, the Champions presented the CPG to the EBPWG for their approval. Changes were made based on feedback from the EBPWG and the guideline was finalized.

The Work Group also produced a set of guideline toolkit materials which included a provider summary, pocket card, and patient summary. The final 2020 VA/DoD Obesity CPG was submitted to the EBPWG in June 2020.

Appendix B: Patient Focus Group Methods and Findings

A. Methods

As part of the effort to update this CPG, VA and DoD Leadership held a patient focus group on March 7, 2019, at the Womack Army Medical Center in Fort Bragg, NC. The aim of the focus group was to further understand and incorporate the perspective of patients with overweight and obesity, who are covered and/or receiving their care through the VA and/or DoD healthcare systems, as these patients are most affected by the recommendations put forth in the CPG. The focus groups explored the patients' perspectives on a set of topics related to their overweight or obesity management, including their priorities, challenges they have experienced, the information they received regarding their care, as well as the impacts of their care on their lives.

Participants for the focus group were recruited by VA and DoD Leadership with assistance from the Obesity CPG Champions. Patient focus group participants were not intended to be a representative sample of VA and DoD patients. However, recruitment focused on eliciting a range of perspectives likely to be relevant and informative in the guideline development process. Patients were not incentivized for their participation or reimbursed for travel expenses.

The Obesity CPG Champions and Work Group, with support from Lewin, developed a set of questions to help guide the focus group. The focus group facilitator led the discussion using the previously prepared questions as a general guide to elicit the most important information from the patients regarding their experiences and views about their treatment and overall care. Given the limited time and the range of interests, knowledge, and information of the focus group participants, not all of the listed questions were addressed.

B. Findings

The following ideas and suggestions about aspects of care that are important to patients with overweight or obesity emerged as recurring themes during the discussions (Table B-1). These concepts were important parts of the participants' care and added to the Work Group's understanding of patient values and perspectives.

Table B-1. Obesity CPG Focus Group Findings

Obesity CPG Patient Focus Group Concepts	
A.	Providers should use shared decision making to develop an individualized, patient-centered lifestyle-modification treatment plan that incorporates both a dietary regimen and exercise routine.
B.	Patients, particularly those in the DoD, face stigmatization and discrimination based on their weight. For active duty Service Members, not meeting their weight requirements can have significant effects on their careers.
C.	Active duty participants expressed concern over the methods used to screen for overweight and obesity. Participants believed the "Tape Test" is inaccurate and prone to human error.
D.	Patients utilized a variety of internet tools and mobile apps to manage their weight loss goals. Providers should offer telemedicine and other technology options to augment care but recognize these options may not align with the preferences of all patients.
E.	Patients would like to receive more education regarding weight loss and effective treatment strategies, including specific types of diet and exercise plans, dietary or herbal supplements, and pharmaceuticals.

a. Providers should use shared decision making to develop an individualized, patient-centered lifestyle-modification treatment plan that incorporates both a dietary regimen and exercise routine.

- Patients expressed a desire for more individualized, patient-centered treatment plans. Providers should use shared decision making to find a treatment plan that works best for each patient.
- Patients varied in their treatment preferences; some patients found weight loss success by changing the types of foods they ate, while others found that the timing of meals was important to their weight loss.
- Patients stated that being surrounded by individuals who share their weight loss goals would be beneficial to their treatment. Additionally, patients avoided group settings where unhealthy food was being eaten in an effort to improve their diet.
- Patients expressed a desire to receive individualized dietary advice but found scheduling appointments with dietitians difficult.
- Patients stated that their family members were affected by their treatment plans and should, therefore, be included in treatment planning and education, not only for the benefit of the patients' health but also for the health of their family members.
- Providers should be mindful of and take into account each patient's co-occurring conditions, particularly mental health conditions, when developing their treatment plan.

b. Patients, particularly those in the DoD, face stigmatization and discrimination based on their weight. For active duty Service Members, not meeting their weight requirements can have significant effects on their careers.

- Patients in the DoD face stigmatization and discrimination based on their weight. This is compounded by mental health stigmas issues many patients face.
- Most participants' military careers have been significantly impacted by their weight.
- Several of the participants expressed that they would do just about anything to meet the military weight criteria that would allow them to move on with their career.
- The main challenge for active duty patients was to have more information and more time to achieve the weight criteria, not that they found the dietary or physical activity changes difficult to implement.

c. Active duty participants expressed concern over the methods used to screen for overweight and obesity. Participants believed the "Tape Test" is inaccurate and prone to human error.

- Some patients expressed their frustration that while they were in the best shape they had ever been in and had no difficulty passing the physical fitness requirements for duty, they were still failing to achieve the "Tape Test" (waist and neck circumferences) standards.
- Patients stated that the "Tape Test" is unfair to individuals with wider hip bones or small neck circumferences and felt that it is not an accurate measure of physical fitness or health. They believe the "Tape Test" is inaccurate, imprecise, and prone to human error.

- Patients agreed that the timeframe given by the military to meet the physical requirements should be adjusted based on an individual's baseline weight.

d. Patients utilized a variety of internet tools and mobile apps to manage their weight loss goals. Providers should offer telemedicine and other technology options to augment care but recognize these options may not align with the preferences of all patients.

- Younger patients used mobile apps and websites to help them track their calories, determine if foods were healthy or not, count their steps, and measure their weight loss progress.
- Patients varied in their desire to use telehealth.

e. Patients would like to receive more education regarding weight loss and effective treatment strategies, including specific types of diet and exercise plans, dietary or herbal supplements, and pharmaceuticals.

- Patients desired more education from their providers regarding their options for effective strategies to treat overweight and obesity.
- Patients used a variety of methods to lose weight, most of which they discovered through their research, word-of-mouth, or online.
- Dietary supplements and OTC weight-loss drugs are used by patients to provide short-term fixes ahead of the "Tape Test"; patients want to learn more about the safety and efficacy of these supplements.
- Patients were receptive to using prescription weight loss medications, even if the side effects could be harmful. Providers should educate patients about the risks and potential benefits of pharmacologic treatment.

Appendix C: Evidence Table

Table C-1. Evidence Table[a,b,c,d]

Recommendation	2014 Grade	Evidence	2020 Strength of Recommendation	Recommendation Category
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.	C, A, I, A, B, C, I, A, B	[2,77-86] **Additional References:** [26,74-76,87-91]	Strong for	Reviewed, New-replaced
2. There is insufficient evidence to recommend a specific number of sessions of a comprehensive lifestyle intervention for patients with overweight or obesity.	B	[2] **Additional References:** [26]	Neither for nor against	Reviewed, New-replaced
3. We suggest offering a comprehensive lifestyle intervention for weight maintenance to patients who have completed a comprehensive lifestyle intervention for weight loss.	B	[2,74,75,92,93]	Weak for	Reviewed, New-replaced
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.	B	[2,75,92,94,95]	Weak for	Reviewed, Amended

[a] 2014 Grade column: The 2014 VA/DoD Obesity CPG used the USPSTF evidence grading system. Inclusion of more than one 2014 Grade indicates that more than one 2014 CPG recommendation is covered under the 2020 recommendation. The strength of recommendations were rated as follows: A- a strong recommendation that the clinicians provide the intervention to eligible patients; B- a recommendation that clinicians provide (the service) to eligible patients; C- no recommendation for or against the routine provision of the intervention is made; D- recommendation is made against routinely providing the intervention; I- the conclusion is that the evidence is insufficient to recommend for or against routinely providing the intervention. "None" indicates that the 2014 VA/DoD Obesity CPG recommendation was not graded. "Not applicable" indicates that the 2020 VA/DoD Obesity CPG recommendation was a new recommendation, and therefore does not have an associated 2014 Grade.

[b] 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 the 2019 evidence review or included in the evidence base for the 2014 VA/DoD Obesity 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 systematically identified through a literature review. These references were not included in the evidence base for the recommendation and, therefore, did not influence the strength and direction of the recommendation.

[c] 2020 Strength of Recommendation column: Refer to the Grading Recommendations section for more information on how the strength of the recommendation was determined using GRADE methodology.

[d] Recommendation Categorization column: Refer to the Recommendation Categorization section for more information on the description of the categorization process and the definition of each category.

Recommendation	2014 Grade	Evidence	2020 Strength of Recommendation	Recommendation Category
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.	I	[2,106,108-111] **Additional References:** [96-107]	Neither for nor against	Reviewed, New-Replaced
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.	A, A, A, EO	[2,89,112-119] **Additional References:** [120,121]	Weak for	Reviewed, New-replaced
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.	A	[2,122-145] **Additional References:** [146]	Strong for	Reviewed, Amended
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.	A	[122,147-150] **Additional References:** [151]	Weak for	Reviewed, New-replaced
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.	A, B	[2,152,154-156,158-164,166,167] **Additional References:** [153,157,165]	Weak for	Reviewed, New-replaced
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.	N/A	[154]	Neither for nor against	Reviewed, New-added
11. We suggest against using dietary supplements or nutraceuticals for clinically meaningful short-term weight loss or long-term weight management.	N/A	[169-176] **Additional References:** [168,177]	Weak against	Reviewed, New-added
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.	N/A	[178,179,187-189] **Additional References:** [180-186]	Weak for	Reviewed, New-added

Recommendation	2014 Grade	Evidence	2020 Strength of Recommendation	Recommendation Category
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).	A, A	[187-196] **Additional References:** [186]	Weak for	Reviewed, New-replaced
14. There is insufficient evidence to recommend for or against metabolic/bariatric surgery to patients over age 65.	I	[197-201]	Neither for nor against	Reviewed, Amended
15. There is insufficient evidence to recommend for or against percutaneous gastrostomy devices for weight loss in patients with obesity.	N/A	[202-205]	Neither for nor against	Reviewed, New-added
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.	N/A	[206-210] **Additional References:** [186]	Weak for	Reviewed, New-added
17. There is insufficient evidence to recommend for or against intragastric balloons for long-term weight loss to support chronic weight management or maintenance.	N/A	[206-210] **Additional References:** [186]	Neither for nor against	Reviewed, New-added
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.	N/A	[130,134,138] **Additional References:** [137,139,141,144,211]	Weak for	Reviewed, New-added

Appendix D: 2014 Recommendation Categorization Table

Table D-1. 2014 Recommendation Categorization Table[a,b,c,d,e]

2014 Location		2014 Recommendation Text	2014 Grade	Recommendation Category	2020 Recommendation
Rec. Number	Page				
1	20	Screen adult patients to establish a diagnosis of overweight or obesity by calculating body mass index (BMI), and document the presence of overweight or obesity in the medical record.	B	Not reviewed, Deleted	–
2	20	Screen for overweight and obesity at least annually.	EO	Not reviewed, Deleted	–
3	20	Assess for the presence of obesity-associated conditions among overweight patients or patients with increased waist circumference.	B	Not reviewed, Deleted	–
4	20	Perform a targeted assessment on overweight and obese patients. In addition to the basic medical history and physical examination, assess for factors contributing to obesity.	EO	Not reviewed, Deleted	–
5	22	Consider providing normal weight patients with information and behavioral counseling regarding healthy diet and physical activity behaviors, in order to maintain a healthy weight.	C	Not reviewed, Deleted	–
6	23	Consider providing overweight patients without obesity-associated conditions with information and behavioral counseling regarding healthy diet and physical activity behaviors, in order to pursue a healthy weight.	C	Reviewed, New-replaced	Recommendation 1
7	23	Offer comprehensive lifestyle intervention to achieve weight loss and to improve blood pressure and/or glucose control in overweight patients.	A	Reviewed, New-replaced	Recommendation 1

[a] 2014 Location columns: The first two columns indicate the location of each recommendation within the 2014 VA/DoD Obesity CPG.

[b] 2014 Recommendation Text column: The 2014 Recommendation Text column contains the wording of each recommendation from the 2014 VA/DoD Obesity CPG.

[c] 2014 Grade column: The 2014 VA/DoD Obesity CPG used the U.S. Preventive Services Task Force (USPSTF) evidence grading system: http://www.uspreventiveservicestaskforce.org. The strength of recommendations were rated as follows: A- a strong recommendation that the clinicians provide the intervention to eligible patients; B- a recommendation that clinicians provide (the service) to eligible patients; C- no recommendation for or against the routine provision of the intervention is made; D- recommendation is made against routinely providing the intervention; I- the conclusion is that the evidence is insufficient to recommend for or against routinely providing the intervention. "N/A" indicates there was no grade assigned to the recommendation in the 2014 VA/DoD Obesity CPG.

[d] Recommendation Category column: This column indicates the way in which each 2014 VA/DoD Obesity CPG recommendation was updated.

[e] 2020 Recommendation column: For recommendations that were carried forward to the 2020 VA/DoD Obesity CPG, this column indicates the new recommendation(s) to which they correspond.

2014 Location		2014 Recommendation Text	2014 Grade	Recommendation Category	2020 Recommendation
Rec. Number	Page				
8	23	Offer comprehensive lifestyle intervention to overweight patients with dyslipidemia for weight loss and to improve lipid levels.	B	Not reviewed, Deleted	–
9	24	Current evidence is insufficient to recommend for or against offering comprehensive lifestyle intervention for weight loss to overweight patients with degenerative joint disease, non-alcoholic fatty liver disease, and/or obstructive sleep apnea to reduce harms of these conditions.	I	Reviewed, New-replaced	Recommendation 1
10	25	Offer obese patients comprehensive lifestyle intervention for weight loss to improve lipid levels, blood pressure, and/or glucose control.	A	Reviewed, New-replaced	Recommendation 1
11	25	Offer obese patients comprehensive lifestyle intervention for weight loss to reduce harms of obstructive sleep apnea.	B	Reviewed, New-replaced	Recommendation 1
12	25	Consider offering obese patients comprehensive lifestyle intervention for weight loss to reduce harms of degenerative joint disease.	C	Reviewed, New-replaced	Recommendation 1
13	25	Current evidence is insufficient to support weight loss through comprehensive lifestyle intervention for reducing harms of non-alcoholic fatty liver disease.	I	Reviewed, New-replaced	Recommendation 1
14	26	Reach a shared understanding with overweight and obese patients about the risks of overweight and obesity, and the benefits of weight management.	EO	Not reviewed, Deleted	–
15	27	Perform an in-depth clinical assessment in order to assess the risks and benefits of different weight management treatments and to develop a weight management plan.	EO	Not reviewed, Deleted	–
16	27	Use motivational interviewing techniques to evoke patient motivation to accept and participate in weight loss treatments.	EO	Reviewed, Deleted	–
17	27	Convey the importance of weight loss and maintenance as a lifelong commitment rather than a brief episode of treatment.	EO	Reviewed, Deleted	–
18	28	Offer patients at least 12 contacts within 12 months of a comprehensive lifestyle intervention that combines dietary, physical activity and behavioral strategies.	B	Reviewed, New-replaced	Recommendation 2
19	29	Plan a net deficit of 500 to 1,000 kcal/day addressing both diet and physical activity to achieve a weight loss of 0.5 to 2 pounds per week, resulting in a 5-10% reduction in body weight over 6 months.	A	Reviewed, New-replaced	Recommendation 1
20	30	Assess adherence to the weight loss program one-to-two times per month by measuring the patient's weight and providing feedback and ongoing support.	EO	Not reviewed, Deleted	–

2014 Location		2014 Recommendation Text	2014 Grade	Recommendation Category	2020 Recommendation
Rec. Number	Page				
21	30	Re-evaluate the treatment plan for patients who have lost an average of less than 0.5pound per week.	EO	Not reviewed, Deleted	–
22	30	Offer patients who have met their weight loss goals a comprehensive maintenance program consisting of behavioral components and ongoing support.	B	Reviewed, New-replaced	Recommendation 3
23	31	Offer comprehensive lifestyle interventions for weight loss, in either individual or group setting.	B	Reviewed, New-replaced	Recommendation 1
24	31	Offer telephone-based comprehensive lifestyle intervention for weight loss, either as an alternative or an adjunct to face-to-face intervention.	B	Reviewed, Amended	Recommendation 4
25	31	There is insufficient evidence for or against offering internet-based comprehensive lifestyle intervention for weight loss, as an alternate or adjunct to face-to-face intervention.	I	Reviewed, New-replaced	Recommendation 5
26	32	Offer any of several diets that produce a caloric deficit and have evidence for weight loss efficacy and safety (e.g., low-carbohydrate, Dietary Approaches to Stop Hypertension (DASH), low-fat).	A	Reviewed, Amended	Recommendation 7
27	32	Offer very-low-calorie diets for weight loss, but only for short durations (12-16 weeks) and under close medical supervision.	B	Not reviewed, Deleted	–
28	32	Offer meal replacements to achieve low-calorie or very low-calorie diets.	A	Reviewed, New-replaced	Recommendation 8
29	34	Offer physical activity elements (e.g., home fitness, lifestyle, or structured/supervised physical activities) that can be combined to produce a caloric deficit leading to weight loss.	A	Reviewed, New-replaced	Recommendation 6
30	34	Offer physical activity options that include short intermittent bursts (at least 10minutes) as well as longer continuous exercise.	A	Reviewed, New-replaced	Recommendation 6
31	34	Offer, as part of a comprehensive lifestyle intervention, moderate-intensity physical activity performed for at least 150 minutes/week to result in weight loss.	A	Reviewed, New-replaced	Recommendation 6
32	34	Offer, as part of comprehensive lifestyle intervention, moderate-intensity physical activity performed for 200-300 minutes per week to prevent weight regain after initial weight loss.	EO	Reviewed, New-replaced	Recommendation 6
33	36	Offer pharmacotherapy with the combination phentermine/topiramate extended-release to patients with a body mass index (BMI) ≥30 kg/m^2 and to those with a BMI≥27 kg/m^2 who also have obesity-associated conditions, as an adjunct to comprehensive lifestyle intervention, when lifestyle interventions alone do not produce the desired weight loss.	A	Reviewed, New-replaced	Recommendation 9

2014 Location		2014 Recommendation Text	2014 Grade	Recommendation Category	2020 Recommendation
Rec. Number	Page				
34	36	Offer pharmacotherapy with orlistat or lorcaserin to patients with a body mass index (BMI) ≥30 kg/m^2 and to those with a BMI ≥27 kg/m^2 who also have obesity-associated conditions, as an adjunct to comprehensive lifestyle intervention, when lifestyle interventions alone do not produce the desired weight loss.	B	Reviewed, New-replaced	Recommendation 9
35	36	Offer pharmacotherapy (i.e., orlistat, lorcaserin, combination phentermine/topiramate extended-release) as an adjunct to comprehensive lifestyle intervention, to patients with obesity-associated conditions, for its beneficial effects on type 2 diabetes, hypertension, and/or dyslipidemia.	B	Reviewed, Deleted	–
36	36	Offer patients who achieve their weight loss goal a program that includes continued use of medication for weight maintenance.	B	Reviewed, Deleted	–
37	38	Offer bariatric surgery, as an adjunct to comprehensive lifestyle intervention, for weight loss in adult patients with a body mass index (BMI) >40 kg/m^2 or those with BMI 35.0-39.9 kg/m^2 with one or more obesity-associated conditions.	A	Reviewed, New-replaced	Recommendation 13
38	38	Offer bariatric surgery, as an adjunct to comprehensive lifestyle intervention, to improve some obesity-associated conditions in adult patients with a body mass index (BMI) >35.0 kg/m^2.	A	Reviewed, New-replaced	Recommendation 13
39	38	Current evidence is insufficient to assess the balance of benefits and harms of offering bariatric surgery as an adjunct to comprehensive lifestyle intervention, for weight loss or to improve some obesity-associated conditions, to patients over age 65 or with a body mass index (BMI) <35 kg/m^2.	I	Reviewed, Amended	Recommendation 14
40	39	Engage all patients who are candidates for bariatric surgery in a general discussion of the benefits and potential risks. If more detailed information is requested by the patient to assist in the decision-making process, a consultation with a bariatric surgical team should occur.	EO	Not reviewed, Deleted	–
41	39	Provide lifelong follow-up after bariatric surgery to monitor adverse effects and complications, dietary restrictions, adherence to weight management behaviors, and psychological health.	EO	Not reviewed, Deleted	–

Appendix E: Participant List

Erin Arra, MS, RD, CSOWM, LD
Primary Care/ALS Dietitian
Facility MOVE! Weight Management Program Coordinator
VA Medical Center
Cleveland, OH

Charolotte K. Baldridge, FNP
Family Nurse Practitioner
San Antonio Military Medical Center
Joint Base San Antonio, TX

Elaine Furmaga, PharmD
National Clinical Pharmacy Program Manager
VA Pharmacy Benefits Management Services
Hines, IL

Earl Gaar, MD
Professor of Surgery
University of Louisville School of Medicine
VA Medical Center
Louisville, KY

Michael G. Goldstein, MD
Associate Chief Consultant
Office of Patient Care Services
VHA National Center for Health Promotion and Disease Prevention (NCP)
Durham, NC

Navjit (Nicky) Goraya, MD
Primary Care Physician
Department of Ambulatory Care
VA Medical Center
Washington, D.C.

LTC Sky D. Graybill, MD
Chief of Endocrinology
Brooke Army Medical Center
Join Base San Antonio, TX

Gwen Hampton, PMHCNS-BC
Chief Nurse for Mental Health
Psychiatric Mental Health Clinical Nurse Specialist
Mental Health & Behavioral Sciences
W.G. Bill Hefner VAMC
Salisbury, NC

CPT Zachary M. Leftwich, PharmD
Deputy Chief, Pharmacy Branch
AMEDD C&S Pharmacology Instructor
Interservice Physician Assistant
Joint Base San Antonio, TX

Stéphanie B. Mayer, MD, MHSc
Associate Professor
Divisions of Endocrinology and Metabolism
Hunter Homes McGuire Veteran Affairs and VCU
Richmond, VA

COL Stephanie A. Meyer, SP, DrPH, MS, RD, LD, CHES
Nutrition Consultant to TSG & Nutrition Program Manager
HQ, US Army Medical Command
Joint Base San Antonio, TX

Susan Raffa, PhD
National Program Director
Supervisory Clinical Psychologist
National Center for Health Promotion and Disease Prevention
Veterans Health Administration
Durham, NC

CPT Scott J. Santos, PsyD
Clinical and Aeromedical Psychologist
Behavioral Health Officer
Fort Bragg, NC

COL Jason L. Silvernail, DPT, DSc
Assistant Chief of Staff
Walter Reed National Military Medical Center
Bethesda, MD

CPT Bryan Stepanenko, MD, MPH
Family Practice Physician
Martin Army Community Hospital
Fort Benning, GA

LTC Christopher L. Tracy, MD, FACP, FACR
Chief, Rheumatology Services
Director, Infusion Treatment Clinic
Womack Army Medical Center
Fort Bragg, NC

Carol Volante, DNP, APRN-C
Nurse Practitioner, Cardiology
SLC VA Medical Center
Salt Lake City, UT

CAPT Gordon G. Wisbach, MD, MBA, FACS, FAMBS, MC, USN
Director, Metabolic & Bariatric Surgery Program
General Surgery Department
Naval Medical Center San Diego
San Diego, CA

Appendix F: Literature Review Search Terms and Strategy

A. EMBASE and Medline in EMBASE.com Syntax (all questions)

Set #	Concept	Strategy
#1	Obesity	'abdominal obesity'/exp OR 'diabetic obesity'/exp OR 'morbid obesity'/exp OR 'obese patient'/exp OR 'obesity'/de OR obes*:ab,ti,kw OR overweight:ab,ti,kw
#2	Weight Loss	'body weight loss'/exp OR 'obesity management'/exp OR (((pound* OR weigh* OR bmi) NEAR/2 (loos* OR loss* OR off* OR reduc* OR shed*)):ab,ti,kw)
#3	Weight Maintenance	('body weight loss'/exp OR obes*:ab,ti,kw OR 'obesity'/de OR 'obesity management'/exp OR 'weight loss':ti OR 'weight loss'/exp) AND ('body weight maintenance'/exp OR longterm*:ab,ti,kw OR 'long-term':ab,ti,kw OR 'maintenance therapy'/exp OR maintain*:ab,ti,kw OR maintenance*:ab,ti,kw OR sustain*:ab,ti,kw) OR (((keep* OR maintain* OR maintenance OR sustain* OR longterm* OR 'long-term') NEAR/3 (weigh* OR pound* OR bmi) NEAR/3 (loos* OR loss* OR off OR reduc* OR shed*)):ab,ti,kw)
#4	Behavioral Treatments (Psychological)	'behavior therapy'/exp OR 'cognitive behavioral therapy'/exp OR 'cognitive therapy'/exp OR 'counseling'/exp OR 'dialectical behavior therapy'/exp OR 'food addiction'/exp OR 'motivation enhancement therapy' OR 'patient counseling'/exp OR 'problem solving therapy'/exp OR 'psychiatric treatment'/exp OR 'psychotherapy'/exp OR (((behavior* OR behaviour* 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,kw) OR ((food* NEAR/2 addict*):ab,ti,kw) OR psychotherap*:ab,ti,kw
#5	Behavioral Treatments (Lifestyle Modifications)	'behavioral economics'/exp OR 'behavior modification'/exp OR 'dietary compliance'/exp OR 'eating habit'/exp OR 'environmental change'/exp OR 'feeding behavior'/exp OR 'food preference'/exp OR 'food seeking behavior'/exp OR 'goal attainment'/exp OR 'habit'/exp OR 'health behavior'/exp OR 'healthy lifestyle'/exp OR 'lifelong learning'/exp OR 'lifestyle modification'/exp OR 'motivation'/exp OR 'motivational interviewing'/exp OR 'patient education'/exp OR 'portion size'/exp OR 'problem solving'/exp OR 'social learning'/exp OR 'social learning theory'/exp OR 'stress management'/exp OR (((adjust* OR adapt* OR adopt* OR alter* OR chang* OR health* OR improv* OR modif* OR new OR overhaul*) NEAR/2 (activ* OR behav* OR environment* OR exercis* OR habit* OR health* OR lifestyle* OR pattern* OR physical* OR regimen* OR routine*)):ab,ti,kw) OR ((behav* NEAR/2 (economic* OR theor*)):ab,ti,kw) OR ((motivat* NEAR/2 interview*):ab,ti,kw) OR ((portion* NEAR/2 (control* OR size*)):ab,ti,kw) OR (((collaborat* OR combin* OR comprehensiv* OR customi* OR group* OR individuali* OR integrat* OR interdisciplin* OR multi* OR personali* OR speciali* OR tailor*) NEAR/2 (approach* OR care OR component* OR deliver* OR method* OR modalit* OR plan* OR program* OR regimen* OR strateg* OR support* OR technique*)):ab,ti,kw) OR ((social* NEAR/2 learn*):ab,ti,kw) OR comprehensiv*:ti OR group*:ti OR program*:ti OR service*:ti OR transtheoretical*

Set #	Concept	Strategy
#6	Modes of Intervention	'face to face support group'/exp OR 'group therapy'/exp OR 'internet'/exp OR 'mobile application'/exp OR 'mobile health application'/exp OR 'mobile phone'/exp OR 'online monitoring'/exp OR 'self care'/exp OR 'self monitoring'/exp OR 'self report'/exp OR 'social media'/exp OR 'support group'/exp OR 'technology assisted health coaching' OR 'teleconsultation'/exp OR 'telehealth'/exp OR 'telemedicine'/exp OR 'telemonitoring'/exp OR 'text messaging'/exp OR 'videorecording'/exp OR 'workplace'/exp OR 'weight loss program'/exp OR android*:ab,ti,kw OR app:ab,ti,kw OR apps:ab,ti,kw OR 'clinical video telehealth':ab,ti,kw OR cvt:ab,ti OR device*:ab,ti,kw OR digital*:ab,ti,kw OR electronic*:ab,ti,kw OR 'e-mail':ab,ti,kw OR email:ab,ti,kw OR 'face-to-face':ab,ti,kw OR facebook:ab,ti,kw OR internet:ab,ti,kw OR iphone*:ab,ti,kw OR 'mobile health':ab,ti,kw OR mhealth:ab,ti,kw OR 'm health':ab,ti,kw OR 'one-on-one':ab,ti,kw OR online:ab,ti,kw OR phone*:ab,ti,kw OR 'in person':ab,ti,kw OR 'in-person':ab,ti,kw OR 'smart-phone':ab,ti,kw OR smartphone*:ab,ti,kw OR 'smart watch':ab,ti,kw OR smartwatch:ab,ti,kw OR 'short message service':ab,ti,kw OR sms:ab,ti,kw OR technolog*:ab,ti,kw OR telephone*:ab,ti,kw OR text*:ab,ti,kw OR video*:ab,ti,kw OR virtual*:ab,ti,kw OR wearable:ab,ti,kw OR web:ab,ti,kw OR 'web site*':ab,ti,kw OR website*:ab,ti,kw OR wireless*:ab,ti,kw OR workplace:ab,ti,kw OR ((self* NEAR/2 (actuali* OR administer* OR care OR deliver* OR direct* OR monitor* OR report*)):ab,ti,kw) OR (((shar* OR group*) NEAR/2 appointment*):ab,ti,kw) OR (((employ* OR work* OR office*) NEAR/2 (based OR environment* OR place OR setting* OR space*)):ab,ti,kw)
#7	Dietary Approaches	'atkins diet'/exp OR 'dash diet'/exp OR 'fasting'/exp OR 'ketogenic diet'/exp OR 'low calorie diet'/exp OR 'low carbohydrate diet'/exp OR 'low fat diet'/exp OR 'mediterranean diet'/exp OR 'paleolithic diet'/exp OR 'time restricted feeding'/exp OR 'very low calorie diet'/exp OR 'very low calorie ketogenic diet'/exp OR (((atkins* OR dash OR keto* OR mediterranean* OR paleo* OR 'south beach') NEAR/3 (ate OR consum* OR diet* OR eat* OR feed* OR food* OR plan* OR regimen* OR style*)):ab,ti,kw) OR (((low* OR minim* OR reduc* OR restrict*) NEAR/2 (calorie* OR carb* OR fat*)):ab,ti,kw) OR ((meal* NEAR/2 (replac* OR substitut*)):ab,ti,kw) OR ((time* NEAR/2 restrict*):ab,ti,kw) OR 'dietary approaches to stop hypertension':ab,ti,kw OR fast*:ab,ti,kw
#8	Physical Activity	'aerobic exercise'/exp OR 'cardio respiratory fitness' OR 'exercise'/exp OR 'exercise intensity'/exp OR 'fitness'/exp OR 'high intensity interval training'/exp OR 'jogging'/exp OR 'martial art'/exp OR 'moderate intensity continuous training'/exp OR 'physical activity'/exp OR 'physical activity, capacity and performance'/exp OR 'pilates'/exp OR 'resistance training'/exp OR 'stretching exercise'/exp OR 'swimming'/exp OR 'tai chi'/exp OR 'training'/exp OR 'treadmill'/exp OR 'treadmill exercise'/exp OR 'walking'/exp OR 'weight lifting'/exp OR 'yoga'/exp OR bicycle*:ab,ti,kw OR bike*:ab,ti,kw OR biking:ab,ti,kw OR cardio:ab,ti,kw OR cycling:ab,ti,kw OR exercis*:ab,ti,kw OR fitness:ab,ti,kw OR jog*:ab,ti,kw OR hike*:ab,ti,kw OR hiking:ab,ti,kw OR 'martial art*':ab,ti,kw OR pilates:ab,ti,kw OR ran:ab,ti,kw OR run:ab,ti,kw OR runner:ab,ti,kw OR runs:ab,ti,kw OR running:ab,ti,kw OR sport*:ab,ti,kw OR swim*:ab,ti,kw OR 'tai chi':ab,ti,kw OR treadmill*:ab,ti,kw OR walk*:ab,ti,kw OR 'weight training':ab,ti,kw OR workout*:ab,ti,kw OR ((work NEXT/1 out*):ab,ti,kw) OR yoga:ab,ti,kw OR (((aerobic* OR physical*) NEAR/2 (exercis* OR fitness)):ab,ti,kw) OR (((activ* OR exercis* OR fitness* OR physical* OR train*) NEAR/2 (boost* OR duration* OR encourag* OR engag* OR enhance* OR frequen* OR improv* OR increas* OR intens* OR interval* OR partake* OR participat* OR plan* OR promot* OR regimen* OR regular* OR routine* OR schedul*)):ab,ti,kw) OR (((desk* OR workstation* OR 'work station*') NEAR/2 (activ* OR adjust* OR stand*)):ab,ti,kw)

Set #	Concept	Strategy
#9	Pharmacotherapy	'amfebutamone'/exp OR 'amfebutamone plus naltrexone'/exp OR 'anorexic agent'/exp OR 'antiobesity agent'/exp OR 'benzphetamine'/exp OR 'liraglutide'/exp OR 'lorcaserin'/exp OR 'naltrexone'/exp OR 'phendimetrazine'/exp OR 'phentermine'/exp OR 'phentermine plus topiramate'/exp OR 'sibutramine'/exp OR 'tetrahydrolipstatin'/exp OR 'topiramate'/exp OR alli:ab,ti,kw OR amfebutamone*:ab,ti,kw OR belviq*:ab,ti,kw OR benzphetamine:ab,ti,kw OR bupropion*:ab,ti,kw OR contrave*:ab,ti,kw OR orlistat*:ab,ti,kw OR diethylpropion:ab,ti,kw OR liraglutide*:ab,ti,kw OR lorcaserin*:ab,ti,kw OR naltrexone*:ab,ti,kw OR phendimetrazine:ab,ti,kw OR phentermine*:ab,ti,kw OR qsymia*:ab,ti,kw OR saxenda*:ab,ti,kw OR sibutramine*:ab,ti,kw OR tetrahydrolipstatin*:ab,ti,kw OR topiramate*:ab,ti,kw OR victoza:ab,ti,kw OR wellbutrin*:ab,ti,kw OR xenical*:ab,ti,kw OR zyban*:ab,ti,kw OR 'appetite suppressant*':ab,ti,kw OR (((‘anti-obesity' OR antiobesity OR 'weight loss') NEAR/1 (agent* OR drug* OR medicat* OR pharm*)):ab,ti,kw)
#10	Dietary Supplements/ Nutraceutical	'beta glucan'/exp OR caffeine/exp OR 'calcium sulfate'/exp OR capsaicin/exp OR carnitine/exp OR 'chinese medicine'/exp OR chitin/exp OR chitosan/exp OR chromium/exp OR cinnamon/exp OR 'cinnamon extract'/exp OR 'cissus quadrangularis'/exp OR cola/exp OR 'conjugated linoleic acid'/exp OR 'dietary fiber'/exp OR 'dietary supplement'/exp OR 'ephedra sinica'/exp OR fucoxanthin/exp OR 'garcinia cambogia'/exp OR 'garcinia cambogia extract'/exp OR germander/exp OR 'guar gum'/exp OR ginseng/exp OR guarana/exp OR 'guarana extract'/exp OR 'herbaceous agent'/exp OR hoodia/exp OR 'hydroxycitric acid'/exp OR 'ilex paraguariensis'/exp OR 'mannan'/exp OR 'mineral supplementation'/exp OR 'nutraceutical'/exp OR 'phaseolus vulgaris'/exp OR 'probiotic agent'/exp OR 'pyruvic acid'/exp OR sinecatechins/exp OR 'sour orange'/exp OR 'sour orange extract'/exp OR supplementation/exp OR trigonella/exp OR 'vitamin d'/exp OR 'vitamin supplementation'/exp OR yohimbine/exp OR (((diet* OR calcium* OR fiber* OR fibre* OR herb* OR mineral* OR nutrient* OR nutrition* OR vitamin*) NEAR/2 supplement*):ab,ti,kw) OR 'african mango':ab,ti,kw OR 'beta-glucan*':ab,ti,kw OR 'bitter orange':ab,ti,kw OR caffeine:ab,ti,kw OR calcium:ab,ti,kw OR 'camellia sinensis':ab,ti,kw OR capsaicin:ab,ti,kw OR carnitine:ab,ti,kw OR chitin:ab,ti,kw OR chitosan:ab,ti,kw OR cinnamon:ab,ti,kw OR 'cissus quadrangularis':ab,ti,kw OR 'citrus aurantium':ab,ti,kw OR 'coffea arabica':ab,ti,kw OR 'coffea canephora':ab,ti,kw OR 'coffea robusta':ab,ti,kw OR 'cola nut*':ab,ti,kw OR chromium:ab,ti,kw OR 'coleus forskohlii':ab,ti,kw OR 'conjugated linoleic acid':ab,ti,kw OR 'cumin':ab,ti,kw OR 'cuminum cyminum l':ab,ti,kw OR dandelion*:ab,ti,kw OR forskolin ab,ti,kw OR fenugreek ab,ti,kw OR fucoxanthin:ab,ti,kw OR 'garcinia cambogia':ab,ti,kw OR germander:ab,ti,kw OR ginseng:ab,ti,kw OR glucomannan:ab,ti,kw OR 'green coffee bean extract':ab,ti,kw OR 'green tea':ab,ti,kw OR 'guar gum':ab,ti,kw OR guarana:ab,ti,kw OR 'gymnema sylvestre'/exp OR 'gymnema sylvestre extract'/exp OR 'gymnema sylvestre':ab,ti,kw OR hoodia:ab,ti,kw OR 'hydroxycitric acid':ab,ti,kw OR 'irvingia gabonensis':ab,ti,kw OR kola:ab,ti,kw OR konjac:ab,ti,kw OR 'l-carnitine':ab,ti,kw OR 'ma huang':ab,ti,kw OR mannan:ab,ti,kw OR mate:ab,ti,kw OR nutraceutical*:ab,ti,kw OR oregano:ab,ti,kw OR 'phaseolus vulgaris':ab,ti,kw OR probiotic*:ab,ti,kw OR pyruvate:ab,ti,kw OR 'raspberry ketone*':ab,ti,kw OR rosemary:ab,ti,kw OR 'rosmarinus officinalis extract'/exp OR 'sour orange':ab,ti,kw OR teucrium:ab,ti,kw OR trigonella:ab,ti,kw OR 'vitamin d':ab,ti,kw OR 'white kidney bean*':ab,ti,kw OR 'yerba mate':ab,ti,kw OR yohimbe:ab,ti,kw

Set #	Concept	Strategy
#11	Bariatric Surgery	'bariatric surgery'/exp OR 'biliopancreatic bypass'/exp OR 'gastric banding'/exp OR 'endoscopic gastric plication' OR 'gastric plication' OR 'gastric bypass surgery'/exp OR 'laparoscopic gastric plication' 'laparoscopic sleeve gastrectomy'/exp OR 'laparoscopic surgery'/exp OR 'percutaneous endoscopic gastrostomy'/exp OR 'roux y anastomosis'/exp OR 'roux-en-y gastric bypass'/exp OR 'sleeve gastrectomy'/exp OR 'biliopancreatic diversion':ab,ti,kw OR 'biliopancreatic diversion with duodenal switch':ab,ti,kw OR 'bpd/ds':ab,ti,kw OR 'bpd-ds':ab,ti,kw OR 'closed loop gastric electrical stimulation':ab,ti,kw OR 'duodenal jejunal':ab,ti,kw OR 'duodenal switch':ab,ti,kw OR 'gastric bypass':ab,ti,kw OR 'gastric by-pass':ab,ti,kw OR 'gastric sleeve':ab,ti,kw OR 'sleeve gastrectomy':ab,ti,kw OR 'roux-n-y':ab,ti,kw OR 'roux-en-y':ab,ti,kw OR rygb:ab,ti,kw OR (((bariatric* OR metabolic OR obes* OR 'weight loss' OR 'weight reduction') NEAR/3 (operat* OR procedur* OR surg*)):ab,ti,kw) OR ((laparoscopic* NEAR/3 band*):ab,ti,kw)
#12	FDA-approved Weight Loss Devices	'digestive surgical device'/exp OR 'gastric balloon'/exp OR 'gastric band'/exp OR 'gastric pacemaker'/exp OR 'implanted vagus nerve stimulator'/exp OR 'stomach bypass device'/exp OR 'weight loss device*':ab,ti,kw OR abiliti:ab,ti,kw OR aspireassist*:ab,ti,kw OR elipse*:ab,ti,kw OR endobarrier*:ab,ti,kw OR enterra*:ab,ti,kw OR heliosphere*:ab,ti,kw OR 'lap band*':ab,ti,kw OR lapband*:ab,ti,kw OR maestro*:ab,ti,kw OR obalon*:ab,ti,kw OR orbera*:ab,ti,kw OR reshape*:ab,ti,kw OR smartbyte*:ab,ti,kw OR vbloc*:ab,ti,kw OR (((balloon* OR band* OR bypass* OR 'by-pass' OR electrostimulat* OR emptying OR fda OR 'food and drug administration' OR gastric* OR 'intra-gastric*' OR intragastric* OR neurostimulat* OR sleeve* OR stimulat*) NEAR/3 (device* OR implant* OR system*)):ab,ti,kw) OR (((nerve* OR vagus OR vagal) NEAR/2 block*):ab,ti,kw)
#13	Study Designs/ Publication Types/ Date and Language Restrictions	[english]/lim AND [2013-2019]/py NOT (abstract:nc OR annual:nc OR 'book'/exp OR 'case report'/exp OR conference:nc OR 'conference abstract':it OR 'conference paper'/exp OR 'conference paper':it OR 'conference proceeding':pt OR 'conference review':it OR congress:nc OR 'editorial'/exp OR editorial:it OR 'erratum'/exp OR letter:it OR 'note'/exp OR note:it OR meeting:nc OR sessions:nc OR 'short survey'/exp OR symposium:nc) AND ([cochrane review]/lim OR 'meta analysis'/de OR metaanaly*:ab,ti,kw OR ((meta* NEXT/1 anal*):ab,ti,kw) OR 'randomized controlled trial'/de OR random*:ti OR pool*:ab,ti,kw OR systematic*:ti OR 'systematic review'/de OR 'systematic review*':ab,ti,kw)
#14	Remove Pediatric/ Pregnant/and Animal Populations	(abortion*:ti OR abortus:ti OR adolescen*:ti OR ((ante* OR post* OR pre*) NEXT/1 (adolesc* OR natal* OR partum)):ti OR antenatal*:ti OR antepartum:ti OR baby:ti OR babies:ti OR birth*:ti OR boy*:ti OR (breast* NEXT/1 (fed* OR feed*)):ti OR child*:ti OR classroom*:ti OR 'day care':ti OR ectopic:ti OR embryo*:ti OR fetal:ti OR fetus:ti OR gestation*:ti OR girl*:ti OR gravid*:ti OR infan*:ti OR juvenil*:ti OR 'in utero':ti OR kinder*:ti OR kid:ti OR kids:ti OR maternal:ti OR maternity:ti OR miscarry:ti OR miscarriage*:ti OR multigravid*:ti OR multipar*:ti OR multip:ti OR neonat*:ti OR newborn*:ti OR nullipar*:ti OR nurser*:ti OR infan*:ti OR obstaetric*:ti OR obstetric*:ti OR paediatric*:ti OR pediatric*:ti OR perinat* OR (post* NEXT/1 (natal* OR partum*)):ti OR postnatal*:ti OR postpartum:ti OR (pre* NEXT/1 (adolesc* OR matur* OR natal* OR pubes* OR teen* OR term*)):ti OR preadolesc*:ti OR preeclamps*:ti OR pregnan*:ti OR prematur*:ti OR prenatal*:ti OR prepubesc*:ti OR preschool*:ti OR preteen*:ti OR preterm*:ti OR primigravid*:ti OR primip*:ti OR pubert*:ti OR pubesc*:ti OR school*:ti OR secundigravid*:ti OR stillbirth*:ti OR teen*:ti OR toddler*:ti OR trimester*:ti OR young*:ti OR youth*:ti OR equine* OR canine* OR cat OR cats OR dog* OR feline OR horse* OR mice OR mouse OR ovine OR pig OR pigs OR porcine OR rabbit* OR rat OR rodent* OR sheep OR swine)
#15	KQ1	(#1 AND #2) AND (#4 OR #5) AND #13 NOT #14 What are the benefits and harms of weight loss behavioral interventions on weight status and health outcomes?

Set #	Concept	Strategy
#16	KQ2	#3 AND (#4 OR #5) AND #13 NOT #14 What is the effectiveness (versus no intervention, wait list, intervention unrelated to weight), comparative effectiveness (versus another weight maintenance behavioral treatment), and safety of weight *maintenance* behavioral treatments on weight maintenance starting after initial weight loss? Does this vary with intervention intensity (number of contacts) or intervention duration?
#17	KQ3	(#2 OR #3) AND #6 AND #13 NOT #14 What is the comparative effectiveness of different modes of delivering behavioral weight loss or maintenance interventions? Including: Technology / virtual versus in-person Group versus individual Self-directed versus professionally-directed Individualized / tailored versus standard
#18	KQ4	#1 AND (#2 OR #3) AND #7 AND #13 NOT #14 What is the comparative effectiveness and safety of various dietary approaches on weight status and health outcomes? Including: Different macronutrient compositions: low-carb / Atkins / South Beach / ketogenic versus low-fat versus balanced low calorie Eating plans: DASH, Mediterranean, paleo Meal replacement Intermittent fasting / time-restricted eating Very low calorie diets
#19	KQ5	#1 AND (#2 OR #3) AND #8 AND #13 NOT #14 What are the benefits and harms of physical activity on initial weight loss and long-term weight status? Does this vary with physical activity type (e.g., aerobic, resistance) or intensity (e.g., frequency, duration)?
#20	KQ6 AND KQ7 (Searched together)	(#1 OR #2 OR #3) AND #9 AND #13 NOT #14 What are the benefits and harms of short term administration of FDA-approved weight *loss* pharmacotherapy on initial (short-term) weight loss and long-term weight status? What are the benefits and harms of chronic administration of FDA-approved weight *loss* pharmacotherapy on weight maintenance and health outcomes?
#21	KQ8	(#1 OR #2 OR #3) AND #10 AND #13 NOT #14 What are the benefits and harms of dietary supplement / nutraceutical on initial weight loss and long-term weight status?
#22	KQ9 AND KQ10 (Searched together)	(#1 OR #2 OR #3) AND #11 AND #13 NOT #14 What are the benefits and harms of bariatric surgery on initial weight loss, long-term weight status, health outcomes, and comorbid conditions (e.g., diabetes, hypertension, or osteoarthritis? Does this vary by: Patient initial BMI: including 30-35, 35-40, >40 Patient initial comorbid conditions: including diabetes, hypertension, osteoarthritis Patient age or "physiological age" What is the comparative effectiveness of different type of bariatric procedures on short and long-term weight loss, health outcomes and comorbid conditions

Set #	Concept	Strategy
#23	KQ11 and KQ12 (Searched together)	(#1 OR #2 OR #3) AND #12 AND #13 NOT #14 What benefits and harms of FDA-approved weight loss devices on initial weight loss, long-term weight status, health outcomes, and comorbid conditions (e.g., diabetes, hypertension, or osteoarthritis)? Does this vary by: Patient initial BMI: including 30-35, 35-40, >40 Patient initial comorbid conditions including diabetes, hypertension, osteoarthritis Patient age or "physiological age" What is the comparative effectiveness and harms od FDA-approved weight loss devices on short and long-term weight loss, health outcomes and comorbid conditions
#24	Combine Concepts	#15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23

B. PsycINFO in OVID Syntax (for KQ1, KQ2, and KQ3 only)

Set #	Concept	Strategy
#1	Obesity	exp obesity/ OR exp overweight/ OR (obes* OR overweight).mp
#2	Weight Loss	exp weight loss/ OR ((obes* OR overweight) ADJ2 manag*).mp. OR ((pound* OR weigh* OR bmi) ADJ2 (loos* OR loss* OR off* OR reduc* OR shed*)).mp.
#3	Weight Maintenance	(exp obesity/ OR exp overweight/ OR exp weight loss/ OR obes*.ab,ti. OR weight loss.ab,ti.) AND (exp maintenance therapy/ OR exp weight control/ OR longterm.ab,ti OR long-term.ab,ti OR maintain*.ab,ti OR maintenance*.ab,ti. OR sustain*.ab,ti.) OR ((keep* OR maintain* OR maintenance OR sustain* OR longterm* OR long-term) ADJ3 (weigh* OR pound* OR bmi) ADJ3 (loos* OR loss* OR off OR reduc* OR shed*)).ab,ti.
#4	Behavioral Treatments (Psychological)	exp cognitive behavior therapy/ OR exp cognitive therapy/ OR exp counseling/ OR exp dialectical behavior therapy/ OR exp mental health services/ OR exp psychotherapy/ OR exp problem solving/ OR exp psychotherapy/ OR ((behavior* OR behaviour* OR cognitive OR dialectical OR emotion* OR "mental health" OR mindful* OR psych*) ADJ2 (coach* OR counsel* OR intervention* OR manag* OR support* OR therap* OR treat* OR train*)).ab,ti. OR (food* ADJ2 addict*).ab,ti. OR psychotherap*.ab,ti.
#5	Behavioral Treatments (Lifestyle Modifications)	exp attitude change/ OR exp behavior change/ OR exp behavior modification/ OR exp behavioral economics/ OR exp client education/ OR exp eating behavior/ OR exp food intake/ OR exp food preferences/ OR exp goals/ OR exp habits/ OR exp health behavior/ OR exp lifestyle/ OR exp lifestyle changes/ OR exp motivation/ OR exp motivational interviewing/ OR exp problem solving/ OR exp social learning/exp OR exp stress management/ OR exp transtheoretical model/ OR exp treatment compliance/ OR ((adjust* OR adapt* OR adopt* OR alter* OR chang* OR health* OR improv* OR modif* OR new OR overhaul*) ADJ2 (activ* OR behav* OR environment* OR exercis* OR habit* OR health* OR lifestyle* OR pattern* OR physical* OR regimen* OR routine*)).ab,ti. OR (behav* ADJ2 (economic* OR theor*)).ab,ti. OR (motivat* ADJ2 interview*).ab,ti. OR (portion* ADJ2 (control* OR size*)).ab,ti. OR ((collaborat* OR combin* OR comprehensiv* OR customi* OR group* OR individuali* OR integrat* OR interdisciplin* OR multi* OR personali* OR speciali* OR tailor*) ADJ2 (approach* OR care OR component* OR deliver* OR method* OR modalit* OR plan* OR program* OR regimen* OR strateg* OR support* OR technique*)).ab,ti. OR (social* ADJ2 learn*).ab,ti. OR comprehensiv*.ti. OR group*.ti. OR program*.ti. OR service*.ti. OR transtheoretical*.ab,ti.

Set #	Concept	Strategy
#6	Modes of Intervention	exp cellular phones/ OR exp digital video/ OR exp group psychotherapy/ OR exp internet/ OR exp internet usage/ OR exp mobile devices/ OR exp monitoring/ OR exp self-report/ OR exp self monitoring/ OR exp social media/ OR exp support groups/ OR exp technology/ OR exp teleconferencing/ OR exp telemedicine/ OR exp text messaging/ OR exp workplace intervention/ OR (android* OR app OR apps OR "clinical video telehealth" OR cvt OR device* OR digital* OR electronic* OR "e-mail" OR email OR "face-to-face" OR facebook OR internet OR iphone* OR "mobile health" OR mhealth OR "m health" OR "one-on-one" OR online OR phone* OR "in person" OR "in-person" OR "smart-phone" OR smartphone* OR "smart watch" OR smartwatch OR "short message service" OR sms OR technolog* OR telephone* OR text* OR video* OR virtual* OR wearable OR web OR "web site*" OR website* OR wireless* OR workplace).ab,ti. OR (self* adj2 (actuali* OR administer* OR care OR deliver* OR direct* OR monitor* OR report*)).ab,ti. OR ((shar* OR group*) adj2 appointment*).ab,ti. OR ((employ* OR work* OR office*) adj2 (based OR environment* OR place OR setting* OR space*)).ab,ti.
#7	Study Designs/ Publication Types/ Date and Language Restrictions	(("randomized controlled trial*" OR "systematic review*" OR "meta analysis" OR "meta analyses" OR metaanaly*).ab,ti. OR (random* OR systematic*).ab,ti.) NOT (exp case report/ OR (authored book OR book OR edited book OR encyclopedia OR dissertation abstract OR electronic collection).pt. OR (abstract collection OR bibliography OR chapter OR clarification OR "column/opinion" OR "comment/reply" OR dissertation OR editorial OR encyclopedia entry OR "erratum/correction" OR letter OR obituary OR poetry OR publication information OR reprint OR retraction OR review-book OR review-media OR review-software & other).dt.)
#8	Remove Pediatric/Pregnant/and Animal Populations	((abortion* OR abortus OR adolescen* OR antenatal* OR antepartum OR baby OR babies OR birth* OR boy* OR child* OR classroom* OR day care OR ectopic OR embryo* OR fetal OR fetus OR gestation* OR girl* OR gravid* OR infan* OR juvenil* OR in utero OR kinder* OR kid OR kids OR maternal OR maternity OR miscarry OR miscarriage* OR multigravid* OR multipar* OR multip OR neonat* OR newborn* OR nullipar* OR nurser* OR infan* OR obstaetric* OR obstetric* OR paediatric* OR pediatric* OR perinat* OR postnatal* OR postpartum OR preadolesc* OR preeclamps* OR pregnan* OR prematur* OR prenatal* OR prepubesc* OR preschool* OR preteen* OR preterm* OR primigravid* OR primip* OR pubert* OR pubesc* OR school* OR secundigravid* OR stillbirth* OR teen* OR toddler* OR trimester* OR young* OR youth*).ti. OR (equine* OR canine* OR cat OR cats OR dog* OR feline OR horse* OR mice OR mouse OR ovine OR pig OR pigs OR porcine OR rabbit* OR rat OR rodent* OR sheep OR swine).ab,ti OR ((ante* OR post* OR pre*) ADJ1 (adolesc* OR natal* OR partum)).ti. OR (breast* ADJ1 (fed* OR feed*)).ti. OR (post* ADJ1 (natal* OR partum*)).ti. OR (pre* ADJ1 (adolesc* OR matur* OR natal* OR pubes* OR teen* OR term*)).ti.)
#9	Combine Concepts and Apply Date and Language Limits	7 NOT 8
#10	Apply Date and Language Limits	limit 9 to (english language and yr="2013 -Current")
#11	KQ1	(1 AND 2) AND (4 OR 5) AND 10 What are the benefits AND harms of weight loss behavioral interventions on weight status AND health outcomes?

Set #	Concept	Strategy
#12	KQ2	3 AND (4 OR 5) AND 10 What is the effectiveness (versus no intervention, wait list, intervention unrelated to weight), comparative effectiveness (versus another weight maintenance behavioral treatment), AND safety of weight *maintenance* behavioral treatments on weight maintenance starting after initial weight loss? Does this vary with intervention intensity (number of contacts) or intervention duration?
#13	KQ3	(2 OR 3) AND 6 AND 10 What is the comparative effectiveness of different modes of delivering behavioral weight loss or maintenance interventions? Including: Technology / virtual versus in-person Group versus individual Self-directed versus professionally-directed Individualized / tailored versus standard
#14	Combine Concepts	11 OR 12 OR 13
#15	Remove Duplicates from 14	

Appendix G: Dietary Approaches

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

The Academy of Nutrition and Dietetics (Academy) Evidence Analysis Library (EAL) Adult Weight Management Guideline (2014) [218] found strong evidence that weight loss, weight maintenance, and a reduced-calorie diet should be part of a comprehensive weight management program that also includes "increasing physical activity and behavioral strategies." This is supported by the 2016 Academy Position Statement for treating overweight and obesity.[219] The Academy EAL guideline further states that, "the registered dietitian should prescribe an individualized diet, including patient preferences and health status, to achieve and maintain nutrient adequacy and reduce caloric intake," and that calorie reduction can be achieved by one of the following:

A. Caloric Recommendations

- 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;
- A 500 to 750 kcal energy deficit/negative energy balance per day; or
- Restriction of certain food types, such as high carbohydrate foods, low fiber foods, or high-fat foods to create an energy deficit/negative energy balance by reducing food consumption [218]

The National Heart, Lung, and Blood Institute's Obesity Expert Panel echoes the Academy EAL, adding that a 30% energy deficit may be used as the basis for estimating calorie reduction versus using the 500 – 750 kcal range to estimate the calorie prescription to achieve negative energy balance.[220] Many different 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; 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 shared decision making to determine the specific dietary approach that considers and addresses patients' "preferences, health, and nutrient status."[219]

Table G-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.

Table G-1. Dietary Approaches to Support Weight Loss

Dietary Approaches	Description
Mediterranean diet[a] [221]	• A dietary pattern that is focused on plant-based food consumption, which includes vegetables, fruits, whole grains, nuts and seeds; minimally processed foods; olive oil as the primary fat source; low to moderate amounts of dairy, fish, and poultry; and minimal amounts of red meat.[220] This dietary approach is evaluated based on the intake of specific food groups with positive health outcomes rather than meeting specific nutrient standards.[221] • An SR of five RCTs (n=998) that compared the Mediterranean diet to low-carbohydrate, low-fat, or the American Diabetes Association diet found that at 12 and 48 months, participants on the Mediterranean diet lost an average of between 3.8 and 10.1 kg, lost more weight at ≥12 months, and lost a comparable amount of weight to the remaining diets.[222]
Dietary Approaches to Stop Hypertension (DASH) diet[b] [219]	• The DASH diet is a dietary pattern that focuses on reducing hypertension and promotes the consumption of vegetables, fruits, whole grains, nuts, legumes, seeds, low-fat dairy foods, and lean meats. It also limits the consumption of sugar-sweetened foods and beverages, sodium, caffeine, and alcohol. • The DASH Diet is low in saturated fats and rich in potassium, calcium, magnesium, dietary fiber, and protein. The sodium levels are between 1,500-2,300 mg daily. This dietary approach is recognized by the USDA as an ideal eating plan for Americans. • A 2016 SR and meta-analysis of 10 studies (n=1,291) found that participants who followed the DASH diet lost more weight than controls (WMD: -1.42 kg), and that DASH diet with and without energy restriction yielded statistically significant weight loss (WMD: -2.27 kg and -0.85 kg respectively). Studies varied between 8 and 24 weeks.[142]
Low-carbohydrate diet	• The definition of low carbohydrate varies based on the specific dietary approach. • The Dietary Guidelines for Americans recommends that 45 – 65% of calories each day come from carbohydrate and sets the RDA at 130 g.[221] Therefore, any recommendation that is less than 130 g of carbohydrate may be considered low carbohydrate. • Adherence to modest carbohydrate reductions may be more achievable than more strict carbohydrate reductions, while still promoting weight loss.[134,138,223] • Low-carbohydrate ketogenic diets (<50 g carbohydrate) are effective for weight loss, but this dietary approach may result in: headache, upset stomach, fatigue and dizzy spells (also called the "keto flu"); constipation; and may require micronutrient supplementation given limitations of vitamin and mineral-rich carbohydrate-containing foods.[123,130,144,224] • Typically, low-carbohydrate, ketogenic diets (induction phase of <20 g of carbohydrate) may be best implemented under medical supervision with attention paid to lifestyle and need for monitoring medications and comorbidities. Medications, especially diuretics and antiglycemic agents, may require adjustment on this diet plan.
Low-fat diet	• The definition of low-fat varies from less than 20 – 30% of total calories from fat, without formally prescribed energy restriction but with an energy deficit.[26] • Studies found that there was significant weight loss in both the low-fat and low-carbohydrate diet groups.[128,130] These findings are consistent with the findings in the 2013 AHA/ACC/TOS Guidelines for the Management of Obesity and Weight Management in Adults.[26]

Dietary Approaches	Description
Alternate day fasting and Intermittent fasting	• Alternate day fasting and intermittent fasting are both forms of intermittent energy restriction using varied plans for when energy is restricted (by day or in the same day). • Current research is limited on this dietary approach. • Studies using an alternate day fasting or intermittent fasting methodology yielded the same results, which was that there was no difference in weight loss when compared to an alternate calorie-restriction method.[125,126,131-133]

[a] For further information about the Mediterranean eating pattern see the 2015-2020 Dietary Guidelines for Americans, available at: https://health.gov/dietaryguidelines/2015/

[b] For further information on the DASH dietary pattern visit: https://www.nhlbi.nih.gov/health-topics/dash-eating-plan and https://health.gov/dietaryguidelines/2015/resources/2015-2020_Dietary_Guidelines.pdf

Abbreviations: ACC: American College of Cardiology; AHA: American Heart Association; DASH: Dietary Approaches to Stop Hypertension; g: grams; kg: kilograms; mg: milligrams; RDA: recommended dietary allowance; SR: systematic review; TOS: The Obesity Society; USDA: United States Department of Agriculture; WMD: weighted mean difference

Appendix H: Pharmacotherapy

A. Medications Approved for Long-term Weight Management

The following table includes prescribing information for the five medications currently FDA-approved for long-term weight management. The information has been compiled from the respective manufacturer's product information. See the individual product information for the most current prescribing information.

Table H-1. Pharmacologic Information for Long-term Weight Management Medications[a, b]

Medication	Dosing	Monitoring	Common Side Effects	Contraindications	Warnings
Phentermine/ topiramate ER (Qsymia®) **Schedule for Controlled Substances: CIV**	• Phentermine 3.75 mg/ topiramate 23 mg capsule each morning for 14 days; then increase to 7.5 mg/46 mg each morning for an additional 12 weeks • Per the product information, 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 to avoid inducing a seizure) • <u>Renal Impairment:</u> ♦ Moderate/severe (CrCl <50 mL/min): ♦ Maximum dose: 7.5 mg/ 46 mg daily • <u>Hepatic Impairment:</u> ♦ Moderate (Child-Pugh score 7 – 9) ♦ Maximum dose: 7.5 mg/ 46 mg daily	• Weight • Blood pressure (orthostatic) and/or signs/symptoms of hypotension • Resting heart rate • Serum bicarbonate, especially if the patient is taking another carbonic anhydrase inhibitor • Serum potassium, especially if the patient is 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 age • Baseline and periodic monitoring of serum creatinine (SCr)/ estimated glomerular filtration rate (eGFR)	• Increased heart rate • Paresthesia • Dizziness • Dysgeusia • Headache • Insomnia • Decreased serum bicarbonate • Xerostomia • Constipation • Upper respiratory tract infection • Nasopharyngitis	• Pregnancy • A REMS program exists to inform prescribers and patients of risks • Glaucoma • Hyperthyroidism • MAOI use during or within 14 days	• Metabolic acidosis • Cognitive impairment • Elevated heart rate • Nephrolithiasis • Hypokalemia • Mood and sleep disorders • Depression or suicidal ideation • Increased creatinine • Adjust hypoglycemic medications to avoid hypoglycemia • Abuse potential: Phentermine is pharmacologically related to amphetamines, which have a high abuse potential; prolonged use may lead to dependency • Anticonvulsants (including topiramate) should not be discontinued abruptly to minimize the possibility of increasing seizure frequency; tapering over at least 1 week is recommended • Avoid concomitant consumption of alcohol due to increased serum concentrations of topiramate which may lead to increased CNS depressant effect • Multiple drug interactions (CYP 2D6)

Medication	Dosing	Monitoring	Common Side Effects	Contraindications	Warnings
Naltrexone/ bupropion ER (Contrave®)	• Naltrexone 8mg/bupropion 90 mg dose-escalation schedule: ♦ Morning Dose/Evening Dose o Week 1: 1 tablet / None o Week 2: 1 tablet / 1 tablet o Week 3: 2 tablets / 1 tablet o Week ≥4: 2 tablets / 2 tablets ♦ Maintenance dose: 2 tablets twice daily (Naltrexone 16 mg/bupropion 180 mg) ♦ Per the product information, discontinue if a 5% weight loss is not achieved by week 12, as it is unlikely that a meaningful weight loss will be achieved and sustained with continued treatment • <u>Renal Impairment:</u> ♦ Moderate/severe: ♦ Maximum dose: 1 tablet twice a day o Not recommended for use in patients with end-stage renal disease. • <u>Hepatic Impairment:</u> ♦ Maximum dose: 1 tablet in the morning.	• Weight • Pregnancy • Glucose and/or signs/symptoms of hypoglycemia in patients with diabetes Blood pressure and/or signs/symptoms of hyper- or hypotension • Heart rate • Signs and symptoms of depression, suicidal thought or behavior, cognitive impairment, or changes in mood • Recommend to add baseline and periodic monitoring of renal and hepatic function	• Headache • Sleep disorder • Nausea • Constipation • Diarrhea • Vomiting • Dizziness • Xerostomia	• Opioid use (agonists or partial agonists) • Pregnancy • Uncontrolled hypertension • Seizure disorder • Bulimia or anorexia nervosa • Abrupt discontinuation of alcohol • Acute opioid withdrawal • Concomitant MAOI use or initiation in patients receiving linezolid or IV methylene blue	• Suicidal thinking/ behavior [U.S. Boxed Warning] • Neuropsychiatric symptoms • May precipitate acute opioid withdrawal in patients receiving opioids • Seizures • Increase blood pressure, heart rate • Hepatotoxicity • Adjust hypoglycemic medications to avoid hypoglycemia

Medication	Dosing	Monitoring	Common Side Effects	Contraindications	Warnings
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 • Renal Impairment: There are no dosage adjustments provided in the manufacturer's labeling • Hepatic Impairment: There are no dosage adjustments provided in the manufacturer's labeling	• Weight • Blood pressure (orthostatic) and/or signs/symptoms of hypotension • 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	• Gastrointestinal effects (e.g., oily rectal leakage, abdominal distress/pain, flatulence with discharge, bowel urgency, steatorrhea). Frequency may decline over time • Headache • Fatigue • Anxiety • Menstrual disease • Neuromuscular and skeletal pain • URTI 26.1% – 38.1% • Influenza 39.7%	• Pregnancy • Chronic malabsorption syndrome • Cholestasis	• Increased urinary oxalate and nephrolithiasis • Hepatotoxicity • Cholelithiasis • Interference with absorption of fat-soluble vitamins, cyclosporine, thyroid hormone, and anticonvulsants • Adjust hypoglycemic drugs to avoid hypoglycemia

Medication	Dosing	Monitoring	Common Side Effects	Contraindications	Warnings
Liraglutide (Saxenda®)	• 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 • Patients on secretagogues (such as sulfonylureas) or insulin: Consider reducing the dose of the secretagogue (e.g., by 50%) or insulin to avoid hypoglycemia • *Dose in Renal Impairment:* Use with caution in renal impairment	• Weight • Blood pressure (orthostatic) and/or signs/symptoms of hypotension • Resting heart rate • Glucose and/or signs/symptoms of hypoglycemia. Use additional caution if the patient is using another glucose-lowering agent. • Mood (symptoms of depression) and sleep disorders	• Increased heart rate • Headache • Hypoglycemia • Nausea • Diarrhea • Constipation • Vomiting • Dyspepsia • Abdominal pain • Fatigue	• Pregnancy • Personal or family history of medullary thyroid carcinoma (U.S. Boxed Warning) or MEN2	• Injection site reactions • Hypersensitivity reactions (caution if previous reactions to GLP-1 agonist) • Thyroid C-cell tumors **[Boxed Warning]** • Gallbladder disease • Pancreatitis (discontinue) • Increased heart rate • Renal impairment • Acute cholelithiasis and cholecystitis • Tachycardia • Acute/chronic renal failure exacerbation • Suicidal behavior and ideation • Adjust hypoglycemia drugs to avoid hypoglycemia

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

[b] In February 2020, the FDA requested the withdrawal of the weight-loss drug Belviq, Belviq XR (lorcaserin) from the U.S. market, citing potential risk of cancer outweighing the benefits of use.

Abbreviations: CIV: Schedule IV controlled substance; CrCl: creatinine clearance; ER: extended-release; GLP-1: glucagon-like peptide-1 receptor; IV: intravenous; MAOI: monoamine oxidase inhibitor; MEN2: multiple endocrine neoplasia type 2; mg: milligram; min: minute; mL: milliliter; REMS: Risk Evaluation and Mitigation Strategy; XR: extended-release

B. Medications and Potential for 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 are overweight, obese, or at risk. Providers should review the patient's current medications for any medications that may be contributing to increased weight. The side effects of weight gain 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 may benefit the patient whose only option is a medication associated with weight gain. The information in the 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.[225-227] 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.[228]

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 – 60 weeks found 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 paresthesias, taste perversion, psychomotor impairment, hypoesthesia, difficulty concentrating, anorexia, memory impairment, and nervousness.[229] In a meta-analysis in patients with obesity and T2DM, topiramate reduced weight and HgA1C; however, serious and total number of adverse events occurred more frequently with treatment.[230]

b. 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 PCOS.[89,231-235] It has also been shown to cause weight loss in patients without DM with antipsychotic-induced weight gain.[236] In patients with T2DM, reductions have persisted for 10 years or more and the most important influence on both weight loss and maintenance is adherence to metformin therapy.[237] Additional data are needed for the use of metformin for weight loss in patients without the aforementioned conditions.[238,239] 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).

c. Glucagon-like Peptide-1 Receptor Agonists (exenatide, dulaglutide, lixisenatide, semaglutide; note: liraglutide 3 mg dose FDA-approved for long-term weight management)

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.[240] 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.[241] 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.[242] 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/1,000 patient-years of observation [PYO]) than in the treatment arm with liraglutide (18, 0.4%, 1.1 events/1,000 PYO).[243] Due to rat and mice 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).

d. Sodium-glucose Cotransporter 2 Inhibitors (empagliflozin, dapagliflozin, canagliflozin, ertugliflozin)

As a class, sodium-glucose cotransporter 2 (SGLT2) inhibitors cause glucosuria by inhibiting 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.[244] 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, as well as rare cases of necrotizing fasciitis.[245,246] There remains a boxed warning for use of canagliflozin in the setting of foot ulcers or amputations. Renal function should be monitored with use.

e. Bupropion

Bupropion, as monotherapy, has been noted to cause weight loss when used in patients with depression or those seeking to abstain from tobacco.[247] 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 placebo.[248-250] 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.

f. 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.

g. Testosterone Replacement Therapy

Testosterone replacement therapy has been advocated to achieve weight loss in hypogonadal men with obesity.[251] 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.[252,253] 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.[254-256] This is an area requiring further review.[257]

h. 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.[258] 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.[259]

i. 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.[260] 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.

j. Thyroid Hormones

Several small studies have evaluated the association between weight loss and the use of levothyroxine and liothyronine replacement in hypothyroid patients.[261] 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., Grave's disease) is a condition that requires treatment to avoid negative health consequences. Latrogenic hyperthyroidism accrues significant harm.

Appendix I: Metabolic/Bariatric Surgery

Metabolic/bariatric surgery frequency has increased over the last decade, paralleling the obesity epidemic in the U.S. Advancement in laparoscopic surgical techniques, surgical instrumentation, and accreditation programs (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. Irrespective of surgical approach, these are major operative procedures with a target population that may have multiple comorbidities. Current operative mortality of <0.5% and major morbidity of <4% are significantly improved.[187,262,263] Nonetheless, all patients considering surgical intervention require careful pre-operative evaluation, paying particular attention to cardio-pulmonary risk factors and pre-habilitation as indicated. Evidence from five RCTs suggests that metabolic/bariatric surgery significantly improves systolic blood pressure, HbA1C, fasting blood glucose, HDL cholesterol, and triglycerides compared to non-surgical lifestyle and/mediation therapy at 1 – 5 years follow-up.[179,187,191,192] A survival benefit has been demonstrated.[264] Evidence from 23 observational studies shows continued absolute and excessive weight loss among overweight and obese adults >10 years after surgical intervention.[265] Evidence from 13 observational studies in one SR suggests that metabolic/bariatric surgery significantly reduces the incidence of hirsutism, menstrual irregularity, and infertility in women with PCOS and obesity at one year and longer follow-up.[266] Counter to this, however, is the finding that morbidity and mortality have been noted to be increased in those patients over the age of 60 who undergo bariatric surgical procedures compared to younger people.[201]

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 the Standards of Care. This includes identification of problematic maladaptive eating patterns that may require further assessment or management. Although nearly all patients with obesity have shortness of breath, if shortness of breath is severe, an assessment for sleep apnea and cardiopulmonary function is warranted to identify any potential contraindications to surgery or health issues that may be correctable or improved prior to surgery.[267] Any biliary symptoms should be evaluated with ultrasonography.[268] Patients who smoke should be encouraged to quit and abstain from smoking due to its deleterious effects on pulmonary function and wound healing. Patients that have active, untreated addictions to drugs or alcohol should not be referred for metabolic/bariatric surgery.[269]

Patients considering metabolic/bariatric surgery 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 a restricted diet, physical activity, and lifestyle changes is essential to long-term maintenance of weight loss after surgery. Patients should receive preoperative nutritional counseling to ensure they understand postoperative dietary requirements and the need for lifestyle alteration. Metabolic/bariatric surgery support groups often facilitate this education both pre-operatively as well as postoperatively. In addition, lifelong medical surveillance after metabolic/bariatric surgery should include monitoring for changes in the status of chronic health conditions and procedure-specific complications such as nutritional deficiencies.[270]

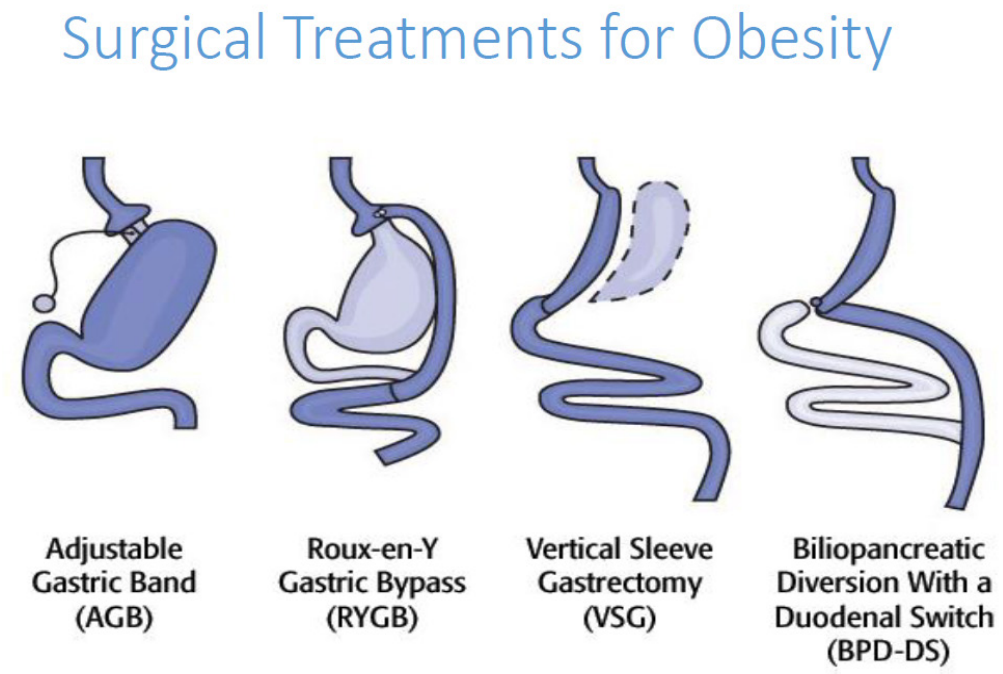
Numerous insurance companies mandate enrollment in a structured weight-loss program for a prescribed period of time before patients can be considered for these procedures. There is conflicting evidence as to

the benefit of such an approach and it has been condemned by the American Society of Metabolic and Bariatric Surgery.[265] The requirement of pre-surgical psycho-social evaluation of patients seeking weight-loss surgery has been adopted by the majority of third-party payers and by over 80% of bariatric programs in the U.S. 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 clinician plays a number of 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.[271]

Classic indications for metabolic/bariatric surgery are patients with a BMI ≥40 kg/m^2 who have failed to achieve significant weight loss by non-surgical means and are fit to withstand a major operative procedure or those with an obesity-related comorbidity and BMI ≥35 kg/m^2. All must commit to long-term follow-up. In this publication, we provide evidence to support the option of metabolic/bariatric surgery in conjunction with a comprehensive lifestyle intervention, for patients with DM and BMI ≥30 kg/m^2 (see Recommendation 13).

Expert consensus states that pregnancy is not recommended during the rapid weight-loss phase after metabolic/bariatric surgery; therefore, counseling and follow-up regarding contraception during this period is important.[272] Other contraindications to metabolic/bariatric surgery 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, active alcohol/substance abuse, and impaired intellectual capacity/inability to follow pre- and postoperative instructions.[273,274] Consultation with the bariatric surgeon should be performed to discuss all possible contraindications for surgery for any specific patient.

Figure I-1: Most Common Types of Metabolic/Bariatric Procedures Performed in the U.S. [275]



A. Non-metabolic Surgery (i.e., Adjustable Gastric Band)

With the adjustable gastric band procedure (AGB), a silastic inflatable band is placed around the cardia of the stomach. A reservoir port placed under the skin is subsequently injected with saline to expand or desufflate a balloon in the band to create more or less restriction to the passage food.[276] The AGB is considered to be a reversible form of the previously popular vertical banded gastroplasty. Reducing the band lumen via band filling is done postoperatively gradually over time with repeated adjustments or "fills". It rapidly became a popular procedure early after its introduction in the U.S. but has been abandoned by many due to its high rate of complications (and associated high rates of removal), and lower effectiveness compared to other procedures.[277,278]

B. Metabolic Surgery

Metabolic surgery includes procedures that involve stapling part of the GI system. There is growing recognition that they contribute to neurohormonal effects on the regulation of energy balance and hunger control.

a. Roux-en-Y Gastric Bypass

The RYGP can be an open, or more commonly, a laparoscopic procedure. It involves creating a 30 mL gastric pouch which empties into a Roux limb of jejunum. A variable distance downstream from this anastomosis (~150 cm), another anastomosis is created with the biliary limb to form a "common channel" that travels to the cecum.[278-280]

b. Laparoscopic Sleeve Gastrectomy

Since the publication of the 2014 VA/DoD Obesity CPG, laparoscopic sleeve gastrectomy (SG) has emerged as the most commonly done operation for obesity.[281] Its origins began as a component of Scopinaro's BPD with a duodenal switch (DS).[278,282-284] In the "super-obese population", sleeve gastrectomy was used as an initial procedure to bring the patient down to a "safer" operative weight when a more definitive by-pass component could be added. Seeing the impressive results of SG alone has established SG as a primary bariatric operative option.

The procedure involves removing 75 – 80% of the greater curvature of the stomach, re-shaping the stomach into a banana or "sleeve" shaped organ. The procedure permanently reduces the size of the stomach though there could be some dilation of the stomach later in life. Resection starts approximately 5 – 6 cm proximal to the pylorus and progresses close to the gastric cardia. It is usually fashioned over a 36 French bougie. It is a relatively simple procedure utilizing a laparoscopic GIA™ stapling device to resect the greater curvature with surgeons often using buttressing material around the staples to minimize postoperative leaks.

Several studies demonstrate that SG and RYGB provide more comparable weight loss than seen after adjustable gastric bands or nonsurgical interventions [187,282] with no reliable conclusion regarding which operation procedures result in the greatest weight loss following surgery. In a randomized trial (RT) conducted by Zhang et al. (2014) in China, SG and RYGB led to similar weight loss at one year, but RYGB was found to be superior at five years.[285] Similar resolution of type II diabetes with both procedures has been observed.[190] SG is associated with significantly fewer major complications within

30 days of surgery compared to RYGB or BPD. Reports of increased incidence of GERD have been noted after sleeve gastrectomy and remission of GERD is seen more often with RYGP.

As with any bariatric procedure, long-term weight regain can occur due to patient non-adherence with postoperative dietary instructions and may require one or more of a variety of re-interventions if applicable.

c. Biliopancreatic Diversion with Duodenal Switch

BPD with DS entails an SG and duodenal bypass affected by a proximal roux-en-y duodeno-jejunostomy. It is the longest studied of all bariatric operations and has the highest efficacy in terms of weight loss and T2DM resolution, but also has a higher risk of complications.[189,286] Technical complexity and long-term nutritional deficiencies have limited its acceptance and popularity in the U.S. The American Society for Metabolic and Bariatric Surgery published estimates from 2011-2014 that BPD comprised only 0.4% of bariatric procedures performed.[287] A lesser performed procedure is the "single anastomosis gastric bypass" or "mini gastric bypass" (MGP), which in essence is an SG combined with a loop gastro-jejunostomy. Reports show impressive results compared to RYGB and SG.[288,289]

C. Mortality Risk

Bariatric procedures have potentially serious complications, and there is a risk of mortality from these procedures. The risk of mortality varies according to the type of procedure performed. With laparoscopic RYGB, in one study of 16,509 patients, mortality was 0.3%.[290] Data from Longitudinal Assessment of Bariatric Surgery Consortium demonstrated 30-day mortality for LAGB, laparoscopic RYGB, and open RYGB of 0% of 1,109 patients, 0.2% of 2,975 patients, and 2.1% of 437 patients, respectively.[291] The Bariatric Outcomes Longitudinal Database 30-day and one-year mortality rate for 128,349 patients undergoing laparoscopic RYGP was 0.13% and 0.23% respectively. For SG, they were 0.06% and 0.11% respectively. BPD carries the highest risk of mortality, with a 30-day mortality at 1.2%.[292] 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.[263,293-295] In most studies, PE is the most frequently reported cause of death.

D. Morbidity Risk

Based upon the Longitudinal Assessment of Bariatric Surgery database including 4776 patients, the rate of failure of discharge from hospital at 30 days was 4.1%.[291] Over-all complication rates have decreased in time from 4.6% (2006) to 3.0% (2013).[286] The type of procedure done is associated with 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 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).[296] Similarly from the same database, open RYGP 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.[292] The following is a list of potential complications associated with the various surgical procedures:

a. Gastric Anastomotic Stricture (RYGB, BPD, LSG, MGP)

An SR (n=230) found that the risk of stricture for RYGB, BPD, and laparoscopic sleeve gastrectomy (LSG) was 3.3%, 1.2%, and 3.5% respectively.[297] Stenosis with a sleeve can occur if the sleeve kinks, twists, or narrows. An anastomotic stricture may form secondary to improper healing of a marginal ulceration of the anastomosis. Anastomotic stricture presents with dysphagia, vomiting, and/or food intolerance. This problem is generally addressed by endoscopic pneumatic balloon dilation. Multiple follow-up dilations may be required, but surgical revision is rarely required.

b. Marginal Ulceration (RYGB, BPD, MGP)

Marginal ulcers are peptic ulcerations that occur at the gastrojejunal anastomosis on the jejunal side of the anastomosis and typically occur within 30 days of the index procedure. A prospective study found the risk to be as high as 12.3% at one month following surgery.[298] The clinical presentation may include hematemesis, hematochezia, obstructive symptoms, and pain. They are felt to be the result of tissue ischemia. Helicobacter pylori, smoking, and usage of NSAIDS are also risk factors. First line treatment is with proton pump inhibitors. Follow-up endoscopy should be performed to document resolution. When refractory to medical treatment, the anastomosis may require operative revision. Marginal ulcer bleeding can be severe but usually responds to endoscopic intervention.

c. Bowel Obstruction/Hernias (all)

As with any operation, adhesive bowel obstruction may occur. Presenting symptoms include vomiting, abdominal distention, and pain. Internal hernias can present more insidiously with intermittent symptoms such as cramping and abdominal pain. Rates for bowel obstruction of 6% have been reported with laparoscopic approaches.[299]

A curious site of intestinal obstruction secondary to internal herniation occurs in “Petersen's Space”, which is the space between the roux limb going to the gastric pouch and the transverse mesocolon. In one study (n=11,918), the incidence of this hernia was 2.51%.[300] Often seen when a roux limb is brought up in a retro-colic position it can cause a closed-loop obstruction. It occurs secondary to failure to close this potential site of internal herniation. Physical findings may be misleading and often a “swirl” sign can be seen on computerized tomography (CT) imaging. The incidence of internal hernias is somewhat higher with laparoscopic procedures compared to open procedures secondary to the relative lack of adhesion formation following laparoscopic procedures.[301]

Port-site hernias may develop in laparoscopic procedures secondary to technical errors in fascial closure. Incisional hernias from open incisions can occur in 6.4% to 8.6% of midline incisions [302,303] compared to 0.47% (port site) with the laparoscopic approach. In the same study,[303] bowel obstructions were seen in 2.91% of patients with the laparoscopic approach, compared to 2.1% with the open approach.

Partial bowel obstructions secondary to postoperative adhesions require admission and intravenous (IV) fluid hydration with initial conservative care. Gastrograffin small bowel studies may be helpful in the localization of a transition point (point of obstruction) and predicting the future need for operative intervention. Most partial obstructions resolve with IV fluid resuscitation and nasogastric tube decompression. Complete bowel obstructions or those with tight transition zones require emergent surgery.

Obstructions around the distal anastomosis (RYGB, BPD) may result in acute "gas bloat" of the distal (partitioned off) stomach. This is a true surgical emergency in that if the distal stomach is not vented, gastric necrosis, perforation, and death may rapidly ensue. Patients often present with epigastric fullness and "hiccups". Diagnosis is suggested by a large gas bubble in the right upper quadrant on plain films. Distal gastric remnant is decompressed via tube gastrostomy and attention directed to the etiology of the distal anastomotic obstruction.

d. Gastrointestinal Bleeding (all)

Gastrointestinal bleeding occurs in approximately 1 – 2% of patients after RYGB (1.92% open versus 0.59% laparoscopic) [303] and usually occurs from one of the various staple lines in the immediate postoperative time period. Pre-operative identification of the site of staple line bleeding may be nearly impossible: the distal anastomosis in an RYGB or BPD may be as far as 150 cm distal to the gastro-jejunostomy proximal anastomosis making endoscopic access to this anastomosis difficult. The gastric pouch and gastric anastomotic staple lines are easily identified with an upper endoscopy. As with most GI bleeding, endoscopic therapy is the preferred method of management. Fortunately, most staple line bleeding in the immediate postoperative time period usually stops with conservative care alone. Bleeding can also occur in the gastric remnant from the partition staple line, which is usually not accessible through normal endoscopy. Many surgeons consider transfusion requirements in excess of 4 units of packed red blood cells as an indication for operative intervention if endoscopy is not revealing. There is no substitute for an experienced bariatric surgeon in these cases. Bleeding can later occur in conjunction with a marginal ulcer as discussed above.

e. Pulmonary Embolism (all)

In one study the incidence with open surgery of PE was 0.41% and with laparoscopic surgery 0.77%.[303] In another study, the overall risk of PE within 90 days of surgery was 0.42% with 27% occurring before discharge and 73% occurring post-discharge. Most occurred within 30 days after surgery, though overall risk can extend past the 30-day postoperative period.[304] While chemical prophylaxis is indicated, there is no substitute for early postoperative ambulation. Risk factors for venous thromboembolism after metabolic/bariatric surgery may include high BMI, advanced age, immobility, prior venous thromboembolism, known hypercoagulable condition, obesity hypoventilation syndrome, pulmonary HTN, venous stasis disease, hormonal therapy, expected long operative time or open approach, and male gender. Most series report postoperative PE as a leading cause of death along with anastomotic leaks.

Prophylactic measures reduce the risk of PE, but they do not completely eliminate the risk. The use of Inferior Vena Cava (IVC) filters as the only method of prophylaxis before metabolic/bariatric surgery is not recommended. Filter placement may be considered in combination with chemical and mechanical prophylaxis for selected high-risk patients in whom the risk of venous thromboembolism (VTE) are determined to be greater than the risks of filter-related complications.[305]

f. Anastomotic Leak/Staple Line Leak (all except AGB)

In a study from 2015 in RYGB patients, leaks were seen in <1% (0.99%) of 4,444 patients studied. Of these, 39 (89%) underwent abdominal reoperation, three (7%) died, and 93% recovered from the event.[306] A high index of suspicion is mandatory as many of these patients with obesity will not exhibit classical peritoneal signs. The risk of leakage is increased with open and revisions surgery.

Another study from 2018 with 133,478 patients, who had either laparoscopic RYGP or SG, found the over-all leak around to be around 0.7%, with fewer leaks seen with SG.[307] Preoperative comorbidities associated with increased risk for anastomotic leak were history of oxygen dependency, hypoalbuminemia, sleep apnea, hypertension, and DM. Gagner in a recent SR of 40,653 SG patients reported an over-all leak rate of 1.5%.[308]

Early hallmarks of leaks are unexplained tachycardia, dyspnea, pain, and a feeling of impending doom. Despite negative imaging studies, persistent symptoms require exploration or diagnostic laparoscopic evaluation. Reoperation at a minimum entails wide surgical drainage. Endoscopically placed stents across a leak may be particularly helpful.

g. Portal/Splenic/Mesenteric Vein Thrombosis (all)

Portomesenteric vein thrombosis occurs most commonly with laparoscopic SG. A prevalence of 0.52% has been cited and ranges from 0.2% to as high as 1.81%.[309] Risk is increased with a personal history of malignancy or T2DM. Abdominal pain is usually the presenting symptom and diagnosis is confirmed with CT scanning with IV contrast. Treatment is with anticoagulation.

h. Pneumonia (all)

All postoperative patients having general anesthesia have some element of atelectasis that usually is addressed with incentive spirometry and vigorous pulmonary toilet. In a meta-analysis comprising (n=185,328) comparing pulmonary complications with both laparoscopic and open procedures, pneumonia was reported in 0.5% of laparoscopic cases and 1.1% in open cases.[310]

i. Complications Specifically Related to Laparoscopic Adjustable Band

Although this procedure is associated with fewer acute peri-operative complications, it has its own set of potential problems stemming from the insertion of a prosthetic “band”. Gastric band slippage (<5%), pouch dilation (12%), persistent GERD (7%), port malfunction (<1%), late port infection (<1%), and band erosion (<1%) are examples of complications that may occur after LAGB.[311,312] Patients may also present with severe food intolerance which may be related to the degree of band over-inflation. Acute stomal obstruction can occur in up to 14% of laparoscopic adjustable band (LAB) patients and may be related to the inclusion of excess perigastric fat under the band, insufficient diameter of band, or acute tissue edema. Persistent symptoms after edema has subsided may require revision or removal.

E. Suicide Risk

In a recent SR by Castenda et al. (2019), evidence from 29 observational studies suggests that mortality by suicide is higher among post-bariatric patients compared to the general population and matched controls (matched on BMI, age, and gender).[188] The post-bariatric suicide event rate was 2.7/1,000 patients, while the suicide/self-harm attempt event rate was 17/1,000 patients. Evidence from seven observational studies included in the SR suggests that suicide or self-harm attempts are higher among post-bariatric patients compared to the general population or matched controls (matched on BMI, age, and gender).[188] As depression is not uncommon before or after metabolic/bariatric surgery, increased vigilance for suicidal ideation and other risk factors for suicide (e.g., alcohol and other substance use disorders) is warranted.

F. Non-insulinoma Pancreatogenous Hypoglycemia Syndrome

After gastric bypass procedures, non-insulinoma pancreatogenous hypoglycemia syndrome (NIPHS), can occur resulting in postprandial hyperinsulinemic hypoglycemia 1-3 hours following a meal, accompanied by neuroglycopenic symptoms. Its incidence is unknown and is probably under-diagnosed as many patients have mild presentations. Post-prandial hypoglycemia appears to be observed after procedures that divert nutrients into the mid-small bowel, such as RYGB, and not purely restrictive procedures such as adjustable gastric banding.[313] Though some may be responsive to an ultra-low-carbohydrate/high-protein diet, a variety of medical treatment options may be required (acarbose, calcium channel blockers, octreotide, and diazoxide).[314] Treatment response is variable. Bypass reversal or conversion to SG, and partial/total pancreatectomy are surgical options.[315] The most appropriate surgical therapy remains undefined.[316]

G. Nutritional Concerns

All patients should be followed regularly and closely for potential nutritional deficiencies. In its evidence-based CPG for endocrine and nutritional management of the post-metabolic/bariatric surgery patient, the Endocrine Society has provided a strong recommendation for periodic clinical and biochemical monitoring for micro- and macro- nutritional deficiencies after metabolic/bariatric surgery.[270,317] Metabolic procedures have the greatest risk for nutritional deficiency, especially the BPD. Less mixing of bile and pancreatic enzymes results in fat and protein malabsorption. Non-metabolic surgeries can also result in nutritional deficiencies since the volume of food intake is markedly reduced; it is best for patients to take a multivitamin and then be monitored for nutritional deficiencies. Furthermore, all postoperative patients should receive an average of 60 – 120 g of protein daily.[317] Those with mal-absorptive components of their procedures require a low carbohydrate diet to avoid “dumping”.

Several nutritional deficiencies are common and supplementation at higher than the usual recommended daily dose may be required. Typical doses of elemental calcium are 1,200 – 2,000 mg daily, preferably as calcium citrate, which is better absorbed in the absence of gastric acid. Vitamin B12 is absorbed in the duodenum, thus, if bypassed, sub-lingual formulations are recommended. Iron deficiency is common and typically all patients undergoing bariatric procedures receive prophylactic therapy in conjunction with vitamin C to enhance absorption. Women with ongoing menstrual losses should receive a higher dose. Folate and B-complex vitamins are usually supplied in the form of a complete multivitamin. Fat-soluble vitamin (K, A, D, and E) status should be monitored by clinical and laboratory methods. Though not as common as in BPD procedures, deficiencies may occur with all procedures, especially of vitamin D deficiency. Together, calcium and vitamin D deficiencies contribute to secondary hyperparathyroidism, which can be seen following metabolic/bariatric surgery and may require higher than typical replacement dosing of both vitamin D (which should be taken with food for best absorption) and elemental calcium, ideally in the form of calcium citrate for best absorption after metabolic/bariatric surgery. Thiamine deficiency can also occasionally occur typically associated with intractable vomiting after surgery.

Table I-1. Post-Surgical Schedule for Clinical/Biochemical Monitoring [317]

	Pre-operative	1 Month	3 Months	6 Months	12 Months	18 Months	24 Months	Continue Annually
Complete blood count	X	X	X	X	X	X	X	X
LFTs	X	X	X	X	X	X	X	X
Glucose	X	X	X	X	X	X	X	X
Creatinine	X	X	X	X	X	X	X	X
Electrolytes	X	X	X	X	X	X	X	X
Iron/ferritin	X			Xa	Xa	Xa	Xa	Xa
Vitamin B12	X			Xa	Xa	Xa	Xa	Xa
Folate	X			Xa	Xa	Xa	Xa	Xa
Calcium	X			Xa	Xa	Xa	Xa	Xa
Intact PTH	X			Xa	Xa	Xa	Xa	Xa
25-D	X			Xa	Xa	Xa	Xa	Xa
Albumin/prealbumin	X			Xa	Xa	Xa	Xa	Xa
Vitamin A	X						+/-	+/-
Zinc	X			+/-	+/-		+/-	+/-
Bone mineral density and body composition	X				Xa		Xa	Xa
Vitamin B1			+/-	+/-	+/-	+/-	+/-	+/-

X: Indicate the suggested schedule for laboratory monitoring after metabolic/bariatric surgery.

Xa: Examinations should be performed after Roux-en-Y gastric bypass

+/-: optional

Abbreviations: LFT: liver function test; PTH: parathyroid hormone

All patients should be monitored routinely by an experienced team to detect nutritional deficiencies (see Table I-1). Due to potentially poor dietary tolerance or reduced intake, monitoring may still be required. The American Association of Clinical Endocrinologists, The Obesity Society, American Society for Metabolic and Bariatric Surgery together, and the Endocrine Society have both issued recommendations for postoperative nutrient deficiency monitoring for various bariatric surgical procedures, and this publication provides a wealth of information beyond the scope of this appendix.[270] Table 1 in Lupilo et al. (2017) contains a suggested schedule of biochemical and nutritional monitoring for various bariatric procedures.[318] The reader is referred to these publications for specific details.

a. Recommended Post-metabolic/Bariatric Surgery Nutritional Supplementation and Medications [319]

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 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 by providers with expertise in clinical nutrition.

Appendix J: 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 the goal and keeping a record of progress with self-monitoring helps the patient monitor progress toward goals that might be modified as goals are attained. Attaining goals motivates 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 behaviors in question. For weight management purposes, individuals record all details of food intake, physical activity, and body weight daily. Record-keeping 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, in this case, eating and/or sedentary behaviors. 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, having walking shoes placed in a convenient spot where they will be noticed, and so on. The overall idea is to eliminate signals for inappropriate eating and substitute cues for helpful weight control behaviors in their place.

D. Positive Reinforcement

Positive reinforcement refers to the provision of rewards for desirable behavior.

E. Contingency Management

Contingency management is establishing a defined schedule for the delivery of either rewards or punishments. Accordingly, a reward is delivered "contingent upon" completion of a specified behavior or performance of a desired behavior (e.g., staying within a certain caloric intake for a day or performing 30 minutes of exercise). Positive reinforcement is generally preferred over punishment to alter weight control behaviors, because people develop a positive association between desirable behaviors and receipt of reward. In this fashion, the desirable behavior eventually becomes self-rewarding. It is recommended to encourage choosing a reward that does not involve calories. Examples might include watching a movie, getting a new CD or comic book, going out bowling or roller-skating, or an activity that you enjoy that does not include food.

F. Stress Management

Stress management is utilized in the treatment of numerous conditions to reduce felt stress because excess stress often stimulates inappropriate or self-defeating behavior. In weight control, excessive stress frequently leads to over-eating and/or failure to exercise. 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 skill training. Taken together, the patient becomes more resistant to becoming overly stressed and more capable of coping with and reducing felt stress when it is noticed.

G. Problem-solving

Problem-solving involves training the patient to effectively analyze problems which might otherwise lead to inappropriate or self-defeating behavior such as over-eating. 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.

H. Skill Training

Skill training refers to training a patient in those skills that are likely to enhance success. For example, weight control patients are taught skills in evaluating the caloric content of various foods and in planning to avoid overly tempting eating situations. Patients might be taught skills in eating more slowly, cooking more healthfully, or refusing offers for second helpings or dessert from relatives or friends who might be pressuring them to overindulge.

I. Social Support

Social support is widely acknowledged to facilitate almost every difficult behavior and to improve coping in troublesome 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 control groups, Alcoholics Anonymous, cancer support groups, and many others.

J. Cognitive Therapy

Cognitive therapy or "cognitive restructuring" is a process whereby individuals are taught to become fully aware of negative or self-defeating thoughts, to counteract those thoughts, and to then replace them with more realistic, adaptive, and positive thoughts. Those thoughts then stimulate more desirable behaviors. Negatively oriented, discouraging, self-defeating, over-reactive, and unrealistic thoughts mediate inappropriate and/or maladaptive behavior. People are frequently not fully aware of thoughts such as "I MUST clean my plate!", "I'll just DIE if I can't have that piece of cake!" or "Taking a walk is really going to HURT!" These thoughts often lead to engaging in undesirable behavior. Cognitive therapy can be used to identify and modify dysfunctional thoughts and attitudes about weight regulation.

K. Relapse-prevention Training

Relapse-prevention training helps people 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 quite negatively to lapses and experience feelings of

guilt or shame, as well as negative, self-defeating 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 helps 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 K: Alternative Text Description of the Algorithm

1. The algorithm begins with Box 1, in the shape of a rounded rectangle: "Adult enrolled in the VA/DoD health system"
2. Box 1 connects to Box 2, in the shape of a rectangle: "Obtain height and weight; calculate BMI to screen for overweight and obesity at medical visits"
3. Box 2 connects to Box 3, in the shape of a hexagon, asks the question: "Is the patient's BMI ≥25 kg/m^{2}[a]?"
    a. If the answer is "Yes" to Box 3, then Box 5, in the shape of a rectangle: "With permission, assess patients (see Sidebar 3) and screen for overweight- and obesity-associated conditions (see Sidebar 1) and obesogenic medications[c]"
    b. If the answer is "No" to Box 3, then Box 4, in the shape of a rectangle: "Offer guidance about healthy eating and physical activity to maintain a healthy weight;[b] consider screening for overweight- and obesity-associated conditions (see Sidebar 1) and obesogenic medications (see Sidebar 2)"
4. Box 5 connects to Box 6, in the shape of a hexagon, asks the question: "Is patient ready to engage with a weight management program?"
    a. If the answer is "Yes" to Box 6, then Box 8, in the shape of a rectangle: "Offer a CLI (see Sidebar 5); Continue to monitor and reassess the patient (see Appendix K); Consider pharmacotherapy and/or bariatric procedure concurrently with CLI (see Sidebar 6)"
    b. If the answer is "No" to Box 6, then Box 7, in the shape of a rectangle: "Offer counseling on nutrition, physical activity, and behavior change; ask for permission to readdress at subsequent visits. (see Sidebar 4)"
        i. Box 7 connects to Box 6, in the shape of a hexagon, asks the question: "Is patient ready to engage with a weight management program?"
5. 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" to Box 9, then Box 10, in the shape of a rectangle: "Continue a CLI and any additional therapy for weight maintenance; reassess periodically including for pharmacotherapy and follow-up for long-term post bariatric procedure management"
    b. If the answer is "No" to Box 9, then Box 6, in the shape of a rectangle: "With permission, assess patients (see Sidebar 3) and screen for overweight- and obesity-associated conditions (see Sidebar 1) and obesogenic medications[c]"

Appendix L: Abbreviations

Abbreviation	Definition
Academy	The Academy of Nutrition and Dietetics
ACEI	angiotensin-converting enzyme inhibitor
AGB	adjustable gastric band
AHRQ	Agency for Healthcare Research and Quality
ALT	alanine transaminase
ARB	angiotensin receptor blocker
AST	aspartate transaminase
BEI	bioelectrical impedance
BMI	body mass index
BP	blood pressure
BPD	biliopancreatic diversion
CCB	calcium channel blocker
CDC	Centers for Disease Control and Prevention
CI	confidence interval
CKD	chronic kidney disease
CLI	comprehensive lifestyle intervention
COI	conflict of interest
CPGs	clinical practice guidelines
CV	cardiovascular
CVD	cardiovascular disease
CVT	clinical video telehealth
DASH	Dietary Approaches to Stop Hypertension
dL	deciliter
DM	diabetes mellitus
DoD	Department of Defense
DS	duodenal switch
EAL	evidence analysis library
ERCP	endoscopic retrograde cholangiopancreatography
FDA	U.S. Food and Drug Administration
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

Abbreviation	Definition
HDL-c	high-density lipoprotein cholesterol
HTN	hypertension
HOMA	homeostatic model assessment
HOMA-β	homeostatic model assessment of β-cell function
HOMA-IR	homeostatic model assessment of insulin resistance
IGB	intragastric balloon
IOM	Institute of Medicine
KQs	key questions
LAGB	laparoscopic adjustable gastric banding
LEADER	Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results
LDL-c	low-density lipoprotein cholesterol
MEN2	multiple endocrine neoplasia type 2
mg	milligrams
MI	myocardial infarction
MTC	medullary thyroid cancer
NAFLD	non-alcoholic fatty liver disease
NAM	National Academy of Medicine
ng	nanogram
NICE	National Institute for Health and Care Excellence
NIH	National Institutes of Health
NASH	non-alcoholic steatohepatitis
NSAID	non-steroidal anti-inflammatory drug
NIPHS	non-insulinoma pancreatogenous hypoglycemia syndrome
OTC	over-the-counter
PAGA	Physical Activity Guidelines for Americans
PCOS	polycystic ovary syndrome
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
RR	risk ratio
RYGB	roux-en-Y gastric bypass
SCr	serum creatinine
SG	sleeve gastrectomy
SIK	subsistence in Kind

Abbreviation	Definition
SR	systematic review
T2DM	type 2 diabetes mellitus
U.K.	United Kingdom
U.S.	United States
USPSTF	U.S. Preventive Services Task Force
WC	waist circumference

References

1. U.S. Department of Veteran Affairs, Department of Defense. Guideline for guidelines. Veterans Health Administration, Office of Quality & Performance, Evidence Review Subgroup; Revised January 29, 2019.
2. LeBlanc EL, Patnode CD, Webber EM, Redmond N, Rushkin M, O'Connor EA. *Behavioral and pharmacotherapy weight loss interventions to prevent obesity-related morbidity and mortality in adults: An updated Systematic review for the U.S. Preventive Services Task Force.* Rockville MD2018.
3. Centers for Disease Prevention and Control, Division of Nutrition, Physical Activity, and Obesity, National Center for Chronic Disease Prevention and Health Promotion. *Defining overweight and obesity*. *Overweight and Obesity* 2012; http://www.cdc.gov/obesity/adult/defining.html. Updated April 12, 2012. Accessed February 13, 2014.
4. Hales CM, Carroll MD, Fryar CD, Ogden CL. Prevalence of obesity among adults and youth: United States, 2015–2016. 2017.
5. National Center for Health Statistics,. *Prevalence of overweight, obesity, and severe obesity among adults aged 20 and over: United States, 1960–1962 through 2015–2016*. 2018; https://www.cdc.gov/nchs/data/hestat/obesity_adult_15_16/obesity_adult_15_16.htm.
6. Flegal KM, Kit BK, Orpana H, Graubard BI. Association of all-cause mortality with overweight and obesity using standard body mass index categories: A systematic review and meta-analysis. *JAMA.* Jan 2 2013;309(1):71-82. PMID: 23280227.
7. Borrell LN, Samuel L. Body mass index categories and mortality risk in U.S. Adults: The effect of overweight and obesity on advancing death. *Am J Public Health.* Mar 2014;104(3):512-519. PMID: 24432921.
8. Aune D, Sen A, Prasad M, et al. BMI and all cause mortality: Systematic review and non-linear dose-response meta-analysis of 230 cohort studies with 3.74 million deaths among 30.3 million participants. *BMJ.* May 4, 2016; 353:i2156. PMID: 27146380.
9. Expert panel report: Guidelines (2013) for the management of overweight and obesity in adults. *Obesity (Silver Spring).* Jul 2014;22 Suppl 2:S41-410. PMID: 24227637.
10. Bhaskaran K, Douglas I, Forbes H, dos-Santos-Silva I, Leon DA, Smeeth L. Body-mass index and risk of 22 specific cancers: A population-based cohort study of 5.24 million UK adults. *Lancet.* Aug 30, 2014;384(9945): 755-765. PMID: 25129328.
11. Biener AI, Decker SL. Medical care use and expenditures associated with adult obesity in the United States. *JAMA.* Jan 16, 2018;319(3):218. PMID: 29340665.
12. Control CfD, Prevention. National diabetes statistics report, 2017. *Atlanta, GA: Centers for Disease Control and Prevention, US Department of Health and Human Services.* 2017.
13. Gregg EW, Zhuo X, Cheng YJ, Albright AL, Narayan KM, Thompson TJ. Trends in lifetime risk and years of life lost due to diabetes in the USA, 1985-2011: A modelling study. *Lancet Diabetes Endocrinol.* Nov 2014;2(11): 867-874. PMID: 25128274.
14. Angulo P, Hui JM, Marchesini G, et al. The NAFLD fibrosis score: A noninvasive system that identifies liver fibrosis in patients with NAFLD. *Hepatology.* Apr 2007;45(4):846-854. PMID: 17393509.
15. Adams LA, Lindor KD. Nonalcoholic fatty liver disease. *Ann Epidemiol.* Nov 2007;17(11):863-869. PMID: 17728149.
16. Estes C, Razavi H, Loomba R, Younossi Z, Sanyal AJ. Modeling the epidemic of nonalcoholic fatty liver disease demonstrates an exponential increase in burden of disease. *Hepatology.* Jan 2018;67(1):123-133. PMID: 28802062.
17. Agopian VG, Kaldas FM, Hong JC, et al. Liver transplantation for nonalcoholic steatohepatitis: The new epidemic. *Ann Surg.* Oct 2012;256(4):624-633. PMID: 22964732.
18. Charlton MR, Burns JM, Pedersen RA, Watt KD, Heimbach JK, Dierkhising RA. Frequency and outcomes of liver transplantation for nonalcoholic steatohepatitis in the United States. *Gastroenterology.* Oct 2011;141(4):1249-1253. PMID: 21726509.

19. Ul-Haq Z, Mackay DF, Fenwick E, Pell JP. Meta-analysis of the association between body mass index and health-related quality of life among adults, assessed by the SF-36. *Obesity (Silver Spring).* Mar 2013;21(3): E322-327. PMID: 23592685.
20. Puhl RM, Heuer CA. The stigma of obesity: A review and update. *Obesity (Silver Spring).* May 2009;17(5):941-964. PMID: 19165161.
21. Biener A, Cawley J, Meyerhoefer C. The high and rising costs of obesity to the US health care system. *J Gen Intern Med.* Apr 2017;32(Suppl 1):6-8. PMID: 28271429.
22. U.S. Army Public Health Center. 2018 health of the force. 2018:1-77.
23. Callahan E. *Understanding and overcoming the challenge of obesity and overweight in the Armed Forces: Proceedings of a workshop.* National Academies Press; 2019.
24. Breland JY, Phibbs CS, Hoggatt KJ, et al. The obesity epidemic in the Veterans Health Administration: Prevalence among key populations of women and men Veterans. *J Gen Intern Med.* Apr 2017;32(Suppl 1):11-17. PMID: 28271422.
25. *Chronic kidney disease surveillance system*. http://www.cdc.gov/ckd.
26. Jensen MD, Ryan DH, Apovian CM, et al. 2013 aha/acc/tos guideline for the management of overweight and obesity in adults: A report of the American College of Cardiology/American Heart Association task force on practice guidelines and the Obesity Society. *J Am Coll Cardiol.* Nov 7, 2013. PMID: 24239920.
27. Andrews JC, Schunemann HJ, Oxman AD, et al. GRADE guidelines: 15. Going from evidence to recommendation-determinants of a recommendation's direction and strength. *J Clin Epidemiol.* Jul 2013;66(7): 726-735. PMID: 23570745.
28. Newberry SJ, Ahmadzai N, Motala A, et al. AHRQ methods for effective health care. *Surveillance and identification of signals for updating systematic reviews: Implementation and early experience*. Rockville (MD): Agency for Healthcare Research and Quality (US); 2013.
29. Guirguis-Blake J, Calonge N, Miller T, Siu A, Teutsch S, Whitlock E. Current processes of the U.S. Preventive Services Task Force: refining evidence-based recommendation development. *Ann Intern Med.* Jul 17, 2007; 147(2):117-122. PMID: 17576998.
30. *The guidelines manual.* London: National Institute for Health and Care Excellence;2012. http://www.nice.org.uk/article/pmg6/resources/non-guidance-the-guidelines-manual-pdf.
31. Martinez Garcia L, McFarlane E, Barnes S, Sanabria AJ, Alonso-Coello P, Alderson P. Updated recommendations: An assessment of NICE clinical guidelines. *Implement Sci.* 2014;9:72. PMID: 24919856.
32. IOM (U.S.) Committee on Standards for Developing Trustworthy Clinical Practice Guidelines, R Graham, M Mancher, D Miller Wolman, et al., editors. *Clinical practice guidelines we can trust.* Washington, DC: National Academies Press;2011.
33. Schunemann HJ, Fretheim A, Oxman AD. Improving the use of research evidence in guideline development: 10. Integrating values and consumer involvement. *Health Res Policy Syst.* 2006;4:22. PMID: 17147811.
34. Robinson JH, Callister LC, Berry JA, Dearing KA. Patient-centered care and adherence: Definitions and applications to improve outcomes. *J Am Acad Nurse Pract.* Dec 2008;20(12):600-607. PMID: 19120591.
35. Stewart M, Brown JB, Donner A, et al. The impact of patient-centered care on outcomes. *J Fam Pract.* Sep 2000;49(9):796-804. PMID: 11032203.
36. Fiscella K, Meldrum S, Franks P, et al. Patient trust: Is it related to patient-centered behavior of primary care physicians? *Med Care.* Nov 2004;42(11):1049-1055. PMID: 15586831.
37. *Crossing the quality chasm: A new health system for the 21st century.* Washington DC: National Academies Press;2001.
38. Society for Medical Decision Making Committee on Standardization of Clinical Algorithms. Proposal for clinical algorithm standards. *Med Decis Making.* Apr-Jun 1992;12(2):149-154. PMID: 1573982.
39. WHO expert consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet.* Jan 10, 2004;363(9403):157-163. PMID: 14726171.

40. Winter JE, MacInnis RJ, Wattanapenpaiboon N, Nowson CA. BMI and all-cause mortality in older adults: A meta-analysis. *The American Journal of Clinical Nutrition.* 2014;99(4):875-890.
41. Obesity: Preventing and managing the global epidemic. Report of a WHO consultation. *World Health Organ Tech Rep Ser.* 2000;894:i-xii, 1-253. PMID: 11234459.
42. Moyer VA, U. S. Preventive Services Task Force. Screening for and management of obesity in adults: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med.* Sep 4, 2012;157(5):373-378. PMID: 22733087.
43. Han TS, Tajar A, Lean ME. Obesity and weight management in the elderly. *Br Med Bull.* 2011;97:169-196. PMID: 21325341.
44. Frankenfield DC, Rowe WA, Cooney RN, Smith JS, Becker D. Limits of body mass index to detect obesity and predict body composition. *Nutrition.* Jan 2001;17(1):26-30. PMID: 11165884.
45. LeBlanc E, O'Connor E, Whitlock EP, Patnode C, Kapka T. Screening for and management of obesity and overweight in adults. Evidence Report No. 89. AHRQ Publication No. 11-05159-EF-1. Rockville, MD: Agency for Healthcare Research and Quality; 2011.
46. Centers for Disease Prevention and Control, Division of Nutrition, Physical Activity, and Obesity, National Center for Chronic Disease Prevention and Health Promotion. *Assessing your weight*. *Healthy Weight - it's not a diet, it's a lifestyle!* 2011; http://www.cdc.gov/healthyweight/assessing/index.html. Updated August 17, 2011. Accessed February 14, 2014.
47. Cao Q, Yu S, Xiong W, et al. Waist-hip ratio as a predictor of myocardial infarction risk: A systematic review and meta-analysis. *Medicine (Baltimore).* Jul 2018;97(30):e11639. PMID: 30045310.
48. Colditz GA, Dart H. Chapter 1: Epidemiology and health and economic consequences of obesity. In: Thomas A Wadden, George A Bray, eds. *Handbook of obesity treatment: Second edition*. 2 ed. New York: Guilford Press; 2018:3-23.
49. Puhl RM, Pearl RL. Psychosocial contributors to and consequences of obesity. *Handbook of Obesity Treatment.* 2018:149.
50. Grossman DC, Bibbins-Domingo K, Curry SJ, et al. Behavioral counseling to promote a healthful diet and physical activity for cardiovascular disease prevention in adults without cardiovascular risk factors: U.S. Preventive Services Task Force recommendation statement. *JAMA.* Jul 11 2017;318(2):167-174. PMID: 28697260.
51. Patnode CD, Evans CV, Senger CA, Redmond N, Lin JS. Behavioral counseling to promote a healthful diet and physical activity for cardiovascular disease prevention in adults without known cardiovascular disease risk factors: Updated evidence report and Systematic review for the U.S. Preventive Services Task Force. *JAMA.* Jul 11, 2017;318(2):175-193. PMID: 28697259.
52. Makoul G, Clayman ML. An integrative model of shared decision making in medical encounters. *Patient Educ Couns.* Mar 2006;60(3):301-312. PMID: 16051459.
53. Palmer S, Tubbs I, Whybrow A. Health coaching to facilitate the promotion of healthy behaviour and achievement of health-related goals. *Int J Health Prom Eval.* 2003;41(3):91-93.
54. Whitlock EP, Orleans CT, Pender N, Allan J. Evaluating primary care behavioral counseling interventions: An evidence-based approach. *Am J Prev Med.* May 2002;22(4):267-284. PMID: 11988383.
55. Goldstein MG, Whitlock EP, DePue J, Planning Committee of the Addressing Multiple Behavioral Risk Factors in Primary Care Project. Multiple behavioral risk factor interventions in primary care. Summary of research evidence. *Am J Prev Med.* Aug 2004;27(2 Suppl):61-79. PMID: 15275675.
56. Rollnick S, Miller W, Butler C. *Motivational interviewing in health care.* New York, NY: The Guilford Press; 2008.
57. Miller W, Rollnick S. *Motivational interviewing: Helping people change.* 3rd ed. New York, NY: The Guilford Press; 2013.
58. Schillinger D, Piette J, Grumbach K, et al. Closing the loop: Physician communication with diabetic patients who have low health literacy. *Arch Intern Med.* Jan 13, 2003;163(1):83-90. PMID: 12523921.
59. Levinson W, Lesser CS, Epstein RM. Developing physician communication skills for patient-centered care. *Health Aff (Millwood).* Jul 2010;29(7):1310-1318. PMID: 20606179.

60. Puhl RM, Phelan SM, Nadglowski J, Kyle TK. Overcoming weight bias in the management of patients with diabetes and obesity. *Clin Diabetes.* Jan 2016;34(1):44-50. PMID: 26807008.
61. Phelan SM, Burgess DJ, Yeazel MW, Hellerstedt WL, Griffin JM, van Ryn M. Impact of weight bias and stigma on quality of care and outcomes for patients with obesity. *Obes Rev.* Apr 2015;16(4):319-326. PMID: 25752756.
62. Burke BL, Arkowitz H, Menchola M. The efficacy of motivational interviewing: A meta-analysis of controlled clinical trials. *J Consult Clin Psychol.* Oct 2003;71(5):843-861. PMID: 14516234.
63. Britt E, Hudson SM, Blampied NM. Motivational interviewing in health settings: A review. *Patient Educ Couns.* May 2004;53(2):147-155. PMID: 15140454.
64. Burton AM, Agne AA, Lehr SM, Davis NJ, Willett LL, Cherrington AL. Training residents in obesity counseling: Incorporating principles of motivational interviewing to enhance patient centeredness. *J Grad Med Educ.* Sep 2011;3(3):408-411. PMID: 22942974.
65. DiLillo V, West DS. Motivational interviewing for weight loss. *Psychiatr Clin North Am.* Dec 2011;34(4):861-869. PMID: 22098809.
66. Hettema J, Steele J, Miller WR. Motivational interviewing. *Annu Rev Clin Psychol.* 2005;1:91-111. PMID: 17716083.
67. Levensky ER, Forcehimes A, O'Donohue WT, Beitz K. Motivational interviewing: An evidence-based approach to counseling helps patients follow treatment recommendations. *Am J Nurs.* Oct 2007;107(10):50-58; quiz 58-59. PMID: 17895731.
68. Williams GC, Minicucci DS, Kouides RW, et al. Self-determination, smoking, diet and health. *Health Educ Res.* Oct 2002;17(5):512-521. PMID: 12408196.
69. Armstrong MJ, Mottershead TA, Ronksley PE, Sigal RJ, Campbell TS, Hemmelgarn BR. Motivational interviewing to improve weight loss in overweight and/or obese patients: A systematic review and meta-analysis of randomized controlled trials. *Obes Rev.* Sep 2011;12(9):709-723. PMID: 21692966.
70. West DS, DiLillo V, Bursac Z, Gore SA, Greene PG. Motivational interviewing improves weight loss in women with type 2 diabetes. *Diabetes Care.* May 2007;30(5):1081-1087. PMID: 17337504.
71. Rosenbaum M, Hirsch J, Gallagher DA, Leibel RL. Long-term persistence of adaptive thermogenesis in subjects who have maintained a reduced body weight. *Am J Clin Nutr.* Oct 2008;88(4):906-912. PMID: 18842775.
72. Knuth ND, Johannsen DL, Tamboli RA, et al. Metabolic adaptation following massive weight loss is related to the degree of energy imbalance and changes in circulating leptin. *Obesity (Silver Spring).* Dec 2014;22(12): 2563-2569. PMID: 25236175.
73. Catenacci VA, Grunwald GK, Ingebrigtsen JP, et al. Physical activity patterns using accelerometry in the national weight control registry. *Obesity (Silver Spring).* Jun 2011;19(6):1163-1170. PMID: 21030947.
74. Leblanc ES, O'Connor E, Whitlock EP, Patnode CD, Kapka T. Effectiveness of primary care-relevant treatments for obesity in adults: A systematic evidence review for the U.S. Preventive Services Task Force. *Ann Intern Med.* Oct 4, 2011;155(7):434-447. PMID: 21969342.
75. Wadden TA, Webb VL, Moran CH, Bailer BA. Lifestyle modification for obesity: New developments in diet, physical activity, and behavior therapy. *Circulation.* Mar 6, 2012;125(9):1157-1170. PMID: 22392863.
76. LeBlanc ES, Patnode CD, Webber EM, Redmond N, Rushkin M, O'Connor EA. Behavioral and pharmacotherapy weight loss interventions to prevent obesity-related morbidity and mortality in adults: Updated evidence report and systematic review for the U.S. Preventive Services Task Force. *JAMA.* Sep 18, 2018;320(11):1172-1191. PMID: 30326501.
77. Aucott L, Poobalan A, Smith WC, Avenell A, Jung R, Broom J. Effects of weight loss in overweight/obese individuals and long-term hypertension outcomes: A systematic review. *Hypertension.* Jun 2005;45(6):1035-1041. PMID: 15897373.
78. Horvath K, Jeitler K, Siering U, et al. Long-term effects of weight-reducing interventions in hypertensive patients: Systematic review and meta-analysis. *Arch Intern Med.* Mar 24, 2008;168(6):571-580. PMID: 18362248.

79. Krukowski RA, Hare ME, Talcott GW, et al. Dissemination of the look ahead intensive lifestyle intervention in the United States military: A randomized controlled trial. *Obesity (Silver Spring).* Oct 2018;26(10):1558-1565. PMID: 30277030.
80. Neter JE, Stam BE, Kok FJ, Grobbee DE, Geleijnse JM. Influence of weight reduction on blood pressure: A meta-analysis of randomized controlled trials. *Hypertension.* Nov 2003;42(5):878-884. PMID: 12975389.
81. Poobalan A, Aucott L, Smith WC, et al. Effects of weight loss in overweight/obese individuals and long-term lipid outcomes--a systematic review. *Obes Rev.* Feb 2004;5(1):43-50. PMID: 14969506.
82. Ratner R, Goldberg R, Haffner S, et al. Impact of intensive lifestyle and metformin therapy on cardiovascular disease risk factors in the diabetes prevention program. *Diabetes Care.* Apr 2005;28(4):888-894. PMID: 15793191.
83. Vitolins MZ, Anderson AM, Delahanty L, et al. Action for health in diabetes (look ahead) trial: Baseline evaluation of selected nutrients and food group intake. *J Am Diet Assoc.* Aug 2009;109(8):1367-1375. PMID: 19631042.
84. Wing RR. Long-term effects of a lifestyle intervention on weight and cardiovascular risk factors in individuals with type 2 diabetes mellitus: Four-year results of the look ahead trial. *Arch Intern Med.* Sep 27, 2010;170(17): 1566-1575. PMID: 20876408.
85. Wing RR, Bolin P, Brancati FL, et al. Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes. *N Engl J Med.* Jul 11, 2013;369(2):145-154. PMID: 23796131.
86. Witham MD, Avenell A. Interventions to achieve long-term weight loss in obese older people: A systematic review and meta-analysis. *Age Ageing.* Mar 2010;39(2):176-184. PMID: 20083615.
87. Lindstrom J, Peltonen M, Eriksson JG, et al. Improved lifestyle and decreased diabetes risk over 13 years: Long-term follow-up of the randomised finnish diabetes prevention study (dps). *Diabetologia.* Feb 2013;56(2):284-293. PMID: 23093136.
88. Tuomilehto J, Lindstrom J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med.* May 3 2001;344(18):1343-1350. PMID: 11333990.
89. Knowler WC, Barrett-Connor E, Fowler SE, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med.* Feb 7 2002;346(6):393-403. PMID: 11832527.
90. Wadden TA, Bray GA. Behavioral treatment of obesity. *Handbook of obesity treatment*: Guilford Publications; 2018:336-348.
91. Miller WR, Rollnick S. *Motivational interviewing: Helping people change.* 3 ed: Guilford press; 2012.
92. Jeffery RW, Drewnowski A, Epstein LH, et al. Long-term maintenance of weight loss: Current status. *Health Psychol.* Jan 2000;19(1S):5-16. PMID: 10709944.
93. Mai K, Brachs M, Leupelt V, et al. Effects of a combined dietary, exercise and behavioral intervention and sympathetic system on body weight maintenance after intended weight loss: Results of a randomized controlled trial. *Metabolism.* Jun 2018;83:60-67. PMID: 29360493.
94. Lutes LD, Damschroder LJ, Masheb R, et al. Behavioral treatment for Veterans with obesity: 24-month weight outcomes from the ASPIRE-VA Small Changes randomized trial. *J Gen Intern Med.* Apr 2017;32(Suppl 1):40-47. PMID: 28271430.
95. Harrigan M, Cartmel B, Loftfield E, et al. Randomized trial comparing telephone versus in-person weight loss counseling on body composition and circulating biomarkers in women treated for breast cancer: The lifestyle, exercise, and nutrition (lean) study. *J Clin Oncol.* Mar 1, 2016;34(7):669-676. PMID: 26598750.
96. Christian JG, Byers TE, Christian KK, et al. A computer support program that helps clinicians provide patients with metabolic syndrome tailored counseling to promote weight loss. *J Am Diet Assoc.* Jan 2011;111(1):75-83. PMID: 21185968.
97. Demark-Wahnefried W, Jones LW, Snyder DC, et al. Daughters and mothers against breast cancer (dames): Main outcomes of a randomized controlled trial of weight loss in overweight mothers with breast cancer and their overweight daughters. *Cancer.* Aug 15, 2014;120(16):2522-2534. PMID: 24804802.

98. Fischer HH, Fischer IP, Pereira RI, et al. Text message support for weight loss in patients with prediabetes: A randomized clinical trial. *Diabetes Care.* Aug 2016;39(8):1364-1370. PMID: 26861922.
99. Godino JG, Merchant G, Norman GJ, et al. Using social and mobile tools for weight loss in overweight and obese young adults (project smart): A 2 year, parallel-group, randomised, controlled trial. *Lancet Diabetes Endocrinol.* Sep 2016;4(9):747-755. PMID: 27426247.
100. Haapala I, Barengo NC, Biggs S, Surakka L, Manninen P. Weight loss by mobile phone: A 1-year effectiveness study. *Public Health Nutr.* Dec 2009;12(12):2382-2391. PMID: 19323865.
101. Little P, Stuart B, Hobbs FR, et al. An internet-based intervention with brief nurse support to manage obesity in primary care (power+): A pragmatic, parallel-group, randomised controlled trial. *Lancet Diabetes Endocrinol.* Oct 2016;4(10):821-828. PMID: 27474214.
102. Morgan PJ, Lubans DR, Collins CE, Warren JM, Callister R. 12-month outcomes and process evaluation of the SHED-IT RCT: An internet-based weight loss program targeting men. *Obesity (Silver Spring).* Jan 2011;19(1): 142-151. PMID: 20523304.
103. Nicklas JM, Zera CA, England LJ, et al. A web-based lifestyle intervention for women with recent gestational diabetes mellitus: A randomized controlled trial. *Obstet Gynecol.* Sep 2014;124(3):563-570. PMID: 25162257.
104. Pacanowski CR, Levitsky DA. Frequent self-weighing and visual feedback for weight loss in overweight adults. *J Obes.* 2015;2015:763680. PMID: 26064677.
105. Patrick K, Calfas KJ, Norman GJ, et al. Outcomes of a 12-month web-based intervention for overweight and obese men. *Ann Behav Med.* Dec 2011;42(3):391-401. PMID: 21822750.
106. Shapiro JR, Koro T, Doran N, et al. Text4diet: A randomized controlled study using text messaging for weight loss behaviors. *Prev Med.* Nov 2012;55(5):412-417. PMID: 22944150.
107. Thomas JG, Raynor HA, Bond DS, et al. Weight loss in Weight Watchers online with and without an activity tracking device compared to control: A randomized trial. *Obesity (Silver Spring).* Jun 2017;25(6):1014-1021. PMID: 28437597.
108. Beleigoli AM, Andrade AQ, Cancado AG, Paulo MN, Diniz MFH, Ribeiro AL. Web-based digital health interventions for weight loss and lifestyle habit changes in overweight and obese adults: Systematic review and meta-analysis. *J Med Internet Res.* Jan 8 2019;21(1):e298. PMID: 30622090.
109. Park SH, Hwang J, Choi YK. Effect of mobile health on obese adults: A systematic review and meta-analysis. *Healthc Inform Res.* Jan 2019;25(1):12-26. PMID: 30788177.
110. Svetkey LP, Batch BC, Lin PH, et al. Cell phone intervention for you (city): A randomized, controlled trial of behavioral weight loss intervention for young adults using mobile technology. *Obesity (Silver Spring).* Nov 2015;23(11):2133-2141. PMID: 26530929.
111. Spring B, Duncan JM, Janke EA, et al. Integrating technology into standard weight loss treatment: A randomized controlled trial. *JAMA Intern Med.* Jan 28, 2013;173(2):105-111. PMID: 23229890.
112. Cheng CC, Hsu CY, Liu JF. Effects of dietary and exercise intervention on weight loss and body composition in obese postmenopausal women: A systematic review and meta-analysis. *Menopause.* Jul 2018;25(7):772-782. PMID: 29533366.
113. Schwingshackl L, Dias S, Hoffmann G. Impact of long-term lifestyle programmes on weight loss and cardiovascular risk factors in overweight/obese participants: A systematic review and network meta-analysis. *Syst Rev.* Oct 30, 2014;3:130. PMID: 25358395.
114. Creasy SA, Rogers RJ, Davis KK, Gibbs BB, Kershaw EE, Jakicic JM. Effects of supervised and unsupervised physical activity programmes for weight loss. *Obes Sci Pract.* Jun 2017;3(2):143-152. PMID: 28713583.
115. Donnelly JE, Blair SN, Jakicic JM, Manore MM, Rankin JW, Smith BK. American college of sports medicine position stand. Appropriate physical activity intervention strategies for weight loss and prevention of weight regain for adults. *Med Sci Sports Exerc.* Feb 2009;41(2):459-471. PMID: 19127177.
116. Slentz CA, Duscha BD, Johnson JL, et al. Effects of the amount of exercise on body weight, body composition, and measures of central obesity: STRRIDE--a randomized controlled study. *Arch Intern Med.* Jan 12, 2004; 164(1):31-39. PMID: 14718319.

117. Miller WC, Koceja DM, Hamilton EJ. A meta-analysis of the past 25 years of weight loss research using diet, exercise or diet plus exercise intervention. *Int J Obes Relat Metab Disord.* Oct 1997;21(10):941-947. PMID: 9347414.

118. Dutheil F, Lac G, Lesourd B, et al. Different modalities of exercise to reduce visceral fat mass and cardiovascular risk in metabolic syndrome: The resolve randomized trial. *Int J Cardiol.* Oct 9 2013;168(4):3634-3642. PMID: 23714599.

119. Fanning J, Walkup MP, Ambrosius WT, et al. Change in health-related quality of life and social cognitive outcomes in obese, older adults in a randomized controlled weight loss trial: Does physical activity behavior matter? *J Behav Med.* Jun 2018;41(3):299-308. PMID: 29168052.

120. Piercy KL, Troiano RP, Ballard RM, et al. The Physical Activity Guidelines for Americans. *JAMA.* Nov 20, 2018; 320(19):2020-2028. PMID: 30418471.

121. U.S. Department of Health and Human Services. *Physical Activity Guidelines for Americans*. 2018; 2nd edition:https://health.gov/paguidelines/second-edition/pdf/Physical_Activity_Guidelines_2nd_edition.pdf. Accessed October 7, 2019.

122. Astbury NM, Piernas C, Hartmann-Boyce J, Lapworth S, Aveyard P, Jebb SA. A systematic review and meta-analysis of the effectiveness of meal replacements for weight loss. *Obes Rev.* Apr 2019;20(4):569-587. PMID: 30675990.

123. Bazzano LA, Hu T, Reynolds K, et al. Effects of low-carbohydrate and low-fat diets: A randomized trial. *Ann Intern Med.* Sep 2, 2014;161(5):309-318. PMID: 25178568.

124. Brinkworth GD, Wycherley TP, Noakes M, Buckley JD, Clifton PM. Long-term effects of a very-low-carbohydrate weight-loss diet and an isocaloric low-fat diet on bone health in obese adults. *Nutrition.* Sep 2016;32(9):1033-1036. PMID: 27157472.

125. Catenacci VA, Pan Z, Ostendorf D, et al. A randomized pilot study comparing zero-calorie alternate-day fasting to daily caloric restriction in adults with obesity. *Obesity (Silver Spring).* Sep 2016;24(9):1874-1883. PMID: 27569118.

126. Headland ML, Clifton PM, Keogh JB. Effect of intermittent compared to continuous energy restriction on weight loss and weight maintenance after 12 months in healthy overweight or obese adults. *Int J Obes (Lond).* Nov 23, 2018. PMID: 30470804.

127. Lutze J, Taylor P, Brinkworth GD, et al. Psychological well-being response to high protein and high carbohydrate weight loss diets in overweight and obese men: A randomised trial. *e-SPEN Journal.* 2013;8(6): e235-e240.

128. Johnston BC, Kanters S, Bandayrel K, et al. Comparison of weight loss among named diet programs in overweight and obese adults: A meta-analysis. *JAMA.* Sep 3, 2014;312(9):923-933. PMID: 25182101.

129. Moreno B, Bellido D, Sajoux I, et al. Comparison of a very low-calorie-ketogenic diet with a standard low-calorie diet in the treatment of obesity. *Endocrine.* Dec 2014;47(3):793-805. PMID: 24584583.

130. Sackner-Bernstein J, Kanter D, Kaul S. Dietary intervention for overweight and obese adults: Comparison of low-carbohydrate and low-fat diets. A Meta-Analysis. *PLoS One.* 2015;10(10):e0139817. PMID: 26485706.

131. Roman YM, Dominguez MC, Easow TM, Pasupuleti V, White CM, Hernandez AV. Effects of intermittent versus continuous dieting on weight and body composition in obese and overweight people: A systematic review and meta-analysis of randomized controlled trials. *Int J Obes (Lond).* Sep 11, 2018. PMID: 30206335.

132. Trepanowski JF, Kroeger CM, Barnosky A, et al. Effects of alternate-day fasting or daily calorie restriction on body composition, fat distribution, and circulating adipokines: Secondary analysis of a randomized controlled trial. *Clin Nutr.* Dec 2018;37(6 Pt A):1871-1878. PMID: 29258678.

133. Sundfor TM, Svendsen M, Tonstad S. Effect of intermittent versus continuous energy restriction on weight loss, maintenance and cardiometabolic risk: A randomized 1-year trial. *Nutr Metab Cardiovasc Dis.* Jul 2018; 28(7):698-706. PMID: 29778565.

134. Zinn C, McPhee J, Harris N, Williden M, Prendergast K, Schofield G. A 12-week low-carbohydrate, high-fat diet improves metabolic health outcomes over a control diet in a randomised controlled trial with overweight defence force personnel. *Appl Physiol Nutr Metab.* Nov 2017;42(11):1158-1164. PMID: 28700832.

135. Ajala O, English P, Pinkney J. Systematic review and meta-analysis of different dietary approaches to the management of type 2 diabetes. *Am J Clin Nutr.* Mar 2013;97(3):505-516. PMID: 23364002.

136. Bravata DM, Sanders L, Huang J, et al. Efficacy and safety of low-carbohydrate diets: A systematic review. *JAMA.* Apr 9, 2003;289(14):1837-1850. PMID: 12684364.

137. Foster GD, Wyatt HR, Hill JO, et al. A randomized trial of a low-carbohydrate diet for obesity. *N Engl J Med.* May 22, 2003;348(21):2082-2090. PMID: 12761365.

138. Hu T, Mills KT, Yao L, et al. Effects of low-carbohydrate diets versus low-fat diets on metabolic risk factors: A meta-analysis of randomized controlled clinical trials. *Am J Epidemiol.* Oct 1, 2012;176 Suppl 7:S44-54. PMID: 23035144.

139. Nordmann AJ, Nordmann A, Briel M, et al. Effects of low-carbohydrate vs low-fat diets on weight loss and cardiovascular risk factors: A meta-analysis of randomized controlled trials. *Arch Intern Med.* Feb 13, 2006; 166(3):285-293. PMID: 16476868.

140. Sacks FM, Bray GA, Carey VJ, et al. Comparison of weight-loss diets with different compositions of fat, protein, and carbohydrates. *N Engl J Med.* Feb 26, 2009;360(9):859-873. PMID: 19246357.

141. Samaha FF, Iqbal N, Seshadri P, et al. A low-carbohydrate as compared with a low-fat diet in severe obesity. *N Engl J Med.* May 22, 2003;348(21):2074-2081. PMID: 12761364.

142. Soltani S, Shirani F, Chitsazi MJ, Salehi-Abargouei A. The effect of dietary approaches to stop hypertension (DASH) diet on weight and body composition in adults: A systematic review and meta-analysis of randomized controlled clinical trials. *Obes Rev.* May 2016;17(5):442-454. PMID: 26990451.

143. Wycherley TP, Buckley JD, Noakes M, Clifton PM, Brinkworth GD. Comparison of the effects of weight loss from a high-protein versus standard-protein energy-restricted diet on strength and aerobic capacity in overweight and obese men. *Eur J Nutr.* Feb 2013;52(1):317-325. PMID: 22406907.

144. Yancy WS, Jr., Olsen MK, Guyton JR, Bakst RP, Westman EC. A low-carbohydrate, ketogenic diet versus a low-fat diet to treat obesity and hyperlipidemia: A randomized, controlled trial. *Ann Intern Med.* May 18, 2004; 140(10):769-777. PMID: 15148063.

145. Klempel MC, Kroeger CM, Norkeviciute E, Goslawski M, Phillips SA, Varady KA. Benefit of a low-fat over high-fat diet on vascular health during alternate day fasting. *Nutr Diabetes.* May 27, 2013;3:e71. PMID: 23712283.

146. Parretti HM, Jebb SA, Johns DJ, Lewis AL, Christian-Brown AM, Aveyard P. Clinical effectiveness of very-low-energy diets in the management of weight loss: A systematic review and meta-analysis of randomized controlled trials. *Obes Rev.* Mar 2016;17(3):225-234. PMID: 26775902.

147. Yoong SL, Carey M, Sanson-Fisher R, Grady A. A systematic review of behavioural weight-loss interventions involving primary-care physicians in overweight and obese primary-care patients (1999-2011). *Public Health Nutr.* Nov 2013;16(11):2083-2099. PMID: 23101456.

148. Anderson JW, Luan J, Hoie LH. Structured weight-loss programs: Meta-analysis of weight loss at 24 weeks and assessment of effects of intervention intensity. *Adv Ther.* Mar-Apr 2004;21(2):61-75. PMID: 15310080.

149. Heymsfield SB, van Mierlo CA, van der Knaap HC, Heo M, Frier HI. Weight management using a meal replacement strategy: Meta and pooling analysis from six studies. *Int J Obes Relat Metab Disord.* May 2003; 27(5):537-549. PMID: 12704397.

150. Noakes M, Foster PR, Keogh JB, Clifton PM. Meal replacements are as effective as structured weight-loss diets for treating obesity in adults with features of metabolic syndrome. *J Nutr.* Aug 2004;134(8):1894-1899. PMID: 15284372.

151. Dietetics AoNa. Adult weight management (awm) guideline (2014). 2014. http://andeal.org/topic.cfm?menu=5276&cat=4688.

152. Khera R, Murad MH, Chandar AK, et al. Association of pharmacological treatments for obesity with weight loss and adverse events: A systematic review and meta-analysis. *JAMA.* Jun 14, 2016;315(22):2424-2434. PMID: 27299618.

153. *FDA requests the withdrawal of the weight-loss drug belviq, belviq xr (lorcaserin) from the market*. 2020; https://www.fda.gov/drugs/drug-safety-and-availability/fda-requests-withdrawal-weight-loss-drug-belviq-belviq-xr-lorcaserin-market.

154. Suplicy H, Boguszewski CL, dos Santos CM, do Desterro de Figueiredo M, Cunha DR, Radominski R. A comparative study of five centrally acting drugs on the pharmacological treatment of obesity. *Int J Obes (Lond).* Aug 2014;38(8):1097-1103. PMID: 24287940.

155. Garvey WT, Ryan DH, Look M, et al. Two-year sustained weight loss and metabolic benefits with controlled-release phentermine/topiramate in obese and overweight adults (SEQUEL): A randomized, placebo-controlled, phase 3 extension study. *Am J Clin Nutr.* Feb 2012;95(2):297-308. PMID: 22158731.

156. Smith SR, Weissman NJ, Anderson CM, et al. Multicenter, placebo-controlled trial of lorcaserin for weight management. *N Engl J Med.* Jul 15, 2010;363(3):245-256. PMID: 20647200.

157. Kyle TK, Dhurandhar EJ, Allison DB. Regarding obesity as a disease: Evolving policies and their implications. *Endocrinol Metab Clin North Am.* Sep 2016;45(3):511-520. PMID: 27519127.

158. Siebenhofer A, Jeitler K, Horvath K, et al. Long-term effects of weight-reducing drugs in people with hypertension. *Cochrane Database Syst Rev.* Mar 2, 2016;3:CD007654. PMID: 26934640.

159. le Roux CW, Astrup A, Fujioka K, et al. 3 years of liraglutide versus placebo for type 2 diabetes risk reduction and weight management in individuals with prediabetes: A randomised, double-blind trial. *Lancet.* Apr 8 2017; 389(10077):1399-1409. PMID: 28237263.

160. Davies MJ, Bergenstal R, Bode B, et al. Efficacy of liraglutide for weight loss among patients with type 2 diabetes: The scale diabetes randomized clinical trial. *JAMA.* Aug 18 2015;314(7):687-699. PMID: 26284720.

161. Bohula EA, Scirica BM, Inzucchi SE, et al. Effect of lorcaserin on prevention and remission of type 2 diabetes in overweight and obese patients (camellia-timi 61): A randomised, placebo-controlled trial. *Lancet.* Nov 24, 2018;392(10161):2269-2279. PMID: 30293771.

162. O'Neil PM, Smith SR, Weissman NJ, et al. Randomized placebo-controlled clinical trial of lorcaserin for weight loss in type 2 diabetes mellitus: The BLOOM-DM study. *Obesity (Silver Spring).* Jul 2012;20(7):1426-1436. PMID: 22421927.

163. Torgerson JS, Hauptman J, Boldrin MN, Sjostrom L. Xenical in the prevention of diabetes in obese subjects (XENDOS) study: A randomized study of orlistat as an adjunct to lifestyle changes for the prevention of type 2 diabetes in obese patients. *Diabetes Care.* Jan 2004;27(1):155-161. PMID: 14693982.

164. Gadde KM, Allison DB, Ryan DH, et al. Effects of low-dose, controlled-release, phentermine plus topiramate combination on weight and associated comorbidities in overweight and obese adults (CONQUER): A randomised, placebo-controlled, phase 3 trial. *Lancet.* Apr 16, 2011;377(9774):1341-1352. PMID: 21481449.

165. Hollander P, Gupta AK, Plodkowski R, et al. Effects of naltrexone sustained-release/bupropion sustained-release combination therapy on body weight and glycemic parameters in overweight and obese patients with type 2 diabetes. *Diabetes Care.* Dec 2013;36(12):4022-4029. PMID: 24144653.

166. Bohula EA, Wiviott SD, McGuire DK, et al. Cardiovascular safety of lorcaserin in overweight or obese patients. *N Engl J Med.* Sep 20, 2018;379(12):1107-1117. PMID: 30145941.

167. Khera R, Pandey A, Chandar AK, et al. Effects of weight-loss medications on cardiometabolic risk profiles: A systematic review and network meta-analysis. *Gastroenterology.* Apr 2018;154(5):1309-1319 e1307. PMID: 29305933.

168. NIH. *NCI dictionary of cancer terms*. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/nutraceutical. Accessed December 11, 2019.

169. Huang LH, Liu CY, Wang LY, Huang CJ, Hsu CH. Effects of green tea extract on overweight and obese women with high levels of low density-lipoprotein-cholesterol (LDL-c): A randomised, double-blind, and cross-over placebo-controlled clinical trial. *BMC Complement Altern Med.* Nov 6, 2018;18(1):294. PMID: 30400924.

170. Mousavi SM, Milajerdi A, Varkaneh HK, Gorjipour MM, Esmaillzadeh A. The effects of curcumin supplementation on body weight, body mass index and waist circumference: A systematic review and dose-response meta-analysis of randomized controlled trials. *Crit Rev Food Sci Nutr.* Oct 29, 2018:1-10. PMID: 30373373.

171. Tripathy P, Karmahapatra P, Palaniyamma D. "Randomized, double-blind, placebo controlled clinical study to evaluate the effects of garcinia caplets in obese subjects" *International Research Journal of Pharmacy.* 2013.

172. Chen W, Liu Y, Yang Q, et al. The effect of protein-enriched meal replacement on waist circumference reduction among overweight and obese chinese with hyperlipidemia. *J Am Coll Nutr.* 2016;35(3):236-244. PMID: 26650434.
173. Nabi BN, Sedighinejad A, Haghighi M, et al. The anti-obesity effects of green tea: A controlled, randomized, clinical trial. *Iranian Red Crescent Medical Journal.* 2018;20(1).
174. Grube B, Chong WF, Chong PW, Riede L. Weight reduction and maintenance with iqp-pv-101: A 12-week randomized controlled study with a 24-week open label period. *Obesity (Silver Spring).* Mar 2014;22(3):645-651. PMID: 24006357.
175. Suzumura EA, Bersch-Ferreira AC, Torreglosa CR, et al. Effects of oral supplementation with probiotics or synbiotics in overweight and obese adults: A systematic review and meta-analyses of randomized trials. *Nutr Rev.* Jun 1, 2019;77(6):430-450. PMID: 30924853.
176. Khazaal FAK, Mosah HA, Sahib H, Hamdi AS. Effect of raspberry ketones and l-carnitine on oxidative stress and body weight in iraqi obese patients. *International Journal of Pharmaceutical Sciences Review and Research.* Jan 1, 2015;31:69-75.
177. FDA. *Information for consumers on using dietary supplements*. 2019; https://www.fda.gov/food/dietary-supplements/information-consumers-using-dietary-supplements. Accessed December 11, 2019.
178. Horwitz D, Saunders JK, Ude-Welcome A, et al. Three-year follow-up comparing metabolic surgery versus medical weight management in patients with type 2 diabetes and BMI 30-35. The role of srage biomarker as predictor of satisfactory outcomes. *Surg Obes Relat Dis.* Aug 2016;12(7):1337-1341. PMID: 27134202.
179. Muller-Stich BP, Senft JD, Warschkow R, et al. Surgical versus medical treatment of type 2 diabetes mellitus in nonseverely obese patients: A systematic review and meta-analysis. *Ann Surg.* Mar 2015;261(3):421-429. PMID: 25405560.
180. Liang Z, Wu Q, Chen B, Yu P, Zhao H, Ouyang X. Effect of laparoscopic roux-en-y gastric bypass surgery on type 2 diabetes mellitus with hypertension: A randomized controlled trial. *Diabetes Res Clin Pract.* Jul 2013;101(1):50-56. PMID: 23706413.
181. Wentworth JM, Playfair J, Laurie C, et al. Multidisciplinary diabetes care with and without bariatric surgery in overweight people: A randomised controlled trial. *Lancet Diabetes Endocrinol.* Jul 2014;2(7):545-552. PMID: 24731535.
182. Dixon JB, O'Brien PE, Playfair J, et al. Adjustable gastric banding and conventional therapy for type 2 diabetes: A randomized controlled trial. *JAMA.* Jan 23, 2008;299(3):316-323. PMID: 18212316.
183. Ikramuddin S, Korner J, Lee WJ, et al. Roux-en-y gastric bypass vs intensive medical management for the control of type 2 diabetes, hypertension, and hyperlipidemia: The diabetes surgery study randomized clinical trial. *JAMA.* Jun 5, 2013;309(21):2240-2249. PMID: 23736733.
184. Courcoulas AP, Goodpaster BH, Eagleton JK, et al. Surgical vs medical treatments for type 2 diabetes mellitus: A randomized clinical trial. *JAMA Surg.* Jul 2014;149(7):707-715. PMID: 24899268.
185. Schauer PR, Kashyap SR, Wolski K, et al. Bariatric surgery versus intensive medical therapy in obese patients with diabetes. *N Engl J Med.* Apr 26, 2012;366(17):1567-1576. PMID: 22449319.
186. Policy on bariatric surgical procedures for Active Duty service members. In: Department of Defense, ed. Washington, D.C.: Department of Defense; 2007.
187. Cheng J, Gao J, Shuai X, Wang G, Tao K. The comprehensive summary of surgical versus non-surgical treatment for obesity: A systematic review and meta-analysis of randomized controlled trials. *Oncotarget.* Jun 28, 2016; 7(26):39216-39230. PMID: 27233078.
188. Castaneda D, Popov VB, Wander P, Thompson CC. Risk of suicide and self-harm is increased after bariatric surgery-a systematic review and meta-analysis. *Obes Surg.* Jan 2019;29(1):322-333. PMID: 30343409.
189. O'Brien PE, Hindle A, Brennan L, et al. Long-term outcomes after bariatric surgery: A systematic review and meta-analysis of weight loss at 10 or more years for all bariatric procedures and a single-centre review of 20-year outcomes after adjustable gastric banding. *Obes Surg.* Jan 2019;29(1):3-14. PMID: 30293134.

190. Yang P, Chen B, Xiang S, Lin XF, Luo F, Li W. Long-term outcomes of laparoscopic sleeve gastrectomy versus roux-en-y gastric bypass for morbid obesity: Results from a meta-analysis of randomized controlled trials. *Surg Obes Relat Dis.* Apr 2019;15(4):546-555. PMID: 30826243.
191. Khorgami Z, Shoar S, Saber AA, Howard CA, Danaei G, Sclabas GM. Outcomes of bariatric surgery versus medical management for type 2 diabetes mellitus: A meta-analysis of randomized controlled trials. *Obes Surg.* Mar 2019;29(3):964-974. PMID: 30402804.
192. Sheng B, Truong K, Spitler H, Zhang L, Tong X, Chen L. The long-term effects of bariatric surgery on type 2 diabetes remission, microvascular and macrovascular complications, and mortality: A systematic review and meta-analysis. *Obes Surg.* Oct 2017;27(10):2724-2732. PMID: 28801703.
193. Yan Y, Sha Y, Yao G, et al. Roux-en-y gastric bypass versus medical treatment for type 2 diabetes mellitus in obese patients: A systematic review and meta-analysis of randomized controlled trials. *Medicine (Baltimore).* Apr 2016;95(17):e3462. PMID: 27124041.
194. Szmulewicz A, Wanis KN, Gripper A, et al. Mental health quality of life after bariatric surgery: A systematic review and meta-analysis of randomized clinical trials. *Clin Obes.* Feb 2019;9(1):e12290. PMID: 30458582.
195. Adil MT, Jain V, Rashid F, Al-Taan O, Whitelaw D, Jambulingam P. Meta-analysis of the effect of bariatric surgery on physical function. *Br J Surg.* Aug 2018;105(9):1107-1118. PMID: 29893414.
196. Zhou X, Yu J, Li L, et al. Effects of bariatric surgery on mortality, cardiovascular events, and cancer outcomes in obese patients: Systematic review and meta-analysis. *Obes Surg.* Nov 2016;26(11):2590-2601. PMID: 26992897.
197. Bhandari M, Mathur W, Fobi M, Kosta S. Outcomes of bariatric surgery in geriatric patients >/= 65 years: Single institution study. *Obes Surg.* May 2019;29(5):1470-1476. PMID: 30721427.
198. Arnold MR, Schlosser KA, Otero J, et al. Laparoscopic weight loss surgery in the elderly: An ACS NSQIP study on the effect of age on outcomes. *Am Surg.* Mar 1, 2019;85(3):273-279. PMID: 30947773.
199. Goldberg I, Yang J, Nie L, et al. Safety of bariatric surgery in patients older than 65 years. *Surg Obes Relat Dis.* Aug 2019;15(8):1380-1387. PMID: 31248793.
200. Koh CY, Inaba CS, Sujatha-Bhaskar S, Nguyen NT. Outcomes of laparoscopic bariatric surgery in the elderly population. *Am Surg.* Oct 1, 2018;84(10):1600-1603. PMID: 30747677.
201. Marczuk P, Kubisa MJ, Swiech M, et al. Effectiveness and safety of roux-en-y gastric bypass in elderly patients-Systematic review and meta-analysis. *Obes Surg.* Feb 2019;29(2):361-368. PMID: 30353247.
202. Thompson CC, Abu Dayyeh BK, Kushner R, et al. Percutaneous gastrostomy device for the treatment of Class II and Class III obesity: Results of a randomized controlled trial. *Am J Gastroenterol.* Mar 2017;112(3):447-457. PMID: 27922026.
203. Ikramuddin S, Blackstone RP, Brancatisano A, et al. Effect of reversible intermittent intra-abdominal vagal nerve blockade on morbid obesity: The recharge randomized clinical trial. *JAMA.* Sep 3, 2014;312(9):915-922. PMID: 25182100.
204. Shikora SA, Wolfe BM, Apovian CM, et al. Sustained weight loss with vagal nerve blockade but not with sham: 18-month results of the recharge trial. *J Obes.* 2015;2015:365604. PMID: 26246907.
205. Apovian CM, Shah SN, Wolfe BM, et al. Two-year outcomes of vagal nerve blocking (vBloc) for the treatment of obesity in the recharge trial. *Obes Surg.* Jan 2017;27(1):169-176. PMID: 27506803.
206. Popov VB, Ou A, Schulman AR, Thompson CC. The impact of intragastric balloons on obesity-related co-morbidities: A systematic review and meta-analysis. *Am J Gastroenterol.* Mar 2017;112(3):429-439. PMID: 28117361.
207. Sullivan S, Swain J, Woodman G, et al. Randomized sham-controlled trial of the 6-month swallowable gas-filled intragastric balloon system for weight loss. *Surg Obes Relat Dis.* Dec 2018;14(12):1876-1889. PMID: 30545596.
208. Tate CM, Geliebter A. Intragastric balloon treatment for obesity: Review of recent studies. *Adv Ther.* Aug 2017; 34(8):1859-1875. PMID: 28707286.
209. Zheng Y, Wang M, He S, Ji G. Short-term effects of intragastric balloon in association with conservative therapy on weight loss: A meta-analysis. *J Transl Med.* Jul 29, 2015;13:246. PMID: 26219459.

210. Trang J, Lee SS, Miller A, et al. Incidence of nausea and vomiting after intragastric balloon placement in bariatric patients - a systematic review and meta-analysis. *Int J Surg.* Sep 2018;57:22-29. PMID: 30031839.

211. Hession M, Rolland C, Kulkarni U, Wise A, Broom J. Systematic review of randomized controlled trials of low-carbohydrate vs. low-fat/low-calorie diets in the management of obesity and its comorbidities. *Obes Rev.* Jan 2009;10(1):36-50. PMID: 18700873.

212. Prevention CfDCa. Percent of adults aged 18 years and older who have obesity. *Nutrition, Physical Activity, and Obesity: Data, Trends, and Maps.* 2018. https://nccd.cdc.gov/dnpao_dtm/rdPage.aspx?rdReport=DNPAO_DTM.ExploreByTopic&islClass=OWS&islTopic=OWS1&go=GO.

213. Padwal RS, Pajewski NM, Allison DB, Sharma AM. Using the edmonton obesity staging system to predict mortality in a population-representative cohort of people with overweight and obesity. *Cmaj.* 2011;183(14): E1059-E1066.

214. Sharma AM, Campbell-Scherer DL. Redefining obesity: Beyond the numbers. *Obesity.* 2017;25(4):660-661.

215. Agency for Health Research and Quality. The effective health care program stakeholder guide appendix d: Research questions & PICO(TS) 2011. https://www.ahrq.gov/research/findings/evidence-based-reports/stakeholderguide/appendixc.html.

216. Guyatt GH, Oxman AD, Kunz R, et al. GRADE guidelines: 2. Framing the question and deciding on important outcomes. *J Clin Epidemiol.* Apr 2011;64(4):395-400. PMID: 21194891.

217. Andrews J, Guyatt G, Oxman AD, et al. GRADE guidelines: 14. Going from evidence to recommendations: The significance and presentation of recommendations. *J Clin Epidemiol.* Jul 2013;66(7):719-725. PMID: 23312392.

218. Academy of Nutrition and Dietetics. *2014 adult weight management evidence-based nutrition practice guideline*. https://www.andeal.org/topic.cfm?menu=5276&cat=4688. Accessed October 9, 2019.

219. Raynor HA, Champagne CM. Position of the Academy of Nutrition and Dietetics: Interventions for the treatment of overweight and obesity in adults. *J Acad Nutr Diet.* Jan 2016;116(1):129-147. PMID: 26718656.

220. National Heart Lung and Blood Institute. *Managing overweight and obesity in adults: Systematic evidence review from the obesity expert panel*. 2013; https://www.nhlbi.nih.gov/health-topics/managing-overweight-obesity-in-adults. Accessed October 8, 2019.

221. Office of Disease Prevention and Health Promotion. Dietary Guidelines for Americans, 2015–2020. 8th edition, 2016:35.

222. Mancini JG, Filion KB, Atallah R, Eisenberg MJ. Systematic review of the Mediterranean diet for long-term weight loss. *Am J Med.* Apr 2016;129(4):407-415 e404. PMID: 26721635.

223. Huntriss R, Campbell M, Bedwell C. The interpretation and effect of a low-carbohydrate diet in the management of type 2 diabetes: A systematic review and meta-analysis of randomised controlled trials. *Eur J Clin Nutr.* Mar 2018;72(3):311-325. PMID: 29269890.

224. *What is the ketogenic diet?* 2019; https://www.eatright.org/health/weight-loss/fad-diets/what-is-the-ketogenic-diet. Updated May 15, 2019. Accessed October 9, 2019.

225. Isidro ML, Cordido F. Approved and off-label uses of obesity medications, and potential new pharmacologic treatment options. *Pharmaceuticals (Basel).* Jan 12, 2010;3(1):125-145. PMID: 27713245.

226. Moyers SB. Medications as adjunct therapy for weight loss: Approved and off-label agents in use. *J Am Diet Assoc.* Jun 2005;105(6):948-959. PMID: 15942547.

227. Hendricks EJ. Off-label drugs for weight management. *Diabetes Metab Syndr Obes.* 2017;10:223-234. PMID: 28652791.

228. Ben-Menachem E, Axelsen M, Johanson EH, Stagge A, Smith U. Predictors of weight loss in adults with topiramate-treated epilepsy. *Obes Res.* Apr 2003;11(4):556-562. PMID: 12690085.

229. Kramer CK, Leitao CB, Pinto LC, Canani LH, Azevedo MJ, Gross JL. Efficacy and safety of topiramate on weight loss: A meta-analysis of randomized controlled trials. *Obes Rev.* May 2011;12(5):e338-347. PMID: 21438989.

230. Paravattil B, Wilby KJ, Turgeon R. Topiramate monotherapy for weight reduction in patients with type 2 diabetes mellitus: A systematic review and meta-analysis. *Diabetes Res Clin Pract.* Apr 2016;114:9-14. PMID: 27103363.

231. Ghandi S, Aflatoonian A, Tabibnejad N, Moghaddam MH. The effects of metformin or orlistat on obese women with polycystic ovary syndrome: A prospective randomized open-label study. *J Assist Reprod Genet.* Jul 2011; 28(7):591-596. PMID: 21484319.

232. Anwary SA, Alfazzaman M, Bari N, Islam MR. Outcome of metformin treatment in polycystic ovary syndrome. *Mymensingh Med J.* Jan 2012;21(1):60-65. PMID: 22314456.

233. Ladson G, Dodson WC, Sweet SD, et al. The effects of metformin with lifestyle therapy in polycystic ovary syndrome: A randomized double-blind study. *Fertil Steril.* Mar 1, 2011;95(3):1059-1066 e1051-1057. PMID: 21193187.

234. Meneghini LF, Orozco-Beltran D, Khunti K, et al. Weight beneficial treatments for type 2 diabetes. *J Clin Endocrinol Metab.* Nov 2011;96(11):3337-3353. PMID: 21900381.

235. Swislocki AL, Siegel D, Jialal I. Pharmacotherapy for the metabolic syndrome. *Curr Vasc Pharmacol.* Mar 2012; 10(2):187-205. PMID: 22022773.

236. Bjorkhem-Bergman L, Asplund AB, Lindh JD. Metformin for weight reduction in non-diabetic patients on antipsychotic drugs: A systematic review and meta-analysis. *J Psychopharmacol.* Mar 2011;25(3):299-305. PMID: 20080925.

237. Long-term safety, tolerability, and weight loss associated with metformin in the diabetes prevention program outcomes study. *Diabetes Care.* Apr 2012;35(4):731-737. PMID: 22442396.

238. Levri KM, Slaymaker E, Last A, et al. Metformin as treatment for overweight and obese adults: A systematic review. *Ann Fam Med.* Sep-Oct 2005;3(5):457-461. PMID: 16189063.

239. Seifarth C, Schehler B, Schneider HJ. Effectiveness of metformin on weight loss in non-diabetic individuals with obesity. *Exp Clin Endocrinol Diabetes.* Jan 2013;121(1):27-31. PMID: 23147210.

240. Shyangdan DS, Royle P, Clar C, Sharma P, Waugh N, Snaith A. Glucagon-like peptide analogues for type 2 diabetes mellitus. *Cochrane Database Syst Rev.* Oct 5 2011(10):CD006423. PMID: 21975753.

241. Ahmann AJ, Capehorn M, Charpentier G, et al. Efficacy and safety of once-weekly semaglutide versus exenatide er in subjects with type 2 diabetes (SUSTAIN 3): A 56-week, open-label, randomized clinical trial. *Diabetes Care.* Feb 2018;41(2):258-266. PMID: 29246950.

242. O'Neil PM, Birkenfeld AL, McGowan B, et al. Efficacy and safety of semaglutide compared with liraglutide and placebo for weight loss in patients with obesity: A randomised, double-blind, placebo and active controlled, dose-ranging, phase 2 trial. *Lancet.* Aug 25, 2018;392(10148):637-649. PMID: 30122305.

243. Steinberg WM, Buse JB, Ghorbani MLM, Orsted DD, Nauck MA. Amylase, lipase, and acute pancreatitis in people with type 2 diabetes treated with liraglutide: Results from the LEADER randomized trial. *Diabetes Care.* Jul 2017;40(7):966-972. PMID: 28476871.

244. Clar C, Gill JA, Court R, Waugh N. Systematic review of SGLT2 receptor inhibitors in dual or triple therapy in type 2 diabetes. *BMJ Open.* 2012;2(5). PMID: 23087012.

245. Liu XY, Zhang N, Chen R, Zhao JG, Yu P. Efficacy and safety of sodium-glucose cotransporter 2 inhibitors in type 2 diabetes: A meta-analysis of randomized controlled trials for 1 to 2 years. *J Diabetes Complications.* Nov-Dec 2015;29(8):1295-1303. PMID: 26365905.

246. Foote C, Perkovic V, Neal B. Effects of SGLT2 inhibitors on cardiovascular outcomes. *Diab Vasc Dis Res.* Apr 2012;9(2):117-123. PMID: 22381403.

247. Anderson JW, Greenway FL, Fujioka K, Gadde KM, McKenney J, O'Neil PM. Bupropion sr enhances weight loss: A 48-week double-blind, placebo- controlled trial. *Obes Res.* Jul 2002;10(7):633-641. PMID: 12105285.

248. Apovian CM, Aronne L, Rubino D, et al. A randomized, phase 3 trial of naltrexone sr/bupropion sr on weight and obesity-related risk factors (cor-ii). *Obesity (Silver Spring).* May 2013;21(5):935-943. PMID: 23408728.

249. Greenway FL, Fujioka K, Plodkowski RA, et al. Effect of naltrexone plus bupropion on weight loss in overweight and obese adults (cor-i): A multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet.* Aug 21, 2010;376(9741):595-605. PMID: 20673995.

250. Wadden TA, Foreyt JP, Foster GD, et al. Weight loss with naltrexone sr/bupropion sr combination therapy as an adjunct to behavior modification: The COR-BMOD trial. *Obesity (Silver Spring).* Jan 2011;19(1):110-120. PMID: 20559296.

251. Saad F, Haider A, Doros G, Traish A. Long-term treatment of hypogonadal men with testosterone produces substantial and sustained weight loss. *Obesity (Silver Spring).* Oct 2013;21(10):1975-1981. PMID: 23512691.

252. Bhasin S, Cunningham GR, Hayes FJ, et al. Testosterone therapy in adult men with androgen deficiency syndromes: An endocrine society clinical practice guideline. *J Clin Endocrinol Metab.* Jun 2006;91(6):1995-2010. PMID: 16720669.

253. Isidori AM, Giannetta E, Greco EA, et al. Effects of testosterone on body composition, bone metabolism and serum lipid profile in middle-aged men: A meta-analysis. *Clin Endocrinol (Oxf).* Sep 2005;63(3):280-293. PMID: 16117815.

254. Basaria S, Coviello AD, Travison TG, et al. Adverse events associated with testosterone administration. *N Engl J Med.* Jul 8, 2010;363(2):109-122. PMID: 20592293.

255. Vigen R, O'Donnell CI, Baron AE, et al. Association of testosterone therapy with mortality, myocardial infarction, and stroke in men with low testosterone levels. *JAMA.* Nov 6, 2013;310(17):1829-1836. PMID: 24193080.

256. Finkle WD, Greenland S, Ridgeway GK, et al. Increased risk of non-fatal myocardial infarction following testosterone therapy prescription in men. *PLoS One.* 2014;9(1):e85805. PMID: 24489673.

257. Mangolim AS, Brito LAR, Nunes-Nogueira VS. Effectiveness of testosterone therapy in obese men with low testosterone levels, for losing weight, controlling obesity complications, and preventing cardiovascular events: Protocol of a systematic review of randomized controlled trials. *Medicine (Baltimore).* Apr 2018;97(17):e0482. PMID: 29703008.

258. Lijesen GK, Theeuwen I, Assendelft WJ, Van Der Wal G. The effect of human chorionic gonadotropin (hcg) in the treatment of obesity by means of the simeons therapy: A criteria-based meta-analysis. *Br J Clin Pharmacol.* Sep 1995;40(3):237-243. PMID: 8527285.

259. Goodbar NH, Foushee JA, Eagerton DH, Haynes KB, Johnson AA. Effect of the human chorionic gonadotropin diet on patient outcomes. *Ann Pharmacother.* May 2013;47(5):e23. PMID: 23606549.

260. Kehagias I, Karamanakos SN, Argentou M, Kalfarentzos F. Randomized clinical trial of laparoscopic roux-en-y gastric bypass versus laparoscopic sleeve gastrectomy for the management of patients with BMI < 50 kg/m2. *Obes Surg.* Nov 2011;21(11):1650-1656. PMID: 21818647.

261. Pearce EN. Thyroid hormone and obesity. *Curr Opin Endocrinol Diabetes Obes.* Oct 2012;19(5):408-413. PMID: 22931855.

262. Cardoso L, Rodrigues D, Gomes L, Carrilho F. Short- and long-term mortality after bariatric surgery: A systematic review and meta-analysis. *Diabetes Obes Metab.* Sep 2017;19(9):1223-1232. PMID: 28244626.

263. Inaba CS, Koh CY, Sujatha-Bhaskar S, et al. One-year mortality after contemporary laparoscopic bariatric surgery: An analysis of the bariatric outcomes longitudinal database. *J Am Coll Surg.* Jun 2018;226(6):1166-1174. PMID: 29551698.

264. Reges O, Greenland P, Dicker D, et al. Association of bariatric surgery using laparoscopic banding, roux-en-y gastric bypass, or laparoscopic sleeve gastrectomy vs usual care obesity management with all-cause mortality. *JAMA.* Jan 16, 2018;319(3):279-290. PMID: 29340677.

265. Kim JJ, Rogers AM, Ballem N, Schirmer B. ASMBS updated position statement on insurance mandated preoperative weight loss requirements. *Surg Obes Relat Dis.* Jun 2016;12(5):955-959. PMID: 27523728.

266. Skubleny D, Switzer NJ, Gill RS, et al. The impact of bariatric surgery on polycystic ovary syndrome: A systematic review and meta-analysis. *Obes Surg.* Jan 2016;26(1):169-176. PMID: 26431698.

267. ASMBS'. Peri-operative management of obstructive sleep apnea. *Surg Obes Relat Dis.* May-Jun 2012;8(3):e27-32. PMID: 22503595.

268. Guzman HM, Sepulveda M, Rosso N, San Martin A, Guzman F, Guzman HC. Incidence and risk factors for cholelithiasis after bariatric surgery. *Obes Surg.* Jul 2019;29(7):2110-2114. PMID: 31001756.

269. Parikh M, Johnson JM, Ballem N. ASMBS position statement on alcohol use before and after bariatric surgery. *Surg Obes Relat Dis.* Feb 2016;12(2):225-230. PMID: 26968500.

270. Mechanick JI, Apovian C, Brethauer S, et al. Clinical practice guidelines for the perioperative nutrition, metabolic, and nonsurgical support of patients undergoing bariatric procedures - 2019 update: Cosponsored by American Association of Clinical Endocrinologists/American College of Endocrinology, the Obesity Society, American Society for Metabolic & Bariatric Surgery, Obesity Medicine Association, and American Society of Anesthesiologists - executive summary. *Endocr Pract.* Dec 2019;25(12):1346-1359. PMID: 31682518.

271. Sogg S, Lauretti J, West-Smith L. Recommendations for the presurgical psychosocial evaluation of bariatric surgery patients. *Surg Obes Relat Dis.* May 2016;12(4):731-749. PMID: 27179400.

272. Kominiarek MA, Jungheim ES, Hoeger KM, Rogers AM, Kahan S, Kim JJ. American Society for Metabolic and Bariatric Surgery position statement on the impact of obesity and obesity treatment on fertility and fertility therapy endorsed by the American College of Obstetricians and Gynecologists and the Obesity Society. *Surg Obes Relat Dis.* May 2017;13(5):750-757. PMID: 28416185.

273. Saltzman E, Anderson W, Apovian CM, et al. Criteria for patient selection and multidisciplinary evaluation and treatment of the weight loss surgery patient. *Obes Res.* Feb 2005;13(2):234-243. PMID: 15800279.

274. Committee SG. SAGES guideline for clinical application of laparoscopic bariatric surgery. *Surg Endosc.* Oct 2008;22(10):2281-2300. PMID: 18791862.

275. National Institutes of Health. *Types of bariatric surgery*. https://www.niddk.nih.gov/health-information/weight-management/bariatric-surgery/types

276. Ren CJ, Fielding GA. Laparoscopic adjustable gastric banding: Surgical technique. *J Laparoendosc Adv Surg Tech A.* Aug 2003;13(4):257-263. PMID: 14561254.

277. Koh CY, Inaba CS, Sujatha-Bhaskar S, Hohmann S, Ponce J, Nguyen NT. Laparoscopic adjustable gastric band explantation and implantation at academic centers. *J Am Coll Surg.* Oct 2017;225(4):532-537. PMID: 28754410.

278. ASMBS. Bariatric surgery procedures. 2018.

279. Torres JC, Oca CF, Garrison RN. Gastric bypass: Roux-en-y gastrojejunostomy from the lesser curvature. *South Med J.* Oct 1983;76(10):1217-1221. PMID: 6623129.

280. Abdeen G, le Roux CW. Mechanism underlying the weight loss and complications of roux-en-y gastric bypass. Review. *Obes Surg.* Feb 2016;26(2):410-421. PMID: 26530712.

281. Angrisani L, Santonicola A, Iovino P, et al. Ifso worldwide survey 2016: Primary, endoluminal, and revisional procedures. *Obes Surg.* Dec 2018;28(12):3783-3794. PMID: 30121858.

282. Ali M, El Chaar M, Ghiassi S, Rogers AM. American Society for Metabolic and Bariatric Surgery updated position statement on sleeve gastrectomy as a bariatric procedure. *Surg Obes Relat Dis.* Oct 2017;13(10):1652-1657. PMID: 29054173.

283. Scopinaro N, Gianetta E, Civalleri D, Bonalumi U, Bachi V. Bilio-pancreatic bypass for obesity: II. Initial experience in man. *Br J Surg.* Sep 1979;66(9):618-620. PMID: 497645.

284. Buchwald H. The evolution of metabolic/bariatric surgery. *Obes Surg.* Aug 2014;24(8):1126-1135. PMID: 25008469.

285. Zhang Y, Zhao H, Cao Z, et al. A randomized clinical trial of laparoscopic roux-en-y gastric bypass and sleeve gastrectomy for the treatment of morbid obesity in China: A 5-year outcome. *Obes Surg.* Oct 2014;24(10): 1617-1624. PMID: 24827405.

286. Chen SY, Stem M, Schweitzer MA, Magnuson TH, Lidor AO. Assessment of postdischarge complications after bariatric surgery: A national surgical quality improvement program analysis. *Surgery.* Sep 2015;158(3):777-786. PMID: 26096563.

287. Ponce J, Nguyen NT, Hutter M, Sudan R, Morton JM. American Society for Metabolic and Bariatric Surgery estimation of bariatric surgery procedures in the United States, 2011-2014. *Surg Obes Relat Dis.* Nov-Dec 2015;11(6):1199-1200. PMID: 26476493.

288. Wang FG, Yu ZP, Yan WM, Yan M, Song MM. Comparison of safety and effectiveness between laparoscopic mini-gastric bypass and laparoscopic sleeve gastrectomy: A meta-analysis and systematic review. *Medicine (Baltimore).* Dec 2017;96(50):e8924. PMID: 29390281.

289. Magouliotis DE, Tasiopoulou VS, Tzovaras G. One anastomosis gastric bypass versus roux-en-y gastric bypass for morbid obesity: A meta-analysis. *Clin Obes.* Jun 2018;8(3):159-169. PMID: 29573175.

290. Aminian A, Brethauer SA, Kirwan JP, Kashyap SR, Burguera B, Schauer PR. How safe is metabolic/diabetes surgery? *Diabetes Obes Metab.* Feb 2015;17(2):198-201. PMID: 25352176.

291. Flum DR, Belle SH, King WC, et al. Perioperative safety in the longitudinal assessment of bariatric surgery. *N Engl J Med.* Jul 30, 2009;361(5):445-454. PMID: 19641201.

292. Nelson DW, Blair KS, Martin MJ. Analysis of obesity-related outcomes and bariatric failure rates with the duodenal switch vs gastric bypass for morbid obesity. *Arch Surg.* Sep 2012;147(9):847-854. PMID: 22987179.

293. Livingston EH, Huerta S, Arthur D, Lee S, De Shields S, Heber D. Male gender is a predictor of morbidity and age a predictor of mortality for patients undergoing gastric bypass surgery. *Ann Surg.* Nov 2002;236(5):576-582. PMID: 12409663.

294. Livingston EH. Procedure incidence and in-hospital complication rates of bariatric surgery in the United States. *Am J Surg.* Aug 2004;188(2):105-110. PMID: 15249233.

295. Melinek J, Livingston E, Cortina G, Fishbein MC. Autopsy findings following gastric bypass surgery for morbid obesity. *Arch Pathol Lab Med.* Sep 2002;126(9):1091-1095. PMID: 12204059.

296. Lancaster RT, Hutter MM. Bands and bypasses: 30-day morbidity and mortality of bariatric surgical procedures as assessed by prospective, multi-center, risk-adjusted acs-nsqip data. *Surg Endosc.* Dec 2008;22(12):2554-2563. PMID: 18806945.

297. Parikh A, Alley JB, Peterson RM, et al. Management options for symptomatic stenosis after laparoscopic vertical sleeve gastrectomy in the morbidly obese. *Surg Endosc.* Mar 2012;26(3):738-746. PMID: 22044967.

298. Csendes A, Burgos AM, Altuve J, Bonacic S. Incidence of marginal ulcer 1 month and 1 to 2 years after gastric bypass: A prospective consecutive endoscopic evaluation of 442 patients with morbid obesity. *Obes Surg.* Feb 2009;19(2):135-138. PMID: 18581192.

299. Clapp B. Small bowel obstruction after laparoscopic gastric bypass with nonclosure of mesenteric defects. *Jsls.* Jan-Mar 2015;19(1):e2014.00257. PMID: 25848176.

300. Iannelli A, Facchiano E, Gugenheim J. Internal hernia after laparoscopic roux-en-y gastric bypass for morbid obesity. *Obes Surg.* Oct 2006;16(10):1265-1271. PMID: 17059733.

301. Higa KD, Ho T, Boone KB. Internal hernias after laparoscopic roux-en-y gastric bypass: Incidence, treatment and prevention. *Obes Surg.* Jun 2003;13(3):350-354. PMID: 12841892.

302. Jones KB, Jr., Afram JD, Benotti PN, et al. Open versus laparoscopic roux-en-y gastric bypass: A comparative study of over 25,000 open cases and the major laparoscopic bariatric reported series. *Obes Surg.* Jun 2006; 16(6):721-727. PMID: 16756731.

303. Podnos YD, Jimenez JC, Wilson SE, Stevens CM, Nguyen NT. Complications after laparoscopic gastric bypass: A review of 3464 cases. *Archives of Surgery.* 2003;138(9):957-961.

304. Winegar DA, Sherif B, Pate V, DeMaria EJ. Venous thromboembolism after bariatric surgery performed by bariatric surgery center of excellence Participants: Analysis of the bariatric outcomes longitudinal database. *Surg Obes Relat Dis.* Mar-Apr 2011;7(2):181-188. PMID: 21421182.

305. ASMBS. ASMBS updated position statement on prophylactic measures to reduce the risk of venous thromboembolism in bariatric surgery patients. *Surg Obes Relat Dis.* Jul-Aug 2013;9(4):493-497. PMID: 23769113.

306. Smith MD, Adeniji A, Wahed AS, et al. Technical factors associated with anastomotic leak after roux-en-y gastric bypass. *Surg Obes Relat Dis.* Mar-Apr 2015;11(2):313-320. PMID: 25595919.

307. Alizadeh RF, Li S, Inaba C, et al. Risk factors for gastrointestinal leak after bariatric surgery: MBASQIP analysis. *J Am Coll Surg.* Jul 2018;227(1):135-141. PMID: 29605723.

308. Gagner M, Kemmeter P. Comparison of laparoscopic sleeve gastrectomy leak rates in five staple-line reinforcement options: A systematic review. *Surg Endosc.* Jan 2020;34(1):396-407. PMID: 30993513.
309. Caruso F, Cesana G, Lomaglio L, et al. Is portomesenteric vein thrombosis after laparoscopic sleeve gastrectomy related to short-course prophylaxis of thromboembolism? A monocentric retrospective analysis about an infrequent but not rare complication and review of the literature. *J Laparoendosc Adv Surg Tech A.* Oct 2017;27(10):987-996. PMID: 28604246.
310. Antoniou SA, Antoniou GA, Koch OO, Kohler G, Pointner R, Granderath FA. Laparoscopic versus open obesity surgery: A meta-analysis of pulmonary complications. *Dig Surg.* 2015;32(2):98-107. PMID: 25765889.
311. Snow JM, Severson PA. Complications of adjustable gastric banding. *Surg Clin North Am.* Dec 2011;91(6):1249-1264, ix. PMID: 22054152.
312. Lattuada E, Zappa MA, Mozzi E, Antonini I, Boati P, Roviaro GC. Injection port and connecting tube complications after laparoscopic adjustable gastric banding. *Obes Surg.* Apr 2010;20(4):410-414. PMID: 18542848.
313. Rabiee A, Magruder JT, Salas-Carrillo R, et al. Hyperinsulinemic hypoglycemia after roux-en-y gastric bypass: Unraveling the role of gut hormonal and pancreatic endocrine dysfunction. *J Surg Res.* May 15 2011;167(2): 199-205. PMID: 21414635.
314. Malik S, Mitchell JE, Steffen K, et al. Recognition and management of hyperinsulinemic hypoglycemia after bariatric surgery. *Obes Res Clin Pract.* Jan-Feb 2016;10(1):1-14. PMID: 26522879.
315. Clancy TE, Moore FD, Jr., Zinner MJ. Post-gastric bypass hyperinsulinism with nesidioblastosis: Subtotal or total pancreatectomy may be needed to prevent recurrent hypoglycemia. *J Gastrointest Surg.* Sep-Oct 2006;10(8): 1116-1119. PMID: 16966030.
316. Mala T. Postprandial hyperinsulinemic hypoglycemia after gastric bypass surgical treatment. *Surg Obes Relat Dis.* Nov-Dec 2014;10(6):1220-1225. PMID: 25002326.
317. Heber D, Greenway FL, Kaplan LM, Livingston E, Salvador J, Still C. Endocrine and nutritional management of the post-bariatric surgery patient: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab.* Nov 2010;95(11):4823-4843. PMID: 21051578.
318. Lupoli R, Lembo E, Saldalamacchia G, Avola CK, Angrisani L, Capaldo B. Bariatric surgery and long-term nutritional issues. *World J Diabetes.* Nov 15 2017;8(11):464-474. PMID: 29204255.
319. Mechanick JI, Apovian C, Brethauer S, et al. Clinical practice guidelines for the perioperative nutrition, metabolic, and nonsurgical support of patients undergoing bariatric procedures - 2019 update: Cosponsored by American Association of Clinical Endocrinologists/American College of Endocrinology, the Obesity Society, American Society for Metabolic and Bariatric Surgery, Obesity Medicine Association, and American Society of Anesthesiologists. *Obesity (Silver Spring).* Apr 2020;28(4):O1-O58. PMID: 32202076.