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AACE/ACE Guidelines

AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND AMERICAN COLLEGE OF ENDOCRINOLOGY CLINICAL PRACTICE GUIDELINES FOR COMPREHENSIVE MEDICAL CARE OF PATIENTS WITH OBESITY – EXECUTIVE SUMMARY

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Keywords: bariatric surgery**;** best practice guidelines**;** clinical practice guidelines**;** evidence-based medicine; lifestyle medicine**;** metabolic syndrome**;** obesity**;** obesity-related complication**;** overweight; weight-loss medications

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American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice are systematically developed statements to assist health care professionals in medical decision-making for specific clinical conditions. Most of the content herein is based on a systematic review
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of evidence published in peer-reviewed literature. In areas where there was some uncertainty, professional judgment was applied.

These guidelines are a working document reflecting the state of the field at the time of publication. Because rapid changes in this area are expected, periodic revisions are inevitable. We encourage medical professionals to use this information in conjunction with their best clinical judgment. The presented recommendations may not be appropriate in all situations. Any decision by practitioners to apply these guidelines must be made in light of local resources and individual patient circumstances.

*A complete list of the Reviewers of the AACE/ACE Obesity Clinical Practice Guidelines can be found in the Supplementary material online.

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Abbreviations:
A1C = hemoglobin A1c; **AACE** = American Association of Clinical Endocrinologists; **ACE** = American College of Endocrinology; **AMA** = American Medical Association; **BEL** = best evidence level; **BMI** = body mass index; **CCO** = Consensus Conference on Obesity; **CPG** = clinical practice guideline; **CSS** = cross-sectional study; **CVD** = cardiovascular disease; **EL** = evidence level; **FDA** = US Food and Drug Administration; **GERD** = gastroesophageal reflux disease; **HDL** = high-density lipoprotein; **HDL-c** = high-density lipoprotein cholesterol; **IFG** = impaired fasting glucose; **IGT** = impaired glucose tolerance; **LDL-c** = low-density lipoprotein cholesterol; **min** = minutes; **MNRCT** = meta-analysis of non-randomized prospective or case-controlled trials; **NE** = no evidence; **PCOS** = polycystic ovary syndrome; **RCT** = randomized controlled trial; **SS** = surveillance study; **US** = United States.

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Abstract

The development of these guidelines is mandated by the AACE Board of Directors and ACE Board of Trustees and adheres with published AACE protocols for the standardized production of clinical practice guidelines (CPGs). Each recommendation is based on a diligent review of the clinical evidence with transparent incorporation of subjective factors. There are 9 broad clinical questions with 123 recommendation numbers with 160 specific statements (85 [53.1%] are strong [Grade A], 48 [30.0%] are intermediate [Grade B], and 11 [6.9%] are weak [Grade C], with 16 [10.0%] based on expert opinion [Grade D]) that build a comprehensive medical care plan for obesity. There were 133 (83.1%) statements based on strong (best evidence level [BEL] 1 = 79 [49.4%]) or intermediate (BEL 2 = 54 [33.7%]) levels of scientific substantiation. There are 34 (23.6%) evidence-based recommendation grades (Grades A-C = 144) that are adjusted based on subjective factors. Among the 1,790 reference citations used in this CPG, 524 (29.3%) are based on strong (evidence level [EL] 1), 605 (33.8%) are based on intermediate (EL 2), and 308 (17.2%) are based on weak (EL 3) scientific studies, with 353 (19.7%) based on reviews and opinions (EL 4). The thrust of the final recommendations is to recognize that obesity is a complex, adiposity-based chronic disease, where management targets both weight-related complications and adiposity to improve overall health and quality of life. The detailed evidence-based recommendations allow for nuance-based clinical decision-making that addresses the multiple aspects of real-world medical care of patients with obesity, including screening, diagnosis, evaluation, selection of therapy, treatment goals, and individualization of care. The goal is to facilitate high-quality care of patients with obesity and provide a rational, scientifically based approach to management that optimizes health outcomes and safety.

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“Corpulence is not only a disease itself, but the harbinger of others.” Hippocrates

I. Introduction and Rationale

Obesity rates have increased sharply over the past 30 years, creating a global public health crisis (1 [EL 3; SS]; 2 [EL 2; MNRCT]; 3 [EL 3; CSS]). Global estimates suggest that 500 million adults have obesity worldwide (2 [EL 2; MNRCT]), with prevalence rates increasing among children and adolescents (3 [EL 3; CSS]; 4 [EL 3; SS]; 5 [EL 3; SS]). Data from the National Health and Nutrition Examination Surveys show that roughly 2 out of 3 United States (US) adults have overweight or obesity, and 1 out of 3 adults has obesity (1 [EL 3; SS]; 2 [EL 2; MNRCT]; 3 [EL 3; CSS]). The impact of obesity on morbidity, mortality, and health care costs is profound. Obesity and weight-related complications exert a huge burden on patient suffering and social costs (6 [EL 3; SS]; 7 [EL 3; SS]). Obesity is estimated to add $3,559 annually (adjusted to 2012 dollars) to per-patient medical expenditures compared with patients who do not have obesity; this includes $1,372 each year for inpatient services, $1,057 for outpatient services, and $1,130 for prescription drugs (6 [EL 3; SS]).

In recent years, exciting advances have occurred in all 3 modalities used to treat obesity: lifestyle intervention, pharmacotherapy, and weight-loss procedures including bariatric surgery (8 [EL 4; NE]). Clinical trials have established the efficacy of lifestyle and behavioral interventions in obesity; moreover, there are now 5 weight-loss medications approved by the US Food and Drug Administration (FDA) for chronic management of obesity (9 [EL 4; NE]; 10 [EL 4; NE]). Bariatric surgical practices have been developed and refined, together with improvements in pre- and postoperative care standards, resulting in better patient outcomes (11 [EL 4; NE]). The FDA has also

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recently approved devices involving electrical stimulation and gastric balloons for the treatment of obesity. In addition to enhanced treatment options, the scientific understanding of the pathophysiology of obesity has advanced, and it is now viewed as a complex chronic disease with interacting genetic, environmental, and behavioral determinants that result in serious complications (10 [EL 4; NE]). Adipose tissue itself is an endocrine organ which can become dysfunctional in obesity and contribute to systemic metabolic disease. Weight loss can be used to prevent and treat metabolic disease concomitant with improvements in adipose tissue functionality. These new therapeutic tools and scientific advances necessitate development of rational medical care models and robust evidenced-based therapeutic approaches, with the intended goal of improving patient well-being and recognizing patients as individuals with unique phenotypes in unique settings.

In 2012, the American Association of Clinical Endocrinologists (AACE) published a position statement designating obesity as a disease and providing the rationale for this designation (12 [EL 4; NE]). Subsequently, AACE was joined by multiple professional organizations in submitting a resolution to the American Medical Association (AMA) to recognize obesity as a disease. In June 2013, following a vote by its House of Delegates, the AMA adopted a policy designating obesity as a chronic disease (13 [EL 4, NE]). These developments have the potential to accelerate scientific study of the multidimensional pathophysiology of obesity and also present an impetus to our health care system to provide effective treatment and prevention.

In May of 2014, AACE and the American College of Endocrinology (ACE) sponsored their first Consensus Conference on Obesity (CCO) in Washington, DC, to

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establish an evidence base that could be used to develop a comprehensive plan to combat obesity (14 [EL 4; NE]). The conference convened a wide array of national stakeholders (the “pillars”) with a vested interest in obesity. The concerted participation of these stakeholders was recognized as necessary to support an effective overall action plan, and they included health professional organizations, government regulatory agencies, employers, health care insurers, pharmaceutical industry representatives, research organizations, disease advocacy organizations, and health profession educators.

A key consensus concept that emerged from the CCO was that a more medically meaningful and actionable definition of obesity was needed. It became clear that diagnosis based solely on body mass index (BMI) lacked the information needed for effective interaction and concerted policy regarding obesity among stakeholders (14 [EL 4; NE]) and was a barrier to the development of acceptable and rational approaches to medical care. It was agreed that the elements for an improved obesity diagnostic process should include BMI alongside an indication of the degree to which excess adiposity negatively affects an individual patient’s health.

In response to this emergent concept from the CCO, AACE proposed an “Advanced Framework for a New Diagnosis of Obesity.” This document features an anthropometric component that is the measure of adiposity (ie, BMI) and a clinical component that describes the presence and severity of weight-related complications (15 [EL 4; NE]). Given the multiple meanings and perspectives associated with the term “obesity” in our society, there was also discussion that the medical diagnostic term for obesity should be “adiposity-based chronic disease” (ABCD).

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The paradigm for obesity care proposed by the National Heart, Lung, and Blood Institute (16 [EL4;NE]), as well as FDA-sanctioned prescribing information for the use of obesity medications (17 [EL 4; NE]), largely bases indications for therapeutic modalities on patient BMI (a BMI-centric approach). As part of the AACE Clinical Practice Guidelines for Developing a Diabetes Mellitus Comprehensive Care Plan (18 [EL 4; NE]), an algorithm for obesity management was proposed wherein the presence and severity of weight-related complications constitute the primary determinants for treatment modality selection and weight-loss therapy intensity (19 [EL 4; NE]). In this new complications-centric approach, the primary therapeutic endpoint is improvement in adiposity-related complications, not a preset decline in body weight (8 [EL 4; NE]). Thus, the main endpoint of therapy is to measurably improve patient health and quality of life. Other organizations such as the American Heart Association, the American College of Cardiology, The Obesity Society (20 [EL 4; NE]), the Obesity Medical Association (21 [EL 4; NE]), and the Endocrine Society (22 [EL 4; NE]) have also developed obesity care guidelines and algorithms incorporating aspects of a complications-centric approach.

This AACE/ACE evidence-based clinical practice guideline (CPG) is structured around a series of *a priori,* relevant, intuitive, and pragmatic questions that address key and germane aspects of obesity care: screening, diagnosis, clinical evaluation, treatment options, therapy selection, and treatment goals. In aggregate, these questions evaluate obesity as a chronic disease and consequently outline a comprehensive care plan to assist the clinician in caring for patients with obesity. This approach may differ from other CPGs. Specifically, in other CPGs:

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- the scientific evidence is first examined and then questions are formulated only when strong scientific evidence exists (eg, randomized controlled trials [RCTs]), and/or
- only certain aspects of management (eg, pharmacotherapy) are chosen for a focused (but not comprehensive) CPG.

Neither of these approaches addresses the totality, multiplicity, or complexity of issues required to provide effective, comprehensive obesity management applicable to real-world patient care. Moreover, the nuances of obesity care in an obesogenic-built environment, which at times have an overwhelming socioeconomic contextualization, require diligent analysis of the full weight of extant evidence.

To this end, these CPGs address multiple aspects of patient care relevant to any individual patient encounter, assess the available evidence base, and provide specific recommendations. The strength of each recommendation is commensurate with the strength of evidence. In this way, these CPGs marshal the best existing evidence to address the key questions and decisions facing clinicians in the real-world practical care of patients with obesity. This methodology is transparent and outlined in multiple AACE/ACE processes for producing guideline protocols (23 [EL 4; NE]; 24 [EL 4; NE]; 25 [EL 4; NE]). Implementing these CPGs should facilitate high-quality care of patients with obesity and provide a rational, scientifically based approach to management that optimizes outcomes and safety. Thus, these CPGs will be useful for all health care professionals involved in the care of patients with, or at risk for, obesity and adiposity-related complications.

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II. Mandate

In 2015, the AACE Executive Committee and the AACE Board of Directors mandated the development of CPGs for obesity to provide a set of evidence-based recommendations for the comprehensive care of patients with overweight or obesity, including an end goal of optimizing patient outcomes. The selection of the chair, primary writers, and reviewers was made by the President of AACE, in consultation with the AACE Executive Committee. The charge was to develop evidence-based CPGs in strict adherence with the process established in the 2004 AACE Protocol for Standardized Production of Clinical Practice Guidelines (23 [EL 4; NE]) and the 2010 and 2014 updates (24 [EL 4; NE]; 25 [EL 4; NE]). The development of these obesity CPGs complements other AACE/ACE activities in obesity medicine, namely the new complications-centric framework for the diagnosis and management of overweight and obesity (15 [EL 4; NE]), bariatric surgery CPGs (11 [EL 4; NE]), healthy eating CPGs (26 [EL 4; NE]), diabetes comprehensive care CPGs (18 [EL 4; NE]; 19 [EL 4; NE]), obesity and nutrition position statements (12 [EL 4; NE]), and other educational programs and white papers (14 [EL 4; NE]).

III. Methods

This AACE/ACE CPG on Obesity is developed according to established AACE/ACE methodology for guidelines development (23 [EL 4; NE]; 24 [EL 4; NE]; 25 [EL 4; NE]) and is characterized by the following salient attributes:

1. Appointment of credentialed experts who have disclosed all multiplicities of interests, vetted by the AACE Publications Committee;
2. Incorporation of middle-range literature searching with: (i) an emphasis on strong evidence and the identification of all relevant RCTs and meta-

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analyses; (ii) inclusion of relevant cohort studies, nested case-control studies, and case series; and (iii) inclusion of more general reviews/opinions, mechanistic studies, and illustrative case reports when considered appropriate;

3. An orientation on questions that are directly relevant to patient care;
4. Use of a technical *a priori* methodology, which maps strength of evidence to recommendation grades and stipulates subjective factors established in the AACE/ACE Protocol for Standardized Production of Clinical Practice Guidelines (23 [EL 4; NE]; 24 [EL 4; NE]; 25 [EL 4; NE]); and
5. Employment of a multilevel review process and high level of diligence.

Task Force Assignments. The logistics and process for task force assignments adhered with the AACE Protocol for Standardized Production of Clinical Practice Guidelines (23 [EL 4; NE]; 24 [EL 4; NE]; 25 [EL 4; NE]). The selection of the chair, primary writing team, and reviewers was based on the expert credentials of these individuals in obesity medicine. All appointees are AACE members and are experts in the field of obesity care. All multiplicities of interests for each individual participant are clearly disclosed and delineated in this document. No appointee is employed by industry, and there was no involvement of industry in the development of these CPGs.

Question/Problem Structure for Guidelines Development. The goal was to develop CPGs that are comprehensive and relevant to clinicians. Therefore, the questions for evidence-based review reflect the multiple aspects of management that must be addressed by clinicians as they evaluate, screen, and diagnose patients with obesity; establish a clinical database; make treatment decisions; and assess therapeutic

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outcomes. The primary writing team drafted questions for evidence-based review and, following multiple and interactive discussions, arrived at a consensus for the final question list addressed in these CPGs.

Evidence-Based Review. Once the questions were finalized, the next step was to conduct a systematic electronic search of the literature pertinent to each question. The task force chair assigned each question to a member of the task force writing team, and the team members executed a systematic electronic search of the published literature from relevant bibliographic databases for each clinical question. The objective was to identify all publications necessary to assign the true strength of evidence, given the totality of evidence available in the literature. The mandate was to include all studies that materially impact the strength of the evidence level. Thus, all RCTs and meta-analyses were to be identified (whether they provided positive or negative data with respect to each question) since these studies would predominate in scoring the strength of evidence. The writing team members also identified relevant nonrandomized interventions, cohort studies, and case-control trials, as well as cross-sectional studies, surveillance studies, epidemiological data, case series, and pertinent studies of disease mechanisms. In the absence of RCTs, recommendations would necessarily rely on lower levels of evidence, which would in turn affect the strength of the ensuing recommendations.

For the systematic review of all clinical trials and meta-analyses, each task force member conducted a search of the Cochrane Library (which includes all references in the Cochrane Central Register of Controlled Trials) (27 [EL 4; NE]). A search was conducted without date limits for all trials, using “obesity” and/or “weight loss” as key

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search terms together with term(s) relevant to the question being addressed. In addition, all relevant trials and meta-analyses were identified in a search of the PubMed database. The task force members culled references for studies that were duplicates or not relevant, as well as papers devoid of original data or analyses that would not contribute to scientific substantiation or alter the evidence level and recommendation strength. In addition to these search strategies, the task force members used other databases, employed literature reviews, and included mechanistic data when this contributed to the discussion of evidence.

References numerically cited in the text were then scored for strength of evidence using definitions provided in Table 1 (24 [EL 4; NE]). There are 4 intuitive levels of evidence based on study design and data quality: 1 = strong, 2 = intermediate, 3 = weak, and 4 = no clinical evidence. Where appropriate, comments were appended to the evidence level regarding judgments or factors that could influence the subsequent grading process (Table 2) (24 [EL 4; NE]). Reference citations in the document text include the reference number, the evidence level numerical descriptor (eg, evidence level [EL] 1, 2, 3, or 4), and a semantic descriptor abbreviation.

Once the evidence base was systematically established and reviewed, task force members summarily described the evidence, including all references that could materially affect the strength-of-evidence assessment and CPG recommendations. Task force members also formulated 1 or more recommendations based on the evidence in response to each question. Clinical questions are labeled “Q,” and recommendations are labeled “R.”

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Formulation of Recommendations. The task force discussed and critiqued each of the evidence reviews and recommendations, which were then revised for consensus approval. The evidence ratings were used to grade the scientific strength of the recommendations. Recommendations (numerically labeled “R1, R2,” etc) are based on strength of evidence, indexed to the best evidence level (BEL), which corresponds to the strongest and most conclusive evidence (when taking the evidence level of all the references in each of the evidence reviews into consideration; Table 1). The BEL is accompanied by a recommendation grade (A, B, C, or D) as shown in Figure 1 and Table 1. This recommendation grade maps to the BEL and can be adjusted upward or downward by 1 level as shown in Table 3 based on judgments and factors listed in Table 4. As prespecified in Table 4, comments may be appended to the recommendation grade and BEL regarding any relevant factors that may have influenced the grading process. Final recommendation grades may be interpreted as being based on strong (Grade A), intermediate (Grade B), weak (Grade C), or no (Grade D) scientific substantiation. The evidence base supporting each recommendation, with accompanying tables, figures, algorithm, and care model, will be provided in a future appendix section.

This transparent process leads to a final recommendation and grade that incorporate complex expert integration of scientific data (and, to a degree, factors reflecting real-world practice) to establish actionable, evidence-based guidelines for optimal clinical decision-making and patient care practices. Again, this document represents only guidelines for clinical practice. Individual patient circumstances and presentations obviously differ, and ultimately clinical management choices should be

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based on individual patients' best interests, including patient input and reasonable clinical judgment by treating clinicians.

Prepublication Review and Critique. These CPGs were first drafted and agreed upon by the task force writing team and then critically reviewed by the AACE Obesity Scientific Committee, the special external reviewer, the AACE Publications Committee, the AACE Board of Directors, and the AACE Executive Committee. Where appropriate, revisions were incorporated at each step of this review process.

Summary. These CPGs include an executive summary consisting of 123 clinical practice recommendations with 160 specific statements, organized in response to 9 broad questions covering the spectrum of obesity management. The objectives of these CPGs are to provide an evidence-based resource addressing rational approaches to the care of patients with obesity and an educational resource for the development of a comprehensive care plan for clinical endocrinologists and other health care professionals who care for patients with obesity. To achieve these goals, these recommendations provide concise, accurate answers to each question, as well as a forthcoming detailed and extensively referenced appendix organized to provide supporting evidence for each recommendation. This format does not attempt to present an encyclopedic citation of all pertinent primary references; however, sufficient key references are provided to designate the BEL for each recommendation. Although many studies rated at the highest evidence level are cited (ie, RCTs and meta-analyses of these trials [EL1]), in the interest of conciseness, derivative EL4 review publications that include many primary evidence citations (EL1, EL2, and EL3) are also included. In addition, rigorously reviewed guidelines by other organizations have been adopted for

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specific issues, such as physical activity guidelines by the American Academy of Sports Medicine (28 [EL 4; NE]), physical activity guidelines by the American Heart Association and the American College of Cardiology (29 [EL 4; NE]), healthy eating guidelines by the American Association of Clinical Endocrinologists and The Obesity Society (30 [EL 4; NE]), and perioperative bariatric surgery guidelines by the American Association of Clinical Endocrinologists, the Obesity Society, and the American Society for Metabolic and Bariatric Surgery (11 [EL 4; NE]). Thus, these CPGs are not intended to serve as an obesity textbook, but rather to complement existing texts, other CPGs, and previously published AACE documents.

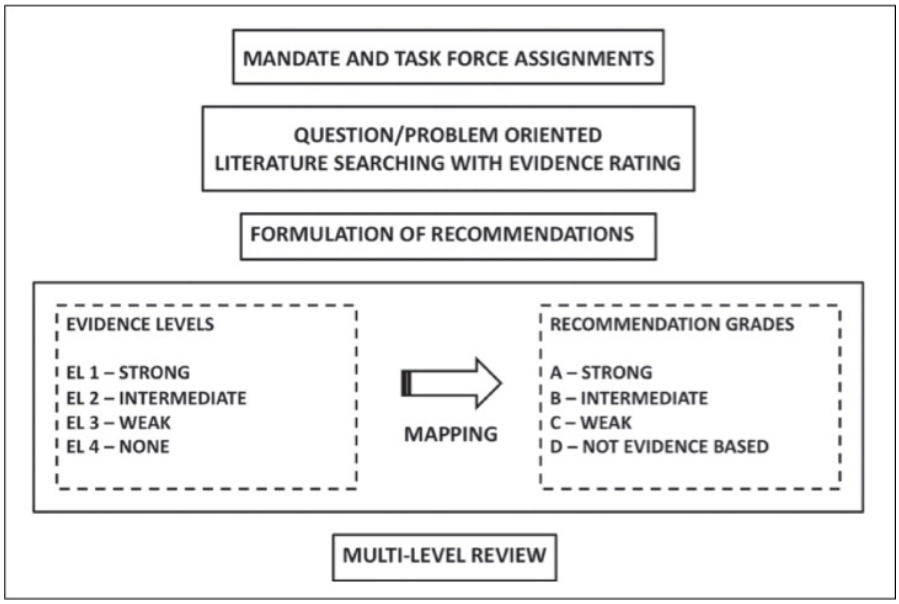

Figure. 1. (24 [EL 4; NE])
2010 American Association of Clinical Endocrinologists (AACE) Clinical Practice Guideline (CPG) methodology. Current AACE CPGs have a problem-oriented focus that results in a shortened production timeline, middle-range literature searching, emphasis on patient-oriented evidence that matters, greater transparency of intuitive evidence rating and qualifications, incorporation of subjective factors into evidence-recommendation mapping, cascades of alternative approaches, and an expedited multilevel review mechanism.

Table 1. 2010 American Association of Clinical Endocrinologists Protocol for Production of Clinical Practice Guidelines—Step I: Evidence Rating (24 [EL 4; NE])

Numeric	Semantic descriptor (reference methodology)

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descriptor (evidence level)[a]	
1	Meta-analysis of randomized controlled trials (MRCT)
1	Randomized controlled trial (RCT)
2	Meta-analysis of nonrandomized prospective or case-controlled trials (MNRCT)
2	Nonrandomized controlled trial (NRCT)
2	Prospective cohort study (PCS)
2	Retrospective case-control study (RCCS)
3	Cross-sectional study (CSS)
3	Surveillance study (registries, surveys, epidemiologic study, retrospective chart review, mathematical modeling of database) (SS)
3	Consecutive case series (CCS)
3	Single case reports (SCR)
4	No evidence (theory, opinion, consensus, review, or preclinical study) (NE)
[a] 1, strong evidence; 2, intermediate evidence; 3, weak evidence; and 4, no evidence.	

Table 2. 2010 American Association of Clinical Endocrinologists Protocol for Production of Clinical Practice Guidelines—Step II: Evidence Analysis and Subjective Factors (24 [EL 4; NE])

Study design	Data analysis	Interpretation of results
Premise correctness	Intent-to-treat	Generalizability
Allocation concealment (randomization)	Appropriate statistics	Logical
Selection bias		Incompleteness
Appropriate blinding		Validity
Using surrogate endpoints (especially in "first-in-its-class" intervention)		
Sample size (beta error)		
Null hypothesis vs Bayesian statistics		

Table 3. 2010 American Association of Clinical Endocrinologists Protocol for Production of Clinical Practice Guidelines—Step III: Grading of Recommendations; How Different Evidence Levels Can Be Mapped to the Same Recommendation Grade[a] (24 [EL 4; NE])

Best evidence level	Subjective factor impact	Two-thirds consensus	Mapping	Recommendation grade
1	None	Yes	Direct	A
2	Positive	Yes	Adjust up	A
2	None	Yes	Direct	B
1	Negative	Yes	Adjust down	B
3	Positive	Yes	Adjust up	B

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3	None	Yes	Direct	C
2	Negative	Yes	Adjust down	C
4	Positive	Yes	Adjust up	C
4	None	Yes	Direct	D
3	Negative	Yes	Adjust down	D
1, 2, 3, 4	NA	No	Adjust down	D

[a] Starting with the left column, best evidence levels (BELs), subjective factors, and consensus map to recommendation grades in the right column. When subjective factors have little or no impact ("none"), then the BEL is directly mapped to recommendation grades. When subjective factors have a strong impact, then recommendation grades may be adjusted up ("positive" impact) or down ("negative" impact). If a two-thirds consensus cannot be reached, then the recommendation grade is D. NA/not applicable (regardless of the presence or absence of strong subjective factors, the absence of a two-thirds consensus mandates a recommendation grade D).

Table 4. 2010 American Association of Clinical Endocrinologists Protocol for Production of Clinical Practice Guidelines—Step IV: Examples of Qualifiers (24 [EL 4; NE])

Cost-effectiveness
Risk-benefit analysis
Evidence gaps
Alternative physician preferences (dissenting opinions)
Alternative recommendations ("cascades")
Resource availability
Cultural factors
Relevance (patient-oriented evidence that matters)

IV. Executive Summary

A. QUESTIONS

The evidence based recommendations for the CPGs were organized in response to the following questions, which provided the structure for evidence review. Readers are referred to the future publication of the appendix for detailed evidence reviews and references that support the recommendations and evidence level ratings for each reference as pertains to each question and associated recommendations. In the 123 numbered recommendations, there are 160 individual statements, of which 85 (53.1%) are Grade A, 48 (30.0%) are Grade B, 11 (6.9%) are Grade C, and 16 (10.0%) are Grade D. There are 133 (83.1%) statements that are Grade A or B indicating a strong or intermediate level of scientific substantiation. There are 34 (23.6%) evidence-based recommendation grades (Grades A-C = 144) that are adjusted based on subjective

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factors. Of these, 19 (55.9%) were due to clinical relevance and 15 (44.1%) were due to evidence gaps (Table 4).

- **Post Hoc Question**: By inductive evaluation of all evidence-based recommendations, what are the core recommendations for medical care of patients with obesity?

Obesity and 3 Phases of Chronic Disease Prevention and Treatment

- Q1. Do the 3 phases of chronic disease prevention and treatment—ie, primary, secondary, and tertiary—apply to the disease of obesity?

The Anthropometric Component of the Diagnosis of Obesity

- Q2. How should the degree of adiposity be measured in the clinical setting?
    - Q2.1. What is the best way to optimally screen or aggressively case-find for overweight and obesity?
    - Q2.2. What are the best anthropomorphic criteria for defining excess adiposity in the diagnosis of overweight and obesity in the clinical setting?
    - Q2.3. Does waist circumference provide information in addition to BMI to indicate adiposity risk?
    - Q2.4. Do BMI and waist circumference accurately capture adiposity risk at all levels of BMI, ethnicities, gender, and age?

The Clinical Component of the Diagnosis of Obesity

- Q3. What are the weight-related complications that are either caused or exacerbated by excess adiposity?
    - Q3.1. Diabetes risk, metabolic syndrome, and prediabetes (IFG, IGT)
    - Q3.2. Type 2 diabetes
    - Q3.3. Dyslipidemia
    - Q3.4. Hypertension
    - Q3.5. Cardiovascular disease and cardiovascular disease mortality
    - Q3.6. Nonalcoholic fatty liver disease/nonalcoholic steatohepatitis
    - Q3.7. Polycystic ovary syndrome (PCOS)
    - Q3.8. Female infertility
    - Q3.9. Male hypogonadism
    - Q3.10. Obstructive sleep apnea
    - Q3.11. Asthma/reactive airway disease
    - Q3.12. Osteoarthritis
    - Q3.13. Urinary stress incontinence
    - Q3.14. Gastroesophageal reflux disease (GERD)
    - Q3.15. Depression
- Q4. Does BMI or other measures of adiposity convey full information regarding the impact of excess body weight on the patient's health?

Therapeutic Benefits of Weight Loss in Patients With Overweight or Obesity

- Q5. Do patients with excess adiposity and related complications benefit more from weight loss than patients without complications, and, if so, how much weight

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loss would be required?

- Q5.1. Is weight loss effective to treat diabetes risk (ie, prediabetes, metabolic syndrome) and prevent progression to type 2 diabetes? How much weight loss would be required?
- Q5.2. Is weight loss effective to treat to type 2 diabetes? How much weight loss would be required?
- Q5.3. Is weight loss effective to treat dyslipidemia? How much weight loss would be required?
- Q5.4. Is weight loss effective to treat hypertension? How much weight loss would be required?
- Q5.5. Is weight loss effective to treat or prevent cardiovascular disease? How much weight loss would be required?
    - Q.5.5.1. Does weight loss prevent cardiovascular disease events or mortality?
    - Q.5.5.2. Does weight loss prevent cardiovascular disease events or mortality in diabetes?
    - Q.5.5.3. Does weight loss improve congestive heart failure?
- Q5.6. Is weight loss effective to treat nonalcoholic fatty liver disease and nonalcoholic steatohepatitis? How much weight loss would be required?
- Q5.7. Is weight loss effective to treat polycystic ovary syndrome (PCOS)? How much weight loss would be required?
- Q5.8. Is weight loss effective to treat infertility in women? How much weight loss would be required?
- Q5.9. Is weight loss effective to treat male hypogonadism? How much weight loss would be required?
- Q5.10. Is weight loss effective to treat obstructive sleep apnea? How much weight loss would be required?
- Q5.11. Is weight loss effective to treat asthma/reactive airway disease? How much weight loss would be required?
- Q5.12. Is weight loss effective to treat osteoarthritis? How much weight loss would be required?
- Q5.13. Is weight loss effective to treat urinary stress incontinence? How much weight loss would be required?
- Q5.14. Is weight loss effective to treat gastroesophageal reflux disease (GERD)? How much weight loss would be required?
- Q5.15. Is weight loss effective to improve symptoms of depression? How much weight loss would be required?

Lifestyle/Behavioral Therapy for Overweight and Obesity

- Q6. Is lifestyle/behavioral therapy effective to treat overweight and obesity, and what components of lifestyle therapy are associated with efficacy?
    - Q6.1. Meal plan and macronutrient composition
    - Q6.2. Physical activity
    - Q6.3. Behavior interventions

Pharmacotherapy for Overweight and Obesity

- Q7. Is pharmacotherapy effective to treat overweight and obesity?
    - Q7.1. Should pharmacotherapy be used as an adjunct to lifestyle therapy?

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- Q7.2. Does the addition of pharmacotherapy produce greater weight loss and weight-loss maintenance compared with lifestyle therapy alone?
- Q7.3. Should pharmacotherapy only be used in the short term to help achieve weight loss or should it be used chronically in the treatment of obesity?
- Q7.4. Are there differences in weight-loss drug efficacy and safety?
- Q7.5. Should combinations of weight-loss medications be used in a manner that is not approved by the US Food and Drug Administration?

Individualization of Pharmacotherapy in the Treatment of Obesity

- Q8. Are there hierarchies of drug preferences in patients with the following disorders or characteristics?
  - Q8.1. Chronic kidney disease
  - Q8.2. Nephrolithiasis
  - Q8.3. Hepatic impairment
  - Q8.4. Hypertension
  - Q8.5. Cardiovascular disease and arrhythmia
  - Q8.6. Depression with or without selective serotonin reuptake inhibitors
  - Q8.7. Anxiety
  - Q8.8. Psychotic disorders with or without medications (lithium, atypical antipsychotics, monoamine oxidase inhibitors)
  - Q8.9. Eating disorders including binge eating disorder
  - Q8.10. Glaucoma
  - Q8.11. Seizure disorder
  - Q8.12. Pancreatitis
  - Q8.13. Opioid use
  - Q8.14. Women of reproductive potential
  - Q8.15. The elderly, age ≥65 years
  - Q8.16. Addiction/alcoholism
  - Q8.17. Post-bariatric surgery

Bariatric Surgery

- Q9. Is bariatric surgery effective to treat obesity?
  - Q9.1. Is bariatric surgery effective to treat obesity and weight-related complications?
  - Q9.2. When should bariatric surgery be used to treat obesity and weight-related complications?

B. RECOMMENDATIONS

Post Hoc Question: By inductive evaluation of all evidence-based recommendations, what are the core recommendations for medical care of patients with obesity?

- **R1.A.** The principal outcome and therapeutic target in the treatment of obesity should be to improve the health of the patient by preventing or treating weight-related complications using weight loss, not the loss of body weight *per se*

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(Grade D).

- **R1.B.** The evaluation of patients for risk and existing burden of weight-related complications is a critical component of care and should be considered in clinical decisions and the therapeutic plan for weight-loss therapy **(Grade D)**.

Obesity and 3 Phases of Chronic Disease Prevention and Treatment

Q1. Do the 3 phases of chronic disease prevention and treatment—ie, primary, secondary, and tertiary— apply to the disease of obesity? (Table 5)

- **R2.** The modality and intensity of obesity interventions should be based on the primary, secondary, and tertiary phases of disease prevention; this 3-phase paradigm for chronic disease aligns with the pathophysiology and natural history of obesity and provides a rational framework for appropriate treatment at each phase of prevention **(Grade C; BEL 4, upgraded due to high relevance to natural history of the disease)**.

Table 5. Definitions, Goals, and Methods for Phases of Prevention in Chronic Disease: General Practices in Chronic Disease and Specific Practices in Obesity

Phase of Intervention	Definition and Goals	Methods of Prevention
Primary Prevention	GENERAL: • Prevent a disease from occurring	GENERAL: • Eliminate risk factors, remove causes, or increase resistance to disease
	OBESITY: • Prevent the development of overweight and obesity	OBESITY: • Educate the public • Built environment • Promote healthy eating and regular physical activity
Secondary Prevention	GENERAL: • Halt the progression of disease from its early stage prior to complications to a more severe stage • Arrest the disease process to prevent complications or sequelae	GENERAL: • Use a screening test and follow-up diagnosis, followed by treatment
	OBESITY: • Prevent future weight gain and the development of weight-related complications in patients with overweight or obesity	OBESITY: • Screen using BMI • Diagnose using BMI and evaluation for complications • Treat with lifestyle/behavioral intervention ± weight-loss medications
Tertiary Prevention	GENERAL: • Use clinical activities that reduce complications and prevent further deterioration	GENERAL: • Use treatment strategies that limit adverse consequences of a disease on health
	OBESITY: • Treat with weight-loss therapy to eliminate or ameliorate weight-related complications and prevent disease progression	OBESITY: • Treat with lifestyle/behavioral intervention plus weight-loss medications • Consider bariatric surgery

Abbreviation: BMI = body mass index.

The Anthropometric Component of the Diagnosis of Obesity

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Q2. How should the degree of adiposity be measured in the clinical setting? (Figure 2)

Q2.1. What is the best way to optimally screen or aggressively case-find for overweight and obesity?

- **R3.** All adults should be screened annually using a BMI measurement; in most populations a cutoff point of ≥25 kg/m^2 should be used to initiate further evaluation of overweight or obesity (**Grade A; BEL 2, upgraded due to high relevance)**.

Q2.2. What are the best anthropomorphic criteria for defining excess adiposity in the diagnosis of overweight and obesity in the clinical setting? (Table 6)

- **R4.** BMI should be used to confirm an excessive degree of adiposity and to classify individuals as having overweight (BMI 25-29.9 kg/m^2) or obesity (BMI ≥30 kg/m^2), after taking into account age, gender, ethnicity, fluid status, and muscularity; therefore, clinical evaluation and judgment must be used when BMI is employed as the anthropometric indicator of excess adiposity, particularly in athletes and those with sarcopenia **(Grade A; BEL 2, upgraded due to high relevance)**.
- **R5.** Other measurements of adiposity (eg, bioelectric impedance, air/water displacement plethysmography, or dual-energy x-ray absorptiometry) may be considered at the clinician's discretion if BMI and physical examination results are equivocal or require further evaluation **(Grade C, BEL 2, downgraded due to evidence gaps)**. However, the clinical utility of these measures is limited by availability, cost, and lack of outcomes data for validated cutoff points **(Grade B; BEL 2)**.

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Table 6. Classification of Overweight and Obesity by BMI and Waist Circumference (31 [EL 4; NE])

Classification	BMI		Waist	
	BMI (kg/m^2)	Comorbidity Risk	Waist Circumference and Comorbidity Risk	
			Men ≤40 in (102 cm) Women ≤35 in (88 cm)	Men >40 in (102 cm) Women >35 in (88 cm)
Underweight	<18.5	Low but other problems		
Normal weight	18.5–24.9	Average		
Overweight	25–29.9	Increased	Increased	High
Obese class I	30–34.9	Moderate	High	Very high
Obese class II	35–39.9	Severe	Very high	Very high
Obese class III	≥40	Very severe	Extremely high	Extremely high

Abbreviations: BMI = body mass index; in = inches.

Q2.3. Does waist circumference provide information in addition to BMI to indicate adiposity risk? (Table 7)

- **R6.** When evaluating patients for adiposity-related disease risk, waist circumference should be measured in all patients with BMI <35 kg/m^2 (**Grade A; BEL 2, upgraded due to high relevance)**. In many populations, a waist circumference cutoff point ≥94 cm in men and ≥80 cm in women should be considered at risk and consistent with abdominal obesity; in the United States and Canada cutoff points that can be used to indicate increased risk are ≥102 cm for men and ≥88 cm for women **(Grade A; BEL 2, upgraded due to high relevance)**.

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Table 7. Waist Circumference Thresholds for Abdominal Obesity (32 [EL4; NE])			
POPULATION	**ORGANIZATION**	**MEN**	**WOMEN**
Europid	IDF	≥94 cm ≥37 inches	≥80 cm ≥31 inches
Caucasian	WHO	≥94 cm (⬆ risk) ≥37 inches ≥102 cm (⬆⬆ risk) ≥40 inches	≥80 cm (⬆ risk) ≥31 inches ≥88 cm (⬆⬆ risk) ≥35 inches
United States	AHA/NHLBI (ATPIII)	≥102 cm ≥40 inches	≥88 cm ≥35 inches
Canada	Health Canada	≥102 cm ≥40 inches	≥88 cm ≥35 inches
European	European Cardiovasc. Societies	≥102 cm ≥40 inches	≥88 cm ≥35 inches
Asian (including Japanese)	IDF	≥90 cm ≥35 inches	≥80 cm ≥31 inches
Asian	WHO	≥90 cm ≥35 inches	≥80 cm ≥31 inches
Japanese	Japanese Obesity Society	≥85 cm ≥33 inches	≥90 cm ≥35 inches
China	Cooperative Task Force	≥85 cm ≥33 inches	≥80 cm ≥31 inches
Middle East, Mediterranean	IDF	≥94 cm ≥37 inches	≥80 cm ≥31 inches
Sub-Saharan African	IDF	≥94 cm ≥37 inches	≥80 cm ≥31 inches
Ethnic Central and South American	IDF	≥90 cm ≥35 inches	≥80 cm ≥31 inches

Abbreviations: AHA = American Heart Association; ATPIII = Adult Treatment Panel III; IDF = International Diabetes Federation; WHO = World Health Organization.

Q2.4. Do BMI and waist circumference accurately capture adiposity risk at all levels of BMI, ethnicities, gender, and age?

- **R7.** A BMI cutoff point value of ≥23 kg/m^2 should be used in the screening and confirmation of excess adiposity in South Asian, Southeast Asian, and East Asian adults (**Grade B; BEL 2)**.
- **R8.** Region- and ethnic-specific cutoff point values for waist circumference should be used as measures of abdominal adiposity and disease risk; in South Asian, Southeast Asian, and East Asian adults, men with values ≥85 cm and women ≥74 to 80 cm should be considered at risk and consistent with abdominal obesity **(Grade B; BEL 2)**.

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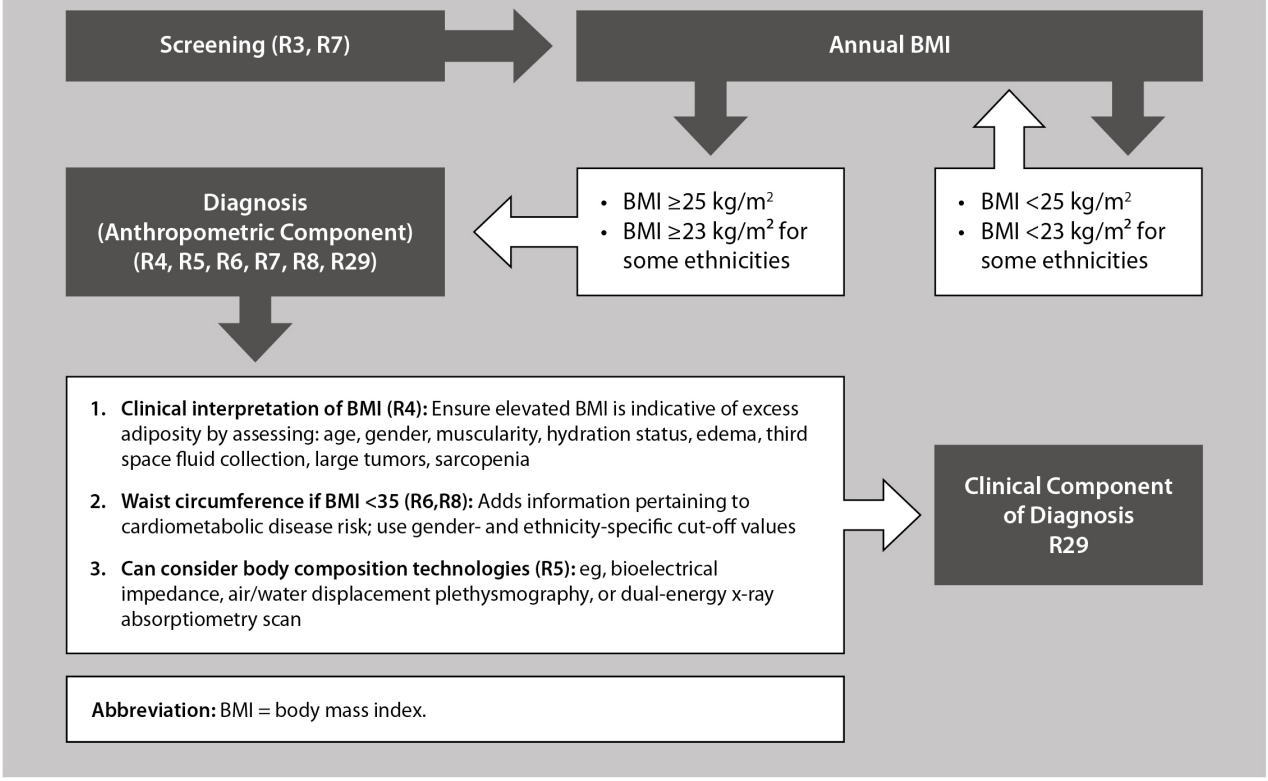
Figure 2. Anthropometric Component of the Medical Diagnosis of Obesity

Evidence-based screening and diagnosis for excess adiposity in clinical settings
Recommendations: Screening R3, R7; Diagnosis R4, R5, R6, R7, R8, R29



The Clinical Component of the Diagnosis of Obesity

Q3. What are the weight-related complications that are either caused or exacerbated by excess adiposity? (Figure 3)

Q3.1. Diabetes risk, metabolic syndrome, and prediabetes (IFG, IGT)

- **R9.** Patients with overweight or obesity and patients experiencing progressive weight gain should be screened for prediabetes and type 2 diabetes and evaluated for metabolic syndrome by assessing waist circumference, fasting glucose, A1C, blood pressure, and lipid panel, including triglycerides and HDL-c **(Grade A; BEL 2, upgraded due to high clinical relevance)**.
- **R10.** Due to variable risk for future diabetes, patients with overweight or obesity should be evaluated for risk of type 2 diabetes, which can be estimated or stratified using indices or staging systems that employ clinical data, glucose tolerance testing, and/or metabolic syndrome traits **(Grade B; BEL 2)**.

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Q3.2. Type 2 diabetes

- **R11.** Patients with type 2 diabetes should be evaluated for the presence of overweight or obesity **(Grade A; BEL 2, upgraded due to high relevance)**.

Q3.3. Dyslipidemia

- **R12.** All patients with overweight or obesity and individuals experiencing progressive weight gain should be screened for dyslipidemia with a lipid panel that includes triglycerides, HDL-c, calculated LDL-c, total cholesterol, and non-HDL cholesterol; all patients with dyslipidemia should be evaluated for the presence of overweight or obesity **(Grade A; BEL 2, upgraded due to high relevance)**.

Q3.4 Hypertension

- **R13.** Blood pressure should be measured in all patients with overweight or obesity as a screen for the presence of hypertension or prehypertension; all patients with hypertension should be evaluated for the presence of overweight or obesity **(Grade A; BEL 2, upgraded due to high relevance)**.

Q3.5. Cardiovascular disease and cardiovascular disease mortality

- **R14.** Risk factors for cardiovascular disease should be assessed in patients with overweight or obesity **(Grade A; BEL 2, upgraded due to high relevance)**.
- **R15.** Patients with overweight or obesity should be screened for active cardiovascular disease by history, physical examination, and with additional testing or expert referral based on cardiovascular disease risk status **(Grade A; BEL 2, upgraded due to high relevance)**.

Q.3.6. Nonalcoholic fatty liver disease and nonalcoholic steatohepatitis

- **R16.** Screening for nonalcoholic fatty liver disease should be performed in all patients with overweight or obesity, type 2 diabetes, or metabolic syndrome with liver function testing, followed by ultrasound or other imaging modality if transaminases are elevated; all patients with nonalcoholic fatty liver disease should be evaluated for the presence of overweight or obesity **(Grade B; BEL 2)**.

Q.3.7. Polycystic ovary syndrome (PCOS)

- **R17.** Premenopausal female patients with overweight or obesity and/or metabolic syndrome should be screened for polycystic ovary syndrome by history and physical examination; all patients with polycystic ovary syndrome should be evaluated for the presence of overweight or obesity **(Grade B; BEL 2)**.

Q.3.8. Female infertility

- **R18.** Women with overweight or obesity should be counseled when appropriate that they are at increased risk for infertility and, if seeking assisted reproduction,

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should be informed of lower success rates of these procedures regarding conception and the ability to carry the pregnancy to live birth **(Grade B; BEL 2)**. All female patients with infertility should be evaluated for the presence of overweight or obesity **(Grade B; BEL 2)**.

Q.3.9. Male hypogonadism

- **R19.** All men who have an increased waist circumference or who have obesity should be assessed for hypogonadism by history and physical examination and be tested for testosterone deficiency if indicated; all male patients with hypogonadism should be evaluated for the presence of overweight or obesity **(Grade B; BEL 2)**.
- **R20.** All male patients with type 2 diabetes should be evaluated to exclude testosterone deficiency **(Grade B; BEL 2)**.

Q3.10. Obstructive sleep apnea

- **R21.** All patients with overweight or obesity should be evaluated for obstructive sleep apnea during medical history and physical examination; this is based on the strong association of these disorders with each other **(Grade B; BEL 2)**. Polysomnography and other sleep studies, at home or in a sleep lab, should be considered for patients at high risk for sleep apnea based on clinical presentation, severity of excess adiposity, and symptomatology **(Grade D)**. All patients with obstructive sleep apnea should be evaluated for the presence of overweight or obesity **(Grade B; BEL 2)**.

Q.3.11. Asthma/reactive airway disease

- **R22.** All patients with overweight or obesity should be evaluated for asthma and reactive airway disease based on the strong association of these disorders with each other **(Grade B; BEL 2)**. Based on medical history, symptomatology, and physical examination, spirometry and other pulmonary function tests should be considered for patients at high risk for asthma and reactive airway disease **(Grade D)**. All patients with asthma should be evaluated for the presence of overweight or obesity **(Grade D)**.

Q.3.12. Osteoarthritis

- **R23.** All patients with overweight or obesity should be screened by symptom assessment and physical examination for osteoarthritis of the knee and other weight-bearing joints **(Grade B; BEL 2)**. All patients with osteoarthritis should be evaluated for the presence of overweight or obesity **(Grade D)**.

Q.3.13. Urinary stress incontinence

- **R24.** All female patients with overweight or obesity should be screened for urinary incontinence by assessing symptomatology, based on the strong association of these disorders with each other; all patients with urinary stress

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incontinence should be evaluated for the presence of overweight or obesity **(Grade B; BEL 2)**.

Q.3.14. Gastroesophageal reflux disease (GERD)

- **R25.** Patients with overweight or obesity or who have increased waist circumferences should be evaluated for symptoms of GERD **(Grade B; BEL 2)**; all patients with GERD should be evaluated for the presence of overweight or obesity **(Grade C; BEL 3)**.
- **R26.** Patients with obesity and GERD symptoms should be evaluated by endoscopy if medical treatment fails to control symptoms **(Grade B; BEL 2)**.
- **R27.** Endoscopy should be considered in patients with obesity and GERD symptoms prior to bariatric surgery **(Grade B; BEL 2)**.

Q.3.15. Depression

- **R28.** Patients with overweight or obesity should be screened for depression; all patients with depression should be evaluated for the presence of overweight or obesity **(Grade B; BEL 2)**.

Figure 3. Clinical Component of the Medical Diagnosis of Obesity

Candidates for weight-loss therapy can present with either excess adiposity (ie, the anthropometric component) or weight-related complications (ie, the clinical component)

Patients Present With Overweight or Obesity (Anthropometric Component)	Candidates for Weight-Loss Therapy	Patients Present With Weight-Related Disease or Complications (Clinical Component)	
Patients present with BMI ≥25 kg/m^2, or ≥23 kg/m^2 in certain ethnicities, and excess adiposity	Evaluate for weight-related complications: R9–R29 → / Evaluate for overweight or obesity: R9–R29 ←	R9, R10	Prediabetes
		R9, R10	Metabolic syndrome
		R11	Type 2 diabetes
		R12	Dyslipidemia
		R13	Hypertension
		R14, R15	Cardiovascular disease
		R16	Nonalcoholic fatty liver disease
		R17	Polycystic ovary syndrome
		R18	Female infertility
		R19, R20	Male hypogonadism
		R21	Obstructive sleep apnea
		R22	Asthma/reactive airway disease
		R23	Osteoarthritis
		R24	Urinary Stress Incontinence
		R25, R26	Gastroesophageal reflux disease
		R28	Depression

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Q4. Do BMI or other measures of adiposity convey full information regarding the impact of excess body weight on the patient's health?

- **R29.** All patients with overweight or obesity should be clinically evaluated for weight-related complications because BMI alone is not sufficient to indicate the impact of excess adiposity on health status; therefore, the diagnostic evaluation of patients with obesity should include an anthropometric assessment of adiposity and a clinical assessment of weight-related complications **(Grade A; BEL 2, upgraded due to high relevance)**. Patients with overweight or obesity should be reevaluated at intervals to monitor for any changes in adiposity and adiposity-related complications over time **(Grade A; BEL 2, upgraded due to high relevance)**.

Therapeutic Benefits of Weight Loss in Patients With Overweight or Obesity

Q5. Do patients with excess adiposity and related complications benefit more from weight loss than patients without complications? Can weight loss be used to treat weight-related complications, and, if so, how much weight loss would be required? (Table 8)

Note: Specific medications are mentioned or recommended below for use in different clinical settings based on available evidence for efficacy and safety. Medications may not be explicitly recommended if there are no data available for use in the specified clinical setting, even though weight loss associated with these medications may produce clinical benefits.

Q5.1. Is weight loss effective to treat diabetes risk (ie, prediabetes, metabolic syndrome) and prevent progression to type 2 diabetes? How much weight loss would be required?

- **R30.** Patients with overweight or obesity and with either metabolic syndrome or prediabetes or patients identified to be at high risk of type 2 diabetes based on validated risk-staging paradigms should be treated with lifestyle therapy to prevent progression to diabetes that includes a reduced-calorie healthy meal plan and a physical activity program incorporating both aerobic and resistance exercise **(Grade A; BEL 1)**. The weight-loss goal should be 10% **(Grade B; BEL 2)**.
- **R31.** Medication-assisted weight loss employing phentermine/topiramate ER, liraglutide 3 mg, or orlistat should be considered in patients at risk for future type 2 diabetes and should be used when needed to achieve 10% weight loss in conjunction with lifestyle therapy **(Grade A; BEL 1)**.
- **R32.** Diabetes medications including metformin, acarbose, and thiazolidinediones can be considered in selected high-risk patients with prediabetes who are not successfully treated with lifestyle and weight-loss medications and who remain glucose intolerant **(Grade A; BEL 1)**.

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Q5.2. Is weight loss effective to treat type 2 diabetes? How much weight loss would be required?

- **R33.** Patients with overweight or obesity and type 2 diabetes should be treated with lifestyle therapy to achieve 5% to 15% weight loss or more as needed to achieve targeted lowering of A1C **(Grade A; BEL 1)**. Weight-loss therapy should be considered regardless of the duration or severity of type 2 diabetes, both in newly diagnosed patients and in patients with longer-term disease on multiple diabetes medications **(Grade A; BEL 1)**.
- **R34.** Weight-loss medications should be considered as an adjunct to lifestyle therapy in all patients with type 2 diabetes as needed for weight loss sufficient to improve glycemic control, lipids, and blood pressure **(Grade A; BEL 1)**.
- **R35.** Patients with obesity (BMI ≥30 kg/m^2) and diabetes who have failed to achieve targeted clinical outcomes following treatment with lifestyle therapy and weight-loss medications may be considered for bariatric surgery, preferably Roux-en-Y gastric bypass, sleeve gastrectomy, or biliopancreatic diversion; also see recommendation 121 **(Grade B; BEL 1, downgraded due to evidence gaps)**.
- **R36.** Diabetes medications that are associated with modest weight loss or are weight-neutral are preferable in patients with obesity and type 2 diabetes, although clinicians should not refrain from insulin or other medications when needed to achieve A1C targets **(Grade A; BEL 2, upgraded due to high relevance)**.

Q5.3. Is weight loss effective to treat dyslipidemia? How much weight loss would be required?

- **R37.** Patients with overweight or obesity and dyslipidemia (elevated triglycerides and reduced HDL-c) should be treated with lifestyle therapy to achieve 5% to 10% weight loss or more as needed to achieve therapeutic targets **(Grade A; BEL 1)**. The lifestyle intervention should include a physical activity program and a reduced-calorie healthy meal plan that minimizes sugars and refined carbohydrates, avoids trans fats, limits alcohol use, and emphasizes fiber **(Grade B; BEL 1, downgraded due to evidence gaps)**.
- **R38.** Patients with overweight or obesity and dyslipidemia should be considered for treatment with a weight-loss medication combined with lifestyle therapy when necessary to achieve sufficient improvements in lipids (ie, elevated triglycerides and reduced HDL-c) **(Grade A; BEL 1)**.

Q5.4. Is weight loss effective to treat hypertension? How much weight loss would be required?

- **R39.** Patients with overweight or obesity and elevated blood pressure or hypertension should be treated with lifestyle therapy to achieve >5% to 15% weight loss or more as necessary to achieve blood pressure reduction goals in a

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program that includes caloric restriction and regular physical activity **(Grade A; BEL 1)**.

- **R40.** Patients with overweight or obesity and elevated blood pressure or hypertension should be considered for treatment with a weight-loss medication combined with lifestyle therapy when necessary to achieve sufficient weight loss for blood pressure reduction **(Grade A; BEL 1)**.
- **R41.** Patients with hypertension considering bariatric surgery should be recommended for Roux-en-Y gastric bypass or sleeve gastrectomy, unless contraindicated, due to greater long-term weight reduction and significantly better remission of hypertension than with laparoscopic adjustable gastric banding **(Grade B; BEL 1, downgraded due to evidence gaps)**.

Q5.5. Is weight loss effective to treat or prevent cardiovascular disease (CVD)? How much weight loss would be required?

Q5.5.1. Does weight loss prevent cardiovascular disease events or mortality?

- **R42.** Weight-loss therapy is not recommended based on available data for the expressed and sole purpose of preventing CVD events or to extend life, although evidence suggests that the degree of weight loss achieved by bariatric surgery can reduce mortality **(Grade B; BEL 2)**. Cardiovascular outcome trials assessing medication-assisted weight loss are currently ongoing or being planned.

Q5.5.2. Does weight loss prevent cardiovascular disease events or mortality in diabetes?

- **R43.** Weight-loss therapy is not recommended based on available data for the expressed and sole purpose of preventing CVD events or to extend life in patients with diabetes **(Grade B; BEL 1, downgraded due to evidence gaps)**. Cardiovascular outcome trials assessing medication-assisted weight loss are currently ongoing or being planned.

Q5.5.3. Does weight loss improve congestive heart failure and prevent cardiovascular disease events or mortality in patients with congestive heart failure?

- **R44.** Weight-loss therapy is not recommended based on available data for the expressed purpose of preventing CVD events or to extend life in patients with congestive heart failure, although evidence suggests that weight loss can improve myocardial function and congestive heart failure symptomatology in the short term **(Grade B; BEL 2)**.

Q5.6. Is weight loss effective to treat nonalcoholic fatty liver disease and nonalcoholic steatohepatitis? How much weight loss would be required?

- **R45.** Patients with overweight or obesity and nonalcoholic fatty liver disease should be primarily managed with lifestyle interventions, involving calorie

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restriction and moderate-to-vigorous physical activity, targeting 4% to10% weight loss (a range over which there is a dose-dependent beneficial effect on hepatic steatosis) **(Grade A; BEL 1)**.

- **R46.** Weight loss as high as 10% to 40% may be required to decrease hepatic inflammation, hepatocellular injury, and fibrosis **(Grade A, BEL 1)**. In this regard, weight loss assisted by orlistat **(Grade B; BEL 2)**, liraglutide **(Grade A; BEL 1)**, and bariatric surgery **(Grade B; BEL 2)** may be effective.
- **R47.** A Mediterranean dietary pattern or meal plan can have a beneficial effect on hepatic steatosis independent of weight loss **(Grade A; BEL 1)**.

Q5.7. Is weight loss effective to treat polycystic ovary syndrome (PCOS)? How much weight loss would be required?

- **R48.** Women with overweight or obesity and PCOS should be treated with lifestyle therapy with the goal of achieving 5% to 15% weight loss or more to improve hyperandrogenism, oligomenorrhea, anovulation, insulin resistance, and hyperlipidemia; clinical efficacy can vary among individual patients **(Grade A; BEL 1)**.
- **R49.** Patients with overweight or obesity and PCOS should be considered for treatment with orlistat, metformin, or liraglutide, alone or in combination, since these medications can be effective in decreasing weight or improving PCOS manifestations including insulin resistance, glucose tolerance, dyslipidemia, hyperandrogenemia, oligomennorrhea, and anovulation **(Grade A; BEL 1)**.
- **R50.** Selected patients with obesity and PCOS should be considered for laparoscopic Roux-en-Y gastric bypass to improve symptomatology including restoration of menses and ovulation **(Grade B; BEL 2)**.

Q5.8. Is weight loss effective to treat infertility in women with overweight and obesity? How much weight loss would be required?

- **R51.** Weight loss is effective to treat infertility in women with overweight and obesity and should be considered as part of the initial treatment to improve fertility; weight loss of ≥10% should be targeted to augment the likelihood of conception and live birth **(Grade A; BEL 1)**.

Q5.9. Is weight loss effective to treat male hypogonadism? How much weight loss would be required?

- **R52.** Treatment of hypogonadism in men with increased waist circumference or obesity should include weight-loss therapy **(Grade B; BEL 2)**. Weight loss of more than 5% to 10% is needed for significant improvement in serum testosterone **(Grade D)**.
- **R53.** Bariatric surgery should be considered as a treatment approach that improves hypogonadism in the majority of patients with obesity, including patients with severe obesity (BMI >50 kg/m^2) and type 2 diabetes **(Grade A; BEL 1)**.

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- **R54.** Men with true hypogonadism and obesity who are not seeking fertility should be considered for testosterone therapy in addition to lifestyle intervention since testosterone in these patients results in weight loss, decreased waist circumference, and improvements in metabolic parameters (glucose, A1C, lipids, and blood pressure) **(Grade A; BEL 1)**.

Q5.10. Is weight loss effective to treat obstructive sleep apnea? How much weight loss would be required?

- **R55.** Patients with overweight or obesity and obstructive sleep apnea should be treated with weight-loss therapy including lifestyle interventions and additional modalities as needed, including phentermine/topiramate ER or bariatric surgery; the weight-loss goal should be at least 7% to 11% or more **(Grade A; BEL 1)**.

Q5.11. Is weight loss effective to treat asthma/reactive airway disease? How much weight loss would be required?

- **R56.** Patients with overweight or obesity and asthma should be treated with weight loss using lifestyle interventions; additional treatment modalities may be considered as needed including bariatric surgery; the weight-loss goal should be at least 7% to 8% **(Grade A; BEL 1)**.

Q5.12. Is weight loss effective to treat osteoarthritis? How much weight loss would be required?

- **R57.** Patients with overweight or obesity and osteoarthritis involving weight-bearing joints, particularly osteoarthritis of the knee, should be treated with weight-loss therapy for symptomatic and functional improvement and reduction in compressive forces during ambulation; the weight-loss goal should be ≥10% of body weight **(Grade A; BEL 1)**. A physical activity program should also be recommended in this setting since the combination of weight-loss therapy achieving 5% to 10% loss of body weight combined with physical activity can effectively improve symptoms and function **(Grade A; BEL 1)**.
- **R58.** Patients with overweight or obesity and osteoarthritis should undergo weight-loss therapy before and after total knee replacement **(Grade C; BEL 2, downgraded due to evidence gaps)**.

Q5.13. Is weight loss effective to treat urinary stress incontinence? How much weight loss would be required?

- **R59.** Women with overweight or obesity and stress urinary incontinence should be treated with weight-loss therapy; the weight-loss goal should be 5% to 10% of body weight or greater **(Grade A; BEL 1)**.

Q5.14. Is weight loss effective to treat gastroesophageal reflux disease (GERD)? How much weight loss would be required?

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- **R60.** Patients who have overweight or obesity and who have gastroesophageal reflux should be treated using weight loss; the weight-loss goal should be 10% of body weight or greater **(Grade A; BEL 1)**.
- **R61.** Proton pump inhibitor therapy should be administered as medical therapy in patients who have overweight or obesity and have persistent gastroesophageal reflux symptoms during weight-loss interventions **(Grade A; BEL 1)**.
- **R62.** Roux-en-Y gastric bypass should be considered as the bariatric surgery procedure of choice for patients who have obesity and have moderate to severe gastroesophageal reflux symptoms, hiatal hernia, esophagitis, or Barrett's esophagus **(Grade B; BEL 2)**. Intragastric balloon for weight loss may increase gastroesophageal reflux symptoms and should not be used for weight loss in patients with established gastroesophageal reflux **(Grade A; BEL 1)**.

Q5.15. Is weight loss effective to improve symptoms of depression? How much weight loss would be required?

R63. Patients with overweight or obesity and depression interested in losing weight should be offered a structured lifestyle intervention **(Grade A; BEL 1)**

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Table 8: Treatment Goals Based on Diagnosis in the Medical Management of Patients With Obesity

	DIAGNOSIS		TREATMENT GOALS		
	Anthropometric Component	**Clinical Component**	**Intervention/ Weight-Loss Goal**	**Clinical Goals**	**Qs & Rs**
PRIMARY PREVENTION					
Primordial Prevention	BMI ≤25 (≤23 in certain ethnicities)	Obesogenic environment	• Public education • Built environment • Access to healthy foods	Decreased incidence of overweight/ obesity in populations	Q1,R2
Primary Prevention	BMI ≤25 (≤23 in certain ethnicities)	High-risk individuals or subgroups based on individual or cultural behaviors, ethnicity, family history, biomarkers, or genetics	• Annual BMI screening • Healthy meal plan • Increased physical activity	Decreased incidence of overweight/ obesity in high-risk individuals or identifiable subgroups	Q1,R2 Q2,R3
SECONDARY PREVENTION					
Overweight	BMI 25–29.9 (BMI 23–24.9 in certain ethnicities)	No clinically significant or detectable weight-related complications	• Prevent progressive weight gain or • Weight loss	• Prevent progression to obesity • Prevent the development of weight-related complications	Q1,R2 Q4,R29
Obesity	BMI ≥30 (≥25 in certain ethnicities)	No clinically significant or detectable weight-related complications	• Weight loss or • Prevent progressive weight gain	Prevent the development of weight-related complications	Q1,R2 Q4,R29
TERTIARY PREVENTION					
Overweight or Obesity	BMI ≥25 (≥23 in certain ethnicities)	Metabolic syndrome	10%	Prevention of T2DM	Q3.1,R9,R10 Q5.1,R30,R31
		Prediabetes	10%	Prevention of T2DM	Q3.1,R9,R10 Q5.1,R30,R31
		T2DM	5% to ≥15%	• Reduction in A1C • Reduction in number and/or doses of glucose lowering medications • Diabetes remission especially when diabetes duration is short	Q3.2,R11 Q5.2,R33,R34
		Dyslipidemia	5% to ≥15%	• Lower triglycerides • Raise HDL-c • Lower non-HDL-c	Q3.3,R12 Q5.3,R37,R38
		Hypertension	5% to ≥15%	• Lower systolic and diastolic BP • Reductions in number and/or doses of antihypertensive medications	Q3.4,R13 Q5.4,R39,R40
		Nonalcoholic fatty liver disease – Steatosis	5% or more	Reduction in intrahepatocellular lipid	Q3.6,R16 Q5.6,R45,R46
		Nonalcoholic fatty liver disease – Steatohepatitis	10% to 40%	Reduction in inflammation and fibrosis	Q3.6,R16 Q5.6,R45,R46
		Polycystic ovary syndrome	5% to 15% or more	• Ovulation • Regularization of menses • Reduced hirsuitism • Enhanced insulin sensitivity • Reduced serum androgen levels	Q3.7,R17 Q5.7,R48,R49
		Female infertility	10% or more	• Ovulation • Pregnancy and live birth	Q3.8,R18 Q5.8,R51
		Male hypogonadism	5% to 10% or more	Increase in serum testosterone	Q3.9,R19,R20 Q5.9,R52
		Obstructive sleep apnea	7% to 11% or more	• Improved symptomatology • Decreased apnea-hypopnea index	Q3.10,R21 Q5.10,R55
		Asthma/reactive airway disease	7% to 8% or more	• Improvement in forced expiratory volume at 1 second • Improved symptomatology	Q3.11,R22 Q5.11,R56
		Osteoarthritis	• ≥10% • 5% to 10% or more when coupled with exercise	• Improvement in symptomatology • Increased function	Q3.12,R23 Q5.12,R57, R58
		Urinary stress incontinence	5% to 10% or more	Reduced frequency of incontinence episodes	Q3.13,R24 Q5.13,R59
		Gastroesophageal reflux disease	10% or more	Reduced symptom frequency and severity	Q3.14,R25, Q15.5,R60
		Depression	Uncertain	• Reduction in depression symptomatology • Improvement in depression scores	Q3.15,R28 Q5.15,R63

Abbreviations: A1C = hemoglobin A1c; BMI = body mass index; BP = blood pressure; HDL-c = high-density lipoprotein cholesterol; T2DM = type 2 diabetes mellitus.

Lifestyle/Behavioral Therapy for Overweight and Obesity

Q6. Is lifestyle/behavioral therapy effective to treat overweight and obesity, and what components of lifestyle therapy are associated with efficacy? (Figure 4)

- **R64.** A structured lifestyle intervention program designed for weight loss (lifestyle therapy) and consisting of a healthy meal plan, physical activity, and behavioral interventions should be available to patients who are being treated for overweight or obesity **(Grade A;BEL1)**.

Q6.1. Reduced-calorie meal plan and macronutrient composition. (Table 9)

- **R65.** Reducing total energy (caloric) intake should be the main component of any weight-loss intervention **(Grade A; BEL 1)**.
- **R66.** Even though the macronutrient composition of meals has less impact on weight loss than adherence rates in most patients, in certain patient populations, modifying macronutrient composition may be considered to optimize adherence, eating patterns, weight loss, metabolic profiles, risk factor reduction, and/or clinical outcomes **(Grade A; BEL 1)**.

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Table 9. Association of Eating Patterns and Macronutrient Composition on Weight-Loss Efficacy

Eating Pattern or Macronutrient Change	Effect	Reference [EL]
Low glycemic index/load	• ⬆ Endothelial function • ⬇ Glycemic variability • Effects on energy expenditure • Decreased adipocyte diameter • No incremental effect on weight loss[1]	33 [EL 1; RCT], 34 [EL 1; RCT], 35 [EL 1; RCT, small N=13], 36 [EL 1; RCT]
Low carbohydrate	• Improved glycemic status and lipids • Improved other cardio-metabolic risk factors • Improved renal function • No incremental effect on weight loss (some studies show more short-term weight loss)[2]	37 [EL 4; NE], 38 [EL 1; RCT], 39 [EL 1; RCT], 40 [EL 1; RCT], 41 [EL 1; RCT], 42 [EL 1; RCT], 43 [EL 2; NRCT], 44 [EL 1; RCT], 45 [EL 1; RCT], 46 [EL 1; RCT], 47 [EL 1; RCT]
High protein	• Longer benefit on WC, %fat • Improved cardio-metabolic risk factors • Decreased adipocyte diameter • Animal (not plant) proteins associated with markers of inflammation • Less relative loss of muscle mass • No incremental effect on weight loss	33 [EL 1; RCT], 38 [EL 1; RCT], 45 [EL 1; RCT], 48 [EL 1; RCT], 49 [EL 1; RCT], 50 [EL 1; RCT], 51 [EL 1; RCT], 52 [EL 1; RCT], 53 [EL 1; RCT]
Moderate carbohydrate – moderate protein	• Improved body composition, lipid, ppINS • No incremental effect on weight loss	37 [EL 4; NE]. 54 [EL 1; RCT]
Low fat	• Beneficial effects on lipids • Benefits on lipids replacing with unsaturated fat • Improved renal function • No incremental effect on weight loss	37 [EL 4; NE], 41 [EL 1; RCT], 47 [EL 1; RCT], 55 [EL 1; RCT], 56 [EL 1; RCT]
High fat	• With lactation: when hypocaloric, great weight loss compared with hypocaloric low-carbohydrate diet	57 [EL 2; PCS]
Mediterranean-style	• Decreased risk certain cancers • EVOO supplementation – no effect on weight • Reduces cardio-metabolic risk factors and MetS • Reduces markers of inflammation • Improves hepatic steatosis and insulin sensitivity • Improves renal function • No incremental effect on weight loss	40 [EL 1; RCT], 58 [EL 1; RCT, post-hoc analysis], 59 [EL 2; PCS, post-hoc analysis], 60 [EL 1; RCT, secondary analysis], 61 [EL 2; PCS], 62 [EL 1; RCT], 63 [EL 1; RCT], 64 [EL 2; PCS], 65 [EL 2; PCS], 66 [EL 1; RCT]

Abbreviations: EL = evidence level; EVOO = extra-virgin olive oil; MetS = metabolic syndrome; ppINS = postprandial insulin response; WC = waist circumference.

[1] Incremental effect in comparison to a isocaloric control diet does not occur or is inconsistent.
[2] Short-term is <1 year.

Q6.2. Physical activity

- **R67.** Aerobic physical activity training should be prescribed to patients with overweight or obesity as a component of lifestyle intervention; the initial prescription may require a progressive increase in the volume and intensity of exercise, and the ultimate goal should be a total of ≥150 min/week of moderate exercise performed during 3 to 5 daily sessions per week **(Grade A; BEL 1)**.
- **R68.** Resistance training should be prescribed to patients with overweight or obesity undergoing weight-loss therapy to help promote fat loss while preserving

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fat-free mass; the goal should be resistance training 2 to 3 times per week consisting of single-set exercises that use the major muscle groups **(Grade A; BEL 1)**.

- **R69.** An increase in non-exercise and active leisure activity should be encouraged to reduce sedentary behavior in all patients with overweight or obesity **(Grade A; BEL 1)**.
- **R70.** The prescription for physical activity should be individualized to include activities and exercise regimens within the capabilities and preferences of the patient, taking into account health-related and physical limitations **(Grade C; BEL4, upgraded due to high relevance)**.
- **R71.** Involvement of an exercise physiologist or certified fitness professional in the care plan should be considered to individualize the physical activity prescription and improve outcomes **(Grade A; BEL 1)**.

Q6.3. Behavior interventions

- **R72.** Lifestyle therapy in patients with overweight or obesity should include behavioral interventions that enhance adherence to prescriptions for a reduced-calorie meal plan and increased physical activity (behavioral interventions can include: self-monitoring of weight, food intake, and physical activity; clear and reasonable goal-setting; education pertaining to obesity, nutrition, and physical activity; face-to-face and group meetings; stimulus control; systematic approaches for problem solving; stress reduction; cognitive restructuring [ie, cognitive behavioral therapy]; motivational interviewing; behavioral contracting; psychological counseling; and mobilization of social support structures) **(Grade A; BEL 1)**.
- **R73.** The behavior intervention package is effectively executed by a multidisciplinary team that includes dietitians, nurses, educators, physical activity trainers or coaches, and clinical psychologists **(Grade C; BEL 4, upgraded due to high relevance)**. Psychologists and psychiatrists should participate in the treatment of eating disorders, depression, anxiety, psychoses, and other psychological problems that can impair the effectiveness of lifestyle intervention programs **(Grade B; BEL 2)**.
- **R74.** Behavioral lifestyle intervention and support should be intensified if patients do not achieve a 2.5% weight loss in the first month of treatment, as early weight reduction is a key predictor of long-term weight-loss success **(Grade A; BEL 1)**. A stepped-care behavior approach should teach skills for problem-solving and should evaluate outcomes **(Grade A; BEL 1)**.
- **R75.** Behavioral lifestyle intervention should be tailored to a patient's ethnic, cultural, socioeconomic, and educational background **(Grade B; BEL 2)**.

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Figure 4. Lifestyle Therapy

Evidence-based lifestyle therapy for treatment of obesity should include 3 components
Recommendations: R64 through R75

Meal Plan (R64, R65, R66)	Physical Activity (R64, R67, R68, R69, R70, R71)	Behavior (R64, R72, R73, R74, R75)
• Reduced-calorie healthy meal plan • ~500–750 kcal daily deficit • Individualize based on personal and cultural preferences • Meal plans can include: Mediterranean, DASH, low-carb, low-fat, volumetric, high protein, vegetarian • Meal replacements • Very low-calorie diet is an option in selected patients and requires medical supervision Team member or expertise: dietitian, health educator	• Voluntary aerobic physical activity progressing to >150 minutes/week performed on 3–5 separate days per week • Resistance exercise: single-set repetitions involving major muscle groups, 2–3 times per week • Reduce sedentary behavior • Individualize program based on preferences and take into account physical limitations Team member or expertise: exercise trainer, physical activity coach, physical/occupational therapist	An interventional package that includes any number of the following: • Self-monitoring (food intake, exercise, weight) • Goal setting • Education (face-to-face meetings, group sessions, remote technologies) • Problem-solving strategies • Stimulus control • Behavioral contracting • Stress reduction • Psychological evaluation, counseling, and treatment when needed • Cognitive restructuring • Motivational interviewing • Mobilization of social support structures Team member or expertise: health educator, behaviorist, clinical psychologist, psychiatrist

Pharmacotherapy for Overweight and Obesity

Q.7. Is pharmacotherapy effective to treat overweight and obesity?

Q7.1. Should pharmacotherapy be used as an adjunct to lifestyle therapy or alone?

- **R76.** Pharmacotherapy for overweight and obesity should be used only as an adjunct to lifestyle therapy and not alone **(Grade A; BEL 1)**.

Q7.2. Does the addition of pharmacotherapy produce greater weight loss and weight-loss maintenance compared with lifestyle therapy alone?

- **R77.** The addition of pharmacotherapy produces greater weight loss and weight-loss maintenance compared with lifestyle therapy alone **(Grade A; BEL 1)**.
- **R78.** The concurrent initiation of lifestyle therapy and pharmacotherapy should be considered in patients with weight-related complications that can be ameliorated by weight loss **(Grade A; BEL 1)**.

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Q7.3. Should pharmacotherapy only be used in the short term to help achieve weight loss or should it be used chronically in the treatment of obesity?

- **R79.** Pharmacotherapy should be offered to patients with obesity, when potential benefits outweigh the risks, for the chronic treatment of their disease **(Grade A; BEL1)**. Short-term treatment (3-6 months) using weight-loss medications has not been demonstrated to produce longer-term health benefits and cannot be generally recommended based on scientific evidence **(Grade B; BEL 1, downgraded due to evidence gaps).**

Q7.4. Are there differences in weight-loss drug efficacy and safety? (Table 10)

- **R80.** In selecting the optimal weight-loss medication for each patient, clinicians should consider differences in efficacy, side effects, cautions, and warnings that characterize medications approved for chronic management of obesity, as well as the presence of weight-related complications and medical history; these factors are the basis for individualized weight-loss pharmacotherapy; a generalizable hierarchical algorithm for medication preferences that would be applicable to all patients cannot currently be scientifically justified **(Grade A; BEL 1)**.
- **R81.** Clinicians and their patients with obesity should have available access to all approved medications to allow for the safe and effective individualization of appropriate pharmacotherapy **(Grade D)**.

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Table 10. Weight-Loss Medications: Key Clinical Trials, Baseline Characteristics, and Weight-Loss Efficacy (67 [EL 1; RCT]; 68 [EL 1; RCT]; 69 [EL 1; RCT]; 70 [EL 1; RCT]; 71 [EL 1; RCT]) *

Generic Name	Naltrexone ER/ Bupropion ER		Liraglutide 3 mg		Locaserin		Orlistat		Phentermine/ Topiramte ER		
Brand Name	Contrave		Saxenda		Belviq		Xenical		Qsymia		
Frequency	Oral, BID		subQ, QD		Oral, BID		Oral, TID		Oral, QD		
Total Daily Dose	32 mg/360 mg		3 mg		20 mg		360 mg		7.5 mg / 46 mg	15 mg / 92 mg	
	Drug	Control	Drug	Control	Drug	Control	Drug	Control	Drug	Drug	Control
Age (years)	44.4	43.7	45.2	45.0	43.8	43.7	43.2	41.6	51.1	51.0	51.2
Gender (% female)	85	85	78.7	78.1	80.5	78.0	79	78	70.0	70.0	70.0
Baseline Weight (kg)	99.7	99.5	106.2	106.2	100.3	100.5	100.5	101.8	102.6	103.0	103.3
Baseline Waist (cm)	108.8	110.0	115.0	114.5	108.9	110.2	n/a	n/a	112.6	113.2	113.4
Baseline BMI	36.1	36.2	38.3	38.3	36.0	35.9	36.0	36.1	36.2	36.6	36.7
Weight-Loss (%) Completers	-8.1	-1.8	-9.2	-3.5	-7.9	-4.0	-8.78	-4.26	-9.6	-12.4	-1.6
Weight Loss (%) ITT LOCF	-6.1	-1.3	-8.0	-2.6	-5.8	-2.8	-7.94	-4.14	-7.8	-9.8	-1.2
5% Weight Loss (in %) ITT LOCF	48	16	63.2	27.1	47.2	25.0	50.5	30.7	62	70	21
10% Weight Loss (in %) ITT LOCF	25	7	33.1	10.6	22.6	9.7	28.6	11.3	37	48	7

*There is a lack of clinical trials with head-to-head direct comparisons among the drugs approved for chronic weight management. For this table, data are delineated from a representative major randomized clinical trial for each drug. Each study was conducted over at least 1 year in duration, enrolled subjects with baseline weights of approximately 100 kg and average BMIs in the range of class II obesity (BMI 35-39.9 kg/m^2), and included data from subjects on the recommended doses for the medication. Each study also had to have data for weight loss % (completers), weight loss % (LOCF), 5% weight loss LOCF and 10% weight loss LOCF to be included in the chart.

Abbreviations: ITT = Intent-to-treat; LOCF = last observation carried forward.

Q7.5. Should combinations of weight-loss medications be used in a manner that is not approved by the US Food and Drug Administration?

- **R82.** Combinations of FDA-approved weight-loss medications should only be used in a manner approved by the FDA **(Grade A; BEL 1)** or when sufficient safety and efficacy data are available to assure informed judgment regarding a favorable benefit-to-risk ratio **(Grade D).**

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Individualization of Pharmacotherapy in the Treatment of Obesity

Q8. Are there hierarchies of drug preferences in patients with the following disorders or characteristics? (Table 11)

Note: Specific medications are mentioned or recommended below for use in different clinical settings based on efficacy, side effects, warnings and contraindications, organ clearance, mechanisms of action, and available data for use of the medication under these specific conditions. Medications may not be explicitly recommended if there are no data available for use in the specified clinical setting, even though weight loss associated with these medications may produce clinical benefits.

Q8.1. Chronic kidney disease

- **R83.** Weight-loss medications should not be used in the setting of end-stage renal failure, with the exception that orlistat and liraglutide 3 mg can be considered in selected patients with a high level of caution **(Grade B; BEL 2)**.
- **R84.** The use of naltrexone ER/bupropion ER, lorcaserin, or phentermine/topiramate ER is not recommended in patients with severe renal impairment (<30 mL/min) **(Grade B; BEL 2)**.
- **R85.** All weight-loss medications can be used with appropriate cautions in patients with mild (50-79 mL/min) and moderate (30-49 mL/min) renal impairment, except that in moderate renal impairment the dose of naltrexone ER/bupropion ER should not exceed 8 mg/90 mg twice a day, and the daily dose of phentermine/topiramate ER should not exceed 7.5 mg/46 mg **(Grade B; BEL 2)**.
- **R86.** Orlistat should not be used in patients with, or at risk of, oxalate nephropathy **(Grade C; BEL 3)**. Liraglutide 3 mg should be discontinued if patients develop volume depletion, for example, due to nausea, vomiting, or diarrhea **(Grade B; BEL 2)**.

Q8.2. Nephrolithiasis

- **R87.** Naltrexone ER/bupropion ER, lorcaserin, and liraglutide 3.0 mg are preferred weight-loss medications in patients with a history, or at risk, of nephrolithiasis (**Grade D)**. Caution should be exercised in treating patients with phentermine/topiramate ER and orlistat who have a history of nephrolithiasis **(Grade A; BEL 1)**.

Q8.3. Hepatic impairment

- **R88.** All weight-loss medications should be used with caution in patients with hepatic impairment and should be avoided in severe hepatic impairment (ie, Child-Pugh score >9) **(Grade C; BEL 3)**.

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- **R89.** Dose adjustments for some medications are warranted in patients with moderate hepatic impairment: specifically, the maximum recommended dose of naltrexone ER/bupropion ER is 1 tablet (8 mg/90 mg) in the morning; the maximum recommended dose of phentermine/topiramate ER is 7.5 mg/46 mg daily **(Grade D)**.
- **R90.** Clinicians should maintain a high index of suspicion for cholelithiasis in patients undergoing weight-loss therapy, regardless of the treatment modality; in high-risk patients, liraglutide 3 mg should be used with caution; effective preventive measures include a slower rate of weight loss, an increase in dietary fat, or administration of ursodeoxycholic acid **(Grade A; BEL 1)**.

Q8.4. Hypertension

- **R91.** In patients with existing hypertension, orlistat, lorcaserin, phentermine/topiramate ER, and liraglutide 3 mg are preferred weight-loss medications **(Grade B; BEL 1, downgraded due to evidence gaps)**. Heart rate should be carefully monitored in patients receiving liraglutide 3 mg and phentermine/topiramate ER **(Grade A; BEL 1)**. Naltrexone ER/bupropion ER should be avoided if other weight-loss medications can be used since weight loss assisted by naltrexone ER/bupropion ER cannot be expected to produce blood pressure lowering, and the drug is contraindicated in uncontrolled hypertension **(Grade B; BEL 1, downgraded due to evidence gaps)**.
- **R92.** Renin-angiotensin system inhibition therapy (angiotensin receptor blocker or angiotensin converting enzyme inhibitor) should be used as the first-line drug for blood pressure control in patients with obesity **(Grade A; BEL 1)**.
- **R93.** Combination antihypertension therapy with calcium channel blockers may be considered as second-tier treatment **(Grade A; BEL 1)**. Beta-blockers and thiazide diuretics may also be considered in some patients but can have adverse effects on metabolism; beta-blockers and alpha-blockers can promote weight gain **(Grade A; BEL 1)**.

Q8.5. Cardiovascular disease and cardiac arrhythmia

- **R94.** In patients with established atherosclerotic cardiovascular disease, orlistat and lorcaserin are preferred weight-loss medications **(Grade A; BEL 1)**. Liraglutide 3 mg, phentermine/topiramate ER, and naltrexone ER/bupropion ER are reasonable to use with caution, and to continue if weight-loss goals are met, with careful monitoring of heart rate and blood pressure **(Grade A; BEL 1)**. Cardiovascular outcome trials are planned or ongoing for all weight-loss medications except orlistat.
- **R95.** Orlistat and lorcaserin are preferred weight-loss medications in patients with a history or risk of cardiac arrhythmia **(Grade B; BEL 1, downgraded due to evidence gaps)**. Naltrexone ER/bupropion ER, liraglutide 3 mg, and phentermine/topiramate ER are not contraindicated but should be used cautiously with careful monitoring of heart rate and rhythm (**Grade A; BEL 1)**.

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Q8.6. Depression with or without selective serotonin reuptake inhibitor therapy

- **R96.** All patients undergoing weight-loss therapy should be monitored for mood disorders, depression, and suicidal ideation **(Grade A; BEL 2, upgraded due to high relevance)**.
- **R97.** Orlistat, liraglutide 3 mg, and phentermine/topiramate ER at initiation (3.75 mg/23 mg) and low treatment (7.5 mg/46 mg) doses may be considered in patients with obesity and depression **(Grade A; BEL 1)**.
- **R98.** Lorcaserin and naltrexone ER/bupropion ER should be used with caution in patients with obesity and depression or avoided if patients are taking medications for depression **(Grade A; BEL 1)**.

Q8.7. Anxiety

- **R99.** Maximal dose (15 mg/92 mg) phentermine/topiramate ER should be used with caution in patients with obesity and anxiety disorders **(Grade A; BEL 1)**.

Q8.8. Psychotic disorders with or without medications (lithium, atypical antipsychotics, monoamine oxidase inhibitors)

- **R100.** Patients with psychotic disorders being treated with antipsychotic medications should be treated with a structured lifestyle intervention to promote weight loss or prevent weight gain **(Grade A; BEL 1)**.
- **R101.** Treatment with metformin may be beneficial in promoting modest weight loss and metabolic improvement in individuals with psychotic disorders who are taking antipsychotic medications **(Grade A; BEL 1)**.
- **R102.** Caution must be exercised in using any weight-loss medication in patients with obesity and a psychotic disorder due to insufficient current evidence assessing safety and efficacy **(Grade D)**.

Q8.9. Eating disorders including binge eating disorder

- **R103.** Patients with overweight or obesity who are being considered for weight-loss therapy should be screened for binge eating disorder and night eating syndrome **(Grade B; BEL 3, upgraded due to high relevance)**.
- **R104.** Patients with overweight or obesity who have binge eating disorder should be treated with a structured behavioral/lifestyle program in conjunction with cognitive behavioral therapy or other psychological interventions **(Grade A; BEL 1)**.
- **R105.** In patients with overweight or obesity and binge eating disorder, treatment with orlistat or approved medications containing topiramate or bupropion may be considered in conjunction with structured lifestyle therapy, cognitive behavioral therapy, and/or other psychological interventions **(Grade A; BEL 1)**.
- **R106.** Structured lifestyle therapy and/or selective serotonin reuptake inhibitor therapy may be considered in patients with obesity and night eating syndrome **(Grade B; BEL 1, downgraded due to evidence gaps)**.

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Q8.10. Glaucoma

- **R107.** Liraglutide 3 mg, orlistat, and lorcaserin should be preferred weight-loss medications in patients with a history, or at risk of, glaucoma **(Grade B; BEL 2)**. Phentermine/topiramate ER should be avoided and naltrexone ER/bupropion ER used with caution in patients with glaucoma **(Grade C; BEL 2, downgraded due to evidence gaps)**.

Q8.11. Seizure disorder

- **R108.** Phentermine/topiramate, lorcaserin, liraglutide, and orlistat should be preferred weight-loss medications in patients with a history, or at risk, of seizure/epilepsy **(Grade B; BEL 1, downgraded due to evidence gaps)**. The use of naltrexone ER/bupropion ER should be avoided in these patients.

Q8.12. Pancreatitis

- **R109.** All patients with obesity should be monitored for typical symptoms of pancreatitis (eg, abdominal pain or gastrointestinal distress) due to a proven association between these diseases **(Grade A; BEL 1)**.
- **R110.** Patients receiving glyburide, orlistat, or incretin-based therapies (glucagon-like peptide-1 receptor agonists or dipeptidyl peptidase 4 inhibitors) should be monitored for the development of pancreatitis **(Grade C; BEL 3)**. Glyburide, orlistat, and incretin-based therapies should be withheld in cases of prior or current pancreatitis; otherwise there are insufficient data to recommend withholding glyburide for glycemic control, orlistat for weight loss, or incretin-based therapies for glycemic control or weight loss due to concerns regarding pancreatitis **(Grade D)**.

Q8.13. Opioid use

- **R111.** In patients requiring chronic administration of opioid or opiate medications, phentermine/topiramate ER, lorcaserin, liraglutide 3 mg, and orlistat should be preferred weight-loss medications, while naltrexone ER/bupropion ER should not be used **(Grade B; BEL 1, downgraded due to evidence gaps)**.

Q8.14. Women of reproductive potential

- **R112.** Weight-loss medications must not be use in pregnancy **(Grade A; BEL 2, upgraded due to high relevance)**.
- **R113.** All weight-loss medications should be used in conjunction with appropriate forms of contraception in women of reproductive potential **(Grade A; BEL 1)**.
- **R114.** Weight-loss medications should not be used in women who are lactating and breast-feeding **(Grade D)**.

Q8.15. The elderly, age ≥65 years

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- **R115.** Elderly patients (≥65 years of age) should be selected for weight-loss therapy involving structured lifestyle interventions that include reduced-calorie meal plans and exercise, with clear health-related goals in mind that include prevention of type 2 diabetes in high-risk patients with prediabetes, blood pressure lowering, and improvements in osteoarthritis, mobility, and physical function **(Grade A; BEL 1)**.
- **R116.** Elderly patients with overweight or obesity being considered for weight-loss therapy should be evaluated for osteopenia and sarcopenia **(Grade B; BEL 2)**.
- **R117.** Weight-loss medications should be used with extra caution in elderly patients with overweight or obesity **(Grade A; BEL 1)**; additional studies are needed to assess efficacy and safety of weight-loss medications in the elderly.

Q8.16. Addiction/alcoholism

- **R118.** In patients with obesity and alcohol or other addictions, consider using orlistat or liraglutide 3 mg **(Grade A; BEL 1)**. Lorcaserin (abuse potential due to euphoria at supra-pharmacological doses) and naltrexone ER/bupropion ER (lowers seizure threshold) should be avoided in patients with alcohol abuse, and naltrexone ER/bupropion ER is contraindicated during alcohol withdrawal **(Grade A; BEL 1)**.

Q8.17. Post-bariatric surgery

- **R119.** Patients who have undergone bariatric surgery should continue to be treated with an intensive lifestyle intervention **(Grade A; BEL 1)**. Patients who have regained excess weight (≥25% of the lost weight) and who have not responded to intensive lifestyle intervention and are not candidates for reoperation may be considered for treatment with liraglutide 1.8 to 3.0 mg or phentermine/topiramate ER; the safety and efficacy of other weight-loss medications have not been assessed in these patients **(Grade D; BEL 3, downgraded due to evidence gaps)**.

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Table 11. Preferred Weight-Loss Medications: Individualization of Therapy

KEY: ☐ PREFERRED DRUG ☐ USE WITH CAUTION ■ AVOID

CLINICAL CHARACTERISTICS OR COEXISTING DISEASES		MEDICATIONS FOR CHRONIC WEIGHT MANAGEMENT				
		Orlistat	Lorcaserin	Phentermine/ topiramate ER	Naltrexone ER/ bupropion ER	Liraglutide 3 mg
Diabetes Prevention (metabolic syndrome, prediabetes)			Insufficient data for T2DM prevention		Insufficient data for T2DM prevention	
Type 2 Diabetes Mellitus						
Hypertension				Monitor heart rate	Monitor BP and heart rate. Contraindicated in uncontrolled HTN	Monitor heart rate
Cardiovascular Disease	CAD			Monitor heart rate	Monitor heart rate, BP	Monitor heart rate
	Arrhythmia		Monitor for bradycardia	Monitor heart rate, rhythm	Monitor heart rate, rhythm, BP	Monitor heart rate, rhythm
	CHF	Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data
Chronic Kidney Disease	Mild (50-79 mL/min)					
	Moderate (30-49 mL/min)			Do not exceed 7.5 mg/46 mg per day	Do not exceed 8 mg/90 mg bid	
	Severe (<30 mL/min)	Watch for oxalate nephropathy	Urinary clearance of drug metabolites	Urinary clearance of drug	Urinary clearance of drug	Avoid vomiting and volume depletion
Nephrolithiasis		Calcium oxalate stones		Calcium phosphate stones		
Hepatic Impairment	Mild-Moderate (Child-Pugh 5–9)	Watch for cholelithiasis	Hepatic metabolism of drug	Do not exceed 7.5 mg/46 mg per day	Do not exceed 8 mg/90 mg in AM	Watch for cholelithiasis
	Severe (Child-Pugh >9)	Not recommended	Not recommended	Not recommended	Not recommended	Not recommended
Depression			Insufficient safety data Avoid combinations of serotonergic drugs	Avoid maximum dose: 15 mg/92 mg per day	Insufficient safety data Avoid in adolescents and young adults	
Anxiety				Avoid max dose: 15 mg/92 mg per day		
Psychoses		Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data
Binge Eating Disorder			Insufficient data. Possible benefit based on reduction in food cravings	Insufficient data. Possible benefit based on studies with topiramate	Insufficient data. Possible benefit based on studies with bupropion Avoid in patients with purging or bulimia nervosa	Insufficient data
Glaucoma				Contraindicated, may trigger angle closure	May trigger angle closure	
Seizure Disorder				If discontinue at dose of 15 mg/92 mg, taper slowly	Bupropion lowers seizure threshold	
Pancreatitis		Monitor for symptoms				Monitor for symptoms Avoid if prior or current disease
Opioid Use					Will antagonize opioids and opiates	
Women of Reproductive Potential	Pregnancy	Use contraception and discontinue orlistat should pregnancy occur	Use contraception and discontinue lorcaserin should pregnancy occur	Use contraception and discontinue phentermine/topiramate should pregnancy occur (perform monthly pregnacy checks to identify early pregnancy	Use contraception and discontinue naltrexone ER/bupropion ER should pregnancy occur	Use contraception and discontinue liraglutide 3mg should pregnancy occur
	Breast-feeding	Not recommended	Not recommended	Not recommended	Not recommended	Not recommended
Age ≥65 years *		Limited data available	Insufficient data	Limited data available	Insufficient data	Limited data available
Alcoholism/ Addiction			Might have abuse potential due to euphoria at high doses	Insufficient data. Topiramate might exert therapeutic benefits	Avoid due to seizure risk and lower seizure threshold on bupropion	
Post-Bariatric Surgery		Insufficient data	Insufficient data	Limited data available	Insufficient data	Data available at 1.8 – 3.0 mg/day

* Use medications only with clear health-related goals in mind; assess patient for osteoporosis and sarcopenia.

Abbreviations: BP = blood pressure; CAD = coronary artery disease; CHF = congestive heart failure; HTN = hypertension; T2DM = Type 2 Diabetes Mellitus.

Bariatric Surgery

Q9. Is bariatric surgery effective to treat obesity?
Note: A de novo evidence-based review of questions pertaining to bariatric surgery was not undertaken. The "Clinical Practice Guidelines for the Perioperative, Nutritional, Metabolic, and Nonsurgical Support of the Bariatric Surgery Patient 2013-Update" from AACE, The Obesity Society, and the American Society for Metabolic & Bariatric Surgery were reviewed and felt to be adequate in their current form. Key recommendations from these guidelines relevant to the questions generated for evidence-based review are copied below.

Q9.1. Is bariatric surgery effective to treat obesity and weight-related complications?

- **R120.** Patients with a BMI of ≥40 kg/m^2 without coexisting medical problems and for whom the procedure would not be associated with excessive risk should be eligible for bariatric surgery **(Grade A; BEL 1)**.

Q9.2. When should bariatric surgery be used to treat obesity and weight-related complications?

- **R121.** Patients with a BMI of ≥35 kg/m^2 and 1 or more severe obesity-related complications, including type 2 diabetes, hypertension, obstructive sleep apnea, obesity-hypoventilation syndrome, Pickwickian syndrome, nonalcoholic fatty liver disease or nonalcoholic steatohepatitis, pseudotumor cerebri, gastroesophageal reflux disease, asthma, venous stasis disease, severe urinary incontinence, debilitating arthritis, or considerably impaired quality of life may also be considered for a bariatric surgery procedure. Patients with BMI of 30 to 34.9 kg/m^2 with diabetes or metabolic syndrome may also be considered for a bariatric procedure, although current evidence is limited by the number of patients studied and lack of long-term data demonstrating net benefit.
    - BMI ≥35 kg/m^2 and therapeutic target of weight control and improved biochemical markers of CVD risk **(Grade A; BEL 1)**.
    - BMI ≥30 kg/m^2 and therapeutic target of weight control and improved biochemical markers of CVD risk **(Grade B; BEL 2)**.
    - BMI ≥30 kg/m^2 and therapeutic target of glycemic control in type 2 diabetes and improved biochemical markers of CVD risk **(Grade C; BEL 3)**.
- **R122.** Independent of BMI criteria, there is insufficient evidence for recommending a bariatric surgical procedure specifically for glycemic control alone, lipid lowering alone, or CVD risk reduction alone **(Grade D)**.
- **R123.** All patients should undergo preoperative evaluation for weight-related complications and causes of obesity, with special attention directed to factors

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that could affect a recommendation for bariatric surgery or be ameliorated by weight loss resulting from the procedure **(Grade A; BEL 1)**.

General Guideline for Diagnosis and Medical Management of Patients with Overweight or Obesity

Figure 5 incorporates and summarizes many of the evidence-based recommendations provided in this document.

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Figure 5. Diagnosis and Medical Management of Obesity

DIAGNOSIS		COMPLICATION-SPECIFIC STAGING AND TREATMENT		
Anthropometric Component (BMI kg/m^2)	**Clinical Component**	**Disease Stage**	**Chronic Disease Phase of Prevention**	**Suggested Therapy (based on clinical judgment)**
<25 <23 in certain ethnicities waist circumference below regional/ ethnic cutoffs		**Normal weight** (no obesity)	**Primary**	• **Healthy lifestyle:** healthy meal plan/ physical activity
25–29.9 23–24.9 in certain ethnicities	Evaluate for presence or absence of adiposity-related complications and severity of complications • Metabolic syndrome • Prediabetes • Type 2 diabetes • Dyslipidemia • Hypertension • Cardiovascular disease • Nonalcoholic fatty liver disease • Polycystic ovary syndrome • Female infertility • Male hypogonadism • Obstructive sleep apnea • Asthma/reactive airway disease • Osteoarthritis • Urinary stress incontinence • Gastroesophageal reflux disease • Depression	**Overweight stage 0** (no complications)	**Secondary**	• **Lifestyle therapy:** Reduced-calorie healthy meal plan/physical activity/ behavioral interventions
≥30 ≥25 in certain ethnicities		**Obesity stage 0** (no complications)	**Secondary**	• **Lifestyle therapy:** Reduced-calorie healthy meal plan/physical activity/ behavioral interventions • **Weight-loss medications:** Consider after lifestyle therapy fails to prevent progressive weight gain. (BMI ≥27)
≥25 ≥23 in certain ethnicties		**Obesity stage 1** (1 or more mild-moderate complications)	**Tertiary**	• **Lifestyle therapy:** Reduced-calorie healthy meal plan/physical activity/ behavioral interventions • **Weight-loss medications:** Consider after lifestyle therapy fails to achieve therapeutic target or initiate concurrent with lifestyle therapy. (BMI ≥27)
≥25 ≥23 in certain ethnicties		**Obesity stage 2** (at least 1 severe complication)	**Tertiary**	• **Lifestyle therapy:** Reduced-calorie healthy meal plan/physical activity/ behavioral interventions • **Add weight-loss medication:** Initiate concurrent with lifestyle therapy. (BMI ≥27) • **Consider bariatric surgery:** (BMI ≥35)

a. All patients with BMI ≥25 have either overweight stage 0, obesity stage 0, obesity stage 1, or obesity stage 2, depending on the initial clinical evaluation for presence and severity of complications. These patients should be followed over time and evaluated for changes in both anthropometric and clinical diagnostic components. The diagnoses of overweight/obesity stage 0, obesity stage 1, and obesity stage 2 are not static, and disease progression may warrant more aggressive weight-loss therapy in the future. BMI values ≥25 have been clinically confirmed to represent excess adiposity after evaluation for muscularity, edema, sarcopenia, etc.

b. Stages are determined using criteria specific to each obesity-related complication; stage 0 = no complication; stage 1 = mild-to-moderate; stage 2 = severe.

c. Treatment plans should be individualized; suggested interventions are appropriate for obtaining the sufficient degree of weight loss generally required to treat the obesity-related complication(s) at the specified stage of severity.

d. BMI ≥27 is consistent with the prescribing information mandated by the US Food and Drug Administration for weight-loss medications.

Abbreviation: BMI = body mass index.

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Appendix 3

AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND AMERICAN COLLEGE OF ENDOCRINOLOGY

OBESITY CHRONIC CARE MODEL

Obesity is a chronic disease, increasingly responsible for patient suffering and social costs worldwide. The conceptualization of obesity as a lifestyle choice and primarily a cosmetic concern is not only debunked by scientific evidence, but has failed our patients and our societies. With improved efficacy and a range of treatment options, it is incumbent that the full force of our medical chronic care model (CCM) be brought to bear on obesity prevention and treatment. This can only be achieved through activated health care systems, as well as regulatory and legislative measures that ensure patient access to therapies of proven benefit. The American Association of Clinical Endocrinologists and American College of Endocrinology Comprehensive Clinical Practice Guidelines for Medical Care of Patients with Obesity represent an evidence-based CCM that emphasizes weight-loss therapy directed at the prevention and treatment of obesity-related complications. This clinical practice guideline (CPG) approaches obesity as a chronic medical illness that is a source of morbidity, mortality, and compromised quality of life. The guidelines target more aggressive treatment for patients with weight-related complications who will benefit

most greatly from weight loss and so optimizes benefit/risk ratios and cost-effectiveness (ie, the "complications-centric" approach). The medical CCM promulgated by these guidelines is not isolated but exists within the context of our larger health care system, communities, governments, and societies. Therefore, a CCM for obesity must become an operational, integral component of the health care system and be embraced by the larger society if it is to optimally benefit patients in particular and public health in general.

The general concept of the CCM for disease management was introduced in the 1990s, designed for primary care practice settings and credited with improving clinical outcomes (1,2). The core aspiration is that patients become activated and empowered, while health care systems become prepared and proactive. In general, there are 3 interrelated settings for the CCM: community, health care system, and provider organization (private practice, health center, integrated system, etc) (3). The 6 integrated components of the AACE/ACE Obesity CCM are:

Component 1: **Built Environment** (contextualization; community resources, laws, and policies; safe public spaces for physical activity, lifestyle education, self-help, and socialization; minimization of adverse obesogenic drivers; includes home and workplace)

Component 2: **Healthcare System** (recognition and prioritization of health promotion and obesity prevention, with a favorable economic model [payment reform] that engages health care professionals [primary care and specialists] and patients, while making comprehensive, evidence-based obesity care affordable and accessible)

Component 3: **Decision Support** (creation and electronic implementation of evidence-based CPGs for comprehensive, complications-centric obesity care)

Component 4: **Delivery System Design** (creation and coordination of an obesity care team, available for routine patient encounters and oriented toward management of both acute and chronic issues; includes lifestyle, pharmacotherapy, and bariatric procedures)

Component 5: **Clinical Information Systems** (routine patient care, CPGs,

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interactive/feedback, and registries)

Component 6: **Self-Management Support** (education, behavioral medicine, follow-up and feedback regarding obesity care; recognition by patient of need for obesity prevention and care)

Effective integration of the components of this CCM is central to successful implementation and realization of superior clinical outcomes in comprehensive, complications-centric obesity care. The specific processes for a CCM have been described as building blocks (4) and are described here in the context of the American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology (ACE) Obesity CCM:

Block 1: **Engaged Leadership** (commitment to transformative care and focus on health promotion, obesity prevention, and comprehensive, complications-centric obesity management to improve patient health)

Block 2: **Data-Driven Improvement** (evidence-based interventions and metrics; use of registries; properly designed clinical trials)

Block 3: **Empanelment** (linking patients with an obesity care team and primary care clinician; basis for performance metrics)

Block 4: **Team-Based Care** (team leaders [primary care physician, endocrinologist, or other obesity specialist AND advanced practice professional] and support [nursing, registered dietitian, behaviorist, psychologist, pharmacist, physical activity trainer, social worker, etc])

Block 5: **Patient-Team Partnership** (empowered, activated patient with a prepared, proactive practice that is empathetic and supportive; physician personal health behaviors; motivational interviewing, shared decision-making, and trusting relationships)

Block 6: **Population-Based Care** (routine health promotion and coaching with preventive services; use of specialized teams for patients with specific weight-related complications; family-oriented care that addresses childhood obesity;

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identification of relevant metrics [eg, weight, body mass index, waist circumference, target blood pressure, target lipids, target renal and liver function, symptom relief, performance, reduction of major adverse cardiac events])

Block 7: **Continuity of Care** (linked to all blocks and necessary for effective CCM; requires payment reform)

Block 8: **Enhanced Access to Care** (includes nights and weekends and adds capacity to meet demand; uses e-visits, phone visits, group visits, telemedicine visits, efficient use of obesity team members, and payment reform)

Block 9: **Comprehensive Coordinated Care** (primary care, weight loss, weight-related complications, other specialized care; accountability by primary care; includes outpatient, inpatient, and long-term care; infrastructure for appointment logistics, transportation, interpretation, comfort and safety, electronic connectivity, and information-sharing)

Block 10: **Alternative Encounters** (payment reforms to drive and facilitate novel modalities for each of the above blocks to optimize obesity care)

In conclusion, a contemporary AACE/ACE Obesity CCM focuses on an upstream approach (3) that promotes general health and prevents obesity as a disease state, while simultaneously providing downstream comprehensive, complications-centric, disease management. The CCM defines a concerted approach, based on evidence-based treatment guidelines for obesity, which is required to stem the increasing suffering and social costs of this disease. The above text, recommendations in the Executive Summary, explanations and evidence base in Appendix 1, and the pictorial algorithm in Appendix 2, each contribute detail to the AACE/ACE Obesity CCM provided in Figure 1.

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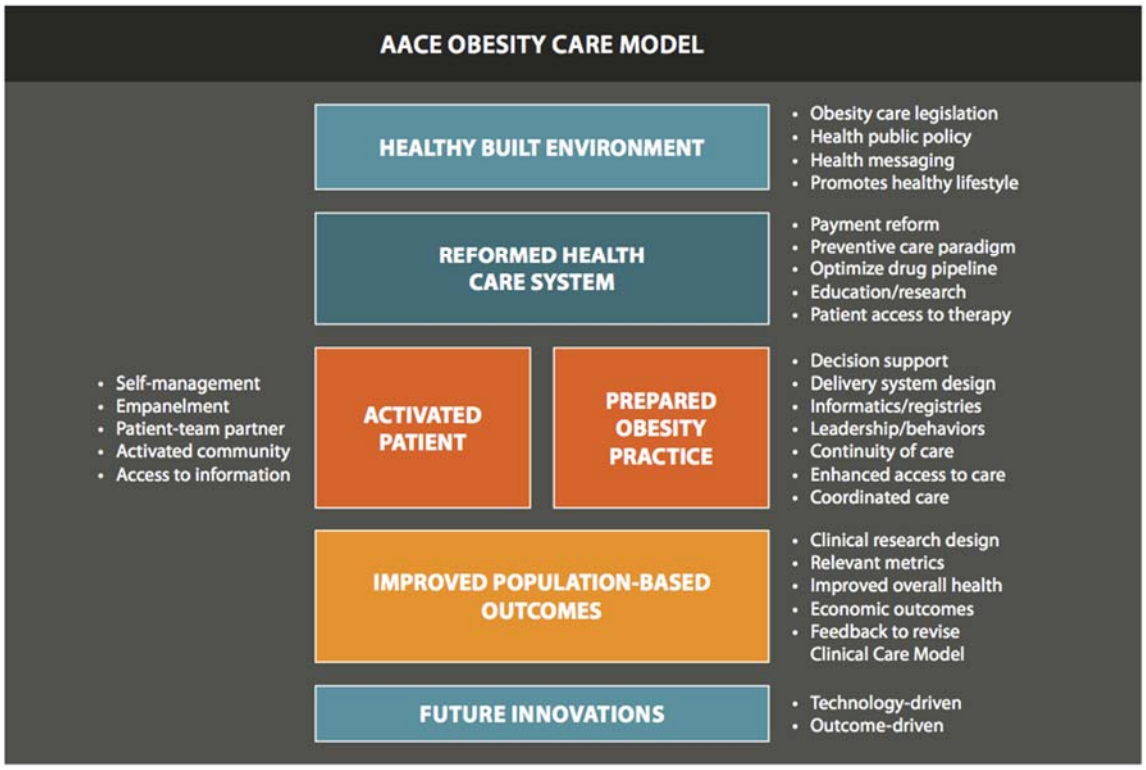
Figure 1. The AACE/ACE Obesity Chronic Care Model*



* see text for details.

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