

**AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND
AMERICAN COLLEGE OF ENDOCRINOLOGY
CONSENSUS CONFERENCE ON OBESITY:
BUILDING AN EVIDENCE BASE FOR COMPREHENSIVE ACTION**

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This document represents the official position of the American Association of Clinical Endocrinologists and the American College of Endocrinology. Where there were no randomized controlled trials or specific U.S. FDA labeling for issues in clinical practice, the participating clinical experts utilized their judgment and experience. Every effort was made to achieve consensus among the committee members. Position statements are meant to provide guidance, but they are not to be considered prescriptive for any individual patient and cannot replace the judgment of a clinician.

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ABSTRACT

Objective/Methods: The American Association of Clinical Endocrinologists/American College of Endocrinology “Consensus conference on obesity: building an evidence base for comprehensive action” convened March 23-25, 2014, in Washington, D.C. The premise of the conference was that by bringing together stakeholders in U.S. obesity care, representing the biomedical and public health models, new information would emerge to formulate actionable recommendations.

Results: Key conference findings include 5 affirmed and 8 emergent concepts. These concepts include the need for a medically meaningful and actionable diagnosis of obesity, research that evaluates and refines a complications-centric clinical approach to obesity, the need for a better understanding of reimbursement mechanisms and the value associated with obesity prevention and management, increased nutrition and obesity education, and enhanced public awareness and health literacy.

Conclusion: Next steps include deriving a more robust medical definition of obesity, translation of the affirmed and emergent concepts into actionable recommendations in the interests of patients with obesity, and developing logistics for effective implementation. (*Endocr Pract.* 2014; 20:956-976)

Abbreviations:

AACE = American Association of Clinical Endocrinologists; **AC** = affirmed concept; **ACE** = American College of Endocrinology; **AHEAD** = Action for Health in Diabetes; **AMA** = American Medical Association; **BMI** = body mass index; **CCO** = Consensus Conference on Obesity; **CMS** = U.S. Center for Medicare & Medicaid Services; **DASH** = Dietary Approaches To Stop Hypertension; **DPP** = Diabetes Prevention Program; **EC** = emergent concept; **ER** = extended release; **FDA** = U.S. Food and Drug Administration; **KF** = key finding; **PHEN/TPM ER** = phentermine/topiramate-extended release; **T2DM** = type 2 diabetes mellitus; **VLCD** = very-low-calorie diet

INTRODUCTION**Rationale for a Consensus Conference on Obesity**

Obesity rates have soared over the past 30 years, creating a global public health crisis (1-3). Data from two National Health and Nutrition Examination Surveys (NHANES) show that, in 1990, adults with obesity made up less than 15% of the population in most U.S. states. Today, roughly 2 out of 3 U.S. adults are overweight or obese (69%), and 1 out of 3 adults are obese (36%) (3,4). Global estimates suggest that 500 million adults are obese

worldwide, and as many as 43 million preschool children are overweight or obese (5,6).

The impact of obesity on morbidity, mortality, and health care costs is profound. Nearly 3 million adults die each year as a result of being overweight or obese (7). In the U.S., the annual cost of managing obesity has been estimated at approximately \$190.2 billion per year, or 20.6% of national health expenditures (8). Other studies project costs up to \$270 billion (9). If these trends continue, health care costs related to obesity could reach \$957 billion by 2030 (10). Obesity is estimated to add \$3,371 annually (adjusted to 2012 dollars) to per-patient medical expenditures, compared with patients who are not obese (including \$1,372 each year for inpatient services, \$1,057 for outpatient services, and \$1,130 for prescription drugs) (8).

In the last 2 decades, accumulating data support the view that, like any other chronic disease, obesity has genetic, environmental, and behavioral determinants that confer increased morbidity and mortality (11). The complications of obesity account for its adverse effects on mortality, morbidity, and quality of life, as well as the burgeoning social costs of the disease (12-15). Obesity-related complications can be broadly categorized as cardiometabolic, biomechanical, and other complications (Table 1).

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 (11). Subsequently, the AACE was joined by multiple organizations in submitting a proposition 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 (16). This has enhanced opportunities to advance our understanding of the complex, multidimensional pathophysiology of obesity and provided an impetus to our health care system to develop more robust medical models for treatment and prevention. In recent years, exciting advances have occurred in all three modalities used to treat obesity: lifestyle intervention, pharmacotherapy, and bariatric surgery. Clinical trials have established that lifestyle and behavioral interventions can produce and sustain weight loss, leading to the prevention and treatment of diabetes and improvements in cardiovascular risk factors (17-19). Principles embodied in these clinical trials have been translated into community-based programs for weight loss (20) and incorporated into effective, structured treatment programs that can be remote or web-based (21), offered commercially (22,23), or used in multidisciplinary clinic-based programs (24).

Until recently, available pharmacotherapy options were limited, consisting of only single-agent phentermine, approved for short-term use, and orlistat. However, in 2012 the U.S. Food and Drug Administration (FDA) approved 2 new drugs as safe and effective for obesity, lorcaserin and phentermine/topiramate extended release (PHEN/TPM

Table 1
Cardiometabolic, Biomechanical, and Other Complications of Obesity

Cardiometabolic Complications	Biomechanical Complications	Other Complications
Cardiovascular disease Dyslipidemia Hypertension Metabolic syndrome Nonalcoholic fatty liver disease Prediabetes Type 2 diabetes mellitus Polycystic ovary syndrome	Disability/Immobility Gastroesophageal reflux disease Osteoarthritis Sleep apnea Urinary stress incontinence	Certain cancers Depression and other psychological disorders Gall bladder disease Infertility Social stigmatization

ER) (25,26). In addition, 2 other medications are currently being evaluated by the FDA for a weight-loss indication (naltrexone/bupropion and high-dose liraglutide) (27,28). Finally, bariatric surgical approaches have been developed and refined, and pre- and postoperative care practices improved. This has enhanced outcomes and reduced medical and surgical complications resulting from these procedures (29-31). These advancements in all obesity treatment modalities have provided clinicians with improved tools to reduce morbidity and improve patient quality of life. In particular, it is clear that the combination of lifestyle intervention combined with pharmacotherapy can induce 5 to 15% weight loss in the majority of patients; this is sufficient to substantially improve a large number of obesity-related complications (13,14,32).

The most commonly followed paradigm for obesity care (33), as well as FDA-sanctioned prescribing information for the use of obesity medications (34), index treatment indications to anthropomorphic metrics such as weight and body mass index (BMI). In contrast, the AACE has formulated a complications-centric approach to management (35), wherein the presence and severity of obesity-related complications are the primary determinants for selection of treatment modality and intensity of weight-loss therapy (36). Moreover, the primary therapeutic endpoint is improvement in the obesity-related complications being treated by weight-loss therapy, not a set decline in body weight. Other organizations, such as the American Heart Association/American College of Cardiology/The Obesity Society (37) and the American Society of Bariatric Physicians (38) have also developed obesity care algorithms that take complications into account.

It is clear from the above discussion that society is experiencing an increased burden of patient suffering and social cost due to obesity. At the same time, we have a more advanced knowledge of pathophysiology pertinent to prevention, as well as improved therapeutic tools. Old-order thinking that obesity is a lifestyle choice has failed us and has allowed us to dismiss or ignore the need to implement a

robust medical model for prevention and treatment. These considerations compelled the AACE to marshal evidence that could inform the development of an effective and comprehensive action plan to combat obesity. However, such a plan required the concerted action of a broad range of stakeholders addressing a common evidence base. Using the analogy of a Greek temple, the AACE viewed 4 groupings of these stakeholders as constituting the 4 “pillars” needed to support a comprehensive strategy that could be represented by the temple’s pediment. Without the concerted participation of all 4 pillars, the pediment would fall to the ground (i.e., render the plan nonviable).

The 4 pillars and the constituencies that comprise each pillar who participated in the AACE/ACE Consensus Conference on Obesity (CCO) are shown in Table 2. The *Biomedical* pillar comprises professional organizations representing the multidisciplinary health care team of professionals participating in the care of patients with obesity. The *Government/Regulatory* pillar includes groups that set health care policy, including disease prevention and management, as well as medical economics and reimbursements. The *Health Care Industry* pillar encompasses pharmaceutical companies developing medications for obesity, large employers that purchase health care insurance plans and are concerned with the adverse health impact of obesity among their employees, and major payers or health care insurance companies. The *Organizations, Education, and Research* pillar includes lay and professional organizations advocating for obesity treatment, federal agencies sponsoring biomedical research, and medical educational organizations.

The goal of the CCO was to develop the evidence base for a comprehensive action plan for the effective prevention and treatment of obesity and to identify points of consensus, along with alternative interpretations, among constituencies across all 4 pillars. The intention was to have the broad range of stakeholders jointly examine the evidence from different perspectives and with different priority emphases. In this sense, the conference was emergent in nature and

Table 2
AACE/ACE Consensus Conference on Obesity—Pillar Participants

PILLAR	PILLAR PARTICIPANTS	
Biomedical Pillar	<p>W. Timothy Garvey, MD, FACE, Co-Moderator Janet B. McGill, MD, FACE, Co-Moderator Harold Bays, MD Lynn Bufka, PhD Alice Fuisz, MD, FACP Angela Golden, DNP, FNP-c, FAANP Lawrence Herman John Jakicic, PhD Suzanne Bennett Johnson, PhD Sheela Magge, MD, MSCE, FAAP David Marrero, PhD</p> <p>Kenneth Miller, PhD, RN, CFNP, FAAN John Morton, MD, MPH, FACS, FASMBS Hollie Raynor, PhD, RD, LDN Adelaide Robb, MD, FAPA Francesco Rubino, MD Jennifer Seger, MD</p>	<p>American Association of Clinical Endocrinologists American Association of Clinical Endocrinologists National Lipid Association American Psychological Association American College of Physicians American Association of Nurse Practitioners American Academy of Physician Assistants American College of Sports Medicine American Psychological Association American Academy of Pediatrics Diabetes Translational Research Center, Indiana University School of Medicine American Association of Nurse Practitioners American Society for Metabolic & Bariatric Surgery Academy of Nutrition and Dietetics American Psychiatric Association</p> <p>American Society of Bariatric Physicians</p>
Government & Regulatory	<p>Jeffrey I. Mechanick, MD, FACP, FACP, FACE, ECNU, Co-Moderator Jonathan D. Leffert, MD, FACP, FACP, FACE, ECNU, Co-Moderator Ann Albright, PhD, RD</p> <p>Patricia Beaston, MD, PhD</p> <p>Helene D. Clayton-Jeter, OD</p> <p>Jackie Haven, MS, RD</p> <p>Susan Kansagra, MD, MBA</p> <p>Elizabeth Koller, MD, FACE</p> <p>Gregory Peterson, DO, FACP</p>	<p>American Association of Clinical Endocrinologists</p> <p>American Association of Clinical Endocrinologists</p> <p>Centers for Disease Control and Prevention, Division of Diabetes Translation U.S. Food and Drug Administration, Office of Device Evaluation U.S. Food and Drug Administration, Office of Constituent Affairs U.S. Department of Agriculture, Center for Nutrition Policy and Promotion Health Promotion and Disease Prevention, NYC Department of Health and Mental Hygiene Centers for Medicaid & Medicare Services, Coverage and Analysis Group American Association of Clinical Endocrinologists</p>
Health Industry & Economics	<p>Alan J. Garber, MD, PhD, FACE, Co-Moderator Daniel Einhorn, MD, FACP, FACE, Co-Moderator Paulos Berhanu, MD, FACE, FHHA Jason Brett, MD Elaine Chiquette, BPharm, PharmD Eric Andrew Finkelstein, PhD, MHA Todd Hobbs, MD Jim Huffman Matthew Maryniak, MBA Mansi Mehta, RD, LDN Karen Miller-Kovach, MBA, MS, RD Andrew Renda, MD, MPH Robert Silverman, MD, FACE Kenneth Snow, MD Jean-Claude Tetreault Barbara Troupin, MD, MBA</p>	<p>American Association of Clinical Endocrinologists American Association of Clinical Endocrinologists Takeda Pharmaceuticals International Novo Nordisk, Inc. GI Dynamics, Inc. Duke-NUS Graduate Medical School, Singapore Novo Nordisk, Inc. Bank of America IMS Health Takeda Pharmaceuticals America, Inc. Weight Watchers International Humana Cigna Healthcare Aetna GI Dynamics, Inc. VIVUS, Inc.</p>
Organizations, Education, & Research	<p>George Grunberger, MD, FACP, FACE, Co-Moderator Yehuda Handelsman, MD, FACP, FACE, FNLA, Co-Moderator Solweig Cunningham, PhD Ann Danoff, MD</p> <p>Scott Kahan, MD, MH Mary Lieh-Lai, MD, FAAP, FCCP</p> <p>Lillian Lien, MD Joe Nadglowski Chiadi Ndumele, MD, MHS Robert Ratner, MD, FACE Tonya Saffer, MPH</p>	<p>American Association of Clinical Endocrinologists American Association of Clinical Endocrinologists Rollins School of Public Health, Emory University Association of Program Directors in Endocrinology, Diabetes & Metabolism (APDEM) STOP Obesity Alliance Accreditation Council for Graduate Medical Education (ACGME) Medical Director, Duke Inpatient Diabetes Management Obesity Action Coalition American College of Cardiology American Diabetes Association National Kidney Foundation</p>
Abbreviations: AACE = American Association of Clinical Endocrinologists; ACE = American College of Endocrinology.		

a process of joint discovery based on the totality of viewpoints. This approach was critical because the action plan will ultimately require concerted action and cooperation among stakeholders based on a consensus interpretation of evidence. The process of “building the evidence base” was viewed as the first step. Subsequent meetings will be planned to translate these findings into actionable, specific recommendations deemed likely to succeed, and the third step will be to implement the comprehensive action plan.

CONFERENCE METHODS AND SCOPE

The CCO was initiated by a directive from the AACE President, followed by an approval vote by the AACE Board of Directors. An AACE leadership task force was charged with conference planning. The first step was to identify the key stakeholders essential to the development of comprehensive solutions. These stakeholders were placed into 4 groups, represented by the 4 pillars. Extensive discussions and consultations were conducted regarding which participants to invite within each pillar, and formal invitations were submitted to the individuals and organizations listed in Table 2. The Biomedical Pillar provided expertise in evaluating data pertaining to the diagnosis of obesity, as well as medical models for effective treatment and prevention. The Government/Regulatory Pillar was qualified to evaluate policies and practices regarding the effective prevention and treatment of obesity, as well as aspects related to reimbursement. Members of the Health Care Industry Pillar were selected for their ability to address the efficacy of treatment options, whether therapy was being optimally utilized to benefit patients with obesity, and how this could be accomplished in a cost-effective manner. The Organizations/Education/Research Pillar was able to identify mechanisms by which research could be funded to fill knowledge gaps and to provide input on how to train the next generation health care professionals in the treatment and prevention of obesity.

To establish and organize the evidence base, the task force established 5 critical questions (Table 3), submitted ahead of the conference to participants in each of the

pillars. Prior to the CCO, all participants provided written answers to the questions and were requested to provide data, published references, and other relevant information in support of their answers. All responses were collated by the AACE staff and disseminated to participants in the weeks leading up to the conference. This process enabled participants across pillars to review and interpret the same data both prior to and in the context of the conference. The CCO convened March 22-23, 2014, in Washington, D.C. at the JW Marriott Hotel. The conference agenda is outlined in Table 4.

The conference began with introductory remarks from the AACE president (Dr. Mechanick), a summary of the AACE’s position statement on obesity as a disease and its complications-centric treatment algorithm (Dr. Garvey), and 3 keynote talks from national leaders in obesity. Pillar breakout sessions were scheduled on the afternoon of the first day. During these breakout sessions, participants within each pillar individually presented their answers to each of the 5 questions using oral statements, hardcopy handouts, and/or slide presentations. Every participant was given up to 10 minutes to respond to each question. This was followed by general discussion and debate, moderated by the co-chairs. For each question, the effort was made to establish points of consensus among participants, as well as to identify alternative viewpoints and knowledge gaps requiring additional research. The proceedings were both recorded and transcribed. To capture salient aspects and conclusions in real time, a team of medical writers and conference leaders integrated information and discussions.

On the morning of the second day, the pillars met together for “among-pillar discussions” so all participants could evaluate and debate the conclusions reached by the individual pillars. The co-chairs assigned to each pillar briefly summarized the points of consensus and alternate views, followed by robust discussion of the evidence pertinent to each question, involving all participants. This facilitated the emergence of consensus across pillars as a prerequisite for development of a concerted action plan. Again, the proceedings were recorded, transcribed, and summarized by onsite medical note-takers.

Question 1	What is obesity?
Question 2	What options are available for obesity management?
Question 3	What is the optimal use of therapeutic modalities?
Question 4	Can the optimal framework be cost-effective?
Question 5	What are the key knowledge gaps, and how can they be filled?
Abbreviations: AACE = American Association of Clinical Endocrinologists; ACE = American College of Endocrinology.	

Table 4	
AACE/ACE Consensus Conference on Obesity—Agenda	
SUNDAY, MARCH 23 2014	
GENERAL SESSION—KEYNOTE SPEAKERS	
MODERATOR: DR. W. TIMOTHY GARVEY	
7:00 AM – 8:00 AM	Registration
8:00 AM - 8:10 AM	Welcome and Introductions Dr. Jeffrey I. Mechanick, AACE President, Obesity Consensus Task Force Co-Chair
8:10 AM - 8:45 AM	Conference Overview & AACE Perspective: “Obesity as a Disease” - Dr. W. Timothy Garvey, Obesity Consensus Task Force Chair
8:45 AM - 9:30 AM	“Building a Consensus: Evidence-Based Long-Term Weight Management” - Dr. John Foreyt, Director, Behavioral Medicine Research Center at Baylor College of Medicine
9:45 AM - 10:30 AM	“Making the Healthy Choice the Easy Choice: Working with Industry to Reduce Childhood Obesity” - Mr. Lawrence Soler, CEO of the Partnership for a Healthier America
10:30 AM - 11:15 AM	“Obesity: Where Do We Go From Here?” - Dr. Patrice Harris, American Medical Association Board of Trustees
11:15 PM - 11:45 AM	Summary and Next Steps Dr. W. Timothy Garvey, Chair
PILLAR BREAKOUT SESSIONS	
12:45 PM - 5:00 PM	Biomedical
	Government & Regulatory
	Health Industry & Economics
	Organizations, Education & Research
MONDAY, MARCH 24, 2014	
PILLAR FORUM	
8:00 AM - 8:10 AM	Welcome Dr. Timothy Garvey, Chair
8:10 AM – 9:00 AM	Question 1: What is Obesity? Dr. Alan J. Garber, Co-Chair
9:00 AM - 9:50 AM	Question 2: What Options are Available for Obesity Management? Dr. W. Timothy Garvey, Chair
10:05 AM - 10:55 AM	Question 3: What is the Optimal Use of Therapeutic Modalities? Dr. W. Timothy Garvey , Chair
10:55 AM – 11:45 AM	Question 4: Can the Optimal Framework be Cost-Effective? Dr. Jeffrey I. Mechanick, Co-Chair
11:45 AM - 12:35 PM	Question 5: What are the Knowledge Gaps and How Can They Be Filled? Dr. Jeffrey I. Mechanick, Co-Chair
12:35 PM - 1:00 PM	Conclusion Dr. W. Timothy Garvey, Chair
1:00 PM - 5:00 PM	Writing Committee Convenes
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Immediately after the conference, a primary writing team analyzed the meeting's transcripts and completed this document summarizing the conference proceedings, along with points of consensus and alternative views. The writing committee identified points of affirmation where the data and related discussions supported previously accepted or validated practices. In addition, new points of emergence arose from the dynamic and multidisciplinary nature of the conference. Both the affirmed and emergent conclusions were sufficient to organize the body of information yielded by the CCO as well as form the basis for actionable recommendations. Thus, the goal of "building an evidence base" for a comprehensive action plan was achieved.

To translate this evidence base via the development of recommended interventions and protocols, subsequent interactions are planned with pillar participants, followed by similar interactions focused on implementation strategies and logistics.

CONSENSUS PERTAINING TO THE 5 CRITICAL QUESTIONS

The following represents points of consensus among the wide array of stakeholders (i.e., all 4 pillars) participating in the conference.

Question 1—What is Obesity?

Obesity, which reflects an unhealthy accumulation of fat mass, is a global epidemic that diminishes the quality and length of life while dramatically increasing individual, national, and global health care costs. In June 2013, the AMA adopted a policy that recognizes obesity as a disease, based on 3 standard criteria (16). Those criteria define a disease as a condition that involves impairment of normal function, has characteristic signs and symptoms, and results in bodily harm. This landmark AMA policy statement should stimulate efforts aimed at advancing our understanding of and developing timely interventions for obesity. The CCO agreed that obesity met these criteria as a chronic disease.

The current definition of obesity is based on the BMI, calculated as weight in kilograms divided by height in meters squared. A BMI ≥ 30 kg/m² defines obesity. However, the accumulation of excess body fat represents a continuum that includes overweight individuals with a lesser degree of excess adiposity that can also adversely impact health. The current BMI cut-off for overweight status is 25.0 to 29.9 kg/m². Additional anthropometric measures may include waist circumference, which can confer risk information independent of BMI, particularly within the BMI range 25 to 35 kg/m² (39).

Overweight and obesity are associated with several debilitating and deadly diseases, including type 2 diabetes mellitus (T2DM), cardiovascular disease, musculoskeletal disorders, and obstructive sleep apnea (see Table 1). A neck

circumference >43 cm (17 inches) in men and >41 cm (16 inches) in women has been associated with increased risk of sleep apnea (2).

Although BMI is currently the most practical and well-validated measure of obesity, it does not fully capture the complexity of the disease, and additional measures, such as waist circumference, assessment of body fat and fitness, and comorbidities are useful in risk stratification (33,35,36). Furthermore, refinements to BMI cut-offs may be necessary to capture risk differences by race, ethnicity, and body type (40,41). Also unclear is a precise determination of the BMI thresholds for onset of various comorbidities, such as T2DM, hypertension, and musculoskeletal disorders. The etiology of obesity is multifactorial, including interplay of genetic, environmental, and lifestyle factors. At each level of BMI, fitness and active lifestyle may mitigate obesity-associated comorbid risks. Sedentary lifestyle clearly exacerbates risk (11). A useful guide in the assessing obesity-related complications is the Edmonton Obesity Staging System, a 5-stage system that is a better long-term predictor of mortality than BMI (42). In addition, the Cardiometabolic Disease Staging system (CMDS) is a quantitative risk engine for predicting future cardiometabolic complication risk, such as T2DM and cardiovascular disease mortality. The CMDS can be used as a guide to the selection and intensity of weight-loss therapy (43).

Question 2—What Options are Available for Obesity Management?

Options in the Treatment of Obesity

Treatment of obesity depends, in part, on how one defines obesity. Currently, the predominant definition is based on the World Health Organization and National Health Lung and Blood Institute BMI stratification (overweight and obesity class I, II, and III) and its associated comorbidities (2,44). Early childhood intervention is likely to be key to the treatment of obesity over the life cycle, as the continuity of excess adiposity from childhood into adulthood is clear (45). Environmental approaches may use a socio-ecological framework to address the levels and sectors of influence on obesity risk. Given the scope of the problem, a multiplicity of sectors will be required to treat obesity, and culturally sensitive approaches are needed (2). Individual implementation of a healthy lifestyle is necessary to both prevent and control obesity. A healthy lifestyle encompasses a diet that does not exceed caloric needs and includes healthy food choices, regular physical activity, and proper sleep hygiene (2). Management of obesity must include strategies at all phases of prevention and treatment of chronic disease as described below (2,37,38):

- Primary = Interventions that prevent the disease from occurring. This includes healthy lifestyle and environmental reductions in obesogenic factors to prevent obesity.

- Secondary = Interventions prior to the emergence of disease complications. These include lifestyle change, behavioral/cognitive therapy, and pharmacotherapy to treat obesity, avoid progressive weight gain, and prevent obesity-related complications.
- Tertiary = Interventions subsequent to the development of complications that treat complications and limit adverse consequences of obesity on health. These include lifestyle change, behavioral/cognitive therapy, pharmacotherapy, and bariatric surgery to treat obesity and its related comorbidities.

If prevention fails, treatment is recommended for those who develop obesity. Lifestyle modification is a volitional approach that requires both patient education and support to maintain adherence for success (2,39,46). Techniques used in lifestyle modification include behavioral/cognitive therapy (delivered via multidisciplinary intensive lifestyle modification programs, internet-based and other remote programs, and other patient education materials), support groups (i.e., professional psychologists, Take Off Pounds Sensibly (TOPS), and Overeaters Anonymous), reduced-calorie diets, meal replacements and planned prescribed meals (i.e., Lean Cuisine, Nutrisystem, and Jenny Craig), and structured commercial programs (i.e., Weight Watchers and the Young Men's Christian Association [YMCA]) (37,47). Many "over-the-counter" nutritional supplements are available, but there are no conclusive data to support the use of these products. Prescribed approaches for weight management include very-low-calorie diets and FDA-approved pharmacotherapy for long-term management. When lifestyle modification and/or pharmacotherapy are insufficient to treat obesity and its complications, surgical options may be indicated (2,37).

Individualizing therapy is essential (32). Therapies should not only be designed to achieve weight loss but to maintain weight loss (37). Appropriate training should be available to improve the ability of the general health care clinician to manage obesity, and to increase the number of specialists in obesity management (11).

Provider Types in the Treatment of Obesity

It is important to recognize that effective treatment of obesity can involve multiple providers in different settings:

1. Parents and/or significant others, by influencing children/adolescents in the home and local environment.
2. Teachers and school boards, by regulating the content of vending machines, physical activities, and school meals.
3. Self-help education materials to include on-line education, in addition to TOPS and Overeaters Anonymous self-help programs.

4. Commercial weight-loss programs, such as Weight Watchers, Nutrisystem, Jenny Craig, Medifast, and Pritikin Centers, in addition to worksite and not-for-profit programs provided by hospitals, churches, the YMCA, and others.
5. Weight-loss centers run by nutritionists, registered dietitians, psychologists, fitness trainers, and others.
6. Medically supervised weight-management programs run by bariatric surgeons, endocrinologists, physicians certified by the American Board of Obesity Medicine (48), general internists, family physicians, obstetricians and gynecologists, pediatricians, psychologists, psychiatrists, osteopathic physicians, nurse practitioners, and physician assistants. Medically-supervised obesity treatment programs optimally involve an integrated team approach that can include dietitians, nurses, educators, exercise therapists/fitness trainers, psychologists, and others.
7. State and Federal Governmental agencies to include: the U.S. Department of Agriculture, by providing standards for school lunch programs, the U.S. FDA, through food labeling requirements, the U.S. Federal Trade Commission, by guaranteeing fair scientifically-based advertisements for weight-loss interventions and limiting television advertising to children, and states via their control of regional nutrition education and health care programs as well as the built environment.

Modalities Available in the Treatment of Obesity

A. Lifestyle Management

Lifestyle management is the cornerstone for the treatment of obesity and includes 3 primary components: healthy eating and caloric restriction, increased energy expenditure from regular physical activity (for example, aerobic exercise) 3 to 5 days per week, and behavioral changes supporting a healthy lifestyle. Numerous clinical trials have established the efficacy of this approach, most notably the Diabetes Prevention Program (DPP) (17,49-53).

Individualizing therapy is essential. Therapies should not only be designed to achieve weight loss, but should also support adherence (to maintain long-term weight loss). Self-monitoring of healthy eating and exercise, and the use of personal logs, daily records, and electronic devices can be helpful tools. Two kinds of nutrition/dietary advice can be provided as part of the management of individuals who are overweight/obese. One type of advice focuses on dietary patterns and the other emphasizes variation in macronutrients to help control caloric intake (32).

1. *Dietary Patterns, Macronutrient Choices, and Diet Comparisons*

Several dietary patterns can be helpful in the management of patients with obesity. These include the Dietary Approaches to Stop Hypertension (DASH) diet, which emphasizes fruits and vegetables, low-fat dairy products, slightly higher protein intake, and reduced consumption of total fat and soft drinks. This dietary pattern can reduce blood pressure in persons with normal and stage I hypertension (54,55). A second dietary pattern is the Mediterranean diet, which emphasizes intake of mono-unsaturated fats, limited intake of red meats, and higher intake of legumes, fish, chicken, and nuts. This dietary pattern has been associated with a lower risk of heart disease (56,57).

Diets focused on varied macronutrients include low-fat, low-carbohydrate/high-protein, low-glycemic-index, balanced-deficit, and very-low-energy diets. However, comparative head-to-head trials suggest no basis for selecting one diet over another, with the exception of possibly better weight loss with a low-carbohydrate diet in premenopausal women. Data from the Look AHEAD (Action for Health in Diabetes) and DPP studies provide evidence that reduced caloric intake is the main driver for weight loss (58-61). In the Look AHEAD trial, the magnitude of weight loss in the first year was related to the frequency of meal replacement use, the amount of physical activity, and the degree of attendance at behavioral sessions (58-60). However, genetic background can also influence treatment response, as has been shown in both the DPP and Preventing Obesity Using Novel Dietary Strategies (POUNDS) Lost Trials (62-63).

Several randomized clinical trials lasting 1 to 2 years have performed head-to-head comparisons of diets for effective weight loss. In one study, 169 individuals with obesity were randomized to the Atkins, Ornish, Weight Watchers, or Zone Diets. Each diet produced about 5 kg weight loss after 1 year, with no significant difference between diets. Adherence to each diet was the single most important criterion of weight loss success, with the Atkins and Ornish diets being the most difficult to adhere to (64). In another trial involving premenopausal overweight and obese women, the Atkins, Lifestyle Exercise Attitudes Relationships Nutrition (LEARN), Ornish, and Zone diets were compared. At 6 and 12 months, the Atkins diet produced more weight loss compared to the other 3 diets. A post-hoc analysis again showed that adherence was the best predictor of weight loss (65). A 2-year study of a predominantly male (86%) worksite population evaluated 3 diets: a low-carbohydrate very-low-calorie diet (VLCD; Atkins-like), a low-fat diet, and a Mediterranean-style diet. The low-carbohydrate VLCD group lost the most weight initially, but in the next 6 months there was an accelerated weight loss in the Mediterranean diet group, and at 2 years, the low-carbohydrate VLCD and Mediterranean diet groups were similar and performed slightly better than

the low-fat diet group (66). The largest study conducted to date randomized 811 men and women to 1 of 4 diets: (1) 20% fat-15% protein, (2) 20% fat-25% protein, (3) 49% fat-15% protein, or (4) 40% fat-25% protein. Weight loss was similar for each diet at 6, 12, and 24 months. Again, the principal determinant of success was dietary adherence (67).

a. VLCDs

VLCDs or very-low-energy diets have energy levels of between 200 and 800 kcal/day. The theory behind them is that lower energy intake results in more rapid loss of body fat and weight. Contrary to this theory are data showing no difference in weight loss between a 400-kcal/day VLCD and an 800-kcal/day diet (68).

b. Balanced-Deficit Diets

Diets that reduce carbohydrate, protein, and fat are called balanced-deficit or prudent diets. A meta-analysis of such low-calorie diets found a 1-year difference in weight (5.31 kg) favoring diet over control subjects (69). A systematic review of 16 diet studies revealed weight loss after 2 to 3 years was usually <5 kg below baseline (3.5 ± 2.4 kg; range, 0.9 to 10.0 kg) and was maintained after 4 to 7 years (3.6 ± 2.6 kg below baseline) in cases where data were available (70). Portion-controlled diets or meal replacements (using packaged foods containing 180 to 350 kcal) can result in early initial weight loss, with weight loss maintained over 4 years in one study (71).

c. Low-Glycemic-Index Diets

The glycemic index is defined as the rise in blood glucose in response to a test food, compared to the glucose rise after a 50-g portion of white bread. The glycemic load is the product of the glycemic index and amount of carbohydrate in the food. The effect of low-glycemic-index diets on weight loss has been studied in a number of randomized clinical trials in adults. Three studies have compared low- versus high-glycemic-index diets (72-74). Other studies have included (1) an ad lib reduced-glycemic-load diet compared with an energy-restricted reduced-fat diet (75-77) or (2) an energy-restricted low-glycemic-index diet with a normal energy-restricted diet (78). Interventions have typically been relatively short, ranging from 5 weeks to 6 months, but a Cochrane Database review found significant differences in body weight (1.1 kg, 95% confidence interval, -2.0 to -0.2), body mass (1.1 kg; $P < .05$), and levels of both total cholesterol and low-density-lipoprotein cholesterol (LDL-C) that favored the low-glycemic-index diet (79).

d. Low-Fat Diets

Low-fat diets are commonly prescribed to help patients lose weight. A meta-analysis of 5 randomized controlled trials of low-fat diets showed a significant weight

loss, but not more so than comparison diets (80). However, a large randomized clinical trial of 48,835 postmenopausal women reported significantly more weight loss from baseline (2.2 kg at 1 year and 0.6 kg after 7.5 years) with a low-fat diet than in the control group (81).

e. **Low-Carbohydrate Diets**

Low-carbohydrate diets contain <50 g of carbohydrate and are designed on the premise that insulin is the driving force behind obesity. In addition, high-protein diets have been touted as weight-loss diets. Several studies of the Atkins diet have provided evidence for the effectiveness of these diets. In general, weight loss in subjects randomized to a low-carbohydrate diet may or may not initially exceed that observed on other diets; however, in randomized trials with longer follow-up (e.g., after 1 year), weight loss tended to be comparable among diets (64,82).

f. **Low-Fat/Higher-Protein Diets**

Higher-protein diets may also enhance weight maintenance. One study compared 15% protein and 25% protein diets as part of a low-fat intake. At 6, 12, and 24 months, weight loss was greater with the higher-protein diet (83). In a randomized study, after 4 weeks of weight loss with a VLCD, daily supplementation of 48.2 g of protein (18% of the diet) resulted in a 50% reduction in body weight regain at 3 months (84).

2. **Physical Activity**

Increased physical activity is the second important component of a healthy lifestyle program, and even daily non-sedentary activities have been shown to improve cardiovascular disease risk factors. The Look AHEAD trial included 2 types of physical activity; ≥ 175 minutes/week of moderately intense activity alongside an increased focus on daily lifestyle activity (e.g., using the stairs instead of elevators and walking instead of riding). Pedometers were provided and participants were instructed to reach a goal of $\geq 10,000$ steps per day. In the intensive lifestyle intervention group, 1-year primary outcomes included greater weight loss (8.6% versus 0.7%) and physical fitness and greater reductions in waist circumference, blood pressure, and glycated hemoglobin (A_{1c}) and high-density-lipoprotein cholesterol (HDL-C) levels (85). After a median follow-up of 9.6 years, weight loss was sustained (6.0% versus 3.5%), but the study was stopped due to no difference in cardiovascular mortality between treatment groups (86).

3. **Behavior Modification**

The third component of lifestyle management is behavior modification. In the Look AHEAD trial, group sessions occurred in the first year, with subsequent individual monthly sessions and phone contact. Behavior modification included self-monitoring of food intake and physical activity, coping with stress and negative thoughts,

eating at regular times, and focus on the act of eating. Self-monitoring of food intake and recording physical activity were the most important strategies for success, and this finding is supported by extensive empirical evidence (2,85). Frequent weighing has also been associated with improved weight loss (87). Other strategies used to keep participants engaged and motivated to promote weight loss and weight maintenance have included refresher courses, campaigns, and incentives.

Several trials have compared behavioral strategies in primary care settings. For example, studies employing either group sessions or remote internet-based programs have demonstrated more than 5% average weight loss (21,59). Additionally, a Cochrane Review found that weight loss is substantially less when a program has a primary emphasis on physical activity (88), suggesting that although physical activity has a role, behavioral and healthy eating strategies should be the main focus of behavioral programs.

B. Pharmacotherapy

If lifestyle interventions fail to produce weight loss after 3 to 6 months, pharmacologic therapy may enhance weight loss. Alternatively, weight-loss medications and a reduced-calorie meal plan can be initiated concomitantly at the outset, particularly in patients that need substantial weight loss to ameliorate obesity related complications. In clinical trials, the addition of weight-loss medication to various lifestyle intervention programs has consistently resulted in greater weight loss than that achieved from the lifestyle intervention alone. In accordance with U.S. FDA prescribing information and the 2014 American Heart Association/American College of Cardiology/The Obesity Society guidelines for weight loss, pharmacologic therapy is indicated for individuals with a BMI of 27 to 30 kg/m² and comorbidities or a BMI >30 kg/m² with or without comorbidities. The first step is to ensure that the patient is not taking drugs that produce weight gain, such as certain diabetes medications, antidepressants, and antiepileptics (37).

Weight-loss drugs approved by the U.S. FDA for long-term use include orlistat, lorcaserin, and PHEN/TPMER (89). Drugs approved for short-term use, usually considered to be 12 weeks or less, include PHEN, benzphetamine, and phendimetrazine (90). Several guiding principles should be followed when prescribing weight loss agents. First, the patient should be familiar with the drug and its potential side effects. Second, effective lifestyle support for weight loss should be provided during drug use. Third, if <5% weight loss is achieved after 3 months on a maximally tolerated dose, the medication should be discontinued and a new treatment plan implemented. Fourth, weight-loss medications should be employed only as an adjunct to lifestyle intervention and a reduced-calorie meal plan (91).

1. *Orlistat*

Orlistat is a selective inhibitor of pancreatic lipase and reduces intestinal digestion of fat; it has been studied in both adolescents and adults. In a 2005 meta-analysis comparing orlistat and placebo added to lifestyle change, patients treated with orlistat lost more than 8 kg, compared to 5 kg with lifestyle modifications alone (92). In a 4-year double-blind, randomized, placebo-controlled trial in 3,304 patients (21% with impaired glucose tolerance), weight loss was greater with orlistat compared to controls (>11% versus 6% at year 1 and 6.9% versus 4.1% at year 4). There was also a 37% reduction in new T2DM onset with the use of orlistat (52).

Safety of orlistat. Orlistat is not significantly absorbed, and its side effects are related to the blockade of triglyceride digestion, to include fecal fat loss and related gastrointestinal (GI) symptoms. Orlistat may cause a small but significant decrease in fat-soluble vitamins, and it is wise to provide a multivitamin routinely with its use. Orlistat does not seem to affect the absorption of other drugs, except acyclovir. Orlistat may cause increased renal excretion of oxalate. Rare cases of severe liver injury have been reported, but a causal relationship has not been established (93).

2. *Lorcaserin*

Nonselective serotonergic drugs have been used in the past but were removed from the market because of heart valve damage. Lorcaserin selectively targets the serotonin 2C receptor in the hypothalamus to reduce food intake, thus avoiding activation of the serotonin 2B receptor expressed in the heart (94). Lorcaserin is prescribed at a dose of 10-mg twice daily. Three major clinical trials have provided evidence for its effectiveness and safety. Placebo-subtracted weight loss approximating ~4% occurred with lorcaserin in all 3 studies, with improvements in cardiovascular risk factors (91,95,96). In patients with T2DM, decreases in A_{1c} (0.9 ± 0.06 versus 0.4 ± 0.06 ; $P < .001$) and fasting glucose (27.4 ± 2.5 mg/dL versus 11.9 ± 2.5 mg/dL; $P < .001$) were greater with lorcaserin than placebo. Weight maintenance was demonstrated, with a small amount of weight regained in the second year (95).

Safety of lorcaserin. Echocardiograms performed in phase III studies on >5,200 subjects found no statistically significant increase in FDA-defined valvulopathy compared to placebo. The most common adverse events include headache, nausea, dizziness, fatigue, dry mouth, and constipation. These symptoms tend to be mild and are often reduced in intensity over time (91). Because of the risk of serotonin syndrome, lorcaserin should be used with caution in patients taking selective serotonin reuptake inhibitors or monoamine oxidase inhibitors (MAOIs).

3. *PHEN/TPM-ER*

The combination of PHEN and TPM as an ER preparation uses lower doses of both drugs than are usually prescribed when either drug is used as a single agent (3.35/23 mg, 7.5/46 mg, and 15/92 mg in the starting, mid, and full doses, respectively). PHEN/TPM ER efficacy and safety were demonstrated in 2 large clinical trials of adult patients, one of which involved obesity ($BMI \geq 35$ kg/m²) (97) and the other overweight or obesity plus ≥ 2 comorbidities (increased waist circumference, hypertension, hypertriglyceridemia, or dysglycemia; the latter defined as impaired fasting glucose, impaired glucose tolerance, or T2DM) (98). Two-year placebo-subtracted weight loss was 7 and 9% in subjects taking the mid and full doses, respectively (98). Weight loss with PHEN/TPM ER was accompanied by improvements in sleep apnea and significant improvements in blood pressure, glycemic control, and HDL-C and triglycerides, with greater benefit observed with increased weight loss. Progression to T2DM was reduced by 79% in patients with either prediabetes and/or metabolic syndrome at baseline treated with full-dose PHEN/TPM ER, compared to subjects treated with lifestyle intervention plus placebo (99,100). Use of PHEN/TPM ER in patients with T2DM led to improved glycemic control with less need for conventional glucose-lowering medications (101).

Safety of PHEN/TPM ER. The most common side effects include paresthesias, dizziness, dysgeusia, insomnia, constipation, and dry mouth (98). Topiramate is associated with oral clefts if used during pregnancy, and like all weight-loss medications, PHEN/TPM ER is contraindicated in pregnancy (97). A rare side effect of TPM is acute glaucoma, consequently the drug is contraindicated in glaucoma, and another potential adverse event is kidney stones (102). PHEN/TPM ER is also contraindicated in hyperthyroidism and within 14 days of treatment with MAOIs.

4. *PHEN and Short-Term Sympathomimetic Drugs*

The sympathomimetic drugs benzphetamine, diethylpropion, phendimetrazine, and PHEN were tested before 1975. The U.S. Drug Enforcement Agency classifies these drugs as schedule III (benzphetamine and phendimetrazine) or schedule IV (PHEN and diethylpropion), indicating the government's belief that they have the potential for abuse/habituation/addiction (103). Most of the data on these drugs come from short-term trials (up to 12 weeks) (99). PHEN at a dose of 15 mg/day produced 4.9% weight loss at 6 months, compared to 2.1% for placebo (104). These drugs are only approved for short-term administration, generally considered to be ≤ 3 months (99).

Safety of sympathomimetic drugs. Sympathomimetic drugs produce central excitation, manifested as insomnia and/or nervousness. This effect is most obvious shortly after drug onset and tends to wane with continued use. Dry mouth is among the most common side effects. These drugs may also increase heart rate and blood pressure to a variable extent (105). However, there is little evidence of quantitative effects on blood pressure and heart rate with PHEN, especially after 6 months or more of treatment (106). Lacking good quantitative data of the effects of phentermine on blood pressure and heart rate, caution should be used in prescribing these drugs, particularly in persons with a history of cardiovascular disease. In addition, patient blood pressure and pulse should be monitored while taking sympathomimetics (107).

5. Medications Under Study

Two additional medications are under consideration for approval by the U.S. FDA for a weight-loss indication, and have the potential to increase options for effective pharmacotherapy in obesity. These medications include the combination naltrexone plus bupropion (both drugs in a sustained-release preparation) and liraglutide 3 mg/day (27,28). Phase III clinical trial data for both of these drugs indicate that placebo-subtracted weight loss is ~6%.

C. Surgical Procedures in the Treatment of Obesity

Currently, bariatric surgery is the most effective treatment for attaining significant and durable weight loss in patients with obesity (36), although this must be considered in the context of inherent risks with these invasive procedures. Because metabolic comorbidities often improve or remit after weight loss following bariatric procedures, the term metabolic surgery can be used interchangeably with bariatric surgery (108,109). In general, bariatric operations alter the GI tract by (1) reducing stomach capacity (gastric-restrictive operations), (2) rerouting nutrient flow to bypass the duodenum and in some instances producing a degree of malabsorption (bypass procedures), or (3) combining both strategies. In terms of frequency of use, 2011 global data indicate the following: Roux-en-Y gastric bypass (46.6%), sleeve gastrectomy (27.8%), adjustable gastric banding (17.8%), and bilio-pancreatic diversion (2.2%) (110).

The 1991 National Institutes of Health guidelines set indications for surgical intervention in patients with a BMI ≥ 40 kg/m² or BMI ≥ 35 kg/m² with obesity-related comorbidities (111). A meta-analysis of mostly short-term (<5 years) weight-loss outcomes after 22,000 bariatric procedures found an overall mean excess weight loss (i.e., percent weight loss of the amount of weight that is above the ideal body weight) of 61.2% (47.5% for adjustable gastric band, 61.6% for Roux-en-Y gastric bypass, 68.2% for gastroplasty, and 70.1% for bilio-pancreatic diversion) (112). The best long-term surgical weight-loss data come from the Swedish Obese Subjects study, a prospective

study with a 90% follow-up rate evaluating the long-term effects of bariatric surgery compared to nonsurgical weight management in patients with severe obesity. At 15 years, total body weight loss was $27 \pm 12\%$ for gastric bypass, $18 \pm 11\%$ for vertical-banded gastroplasty, and $13 \pm 14\%$ for adjustable gastric band, compared to slight weight gain in the control group (31). In addition to bariatric surgery, several new implantable devices are in research testing and may provide utility in the future (113). These surgical procedures require lifelong medical follow-up and are accompanied by mortality rates generally <0.5%, as well as perioperative and postoperative morbidity.

Question 2—Summary

A healthy lifestyle is the foundation for all modalities in the prevention and management of obesity. The therapeutic modalities and choices within each modality should be based on risk stratification during the initial assessment, to include the degree of obesity and the presence and severity of obesity-related complications. Therapy should be intensified based on risk stratification to achieve therapeutic goals/targets, and the goals/targets will differ based on the individual's risk assessment and burden of complications. Patients need appropriate access to therapeutic modalities for weight loss and weight maintenance, to include lifestyle behavior modifications, pharmacotherapy, and bariatric surgery as appropriate. Key factors in obesity management include patient education, support for increased public awareness, and ongoing education.

There are knowledge gaps in the predictors of response for patients with obesity that require attention. Long-term outcomes data are required to design effective treatment algorithms that include the proper duration, sequence, and combination of therapy. Appropriate research to understand obesity pathophysiology for prevention and management at the basic, clinical, and translational levels will help improve treatment intervention. The optimal timing of lifestyle and pharmacotherapy interventions, whether sequential or simultaneous, should be further studied. In addition, with the recent diagnosis of obesity as a disease, novel reimbursement mechanisms for obesity-related clinical care are needed. And equally important, appropriate training should be available to improve the ability of physicians and other health care professionals to manage the growing number of patients with obesity.

Question 3—What is the Optimal Use of Therapeutic Modalities?

A healthy lifestyle is the foundation for all therapeutic modalities. The choice of therapeutic modality should be based on risk stratification during the initial assessment: (1) the presence/severity of obesity-related complications during the initial assessment, and (2) the response to therapy. Therapy should be intensified based on risk stratification and the presence and severity of obesity-related

complications in order to achieve individualized goals and outcomes, optimal benefit to risk ratio, and enhanced cost effectiveness (36), as exemplified by the AACE complications-centric obesity treatment algorithm (35). This will assure that weight loss therapy is intensified commensurate with the severity of the disease and will target more aggressive interventions to those individuals who will derive the greatest benefit.

Several multicenter, randomized controlled lifestyle-intervention studies have shown the efficacy of lifestyle intervention as a therapeutic modality. A multidisciplinary team can most effectively implement the program whether in-person, in a group setting, or delivered remotely (telemedicine). The Look AHEAD and other lifestyle intervention programs have reported that combined behavioral, nutrition (including meal replacements), and physical activity are successful in achieving and maintaining health outcomes (47,49,58). A stepped care approach with rapid escalation to combination lifestyle modification and medical therapy is frequently needed to achieve weight loss and prevent weight regain (114). More aggressive intervention, including weight-loss medications, should be targeted to patients with obesity-related complications who can benefit the most from weight loss (35). Bariatric surgery is an option for patients with BMI ≥ 40 kg/m² and those with BMI ≥ 35 kg/m² and severe obesity-related comorbidities (37).

All patients who are overweight or obese should undergo evaluation and management of comorbidities, including prediabetes, metabolic syndrome, T2DM, hypertension, dyslipidemia, biomechanical complications, and sleep disorders (37). In addition, psychiatric disorders such as depression, stress, addiction, and disordered eating require special evaluation and treatment.

The key to successful implementation of treatment for obesity includes adequate reimbursement, affordability, and access to nutrition education, medications, and other therapeutic modalities. To effectively evaluate and implement a comprehensive treatment plan and take the lead in providing long-term care, health care providers should ideally be trained in the management of obesity. Critical to the success of obesity management regimens is the optimization of health literacy and patient adherence.

Question 4—Can the Optimal Framework be Cost Effective?

The medical and financial benefits of treating obesity can be determined from several sources. The first relates to the treatment of obesity-related complications and the extent to which reduction in weight and/or adiposity ameliorates these conditions. These therapeutic effects will predictably lower the direct and indirect costs of obesity associated with dyslipidemia, high blood pressure, malignancies, mobility disorders, osteoarthritis, sleep apnea, T2DM, etc. The second is in the prevention of T2DM.

Increasing evidence indicates that lifestyle intervention with weight loss, or lifestyle intervention plus a weight-loss medication, are highly effective strategies for preventing T2DM in susceptible populations (49-53,90,115). This approach prevents or delays the costs of medical care for a person with T2DM, which are known to be 2- to 3-fold higher than for a person without T2DM (116). Every year that T2DM is prevented has financial value. The third medical and financial benefit can be determined by examining the impact of BMI and/or adiposity on life expectancy. Class I obesity (BMI of 30 to 34.9 kg/m²) subtracts 2 to 3 years from life expectancy. A BMI >40 kg/m² reduces life expectancy by $>8\%$, a reduction comparable to smoking. For each 5-point increase in BMI, a 30% excess mortality and 40% excess vascular death is observed (117). This approach also applies to efforts to use global economic metrics to calculate a cost benefit.

The expenditure of resources to accomplish weight loss has been analyzed and varies widely in terms of dollars per kilogram loss of body weight. These range from free web-based programs, inexpensive apps and wearables (pedometers, fitness bands, etc.), up to intensive structured lifestyle-intervention programs, medication, and surgery. Choice of intervention obviously factors into the cost-benefit analysis. A key to enhancing cost-effectiveness is to target at-risk patients based on their risk profile and the presence of complications that can be ameliorated by weight-loss therapy. In this way, more aggressive care can be delivered to those patients who would benefit the most from weight loss. A second issue is to identify patients who are responsive to the intervention, generally based on direct results in the first weeks after initiating the intervention. The data are convincing that lifestyle intervention programs, together with weight-loss medications, can achieve 5 to 15% weight loss in many patients (49-53,115).

For many illnesses, a cost-effectiveness analysis is demanded (usually by payers) to justify the costs of interventions and treatments. For many obesity-related diseases such as T2DM, hypertension, and dyslipidemia, Major Adverse Cardiac Event endpoints are not practical because the studies would need to be quite long and therefore difficult to control. Instead, it is more reasonable to approximate the utility of weight loss or adiposity reduction using validated surrogates such as blood pressure, LDL-C, and the appearance of T2DM. The costs resulting from the appearance of T2DM have been well documented (118) and can therefore be used to estimate the value of weight loss in patients resulting from a comprehensive effort to prevent T2DM. Such analyses have been conducted and have shown the utility of weight reduction (119). Many health economic studies pertaining to the care of patients with obesity assess all patients over a certain range of BMIs. More data are needed to evaluate how a complications-centric approach can impact the cost-effectiveness equation, where more aggressive therapies are targeted to

patients with complications, patients who will experience the greatest benefit from weight loss.

For other medical conditions, such as cancer, we typically do not ask whether treatment is cost-effective. We ask whether it has value to improve the disease course or outcome. To that extent, we have treatments for obesity that meet this standard and have been approved as safe and effective. The rationale is not clear why obesity should be considered any differently from other diseases in coverage decisions for new effective therapies. Furthermore, in areas of public health such as smoking cessation, avoiding drunk driving, and substance abuse treatment, we recognize the value without demanding a cost-effectiveness determination. Most importantly, the references provided in this document present published experience to guide payers, including U.S. Center for Medicare & Medicaid Services (CMS) regulators. Although there is reason to request further study, sufficient and compelling data are already available and should be employed to attack the epidemic of obesity in the U.S.

Question 5—What Are the Knowledge Gaps and How Can They be Filled?

Overweight and obesity are related to increased morbidity and mortality, with hazards that are comparable to those of cigarettes (120). However, several knowledge gaps still exist. To achieve a positive impact on the obesity epidemic will require policy changes and associated incentives that provide a supportive environment for effective prevention and treatment, with collective participation of government, communities, health systems, payers, the food industry, and others.

One of the major drawbacks to achieving new knowledge, as well as the application of existing knowledge, relates to the current lack of reimbursement for the treatments of obesity. To convince third-party payers, businesses, and the government that weight loss has true value to individuals and society may require clinical and economic data with 2 to 5 years of follow-up.

With respect to research, it would be useful to quantify the effects of the prevalence of obesity in childhood on adult mortality in different ethnic groups.

Among adults with obesity, there are often large gaps in general knowledge about obesity due to a lack of health literacy and personal health education (121,122). For example, in a study of 200 patients with T2DM attending a teaching hospital, most individuals with obesity lacked awareness of their own health status (122). Education can be a meaningful step toward engaging patients with obesity in making positive choices; for example, as part of a corporate wellness program, information can be provided about BMI and its impact on overall health.

In addition, knowledge gaps exist among health care providers due to a lack of education about optimal management of patients with obesity (11). There was broad-based

acknowledgment that improvements in education concerning the disease of obesity must be enacted at all stages in the training of health care professionals. Education and training in the use of therapeutic lifestyle changes involving healthy eating and regular physical activity, as well as drug therapies and surgical interventions are needed. Finally, most guidelines mention the critical importance of addressing obesity but lack specific direction for the health care provider. Adding guidelines for the management of obesity into clinical guidelines in general, and guidelines specific to obesity-related complications in particular, should facilitate greater awareness and competency for the effective management of obesity.

Although the value of treatment to manage obesity appears self-evident, gaps exist in data that address the degree to which treatments for obesity can be cost-effective (123,124). Existing data do support the value and cost-effectiveness of treating individuals with complications of overweight or obesity (69,125). Reliable data on the societal costs and the adverse impact of obesity in the workplace are also available (126,127). It is more difficult to quantify the personal impact of obesity and the impact on family and society. Enhancing cost-effectiveness includes targeting those at greatest risk from complications and those who demonstrate greatest responsiveness. It also means judicious choice of therapies based in part on their relative cost per amount of weight lost and/or the relative ability to improve obesity-related complications. If reimbursement for the treatment of obesity becomes a reality, we will witness “crowd-sourcing” for creative solutions by the legion of clinicians and individuals with obesity who will finally have access to the medical care they need.

Analysis

The evidence base and conclusions derived from the 5-question, 4-pillar matrix served as discussion points for “among-pillar” moderated sessions. Information from these discussions was analyzed by writing committee members to generate the following affirmed and emergent concepts, as defined below.

Affirmed Concepts (ACs)

Many concepts, with varying levels of validation, have been generally accepted by the scientific and medical communities and also supported by the AACE/ACE previously in treatment recommendations. These concepts were the subject of analysis at the CCO and were discussed in terms of their accuracy, relevance, and utility. These concepts were affirmed, or slightly modified, and found to be consistent with the evidence base established at the CCO. These ACs are included here because they were affirmed in the multidisciplinary CCO format involving a broad array of stakeholders vested in the problem of obesity. In addition, the affirmed concepts were deemed, through

consensus, to have sufficient potential to generate actionable recommendations.

AC.1. Obesity is a chronic disease. There was consensus that this precept is scientifically justified and critical to efforts to combat obesity.

AC.2. Treatment of obesity should be guided by a complications-centric approach, such as the AACE/ACE Obesity Algorithm, wherein therapeutic decisions are based on the presence and severity of obesity-related complications that can be ameliorated by weight-loss therapy. Safe and effective treatment modalities for overweight/obesity based on complications-centric risk stratification include intensive lifestyle intervention, meal replacements in the context of reduced-calorie diets, pharmaceuticals, and surgery. This approach will assure that more aggressive interventions will be targeted to patients with obesity-related complications who will benefit most from weight loss therapy (i.e., enhanced benefit to risk ratio and cost-effectiveness). Recommended team approaches utilize a physician trained in the care of the patient with obesity, nurse practitioners and physician assistants, and, importantly, other health care professionals as represented by participants at the CCO. Patients who are overweight/obese should also be managed using a complications-centric approach, such as the AACE/ACE Obesity Algorithm, and may be situated on a physiologic continuum of insulin resistance and/or adipocyte dysfunction associated with an increased risk for cardiometabolic and other obesity-related complications.

AC.3. Lifestyle intervention is critical to a comprehensive obesity care plan. Lifestyle interventions include behavioral modification, healthy eating patterns, increased physical activity, and sleep hygiene, and have been shown to be efficacious in multiple studies. Reimbursement for long-term, individualized, high-intensity structured lifestyle interventions is necessary, especially in the context of reducing disparities in health care accessibility.

AC.4. The obesogenic factors in the environment need to be reduced. The obese phenotype results from an interaction of the built environment, behavior, and genotype (inheritance of obesity susceptibility genes). Efforts to reduce the obesogenic nature of our environment will require participation from stakeholders in the biomedical, government and regulatory, industry and economic, and society/education/research pillars. These efforts include better nutritional messaging, more health literacy initiatives, public policy, public awareness, and advocacy regarding the dangers of untreated overweight/obesity and the rewards of a healthy lifestyle and body. The role of more aggressive antiobesity legislation requires further study.

AC.5. Primary and secondary prevention strategies are critically important. In addition to tertiary interventions, preventive strategies at early pathophysiologic

stages are essential for a comprehensive action plan to combat obesity.

Emergent Concepts (ECs)

New concepts emerged from multidisciplinary discussions of the evidence base at the CCO. These concepts may not have become evident upon analyses of the data in a conference featuring focused expertise, for example only biomedical experts, but did emerge in the context of discussions involving the broad array of conference stakeholders. These ECs have not been entirely validated, but are deemed through consensus to have sufficient potential to generate actionable recommendations.

EC.1. The definition of obesity needs to be improved. Obesity is currently defined as a chronic disease by many organizations, but nearly all discussions at the CCO, involving all pillars discussing all 5 questions, centered on the need for a better definition of obesity that would constitute a medical diagnosis as a chronic disease. The imprecision and uncertainties regarding the current diagnosis of obesity based solely on BMI and the need for a diagnosis that was more medically meaningful and actionable, clearly emerged as major impediments to concerted action and were responsible for a degree of immobilization across pillars. The analogy is a hub representing the definition of obesity as a central limitation that reaches out as spokes to each pillar and participating organizations to diminish the potential for concerted action. It was recognized that BMI may be predictive for risk as a single metric, but as an anthropometric measure, BMI may not reflect the impact of weight gain on the health or well-being of the individual. Furthermore, the predictive power of BMI varies among different ethnicities, body types, and specific obesity-related complications. An improved medically relevant definition will facilitate a greater degree of concerted action among CCO participants and access to lifestyle interventions, weight-loss medications, and bariatric surgery. An actionable diagnosis will also enhance and inform regulatory agency processes, appropriate investigative research designs, education, public awareness and health literacy, and policy effectiveness. A more meaningful definition of obesity will require further study; however, there was consensus at the CCO that the framework for a medical definition of obesity would consist of the continued use of BMI together with other anthropometrics (e.g., waist circumference) and an assessment of the presence and severity of obesity-related complications. For greater accuracy, such a definition would need to consider variables, such as ethnicity and age.

EC.2. Regulatory, governmental, and insurance organizations require different thresholds of evidence based on specific mandates and decision processes. For instance, the U.S. Centers for Disease Control and Prevention National Diabetes Prevention Program and

similar programs can operate based on the existing evidence base due to the strength of that evidence and the urgency of the problem, whereas the FDA requires additional structured evidence to evaluate and approve anti-obesity pharmaceuticals and devices. The CMS has several requirements for coverage determinations, including whether there is a statutory benefit category for the item and service and requires evidence and outcomes most relevant to the Medicare population. For example, for certain prevention and screening items and services, the U.S. Preventive Services Task Force must recommend the preventive service with a grade A or B to be eligible for coverage. Some private insurance carriers rely on evidence demonstrating health benefits, especially over a 2- to 5-year period. The emergent concept was that these particulars were impairing a more concerted and uniform action plan that would make effective treatment modalities available in a more consistent way among different population groups. Resolution of these issues is needed for a comprehensive action plan to combat obesity.

EC.3. Public awareness can change private insurance carriers' reimbursement strategies and health care coverage provided by employers. Social contracts, primarily between employers and private insurance carriers, can be modified to include reimbursement for components of obesity comprehensive care plans (structured lifestyle intervention, pharmaceuticals, and surgery as medically indicated). However, to varying degrees, these components of care are often not made available to employees. This represents an important limitation in developing a comprehensive care plan for obesity. Change can be affected by greater public awareness and advocacy for obesity as a potentially dangerous chronic disease when left untreated. Research is needed to examine the impact of therapy and prevention of obesity on employee health, health care expenses, absenteeism, morale, and productivity.

EC.4. Intergenerational obesity must be prevented through intervention in pregnancy to manage excessive maternal weight gain, in infants (0 to 24 months old) and children, and in young reproductive-age females. The transmission of risk for obesity is propagated via maternal weight gain to the in utero environment, promoting obesity in children, who become adults with obesity. A comprehensive action plan will require a primary prevention care model, with interventions applied early in the lifecycle to include families and social groups in addition to larger populations and individual patients.

EC.5. Understanding the value of obesity care is important for patients, physicians, payers, and employers. "Value" relates to cost-effectiveness regarding a favorable impact on health outcomes and impact regarding quality of life improvements (e.g., quality adjusted life-years), including both perceived and documented health benefits. "Value" stands in contrast to cost-utility analyses, which relate only to monetary outcomes and cost-benefit ratios

measured in dollars. The "value" of different treatment and prevention modalities for obesity should receive greater emphasis in reimbursement decisions, and obesity should not be different from any other disease in the general consideration of factors determining coverage decisions.

EC.6. Greater emphasis on medical education and training regarding obesity. There is an underrepresentation of formalized obesity education in the training of health care professionals. This needs to be addressed to optimize the competency of the next generation of health care professionals entrusted with the care of patients with obesity and to assure high-quality, comprehensive care. A comprehensive action plan to combat obesity must include increased education and training in the evaluation and management of obesity in medical school, residencies, and fellowships for medical doctors, and in training programs for health care professionals who are vital members of the multidisciplinary health care team.

EC.7. The need to standardize core elements of lifestyle intervention programs. The operational definition of lifestyle intervention programs has not been standardized. Different approaches and intensities of lifestyle intervention should be defined around core essential programmatic elements. This will give meaning to these programs' descriptors, allow for evaluation of efficacy and outcomes across multiple studies (together with efficacy comparisons for different program types), provide clinicians with better information regarding patient referrals for these interventions, and permit payers and employers to make more strategic coverage decisions.

EC.8. The need for additional data addressing the optimal management of obesity in elderly patients. More studies are needed to elucidate how the diagnostic and treatment paradigm for obesity should be modified for elderly patients (e.g., >70 years of age). Does advancing age alter the priority of obesity-related complications effectively treated by weight loss? How does aging affect the relationship between adiposity, complications, and longevity? What are the appropriate endpoints and desired outcomes of weight loss therapy in the elderly? How does the presence of sarcopenic obesity impact the treatment plan? These and other questions are highly relevant to the management of obesity in a segment of the population that is increasing in numbers and to a concerted action plan involving CCO participants (e.g., coverage of therapy by CMS for Medicare beneficiaries).

Key Findings (KFs)

The writing committee has reviewed the ACs and ECs above and formulated KFs that can efficiently represent the results of the CCO.

KF.1. Obesity is a chronic disease, and once diagnosed, should be managed using a complications-centric approach, as typified by the AACE/ACE Obesity Algorithm, which includes structured lifestyle

intervention, meal replacements, pharmacotherapy, and surgery.

KF.2. A preventive medicine paradigm is necessary to improve outcomes in overweight/obesity and consists of structured lifestyle intervention, behavior change, and alterations in the built environment.

KF.3. Comprehensive interventions producing improved outcomes for patients who are overweight/obese require demonstration of value in a combined biomedical and public health model.

CONCLUSION

This immediate CCO deliverable includes evidence from 4 stakeholder pillars as part of a composite biomedical and public health disease model of obesity care. The evidence has been organized around answers to 5 relevant and pragmatic questions. Analysis of the evidence base has produced statements corresponding to ACs, ECs, and KFs. In conjunction with our pillar partners, the AACE plans to translate this body of information into actionable recommendations that will strategically and efficiently provide net benefit and value to patients requiring comprehensive management of obesity. Subsequently, the AACE, together with CCO participants, plans to devise implementation logistics and strategies for these specific recommendations to realize a concerted approach for effective prevention and treatment of obesity.

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