

## The Obesity Epidemic and Potential Interventions

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**O**besity is a growing public health problem that leads to multiple comorbidities and mortality. The health-care-related cost of overweight and obesity in the United States is estimated at \$270 billion yearly and is expected to increase to \$500-800 billion in 2030, if unchanged. Despite being one of the fastest growing health problems, obesity is often unrecognized by healthcare providers and the public. There is wide heterogeneity in the causes and manifestations of obesity that leads to wide patient-to-patient variability in the response to anti-obesity therapies. In this article, we discuss underlying causes of obesity, how to address the complex issues of obesity using a team-based approach, potential medical and surgical treatments, and emerging therapies.

The prevalence of obesity has significantly increased worldwide over the past three decades, creating a global public health crisis. Based on data from the National Health and Nutrition Examination Surveys (NHANES), approximately 68% of adults in the United States are overweight and 35% are obese. It is projected that between 2010 and 2030, the incidence of obesity will rise from 35% to 50%.

The cause of obesity is multifactorial. Although genetically influenced, obesity is not a simple Mendelian trait disease. As of October 2005, only 176 different human obesity cases due to single gene defects were found. Cultural and society factors play an important role in obesity prevalence. Adipose tissue itself is an endocrine organ, which can become dysfunctional in obesity and contribute to systemic metabolic disease. In 2012, the American Association

of Clinical Endocrinologists (AACE) published a position statement designating obesity as a disease. Other organizations such as the American Heart Association, the American College of Cardiology, The Obesity Society, the Obesity Medical Association, and the Endocrine Society have also developed obesity care guidelines and algorithms incorporating care plan of a complications-centric approach. These guideline developments accelerate further scientific study of obesity and demand for obesity management. It is expected that general internists and primary care providers be at the front line of screening, prevention, diagnosis, and treatment for patients with obesity and its related complications.

In recent years, many new modalities have emerged to treat obesity, although lifestyle and behavioral interventions do remain the mainstay of treatment. The U.S. Food and Drug Administration (FDA) has approved five weight-loss medications for long-term management of obesity. The following medications target different neurochemical and hormonal pathways to promote satiety, reduce hunger, and decrease energy intake:

- Orlistat (Xenical or Alli) works by inhibiting enzyme lipase at the intestinal brush border that in turn causes fat malabsorption and decreased energy intake.
- Lorcaserine (Belviq) is a selective serotonin receptor agonist (5HT<sub>2c</sub>) which promotes satiety and appetite control.
- Phentermine/Topiramate ER (Qsymia) is a combination of sympathomimetic and anti-seizure medication that affects

appetite control and satiety.

- Naltrexone/Bupropion (Contrave) is a combination of an opioid receptor antagonist and a norepinephrine-dopamine reuptake inhibitor that works at neurotransmitters in the brain to control appetite and promote satiety.
- Liraglutide (Saxenda) is a glucagon-like peptide-1 receptor agonist, also known as GLP-1 receptor agonist or incretin mimetic. This class of drugs includes exenatide (Byetta/Bydureon), albiglutide (Tanzeum), and dulaglutide (Trulicity) which are used for treatment of type 2 diabetes as they increase insulin secretion. However, most of them have additional effects on appetite, satiety, and gastric emptying which promote weight loss. Nevertheless, Saxenda is the only one in its class that is approved for weight loss treatment.

Providers need to monitor patient's response and side effects closely in order to appropriately titrate treatment regimen. To choose the proper treatment regimen, a good understanding of the mechanism of action and side effects of each medication is required. Primary care providers need to gain experience and develop expertise in obesity treatment to use these medications effectively and comfortably.

In addition, surgical treatment for weight loss has been developed and refined with significantly lower morbidity and mortality. The two most common surgical procedures include

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laparoscopic sleeve gastrectomy and roux-en-Y gastric bypass, which usually lead to 50-55% and 60-70% of excess weight loss, respectively. Both procedures promote significant weight loss and improve various metabolic parameters through restrictive and malabsorptive effects. A proper evaluation by bariatric team members is crucial and usually requires a comprehensive psychiatric and medical evaluation. Other emerging procedures include endoscopically implant intra-gastric balloons, bypass liners or endo-barriers, aspiration therapy using gastronomy tubes, etc. There is no adequate study and outcome data to support their uses at this time.

How we approach the complex issues of obesity requires a comprehensive and team-based approach that is applicable to real-world patient care. Having a good understanding of pathophysiology of obesity can help us manage patients appropriately. Obesity is a complex and multifactorial disease with multiple signals and hormones influencing the brain and appetite. Diet and lifestyle intervention only works for certain levels of weight loss. The human body fights against weight loss by disproportionate response in energy expenditure, appetite regulation and gut hormone adaptations. Therefore, treatment with anti-obesity medications and/or surgical weight loss may be required for selected population to achieve the goal.

Regulation of obesity and energy balance is much more complex and comprise of physiology involving multiple signaling and homeostasis rather than just the physics of calories in and calories out. Reducing

total caloric intake is still the main component of any weight loss intervention. There is no specific diet that provides highest weight loss. The key to success is an adherence to an individualized low calorie diet. Aerobic physical activity should be prescribed for patients as a component to lifestyle intervention. Progressive increase in the volume and intensity of exercise may be needed with an ultimate goal of moderate exercise of more than 150 minutes per week.

General internists should work as a team with endocrinologists, nutritionists, exercise physiologists, behavioral health providers, midlevel providers, and bariatric surgeons to elaborate a care plan for obese patients. Rather than focusing on a preset decline in body weight, the primary therapeutic endpoint for patient's health and quality of life. Data shows that approximately 10% weight loss from baseline body weight improves obesity-related health conditions, such as hypertension, type 2 diabetes, coronary artery disease, obstructive sleep apnea, infertility, osteoarthritis, and chronic pain.

Weight maintenance is the most difficult aspect of a weight-loss journey. After a successful weight loss, primary care providers are vital in the transition process for surveillance and follow-up. A good long-term relationship with patients is pivotal in the continuum of care to prevent weight regain. Patients with obesity generally have poor access to health care. Providers are also less likely to build emotional rapport with obese patients. Treating the patient, not just the condition, is critical and providers should approach

patients in a confident, supportive and non-judgmental fashion.

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