

Obesity continues to be an epidemic with approximately 42.4% of all adults in the United States deemed obese and 9.2% with severe obesity.<sup>1</sup> In 2 decades, the prevalence of obesity in the United States has increased by 39% (from 30.5% to 42.4%) and the prevalence of severe obesity has increased by more than 96% (from 4.7% to 9.2%).1 From 2017 to 2018, the age-adjusted prevalence of obesity was reported to be 42.1% in females and 43.0% in males.<sup>1</sup> The prevalence of obesity in the United States is highest among non-Hispanic Black adults (49.6%) and lowest among non-Hispanic Asian adults (17.4%).<sup>2</sup> If current trends continue, it is projected that by the year 2030, nearly 1 in 2 adults will be affected by obesity (48.9%; 95% confidence interval [CI], 47.7% to 50.1%), and nearly 1 in 4 adults is projected to be affected with severe obesity (24.2%; 95% CI 22.9% to 25.5%).3 Considering the prevalence of obesity and its associated comorbidities (eg, diabetes, cardiovascular disease, hypertension, osteoarthritis), the economic burden is substantial.4-8 Annual medical expenditures associated with obesity totaled \$248 billion in 2020, equating to 6.2% of total health care expenditures.9 Individuals with obesity spend an estimated \$628 to \$756 more on health care annually compared to individuals in a healthy weight range.<sup>10</sup> Persons with obesity and diabetes, or metabolic syndrome, have been shown to have a lower healthrelated quality of life (QOL).<sup>11</sup> Specifically, obesity is a major contributor to the type 2 diabetes (T2D) epidemic with nearly 88% of persons with T2D considered overweight or obese.6-8 Despite the increased risk of poor clinical outcomes and negative impact on QOL, only one-half of persons with diabetes and other chronic conditions receive counseling on diet and/or exercise from their health care professionals (HCPs).<sup>12,13</sup>

## **Diabetes and Obesity Connection**

Obesity is a multifactorial disease<sup>14</sup> that is likely to occur when energy intake exceeds energy expenditure over a long period. Genetic, environmental, and health behavior factors impact the energy and body weight status, such as hormones signaling hunger, availability of palatable foods, habit-forming preferences, and the gut microbiome.

Epidemiological research has documented the association between nutritional status early in life and health behavior habits with the

development of obesity and chronic diseases. Eating behavior is regulated by 2 competing mechanisms: the homeostatic and hedonic drive to eat. The homeostatic mechanism is biological control compared to the hedonic, which is the reward means for managing appetite. Research points to an *obesogenic environment*, meaning there are external factors contributing to hormonal imbalances, overeating, and alterations in the hedonic response to food. For example, sleep deprivation leads to an alteration in appetite-regulating hormones, particularly ghrelin thus increasing hunger and heightening hedonic response.<sup>15</sup> Just extending sleep to 6 hours improved body composition by decreasing fat mass gain.

Weight gain is decreased by leptin and other hormones that induce satiety, including gut-derived hormones. Leptin is generated from the adipocytes and is key to regulating body fat mass and weight. Leptin levels decrease with weight loss. This decrease results in compensatory mechanisms that reduce energy expenditure and encourage weight (re)gain.<sup>16,17</sup>

Leptin and ghrelin are endocrine hormones involved in energy and appetite signaling. Leptin is secreted by adipocytes in proportion to a person's triglyceride content and is associated with maintaining long-term energy status. The typical signaling of leptin works to decrease food intake by decreasing appetite to increase energy expenditure.<sup>16-18</sup> During energy restriction and weight loss, leptin levels are decreased and are associated with numerous metabolic abnormalities related to visceral obesity (eg, hunger, decreased metabolic rate, insulin resistance). Paradoxically, obesity is often correlated with increased leptin levels giving rise to the hypothesis of *leptin resistance*.<sup>16-18</sup> Ghrelin is a gut hormone associated with short-term energy maintenance through signaling in meal initiation and termination. The typical signaling of ghrelin works to stimulate appetite, followed by a corresponding fall in circulating ghrelin levels in response to dietary consumption. This postprandial reduction of ghrelin has been shown to be blunted, or even absent in persons with obesity.<sup>18</sup>

The relationship between hyperinsulinemia, insulin resistance, and obesity has remained unresolved for decades. Insulin is responsible for postprandial use and storage of nutrients, which includes inhibiting fatty acid oxidation and increased lipogenesis. Fasting and postprandial hyperinsulinemia occur as a response to systemic insulin resistance in an attempt to maintain glucose homeostasis.<sup>19</sup> Hyperinsulinemia directly contributes to the development of excess lipid accumulation [obesity] in several tissues. Genetic research has shown this as a cyclic positive feedback loop where hyperinsulinemia promotes obesity, which in turn increases insulin resistance and encourages obesity.<sup>19</sup>

The gut microbiome plays a pivotal role in macronutrient metabolism, insulin resistance, and inflammation. Bacteria in the gut are required for maintaining energy homeostasis, insulin signaling, immunity, and modulating inflammation. Alterations in gut microbiota can lead to dysbiosis contributing to metabolic disorders such as T2D separately and in concurrence with obesity.<sup>20</sup> Research demonstrates that dietary and environmental factors affect gut microbiota, with low diversity being associated with changes in metabolic markers including increased serum leptin, insulin resistance, increased high-sensitive C-reactive protein, and decreased adiponectin.<sup>21-23</sup> The importance of these changes leads to gut-derived metabolites and microbes such as lipopolysaccharides and short-chain fatty acids influencing metabolic pathways, such as insulin signaling, appetite regulation, incretin production, and inflammation. Gut dysbiosis can be attenuated through dietary modifications. Dietary or supplemental intake of pre- and probiotics cause positive changes in gut integrity, increased satiety, improved insulin sensitivity, improved energy homeostasis, and excess body weight loss The effects of dietary and environmental factors, medications can also influence gut flora and in turn, inhibit weight loss through mechanisms of increased inflammation and decreased insulin sensitivity.24,25

### Classification

The American Association of Clinical Endocrinologists (AACE) and the American College of Endocrinology (ACE) clinical practice Guidelines recommend all adults be screened annually for overweight and obesity.<sup>26</sup> The recommended approach is to use body mass index (BMI), which is calculated as weight in kilograms divided by height in meters squared. Normal BMI is 18.5 to 24.9 kg/m<sup>2</sup>. A cutoff of  $\geq$ 23 kg/m<sup>2</sup> defines those individuals who should be screened and further evaluated for diagnosis in South Asian, Southeast Asian, and East Asian adults, and a cutoff of  $\geq 25 \text{ kg/m}^2$  for everyone else. Adults with a BMI between 25 and 29.9kg/m<sup>2</sup> are classified as overweight and those with a BMI greater than or equal to 30 kg/m<sup>2</sup> are considered obese. Obesity is further defined by class I (30 to 34.9 kg/m<sup>2</sup>), class II (35 to 39.9 kg/m<sup>2</sup>), and class III (≥40 kg/m<sup>2</sup>). To further assess disease risk associated with obesity, the AACE/ACE Guidelines recommend measuring the waist circumference in adults classified as overweight or class I obese, when BMI is <35 kg/m<sup>2</sup>. For males, the waist circumference cutoff for increased risk is  $\geq 94$  cm (37 in), and for females it is  $\geq 80$  cm (31.5 in). For the Asian population, the waist circumference cutoff for males is

 $\geq$ 85 cm (33.5 in) and the cutoff for females is  $\geq$ 74 to 80 cm (29 in to 31 in).

#### **Obesity and Diabetes Progression**

The prevalence of prediabetes in US adults from 2017 to 2020 was 38.0%.<sup>27</sup> The prevalence of metabolic syndrome in 2016 was 34.7%. Although the overall increase in metabolic syndrome prevalence among US adults from 2011 to 2012 and 2015 to 2016 did not meet statistical significance, there was a significant increase observed among young adults and Hispanic and Asian individuals.<sup>28</sup> Metabolic syndrome is a cluster of interrelated metabolic risk factors including abdominal obesity and arguably has been labeled a prediabetes state.<sup>29</sup> Individuals with metabolic syndrome have a fivefold increase in diabetes risk. Undeniably, reducing the risk of or delaying diabetes can be achieved by adopting and maintaining healthy behaviors, like those described in the National Diabetes Prevention Program (DPP).<sup>30</sup> Several long-term follow-ups of key trials demonstrated intensive health behavior interventions targeting a 5% to 10% reduction in total body weight coupled with 150 minutes (2 hrs and 30 min) or more of physical activity per week may reduce the incidence of T2D by anywhere from 34% to 58%.<sup>31-33</sup> Incorporating 150 minutes of moderate-intensity physical activity per week has been shown to have many positive effects on managing prediabetes including improved insulin sensitivity and reduced abdominal fat.34-36

Obesity is also a major risk factor for cardiovascular disease (CVD).37 Individuals with obesity are at greater risk of CVD compared with individuals of normal weight.<sup>38</sup> Maintaining a weight loss of just 5% to 10% of body weight can result in decreased triglycerides, systolic blood pressure, low-density lipoprotein, and an increase in high-density lipoprotein; all of which reduce the risk of CVD.<sup>38,39</sup> Reduced weight and sustained weight loss can improve glycemic management and decrease the number of medications an individual takes.<sup>40</sup> Findings from the Action for Health in Diabetes (Look AHEAD) trial demonstrated that weight loss and physical activity corresponded to a marked decline in A1C and improvements in CVD risk factors.<sup>41,42</sup> Weight loss at any age after 20 years has been shown to have lifetime cost savings ranging from \$16,882 to \$36,278 due to several factors that include reducing the number of medications, hospitalizations, outpatient visits, and emergency department visits.43

## Managing Obesity in the Person With Diabetes

Effective education and counseling provided by diabetes care and education specialists (DCES) as part of a comprehensive health care plan can yield important clinical benefits while improving cost savings to both the individual and the health care system.<sup>44</sup> The American Medical Association recognizes obesity as a disease<sup>14</sup> that requires a range of medical interventions for treatment and prevention. The AACE and ACE further support

this classification emphasizing the role multifactorial approaches have along with diet and exercise for treating overweight and obesity.<sup>26</sup> Diabetes care and education specialists are in a unique role to provide continued support for health behavior changes in persons with obesity and diabetes.<sup>26</sup>

### Addressing Weight Stigma and Bias

Weight stigma or bias is a conscious or unconscious negative behavior by HCPs that elicits distress from the person with obesity.45 Weight-associated stereotypes that place personal responsibility on the individual for excess weight as a consequence of laziness, noncompliance, and lack of willpower are common weight stigmas among HCPs.<sup>46</sup> Weight stigma is prevalent in the United States and international health care settings and contributes to unfavorable perceptions of HCPs and general dissatisfaction with health care experiences. This contributes to poor uptake of health-related recommendations and reducing risks and illness care among persons with overweight and obesity.<sup>46,47</sup> Forty-four percent of adults in the general population and 52% of adults with obesity internalize weight stigma.<sup>48</sup> When internalized, weight stigma has been associated with mental health conditions including low selfesteem, depression, suicidality, anxiety, substance misuse, and disordered eating.<sup>46,49-51</sup> A health-focused, weight-inclusive approach to the care of individuals with higher weight is preferable to the traditional weight-centric environments of most health care settings.<sup>52</sup> Conventional weight-normative approaches to care equate weight with health and well-being and emphasize targeted weight goals for treatment, contributing to weight stigma. In contrast, weight-inclusive approaches to care appreciate the multifactorial complexity of weight and create environments that focus on health care access and reducing weight stigma.53 Goals of weight-inclusive care address health behaviors that are accessible to most people including eating nutritious foods when hungry, ending the meal when full, participating in enjoyable physical activity, and establishing effective sleep hygiene habits.53

Diabetes care and education specialists possess the knowledge and skills to collaboratively guide persons with overweight, obesity, and associated cardiometabolic conditions. Specifically, the ADCES7 Self-Care Behaviors<sup>®</sup> provide a person-centered framework by which DCES can partner with these individuals within the context of their personal lives to support successful health behavior change.<sup>54</sup> Diabetes care and education specialists must establish person/HCPs relationships that are free of weight bias and provide care environments that are respectful and welcoming for all individuals, including those with higher weights.

A person-centered approach to care is essential in supporting the overall health and wellness of persons with overweight and obesity. Using person-first language to replace traditional descriptions of people with higher weight as obese people to persons with obesity or persons affected by obesity helps to limit weight-related biases.<sup>55,56</sup> Persons with higher weight appreciate sensitive, direct HCPs-led discussions about weight,<sup>57</sup> prefer clinical conversations using terms such as *weight, weight problem,* and *unhealthy weight.*<sup>58</sup> Persons with overweight and obesity are more likely to experience realistic weight-related expectations, display motivation and confidence, and adopt behavior change strategies that support weight loss when they engage in collaborative partnerships with HCPs.<sup>59</sup>

Diabetes care and education specialists have an obligation to deliver and advocate for health care delivery that is weightinclusive. Clinical interventions that address the multidimensional nature of weight gain that extend beyond basic advice on food and physical activity are indicated because many individuals with overweight and obesity have prior knowledge and experience in these areas.<sup>59</sup> The person's health history, weight history including any experiences with eating disorders, comorbid profile, family history, psychosocial history, long-term prognosis, and personal desires including the right to decline or defer in weight-related discussions should guide collaborative care planning.<sup>50</sup> Attention to the care environment is imperative in reducing weight stigma and promoting weight-inclusive care. Creating a weight-inclusive clinical setting for persons with higher weight supports a positive health care experience and provides a foundation for effective relationship building between the person with higher weight and the DCES. All furniture, and the arrangement of furniture in care areas, should easily accommodate a person of higher weight. Diabetes care and education specialists should exhibit sensitivity when weighing individuals, including having a private location for scales, having a process for how office staff gathers individuals' weight measurements, practices involving a person's refusal to be weighed, and the ready availability of equipment and supplies, such as scales, gowns, and blood pressure cuff sizes that are appropriate for individuals across the weight spectrum support weight-inclusive care and limit weight-related stigma.<sup>53</sup> Health care professionals, especially DCES, must own and reflect on any weight biases they may have when working with persons with higher weights.60

#### **Ethnic and Cultural Considerations**

Black/African American and Hispanic adults have the highest rates of obesity in the United States and are at the greatest risk of receiving disparate diabetes health care.<sup>1</sup> To ensure equitable care, it is essential that DCES understand the cultural context in which these ethnic groups view overweight and obesity.

Appreciating cultural nuances can increase the likelihood that the person will accept weight management advice.

When discussing how to increase weight loss with Black/African American and Hispanic adults, consider these cultural factors:

- » Food: Some cultural behaviors around food can impact weight goals. For example, it is common for Hispanics to give treats as a sign of love or to continue eating when full of respect for older adults.<sup>61</sup>
- » Body Image: The perception of being overweight or obese can vary from culture to culture. A curvy or *thick* body is generally celebrated in Black/African American and Hispanic cultures.<sup>61,62</sup>
- » Trust: Some Blacks/African Americans may have a medical distrust that can be traced back to studies such as the Tuskegee Syphilis Study.<sup>63</sup> Diabetes care and education specialists who are not knowledgeable and sensitive to these experiences may find it challenging, but not impossible, to gain the trust and confidence of this community.<sup>64</sup>
- » Spirituality: In the Hispanic community, the cultural value of *fatalismo* can impact health-related attitudes. Fatalism, aka fatalism, is a general belief that the course of life events, including a decline in health or illness is unavoidable regardless of the person's actions. Similarly, some Black/ African Americans may believe they can rely on their faith to bring blessings into their lives or push unwanted circumstances away.<sup>61-63</sup>

## Diabetes Self-Management Education and Support

The DCES needs to address obesity as a comorbidity of diabetes through self-management and behavior change. The ADCES7 Self-Care Behaviors is a tool that can be beneficial in helping persons diagnosed with diabetes manage their weight.65 For example, promoting healthy eating and being active are 2 self-care behaviors that can help achieve weight loss and should be used as a first-line treatment strategy for persons with obesity during diabetes self-management education and support (DSMES).44 Healthy coping should also be included because managing stress and other psychosocial aspects can impact a person's success with weight loss. People with diabetes and DCES should collaboratively develop strategies (problem solving) for achieving behavior change (reducing risks) through appropriate goal setting based on the person's readiness to change and current abilities. Success should be measured not only in the weight loss achieved through this process but more importantly in gradual improvements in health and well-being.

## **Healthy Eating**

The National Standards for DSMES include a nutrition education component as part of the required curriculum.<sup>65</sup> Diabetes care and education specialists can assist people with diabetes in gaining knowledge about the effect of food on glucose levels, carbohydrate sources, protein and fat, and appropriate meal planning and resources for making healthy food choices. Diabetes care and

education specialists help people to understand portion sizes, read food labels, plan and prepare meals, and recognize the best times to eat to match their medication taking behavior. This knowledge is central to managing diabetes and addressing barriers to healthy eating.<sup>48</sup> Medical nutrition therapy (MNT) provided by registered dietitians (RDs), in combination with DSMES may further benefit people with obesity and prediabetes or diabetes. Medical nutrition therapy involves a comprehensive nutrition assessment and addresses individualized nutrition plans considering comorbidities, personal food preferences, eating habits, and cultural environment all aimed to achieve the individual's desired clinical outcomes.<sup>49</sup> Diabetes care and education specialists who are not RDs should consider recommending physician referrals for MNT and adding RDs to their diabetes care team.<sup>50</sup>

#### **Physical Activity**

Increased energy expenditure through physical activity is essential for weight management and overall health.7 Benefits may include preserving fat-free mass during weight loss and enhanced fitness along with improvements in insulin sensitivity, cardiovascular disease risk factors, and QOL. While all persons should strive for the accumulation of 150 minutes/week of moderate-intensity physical activity (equivalent to a brisk walk) to improve chronic conditions, DCES must recognize that these amounts alone may result in minimal weight loss (~2 to 3kg).<sup>51,52</sup> Indeed, exercise for a longer time can provide clinically significant weight loss or minimize weight regain long-term (ie, 200 to 300 minutes/week) and may be recommended.53 However, matching physical activity to the person's abilities, interests, resources, and health status are important considerations when working with people ready to change their activity behavior. For in-depth physical activity prescription or advanced exercise considerations, consulting with an exercise physiologist can help the DCES safely and effectively prescribe exercise for the person with obesity, prediabetes, or diabetes.

#### **Healthy Coping**

Diabetes care and education specialists and people with diabetes collaboratively develop strategies for maintaining sustained weight loss with long-term health behavior alterations. For example, when weight loss occurs there is a 20% to 25% decline in 24-hour energy expenditure an individual who was formerly obese would require at least 300 kcal less per day to maintain the same body weight as an individual who never had obesity with the same current body weight. The latter illustrates how continued partnership can allow the DCES to work with the person in navigating these physiological changes and improve overall health and well-being.<sup>54,55</sup> Ongoing counseling is essential, in all stages of the weight-loss program, to encourage a support system for weight loss and maintenance as well as discuss expectations.50 Those who have a strong support system

are more successful in maintaining their weight loss. Research demonstrates that 33% of people who fall in the obese category achieve long-term weight loss if counseling is included as part of the program<sup>55</sup> and assessing psychosocial influences should be considered for tailoring and individualizing weight loss maintenance programs.<sup>56</sup> Often individuals experiencing obesity and diabetes not only struggle with the stress related to self-care of diabetes, known as *diabetes distress syndrome*, but they also struggle with obesity-related concerns, such as body image, guilt, society acceptance, and bias.<sup>57,58</sup> Therefore, establishing a referral system that includes a mental health professional as a care team member should be considered for those struggling with the psychosocial issues of both diabetes and weight management.57 It is recommended that the treatment plan be evaluated on an ongoing basis for changes in eating patterns and behavior.57 For individuals who have undergone metabolic surgery it is recommended to assess how well the person with diabetes is adapting to the medical and psychosocial changes following surgery and the need to include mental health services.5

#### Pharmacotherapy

As noted, the importance of promoting and maintaining healthy eating patterns and physical activity in persons with obesity and diabetes is paramount and should always be encouraged. However, for persons assessed as *high risk* and persons for whom nutrition therapy and physical activity have not been successful, treatment options may also include pharmacologic interventions specific to weight loss.<sup>66,67</sup>

Pharmacotherapy for obesity may be considered for individuals who: (1) fail to achieve a minimum of 5% weight loss after 6 months of a comprehensive health behavior intervention; (2) have a BMI greater than or equal to 30kg/m<sup>2</sup>; or (3) have a BMI between 27 and 29.9 kg/m<sup>2</sup> with at least 1 indication for increased risk of CVD. Pharmacotherapy helps to reinforce health behavior interventions and should always be in adjunct to diet, physical activity, and behavior therapy<sup>68-70</sup> (see **Table 1:** Pharmacotherapy for detailed information on medication options).

Diabetes care and education specialists can play a pivotal role in providing evidence-based medication management.<sup>26,65,67,71</sup> Therefore, in addition to glycemic management, DCES should collaboratively work with the care team when considering the effects of various therapeutic options on body weight and when recommending treatment strategies. Medications commonly associated with weight gain include glucocorticoids, certain diabetes-related medications (sulfonylureas, insulin, thiazolidinediones), antidepressants (amitriptyline, imipramine, nortriptyline, SSRIs), antipsychotics (clozapine, quetiapine, risperidone), and antiepileptic medications (gabapentin, carbamazepine, and valproic acid).<sup>68,69</sup> Weight gain is observed through the slowing of the metabolic rate, appetite stimulation, fluid retention, hypoglycemia, or decrease in glycosuria.<sup>69</sup> Intensive glycemic management through pharmacotherapy (ie, sulfonylureas, TZDs, insulin) has been linked to weight gain in both T1D and T2D.<sup>70,72</sup> This weight gain can promote hyperglycemia (through insulin resistance), hypertension, hyperlipidemia, and additional cardiac risk factors and comorbid conditions.<sup>73</sup> Hence, treating diabetes in persons with obesity with medications that are weight neutral (ie, metformin, DPP-4 inhibitors, SGLT-2), induce weight loss (ie, GLP-1RA), or minimize weight gain should be advised when appropriate.<sup>73</sup>

Current US Food and Drug Administration (FDA) approved pharmacotherapy includes Adipex-P and Lomaira (phentermine), Qsymia (phentermine/topiramate extendedrelease [ER]), Contrave (naltrexone/bupropion ER), Xenical and Alli (orlistat), Saxenda (liraglutide) and Wegovy (semaglutide).74 The pharmacological actions of these medications vary and require the person to deliberately alter their behavior and consciously for significant weight loss to occur. Diabetes care and education specialists often encounter people with diabetes who have higher weight or obesity who are eligible for weight loss medications. It is important for DCES to be familiar with the available weight loss medications along with their mechanism of action, dosages, adverse effects, contraindications, and special considerations (see Table 1). A DCES who is familiar with these medications can be an advocate for the person and make suggestions for potential weight loss medications when appropriate. Weight loss medications may be particularly beneficial for weight loss maintenance in those persons who have weight loss via intensive health behavior strategies.

The choice of medication is often made by considering efficacy with cost, the person's preference, and specific safety issues or potential for adverse effects. In most cases, medications will need to be long-term therapy rather than short-term courses.75 Important to note is that there are existing policy barriers limiting access to current evidence-based obesity treatments for private and public health-insured beneficiaries. In a 2019 report by the US Government Accountability Office, two-thirds (68%) of obesity drug payments were out-of-pocket, and only one-fourth (25%) was paid by private insurers.<sup>76</sup> The statutory prohibition of drugs for weight loss, even if used for a noncosmetic purpose, is excluded from the definition of a Part D drug covered under Medicare Part D, which sets a precedent for all payors to restrict their coverage and therefore access. Diabetes care and education specialists should become familiar with the pharmacy benefits managers and their formulary policies to advocate for improved access to evidence-based and FDA-approved medications for the treatment of obesity-now recognized as a chronic disease.77

Table 1. Pharmacotherapy Options—FDA APPROVED AGENTS FOR OBESITY MANAGEMENT IN ADULTS-OCTOBER 2023

Medication (Brand Name)	Phentermine (Adipex-P <sup>®</sup> , Lomaira™)	Phentermine/ Topiramate ER (Qsymia®)	Naltrexone/ buproprion ER (Contrave®)	Orlistat(Alli™ OTC, Xenical® Rx)	Liraglutide (Saxenda®)*†	Semaglutide (Wegovy®)*†
Drug Class	Sympatho- mimetic anorectic/ stimulant	Sympatho-mimetic anorectic/ antiepileptic combination	Opioid antagonist/ aminoketone antidepressant combination	Lipase inhibitor	Glucagon- like peptide 1 receptor agonist (GLP-1 RA)*†	Glucagon- like peptide 1 receptor agonist (GLP-1 RA)*†
Mechanism of Action	Adrenergic agonist that promotes weight loss by activation of the sympathetic nervous system	Sympathomimetic; amine/GABA modulator and carbonic anhydrase inhibitor	Opioid receptor antagonist; dopamine & norepinephrine reuptake inhibitor	Pancreatic and gastric lipase inhibitor	GLP-1 receptor agonist (RA)	GLP-1 receptor agonist (RA)
Recommended Dose and Route of Administration	37.5 mg by mouth daily or 8 mg three (3) times daily. Only for short-term use, less than or equal to 12 weeks.	3.75 mg/23 mg by mouth once daily for 14 days, titrated to 7.5 mg/46 mg for 12 wks. If at least 3% weight loss, discontinue, or titrate to 11.25 mg/69 mg for 14 dys, then titrate to 15 mg/92 mg	8 mg/90 mg by mouth in the morning for 1 week, titrated to 8 mg/90 mg twice daily for 1 week, then to 16 mg/180 mg in the AM and 8 mg/90 mg in the evening for 1 week, and then 16 mg/180 mg, 2 times daily	60 mg by mouth three times daily (OTC). 120 mg 3 times daily (prescription)	Initiate 0.6 mg injected subcutaneously (subQ) once DAILY for 1 week, titrate by 0.6 mg daily at weekly intervals until 3 mg target is reached	Initiate 0.25 mg injected subcutaneously (subQ) once WEEKLY for 4 weeks, then 0.5 mg weekly for 4 weeks, then 1 mg weekly for 4 weeks, the 1.7 mg weekly for 4 weeks, then target dose of 2.4 mg weekly
Mechanism of Action	Adrenergic agonist that promotes weight loss by activation of the sympathetic nervous system	Sympathomimetic; amine/GABA modulator and carbonic anhydrase inhibitor	Opioid receptor antagonist; dopamine & norepinephrine reuptake inhibitor	Pancreatic and gastric lipase inhibitor	GLP-1 receptor agonist (RA)	GLP-1 receptor agonist (RA)
Contraindications	Contraindicated for use in combination with monoamine oxidase inhibitors (MAO's), pregnancy	Hyperthyroidism, glaucoma, within 14-days of MAOI therapy, pregnancy	Concomitant use of bupropion-containing products, chronic opioid use, opiate agonist, acute opioid withdrawal, uncontrolled hypertension, seizure disorder, bulimia, abrupt discontinuation of alcohol, use with benzodiazepines, barbiturates, antiepileptic drugs, MAOI, initiation of naltrexone/ bupropion, or pregnancy	Chronic malabsorption syndrome, cholestasis, pregnancy	Person's history or family history of medullary thyroid cancer (MTC), multiple endocrine neoplasia syndrome type 2 (MENS2), pregnancy. AVOID DPP-4 meds as there is not an added benefit, increase cost	Person's history or family history of medullary thyroid cancer (MTC), multiple endocrine neoplasia syndrome type 2 (MENS2), pregnancy. AVOID DPP-4 meds as there is not an added benefit, increase cost

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Common Adverse Effects(a)	Dry mouth, insomnia, dizziness, irritability, pressure, elevated heart rate, headache	Insomnia, dry mouth, constipation, paresthesia, xerostomia, increased heart rate (dose dependent) insomnia, dizziness, dysgeusia, headache	Nausea constipation, headache, vomiting, dizziness, insomnia	Oily rectal leakage, flatulence with discharge, abdominal distress, steatorrhea, bowel urgency, oily evacuation, fecal incontinence, headache	Nausea, vomiting, diarrhea, esophageal reflux, constipation, headache, increased heart rate, hypo- glycemia, injection site reactions	Nausea, vomiting, diarrhea, esophageal reflux, constipation, headache, increased heart rate, hypo- glycemia, injection site reactions
Serious Adverse Effects (a)	Dyspnea, angina, severe hypertension	Topiramate is teratogenic (birth defects), cognitive impairment, acute angle-closure glaucoma	Depression, precipitation, or mania <b>BLACK BOX</b> <b>WARNING</b> : Risk of suicidal behavior/ ideation in a person with depression <24 years	Liver failure, oxalate nephropathy	Pancreatitis, acute kidney injury <b>BLACK BOX</b> <b>WARNING</b> : Risk of thyroid C-cell tumors in rodents; human relevance not determined	Pancreatitis, acute kidney injury <b>BLACK BOX</b> <b>WARNING</b> : Risk of thyroid C-cell tumors in rodents; human relevance not determined
Comments	Only use for < =12 weeks; Give 30 min before meals (breakfast or all 3 meals depending on dosage/ formulation)	Administer in the morning without regard to meals	Contraindicated in people with diabetes and with a seizure disorder; Do not give high-fat meals	Give with each meal containing fat; May result in malabsorption of fat-soluble vitamins & some medications	Administer without regard to meals	Allow at least 2 days between doses if changing day of administration
Average 1-yr Weight Loss: Mean Weight Ioss in clinical trials(b)	N/A ONLY USED SHORT-TERM	7.5/46mg: 6.7 kg 15/92mg: 9.9 kg ~5.1-10.9%	2-4.1 kg ~8.2-11.5%	60 mg: 2.5 kg 120 mg: 3.4 kg ~3 kg	5.8 to 5.9 kg ~6-8%	15.3 kg (in 68 wks) ~5.9%-3 mon; ~10.9%-6 mon

Limited safety and side effect information is provided; for a comprehensive discussion of safety considerations, please refer to the prescribing information for each medication. Pharmacotherapy for overweight and obesity should be used only as an adjunct to lifestyle therapy and not alone.

 ${\sf ER}{\sf =} {\sf extended release; N/A{\sf =} not applicable; OTC{\sf =} over the counter; Rx{\sf =} prescription$ 

\*Drug classes current at the time of writing.

<sup>†</sup>On November 8, 2023, a new dual-targeted, Glucagon-like peptide 1 receptor agonist (GLP-1 RA) and glucose-dependent insulinotropic polypeptide receptor (GIP), Tirzepatide (Zepbound<sup>™</sup>) injection was approved for the treatment for adults with obesity (BMI >= 30kg/m<sup>2</sup>) or overweight (BMI >= 27kg/m<sup>2</sup>) and also have weight-related medical problems.

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## **Surgical Considerations**

Bariatric surgery can reduce the size of the stomach reservoir, limiting the amount of food that can be eaten as well as affecting the absorption of nutrients.<sup>78-82</sup> Common types of bariatric surgery procedures include laparoscopic adjustable gastric banding (LAGB), laparoscopic sleeve gastrectomy (LSG), laparoscopic Roux-en-Y gastric bypass (RYGB), and laparoscopic biliopancreatic diversion (BPD), BPD/duodenal switch (BPD-DS). Each procedure has different processes and end results. The LAGB procedure places a band around the stomach, semipermanently altering the size.<sup>81</sup> The LSG procedure resects the stomach permanently removing about 80% of the stomach. The RYGB transects the stomach to form a smaller pouch reducing both volume and decreasing absorption and the BPD-DS procedure combines the previous transection with about 75% removal of the stomach.

People are considered candidates for evaluation for bariatric surgery if they meet 1 of the 3 following conditions: (1) a BMI

greater than or equal to 40 kg/m<sup>2</sup> without coexisting medical conditions; (2) a BMI greater than or equal to 35 kg/m2 with 1 or more obesity-related comorbidities including, but not limited to, T2D, hypertension, hyperlipidemia, obstructive sleep apnea, asthma, severe urinary incontinence, and debilitating arthritis; or (3) a BMI 30 to 34.9 kg/m<sup>2</sup> with diabetes or metabolic syndrome.<sup>26</sup> These procedures have shown major benefits to health, survival, and QOL, primarily through the impressive weight loss outcomes reporting reductions as great as 30 to 40 kg.79 Of note, bariatric procedures will affect drug absorption either through pH or surface area available for absorption.<sup>80</sup> For people with diabetes, insulin and insulin secretagogue doses should be adjusted to minimize the risk of hypoglycemia. Metformin, however, can be continued at preoperative doses.74 While the complete effects of bariatric surgery on diabetes are yet to be elucidated, reports have indicated the potential remission of T2D following surgery.79

	Expected % excess body weight at 2 years	Optimal benefits likely for those with:	Pros	Cons	Comments
Vertical Sleeve Gastric Bypass (VSG)	50% to 70% (3-year data)	Metabolic Disease	Improves metabolic disease, maintains small intestine anatomy, micronutrient deficiencies infrequent	No long-term data	Most common first step of the stage approach
Laparoscopic Adjustable Gastric Banding	30% to 50%	Lower BMI; no metabolic disease	Least invasive; removable	25% to 40% 5-year removal rate internationally	Metabolic benefits achieved are dependent on weight loss
Roux-en-Y Gastric Bypass	60% to 75%	Higher BMI, GERD, Type 2 Diabetes	Greater improvement in metabolic disease	Increased risk of malabsorptive complications	Largest data set but the most technically challenging
Loop Duodenal Switch	70% to 80%	Higher BMI, Type 2 Diabetes	Potentially simpler and safer than BD-DS with less micronutrient deficiencies	No long-term data available	2-step procedure VSG followed by single anastomosis
Biliopancreatic Diversion with Duodenal Switch (BD-DS)	70% to 80%	Higher BMI, Type 2 Diabetes	Greatest amount of weight loss and reduction of metabolic disease	Higher increased risk of macro and micronutrient deficiencies than bypass	Most technically challenging

Excess body weight = total body weight - lean body weight

## Conclusion

Diabetes care and education specialists should address obesity as a component of diabetes self-management to empower people with diabetes to adopt appropriate health behavior changes. The most effective behavioral weight loss treatment is in-person, high-intensity (ie,  $\geq$ 14 sessions in 6 months) comprehensive weight loss interventions provided in individual or group sessions.<sup>53</sup>

The following is a list of recommendations within this advisory that has been compiled to help guide the DCES during counseling with the person with overweight or obesity to help them manage, reduce the risk of, or delay diabetes.

- » Establish a positive person-centered partnership using nonjudgmental bias, empathetic communication, and counseling strategies
- » Discuss factors influencing body weight and individualize nutrition-related, physical activity, and weight management goals
- » Discuss weight loss treatment options
- » Communicate with physicians to consider medications for diabetes that are weight neutral or may favorably impact weight loss
- » Create a support system by communicating with physicians and other HCPs to encourage and support health behavior change in persons with obesity and diabetes or who are at risk for diabetes
- » Refer to community resources and programs for obtaining affordable, healthy food and beverages and opportunities for physical activity
- » Promote strategies for healthy coping to overcome barriers affecting goal attainment

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