

Treatment of Obesity in Patients With Diabetes

Carolyn T. Bramante,¹ Clare J. Lee,² and Kimberly A. Gudzone^{1,3}

■ **IN BRIEF** More than 90% of patients with diabetes have overweight or obesity. Whereas weight gain and obesity worsen insulin resistance, weight loss slows the progression of diabetes complications. Given the elevated risk for diabetes complications in patients with obesity, clinicians must understand how to treat obesity in their patients with diabetes, including providing counseling and behavioral management, referral to weight loss programs, and medication management. This article summarizes guidelines for diagnosing and managing obesity in people with diabetes.

More than 90% of patients with type 2 diabetes have a BMI ≥ 25.0 kg/m² (1). In 2013, the American Medical Association designated obesity as a chronic disease (2), and there is growing appreciation of obesity as a complex chronic condition caused by multiple factors, including behaviors, genetics, and the environment. Adipose tissue is an endocrine organ, releasing and responding to hormones that contribute to metabolic disease, including diabetes (2). Obesity affects all organ systems, causing increased rates of cardiovascular and renal disease, certain cancers, arthritis, and sleep apnea (3–6). Given the high prevalence of concomitant disease, most clinicians will have patients with both diabetes and obesity.

Previous studies have shown that a lack of time and training limits clinicians' desire to engage patients in weight management discussions (7,8). However, research shows that clinicians can successfully provide behavioral counseling for obesity and also have important roles in referring to weight loss programs as needed, following up on patients' weight loss

goals, and providing ongoing support and encouragement (9–13). Thus, it is important for clinicians to understand obesity treatment in patients with diabetes because modest weight losses of 3–5% of initial body weight improve glucose intolerance and A1C, slow complications of diabetes, reduce the need for glucose-lowering agents, and prevent the progression of prediabetes to type 2 diabetes (3,14,15). This article will summarize guidelines for nonsurgical treatment of obesity in patients with diabetes.

Diagnosing Obesity

Obesity is traditionally diagnosed by BMI, which is an accurate approximation of adiposity for most individuals. Recent guidelines from the American Academy of Clinical Endocrinologists (AACE) and the American Heart Association/American College of Cardiology/The Obesity Society (AHA/ACC/TOS) recommend that clinicians evaluate metabolic health in addition to BMI (2,3). Patients should be screened for obesity with annual calculation of BMI after measuring both height and weight (2,3). For patients with a BMI ≥ 25 kg/m² (≥ 23 kg/m² in those

¹Division of General Internal Medicine, ²Division of Endocrinology, Diabetes, and Metabolism, and ³The Welch Center for Prevention, Epidemiology and Clinical Research, The Johns Hopkins University, Baltimore, MD

Corresponding author: Carolyn T. Bramante, cb@jhmi.edu

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TABLE 1. Weight-Related Complications Caused/Exacerbated by Excess Adiposity (2)

| | |
|-----------------------------|------------------------------------|
| • Elevated blood pressure | • Reactive airway disease |
| • Hypertriglyceridemia | • Nonalcoholic fatty liver disease |
| • Hypercholesterolemia | • Gastroesophageal reflux disease |
| • Decreased HDL cholesterol | • Male hypogonadism |
| • Osteoarthritis | • Female infertility |
| • Depression | • Polycystic ovary disease |
| • Sleep apnea | • Stress urinary incontinence |

TABLE 2. The 5 A's Model for Behavior Change and Its Use for Weight Management in Practice (22)

| | |
|------------|---|
| 1. Assess | <ul style="list-style-type: none"> • Assess patients for obesity or overweight with metabolic risk factors • Assess for patients' readiness and ability to make change at this time |
| 2. Advise | <ul style="list-style-type: none"> • Advise patients about the increased risks of cardiovascular disease with excess adiposity • Advise patients of the health benefits of weight loss and lifestyle change |
| 3. Agree | <ul style="list-style-type: none"> • Agree with patients on a quantifiable and achievable weight loss goal that will lead to health benefits (i.e., a goal of losing 5% of initial body weight in 6 months) |
| 4. Assist | <ul style="list-style-type: none"> • Assist patients in defining a weight management strategy (i.e., practice-based weight loss counseling vs. referral to a weight loss program) |
| 5. Arrange | <ul style="list-style-type: none"> • Arrange follow-up to create a structure for accountability and feedback on progress |

of Asian ethnicities), clinicians should assess for excess adiposity by taking into account muscularity, hydration status, edema, and sarcopenia (2). For patients with a BMI ≥ 25 kg/m² but < 35 kg/m², clinicians should assess waist circumference to further stratify patients by risk. In the United States, a waist circumference ≥ 88 cm (35 inches) in women and ≥ 102 cm (40 inches) in men indicates abdominal adiposity and increased risk for cardiometabolic disease (2). In Southeast Asian and East Asian populations, a waist circumference ≥ 80 cm (31 inches) for women and ≥ 85 cm (33 inches) for men indicate higher risk (2). Staging obesity via associated comorbid conditions and weight-related health and functional limitations has been recommended but is not yet codified in most published guidelines.

Patients who are diagnosed with overweight or obesity should also be

screened for, at minimum, the comorbidities listed in Table 1, which are associated with increased adiposity (2).

Approaching the Weight Loss Discussion

Clinicians should be sensitive when discussing the diagnosis of obesity with patients. Several studies have shown that patients with obesity are regarded with less respect than normal-weight patients (16); experiencing such biased interactions has been shown to negatively affect weight-related behaviors such as binge-eating, weight trajectory, and health outcomes (17). Approaching discussions about weight loss with the 5 A's model for behavior change has been shown to increase patients' motivation to lose weight and improve their success at weight loss (18–21). The 5 A's, described in Table 2 (22), are an important framework regardless of

whether clinicians will provide weight loss support in their practice or will be referring patients to a weight loss program.

Weight Loss Goals

Weight loss of 5–10% of baseline body weight is recommended as an initial goal of treatment, and this amount of weight loss is associated with a 0.6–1.0% reduction in A1C and numerous other health improvements (3). However, weight loss of as little as 2–5% produces a clinically meaningful reduction in fasting blood glucose (20 mg/dL) (3). The American Diabetes Association (ADA) recommends that patients with prediabetes lose 7% of baseline body weight to avoid developing diabetes (23).

In adult patients with type 2 diabetes, cohort studies have shown that individuals who lost 9–13 kg had a 25% reduction in all-cause mortality compared to weight-neutral patients (3). In the Look AHEAD (Action for Health in Diabetes) trial, adults with type 2 diabetes and overweight/obesity who were randomized to an intensive lifestyle intervention for weight loss had a 6.0% weight loss at 9 years compared to a 3.5% weight loss in the control group. Although the intervention group did not achieve a significant reduction in cardiovascular events compared to the control group, numerous other health improvements occurred, including reduced sleep apnea, lower A1C, reduced need for diabetes medications, improved mobility and quality of life, fewer hospitalizations, and reduced health care costs (24,25). Moreover, a secondary analysis of participants who lost and sustained $\geq 10\%$ of their body weight, which included $> 25\%$ of intervention subjects, did show significant improvements in cardiovascular morbidity and mortality (26–29). A sustained 7% weight loss improves many other outcomes in patients with diabetes and overweight/obesity, including fitness, waist cir-

TABLE 3. Common Commercial Weight Loss Programs' Weight Loss and Glycemic Outcomes In RCTs

| | Time Point | Mean Weight Loss at Time Point (kg) | RCTs Conducted in Patients With Diabetes? | A1C Change at Time Point (%) | Patients Who Reduced Diabetes Medications at Time Point (%) |
|-----------------|------------|-------------------------------------|---|------------------------------|---|
| Weight Watchers | 12 Months | -3.0 to -9.1 | No | — | — |
| Jenny Craig | 12 Months | -6.6 to -10.1 | Yes | -0.3 to -0.7 | 30-39 (oral); 63-90 (insulin) |
| Nutrisystem | 6 Months | -7.3 to -10.8 | Yes | -0.7 | 28 (all medications) |

cumference, blood pressure, sexual functioning, and reported peripheral neuropathy symptoms (15,26,27,30).

Clinician-Managed Weight Loss Support Versus Referral to a Weight Loss Program

When patients are ready to discuss weight loss strategies, clinicians should determine whether they are able to provide intensive counseling and follow-up for weight loss in their clinical practice or whether they should instead refer patients to an outside weight loss program. The 2016 ADA guidelines and the 2013 AHA/ACC/TOS guidelines recommend that clinicians refer patients with obesity and type 2 diabetes to high-intensity programs (3,23,31). Per these guidelines, high-intensity programs involve at least 14–16 visits over 6 months. In-person programs result in more weight loss than electronically delivered interventions, but both produce more weight loss than no program (3). Whether clinicians provide intensive support for weight loss or refer patients to a high-intensity program, they should see patients at least every 3 months to monitor their blood glucose control because patients may require decreased doses of glucose-lowering medications as they lose weight (23).

Clinicians can consider managing weight loss in their patients if they are able to provide the high frequency of visits, as well as the necessary behavioral and nutritional support. Individualized weight loss support is also contingent on

clinicians having enough time to take in-depth histories of patients' daily routines and eating behaviors (22). The AACE/ACE guidelines recommend that a weight loss intervention involve behavioral therapy focusing on goal-setting, education, self-monitoring, problem-solving strategies, stimulus control, behavioral contracting, stress reduction, psychological evaluation (with treatment if indicated), cognitive restructuring, motivational interviewing, and mobilization of social support structures (2,32). Medicare covers obesity screening and intensive counseling in the primary care setting, which may encourage clinicians to provide these services (33,34).

Given the intensity of follow-up required, many clinicians may prefer to refer patients to evidence-based weight loss programs in their community. However, these clinicians need to be aware that guideline-adherent community weight loss programs may be difficult to find (35). Popular commercial weight loss programs are available in many communities, and guidelines suggest that referral to an evidence-based commercial weight loss program that has documented efficacy via rigorous scientific studies is an acceptable strategy (3).

Table 3 summarizes outcomes with Weight Watchers, Jenny Craig, and Nutrisystem, which typically comprise the majority market share in the commercial weight loss industry (31,36–41). Both Weight Watchers and Jenny Craig have had randomized, controlled trials (RCTs)

documenting their long-term weight loss efficacy, and Jenny Craig has demonstrated long-term glycemic benefits among patients with diabetes (3,42–44).

Another community referral option is the Centers for Disease Control and Prevention (CDC) National Diabetes Prevention Program (DPP), which is based on the Diabetes Prevention Program RCT, in which an intensive behavioral program delayed the development of type 2 diabetes and showed a 58% reduced progression to diabetes compared to a control group (45,46). Patients with prediabetes can be referred to a clinical center or YMCA that has a certified National DPP program. Beginning in January 2018, National DPP interventions will be covered by Medicare, which is a significant benefit for Medicare patients with prediabetes (47).

Behavioral Components of Weight Loss and Weight Loss Maintenance

The goal of weight-related behavioral changes and programs should be to achieve a caloric deficit of 500–750 kcal/day (3,23). Dietary approaches that selectively restrict fat or carbohydrates or selectively increase protein or fiber are equally effective in producing weight loss if they meet the targeted reduction in calories (Table 4) (3,23). Each of these dietary approaches is considered safe for patients with diabetes, and each is effective if patients are able to adhere to the caloric restrictions (2,23). Patients may believe that they will have a higher likelihood of

TABLE 4. Eating Patterns With Equivalent Effects on Weight Loss (2)

| | |
|--|---|
| <ul style="list-style-type: none"> • Low glycemic index/load • High protein • Low fat | <ul style="list-style-type: none"> • Low carbohydrate • Moderate carbohydrate–moderate protein • Mediterranean style |
|--|---|

success if they use a meal-replacement option, and this option may be particularly helpful to patients who have limited time or ability to prepare food. As patients achieve caloric reduction, they may need to monitor their blood glucose more often depending on which glucose-lowering medication(s) they take.

It is important to understand that reducing caloric intake is more effective at achieving initial weight loss than only increasing exercise (48,49). Patients who made dietary changes alone lost 7 kg more at the 6-month follow-up than patients who added physical activity alone (49). Physical activity remains important for maintaining weight loss but should not be the primary focus of behavioral change for weight loss. Patients on insulin should increase glucose monitoring when starting a new exercise regimen to avoid hypoglycemia during or after exercise. The CDC does recommend that all adults, regardless of their weight or diabetes status, get 150 min/week of moderate aerobic activity and perform resistance exercise twice per week (32). Achieving this amount of physical activity, as well as avoiding long periods of inactivity, are good initial goals for patients who are not physically active (2).

Self-monitoring is another important tool in weight loss and weight maintenance efforts (50). Daily self-weighing has been shown to improve individuals' ability to refrain from excess caloric intake (51) and thus promotes weight loss (52). Breaks in daily weighing are associated with weight regain (52). Additionally, both the AHA/ACC/TOS and AACE/ACE guidelines rec-

ommend monitoring physical activity and food intake (3,53).

For maintaining weight loss, the ADA guidelines recommend that patients with diabetes be referred to a long-term (at least 1 year) weight maintenance program that involves at least monthly visits, at least weekly weight measurements, and at least 200–300 min/week of physical activity (23).

Medication Management

In addition to promoting patients' healthy lifestyle changes, managing medications is an important role for clinicians in treating patients with type 2 diabetes and obesity. Clinicians should consider altering the diabetes medication regimen and using weight loss medications for these patients.

First, clinicians should consider using the following glucose-lowering medications that are weight neutral or may promote weight loss: metformin, pramlintide, glucagon-like peptide 1 (GLP-1) receptor agonists, dipeptidyl peptidase 4 (DPP-4) inhibitors, and sodium–glucose cotransporter 2 (SGLT2) inhibitors. Metformin has been associated with a 3-kg weight loss (23,54–56). In addition to being associated with a 3.7-kg weight loss, pramlintide can also lower daily insulin requirements in patients with diabetes on insulin therapy (57). GLP-1 receptor agonists have been associated with a 5.3-kg weight loss (58). DPP-4 inhibitors are generally weight neutral (59,60). Finally, SGLT2 inhibitors can promote a 2.4-kg weight loss and lower insulin requirements (61). Of note, there is generally no benefit to using DPP-4 inhibitors and GLP-1 receptor agonists simultaneously because they work on the same pathway. Further

discussion on pharmacotherapy for obesity in patients with diabetes is covered elsewhere in this issue (p. 250).

In addition to avoiding diabetes medications that are associated with weight gain (e.g., sulfonylureas, thiazolidinediones, and insulin), clinicians should also assess for other medications that are associated with weight gain. When possible, clinicians should attempt to reduce or find alternatives to common medications that can increase appetite and promote weight gain, including sedating antihistamines, steroids, some selective serotonin reuptake inhibitors, beta-blockers, and most antipsychotic agents (62).

The AACE/ACE guidelines recommend that patients with diabetes and a BMI ≥ 27 kg/m² be prescribed weight loss medications (53). Treatment of obesity through pharmacotherapy, in conjunction with a healthy lifestyle, directly improves glycemic control (63,64). Five medications are now approved by the U.S. Food and Drug Administration (FDA) for long-term use for weight loss. Table 5 provides an overview of their weight loss and A1C outcomes and their side effects (62,65–69). Additionally, sympathomimetic appetite suppressant medications are approved for short-term use (up to 12 weeks). To avoid weight regain, the ADA recommends long-term use of weight loss medication for patients who successfully lose weight on the medication. Therefore, this article will focus only on medications approved for long-term use (70). For patients whose weight loss is <5% of initial body weight after the initial treatment period on a given medication (various medications have different initial treatment periods), the medication should be discontinued and an alternative medication or approach should be tried (23). The AACE/ACE guidelines recommend monitoring patients who are on insulin or sulfonylureas for hypoglycemia after starting any weight loss medication (2,53). When considering these

TABLE 5. Medications Approved by the FDA for Long-Term Use for Weight Management

| Medication (Trade Names) | Mechanism of Action | Five Most Common Side Effects | Possible Safety Concerns* | Mean 1-Year Weight Loss Compared to Placebo (Dose) | A1C Change in Patients With Diabetes (%) |
|---------------------------------|--|--|---|---|--|
| Decreases absorption | | | | | |
| Orlistat (Alli, Xenical) | Lipase inhibitor | Abdominal pain, flatulence, fecal urgency, back pain, and headache | Fat-soluble vitamin deficiencies, altered absorption of medications, cholelithiasis, nephrolithiasis | 3.4 kg, 4.0% (120 mg TID) | -0.7 |
| Suppresses appetite | | | | | |
| Lorcaserin (Belviq) | Serotonin receptor agonist | Headache, nausea, dizziness, fatigue, and nasopharyngitis | Serotonin syndrome, hypertension, edema, avoid in liver and renal failure | 3.3 kg, 3.6% (10 mg BID) | -1.1† |
| Phentermine/Topiramate (Qsymia) | Norepinephrine release, GABA receptor modulation | Constipation, paresthesia, insomnia, nasopharyngitis, and xerostomia | Birth defects, cognitive impairment, acute angle-closure glaucoma, lactic acidosis with metformin, avoid in renal failure | 6.7 kg, 6.6% (7.5/46 mg daily) 8.9 kg, 9.0% (15/92 mg daily) | -0.4 |
| Naltrexone/Bupropion (Contrave) | Opiate antagonist, decreased re-uptake of norepinephrine | Constipation, nausea, headache, xerostomia, and insomnia | Depression, anxiety, acute angle-closure glaucoma, avoid in patients with uncontrolled hypertension and renal failure | 4.1 kg, 5.2% (16/80 mg BID) | -0.6 |
| Liraglutide (Saxenda) | GLP-1 receptor agonist | Hypoglycemia, constipation, nausea, headache, and indigestion | Gastroparesis, suicidal ideation, increased heart rate, caution in pancreatitis and cholelithiasis | 4.5 kg, 5.6% (3 mg daily) | -0.6 to -1.8 |

*A comprehensive list of safety concerns can be found in each medication's package insert, which is available from the manufacturing pharmaceutical company. †A1C change has only been assessed in patients with prediabetes (66). BID, twice daily; GABA, gamma-aminobutyric acid; TID, three times daily.

medications, clinicians should discuss typical weight loss results, side effects, and medication costs with their patients.

Obesity Treatment in Type 1 Diabetes

Obesity is increasingly common in patients with type 1 diabetes; in 1988, 25% of 40- to 49-year-olds with type 1 diabetes had overweight or obesity compared to 68% in 2007 (71). Patients with type 1 diabetes will need to continue to take their insulin and strive for a caloric reduction of 500–700 kcal/day to lose weight. The ADA recommends that adults with type 1 diabetes meet the CDC recommendations for physical activity for all adults—150 min/week of moderate aerobic activity and two sessions of resistance training per week (23). Patients with type 1 diabetes starting a new exercise regimen or caloric reduction will need to monitor closely for hypoglycemia. In addition, the weight loss medications described above can also be considered for patients with type 1 diabetes. Pramlintide may be considered in patients with type 1 diabetes as a means of reducing their insulin requirements and promoting weight loss.

Conclusion

Weight loss is particularly important for individuals who have both diabetes and obesity. Because of the high prevalence of their co-occurrence, clinicians should be aware of the guidelines for treating obesity in patients with type 2 diabetes. The ADA, AACE/ACE, and AHA/ACA/TOS guidelines all recommend referring patients to high-intensity weight loss programs. Caloric reduction is the mainstay of weight loss, and increased exercise is crucial for maintaining weight loss. Medication management is also important for these patients, whether that involves selecting diabetes medications that promote weight loss or are weight neutral, prescribing medications approved for weight loss, or both.

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Duality of Interest

No potential conflicts of interest relevant to this article were reported.

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