



American Diabetes Association

6. Obesity Management for the Treatment of Type 2 Diabetes

Diabetes Care 2016;39(Suppl. 1):S47–S51 | DOI: 10.2337/dc16-S009

There is strong and consistent evidence that obesity management can delay progression from prediabetes to type 2 diabetes (1,2) and may be beneficial in the treatment of type 2 diabetes. In overweight and obese patients with type 2 diabetes, modest and sustained weight loss has been shown to improve glycemic control and to reduce the need for glucose-lowering medications (3–5). Small studies have demonstrated that in obese patients with type 2 diabetes more extreme dietary energy restriction with very low-calorie diets can reduce A1C to <6.5% (48 mmol/mol) and fasting glucose to <126 mg/dL (7.0 mmol/L) in the absence of pharmacological therapy or ongoing procedures (6,7). Weight loss–induced improvements in glycemia are most likely to occur early in the natural history of type 2 diabetes when obesity-associated insulin resistance has caused reversible β -cell dysfunction but insulin secretory capacity remains relatively preserved (5,8). Although the Action for Health in Diabetes (Look AHEAD) trial did not show that an intensive lifestyle intervention reduced cardiovascular events in overweight or obese adults with type 2 diabetes (9), it did show the feasibility of achieving and maintaining long-term weight loss in patients with type 2 diabetes.

LOOK AHEAD

In the Look AHEAD intensive lifestyle intervention group, mean weight loss was 4.7% (SE 0.2) at 8 years (10). Approximately 50% of intensive lifestyle intervention participants lost $\geq 5\%$ and 27% lost $\geq 10\%$ of their initial body weight at 8 years (10). Participants randomly assigned to the intensive lifestyle group achieved equivalent risk factor control but required fewer glucose-, blood pressure-, and lipid-lowering medications than those randomly assigned to standard care. Secondary analyses of the Look AHEAD trial and other large cardiovascular outcome studies document other benefits of weight loss in patients with type 2 diabetes, including improvements in mobility, physical and sexual functioning, and health-related quality of life (11). The goal of this section is to provide evidence-based recommendations for dietary, pharmacological, and surgical interventions for obesity management as treatments for hyperglycemia in type 2 diabetes.

ASSESSMENT

Recommendation

- At each patient encounter, BMI should be calculated and documented in the medical record. **B**

At each routine patient encounter, BMI should be calculated from the height and weight. BMI should be classified to determine the presence of overweight or obesity, discussed with the patient, and documented in the patient record (**Table 6.1**). In Asian Americans, the BMI cutoff points to define overweight and obesity are lower: normal (<23 kg/m²), overweight (23.0–27.4 kg/m²), obese (27.5–37.4 kg/m²), and extremely obese (≥ 37.5 kg/m²) (12). Providers should advise overweight and obese patients that higher BMIs increase the risk of cardiovascular disease and all-cause mortality. Providers should assess each patient's readiness to achieve weight loss and jointly determine weight loss goals and intervention strategies. Strategies include diet, physical activity, behavioral therapy, pharmacological therapy, and bariatric surgery (**Table 6.1**). The latter two strategies may be prescribed for carefully selected patients as adjuncts to diet, physical activity, and behavioral therapy.

Suggested citation: American Diabetes Association. Obesity management for the treatment of type 2 diabetes. Sec. 6. In Standards of Medical Care in Diabetes—2016. Diabetes Care 2016; 39(Suppl. 1):S47–S51

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DIET, PHYSICAL ACTIVITY, AND BEHAVIORAL THERAPY

Recommendations

- Diet, physical activity, and behavioral therapy designed to achieve 5% weight loss should be prescribed for overweight and obese patients with type 2 diabetes ready to achieve weight loss. **A**
- Such interventions should be high intensity (≥ 16 sessions in 6 months) and focus on diet, physical activity, and behavioral strategies to achieve a 500–750 kcal/day energy deficit. **A**
- Diets that provide the same caloric restriction but differ in protein, carbohydrate, and fat content are equally effective in achieving weight loss. **A**
- For patients who achieve short-term weight loss goals, long-term (≥ 1 -year) comprehensive weight maintenance programs should be prescribed. Such programs should provide at least monthly contact and encourage ongoing monitoring of body weight (weekly or more frequently), continued consumption of a reduced calorie diet, and participation in high levels of physical activity (200–300 min/week). **A**
- To achieve weight loss of $> 5\%$, short-term (3-month) high-intensity lifestyle interventions that use very low-calorie diets (≤ 800 kcal/day) and total meal replacements may be prescribed for carefully selected patients by trained practitioners in medical care settings with close medical monitoring. To maintain weight loss, such programs must incorporate long-term comprehensive weight maintenance counseling. **B**

Among overweight or obese patients with type 2 diabetes and inadequate glycemic, blood pressure and lipid

control, and/or other obesity-related medical conditions, lifestyle changes that result in modest and sustained weight loss produce clinically meaningful reductions in blood glucose, A1C, and triglycerides (3–5). Greater weight loss produces even greater benefits, including reductions in blood pressure, improvements in LDL and HDL cholesterol, and reductions in the need for medications to control blood glucose, blood pressure, and lipids (9,10).

Lifestyle Interventions

Weight loss can be attained with lifestyle programs that achieve a 500–750 kcal/day energy deficit or provide approximately 1,200–1,500 kcal/day for women and 1,500–1,800 kcal/day for men, adjusted for the individual’s baseline body weight. Although benefits may be seen with as little as 5% weight loss, sustained weight loss of $\geq 7\%$ is optimal.

These diets may differ in the types of foods they restrict (such as high-fat or high-carbohydrate foods) but are effective if they create the necessary energy deficit (13–16). The diet choice should be based on the patient’s health status and preferences.

Intensive behavioral lifestyle interventions should include ≥ 16 sessions in 6 months and focus on diet, physical activity, and behavioral strategies to achieve an ~ 500 –750 kcal/day energy deficit. Interventions should be provided by trained interventionists in either individual or group sessions (17).

Overweight and obese patients with type 2 diabetes who have lost weight during the 6-month intensive behavioral lifestyle intervention should be enrolled in long-term (≥ 1 -year) comprehensive weight loss maintenance programs that provide at least monthly contact with a trained interventionist and focus on ongoing monitoring of body weight (weekly or more frequently), continued

consumption of a reduced calorie diet, and participation in high levels of physical activity (200–300 min/week). Some commercial and proprietary weight loss programs have shown promising weight loss results (18).

When provided by trained practitioners in medical care settings with close medical monitoring, short-term (3-month) high-intensity lifestyle interventions that use very low-calorie diets (defined as ≤ 800 kcal/day) and total meal replacements may achieve greater short-term weight loss (10–15%) than intensive behavioral lifestyle interventions that typically achieve 5% weight loss. Weight regain following the cessation of high-intensity lifestyle interventions is greater than following intensive behavioral lifestyle interventions unless a long-term comprehensive weight loss maintenance program is provided (19,20).

PHARMACOTHERAPY

Recommendations

- When choosing glucose-lowering medications for overweight or obese patients with type 2 diabetes, consider their effect on weight. **E**
- Whenever possible, minimize the medications for comorbid conditions that are associated with weight gain. **E**
- Weight loss medications may be effective as adjuncts to diet, physical activity, and behavioral counseling for selected patients with type 2 diabetes and $BMI \geq 27$ kg/m². Potential benefits must be weighed against the potential risks of the medications. **A**
- If a patient’s response to weight loss medications is $< 5\%$ after 3 months or if there are any safety or tolerability issues at any time, the medication should be discontinued and alternative medications or treatment approaches should be considered. **A**

When considering pharmacological treatments for overweight or obese patients with type 2 diabetes, providers should first consider their choice of glucose-lowering medications. Whenever possible, medications should be chosen to promote weight loss or to be weight neutral. Agents associated with weight loss include metformin, α -glucosidase inhibitors, glucagon-like peptide 1 agonists, amylin mimetics, and sodium–glucose cotransporter 2 inhibitors. Dipeptidyl

Table 6.1—Treatment for overweight and obesity in type 2 diabetes

Treatment	BMI category (kg/m ²)				
	23.0* or 25.0–26.9	27.0–29.9	30.0–34.9	35.0–39.9	≥ 40
Diet, physical activity, and behavioral therapy	†	†	†	†	†
Pharmacotherapy		†	†	†	†
Bariatric surgery				†	†

†Treatment may be indicated for selected motivated patients.

*Cutoff points for Asian American individuals.

peptidase 4 inhibitors appear to be weight neutral. Unlike these agents, insulin secretagogues, thiazolidinediones, and insulin have often been associated with weight gain (see Section 7 “Approaches to Glycemic Treatment”).

Concomitant Medications

Providers should carefully review the patient’s concomitant medications and, whenever possible, minimize or provide alternatives for medications that promote weight gain. The latter include atypical antipsychotics (clozapine, olanzapine, risperidone, etc.) and antidepressants (tricyclic antidepressants, selective serotonin reuptake inhibitors, and monoamine oxidase inhibitors), glucocorticoids, oral contraceptives that contain progestins, anticonvulsants including gabapentin, and a number of antihistamines and anticholinergics.

Approved Medications

The U.S. Food and Drug Administration (FDA) has approved five weight loss medications (or combination medications) for long-term use by patients with BMI ≥ 27 kg/m² with one or more obesity-associated comorbid conditions and by patients with BMI ≥ 30 kg/m² who are motivated to lose weight (21–23). Medications approved for long-term weight loss and weight loss maintenance and their advantages and disadvantages are summarized in **Table 6.2**. The rationale for weight loss medications is to help patients to more consistently adhere to low-calorie diets and to reinforce lifestyle changes including physical activity. Providers should be knowledgeable about the product label and should balance the potential benefits of successful weight loss against the potential risks of the medication for each patient. All medications are FDA pregnancy category X. These medications are contraindicated in women who are or may become pregnant. Women in their reproductive years must be cautioned to use a reliable method of contraception.

Assessing Efficacy and Safety

Efficacy and safety should be assessed at least monthly for the first 3 months of treatment. If a patient’s response is deemed insufficient (weight loss $< 5\%$) or if there are any safety or tolerability issues at any time, the medication should be discontinued and alternative medications or treatment approaches should be considered.

In general, pharmacological treatment of obesity has been limited by low adherence, modest efficacy, adverse effects, and weight regain after medication cessation (21).

BARIATRIC SURGERY

Recommendations

- Bariatric surgery may be considered for adults with BMI > 35 kg/m² and type 2 diabetes, especially if diabetes or associated comorbidities are difficult to control with lifestyle and pharmacological therapy. **B**
- Patients with type 2 diabetes who have undergone bariatric surgery need lifelong lifestyle support and annual medical monitoring, at a minimum. **B**
- Although small trials have shown a glycemic benefit of bariatric surgery in patients with type 2 diabetes and BMI 30–35 kg/m², there is currently insufficient evidence to generally recommend surgery in patients with BMI ≤ 35 kg/m². **E**

Bariatric and metabolic surgeries, either gastric banding or procedures that involve resecting, bypassing, or transposing sections of the stomach and small intestine, can be effective weight loss treatments for severe obesity when performed as part of a comprehensive weight management program with lifelong lifestyle support and medical monitoring. In one meta-analysis, gastric banding resulted in less weight loss than sleeve gastrectomy and Roux-en-Y gastric bypass (1-year excess weight loss $\sim 33\%$ vs. $\sim 70\%$) (24). National guidelines support consideration of bariatric surgery for people with type 2 diabetes with BMI > 35 kg/m².

Advantages

Treatment with bariatric surgery has been shown to achieve near or complete normalization of glycemia 2 years following surgery in 72% of patients (compared with 16% in a matched control group treated with lifestyle and pharmacological interventions) (25). A study evaluated the effectiveness of surgical intervention (Roux-en-Y gastric bypass or sleeve gastrectomy) and medical therapy compared with medical therapy alone (quarterly visits, pharmacological therapy, self-monitoring of blood glucose, diabetes

education, lifestyle counseling, and encouragement to participate in Weight Watchers) in achieving a target A1C $\leq 6\%$ (42 mmol/mol) at 3 years among obese patients with uncontrolled type 2 diabetes (mean A1C 9.3% [78 mmol/mol]). This A1C target was achieved by 38% ($P < 0.001$) in the gastric bypass group, 24% ($P = 0.01$) in the sleeve gastrectomy group, and 5% in the group that received only medical therapy (26). Diabetes remission rates tend to be higher with procedures that bypass portions of the small intestine and lower with procedures that only restrict the stomach.

Younger age, shorter duration of type 2 diabetes, lower A1C, higher serum insulin levels, and nonuse of insulin have all been associated with higher remission rates after bariatric surgery (27).

Although bariatric surgery has been shown to improve the metabolic profiles of morbidly obese patients with type 1 diabetes, the role of bariatric surgery in such patients will require larger and longer studies (28).

Disadvantages

Bariatric surgery is costly and has associated risks. Morbidity and mortality rates directly related to the surgery have decreased considerably in recent years, with 30-day mortality rates now 0.2% for laparoscopic procedures, similar to those for laparoscopic cholecystectomy, and 2.1% for open procedures (29,30). Outcomes vary depending on the procedure and the experience of the surgeon and center. Longer-term concerns include dumping syndrome (nausea, colic, diarrhea), vitamin and mineral deficiencies, osteoporosis, and, rarely, severe hypoglycemia from insulin hypersecretion. More recent studies also suggest that patients who undergo bariatric surgery may be at increased risk for substance use, including drug and alcohol use and cigarette smoking (31). Cohort studies attempting to match surgical and nonsurgical subjects suggest that the procedure may reduce longer-term mortality (25).

In contrast, a propensity score-adjusted analysis of older, severely obese patients in Veterans Affairs Medical Centers found that bariatric surgery was not associated with decreased mortality compared with usual care (mean follow-up 6.7 years) (32). Retrospective analyses

Table 6.2—Medications approved by the FDA for the long-term treatment of obesity

Generic drug name, (proprietary name[s]) and dosage strength and form	1-Year weight change status ²⁻⁵			Adverse effects ^{2,6-12}
	Average wholesale price (per month) ⁴	Average weight loss relative to placebo	% Patients with $\geq 5\%$ loss of baseline weight	
Lipase inhibitor				
Orlistat (Alli) 60 mg caps or orlistat (Xenical) 120 mg caps	\$41–82 (60 mg) \$615 (120 mg)	2.5 kg (60 mg) 3.4 kg (120 mg)	35–73%	Common ⁷ Abdominal pain/discomfort, oily spotting/stool, fecal urgency, malabsorption of fat-soluble vitamins (A, D, E, K) and medications (e.g., cyclosporine, thyroid hormone replacement, or anticonvulsants), potentiation of the effects of warfarin Serious ⁷ Liver failure and oxalate nephropathy
Selective serotonin (5-HT)_{2C} receptor agonist				
Lorcaserin (Belviq) 10 mg tabs	\$263	3.2 kg	38–48%	Common ⁷ Hypoglycemia, headache, fatigue Serious ⁷ Serotonin syndrome or NMS-like reactions, heart valve disorder (<2.4%), bradycardia
Sympathomimetic amine anorectic/antiepileptic combination				
Phentermine/topiramate ER (Qsymia) 3.75 mg/23 mg caps, 7.5 mg/46 mg caps, 11.25 mg/69 mg caps, 15 mg/92 mg caps	\$239 (maximum dose using the highest strength)	6.7 kg (7.5 mg/46 mg) 8.9 kg (15 mg/92 mg)	45–70%	Common ⁷ Paresthesia, xerostomia, constipation, headache Serious ⁷ Topiramate is teratogenic and has been associated with cleft lip/palate
Opioid antagonist/amino ketone antidepressant combination				
Naltrexone/bupropion (Contrave) 8 mg/90 mg tabs	\$239 (maximum dose)	2.0–4.1 kg (32 mg/360 mg)	36–57%	Common ⁷ Nausea, constipation, headache, vomiting Serious ⁷ Depression, precipitation of mania
Acylated human glucagon-like peptide 1 receptor agonist				
Liraglutide (Saxenda) 6 mg/mL pre-filled pen	\$1,282	5.8–5.9 kg	51–73%	Common ⁷ Hypoglycemia, nausea, vomiting, diarrhea, constipation, headache Serious ⁷ Pancreatitis, thyroid C-cell tumors in rodents, contraindicated in patients with personal/family history of MTC or MEN2, acute renal failure

All medications are FDA pregnancy category X; these medications are contraindicated in women who are or may become pregnant. Women in their reproductive years must be cautioned to use a reliable method of contraception. Caps, capsules; ER, extended release; MEN2, multiple endocrine neoplasia type 2; MTC, medullary thyroid carcinoma; NMS, neuroleptic malignant syndrome; s.c., subcutaneous; tabs, tablets.

¹RED BOOK Online. Micromedex 2.0 (electronic version). Truven Health Analytics, Greenwood Village, CO.

²Physicians' Desk Reference. PDR Network, LLC (electronic version). Truven Health Analytics, Greenwood Village, CO.

³Yanovski SZ, Yanovski JA. Long-term drug treatment for obesity: a systematic and clinical review. *JAMA* 2014;311:74–86.

⁴Astrup A, Carraro R, Finer N, et al; NN8022-1807 Investigators. Safety, tolerability and sustained weight loss over 2 years with the once-daily human GLP-1 analog, liraglutide. *Int J Obes (Lond)* 2012;36:843–854.

⁵Wadden TA, Hollander P, Klein S, et al; NN8022-1923 Investigators. Weight maintenance and additional weight loss with liraglutide after low-calorie-diet-induced weight loss: the SCALE Maintenance randomized study. *Int J Obes (Lond)* 2013;37:1443–1451.

⁶DrugPoints System (electronic version). Truven Health Analytics, Greenwood Village, CO.

⁷Selective common (defined as an incidence of $>5\%$) and serious adverse effects are noted. Refer to the medication package inserts for full information about adverse effects, cautions, and contraindications.

⁸Data of common adverse effects for Xenical were derived from seven double-blind, placebo-controlled clinical trials in mixed-type study populations (i.e., patients with or without type 2 diabetes), but the percentage of patients with type 2 diabetes was not reported. In clinical trials in obese patients with diabetes, hypoglycemia and abdominal distension were also observed.

⁹Data of common adverse effects for Belviq were derived from placebo-controlled clinical trials in patients with type 2 diabetes.

¹⁰Data of common adverse effects for Qsymia were derived from four clinical trials in mixed-type study populations (i.e., patients with or without type 2 diabetes); 13% had type 2 diabetes.

¹¹Data of common adverse effects for Contrave were derived from five double-blind, placebo-controlled clinical trials in mixed-type study populations (i.e., patients with or without type 2 diabetes); 13% had type 2 diabetes.

¹²Data of common adverse effects for Saxenda were derived from clinical trials in mixed-type study populations (i.e., patients with or without type 2 diabetes). Percentage of patients with type 2 diabetes was not reported.

and modeling studies suggest that bariatric surgery may be cost-effective or even cost-saving for patients with type 2 diabetes, but the results are largely dependent on assumptions about the long-term effectiveness and safety of the procedures (33,34). Understanding the long-term benefits and risks of bariatric surgery in individuals with type 2 diabetes, especially those who are not severely obese, will require well-designed clinical trials, with optimal medical therapy as the comparator (35). Unfortunately, such studies may not be feasible (36).

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