



American Diabetes Association

7. Obesity Management for the Treatment of Type 2 Diabetes

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There is strong and consistent evidence that obesity management can delay the progression from prediabetes to type 2 diabetes (1,2) and may be beneficial in the treatment of type 2 diabetes (3–8). 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 (7,9,10). 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 (5,8,10). 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. In Asian Americans, the BMI cutoff points to define overweight and obesity are lower than in other populations (**Table 7.1**) (11,12). 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 metabolic surgery (**Table 7.1**). The latter two strategies may be prescribed for carefully selected patients as adjuncts to diet, physical activity, and behavioral therapy.

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 should be individualized, as those 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

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Table 7.1—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	27.5* or 30.0–34.9	35.0–39.9	≥40
Diet, physical activity, and behavioral therapy	†	†	†	†	†
Pharmacotherapy		†	†	†	†
Metabolic surgery			†	†	†

*Cutoff points for Asian American individuals.

†Treatment may be indicated for selected motivated patients.

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) 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 (13,14).

Look AHEAD Trial

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 (13), it did show the feasibility of achieving and maintaining long-term weight loss in patients with type 2 diabetes. In the Look AHEAD intensive lifestyle intervention group, mean weight loss was 4.7% at 8 years (14). Approximately 50% of intensive lifestyle intervention participants lost ≥5% and

27% lost ≥10% of their initial body weight at 8 years (14). 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 (15).

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 ≥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 (16–19). Use of meal replacement plans prescribed by trained practitioners, with close patient monitoring, can be beneficial. Within the intensive lifestyle intervention group of the Look AHEAD trial, for example, use of a partial meal replacement plan was associated with improvements in diet quality (20). 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 (21).

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 (22).

When provided by trained practitioners in medical care settings with close medical monitoring, short-term (3-month) 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 very low-calorie diets is greater than following intensive behavioral lifestyle interventions unless a long-term comprehensive weight loss maintenance program is provided (23,24).

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 ≥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% weight loss 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**

Antihyperglycemic Therapy

When evaluating 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, sodium–glucose cotransporter 2 inhibitors, glucagon-like peptide 1 agonists, and amylin mimetics. Dipeptidyl 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 8 “Pharmacologic 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. Medications associated with weight gain include atypical antipsychotics (e.g., clozapine, olanzapine, risperidone, etc.) and antidepressants (e.g., 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 Weight Loss Medications

The U.S. Food and Drug Administration (FDA) has approved five weight loss medications (or combination medications) for long-term use (more than a few weeks) by patients with BMI ≥ 27 kg/m² with one or more obesity-associated comorbid conditions (e.g., type 2 diabetes, hypertension, and dyslipidemia) and by patients with BMI ≥ 30 kg/m² who are motivated to lose weight (25–27). Medications approved for long-term weight loss and weight loss maintenance and their advantages and disadvantages are summarized in **Table 7.2**. 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. 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 (25).

METABOLIC SURGERY

Recommendations

- Metabolic surgery should be recommended to treat type 2 diabetes in appropriate surgical candidates with BMI ≥ 40 kg/m² (BMI ≥ 37.5 kg/m² in Asian Americans), regardless of the level of glycemic control or complexity of glucose-lowering regimens, and in adults with BMI 35.0–39.9 kg/m² (32.5–37.4 kg/m² in Asian Americans) when hyperglycemia is inadequately controlled despite lifestyle and optimal medical therapy. **A**
- Metabolic surgery should be considered for adults with type 2 diabetes and BMI 30.0–34.9 kg/m² (27.5–32.4 kg/m² in Asian Americans) if hyperglycemia is inadequately controlled despite optimal medical control by either oral or injectable medications (including insulin). **B**
- Metabolic surgery should be performed in high-volume centers with multidisciplinary teams that understand and are experienced in the management of diabetes and gastrointestinal surgery. **C**
- Long-term lifestyle support and routine monitoring of micronutrient

and nutritional status must be provided to patients after surgery, according to guidelines for postoperative management of metabolic surgery by national and international professional societies. **C**

- People presenting for metabolic surgery should receive a comprehensive mental health assessment. **B** Surgery should be postponed in patients with histories of alcohol or substance abuse, significant depression, suicidal ideation, or other mental health conditions until these conditions have been fully addressed. **E**
- People who undergo metabolic surgery should be evaluated to assess the need for ongoing mental health services to help them adjust to medical and psychosocial changes after surgery. **C**

Several gastrointestinal (GI) operations promote dramatic and durable improvement of type 2 diabetes. Given the magnitude and rapidity of the effect of GI surgery on hyperglycemia, and experimental evidence that rearrangements of GI anatomy similar to those in some metabolic procedures directly affect glucose homeostasis (28), GI interventions have been suggested as treatments for type 2 diabetes, and in that context are termed “metabolic surgery.”

A substantial body of evidence has now accumulated, including data from numerous randomized controlled clinical trials, demonstrating that metabolic surgery achieves superior glycemic control and reduction of cardiovascular risk factors in obese patients with type 2 diabetes compared with various lifestyle/medical interventions (29). Improvements in micro- and macrovascular complications of diabetes, cardiovascular disease, and cancer have been observed only in nonrandomized observational studies (30–37). Cohort studies attempting to match surgical and nonsurgical subjects suggest that the procedure may reduce longer-term mortality (31).

On the basis of this mounting evidence, several organizations and government agencies have recommended expanding the indications for metabolic surgery to include patients with inadequately controlled type 2 diabetes and BMI as low as 30 kg/m² (27.5 kg/m² for

Table 7.2—Medications approved by the FDA for the long-term (more than a few weeks) 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) ¹	Average weight loss relative to placebo	% Patients with $\geq 5\%$ loss of baseline weight	Common ⁷	Serious ⁷
Lipase inhibitor					
Orlistat (Alli) 60 mg caps or orlistat (Xenical) 120 mg caps	\$43-86 (60 mg); \$670 (120 mg)	2.5 kg (60 mg); 3.4 kg (120 mg)	35-73%	Abdominal pain/discomfort, oily spotting/stool, fecal urgency, flatulence, 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	Liver failure and oxalate nephropathy
Selective serotonin (5-HT) 5-HT_{2c} receptor agonist					
Lorcaserin (Belviq) 10 mg tabs	\$263	3.2 kg	38-48%	Hypoglycemia, headache, fatigue	Serotonin syndrome or NMS-like reactions, suicidal ideation, heart valve disorder (<2.4%), bradycardia
Sympathomimetic amine anorectic/antiepileptic combination					
Phentermine/topiramate ER (Qsymia)	\$239 (maximum dose using the highest strength)	6.7 kg (7.5 mg/46 mg); 8.9 kg (15 mg/92 mg)	45-70%	Paresthesia, xerostomia, constipation, headache	Topiramate is teratogenic and has been associated with cleft lip/palate
3.75 mg/23 mg caps, 7.5 mg/46 mg caps, 11.25 mg/69 mg caps, 15 mg/92 mg caps					
Opioid antagonist/amino ketone antidepressant combination					
Naltrexone/bupropion (Contrave) 8 mg/90 mg tabs	\$251 (maximum dose)	2.0-4.1 kg (32 mg/360 mg)	36-57%	Nausea, constipation, headache, vomiting	Depression, precipitation of mania, contraindicated in patients with a seizure disorder
Acylated human glucagon-like peptide 1 receptor agonist					
Liraglutide (Saxenda) 6 mg/ml pre-filled pen	\$1,385	5.8-5.9 kg	51-73%	Hypoglycemia, nausea, vomiting, diarrhea, constipation, headache	Pancreatitis, thyroid C-cell tumors in rodents, contraindicated in patients with personal/family history of MTC or MEN2, acute renal failure

All 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 $\geq 5\%$) 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.

Asian Americans) (38–41). Please refer to the American Diabetes Association consensus report “Metabolic Surgery in the Treatment Algorithm for Type 2 Diabetes: A Joint Statement by International Diabetes Organizations” for a thorough review (29).

Randomized controlled trials with postoperative follow-up ranging from 1 to 5 years have documented sustained diabetes remission in 30–63% of patients (29). Available data suggest an erosion of diabetes remission over time: 35–50% or more of patients who initially achieve remission of diabetes eventually experience recurrence. However, the median disease-free period among such individuals following Roux-en-Y gastric bypass (RYGB) is 8.3 years (42,43). With or without diabetes relapse, the majority of patients who undergo surgery maintain substantial improvement of glycemic control from baseline for at least 5 (44) to 15 (31,32,43,45–47) years.

Younger age, shorter duration of diabetes (e.g., <8 years) (48), nonuse of insulin, and better glycemic control are consistently associated with higher rates of diabetes remission and/or lower risk of recidivism (31,46,48). Greater baseline visceral fat area may also help to predict better postoperative outcomes, especially among Asian American patients with type 2 diabetes, who typically have more visceral fat compared with Caucasians with diabetes of the same BMI (49).

Beyond improving glycemia, metabolic surgery has been shown to confer additional health benefits in randomized controlled trials, including greater reductions in cardiovascular disease risk factors (29) and enhancements in quality of life (44,48,50).

The safety of metabolic surgery has improved significantly over the past two decades, with continued refinement of minimally invasive approaches (laparoscopic surgery), enhanced training and credentialing, and involvement of multidisciplinary teams. Mortality rates with metabolic operations are typically 0.1–0.5%, similar to cholecystectomy or hysterectomy (51–55). Morbidity has also dramatically declined with laparoscopic approaches. Major complications rates are 2–6%, with minor complications in up to 15% (51–59), comparing favorably with other commonly performed elective operations (55). Empirical data

suggest that proficiency of the operating surgeon is an important factor for determining mortality, complications, reoperations, and readmissions (60).

Although metabolic surgery has been shown to improve the metabolic profiles of morbidly obese patients with type 1 diabetes, establishing the role of metabolic surgery in such patients will require larger and longer studies (61).

Retrospective analyses and modeling studies suggest that metabolic 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 (62,63).

Adverse Effects

Metabolic surgery is costly and has associated risks. Longer-term concerns include dumping syndrome (nausea, colic, diarrhea), vitamin and mineral deficiencies, anemia, osteoporosis, and, rarely (64), severe hypoglycemia from insulin hypersecretion. Long-term nutritional and micronutrient deficiencies and related complications occur with variable frequency depending on the type of procedure and require lifelong vitamin/nutritional supplementation (65,66). Postprandial hypoglycemia is most likely to occur with RYGB (66,67). The exact prevalence of symptomatic hypoglycemia is unknown. In one study, it affected 11% of 450 patients who had undergone RYGB or vertical sleeve gastrectomy (67). Patients who undergo metabolic surgery may be at increased risk for substance use, including drug and alcohol use and cigarette smoking (68).

People with diabetes presenting for metabolic surgery also have increased rates of depression and other major psychiatric disorders (69). Candidates for metabolic surgery with histories of alcohol or substance abuse, significant depression, suicidal ideation, or other mental health conditions should therefore first be assessed by a mental health professional with expertise in obesity management prior to consideration for surgery (70). Individuals with preoperative psychopathology should be assessed regularly following metabolic surgery to optimize mental health management and to ensure psychiatric symptoms do not interfere with weight loss and lifestyle changes.

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