



## 8. Obesity and Weight Management for the Prevention and Treatment of Type 2 Diabetes: *Standards of Care in Diabetes—2023*

*Diabetes Care* 2023;46(Suppl. 1):S128–S139 | <https://doi.org/10.2337/dc23-S008>

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The American Diabetes Association (ADA) “Standards of Care in Diabetes” includes the ADA’s current clinical practice recommendations and is intended to provide the components of diabetes care, general treatment goals and guidelines, and tools to evaluate quality of care. Members of the ADA Professional Practice Committee, a multidisciplinary expert committee, are responsible for updating the Standards of Care annually, or more frequently as warranted. For a detailed description of ADA standards, statements, and reports, as well as the evidence-grading system for ADA’s clinical practice recommendations and a full list of Professional Practice Committee members, please refer to Introduction and Methodology. Readers who wish to comment on the Standards of Care are invited to do so at [professional.diabetes.org/SOC](http://professional.diabetes.org/SOC).

Obesity is a chronic and often progressive disease with numerous medical, physical, and psychosocial complications, including a substantially increased risk for type 2 diabetes (1). There is strong and consistent evidence that obesity management can delay the progression from prediabetes to type 2 diabetes (2–6) and is highly beneficial in treating type 2 diabetes (7–18). In people with type 2 diabetes and overweight or obesity, modest weight loss improves glycemia and reduces the need for glucose-lowering medications (7–9), and larger weight loss substantially reduces A1C and fasting glucose and has been shown to promote sustained diabetes remission through at least 2 years (11,19–23). Several modalities, including intensive behavioral counseling, obesity pharmacotherapy, and bariatric surgery, may aid in achieving and maintaining meaningful weight loss and reducing obesity-associated health risks. Metabolic surgery strongly improves glycemia and often leads to remission of diabetes, improved quality of life, improved cardiovascular outcomes, and reduced mortality. The importance of addressing obesity is further heightened by numerous studies showing that both obesity and diabetes increase the risk for more severe coronavirus disease 2019 (COVID-19) infections (24–27). This section aims to provide evidence-based recommendations for obesity management, including behavioral, pharmacologic, and surgical interventions, in people with type 2 diabetes and in those at risk. This section focuses on obesity management in adults; further discussion on obesity in older individuals and children can be found in Section 13, “Older Adults,” and Section 14, “Children and Adolescents,” respectively.

Disclosure information for each author is available at <https://doi.org/10.2337/dc23-SDIS>.

Suggested citation: ElSayed NA, Aleppo G, Aroda VR, et al., American Diabetes Association. 8. Obesity and weight management for the prevention and treatment of type 2 diabetes: Standards of Care in Diabetes—2023. *Diabetes Care* 2023;46(Suppl. 1):S128–S139

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## ASSESSMENT

### Recommendations

- 8.1** Use person-centered, nonjudgmental language that fosters collaboration between individuals and health care professionals, including person-first language (e.g., “person with obesity” rather than “obese person”). **E**
- 8.2** Measure height and weight and calculate BMI at annual visits or more frequently. Assess weight trajectory to inform treatment considerations. **E**
- 8.3** Based on clinical considerations, such as the presence of comorbid heart failure or significant unexplained weight gain or loss, weight may need to be monitored and evaluated more frequently. **B** If deterioration of medical status is associated with significant weight gain or loss, inpatient evaluation should be considered, especially focused on associations between medication use, food intake, and glycemic status. **E**
- 8.4** Accommodations should be made to provide privacy during weighing. **E**
- 8.5** Individuals with diabetes and overweight or obesity may benefit from modest or larger magnitudes of weight loss. Relatively small weight loss (approximately 3–7% of baseline weight) improves glycemia and other intermediate cardiovascular risk factors. **A** Larger, sustained weight losses (>10%) usually confer greater benefits, including disease-modifying effects and possible remission of type 2 diabetes, and may improve long-term cardiovascular outcomes and mortality. **B**

A person-centered communication style that uses inclusive and nonjudgmental language and active listening to elicit individual preferences and beliefs and assesses potential barriers to care should be used to optimize health outcomes and health-related quality of life. Use person-first language (e.g., “person with obesity” rather than “obese person”) to avoid defining people by their condition (28–30).

Height and weight should be measured to calculate BMI annually or more frequently when appropriate (20). BMI, calculated as weight in kilograms divided by the square of height in meters ( $\text{kg}/\text{m}^2$ ), is calculated automatically by most electronic medical records. Use BMI to document weight status (overweight: BMI 25–29.9  $\text{kg}/\text{m}^2$ ; obesity class I: BMI 30–34.9  $\text{kg}/\text{m}^2$ ; obesity class II: BMI 35–39.9  $\text{kg}/\text{m}^2$ ; obesity class III: BMI  $\geq 40$   $\text{kg}/\text{m}^2$ ) but note that misclassification can occur, particularly in very muscular or frail individuals. In some groups, notably Asian and Asian American populations, the BMI cut points to define overweight and obesity are lower than those in other populations due to differences in body composition and cardiometabolic risk (Table 8.1) (30,31). Clinical considerations, such as the presence of comorbid heart failure or unexplained weight change, may warrant more frequent weight measurement and evaluation (32,33). If weighing is questioned or refused, the practitioner should be mindful of possible prior stigmatizing experiences and query for concerns, and the value of weight monitoring should be explained as a part of the medical evaluation process that helps to inform treatment decisions (34,35). Accommodations should be made to ensure privacy during weighing, particularly for those individuals who report or exhibit a high level of weight-related distress or dissatisfaction. Scales should be situated in a private area or room. Weight should be measured and reported nonjudgmentally. Care should be taken to regard a person’s weight (and weight changes) and BMI as sensitive health information. In addition to weight and BMI, assessment of weight distribution (including propensity for central/visceral adipose deposition) and weight gain pattern and trajectory can further inform risk stratification and treatment options (36).

Health care professionals should advise individuals with overweight or obesity and those with increasing weight trajectories that, in general, higher BMIs increase the risk of diabetes, cardiovascular disease, and all-cause mortality, as well as other adverse health and quality of life outcomes. Health care professionals should assess readiness to engage in behavioral changes for weight loss and jointly determine behavioral and weight loss goals and individualized intervention strategies (37). Strategies may include nutrition changes, physical activity, behavioral

counseling, pharmacologic therapy, medical devices, and metabolic surgery (Table 8.1). The latter three strategies may be considered for carefully selected individuals as adjuncts to nutrition changes, physical activity, and behavioral counseling.

Among people with type 2 diabetes and overweight or obesity who have inadequate glycemic, blood pressure, and lipid control and/or other obesity-related medical conditions, modest and sustained weight loss improves glycemia, blood pressure, and lipids and may reduce the need for medications (7–9,38). Greater weight loss may produce even greater benefits (21,22).

As little as 3–7% weight loss reduces the risk for diabetes in people at risk and improves glycemia in those with diabetes (2,7,8,39,40). Given the challenge of losing weight and maintaining weight loss, aiming for relatively small and attainable weight loss is often an effective clinical strategy, particularly for individuals who feel overwhelmed by larger weight loss targets. Nevertheless, mounting data from intensive nutrition and behavioral change interventions, pharmacotherapy, and bariatric surgery have shown that more substantial weight loss usually confers still greater benefits on glycemia and possibly disease remission as well as other cardiometabolic and quality-of-life outcomes (6,21–23,41–50).

With the increasing availability of more effective obesity treatments, individuals with diabetes and overweight or obesity should be informed of the potential benefits of both modest and more substantial weight loss and guided in the range of available treatment options, as discussed in the sections below. Shared decision-making should be used when counseling on behavioral changes, intervention choices, and weight management goals.

## NUTRITION, PHYSICAL ACTIVITY, AND BEHAVIORAL THERAPY

### Recommendations

- 8.6** Nutrition, physical activity, and behavioral therapy to achieve and maintain  $\geq 5\%$  weight loss are recommended for most people with type 2 diabetes and overweight or obesity. Additional weight loss usually results in further improvements in the management of diabetes and cardiovascular risk. **B**

**Table 8.1—Treatment options for overweight and obesity in type 2 diabetes**

| Treatment   | BMI category (kg/m <sup>2</sup> ) |                           |                   |
|---|-----------------------------------|---------------------------|-------------------|
|   | 25.0–26.9 (or 23.0–24.9*)         | 27.0–29.9 (or 25.0–27.4*) | ≥30.0 (or ≥27.5*) |
| Nutrition, physical activity, and behavioral counseling | †                                 | †                         | †                 |
| Pharmacotherapy   |                                   | †                         | †                 |
| Metabolic surgery                                       |                                   |                           | †                 |

\*Recommended cut points for Asian American individuals (expert opinion). †Treatment may be indicated for select motivated individuals.

- 8.7** Such interventions should include a high frequency of counseling (≥16 sessions in 6 months) and focus on nutrition changes, physical activity, and behavioral strategies to achieve a 500–750 kcal/day energy deficit. **A**
- 8.8** An individual’s preferences, motivation, and life circumstances should be considered, along with medical status, when weight loss interventions are recommended. **C**
- 8.9** Behavioral changes that create an energy deficit, regardless of macronutrient composition, will result in weight loss. Nutrition recommendations should be individualized to the person’s preferences and nutritional needs. **A**
- 8.10** Evaluate systemic, structural, and socioeconomic factors that may impact nutrition patterns and food choices, such as food insecurity and hunger, access to healthful food options, cultural circumstances, and social determinants of health. **C**
- 8.11** For those who achieve weight loss goals, long-term (≥1 year) weight maintenance programs are recommended when available. Such programs should, at minimum, provide monthly contact and support, recommend ongoing monitoring of body weight (weekly or more frequently) and other self-monitoring strategies, and encourage regular physical activity (200–300 min/week). **A**
- 8.12** Short-term nutrition intervention using structured, very-low-calorie meals (800–1,000 kcal/day) may be prescribed for carefully selected individuals by trained

practitioners in medical settings with close monitoring. Long-term, comprehensive weight maintenance strategies and counseling should be integrated to maintain weight loss. **B**

**8.13** There is no clear evidence that nutrition supplements are effective for weight loss. **A**

For a more detailed discussion of lifestyle management approaches and recommendations, see Section 5, “Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes.” For a detailed discussion of nutrition interventions, please also refer to “Nutrition Therapy for Adults With Diabetes or Prediabetes: A Consensus Report” (127).

**Look AHEAD Trial**

Although the Action for Health in Diabetes (Look AHEAD) trial did not show that the intensive lifestyle intervention reduced cardiovascular events in adults with type 2 diabetes and overweight or obesity (39), it did confirm the feasibility of achieving and maintaining long-term weight loss in people with type 2 diabetes. In the intensive lifestyle intervention group, mean weight loss was 4.7% at 8 years (40). Approximately 50% of intensive lifestyle intervention participants lost and maintained ≥5% of their initial body weight, and 27% lost and maintained ≥10% of their initial body weight at 8 years (40). Participants assigned to the intensive lifestyle group 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 additional weight loss benefits in people with type 2 diabetes, including improved mobility, physical and

sexual function, and health-related quality of life (32). Moreover, several subgroups had improved cardiovascular outcomes, including those who achieved >10% weight loss (41) and those with moderately or poorly managed diabetes (A1C >6.8%) at baseline (42).

**Behavioral Interventions**

Significant weight loss can be attained with lifestyle programs that achieve a 500–750 kcal/day energy deficit, which in most cases is 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. Clinical benefits typically begin upon achieving 3–5% weight loss (20,51), and the benefits of weight loss are progressive; more intensive weight loss goals (>5%, >7%, >15%, etc.) may be pursued if needed to achieve further health improvements and/or if the individual is more motivated and more intensive goals can be feasibly and safely attained.

Nutrition interventions may differ by macronutrient goals and food choices as long as they create the necessary energy deficit to promote weight loss (20,52–54). Using meal replacement plans prescribed by trained practitioners, with close monitoring, can be beneficial. Within the intensive lifestyle intervention group of the Look AHEAD trial, for example, the use of a partial meal replacement plan was associated with improvements in nutrition quality and weight loss (51). The nutrition choice should be based on the individual’s health status and preferences, including a determination of food availability and other cultural circumstances that could affect nutrition patterns (55).

Intensive behavioral interventions should include ≥16 sessions during the initial 6 months and focus on nutrition changes, 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 (51). Assessing an individual's motivation level, life circumstances, and willingness to implement behavioral changes to achieve weight loss should be considered along with medical status when weight loss interventions are recommended and initiated (37,56).

People with type 2 diabetes and overweight or obesity who have lost weight should be offered long-term ( $\geq 1$  year) comprehensive weight loss maintenance programs that provide at least monthly contact with trained interventionists and focus on ongoing monitoring of body weight (weekly or more frequently) and/or other self-monitoring strategies such as tracking intake, steps, etc.; continued focus on nutrition and behavioral changes; and participation in high levels of physical activity (200–300 min/week) (57). Some commercial and proprietary weight loss programs have shown promising weight loss results. However, most lack evidence of effectiveness, many do not satisfy guideline recommendations, and some promote unscientific and possibly dangerous practices (58,59).

When provided by trained practitioners in medical settings with ongoing monitoring, short-term (generally up to 3 months) intensive nutrition intervention may be prescribed for carefully selected individuals, such as those requiring weight loss before surgery and those needing greater weight loss and glycemic improvements. When integrated with behavioral support and counseling, structured very-low-calorie meals, typically 800–1,000 kcal/day, utilizing high-protein foods and meal replacement products, may increase the pace and/or magnitude of initial weight loss and glycemic improvements compared with standard behavioral interventions (21,22). As weight regain is common, such interventions should include long-term, comprehensive weight maintenance strategies and counseling to maintain weight loss and behavioral changes (60,61).

Despite widespread marketing and exorbitant claims, there is no clear evidence that nutrition supplements (such as herbs and botanicals, high-dose vitamins and minerals, amino acids, enzymes, antioxidants, etc.) are effective for obesity management or weight loss (62–64). Several large systematic reviews show that most trials evaluating nutrition supplements for weight loss are of low quality and at high risk for bias. High-quality published studies show

little or no weight loss benefits. In contrast, vitamin/mineral (e.g., iron, vitamin B12, vitamin D) supplementation may be indicated in cases of documented deficiency, and protein supplements may be indicated as adjuncts to medically supervised weight loss therapies.

Health disparities adversely affect people who have systematically experienced greater obstacles to health based on their race or ethnicity, socioeconomic status, gender, disability, or other factors. Overwhelming research shows that these disparities may significantly affect health outcomes, including increasing the risk for obesity, diabetes, and diabetes-related complications. Health care professionals should evaluate systemic, structural, and socioeconomic factors that may impact food choices, access to healthful foods, and nutrition patterns; behavioral patterns, such as neighborhood safety and availability of safe outdoor spaces for physical activity; environmental exposures; access to health care; social contexts; and, ultimately, diabetes risk and outcomes. For a detailed discussion of social determinants of health, refer to “Social Determinants of Health: A Scientific Review” (65).

## PHARMACOTHERAPY

### Recommendations

- 8.14** When choosing glucose-lowering medications for people with type 2 diabetes and overweight or obesity, consider the medication's effect on weight. **B**
- 8.15** Whenever possible, minimize medications for comorbid conditions that are associated with weight gain. **E**
- 8.16** Obesity pharmacotherapy is effective as an adjunct to nutrition, physical activity, and behavioral counseling for selected people with type 2 diabetes and BMI  $\geq 27$  kg/m<sup>2</sup>. Potential benefits and risks must be considered. **A**
- 8.17** If obesity pharmacotherapy is effective (typically defined as  $\geq 5\%$  weight loss after 3 months' use), further weight loss is likely with continued use. When early response is insufficient (typically  $< 5\%$  weight loss after 3 months' use) or if there are significant safety or tolerability issues, consider

discontinuation of the medication and evaluate alternative medications or treatment approaches. **A**

### Glucose-Lowering Therapy

A meta-analysis of 227 randomized controlled trials of glucose-lowering treatments in type 2 diabetes found that A1C changes were not associated with baseline BMI, indicating that people with obesity can benefit from the same types of treatments for diabetes as normal-weight individuals (66). As numerous effective medications are available when considering medication plans, health care professionals should consider each medication's effect on weight. Agents associated with varying degrees of weight loss include metformin,  $\alpha$ -glucosidase inhibitors, sodium–glucose cotransporter 2 inhibitors, glucagon-like peptide 1 receptor agonists, dual glucagon-like peptide 1/glucose–dependent insulinotropic polypeptide receptor agonist (tirzepatide), and amylin mimetics. Dipeptidyl peptidase 4 inhibitors are weight neutral. In contrast, insulin secretagogues, thiazolidinediones, and insulin are often associated with weight gain (see Section 9, “Pharmacologic Approaches to Glycemic Treatment”).

### Concomitant Medications

Health care professionals should carefully review the patient's concomitant medications and, whenever possible, minimize or provide alternatives for medications that promote weight gain. Examples of medications associated with weight gain include antipsychotics (e.g., clozapine, olanzapine, risperidone), some antidepressants (e.g., tricyclic antidepressants, some selective serotonin reuptake inhibitors, and monoamine oxidase inhibitors), glucocorticoids, injectable progestins, some anticonvulsants (e.g., gabapentin, pregabalin), and possibly sedating antihistamines and anticholinergics (67).

### Approved Obesity Pharmacotherapy Options

The U.S. Food and Drug Administration (FDA) has approved medications for both short-term and long-term weight management as adjuncts to nutrition, physical activity and behavioral therapy. Nearly all

FDA-approved obesity medications have been shown to improve glycemia in people with type 2 diabetes and delay progression to type 2 diabetes in at-risk individuals (23). Phentermine and other older adrenergic agents are indicated for short-term ( $\leq 12$  weeks) treatment (68). Five medications are FDA approved for long-term use ( $> 12$  weeks) in adults with BMI  $\geq 27$  kg/m<sup>2</sup> with one or more obesity-associated comorbid conditions (e.g., type 2 diabetes, hypertension, and/or dyslipidemia) who are motivated to lose weight (23). (Refer to Section 14, “Children and Adolescents,” for medications approved for adolescents with obesity.) Medications approved by the FDA for the treatment of obesity, summarized in **Table 8.2**, include orlistat, phentermine/topiramate ER, naltrexone/bupropion ER, liraglutide 3 mg, and semaglutide 2.4 mg. (In addition, setmelanotide, a melanocortin 4 receptor agonist, is approved for use in cases of rare genetic mutations resulting in severe hyperphagia and extreme obesity, such as leptin receptor deficiency and proopiomelanocortin deficiency.) In principle, medications help improve adherence to nutrition recommendations, in most cases by modulating appetite or satiety. Health care professionals should be knowledgeable about the product label and balance the potential benefits of successful weight loss against the potential risks of the medication for each individual. These medications are contraindicated in individuals who are pregnant or actively trying to conceive and not recommended for use in women who are nursing. Individuals of reproductive potential should receive counseling regarding the use of reliable methods of contraception. Of note, while weight loss medications are often used in people with type 1 diabetes, clinical trial data in this population are limited.

### Assessing Efficacy and Safety

Upon initiating weight loss medication, assess efficacy and safety at least monthly for the first 3 months and at least quarterly thereafter. Modeling from published clinical trials consistently shows that early responders have improved long-term outcomes (69–71). Unless clinical circumstances (such as poor tolerability) or other considerations (such as financial expense or individual preference) suggest otherwise, those who achieve sufficient early weight loss upon starting a chronic weight loss medication (typically defined as  $> 5\%$  weight loss after 3 months' use) should

continue the medication. When early use appears ineffective (typically  $< 5\%$  weight loss after 3 months' use), it is unlikely that continued use will improve weight outcomes; as such, it should be recommended to discontinue the medication and consider other treatment options.

### MEDICAL DEVICES FOR WEIGHT LOSS

While gastric banding devices have fallen out of favor in recent years, since 2015, several minimally invasive medical devices have been approved by the FDA for short-term weight loss, including implanted gastric balloons, a vagus nerve stimulator, and gastric aspiration therapy (72). Given the current high cost, limited insurance coverage, and paucity of data in people with diabetes, medical devices for weight loss are rarely utilized at this time, and it remains to be seen how they may be used in the future (73).

An oral hydrogel (Plenity) has recently been approved for long-term use in those with BMI  $> 25$  kg/m<sup>2</sup> to simulate the space-occupying effect of implantable gastric balloons. Taken with water 30 min before meals, the hydrogel expands to fill a portion of the stomach volume to help decrease food intake during meals. Though average weight loss is relatively small (2–3% greater than placebo), the subgroup of participants with prediabetes or diabetes at baseline had improved weight loss outcomes (8.1% weight loss) compared with the overall treatment (6.4% weight loss) and placebo (4.4% weight loss) groups (74).

### METABOLIC SURGERY

#### Recommendations

- 8.18** Metabolic surgery should be a recommended option to treat type 2 diabetes in screened surgical candidates with BMI  $\geq 40$  kg/m<sup>2</sup> (BMI  $\geq 37.5$  kg/m<sup>2</sup> in Asian American individuals) and in adults with BMI 35.0–39.9 kg/m<sup>2</sup> (32.5–37.4 kg/m<sup>2</sup> in Asian American individuals) who do not achieve durable weight loss and improvement in comorbidities (including hyperglycemia) with nonsurgical methods. **A**
- 8.19** Metabolic surgery may be considered as an option to treat type 2 diabetes in adults

with BMI 30.0–34.9 kg/m<sup>2</sup> (27.5–32.4 kg/m<sup>2</sup> in Asian American individuals) who do not achieve durable weight loss and improvement in comorbidities (including hyperglycemia) with nonsurgical methods. **A**

- 8.20** Metabolic surgery should be performed in high-volume centers with multidisciplinary teams knowledgeable about and experienced in managing obesity, diabetes, and gastrointestinal surgery. **E**
- 8.21** People being considered for metabolic surgery should be evaluated for comorbid psychological conditions and social and situational circumstances that have the potential to interfere with surgery outcomes. **B**
- 8.22** People who undergo metabolic surgery should receive long-term medical and behavioral support and routine micronutrient, nutritional, and metabolic status monitoring. **B**
- 8.23** If postbariatric hypoglycemia is suspected, clinical evaluation should exclude other potential disorders contributing to hypoglycemia, and management includes education, medical nutrition therapy with a dietitian experienced in postbariatric hypoglycemia, and medication treatment, as needed. **A** Continuous glucose monitoring should be considered as an important adjunct to improve safety by alerting individuals to hypoglycemia, especially for those with severe hypoglycemia or hypoglycemia unawareness. **E**
- 8.24** People who undergo metabolic surgery should routinely be evaluated to assess the need for ongoing mental health services to help with the adjustment to medical and psychosocial changes after surgery. **C**

Surgical procedures for obesity treatment—often referred to interchangeably as bariatric surgery, weight loss surgery, metabolic surgery, or metabolic/bariatric surgery—can promote significant and durable weight loss and improve type 2

**Table 8.2—Medications approved by the FDA for the treatment of overweight or obesity in adults**

| Medication name  | Typical adult maintenance dose            | Average wholesale price (30-day supply) (128) | National Average Drug Acquisition Cost (30-day supply) (129) | 1-Year (52- or 56-week) mean weight loss (% loss from baseline) |                                    | Common side effects (130–134)  | Possible safety concerns/considerations (130–134)  |
|--|---|---|--|---|------------------------------------|--|--|
|  |   |   |  | Treatment arms  | Weight loss (% loss from baseline) |  |  |
| <b>Short-term treatment (≤12 weeks)</b>                          |   |   |  |   |                                    |  |  |
| <b>Sympathomimetic amine anorectic</b>                           |   |   |  |   |                                    |  |  |
| Phentermine (135)  | 8–37.5 mg q.d.*                           | \$5–\$56 (37.5 mg dose)                       | \$2–\$3 (37.5 mg dose)                                       | 15 mg q.d.†<br>7.5 mg q.d.†<br>PBO                              | 6.1<br>5.5<br>1.2                  | Dry mouth, insomnia, dizziness, irritability, increased blood pressure, elevated heart rate  | <ul style="list-style-type: none"> <li>Contraindicated for use in combination with monoamine oxidase inhibitors</li> </ul>   |
| <b>Long-term treatment (&gt;12 weeks)</b>                        |   |   |  |   |                                    |  |  |
| <b>Lipase inhibitor</b>  |   |   |  |   |                                    |  |  |
| Orlistat (4)   | 60 mg t.i.d. (OTC)<br>120 mg t.i.d. (Rx)  | \$41–\$82<br>\$781–\$904                      | NA<br>\$722  | 120 mg t.i.d.‡<br>PBO   | 9.6<br>5.6                         | Abdominal pain, flatulence, fecal urgency  | <ul style="list-style-type: none"> <li>Potential malabsorption of fat-soluble vitamins (A, D, E, K) and of certain medications (e.g., cyclosporine, thyroid hormone, anticonvulsants, etc.)</li> <li>Rare cases of severe liver injury reported</li> <li>Cholelithiasis</li> <li>Nephrolithiasis</li> </ul>  |
| <b>Sympathomimetic amine anorectic/antiepileptic combination</b> |   |   |  |   |                                    |  |  |
| Phentermine/topiramate ER (45)                                   | 7.5 mg/46 mg q.d.§<br>16 mg/180 mg b.i.d. | \$223 (7.5 mg/46 mg dose)<br>\$750            | \$179 (7.5 mg/46 mg dose)<br>\$599                           | 15 mg/92 mg q.d.  <br>7.5 mg/46 mg q.d.  <br>PBO                | 9.8<br>7.8<br>1.2                  | Constipation, paresthesia, insomnia, nasopharyngitis, xerostomia, increased blood pressure   | <ul style="list-style-type: none"> <li>Contraindicated for use in combination with monoamine oxidase inhibitors</li> <li>Birth defects</li> <li>Cognitive impairment</li> <li>Acute angle-closure glaucoma</li> <li>Contraindicated in people with unmanaged hypertension and/or seizure disorders</li> <li>Contraindicated for use with chronic opioid therapy</li> <li>Acute angle-closure glaucoma</li> </ul> |
| <b>Opioid antagonist/antidepressant combination</b>              |   |   |  |   |                                    |  |  |
| Naltrexone/bupropion ER (16)                                     | 16 mg/180 mg b.i.d.                       | \$750   | \$599  | 16 mg/180 mg b.i.d.<br>PBO                                      | 5.0<br>1.8                         | Constipation, nausea, headache, xerostomia, insomnia, elevated heart rate and blood pressure | <ul style="list-style-type: none"> <li>Contraindicated for use with chronic opioid therapy</li> <li>Acute angle-closure glaucoma</li> </ul> <p><b>Black box warning:</b></p> <ul style="list-style-type: none"> <li>Risk of suicidal behavior/ideation in people younger than 24 years old who have depression</li> </ul>  |

Continued on p. S134

**Table 8.2—Continued**

| Medication name  | Typical adult maintenance dose | Average wholesale price (30-day supply) (128) | National Average Drug Acquisition Cost (30-day supply) (129) | 1-Year (52- or 56-week) mean weight loss (% loss from baseline) |                                    | Common side effects (130–134)  | Possible safety concerns/considerations (130–134)   |
|--|--------------------------------|---|--|---|------------------------------------|--|---|
|  |                                |   |  | Treatment arms  | Weight loss (% loss from baseline) |  |   |
| Glucagon-like peptide 1 receptor agonist<br>Liraglutide (17)** | 3 mg q.d.                      | \$1,619                                       | \$1,295  | 3.0 mg q.d.<br>1.8 mg q.d.<br>PBO                               | 6.0<br>4.7<br>2.0                  | Gastrointestinal side effects (nausea, vomiting, diarrhea, esophageal reflux), injection site reactions, elevated heart rate, hypoglycemia | <ul style="list-style-type: none"> <li>Pancreatitis has been reported in clinical trials, but causality has not been established. Discontinue if pancreatitis is suspected.</li> <li>Use caution in people with kidney disease when initiating or increasing dose due to potential risk of acute kidney injury.</li> <li>May cause cholelithiasis and gallstone-related complications.</li> </ul> <p><b>Black box warning:</b></p> <ul style="list-style-type: none"> <li>Risk of thyroid C-cell tumors in rodents; human relevance not determined</li> </ul> |
| Semaglutide (46,47)  | 2.4 mg once weekly             | \$1,619                                       | \$1,295  | 2.4 mg weekly<br>PBO  | 9.6<br>3.4                         | Gastrointestinal side effects (nausea, vomiting, diarrhea, esophageal reflux), injection site reactions, elevated heart rate, hypoglycemia | <ul style="list-style-type: none"> <li>Pancreatitis has been reported in clinical trials, but causality has not been established. Discontinue if pancreatitis is suspected.</li> <li>May cause cholelithiasis and gallstone-related complications.</li> </ul> <p><b>Black box warning:</b></p> <ul style="list-style-type: none"> <li>Risk of thyroid C-cell tumors in rodents; human relevance not determined</li> </ul>   |

All medications are contraindicated in individuals who are or may become pregnant. Individuals of reproductive potential must be counseled regarding the use of reliable methods of contraception. Select safety and side effect information is provided; for a comprehensive discussion of safety considerations, please refer to the prescribing information for each agent. b.i.d., twice daily; ER, extended release; OTC, over the counter; NA, data not available; PBO, placebo; q.d., daily; Rx, prescription; t.i.d., three times daily. \*Use lowest effective dose; maximum appropriate dose is 37.5 mg. †Duration of treatment was 28 weeks in a general adult population with obesity. ‡Enrolled participants had normal (79%) or impaired (21%) glucose tolerance. §Maximum dose, depending on response, is 15 mg/92 mg q.d. ||Approximately 68% of enrolled participants had type 2 diabetes or impaired glucose tolerance. \*\*Agent has demonstrated cardiovascular safety in a dedicated cardiovascular outcome trial (47).

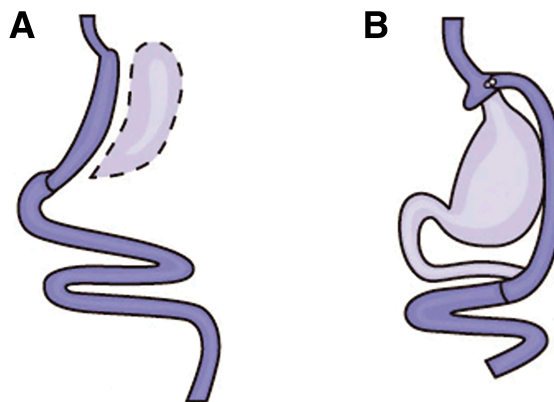
diabetes. Given the magnitude and rapidity of improvement of hyperglycemia and glucose homeostasis, these procedures have been suggested as treatments for type 2 diabetes even in the absence of severe obesity and will be referred to here as “metabolic surgery.”

A substantial body of evidence, including data from numerous large cohort studies and randomized controlled (non-blinded) clinical trials, demonstrates that metabolic surgery achieves superior glycemic control and reduction of cardiovascular risk in people with type 2 diabetes and obesity compared with nonsurgical intervention (18). In addition to improving glycemia, metabolic surgery reduces the incidence of microvascular disease (75), improves quality of life (43,76,77), decreases cancer risk, and improves cardiovascular disease risk factors and long-term cardiovascular events (78–89). Cohort studies that match surgical and nonsurgical subjects strongly suggest that metabolic surgery reduces all-cause mortality (90,91).

The overwhelming majority of procedures in the U.S. are vertical sleeve gastrectomy (VSG) and Roux-en-Y gastric bypass (RYGB). Both procedures result in an anatomically smaller stomach pouch and often robust changes in enteroendocrine hormones. In VSG, ~80% of the stomach is removed, leaving behind a long, thin sleeve-shaped pouch. RYGB creates a much smaller stomach pouch (roughly the size of a walnut), which is then attached to the distal small intestine, thereby bypassing the duodenum and jejunum (Fig. 8.1).

Several organizations recommend lowering the BMI criteria for metabolic surgery to 30 kg/m<sup>2</sup> (27.5 kg/m<sup>2</sup> for Asian American individuals) for people with type 2 diabetes who have not achieved sufficient weight loss and improved comorbidities (including hyperglycemia) with reasonable nonsurgical treatments. Studies have documented diabetes remission after 1–5 years in 30–63% of patients with RYGB (18,93).

Most notably, the Surgical Treatment and Medications Potentially Eradicate Diabetes Efficiently (STAMPEDE) trial, which randomized 150 participants with unmanaged diabetes to receive either metabolic surgery or medical treatment, found that 29% of those treated with RYGB and 23% treated with VSG achieved A1C of 6.0% or lower after 5 years (43). Available data suggest an erosion of



**Figure 8.1**—A: Vertical sleeve gastrectomy. B: Roux-en-Y gastric bypass surgery. Images reprinted from National Institute of Diabetes and Digestive and Kidney Diseases (92).

diabetes remission over time (44); at least 35–50% of patients who initially achieve remission of diabetes eventually experience recurrence. Still, the median disease-free period among such individuals following RYGB is 8.3 years (94,95), and the majority of those who undergo surgery maintain substantial improvement of glycemia from baseline for at least 5–15 years (43,76,79,80,95–98).

Exceedingly few presurgical predictors of success have been identified, but younger age, shorter duration of diabetes (e.g., <8 years) (70), and lesser severity of diabetes (better glycemic control, non-use of insulin) are associated with higher rates of diabetes remission (43,79,97,99). Greater baseline visceral fat area may also predict improved postoperative outcomes, especially among Asian American people with type 2 diabetes (100).

Although surgery has been shown to improve the metabolic profiles of people with type 1 diabetes, larger and longer-term studies are needed to determine the role of metabolic surgery in such individuals (101).

Whereas metabolic surgery has greater initial costs than nonsurgical obesity treatments, retrospective analyses and modeling studies suggest that surgery may be cost-effective or even cost-saving for individuals with type 2 diabetes. However, these results largely depend on assumptions about the long-term effectiveness and safety of the procedures (102,103).

#### Potential Risks and Complications

The safety of metabolic surgery has improved significantly with continued refinement of minimally invasive (laparoscopic)

approaches, enhanced training and credentialing, and involvement of multidisciplinary teams. Perioperative mortality rates are typically 0.1–0.5%, similar to those of common abdominal procedures such as cholecystectomy or hysterectomy (104–108). Major complications occur in 2–6% of those undergoing metabolic surgery, which compares favorably with the rates for other commonly performed elective operations (108). Postsurgical recovery times and morbidity have also dramatically declined. Minor complications and need for operative reoperation occur in up to 15% (104–113). Empirical data suggest that the proficiency of the operating surgeon and surgical team is an important factor in determining mortality, complications, reoperations, and readmissions (114). Accordingly, metabolic surgery should be performed in high-volume centers with multidisciplinary teams experienced in managing diabetes, obesity, and gastrointestinal surgery.

Beyond the perioperative period, longer-term risks include vitamin and mineral deficiencies, anemia, osteoporosis, dumping syndrome, and severe hypoglycemia (115). Nutritional and micronutrient deficiencies and related complications occur with a variable frequency depending on the type of procedure and require routine monitoring of micronutrient and nutritional status and lifelong vitamin/nutritional supplementation (115). Dumping syndrome usually occurs shortly (10–30 min) after a meal and may present with diarrhea, nausea, vomiting, palpitations, and fatigue; hypoglycemia is usually not present at the time of symptoms but, in some cases, may develop several hours later.



Postbariatric hypoglycemia (PBH) can occur with RYGB, VSG, and other gastrointestinal procedures and may severely impact quality of life (116–118). PBH is driven in part by altered gastric emptying of ingested nutrients, leading to rapid intestinal glucose absorption and excessive postprandial secretion of glucagon-like peptide 1 and other gastrointestinal peptides. As a result, overstimulation of insulin release and a sharp drop in plasma glucose occur, most commonly 1–3 h after a high-carbohydrate meal. Symptoms range from sweating, tremor, tachycardia, and increased hunger to impaired cognition, loss of consciousness, and seizures. In contrast to dumping syndrome, which often occurs soon after surgery and improves over time, PBH typically presents >1 year post-surgery. Diagnosis is primarily made by a thorough history, detailed records of food intake, physical activity, and symptom patterns, and exclusion of other potential causes (e.g., malnutrition, side effects of medications or supplements, dumping syndrome, and insulinoma). Initial management includes education to facilitate reduced intake of rapidly digested carbohydrates while ensuring adequate intake of protein and healthy fats, and vitamin/nutrient supplements. When available, patients should be offered medical nutrition therapy with a dietitian experienced in PBH and the use of continuous glucose monitoring (ideally real-time continuous glucose monitoring, which can detect dropping glucose levels before severe hypoglycemia occurs), especially for those with hypoglycemia unawareness. Medication treatment, if needed, is primarily aimed at slowing carbohydrate absorption (e.g., acarbose) or reducing glucagon-like peptide 1 and insulin secretion (e.g., diazoxide, octreotide) (119).

People who undergo metabolic surgery may also be at increased risk for substance abuse, worsening or new-onset depression and/or anxiety disorders, and suicidal ideation (115,120–125). Candidates for metabolic surgery should be assessed by a mental health professional with expertise in obesity management prior to consideration for surgery (126). Surgery should be postponed in individuals with alcohol or substance use disorders, severe depression, suicidal ideation, or other significant

mental health conditions until these conditions have been sufficiently addressed. Individuals with preoperative or new-onset psychopathology should be assessed regularly following surgery to optimize mental health and postsurgical outcomes.

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