

## 8. Obesity and Weight Management for the Prevention and Treatment of Type 2 Diabetes: *Standards of Medical Care in Diabetes—2022*

American Diabetes Association  
Professional Practice Committee\*

*Diabetes Care* 2022;45(Suppl. 1):S113–S124 | <https://doi.org/10.2337/dc22-S008>

The American Diabetes Association (ADA) “Standards of Medical 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 (<https://doi.org/10.2337/dc22-SPPC>), 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, please refer to the Standards of Care Introduction (<https://doi.org/10.2337/dc22-SINT>). Readers who wish to comment on the Standards of Care are invited to do so at [professional.diabetes.org/SOC](https://professional.diabetes.org/SOC).

There is strong and consistent evidence that obesity management can delay the progression from prediabetes to type 2 diabetes (1–5) and is highly beneficial in the treatment of type 2 diabetes (6–17). In patients with type 2 diabetes and overweight or obesity, modest weight loss improves glycemic control and reduces the need for glucose-lowering medications (6–8), and more intensive dietary energy restriction can substantially reduce A1C and fasting glucose and promote sustained diabetes remission through at least 2 years (10,18–22). Metabolic surgery strongly improves glycemic control 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 risk for more severe coronavirus disease 2019 (COVID-19) infections (23–26). The goal of this section is to provide evidence-based recommendations for obesity management, including behavioral, pharmacologic, and surgical interventions, in patients with type 2 diabetes. 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” (<https://doi.org/10.2337/dc22-S013>), and Section 14, “Children and Adolescents” (<https://doi.org/10.2337/dc22-S014>), respectively.

### ASSESSMENT

#### Recommendations

- 8.1** Use person-centered, nonjudgmental language that fosters collaboration between patients and providers, including people-first language (e.g., “person with obesity” rather than “obese person”). **E**

\*A complete list of members of the American Diabetes Association Professional Practice Committee can be found at <https://doi.org/10.2337/dc22-SPPC>.

Suggested citation: American Diabetes Association Professional Practice Committee. 8. Obesity and weight management for the prevention and treatment of type 2 diabetes: Standards of Medical Care in Diabetes—2022. *Diabetes Care* 2022;45(Suppl. 1):S113–S124

© 2021 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered. More information is available at <https://diabetesjournals.org/journals/pages/license>.

**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**

A person-centered communication style that uses inclusive and nonjudgmental language and active listening, elicits patient preferences and beliefs, and assesses potential barriers to care should be used to optimize patient health outcomes and health-related quality of life. Use people-first language (e.g., “person with obesity” rather than “obese person”) to avoid defining patients by their condition (27–29).

Height and weight should be measured and used to calculate BMI annually or more frequently when appropriate (19). 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 in other populations due to differences in body composition and cardio-metabolic 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 patients 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 patient’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). Providers should advise patients 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. Providers should assess readiness to engage in behavioral changes for weight loss and jointly determine behavioral and weight loss goals and patient-appropriate intervention strategies (37). Strategies may include dietary 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 patients as adjuncts to dietary changes, physical activity, and behavioral counseling.

## DIET, PHYSICAL ACTIVITY, AND BEHAVIORAL THERAPY

### Recommendations

**8.5** Diet, physical activity, and behavioral therapy to achieve and maintain  $\geq 5\%$  weight loss is recommended for most people with type 2 diabetes and overweight or obesity. Additional weight loss usually results in further improvements in control

of diabetes and cardiovascular risk. **B**

**8.6** Such interventions should include a high frequency of counseling ( $\geq 16$  sessions in 6 months) and focus on dietary changes, physical activity, and behavioral strategies to achieve a 500–750 kcal/day energy deficit. **A**

**8.7** An individual’s preferences, motivation, and life circumstances should be considered, along with medical status, when weight loss interventions are recommended. **C**

**8.8** Behavioral changes that create an energy deficit, regardless of macronutrient composition, will result in weight loss. Dietary recommendations should be individualized to the patient’s preferences and nutritional needs. **A**

**8.9** Evaluate systemic, structural, and socioeconomic factors that may impact dietary patterns and food choices, such as food insecurity and hunger, access to healthful food options, cultural circumstances, and social determinants of health. **C**

**8.10** For those who achieve weight loss goals, long-term ( $\geq 1$  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**

**8.11** Short-term dietary intervention using structured, very-low-calorie diets (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**

**8.12** There is no clear evidence that dietary supplements are effective for weight loss. **A**

**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*)
Diet, physical activity, and behavioral counseling	†	†	†
Pharmacotherapy		†	†
Metabolic surgery			†

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

Among patients with both 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 glycemic control, blood pressure, and lipids and may reduce the need for medications to control these risk factors (6–8,38). Greater weight loss may produce even greater benefits (20,21). For a more detailed discussion of lifestyle management approaches and recommendations see Section 5, “Facilitating Behavior Change and Well-being to Improve Health Outcomes” (<https://doi.org/10.2337/dc22-5005>). For a detailed discussion of nutrition interventions, please also refer to “Nutrition Therapy for Adults With Diabetes or Prediabetes: A Consensus Report” (39).

#### 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 (40), it did confirm the feasibility of achieving and maintaining long-term weight loss in patients with type 2 diabetes. In the intensive lifestyle intervention group, mean weight loss was 4.7% at 8 years (41). 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 (41). 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 benefits of weight loss in patients with type 2 diabetes, including improvements in 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 (42) and those with moderately or poorly controlled diabetes (A1C >6.8%) at baseline (43).

#### 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 (19,44), 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 patient is more motivated and more intensive goals can be feasibly and safely attained.

Dietary interventions may differ by macronutrient goals and food choices as long as they create the necessary energy deficit to promote weight loss (19,45–47). 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 and weight loss (44). The diet choice should be based on the patient’s health status and preferences, including a determination of food availability and other cultural circumstances that could affect dietary patterns (48).

Intensive behavioral interventions should include ≥16 sessions during the initial 6 months and focus on dietary 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 (44). 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 (37,49).

Patients with type 2 diabetes and overweight or obesity who have lost weight should be offered long-term (≥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 dietary and behavioral changes; and participation in high levels of physical activity (200–300 min/week) (50). Some commercial and proprietary weight loss programs have shown promising weight loss results, though most lack evidence of effectiveness, many do not satisfy guideline recommendations, and some promote unscientific and possibly dangerous practices (51,52).

When provided by trained practitioners in medical settings with ongoing monitoring, short-term (generally up to 3 months) intensive dietary intervention may be prescribed for carefully selected patients, such as those requiring weight loss prior to surgery and those needing greater weight loss and glycemic improvements. When integrated with behavioral support and counseling, structured very-low-calorie diets, 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 (20,21). As weight regain is common,

such interventions should include long-term, comprehensive weight maintenance strategies and counseling to maintain weight loss and behavioral changes (53,54).

Despite widespread marketing and exorbitant claims, there is no clear evidence that dietary supplements (such as herbs and botanicals, high-dose vitamins and minerals, amino acids, enzymes, antioxidants, etc.) are effective for obesity management or weight loss (55–57). Several large systematic reviews show that most trials evaluating dietary 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 regimens.

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 providers should evaluate systemic, structural, and socioeconomic factors that may impact food choices, access to healthful foods, and dietary 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” (58).

## PHARMACOTHERAPY

### Recommendations

- 8.13** When choosing glucose-lowering medications for people with type 2 diabetes and overweight or obesity, consider the medication’s effect on weight. **B**
- 8.14** Whenever possible, minimize medications for comorbid conditions that are associated with weight gain. **E**

**8.15** Weight loss medications are effective as adjuncts to diet, 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**

**8.16** If a patient’s response to weight loss medication is effective (typically defined as  $>5\%$  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 patients (59). As numerous effective medications are available, when considering medication regimens health care providers 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, 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,” <https://doi.org/10.2337/dc22-S009>).

### Concomitant Medications

Providers 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, etc.), 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 (60).

### Approved Weight Loss Medications

The U.S. Food and Drug Administration (FDA) has approved medications for both short-term and long-term weight management as adjuncts to diet, exercise, and behavioral therapy. Nearly all FDA-approved medications for weight loss have been shown to improve glycemic control in patients with type 2 diabetes and delay progression to type 2 diabetes in patients at risk (22). Phentermine and other older adrenergic agents are indicated for short-term ( $\leq 12$  weeks) treatment (61). Five weight loss medications are FDA approved for long-term use ( $>12$  weeks) in adult patients with BMI  $\geq 27$  kg/m<sup>2</sup> with one or more obesity-associated comorbid condition (e.g., type 2 diabetes, hypertension, and/or dyslipidemia) who are motivated to lose weight (22). 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 dietary recommendations, in most cases by modulating appetite or satiety. Providers 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 patient. These medications are contraindicated in women who are pregnant or actively trying to conceive and not recommended for use in women who are nursing. Women of reproductive potential should receive counseling regarding the use of reliable methods of contraception. Of note, while weight loss medications are often used in patients with type 1 diabetes, clinical trial data in this population are limited.

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

Medication name	Typical adult maintenance dose	Average wholesale price (30-day supply) (130)	National Average Drug Acquisition Cost (30-day supply) (131)	1-Year (52- or 56-week) mean weight loss (% loss from baseline)		Common side effects (132–136)	Possible safety concerns/considerations (132–136)
				Treatment arms	Weight loss (% loss from baseline)		
<b>Short-term treatment (≤12 weeks)</b>							
<b>Sympathomimetic amine anorectic</b>							
Phentermine (137)	8–37.5 mg q.d.*	\$5–\$44 (37.5 mg dose)	\$3 (37.5 mg dose)	15 mg q.d.† 7.5 mg q.d.† PBO	6.1 5.5 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 (3)	60 mg t.i.d. (OTC) 120 mg t.i.d. (Rx)	\$41–\$82 \$823	\$41 \$659	120 mg t.i.d.‡ PBO	9.6 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 (138)	7.5 mg/46 mg q.d.§ 7.5 mg/46 mg q.d.¶	\$223 (7.5 mg/46 mg dose)	\$179 (7.5 mg/46 mg dose)	15 mg/92 mg q.d.   7.5 mg/46 mg q.d.   PBO	9.8 7.8 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> </ul>
<b>Opioid antagonist/antidepressant combination</b>							
Naltrexone/bupropion ER (15)	16 mg/180 mg b.i.d.	\$364	\$291	16 mg/180 mg b.i.d. PBO	5.0 1.8	Constipation, nausea, headache, xerostomia, insomnia, elevated heart rate and blood pressure	<ul style="list-style-type: none"> <li>Contraindicated in patients with uncontrolled hypertension and/or seizure disorders</li> <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. S118

**Table 8.2—Continued**

Medication name	Typical adult maintenance dose	Average wholesale price (30-day supply) (130)	National Average Drug Acquisition Cost (30-day supply) (131)	1-Year (52- or 56-week) mean weight loss (% loss from baseline)		Common side effects (132–136)	Possible safety concerns/considerations (132–136)
				Treatment arms	Weight loss (% loss from baseline)		
<b>Glucagon-like peptide 1 receptor agonist</b>							
Liraglutide (16)**	3 mg q.d.	\$1,619	\$1,296	3.0 mg q.d. 1.8 mg q.d. PBO	6.0 4.7 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 patients with kidney disease when initiating or increasing dose due to potential risk of acute kidney injury</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 (139)	2.4 mg once weekly	\$1,619	\$1,302	2.4 mg weekly PBO	9.6 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> </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 women who are or may become pregnant. Women 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; N/A, not applicable; OTC, over the counter; 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. \*\*Agent has demonstrated cardiovascular safety in a dedicated cardiovascular outcome trial (140). ‡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.

### 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 (62–64). Unless clinical circumstances (such as poor tolerability) or other considerations (such as financial expense or patient 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 (65). 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 (66).

Recently, an oral hydrogel (Plenity) has 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 (67).

### METABOLIC SURGERY

#### Recommendations

- 8.17** 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 Americans) 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 Americans) who do not achieve durable weight loss and improvement in comorbidities (including hyperglycemia) with nonsurgical methods. **A**
- 8.18** 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 Americans) who do not achieve durable weight loss and improvement in comorbidities (including hyperglycemia) with nonsurgical methods. **A**
- 8.19** Metabolic surgery should be performed in high-volume centers with multidisciplinary teams knowledgeable about and experienced in the management of obesity, diabetes, and gastrointestinal surgery. **E**
- 8.20** 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**
- 8.21** People who undergo metabolic surgery should receive long-term medical and behavioral support and routine monitoring of micronutrient, nutritional, and metabolic status. **B**
- 8.22** 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

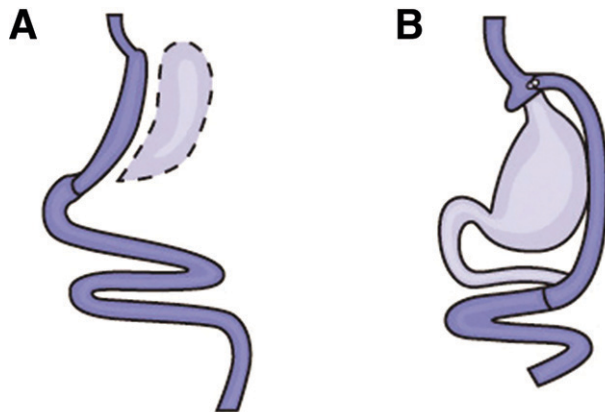
alerting patients to hypoglycemia, especially for those with severe hypoglycemia or hypoglycemia unawareness. **E**

- 8.23** 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 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 patients with type 2 diabetes and obesity compared with nonsurgical intervention (17). In addition to improving glycemia, metabolic surgery reduces the incidence of microvascular disease (68), improves quality of life (69–71), decreases cancer risk, and improves cardiovascular disease risk factors and long-term cardiovascular events (72–83). Cohort studies that match surgical and nonsurgical subjects strongly suggest that metabolic surgery reduces all-cause mortality (84,85).

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



**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 (141).

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 Americans) for people with type 2 diabetes who have not achieved sufficient weight loss and improved comorbidities (including hyperglycemia) with reasonable nonsurgical treatments (86–93). Studies have documented diabetes remission after 1–5 years in 30–63% of patients with RYGB (17,94). Most notably, the Surgical Treatment and Medications Potentially Eradicate Diabetes Efficiently (STAMPEDE) trial, which randomized 150 participants with uncontrolled 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 (95). Available data suggest an erosion of diabetes remission over time (96); 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 (97,98), and the majority of those who undergo surgery maintain substantial improvement of glycemic control from baseline for at least 5–15 years (69,73,74,95,98–101).

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, nonuse of insulin) are associated with higher rates of

diabetes remission (70,73,100,102). Greater baseline visceral fat area may also predict improved postoperative outcomes, especially among Asian American patients with type 2 diabetes, who typically have greater visceral fat compared with Caucasians (103).

Although surgery has been shown to improve the metabolic profiles of patients with type 1 diabetes, larger and longer-term studies are needed to determine the role of metabolic surgery in such patients (104).

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 are largely dependent on assumptions about the long-term effectiveness and safety of the procedures (105,106).

#### 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 (107–111). Major complications occur in 2–6% of those undergoing metabolic surgery, which compares favorably with the rates for other commonly performed elective operations (111). Postsurgical recovery times and morbidity have also dramatically declined. Minor complications and need

for operative reintervention occur in up to 15% (107–116). Empirical data suggest that proficiency of the operating surgeon and surgical team is an important factor for determining mortality, complications, reoperations, and readmissions (117). Accordingly, metabolic surgery should be performed in high-volume centers with multidisciplinary teams experienced in the management of diabetes, obesity, and gastrointestinal surgery.

Beyond the perioperative period, longer-term risks include vitamin and mineral deficiencies, anemia, osteoporosis, dumping syndrome, and severe hypoglycemia (118). Nutritional and micronutrient deficiencies and related complications occur with variable frequency depending on the type of procedure and require routine monitoring of micronutrient and nutritional status and lifelong vitamin/nutritional supplementation (118). 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 (119–121). 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 occurs, 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 postsurgery. 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, insulinoma). Initial management includes patient 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 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) (122).

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 (118,123–128). Candidates for metabolic surgery should be assessed by a mental health professional with expertise in obesity management prior to consideration for surgery (129). Surgery should be postponed in patients 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.

## References

- Knowler WC, Barrett-Connor E, Fowler SE, et al.; Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 2002;346:393–403
- Garvey WT, Ryan DH, Henry R, et al. Prevention of type 2 diabetes in subjects with prediabetes and metabolic syndrome treated with phentermine and topiramate extended release. *Diabetes Care* 2014;37:912–921
- Torgerson JS, Hauptman J, Boldrin MN, Sjöström L. XENical in the prevention of diabetes in obese subjects (XENDOS) study: a randomized study of orlistat as an adjunct to lifestyle changes for the prevention of type 2 diabetes in obese patients. *Diabetes Care* 2004;27:155–161
- le Roux CW, Astrup A, Fujioka K, et al.; SCALE Obesity Prediabetes NN8022-1839 Study Group. 3 years of liraglutide versus placebo for type 2 diabetes risk reduction and weight management in individuals with prediabetes: a randomised, double-blind trial. *Lancet* 2017;389:1399–1409
- Booth H, Khan O, Prevost T, et al. Incidence of type 2 diabetes after bariatric surgery: population-based matched cohort study. *Lancet Diabetes Endocrinol* 2014;2:963–968
- UKPDS Group. UK Prospective Diabetes Study 7: response of fasting plasma glucose to diet therapy in newly presenting type II diabetic patients. *Metabolism* 1990;39:905–912
- Goldstein DJ. Beneficial health effects of modest weight loss. *Int J Obes Relat Metab Disord* 1992;16:397–415
- Pastors JG, Warshaw H, Daly A, Franz M, Kulkarni K. The evidence for the effectiveness of medical nutrition therapy in diabetes management. *Diabetes Care* 2002;25:608–613
- Lim EL, Hollingsworth KG, Aribisala BS, Chen MJ, Mathers JC, Taylor R. Reversal of type 2 diabetes: normalisation of beta cell function in association with decreased pancreas and liver triacylglycerol. *Diabetologia* 2011;54:2506–2514
- Jackness C, Karmally W, Febres G, et al. Very low-calorie diet mimics the early beneficial effect of Roux-en-Y gastric bypass on insulin sensitivity and  $\beta$ -cell function in type 2 diabetic patients. *Diabetes* 2013;62:3027–3032
- Rothberg AE, McEwen LN, Kraftson AT, Fowler CE, Herman WH. Very-low-energy diet for type 2 diabetes: an underutilized therapy? *J Diabetes Complications* 2014;28:506–510
- Hollander PA, Elbein SC, Hirsch IB, et al. Role of orlistat in the treatment of obese patients with type 2 diabetes. A 1-year randomized double-blind study. *Diabetes Care* 1998;21:1288–1294
- Garvey WT, Ryan DH, Bohannon NJV, et al. Weight-loss therapy in type 2 diabetes: effects of phentermine and topiramate extended release. *Diabetes Care* 2014;37:3309–3316
- O'Neil PM, Smith SR, Weissman NJ, et al. Randomized placebo-controlled clinical trial of lorcaserin for weight loss in type 2 diabetes mellitus: the BLOOM-DM study. *Obesity (Silver Spring)* 2012;20:1426–1436
- Hollander P, Gupta AK, Plodkowski R, et al.; COR-Diabetes Study Group. Effects of naltrexone sustained-release/bupropion sustained-release combination therapy on body weight and glycemic parameters in overweight and obese patients with type 2 diabetes. *Diabetes Care* 2013;36:4022–4029
- Davies MJ, Bergenstal R, Bode B, et al.; NN8022-1922 Study Group. Efficacy of liraglutide for weight loss among patients with type 2 diabetes: the SCALE diabetes randomized clinical trial. *JAMA* 2015;314:687–699
- Rubino F, Nathan DM, Eckel RH, et al.; Delegates of the 2nd Diabetes Surgery Summit. Metabolic surgery in the treatment algorithm for type 2 diabetes: a joint statement by international diabetes organizations. *Diabetes Care* 2016;39:861–877
- Steven S, Hollingsworth KG, Al-Mrabeh A, et al. Very low-calorie diet and 6 months of weight stability in type 2 diabetes: pathophysiological changes in responders and nonresponders. *Diabetes Care* 2016;39:808–815
- Jensen MD, Ryan DH, Apovian CM, et al.; American College of Cardiology/American Heart Association Task Force on Practice Guidelines; Obesity Society. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. *J Am Coll Cardiol* 2014;63(25 Pt B):2985–3023
- Lean ME, Leslie WS, Barnes AC, et al. Primary care-led weight management for remission of type 2 diabetes (DIRECT): an open-label, cluster-randomised trial. *Lancet* 2018;391:541–551
- Lean MEJ, Leslie WS, Barnes AC, et al. Durability of a primary care-led weight-management intervention for remission of type 2 diabetes: 2-year results of the DIRECT open-label, cluster-randomised trial. *Lancet Diabetes Endocrinol* 2019;7:344–355
- Kahan S, Fujioka K. Obesity pharmacotherapy in patients with type 2 diabetes. *Diabetes Spectr* 2017;30:250–257
- Cao P, Song Y, Zhuang Z, et al. Obesity and COVID-19 in adult patients with diabetes. *Diabetes* 2021;70:1061–1069
- Richardson S, Hirsch JS, Narasimhan M, et al.; the Northwell COVID-19 Research Consortium. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. *JAMA* 2020;323:2052–2059
- Chu Y, Yang J, Shi J, Zhang P, Wang X. Obesity is associated with increased severity of disease in COVID-19 pneumonia: a systematic review and meta-analysis. *Eur J Med Res* 2020;25:64
- Popkin BM, Du S, Green WD, et al. Individuals with obesity and COVID-19: a global perspective on the epidemiology and biological relationships. *Obes Rev* 2020;21:e13128
- AMA Manual of Style Committee. *AMA Manual of Style: A Guide for Authors and Editors*. 11th ed. New York, Oxford University Press, 2020
- American Medical Association. *Person-First Language for Obesity H-440.821*. Accessed 12 October 2021. Available from <https://policy-search.ama-assn.org/policyfinder/detail/obesity?uri=%2FAMADoc%2FHOD.xml-H-440.821.xml>
- Rubino F, Puhl RM, Cummings DE, et al. Joint international consensus statement for ending stigma of obesity. *Nat Med* 2020;26:485–497
- WHO Expert Consultation. *Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies*. *Lancet* 2004;363:157–163
- Araneta MRG, Kanaya A, Hsu WC, et al. Optimum BMI cutpoints to screen Asian Americans for type 2 diabetes. *Diabetes Care* 2015;38:814–820
- Yancy CW, Jessup M, Bozkurt B, et al.; American College of Cardiology Foundation; American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2013;62:e147–e239
- Bosch X, Monclús E, Escoda O, et al. Unintentional weight loss: Clinical characteristics and outcomes in a prospective cohort of 2677 patients. *PLoS One* 2017;12:e0175125
- Wilding JPH. The importance of weight management in type 2 diabetes mellitus. *Int J Clin Pract* 2014;68:682–691
- Van Gaal L, Scheen A. Weight management in type 2 diabetes: current and emerging approaches to treatment. *Diabetes Care* 2015;38:1161–1172
- Kushner RF, Batsis JA, Butsch WS, et al. Weight history in clinical practice: the state of the science and future directions. *Obesity (Silver Spring)* 2020;28:9–17

37. Warren J, Smalley B, Barefoot N. Higher motivation for weight loss in African American than Caucasian rural patients with hypertension and/or diabetes. *Ethn Dis* 2016;26:77–84
38. Rothberg AE, McEwen LN, Kraftson AT, et al. Impact of weight loss on waist circumference and the components of the metabolic syndrome. *BMJ Open Diabetes Res Care* 2017;5:e000341
39. Evert AB, Dennison M, Gardner CD, et al. Nutrition therapy for adults with diabetes or prediabetes: a consensus report. *Diabetes Care* 2019;42:731–754
40. Wing RR, Bolin P, Brancati FL, et al.; Look AHEAD Research Group. Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes. *N Engl J Med* 2013;369:145–154
41. Look AHEAD Research Group. Eight-year weight losses with an intensive lifestyle intervention: the Look AHEAD study. *Obesity (Silver Spring)* 2014;22:5–13
42. Gregg EW, Jakicic JM, Blackburn G, et al.; Look AHEAD Research Group. Association of the magnitude of weight loss and changes in physical fitness with long-term cardiovascular disease outcomes in overweight or obese people with type 2 diabetes: a post-hoc analysis of the Look AHEAD randomised clinical trial. *Lancet Diabetes Endocrinol* 2016;4:913–921
43. Baum A, Scarpa J, Bruzelius E, Tamler R, Basu S, Faghmous J. Targeting weight loss interventions to reduce cardiovascular complications of type 2 diabetes: a machine learning-based post-hoc analysis of heterogeneous treatment effects in the Look AHEAD trial. *Lancet Diabetes Endocrinol* 2017;5:808–815
44. Franz MJ, Boucher JL, Rutten-Ramos S, VanWormer JJ. Lifestyle weight-loss intervention outcomes in overweight and obese adults with type 2 diabetes: a systematic review and meta-analysis of randomized clinical trials. *J Acad Nutr Diet* 2015;115:1447–1463
45. Sacks FM, Bray GA, Carey VJ, et al. Comparison of weight-loss diets with different compositions of fat, protein, and carbohydrates. *N Engl J Med* 2009;360:859–873
46. de Souza RJ, Bray GA, Carey VJ, et al. Effects of 4 weight-loss diets differing in fat, protein, and carbohydrate on fat mass, lean mass, visceral adipose tissue, and hepatic fat: results from the POUNDS LOST trial. *Am J Clin Nutr* 2012;95:614–625
47. Johnston BC, Kanters S, Bandayrel K, et al. Comparison of weight loss among named diet programs in overweight and obese adults: a meta-analysis. *JAMA* 2014;312:923–933
48. Leung CW, Epel ES, Ritchie LD, Crawford PB, Laraia BA. Food insecurity is inversely associated with diet quality of lower-income adults. *J Acad Nutr Diet* 2014;114:1943–53.e2
49. Kahan S, Manson JE. Obesity treatment, beyond the guidelines: practical suggestions for clinical practice. *JAMA* 2019;321:1349–1350
50. Donnelly JE, Blair SN, Jakicic JM, Manore MM, Rankin JW; American College of Sports Medicine. American College of Sports Medicine Position Stand. Appropriate physical activity intervention strategies for weight loss and prevention of weight regain for adults. *Med Sci Sports Exerc* 2009;41:459–471
51. Gudzone KA, Doshi RS, Mehta AK, et al. Efficacy of commercial weight-loss programs: an updated systematic review. *Ann Intern Med* 2015;162:501–512
52. Bloom B, Mehta AK, Clark JM, Gudzone KA. Guideline-concordant weight-loss programs in an urban area are uncommon and difficult to identify through the internet. *Obesity (Silver Spring)* 2016;24:583–588
53. Tsai AG, Wadden TA. The evolution of very-low-calorie diets: an update and meta-analysis. *Obesity (Silver Spring)* 2006;14:1283–1293
54. Johansson K, Neovius M, Hemmingsson E. Effects of anti-obesity drugs, diet, and exercise on weight-loss maintenance after a very-low-calorie diet or low-calorie diet: a systematic review and meta-analysis of randomized controlled trials. *Am J Clin Nutr* 2014;99:14–23
55. Batsis JA, Apolzan JW, Bagley PJ, et al. A systematic review of dietary supplements and alternative therapies for weight loss. *Obesity (Silver Spring)* 2021;29:1102–1113
56. Bessell E, Maunder A, Lauche R, Adams J, Sainsbury A, Fuller NR. Efficacy of dietary supplements containing isolated organic compounds for weight loss: a systematic review and meta-analysis of randomised placebo-controlled trials. *Int J Obes* 2021;45:1631–1643
57. Maunder A, Bessell E, Lauche R, Adams J, Sainsbury A, Fuller NR. Effectiveness of herbal medicines for weight loss: a systematic review and meta-analysis of randomized controlled trials. *Diabetes Obes Metab* 2020;22:891–903
58. Hill-Briggs F, Adler NE, Berkowitz SA, et al. Social determinants of health and diabetes: a scientific review. *Diabetes Care* 2021;44:258–279
59. Cai X, Yang W, Gao X, Zhou L, Han X, Ji L. Baseline body mass index and the efficacy of hypoglycemic treatment in type 2 diabetes: a meta-analysis. *PLoS One* 2016;11:e0166625
60. Domecq JP, Prutsky G, Leppin A, et al. Clinical review: drugs commonly associated with weight change: a systematic review and meta-analysis. *J Clin Endocrinol Metab* 2015;100:363–370
61. Drugs.com. Phentermine [FDA prescribing information]. Accessed 12 October 2021. Available from <https://www.drugs.com/pro/phentermine.html>
62. Apovian CM, Aronne LJ, Bessesen DH, et al.; Endocrine Society. Pharmacological management of obesity: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2015;100:342–362
63. Fujioka K, O'Neil PM, Davies M, et al. Early weight loss with liraglutide 3.0 mg predicts 1-year weight loss and is associated with improvements in clinical markers. *Obesity (Silver Spring)* 2016;24:2278–2288
64. Fujioka K, Plodkowski R, O'Neil PM, Gilder K, Walsh B, Greenway FL. The relationship between early weight loss and weight loss at 1 year with naltrexone ER/bupropion ER combination therapy. *Int J Obes* 2016;40:1369–1375
65. Sullivan S. Endoscopic medical devices for primary obesity treatment in patients with diabetes. *Diabetes Spectr* 2017;30:258–264
66. Kahan S, Saunders KH, Kaplan LM. Combining obesity pharmacotherapy with endoscopic bariatric and metabolic therapies. *Techniques nnov Gastrointest Endosc* 2020;22:154–158
67. Greenway FL, Aronne LJ, Raben A, et al. A randomized, double-blind, placebo-controlled study of Gelesis100: a novel nonsystemic oral hydrogel for weight loss. *Obesity (Silver Spring)* 2019;27:205–216
68. O'Brien R, Johnson E, Haneuse S, et al. Microvascular outcomes in patients with diabetes after bariatric surgery versus usual care: a matched cohort study. *Ann Intern Med* 2018;169:300–310
69. Mingrone G, Panunzi S, De Gaetano A, et al. Bariatric-metabolic surgery versus conventional medical treatment in obese patients with type 2 diabetes: 5 year follow-up of an open-label, single-centre, randomised controlled trial. *Lancet* 2015;386:964–973
70. Schauer PR, Bhatt DL, Kirwan JP, et al.; STAMPEDE Investigators. Bariatric surgery versus intensive medical therapy for diabetes—3-year outcomes. *N Engl J Med* 2014;370:2002–2013
71. Halperin F, Ding S-A, Simonson DC, et al. Roux-en-Y gastric bypass surgery or lifestyle with intensive medical management in patients with type 2 diabetes: feasibility and 1-year results of a randomized clinical trial. *JAMA Surg* 2014;149:716–726
72. Sjöström L, Lindroos A-K, Peltonen M, et al.; Swedish Obese Subjects Study Scientific Group. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. *N Engl J Med* 2004;351:2683–2693
73. Sjöström L, Peltonen M, Jacobson P, et al. Association of bariatric surgery with long-term remission of type 2 diabetes and with microvascular and macrovascular complications. *JAMA* 2014;311:2297–2304
74. Adams TD, Davidson LE, Litwin SE, et al. Health benefits of gastric bypass surgery after 6 years. *JAMA* 2012;308:1122–1131
75. Sjöström L, Narbro K, Sjöström CD, et al.; Swedish Obese Subjects Study. Effects of bariatric surgery on mortality in Swedish obese subjects. *N Engl J Med* 2007;357:741–752
76. Sjöström L, Gummesson A, Sjöström CD, et al.; Swedish Obese Subjects Study. Effects of bariatric surgery on cancer incidence in obese patients in Sweden (Swedish Obese Subjects Study): a prospective, controlled intervention trial. *Lancet Oncol* 2009;10:653–662
77. Sjöström L, Peltonen M, Jacobson P, et al. Bariatric surgery and long-term cardiovascular events. *JAMA* 2012;307:56–65
78. Adams TD, Gress RE, Smith SC, et al. Long-term mortality after gastric bypass surgery. *N Engl J Med* 2007;357:753–761
79. Arterburn DE, Olsen MK, Smith VA, et al. Association between bariatric surgery and long-term survival. *JAMA* 2015;313:62–70
80. Adams TD, Arterburn DE, Nathan DM, Eckel RH. Clinical outcomes of metabolic surgery: microvascular and macrovascular complications. *Diabetes Care* 2016;39:912–923
81. Sheng B, Truong K, Spitzer H, Zhang L, Tong X, Chen L. The long-term effects of bariatric surgery on type 2 diabetes remission, microvascular and macrovascular complications, and mortality: a systematic review and meta-analysis. *Obes Surg* 2017;27:2724–2732
82. Fisher DP, Johnson E, Haneuse S, et al. Association between bariatric surgery and macrovascular disease outcomes in patients with type 2 diabetes and severe obesity. *JAMA* 2018;320:1570–1582
83. Billeter AT, Scheurlen KM, Probst P, et al. Meta-analysis of metabolic surgery versus

- medical treatment for microvascular complications in patients with type 2 diabetes mellitus. *Br J Surg* 2018;105:168–181
84. Aminian A, Zajichek A, Arterburn DE, et al. Association of metabolic surgery with major adverse cardiovascular outcomes in patients with type 2 diabetes and obesity. *JAMA* 2019;322:1271–1282
85. Syn NL, Cummings DE, Wang LZ, et al. Association of metabolic-bariatric surgery with long-term survival in adults with and without diabetes: a one-stage meta-analysis of matched cohort and prospective controlled studies with 174 772 participants. *Lancet* 2021;397:1830–1841
86. Rubino F, Kaplan LM, Schauer PR, Cummings DE; Diabetes Surgery Summit Delegates. The Diabetes Surgery Summit consensus conference: recommendations for the evaluation and use of gastrointestinal surgery to treat type 2 diabetes mellitus. *Ann Surg* 2010;251:399–405
87. Cummings DE, Cohen RV. Beyond BMI: the need for new guidelines governing the use of bariatric and metabolic surgery. *Lancet Diabetes Endocrinol* 2014;2:175–181
88. Zimmet P, Alberti KGMM, Rubino F, Dixon JB. IDF's view of bariatric surgery in type 2 diabetes. *Lancet* 2011;378:108–110
89. Kasama K, Mui W, Lee WJ, et al. IFSO-APC consensus statements 2011. *Obes Surg* 2012;22:677–684
90. Wentworth JM, Burton P, Laurie C, Brown WA, O'Brien PE. Five-year outcomes of a randomized trial of gastric band surgery in overweight but not obese people with type 2 diabetes. *Diabetes Care* 2017;40:e44–e45
91. Cummings DE, Arterburn DE, Westbrook EO, et al. Gastric bypass surgery vs intensive lifestyle and medical intervention for type 2 diabetes: the CROSSROADS randomised controlled trial. *Diabetologia* 2016;59:945–953
92. Liang Z, Wu Q, Chen B, Yu P, Zhao H, Ouyang X. Effect of laparoscopic Roux-en-Y gastric bypass surgery on type 2 diabetes mellitus with hypertension: a randomized controlled trial. *Diabetes Res Clin Pract* 2013;101:50–56
93. Aminian A, Chang J, Brethauer SA; American Society for Metabolic and Bariatric Surgery Clinical Issues Committee. ASBMS updated position statement on bariatric surgery in class I obesity (BMI 30–35 kg/m<sup>2</sup>). *Surg Obes Relat Dis* 2018;14:1071–1087
94. Isaman DJM, Rothberg AE, Herman WH. Reconciliation of type 2 diabetes remission rates in studies of Roux-en-Y gastric bypass. *Diabetes Care* 2016;39:2247–2253
95. Schauer PR, Bhatt DL, Kirwan JP, et al.; STAMPEDE Investigators. Bariatric surgery versus intensive medical therapy for diabetes—5-year outcomes. *N Engl J Med* 2017;376:641–651
96. Ikramuddin S, Korner J, Lee W-J, et al. Durability of addition of Roux-en-Y gastric bypass to lifestyle intervention and medical management in achieving primary treatment goals for uncontrolled type 2 diabetes in mild to moderate obesity: a randomized control trial. *Diabetes Care* 2016;39:1510–1518
97. Sjöholm K, Pajunen P, Jacobson P, et al. Incidence and remission of type 2 diabetes in relation to degree of obesity at baseline and 2 year weight change: the Swedish Obese Subjects (SOS) study. *Diabetologia* 2015;58:1448–1453
98. Arterburn DE, Bogart A, Sherwood NE, et al. A multisite study of long-term remission and relapse of type 2 diabetes mellitus following gastric bypass. *Obes Surg* 2013;23:93–102
99. Cohen RV, Pinheiro JC, Schiavon CA, Salles JE, Wajchenberg BL, Cummings DE. Effects of gastric bypass surgery in patients with type 2 diabetes and only mild obesity. *Diabetes Care* 2012;35:1420–1428
100. Brethauer SA, Aminian A, Romero-Talamás H, et al. Can diabetes be surgically cured? Long-term metabolic effects of bariatric surgery in obese patients with type 2 diabetes mellitus. *Ann Surg* 2013;258:628–636; discussion 636–637
101. Hsu C-C, Almulaifi A, Chen J-C, et al. Effect of bariatric surgery vs medical treatment on type 2 diabetes in patients with body mass index lower than 35: five-year outcomes. *JAMA Surg* 2015;150:1117–1124
102. Hariri K, Guevara D, Jayaram A, Kini SU, Herron DM, Fernandez-Ranvier G. Preoperative insulin therapy as a marker for type 2 diabetes remission in obese patients after bariatric surgery. *Surg Obes Relat Dis* 2018;14:332–337
103. Yu H, Di J, Bao Y, et al. Visceral fat area as a new predictor of short-term diabetes remission after Roux-en-Y gastric bypass surgery in Chinese patients with a body mass index less than 35 kg/m<sup>2</sup>. *Surg Obes Relat Dis* 2015;11:6–11
104. Kirwan JP, Aminian A, Kashyap SR, Burguera B, Brethauer SA, Schauer PR. Bariatric surgery in obese patients with type 1 diabetes. *Diabetes Care* 2016;39:941–948
105. Rubin JK, Hinrichs-Krapels S, Hesketh R, Martin A, Herman WH, Rubino F. Identifying barriers to appropriate use of metabolic/bariatric surgery for type 2 diabetes treatment: Policy Lab results. *Diabetes Care* 2016;39:954–963
106. Fouse T, Schauer P. The socioeconomic impact of morbid obesity and factors affecting access to obesity surgery. *Surg Clin North Am* 2016;96:669–679
107. Flum DR, Belle SH, King WC, et al.; Longitudinal Assessment of Bariatric Surgery (LABS) Consortium. Perioperative safety in the longitudinal assessment of bariatric surgery. *N Engl J Med* 2009;361:445–454
108. Courcoulas AP, Christian NJ, Belle SH, et al.; Longitudinal Assessment of Bariatric Surgery (LABS) Consortium. Weight change and health outcomes at 3 years after bariatric surgery among individuals with severe obesity. *JAMA* 2013;310:2416–2425
109. Arterburn DE, Courcoulas AP. Bariatric surgery for obesity and metabolic conditions in adults. *BMJ* 2014;349:g3961
110. Young MT, Gebhart A, Phelan MJ, Nguyen NT. Use and outcomes of laparoscopic sleeve gastrectomy vs laparoscopic gastric bypass: analysis of the American College of Surgeons NSQIP. *J Am Coll Surg* 2015;220:880–885
111. Aminian A, Brethauer SA, Kirwan JP, Kashyap SR, Burguera B, Schauer PR. How safe is metabolic/diabetes surgery? *Diabetes Obes Metab* 2015;17:198–201
112. Birkmeyer NJO, Dimick JB, Share D, et al.; Michigan Bariatric Surgery Collaborative. Hospital complication rates with bariatric surgery in Michigan. *JAMA* 2010;304:435–442
113. Altieri MS, Yang J, Telem DA, et al. Lap band outcomes from 19,221 patients across centers and over a decade within the state of New York. *Surg Endosc* 2016;30:1725–1732
114. Hutter MM, Schirmer BD, Jones DB, et al. First report from the American College of Surgeons Bariatric Surgery Center Network: laparoscopic sleeve gastrectomy has morbidity and effectiveness positioned between the band and the bypass. *Ann Surg* 2011;254:410–420; discussion 420–422
115. Nguyen NT, Slone JA, Nguyen X-MT, Hartman JS, Hoyt DB. A prospective randomized trial of laparoscopic gastric bypass versus laparoscopic adjustable gastric banding for the treatment of morbid obesity: outcomes, quality of life, and costs. *Ann Surg* 2009;250:631–641
116. Courcoulas AP, King WC, Belle SH, et al. Seven-year weight trajectories and health outcomes in the Longitudinal Assessment of Bariatric Surgery (LABS) study. *JAMA Surg* 2018;153:427–434
117. Birkmeyer JD, Finks JF, O'Reilly A, et al.; Michigan Bariatric Surgery Collaborative. Surgical skill and complication rates after bariatric surgery. *N Engl J Med* 2013;369:1434–1442
118. Mechanick JI, Apovian C, Brethauer S, et al. Clinical practice guidelines for the perioperative nutrition, metabolic, and nonsurgical support of patients undergoing bariatric procedures – 2019 update: cosponsored by American Association of Clinical Endocrinologists/American College of Endocrinology, The Obesity Society, American Society for Metabolic & Bariatric Surgery, Obesity Medicine Association, and American Society of Anesthesiologists – executive summary. *Endocr Pract* 2019;25:1346–1359
119. Service FJ, Thompson GB, Service FJ, Andrews JC, Collazo-Clavell ML, Lloyd RV. Hyperinsulinemic hypoglycemia with nesidioblastosis after gastric-bypass surgery. *N Engl J Med* 2005;353:249–254
120. Sheehan A, Patti ME. Hypoglycemia after upper gastrointestinal surgery: clinical approach to assessment, diagnosis, and treatment. *Diabetes Metab Syndr Obes* 2020;13:4469–4482
121. Lee D, Dreyfuss JM, Sheehan A, Puleio A, Mulla CM, Patti ME. Glycemic patterns are distinct in post-bariatric hypoglycemia after gastric bypass (PBH-RYGB). *J Clin Endocrinol Metab* 2021;106:2291–2303
122. Salehi M, Vella A, McLaughlin T, Patti M-E. Hypoglycemia after gastric bypass surgery: current concepts and controversies. *J Clin Endocrinol Metab* 2018;103:2815–2826
123. Conason A, Teixeira J, Hsu C-H, Puma L, Knafo D, Geliebter A. Substance use following bariatric weight loss surgery. *JAMA Surg* 2013;148:145–150
124. Bhatti JA, Nathens AB, Thiruchelvam D, Grantcharov T, Goldstein BI, Redelmeier DA. Self-harm emergencies after bariatric surgery: a population-based cohort study. *JAMA Surg* 2016;151:226–232
125. Peterhänsel C, Petroff D, Klinitzke G, Kersting A, Wagner B. Risk of completed suicide after bariatric surgery: a systematic review. *Obes Rev* 2013;14:369–382
126. Jakobsen GS, Småstuen MC, Sandbu R, et al. Association of bariatric surgery vs medical obesity treatment with long-term medical

- complications and obesity-related comorbidities. *JAMA* 2018;319:291–301
127. King WC, Chen J-Y, Mitchell JE, et al. Prevalence of alcohol use disorders before and after bariatric surgery. *JAMA* 2012;307:2516–2525
128. Young-Hyman D, Peyrot M. *Psychosocial Care for People with Diabetes*. 1st ed. Alexandria, VA, American Diabetes Association, 2012
129. Greenberg I, Sogg S, M Perna F. Behavioral and psychological care in weight loss surgery: best practice update. *Obesity* (Silver Spring) 2009;17:880–884
130. Truven Health Analytics. *Micromedex 2.0. Introduction to RED BOOK Online*. Accessed 15 October 2021. Available from [https://www.micromedexsolutions.com/micromedex2/4.34.0/WebHelp/RED\\_BOOK/Introduction\\_to\\_REDB\\_BOOK\\_Online.htm](https://www.micromedexsolutions.com/micromedex2/4.34.0/WebHelp/RED_BOOK/Introduction_to_REDB_BOOK_Online.htm)
131. Data.Medicare.gov. NADAC (National Average Drug Acquisition Cost) 2021. U.S. Centers for Medicare & Medicaid Services. Accessed 15 October 2021. Available from <https://data.medicare.gov/dataset/d5eaf378-dcef-5779-83de-acdd8347d68e>
132. U.S. National Library of Medicine. Phen-termine - phentermine hydrochloride capsule. Accessed 13 October 2021. Available from <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=737eef3b-9a6b-4ab3-a25c-49d84d2a0197>
133. Nalpropion Pharmaceuticals. *Contrave* (naltrexone HCl/bupropion HCl) extended-release tablets. Accessed 13 October 2021. Available at <https://contrave.com>
134. CHEPLAPHARM and H2-Pharma. *Xenical* (orlistat). Accessed 13 October 2021. Available from <https://xenical.com>
135. Vivus. *Qsymia* (phentermine and topiramate extended-release) capsules. Accessed 13 October 2021. Available from <https://qsymia.com>
136. Novo Nordisk. *Saxenda* (liraglutide injection 3 mg). Accessed 13 October 2021. Available from <https://www.saxenda.com>
137. Aronne LJ, Wadden TA, Peterson C, Winslow D, Odeh S, Gadde KM. Evaluation of phentermine and topiramate versus phen-termine/topiramate extended-release in obese adults. *Obesity* (Silver Spring) 2013;21:2163–2171
138. Gadde KM, Allison DB, Ryan DH, et al. Effects of low-dose, controlled-release, phentermine plus topiramate combination on weight and associated comorbidities in overweight and obese adults (CONQUER): a randomised, placebo-controlled, phase 3 trial. *Lancet* 2011; 377:1341–1352
139. Davies M, Færch L, Jeppesen OK, et al.; STEP 2 Study Group. Semaglutide 2.4 mg once a week in adults with overweight or obesity, and type 2 diabetes (STEP 2): a randomised, double-blind, double-dummy, placebo-controlled, phase 3 trial. *Lancet* 2021;397:971–984
140. Marso SP, Daniels GH, Brown-Frandsen K, et al.; LEADER Steering Committee; LEADER Trial Investigators. Liraglutide and cardiovascular outcomes in type 2 diabetes. *N Engl J Med* 2016;375:311–322
141. National Institute of Diabetes and Digestive and Kidney Diseases. *Types of Weight-loss Surgery*. Accessed 31 August 2021. Available from <https://www.niddk.nih.gov/health-information/weight-management/bariatric-surgery/types>