8. Obesity and Weight Management for the Prevention and Treatment of Type 2 Diabetes: *Standards of Care in Diabetes–2024*

*American Diabetes Association Professional Practice Committee**

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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, an interprofessional 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.

Obesity is a chronic, often relapsing disease with numerous metabolic, 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 (7–17). 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 may promote sustained diabetes remission (11,18–22). Metabolic surgery, which induces on average >20% of body weight loss, strongly improves glycemia and often leads to remission of diabetes, improved quality of life, improved cardiovascular outcomes, and reduced mortality (23,24). Several modalities, including intensive behavioral and lifestyle counseling, obesity pharmacotherapy, and metabolic surgery, may aid in achieving and maintaining meaningful weight loss and reducing obesity-associated health risks. This section aims to provide evidence-based recommendations for obesity management, including behavioral, pharmacologic, and surgical interventions, in people with, or at high risk of, type 2 diabetes. Additional considerations regarding weight management in older individuals and children can be found in Section 13, "Older Adults," and Section 14, "Children and Adolescents," respectively.

ASSESSMENT AND MONITORING OF THE INDIVIDUAL WITH OVERWEIGHT AND OBESITY

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" and "person with diabetes" rather than "diabetic person"). **E**

**A complete list of members of the American Diabetes Association Professional Practice Committee can be found at https://doi.org/10.2337/dc24-SINT.*

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8.2a To support the diagnosis of obesity, measure height and weight to calculate BMI and perform additional measurements of body fat distribution, like waist circumference, waist-to-hip ratio, and/or waist-to-height ratio. **E**

8.2b Monitor obesity-related anthropometric measurements at least annually to inform treatment considerations. **E**

8.3 Accommodations should be made to provide privacy during anthropometric measurements. **E**

8.4 In people with type 2 diabetes and overweight or obesity, weight management should represent a primary goal of treatment along with glycemic management. **A**

8.5 People with diabetes and overweight or obesity may benefit from any magnitude of weight loss. Weight loss of 3–7% of baseline weight improves glycemia and other intermediate cardiovascular risk factors. **A** Sustained loss of >10% of body weight usually confers greater benefits, including disease-modifying effects and possible remission of type 2 diabetes, and may improve long-term cardiovascular outcomes and mortality. **B**

8.6 Individualize initial treatment approaches for obesity (i.e., lifestyle and nutritional therapy, pharmacologic agents, or metabolic surgery) **A** based on the person's medical history, life circumstances, preferences, and motivation. **C** Consider combining treatment approaches if appropriate. **E**

Obesity is defined by the World Health Organization as an abnormal or excessive fat accumulation that presents a risk to health (25). BMI (calculated as weight in kilograms divided by the square of height in meters [kg/m^2]) has been used widely to diagnose and stage obesity (overweight: BMI 25–29.9 kg/m^2; obesity class I: BMI 30–34.9 kg/m^2; obesity class II: BMI 35–39.9 kg/m^2; obesity class III: BMI ≥40 kg/m^2); however, BMI should not be relied on as a sole diagnostic and staging tool (19). Despite its ease of measurement, BMI is at most an imperfect measure of adipose tissue mass and does not measure adipose tissue distribution or function, nor does it factor in the presence of weight-related health or well-being consequences (26,27). BMI is especially prone to misclassification in individuals who are very muscular or frail, as well as in populations with different body composition and cardiometabolic risk (28). A diagnosis of obesity should be made based on an overall assessment of the individual's adipose tissue mass (BMI can be used as a general guidance), distribution (using other anthropometric measurements like waist circumference, waist-to-hip circumference ratio, or waist-to-height ratio), or function and, importantly, the presence of associated health or well-being consequences: metabolic, physical, or psychological/well-being (29).

Obesity is a key pathophysiologic driver of diabetes, other cardiovascular risk factors (e.g., hypertension, hyperlipidemia, nonalcoholic fatty liver disease, and inflammatory state), and ultimately cardiovascular and kidney disease (30). Diabetes can further exacerbate obesity, setting up a vicious cycle that contributes to disease progression and occurrence of microvascular and macrovascular complications. As such, treatment goals for both glycemia and weight are recommended in people with diabetes to address both hyperglycemia and its underlying pathophysiologic driver (obesity) and therefore benefit the person holistically.

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 (26,31,32). Measurement of weight and height (to calculate BMI) and other anthropometric measurements should be performed at least annually to aid the diagnosis of obesity and to monitor its progression and response to treatment (33). Clinical considerations, such as the presence of comorbid heart failure or unexplained weight change, may warrant more frequent evaluation (34,35). If such measurements are questioned or declined by the individual, the practitioner should be mindful of possible prior stigmatizing experiences and query for concerns, and the value of monitoring should be explained as a part of the medical evaluation process that helps to inform treatment decisions (36,37). Accommodations should be made to ensure privacy during weighing and other anthropometric measurements, particularly for those individuals who report or exhibit a high level of disease-related distress or dissatisfaction. Anthropometric measurements should be performed and reported nonjudgmentally; such information should be regarded as sensitive health information.

Health care professionals should advise individuals with overweight or obesity and those with increasing weight trajectories that, in general, greater fat accumulation increases the risk of diabetes, cardiovascular disease, and all-cause mortality and has multiple adverse health and quality of life consequences. 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 using shared decision-making (38). Strategies may include nutrition and dietary changes, physical activity and exercise, behavioral counseling, pharmacotherapy, medical devices, and metabolic surgery. The initial and subsequent therapeutic choice should be individualized based on the person's medical history, life circumstances, preferences, and motivation (39). Combination treatment approaches may be appropriate in higher-risk individuals.

Among people with type 2 diabetes and overweight or obesity who have inadequate glycemic, blood pressure, and lipid management and/or other obesity-related metabolic complications, modest and sustained weight loss (3–7% of body weight) improves glycemia, blood pressure, and lipids and may reduce the need for disease-specific medications (7–9,40). In people at risk, 3–7% weight loss reduces progression to diabetes (2,7,8,41,42). Greater weight loss may produce additional benefits (20,21). Mounting data have shown that >10% body weight loss usually confers greater benefits on glycemia and possibly diabetes remission and improves other metabolic comorbidities, including cardiovascular outcomes, nonalcoholic steatohepatitis, nonalcoholic fatty liver disease, adipose tissue inflammation, and sleep apnea, as well as physical comorbidities and quality of life (6,20,21,30,41,43–52).

With the increasing availability of more effective 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

8.7 Nutrition, physical activity, and behavioral therapy to achieve and maintain ≥5% weight loss are recommended for people with type 2 diabetes and overweight or obesity. **B**

8.8a Interventions including high frequency of counseling (≥16 sessions in 6 months) with focus on nutrition changes, physical activity, and behavioral strategies to achieve a 500–750 kcal/day energy deficit have been shown to be beneficial for weight loss and should be considered when available. **A**

8.8b Consider structured programs delivering behavioral counseling (face-to-face or remote) to address barriers to access. **E**

8.9 Nutrition recommendations should be individualized to the person's preferences and nutritional needs. Use nutritional plans that create an energy deficit, regardless of macronutrient composition, to achieve weight loss. **A**

8.10 When developing a plan of care, consider 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 other social determinants of health. **C**

8.11a For those who achieve weight loss goals, long-term (≥1 year) weight maintenance programs are recommended, when available. Effective programs 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**

8.11b For those who achieve weight loss goals, continue to monitor progress periodically, provide ongoing support, and recommend continuing adopted interventions to maintain goals long term. **E**

8.12 When short-term nutrition intervention using structured, very-low-calorie meals (800–1,000 kcal/day) is considered, it should be prescribed to 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 Nutritional supplements have not been shown to be effective for weight loss and are not recommended. **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 Pre-diabetes: A Consensus Report" (53).

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 (41), 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 (42). 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 (42). 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 (34). Moreover, several subgroups had improved cardiovascular outcomes, including those who achieved >10% weight loss (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 5% weight loss (19,54), and the benefits of weight loss are progressive; more intensive weight loss goals (>7%, >10%, >15%, etc.) may be pursued to achieve further health improvements if the individual is 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 (19,55–57). 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 (54), and improvement in cardiovascular risk factors (41). In a systematic review and meta-analysis, efficacy and safety of meal replacements (partial or total meal replacement) as compared with conventional diets showed improvements in A1C, FBG, body weight, and BMI (58). 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 (59).

Proven intensive behavioral interventions included ≥16 sessions during an initial 6 months and focus on nutritional changes, physical activity, and behavioral strategies to achieve an ~500–750 kcal/day energy deficit. Such interventions should be provided by trained individuals and can be conducted in either individual or group sessions (54). Assessing a person's motivation level, life circumstances, and willingness to implement behavioral changes to achieve weight loss should be considered along with medical status when such interventions are recommended and initiated (38,60). If such intensive behavioral interventions are not available or accessible, structured programs delivering behavioral counseling (face-to-face or remote) can be considered; however, their effectiveness varies (61,62).

People 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 individuals 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) (63,64). Some commercial and proprietary weight loss programs have shown promising weight loss results; however, results vary across these programs, most lack evidence of effectiveness, many do not satisfy guideline recommendations, and some promote unscientific and possibly dangerous practices (65,66).

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 (20,21). However, such an intensive nutritional intervention should be provided only by trained practitioners in medical settings with close ongoing monitoring and integration with behavioral support and counseling, and only for short term (generally up to 3 months). Furthermore, due to the high risk of complications (electrolyte abnormalities, severe fatigue, cardiac arrhythmias, etc.), such intensive intervention should be prescribed only to carefully selected individuals, such as those requiring weight loss and/or glycemic management before a needed surgery, if the benefits exceed the potential risks (67–69). As weight recurrence is common, such interventions should include long-term, comprehensive weight maintenance strategies and counseling to maintain weight loss and behavioral changes (70,71).

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 (72–75). 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 (76), and protein supplements may be indicated as adjuncts to medically supervised weight loss therapies (77,78).

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" (79).

PHARMACOTHERAPY

Recommendations

8.14 Whenever possible, minimize medications for comorbid conditions that are associated with weight gain. **E**

8.15 When choosing glucose-lowering medications for people with type 2 diabetes and overweight or obesity, prioritize medications with beneficial effect on weight. **B**

8.16 Obesity pharmacotherapy should be considered for people with diabetes and overweight or obesity along with lifestyle changes. Potential benefits and risks must be considered. **A**

8.17 In people with diabetes and overweight or obesity, the preferred pharmacotherapy should be a glucagon-like peptide 1 receptor agonist or dual glucose-dependent insulinotropic polypeptide and glucagon-like peptide 1 receptor agonist with greater weight loss efficacy (i.e., semaglutide or tirzepatide), especially considering their added weight-independent benefits (e.g., glycemic and cardiometabolic). **A**

8.18 To prevent therapeutic inertia, for those not reaching goals, reevaluate weight management therapies and intensify treatment with additional approaches (e.g., metabolic surgery, additional pharmacologic agents, and structured lifestyle management programs). **A**

Glucose-Lowering Therapy

Numerous effective glucose-lowering medications are currently available. However, to achieve both glycemic and weight management goals for diabetes treatment, health care professionals should prioritize the use of glucose-lowering medications with a beneficial effect on weight. Agents associated with clinically meaningful weight loss include glucagon-like peptide 1 (GLP-1) receptor agonists, dual glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 receptor agonist (tirzepatide), sodium–glucose cotransporter 2 inhibitors, metformin, and amylin mimetics. Dipeptidyl peptidase 4 inhibitors, centrally acting dopamine agonist (bromocriptine), α-glucosidase inhibitors, and bile acid sequestrants (colesevelam) are considered weight neutral. In contrast, insulin secretagogues (sulfonylureas and meglitinides), 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 individual'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 and pregabalin), β-blockers, and possibly sedating antihistamines and anticholinergics (80).

Approved Obesity Pharmacotherapy

The U.S. Food and Drug Administration (FDA) has approved several medications for weight management as adjuncts to reduced calorie diet and increased physical activity in individuals with a BMI $\geq$30 kg/m^2 or $\geq$27 kg/m^2 with one or more obesity-associated comorbid conditions (e.g., type 2 diabetes, hypertension, and/or dyslipidemia). 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 (22), and some of these agents (e.g., liraglutide and semaglutide) have an indication for glucose lowering as well as weight management. Phentermine and other older adrenergic agents are approved for short-term treatment (≤12 weeks) (81), while all others are approved for long-term treatment (>12 weeks) (22) (**Table 8.1**). (Refer to Section 14, "Children and Adolescents," for medications approved for adolescents with obesity.) 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 people with type 2 diabetes and overweight or obesity, agents with both glucose-lowering and weight loss effects are preferred (refer to Section 9, "Pharmacologic Approaches to Diabetes Treatment"), which include agents from the GLP-1 receptor agonist class and the dual GIP and GLP-1 receptor agonist class. Should use of these medications not result in achievement of weight management goals, or if they are not tolerated or contraindicated, other obesity treatment approaches should be considered. Two phase 3 trials have demonstrated the potential for use of the dual GIP and GLP-1 receptor agonist (tirzepatide) for obesity (SURMOUNT-1, individuals with obesity, and SURMOUNT-2, individuals with obesity and type 2 diabetes) (82,83). In the SURMOUNT-2 trial, tirzepatide resulted in body weight loss of 9.6% and 11.6% more than placebo and A1C lowering of 1.55% and 1.57% more than placebo after 72 weeks of treatment with the 10 mg and 15 mg doses, respectively, with adverse effects similar to those seen with the GLP-1 receptor agonist class (83).

Health care professionals should be knowledgeable about the benefits, dosing, and risks for each treatment option to balance the potential benefits of successful weight loss against the potential risks for each individual. The high risk and prevalence of cardiovascular disease in people with diabetes has to be balanced against the lack of long-term cardiovascular outcomes trial data for agents like naltrexone-bupropion and phentermine-topiramate. All these medications are contraindicated in individuals who are pregnant or actively trying to conceive and are not recommended for use in individuals who are nursing. Individuals of childbearing 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 of Obesity Pharmacotherapy

Upon initiating medications for obesity, assess their 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 (84,85); however, it is notable that the response rate with the latest generation of obesity pharmacotherapies is much higher (48,83). 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 obesity medication (typically defined as >5% weight loss after 3 months of use) should continue the medication long term. When early weight loss results are modest (typically <5% weight loss after 3 months of use), the benefits of ongoing treatment need to be balanced in the context of the glycemic response, the availability of other potential treatment options, treatment tolerance, and overall treatment burden.

Ongoing monitoring of the achievement and maintenance of weight management goals is recommended. For those not reaching or maintaining weight-related treatment goals, reevaluate weight management therapies and intensify treatment with additional approaches (e.g., metabolic surgery, additional pharmacologic agents, and structured lifestyle management programs).

MEDICAL DEVICES FOR WEIGHT LOSS

While gastric banding devices have fallen out of favor due to their limited long-term efficacy and high rate of complications, 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 (86). High cost, limited insurance coverage, and limited data supporting the efficacy of these devices in the treatment of individuals with diabetes has created uncertainty for their current use (87).

An oral hydrogel (cellulose and citric acid) has been approved for long-term use in those with BMI >25 kg/m^2 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. The average weight loss was relatively small (2.1% greater than placebo), and very few participants had diabetes at baseline (~10%) (88).

METABOLIC SURGERY

Recommendations

8.19 Consider metabolic surgery as a weight and glycemic management approach in people with diabetes with BMI ≥30.0 kg/m^2 (or ≥27.5 kg/m^2 in Asian American individuals) who are otherwise good surgical candidates. **A**

8.20 Metabolic surgery should be performed in high-volume centers with interprofessional teams knowledgeable about and experienced in managing obesity, diabetes, and gastrointestinal surgery (www.facs.org/quality-programs/accreditation-and-verification/metabolic-and-bariatric-surgery-accreditation-and-quality-improvement-program/). **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 post–metabolic surgery hypoglycemia is suspected, clinical evaluation should exclude other potential disorders contributing to hypoglycemia, and management should include education, medical nutrition therapy with a registered dietitian/nutritionist experienced in post–metabolic surgery 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

Table 8.1—Obesity pharmacotherapy

Medication name and typical adult maintenance dose	Average wholesale price (median and range for 30-day supply) (142)	National Average Drug Acquisition Cost (30-day supply) (143)	Treatment arms	Weight loss (% loss from baseline)	Common side effects (144–149)	Possible safety concerns and considerations (144–149)
Short-term treatment (12 weeks)						
Sympathomimetic amine anorectic						
Phentermine (150)						
8–37.5 mg q.d.*	$43 ($5–$90), 37.5 mg/day	$2 (37.5 mg dose)	15 mg q.d. 7.5 mg q.d. Placebo	5.0 4.9 1.9	Dry mouth, insomnia, dizziness, irritability, increased blood pressure, elevated heart rate	• Contraindicated for use in combination with monoamine oxidase inhibitors
Long-term treatment (52 or 56 weeks)						
Lipase inhibitor						
Orlistat (4)						
60 mg t.i.d. (OTC)	$52 ($41–$82)	NA	120 mg t.i.d.†	9.6	Abdominal pain, flatulence, fecal urgency	• Potential malabsorption of fat-soluble vitamins (A, D, E, K) and of certain medications (e.g., cyclosporine, thyroid hormone, anticonvulsants) • Rare cases of severe liver injury reported • Cholelithiasis • Nephrolithiasis
120 mg t.i.d. (Rx)	$843 ($781–$904)	$722	Placebo	5.6		
Sympathomimetic amine anorectic/antiepileptic combination						
Phentermine/topiramate ER (47)						
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.§ Placebo	9.8 7.8 1.2	Constipation, paresthesia, insomnia, nasopharyngitis, xerostomia, increased blood pressure	• Contraindicated for use in combination with monoamine oxidase inhibitors • Birth defects • Cognitive impairment • Acute angle-closure glaucoma
Opioid antagonist/antidepressant combination						
Naltrexone/bupropion ER (15)						
16 mg/180 mg b.i.d.	$750	$599	16 mg/180 mg b.i.d. Placebo	5.0 1.8	Constipation, nausea, headache, xerostomia, insomnia, elevated heart rate and blood pressure	• Contraindicated in people with unmanaged hypertension and/or seizure disorders • Contraindicated for use with chronic opioid therapy • Acute angle-closure glaucoma **Black box warning:** • Risk of suicidal behavior/ideation in people younger than 24 years old who have depression

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Table 8.1—Continued

Medication name and typical adult maintenance dose	Average wholesale price (median and range for 30-day supply) (142)	National Average Drug Acquisition Cost (30-day supply) (143)	Treatment arms	Weight loss (% loss from baseline)	Common side effects (144–149)	Possible safety concerns and considerations (144–149)
Glucagon-like peptide 1 receptor agonist						
Liraglutide (16,49)‖						
3 mg q.d.	$1,619	$1,294	3.0 mg q.d. 1.8 mg q.d. Placebo	6.0 4.7 2.0	Gastrointestinal side effects (nausea, vomiting, diarrhea, esophageal reflux), injection site reactions, elevated heart rate, hypoglycemia	• Pancreatitis has been reported in clinical trials, but causality has not been established. Discontinue if pancreatitis is suspected. • Use caution in people with kidney disease when initiating or increasing dose due to potential risk of acute kidney injury. • May cause cholelithiasis and gallstone-related complications. • Gastrointestinal disorders (severe constipation and small bowel obstruction/ileus progression) • Monitor for potential consequences of delayed absorption of oral medications. **Black box warning:** • Risk of thyroid C-cell tumors in rodents; human relevance not determined
Semaglutide (48,151)‖						
2.4 mg once weekly	$1,619	$1,295	2.4 mg weekly 1.0 mg weekly Placebo	9.6 7.0 3.4	Gastrointestinal side effects (nausea, vomiting, diarrhea, esophageal reflux), injection site reactions, elevated heart rate, hypoglycemia	• Pancreatitis has been reported in clinical trials, but causality has not been established. Discontinue if pancreatitis is suspected. • Use caution in people with kidney disease when initiating or increasing dose due to potential risk of acute kidney injury. • May cause cholelithiasis and gallstone-related complications. • Gastrointestinal disorders (severe constipation and small bowel obstruction/ileus progression) • Monitor for potential consequences of delayed absorption of oral medications. **Black box warning:** • Risk of thyroid C-cell tumors in rodents; human relevance not determined

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Table 8.1—Continued

Medication name and typical adult maintenance dose	Average wholesale price (median and range for 30-day supply) (142)	National Average Drug Acquisition Cost (30-day supply) (143)	Treatment arms	Weight loss (% loss from baseline)	Common side effects (144–149)	Possible safety concerns and considerations (144–149)
Dual glucose-dependent insulinotropic polypeptide and glucagon-like peptide 1 receptor agonist						
Tirzepatide (83)						
5 mg, 10 mg, or 15 mg once weekly	NA	NA	10 mg weekly 15 mg weekly Placebo	12.8 14.7 3.2	Gastrointestinal side effects (nausea, vomiting, diarrhea, esophageal reflux), injection site reactions, elevated heart rate, hypoglycemia	• Pancreatitis has been reported in clinical trials, but causality has not been established. Discontinue if pancreatitis is suspected. • Use caution in people with kidney disease when initiating or increasing dose due to potential risk of acute kidney injury. • May cause cholelithiasis and gallstone-related complications. • Gastrointestinal disorders (severe constipation and small bowel obstruction/ileus progression) • Monitor effects of oral medications with narrow therapeutic index (warfarin) or whose efficacy is dependent on threshold concentration. • Advise those using oral hormonal contraception to use or add a non-oral contraception method for 4 weeks after initiation and dose escalations. **Black box warning:** • Risk of thyroid C-cell tumors in rodents; human relevance not determined.

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; Rx, prescription; t.i.d., three times daily, p.o., by mouth; SC, subcutaneous injection; AWP, average wholesale price; NADAC, National Average Drug Acquisition Cost. *Use lowest effective dose; maximum appropriate dose is 37.5 mg. Weight loss data were extracted from the 12-week time point, as phentermine is approved for use for up to 12 weeks. †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 indication for reduction of cardiovascular events (49,151). AWP and NADAC prices for 30-day supply of maximum or maintenance dose as of 6 September 2023.

for those with severe hypoglycemia or hypoglycemia unawareness. **E**

8.24 In people who undergo metabolic surgery, routinely screen for psychosocial and behavioral health changes and refer to a qualified behavioral health professional as needed. **C**

8.25 Monitor individuals who have undergone metabolic surgery for insufficient weight loss or weight recurrence at least every 6–12 months. **E** In those who have insufficient weight loss or experience weight recurrence, assess for potential predisposing factors and, if appropriate, consider additional weight loss interventions (e.g., obesity pharmacotherapy). **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, hence the current preferred terminology of "metabolic surgery" (89).

A substantial body of evidence, including data from numerous large cohort studies and randomized controlled (nonblinded) clinical trials, demonstrates that metabolic surgery achieves superior glycemic management and reduction of cardiovascular risk in people with type 2 diabetes and obesity compared with nonsurgical intervention (45). In addition to improving glycemia, metabolic surgery reduces the incidence of microvascular disease (90), improves quality of life (45,91,92), decreases cancer risk, and improves cardiovascular disease risk factors and long-term cardiovascular events (93–104). Cohort studies that match surgical and nonsurgical subjects strongly suggest that metabolic surgery reduces all-cause mortality (105,106).

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.

Metabolic surgery has been demonstrated to have beneficial effects on type 2 diabetes irrespective of the presurgical BMI (107). The American Society for Metabolic and Bariatric Surgery is now recommending metabolic surgery for people with type 2 diabetes and a BMI $\geq$30 kg/m^2 (or $\geq$27.5 kg/m^2 for Asian American individuals) in surgically eligible individuals. Studies have documented diabetes remission after 1–5 years in 30–63% of individuals with RYGB (17,108).

Most notably, the Surgical Treatment and Medications Potentially Eradicate Diabetes Efficiently (STAMPEDE) trial, which randomized 150 participants with poorly managed 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 (45). Available data suggest an erosion of diabetes remission over time (46); at least 35–50% of individuals who initially achieve remission of diabetes eventually experience recurrence. Still, the median disease-free period among such individuals following RYGB is 8.3 years (109,110), and the majority of those who undergo surgery maintain substantial improvement of glycemia from baseline for at least 5–15 years (45,91,94,95,110–113).

Exceedingly few presurgical predictors of success have been identified, but younger age, shorter duration of diabetes (e.g., <8 years) (84), and lesser severity of diabetes (better glycemic control, not using insulin) are associated with higher rates of diabetes remission (45,94,112,114). Greater baseline visceral fat area may also predict improved postoperative outcomes, especially among Asian American people with type 2 diabetes (115).

Although surgery has been shown to improve the metabolic profiles and cardiovascular risk of people with type 1 diabetes, larger and longer-term studies are needed to determine the role of metabolic surgery in such individuals (116).

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 (117,118).

The safety of metabolic surgery has improved significantly with continued refinement of minimally invasive (laparoscopic) approaches, enhanced training and credentialing, and involvement of interprofessional teams. Perioperative mortality rates are typically 0.1–0.5%, similar to those of common abdominal procedures such as cholecystectomy or hysterectomy (119–123). Major complications occur in 2–6% of those undergoing metabolic surgery, which compares favorably with the rates for other commonly performed elective operations (123). Postsurgical recovery times and morbidity have also dramatically declined. Minor complications and need for operative reintervention occur in up to 15% (119–128). Empirical data suggest that the proficiency of the operating surgeon and surgical team is an important factor in determining mortality, complications, reoperations, and readmissions (129). Accordingly, metabolic surgery should be performed in high-volume centers with interprofessional teams experienced in managing diabetes, obesity, and gastrointestinal surgery. Refer to the American College of Surgeons website for information on accreditation and to locate an accredited program (https://www.facs.org/quality-programs/accreditation-and-verification/metabolic-and-bariatric-surgery-accreditation-and-quality-improvement-program/).

Beyond the perioperative period, longer-term risks include vitamin and mineral deficiencies, anemia, osteoporosis, dumping syndrome, and severe hypoglycemia (130). 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 (130). 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. Post–metabolic surgery hypoglycemia can occur with RYGB, VSG, and other gastrointestinal procedures and may severely impact quality of life (131–133). Post–metabolic

surgery hypoglycemia is driven in part by altered gastric emptying of ingested nutrients, leading to rapid intestinal glucose absorption and excessive postprandial secretion of GLP-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, post–bariatric surgery hypoglycemia 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, individuals should be offered medical nutrition therapy with a dietitian experienced in post–bariatric surgery hypoglycemia 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 GLP-1 and insulin secretion (e.g., diazoxide, octreotide) (134).

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 (130,135–140). Candidates for metabolic surgery should be assessed by a behavioral health professional with expertise in obesity management prior to consideration for surgery (141). Surgery should be postponed in individuals with alcohol or substance use disorders, severe depression, suicidal ideation, or other significant behavioral health conditions until these conditions have been sufficiently addressed. Individuals with preoperative or new-onset psychopathology should be assessed regularly following surgery to optimize behavioral health and postsurgical outcomes.

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