

8. Obesity and Weight Management for the Prevention and Treatment of Type 2 Diabetes: Standards of Care in Diabetes-2025

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American Diabetes Association Professional Practice Committee*

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 the development and progression of 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 (7-15). In people with type 2 diabetes and overweight or obesity, modest weight loss improves glycemia and reduces the need for glucose-lowering medications (7,16,17), and greater weight loss substantially reduces A1C and fasting glucose and may promote sustained diabetes remission (9,18-22). Metabolic surgery, which results in an average >20% body weight loss, greatly improving glycemia and often leading to remission of diabetes, improved quality of life, improved cardiovascular outcomes, and reduced mortality (23,24). Several therapeutic modalities, including intensive behavioral and lifestyle counseling, weight management 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."

ASSESSMENT AND MONITORING OF THE INDIVIDUAL WITH OVERWEIGHT OR OBESITY

Recommendations

8.1 Use person-centered, nonjudgmental language that fosters collaboration between individuals and health care professionals, including person-first language (e.g.,

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"person with obesity" rather than "obese person" and "person with diabetes" rather than "diabetic person"). E 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 if BMI is indeterminant. E

- 8.2b Monitor obesity-related anthropometric measurements at least annually to inform treatment considerations. During active weight management treatment, increase monitoring to at least every 3 months. 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 Provide weight management treatment, aiming for 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/m²]) has been used widely to diagnose and stage obesity (overweight: BMI 25-29.9 kg/m²; obesity class I: BMI 30-34.9 kg/m²; obesity class II: BMI 35-39.9 kg/m²; obesity class III: BMI ≥40 kg/m²); 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, and it does not 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 and 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 guide), distribution (using other anthropometric measurements, like waist circumference, waist-to-hip circumference ratio, or waistto-height ratio), or function and, importantly, the presence of associated health or well-being consequences: metabolic, physical, or psychological (29).

Obesity is a key pathophysiologic driver of diabetes, other cardiovascular risk factors (e.g., hypertension, hyperlipidemia, metabolic dysfunction-associated steatotic liver disease [MASLD], and inflammatory state), and ultimately cardiovascular and kidney disease (30). Diabetes can further exacerbate obesity, including through the use of glucose-lowering therapies that lead to weight gain (e.g., insulin, sulfonylurea, and pioglitazone), and obesity can exacerbate hyperglycemia and diabetes, thereby 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.

Weight stigma, fat bias, and anti-fat bias are ways to describe the bias toward people living in larger bodies. Fat bias is prevalent among health care professionals and the general public. Health care professionals are strongly encouraged to increase their awareness of implicit and explicit weight-biased attitudes (31). Increasing empathy and understanding about the complexity of weight management among health care professionals is a useful avenue to help reduce weight bias (32).

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 healthrelated quality of life. Use person-first language (e.g., "person with obesity"

rather than "obese person") to avoid defining people by their condition (26,33,34). Measurement of weight and height (to calculate BMI) and other anthropometric measurements should be performed at least annually to aid the diagnosis of obesity. More frequent assessments (at least every 3 months) should be undertaken to monitor response to treatment during active weight management (35). Clinical considerations, such as the presence of comorbid heart failure or unexplained weight change, may warrant more frequent evaluation (36,37). If such measurements are questioned or declined by the individual, the health care professional 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 (38,39). 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 also 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 (40). Strategies may include nutrition and eating pattern changes, physical activity and exercise, behavioral counseling, pharmacotherapy, medical devices, and metabolic surgery. The initial and subsequent therapeutic choices should be individualized based on the person's medical history, life circumstances, preferences, and motivation (41). Combination treatment approaches may be appropriate in higherrisk 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 (7,16,17,42). In people at risk, 3-7% weight loss reduces progression to diabetes (2,16,17,43,44). Greater weight loss produces additional benefits (20,21). Mounting data have shown that >10% body weight loss usually confers greater benefits on glycemia and diabetes remission and improves other metabolic comorbidities, including cardiovascular outcomes, metabolic dysfunctionassociated steatohepatitis (MASH), MASLD, adipose tissue inflammation, and sleep apnea, as well as physical comorbidities and quality of life (6,20,21,30,43,45-54).

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 are recommended for people with type 2 diabetes and overweight or obesity to achieve both weight and health outcome goals. 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 should be recommended for weight loss and should be considered when available. A

8.8b If access to such interventions is limited, consider alternative structured programs delivering behavioral counseling (face-to-face or remote). **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, cultural, and socioeconomic factors

that may impact nutrition patterns and food choices, such as food insecurity and hunger, access to healthful food options, and other social determinants of health. C

8.11 For those who achieve weight loss goals, continue to monitor progress, provide ongoing support, and recommend continuing interventions to maintain weight goals long term. E Effective long-term (≥1 year) weight maintenance programs provide monthly contact and support, include frequent self-monitoring of body weight (weekly or more frequently) and other selfmonitoring strategies (e.g., food diaries or wearables), and encourage regular physical activity (200-300 min/week). A **8.12** Short-term nutrition intervention using structured, very-low-calorie meals (800-1,000 kcal/day) should be prescribed only to carefully selected individuals by trained practitioners in medical settings with close monitoring. Longterm, 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-specific interventions, please refer to "Nutrition Therapy for Adults With Diabetes or Prediabetes: A Consensus Report" (55).

Behavioral Interventions

Numerous behavioral interventions have demonstrated positive effects from reducing energy intake, increasing physical activity, or some combination of these key lifestyle behaviors (56). The Look AHEAD (Action for Health in Diabetes) trial confirmed the feasibility of achieving and maintaining long-term weight loss in people with type 2 diabetes. Approximately half of intensive lifestyle intervention participants lost and maintained ≥5% of their initial body weight (44). Tailoring behavioral interventions to cultural context could be an additional useful tool for improving the impact of interventions (57–59).

To achieve significant weight loss with lifestyle change programs, creating a 500–750 kcal/day energy deficit is recommended. For most women, this is equal to approximately 1,200-1,500 kcal/day, and for most men, this is equal to approximately 1,500-1,800 kcal/day, with adjustment for the individual's baseline body weight. Clinical benefits of weight loss typically begin upon achieving 3% weight loss (19,60), but these benefits are progressive; more intensive weight loss goals (>7%, >10%, >15%, etc.) can achieve further health improvements if these goals can be feasibly and safely attained. Almost one-third of the Look AHEAD intensive lifestyle group participants lost and maintained ≥10% of their initial body weight at 8 years (44) and required fewer glucose-, blood pressure-, and lipidlowering medications than those randomly assigned to standard care.

Nutrition interventions can create the necessary energy deficit to promote weight loss in many ways, and no single way is best (19,61-63). Altering macronutrient content and using meal replacement plans prescribed by trained professionals are two commonly used approaches (64). Reducing processed and ultraprocessed food intake is also an encouraging area of ongoing weight loss research. The Preventing Overweight Using Novel Dietary Strategies (POUNDS) Lost trial reported small but significant improvements when ultraprocessed foods were replaced isocalorically by less processed foods, with improved trunk fat loss (β = 3.9, 95% CI -7.01 to -0.70, P = 0.02) (65). The specific nutrition and lifestyle choices should be based on the individual's health status, clinical considerations, social determinants of health, overall preferences, and other cultural and personal circumstances that affect eating and activity patterns (66) (see Section 5, "Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes," for more discussion on processed and ultraprocessed foods).

Based on evidence from the Diabetes Prevention Program (DPP) and Look AHEAD, proven intensive behavioral interventions generally include ≥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

face-to-face or remotely and on an individual or group basis (60,67,68). Assessing a person's motivation level, life circumstances, cultural considerations, socioeconomic factors, and ability to implement behavioral changes to achieve weight loss should be considered along with medical status when such interventions are recommended and initiated (40.69).

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. Weight loss maintenance programs should be delivered by an interprofessional team with appropriate training and experience in implementing long-term weight maintenance programs. While we acknowledge that most insurers, Medicare, and Medicaid are not currently covering many long-term weight maintenance programs, there is evidence to support their effectiveness and benefits (44,60,70) on both personal and population levels. Weight maintenance programs should include 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 food and beverage intake and steps; continued focus on nutrition and behavioral changes; and participation in high levels of physical activity (200-300 min/week) (71,72). Some commercial and proprietary weight loss programs have shown promising weight loss results; however, results vary across programs, most lack evidence of effectiveness, many do not satisfy guideline recommendations, and some promote unscientific and possibly dangerous practices (73,74).

Structured, very-low-calorie eating patterns, typically 800-1,000 kcal/day, using 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 intensive nutritional interventions should be provided only by trained and experienced professionals in medical settings with close ongoing monitoring and integration with behavioral support and counseling, and only for a short term (generally up to 3 months). Furthermore, due to the high risk of complications (electrolyte abnormalities, severe fatigue, cardiac arrhythmias, etc.), such intensive interventions should be prescribed only to carefully selected individuals, such as

those requiring weight loss and/or glycemic management before surgery, if benefits exceed potential risks (75–77). As weight regain is common, such interventions should include long-term, comprehensive weight maintenance strategies and counseling to maintain weight loss and behavioral changes (78,79).

Despite widespread marketing and exorbitant claims, there is no clear evidence that nutrition supplements (e.g., herbs, vitamins and minerals, amino acids, enzymes, and antioxidants) are effective for obesity management or weight loss (80–82). Several large systematic reviews show that most trials evaluating nutrition supplements for weight loss are of low quality and at high risk for bias. Highquality published studies show little or no weight loss benefits. In contrast, vitamin and mineral supplementation (e.g., iron, vitamin B12, and vitamin D) may be indicated in cases of documented deficiency (83), and protein supplements may be indicated as adjuncts to medically supervised weight loss therapies (84). See METABOLIC SURGERY, below, for more details on nutrition guidance for people who have undergone metabolic surgery.

Health disparities adversely affect people who have systematically experienced greater obstacles to health based on their race or ethnicity, socioeconomic status, gender identity, disability, or other factors. Overwhelming research shows that these disparities can 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" (85).

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 Weight management 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 glucagonlike 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 Screen people with diabetes and obesity who have lost significant weight for malnutrition, especially those who have undergone metabolic surgery A and those treated with weight management pharmacologic therapy. B
- 8.19 Weight management pharmacotherapy indicated for chronic therapy should be continued beyond reaching weight loss goals to maintain the health benefits. Sudden discontinuation of weight management pharmacotherapy often results in weight gain and worsening of cardiometabolic risk factors. A
- **8.20** For those not reaching treatment 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 (RAs) and a dual glucosedependent insulinotropic polypeptide (GIP) and GLP-1 RA (tirzepatide). Sodium-glucose

cotransporter 2 inhibitors, metformin, acarbose, and amylin mimetics are also associated with weight loss, although the magnitude of weight loss is much smaller (<5% body weight loss). 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 (86). Examples of medications associated with weight gain include antipsychotics (e.g., clozapine, olanzapine, and 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 (e.g., atenolol, metoprolol, and propranolol), and possibly sedating antihistamines and anticholinergics (87).

Approved Weight Management Pharmacotherapy

The U.S. Food and Drug Administration (FDA) has approved several medications for weight management as adjuncts to a reduced-calorie eating pattern and increased physical activity in individuals with BMI \geq 30 kg/m² or \geq 27 kg/m² with one or more obesity-associated comorbid conditions (e.g., type 2 diabetes, hypertension, and/or dyslipidemia). Nearly all FDA-approved weight management 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, semaglutide, and tirzepatide) have an indication for glucose lowering as well as weight management. Phentermine and other older adrenergic agents are approved for short-term treatment (88), while all others are approved for long-term treatment (22) (Tables 8.1 and 8.2). (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") and include agents from the GLP-1 RA class and the dual GIP and GLP-1 RA class (collectively referred to as nutrient-stimulated hormone-based therapeutics, a class that also includes other investigational agents that act on various nutrient-stimulated hormonal pathways, like glucagon and amylin). Should use of these medications not result in achievement of weight management goals, or if they are not tolerated or are contraindicated, other obesity treatment approaches should be considered. In the Effect and Safety of Semaglutide 2.4 mg Once-Weekly in Subjects With Overweight or Obesity and Type 2 Diabetes (STEP 2) trial, semaglutide 2.4 mg resulted in a body weight loss of 6.2% more than placebo and A1C lowering of 1.2% more than placebo after 68 weeks (50). In the Efficacy and Safety of Tirzepatide Once Weekly in Participants With Type 2 Diabetes Who Have Obesity or Are Overweight: A Randomized, Double-Blind, Placebo-Controlled Trial (SURMOUNT-2), 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 RA class (89). The observed weight loss with weight management pharmacotherapy is lower in people with diabetes than in those of similar baseline weight without diabetes; therefore, it is important to appropriately manage expectations of individuals with diabetes and health care professionals.

Weight management pharmacotherapy has demonstrated multiple additional benefits beyond weight loss and improvement in glucose management. Some such examples include improvements or potential improvements in cardiovascular risk factors (e.g., blood pressure and lipids), inflammation, obstructive sleep apnea, MASLD and MASH, and symptoms related to heart failure with preserved ejection fraction (90–93). Liraglutide 1.8 mg

and semaglutide 1 mg (doses approved for type 2 diabetes, which are lower than those approved for the treatment of obesity) demonstrated reduction in cardiovascular events in people with type 2 diabetes who are either at high risk for cardiovascular disease or have cardiovascular disease (51,94). Additionally, semaglutide 2.4 mg (dose approved for the treatment of obesity) also demonstrated reduction in cardiovascular events in people with overweight or obesity and preexistent cardiovascular disease but without diabetes (95).

Health care professionals should be knowledgeable about the dosing, benefits, 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 must be balanced against the lack of long-term cardiovascular outcomes trial data for agents like combination naltrexone and bupropion and combination phentermine and topiramate. The response to all weight management medications is highly heterogeneous; therefore, their weight loss effectiveness should be reevaluated after initiation and therapy adjustments should be considered, if needed. 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 while using weight loss medications. Tirzepatide in particular may reduce the efficacy of oral hormonal contraceptives due to delayed gastric emptying, an effect that is largest after the first dose and diminishes over time. Individuals using oral hormonal contraceptives should switch to a nonoral contraceptive method or add a barrier method of contraception for 4 weeks after initiation and for 4 weeks after each dose escalation. Of note, while weight loss medications are often used in people with type 1 diabetes, clinical trial data in this population are limited.

Incretin pharmacotherapies and metabolic surgery options for weight loss may increase the risk for malnutrition and sarcopenia (96). Health care professionals should encourage resistance training (97) and sufficient protein intake. Individuals with diabetes who are experiencing significant (>20%) or rapid (>4 kg/month) weight loss should be screened for

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Table 8.1-Weight management pharmacotherapy	macotherapy			
Medication name	Treatment arm; weight loss from baseline	Time frame for weight loss (weeks)*	Common side effects	Possible safety concerns and considerations
Sympathomimetic amine anorectic: approved for short-term use only Phentermine (160,161)†	15 mg q.d.; 7.4%7.5 mg q.d.; 6.6%Placebo; 2.3%	78	Dry mouth, insomnia, dizziness, irritability, increased blood pressure, elevated heart rate	 Contraindicated for use in combination with monoamine oxidase inhibitors Caution with cardiovascular disease Do not use if at high risk for glaucoma due to risk of acute angleclosure glaucoma
Lipase inhibitor Orlistat (4,162)‡	 120 mg t.i.d.; 9.6% Placebo; 5.6% 	52	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
Sympathomimetic amine anorectic/ antiepileptic combination Phentermine/topiramate ER (49,163)§	 15 mg/92 mg q.d.; 9.8% 7.5 mg/46 mg q.d.; 7.8% Placebo; 1.2% 	99	Constipation, paresthesia, insomnia, nasopharyngitis, xerostomia, increased blood pressure, nephrolithiasis	 Contraindicated for use in combination with monoamine oxidase inhibitors Birth defects Cognitive impairment Caution with cardiovascular disease Do not use if at high risk for glaucoma due to risk of acute angleclosure glaucoma
Opioid antagonist/antidepressant combination Naltrexone/bupropion ER (13,164)	• 16 mg/180 mg b.i.d.; 5% • Placebo; 1.8%	26	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
Glucagon-like peptide 1 receptor agonist Liraglutide (14,51,165)	3.0 mg q.d.; 6%1.8 mg q.d.; 4.7%Placebo; 2%	99	Gastrointestinal side effects (nausea, vomiting, diarrhea, esophageal reflux)	 Hypoglycemia (with concomitant use of insulin or sulfonylurea) 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 increased risk of gastrointestinal side effects and potential risk of acute kidney injury from dehydration
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Table 8.1—Continued				
Medication name	Treatment arm; weight loss from baseline	Time frame for weight loss (weeks)*	Common side effects	Possible safety concerns and considerations
Semaglutide (50,94)	 2.4 mg weekly; 9.6% 1.0 mg weekly; 7% Placebo; 3.4% 			 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 May cause injection site reactions May cause elevated heart rate Black box warning: Risk of thyroid C-cell tumors in rodents; human relevance not determined; do not use in individuals with personal or family history of medullary thyroid cancer or multiple endocrine neoplasia type 2
Dual glucose-dependent insulinotropic polypeptide and glucagon-like peptide 1 receptor agonist Tirzepatide (89,166)	15 mg weekly; 14.7%10 mg weekly; 12.8%Placebo; 3.2%	72	Gastrointestinal side effects (nausea, vomiting, diarrhea, esophageal reflux)	 Same as for GLP-1 receptor agonists Monitor effects of oral medications with narrow therapeutic index (warfarin) or whose efficacy is dependent on threshold concentration Advise females using oral contraceptives to switch to a nonoral contraceptive method or add a barrier method of contraception for 4 weeks after initiation and for 4 weeks after each dose escalation Black box warning: Risk of thyroid C-cell tumors in rodents; human relevance not determined; do not use in individuals with personal or family history of medullary thyroid cancer or multiple endocrine neoplasia type 2

reaching weight loss goals. †Phentermine was evaluated in a general adult population with obesity. As monotherapy, phentermine is only approved for short-term use. Use lowest effective dose; maximum appropriate dose is 37.5 mg. ‡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 (51,94). 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; q.d., every day; Rx, prescription; t.i.d., three times daily, p.o., by mouth. *Time frames used in clinical trials. Medications approved for long-term use should be continued as indicated beyond

Table 8.2—Median monthly (30-day) AWP and NADAC of maximum or maintenance dose of weight management pharmacotherapies Typical adult AWP (median and range NADAC (median and Medication name maintenance dose for 30-day supply) range for 30-day supply) Sympathomimetic amine anorectic: approved for short-term use only Phentermine 8-37.5 mg q.d. \$43 (\$9-\$98)* \$3 (\$3, \$79)* Lipase inhibitor Orlistat 60 mg t.i.d. (OTC) \$58 (\$41-\$82) NA 120 mg t.i.d. (Rx) \$843 (\$781-\$904) \$677 (\$629-\$724) Sympathomimetic amine anorectic/ antiepileptic combination Phentermine/topiramate ER 7.5 mg/46 mg q.d. \$237 NA Opioid antagonist/antidepressant combination Naltrexone/bupropion ER 16 mg/180 mg b.i.d. \$750 NA Glucagon-like peptide 1 receptor agonist Liraglutidet \$1,619 \$1.296 3 mg q.d. Semaglutide 2.4 mg once weekly \$1,619 \$1,296 Dual glucose-dependent insulinotropic

The costs listed in this table are representative of costs at a national level. These costs may not be representative of an individual's cost and do not account for medication coverage or available discounts. AWP, average wholesale price; b.i.d., twice daily; ER, extended release; NA, data not available; NADAC, National Average Drug Acquisition Cost; OTC, over the counter; q.d., every day; Rx, prescription; t.i.d., three times daily. AWP and NA-DAC prices are for a 30-day supply of maximum or maintenance dose as of 1 July 2024 (167,168). *Data are for 37.5 mg q.d. dose. +New generic liraglutide pricing was not available on 1 July 2024.

\$1.272

5, 10, or 15 mg once weekly

malnutrition. While no single method is best to screen for both malnutrition and sarcopenia, instruments are available to screen for each condition, including the Simplified Nutritional Appetite Questionnaire (SNAQ) and the Malnutrition Universal Screening Tool (MUST) (98-100). For a more detailed discussion of malnutrition in the context of diabetes and weight loss, see Section 5, "Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes."

polypeptide and glucagon-like peptide 1

receptor agonist Tirzepatide

Thus, choice of therapy should be guided by person-centered treatment factors, including comorbidities, considerations of adverse effects and treatment burden, treatment cost and accessibility, and the individual's therapeutic goals and preferences. Medication cost and insurance coverage considerations often influence treatment decisions, and payors should cover evidence-based obesity treatments for people with diabetes and prediabetes to reduce barriers to treatment access. It is also essential that health care teams are knowledgeable about insurance coverage requirements and establish systems to support clinicians in prescribing evidencebased weight management medications

and to reduce financial hardship of treatment for individuals, including formulary and medication coverage requirements, eligibility for medication assistance programs, and availability of copayment reduction cards (see Section 1, "Improving Care and Promoting Health in Populations").

Assessing Efficacy and Safety of Weight Management Pharmacotherapy

Upon initiating medications for obesity, assess their effectiveness 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 (101,102); however, it is notable that the response rate with the latest generation of weight management pharmacotherapies is much higher (50,89). Unless clinical circumstances (such as poor tolerability) or other considerations (such as financial expense or individual preference) suggest otherwise, those who achieve sufficient early weight loss upon starting a chronic weight management 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 examined 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. Sudden discontinuation of semaglutide and tirzepatide results in regain of one-half to two-thirds of the weight loss within 1 year (103-105). Shared decision-making should be used to determine the best long-term weight management approach, such as continuing pharmacotherapy on the lowest effective dose, using intermittent therapy, or stopping medication followed by close weight monitoring.

\$1,017

For those not reaching or maintaining weight-related treatment goals, avoid treatment inertia by reevaluating ongoing 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 longterm 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 (106). 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 and led to the voluntary removal of several of these medical devices from the U.S. market (107).

METABOLIC SURGERY

Recommendations

8.21 Consider metabolic surgery as a weight and glycemic management approach in people with diabetes with BMI ≥30.0 kg/m² (or ≥27.5 kg/m² in Asian American individuals) who are otherwise good surgical candidates. **A**

8.22 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**

8.23 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**

8.24 People who undergo metabolic surgery should receive long-term medical and behavioral support and routine micronutrient, nutritional, and metabolic status monitoring. **B**

8.25 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 In individuals with postmetabolic surgery hypoglycemia, use

continuous glucose monitoring to improve safety. **C**

8.26 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**

8.27 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., weight management 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 glycemic management and long-term outcomes in those with 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" (108).

A substantial body of evidence, including data from 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 (47). In addition to improving glycemia, metabolic surgery reduces the incidence of microvascular disease (109), improves quality of life (47,110,111), decreases cancer risk, improves cardiovascular disease risk factors and long-term cardiovascular events (111-119), and decreases all-cause mortality (120). Cohort studies that match surgical and nonsurgical subjects strongly suggest that metabolic surgery reduces all-cause mortality (121,122). Studies have also shown that metabolic surgery can improve liver outcomes among individuals with MASH, including biopsy-proven disease (123–125).

The overwhelming majority of procedures performed in the U.S. are vertical sleeve gastrectomy (VSG) and Roux-en-Y gastric bypass (RYGB). Both procedures

result in a smaller stomach pouch and often robust changes in enteroendocrine hormones. In VSG, \sim 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 (126). The American Society for Metabolic and Bariatric Surgery recommends metabolic surgery for people with type 2 diabetes and a BMI \geq 30 kg/m²(or \geq 27.5 kg/m² for Asian American individuals) in surgically eligible individuals. A real-world data analysis through the National Patient-Centered Outcomes Research Network (PCORnet) in the U.S. compared surgical outcomes between 6,233 individuals with type 2 diabetes who underwent RYGB and 3,477 who underwent VSG. At 1 year after surgery, those who had RYGB lost on average 29.1% of their total body weight, while those who had VSG lost on average 22.8% of their total body weight. At 5 years after surgery, the total body weight loss was 24.1% for those who had RYGB and 16.1% for those who had VSG, with 86.1% of individuals experiencing type 2 diabetes remission after RYGB and 83.5% of individuals experiencing type 2 diabetes remission after VSG. Among the 6,141 individuals who experienced type 2 diabetes remission, the subsequent type 2 diabetes relapse rate was lower for those who had RYGB than for those who had VSG (hazard ratio 0.75 [95% CI 0.67-0.84]). Estimated relapse rates for those who had RYGB and VSG were 33.1% and 41.6%, respectively, at 5 years after surgery. At 5 years, compared with baseline, A1C was reduced, on average, 0.4 percentage points more for individuals who had RYGB than for individuals who had VSG (127). Most notably, the Surgical Treatment and Medications Potentially Eradicate Diabetes Efficiently (STAMPEDE) trial, which randomized 150 participants with type 2 diabetes, A1C >7.0%, and BMI 27–43 kg/m² to receive either metabolic surgery or medical treatment for type 2 diabetes using glucose-lowering agents, found that 29% of those treated with RYGB and 23% of those treated with VSG achieved A1C of \leq 6.0% after 5 years (47). Available data suggest an erosion of diabetes remission over time (48); 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 (128,129), and the majority of those who undergo surgery maintain substantial improvement of glycemia from baseline for at least 5-15 years (47,110,111,113).

Exceedingly few presurgical predictors of diabetes remission have been identified. However, younger age, shorter duration of diabetes (e.g., <8 years) (101), and lesser severity of diabetes (better glycemic management, not using insulin) are associated with higher rates of diabetes remission (47,111,130,131). Greater baseline visceral fat area may also predict diabetes remission, especially among Asian American people with type 2 diabetes (132).

A review of case series and reports suggests that metabolic surgery also improves the metabolic profiles and cardiovascular risk of people with type 1 diabetes, but larger and longer-term studies with better designs are needed to determine the role of metabolic surgery in such individuals (133).

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, the specific medications being compared, the time horizon for cost-effectiveness assessments, and the population examined (e.g., duration and severity of diabetes) (134,135).

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 for common abdominal procedures such as cholecystectomy and hysterectomy (136,137). Major complications occur in 2-6% of those undergoing metabolic surgery, which compares favorably with the rates for other commonly performed elective operations (137). Postsurgical recovery times and morbidity have also dramatically declined. Minor complications and need for operative reintervention occur in up to 15% (136,138-143). Empirical data suggest that the proficiency of the operating surgeon and

surgical team is a key determinant of mortality, complications, reoperations, and readmissions (144). 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 locations of accredited programs (https://www.facs. org/quality-programs/accreditation-andverification/metabolic-and-bariatric-surgeryaccreditation-and-quality-improvementprogram/).

Beyond the perioperative period, longer-term risks include vitamin and mineral deficiencies, anemia, osteoporosis, dumping syndrome, and severe hypoglycemia (145). Nutritional and micronutrient deficiencies and related complications occur with variable frequency depending on the type of surgical procedure and require routine monitoring of micronutrient and nutritional status and lifelong vitamin/nutritional supplementation (145). 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 (146-148). 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-metabolic surgery hypoglycemia typically presents >1 year after surgery. Diagnosis is primarily made by a thorough examination of history, detailed records of food intake, physical activity, and symptom patterns, and exclusion of other potential causes of hypoglycemia (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, healthy fats, and vitamin and nutrient supplements. When available, individuals should be offered medical nutrition therapy with a registered dietitian nutritionist experienced in post-metabolic 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 impaired hypoglycemia awareness. 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) (149).

People who undergo metabolic surgery may be at increased risk for substance use, worsening or new-onset depression and/or anxiety disorders, and suicidal ideation (150-154). Candidates for metabolic surgery should be assessed by a behavioral health professional with expertise in obesity management prior to consideration for surgery (155). 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.

Finally, no definitive evidence supports the pre- and post-metabolic surgery use of nutrient-stimulated hormone-based therapeutics for chronic obesity. Existing studies suggest that among individuals with a BMI >50 kg/m², GLP-1 RAs are associated with significant weight loss prior to surgery with no increase in complications or time to surgery (156). Nutrientstimulated hormone-based therapeutics can be considered as adjuvants after metabolic surgery to augment initial weight loss either shortly after surgery or when weight loss has plateaued (157). Studies have also shown that GLP-1 RAs can effectively treat weight regain after metabolic surgery and therefore could be considered as an alternative to revisional surgery (158). Long-term outcomes, however, are lacking in terms of durability of weight loss, effect on weight regain when medications are stopped, and long-term side

effects with use and after discontinuation (159).

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