



American Diabetes Association
Professional Practice Committee*

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

Diabetes Care 2024;47(Suppl. 1):S145–S157 | <https://doi.org/10.2337/dc24-S008>

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>. Duality of interest information for each author is available at <https://doi.org/10.2337/dc24-SDIS>.

This section has received endorsement from The Obesity Society.

Suggested citation: American Diabetes Association Professional Practice Committee. 8. Obesity and weight management for the prevention and treatment of type 2 diabetes: Standards of Care in Diabetes—2024. *Diabetes Care* 2024;47(Suppl. 1):S145–S157

© 2023 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered. More information is available at <https://www.diabetesjournals.org/journals/pages/license>.

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 $\geq 40 \text{ kg}/\text{m}^2$); 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 $\geq 5\%$ 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 $\geq 5\%$ of their initial body weight, and 27% lost and maintained $\geq 10\%$ 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 $\geq 30 \text{ kg/m}^2$ or $\geq 27 \text{ kg/m}^2$ 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 $BMI > 25 \text{ kg/m}^2$ 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 ($\sim 10\%$) (88).

METABOLIC SURGERY

Recommendations

8.19 Consider metabolic surgery as a weight and glycemic management approach in people with diabetes with $BMI \geq 30.0 \text{ kg/m}^2$ (or $\geq 27.5 \text{ kg/m}^2$ 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) 120 mg t.i.d. (Rx)	\$52 (\$41–\$82) \$843 (\$781–\$904)	NA \$722	120 mg t.i.d.† Placebo	9.6 5.6	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
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

Continued on p. S51

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	<ul style="list-style-type: none"> 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. <p>Black box warning:</p> <ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> 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. <p>Black box warning:</p> <ul style="list-style-type: none"> Risk of thyroid C-cell tumors in rodents; human relevance not determined

Continued on p. S152

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	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 (non-blinded) 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 non-surgical 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 $\geq 30 \text{ kg/m}^2$ (or $\geq 27.5 \text{ kg/m}^2$ 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.

References

- Narayan KM, Boyle JP, Thompson TJ, Gregg EW, Williamson DF. Effect of BMI on lifetime risk for diabetes in the U.S. *Diabetes Care* 2007;30:1562–1566
- Knowler WC, Barrett-Connor E, Fowler SE, et al.; Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 2002;346:393–403
- Garvey WT, Ryan DH, Henry R, et al. Prevention of type 2 diabetes in subjects with prediabetes and metabolic syndrome treated with phentermine and topiramate extended release. *Diabetes Care* 2014;37:912–921
- Torgerson JS, Hauptman J, Boldrin MN, Sjöström L. XENical in the prevention of diabetes in obese subjects (XENDOS) study: a randomized study of orlistat as an adjunct to lifestyle changes for the prevention of type 2 diabetes in obese patients. *Diabetes Care* 2004;27:155–161
- Le Roux CW, Astrup A, Fujioka K, et al.; SCALE Obesity Prediabetes NN8022-1839 Study Group. 3 years of liraglutide versus placebo for type 2 diabetes risk reduction and weight management in individuals with prediabetes: a randomised, double-blind trial. *Lancet* 2017;389:1399–1409
- Booth H, Khan O, Prevost T, et al. Incidence of type 2 diabetes after bariatric surgery: population-based matched cohort study. *Lancet Diabetes Endocrinol* 2014;2:963–968
- UKPDS Group. UK Prospective Diabetes Study 7: response of fasting plasma glucose to diet therapy in newly presenting type II diabetic patients. *Metabolism* 1990;39:905–912
- Goldstein DJ. Beneficial health effects of modest weight loss. *Int J Obes Relat Metab Disord* 1992;16:397–415
- Pastors JG, Warshaw H, Daly A, Franz M, Kulkarni K. The evidence for the effectiveness of medical nutrition therapy in diabetes management. *Diabetes Care* 2002;25:608–613
- Lim EL, Hollingsworth KG, Arbisala BS, Chen MJ, Mathers JC, Taylor R. Reversal of type 2 diabetes: normalisation of beta cell function in association with decreased pancreas and liver triacylglycerol. *Diabetologia* 2011;54:2506–2514
- Jackness C, Karmally W, Febres G, et al. Very low-calorie diet mimics the early beneficial effect of Roux-en-Y gastric bypass on insulin sensitivity and β-cell function in type 2 diabetic patients. *Diabetes* 2013;62:3027–3032
- Rothberg AE, McEwen LN, Kraftson AT, Fowler CE, Herman WH. Very-low-energy diet for type 2 diabetes: an underutilized therapy? *J Diabetes Complications* 2014;28:506–510
- Hollander PA, Elbein SC, Hirsch IB, et al. Role of orlistat in the treatment of obese patients with type 2 diabetes: a 1-year randomized double-blind study. *Diabetes Care* 1998;21:1288–1294
- Garvey WT, Ryan DH, Bohannon NJ, et al. Weight-loss therapy in type 2 diabetes: effects of phentermine and topiramate extended release. *Diabetes Care* 2014;37:3309–3316
- Hollander P, Gupta AK, Plodkowski R, et al.; COR-Diabetes Study Group. Effects of naltrexone sustained-release/bupropion sustained-release combination therapy on body weight and glycemic parameters in overweight and obese patients with type 2 diabetes. *Diabetes Care* 2013;36:4022–4029
- Davies MJ, Bergenstal R, Bode B, et al.; NN8022-1922 Study Group. Efficacy of liraglutide for weight loss among patients with type 2 diabetes: the SCALE diabetes randomized clinical trial. *JAMA* 2015;314:687–699
- Rubino F, Nathan DM, Eckel RH, et al.; Delegates of the 2nd Diabetes Surgery Summit. Metabolic surgery in the treatment algorithm for type 2 diabetes: a joint statement by international diabetes organizations. *Obes Surg* 2017;27:2–21
- Steven S, Hollingsworth KG, Al-Mrabeh A, et al. Very low-calorie diet and 6 months of weight stability in type 2 diabetes: pathophysiological changes in responders and nonresponders. *Diabetes Care* 2016;39:808–815
- Jensen MD, Ryan DH, Apovian CM, et al.; American College of Cardiology/American Heart Association Task Force on Practice Guidelines; Obesity Society. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. *J Am Coll Cardiol* 2014;63(25 Pt B):2985–3023
- Lean ME, Leslie WS, Barnes AC, et al. Primary care-led weight management for remission of type 2 diabetes (DiRECT): an open-label, cluster-randomised trial. *Lancet* 2018;391:541–551
- Lean MEJ, Leslie WS, Barnes AC, et al. Durability of a primary care-led weight-management intervention for remission of type 2 diabetes: 2-year results of the DiRECT open-label, cluster-randomised trial. *Lancet Diabetes Endocrinol* 2019;7:344–355
- Kahan S, Fujioka K. Obesity pharmacotherapy in patients with type 2 diabetes. *Diabetes Spectr* 2017;30:250–257
- Wiggins T, Guidozzi N, Welbourn R, Ahmed AR, Markar SR. Association of bariatric surgery with all-cause mortality and incidence of obesity-related disease at a population level: a systematic review and meta-analysis. *PLoS Med* 2020;17:e1003206
- Aminian A, Wilson R, Zajicek A, et al. Cardiovascular outcomes in patients with type 2 diabetes and obesity: comparison of gastric bypass, sleeve gastrectomy, and usual care. *Diabetes Care* 2021;44:2552–2563
- World Health Organization. *Obesity*, 2023. Accessed 3 September 2023. Available from https://www.who.int/health-topics/obesity#tab=tab_1
- WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet* 2004;363:157–163
- Araneta MR, Kanaya AM, Hsu WC, et al. Optimum BMI cut points to screen Asian Americans for type 2 diabetes. *Diabetes Care* 2015;38:814–820
- Aggarwal R, Bibbins-Domingo K, Yeh RW, et al. Diabetes screening by race and ethnicity in the United States: equivalent body mass index and age thresholds. *Ann Intern Med* 2022;175:765–773
- Rubino F, Batterham RL, Koch M, et al. Lancet Diabetes & Endocrinology Commission on the definition and diagnosis of clinical obesity. *Lancet Diabetes Endocrinol* 2023;11:226–228

30. Klein S, Gastaldelli A, Yki-Järvinen H, Scherer PE. Why does obesity cause diabetes? *Cell Metab* 2022;34:11–20
31. American Medical Association. *AMA Manual of Style: A Guide for Authors and Editors*. Oxford University Press, 2019
32. American Medical Association. Person-First Language for Obesity H-440.821. Accessed 15 October 2023. Available from: <https://policysearch.ama-assn.org/policyfinder/detail/obesity?uri=%2FAMADoc%2FHOD.xml-H-440.821.xml>
33. Kushner RF, Batsis JA, Butsch WS, et al. Weight history in clinical practice: the state of the science and future directions. *Obesity* (Silver Spring) 2020;28:9–17
34. Yancy CW, Jessup M, Bozkurt B, et al. 2017 ACC/AHA/HFSA focused update of the 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. *J Am Coll Cardiol* 2017;70: 776–803
35. Bosch X, Monclús E, Escoda O, et al. Unintentional weight loss: clinical characteristics and outcomes in a prospective cohort of 2677 patients. *PLoS One* 2017;12:e0175125
36. Wilding JP. The importance of weight management in type 2 diabetes mellitus. *Int J Clin Pract* 2014;68:682–691
37. Van Gaal L, Scheen A. Weight management in type 2 diabetes: current and emerging approaches to treatment. *Diabetes Care* 2015;38:1161–1172
38. Warren J, Smalley B, Barefoot N. Higher motivation for weight loss in African American than Caucasian rural patients with hypertension and/or diabetes. *Ethn Dis* 2016;26:77–84
39. Stoops H, Dar M. Equity and obesity treatment - expanding medicaid-covered interventions. *N Engl J Med* 2023;388:2309–2311
40. Rothberg AE, McEwen LN, Kraftson AT, et al. Impact of weight loss on waist circumference and the components of the metabolic syndrome. *BMJ Open Diabetes Res Care* 2017;5:e000341
41. Wing RR, Bolin P, Brancati FL, et al.; Look AHEAD Research Group. Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes. *N Engl J Med* 2013;369:145–154
42. Look AHEAD Research Group. Eight-year weight losses with an intensive lifestyle intervention: the Look AHEAD study. *Obesity* (Silver Spring) 2014;22:5–13
43. Gregg EW, Jakicic JM, Blackburn G, et al.; Look AHEAD Research Group. Association of the magnitude of weight loss and changes in physical fitness with long-term cardiovascular disease outcomes in overweight or obese people with type 2 diabetes: a post-hoc analysis of the Look AHEAD randomised clinical trial. *Lancet Diabetes Endocrinol* 2016;4:913–921
44. Baum A, Scarpa J, Bruzelius E, Tamler R, Basu S, Faghmous J. Targeting weight loss interventions to reduce cardiovascular complications of type 2 diabetes: a machine learning-based post-hoc analysis of heterogeneous treatment effects in the Look AHEAD trial. *Lancet Diabetes Endocrinol* 2017;5:808–815
45. Schauer PR, Bhatt DL, Kirwan JP, et al.; STAMPEDE Investigators. Bariatric surgery versus intensive medical therapy for diabetes - 5-year outcomes. *N Engl J Med* 2017;376:641–651
46. Ikramuddin S, Korner J, Lee WJ, et al. Durability of addition of Roux-en-Y gastric bypass to lifestyle intervention and medical management in achieving primary treatment goals for uncontrolled type 2 diabetes in mild to moderate obesity: a randomized control trial. *Diabetes Care* 2016;39: 1510–1518
47. Gadde KM, Allison DB, Ryan DH, et al. Effects of low-dose, controlled-release, phentermine plus topiramate combination on weight and associated comorbidities in overweight and obese adults (CONQUER): a randomised, placebo-controlled, phase 3 trial. *Lancet* 2011;377:1341–1352
48. Davies M, Færch L, Jeppesen OK, et al.; STEP 2 Study Group. Semaglutide 2·4 mg once a week in adults with overweight or obesity, and type 2 diabetes (STEP 2): a randomised, double-blind, double-dummy, placebo-controlled, phase 3 trial. *Lancet* 2021;397:971–984
49. Marso SP, Daniels GH, Brown-Frandsen K, et al.; LEADER Steering Committee; LEADER Trial Investigators. Liraglutide and cardiovascular outcomes in type 2 diabetes. *N Engl J Med* 2016;375:311–322
50. Rosenstock J, Wysham C, Frías JP, et al. Efficacy and safety of a novel dual GIP and GLP-1 receptor agonist tirzepatide in patients with type 2 diabetes (SURPASS-1): a double-blind, randomised, phase 3 trial. *Lancet* 2021;398:143–155
51. Frías JP, Davies MJ, Rosenstock J, et al.; SURPASS-2 Investigators. Tirzepatide versus semaglutide once weekly in patients with type 2 diabetes. *N Engl J Med* 2021;385:503–515
52. Magkos F, Fraterrigo G, Yoshino J, et al. Effects of moderate and subsequent progressive weight loss on metabolic function and adipose tissue biology in humans with obesity. *Cell Metab* 2016;23:591–601
53. Evert AB, Dennison M, Gardner CD, et al. Nutrition therapy for adults with diabetes or prediabetes: a consensus report. *Diabetes Care* 2019;42:731–754
54. Franz MJ, Boucher JL, Rutten-Ramos S, VanWormer JJ. Lifestyle weight-loss intervention outcomes in overweight and obese adults with type 2 diabetes: a systematic review and meta-analysis of randomized clinical trials. *J Acad Nutr Diet* 2015;115:1447–1463
55. Sacks FM, Bray GA, Carey VJ, et al. Comparison of weight-loss diets with different compositions of fat, protein, and carbohydrates. *N Engl J Med* 2009;360:859–873
56. de Souza RJ, Bray GA, Carey VJ, et al. Effects of 4 weight-loss diets differing in fat, protein, and carbohydrate on fat mass, lean mass, visceral adipose tissue, and hepatic fat: results from the POUNDS LOST trial. *Am J Clin Nutr* 2012;95: 614–625
57. Johnston BC, Kanters S, Bandayrel K, et al. Comparison of weight loss among named diet programs in overweight and obese adults: a meta-analysis. *JAMA* 2014;312:923–933
58. Ye W, Xu L, Ye Y, et al. The efficacy and safety of meal replacement in patients with type 2 diabetes. *J Clin Endocrinol Metab* 2023;108: 3041–3049
59. Leung CW, Epel ES, Ritchie LD, Crawford PB, Laraia BA. Food insecurity is inversely associated with diet quality of lower-income adults. *J Acad Nutr Diet* 2014;114:1943–1953.e1942
60. Kahan S, Manson JE. Obesity treatment, beyond the guidelines: practical suggestions for clinical practice. *JAMA* 2019;321:1349–1350
61. Hoerster KD, Hunter-Merrill R, Nguyen T, et al. Effect of a remotely delivered self-directed behavioral intervention on body weight and physical health status among adults with obesity: the D-ELITE randomized clinical trial. *JAMA* 2022;328:2230–2241
62. Appel LJ, Clark JM, Yeh HC, et al. Comparative effectiveness of weight-loss interventions in clinical practice. *N Engl J Med* 2011;365:1959–1968
63. Wadden TA, Tronieri JS, Butryn ML. Lifestyle modification approaches for the treatment of obesity in adults. *Am Psychol* 2020;75:235–251
64. Donnelly JE, Blair SN, Jakicic JM, Manore MM, Rankin JW; American College of Sports Medicine. American College of Sports Medicine position stand. Appropriate physical activity intervention strategies for weight loss and prevention of weight regain for adults. *Med Sci Sports Exerc* 2009;41:459–471
65. Gudzune KA, Doshi RS, Mehta AK, et al. Efficacy of commercial weight-loss programs: an updated systematic review. *Ann Intern Med* 2015; 162:501–512
66. Bloom B, Mehta AK, Clark JM, Gudzune KA. Guideline-concordant weight-loss programs in an urban area are uncommon and difficult to identify through the internet. *Obesity* (Silver Spring) 2016; 24:583–588
67. Muscogiuri G, Barrea L, Laudisio D, et al. The management of very low-calorie ketogenic diet in obesity outpatient clinic: a practical guide. *J Transl Med* 2019;17:356
68. Saris WH. Very-low-calorie diets and sustained weight loss. *Obes Res* 2001;9(Suppl. 4):295S–301S
69. Gardner CD, Kim S, Bersamin A, et al. Micronutrient quality of weight-loss diets that focus on macronutrients: results from the A TO Z study. *Am J Clin Nutr* 2010;92:304–312
70. Tsai AG, Wadden TA. The evolution of very-low-calorie diets: an update and meta-analysis. *Obesity* (Silver Spring) 2006;14:1283–1293
71. Johansson K, Neovius M, Hemmingsson E. Effects of anti-obesity drugs, diet, and exercise on weight-loss maintenance after a very-low-calorie diet or low-calorie diet: a systematic review and meta-analysis of randomized controlled trials. *Am J Clin Nutr* 2014;99:14–23
72. Batsis JA, Apolzan JW, Bagley PJ, et al. A systematic review of dietary supplements and alternative therapies for weight loss. *Obesity* (Silver Spring) 2021;29:1102–1113
73. Bessell E, Maunder A, Lauche R, Adams J, Sainsbury A, Fuller NR. Efficacy of dietary supplements containing isolated organic compounds for weight loss: a systematic review and meta-analysis of randomised placebo-controlled trials. *Int J Obes* 2021;45:1631–1643
74. Maunder A, Bessell E, Lauche R, Adams J, Sainsbury A, Fuller NR. Effectiveness of herbal medicines for weight loss: a systematic review and meta-analysis of randomized controlled trials. *Diabetes Obes Metab* 2020;22:891–903
75. Zhang FF, Barr SI, McNulty H, Li D, Blumberg JB. Health effects of vitamin and mineral supplements. *BMJ* 2020;369:m2511
76. Mallard SR, Howe AS, Houghton LA. Vitamin D status and weight loss: a systematic review and meta-analysis of randomized and nonrandomized

- controlled weight-loss trials. *Am J Clin Nutr* 2016; 104:1151–1159
77. Moon J, Koh G. Clinical evidence and mechanisms of high-protein diet-induced weight loss. *J Obes Metab Syndr* 2020;29:166–173
78. Kim JE, O'Connor LE, Sands LP, Sledodenik MB, Campbell WW. Effects of dietary protein intake on body composition changes after weight loss in older adults: a systematic review and meta-analysis. *Nutr Rev* 2016;74:210–224
79. Hill-Briggs F, Adler NE, Berkowitz SA, et al. Social determinants of health and diabetes: a scientific review. *Diabetes Care* 2020;44:258–279
80. Domecq JP, Prutsky G, Leppin A, et al. Clinical review: drugs commonly associated with weight change: a systematic review and meta-analysis. *J Clin Endocrinol Metab* 2015;100:363–370
81. Drugs.com. Phentermine prescribing information. Accessed 15 October 2023. Available from <https://www.drugs.com/pro/phentermine.html>
82. Jastreboff AM, Aronne LJ, Ahmad NN, et al.; SURMOUNT-1 Investigators. Tirzepatide once weekly for the treatment of obesity. *N Engl J Med* 2022; 387:205–216
83. Garvey WT, Frias JP, Jastreboff AM, et al.; SURMOUNT-2 investigators. Tirzepatide once weekly for the treatment of obesity in people with type 2 diabetes (SURMOUNT-2): a double-blind, randomised, multicentre, placebo-controlled, phase 3 trial. *Lancet* 2023;402:613–626
84. Fujioka K, O'Neil PM, Davies M, et al. Early weight loss with liraglutide 3.0 mg predicts 1-year weight loss and is associated with improvements in clinical markers. *Obesity (Silver Spring)* 2016;24:2278–2288
85. Fujioka K, Plodkowski R, O'Neil PM, Gilder K, Walsh B, Greenway FL. The relationship between early weight loss and weight loss at 1 year with naltrexone ER/bupropion ER combination therapy. *Int J Obes* 2016;40:1369–1375
86. Sullivan S. Endoscopic medical devices for primary obesity treatment in patients with diabetes. *Diabetes Spectr* 2017;30:258–264
87. Kahan S, Saunders KH, Kaplan LM. Combining obesity pharmacotherapy with endoscopic bariatric and metabolic therapies. Techniques and Innovations in Gastrointestinal Endoscopy 2020;22: 154–158
88. Greenway FL, Aronne LJ, Raben A, et al. A randomized, double-blind, placebo-controlled study of Gelesis100: a novel nonsystemic oral hydrogel for weight loss. *Obesity (Silver Spring)* 2019;27:205–216
89. Eisenberg D, Shikora SA, Aarts E, et al. 2022 American Society for Metabolic and Bariatric Surgery (ASMBS) and International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO): indications for metabolic and bariatric surgery. *Surg Obes Relat Dis* 2022;18:1345–1356
90. O'Brien R, Johnson E, Haneuse S, et al. Microvascular outcomes in patients with diabetes after bariatric surgery versus usual care: a matched cohort study. *Ann Intern Med* 2018;169:300–310
91. Mingrone G, Panunzi S, De Gaetano A, et al. Bariatric-metabolic surgery versus conventional medical treatment in obese patients with type 2 diabetes: 5 year follow-up of an open-label, single-centre, randomised controlled trial. *Lancet* 2015;386:964–973
92. Aminian A, Kashyap SR, Wolski KE, et al. Patient-reported outcomes after metabolic surgery versus medical therapy for diabetes: insights from the STAMPEDE randomized trial. *Ann Surg* 2021; 274:524–532
93. Sjöström L, Lindroos AK, Peltonen M, et al.; Swedish Obese Subjects Study Scientific Group. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. *N Engl J Med* 2004;351:2683–2693
94. Sjöström L, Peltonen M, Jacobson P, et al. Association of bariatric surgery with long-term remission of type 2 diabetes and with microvascular and macrovascular complications. *JAMA* 2014;311:2297–2304
95. Adams TD, Davidson LE, Litwin SE, et al. Health benefits of gastric bypass surgery after 6 years. *JAMA* 2012;308:1122–1131
96. Sjöström L, Narbro K, Sjöström CD, et al.; Swedish Obese Subjects Study. Effects of bariatric surgery on mortality in Swedish obese subjects. *N Engl J Med* 2007;357:741–752
97. Sjöström L, Gummesson A, Sjöström CD, et al.; Swedish Obese Subjects Study. Effects of bariatric surgery on cancer incidence in obese patients in Sweden (Swedish Obese Subjects Study): a prospective, controlled intervention trial. *Lancet Oncol* 2009;10:653–662
98. Sjöström L, Peltonen M, Jacobson P, et al. Bariatric surgery and long-term cardiovascular events. *JAMA* 2012;307:56–65
99. Adams TD, Gress RE, Smith SC, et al. Long-term mortality after gastric bypass surgery. *N Engl J Med* 2007;357:753–761
100. Arterburn DE, Olsen MK, Smith VA, et al. Association between bariatric surgery and long-term survival. *JAMA* 2015;313:62–70
101. Adams TD, Arterburn DE, Nathan DM, Eckel RH. Clinical outcomes of metabolic surgery: microvascular and macrovascular complications. *Diabetes Care* 2016;39:912–923
102. Sheng B, Truong K, Spitler H, Zhang L, Tong X, Chen L. The long-term effects of bariatric surgery on type 2 diabetes remission, microvascular and macrovascular complications, and mortality: a systematic review and meta-analysis. *Obes Surg* 2017;27:2724–2732
103. Fisher DP, Johnson E, Haneuse S, et al. Association between bariatric surgery and macrovascular disease outcomes in patients with type 2 diabetes and severe obesity. *JAMA* 2018;320: 1570–1582
104. Billeter AT, Scheurten KM, Probst P, et al. Meta-analysis of metabolic surgery versus medical treatment for microvascular complications in patients with type 2 diabetes mellitus. *Br J Surg* 2018;105:168–181
105. Aminian A, Zajicek A, Arterburn DE, et al. Association of metabolic surgery with major adverse cardiovascular outcomes in patients with type 2 diabetes and obesity. *JAMA* 2019;322: 1271–1282
106. Syn NL, Cummings DE, Wang LZ, et al. Association of metabolic-bariatric surgery with long-term survival in adults with and without diabetes: a one-stage meta-analysis of matched cohort and prospective controlled studies with 174 772 participants. *Lancet* 2021;397:1830–1841
107. Li Y, Gu Y, Jin Y, Mao Z. Is bariatric surgery effective for Chinese patients with type 2 diabetes mellitus and body mass index < 35 kg/m²? A systematic review and meta-analysis. *Obes Surg* 2021;31:4083–4092
108. Isaman DJ, Rothberg AE, Herman WH. Reconciliation of type 2 diabetes remission rates in studies of Roux-en-Y gastric bypass. *Diabetes Care* 2016;39:2247–2253
109. Sjöholm K, Pajunen P, Jacobson P, et al. Incidence and remission of type 2 diabetes in relation to degree of obesity at baseline and 2 year weight change: the Swedish Obese Subjects (SOS) study. *Diabetologia* 2015;58:1448–1453
110. Arterburn DE, Bogart A, Sherwood NE, et al. A multisite study of long-term remission and relapse of type 2 diabetes mellitus following gastric bypass. *Obes Surg* 2013;23:93–102
111. Cohen RV, Pinheiro JC, Schiavon CA, Salles JE, Wajchenberg BL, Cummings DE. Effects of gastric bypass surgery in patients with type 2 diabetes and only mild obesity. *Diabetes Care* 2012;35:1420–1428
112. Brethauer SA, Aminian A, Romero-Talamás H, et al. Can diabetes be surgically cured? Long-term metabolic effects of bariatric surgery in obese patients with type 2 diabetes mellitus. *Ann Surg* 2013;258:628–636; discussion 636–637
113. Hsu CC, Almulaifi A, Chen JC, et al. Effect of bariatric surgery vs medical treatment on type 2 diabetes in patients with body mass index lower than 35: five-year outcomes. *JAMA Surg* 2015;150: 1117–1124
114. Hariri K, Guevara D, Jayaram A, Kini SU, Herron DM, Fernandez-Ranvier G. Preoperative insulin therapy as a marker for type 2 diabetes remission in obese patients after bariatric surgery. *Surg Obes Relat Dis* 2018;14:332–337
115. Yu H, Di J, Bao Y, et al. Visceral fat area as a new predictor of short-term diabetes remission after Roux-en-Y gastric bypass surgery in Chinese patients with a body mass index less than 35 kg/m². *Surg Obes Relat Dis* 2015;11:6–11
116. Kirwan JP, Aminian A, Kashyap SR, Burguera B, Brethauer SA, Schauer PR. Bariatric surgery in obese patients with type 1 diabetes. *Diabetes Care* 2016;39:941–948
117. Rubin JK, Hinrichs-Krapels S, Hesketh R, Martin A, Herman WH, Rubino F. Identifying barriers to appropriate use of metabolic/bariatric surgery for type 2 diabetes treatment: policy lab results. *Diabetes Care* 2016;39:954–963
118. Fouse T, Schauer P. The socioeconomic impact of morbid obesity and factors affecting access to obesity surgery. *Surg Clin North Am* 2016;96:669–679
119. Flum DR, Belle SH, King WC, et al.; Longitudinal Assessment of Bariatric Surgery (LABS) Consortium. Perioperative safety in the longitudinal assessment of bariatric surgery. *N Engl J Med* 2009;361:445–454
120. Courcoulas AP, Christian NJ, Belle SH, et al.; Longitudinal Assessment of Bariatric Surgery (LABS) Consortium. Weight change and health outcomes at 3 years after bariatric surgery among individuals with severe obesity. *JAMA* 2013;310: 2416–2425
121. Arterburn DE, Courcoulas AP. Bariatric surgery for obesity and metabolic conditions in adults. *BMJ* 2014;349:g3961
122. Young MT, Gebhart A, Phelan MJ, Nguyen NT. Use and outcomes of laparoscopic sleeve gastrectomy vs laparoscopic gastric bypass: analysis of the American College of Surgeons NSQIP. *J Am Coll Surg* 2015;220:880–885
123. Aminian A, Brethauer SA, Kirwan JP, Kashyap SR, Burguera B, Schauer PR. How safe is

- metabolic/diabetes surgery? *Diabetes Obes Metab* 2015;17:198–201
124. Birkmeyer NJ, Dimick JB, Share D, et al.; Michigan Bariatric Surgery Collaborative. Hospital complication rates with bariatric surgery in Michigan. *JAMA* 2010;304:435–442
125. Altieri MS, Yang J, Telem DA, et al. Lap band outcomes from 19,221 patients across centers and over a decade within the state of New York. *Surg Endosc* 2016;30:1725–1732
126. Hutter MM, Schirmer BD, Jones DB, et al. First report from the American College of Surgeons Bariatric Surgery Center Network: laparoscopic sleeve gastrectomy has morbidity and effectiveness positioned between the band and the bypass. *Ann Surg* 2011;254:410–420; discussion 420–422
127. Nguyen NT, Slone JA, Nguyen XM, Hartman JS, Hoyt DB. A prospective randomized trial of laparoscopic gastric bypass versus laparoscopic adjustable gastric banding for the treatment of morbid obesity: outcomes, quality of life, and costs. *Ann Surg* 2009;250:631–641
128. Courcoulas AP, King WC, Belle SH, et al. Seven-year weight trajectories and health outcomes in the Longitudinal Assessment of Bariatric Surgery (LABS) study. *JAMA Surg* 2018;153:427–434
129. Birkmeyer JD, Finks JF, O'Reilly A, et al.; Michigan Bariatric Surgery Collaborative. Surgical skill and complication rates after bariatric surgery. *N Engl J Med* 2013;369:1434–1442
130. Mechanick JJ, Apovian C, Brethauer S, et al. Clinical practice guidelines for the perioperative nutrition, metabolic, and nonsurgical support of patients undergoing bariatric procedures - 2019 update: cosponsored by American Association of Clinical Endocrinologists/American College of Endocrinology, The Obesity Society, American Society for Metabolic & Bariatric Surgery, Obesity Medicine Association, and American Society of Anesthesiologists - executive summary. *Endocr Pract* 2019;25:1346–1359
131. Service GJ, Thompson GB, Service FJ, Andrews JC, Collazo-Clavell ML, Lloyd RV. Hyperinsulinemic hypoglycemia with nesidioblastosis after gastric bypass surgery. *N Engl J Med* 2005;353:249–254
132. Sheehan A, Patti ME. Hypoglycemia after upper gastrointestinal surgery: clinical approach to assessment, diagnosis, and treatment. *Diabetes Metab Syndr Obes* 2020;13:4469–4482
133. Lee D, Dreyfuss JM, Sheehan A, Puleio A, Mulla CM, Patti ME. Glycemic patterns are distinct in post-bariatric hypoglycemia after gastric bypass (PBH-RYGB). *J Clin Endocrinol Metab* 2021;106:2291–2303
134. Salehi M, Vella A, McLaughlin T, Patti ME. Hypoglycemia after gastric bypass surgery: current concepts and controversies. *J Clin Endocrinol Metab* 2018;103:2815–2826
135. Conanson A, Teixeira J, Hsu CH, Puma L, Knafo D, Geliebter A. Substance use following bariatric weight loss surgery. *JAMA Surg* 2013;148:145–150
136. Bhatti JA, Nathens AB, Thiruchelvam D, Grantcharov T, Goldstein BI, Redelman DA. Self-harm emergencies after bariatric surgery: a population-based cohort study. *JAMA Surg* 2016;151:226–232
137. Peterhänsel C, Petroff D, Klinitzke G, Kersting A, Wagner B. Risk of completed suicide after bariatric surgery: a systematic review. *Obes Rev* 2013;14:369–382
138. Jakobsen GS, Småstuen MC, Sandbu R, et al. Association of bariatric surgery vs medical obesity treatment with long-term medical complications and obesity-related comorbidities. *JAMA* 2018;319:291–301
139. King WC, Chen JY, Mitchell JE, et al. Prevalence of alcohol use disorders before and after bariatric surgery. *JAMA* 2012;307:2516–2525
140. Young-Hyman D, Peyrot M. *Psychosocial Care for People with Diabetes*. 1st ed. Alexandria, VA, American Diabetes Association, 2012
141. Greenberg I, Sogg S, M Perna F. Behavioral and psychological care in weight loss surgery: best practice update. *Obesity (Silver Spring)* 2009;17:880–884
142. Merative Micromedex. RED BOOK (electronic version). Merative, Ann Arbor, Michigan. Accessed 6 September 2023. Available from <https://www.micromedexsolutions.com>
143. Data.Medicaid.gov. NADAC (National Average Drug Acquisition Cost). Accessed 6 September 2023. Available from <https://data.medicaid.gov/dataset/dfa2ab14-06c2-457a-9e36-5cb6d80f8d93>
144. U.S. National Library of Medicine. Phentermine-phentermine hydrochloride capsule. Accessed 15 October 2023. Available from <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=737eeef3b-9a6b-4ab3-a25c-49d8-4d2a0197>
145. Currrax Pharmaceuticals. Contrave (naltrexone HCl/bupropion HCl) extended-release tablets. Accessed 15 October 2023. Available from <https://contrave.com>
146. CHEPLAPHARM and H2-Pharma. Xenical (orlistat). Accessed 15 October 2023. Available from <https://xenical.com>
147. Vivus. Qsymia (phentermine and topiramate extended-release capsules). Accessed 15 October 2023. Available from <https://qsymia.com>
148. Novo Nordisk. Saxenda (liraglutide injection 3 mg). Accessed 15 October 2023. Available from <https://www.saxenda.com>
149. Eli Lilly and Company. Zepbound (tirzepatide). Accessed 8 November 2023. Available from <https://pi.lilly.com/us/zepbound-uspi.pdf>
150. Aronne LJ, Wadden TA, Peterson C, Winslow D, Odeh S, Gadde KM. Evaluation of phentermine and topiramate versus phentermine/topiramate extended-release in obese adults. *Obesity (Silver Spring)* 2013;21:2163–2171
151. Marso SP, Bain SC, Consoli A, et al.; SUSTAIN-6 Investigators. Semaglutide and cardiovascular outcomes in patients with type 2 diabetes. *N Engl J Med* 2016;375:1834–1844