



## 8. Obesity Management for the Treatment of Type 2 Diabetes: Standards of Medical Care in Diabetes—2021

American Diabetes Association

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The American Diabetes Association (ADA) “Standards of Medical Care in Diabetes” includes the ADA’s current clinical practice recommendations and is intended to provide the components of diabetes care, general treatment goals and guidelines, and tools to evaluate quality of care. Members of the ADA Professional Practice Committee, a multidisciplinary expert committee (<https://doi.org/10.2337/dc21-SPPC>), are responsible for updating the Standards of Care annually, or more frequently as warranted. For a detailed description of ADA standards, statements, and reports, as well as the evidence-grading system for ADA’s clinical practice recommendations, please refer to the Standards of Care Introduction (<https://doi.org/10.2337/dc21-SINT>). Readers who wish to comment on the Standards of Care are invited to do so at [professional.diabetes.org/SOC](https://professional.diabetes.org/SOC).

There is strong and consistent evidence that obesity management can delay the progression from prediabetes to type 2 diabetes (1–5) and is highly beneficial in the treatment of type 2 diabetes (6–17). In patients with type 2 diabetes who also have overweight or obesity, modest and sustained weight loss has been shown to improve glycemic control and reduce the need for glucose-lowering medications (6–8). Several studies have demonstrated that in patients with type 2 diabetes and obesity, more intensive dietary energy restriction with very-low-calorie diets can substantially reduce A1C and fasting glucose and promote sustained diabetes remission through at least 2 years (10,18–21). The goal of this section is to provide evidence-based recommendations for obesity management, including dietary, behavioral, pharmacologic, and surgical interventions, in patients with type 2 diabetes. This section focuses on obesity management in adults. Further discussion on obesity in older individuals and children can be found in Section 12 “Older Adults” (<https://doi.org/10.2337/dc21-S012>) and Section 13 “Children and Adolescents” (<https://doi.org/10.2337/dc21-S013>), respectively.

### ASSESSMENT

#### Recommendations

- 8.1** Use patient-centered, nonjudgmental language that fosters collaboration between patients and providers, including people-first language (e.g., “person with obesity” rather than “obese person”). **E**
- 8.2** Measure height and weight and calculate BMI at annual visits or more frequently. Assess weight trajectory to inform treatment considerations. **E**

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**8.3** Based on clinical considerations, such as the presence of comorbid heart failure or significant unexplained weight gain or loss, weight may need to be monitored and evaluated more frequently. **B** If deterioration of medical status is associated with significant weight gain or loss, inpatient evaluation should be considered, especially focused on associations between medication use, food intake, and glycemic status. **E**

**8.4** Accommodations should be made to provide privacy during weighing. **E**

A patient-centered communication style that uses inclusive and nonjudgmental language and active listening, elicits patient preferences and beliefs, and assesses potential barriers to care should be used to optimize patient health outcomes and health-related quality of life. Use people-first language (e.g., “person with obesity” rather than “obese person”) to avoid defining patients by their condition (22,23,23a).

Height and weight should be measured and used to calculate BMI at annual visits or more frequently when appropriate (19). BMI, calculated as weight in kilograms divided by the square of height in meters ( $\text{kg}/\text{m}^2$ ), will be calculated automatically by most electronic medical records. Use BMI to document weight status (overweight: BMI 25–29.9  $\text{kg}/\text{m}^2$ ; obesity class I: BMI 30–34.9  $\text{kg}/\text{m}^2$ ; obesity class II: BMI 35–39.9  $\text{kg}/\text{m}^2$ ; obesity class III: BMI  $\geq 40$   $\text{kg}/\text{m}^2$ ). Note that misclassification can occur, particularly in very muscular or frail individuals. In some populations, notably Asian and Asian American populations, the BMI cut points to define overweight and obesity are lower than in other populations due to differences in body composition and cardiometabolic risk (Table 8.1) (24,25). Clinical considerations, such as the presence of comorbid heart failure or unexplained weight change, may warrant more frequent weight measurement and evaluation (26,27). If weighing is questioned or refused, the practitioner should be mindful of possible prior stigmatizing experiences and query for concerns, and the value of weight monitoring should be explained as a part of the medical evaluation process that helps to inform treatment decisions (28,29). Accommodations should be made to ensure privacy during

weighing, particularly for those patients who report or exhibit a high level of weight-related distress or dissatisfaction. Scales should be situated in a private area or room. Weight should be measured and reported nonjudgmentally. Care should be taken to regard a patient’s weight (and weight changes) and BMI as sensitive health information. Additionally, assessing weight gain pattern and trajectory can further inform risk stratification and treatment options (30). Providers should advise patients with overweight or obesity and those with increasing weight trajectories that, in general, higher BMIs increase the risk of diabetes, cardiovascular disease, and all-cause mortality, as well as other adverse health and quality of life outcomes. Providers should assess readiness to engage in behavioral changes for weight loss and jointly determine behavioral and weight-loss goals and patient-appropriate intervention strategies (31). Strategies may include dietary changes, physical activity, behavioral therapy, pharmacologic therapy, medical devices, and metabolic surgery (Table 8.1). The latter three strategies may be prescribed for carefully selected patients as adjuncts to dietary changes, physical activity, and behavioral counseling.

## DIET, PHYSICAL ACTIVITY, AND BEHAVIORAL THERAPY

### Recommendations

**8.5** Diet, physical activity, and behavioral therapy designed to achieve and maintain  $\geq 5\%$  weight loss is recommended for most patients with type 2 diabetes who have overweight or obesity and are ready to achieve weight loss. Greater benefits in control of diabetes and cardiovascular risk may be gained from even greater weight loss. **B**

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

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

**8.8** Behavioral changes that create an energy deficit, regardless of

macronutrient composition, will result in weight loss. Dietary recommendations should be individualized to the patient’s preferences and nutritional needs. **A**

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

**8.10** For patients who achieve short-term weight-loss goals, long-term ( $\geq 1$  year) weight-maintenance programs are recommended when available. Such programs should, at minimum, provide monthly contact and support, recommend ongoing monitoring of body weight (weekly or more frequently) and other self-monitoring strategies, and encourage high levels of physical activity (200–300 min/week). **A**

**8.11** Short-term dietary intervention using structured, very-low-calorie diets (800–1,000 kcal/day) may be prescribed for carefully selected patients 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**

Among patients with both type 2 diabetes and overweight or obesity who have inadequate glycemic, blood pressure, and lipid control and/or other obesity-related medical conditions, modest and sustained weight loss improves glycemic control, blood pressure, and lipids and may reduce the need for medications to control these risk factors (6–8,32). Greater weight loss may produce even greater benefits (20,21). For a more detailed discussion of lifestyle management approaches and recommendations see Section 5 “Facilitating Behavior Change and Well-being to Improve Health Outcomes” (<https://doi.org/10.2337/dc21-S005>). For a detailed discussion of nutrition interventions, please also refer to “Nutrition Therapy for Adults With Diabetes or Prediabetes: A Consensus Report” (33).

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

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

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

### 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 (34), it did confirm the feasibility of achieving and maintaining long-term weight loss in patients with type 2 diabetes. In the intensive lifestyle intervention group, mean weight loss was 4.7% at 8 years (35). Approximately 50% of intensive lifestyle intervention participants lost and maintained ≥5% of their initial body weight, and 27% lost and maintained ≥10% of their initial body weight at 8 years (35). Participants assigned to the intensive lifestyle group required fewer glucose-, blood pressure-, and lipid-lowering medications than those randomly assigned to standard care. Secondary analyses of the Look AHEAD trial and other large cardiovascular outcome studies document additional benefits of weight loss in patients with type 2 diabetes, including improvements in mobility, physical and sexual function, and health-related quality of life (26). Moreover, several subgroups had improved cardiovascular outcomes, including those who achieved >10% weight loss (36) and those with moderately or poorly controlled diabetes (A1C >6.8%) at baseline (37).

### Lifestyle Interventions

Significant weight loss can be attained with lifestyle programs that achieve a 500–750 kcal/day energy deficit, which in most cases is approximately 1,200–1,500 kcal/day for women and 1,500–1,800 kcal/day for men, adjusted for the individual's baseline body weight. Clinical benefits typically begin upon achieving 3–5% weight loss (19,38), and the benefits of weight loss are progressive; more intensive weight-loss goals (>5%, >7%, >15%, etc.) may be pursued if needed to achieve further health improvements and/or if the patient is more

motivated and more intensive goals can be feasibly and safely attained.

Dietary interventions may differ by macronutrient goals and food choices as long as they create the necessary energy deficit to promote weight loss (19,39–41). Use of meal replacement plans prescribed by trained practitioners, with close patient monitoring, can be beneficial. Within the intensive lifestyle intervention group of the Look AHEAD trial, for example, use of a partial meal replacement plan was associated with improvements in diet quality and weight loss (38). The diet choice should be based on the patient's health status and preferences, including a determination of food availability and other cultural circumstances that could affect dietary patterns (42).

Intensive behavioral lifestyle interventions should include ≥16 sessions in 6 months and focus on dietary changes, physical activity, and behavioral strategies to achieve an ~500–750 kcal/day energy deficit. Interventions should be provided by trained interventionists in either individual or group sessions (38). Assessing an individual's motivation level, life circumstances, and willingness to implement lifestyle changes to achieve weight loss should be considered along with medical status when weight-loss interventions are recommended and initiated (31,43).

Patients with type 2 diabetes and overweight or obesity who have lost weight should be offered long-term (≥1 year) comprehensive weight-loss maintenance programs that provide at least monthly contact with trained interventionists and focus on ongoing monitoring of body weight (weekly or more frequently) and/or other self-monitoring strategies such as tracking intake, steps, etc.; continued focus on dietary and behavioral changes; and participation in high levels of physical activity (200–300 min/week) (44). Some commercial and proprietary weight-loss programs have shown promising weight-loss results, though most lack

evidence of effectiveness, many do not satisfy guideline recommendations, and some promote unscientific and possibly dangerous practices (45,46).

When provided by trained practitioners in medical settings with ongoing monitoring, short-term (generally up to 3 months) intensive dietary intervention may be prescribed for carefully selected patients, such as those requiring weight loss prior to surgery and persons needing greater weight loss and glycemic improvements. When integrated with behavioral support and counseling, structured very-low-calorie diets, typically 800–1,000 kcal/day utilizing high-protein foods and meal replacement products, may increase the pace and/or magnitude of initial weight loss and glycemic improvements compared with standard behavioral interventions (20,21). As weight regain is common, such interventions should include long-term, comprehensive weight-maintenance strategies and counseling to maintain weight loss and behavioral changes (47,48).

Health disparities adversely affect groups of 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 diabetes and diabetes-related complications. Health care providers should evaluate systemic, structural, and socioeconomic factors that may impact food choices, access to healthful foods, and dietary patterns; other 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, please refer to "Social Determinants of Health: A Scientific Review" (49).

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

Medication name	Typical adult maintenance dose	Average wholesale price (30-day supply) (118)	National Average Drug Acquisition Cost (30-day supply) (119)	1-Year (52- or 56-week) mean weight loss (% loss from baseline)		Possible safety concerns/considerations (120–124)
				Treatment arms	Weight loss (% loss from baseline)	
<b>Short-term treatment (≤12 weeks)</b>						
<i>Sympathomimetic amine anorectic</i>						
Phentermine (125)	8–37.5 mg q.d.*	\$5–\$46 (37.5 mg dose)	\$3 (37.5 mg dose)	15 mg q.d.† 7.5 mg q.d.† PBO	6.1 5.5 1.2	• Contraindicated for use in combination with monoamine oxidase inhibitors
<b>Long-term treatment (&gt;12 weeks)</b>						
<i>Lipase inhibitor</i>						
Orlistat (3)	60 mg t.i.d. (OTC) 120 mg t.i.d. (Rx)	\$41–\$82 \$823	\$41 \$556	120 mg t.i.d.‡ PBO	9.6 5.6	• Potential malabsorption of fat-soluble vitamins (A, D, E, K) and of certain medications (e.g., cyclosporine, thyroid hormone, anticonvulsants, etc.) • Rare cases of severe liver injury reported • Cholelithiasis • Nephrolithiasis
<i>Sympathomimetic amine anorectic/antiepileptic combination</i>						
Phentermine/topiramate ER (126)	7.5 mg/46 mg q.d.§	\$223 (7.5 mg/46 mg dose)	\$179 (7.5 mg/46 mg dose)	15 mg/92 mg q.d.   7.5 mg/46 mg q.d.   PBO	9.8 7.8 1.2	• Contraindicated for use in combination with monoamine oxidase inhibitors • Birth defects • Cognitive impairment • Acute angle-closure glaucoma
<i>Opioid antagonist/antidepressant combination</i>						
Naltrexone/bupropion ER (15)	16 mg/180 mg b.i.d.	\$334	\$266	16 mg/180 mg b.i.d. PBO	5.0 1.8	• Contraindicated in patients with uncontrolled hypertension and/or seizure disorders • Contraindicated for use with chronic opioid therapy • Acute angle-closure glaucoma <b>Black box warning:</b> • Risk of suicidal behavior/ideation in persons younger than 24 years old who have depression

*Continued on p. S104*

**Table 8.2—Continued**

Medication name	Typical adult maintenance dose	Average wholesale price (30-day supply) (118)	National Average Drug Acquisition Cost (30-day supply) (119)	1-Year (52- or 56-week) mean weight loss (% loss from baseline)		Possible safety concerns/considerations (120–124)
				Treatment arms	Weight loss (% loss from baseline)	
Glucagon-like peptide 1 receptor agonist						
Liraglutide (16)**	3 mg q.d.	\$1,557	\$1,243	3.0 mg q.d. 1.8 mg q.d. PBO	6.0 4.7 2.0	<p>Common side effects (120–124)</p> <ul style="list-style-type: none"> <li>Gastrointestinal side effects (nausea, vomiting, diarrhea, esophageal reflux), injection site reactions, elevated heart rate</li> </ul> <p>Possible safety concerns/considerations (120–124)</p> <ul style="list-style-type: none"> <li>Pancreatitis has been reported in clinical trials but causality has not been established. Discontinue if pancreatitis is suspected.</li> <li>Use caution in patients with kidney disease when initiating or increasing dose due to potential risk of acute kidney injury</li> </ul> <p><b>Black box warning:</b></p> <ul style="list-style-type: none"> <li>Risk of thyroid C-cell tumors in rodents; human relevance not determined</li> </ul>

All medications are contraindicated in women who are or may become pregnant. Women of reproductive potential must be counseled regarding the use of reliable methods of contraception. Select safety and side effect information is provided; for a comprehensive discussion of safety considerations, please refer to the prescribing information for each agent. b.i.d., twice daily; ER, extended release; OTC, over the counter; PBO, placebo; q.d., daily; Rx, prescription; t.i.d., three times daily. \* Use lowest effective dose; maximum appropriate dose is 37.5 mg. † Duration of treatment was 28 weeks in a general obese adult population. \*\* Agent has demonstrated cardiovascular safety in a dedicated cardiovascular outcome trial (127). ‡ 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.

## PHARMACOTHERAPY

### Recommendations

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

### Glucose-Lowering Therapy

A meta-analysis of 227 randomized controlled trials of glucose-lowering treatments in type 2 diabetes found that A1C changes were not associated with baseline BMI, indicating that patients with obesity can benefit from the same types of treatments for diabetes as normal-weight patients (50). As numerous effective medications are available, when considering medication regimens health care providers should consider each medication's effect on weight. Agents associated with varying degrees of weight loss include metformin,  $\alpha$ -glucosidase inhibitors, sodium-glucose cotransporter 2 inhibitors, glucagon-like peptide 1 receptor agonists, and amylin mimetics. Dipeptidyl peptidase 4 inhibitors are weight neutral. In contrast, insulin secretagogues, thiazolidinediones, and insulin are often associated with weight gain (see Section 9 "Pharmacologic Approaches to Glycemic Treatment," <https://doi.org/10.2337/dc21-s009>).

### Concomitant Medications

Providers should carefully review the patient's concomitant medications and, whenever possible, minimize or provide alternatives for medications that promote weight gain. Examples of medications associated with weight gain include antipsychotics (e.g., clozapine, olanzapine, risperidone, etc.), some antidepressants (e.g., tricyclic antidepressants, some selective serotonin reuptake inhibitors, and monoamine oxidase inhibitors), glucocorticoids, injectable progestins, some anticonvulsants (e.g., gabapentin, pregabalin), and possibly sedating antihistamines and anticholinergics (51).

### Approved Weight-Loss Medications

The U.S. Food and Drug Administration (FDA) has approved medications for both short-term and long-term weight management as adjuncts to diet, exercise, and behavioral therapy. Nearly all FDA-approved medications for weight loss have been shown to improve glycemic control in patients with type 2 diabetes and delay progression to type 2 diabetes in patients at risk (52). Phentermine and other older adrenergic agents are indicated for short-term ( $\leq 12$  weeks) treatment (53). Four weight-loss medications are FDA approved for long-term use ( $>12$  weeks) in patients with BMI  $\geq 27$  kg/m<sup>2</sup> with one or more obesity-associated comorbid condition (e.g., type 2 diabetes, hypertension, and/or dyslipidemia) who are motivated to lose weight (52). Medications approved by the FDA for the treatment of obesity are summarized in **Table 8.2**. The rationale for weight-loss medication use is to help patients adhere to dietary recommendations, in most cases by modulating appetite or satiety. Providers should be knowledgeable about the product label and should balance the potential benefits of successful weight loss against the potential risks of the medication for each patient. These medications are contraindicated in women who are pregnant or actively trying to conceive and not recommended for use in women who are nursing. Women of reproductive potential should receive counseling regarding the use of reliable methods of contraception.

### Assessing Efficacy and Safety

Upon initiating weight-loss medication, assess efficacy and safety at least monthly for the first 3 months and at least quarterly

thereafter. Modeling from published clinical trials consistently shows that early responders have improved long-term outcomes (54–56). Unless clinical circumstances (such as poor tolerability) or other considerations (such as financial expense or patient preference) suggest otherwise, those who achieve sufficient early weight loss upon starting a chronic weight-loss medication (typically defined as  $>5\%$  weight loss after 3 months' use) should continue the medication. When early use appears ineffective (typically  $<5\%$  weight loss after 3 months' use), it is unlikely that continued use will improve weight outcomes; as such, it should be recommended to discontinue the medication and consider other treatment options.

## MEDICAL DEVICES FOR WEIGHT LOSS

Several minimally invasive medical devices have been approved by the FDA for short-term weight loss (57,58). It remains to be seen how these are used for obesity treatment. Given the high cost, limited insurance coverage, and paucity of data in people with diabetes at this time, medical devices for weight loss are currently not considered to be the standard of care for obesity management in people with type 2 diabetes.

## METABOLIC SURGERY

### Recommendations

- 8.16** Metabolic surgery should be a recommended option to treat type 2 diabetes in screened surgical candidates with BMI  $\geq 40$  kg/m<sup>2</sup> (BMI  $\geq 37.5$  kg/m<sup>2</sup> in Asian Americans) and in adults with BMI 35.0–39.9 kg/m<sup>2</sup> (32.5–37.4 kg/m<sup>2</sup> in Asian Americans) who do not achieve durable weight loss and improvement in comorbidities (including hyperglycemia) with nonsurgical methods. **A**
- 8.17** Metabolic surgery may be considered as an option to treat type 2 diabetes in adults with BMI 30.0–34.9 kg/m<sup>2</sup> (27.5–32.4 kg/m<sup>2</sup> in Asian Americans) who do not achieve durable weight loss and improvement in comorbidities (including hyperglycemia) with nonsurgical methods. **A**

- 8.18** Metabolic surgery should be performed in high-volume centers with multidisciplinary teams knowledgeable about and experienced in the management of diabetes and gastrointestinal surgery. **E**
- 8.19** Long-term lifestyle support and routine monitoring of micronutrient and nutritional status must be provided to patients after surgery, according to guidelines for postoperative management of metabolic surgery by national and international professional societies. **C**
- 8.20** People being considered for metabolic surgery should be evaluated for comorbid psychological conditions and social and situational circumstances that have the potential to interfere with surgery outcomes. **B**
- 8.21** People who undergo metabolic surgery should routinely be evaluated to assess the need for ongoing mental health services to help with the adjustment to medical and psychosocial changes after surgery. **C**

Several gastrointestinal (GI) operations, including partial gastrectomies and bariatric procedures (44), promote dramatic and durable weight loss and improvement of type 2 diabetes in many patients. Given the magnitude and rapidity of the effect of GI surgery on hyperglycemia and experimental evidence that rearrangements of GI anatomy similar to those in some metabolic procedures directly affect glucose homeostasis (45), GI interventions have been suggested as treatments for type 2 diabetes, and in that context they are termed “metabolic surgery.”

A substantial body of evidence has now been accumulated, including data from numerous randomized controlled (nonblinded) clinical trials, demonstrating that metabolic surgery achieves superior glycemic control and reduction of cardiovascular risk factors in patients with type 2 diabetes and obesity compared with various lifestyle/medical interventions (17). Improvements in microvascular complications of diabetes, cardiovascular disease, and cancer have been observed only in nonrandomized

observational studies (59–70). Cohort studies attempting to match surgical and nonsurgical subjects suggest that the procedure may reduce longer-term mortality (60,71).

While several surgical options are available, the overwhelming majority of procedures in the U.S. are vertical sleeve gastrectomy and Roux-en-Y gastric bypass (RYGB). Both procedures result in an anatomically smaller stomach pouch and often robust changes in enteroendocrine hormones. On the basis of this mounting evidence, several organizations and government agencies have recommended expanding the indications for metabolic surgery to include patients with type 2 diabetes who do not achieve durable weight loss and improvement in comorbidities (including hyperglycemia) with reasonable nonsurgical methods at BMIs as low as 30 kg/m<sup>2</sup> (27.5 kg/m<sup>2</sup> for Asian Americans) (72–79). Randomized controlled trials have documented diabetes remission during postoperative follow-up ranging from 1 to 5 years in 30–63% of patients with RYGB, which generally leads to greater degrees and lengths of remission compared with other bariatric surgeries (17,80). Available data suggest an erosion of diabetes remission over time (81): 35–50% or more of patients who initially achieve remission of diabetes eventually experience recurrence. However, the median disease-free period among such individuals following RYGB is 8.3 years (82,83). With or without diabetes relapse, the majority of patients who undergo surgery maintain substantial improvement of glycemic control from baseline for at least 5 years (84,85) to 15 years (60,61,83,86–88).

Exceedingly few presurgical predictors of success have been identified, but younger age, shorter duration of diabetes (e.g., <8 years) (89), nonuse of insulin, maintenance of weight loss, and better glycemic control are consistently associated with higher rates of diabetes remission and/or lower risk of weight regain (60,87,89,90). Greater baseline visceral fat area may also help to predict better postoperative outcomes, especially among Asian American patients with type 2 diabetes, who typically have more visceral fat compared with Caucasians with diabetes of the same BMI (91). Beyond improving glycemia, metabolic surgery has been shown to confer additional health benefits in

randomized controlled trials, including substantial reductions in cardiovascular disease risk factors (17), reductions in incidence of microvascular disease (92), and enhancements in quality of life (84,89,93).

Although metabolic surgery has been shown to improve the metabolic profiles of patients with type 1 diabetes and morbid obesity, establishing the role of metabolic surgery in such patients will require larger and longer studies (94).

Metabolic surgery is more expensive than nonsurgical management strategies, but retrospective analyses and modeling studies suggest that metabolic surgery may be cost-effective or even cost-saving for patients with type 2 diabetes. However, results are largely dependent on assumptions about the long-term effectiveness and safety of the procedures (95,96).

#### Adverse Effects

The safety of metabolic surgery has improved significantly over the past several decades, with continued refinement of minimally invasive approaches (laparoscopic surgery), enhanced training and credentialing, and involvement of multidisciplinary teams. Mortality rates with metabolic operations are typically 0.1–0.5%, similar to cholecystectomy or hysterectomy (97–101). Morbidity has also dramatically declined with laparoscopic approaches. Major complications and need for operative reintervention occur in 2–6% of those undergoing bariatric surgery, with other minor complications in up to 15% (97–106). These rates compare favorably with those for other commonly performed elective operations (101). Empirical data suggest that proficiency of the operating surgeon is an important factor for determining mortality, complications, reoperations, and readmissions (107). Accordingly, metabolic surgery should be performed in high-volume centers with multidisciplinary teams knowledgeable about and experienced in the management of diabetes and GI surgery.

Longer-term concerns include dumping syndrome (nausea, colic, and diarrhea), vitamin and mineral deficiencies, anemia, osteoporosis, and severe hypoglycemia (108). Long-term nutritional and micronutrient deficiencies and related complications occur with variable frequency

depending on the type of procedure and require lifelong vitamin/nutritional supplementation; thus, long-term lifestyle support and routine monitoring of micronutrient and nutritional status should be provided to patients after surgery (109,110). Postprandial hypoglycemia is most likely to occur with RYGB (110,111). The exact prevalence of symptomatic hypoglycemia is unknown. In one study, it affected 11% of 450 patients who had undergone RYGB or vertical sleeve gastrectomy (108). Patients who undergo metabolic surgery may be at increased risk for substance use, including drug and alcohol use and cigarette smoking. Additional potential risks of metabolic surgery that have been described include worsening or new-onset depression and/or anxiety, need for additional GI surgery, and suicidal ideation (112–115).

People with diabetes presenting for metabolic surgery also have increased rates of depression and other major psychiatric disorders (116). Candidates for metabolic surgery with histories of alcohol, tobacco, or substance abuse or significant depression, suicidal ideation, or other mental health conditions should therefore first be assessed by a mental health professional with expertise in obesity management prior to consideration for surgery (117). Surgery should be postponed in patients with alcohol or substance abuse disorders, significant depression, suicidal ideation, or other mental health conditions until these conditions have been fully addressed. Individuals with preoperative psychopathology should be assessed regularly following metabolic surgery to optimize mental health management and to ensure that psychiatric symptoms do not interfere with weight loss and lifestyle changes.

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