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Effective Diabetes Prevention for Adults:

Medical and Surgical Treatment of Obesity, Part 2

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Approximately 85% of adult patients with prediabetes have overweight or obesity, and treatment should be individualized to reflect the severity of both conditions.[1]

Obesity is a chronic, relapsing condition most effectively addressed with healthy lifestyle behaviors plus medical and/or surgical treatments to provide durable results that prevent or improve co-morbidities, such as diabetes.[2-6] The American Diabetes Association (ADA) recommends annual obesity screening for all adults using body mass index (BMI) as a primary measure, with treatment offered based on patient readiness to engage, the presence of related medical issues, and the severity of disease.[7-10] Treating prediabetes within the context of obesity treatment is strongly recommended, as delaying or preventing diabetes has been shown to reduce morbidity, mortality, and overall health care costs.[2,6,7,10]

This document provides clinicians with evidence-based guidance and resources to support integrated care for patients with coexisting prediabetes and obesity, using both medical and surgical treatment options. For reviews of screening protocols and behavioral treatments for prediabetes and obesity, see the companion document, "Effective Diabetes Prevention for Adults: Prediabetes Screening and Treatment, Part 1."

Overview of Treatment Approaches for Prediabetes and Obesity

An individual's ability to engage in dietary modifications and physical activity impacts the effectiveness of both pharmacologic and surgical treatments for obesity and prediabetes. For this reason, interventions should be tailored to each patient's circumstances. Table 1 summarizes and compares the typical weight loss outcomes, additional benefits, side-effects and precautions, and costs associated with lifestyle interventions, pharmacotherapy, and bariatric surgery.[11] Considerations specific to women in childbearing years and older adult patients are shown in Table 2.[12-16]

The landmark Diabetes Prevention Program (DPP) trial demonstrated that adults with prediabetes who participated in an intensive lifestyle intervention achieved a 58% reduction in diabetes risk, rising to 71% among those older than 70 years. While lifestyle intervention was most effective, metformin combined with standard diet and physical activity counseling reduced diabetes risk by 31%, offering a more accessible alternative for many patients.[17-21] Despite its effectiveness, participation in DPP programs may be limited by access barriers and individual constraints.[22,23]

Although intensive lifestyle interventions reduce the risk for progression from prediabetes to diabetes, they have not been proven to reduce cardiovascular disease. Moreover, there are significant barriers to accessing an accredited diabetes prevention program and sustaining the intervention after a year. Combinations of lifestyle interventions with medical treatments or surgical therapies for obesity and prediabetes have been shown to lead to better and more sustained results (2 or more years after surgery) than with any of these treatments alone.

Evidence shows that weight loss is the most effective factor for diabetes prevention. While a 4% to 10% reduction in body weight improves outcomes, especially within normal and overweight BMI ranges, the best medical outcomes in moderate or severe obesity (Class II-III) occur with weight losses of 15% to 25% or more. This amount of weight loss is rarely achieved and sustained through lifestyle changes alone but is often achievable when lifestyle changes are combined with obesity management medications and/or bariatric surgery.[2-6,24-26] The American Association of Clinical Endocrinology has published simple algorithms for the assessment and treatment of prediabetes and overweight/obesity (See Additional Resources).[6]

Table 1. Obesity Management Comparison Chart

	Lifestyle Intervention	GLP-1-Based Therapy	Bariatric Surgery
BMI Threshold (kg/m^2)	≥25	≥30 or ≥27 + comorbidity	≥35 or ≥30+ comorbidity; In high-risk ethnic populations consider lower threshold of ≥30 or ≥27.5 +comorbidity
Weight			
Expected Weight Loss, 1 Year	4%-8%	6.1%-25.8%	25.2%-31.2%
Long-Term Weight Loss	-8.4 to +6.7% at 5 years	10.2% 4 years (semaglutide)	18.8%-25.5% at 5 years
Weight Regain	71.2%-88.8% regained at 2-3 years	53%-58.2% regained at 1 year	19.5%-26% regained at 5 years
Other Benefits			
Type 2 Diabetes	41%-61% remission	64%-80% achieve A1C <6.5%	55%-86.6% with improvement or remission
Blood Pressure	48% stopped medication	34% reduced or stopped medication	60%-66.7% with improvement or resolution
Cholesterol	17.5% stopped medication (5% weight loss)	21% reduced or stopped medication	76% with improvement or resolution, 88% stopped medication
Cardiovascular Disease	21% reduction in cardiovascular risk with 10% weight loss	20%-22% lower risk of cardiovascular death	45% lower risk of cardiovascular death
Precautions/Side Effects			
Serious	Cholecystitis	Pancreatitis, bowel obstruction, medullary thyroid cancer, gastroparesis, cholecystitis, acute kidney injury, worsening retinopathy	Anesthesia risk, bowel obstruction, hernia, intussusception, dumping syndrome, cholecystitis
Common	Insufficient weight loss, loss of muscle mass with diet alone	Nausea, vomiting, constipation, diarrhea, injection site reaction, increased heart rate	Pain, nausea, vomiting, surgical site infection
Long-Term	Weight regain, nutrition deficiency	Weight regain after discontinuation	Vitamin deficiency, hypoglycemia, fistula, insufficient loss or regain, reflux
Cost	$	$$$	$$

Adapted from *Obesity Management Comparison Chart.*[11]

Table 2. Special Considerations for Specific Populations

Population / Issue	Key Points and Recommendations
Women With Obesity and Prediabetes in Child-Bearing Years[12-15]	▪ Obesity increases the risk for gestational diabetes and other pregnancy/birth complications. ▪ Weight loss improves fertility, increasing the risk of unintended pregnancy. Counsel patients and implement contraception before starting the treatment. ▪ Delay pregnancy 12-24 months after bariatric surgery to optimize micronutrient levels and pregnancy outcomes. ▪ All OMM are U.S. Food and Drug Administration Category C or higher risk for pregnancy. ▪ Metformin is the only safe option for women at risk for diabetes during pregnancy (i.e., not an OMM). ▪ Long-acting reversible contraception (i.e., IUD or implant) is preferred for women on OMM or post-bariatric surgery. ▪ Oral contraceptive absorption may be reduced after malabsorptive bariatric surgery (e.g., RYGB) or with GLP-1 RA therapy. ▪ For women with moderate to severe obesity desiring pregnancy, bariatric surgery can improve fertility and lower pregnancy risks when conception occurs ≥12 months post-surgery and micronutrient status is optimized. ▪ OMM must be discontinued before pregnancy, often resulting in some weight regain and return of comorbidities.
Intentional Weight Loss in Adults ≥65 Years of Age[16]	▪ Intentional weight loss is not harmful in older adults with obesity and prediabetes. ▪ Older adults are at risk for age related sarcopenia and osteopenia, which could be exacerbated by weight loss. ▪ Weight loss affects both lean and fat mass, but aerobic plus resistance exercise and adequate protein intake maximizes fat loss and preserves muscle. ▪ Exercise improves muscle quality, strength, and bone health.

IUD = intrauterine device; OMM=obesity management medications; RYGB=Roux-en-Y gastric bypass.

Pharmacotherapy

Medications should be considered as part of an obesity and prediabetes treatment plan that also includes individualized lifestyle modification, especially a DPP.[6] Consider adding medication to prevent diabetes and treat obesity for patients with prediabetes and the following:

- Weight loss medications if BMI ≥ 30 kg/m^2, or 27 kg/m^2 with at least one obesity-associated comorbid condition[7]
- Metformin if age 25-59 years with BMI ≥ 35 kg/m^2, higher fasting plasma glucose (e.g., ≥110 mg/dL), higher A1C (e.g., ≥ 6.0%), OR prior gestational diabetes mellitus[10]

Medication for Diabetes Prevention

Metformin has the strongest evidence base for long-term safety when used as pharmacologic therapy for type 2 diabetes prevention, but it does not result in significant weight loss.

Obesity Management Medications

While obesity management medications are less efficacious than bariatric surgery and supported by shorter-term evidence, they significantly increase the amount and durability of weight loss beyond what behavioral change alone can achieve when used on a long-term basis. Several obesity management medications have demonstrated ability to prevent or treat type 2 diabetes, reduce the risk of major adverse cardiovascular events (MACE), and improve blood pressure, lipid levels, obstructive sleep apnea, and metabolic dysfunction-associated steatohepatitis (MASH).[27-30]

Compared to a 4% to 7% weight loss with intensive lifestyle change only, obesity management medications typically increase weight loss by 2% to 9% for non-glucagonlike peptide-1 receptor agonists (GLP-1 RA)-based obesity management medications and up to 10% to 20% for GLP-1 RA-based medications. Adults with prediabetes and obesity treated with tirzepatide for 3 years have a 95% reduction in the progression to diabetes at all doses compared to placebo. Of note, tirzepatide and semaglutide studies also show their effectiveness for the treatment of obstructive sleep apnea and reduction in the risk for MACE, heart failure with preserved ejection fraction, metabolic dysfunction-associated steatotic liver disease (MASLD), and potentially dementia.[27-32]

GLP-1 RA side effects are summarized in Tables 3 and Table 4. Patients prescribed GLP-1 RAs tend to eat less, so it is important to provide them with information on maintaining proper nutrition and hydration while using these medications for their safety and tolerance.[31-33] If discontinued, more than half of weight lost with GLP-1 RA treatment is typically regained within one year, and weight gain continues after that time.[34-36] Lifestyle interventions that start during treatment and continue after a year, particularly those including exercise, slow regain and help retain improvements in body composition.[37]

A recent study reported that 80% of people starting a GLP-1-based treatment for weight loss discontinued it within a year, limiting impact.[38] Long-acting GLP-1-based therapies used as obesity management medications typically produce a long-term weight loss of 9% to 20%, which is substantial but generally less than that achieved with bariatric surgery. Evidence of the long-term medical impact of GLP-1 RA treatments is just emerging.[27-32] Some older non-GLP-1-based obesity management medications are cost-effective, but the GLP-1 RAs have not yet been shown to be cost-effective for obesity treatment.[39] Bariatric surgery is shown to be cost-effective or cost-saving, particularly in younger patients.[40]

Table 3. GLP-1 RA Common Side Effects[a]

Side Effect	Frequency	Onset	Characteristics
Nausea	15%-50%; experienced by up to 50%-60% of patients in some studies	Frequent in the first few weeks, decreasing over time	Most common adverse effect; dose-dependent and often mild to moderate
Vomiting	5%-20%; experienced by up to 25% of people with obesity in some trials	Occurs during the initial treatment phase	Usually transient and disappears within days
Diarrhea	5%–25%; may be more common with long-acting GLP-1 RAs	Most frequent in the first 4 weeks, declining afterward	Typically transient, resolving after a few days
Constipation	4%-12% in general trials, but up to 25%-35% in obesity trials	May occur within the first 16 weeks of treatment	Tends to last longer than other GI side effects
Abdominal Pain	4%-41% depending on the study, with a high percentage reported in some "real-world" cohorts	Occurs during early treatment	Usually mild but requires monitoring to rule out more serious cause
Injection Site Reactions	>1%; varies depending on the specific drug, but most are mild and transient	Can occur with any injectable GLP-1 RA	May include redness, rash, or itching at the injection site

GI = gastrointestinal; GLP-1 RA = glucagon-like peptide-1 receptor agonist.

[a]Typically mild to moderate and often managed by adjusting dosage or through supportive care.

Table 4. GLP-1 RA Less Common to Rare Side Effects for Serious Events[a]

Side Effect	Frequency	Other Considerations
Pancreatitis	Overall incidence is very low (less than 1%); potential link exists, although data from large clinical trials have not consistently shown an increased risk	Symptoms include severe abdominal pain, nausea, and vomiting; risk may be higher with rapid weight loss leading to gallstones
Acute Kidney Injury (AKI)	Not significantly increased on a population level; post-marketing reports have noted AKI, particularly in patients with severe gastrointestinal side effects and dehydration	Requires caution in patients with existing chronic kidney disease or severe vomiting or diarrhea
Gallbladder Problems	May occur in up to 3% of participants; risk increases with rapid weight loss	Includes cholelithiasis (gallstones) and cholecystitis (gallbladder inflammation)
Thyroid Tumors	Conflicting evidence exists regarding the risk in humans, but animal studies and some observational data show a possible link	A U.S. boxed warning exists for medullary thyroid carcinoma, which is the reason glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are not recommended for patients with a personal or family history of medullary thyroid cancer
Immunogenicity and Hypersensitivity	Varies by medication; severe anaphylactic reactions are rare, but other immune-related responses have been reported	May involve the development of antibodies to the drug, which has been linked to injection site reactions
Bowel Obstruction	A small increased risk has been observed, with some studies showing a higher risk compared with other weight-loss drugs	May cause symptoms such as severe cramping and inability to pass gas or stool

[a]Less frequent, but patients should be aware of the symptoms and seek medical attention if they occur.

Bariatric Surgery

Supported by more than 30 years of evidence, bariatric surgery remains the most effective treatment for moderate and severe obesity and is associated with a markedly reduced risk of new-onset diabetes after surgery (90% risk reduction at 15 years), as well as reduced rates of diabetes complications and premature death.[26,41] Bariatric surgery is also associated with improvements in, prevention of, or delayed onset of hypertension, heart failure, stroke, dyslipidemia, sleep apnea, asthma, at least nine obesity-related cancers, Alzheimer's-type dementia, and osteoarthritis of weight-bearing joints. These benefits translate to reduced all-cause and cardiovascular mortality risk, lower rates of disability, and improved quality of life.[41-45]

Given the broad medical benefits of bariatric surgery, clinical guidelines strongly recommend that bariatric procedures be considered and offered to patients younger than 65 years of age who meet the following criteria:

- BMI ≥ 40 regardless of comorbid medical conditions
- BMI ≥ 35 with medical comorbidities improved by weight loss, including prediabetes
- BMI ≥ 30 with uncontrolled type 2 diabetes or any obesity-related comorbidity.[46]

The expanded eligibility criteria established in the 2022 guideline from the American Society for Metabolic and Bariatric Surgery (ASMBS) and International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) are rarely reflected in insurance coverage, which often rely on the 1991 National Institutes of Health guidelines as the basis for coverage determination.[47]

The two most proven, safe, and frequently performed bariatric procedures in the United States are Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG), both of which are typically performed laparoscopically and, with increasing frequency, robotically. In addition to some anatomic restriction, the mechanisms by which bariatric surgery leads to higher levels of sustained weight loss are linked to postoperative changes in incretin levels, such as GLP-1 and ghrelin, making bariatric surgery the first multi-incretin-based treatment for obesity.[48]

Providers should help their patients understand that while bariatric surgery is the most effective treatment for obesity available today, especially severe obesity, it is not a cure. Obesity management remains a lifelong necessity following surgery.[49] As with all medical and behavioral treatments, individual responses to surgery vary considerably. Weight gain is a natural consequence of aging, and approximately half of the people who have had bariatric surgery experience some post-operative weight regain, especially in the 2 to 5 years after surgery.[50] This does not mean surgery is not effective, but underscores the need for ongoing obesity management to support the health benefits from and prevent complications.

To date, there is not unified guidance for the detection and management of non-response and/or weight regain after bariatric surgery. Providers and patients should monitor for weight loss of less than 25%, which is considered insufficient loss, and weight regain of more than 10%. Long-term follow-up with an obesity medicine specialist, the surgical team, or other trained providers is essential to managing setbacks and support best outcomes.[51] The approach to weight regain typically involves re-engagement in lifestyle management, adjunct use of obesity management medications, particularly GLP-1 RAs, and, in some cases, revision procedures.[52] Lifelong micronutrient monitoring and supplementation is also necessary after bariatric surgery.[49]

Challenges to Treatment

With the growing availability of effective obesity management medications, the well-established cardiometabolic benefits of bariatric surgery, and the broad reach of the DPP, primary care clinicians need practical, evidence-based resources to guide treatment decisions. This includes tools to support initiation or referral to appropriate therapies, as well as guidance for managing or co-managing patients after bariatric surgery to sustain long-term benefits and prevent complications.

Despite strong evidence, effective treatments for obesity and prediabetes remain underutilized.[53,54] Contributing factors include limited recognition among clinicians and patients that these are chronic conditions requiring active management, as well as gaps in awareness of evidence-based options such as obesity management medications, bariatric surgery, and intensive lifestyle interventions like the DPP. Treatment is further limited by variable insurance coverage and benefit exclusions for these services.

In addition, many primary care clinicians may have limited experience initiating and monitoring obesity pharmacotherapy or delivering high-intensity lifestyle interventions.[55] When appropriate, consider referral to an obesity medicine specialist (See Additional Resources) and/or to a structured lifestyle program, such as the DPP, or an evidence-based commercial program when accessible and affordable.

Management of Other Health Conditions

Assessment and management of medically-related conditions, such as hypertension, hyperlipidemia, and sleep apnea, reduce a person's overall cardiovascular risk and, in the case of sleep apnea, may reduce progression to diabetes.[56] In addition, the dietary, activity, and weight management recommendations for prediabetes are consistent with managing related conditions, as well.[2,4,7,10] Screening, assessing, and optimizing treatment of mood disorders is often essential for patients to engage in lifestyle changes. It is important to identify medications that may promote weight gain and, if possible, replace them with more weight-friendly options. Common examples include corticosteroids or antipsychotics and medications for depression with anticholinergic effects associated with weight gain.[2-5]

Additional Resources

- **American Association of Clinical Endocrinology**
  - **Algorithm Figure 2 - Adiposity-Based Chronic Disease (ABCD)**
    endocrinepractice.org/article/S1530-891X(23)00034-4/fulltext#fig2
  - **Algorithm Figure 3 - Prediabetes**
    endocrinepractice.org/article/S1530-891X(23)00034-4/fulltext#fig3
- **American Board of Obesity Medicine**
  abom.org
- **Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program (MBSAQIP)**
  facs.org/quality-programs/mbsaqip
- **National Diabetes Prevention Program (National DPP) Locator Map**
  data.ohio.gov/wps/portal/gov/data/view/national-diabetes-prevention-program-_national-dpp_-locator-map

Additional Cardi-OH Resources

- **Capsule 63 - Strength Training for Older Adults**
  cardi-oh.org/resources/capsule-63--strength-training-for-older-adults
- **Capsule 65 - Maintaining Muscle Mass While Taking GLP-1s**
  cardi-oh.org/resources/capsule-65--maintaining-muscle-mass-while-taking-glp-1s
- **Effective Diabetes Prevention for Adults: Prediabetes Screening and Treatment**
  cardi-oh.org/resources/effective-diabetes-prevention-for-adults-prediabetes-screening-and-treatment
- **Helping Patients Achieve an Active Lifestyle**
  cardi-oh.org/resources/helping-patients-achieve-an-active-lifestyle
- **Podcast 43 - Obesity and Weight Loss Management: Pharmacotherapy, Part 1**
  cardi-oh.org/resources/podcast-43--obesity-and-weight-loss-management-pharmacotherapy-part-1
- **Podcast 44 - Obesity and Weight Loss Management: Surgical Interventions, Part 2**
  cardi-oh.org/resources/podcast-44--obesity-and-weight-loss-management-surgical-interventions-part-2
- **Talking With Your Patients About Diabetes Pharmacotherapy: Side Effects and Adverse Events**
  cardi-oh.org/resources/talking-with-your-patients-about-diabetes-pharmacotherapy-side-effects-and-adverse-events
- **SMART Goals for Healthy Weight**
  cardi-oh.org/resources/smart-goals-for-healthy-weight

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