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Clinician Update

Weight Management

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Content reviewed by:

AACE®

BEYOND BMI: Using more accurate tools to diagnose obesity

Experts now say BMI tells only part of the story. Here, insights on other metrics that physicians employ to determine a patient's true weight picture.

For years, body mass index (BMI) has been used to diagnose obesity by identifying increased levels of adiposity. But there is now growing recognition that reliance on BMI alone is inadequate in determining if a patient's weight is unhealthy and whether they have other health risks, such as cardiovascular disease (CVD) and diabetes.[1] "BMI is a good approximation, but it doesn't give information about the complete health of a patient," says Wajahat Mehal, MD, director of the Yale Metabolic Health & Weight Loss Program. "It comes down to the fact that all BMI measures is height and weight. It's as useful as a blood pressure reading, but it's only one data point to get a picture of a patient's health."

In addition, using BMI alone as a diagnostic tool for obesity doesn't measure how much of a patient's weight is fat versus muscle and also doesn't identify abdominal fat, which is associated with increased risk of CVD, metabolic disease and insulin resistance.[2] "Someone can have a high weight because they have a lot of central adiposity–a huge abdomen–or they are very muscular," says Dr. Mehal. "When Arnold Schwarzenegger was a bodybuilder, he had a BMI of 31 or 32, which would be diagnosed as obesity."

For those and other reasons outlined below, an increasing number of healthcare providers are using BMI with additional metrics when diagnosing obesity. Dr. Mehal says one can get a more comprehensive picture of a patient's health when BMI is used along with measurements of waist circumference, blood pressure, cholesterol and blood sugar levels.

Experts also say that clinicians need to use a more ethnically appropriate approach when diagnosing obesity. The BMI formula was created almost 200 years ago by a Belgian mathematician, primarily using data from white European men–no women included–to establish quantifiable characteristics of the "normal man." As the American Medical Association (AMA) noted in its 2023 guidelines, BMI doesn't account for racial, ethnic, sex, gender and age differences in body fat.[3] Similarly, the American Association of Clinical Endocrinology (AACE) guidelines state that classification categories of obesity should include improved nomenclature across the spectrum of BMI using ethnically-specific ranges for BMI and waist circumference.[4]

Given this inherent ethnic and gender bias, clinicians need to consider more than just BMI when diagnosing obesity. For example, the World Health Organization (WHO) guidelines classify BMI ≥25 kg/m² as obesity in Asia-Pacific populations.[5] "Asian people tend to have higher body fat percentages at lower BMI values than White people,"[6] says Stephanie Page, DO, a diabetologist and obesity medicine specialist with Carteret Health Care Medical Group in Morehead City, NC. Using BMI alone also can prevent patients from obtaining insurance approvals for lifesaving anti-obesity medications. Even if they have a relatively low level of BMI, Asian persons are at higher risk of type 2 diabetes, hypertension and hyperlipidemia.

Moving focus away from pounds alone

The AMA advocates using BMI with other measurements for visceral fat (belly fat found deep within the abdominal cavity), such as the body adiposity index

Illustration by Marta Lebek / Stocksy / Adobe Stock Images

(BAI; calculated from height and hip measurements), body composition (the percentage of fat, bone and muscles), relative fat mass, waist circumference and genetic/metabolic factors. BMI, the AMA states, "is significantly correlated with the amount of fat mass in the general population but loses predictability when applied on the individual level."

Simple measures that go beyond BMI

Here, experts offer insights into the techniques they use to complement the basic information provided by BMI.

"BMI is a good approximation, but it doesn't give information about the complete health of a patient."
—Wajahat Mehal, MD

Waist circumference

"One of the things that's easy to do is to measure waist circumference," says Dr. Mehal. Carrying more belly fat signifies that patients have more visceral fat. "Patients with more visceral fat have a greater chance of developing heart disease, type 2 diabetes, high blood pressure and fatty liver," Dr. Page says.[7] This risk increases with a waist size greater than 35 inches for women and 40 inches for men.[8] For Asian persons, these numbers are lower. "Due to higher risk factors in men and women of Asian descent, the ideal waist circumference is less than 31 inches for women and less than 35 inches for men," says Dr. Page.[9]

When working with patients to achieve weight loss, Dr. Page says she always considers waist circumference and where they're losing their body fat. "I discuss with patients that we need to look at their fat distribution," she says. "And if their waist circumferences are above what the normal should be, we focus on that." She adds, "Sometimes people come in and they've only lost a pound, but they've lost an inch on their midsection—that's a huge deal. That means they're losing fat in the right place. It only takes an extra minute or two to do that extra vital sign."

Body roundness index (BRI)

BRI is a calculation that uses height and waist circumference (rather than the BMI's height and weight), which can provide a better estimate of abdominal fat.[10] "Essentially, it's assessing the level of visceral adipose tissue," Dr. Mehal says, noting that a higher BRI value indicates a more spherical body shape associated with higher visceral fat and increased metabolic risk. "When you're measuring the waist, you're basically getting the body roundness index. The body roundness index does a calculation, just like the BMI does a calculation of height and weight." A BRI calculator can be found at *mdcalc.com/calc/10575/body-roundness-index-bri*.

Waist-hip ratio

The waist-hip ratio is the circumference of the waist divided by the circumference of the hips (measured at the widest part of the hips). Experts say this may be a better barometer for obesity-related health risks than BMI or waist circumference alone.[11] "Doing a waist and hip circumference is a super easy way to assess a person's health—and I do it with all my patients," Dr Page says. "I use this as an additional vital and I encourage providers to add waist and hip circumference as a normal vital sign." Guidelines suggest that less than 0.95 in men and less than 0.80 in women means a patient is at a lower risk of developing health issues such as heart disease, notes Dr. Page.[12] A waist-hip ratio calculator can be found at *omnicalculator.com/health/waist-hip-ratio*.

Refining the picture by measuring body composition

While measuring waist circumference and body mass provides a basic indication of fat distribution, measuring body composition provides additional insight by breaking down the components of a patient's body weight—specifically distinguishing between muscle, bone and fat mass—giving a more detailed picture of body makeup. The following are some tools clinicians can use to measure body composition along with expert opinions on the pros and cons of each:

DEXA scan

Whole-body densitometry using dual-energy X-ray absorptiometry (DEXA), often referred to as a bone-density scan, is a noninvasive method for a highly accurate assessment of bone mineral content, lean body and fat mass.[13]

Pros: "It's the best way to assess body composition," says Dr. Page. "If the patient is over 65, most insurance plans will pay for it because it's used for osteoporosis screening. And most machines can now do a body composition analysis with the bone density portion of the imaging study." Providers can refer patients out to a radiology center or an OB-GYN clinic that offers DEXA scans, she adds.

Cons: The scans can be costly. "It's not a simple test, and you can't do it for the millions of people who need it measured," Dr. Page says she has a DEXA machine in her practice and charges a $50 fee for a scan. "Not everyone can pay for the DEXA machine scan," she says. If cost is an issue, she suggests using waist-hip circumference measurements instead.

Bioimpedance scale

The bioimpedance scale passes a very low-voltage electrical circuit through a patient's body. Because muscle and fat conduct electricity at different rates, the scale reveals the difference between a patient's muscle and fat content and provides information on a patient's total body weight and the percentages of lean muscle body fat and visceral fat.

Pros: "This is a fast and easy way to assess body composition—measuring muscle mass, body fat and visceral fat," says Dr. Page. "When I talk to patients, especially if they're at a borderline weight, I say, 'Let's see where your body composition is at, especially if you want to work toward weight loss, because we also want to see where your muscle mass is."

Cons: "The problem is cost, because scales can be a few thousand dollars," says Dr. Page, whose current practice does not have a bioimpedance scale and refers patients out, if needed. They can also be inaccurate. "The trouble is that they give numbers that seem precise, but they're not," says Dr. Mehal. "One day it will say that body fat is 24 percent. And two weeks later it might say body fat is 20 percent. You might think there's a genuine 4 percent change, but you could stand on it three times on the same day, and it'll give you slightly different numbers." If using this scale, Dr. Page says clinicians should advise patients to avoid strenuous exercise within 12 hours prior to the measurement, avoid eating or drinking anything substantial for at least 2-3 hours before the test, wear light clothing, remove all metal objects such as jewelry and watches and use the bathroom before stepping on the scale. All these factors can affect analysis.

Dr. Page says clinicians should also advise patients not to focus so much on the numbers on the scale. "Patients tend to be hyper-focused on just the pounds lost," she continues. "Of coure, everybody wants to see the scale move, but we really need to educate our patients on the benefits of losing weight. We should let them know why we look at metabolic markers and blood lipid panels as well as the inches lost." ●

—by Diane Herbst

Tips for measuring waist circumference

Properly measuring waist circumferences involves placing a tape measure around a patient's middle, just above the hipbones. Ensure that the tape is snug (but does not compress the skin) and is parallel to the floor, and take the measurement just after the patient breathes out.[10]

"Teach your team to educate the patient as to why they are doing it," says Stephanie Page, DO, a diabetologist and obesity medicine specialist with Carteret Health Care Medical Group in North Carolina. "They can say, 'We're doing this because the doctor's going to talk to you about assessing where you're carrying your weight, which can mean that you're at risk for diabetes and high blood pressure and fatty liver disease.' "

Your medical assistant will have had the discussion, which took five minutes away from your visit, notes Wajahat Mehal, MD, director of the Yale Metabolic Health & Weight Loss Program. "There are online videos on how to properly measure waist circumference." (See *youtube.com/@TheFranceFoundation* for more information.)

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Tailoring obesity treatment to the patient

The underlying factors that contribute to weight gain vary from patient to patient. Identifying and addressing them can make all the difference.

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Research has confirmed that obesity is a chronic, progressive, relapsing disease that may not adequately respond to combined lifestyle interventions alone. Many patient characteristics—biological, behavioral and environmental—converge with unhealthy eating patterns and lack of physical activity to compound weight gain. These vary from patient to patient, so weight-loss treatment also needs to be individualized to effectively address underlying factors that are contributing to weight gain (see Figure 1 on p. 10).[1-3]

In practice, however, many healthcare professionals find it challenging to address weight loss with patients, particularly within the framework of a 15-minute office visit. "Physicians want to treat overweight and obesity, but they may not have the comfort level, knowledge, resources or time," says Ken Fujioka, MD, an endocrinologist and weight-loss expert with the Scripps Clinic in San Diego. "Clearly, physicians need to learn how to treat these patients in a limited time slot."

The case for personalized weight loss

The American Association of Clinical Endocrinology (AACE) recognizes the complexity of obesity management and has published guidelines to help clinicians diagnose and treat overweight/obesity based on the stage of disease, complications and other patient factors. The pathophysiology of obesity is so heterogenous that some researchers suggest tailoring strategies for weight loss based on the subgroups patients may belong to, stratified by age, sex, and physical and mental health status (e.g., patients with depression or patients with heavy alcohol use).[4] Obesity medicine specialist Lee Kaplan, MD, at Massachusetts General Hospital estimates there are likely dozens of obesity types based on genetic and environmental variations (e.g., weight gain triggered by sleep deprivation, lack of exercise, increased hunger). Therefore, multiple treatment modalities are needed to help patients reach their goals.[5]

Jennifer McCauley, MD, has experienced this firsthand. "Each patient has a story that is particular to his or her struggles with obesity," says Dr. McCauley, an internist with UNC Health, Chapel Hill, who specializes in overweight/obesity treatment. "During a weight management session, I can see four new patients, and each one may have a different etiology and treatment strategy."

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Yet while the aggravating factors behind obesity are specific to each patient, they all share one characteristic: metabolic adaptation. "As patients lose weight, the body adjusts hormones to decrease its metabolic rate," Dr. Fujioka says. "Not only is metabolism lowered when patients try to lose weight, but the hormones that drive hunger also increase in response to weight loss. So, when those patients eat, they're not as satisfied as before and they start eating bigger portions. This is a permanent biologic change that drives the patient's weight back to its previous highest level." Fortunately, newer weight-loss agents have different mechanisms of action to help control hunger, which helps patients adhere to their plan. "The patient, however, still must control food intake and increase calorie expenditure by exercise, and this part of treatment is unique to each patient," Dr. Fujioka adds.

Setting treatment goals

After you've diagnosed a patient with overweight or obesity, initiating a weight-loss plan based on the following components can help ensure that goals are achieved:

Educate

It's important to get permission from patients first, such as, "Would it be okay if we discuss your weight?" If they're agreeable, start by providing education. Many individuals may not be aware of the interplay of hormones and metabolic dysfunction causing weight gain—and they've heard repeatedly that eating less and exercising more will solve the problem. "Time needs to be spent educating patients about the complexity of obesity," Dr. McCauley says.

Evaluate

Assess the patient's motivation for losing weight, their weight-loss goals and the individual barriers they face to achieving them. Patients' lifestyles and their ability to adhere to a particular plan should be covered in the initial interview. "It's important to understand the patient's barriers to meal planning and buying healthy foods," Dr. McCauley says. "I will ask patients about their current dietary habits and how we might make specific changes to improve dietary quality. Knowing a patient's baseline habits allows us to suggest reasonable, clear, actionable steps." In addition, asking certain questions can also uncover individual risk factors that may be driving weight gain, such as:

- "What time do you go to bed and wake up?"
- "What type of physical activity do you do and how often?"
- "Do you have any particular food cravings?"

"I first try to see what is missing in the patient's attempt to lose weight—for example, is the patient sleeping properly or getting enough exercise—and start with that," says Dr. Fujioka. "I look at the entire treatment plan on the first visit and on subsequent visits will address the challenging components."

Some patients, however, may be hesitant to disclose specific reasons for their weight gain, often out of embarrassment, guilt or shame. For that reason, it's best to start the lifestyle conversation by reassuring patients that your office is a judgment-free zone. "If patients can't disclose details behind their weight gain, sometimes I will explain common eating patterns that may contribute," Dr. McCauley says. "Binge eating, for example, is often accompanied by feelings of shame. When you explain that you've encountered many patients who binge eat, patients then realize they are not the first to do this. This will also give them a clearer understanding of what is happening while they binge eat. Naming and defining the issue and removing the shame can be critical in changing behavior." (Referral to a psychologist is recommended to address eating-disordered behavior.)

Review

The AACE guidelines note the importance of assessing patients for weight-related complications (see Table 1). Also, research shows depression and anxiety often occur in patients with obesity, and interventions to improve weight loss may benefit from treating the underlying psychiatric disorder.[6] Some agents used to treat obesity can affect mood and interact with psychiatric medications. On the other hand, many anxiolytics, antidepressants and antipsychotics can cause significant weight gain but may be necessary for treatment of the underlying mood disorder. Therefore, make sure the patient's depression or anxiety is being adequately treated, as mood disorders can dampen their motivation to lose weight, advises Dr. McCauley. Consult with the patient's psychiatrist to limit obesogenic medications when possible, and counsel patients to never discontinue or change any medication until they speak with their prescribing physician.

Continued on next page ►

Table 1.

Assessment of weight-related complications*[1]

Complication	Identification based on information available in initial evaluation
Metabolic syndrome	Waist circumference, blood pressure, triglycerides, HDL cholesterol, fasting glucose (presence of 3 or more)
Prediabetes	Fasting glucose, A1C
Type 2 diabetes	Fasting glucose, A1C
Dyslipidemia	Fasting triglycerides and HDL with lipid panel
Hypertension	Systolic and diastolic sitting blood pressures
Metabolic dysfunction-associated steatotic liver disease (MASLD)	Liver function tests, imaging studies
Polycystic ovary syndrome	Physical exam, review of systems
Obstructive sleep apnea	Physical exam, review of systems
Osteoarthritis	Physical exam, review of systems
Urinary stress incontinence	Physical exam, review of systems
Gastroesophageal reflux disease	Physical exam, review of systems
Disability/ immobility	Physical exam, review of systems
Psychological disorder and/or stigmatization	Physical exam, review of systems
Obesity secondary to genetic syndromes, hormonal disease, iatrogenic medications	Physical exam, review of systems, review of medications and supplements, family history

*Initial evaluation includes: history, physical exam, review of systems, blood pressure, waist circumference, fasting glucose, fasting lipid panel, creatinine and hepatic transaminases, and lab tests and imaging studies when applicable. See AACE guidelines for full recommendations (*pro.aace.com*).

Though not approved for depression, the antidepressant component in naltrexone/bupropion may help some patients with obesity and comorbid depression, adds Dr. Fujioka.

Another common stumbling block is chronic pain: It hurts to move, so patients gain weight from lack of physical activity and, in turn, the excess weight compounds their pain. However, evidence suggests that exercise can reduce most forms of chronic pain, particularly back pain and osteoarthritis-related pain.[7,8] Educating patients about the importance of physical activity is crucial, and a detailed discussion about their specific barriers to movement can help you collaborate on a plan to increase physical activity, says Dr. McCauley. In some cases, referral to a physical therapist may be necessary to help patients find a safe form of exercise.

Collaborating on a regimen

Once you've determined a patient's weight-related complications and barriers to weight loss, you can work together to create a mutually agreed upon treatment plan. Good places to start:

- **Help them find the right meal plan.** While diets low in saturated fat and simple carbohydrates and moderate in protein generally aid weight loss, no single diet is best for all patients.[1,2] "People often have specific ideas about what diets have worked in the past and what may work in the future," Dr. McCauley says. "The diet the patient sticks to is the one that works." It often hinges on the patient's lifestyle, notes Dr. Fujioka. For example, if the patient lacks time to prepare meals, consider including protein shakes in the plan. For patients who enjoy cooking, planning meals with a focus on portion control may be easier. However, all patients with obesity should receive individualized nutrition therapy provided by a registered dietitian when possible.
- **Set reasonable goals for physical activity.** Involve patients in planning an exercise program that reflects their preferences and physical abilities, advises Dr. Fujioka. For sedentary patients, this can be as simple as walking laps around their house, with gradual progression to walking around the neighborhood. For a working mother with little spare time, encourage short exercise sessions during lunch hour or while the kids are playing sports. Eventually, patients may require both cardiovascular and resistance training to achieve and maintain their goal weight.
- **Add weight-loss medication to lifestyle changes as necessary.** "Some patients are motivated to work on lifestyle measures alone," Dr. McCauley says. "I will follow these patients closely and if they experience a plateau or weight gain, we can discuss medication." For some patients, medication can be started in conjunction with nutrition and lifestyle interventions—e.g., those who struggle with increased appetite can benefit from weight-loss medication early on.

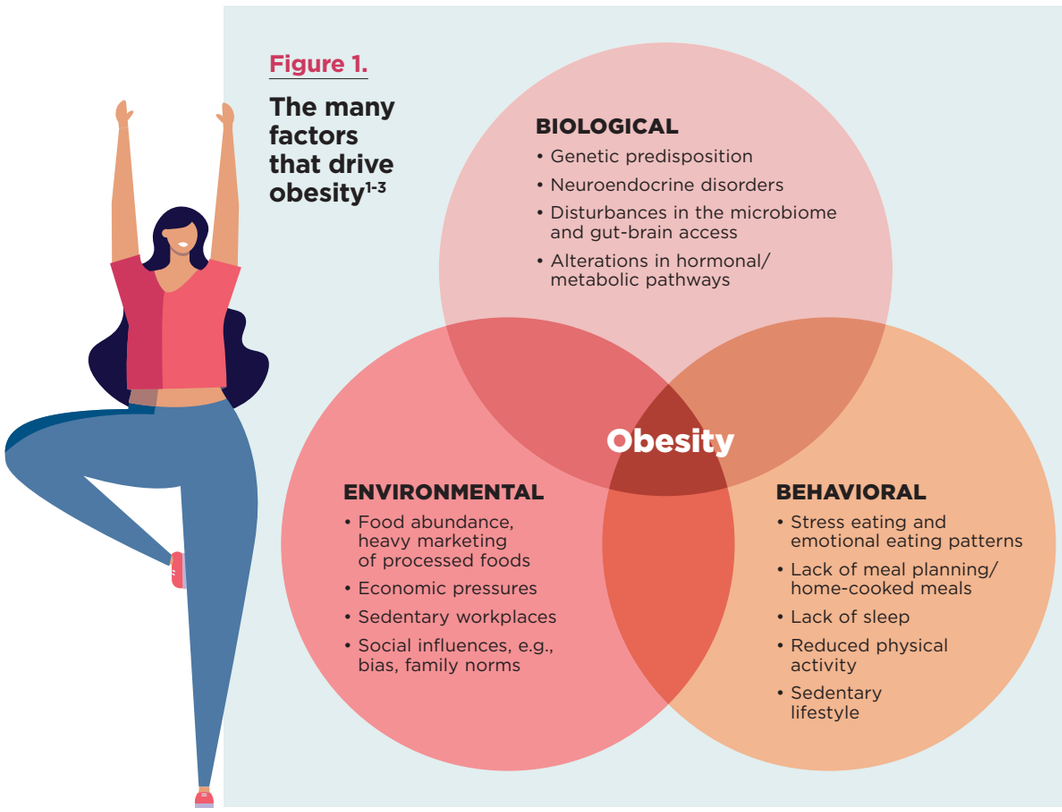
  In addition, Dr. Fujioka notes the importance of reviewing the labeling, since a patient's medical conditions or potential drug interactions may rule out certain options.[9,10] Also, avoid using phentermine/topiramate in women of childbearing age, as the combination agent increases the risk of birth defects and the FDA requires a Risk Evaluation and Mitigation Strategy (obtaining a negative pregnancy test before treatment and monthly testing thereafter) before prescribing it. Note: There are no weight-loss agents approved for treating chronic obesity during pregnancy and breastfeeding.

  Optimal response to pharmacotherapy varies by agent, says Dr. Fujioka. Generally, the goal is to lose 3% to 5% of body weight after 3 to 4 months of treatment. "If patients have the designated amount of weight loss at the prescribed time, they stay on the medication and will often have excellent weight loss over the next year," Dr. Fujioka says. "If they don't, we make sure they have been taking the medication regularly, and if that's the case, we stop the agent and try something else."
- **Set a follow-up schedule.** Until the goal is reached, it's advised that follow-ups occur at least monthly. However, some patients may benefit from weekly or biweekly visits to keep them on track. Once patients have achieved their goals, following up every 3 months is reasonable, but this also is variable. "I'll suggest they follow up in 3 months, only to hear they want to come back in a month," Dr. McCauley says. "Many patients desire accountability, and having a specific weight-management visit duration that suits their needs allows this to happen."

—by Pete Kelly

Figure 1.

The many factors that drive obesity[1-3]



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STEP 5 Study Design: A 104-week trial of 304 adults with obesity (BMI ≥30 kg/m²) or with overweight (BMI 27 kg/m²-29.9 kg/m²) and at least one weight-related comorbid condition, such as treated or untreated dyslipidemia or hypertension, cardiovascular disease, or obstructive sleep apnea; patients with diabetes mellitus were excluded. Patients were randomized in a 1:1 ratio to either once-weekly Wegovy® 2.4 mg or placebo (with a 16-week dose escalation), both in conjunction with a reduced-calorie diet and increased physical activity. Discontinuation rate: 13% Wegovy®; 27% placebo.[2]

†*p*<0.0001 (unadjusted 2-sided) for superiority.
‡Supportive secondary end points were not included in the statistical testing hierarchy and, as such, not controlled for multiplicity.
§Observed data include only patients who had a body weight assessment at week 104 (144 of 152 for Wegovy® arm and 128 of 152 for placebo arm) and do not include all randomized patients.

SELECT Study Design: Multi-national, double-blind, placebo-controlled, event-driven superiority CVOT (N=17,604) for adults with BMI ≥27 kg/m² and established CVD (prior MI, prior stroke, or PAD), without diabetes, randomized 1:1 to receive once-weekly Wegovy® 2.4 mg or placebo. Both groups received SOC for CV risk reduction (medical management and individualized healthy lifestyle counseling, including diet and physical activity). Median duration of follow-up: 41.8 months. Discontinuation rate: 31% Wegovy®; 27% placebo. Adverse event discontinuation: 16% Wegovy®; 8% placebo.[1,3]

Primary composite end point: time from randomization to first occurrence of a 3-part composite MACE, defined as CV death, non-fatal MI, or non-fatal stroke.[3]

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- **Risk of Thyroid C-Cell Tumors:** Patients should be further evaluated if serum calcitonin is measured and found to be elevated or thyroid nodules are noted on physical examination or neck imaging
- **Acute Pancreatitis:** Acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis, has been observed in patients treated with GLP-1 receptor agonists, including Wegovy®. Observe patients carefully for signs and symptoms of acute pancreatitis (including persistent severe abdominal pain, sometimes radiating to the back, and which may or may not be accompanied by vomiting). If acute pancreatitis is suspected, discontinue Wegovy® and initiate appropriate management
- **Acute Gallbladder Disease:** Treatment with Wegovy® is associated with an increased occurrence of cholelithiasis and cholecystitis. The incidence of cholelithiasis and cholecystitis was higher in Wegovy® pediatric patients aged 12 years and older than in Wegovy® adults. In clinical trials in adult patients, cholelithiasis was reported by 1.6% of Wegovy® patients and 0.7% of placebo patients. Cholecystitis was reported by 0.6% of Wegovy® patients and 0.2% of placebo patients. In a clinical trial in pediatric patients aged 12 years and older, cholelithiasis was reported by 3.8% of Wegovy® patients and 0% placebo patients. Cholecystitis was reported by 0.8% of Wegovy® pediatric patients and 0% placebo patients. Substantial or rapid weight loss can increase the risk of cholelithiasis; however, the incidence of acute gallbladder disease was greater in Wegovy® patients than in placebo patients, even after accounting for the degree of weight loss. If cholelithiasis is suspected, gallbladder studies and appropriate clinical follow-up are indicated
- **Hypoglycemia:** Wegovy® lowers blood glucose and can cause hypoglycemia. In a trial of adult patients with type 2 diabetes, hypoglycemia was reported in 6.2% of Wegovy® patients versus 2.5% of placebo patients. Patients with diabetes taking Wegovy® with an insulin or insulin secretagogue (e.g. sulfonylurea) may have an increased risk of hypoglycemia, including severe hypoglycemia. The use of Wegovy® in patients with type 1 diabetes or in combination with insulin has not been evaluated. Inform patients of the risk of hypoglycemia and educate them on the signs and symptoms. Monitor blood glucose in patients with diabetes
- **Acute Kidney Injury:** There have been postmarketing reports of acute kidney injury and worsening of chronic renal failure, which in some cases required hemodialysis, in patients treated with semaglutide. Patients with renal impairment may be at a greater risk of acute kidney injury, but some events have been reported in patients without known underlying renal disease. A majority of the events occurred in patients who experienced nausea, vomiting, or diarrhea, leading to volume depletion. Monitor renal function when initiating or escalating doses of Wegovy® in patients reporting severe adverse gastrointestinal reactions and in patients with renal impairment reporting any adverse reactions that could lead to volume depletion
- **Severe Gastrointestinal Adverse Reactions:** Use of Wegovy® has been associated with gastrointestinal adverse reactions, sometimes severe. In clinical trials, severe gastrointestinal adverse reactions were reported more frequently among patients receiving Wegovy® (4.1%) than placebo (0.9%). Wegovy® is not recommended in patients with severe gastroparesis
- **Hypersensitivity Reactions:** Serious hypersensitivity reactions (e.g., anaphylaxis, angioedema) have been reported with Wegovy®. If hypersensitivity reactions occur, discontinue use of Wegovy®, treat promptly per standard of care, and monitor until signs and symptoms resolve. Use caution in a patient with a history of anaphylaxis or angioedema with another GLP-1 receptor agonist
- **Diabetic Retinopathy Complications in Patients with Type 2 Diabetes:** In a trial of adult patients with type 2 diabetes, diabetic retinopathy was reported by 4.0% of Wegovy® patients and 2.7% of placebo patients. Rapid improvement in glucose control has been associated with a temporary worsening of diabetic retinopathy. Patients with a history of diabetic retinopathy should be monitored for progression of diabetic retinopathy
- **Heart Rate Increase:** Mean increases in resting heart rate of 1 to 4 beats per minute (bpm) were observed in Wegovy® adult patients compared to placebo in clinical trials. More Wegovy® adult patients compared with placebo had maximum changes from baseline of 10 to 19 bpm (41% versus 34%) and 20 bpm or more (26% versus 16%). In a clinical trial in pediatric patients aged 12 years and older with normal baseline heart rate, more patients treated with Wegovy® compared to placebo had maximum changes in heart rate of 20 bpm or more (54% versus 39%). Monitor heart rate at regular intervals and instruct patients to report palpitations or feelings of a racing heartbeat while at rest. If patients experience a sustained increase in resting heart rate, discontinue Wegovy®
- **Suicidal Behavior and Ideation:** Suicidal behavior and ideation have been reported in clinical trials with other weight management products. Monitor patients for depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior. Discontinue Wegovy® in patients who experience suicidal thoughts or behaviors and avoid in patients with a history of suicidal attempts or active suicidal ideation
- **Pulmonary Aspiration During General Anesthesia or Deep Sedation:** Wegovy® delays gastric emptying. There have been rare postmarketing reports of pulmonary aspiration in patients receiving GLP-1 receptor agonists undergoing elective surgeries or procedures requiring general anesthesia or deep sedation who had residual gastric contents despite reported adherence to preoperative fasting recommendations. Instruct patients to inform healthcare providers prior to any planned surgeries or procedures if they are taking Wegovy®

Adverse Reactions

- Most common adverse reactions (incidence ≥5%) are: nausea, diarrhea, vomiting, constipation, abdominal pain, headache, fatigue, dyspepsia, dizziness, abdominal distention, eructation, hypoglycemia in patients with type 2 diabetes, flatulence, gastroenteritis, gastroesophageal reflux disease, and nasopharyngitis

Drug Interactions

- The addition of Wegovy® in patients treated with insulin has not been evaluated. When initiating Wegovy®, consider reducing the dose of concomitantly administered insulin secretagogues (such as sulfonylureas) or insulin to reduce the risk of hypoglycemia
- Wegovy® causes a delay of gastric emptying and has the potential to impact the absorption of concomitantly administered oral medications. Monitor the effects of oral medications concomitantly administered with Wegovy®

Use in Specific Populations

- **Pregnancy:** May cause fetal harm. When pregnancy is recognized, discontinue Wegovy®. Discontinue Wegovy® in patients at least 2 months before a planned pregnancy
- **Pediatric:** Adverse reactions with Wegovy® in pediatric patients aged 12 years and older were similar to those reported in adults. Pediatric patients ≥12 years of age treated with Wegovy® had greater incidences of cholelithiasis, cholecystitis, hypotension, rash, and urticaria compared to adults treated with Wegovy®. There are insufficient data in pediatric patients with type 2 diabetes treated with Wegovy® for obesity to determine if there is an increased risk of hypoglycemia with Wegovy® treatment similar to that reported in adults
- **Geriatric:** In the cardiovascular outcomes trial, patients aged 75 years and older reported more hip and pelvis fractures on Wegovy® than placebo. Patients aged 75 years and older (Wegovy® and placebo) reported more serious adverse reactions overall compared to younger adult patients

Please see the Brief Summary of Prescribing Information about Wegovy® on the following pages.

ARR, absolute risk reduction; BMI, body mass index; CI, confidence interval; CV, cardiovascular; CVD, cardiovascular disease; CVOT, cardiovascular outcomes trial; HR, hazard ratio; MACE, major adverse cardiovascular events; MI, myocardial infarction; PAD, peripheral arterial disease; RRR, relative risk reduction; SOC, standard of care.

References: 1. Wegovy® [package insert]. Plainsboro, NJ: Novo Nordisk Inc. **2.** Garvey WT, Batterham RL, Bhatta M, et al. Two-year effects of semaglutide in adults with overweight or obesity: the STEP 5 trial. *Nat Med*. 2022;28(10):2083-2091. **3.** Lincoff AM, Brown-Frandsen K, Colhoun HM, et al. Semaglutide and cardiovascular outcomes in obesity without diabetes. *N Engl J Med*. 2023;389(24):2221-2232. **4.** Data on file. Novo Nordisk Inc.; Plainsboro, NJ.

US24SEMO01686 December 2024

novo nordisk®

WEGOVY® (semaglutide) injection

Rx Only

BRIEF SUMMARY: Please consult package insert for full prescribing information.

WARNING: RISK OF THYROID C-CELL TUMORS: In rodents, semaglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures. It is unknown whether WEGOVY® causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans as human relevance of semaglutide-induced rodent thyroid C-cell tumors has not been determined *[see Warnings and Precautions]*. WEGOVY® is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2) *[see Contraindications]*. Counsel patients regarding the potential risk for MTC with the use of WEGOVY® and inform them of symptoms of thyroid tumors (e.g. a mass in the neck, dysphagia, dyspnea, persistent hoarseness). Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with WEGOVY® *[see Contraindications and Warnings and Precautions]*.

INDICATIONS AND USAGE: WEGOVY® is indicated in combination with a reduced calorie diet and increased physical activity: to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with established cardiovascular disease and either obesity or overweight; to reduce excess body weight and maintain weight reduction long term in: Adults and pediatric patients aged 12 years and older with obesity; Adults with overweight in the presence of at least one weight-related comorbid condition. Limitations of Use: WEGOVY® contains semaglutide. Coadministration with other semaglutide-containing products or with any other GLP-1 receptor agonist is not recommended. **Important Monitoring and Administration Instructions:** In patients with type 2 diabetes mellitus, monitor blood glucose prior to starting WEGOVY® and during WEGOVY® treatment *[see Warnings and Precautions]*; Prior to initiation of WEGOVY®, train patients on proper injection technique. Refer to the accompanying Instructions for Use for complete administration instructions with illustrations; Inspect WEGOVY® visually prior to each injection. Only use if solution is clear, colorless, and contains no particles; Administer WEGOVY® in combination with a reduced-calorie diet and increased physical activity; Administer WEGOVY® once weekly, on the same day each week, at any time of day, with or without meals; Inject WEGOVY® subcutaneously in the abdomen, thigh, or upper arm. The time of day and the injection site can be changed without dose adjustment.

CONTRAINDICATIONS: WEGOVY® is contraindicated in the following conditions: A personal or family history of MTC or in patients with MEN 2 *[see Warnings and Precautions]*; A prior serious hypersensitivity reaction to semaglutide or to any of the excipients in WEGOVY®. Serious hypersensitivity reactions, including anaphylaxis and angioedema, have been reported with WEGOVY® *[see Warnings and Precautions]*.

WARNINGS AND PRECAUTIONS: Risk of Thyroid C-Cell Tumors: In mice and rats, semaglutide caused a dose-dependent and treatment-duration-dependent increase in the incidence of thyroid C-cell tumors (adenomas and carcinomas) after lifetime exposure at clinically relevant plasma exposures. It is unknown whether WEGOVY® causes thyroid C-cell tumors, including MTC, in humans, as human relevance of semaglutide-induced rodent thyroid C-cell tumors has not been determined. Cases of MTC in patients treated with liraglutide, another GLP-1 receptor agonist, have been reported in the postmarketing period; the data in these reports are insufficient to establish or exclude a causal relationship between MTC and GLP-1 receptor agonist use in humans. WEGOVY® is contraindicated in patients with a personal or family history of MTC or in patients with MEN 2. Counsel patients regarding the potential risk for MTC with the use of WEGOVY® and inform them of symptoms of thyroid tumors (e.g., a mass in the neck, dysphagia, dyspnea, persistent hoarseness). Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with WEGOVY®. Such monitoring may increase the risk of unnecessary procedures, due to the low-test specificity for serum calcitonin and a high background incidence of thyroid disease. Significantly elevated serum calcitonin value may indicate MTC and patients with MTC usually have calcitonin values greater than 50 ng/L. If serum calcitonin is measured and found to be elevated, the patient should be further evaluated. Patients with thyroid nodules noted on physical examination or neck imaging should also be further evaluated. **Acute Pancreatitis:** Acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis, has been observed in patients treated with GLP-1 receptor agonists, including WEGOVY® *[see Adverse Reactions]*. After initiation of WEGOVY®, observe patients carefully for signs and symptoms of acute pancreatitis (including persistent severe abdominal pain, sometimes radiating to the back, and which may or may not be accompanied by vomiting). If acute pancreatitis is suspected, discontinue WEGOVY® and initiate appropriate management. **Acute Gallbladder Disease:** Treatment with WEGOVY® is associated with an increased occurrence of cholelithiasis and cholecystitis. The incidence of cholelithiasis and cholecystitis was higher in WEGOVY®-treated pediatric patients aged 12 years and older than in WEGOVY®-treated adults. In randomized clinical trials in adult patients, cholelithiasis was reported by 1.6% of WEGOVY®-treated patients and 0.7% of placebo-treated patients. Cholecystitis was reported by 0.6% of WEGOVY®-treated adult patients and 0.2% of placebo-treated patients. In a clinical trial in pediatric patients aged 12 years and older, cholelithiasis was reported by 3.8% of WEGOVY®-treated patients and 0% placebo-treated patients. Cholecystitis was reported by 0.8% of WEGOVY®-treated pediatric patients and 0% placebo-treated patients *[see Adverse Reactions]*. Substantial or rapid weight loss can increase the risk of cholelithiasis; however, the incidence of acute gallbladder disease was greater in WEGOVY®-treated patients than in placebo-treated patients, even after accounting for the degree of weight loss. If cholelithiasis is suspected, gallbladder studies and appropriate clinical follow-up are indicated. **Hypoglycemia:** WEGOVY® lowers blood glucose and can cause hypoglycemia. In a trial of adult patients with type 2 diabetes and body mass index (BMI) greater than or equal to 27 kg/m^2, hypoglycemia (defined as a plasma glucose less than 54 mg/dL) was reported in 6.2% of WEGOVY®-treated patients versus 2.5% of placebo-treated patients. One episode of severe hypoglycemia (requiring the assistance of another person) was reported in one WEGOVY®-treated patient versus no placebo-treated patients. Patients with diabetes mellitus taking WEGOVY® in combination with insulin or an insulin secretagogue (e.g., sulfonylurea) may have an increased risk of hypoglycemia, including severe hypoglycemia. Hypoglycemia has been observed in patients treated with semaglutide at doses of 0.5 and 1 mg in combination with insulin. The use of WEGOVY® (semaglutide 2.4 mg or 1.7 mg once weekly) in patients with type 1 diabetes mellitus or in combination with insulin has not been evaluated. Inform patients of the risk of hypoglycemia and educate them on the signs and symptoms of hypoglycemia. In patients with diabetes, monitor blood glucose prior to starting WEGOVY® and during WEGOVY® treatment. When initiating WEGOVY®, consider reducing the dose of concomitantly administered insulin or insulin secretagogue (such as sulfonylureas) to reduce the risk of hypoglycemia *[see Drug Interactions]*. **Acute Kidney Injury:** There have been postmarketing reports of acute kidney injury and worsening of chronic renal failure, which have in some cases required hemodialysis, in patients treated with semaglutide. Patients with renal impairment may be at greater risk of acute kidney injury, but some of these events have been reported in patients without known underlying renal disease. A majority of the reported events occurred in patients who had experienced nausea, vomiting, or diarrhea, leading to volume depletion *[see Adverse Reactions]*. Monitor renal function when initiating or escalating doses of WEGOVY® in patients reporting severe adverse gastrointestinal reactions. Monitor renal function in patients with renal impairment reporting any adverse reactions that could lead to volume depletion **Severe Gastrointestinal Adverse Reactions:** Use of WEGOVY® has been associated with gastrointestinal adverse reactions, sometimes severe *[see Adverse Reactions]*. In WEGOVY® clinical trials, severe gastrointestinal adverse reactions were reported more frequently among patients receiving WEGOVY® (4.1%) than placebo (0.9%). WEGOVY® is not recommended in patients with severe gastroparesis. **Hypersensitivity Reactions:** Serious hypersensitivity reactions (e.g., anaphylaxis, angioedema) have been reported with WEGOVY®. If hypersensitivity reactions occur, discontinue use of WEGOVY®, treat promptly per standard of care, and monitor until signs and symptoms resolve. WEGOVY® is contraindicated in patients with a prior serious hypersensitivity reaction to semaglutide or to any of the excipients in WEGOVY® *[see Adverse Reactions]*. Anaphylaxis and angioedema have been reported with other GLP-1 receptor agonists. Use caution in a patient with a history of anaphylaxis or angioedema with another GLP-1 receptor agonist because it is unknown whether such patients will be predisposed to these reactions with WEGOVY®. **Diabetic Retinopathy Complications in Patients with Type 2 Diabetes:** In a trial of adult patients with type 2 diabetes and BMI greater than or equal to 27 kg/m^2, diabetic retinopathy was reported by 4% of WEGOVY®-treated patients and 2.7% placebo-treated patients. In a 2-year trial with semaglutide 0.5 mg and 1 mg once-weekly injection in adult patients with type 2 diabetes and high cardiovascular risk, diabetic retinopathy complications (which was a 4-component adjudicated endpoint) occurred in patients treated with semaglutide injection (3%) compared to placebo (1.8%). The absolute risk increase for diabetic retinopathy complications was larger among patients with a history of diabetic retinopathy at baseline (semaglutide injection 8.2%, placebo 5.2%) than among patients without a known history of diabetic retinopathy (semaglutide injection 0.7%, placebo 0.4%). Rapid improvement in glucose control has been associated with a temporary worsening of diabetic retinopathy. The effect of long-term glycemic control with semaglutide on diabetic retinopathy complications has not been studied. Patients with a history of diabetic retinopathy should be monitored for progression of diabetic retinopathy. **Heart Rate Increase:** Treatment with WEGOVY® was associated with increases in resting heart rate. Mean increases in resting heart rate of 1 to 4 beats per minute (bpm) were observed in WEGOVY®-treated adult patients compared to placebo in clinical trials. More adult patients treated with WEGOVY® compared with placebo had maximum changes from baseline at any visit of 10 to 19 bpm (41% versus 34%, respectively) and 20 bpm or more (26% versus 16%, respectively). In a clinical trial in pediatric patients aged 12 years and older with normal baseline heart rate, more patients treated with WEGOVY® compared to placebo had maximum changes in heart rate of 20 bpm or more (54% versus 39%) *[see Adverse Reactions]*. Monitor heart rate at regular intervals consistent with usual clinical practice. Instruct patients to inform their healthcare providers of palpitations or feelings of a racing heartbeat while at rest during WEGOVY® treatment. If patients experience a sustained increase in resting heart rate, discontinue WEGOVY®.**Suicidal Behavior and Ideation:** Suicidal behavior and ideation have been reported in clinical trials with other weight management products. Monitor patients treated with WEGOVY® for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior. Discontinue WEGOVY® in patients who experience suicidal thoughts or behaviors. Avoid WEGOVY® in patients with a history of suicidal attempts or active suicidal ideation. **Pulmonary Aspiration During General Anesthesia or Deep Sedation:** WEGOVY® delays gastric emptying. There have been rare postmarketing reports of pulmonary aspiration in patients receiving GLP-1 receptor agonists undergoing elective surgeries or procedures requiring general anesthesia or deep sedation who had residual gastric contents despite reported adherence to preoperative fasting recommendations. Available data are insufficient to inform recommendations to mitigate the risk of pulmonary aspiration during general anesthesia or deep sedation in patients taking WEGOVY®, including whether modifying preoperative fasting recommendations or temporarily discontinuing WEGOVY® could reduce the incidence of retained gastric contents. Instruct patients to inform healthcare providers prior to any planned surgeries or procedures if they are taking WEGOVY®.

ADVERSE REACTIONS: The following serious adverse reactions are described below or elsewhere in the prescribing information: Risk of Thyroid C-Cell Tumors *[see Warnings and Precautions]*; Acute Pancreatitis *[see Warnings and Precautions]*; Acute Gallbladder Disease *[see Warnings and Precautions]*; Hypoglycemia *[see Warnings and Precautions]*; Acute Kidney Injury *[see Warnings and Precautions]*; Severe Gastrointestinal Adverse Reactions *[see Warnings and Precautions]*; Hypersensitivity Reactions *[see Warnings and Precautions]*; Diabetic Retinopathy Complications in Patients with Type 2 Diabetes *[see Warnings and Precautions]*; Heart Rate Increase *[see Warnings and Precautions]*; Suicidal Behavior and Ideation *[see Warnings and Precautions]*; Pulmonary Aspiration During General Anesthesia or Deep Sedation *[see Warnings and Precautions]*. **Clinical Trials Experience:** Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice. **Adverse Reactions in Clinical Trials in Adults with Obesity or Overweight:** *WEGOVY® 2.4 mg Subcutaneous Weekly Dosage:* WEGOVY® was evaluated for safety in 3 randomized, double-blind, placebo-controlled trials that included 2,116 adult patients with obesity or overweight treated with 2.4 mg WEGOVY® for up to 68 weeks and a 7 week off-drug follow-up period. Baseline characteristics included a mean age of 48 years, 71% female, 72% White, 14% Asian, 9% Black or African American, and 5% reported as other or unknown; and 85% were not Hispanic or Latino ethnicity, 13% were Hispanic or Latino ethnicity, and 2% reported as unknown. The baseline characteristics were 42% with hypertension, 19% with type 2 diabetes, 43% with dyslipidemia, 28% with a BMI greater than 40 kg/m^2, and 4% with cardiovascular disease. In these clinical trials, 6.8% of patients treated with 2.4 mg WEGOVY® and 3.2% of patients treated with placebo permanently discontinued treatment as a result of adverse reactions. The most common adverse reactions leading to discontinuation were nausea (1.8% versus 0.2%), vomiting (1.2% versus 0%), and diarrhea (0.7% versus 0.1%) for WEGOVY® and placebo, respectively. Adverse reactions reported in clinical trials in adults and greater than or equal to 2% of WEGOVY®-treated patients and more frequently than in placebo-treated patients are shown in **Table 2**.

Table 2. Adverse Reactions (≥2% and Greater Than Placebo) in WEGOVY®-treated Adults with Obesity or Overweight

	Placebo N=1,261 %	WEGOVY® 2.4 mg N=2,116 %
Nausea	16	44
Diarrhea	16	30
Vomiting	6	24
Constipation	11	24
Abdominal Pain[a]	10	20
Headache	10	14
Fatigue[b]	5	11
Dyspepsia	3	9
Dizziness	4	8
Abdominal Distension	5	7
Eructation	<1	7
Hypoglycemia in T2DM[c]	2	6
Flatulence	4	6
Gastroenteritis	4	6
Gastroesophageal Reflux Disease	3	5
Gastritis[d]	1	4
Gastroenteritis Viral	3	4
Hair Loss	1	3
Dysesthesia[e]	1	2

[a]Includes abdominal pain, abdominal pain upper, abdominal pain lower, gastrointestinal pain, abdominal tenderness, abdominal discomfort and epigastric discomfort
[b]Includes fatigue and asthenia
[c]Defined as blood glucose <54 mg/dL with or without symptoms of hypoglycemia or severe hypoglycemia (requiring the assistance of another person) in patients with type 2 diabetes not on concomitant insulin (Study 3, WEGOVY® N=403, Placebo N=402). See text below for further information regarding hypoglycemia in patients with and without type 2 diabetes. T2DM = type 2 diabetes mellitus
[d]Includes chronic gastritis, gastritis, gastritis erosive, and reflux gastritis
[e]Includes paresthesia, hyperesthesia, burning sensation, allodynia, dysesthesia, skin burning sensation, pain of skin, and sensitive skin

In a cardiovascular outcomes trial, 8,803 patients were exposed to WEGOVY® for a median of 37.3 months and 8,801 patients were exposed to placebo for a median of 38.6 months. Safety data collection was limited to serious adverse events (including death), adverse events leading to discontinuation, and adverse events of special interest. Sixteen percent (16%) of WEGOVY®-treated patients and 8% of placebo-treated patients, respectively, discontinued study drug due to an adverse event. Additional information from this trial is included in subsequent sections below when relevant. **Adverse Reactions in a Clinical Trial of Pediatric Patients Aged 12 Years and Older with Obesity:** WEGOVY® was evaluated in a 68-week, double-blind, randomized, parallel group, placebo-controlled, multi-center trial in 201 pediatric patients aged 12 years and older with obesity. Baseline characteristics included a mean age of 15.4 years; 38% of patients were male; 79% were White, 8% were Black or African American, 2% were Asian, and 11% were of other or unknown race; and 11% were of Hispanic or Latino ethnicity. The mean baseline body weight was 107.5 kg, and mean BMI was 37 kg/m^2. **Table 3** shows adverse reactions reported in greater than or equal to 3% of WEGOVY®-treated pediatric patients and more frequently than in the placebo group from a study in pediatric patients aged 12 years and older.

Table 3. Adverse Reactions (≥3% and Greater than Placebo) in WEGOVY®-Treated Pediatric Patients Aged 12 Years and Older with Obesity

	Placebo N=67 %	WEGOVY® 2.4 mg N=133 %
Nausea	18	42
Vomiting	10	36
Diarrhea	19	22
Headache	16	17
Abdominal Pain	6	15
Nasopharyngitis	10	12
Dizziness	3	8
Gastroenteritis	3	7
Constipation	2	6
Gastroesophageal Reflux Disease	2	4
Sinusitis	2	4
Urinary tract infection	2	4
Ligament sprain	2	4
Anxiety	2	4
Hair Loss	0	4
Cholelithiasis	0	4
Eructation	0	4
Influenza	0	3
Rash	0	3
Urticaria	0	3

Other Adverse Reactions in Adults and/or Pediatric Patients: *Acute Pancreatitis:* In WEGOVY® clinical trials in adults, acute pancreatitis was confirmed by adjudication in 4 WEGOVY®-treated patients (0.2 cases per 100 patient years) versus 1 in placebo-treated patients (less than 0.1 cases per 100 patient years). One additional case of acute pancreatitis was confirmed in a patient treated with WEGOVY® in another clinical trial. *Acute Gallbladder Disease:* In WEGOVY® clinical trials in adults, cholelithiasis was reported by 1.6% of WEGOVY®-treated patients and 0.7% of placebo-treated patients. Cholecystitis was reported by 0.6% of WEGOVY®-treated adult patients and 0.2% of placebo-treated patients. In a clinical trial in pediatric patients aged 12 years and older, cholelithiasis was reported by 3.8% of WEGOVY®-treated patients and 0% placebo-treated patients. Cholecystitis was reported by 0.8% of WEGOVY®-treated pediatric patients and 0% placebo-treated patients. *Hypoglycemia: Patients with Type 2 Diabetes:* In a trial of adult patients with type 2 diabetes and BMI greater than or equal to 27 kg/m^2, clinically significant hypoglycemia (defined as a plasma glucose less than 54 mg/dL) was reported in 6.2% of WEGOVY®-treated patients versus 2.5% of placebo-treated patients. A higher rate of clinically significant hypoglycemic episodes was reported with WEGOVY® (semaglutide 2.4 mg) versus semaglutide 1 mg (10.7 vs. 7.2 episodes per 100 patient years of exposure, respectively); the rate in the placebo-treated group was 3.2 episodes per 100 patient years of exposure. In addition, one episode of severe hypoglycemia requiring intravenous glucose was reported in a WEGOVY®-treated patient versus none in placebo-treated patients. The risk of hypoglycemia was increased when WEGOVY® was used with a sulfonylurea. *Patients without Type 2 Diabetes:* Episodes of hypoglycemia have been reported with GLP-1 receptor agonists in adult patients without type 2 diabetes mellitus. In WEGOVY® clinical trials in adult patients without type 2 diabetes mellitus, there was no systematic capturing or reporting of hypoglycemia. In a cardiovascular outcomes trial in adult patients without type 2 diabetes, 3 episodes of serious hypoglycemia were reported in WEGOVY®-treated patients versus 1 episode in placebo. Patients with a history of bariatric surgery (a risk factor for hypoglycemia) had more events of serious hypoglycemia while taking WEGOVY® (2.3%, 2/87) than placebo (0%, 0/97). *Acute Kidney Injury:* Acute kidney injury occurred in clinical trials in 7 adult patients (0.4 cases per 100 patient years) receiving WEGOVY® versus 4 patients (0.2 cases per 100 patient years of exposure) receiving placebo. Some of these adverse reactions occurred in association with gastrointestinal adverse reactions or dehydration. In addition, 2 patients treated with WEGOVY® had acute kidney injury with dehydration in other clinical trials. The risk of renal adverse reactions with WEGOVY® was increased in adult patients with a history of renal impairment (trials included 65 patients with a history of moderate or severe renal impairment at baseline), and occurred more frequently during dose titration. *Retinal Disorders in Patients with Type 2 Diabetes:* In a trial of adult patients with type 2 diabetes and BMI greater than or equal to 27 kg/m^2, retinal disorders were reported by 6.9% of patients treated with WEGOVY® (semaglutide 2.4 mg), 6.2% of patients treated with semaglutide 1 mg, and 4.2% of patients treated with placebo. The majority of events were reported as diabetic retinopathy (4%, 2.7%, and 2.7%, respectively) and non-proliferative retinopathy (0.7%, 0%, and 0%, respectively). *Increase in Heart Rate:* Mean increases in resting heart rate of 1 to 4 beats per minute (bpm) were observed with routine clinical monitoring in WEGOVY®-treated adult patients compared to placebo in clinical trials. In trials in which adult patients were randomized prior to dose-escalation, more patients treated with WEGOVY®, compared with placebo, had maximum changes from baseline at any visit of 10 to 19 bpm (41% versus 34%, respectively) and 20 bpm or more (26% versus 16%, respectively). In a clinical trial in pediatric patients aged 12 years and older with normal baseline heart rate, more patients treated with WEGOVY® compared to placebo had maximum changes in heart rate of 20 bpm or more (54% versus 39%). *Hypotension and Syncope:* Adverse reactions related to hypotension (hypotension, orthostatic hypotension, and decreased blood pressure) were reported in 1.3% of WEGOVY®-treated adult patients versus 0.4% of placebo-treated patients and syncope was reported in 0.8% of WEGOVY®-treated patients versus 0.2% of placebo-treated patients. Some reactions were related to gastrointestinal adverse reactions and volume loss associated with WEGOVY®. Hypotension and orthostatic hypotension were more frequently seen in patients on concomitant antihypertensive therapy. In a clinical trial in pediatric patients aged 12 years and older, hypotension was reported in 2.3% of WEGOVY®-treated patients versus 0% in placebo-treated patients. *Appendicitis:* Appendicitis (including perforated appendicitis) occurred in 10 (0.5%) WEGOVY®-treated adult patients and 2 (0.2%) patients receiving placebo. *Gastrointestinal Adverse Reactions:* In clinical trials in adults, 73% of WEGOVY®-treated patients and 47% of patients receiving placebo reported gastrointestinal adverse reactions, including severe reactions that were reported more frequently among patients receiving WEGOVY® (4.1%) than placebo (0.9%). The most frequently reported reactions were nausea (44% vs. 16%), vomiting (25% vs. 6%), and diarrhea (30% vs. 16%). Other reactions that occurred at a higher incidence among WEGOVY®-treated adult patients included dyspepsia, abdominal pain, abdominal distension, eructation, flatulence, gastroesophageal reflux disease, gastritis, hemorrhoids, and hiccups. These reactions were most frequently reported during dosage escalation. In the pediatric clinical trial, 62% of WEGOVY®-treated patients and 42% of placebo-treated patients reported gastrointestinal adverse reactions. The most frequently reported reactions were nausea (42% vs. 18%), vomiting (36% vs. 10%), and diarrhea (22% vs. 19%). Other gastrointestinal-related reactions that occurred at a higher incidence than placebo among WEGOVY®-treated pediatric patients included abdominal pain, constipation, eructation, gastroesophageal reflux disease, dyspepsia, and flatulence. Permanent discontinuation of treatment as a result of a gastrointestinal adverse reaction occurred in 4.3% of WEGOVY®-treated adult patients versus 0.7% of placebo-treated patients. In a pediatric clinical trial, 2.3% of patients treated with WEGOVY® versus 1.5% of patients who received placebo discontinued treatment as a result of gastrointestinal adverse reactions. *Injection Site Reactions:* In clinical trials in adults, 1.4% of WEGOVY®-treated patients and 1% of patients receiving placebo experienced injection site reactions (including injection site pruritus, erythema, inflammation, induration, and irritation).

Hypersensitivity Reactions: Serious hypersensitivity reactions (e.g., anaphylaxis, angioedema) have been reported with WEGOVY®. In a pediatric clinical trial, rash was reported in 3% of WEGOVY®-treated patients and 0% of placebo-treated patients, and urticaria was reported in 3% of WEGOVY®-treated patients and 0% of placebo-treated patients. In adult clinical trials, allergic reactions occurred in 16% (8/50) of WEGOVY®-treated patients with anti-semaglutide antibodies and in 7% (114/1659) of WEGOVY®-treated patients who did not develop anti-semaglutide antibodies. *Fractures:* In the cardiovascular outcomes trial in adults, more fractures of the hip and pelvis were reported on WEGOVY® than on placebo in female patients: 1% (24/2448) vs. 0.2% (5/2424), and in patients ages 75 years and older: 2.4% (17/703) vs. 0.6% (4/663), respectively. *Urolithiasis:* In a cardiovascular outcomes trial, 1.2% of WEGOVY®-treated patients and 0.8% of patients receiving placebo reported urolithiasis, including serious reactions that were reported more frequently among patients receiving WEGOVY® (0.6%) than placebo (0.4%). *Dysgeusia:* In clinical trials in adults, 1.7% of WEGOVY®-treated patients and 0.5% of placebo-treated patients reported dysgeusia. *Laboratory Abnormalities: Amylase and Lipase:* Adult and pediatric patients treated with WEGOVY® had a mean increase from baseline in amylase of 15 to 16% and lipase of 39%. These changes were not observed in the placebo group. The clinical significance of elevations in lipase or amylase with WEGOVY® is unknown in the absence of other signs and symptoms of pancreatitis. *Liver Enzymes:* In a pediatric clinical trial, increases in alanine aminotransferase (ALT) greater than or equal to 5 times the upper limit of normal were observed in 4 (3%) WEGOVY®-treated patients compared with 0% of placebo-treated patients. In some patients, increases in ALT and AST were associated with other confounding factors (such as gallstones). In the cardiovascular outcomes trial in adults, increases in total bilirubin greater than or equal to 3 times the upper limit of normal were observed in 0.3% (30/8585) of WEGOVY®-treated patients versus 0.2% (14/8579) of placebo-treated patients. **Postmarketing Experience:** The following adverse reactions have been reported during post-approval use of semaglutide, the active ingredient of WEGOVY®. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. *Gastrointestinal Disorders:* acute pancreatitis and necrotizing pancreatitis, sometimes resulting in death; ileus; *Hypersensitivity:* anaphylaxis, angioedema, rash, urticaria; *Pulmonary:* Pulmonary aspiration has occurred in patients receiving GLP-1 receptor agonists undergoing elective surgeries or procedures requiring general anesthesia or deep sedation; *Renal and Urinary Disorders:* acute kidney injury.

DRUG INTERACTIONS: Concomitant Use with Insulin or an Insulin Secretagogue (e.g., Sulfonylurea): WEGOVY® lowers blood glucose and can cause hypoglycemia. The risk of hypoglycemia is increased when WEGOVY® is used in combination with insulin or insulin secretagogues (e.g., sulfonylureas). The addition of WEGOVY® in patients treated with insulin has not been evaluated. When initiating WEGOVY®, consider reducing the dose of concomitantly administered insulin secretagogue (such as sulfonylureas) or insulin to reduce the risk of hypoglycemia *[see Warnings and Precautions and Adverse Reactions].* **Oral Medications:** WEGOVY® causes a delay of gastric emptying and thereby has the potential to impact the absorption of concomitantly administered oral medications. In clinical pharmacology trials with semaglutide 1 mg, semaglutide did not affect the absorption of orally administered medications. Nonetheless, monitor the effects of oral medications concomitantly administered with WEGOVY®.

USE IN SPECIFIC POPULATIONS: Pregnancy: Pregnancy Exposure Registry: There will be a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to semaglutide during pregnancy. Pregnant women exposed to WEGOVY® and healthcare providers are encouraged to contact Novo Nordisk at 1-877-390-2760 or www.wegovypregnancyregistry.com. Risk Summary: Based on animal reproduction studies, there may be potential risks to the fetus from exposure to semaglutide during pregnancy. Additionally, weight loss offers no benefit to a pregnant patient and may cause fetal harm. When a pregnancy is recognized, advise the pregnant patient of the risk to a fetus, and discontinue WEGOVY® *(see Clinical Considerations).* Available pharmacovigilance data and data from clinical trials with WEGOVY® use in pregnant patients are insufficient to establish a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. In pregnant rats administered semaglutide during organogenesis, embryofetal mortality, structural abnormalities and alterations to growth occurred at maternal exposures below the maximum recommended human dose (MRHD) based on AUC. In rabbits and cynomolgus monkeys administered semaglutide during organogenesis, early pregnancy losses and structural abnormalities were observed at below the MRHD (rabbit) and greater than or equal to 2-fold the MRHD (monkey). These findings coincided with a marked maternal body weight loss in both animal species (see Data). The estimated background risk of major birth defects and miscarriage for the indicated population are unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Clinical Considerations: *Disease-associated maternal and/or embryo/fetal risk:* Appropriate weight gain based on pre-pregnancy weight is currently recommended for all pregnant patients, including those who already have overweight or obesity, because of the obligatory weight gain that occurs in maternal tissues during pregnancy. Data: *Animal Data:* In a combined fertility and embryofetal development study in rats, subcutaneous doses of 0.01, 0.03 and 0.09 mg/kg/day (0.04-, 0.1-, and 0.4-fold the MRHD) were administered to males for 4 weeks prior to and throughout mating and to females for 2 weeks prior to mating, and throughout organogenesis to Gestation Day 17. In parental animals, pharmacologically mediated reductions in body weight gain and food consumption were observed at all dose levels. In the offspring, reduced growth and fetuses with visceral (heart blood vessels) and skeletal (cranial bones, vertebra, ribs) abnormalities were observed at the human exposure. In an embryofetal development study in pregnant rabbits, subcutaneous doses of 0.0010, 0.0025 or 0.0075 mg/kg/day (0.01-, 0.1-, and 0.9-fold the MRHD) were administered throughout organogenesis from Gestation Day 6 to 19. Pharmacologically mediated reductions in maternal body weight gain and food consumption were observed at all dose levels. Early pregnancy losses and increased incidences of minor visceral (kidney, liver) and skeletal (sternebra) fetal abnormalities were observed at greater than or equal to 0.0025 mg/kg/day, at clinically relevant exposures. In an embryofetal development study in pregnant cynomolgus monkeys, subcutaneous doses of 0.015, 0.075, and 0.15 mg/kg twice weekly (0.4-, 2-, and 6-fold the MRHD) were administered throughout organogenesis, from Gestation Day 16 to 50. Pharmacologically mediated, marked initial maternal body weight loss and reductions in body weight gain and food consumption coincided with the occurrence of sporadic abnormalities (vertebra, sternebra, ribs) at greater than or equal to 0.075 mg/kg twice weekly (greater than or equal to 2 times human exposure). In a pre- and postnatal development study in pregnant cynomolgus monkeys, subcutaneous doses of 0.015, 0.075, and 0.15 mg/kg twice weekly (0.2-, 1-, and 3-fold the MRHD) were administered from Gestation Day 16 to 140. Pharmacologically mediated marked initial maternal body weight loss and reductions in body weight gain and food consumption coincided with an increase in early pregnancy losses and led to delivery of slightly smaller offspring at greater than or equal to 0.075 mg/kg twice weekly (greater than or equal to 1 time human exposure). **Lactation:** Risk Summary: There are no data on the presence of semaglutide or its metabolites in human milk, the effects on the breastfed infant, or the effects on milk production. Semaglutide was present in the milk of lactating rats. When a drug is present in animal milk, it is likely that the drug will be present in human milk *(see Data).* The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for WEGOVY® and any potential adverse effects on the breastfed infant from WEGOVY® or from the underlying maternal condition. Data: In lactating rats, semaglutide was detected in milk at levels 3-12 fold lower than in maternal plasma. **Females and Males of Reproductive Potential:** Because of the potential for fetal harm, discontinue WEGOVY® in patients at least 2 months before they plan to become pregnant to account for the long half-life of semaglutide *[see Use in Specific Populations].* **Pediatric Use:** The safety and effectiveness of WEGOVY® as an adjunct to a reduced calorie diet and increased physical activity for weight reduction and long-term maintenance have been established in pediatric patients aged 12 years and older with obesity. Use of WEGOVY® for this indication is supported by a 68-week, double-blind, placebo-controlled clinical trial in 201 pediatric patients aged 12 years and older with a BMI corresponding to ≥95th percentile for age and sex and from studies in adult patients with obesity. Use of the 1.7 mg once weekly maintenance dosage of WEGOVY® in pediatric patients is also supported by additional exposure-efficacy and safety analyses in pooled adult and pediatric patients. Adverse reactions with WEGOVY® treatment in pediatric patients aged 12 years and older were generally similar to those reported in adults. Pediatric patients aged 12 years and older treated with WEGOVY® had greater incidences of cholelithiasis, cholecystitis, hypotension, rash, and urticaria compared to adults treated with WEGOVY® *[see Adverse Reactions].* There are insufficient data in pediatric patients with type 2 diabetes treated with WEGOVY® for obesity to determine if there is an increased risk of hypoglycemia with WEGOVY® treatment similar to that reported in adults. Inform patients of the risk of hypoglycemia and educate them on the signs and symptoms of hypoglycemia. In pediatric patients aged 12 years and older with type 2 diabetes, monitor blood glucose prior to starting WEGOVY® and during WEGOVY® treatment. When initiating WEGOVY® in pediatric patients aged 12 years and older with type 2 diabetes, consider reducing the dose of concomitantly administered insulin secretagogue (such as sulfonylureas) or insulin to reduce the risk of hypoglycemia *[see Warnings and Precautions].* The safety and effectiveness of WEGOVY® have not been established in pediatric patients less than 12 years of age. **Geriatric Use:** In the WEGOVY® clinical trials for weight reduction and long-term maintenance, 233 (9%) WEGOVY®-treated patients were aged 65 to 75 years and 23 (1%) WEGOVY®-treated patients were aged 75 years and older. In a cardiovascular outcomes trial, 2656 (30%) WEGOVY®-treated patients were aged 65 to 75 years and 703 (8%) WEGOVY®-treated patients were aged 75 years and older. No overall difference in effectiveness was observed between patients aged 65 years and older and younger adult patients. In the cardiovascular outcomes trial, patients aged 75 years and older reported more fractures of the hip and pelvis on WEGOVY® than on placebo. Patients aged 75 years and older (WEGOVY®-treated and placebo-treated) reported more serious adverse reactions overall compared to younger adult patients *[see Adverse Reactions].* **Renal Impairment:** The recommended dosage of WEGOVY® in patients with renal impairment is the same as those with normal renal function. In a study in patients with renal impairment, including end-stage renal disease, no clinically relevant change in semaglutide pharmacokinetics was observed. **Hepatic Impairment:** The recommended dosage of WEGOVY® in patients with hepatic impairment is the same as those with normal hepatic function. In a study in patients with different degrees of hepatic impairment, no clinically relevant change in semaglutide pharmacokinetics was observed.

OVERDOSAGE: Overdoses have been reported with other GLP-1 receptor agonists. Effects have included severe nausea, severe vomiting, and severe hypoglycemia. In the event of overdose, appropriate supportive treatment should be initiated according to the patient's clinical signs and symptoms. In the event of an overdose of WEGOVY®, consider contacting the Poison Help line (1-800-222-1222) or a medical toxicologist for additional overdosage management recommendations. A prolonged period of observation and treatment for these symptoms may be necessary, taking into account the long half-life of WEGOVY® of approximately 1 week.

More detailed information is available upon request.

Manufactured by: Novo Nordisk A/S, DK-2880 Bagsvaerd, Denmark

For additional information about WEGOVY® contact: Novo Nordisk Inc., 800 Scudders Mill Road, Plainsboro, NJ 08536, 1-833-934-6891

Version: 6

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PATENT INFORMATION: http://www.novonordisk-us.com/products/product-patents.html

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wegovy®
semaglutide injection 2.4 mg

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Illustration by Jeannie Phan

PATIENT ENGAGEMENT

Improving adherence to behavioral interventions

These practical strategies can help patients adopt—and maintain—healthy lifestyle habits.

For the more than 35% of men and 40% of women in the United States with obesity, the health ramifications are staggering. They're at increased risk for numerous comorbidities, including cardiovascular disease (CVD), type 2 diabetes, metabolic syndrome, gallbladder disease, osteoarthritis and sleep apnea.[1,2]

The serious consequences to public health led the U.S. Preventive Services Task Force to issue a statement recommending intensive multicomponent behavioral interventions for adults with a body mass index (BMI) of 30 or higher. They include proven techniques that were found to improve weight loss.[2]

However, knowing what interventions may work in studies is very different than actually helping patients implement and succeed in changing what may be decades of ingrained behaviors. "Usually people are acutely aware that they need to make changes but don't know how or have tried 'everything' and don't know where to go from here," says Elizabeth Lowden, MD, a bariatric endocrinologist in Chicago. Here, experts offer ways to promote lasting behavioral changes in patients who struggle with weight loss.

Frame it as a medical issue, not a failure.

It's crucial to broach the subject of weight in an empathetic, nonjudgmental way, says Jennifer Seger, MD, founder of the medical weight management program at BMI of Texas, a San Antonio-based bariatric medical institute. "I show them where they are on the BMI chart and explain that obesity is a complicated disease and, as a physician, I am concerned about what that

might lead to," she says. "If they have comorbidities, I tie that in and help the patient understand that it doesn't have to be this way."

Dr. Lowden also stresses compassion. "Tone is important," she says. "We try to use a positive or neutral tone when we ask questions." For example, try saying, "What do you feel like you struggle with?" instead of "Why haven't you lost weight in the past?" Says Dr. Lowden: "We as physicians have the capacity to be empathetic and understanding. This is a medical issue that can be very difficult for people."

"Helping patients identify their motivation will help them make changes because they can see their long-term goal."
—Elizabeth Lowden, MD

Explore the patient's level of readiness.

If patients aren't on board to change their habits, the changes won't stick. That's why Dr. Seger asks patients whether they're ready to make adjustments. Instead of asking whether they're ready to eat less and exercise more, she'll ask, "Are you interested in exploring how we can help you turn this around, so you feel better and have more energy?" Most patients will say yes to that, which means you have them on board to create a plan.

Tip: Dr. Seger takes notes throughout the appointment and gives the patient a copy of what they've agreed to.

Ask the right questions.

At the first appointment, Dr. Lowden discusses patients' weight history: ups and downs, methods they've tried, what's worked and what hasn't and what they've struggled with. "You may be dealing with someone who's always hungry versus someone who struggles with emotional eating—there are different strategies for each," she says. "Most people have excess weight because they're eating too much or there's a mismatch between calorie intake and output, but it's the nuances behind why they're eating too much that allow you to help them."

Address any reasons for "no."

If patients express reservations about trying to lose weight, Dr. Seger meets them at their specific area of concern. If they say, "I've got too much on my plate and can't fathom thinking about a diet," for example, she'll say, "This isn't really a diet. It's more about learning about food and how it interacts with your body and figuring out workarounds to your challenges." If they say they don't have time to cook? "You don't need to know how to cook. We can work with convenience foods," notes Dr. Seger. Examples include precut vegetables, prepared salads and store-made rotisserie chickens.

Help patients find their motivation.

"Many people will be motivated by the threat of worsening medical conditions, but that doesn't motivate everybody," says Dr. Lowden. "Instead, they'll say, 'I want to sit on the ground and play with my grandchildren' or 'I want to be able to walk farther so we can go to Disney World.' Helping them identify their motivation will help them make changes because they can see their long-term goal," she says.

Make food tracking easier.

"When someone struggles with weight, they often have a misconception about how much food they're taking in," says Dr. Lowden. She recommends the app My Fitness Pal to keep track of calories. "It's an effective , low-cost way of helping people become more mindful about what they're eating. People may be over the limit without realizing it." In general, a deficit of at least 500 calories a day is recommended.

Simplify nutrition.

Rather than promote a complicated eating plan, Dr. Seger asks her patients to think about two general principles: First, eat food in its natural state as often as you can. And second, get the obvious villains out: sweetened beverages and highly refined, processed foods. Dr. Lowden positions this as a lifestyle change rather than dieting "because we know diets don't work," she says.

Start small.

"I'll begin by asking patients to make one change," Dr. Seger says. A soda habit is particularly harmful, for example: In a systematic review of 30 studies, 93% found a positive association between the consumption of sugar-sweetened beverages and increased obesity measures (as reflected by BMI or body weight) in children and adults.[3] So that's often where Dr. Seger starts, with a goal of gradually eliminating them. If the patient is drinking two or three sodas a day, she suggests cutting that to one or two per week. Once the patient has adapted to that, switch to seltzer water flavored with mint, fresh ginger, lemon or lime. Ultimately, says Dr. Seger, the goal is to get patients to make plain water their drink of choice.

When recommending swaps, Dr. Lowden goes with what the patient likes. If she sees that a patient isn't getting enough protein at breakfast, for example, she'll ask, "What sort of proteins do you like to eat?" If the patient says, "I hate eggs, but I love string cheese," she incorporates that into the plan for breakfast.

Stress "movement," not "exercise."

For someone who has been sedentary for years, thinking about exercising can be overwhelming. Dr. Seger finds that calling it "movement" can be much more palatable. Research shows that adding either resistance or aerobic training to calorie restriction has been found to enhance total body fat mass loss.[4]

Likewise, her patients' eyes often light up when she tells them they don't have to go to a gym to get their movement in. "I don't ask them to do CrossFit at 6 AM but rather just be more active," she says. "This takes the pressure off." Achievable actions she recommends: Park farther from the building entrance, ask your employer for a standing desk, take the stairs ("If you can't do five flights, do two"). It's good to track daily steps so they can start to raise the bar—using a simple pedometer or technology such as a Fitbit or smartphone app. Dr. Seger explains why these small steps matter. "Before I understood the science around obesity, I thought taking the stairs and parking away from the entrance wouldn't accomplish anything," she says. Now, she's changed her philosophy. "I tell my patients that every move they make is forward progress."

Demonstrate easy fitness moves.

Dr. Seger keeps resistance bands and hand weights in her office so she can show patients how to use them, and she also demonstrates proper form for exercises she thinks they can do—wall sits and wall pushups, for example, so they don't have to get down on the floor. "I want them to see how easy it can be," she says. "I tell them that having more muscle tone will help them burn fat more efficiently, and I ask them to give me 10 minutes of these exercises three or four times a week for the first month."

Encourage sleep hygiene.

Research has found that people who sleep fewer than 7 hours per night were more likely to develop obesity than those who sleep more.[5] Many of Dr. Seger's patients are surprised to hear this. "I explain that when you don't get enough sleep, the body is not as efficient at secreting leptin, a hormone that regulates metabolism and appetite," she says. "Most will say, 'I didn't realize that.'" To improve sleep habits, Dr. Seger recommends setting a hard limit on when patients turn off the TV or computer and move it up by 30 minutes until they get to a bedtime that will ensure sufficient sleep.

Discuss how to relieve stress.

Chronically elevated levels of cortisol are positively correlated with weight and waist circumference, as well as with the persistence of obesity over time.[6] To address chronic stress, Dr. Seger suggests that patients take slow, deep breaths throughout the day. She also encourages them to disconnect from technology. "I suggest having an hour at least once a week when you can't see the phone or TV or computer," Dr. Seger says. Once patients get comfortable with that, she asks if they could do it every night after dinner.

Dr. Lowden agrees and brainstorms with patients: "I'll say, 'What is something you'd love to do if you had the time?' " It might be getting a manicure, reading a book or playing a game with their kids. "If you can identify a couple of things people enjoy and have them write them down, they'll have something to refer back to when they need to relieve stress." And for patients who say they don't have time? "I like to use the oxygen mask analogy," Dr. Lowden says, referring to the instructions given on a plane to put your mask on first before helping others put on theirs. "I tell my patients that's the way they need to live their life as well. They can't take care of other people without taking care of themselves first." ●

—by Andrea Barbalich

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PATIENT: DANIELLE, 32, HAD OBESITY, PREDIABETES AND FEATURES OF METABOLIC SYNDROME.

"We need to consider more than just BMI for diagnosis of obesity"

NURSE PRACTITIONER:
Thomas George, Jr., DNP, CRNP, FNP-C
Assistant Professor, Frontier Nursing University; Doctor of Nursing Practice, Obesity Medicine Association Fellow, Director, Wellspring Weight and Wellness, Shelley, ID

History:
At her initial visit, Danielle, who was of Filipino descent, was concerned about her unsuccessful weight loss despite 6 weeks of lifestyle modifications. She had a history of prediabetes (BMI 27.5), hypertension and dyslipidemia. She also displayed central adiposity (waist circumference 33 inches, body fat 40%) and metabolic syndrome features, including an AIC of 6.2%, elevated fasting glucose (123 mg/dL) and insulin resistance (HOMA-IR 9.1). Danielle met the criteria for obesity according to World Health Organization (WHO) guidelines, which classify BMI ≥25 as obesity in Asia-Pacific populations. Her metabolic dysfunction, body composition and waist circumference further reinforced the need for early intervention. She said she was on a low-carb ketogenic diet that did not result in significant weight loss, and that her anxiety about work and family sometimes led her to overeat and lose sleep. Her main goals were to lose weight and reduce her health risks.

Initiating treatment:
I took a patient-centered approach with Danielle that included integrated nutritional, physical, behavioral and pharmacologic interventions. I recommended that she switch from a ketogenic diet to a Mediterranean diet with a balanced, high-protein, fiber-rich plan and a 500 kcal/day deficit, along with resistance training three times a week and moderate-intensity aerobic exercise. We discussed stress-related eating and improving her sleep hygiene with cognitive behavioral therapy (CBT), and I also suggested that she download and watch a diabetes prevention program app for motivation. To help with her goals, I wanted to start her on a newer type of GLP-1 receptor agonist–alongside lifestyle interventions. Her insurance company denied the initial prescription saying that she didn't have obesity, but I appealed the decision and convinced a medical review board that Danielle did, indeed, have obesity and several obesity-related conditions.

I started her on a lower dose of the newer GLP-1-RA and, after 12 weeks, Danielle had a significant therapeutic response to a lower dose than expected for benefit, and all parameters improved. She achieved a 6% body weight reduction. At 36 weeks, she discontinued anti-hypertensive and anti-obesity medications, normalized her blood pressure and reduced body fat to 29%. By 13 months, she sustained a 16.8% weight loss, increased skeletal muscle mass and demonstrated metabolic improvements.

Considerations:
Long-term weight maintenance requires ongoing metabolic and behavioral monitoring, lifestyle adherence and medical interventions that optimize continued success. Danielle's case illustrates the importance of individualized obesity care that takes ethnic variations and patient-centered decision-making into account. We need to consider more than just BMI for diagnosis of obesity and use a more ethnically appropriate approach. Lastly, we must always advocate for our patients, which sometimes requires gentle urging, leveraging data and persisting until resolution occurs.

NEW!
KOL ON DEMAND VIDEO
Scan here for more insight on Danielle's case.

PATIENT: YUSSEF, 49, WAS DIAGNOSED WITH OBESITY AND MULTIPLE WEIGHT-RELATED COMPLICATIONS.

"He was concerned about maintaining weight loss without medication"

History:
Yussef, a widower of Middle Eastern/North African descent, was diagnosed with Class 1 obesity (BMI 33.6), dyslipidemia, hypertension, insulin resistance, GERD, osteoarthritis (OA) and obstructive sleep apnea (OSA) requiring CPAP therapy. He weighed 257 lbs. (BP 118/70) with 24% body fat and a waist circumference of 34 inches. Yussef successfully lost weight while on a GLP-1 receptor agonist (GLP-1 RA). His other medications included a statin, NSAIDs for knee pain, a proton pump inhibitor (PPI), OTC fish oil, turmeric and multivitamin.

After losing the weight, Yussef experienced a resolution of hypertension, reduced GERD symptoms and improved sleep. He discontinued the NSAIDs, PPI and CPAP therapy. He told me the weight loss made him feel like "a new man," and he was able to resume the athletic activities he enjoyed, like pickleball, soccer and lifting weights.

When he changed jobs, however, he had to stop the GLP-1 RA because it was no longer covered by his insurance. He was worried that he would regain weight without the medication and asked about options to prevent obesity-related conditions.

Initiating treatment:
I suggested that Yussef engage in a structured weight management program that included dietary modifications emphasizing whole foods and lean proteins, such as the Mediterranean diet, with some intermittent fasting and supplemental protein shakes. We also discussed engaging in moderate aerobic exercise daily and resistance training 3-4 times a week. I gave him goal-setting literature and he agreed to attend weight-loss seminars and his church's wellness group.

Because Yussef's new insurance didn't cover GLP-1 RAs, we explored alternative pharmacologic options. A recent study demonstrated that patients using phentermine post-GLP-1 RA therapy were 29% less likely to experience full weight regain at one year compared with those without adjunct pharmacotherapy. However, weight loss history influences outcomes, with individuals losing ≥20 lbs. on GLP-1 RAs at higher risk of partial regain. After reviewing efficacy, safety profiles and cost considerations, Yussef opted to initiate phentermine. Side effects were monitored with initial reports of dry mouth and jitteriness, which resolved after eliminating caffeine-containing protein shakes and switching to decaffeinated beverages.

At a six-month follow-up, Yussef had a modest weight gain of 3 lbs., which was attributed to increased holiday food intake. Dose titration restored appetite control, and Yussef was able to maintain his weight at 197 lbs. We discussed long-term management options, including phentermine dose escalation or transitioning to naltrexone-bupropion. A year post-GLP-1 RA cessation, Yussef successfully maintained his weight loss through phentermine and intensive lifestyle interventions.

Considerations:
Yussef's case highlights the importance of a multifaceted approach to obesity treatment and the need for patient-centered, evidence-based obesity management with medical, lifestyle and behavioral strategies. Despite insurance restrictions, proactive treatment adaptation enabled successful long-term weight maintenance post-GLP-1 RA therapy. Further research is needed to fully understand the long-term impact of switching from a GLP-1 RA to older anti-obesity medications (AOM) for weight maintenance. It's also important to note that phentermine is indicated for short-term use, and prescribers should be aware of local regulations regarding extended use. Finally, insurance barriers necessitate advocacy for continued pharmacologic and non-pharmacologic interventions, even when a patient's BMI falls below traditional AOM eligibility thresholds.

Illustration by Juhee Kim

Q&A

Expert insight on managing overweight/obesity

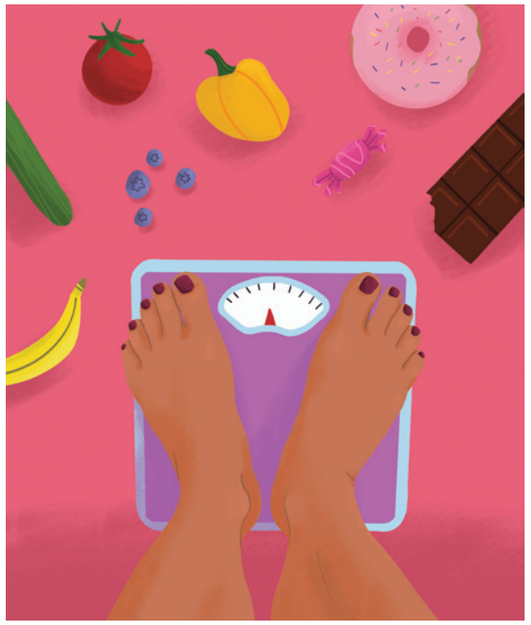

Illustration by fStop / Adobe Stock Images

Addressing weight-loss frustration

Q: How do you counsel patients who struggle with weight loss without making them feel like a "failure"?

A: The method I use to counsel patients who are feeling defeated follows specific steps that I've developed, which are grounded in a comprehensive understanding of each patient's unique situation, specifically:

Step 1: Make them feel heard. I allow patients to express what they need to say while I remain silent. Before offering any advice, I always say, "I hear you." People need to feel safe in a space where they feel vulnerable and frustrated. Creating this environment fosters trust and openness.

Step 2: Reframe the situation. I help patients view their journey from a positive angle by highlighting their progress. This shifts their mindset from seeing the cup as half empty to half full. As the conversation flows, they begin contributing their own solutions, moving toward a problem-solving and solution-oriented approach. The key skill here is guiding patients to develop their own strategies, rather than simply providing advice without their input.

Step 3: Address the mechanics. As a medical weight-loss expert, I help patients understand that many obstacles are rooted in metabolic issues, not personal shortcomings or "doing something wrong." My favorite analogy is: Even if you follow all the safety rules when driving a car—wearing a seatbelt, observing speed limits and checking both ways—you won't get far if the car has a mechanical problem, such as a smoking engine.

Understanding their medical issues can help patients overcome the emotional challenges and redirect them toward a solvable problem. Once the underlying issue or diagnosis is identified, treatment becomes much more manageable.

–Angela Tran, *DO, Founder of Med-Fit Weight Loss Center, Denver, CO*

When to switch therapy

Q: What's your approach when a patient says their obesity medication isn't working?

A: Before deciding whether a medication isn't working, it's essential to cover the basics. Start by asking questions to better understand what the patient is doing regarding their diet and exercise. Are there any factors interfering with their plan? Do they acknowledge any gaps in their nutrition—are they able to follow the plan consistently? I often listen for specific answers, such as data on calories, macros or other measurable information. If their responses are vague, I ask additional questions, because this often indicates an underlying problem.

If the patient adheres to their nutrition and exercise plan, and I haven't uncovered any hidden factors that need to be addressed, I move on to questions about the medication itself. How are they taking it? Are they missing doses? Are they experiencing any side effects that may have led them to deviate from their regimen? It's also important to clarify what they mean when they say the medication isn't working. Does this refer to side effects, insufficient hunger control or another reason? Identifying these factors helps distinguish issues beyond the simple mechanism of action of the medication.

Often the medication is effective, but other factors may give the appearance that it isn't working. Once it's confirmed that the medication itself is not providing the intended chemical benefit, we discuss alternative options. Typically, we consider increasing the dose. I may switch medications if the patient experiences side effects or has reached the maximum dose without progress. Health coaching plays a crucial role in helping patients feel more empowered and regain momentum in their progress.

–Angela Tran, DO

Creating a treatment plan

Q: What advice do you have for patients around setting goals?

A: The first and most important step in helping patients set treatment goals is identifying the real benefits they will gain. We begin by exploring their lifestyle goals: Do they want more energy? Greater confidence? To fit into a specific clothing size? Do they have a fitness milestone in mind? It's crucial to elicit what truly matters to them, as this establishes the motivation behind their effort.

It's important to create a space where they feel comfortable sharing openly. I like to set realistic goals and to share examples of what typical patients achieve in our program to help them envision what's truly possible. I emphasize that the most important treatment goal is sustainability. We discuss what is realistically achievable, and I walk them through how I can help them map this out. This process includes vision casting—envisioning where they could be in six months—such as having more energy, enjoying a vacation or feeling less pain in their knees.

Finally, I remind them that goals will need to adapt over time. I conclude by expressing my belief in their ability to succeed, based on my experience with many other patients who have successfully reached their own milestones.

–Angela Tran, DO

Advice for lifestyle changes

Q: How do you counsel patients on behavior modification?

A: I start by reassuring them that I'll be their partner throughout the process. I use language like "healthy eating" and "physical activity" instead of "diet and exercise." I also suggest patients keep a daily food and activity diary, which makes them aware of what, when and how they're eating, and how much of their day is spent being sedentary. When they come back for follow-up, we review their diary, which is a great way to build their confidence because they can see when they've been successful. We focus on what's working.

We also discuss how to reframe negative thinking so it doesn't derail their plan. For example, instead of "I can't have donuts for breakfast," I encourage them to focus on what they can have, such as "I'm going to have oatmeal and yogurt." It's subtle but gives them a sense of control over their situation.

–Angela Golden, DNP, *Co-owner of NP From Home, and NP Obesity Treatment Clinic, Flagstaff, AZ*

SPECIAL THANKS TO OUR MEDICAL REVIEWER:
Samantha Harris, MD, Endocrinologist and instructor of medicine, John T. Milliken Department of Medicine, Washington University, St. Louis

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Health Monitor

Clinician Update

EXAM TOOL

Screening for overweight/obesity

The American Association of Clinical Endocrinology recognizes obesity as a chronic disease and recommends annual screening of BMI and other health parameters. When a patient presents with excess weight, use the checklist below to gauge the need for medical intervention, including lifestyle therapy and, when appropriate, obesity medication or surgery. And keep in mind: The success of treatment should be measured not solely by number of pounds lost but also by improvements in weight-related complications and overall health.

1. **Does the patient have a body mass index (BMI) and weight-related complications that meet indications for prescribing obesity medication?**

- ☐ **BMI ≥30** (obesity) (all BMI cutoffs may be lower in certain ethnicities)
- ☐ **BMI ≥27** (overweight) with at least one weight-related complication, such as:
  - Prediabetes or type 2 diabetes
  - Metabolic syndrome
  - Hypertension
  - Dyslipidemia
  - Cardiovascular disease
  - Metabolic dysfunction-associated steatotic liver disease (MASLD)
  - Obstructive sleep apnea
  - Asthma/reactive airway disease
  - Osteoarthritis
  - Hormonal issues (e.g., polycystic ovarian syndrome)
  - GERD
  - Urinary stress incontinence

2. **If BMI <35, is waist circumference indicative of cardiometabolic disease? (Use gender- and ethnicity-specific cutoffs.)**

- ☐ **Women: ≥35 inches**
- ☐ **Men: ≥40 inches**

3. **Has the patient attempted lifestyle therapy, including nutritional and behavioral changes and increased physical activity)?**

- ☐ **Yes:** Measures tried: _____
- ☐ **No**

4. **Is the patient aware obesity is a chronic disease caused by genetic, metabolic, behavioral and environmental factors?**

- ☐ **Yes**
- ☐ **No**

5. **Is the patient motivated to set weight-loss goals and work with you on a personalized treatment plan?**

- ☐ **Yes**
- ☐ **No**

Note: For detailed recommendations on weight management, see Garvey WT, et al. AACE/ACE Comprehensive Clinical Practice Guidelines for Medical Care of Patients with Obesity. *Endocrine Pract.* 2016;22(Suppl 3):1-203.