

# Pharmacy Tech Topics™

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## **The Skinny on Obesity**

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### **LEARNING OBJECTIVES**

*Upon completion of this module, the subscriber will be able to:*

1. Classify the difference between obesity and being overweight.
2. Recognize appropriate weight loss goals for patients.
3. State non-pharmacological (non-medication) methods for weight loss.
4. Identify medications which can cause weight gain.
5. Recognize medications used for weight loss and their common side effects.



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# The Skinny on Obesity

## INTRODUCTION

Obesity is a very common disease affecting over a third of adult Americans. Costs due to obesity were estimated to be \$147 billion in 2008. While the incidence of pediatric obesity has increased significantly since 1980 and has the potential to have a significant effect on public health, the focus of this chapter will be primarily on adult obesity.<sup>1</sup>

## Classifying Obesity

Weight is generally classified using a body mass index (BMI). This is a ratio of weight (in kilograms [kg]) to height (in meters<sup>2</sup> [m<sup>2</sup>]) and is calculated with the following equation<sup>2</sup>:

$$\text{BMI} = \text{weight (kg)} \div \text{height}^2 \text{ (m}^2\text{)}$$

To convert from pounds to kilograms, one can multiply the pounds by 0.45 or divide by 2.2 (although dividing by 2.2 is more commonly seen). Both of these conversions are approximate. For example, if someone weighs 150 pounds:

$$\begin{aligned} 150 \times 0.45 &= 67.5 \text{ kg} \\ 150 \div 2.2 &= 68.2 \text{ kg} \end{aligned}$$

To convert from inches to meters, divide the number of inches by 39.37 (or multiply inches by 0.0254). Most people report height in feet and inches; there are 12 inches in every foot. For someone 6 feet tall, multiply 6 × 12 to get 72 inches. To convert to meters:

$$72 \div 39.37 = 1.83 \text{ meters}$$

To make the BMI calculation simpler, there is an equation that does not have to convert pounds to kilograms or inches to meters. You will still need to convert height in feet to inches (**Table 1**).

$$\text{BMI} = [\text{Weight (pounds)} \times 703] \div \text{height (inches)}^2$$

From	To	Multiply by
Inch	Meter	0.0254
Feet	Inches	12
Pounds	Kilograms	0.45

For example, a patient who weighs 250 pounds and is 5 feet tall (60 inches), BMI is calculated as:

$$(250 \text{ lbs.} \times 703) \div (60 \text{ inches} \times 60 \text{ inches}) = 48.8 \text{ kg/m}^2$$

While other methods of classifying weight are used (and described later in this section), BMI is commonly used and relatively easy to measure with low cost.<sup>3</sup> Based on a patient's BMI, their weight is categorized as "underweight", "normal", "overweight", "obese" or "morbidly obese" (**Table 2**). This classification is only used for adults aged 20 years or greater. For children and teens, the BMI is classified as a percentile. For the patient above with a BMI of 48.8 kg/m<sup>2</sup>, their BMI is classified as morbidly obese.

### Test Your Knowledge #1

For a patient who weighs 150 pounds and is 5'10", what is their BMI? What is their classification?

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What if the patient was the same weight but 5'2" tall? What would the patient's BMI and classification be?

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\_\_\_\_\_

*Answers on page 28.*

**Table 2. Weight Classification by body mass index (BMI) for Adults<sup>3</sup>**

BMI *	Classification
<18.5	Underweight
18.5-24.9	Normal
25-29.9	Overweight
≥30	Obese
≥40	Morbidly obese

\* kilograms/meter<sup>2</sup> (kg/m<sup>2</sup>)  
 < less than  
 ≥ greater than or equal to

Alternatives to BMI include waist circumference (WC) and percent body fat. Waist circumference should be measured at the navel, and can be done easily with a tape measure. For WC, classification depends on whether the patient is male or female. Men with a WC of greater than or equal to 40 inches (102 cm) and women with a WC greater than or equal to 35 inches (88 cm) are considered to have abdominal obesity. A lower cut-off point may be appropriate for Asian men and women. For percent body fat, obesity is defined as greater than 25% body fat for men and greater than 32% body fat for women. Percent body fat is a more complex measurement, which is assessed either with a skin-fold measurement (which requires a trained person to measure the body at specific spots, or with a skin-fold device which can be done at home) or with bioelectrical impedance analysis. This is more complex and cannot be measured easily like BMI or waist circumference.<sup>3</sup>

There are some limitations to using each of these criteria to classify patients' weight. For example, think of a professional athlete with a muscular frame. Because muscle weighs more than fat, they may have a higher weight, and therefore a higher BMI, but they have minimal fat and a low waist circumference. Percent body fat may specifically assess body fat, but may be more expensive and is less validated to predict metabolic risk for diseases like hypertension and diabetes. While waist circumference is quick and inexpensive, the racial differences may limit its use.<sup>3</sup>

The goal of classifying patients is to identify if the patient is at risk of the comorbid conditions that come with risk. These comorbidities are discussed later in the chapter (Obesity Complications).

**Test Your Knowledge #2**

What is your weight, height and waist circumference? Calculate your BMI and classify yourself with your BMI and waist circumference. Are you in the same category with both systems?

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**Risk Factors for Obesity**

Some risk factors for obesity are modifiable and others are not. Female gender is a risk factor, as is being African American or Hispanic. Additionally, some people have a genetic predisposition to being overweight. There are also regions of the United States (U.S.) that have higher rates of obesity, with Midwestern and Southern states having the highest rates of obesity. Several states in these regions have rates above 30%. Those patients with lower education or lower incomes are also more likely to be obese, although this increase is not true for all groups of people.<sup>1</sup>

**Interactive Learning**  
(for those with internet access)

Go to <http://www.cdc.gov/obesity/data/adult.html> and look at the rates of adult obesity.

For the state in which you live, what was the 2012 prevalence of obesity among adults in that state? How did that compare to 2010?

\_\_\_\_\_

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Some diseases increase the risk of obesity. These include medical conditions such as immobility (unable to move; sometimes this can happen when patients are bedridden or in a wheelchair), Cushing's disease, sleep apnea, and some psychological diseases.<sup>3</sup> Several medications can also cause weight gain; some examples are provided in **Table 3**. Additional examples include hormones (e.g. estrogen hormones which can be used for contraception or in hormone replacement therapy), antihistamines (e.g. diphenhydramine [Benadryl]), corticosteroids (e.g. prednisone), and non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen (Motrin/Advil). Modification of these diseases and/or medications which increase obesity risk may reduce the patient's weight. While avoiding medications which can cause weight gain may not always be an option, it may be possible to use lower doses or medications in the same class which have less risk of weight gain. Several medications used for other medical conditions may reduce weight; these will be discussed in the Treatment section.<sup>3</sup>

**Table 3. Medications that may influence weight<sup>4-11</sup>**

Class of Medication	Examples of Medication Names	Expected Weight Effect
Insulin	NPH insulin (Novolin/Humulin) and several others	Up to 6.6 kg gain
Sulfonylureas	glimepiride (Amaryl), glyburide (Diabeta, Micronase), others	Loss of 0.3 kg with glimepiride to gain of 3.8 kg
Thiazolidinediones	pioglitazone (Actos), rosiglitazone (Avandia)	Loss of 0.95 to gain of 1.9 kg
Antipsychotics	olanzapine (Zyprexa), clozapine (Clozaril), ziprasidone (Geodon), several others	Loss of 3.2 kg with ziprasidone; gain of up to 9.9 kg with most other antipsychotics
Antiseizure	valproate (Depakote), carbamazepine (Tegretol, others), several others	Up to 5.8 kg gain
Antidepressants	mirtazapine (Remeron), nortriptyline (Pamelor), bupropion (Wellbutrin), others	Potential weight loss with bupropion; up to 3.7 kg gain with nortriptyline

**Test Your Knowledge #3**

Samantha is a 55 year old woman. She fell at work and since then hasn't been able to walk much and now spends more time on the couch. When she does walk, she sometimes needs a cane. She has also developed depression and started taking bupropion. Since the fall she has gained 10 pounds. Which risk factor(s) for obesity and/or weight gain does she have?

- A. Immobility and bupropion
- B. Immobility only
- C. Bupropion only

*Answers on page 28.*

cancer, and gout. Patients who are obese are at a higher risk of cancer, heart disease and stroke than patients who are not obese, and obesity is one of the leading causes of preventable death.<sup>1,3</sup> Obesity can also have psychosocial effects such as increased risk of depression and other psychological diseases, decreased work productivity, biases (such as in the workplace or society), and negative perceptions.<sup>3</sup> Some of the complications from obesity may be “silent” (meaning, the patient doesn't feel different) like hypertension, or the complications may affect what the patient can do (for example, decreased ability to exercise or do activities of daily living due to breathing problems or arthritis). The decreased ability to do what the patient wants to may affect their quality of life. Health-related quality of life (HRQOL) is a concept which reflects how health (both physical and mental) impacts (both positively and negatively) our lives.<sup>12</sup>

**Obesity Complications**

Many of the complications of obesity can be categorized as either due to the physical weight changes (sometimes called “fat mass disease”) or due to the metabolic changes that happen due to excess weight (sometimes call “sick fat disease”). The effects of physical weight changes include complications such as varicose veins; increased risk of thromboembolic events such as stroke or clots; asthma; obstructive sleep apnea; osteoarthritis; and immobility. The metabolic complications include high blood pressure (hypertension), type 2 diabetes mellitus, dyslipidemia, polycystic ovarian syndrome, infertility, some types of

**Goals of Treatment**

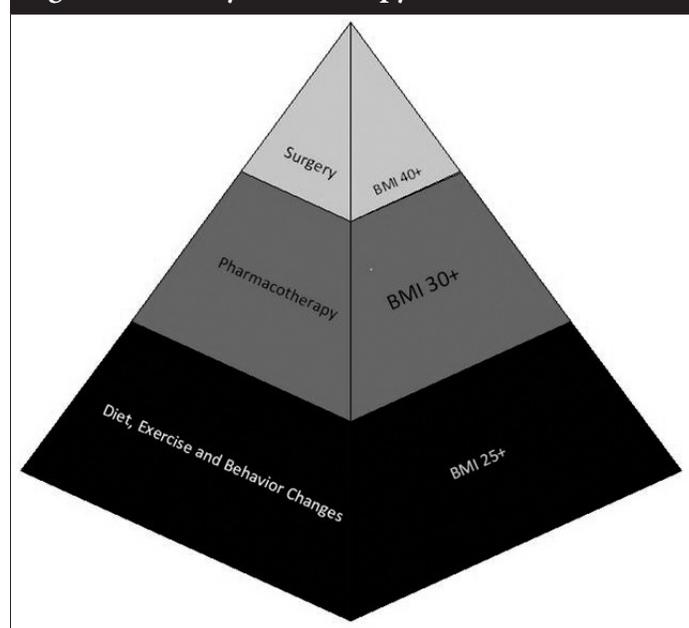
The goals of treatment for obesity or being overweight are to improve the patient's health (by reducing the presence or risk of complications), improve the patient's quality of life, and to improve the patient's body weight and body composition. By improving the patient's health or reducing the patient's weight, quality of life can improve due to psychosocial changes that follow.<sup>3</sup>

Generally, an appropriate weight loss goal is 1-2 pounds per week leading to 5-10% weight loss.<sup>13</sup> Previous studies have shown that a 10% weight loss can improve several

of the complications of obesity, including blood pressure, blood sugar and cholesterol. Many people may have more extreme weight loss goals, but this is often not realistic or appropriate.<sup>14</sup> For example, a patient, MJ, who weighs 300 pounds, should try to lose 1-2 pounds a week, so that after 3 months she now weighs 275 pounds. This is a 9% reduction in weight. If the patient is 5'6", her initial BMI is 48.4 kg/m<sup>2</sup> and her new BMI is 44.4 kg/m<sup>2</sup>. Both BMI readings place the patient in the morbidly obese category, but with this weight loss, the patient will likely still see benefit to her health or quality of life. At 5'6", MJ would need to weigh 154 pounds to have a BMI in the "normal" category. Even with different types of weight loss surgeries, which are generally called bariatric surgery, this may be a difficult weight loss to achieve, as it is nearly a 50% weight loss. Instead of focusing on the "number", it may be helpful to encourage MJ to think about what she is now able to do. She may be able to walk up stairs or dance at a wedding. Sometimes having goals of weight loss besides a number can help people keep from being frustrated.

Since improved health is also a goal of weight loss treatment, it may be appropriate to measure obesity-related comorbidities (disease that develops as a result of the original medical problem, which in this case is obesity). For example, a patient with type 2 diabetes mellitus may see improvements in blood sugar when they are measuring at home, and eventually this improvement leads to better A1C (a measure of longer-term blood sugar control) and then a decreased need for medication for diabetes. For a patient with hypertension, blood pressure may decrease and along with that, the need for medication may also decrease. Many pharmacotherapy (medication therapy) and bariatric surgery studies not only measured weight loss, but also the presence of comorbidities, control of the comorbidity, and the use of medication for the comorbidity. Additionally, studies may also measure the development of new comorbidities. Some of the medications used for weight loss have been shown to delay or decrease the onset of type 2 diabetes. The FDA requires that prior to approval, a weight-management product should be evaluated to see how it affects metabolic parameters, which measure some types of obesity-related comorbidities. Examples of metabolic parameters which should be measured include blood pressure, pulse, lipids (cholesterol), fasting glucose and A1C. Additionally, quality of life (QOL) may improve with weight loss. This is also measured in many clinical trials, and may be included in clinical trials before a medication receives FDA approval.<sup>15</sup>

**Figure 1. Obesity treatment pyramid**



## TREATMENT

Changes in lifestyle are appropriate for most people who desire to be healthier, but are specifically recommended for anyone with a BMI greater or equal to 25. Lifestyle changes may include changes in diet, exercise, and/or behavior modifications. Patients may have the best results with the combination of all three. Pharmacotherapy may be appropriate for patients with a BMI of 30 or greater, or a BMI of 27 and greater if the patient has obesity comorbidities. Bariatric surgery may be an option for patients with a BMI of 40 or greater, or 35 and greater with obesity comorbidities.<sup>13</sup> See **Figure 1**.

## Lifestyle Changes

### Diet

Many different diets have been studied for weight loss. Some options include carbohydrate-restriction ("low carb diet" such as Adkins), fat restriction ("low fat diet"), and very low calorie diets which often involve use of commercially prepared meal replacements.<sup>3</sup> Low carb diets generally involve limiting food intake so that only 50 to 150 grams of carbohydrate are eaten each day; sometimes the intake is even lower. This diet may have better initial results compared to a low fat diet, but the long-term effect may be similar.<sup>3</sup> Low-carbohydrate diets generally have a higher protein intake, which is thought to help patients feel fuller longer.<sup>16</sup>

Low fat diets generally limit the total calories from fat to 20-35%.<sup>3</sup> Low fat diets include the Ornish diet and are recommended by the American Heart Association.<sup>16</sup> These diets generally have 10-20% of calories from fat, and recommend intake of grains, fruits and vegetables.<sup>16</sup>

Very low calorie diets generally limit intake to 400-800 calories a day and may have more potential risks than other diets, but can also produce quicker weight loss than other diets; as a result, they are generally only recommended when the patient is supervised by a healthcare provider with experience monitoring these patients.<sup>3</sup>

In addition to the diets described above, the Mediterranean-type diet involves a higher intake of olive oil, nuts, and fish, as well as fruits, vegetables and whole grains. Some patients follow portion-controlled diets, which usually have meals replaced by high-protein liquid “meals.” This diet can be beneficial in that there is less meal preparation or calorie counting needed. Some patients elect to use a low-glycemic load diet. This diet recommends low-glycemic foods. Clinical trials did not result in a difference in weight loss, but there was an improvement in diabetes control.<sup>16</sup>

For the most part, as long as a patient cuts calories, any of the diets that reduce calories can result in weight loss. One study compared the Adkins, Zone, Ornish, and Weight Watchers diets and found that there was no significant difference in weight between the groups after a year, but there were differences in adherence to the diets.<sup>16</sup> Some patients may prefer one type of diet more than another, or may have a medical condition which affects which type of diet may be best for them. For a patient who is on-the-go and doesn't like cooking, a portion-control diet with meal replacements may be a good fit. A patient with high cholesterol may not be a good candidate for a low-carbohydrate diet if the patient will have a diet high in protein sources which are high in cholesterol. Patients with diabetes may see additional improvements in blood sugar if they choose a low-glycemic load diet. Regardless of the diet chosen, most patients will see weight loss with reduced portion sizes, decreased energy density in the diet (meaning choosing lower calorie foods that make you feel full rather than high calorie foods that do not provide a lasting feeling of fullness), and counting calories.<sup>16</sup>

### *Physical Activity*

In addition to potential weight loss, physical activity (exercise) can improve some cardiovascular risk factors, pulmonary health, mental health, and sexual health.<sup>3</sup> Sometimes patients get frustrated with exercise because it may not lead to much weight loss, but can change body composition so that there is less fat and more muscle. Clothes may fit better or the patient may need to wear a lower size in clothing. Exercise can also improve the patient's health even if weight is not significantly changed. It can be important to continue to encourage patients who are doing physical activity but are not seeing weight loss.

Many organizations including the Center for Disease Control (CDC), recommend at least 150 minutes/week of moderate intensity aerobic exercise plus muscle-strengthening activities twice weekly for adults. Moderate intensity aerobics would be an activity like brisk walking or doing water aerobics, which leads to a higher heart rate and the exerciser to break a sweat. If the patient does vigorous-intensity exercise like running or playing basketball, the recommendation is for 75 minutes weekly. The exercise can be broken down to 10 minute increments. For example, a patient can walk at a moderate pace for 10 minutes three times a day, five days a week. The patient could also walk for 50 minutes three days a week. For more robust weight loss and greater health benefits, patients may need to do 300 minutes/week of moderate activity or 150 minutes of vigorous intensity exercise. For some obese patients, they may have physical limitations which prevents them from doing this type of activity. These patients can do seated exercise programs or aquatic exercises, and may benefit from seeing a physical therapist to help develop an exercise plan that works for them.<sup>17</sup>

#### ***Test Your Knowledge #4***

A patient wants to get the most “bang for his buck” with exercise (biggest benefit, least amount of time needed). Which might be his best choice for exercise for weight loss and cardiovascular benefits?

- A. Play basketball
- B. Low-intensity activity like yoga
- C. Walk briskly
- D. Yard work

*Answers on page 28.*

Muscle-strengthening activities should work the major muscle groups, which include the legs, hips, back, chest, abdomen, shoulders and arms. Strength activities can be done at a gym, or at home using weights, resistance bands, body weight for resistance (such as pushups or sit ups), or with yoga.<sup>17</sup>

### *Behavior*

Behavior therapy may be helpful for patients who need education, assistance in setting goals, controlling triggers, and/or support. It may be helpful for a patient to see a medical professional such as a psychologist to better identify and manage these behaviors. This may be done by using web-based programs and mobile applications. Behavior modifications may include identification of triggers for overeating, then modifying those factors or keeping a food and beverage diary.<sup>3</sup> For example, a patient may realize that they eat more during a stressful day, or drink more calorie-filled sodas than expected. Once the patient is aware of these behaviors, they may be able to manage their diet better.

Examples of behavior modifications include:<sup>3</sup>

- Keep an exercise journal
- Set realistic goals for exercise, diet and weight loss
- Decide on healthy rewards
- Choose healthy snacks
- Weigh daily or weekly
- Set appropriate weight loss goals

One long-term study set out to evaluate intensive lifestyle intervention through diet and exercise on cardiovascular morbidity (health) and mortality (death). Patients in this study all had type 2 diabetes and were either overweight or obese adults aged 45 to 75 years. The patients were assigned to either diabetes support and education (control group) or intensive lifestyle intervention (intervention group). The intervention group had a first year minimum weight loss of 7%, with individual goals of 10% weight loss. Patients were prescribed a diet with 30% reduction in calories the first two weeks, and then calorie-specific diets based on weight. Diets changed over time, but frequently involved meal replacements and other portion control measures. Patients were started on physical activity of 50 minutes per week and increased to 175 minutes of moderate intensity exercise.<sup>18</sup> Despite these interventions, after nearly ten years, the trial was stopped early since it was unlikely to show benefit. Patients in the intervention group were more successful in weight loss (8.6%

weight loss compared to 0.7% weight loss for the control group after the first year), diabetes control, and cardiovascular risk factors, but no benefit was seen for the incidence of cardiovascular death or events.<sup>19</sup> Some have interpreted these results to mean that lifestyle interventions are not helpful to reduce cardiovascular disease; whereas others have argued that this study waited too late to begin to make changes and patients should make changes in lifestyle earlier in life.

### **Pharmacotherapy**

The general rule of thumb is that weight loss can be achieved from two simplified mechanisms: the patient can either have a decrease in caloric intake (meaning the patient eats less) or by an increase in metabolism (meaning calories are burned faster). Medications can target either alone or both mechanisms to lead to weight loss. Pharmacotherapy can be used as an adjunct (in addition) to lifestyle modifications (behavior modification, diet, and physical activity) for weight loss, as shown in **Figure 1**, among patients with a BMI greater than or equal to 30. Pharmacotherapy can also be used if the patient has a BMI of 27 or more and has an obesity-related complication such as type 2 diabetes, hypertension, or dyslipidemia.<sup>3</sup> There are several other Food and Drug Administration (FDA)-approved medications which have been studied and have been found to cause some weight loss, but are not approved by the FDA for weight loss as of August, 2014. Additionally, some herbal or complementary and alternative medications (CAM) are used for weight loss and will be discussed in this section.

Historically, some medications improved weight but had negative effects on some health-related comorbidities. Fenfluramine (Pondimin) and dexfenfluramine (Redux) were medications known as Fen-Phen which increased the risk of a change in function of heart valves called valvulopathy, which is seen on a heart test called an echocardiogram. These medications have not been available in the United States since 1997.<sup>20</sup>

Another medication was removed from the market due to negative cardiovascular effects. Sibutramine (Meridia) was a medication which caused weight loss, but also increased cardiovascular risk. Patients in one study had an increase in heart attacks, strokes, cardiac arrest and cardiovascular death. After this study was released, the FDA recommended that the medication be removed from the market.<sup>21</sup>

## Complementary and Alternative Medications (CAM)

Many different CAM products are available without a prescription. CAM products often have several different ingredients, often called a proprietary blend. These medications are not regulated the same way as prescription medications or as over-the-counter (OTC) medications. These products do not have to prove safety or efficacy before being available on the market. Often the evidence for using one of these products or ingredients comes from animal studies, or no studies at all (only historical use). There are some clinical trials of various CAM products, with varying levels of quality among the studies. Frequently, adverse effects are not fully reported, the duration of studies is usually short, and the number of participants is small.<sup>22</sup> One systematic review done in 2008 of herbal medications used for the management of obesity found only 17 randomized clinical trials out of the 915 trials reviewed. Few of the products studied reported adverse effects.<sup>23</sup> While the number of products marketed for weight loss is large, only a few will be discussed in this review. Additionally, while CAM products are commonly used (for obesity and other medical conditions), frequent use does not mean the product is safe or effective. It is important that patients be educated on the potential risks with supplements and that patients report CAM use to pharmacists and other healthcare providers.

Sometimes CAM products are removed from the market because they have additional ingredients that are prohibited by the FDA. Sometimes these are prescription drug ingredients, controlled substances, not-yet approved medications, or products which have been removed from the market or rejected by the FDA. Several recent products recalled contained sibutramine, which was a prescription medication removed from the market due to safety concerns. The FDA regularly updates the public of these products and has a website with information about potential harms from these dietary supplements. The FDA does note that since it does not test all products, additional products may also be unsafe.<sup>24</sup>

Another CAM ingredient which was used was ephedra (also called Ma Huang), which was frequently sold with other ingredients in combination products. Ephedra was historically boiled and served as a hot tea. The active chemicals of ephedra are ephedrine and pseudoephedrine. Due to concerns with elevations in blood pressure and increased cardiovascular risk, ephedra was banned by the FDA. Additionally, the substance has some psy-

chiatric, autonomic and gastrointestinal adverse effects.<sup>22</sup> Caffeine, a stimulant, is often included in combination products. Many sources of caffeine are found in Western diets, such as coffee, tea, soda and energy drinks. The amount of caffeine in drinks varies on the product and the way the drink is made. An average 8-ounce cup of coffee may contain 100 mg of caffeine. Caffeine is a well-known central nervous system (CNS) stimulant, with effects on mood, alertness, and physical activity. Many of the clinical studies of caffeine used combination products, often with ephedra. One study compared placebo to caffeine 200 mg three times a day plus ephedra 20 mg three times a day, and showed benefit with weight loss. Another study followed people who consumed caffeine and over 12 years showed a benefit to consuming caffeine on reduced weight gain. The studies which show weight benefits generally used more than 300 mg daily of caffeine. Doses greater than 300 mg daily tended to be associated with caffeine's adverse effects, which include tremors, insomnia, and dizziness. Additionally, some of the caffeine dietary sources may have had calories, which negated weight loss potential.<sup>22</sup>

Teas are consumed for potential health benefits, in addition to the potential weight loss from caffeine which is found in teas. *Camellia sinensis* is a tea plant and its leaves are processed to become green tea, black tea or oolong tea. Teas have potential antioxidative, anticarcinogenic (cancer), antidiabetogenic (diabetes), and antiobesogenic (obesity) effects. These effects are thought to come from the polyphenolic compounds called catechins. A review (meta-analysis) of clinical trials showed a small benefit of green tea catechin-caffeine mixtures in preventing weight gain, however, not all studies showed benefit.<sup>22</sup>

The Chinese herbal ginseng has been used for weight loss, and has documented use going back thousands of years. There are different types of ginseng extracts, but the American ginseng (*Panax quinquefolius*) is traditionally used as a stimulant, and animal studies have suggested potential weight loss by reducing food intake.<sup>22</sup>

*Cissus quadrangularis* (CQ) is a vine found in west Africa and southeast Asia. In one study, when the herb was combined with *Irvingia gabonensis*, patients taking the combination had a reduction in body weight and waist circumference.<sup>22</sup>

## Medications Which Can Cause Weight Loss

Some medications which may positively influence weight (leading to some amount of weight loss) include some diabetes medications, as well as some neurologic agents, which primarily work in the brain. The diabetes medications include the biguanide metformin (Glucophage); glucagon-like peptide-1 (GLP-1) agonists exenatide (Byetta) and liraglutide (Victoza); and a new class of medications, the sodium glucose co-transporter 2 (SLGT2) inhibitors canagliflozin (Invokana) and dapagliflozin (Farxiga).<sup>3</sup> Neurologic agents topiramate (Topamax)<sup>25</sup> and bupropion (Wellbutrin) also have weight loss benefits. Topiramate is available in a combination pill (Qsymia) with phentermine (Adipex) for weight loss and is discussed below.<sup>3</sup> A combination product containing bupropion and naloxone is under investigation for its weight loss potential. Sometimes these medications are used “off-label” (non-FDA approved) for their weight loss effect in patients who do not have the disease for which they were FDA approved. Other times they may be an appropriate medication to treat the patient’s medical condition with an extra benefit of weight loss.

## FDA-approved Medications for Weight Loss

The FDA approves medications for use in the U.S. and also regulates medications’ safe use. There are several medications which are approved for short-term use (a few weeks), and three medications approved for long-term use (studied up to 2 to 4 years depending on the medication).<sup>3,26-31</sup> See **Table 4**. While these medications undergo similar FDA approval processes proving safety and efficacy, many insurance companies do not cover weight loss medications like other chronic medications, so frequently patients will have to pay for these medications out of pocket.<sup>32</sup>

The FDA has categorized all pharmacotherapy medications for weight loss as Pregnancy Category X, meaning the risk to the fetus outweighs the benefits of the medication, and therefore pregnant women should not use these medications. All pharmacotherapy medications are Pregnancy Category X since pregnant women should not generally be attempting weight loss during pregnancy, although some of the medications have additional risks in pregnancy.<sup>26-31</sup>

## Short-term Medications

There are several sympathomimetic amines which are FDA-approved for short-term use only. Phentermine and diethylpropion will be discussed with detail in this section. Phendimetrazine and benzphetamine are also available but less commonly prescribed and will not be discussed. These medications are also regulated by the Drug Enforcement Administration (DEA) as Schedule III medications. All of the short-term medications act by increasing satiety (making the patient feel full). Since these have stimulating properties, their common adverse effects include insomnia, palpitations, tachycardia, and increased blood pressure.<sup>3</sup>

### Phentermine

Phentermine (Adipex-P) was initially approved for use in the U.S. in 1959, and is generically available as both 37.5 mg tablets and capsules.<sup>29</sup> Additionally, an orally disintegrating tablet (ODT) is available in 10 mg, 30 mg and 37.5 mg strengths as Suprenza.<sup>30</sup> All formulations of phentermine monotherapy are approved only for short-term use (a few weeks) and not for long-term use. Phentermine is a sympathomimetic amine and has similar activity to amphetamine. It is generally classified as an anorectic, and may work by suppressing appetite, although its precise mechanism is not fully known. Phentermine is a Schedule IV controlled substance federally, given its similar effect to amphetamines which are stimulants.<sup>29-30</sup>

Phentermine’s recommended dose is 37.5 mg once daily before breakfast or 1-2 hours after breakfast. The dose may be lowered to ½ tablet daily, and some patients take ½ tablet twice daily.<sup>29</sup> Phentermine ODT should be placed on the top of the tongue where it dissolves. It can then be swallowed with or without water.<sup>30</sup> Phentermine is approved for ages 17 years and up.<sup>29-30</sup>

Phentermine has several contraindications that prevent many patients from being able to take it. Phentermine should not be used in patients who are pregnant, nursing, have glaucoma, hyperthyroidism, or a history of hypersensitivity reactions to sympathomimetic amines such as pseudoephedrine or amphetamine. Patients with a history of drug abuse or have an agitated state should not use the product either. Phentermine must also be separated from monoamine oxidase inhibitors (MAOIs) by at least 14 days. Examples of MAOIs are provided in **Table 5**. Any patient with a history of cardiovascular disease should not take phentermine, and

included in this category is anyone with a history of coronary artery disease (a heart attack or stent, for example), stroke, arrhythmias (abnormal heart rate/rhythm), congestive heart failure, or hypertension.<sup>29-30</sup> Given the high rate of hypertension among patients with obesity, this limits its use significantly since phentermine can worsen blood pressure. Additionally, the medication has a warning regarding the risk of pulmonary hypertension and valvular heart disease. Common adverse effects include overstimulation, restlessness, tachycardia, and increased blood pressure.<sup>29-30</sup>

The FDA-approved prescribing information limits the use of phentermine to short term use.<sup>29-30</sup> In one early study, phentermine was studied for 36 weeks, comparing its use with placebo and an alternating placebo and phentermine regimen. Among those given placebo who completed the study, they lost an average of 10.5 pounds (4.8 kg), but those given phentermine lost 27 pounds (12.2 kg) and those given alternating phentermine and placebo lost 28.7 pounds (13 kg). This study only reported weight loss among those who completed the trial and was published in 1968.<sup>33</sup> In this trial, six participants withdrew due to adverse reactions related to central nervous system (CNS) stimulation, with symptoms such as insomnia, irritability, agitation, tension and anxiety.<sup>33</sup>

### Diethylpropion

Diethylpropion has a similar mechanism of action as phentermine and has similar contraindications and precautions for use. It is also a Schedule IV federally controlled substance. Diethylpropion is chemically similar to bupropion, the antidepressant, and must be used with severe caution when given to patients with epilepsy (seizures). It is dosed as one 75 mg controlled release tablet daily, taken in the mid-morning. Since the tablet is controlled release, it should not be cut in half or crushed.<sup>31</sup>

### *Long-term Medications*

There are three medications that are currently approved by the FDA as adjunct (in addition) to lifestyle modifications for long-term weight loss. These three medications, with orlistat having two different products, and their dosage forms, strengths, usual doses, generic availability, controlled substance status, and prescription status are provided in **Table 4**.<sup>26-28,34</sup>

### Orlistat

Orlistat (Xenical/Alli) is a gastrointestinal lipase inhibitor, first FDA-approved in 1999. It decreases the absorption of fat in the small intestines. By reducing the amount of fat absorbed, fewer calories are absorbed from a given

**Table 4. Medications FDA-approved for long-term weight loss**<sup>26-28,34</sup>

Generic Name	Trade Name	Dosage Form	Tablet/Capsule Size(s)	Usual Dosage Range	Generic Availability?	Controlled Substance?	Prescription or OTC?
orlistat	Xenical	Capsule	120 mg	120 mg TID with meals	No	No	Rx
orlistat	Alli	Capsule	60 mg	60 mg TID with meals	No	No	OTC
lorcaserin	Belviq	Tablet	10 mg	10 mg BID	No	Yes: C IV	Rx
phentermine/topiramate	Qsymia	Extended-release capsule	<ul style="list-style-type: none"> <li>• 3.75 mg/23 mg</li> <li>• 7.5 mg/46 mg</li> <li>• 11.25 mg/69 mg</li> <li>• 15 mg/92 mg</li> </ul>	3.75 mg/23 mg initially; titrate to 15 mg/92 mg once daily	No	Yes: C IV	Rx

TID= three times a day; Rx=prescription; OTC=over the counter; BID=twice daily; C IV= controlled substance category IV (four) by federal law

meal. Orlistat itself is minimally absorbed, so most of its drug-drug interactions and adverse effects occur in the gastrointestinal track, rather than in the rest of the body. Unlike many medications, no dose adjustment is recommended for patients with kidney or liver disease, since the medication has limited absorption. If a drug is not significantly absorbed, then there is minimal concentration in the blood to be eliminated through the kidneys via filtration or liver via metabolism.<sup>26</sup>

Orlistat is the only weight loss medication approved by the FDA for OTC sale. The OTC orlistat is a lower dose than the prescription-only version of orlistat and is sold under the brand name of Alli; prescription-only orlistat is marketed as Xenical.<sup>26,34</sup> Orlistat should be taken three times a day with a main meal, however if the meal is a high-fat meal, the patient may experience significant adverse effects related to its mechanism of action. Since the drug works by blocking the absorption of fat, the fat that is not absorbed passes on to the stool. The most common adverse effects with orlistat are fatty/oily stool, fecal urgency, oily spotting, flatus with discharge and increased defecation. Most of these adverse effects can be decreased by limiting the amount of fat in the meal to less than 30% of the daily calories or by increasing dietary fiber, although some patients (8% in studies) will find these adverse effects to be bothersome enough to discontinue the medication. In addition to these side effects from orlistat, rare adverse events include urolithiasis (urinary or bladder stones) and cholelithiasis (gallstones). Rarely, liver injury has occurred with orlistat use.<sup>35</sup>

Due to the mechanism of orlistat, use of orlistat can decrease absorption of fat-soluble vitamins (A, D, E, and K), as well as beta-carotene. These vitamins should be supplemented with a multivitamin to prevent vitamin deficiencies, but patients should separate the multivitamin from orlistat by at least 2 hours. In addition to decreased absorption of fat-soluble vitamins, orlistat may decrease the amount or effect of medications such as cyclosporine, levothyroxine and warfarin. The concentrations of cyclosporine, the clinical effect of levothyroxine (by thyroid function monitoring) and the clinical effect of warfarin (by monitoring anticoagulation with international normalized ratio [INR]) should be monitored while the patient uses orlistat. Since orlistat can be purchased without a prescription, patients should be encouraged to tell all providers that they are taking the medication.<sup>26</sup>

In clinical studies of orlistat, orlistat has a relatively small effect on weight. One study saw a 3.69 kg (8.2 pound)

weight loss with orlistat compared to placebo at 24 weeks. This net benefit of orlistat is about 1/3 a pound a week. Among several year-long studies of orlistat, the net weight loss difference between placebo and orlistat was 3%. This means if two people weigh the same and one takes placebo and the other orlistat, the patient taking orlistat can expect to lose 3% more of their baseline weight than the patient taking placebo. In one study, 42.6% of patients taking orlistat lost at least 5% of their weight, compared to 22.4% with placebo. In the same study, 17.7% of patients taking orlistat lost at least 10% of their weight compared to 9.9% with placebo. For most people, their weight loss goal should be 5-10% of their baseline weight, so less than half of the patients in the studies met this goal.<sup>35</sup>

In addition to weight loss, orlistat has shown some benefits in improving some of obesity's complications. Improvements have been seen in cholesterol levels, delaying the onset of type 2 diabetes, improving blood sugar control in patients with type 2 diabetes, and blood pressure in patients with hypertension. These additional benefits in some of the obesity-related comorbidities may reduce cardiovascular disease, although no studies have been done to evaluate this. Orlistat has been studied for use up to four years, so long-term use is safe.<sup>26</sup>

Given the relatively small amount of weight loss with orlistat, and the common frequency of adverse effects, many patients may not be willing to continue to take the medication. It is important that patients have realistic expectations for weight loss and side effects with orlistat. There is a support program for patients who take Alli called myalliplan<sup>®</sup>, as well as an online community forum for users.<sup>36</sup>

### ***Test Your Knowledge #5***

Case example: Ashley has a BMI of 42 and is thinking about starting orlistat over the counter. Which medications would not be expected to have the potential to be affected by her taking orlistat?

- A. Levothyroxine
- B. Vitamin D
- C. Vitamin B
- D. Warfarin

*Answers on page 28.*

## Lorcaserin

Lorcaserin (Belviq) is a selective serotonin 2c (5-HT<sub>2c</sub>) receptor agonist (stimulates receptor). Serotonin 2c receptors are found in the brain. This receptor regulates food intake, so patients taking serotonin 2c receptor agonists can expect to feel less hungry, and therefore eat less. There are different types of serotonin receptors, and other receptors can have different effects that can lead to potentially serious side effects. Serotonin 2A receptors, if activated, could lead to hallucinations and activation of 5-HT<sub>2B</sub> may lead to heart valve disease (valvulopathy) and pulmonary hypertension. Both valvulopathy and pulmonary hypertension are very serious problems and were adverse effects of a weight loss product which activated 5-HT<sub>2B</sub> that is no longer available. Studies have shown that lorcaserin was much more selective for 5-HT<sub>2C</sub> than 5-HT<sub>2A</sub> and 5-HT<sub>2B</sub>, but the FDA will be monitoring closely for these effects.<sup>28,32</sup>

Because lorcaserin is a selective serotonin 2c receptor agonist, there is a potential interaction with other medications that affect serotonin. Other serotonergic medications include selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, monoamine oxidase inhibitors, triptans, bupropion, dextromethorphan, meperidine (Demerol) and St. John's Wort. Many of these medications are used for depression and anxiety (and other conditions), although triptans are used for migraines, dextromethorphan is an OTC cold and cough ingredient, and meperidine is a pain medicine. If more than one serotonergic medication is used at the same time, the patient may have a rare but serious event called serotonin syndrome.<sup>28,32</sup>

Examples of serotonergic medications are provided in **Table 5**.<sup>28,32,37</sup> Serotonin syndrome symptoms include agitation, diarrhea, a fast heartbeat, high blood pressure, an increase in temperature, overactive reflexes, and nausea and vomiting. Serotonin syndrome can be an emergency and if patients have these symptoms, they should contact their healthcare provider immediately.<sup>38</sup>

Lorcaserin is dosed as 10 mg (one tablet) twice daily. Patients can take lorcaserin with or without food. Lorcaserin can be taken by people with kidney or liver disease, but if it is severe, use of lorcaserin should be done with caution or should be avoided.<sup>28,32</sup>

Lorcaserin is a controlled substance (category IV federally). As a result, only a maximum 30 day supply can be

**Table 5. Examples of Potential Drug-Drug Interactions with Lorcaserin**<sup>28,32,37</sup>

Class of Medication	Examples
selective serotonin reuptake inhibitors (SSRI)	fluoxetine (Prozac) citalopram (Celexa) sertraline (Zoloft) paroxetine (Paxil)
serotonin-norepinephrine reuptake inhibitors (SNRI)	venlafaxine (Effexor) duloxetine (Cymbalta) milnacipran (Savella)
monoamine oxidase inhibitors (MAOI)	phenelzine (Nardil) selegiline (Emsam and others) tranylcypromine (Parnate)
triptans (also called serotonin 5-HT <sub>1B</sub> , 1D receptor agonists)	eletriptan (Relpax) sumatriptan (Imitrex) zolmitriptan (Zomig)
Note: list of examples is not complete, as there are several options in these classes of medications	

dispensed at one time and the prescription is only good for 6 months after the initial date of the prescription, according to federal law.<sup>28,32</sup>

In clinical trials, lorcaserin was studied up to 104 weeks. In this study, after 52 weeks, the mean percent weight loss was 5.81% with lorcaserin, compared to 2.16% with placebo, which is a net percent weight loss of 3.65%. This is similar to the percent weight loss with orlistat. In this trial, 47.5% of patients taking lorcaserin lost at least 5% of their baseline weight at 52 weeks, compared to 20.3% with placebo. The percent who lost at least 10% of baseline weight at 52 weeks was 22.6% with lorcaserin and 7.7% with placebo. The mean weight loss after 52 weeks in this trial was 5.8 kg (12.76 pounds) with lorcaserin compared to 2.2 kg (4.84 pounds) with placebo (net weight loss of 3.6 kg [7.92 pounds]). This study reassigned some patients who originally received lorcaserin to placebo after the first 52 weeks, whereas other patients continued to take their originally assigned medication of either lorcaserin or placebo. The patients who were reassigned to placebo for the second half of the study ended up with no difference in weight loss from the original placebo arm. This means that with lorcaserin, patients can expect to lose an average of 8 pounds more than doing lifestyle alone, and once they stop taking the medication, their weight will be about what it would have been if they had never started taking lorcaserin, but just attempted to lose

weight with lifestyle modifications. Among several of the clinical trials of lorcaserin, the bulk of the weight loss was by 12 weeks, but patients continued to lose a little more weight, until about week 32-40, at which time the weight loss plateaued.

If patients do not lose at least 5% of their baseline weight by 12 weeks, they should stop taking the medication since significant additional weight loss is unlikely.<sup>28,32</sup>

### Test Your Knowledge #6

Case example: Heather weighs 190 pounds and is 65 inches tall (BMI=31.6 kg/m<sup>2</sup>). She has tried diet and exercise and initially lost 5 pounds, but after several months, she regained the 5 pounds and weighs 193 pounds. Her doctor decides she might benefit from lorcaserin. She started taking it on New Year's Day as part of a New Year's resolution. After 3 months, she comes in for an evaluation and her current weight is 188 pounds. Should she continue to take lorcaserin?

\_\_\_\_\_

\_\_\_\_\_

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Answers on page 28.

Lorcaserin has potential benefits in addition to weight loss. These cardiovascular and metabolic risk marker changes were not consistently seen in all clinical trials, but there may be benefits for blood pressure, total cholesterol, low density lipoprotein (LDL), triglycerides, high density lipoprotein (HDL), and hemoglobin A1C. Some patients are able to stop taking hypertension, cholesterol and/or diabetes medications while on lorcaserin. Patients were also surveyed with the Impact of Weight on Quality of Life-Lite (IWQOL-Lite) tool. IWQOL-Lite measures perception of how weight affects day-to-day life. Patients who took lorcaserin had inconsistent improvement in scores in the different studies.<sup>28,32</sup>

In addition to the more theoretical concerns with valvulopathy and serotonin syndrome, the common adverse effects of lorcaserin in clinical trials were headache, nausea, dizziness, back pain and nasopharyngitis (also known as the common cold). Some patients with diabetes may see

an improvement in their blood sugar while taking lorcaserin; for some patients this lowering of blood sugar may lead to symptomatic hypoglycemia (low blood sugar).<sup>28,32</sup>

### Phentermine/topiramate

Qsymia is a combination product first FDA approved in 2012 which contains phentermine and topiramate extended-release (ER).<sup>27</sup> Phentermine's weight loss effects and mechanism have already been described above. Topiramate is a medication already available as Topamax to treat epilepsy and for migraine prophylaxis to prevent migraine headaches in patients who have them frequently.<sup>25</sup> One of topiramate's "adverse reactions" noted in clinical trials was weight loss.<sup>25</sup> As a result, some providers would use topiramate "off label" or in patients with migraines or epilepsy who could benefit from weight loss. The mechanism of topiramate's weight loss is not known, but is thought to be related to appetite suppression and making the patient feel full (satiety). Topiramate has multiple properties and sites of action including sodium channels, gamma-aminobutyrate (GABA) receptors, glutamate receptors, and carbonic anhydrase enzymes.<sup>25,27</sup>

The doses of phentermine and topiramate in Qsymia are different than the doses for the individual products, and Topamax is not an ER formulation. Qsymia is available as capsules. The Qsymia dose titration schedule is somewhat complex, so it is provided in **Table 6**.<sup>27</sup>

Qsymia should be taken once daily in the morning; if taken at night, it may cause insomnia. Qsymia can be taken with or without food. Patients should start at the lowest dose (3.75 mg/23 mg) for two weeks, and then increase to the next dose (7.5 mg/46 mg). Patients will take the 7.5 mg/46 mg dose for 12 weeks, and then will be evaluated by their prescriber to see how effective the medication is. If the patient has not lost at least 3% of their baseline

**Table 6. Qsymia Dose Titration Schedule<sup>27</sup>**

Phentermine	Topiramate (ER)	Length of use
3.75 mg	23 mg	14 days
7.5 mg	46 mg	12 weeks; then evaluate dose
11.25 mg	69 mg	14 days
15 mg	92 mg	12 weeks; then evaluate dose
ER=extended release		

body weight, then the patient can either discontinue Qsymia or increase the dose further. If the patient and provider agree to increase the dose, then the patient takes the 11.25 mg/69 mg capsules for 14 days, then increases to 15 mg/92 mg. The patient should be evaluated by their prescriber after 12 weeks of taking 15 mg/92 mg. If the patient has not lost at least 5% of their baseline bodyweight, then the patient should discontinue Qsymia. Both the 3.75 mg/23 mg and 11.25 mg/69 mg capsules are only for titrating to the next higher dose. Since the 3.75 mg/23 mg dose is only taken for two weeks, it is available in bottles of 14 for easy dispensing, as well as a starter pack which has 14 capsules of each of the two lower doses. There is also a dose escalation pack which has 28 total capsules of the 11.25 mg/69 mg and 15 mg/92 mg capsules.

If a patient needs to discontinue the 15 mg/92 mg strength, then the patient should not stop the medication abruptly. The patient should take the dose every other day for at least one week to prevent precipitating a seizure. The dose of Qsymia should be adjusted for renal and hepatic impairment.<sup>27</sup>

Qsymia should not be used in patients who are pregnant, have glaucoma, hyperthyroidism, or a history of hypersensitivity reactions to sympathomimetic amines. Qsymia must also be separated from MAOIs by at least 14 days. Additional warnings and precautions for Qsymia include the risk of increased heart rate, suicidal ideations and behavior, acute glaucoma, mood and sleep disorders, cognitive impairment, metabolic acidosis, increased creatinine, and hypoglycemia among patients taking anti-diabetic medications. The most common adverse effects of Qsymia are paresthesia (abnormal skin sensations, especially tingling in the hands, feet or face), dizziness, dysgeusia (changes in taste sensation, especially a metallic taste), insomnia, constipation, and dry mouth.<sup>27</sup>

Topiramate exposure in the first trimester of pregnancy has been shown to increase the risk of oral clefts (cleft lip and/or cleft palate). Like all weight loss medications, Qsymia is a Pregnancy Category X medication, but it has additional restrictions and recommendations to reduce the risk of fetal harm. Since the risk of oral clefts occurs early in pregnancy, female patients should have a negative pregnancy test prior to starting Qsymia, then every month while taking the medication. Female patients also need to use effective contraception during therapy. Qsymia also has a Risk Evaluation and Mitigation Strategy (REMS).<sup>27</sup> This REMS requires that the medication

only be dispensed by certified pharmacies, who must process the prescription through the pharmacy management system. Some pharmacies are also mail-order pharmacies. These pharmacies must complete the Pharmacy Training Program and Knowledge Assessment, and then complete the enrollment process. All prescriptions must be dispensed with a Medication Guide and the Risk of Birth Defects with Qsymia brochure, regardless of patient age or sex. The prescriber must be enrolled in the REMS program, as well as the patient.<sup>39</sup> In addition to the dispensing regulations from the REMS, Qsymia is also a Schedule IV federally drug due to the phentermine component, so DEA regulations apply and dispensing limitations are the same as those for lorcaserin which were described above.<sup>27</sup>

Although women should be using effective contraception, women taking oral contraceptives may have irregular bleeding while taking Qsymia; the interaction does not appear to increase the risk of pregnancy, though, and women should continue to take the oral contraceptive. Since one of the adverse effects of Qsymia is cognitive (mental) impairment, medications which are central nervous system depressants (including alcohol) should be avoided to reduce this risk. Examples of CNS depressants include barbiturates, benzodiazepines, and many sleep medications. Because topiramate inhibits carbonic anhydrase, it can lower serum potassium (hypokalemia) and this risk is higher among those who are taking a diuretic with hypokalemia risk. These diuretics include commonly prescribed medications such as furosemide and hydrochlorothiazide.<sup>27,32</sup>

Qsymia efficacy has been evaluated in three large clinical trials, with the longest trial lasting 108 weeks. In these trials, low-dose and high-dose Qsymia were compared to placebo. In the EQUIP study, 66.7% of patients taking high-dose Qsymia achieved at least 5% weight loss and 47.2% achieved at least 10% weight loss after 56 weeks.<sup>40</sup> Patients taking high-dose Qsymia lost a mean (average) of 10.9% of their baseline body weight. Weight loss with low-dose Qsymia was not as much as with the higher dose. In the CONQUER trial, percent weight loss was similar, and the mean weight loss with high-dose Qsymia was 10.2 kg (22.4 pounds), compared to 1.2 kg (2.64 pounds) with placebo.<sup>41</sup>

In addition to weight loss, high-dose Qsymia was associated with improvements in blood pressure, fasting blood glucose, triglycerides, total cholesterol, LDL cho-

lesterol and HDL cholesterol, although some of these benefits were not seen in the second year of treatment in the SEQUEL trial. In this 108-week trial, among patients without type 2 diabetes at baseline, fewer patients given Qsymia developed type 2 diabetes compared to placebo.<sup>42</sup> Additionally, the use of medications for hypertension, dyslipidemia and diabetes decreased in clinical studies.<sup>32</sup>

### Test Your Knowledge #7

Case example: HP is a 38 year old female who presents to the pharmacy with a prescription for Qsymia. The pharmacy is not enrolled in the Qsymia REMS program, but the patient states that because she has had her “tubes tied” and can’t get pregnant, she doesn’t think she has to “jump through those hoops.” What should you tell the patient?

- You’re right. We’ll get that filled immediately.
- The patient can get the prescription filled wherever she wants as long as she and the prescriber are enrolled in the Qsymia REMS program.
- The pharmacy, the patient, and the prescriber have to be enrolled in the Qsymia REMS program. It doesn’t matter if she can get pregnant or not.

Answers on page 28.

## Bariatric Surgery

When lifestyle changes and medication are unsuccessful in achieving weight loss goals, bariatric surgery may be an option for patients to lose more weight. Different organizations have different criteria for surgical eligibility, but in general, patients whose BMI is greater than 35 (or 30 with some guidelines) with obesity-related comorbidities or whose BMI is greater than 40 are potential bariatric surgery candidates.<sup>3,43</sup>

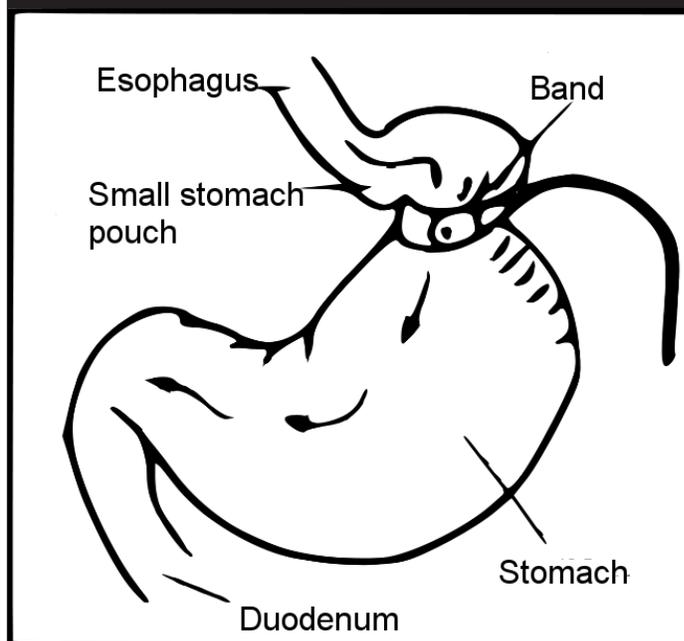
Prior to surgery, patients should have several different evaluations to make sure they are an appropriate candidate for surgery. These include medical, surgical, mental health, nutritional and educational evaluations. Additionally, depending on the patient’s past medical history and risk factors, additional evaluations like cardiology, pulmonology and gastroenterology may be needed.<sup>3,43</sup>

## Types of Surgery

The most common types of surgery are gastric banding (with products such as Lap-Band and Realize bands), vertical sleeve gastrectomy, and gastric bypass. Surgeries can either be done laparoscopically (meaning a small incision is made and then a telescope is used to help the surgeon see the internal organs) or open (meaning a larger cut is made). All surgeries have risk for acute complications such as deep vein thrombosis, infection, gastrointestinal bleeding and death.<sup>3,43</sup>

Gastric banding surgery is usually done laparoscopically, where a band is placed around the upper part of the stomach to make a smaller pouch (see **Figure 2**). This is considered a “restrictive” procedure since the band restricts the size of the stomach pouch. The band is adjustable (there is a small port through which saline can be added or removed to make the pouch smaller or larger). Because it is adjustable, the pouch can be made larger in case the patient needs a short-term change (for example, in pregnancy). Gastric banding is generally an outpatient procedure and does not have some of the nutritional complications other bariatric surgeries may have, but device-related complications are possible (such as band slippage, ulceration, and port infection). Banding surgery is more likely to be associated with weight gain or no weight loss.<sup>3,43</sup>

Figure 2. Gastric Banding Surgery



Source: [http://commons.wikimedia.org/wiki/File:Adjustable\\_gastric\\_banding](http://commons.wikimedia.org/wiki/File:Adjustable_gastric_banding). November 14, 2010. Steven Fruitsmaak.

Sleeve gastrectomy is a type of surgery where a part of the stomach is removed, leaving a sleeve or tube-like structure which is approximately 25% of the previous size of the stomach. See **Figure 3**. This procedure is also considered restrictive, but is more restrictive than gastric banding. This surgery usually involves a hospital stay. Some nutritional complications, such as calcium, iron, protein, and vitamin deficiencies are possible. Additionally, procedure related complications such as fistulas (an abnormal connection between an organ, vessel, or intestine and another structure), esophageal dilation, and gallstones are possible.<sup>3,43</sup>

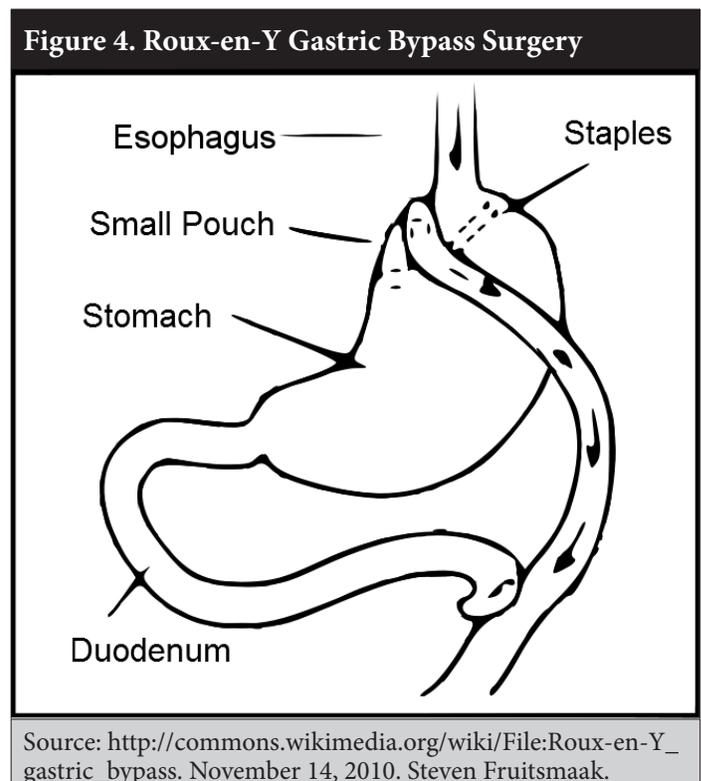
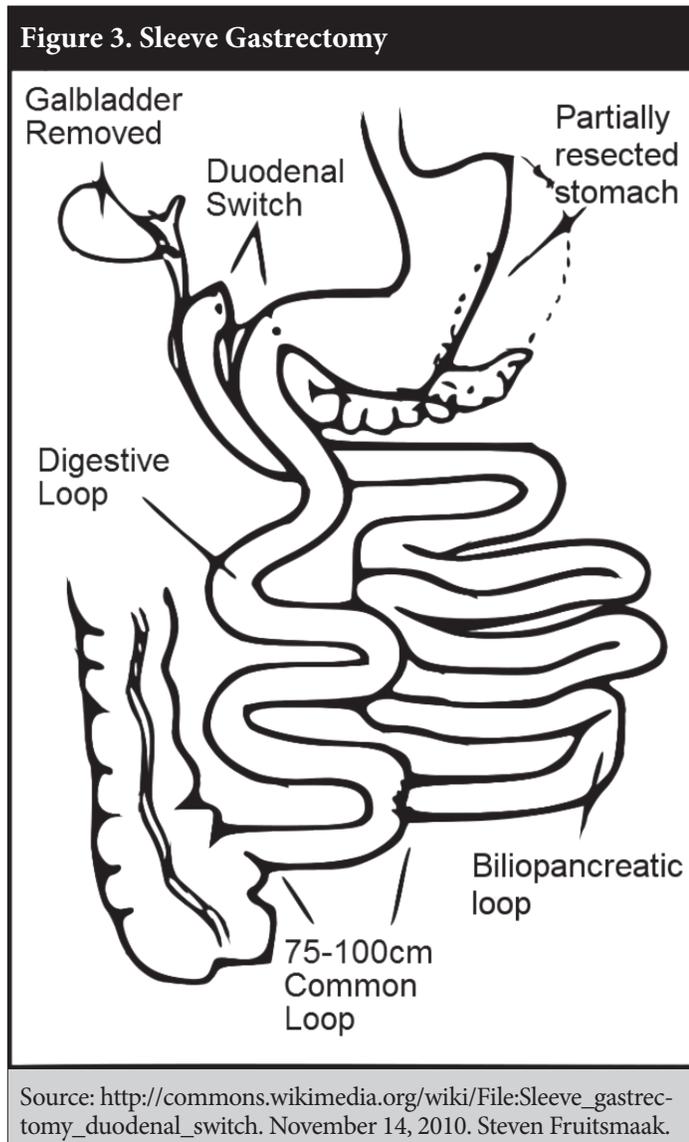
Gastric bypass is a combination restrictive and malabsorptive procedure, where the stomach is cut to make a smaller pouch attached to a now-slightly shorter small intestine, with part of the duodenum removed. This com-

mon form of gastric bypass surgery is called a Roux-en-Y gastric bypass and is shown in **Figure 4**. This surgery also needs a hospitalization and has many of the same complications as sleeve gastrectomy, although there is greater risk for many of the complications, especially related to nutritional deficiencies as a result of the reduced small intestine size.<sup>3,43</sup>

### Benefits and Risks of Surgery

On average, patients who have bariatric surgery lose between 20-35% of their weight after 2-3 years. At 10 years, weight loss of 16% was maintained in one study, the Swedish Obese Subjects (SOS) study.<sup>44</sup> This study compared patients who had surgery to matched control patients who did not. Patients who had surgery had a reduced rate of cardiovascular death, first cardiovascular event, and improvements in diabetes, cancer and overall mortality. There were increased risks with surgery, which included post-op complications (bleeding, embolism/thrombosis, and wounds/infections). In the 90 days post-operation, the rate of death was higher for surgery compared to control. While the immediate risk of death was increased, the long-term mortality was improved.<sup>44-46</sup>

Prior to surgery, efforts to reduce complication risk should be made. Prior to surgery clearance, chronic



conditions should be managed if possible. Patients with diabetes should work with healthcare providers to control their blood sugar, blood pressure and cholesterol. Patients who smoke should be encouraged to quit and provided smoking cessation services. Additionally, medications which increase complications should be avoided, including estrogen. In the hospital, patients will need venous thromboembolism (VTE) prophylaxis and antimicrobial prophylaxis with antibiotics.<sup>3,43</sup>

Nutritional complications after bariatric surgery are possible as with any surgery type, but it is especially common for patients to develop B12, iron, and thiamine deficiency after gastric bypass surgery. Less common deficiencies are folate, fat-soluble vitamin (A, D, E, K) and calcium. Severe malnutrition and fat malabsorption are also possible but less common.<sup>47</sup> All bariatric patients will need to be monitored for the presence of iron and B12 deficiencies. Folic acid, iron studies, vitamin D, and parathyroid monitoring is recommended for patients who have had gastric bypass. Additionally, all bariatric patients should take a multivitamin with folic acid, thiamine and copper to prevent deficiencies. Some vitamins may not be absorbed in the same way as prior to surgery. Calcium is better absorbed if given as calcium citrate. Oral B12 may not be absorbed adequately, so intranasal or parenteral B12 may be needed.<sup>43</sup>

### Post-Surgery Management

After surgery, often obesity complications begin to improve. This means patients' need for medications to control these conditions will decrease. For example, insulin doses will likely decrease or maybe even no longer needed. For patients who have gastric bypass, their changes in gastrointestinal physiology may lead to some pharmacokinetic changes with some medications. The changes in pH, small intestine length, and gastrointestinal enzymes can affect absorption of the drug into the body as well as metabolism. The knowledge of specific changes with medications is still an evolving science, but some basic principles are recommended. Due to increased risk of GI ulceration, nonsteroidal anti-inflammatory drugs (NSAIDs) and aspirin should be avoided. NSAIDs include common OTC medications like ibuprofen (Motrin and Advil) and naproxen (Aleve), as well as prescription medications often used to treat pain and inflammation. Oral bisphosphonates, which are used to treat and prevent osteoporosis, should be avoided. Due to the decreased intestinal length after gastric bypass surgery, ex-

tended-release and delayed-release medications may not be dissolved or absorbed in the manner expected with that formulation so they may not have the intended effect. Additionally, medications which are enteric or film-coated may not dissolve correctly in patients after gastric bypass surgery. Some medications may have a shorter GI transit time (less time in the GI tract due to shorter intestines), so may not have enough time to fully dissolve or absorb. As a result, sometimes oral solutions and suspensions are preferred over tablets or capsules. Some medications are also given as sublingual (under the tongue) or injectable formulations to avoid dissolution and absorption issues.<sup>48</sup> A review of medications to avoid after surgery is provided in **Table 7**.<sup>43</sup> Most medications should be monitored closely after surgery to ensure the patient still has the same need for the medication and that the benefit is still seen.

In one study, one year post-bariatric surgery, there was a 76% reduction in diabetes medication use, a 51% reduction in hypertension medication use, and a 59% reduction in dyslipidemia medication use. There was minimal change in the use of thyroid, antihistamine, or antidepressants.<sup>49</sup> Warfarin (Coumadin) is a blood thinner which is monitored with a test called international normalized ratio (INR) to see if dose changes are needed. In patients who had bariatric surgery at one site, 74.1% of patients needed warfarin dose decreases of at least 20%, compared to 32.2% of control patients.<sup>50</sup>

Pregnancy after bariatric surgery needs to be monitored for closely. Guidelines recommend against pregnancy in the first 12 to 18 months after bariatric surgery. Of note, patients who have gastric bypass may be especially at risk

**Table 7. Medications to Avoid after Bariatric Surgery<sup>43</sup>**

Medication Class or Property	Example
NSAIDS	ibuprofen, naproxen, aspirin
Bisphosphonates	alendronate (Fosamax), ibandronate (Boniva)
Extended- or delayed-release medications	metformin XR (Glucophage XR), bupropion XL (Wellbutrin XL)
Enteric- or film-coated medications	enteric coated Bayer aspirin, some fish oil and garlic supplements
XR=extended release; XL= extended release	

for unintentional pregnancy as they may see decreased efficacy from oral contraceptives. When a patient is pregnant, there is a need for increased monitoring for nutritional complications during each trimester. Patients who have had gastric banding surgery may need additional band adjustments.<sup>3,43</sup>

## PEDIATRIC OBESITY

Pediatric obesity is also a public health problem.<sup>51</sup> Children are assessed by measuring BMI, with the same calculation used for adults, but the criteria for obesity are based on BMI-for age percentile, using the CDC's BMI-for-age growth charts ([http://www.cdc.gov/growthcharts/clinical\\_charts.htm](http://www.cdc.gov/growthcharts/clinical_charts.htm)).<sup>51-52</sup> The criteria takes into account both age and sex. **Table 8** provides weight status categories based on percentiles. The CDC's BMI-for-age growth chart is applicable to children aged 2 to 20 years.<sup>52</sup>

Even with two children with the same BMI, if they are different ages or different sexes, then they are classified differently.<sup>52</sup> For example, two boys, aged 11 and 13, could both have a BMI of 21, but the 11-year old boy is between the 85th and 95th percentile so he is classified as overweight, and the 13-year old boy is between the 5th and 84.9th percentile so is classified as healthy weight. The use of the adult classification system would not be appropriate.

### Treatment of Pediatric Patients

Like with adults, lifestyle changes are the foundation for prevention and treatment of being overweight and obese. Dietary recommendations include avoiding sweetened beverages, using portion control, and increasing the intake of dietary fiber, fruits and vegetables. Dietary modi-

fications are appropriate for the whole family. Pediatric obese patients should also get 60 minutes of moderate to vigorous physical activity daily, and sedentary activities like watching television or playing video games should be limited to 1-2 hours daily.<sup>51</sup>

The Endocrine Society only recommends the use of pharmacotherapy if lifestyle changes are unsuccessful or the patient has co-morbidities. Additionally, overweight children should not be treated with medications unless there are significant, severe comorbidities.<sup>43</sup> Many of the prescription medications are not approved for use or studied in those under the age of 18 years. See **Table 9** for the minimum age of each prescription medication, as recommended by the FDA.<sup>26-31</sup>

One example of a study evaluating a medication currently approved for diabetes for weight loss is with the GLP-1 agonist exenatide (Byetta). This medication was studied in 26 adolescents aged 12 to 19 years with severe obesity (defined as a BMI greater than or equal to 1.2 times the 95th percentile or a BMI greater than or equal to 35). None of the patients in this study had diabetes. Compared to placebo, exenatide reduced BMI at three months.<sup>53</sup> This study had a very small sample size, but studies like it are needed before larger-scale studies are done or use of the medication for weight loss becomes general; and the medication is not FDA-approved for weight loss in adults.

Bariatric surgery should only be used in pediatric patients after puberty, and the criteria for surgery should be a BMI greater than 50 or greater than 40 with severe comorbidities.<sup>51</sup>

**Table 8. Pediatric BMI Classifications<sup>52</sup>**

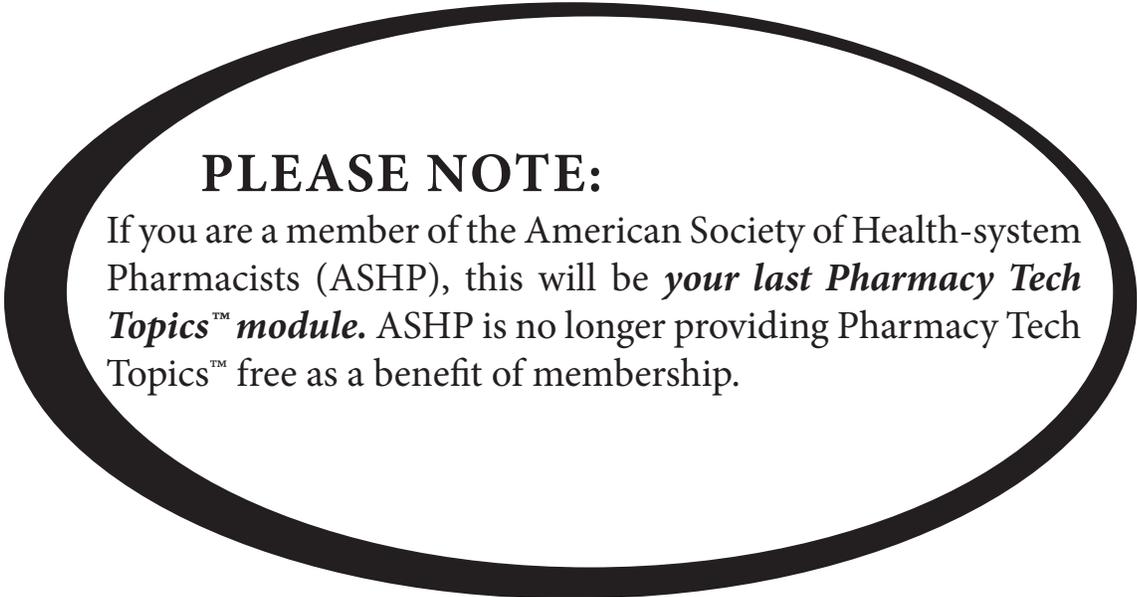
BMI Percentile Range	Classification
<5th percentile	Underweight
5th percentile to <85th percentile	Healthy weight
85th percentile to <95th percentile	Overweight
≥95th percentile	Obese
BMI: Body Mass Index	
< less than	
≥ greater than or equal to	

**Table 9. Minimum age for Pharmacotherapy<sup>26-31</sup>**

Medication Generic Name	Minimum Age Approved For Use
orlistat	12 years
diethylpropion	17 years
phentermine	17 years
lorcaserin	18 years
phentermine/topiramate	18 years

## CONCLUSIONS

Obesity is a complex problem, with multiple causes and potential treatments. All patients benefit from lifestyle changes, which include changes in diet, physical activity, and behaviors. Some patients may benefit from pharmacotherapy, and some patients who meet criteria can have significant benefits from bariatric surgery. Despite multiple potential treatments, many interventions need long-term follow-up and patients need ongoing support to meet long-term weight loss and health goals.



### PLEASE NOTE:

If you are a member of the American Society of Health-system Pharmacists (ASHP), this will be *your last Pharmacy Tech Topics™ module*. ASHP is no longer providing Pharmacy Tech Topics™ free as a benefit of membership.

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ANSWER KEY: TEST YOUR KNOWLEDGE  
EXERCISES

**Exercise #1:**

$[150 \text{ lbs.} \times 703] \div [70 \times 70] = 21.5 \text{ kg/m}^2$ , which classifies the patient as normal;  $[150 \times 703] \div [62 \text{ inches} \times 62 \text{ inches}] = 27.43 \text{ kg/m}^2$ , which classifies the patient as overweight

**Exercise #2:**

Answers vary.

**Exercise #3:**

B. Immobility is a risk factor for obesity. Bupropion can lead to weight loss, so might be helpful for her to lose some of the weight she has recently gained. Additionally, her depression may increase her risk of obesity, although some patients with depression lose weight due to a decreased appetite.

**Exercise #4:**

A. While each activity is beneficial, playing basketball is high intensity, and so the patient only needs 75 minutes per week to meet the CDC recommendation, or 150 minutes for more robust weight loss.

**Exercise #5:**

C. Levothyroxine and warfarin have known drug interactions. Additionally, all fat-soluble vitamins may not be absorbed if taken at the same time as orlistat and vitamin D is a fat-soluble vitamin.

**Exercise #6:**

No. Patients should discontinue lorcaserin if they don't lose at least 5% of their baseline weight after 12 weeks (about 3 months). Heather lost 5 pounds but this is less than 3% of her baseline weight.

How to calculate percent weight loss:

Option A:  $1 - [\text{Current weight (188 pounds)} \div \text{previous weight (193 pounds)}]$

Example:  $1 - [188 \div 193] = 1 - 0.974 = 0.026$

Option B: Change in weight divided by old weight

Example:  $(193 - 188) \div 193 = 5 \div 193 = 0.026$

Remember that percent change is percent of 100, so you move the decimal place over two spots to get 2.6% for both options A and B.

**Exercise #7:**

C. The Qsymia REMS applies regardless of patient age or sex. Patients who have had tubal ligation ("tubes tied") must still be in the program. Pharmacies must also enroll in the pharmacy management system.