Cleveland Clinic

Disease Management Project

October 2013

Physician's Guide to Obesity

In collaboration with

BulletinHealthcare

Cleveland Clinic

Disease Management Project

Dear Healthcare Professional,

Welcome to the Cleveland Clinic *Physician's Guide to Obesity*, an information-packed tool brought to you by the Cleveland Clinic's Disease Management Project (DMP) in collaboration with BulletinHealthcare, the leading provider of medical news updates to healthcare professionals like yourself.

This guide covers a wide range of topics, from signs and symptoms and comorbidities to treatment options including lifestyle modification, medications, surgery, and more. And it was researched and written by leading experts in the field—Dr. Stacy Brethauer, Dr. Sangeeta Kashyap, and Dr. Philip Schauer.

We hope you find the Cleveland Clinic *Physician's Guide to Obesity* to be helpful, informative, and of value in your efforts to diagnose, treat, and provide positive patient outcomes. We look forward to hearing your thoughts about this content. Please send me your comments at *diseasemanagement@ccf.org*.

William Carey, MD
Editor-in-Chief
Disease Management Project
Cleveland Clinic

Contents

Introduction 1

Signs, Symptoms, and Related Diseases 2

Diagnosis and Evaluation of Comorbidities 2

Treatment 3

Outcomes 13

Summary 14

Suggested Readings & References 16

Introduction

Definition and Etiology

Obesity has become an important public-health problem in industrialized countries throughout the world. The body mass index (BMI = weight (in kg/height^2 [in m^2]) is the primary measurement used to categorize obese patients (Table 1). Excess body weight (EBW) is defined as the amount of weight that is in excess of the ideal body weight (IBW). Ideal body weight is conventionally determined by the Metropolitan Life Tables, or as a BMI of 25 kg/m^2. In 1991, the National Institutes of Health defined morbid obesity as a BMI of ≥ 35 kg/m^2 and severe, obesity-related comorbidity as a BMI of ≥ 40 kg/m^2.[1]

Table 1 Definitions of Obesity

Category	Body Mass Index (kg/m^2)	Over Ideal Body Weight
Underweight	<18.5	
Normal	18.5-24.9	
Overweight	25.0-29.9	
Obesity (class 1)	30-34.9	>20%
Severe obesity (class 2)	35-39.9	>100%
Severe obesity (class 3)	40-49.9	
Superobesity	>50	>250%

The development of obesity involves the interactions between excessive caloric intake, inefficient use of food energy, reduced metabolic activity, a reduction in the thermogenic response to meals, and an abnormally high set point for body weight. Genetic, environmental, and psychosocial factors all contribute to this problem.

Prevalence and Risk Factors

The prevalence of obesity in the United States has increased from 15% in 1980 to 36% in 2010.[2] The prevalence of extreme obesity (BMI ≥ 40 kg/m2) is 4.4% in men and 8.2% in women. The prevalence of childhood and adolescent obesity has tripled since 1980 and, currently, 17% of U.S. children and adolescents are obese.[3] Obesity and morbid obesity affect women and minorities (particularly middle-aged black and Hispanic women) more than white males. However, in almost every age and ethnic group, the prevalence of overweight or obesity exceeds 50%.

Recent studies also have delineated the influence of childhood weight on adulthood weight. Being overweight during older childhood is highly predictive of adult obesity, especially if a parent also is obese. Being overweight during the adolescent years is an even greater predictor of adult obesity. Obesity is now the second-leading cause of preventable death in the U.S. after cigarette smoking, despite expenditures of over $45 billion annually on weight-loss products.[4]

Pathophysiology and Natural History

Adipose tissue is primarily stored subcutaneously and in the abdominal cavity. In general, females are more likely to deposit fat in the peripheral tissues; males tend to deposit it in the abdominal compartment. As obesity develops, the size and number of fat cells increase. As fat cells grow, they release increasing amounts of cytokines and lower amounts of adiponectin. These changes have deleterious effects on glucose and lipid metabolism, and contribute to the proinflammatory state associated with obesity.

Obesity shortens the life span of those who suffer with it. The mortality rate of an individual with a BMI $\geq$ 40 kg/m^2 is double that of a normal-weight individual.[5] It is estimated that a man in his 20s with a BMI $\geq$ 45 kg/m^2 has a 22% reduction in life expectancy, a decrease of 13 years.[6] Most obesity-related deaths result from complications related to diabetes, cancer, and cardiovascular disease. Worldwide, approximately 2.5 million deaths occur annually because of obesity-related comorbidities.

Signs, Symptoms, and Related Diseases

There are more than 30 comorbid conditions associated with severe obesity. Insulin resistance and diabetes mellitus occur in 15% to 25% of obese patients. Increased abdominal fat in obese patients raises the intra-abdominal pressure and contributes to gastroesophageal reflux, stress urinary incontinence, venous stasis disease, and abdominal hernia. Fatty deposits in the liver can progress to nonalcoholic steatohepatitis (NASH) and, ultimately, to liver failure. Excess weight causes joint and back stress that can lead to debilitating joint disease.

The low-grade inflammatory state associated with morbid obesity has been implicated in the development of vascular and coronary artery disease, and the hypercoagulable state seen in these patients. Obese patients have impaired pulmonary function, particularly decreased functional residual capacity, and frequently suffer from asthma, obstructive sleep apnea, and obesity hypoventilation syndrome (also known as Pickwickian syndrome and encompassing chronic hypoxemia, hypercarbia, pulmonary hypertension, and polycythemia). Other comorbidities include hypertension, dyslipidemia, asthma, and sex-hormone dysfunction. Obesity is associated with an increased incidence of cancer of the uterus, breast, ovaries, prostate, and colon; skin infections; urinary-tract infections; migraine headaches; depression; and pseudotumor cerebri.

Diagnosis and Evaluation of Comorbidities

The diagnosis of morbid obesity is established by determining the patient's BMI and the presence of any significant comorbid conditions. A thorough history, physical examination, and focused testing will uncover previously undiagnosed comorbidities in up to two-thirds of obese patients.

Visceral, or central, fat is more metabolically active than peripheral fat and is associated with type 2 diabetes, dyslipidemia (elevated triglyceride and reduced high-density lipoprotein [HDL] levels), high blood pressure, and increased risk for cardiovascular atherosclerotic disease. The waist-to-hip ratio helps to identify patients with excess visceral adiposity. Women with a waist-to-hip ratio >0.8 and men with a ratio >1.0 are considered to have excess central adiposity that confers risk for developing the metabolic syndrome. The diagnostic criteria for the metabolic syndrome are shown in Table 2.

Table 2 Adult Treatment Panel III Criteria for the Metabolic Syndrome*

Parameter	Criterion
Central obesity	
Waist circumference in men	>102 cm
Waist circumference in women	>88 cm
Hypertriglyceridemia	≥150 mg/dL
Low high-density lipoprotein cholesterol	
Men	<40 mg/dL
Women	<50 mg/dL
High blood pressure	≥130/≥85 mmHg
Fasting blood glucose	≥110 mg/dL

*Three or more of these criteria need to be present.

Adapted with permission from: National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III): Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation 2002;106:3143-3421.

The pretreatment evaluation performed at the Cleveland Clinic is consistent with published guidelines.[7] Because obese persons are at greater risk for cardiovascular disease, a baseline electrocardiogram (ECG) should be performed. Cardiology evaluation is carried out when there is evidence of cardiac disease based on clinical symptoms or ECG findings. Chest radiography and baseline laboratory testing, including a complete blood count, chemistry panel, liver-function tests, thyroid-function tests, and a lipid profile, should be obtained as well.

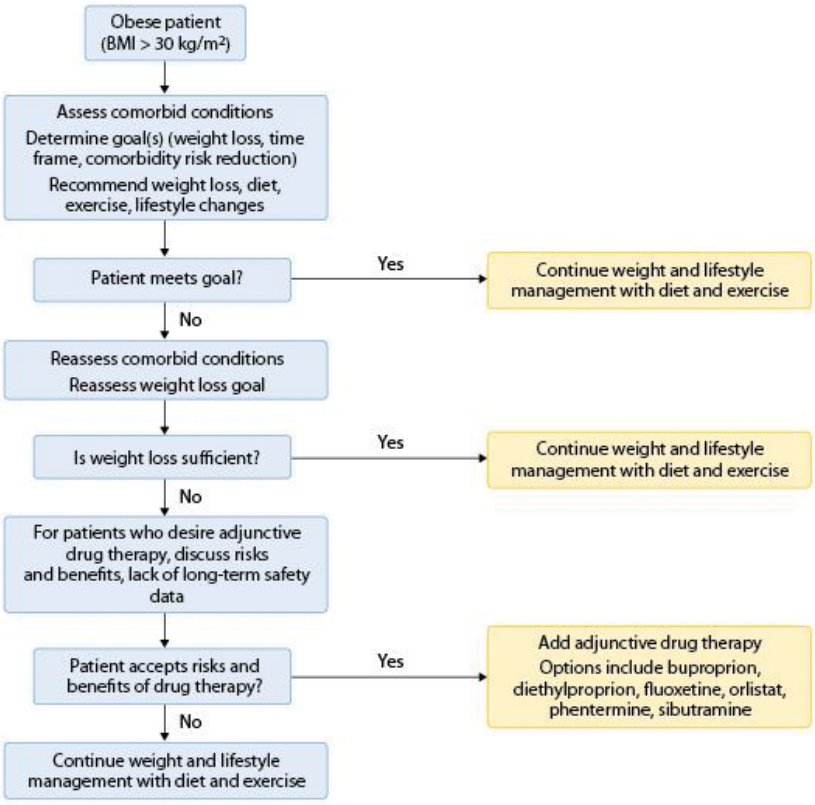
Obstructive sleep apnea frequently goes unrecognized in this patient population until a thorough history prompts further evaluation. Patients with symptoms of loud snoring, daytime hypersomnolence, or a neck circumference ≥ 43 cm should undergo polysomnography and, if positive, be treated with continuous positive airway pressure (CPAP). Asthma and obesity hypoventilation syndrome also are severe pulmonary complications of obesity and should be evaluated by a pulmonologist. Dietary counseling and psychological testing are required for patients who are referred for bariatric surgery.

Treatment

Lifestyle Modifications

According to the clinical guidelines published by the American College of Physicians, all patients with a BMI ≥ 30 kg/m^2 should be counseled intensively on lifestyle and behavior modifications, such as appropriate diet and exercise.[8,9] An algorithm published by the American College of Physicians for medical management of an obese patient is shown in Figure 1.[9] The patient's goals for weight loss should be individually determined and may encompass other related parameters, such as decreasing blood pressure or fasting blood glucose levels. When establishing realistic weight-loss goals, it is important to realize that modest weight loss (10%-15%) is sufficient to result in health benefits.[10,11]

Figure 1 Algorithm for the Medical Management of Obesity



General dietary guidelines for achieving and maintaining a healthy weight include direction to eat a variety of nutritious foods in order to avoid vitamin deficiencies. The patient should be advised to avoid foods that are high in fat and simple sugars, and to increase dietary fiber intake. Meal-replacement shakes and behavior-modification strategies can increase adherence. The patient should be directed to maintain a diet in which 50% to 55% of calories come from complex carbohydrates. In addition, it is helpful to educate the patient about appropriate portion sizes and the caloric content of foods, as recommended by several national scientific organizations, such as the American Dietetic Association and American Diabetes Association. Referral to a registered dietitian can help the patient initiate and adhere to these dietary guidelines.

Every physician should include a graded exercise regimen as part of a comprehensive lifestyle-modification plan. Moderate exercise has been shown to decrease blood pressure; increase HDL levels and reduce triglyceride levels; and is predictive of maintenance of weight loss and delaying onset of type 2 diabetes.[12] General exercise recommendations include 20 to 30 minutes of moderate exercise 5 to 7 days a week, up to 60 minutes per day most days of the week for maintenance of weight, and 90 minutes a day for achieving weight loss.

Medical Options

Pharmacologic therapy can be considered in an obese patient who has significant comorbidities or has failed to achieve weight-loss goals through lifestyle modification alone. Before initiating therapy, however, the clinician must inform the patient of any side effects associated with the drug, the lack of long-term safety data, and the temporary nature of the weight loss achieved through the use of medications. Table 3 lists the medications reviewed in the 2013 American College of Physicians clinical practice guideline for obesity management. Cardiovascular side effects were noted with the appetite suppressant sibutramine, resulting in its removal from the market.

Table 3 Medications Used for Weight Loss

Drug	Mechanism of Action	Side Effects
Phentermine/Topiramate	Appetite suppressant	Dizziness, dry mouth, constipation
Lorcaserin	Appetite suppressant	Nausea, dizziness
Phentermine	Appetite suppressant: sympathomimetic amine	Cardiovascular, gastrointestinal
Diethylpropion	Appetite suppressant: sympathomimetic amine	Palpitations, tachycardia, insomnia, gastrointestinal
Orlistat	Lipase inhibitor: decreased absorption of fat	Diarrhea, flatulence, bloating, abdominal pain, dyspepsia
Bupropion	Appetite suppressant: mechanism unknown	Paresthesia, insomnia, central nervous system effects
Fluoxetine	Appetite suppressant: selective serotonin reuptake inhibitor	Agitation, nervousness, gastrointestinal
Sertraline	Appetite suppressant: selective serotonin reuptake inhibitor	Agitation, nervousness, gastrointestinal
Topiramate	Mechanism unknown	Paresthesia, changes in taste
Zonisamide	Mechanism unknown	Somnolence, dizziness, nausea

The choice of agent depends on the side-effect profile and the patient's ability to tolerate those side effects. The amount of weight loss achieved through pharmacologic therapy is generally modest (< 5 kg at 1 year). However, even modest weight loss can slow the progression of diabetes and reduce cardiovascular risk factors. However, there is no evidence that modest weight loss reduces mortality rates in these patients.

The optimal duration of treatment with obesity medications has not yet been determined. Data from randomized controlled trials are only available for up to 12 months of therapy. There are no long-term data on whether these drugs decrease morbidity or mortality from obesity-related conditions.

Indication

BELVIQ is indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults with an initial body mass index (BMI) of:

- 30 kg/m^2 or greater (obese), or
- 27 kg/m^2 or greater (overweight) in the presence of at least one weight-related comorbid condition (eg, hypertension, dyslipidemia, type 2 diabetes).

Limitations of Use

- The safety and efficacy of coadministration of BELVIQ with other products intended for weight loss, including prescription drugs (eg, phentermine), over-the-counter drugs, and herbal preparations, have not been established.
- The effect of BELVIQ on cardiovascular morbidity and mortality has not been established.

Important Safety Information

Contraindication

- BELVIQ should not be taken during pregnancy or by women who are planning to become pregnant.

Warnings and Precautions

- BELVIQ is a serotonergic drug. The development of potentially life-threatening serotonin syndrome or Neuroleptic Malignant Syndrome (NMS)-like reactions have been reported during use of serotonergic drugs, including, but not limited to, selective serotonin-norepinephrine reuptake inhibitors, and selective serotonin reuptake inhibitors, tricyclic antidepressants, bupropion, triptans, dietary supplements such as St. John's Wort and tryptophan, drugs that impair metabolism of serotonin (including monoamine oxidase inhibitors), dextromethorphan, lithium, tramadol, antipsychotics or other dopamine antagonists,

NEW in chronic weight management

Make weight loss matter

Introducing BELVIQ®, the first and only selective 5-HT_{2C} receptor agonist for chronic weight management[1,2]

- Prescription therapy for use in conjunction with a reduced-calorie diet and increased physical activity[1]
- Novel mechanism of action believed to promote satiety. The exact mechanism of action is not known[1,2]

Visit **BELVIQhcp.com** for information and offers.

particularly when used in combination. Patients should be monitored for the emergence of serotonin syndrome symptoms or NMS-like reactions, including agitation, hallucinations, coma, tachycardia, labile blood pressure, hyperthermia, hyperreflexia, incoordination, nausea, vomiting, diarrhea, and muscle rigidity. Treatment with BELVIQ and any concomitant serotonergic or antidopaminergic agents should be discontinued immediately if the above events occur, and supportive symptomatic treatment should be initiated.

- Patients should not take BELVIQ in combination with drugs that have been associated with valvular heart disease (eg, cabergoline). In clinical trials, 2.4% of patients taking BELVIQ and 2.0% of patients taking placebo developed valvular regurgitation: none of these patients were symptomatic. BELVIQ should be used with caution in patients with congestive heart failure (CHF). Patients who develop signs and symptoms of valvular heart disease, including dyspnea, dependent edema, CHF, or a new cardiac murmur, should be evaluated and discontinuation of BELVIQ should be considered.
- Impairment in attention, memory, somnolence, confusion, and fatigue, have been reported in patients taking BELVIQ. Patients should not drive a car or operate heavy machinery until they know how BELVIQ affects them.
- The recommended dose of 10 mg twice daily should not be exceeded, as higher doses may cause euphoria, hallucination, and dissociation. Monitor patients for the development or worsening of depression, suicidal thoughts or behaviors, and/or any changes in mood. Discontinue BELVIQ in patients who develop suicidal thoughts or behaviors.
- Weight loss may increase the risk of hypoglycemia in patients with type 2 diabetes mellitus who are being treated with antidiabetic medications, so measurement of blood sugar levels before and during treatment with BELVIQ is recommended. Decreases in doses of antidiabetic medications or changes in medication regimen should be considered.
- Men who experience priapism should immediately discontinue BELVIQ and seek emergency medical attention. BELVIQ should be used with caution with erectile dysfunction medications. BELVIQ should be used with caution in men who have conditions that might predispose them to priapism (eg, sickle cell anemia, multiple myeloma, or leukemia), or in men with anatomical deformation of the penis (eg, angulation, cavernosal fibrosis, or Peyronie's disease).
- Because BELVIQ may cause a slow heartbeat, it should be used with caution in patients with a history of bradycardia or heart block greater than first degree.
- Consider monitoring for CBC changes, prolactin excess, and pulmonary hypertension.

Most Common Adverse Reactions

- In patients without diabetes: headache (17%), dizziness (9%), fatigue (7%), nausea (8%), dry mouth (5%), and constipation (6%).
- In patients with diabetes: hypoglycemia (29%), headache (15%), back pain (12%), cough (8%), and fatigue (7%).

Nursing Mothers

- BELVIQ should not be taken by women who are nursing.

BELVIQ is a federally controlled substance (CIV) because it may be abused or lead to dependence.

Please see Brief Summary of Prescribing Information and references on adjacent pages.

BELVIQ® (lorcaserin HCl) IV

BELVIQ®
(lorcaserin HCl)

BRIEF SUMMARY:
For prescribing information, see package insert.

INDICATIONS AND USAGE
BELVIQ is indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adult patients with an initial body mass index (BMI) of:
- 30 kg/m^2 or greater (obese), or
- 27 kg/m^2 or greater (overweight) in the presence of at least one weight related comorbid condition (e.g., hypertension, dyslipidemia, type 2 diabetes)

Limitations of Use:
- The safety and efficacy of coadministration of BELVIQ with other products intended for weight loss including prescription drugs (e.g., phentermine), over-the-counter drugs, and herbal preparations have not been established
- The effect of BELVIQ on cardiovascular morbidity and mortality has not been established

DOSAGE AND ADMINISTRATION
The recommended dose of BELVIQ is 10 mg administered orally twice daily. Do not exceed recommended dose. BELVIQ can be taken with or without food. Response to therapy should be evaluated by week 12. If a patient has not lost at least 5% of baseline body weight, discontinue BELVIQ, as it is unlikely that the patient will achieve and sustain clinically meaningful weight loss with continued treatment.

CONTRAINDICATION
- Pregnancy

WARNINGS AND PRECAUTIONS
Serotonin Syndrome or Neuroleptic Malignant Syndrome (NMS)-like Reactions. BELVIQ is a serotonergic drug. The development of a potentially life-threatening serotonin syndrome or Neuroleptic Malignant Syndrome (NMS)-like reactions have been reported during use of serotonergic drugs, including, but not limited to, selective serotonin-norepinephrine reuptake inhibitors (SNRIs) and selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), bupropion, triptans, dietary supplements such as St. John's Wort and tryptophan, drugs that impair metabolism of serotonin (including monoamine oxidase inhibitors [MAOIs]), dextromethorphan, lithium, tramadol, antipsychotics or other dopamine antagonists, particularly when used in combination.
Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (e.g., hyperreflexia, incoordination) and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea). Serotonin syndrome, in its most severe form, can resemble neuroleptic malignant syndrome, which includes hyperthermia, muscle rigidity, autonomic instability with possible rapid fluctuation of vital signs, and mental status changes. Patients should be monitored for the emergence of serotonin syndrome or NMS-like signs and symptoms.
The safety of BELVIQ when coadministered with other serotonergic or antidopaminergic agents, including antipsychotics, or drugs that impair metabolism of serotonin, including MAOIs, has not been systematically evaluated and has not been established.
If concomitant administration of BELVIQ with an agent that affects the serotonergic neurotransmitter system is clinically warranted, extreme caution and careful observation of the patient is advised, particularly during treatment initiation and dose increases. Treatment with BELVIQ and any concomitant serotonergic or antidopaminergic agents, including antipsychotics, should be discontinued immediately if the above events occur and supportive symptomatic treatment should be initiated.
Valvular Heart Disease. Regurgitant cardiac valvular disease, primarily affecting the mitral and/or aortic valves, has been reported in patients who took serotonergic drugs with 5-HT$_{2B}$ receptor agonist activity. The etiology of the regurgitant valvular disease is thought to be activation of 5-HT$_{2B}$ receptors on cardiac interstitial cells. At therapeutic concentrations, BELVIQ is selective for 5-HT$_{2C}$ receptors as compared to 5-HT$_{2B}$ receptors. In clinical trials of 1-year duration, 2.4% of patients receiving BELVIQ and 2.0% of patients receiving placebo developed echocardiographic criteria for valvular regurgitation at one year (mild or greater aortic regurgitation and/or moderate or greater mitral regurgitation): none of these patients was symptomatic.
BELVIQ has not been studied in patients with congestive heart failure or hemodynamically-significant valvular heart disease. Preliminary data suggest that 5HT$_{2B}$ receptors may be overexpressed in congestive heart failure. Therefore, BELVIQ should be used with caution in patients with congestive heart failure.
BELVIQ should not be used in combination with serotonergic and dopaminergic drugs that are potent 5-HT$_{2B}$ receptor agonists and are known to increase the risk for cardiac valvulopathy (e.g., cabergoline).
Patients who develop signs or symptoms of valvular heart disease, including dyspnea, dependent edema, congestive heart failure, or a new cardiac murmur while being treated with BELVIQ should be evaluated and discontinuation of BELVIQ should be considered.
Cognitive Impairment. In clinical trials of at least one year in duration, impairments in attention and memory were reported adverse reactions associated with 1.9% of patients treated with BELVIQ and 0.5% of patients treated with placebo, and led to discontinuation in 0.3% and 0.1% of these patients, respectively. Other reported adverse reactions associated with BELVIQ in clinical trials included confusion, somnolence, and fatigue.
Since BELVIQ has the potential to impair cognitive function, patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that BELVIQ therapy does not affect them adversely.
Psychiatric Disorders. Events of euphoria, hallucination, and dissociation were seen with BELVIQ at supratherapeutic doses in short-term studies. In clinical trials of at least 1-year in duration, 6 patients (0.2%) treated with BELVIQ developed euphoria, as compared with 1 patient (<0.1%) treated with placebo. Doses of BELVIQ should not exceed 10 mg twice a day.
Some drugs that target the central nervous system have been associated with depression or suicidal ideation. Patients treated with BELVIQ should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior. Discontinue BELVIQ in patients who experience suicidal thoughts or behaviors.
Potential Risk of Hypoglycemia in Patients with Type 2 Diabetes Mellitus on Anti-diabetic Therapy. Weight loss may increase the risk of hypoglycemia in patients with type 2 diabetes mellitus treated with insulin and/or insulin secretagogues (e.g., sulfonylureas); hypoglycemia was observed in clinical trials with BELVIQ. BELVIQ has not been studied in combination with insulin. Measurement of blood glucose levels prior to starting BELVIQ and during BELVIQ treatment is recommended in patients with type 2 diabetes. Decreases in medication doses for anti-diabetic medications which are non-glucose-dependent should be considered to mitigate the risk of hypoglycemia. If a patient develops hypoglycemia after starting BELVIQ, appropriate changes should be made to the anti-diabetic drug regimen.
Priapism. Priapism (painful erections greater than 6 hours in duration) is a potential effect of 5-HT$_{2C}$ receptor agonism.
If not treated promptly, priapism can result in irreversible damage to the erectile tissue. Men who have an erection lasting greater than 4 hours, whether painful or not, should immediately discontinue the drug and seek emergency medical attention.
BELVIQ should be used with caution in men who have conditions that might predispose them to priapism (e.g., sickle cell anemia, multiple myeloma, or leukemia), or in men with anatomical deformation of the penis (e.g., angulation, cavernosal fibrosis, or Peyronie's disease). There is limited experience with the combination of BELVIQ and medication indicated for erectile dysfunction (e.g., phosphodiesterase type 5 inhibitors). Therefore, the combination of BELVIQ and these medications should be used with caution.
Heart Rate Decreases. In clinical trials of at least 1-year in duration, the mean change in heart rate (HR) was -1.2 beats per minute (bpm) in BELVIQ and -0.4 bpm in placebo-treated patients without diabetes and -2.0 beats per minute (bpm) in BELVIQ and -0.4 bpm in placebo-treated patients with type 2 diabetes. The incidence of HR less than 50 bpm was 5.3% in BELVIQ and 3.2% in placebo-treated patients without diabetes and 3.6% in BELVIQ and 2.0% in placebo-treated patients with type 2 diabetes. In the combined population, adverse reactions of bradycardia occurred in 0.3% of BELVIQ and 0.1% of placebo-treated patients. Use with caution in patients with bradycardia or a history of heart block greater than first degree.
Hematological Changes. In clinical trials of at least one year in duration, adverse reactions of decreases in white blood cell count (including leukopenia, lymphopenia, neutropenia, and decreased white cell count) were reported in 0.4% of patients treated with BELVIQ as compared to 0.2% of patients treated with placebo. Adverse reactions of decreases in red blood cell count (including anemia and decreases in hemoglobin and hematocrit) were reported by 1.3% of patients treated with BELVIQ as compared to 1.2% treated with placebo. Consider periodic monitoring of complete blood count during treatment with BELVIQ.
Prolactin Elevation. Lorcaserin moderately elevates prolactin levels. In a subset of placebo-controlled clinical trials of at least one year in duration, elevations of prolactin greater than the upper limit of normal, two times the upper limit of normal, and five times the upper limit of normal, measured both before and 2 hours after dosing, occurred in 6.7%, 1.7%, and 0.1% of BELVIQ-treated patients and 4.8%, 0.8%, and 0.0% of placebo-treated patients, respectively. Prolactin should be measured when symptoms and signs of prolactin excess are suspected (e.g., galactorrhea, gynecomastia). There was one patient treated with BELVIQ who developed a prolactinoma during the trial. The relationship of BELVIQ to the prolactinoma in this patient is unknown.
Pulmonary Hypertension. Certain centrally-acting weight loss agents that act on the serotonin system have been associated with pulmonary hypertension, a rare but lethal disease. Because of the low incidence of this disease, the clinical trial experience with BELVIQ is inadequate to determine if BELVIQ increases the risk for pulmonary hypertension.

ADVERSE REACTIONS
Clinical Trials Experience. In the BELVIQ placebo-controlled clinical database of trials of at least one year in duration, of 6888 patients (3451 BELVIQ vs. 3437 placebo; age range 18-66 years, 79.3% women, 66.6% Caucasians, 19.2% Blacks, 11.8% Hispanics, 2.4% other, 7.4% type 2 diabetics), a total of 1969 patients were exposed to BELVIQ 10 mg twice daily for 1 year and 426 patients were exposed for 2 years.
In clinical trials of at least one year in duration, 8.6% of patients treated with BELVIQ prematurely discontinued treatment due to adverse reactions, compared with 6.7% of placebo-treated patients. The most common adverse reactions leading to discontinuation more often among BELVIQ treated patients than placebo were headache (1.3% vs. 0.8%), depression (0.9% vs. 0.5%) and dizziness (0.7% vs. 0.2%).

Most Common Adverse Reactions

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 trials of another drug and may not reflect the rates observed in practice.
The most common adverse reactions for non-diabetic patients (greater than 5% and more commonly than placebo) treated with BELVIQ compared to placebo were headache, dizziness, fatigue, nausea, dry mouth, and constipation. The most common adverse reactions for diabetic patients were hypoglycemia, headache, back pain, cough, and fatigue. Adverse reactions that were reported by greater than or equal to 2% of patients and were more frequently reported by patients taking BELVIQ compared to placebo are summarized in Table 1 (non-diabetic subjects) and Table 2 (subjects with type 2 diabetes mellitus).

Table 1. Adverse Reactions Reported by Greater Than or Equal to 2% of BELVIQ Patients and More Commonly than with Placebo in Patients without Diabetes Mellitus

	Number of Patients (%)	
Adverse Reaction	**BELVIQ 10 mg BID N=3195**	**Placebo N=3185**
Gastrointestinal Disorders		
Nausea	264 (8.3)	170 (5.3)
Diarrhea	207 (6.5)	179 (5.6)
Constipation	186 (5.8)	125 (3.9)
Dry mouth	169 (5.3)	74 (2.3)
Vomiting	122 (3.8)	83 (2.6)
General Disorders And Administration Site Conditions		
Fatigue	229 (7.2)	114 (3.6)
Infections And Infestations		
Upper respiratory tract infection	439 (13.7)	391 (12.3)
Nasopharyngitis	414 (13.0)	381 (12.0)
Urinary tract infection	207 (6.5)	171 (5.4)
Musculoskeletal And Connective Tissue Disorders		
Back pain	201 (6.3)	178 (5.6)
Musculoskeletal pain	65 (2.0)	43 (1.4)
Nervous System Disorders		
Headache	537 (16.8)	321 (10.1)
Dizziness	270 (8.5)	122 (3.8)
Respiratory, Thoracic And Mediastinal Disorders		
Cough	136 (4.3)	109 (3.4)
Oropharyngeal pain	111 (3.5)	80 (2.5)
Sinus congestion	93 (2.9)	78 (2.4)
Skin And Subcutaneous Tissue Disorders		
Rash	67 (2.1)	58 (1.8)

Table 2. Adverse Reactions Reported by Greater Than or Equal to 2% of BELVIQ Patients and More Commonly than with Placebo in Patients with Type 2 Diabetes Mellitus

	Number of Patients (%)	
Adverse Reaction	**BELVIQ 10 mg BID N=256**	**Placebo N=252**
Gastrointestinal Disorders		
Nausea	24 (9.4)	20 (7.9)
Toothache	7 (2.7)	0

(Table continues)

Table 2. (cont'd.)

Adverse Reaction	Number of Patients (%)	
	BELVIQ 10 mg BID N=256	Placebo N=252
General Disorders And Administration Site Conditions		
Fatigue	19 (7.4)	10 (4.0)
Peripheral edema	12 (4.7)	6 (2.4)
Immune System Disorders		
Seasonal allergy	8 (3.1)	2 (0.8)
Infections And Infestations		
Nasopharyngitis	29 (11.3)	25 (9.9)
Urinary tract infection	23 (9.0)	15 (6.0)
Gastroenteritis	8 (3.1)	5 (2.0)
Metabolism And Nutrition Disorders		
Hypoglycemia	75 (29.3)	53 (21.0)
Worsening of diabetes mellitus	7 (2.7)	2 (0.8)
Decreased appetite	6 (2.3)	1 (0.4)
Musculoskeletal And Connective Tissue Disorders		
Back pain	30 (11.7)	20 (7.9)
Muscle spasms	12 (4.7)	9 (3.6)
Nervous System Disorders		
Headache	37 (14.5)	18 (7.1)
Dizziness	18 (7.0)	16 (6.3)
Psychiatric Disorders		
Anxiety	9 (3.5)	8 (3.2)
Insomnia	9 (3.5)	6 (2.4)
Stress	7 (2.7)	3 (1.2)
Depression	6 (2.3)	5 (2.0)
Respiratory, Thoracic And Mediastinal Disorders		
Cough	21 (8.2)	11 (4.4)
Vascular Disorders		
Hypertension	13 (5.1)	8 (3.2)

Other Adverse Reactions

Serotonin-associated Adverse Reactions. SSRIs, SNRIs, bupropion, tricyclic antidepressants, and MAOIs were excluded from the BELVIQ trials. Triptans and dextromethorphan were permitted: 2% and 15%, respectively, of patients without diabetes and 1% and 12%, respectively, of patients with type 2 diabetes experienced concomitant use at some point during the trials. Two patients treated with BELVIQ in the clinical program experienced a constellation of symptoms and signs consistent with serotonergic excess, including one patient on concomitant dextromethorphan who reported an event of serotonin syndrome. Some symptoms of possible serotonergic etiology that are included in the criteria for serotonin syndrome were reported by patients treated with BELVIQ and placebo during clinical trials of at least 1 year in duration. In both groups, chills were the most frequent of these events (1.0% vs. 0.2%, respectively), followed by tremor (0.3% vs. 0.2%), confusional state (0.2% vs. less than 0.1%), disorientation (0.1% vs. 0.1%) and hyperhidrosis (0.1% vs. 0.2%). Because serotonin syndrome has a very low incidence, an association between BELVIQ and serotonin syndrome cannot be excluded on the basis of clinical trial results.

Hypoglycemia in Patients with Type 2 Diabetes. In a clinical trial of patients with type 2 diabetes mellitus, hypoglycemia requiring the assistance of another person occurred in 4 (1.6%) of BELVIQ-treated patients and in 1 (0.4%) placebo-treated patient. Of these 4 BELVIQ-treated patients, all were concomitantly using a sulfonylurea (with or without metformin). BELVIQ has not been studied in patients taking insulin. Hypoglycemia defined as blood sugar less than or equal to 65 mg/dL and with symptoms occurred in 19 (7.4%) BELVIQ-treated patients and 16 (6.3%) placebo-treated patients.

Cognitive Impairment. In clinical trials of at least 1-year duration, adverse reactions related to cognitive impairment (e.g., difficulty with concentration/attention, difficulty with memory, and confusion) occurred in 2.3% of patients taking BELVIQ and 0.7% of patients taking placebo.

Psychiatric Disorders. Psychiatric disorders leading to hospitalization or drug withdrawal occurred more frequently in patients treated with BELVIQ (2.2%) as compared to placebo (1.1%) in non-diabetic patients.

Euphoria. In short-term studies with healthy individuals, the incidence of euphoric mood following supratherapeutic doses of BELVIQ (40 and 60 mg) was increased as compared to placebo. In clinical trials of at least 1-year duration in obese patients, euphoria was observed in 0.17% of patients taking BELVIQ and 0.03% taking placebo.

Depression and Suicidality. In trials of at least one year in duration, reports of depression/mood problems occurred in 2.6% BELVIQ-treated vs. 2.4% placebo-treated and suicidal ideation occurred in 0.6% BELVIQ-treated vs. 0.4% placebo-treated patients. 1.3% of BELVIQ patients vs. 0.6% of placebo patients discontinued drug due to depression-, mood-, or suicidal ideation-related events.

Laboratory Abnormalities. *Lymphocyte and Neutrophil Counts.* In clinical trials of at least 1-year duration, lymphocyte counts were below the lower limit of normal in 12.2% of patients taking BELVIQ and 9.0% taking placebo, and neutrophil counts were low in 5.6% and 4.3%, respectively. *Hemoglobin.* In clinical trials of at least 1-year duration, 10.4% of patients taking BELVIQ and 9.3% taking placebo had hemoglobin below the lower limit of normal at some point during the trials.

Prolactin. In clinical trials, elevations of prolactin greater than the upper limit of normal, two times the upper limit of normal, and five times the upper limit of normal, occurred in 6.7%, 1.7%, and 0.1% of BELVIQ-treated patients and 4.8%, 0.8%, and 0.0% of placebo-treated patients, respectively.

Eye Disorders. More patients on BELVIQ reported an eye disorder than patients on placebo in clinical trials of patients without diabetes (4.5% vs. 3.0%) and with type 2 diabetes (6.3% vs. 1.6%). In the population without diabetes, events of blurred vision, dry eye, and visual impairment occurred in BELVIQ-treated patients at an incidence greater than that of placebo. In the population with type 2 diabetes, visual disorders, conjunctival infections, irritations, and inflammations, ocular sensation disorders, and cataract conditions occurred in BELVIQ-treated patients at an incidence greater than placebo.

Echocardiographic Safety Assessments

The possible occurrence of regurgitant cardiac valve disease was prospectively evaluated in 7794 patients in three clinical trials of at least one year in duration, 3451 of whom took BELVIQ 10 mg twice daily. The primary echocardiographic safety parameter was the proportion of patients who developed echocardiographic criteria of mild or greater aortic insufficiency and/or moderate or greater mitral insufficiency from baseline to 1 year. At 1 year, 2.4% of patients who received BELVIQ and 2.0% of patients who received placebo developed valvular regurgitation. The relative risk for valvulopathy with BELVIQ is summarized in Table 3. BELVIQ was not studied in patients with congestive heart failure or hemodynamically-significant valvular heart disease.

Table 3. Incidence of FDA-Defined Valvulopathy at Week 52 by Treatment Group[1]

	Study 1		Study 2		Study 3	
	BELVIQ N=1278	Placebo N=1191	BELVIQ N=1208	Placebo N=1153	BELVIQ N=210	Placebo N=209
FDA-defined Valvulopathy, n (%)	34 (2.7)	28 (2.4)	24 (2.0)	23 (2.0)	6 (2.9)	1 (0.5)
Relative Risk (95% CI)	1.13 (0.69, 1.85)		1.00 (0.57, 1.75)		5.97 (0.73, 49.17)	
Pooled RR (95% CI)	**1.16 (0.81, 1.67)**					

[1] Patients without valvulopathy at baseline who received study medication and had a post-baseline echocardiogram; ITT-intention-to-treat; LOCF-last observation carried forward.

DRUG INTERACTIONS

Use with Other Agents that Affect Serotonin Pathways. Based on the mechanism of action of BELVIQ and the theoretical potential for serotonin syndrome, use with extreme caution in combination with other drugs that may affect the serotonergic neurotransmitter systems, including, but not limited to, triptans, monoamine oxidase inhibitors (MAOIs, including linezolid, an antibiotic which is a reversible non-selective MAOI), selective serotonin reuptake inhibitors (SSRIs), selective serotonin-norepinephrine reuptake inhibitors (SNRIs), dextromethorphan, tricyclic antidepressants (TCAs), bupropion, lithium, tramadol, tryptophan, and St. John's Wort.
Cytochrome P450 (2D6) substrates. Use caution when administering BELVIQ together with drugs that are CYP 2D6 substrates, as BELVIQ can increase exposure of these drugs.

USE IN SPECIFIC POPULATIONS

Pregnancy. Pregnancy Category X.

Risk Summary. BELVIQ is contraindicated during pregnancy, because weight loss offers no potential benefit to a pregnant woman and may result in fetal harm. Maternal exposure to lorcaserin in late pregnancy in rats resulted in lower body weight in offspring which persisted to adulthood. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard of maternal weight loss to the fetus.

Clinical Considerations. A minimum weight gain, and no weight loss, is currently recommended for all pregnant women, including those who are already overweight or obese, due to the obligatory weight gain that occurs in maternal tissues during pregnancy.

Animal Data. Reproduction studies were performed in pregnant rats and rabbits that were administered lorcaserin during the period of embryofetal organogenesis. Plasma exposures up to 44 and 19 times human exposure in rats and rabbits, respectively, did not reveal evidence of teratogenicity or embryolethality with lorcaserin hydrochloride.

In a pre- and postnatal development study, maternal rats were dosed from gestation through post-natal day 21 at 5, 15, and 50mg/kg lorcaserin; pups were indirectly exposed in utero and throughout lactation. The highest dose (~44 times human exposure) resulted in stillborns and lower pup viability. All doses lowered pup body weight similarly at birth which persisted to adulthood; however, no developmental abnormalities were observed and reproductive performance was not affected at any dose.

Nursing Mothers. It is not known whether BELVIQ is excreted in human milk. Because many drugs are excreted in human milk, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use. The safety and effectiveness of BELVIQ in pediatric patients below the age of 18 have not been established and the use of BELVIQ is not recommended in pediatric patients.

Geriatric Use. In the BELVIQ clinical trials, a total of 135 (2.5%) of the patients were 65 years of age and older. Clinical studies of BELVIQ did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects, but greater sensitivity of some older individuals cannot be ruled out.

Since elderly patients have a higher incidence of renal impairment, use of BELVIQ in the elderly should be made on the basis of renal function. Elderly patients with normal renal function should require no dose adjustment.

Renal Impairment. No dose adjustment of BELVIQ is required in patients with mild renal impairment. Use BELVIQ with caution in patients with moderate renal impairment. Use of BELVIQ in patients with severe renal impairment or end stage renal disease is not recommended.

Hepatic Impairment. Dose adjustment is not required for patients with mild hepatic impairment (Child-Pugh score 5-6) to moderate hepatic impairment (Child-Pugh score 7-9). The effect of severe hepatic impairment on lorcaserin was not evaluated. Use lorcaserin with caution in patients with severe hepatic impairment.

DRUG ABUSE AND DEPENDENCE

Controlled Substance. BELVIQ is listed in Schedule IV of the Controlled Substances Act.

Abuse. In a human abuse potential study in recreational drug abusers, supratherapeutic oral doses of lorcaserin (40 and 60 mg) produced up to two- to six-fold increases on measures of "High", "Good Drug Effects", "Hallucinations" and "Sedation" compared to placebo. These responses were similar to those produced by oral administration of the positive control drugs, zolpidem (15 and 30 mg) and ketamine (100 mg). In this study, the incidence of the adverse reaction of euphoria following lorcaserin administration (40 and 60 mg; 19%) is similar to the incidence following zolpidem administration (13-16%), but less than the incidence following ketamine administration (50%). The duration of euphoria following lorcaserin administration persisted longer (> 9 hours) than that following zolpidem (1.5 hours) or ketamine (2.5 hours) administration.

Overall, in short-term studies with healthy individuals, the rate of euphoria following oral administration of lorcaserin was 16% following 40 mg (n = 11 of 70) and 19% following 60 mg (n = 6 of 31). However, in clinical studies with obese patients with durations of 4 weeks to 2 years, the incidence of euphoria and hallucinations following oral doses of lorcaserin up to 40 mg was low (< 1.0%).

Dependence. There are no data from well-conducted animal or human studies that evaluate whether lorcaserin can induce physical dependence, as evidenced by a withdrawal syndrome. However, the ability of lorcaserin to produce hallucinations, euphoria, and positive subjective responses at supratherapeutic doses suggests that lorcaserin may produce psychic dependence.

OVERDOSAGE

No experience with overdose of BELVIQ is available. In clinical studies that used doses that were higher than the recommended dose, the most frequent adverse reactions associated with BELVIQ were headache, nausea, abdominal discomfort, and dizziness. Single 40- and 60-mg doses of BELVIQ caused euphoria, altered mood, and hallucination in some subjects. Treatment of overdose should consist of BELVIQ discontinuation and general supportive measures in the management of overdosage. BELVIQ is not eliminated to a therapeutically significant degree by hemodialysis.

References: 1. BELVIQ [package insert]. Woodcliff Lake, NJ: Eisai Inc; 2012. **2.** Thomsen WJ, Grottick AJ, Menzaghi F, et al. Lorcaserin, a novel selective human 5-hydroxytryptamine$_{2C}$ agonist: in vitro and in vivo pharmacological characterization. *J Pharmacol Exp Ther.* 2008;325(2):577-587.

Surgical Options

Indications

Patients with a BMI >35 kg/m^2 with obesity-related comorbidities, and those with a BMI >40 kg/m^2 with or without comorbidities are currently eligible for bariatric surgery (Figure 2).[1]

Figure 2 Candidates for Bariatric Surgery

- BMI >40 kg/m^2, or BMI >35 kg/m^2 with significant obesity-related comorbidities
- Acceptable operative risk
- Documented failure of nonsurgical weight-loss programs
- Psychologically stable, with realistic expectations
- Well-informed and motivated patient
- Supportive family and social environment
- Absence of active alcohol or substance abuse
- Absence of uncontrolled psychotic or depressive disorder

BMI, body mass index.

For a patient to be appropriate for bariatric surgery he or she must have attempted a medical weight-loss program and should be highly motivated to make postsurgical lifestyle changes. In 1991, the National Institutes of Health (NIH) guidelines recommended that bariatric surgery be limited to patients aged 18 to 60 years. At that time, there was insufficient evidence to make recommendations about surgery for patients at the extremes of age. Although advanced age has been a predictor of increased mortality after bariatric surgery in some studies,[13,14] there is evidence from case studies that bariatric surgery can be safe and effective in carefully selected adolescent and older patients.

Contraindications

Patients who cannot tolerate general anesthesia because of cardiac, pulmonary, or hepatic insufficiency are not candidates for surgery. Additionally, patients must be able to understand the consequences of the surgery and comply with the extensive preoperative evaluation and postoperative lifestyle changes, diet, vitamin supplementation, and follow-up program. Patients who have ongoing substance-abuse issues or unstable psychiatric illness are also poor candidates.

Follow-up

Bariatric surgery patients require lifetime follow-up.[1] Early postoperative visits focus on potential complications or difficulties and the dramatic changes in dietary habits. Later follow-up visits focus on psychological support, nutritional assessment and vitamin supplementation, and adherence to an exercise program. Patients who present with new-onset abdominal pain, vomiting, or gastroesophageal reflux months to years after bariatric surgery should be referred to a bariatric surgeon. These symptoms may result from an anastomotic ulcer or stricture, or an intermittent bowel obstruction after Roux-en-Y gastric bypass (RYGB). Following laparoscopic adjustable gastric banding (LAGB), a new onset of gastroesophageal reflux or dysphagia may suggest gastric prolapse through the band. A patient who exhibits these signs requires prompt evaluation and treatment.

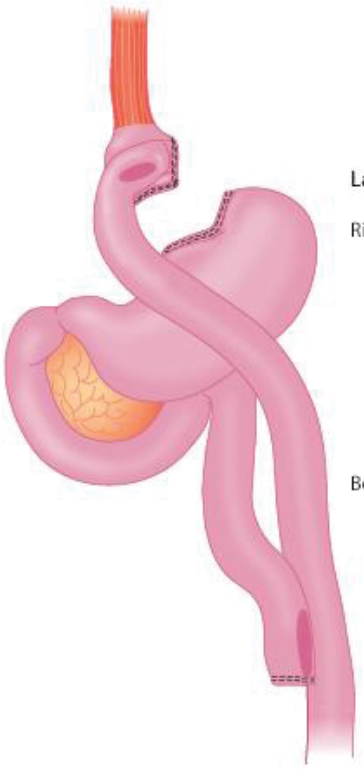
Procedures

Roux-en-Y Gastric Bypass. RYGB combines a restrictive component and a limited proximal intestinal bypass, and is the most common bariatric procedure performed in the U.S. (80% of all bariatric procedures). Most RYGB procedures are now performed laparoscopically, resulting in faster recovery and fewer pulmonary and wound complications when compared with open surgery. A small, 15- to 30-mL gastric pouch is created to restrict food intake, and a Roux-en-Y anastomosis bypasses the duodenum and proximal jejunum (about 150 cm). The risks and benefits associated with RYGB are shown in Figure 3. RYGB results in superior weight loss and comorbidity resolution with excellent long-term excess weight loss (EWL) of 50% to 55% after 10 years. RYGB has unique effects on gut hormones and glucose homeostasis that are weight-loss independent. These incretin effects and a rapid improvement in diabetes have been observed in patients with mild, moderate, and severe obesity.

Laparoscopic Adjustable Gastric Banding. The first device for laparoscopic adjustable gastric banding (LAGB) was approved for use in the U.S. in 2001 after demonstrating excellent results in Europe and Australia. In this procedure, a silicone band with an inflatable inner collar is placed around the upper portion of the stomach to create a small gastric pouch and to restrict the gastric cardia. The band is connected to a port that is placed in the subcutaneous tissue of the abdominal wall. The inner diameter of the band can be adjusted by injecting saline through the port.

The adjustability of LAGB is a major advantage over vertical-banded gastroplasty. Band adjustments are made according to weight loss, hunger, and satiety by injecting or removing saline via the subcutaneous port. Severe complications and mortality rates are lower for LAGB than for RYGB, but LAGB typically results in less weight loss that occurs more gradually. Common risks and benefits of LAGB are shown in Figure 4.

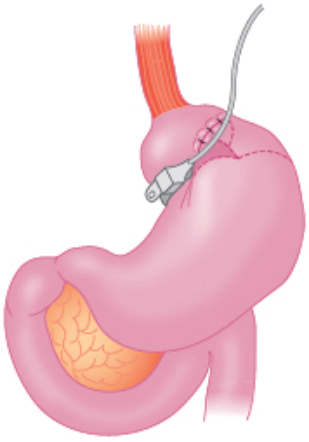
Figure 3 Risks and Benefits of Roux-en-Y Gastric Bypass



Laparascopic Roux-en-Y Gastric Bypass

Risks:	1-2% anastomotic leak rate
	2-15% anastomotic ulcer/stricture rate
	1-5% late bowel obstruction rate
	0.16% mortality rate
	Micronutrient deficiencies (iron, B12, calcium, vitamin D), if not supplemented and followed long-term
Benefits:	65-80% excess weight loss
	84% resolution of diabetes
	97% improvement in hyperlipidemia
	68% resolution of hypertension
	78% resolution of sleep apnea

Figure 4 Risks and Benefits of Laparoscopic Adjustable Gastric Banding



Laparascopic Adjustable Gastric Banding

Risks:	2-25% slip/prolapse rate
	0-2% band erosion rate
	20-30% inadequate weight loss
	15-30% late re-operation rate for failures/complications
Benefits:	40-60% excess weight loss
	55% resolution of diabetes
	60% improvement in hyperlipidemia
	45% resolution of hypertension
	95% resolution of sleep apnea

Sleeve Gastrectomy. Laparoscopic sleeve gastrectomy (LSG) has been used as a weight-loss procedure in a variety of patient groups for more than 10 years. The risks and benefits of this procedure are described in Figure 5. This operation involves a vertical resection and removal of the body and fundus of the stomach, leaving a tubular gastric lumen from the gastroesophageal junction to the antrum. The pylorus is left intact and there is no device or bypass associated with this procedure. Initially, LSG was used as part of a risk-management strategy for high-risk and very high BMI patients. After achieving substantial weight loss and improved health status following LSG, these patients underwent an RYGB or duodenal switch procedure to continue the weight loss. In the past several years, LSG has gained acceptance as a primary bariatric procedure for lower BMI patients, as well. Early complications include leaks at the gastric staple line in 1% to 2% of patients, bleeding, and strictures or narrowing at the gastric incisura. The re-operation and late complication rates for LSG are lower than for LAGB and RYGB, but overall LSG has been shown to fall between LAGB and RYGB in terms of risks, benefits, and weight loss.

Figure 5 Risks and Benefits of Laparoscopic Sleeve Gastrectomy

Risks:

- 1-2% leak rate
- 1-2% stenosis/stricture rate
- 20-30% incidence of GERD long-term
- 5% re-operation rate
- 0.1% mortality rate

Benefits:

- 50-60% excess weight loss long-term (>5 years)
- 50-60% remission of diabetes
- 75% remission of sleep apnea
- 60-75% remission hypertension

Biliopancreatic Diversion. Biliopancreatic diversion is a malabsorptive procedure performed by less than 3% of bariatric surgeons in the U.S. This procedure is designed to limit intestinal energy absorption to the length of the distal common channel. Although these procedures offer the best and most durable weight-loss results of any bariatric procedure performed today, higher complication rates, nutritional deficiencies, and a higher mortality rate have limited their widespread use.

Outcomes

In a meta-analysis of 29 studies of the drug orlistat (also called tetrahydrolipstatin), the pooled mean weight loss for orlistat-treated patients was 2.59 kg at 6 months and 2.89 kg at 12 months. The average age of patients enrolled was 48 years, and the average BMI was 36.7 kg/m^2.[15]

Other agents—such as phentermine, diethylpropion, and fluoxetine—result in a 3.0- to 3.6-kg weight loss after 1 year when used in combination with lifestyle modifications. There are limited data on sertraline, bupropion, topiramate, and zonisamide with regard to weight-loss outcomes. Therefore, recommendations cannot be made until further studies have been completed.[16]

A randomized, controlled trial evaluating the use of the laparoscopic adjustable gastric band (lap-band) for mild to moderate obesity (BMI 30 kg/m^2 to 35 kg/m^2) has demonstrated significantly greater weight loss and comorbidity resolution among patients in the surgical group compared with those enrolled in an aggressive medical weight-loss program. After 2 years, EWL was 87% in the surgical group and 21% in the nonsurgical group. Metabolic syndrome resolved in 93% of surgical patients and in 47% of nonsurgical patients.[17]

A large, prospective, matched cohort study (Swedish Obese Subjects Study) demonstrated the durability of weight loss and comorbidity reduction 10 years after bariatric surgery[18] and a 30% reduction in all-cause mortality in the surgery group.[19] Another large, matched cohort study demonstrated a significant reduction in mortality (40% reduction in all-cause mortality) 7 years after gastric-bypass surgery.[20]

A meta-analysis analyzing 22,094 patients in 136 studies found that for all bariatric procedures, the average EWL was 61.2%. Biliopancreatic diversion or duodenal switch procedures had the highest overall EWL (70%), followed by gastric bypass (61%), and gastric banding (47%). Overall, diabetes improved or resolved in 86% of patients, hyperlipidemia improved in 70%, hypertension improved or resolved in 78.5%, and obstructive sleep apnea improved or resolved in 83.6% of patients.[21] Two recent randomized controlled trials have demonstrated the efficacy of bariatric surgery over medical therapy for the treatment of type 2 diabetes, often eliminating the need for hypoglycemic and cardiovascular drugs.[22,23]

In a meta-analysis of more than 85,000 patients, the overall postoperative mortality after bariatric surgery (<30 days) was 0.3%. The operative mortality rates for laparoscopic restrictive procedures and laparoscopic gastric bypass were 0.07% and 0.16%, respectively.[24] Mortality after bariatric surgery is primarily the result of pulmonary embolism, anastomotic leak, or septic complications.

Summary

- Severe obesity can adversely affect every organ system.
- Detailed evaluation of symptoms can uncover serious comorbidities.
- Diabetes, cancer, and cardiovascular disease are common in obese patients.
- Central adiposity is associated with the presence of the metabolic syndrome.
- All obese patients (BMI >30 kg/m^2) should be counseled on lifestyle and behavioral modifications, such as appropriate diet and exercise.
- Pharmacologic therapy can be offered to obese patients who have failed to lose weight through exercise and changes in diet.
- Bariatric surgery should be considered for morbidly obese patients in whom medical weight loss programs—diet and exercise, with or without pharmacotherapy—have failed. Patients with a BMI >40 kg/m^2, or >35 kg/m^2 with obesity-related comorbidities, are candidates for bariatric surgery.
- Bariatric surgery should be considered for the treatment of type 2 diabetes in severely and moderately obese individuals.

practice fusion®

Thousands of patient records at your fingertips

Free, intuitive features:

- Charting
- Scheduling
- Lab Integration
- e-Prescribing

Practice Fusion's 100% free, web-based EMR gives you the flexibility to chart patient visits anywhere. Learn why over 150,000 medical professionals trust Practice Fusion.

Get started with your free EMR today!

www.practicefusion.com/emr

Suggested Readings & References

Suggested Readings

- Arterburn DE, Crane PK, Veenstra DL: The efficacy and safety of sibutramine for weight loss: A systematic review. Arch Intern Med 2004;164:994-1003.
- Buchwald H, Avidor Y, Braunwald E, et al: Bariatric surgery: A systematic review and meta-analysis. JAMA 2004;292:1724-1737.
- Christou NV, Sampalis JS, Liberman M, et al: Surgery decreases long-term mortality, morbidity, and health care use in morbidly obese patients. Ann Surg 2004;240:416-423.
- Consensus Development Conference Panel: NIH conference. Gastrointestinal surgery for severe obesity. Ann Intern Med 1991;115:956-961.
- Demaria EJ, Jamal MK: Surgical options for obesity. Gastroenterol Clin North Am 2005;34:127-142.
- Flegal KM, Graubard BI, Williamson DF, Gail MH: Excess deaths associated with underweight, overweight, and obesity. JAMA 2005;293:1861-1867.
- Flum DR, Salem L, Elrod JA, et al: Early mortality among Medicare beneficiaries undergoing bariatric surgical procedures. JAMA 2005;294:1903-1908.
- Fontaine KR, Redden DT, Wang C, et al: Years of life lost due to obesity. JAMA 2003;289:187-193.
- Haddock CK, Poston WS, Dill PL, et al: Pharmacotherapy for obesity: A quantitative analysis of four decades of published randomized clinical trials. Int J Obes Relat Metab Disord 2002;26:262-273.
- Harris MI, Flegal KM, Cowie CC, et al: Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults. The Third National Health and Nutrition Examination Survey, 1988-1994. Diabetes Care 1998;21:518-524.
- Knowler WC, Barrett-Connor E, Fowler SE, et al: Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002;346:393-403.
- Livingston EH, Huerta S, Arthur D, et al: Male gender is a predictor of morbidity and age a predictor of mortality for patients undergoing gastric bypass surgery. Ann Surg 2002;236:576-582.
- McTigue KM, Harris R, Hemphill B, et al: Screening and interventions for obesity in adults: Summary of the evidence for the U.S. Preventive Services Task Force. Ann Intern Med 2003;139:933-949.
- National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III): Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation 2002;106:3143-3421.

- Ogden CL, Carroll MD, Curtin LR, et al: Prevalence of overweight and obesity in the United States, 1999-2004. JAMA 2006;295:1549-1555.
- Pi-Sunyer FX. A review of long-term studies evaluating the efficacy of weight loss in ameliorating disorders associated with obesity. Clin Ther 1996;18:1006-1035.
- Sauerland S, Angrisani L, Belachew M, et al: Obesity surgery: Evidence-based guidelines of the European Association for Endoscopic Surgery (EAES). Surg Endosc 2005;19:200-221.
- Sjostrom L, Lindroos AK, Peltonen M, et al: Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. N Engl J Med 2004;351:2683-2693.
- Snow V, Barry P, Fitterman N, et al: Pharmacologic and surgical management of obesity in primary care: A clinical practice guideline from the American College of Physicians. Ann Intern Med 2005;142:525-531.
- Wadden TA, Bartlett SJ, Foster GD, et al: Sertraline and relapse prevention training following treatment by very-low-calorie diet: A controlled clinical trial. Obes Res 1995;3:549-557.
- Wolf AM, Colditz GA: The cost of obesity: The U.S. perspective. Pharmacoeconomics 1994;5(Suppl 1):34-37.

References

1. NIH conference. Gastrointestinal surgery for severe obesity. Consensus Development Conference Panel. Ann Intern Med 1991; 115(12):956-61.
2. Flegal KM, Carroll MD, Kit BK, Ogden CL. Prevalence of obesity and trends in the distribution of body mass index among US adults, 1999-2010. Jama; 307(5):491-7.
3. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of obesity and trends in body mass index among US children and adolescents, 1999-2010. Jama; 307(5):483-90.
4. Wolf AM, Colditz GA. The cost of obesity: the US perspective. Pharmacoeconomics 1994; 5(Suppl 1):34-7.
5. Flegal KM, Graubard BI, Williamson DF, Gail MH. Excess deaths associated with underweight, overweight, and obesity. Jama 2005; 293(15):1861-7.
6. Fontaine KR, Redden DT, Wang C, et al. Years of life lost due to obesity. Jama 2003; 289(2):187-93.
7. Sauerland S, Angrisani L, Belachew M, et al. Obesity surgery: evidence-based guidelines of the European Association for Endoscopic Surgery (EAES). Surg Endosc 2005; 19(2):200-21.
8. Snow V, Barry P, Fitterman N, et al. Pharmacologic and surgical management of obesity in primary care: a clinical practice guideline from the American College of Physicians. Ann Intern Med 2005; 142(7):525-31.
9. McTigue KM, Harris R, Hemphill B, et al. Screening and interventions for obesity in adults: summary of the evidence for the U.S. Preventive Services Task Force. Ann Intern Med 2003; 139(11):933-49.
10. Pi-Sunyer FX. A review of long-term studies evaluating the efficacy of weight loss in ameliorating disorders associated with obesity. Clin Ther 1996; 18(6):1006-35; discussion 1005.
11. Harris MI, Flegal KM, Cowie CC, et al. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults. The Third National Health and Nutrition Examination Survey, 1988-1994. Diabetes Care 1998; 21(4):518-24.
12. Knowler WC, Barrett-Connor E, Fowler SE, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002; 346(6):393-403.
13. Flum DR, Salem L, Elrod JA, et al. Early mortality among Medicare beneficiaries undergoing bariatric surgical procedures. Jama 2005; 294(15):1903-8.
14. Livingston EH, Huerta S, Arthur D, et al. Male gender is a predictor of morbidity and age a predictor of mortality for patients undergoing gastric bypass surgery. Ann Surg 2002; 236(5):576-82.
15. Haddock CK, Poston WS, Dill PL, et al. Pharmacotherapy for obesity: a quantitative analysis of four decades of published randomized clinical trials. Int J Obes Relat Metab Disord 2002; 26(2):262-73.
16. Wadden TA, Bartlett SJ, Foster GD, et al. Sertraline and relapse prevention training following treatment by very-low-calorie diet: a controlled clinical trial. Obes Res 1995; 3(6):549-57.

17. O'Brien PE, Dixon JB, Laurie C, et al. Treatment of mild to moderate obesity with laparoscopic adjustable gastric banding or an intensive medical program: a randomized trial. Ann Intern Med 2006; 144(9):625-33.
18. Sjostrom L, Lindroos AK, Peltonen M, et al. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. N Engl J Med 2004; 351(26):2683-93.
19. Sjostrom L, Narbro K, Sjostrom CD, et al. Effects of bariatric surgery on mortality in Swedish obese subjects. N Engl J Med 2007; 357(8):741-52.
20. Adams TD, Gress RE, Smith SC, et al. Long-term mortality after gastric bypass surgery. N Engl J Med 2007; 357(8):753-61.
21. Buchwald H, Avidor Y, Braunwald E, et al. Bariatric surgery: a systematic review and meta-analysis. Jama 2004; 292(14):1724-37.
22. Mingrone G, Panunzi S, De Gaetano A, et al. Bariatric surgery versus conventional medical therapy for type 2 diabetes. N Engl J Med; 366(17):1577-85.
23. Schauer PR, Kashyap SR, Wolski K, et al. Bariatric surgery versus intensive medical therapy in obese patients with diabetes. N Engl J Med; 366(17):1567-76.
24. Buchwald H, Estok R, Fahrbach K, et al. Trends in mortality in bariatric surgery: a systematic review and meta-analysis. Surgery 2007; 142(4):621-32; discussion 632-5.

Notes

Notes

Software Advice

THE AUTHORITY ON SOFTWARE SELECTION

Compare Over 125 Leading Medical Software Systems

- Unbiased Reviews
- Free Price Quotes
- Free Online Demos

Software Categories

- Electronic Medical Records
- Practice Management
- Medical Billing
- Patient Scheduling
- Medical Accounting
- Over 30 Different Medical Specialties

Find The Right System for Your Needs

Software Advice has connected over 40,000 companies and 100,000 buyers with the software products best suited to their needs.

How we do it: Our software experts match you with products that fit your needs

Why it's free: When we make a "good match" between a software buyer and a software vendor, we get paid by the vendor (it's free for you!).

What we hear: software buyers and vendors tell us every day how happy they are with our ability to simplify the software selection process.

Let us help you find the right system by visiting our website at softwareadvice.com/medical or calling our medical software analysts directly at (800) 234-5103.

Software Advice
200 Academy Drive, Suite 120
Austin, TX 78704

softwareadvice.com/medical **(800) 234-5103**