

in the clinic

Obesity

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The content of *In the Clinic* is drawn from the clinical information and education resources of the American College of Physicians (ACP), including PIER (Physicians' Information and Education Resource) and MKSAP (Medical Knowledge and Self-Assessment Program). *Annals of Internal Medicine* editors develop *In the Clinic* from these primary sources in collaboration with the ACP's Medical Education and Publishing Division and with the assistance of science writers and physician writers. Editorial consultants from PIER and MKSAP provide expert review of the content. Readers who are interested in these primary resources for more detail can consult <http://pier.acponline.org> and other resources referenced in each issue of *In the Clinic*.

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Health Consequences

More than 30% of U.S. adults are obese (1). Generally defined as a body mass index (BMI) greater than 30 kg/m², obesity is a serious chronic problem that is difficult to treat. Obesity is associated with increased all-cause mortality and increased risk for serious medical conditions, including type 2 diabetes, dyslipidemia, hypertension, and sleep apnea. People who are obese may also experience social stigmatization. Although weight loss is difficult to achieve and maintain, several approaches are available for losing weight. Even a loss of 5% body weight can substantially reduce the risks associated with obesity.

What health problems are associated with being overweight?

Excess body fat, particularly visceral fat, increases the risk for numerous diseases. The increased risk results from either the metabolic consequence of the enlarged fat cells or from the increased mass of fat (Table 1).

The increased risk from the diseases associated with obesity substantially increases the risk for mortality. In essentially all studies, mortality and BMI have a J-shaped relationship.

Among more than 90 000 women in the Women's Health Initiative, there was a graded increase in the risk for death as BMI increased from normal levels to greater than 40 kg/m² (2).

Another U.S. cohort of more than 80 000 men and women was monitored for more than 14.7 years with more than 1.23 million person-years of follow-up. Excluding deaths

in the first 5 years, risk for death in patients younger than 55 years of age was directly related to BMI in both men and women, beginning at a BMI of 21 kg/m² in women and 23 kg/m² in men. In those older than 55 years of age, the increase in mortality occurred at a higher BMI, beginning at 25 kg/m² in women and 30 kg/m² in men (3).

What is the evidence that weight loss improves health outcomes?

There is good evidence that obese patients who lose weight reduce their risk for comorbid diseases, including diabetes, hypertension, sleep apnea, and cardiovascular disease, and experience improved overall quality of life. Even modest reductions in weight lead to improvement in health outcomes.

Of 3234 study participants with impaired glucose tolerance randomly assigned to either intensive lifestyle modification (n = 1079), metformin (n = 1073), or placebo (n = 1062), those in the intensive lifestyle

1. Ogden CL, Carroll MD, Curtin LR, et al. Prevalence of overweight and obesity in the United States, 1999-2004. *JAMA*. 2006;295:1549-55. [PMID: 16595758]
2. McTigue K, Larson JC, Valoski A, et al. Mortality and cardiac and vascular outcomes in extremely obese women. *JAMA*. 2006;296:79-86. [PMID: 16820550]
3. Freedman DM, Ron E, Ballard-Barbash R, et al. Body mass index and all-cause mortality in a nationwide US cohort. *Int J Obes (Lond)*. 2006;30:822-9. [PMID: 16404410]
4. Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med*. 2002;346:393-403. [PMID: 11832527]

Table 1. Obesity-Associated Health Problems

Resulting from the metabolic effects of enlarged fat cells and visceral fat

Type 2 diabetes

Hypertension
Dyslipidemia (low HDL-cholesterol levels and high triglyceride levels)

Cardiovascular disease (coronary artery disease, stroke, heart failure, and atrial fibrillation)

Cancer (in men: liver, stomach, pancreas, esophagus, multiple myeloma, rectum, and gall bladder; in women: uterus, kidney, cervix, pancreas, esophagus, gallbladder, breast, liver, ovary, colon, and rectum)

Gastrointestinal disease (GERD, erosive gastritis, gall bladder disease, gall stones, cholecystectomy, and nonalcoholic steatohepatitis)

Kidney disease (kidney stones, chronic renal disease, and end-stage renal disease)

Endocrine changes (hyperinsulinemia and insulin resistance, disturbed menstrual cycles, and altered cortisol metabolism)

Infertility (the polycystic ovarian syndrome)

Obstetrical risks (Caesarean section, hypertension, stillbirth, and neonatal mortality)

Resulting from increased body mass

Bone and joint diseases (osteoarthritis and hospitalization for back disorders)

Pulmonary disease (sleep apnea, pulmonary embolism, and sleep-disordered breathing)

Social stigmatization

GERD = gastroesophageal reflux disease; HDL = high-density lipoprotein.

modification group experienced the best outcome, losing 7% or more of their body weight at 24 weeks, and 38% had a weight loss of 7% at average follow-up of 2.8 years. They had a 58% reduction in the risk for diabetes compared with patients in the placebo group (95% CI, 48% to 66%) (4).

In the Framingham study, a modest weight loss of 6.8 kg or more led to a 28% reduction in the risk for hypertension among middle-age adults and a 37% reduction among older adults (5).

In a clinical trial using lifestyle interventions to lower blood pressure (TOPH II), the risk for hypertension decreased by 65% in those who maintained their weight loss of 4.5 kg for 30 months (6).

In a systematic review of long-term weight-loss studies in obese adults, both dietary and lifestyle approaches and pharmacologic interventions improved markers of cardiovascular disease, particularly in patients with cardiovascular risk factors at the beginning of the study (7).

Health Consequences... Obesity increases the risk for numerous diseases, including type 2 diabetes, cardiovascular disease, pulmonary disease, and cancer. It also increases the risk for mortality, with risk increasing linearly with BMI. Even limited weight loss can substantially lower these risks.

CLINICAL BOTTOM LINE

Should clinicians routinely screen patients for overweight or obesity?

The U.S. Preventive Services Task Force recommends that clinicians screen all adult patients for obesity and offer intensive counseling and behavioral interventions to promote sustained weight loss for obese adults (8). The National Heart, Lung, and Blood Institute also recommends determining both height and weight in order to calculate BMI in all patients (see Box).

The accepted definition of obesity is a BMI greater than 30 kg/m², and overweight is defined as a BMI from 25.0 to 29.9 kg/m² (9).

Which health behaviors reduce the risk for becoming overweight?

Certain health behaviors at different stages of life can reduce the risk for becoming overweight. Even during infancy and early childhood, risk factors for obesity may be present, and some of them are modifiable.

Women can make certain efforts to lower the risk that their children will become overweight, including maintaining normal weight gain

during pregnancy, not smoking, and extending duration of breast feeding (10, 11).

Key factors predicting weight gain in children include high parental BMI, excessive weight gain in the first year, and a rise in BMI before ages 4 to 6 years (12). In addition to avoiding weight gain themselves, parents can encourage certain healthy habits in their children by making sure that they eat breakfast, limiting their intake of high sugar foods (including soft drinks and fruit drinks), reducing their time spent in such sedentary activities as watching television, and encouraging adequate sleep (13–16).

In people of all ages, monitored food intake and increased levels of activity, particularly walking and other forms of exercise, are associated with less future weight gain and should be encouraged (17).

Some drugs are associated with weight gain (see Box), and clinicians may be able to substitute a medication that produces less weight gain to help patients avoid becoming overweight.

Screening and Prevention

Body Mass Index = kilograms of body weight divided by the square of the height in meters (kg/m²)

Drugs that Produce Weight Gain

- Thioridazine
- Olanzapine
- Quetiapine
- Risperidone
- Clozapine
- Amitriptyline
- Nortriptyline
- Imipramine
- Mirtazapine
- Paroxetine
- Valproate
- Carbamazepine
- Gabapentin
- Insulin
- Sulfonylureas
- Thiazolidinediones
- Pizotifen
- Cyproheptadine
- Propranolol
- Terazosin
- Contraceptives
- Glucocorticoids
- Progestational steroids

Screening and Prevention... Clinicians should measure BMI in all patients. Certain health behaviors, such as controlling caloric intake and engaging in regular physical activity, can reduce the risk for becoming overweight in adults and children. Some medications are associated with weight gain and should be avoided in patients at high risk for becoming overweight.

CLINICAL BOTTOM LINE

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Diagnosis

How does one make the diagnosis of overweight and obesity?

Clinicians should calculate the patient's BMI and follow it over time because BMI is easy to determine, very reliable, closely correlated with body fat, and linked with the broadest range of health outcomes (8, 18). The National Heart, Lung, and Blood Institute and the World Health Organization have adopted BMI as the criterion for defining overweight and obesity (9, 19). Both groups define a BMI of 18.5 to 24.9 kg/m² as normal weight, a BMI of 25 to 29.9 kg/m² as overweight, and a BMI greater than 30 kg/m² as obesity. The Asia-Oceania Criteria differ slightly: Normal weight is 18.5 to 22.9 kg/m², overweight is 23 to 24.9 kg/m², and obesity is greater than 25 kg/m² (20). At the same BMI, body fat is about 12% higher in women than in men (21).

In what types of patients might BMI measurement be misleading?

BMI may not be the best predictor of weight-related health problems in certain ethnic groups, such as African Americans and Hispanic-American women, who may have more fat-free mass in bone and muscle compared with Caucasians and thus misleadingly high BMI measurements. BMI may also be misleading in children, elderly patients, and athletes because of differences in height and proportions of fat and fat-free mass. In children, height-weight relationships are continually changing. During the first 5 to 7 years of life, BMI declines, reaches a nadir, and

then begins to rise toward adult levels. BMI can be confusing in elderly individuals who have lost height, which makes the BMI seem higher than it really is. Because of decreased muscle mass in some older people, BMI may underestimate body fat. However, the effect of loss of height is more substantial. Similarly, athletes who have increased muscle mass and reduced fat mass may seem to have a high BMI but have little risk for obesity-associated diseases, such as cardiovascular disease or diabetes.

When should clinicians measure waist circumference or waist-to-hip ratio in evaluating overweight and obese patients?

Clinicians should consider measuring waist circumference and waist-to-hip ratio in most, if not all, overweight patients. Waist circumference may be a better measure of central adiposity, a correlate of visceral adiposity that is related to cardiovascular risk (although waist circumference does not improve prediction of cardiovascular risk in patients with a BMI of 35 or greater). Waist circumference is also a component of the metabolic syndrome as defined by the Adult Treatment Panel III of the National Cholesterol Education Program (22, 23). Table 2 shows criteria for the upper limits of normal waist circumference.

For individuals older than 75 years, the waist-to-hip ratio (waist circumference divided by hip circumference) may be a better predictor of death than either body mass

Table 2. Criteria for Central Adiposity

Organization	Waist Circumference Cut-Points*	
	Men	Women
National Heart, Lung and Blood Institute (United States)	102 cm (40 in)	88 cm (35 in)
International Diabetes Federation (Europe)	94 cm (37 in)	80 cm (31 in)
International Diabetes Federation (South Asia, China, and Japan)	90 cm (33 in)	80 cm (31 in)

* Values above these levels are considered abnormal (22, 25).

index or waist circumference alone (24). Waist-to-hip ratios greater than 0.95 in men and 0.85 in women are considered elevated.

Other measurements of fat mass, such as sagittal diameter and skin-fold thickness, can be made at the time of physical examination but are impractical in everyday clinical practice.

What other factors and conditions should clinicians consider when evaluating overweight and obese patients?

It is important to determine the patient's ethnicity and social situation; if the patient's parents were overweight; if there has been a recent life event that may affect weight, such as pregnancy, recent surgery, or disability; the level of physical activity; and medication history.

On physical examination, clinicians should look for evidence of conditions associated with increased weight, including hypertension, evidence of endocrinopathies (such as hypercortisolism or hypothyroidism), reproductive disorders (such as the polycystic ovary syndrome), and phenotypic abnormalities suggestive of uncommon genetic disorders associated with obesity.

Genetic syndromes associated with obesity include the Prader-Willi syndrome, which results from a paternal chromosomal abnormality, and the Bardet-Biedl syndrome, the Ahlstrom syndrome, the Carpenter syndrome, and the Cohen syndrome, all of which result from

autosomal recessive abnormalities. Other genetic causes of obesity include melanocortin-4 receptor defects and leptin deficiency or leptin receptor deficiency (26).

Which laboratory tests should clinicians consider in overweight and obese patients?

Clinicians should use laboratory testing to evaluate overweight and obese patients who may be at high risk for cardiovascular disease, diabetes, and thyroid disease. Some pertinent tests to consider are fasting plasma glucose or 2-hour postprandial glucose levels and serum lipid levels. Thyroid-stimulating hormone may be helpful in excluding hypothyroidism, particularly in older women. Urinary free cortisol can be obtained if hypercortisolism is suspected.

Other tests to consider depend on clinical assessment and include ultrasound for hepatic steatosis, gallstones, and the polycystic ovary syndrome; electrocardiography in patients at high risk for cardiovascular disease; polysomnography for patients with possible sleep apnea; and head computed tomography or magnetic resonance imaging when pituitary or hypothalamic disorders are suspected. Genetic testing is needed to confirm the diagnosis in patients with rare genetic disorders.

Although there are a variety of more-sophisticated laboratory techniques for gathering additional information about body fat and fat distribution, including bioelectrical impedance, dual-energy X-ray absorptiometry, and total body water determination, none of these

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techniques is recommended for general clinical evaluation. The gold standard test for measuring central and visceral fat is with

abdominal computed tomography or magnetic resonance imaging with cross-sectional cuts at L-4/L-5, but both are costly.

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Diagnosis... Although BMI is used to define overweight (25 to 29.9 kg/m²) and obesity (BMI >30 kg/m²), it may not be the best predictor of weight-related health problems in children, older people, and athletes. Waist circumference and the waist-to-hip ratio may correlate better with increased cardiovascular risk. Laboratory testing should be based on clinical evaluation and used to assess risk for diseases associated with obesity. Clinicians should consider the possible role of endocrine, neuroendocrine, or genetic disorders as causes of obesity.

CLINICAL BOTTOM LINE

Treatment

What counseling should clinicians provide patients about losing weight?

Clinicians should assess whether the patient is ready to make lifestyle changes and encourage attainable weight-loss goals. Patients often have a “dream weight” that involves a weight loss of nearly 30% of their initial body weight. However, weight losses of 5% to 10% are more realistically attainable and are still associated with proven health benefits. For instance, several studies have demonstrated that a weight reduction of 5% or more in “at-risk” individuals can reduce the risk for diabetes (4, 7, 27). Although additional weight loss further reduces risk (28), setting reasonable goals with the patient is one of the initial key steps in treatment (Figure).

Why is it difficult for many people to lose weight?

Body weight is controlled through a carefully regulated feedback system designed to maintain homeostasis and resist change. Even after people lose an initial amount of weight, they reach a “plateau” and stop losing any more weight, regardless of weight-loss program or treatment. Further weight loss is difficult to achieve and initial weight loss difficult to sustain. Only a small minority of people who lose weight are able to

maintain their full weight loss at 3 years.

Lack of adherence to diet is another major reason for difficulty in losing weight and maintaining it. Hunger may increase over time with reduced body weight, serving as a mechanism to signal loss of energy stores and thwart efforts to lose more weight. A drop in circulating leptin may be another factor in maintaining the plateau in body weight.

What behavioral modifications are used in the treatment of obesity?

Behavior therapy is one of the cornerstones of treatment for obesity. People who are successful in losing weight and maintaining weight loss tend to monitor their behavior, eat less, increase their physical activity, and practice positive self-thinking and techniques to reduce stress (29).

Behavior modification strategies include keeping a food diary, which helps patients learn to monitor their eating behavior by recording what is eaten, determining the setting in which they eat, and identifying the situations that trigger eating. With this information, the health-care provider can help patients change their eating habits and adopt a defined eating plan.

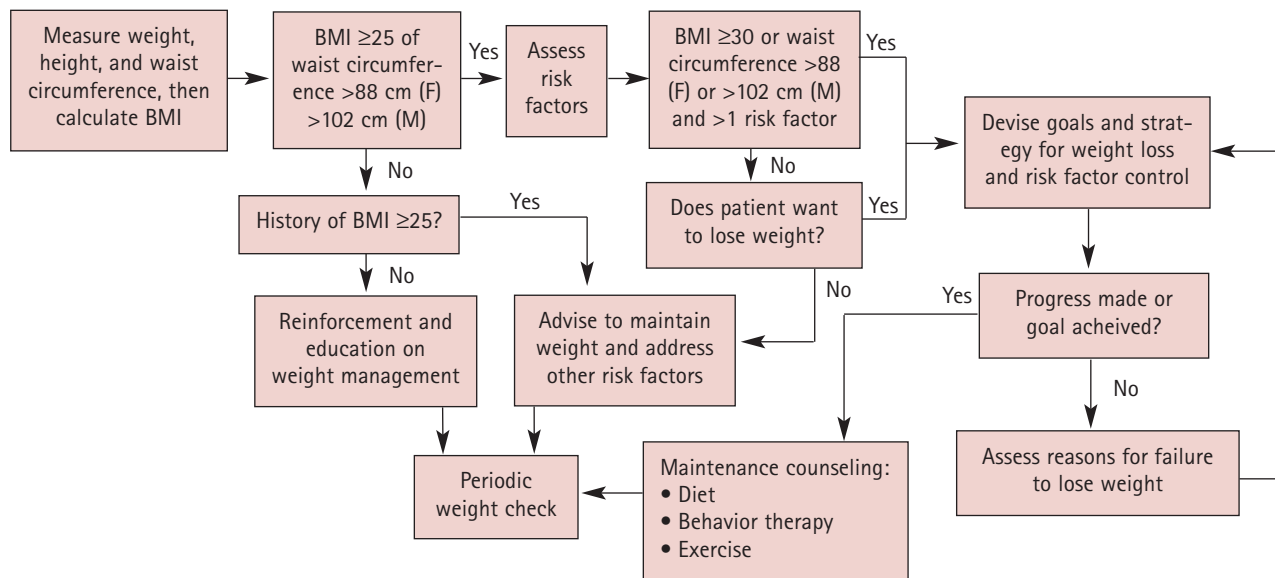


Figure. Treatment algorithm. Adapted from (9).

Exercise offers a strategy for balancing energy intake and expenditure, whether as a primary treatment for weight loss or for preventing patients from regaining weight.

Generally, people who are trying to lose weight should increase their walking or other comparable activities to 30 to 60 minutes 5 or more days a week.

One study found that moderate-to-vigorous exercise for 60 minutes per day, 6 days per week, produced weight loss of 1.4 kg in women and 1.8 kg in men compared with nonexercisers over 12 months (30).

Exercise alone, however, is often inadequate as a primary treatment for weight loss. A meta-analysis of weight loss trials found that exercise alone resulted in a 3-kg weight loss compared with an 11-kg loss with diet (31). This is because it takes a lot of exercise to lose weight. A person who wishes to lose 1 pound per week through exercise needs to walk approximately 5 miles per day 7 days per week in order to achieve a deficit of 3500 kcal. For individuals wanting to monitor their exercise, inexpensive pedometers can be worn on the belt. A mile is about 2000 steps.

Counseling may help people lose weight, and simple dietary advice given by the physicians in the office may be as effective as formal nutrition counseling.

A meta-analysis of 46 studies of dietary counseling showed a maximum net treatment effect of -1.9 (CI, -2.3 to -1.5) BMI units (approximately 6% weight loss over 12 months). There was a decrease of about 0.1 BMI unit per month for the 12 months of active treatment and an increase of about 0.02 to 0.03 BMI units per month during subsequent phases. Different strategies were used in the various studies, and there was no clear basis for selecting one over the other (32).

What dietary modifications are used in the treatment of obesity?

To lose weight, a person must consume fewer calories by eating less food than the body needs for resting metabolic rate and daily activities. The amount and rate of weight loss depends on an individual's degree of adherence to a diet. Many diet plans are available for overweight individuals. These can be grouped into those that are low in fat; those that are low in carbohydrate; those that restrict most nutrients (so-called balanced deficit diets); those that highlight one particular type of food, such as the low-glycemic-index diet; and those

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that highlight specific foods, such as the “grapefruit diet”.

However, diet composition is generally less important than total calories consumed. The standard initial weight loss diet is a balanced low-calorie diet, and use of other types of diets should be based on patient preference. For example, some patients find that diets high in protein and fiber enhance satiety. Patients with dyslipidemia may benefit from low fat diets. Portion-controlled meals provide an easy way to count calories and avoid meal preparation. Whatever diet type, eating at regular intervals throughout the day is important.

Low-Fat Diets

Low-fat diets are effective in helping patients lose weight but are probably not more effective than other types of diets (33). One advantage of very-low fat intake is slowing or reversal of coronary artery atherosclerosis (34).

A large randomized clinical trial of low-fat versus control diets randomly assigned 48835 women to low-fat or control diets and found that weight loss was 2.2 kg below baseline at 1 year and 0.6 kg below baseline at a mean of 7.5 years, and at both times was significantly greater in those on the low-fat diet. There was a clear relationship between the decrease in percent fat and weight loss ($P < 0.001$ for trend) (35).

In a meta-analysis of 19 studies, low-fat diets produced a mean reduction of 10.2% in dietary fat and a weight loss of 3.2 kg more than in the control group. A 1-kg greater pre-diet weight was associated with an additional 2-kg weight loss in those on low-fat diets (36).

Low-Energy-Density Diets

The rationale for recommending low-energy-density diets is based on the theory that filling the stomach with low-fat, high-fiber foods—low-energy-density foods—will reduce hunger and produce satiety. People eat larger amounts of food in experimental settings

when it is more energy dense with more calories per unit weight (37, 38).

Low-Carbohydrate Diets

The most popular diets today are the low-carbohydrate, high-protein, high-fat diets. Carbohydrate content in some of these diets is as low as 13 g/d. When carbohydrate intake is less than 50 g/d, ketosis develops. In short-term metabolic ward studies, patients do not increase the intake of other foods to compensate for the lower calories in a very-low-carbohydrate diet (39). Several randomized clinical trials have reported greater weight loss in patients on low-carbohydrate diets at 6 months, but it is unclear whether differences can be sustained in the long-term (40).

Two recent clinical trials compared a range of low-carbohydrate diets.

In a trial that randomly assigned 160 participants to 1 of 4 popular diets, there were no significant differences in weight loss at 1 year. Weight loss was 3.9 ± 6 kg (CI, 8.58 \pm 13.2 lb) with the Atkins Diet, 4.9 ± 6.9 kg (CI, 10.78 \pm 15.18 lb) with the Zone Diet, 4.6 ± 5.4 kg (10.12 \pm 11.88 lb) with the Weight Watchers Diet, and 6.6 ± 9.3 kg (CI, 14.52 \pm 20.46 lb) with the Ornish Diet. The principal determinant of weight loss was the degree of adherence to the diet and not the diet itself (41).

In the other 1-year trial, 311 premenopausal women were randomly assigned to 1 of 4 diets. The Atkins diet produced more weight loss at 12 months (4.7 kg) compared with the other 3 diets (Zone, 1.6 kg; LEARN, 2.6 kg; Ornish, 2.2 kg). Differences in weight loss among the Zone, LEARN, and Ornish diets were not statistically significant (42).

Commercial Weight-Loss Programs

Several commercial and self-help programs, including Overeaters Anonymous, TOPS (Take Off Pounds Sensibly), Weight Watchers, Jenny Craig, Herbalife, OPTI-FAST, LA Health, and e-Diets, are available. These generally combine diet with self-help programs, some of which are available on the

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Internet. Only a few studies have demonstrated their effectiveness.

In a review of studies of these programs, those that included very-low-calorie diets were associated with high costs, high attrition rates, and a high probability of regaining 50% or more of lost weight in 1 to 2 years, and interventions available over the Internet and organized self-help programs produced minimal weight loss (43).

A 2-year trial involving 423 participants showed that those in the intervention group who attended the Weight Watchers meetings (n = 211) experienced a mean weight loss of 5.3% at 1 year and 3.2% at 2 years, compared with 1.5% at 1 year and 0% at 2 years in those in the control group who received a self-help intervention with 2 visits to a dietitian (44).

When should clinicians consider prescribing very-low-calorie diets?

Clinicians may consider the use of very-low-calorie diets, such as those with energy intake below 800 kcal/d, if needed for rapid weight loss before a major surgical procedure. In other settings, however, the rebound in weight that usually occurs at the end of such programs does not make them worth the extra cost.

A meta-analysis of 29 studies of very-low-calorie diets found that those on diets for at least 2 years lost substantially more weight than those eating hypoenergetic balanced diets (45).

Today, very-low-calorie diets have been largely replaced by portion-controlled diets in which calories are provided from beverages, bars, or frozen meals for use at breakfast or lunch and are fixed by the manufacturer.

In a study of such a diet compared with a 1200- to 1500-kcal control diet in 100 patients, weight loss was substantially greater at 3 months in patients on the diet with meal and snack replacements than in those on the control diet. Thereafter, patients in both groups were given meal replacements and maintained weight losses of 5% or greater at 4 years (46).

Are alternative natural or herbal therapies marketed for weight loss effective and safe?

Many different natural and herbal products are available and purported to facilitate weight loss (see Box) (47). Whether they are safe and effective is unknown in many cases. Clinicians should question patients about use of such products and caution them about uncertainties regarding effectiveness and safety.

When should clinicians consider pharmacological therapy for overweight and obese patients?

Clinicians should consider drug treatment for obesity in patients with a BMI greater than 30 kg/m² and no associated diseases or with a BMI greater than 27 kg/m² if there are associated health problems, such as diabetes, osteoarthritis, hypertension, dyslipidemia, or cardiovascular disease. Because obesity is a long-term problem, current medications should be used as part of a complete program including diet, lifestyle change, and regular physical activity. Guidelines from the American College of Physicians emphasize that pharmacologic therapy should be recommended only when patients fail to meet individualized goals with counseling on lifestyle and behavior modifications, and that physicians should discuss the limitations and adverse effects of available drugs (48).

What pharmacologic therapies are effective in the treatment of overweight and obese patients?

The U.S. Food and Drug Administration (FDA) has approved several drugs for treatment of obesity (Table 3) (49). Two of them, sibutramine and orlistat, are approved for induction and ongoing maintenance of weight loss whereas the others are approved for up to approximately 12 weeks of use.

Metabolic and Herbal Dietary Supplements Marketed to Facilitate Weight Loss

- Chromium picolinate
- Hydroxymethyl butyrate
- Pyruvate
- Conjugated linoleic acid
- Calcium
- Ephedra
- Green tea extract
- Garcinia cambogia
- Yohimbine
- Hoodia
- Bitter orange
- Chitosan
- Glucomannan
- Guar gum
- Psyllium

42. Gardner CD, Kiazand A, Alhassan S, et al. Comparison of the Atkins, Zone, Ornish, and LEARN diets for change in weight and related risk factors among overweight premenopausal women: the A TO Z Weight Loss Study: a randomized trial. *JAMA*. 2007;297:969-77. [PMID: 17341711]
43. Tsai AG, Wadden TA. Systematic review: an evaluation of major commercial weight loss programs in the United States. *Ann Intern Med*. 2005;142:56-66. [PMID: 15630109]
44. Heshka S, Anderson JW, Atkinson RL, et al. Weight loss with self-help compared with a structured commercial program: a randomized trial. *JAMA*. 2003;289:1792-8. [PMID: 12684357]
45. Anderson JW, Konz EC, Frederich RC, Wood CL. Long-term weight-loss maintenance: a meta-analysis of US studies. *Am J Clin Nutr*. 2001;74:579-84. [PMID: 11684524]
46. Flechtner-Mors M, Ditschuneit HH, Johnson TD, et al. Metabolic and weight loss effects of long-term dietary intervention in obese patients: four-year results. *Obes Res*. 2000;8:399-402. [PMID: 10968732]

Table 3. Drug Treatments for Obesity

Agent	Mechanism of Action	Dosage	Side Effects	Notes
Diethylpropion	Sympathomimetic	25 mg tid with meals or 75 mg controlled release in a.m.	Dry mouth, constipation, insomnia, asthenia	FDA schedule IV; approved for short-term use
Phentermine HCl	Sympathomimetic	18.7 to 37.5 mg before meals	Dry mouth, constipation, insomnia, asthenia	FDA schedule IV; approved for short-term use
Phentermine resin	Sympathomimetic	15 to 30 mg in a.m.	Dry mouth, constipation, insomnia, asthenia	FDA schedule IV; approved for short-term use
Sibutramine	Sympathomimetic; serotonergic	5 to 15 mg	Dry mouth, constipation, insomnia, asthenia, increase in blood pressure	FDA schedule IV; approved for long-term use and maintenance
Benzphetamine	Sympathomimetic	25 or 50 mg before breakfast	Dry mouth, constipation, insomnia, asthenia	FDA schedule III; approved for short-term use
Phendimetrazine	Sympathomimetic	35 mg before meals or 105 mg sustained release in a.m.	Dry mouth, constipation, insomnia, asthenia	FDA schedule III; approved for short-term use
Orlistat	Lipase inhibitor	120 mg tid	Bloating; decreased fat-soluble vitamin levels	Nonscheduled; FDA-approved for long-term use and maintenance

FDA = Food and Drug Administration; tid = three times daily.

Sibutramine

Sibutramine primarily promotes satiety but may also increase energy expenditure by blocking the reduction in metabolic rate that accompanies weight loss. Sibutramine is also effective in weight maintenance.

The STORM (Sibutramine Trial of Obesity Reduction and Maintenance) study, which began with a 6-month open-label phase to induce weight loss by using diet and sibutramine (10 mg/d), then randomly assigned patients with greater than 5% weight loss to sibutramine (10 mg/d, increased up to 20 mg/d if weight was regained) or placebo for a further 18 months. Of those who completed the trial, 43% of the sibutramine group and 16% of the placebo group maintained 80% or greater of their weight loss (odds ratio, 4.64; P < 0.001) (50).

A meta-analysis of clinical trials on the long-term effect of anti-obesity drugs found that sibutramine produced a weighted mean weight loss of 6.35 ± 6.47 kg (13.9 lb) compared with 2.18 ± 5.23 kg (4.8 lb) in the placebo group, giving a net effect—what is often called the placebo-subtracted weight loss—of 4.16 kg (CI, 4.73 to 3.59) (51).

Sibutramine, like other sympathomimetic drugs, produces a small increase in mean heart rate and

blood pressure level, which accounted for inability to tolerate the drug in about 5% of patients in clinical trials. Other side effects include dry mouth, insomnia, and asthenia and are similar to those of other noradrenergic drugs. Sibutramine is not associated with valvular heart disease, primary pulmonary hypertension, or substance abuse. Sibutramine should be used with caution in patients with cardiovascular disease and in individuals taking selective serotonin reuptake inhibitors. It should not be used within 2 weeks of taking monoamine oxidase inhibitors and should not be used with other noradrenergic agents.

Orlistat

Orlistat inhibits the enzymatic action of pancreatic lipase and thereby reduces fat absorption in the small intestine.

In a 3-year study, patients who lost 5% or more of their body weight after 8 weeks on a diet were randomly assigned to lifestyle advice or lifestyle advice plus orlistat. Weight loss continued to decline for 3 months and remained below randomization levels at 12 months in the orlistat group but increased above randomization levels by 6 months in the lifestyle control

47. Pittler MH, Ernst E. Complementary therapies for reducing body weight: a systematic review. *Int J Obes (Lond)*. 2005;29:1030-8. [PMID: 15925954]
48. Clinical Efficacy Assessment Subcommittee of the American College of Physicians. Pharmacologic and surgical management of obesity in primary care: a clinical practice guideline from the American College of Physicians. *Ann Intern Med*. 2005;142:525-31. [PMID: 15809464]
49. Bray GA, Greenway FL. Pharmacological treatment of the overweight patient. *Pharmacol Rev*. 2007;59:151-84. [PMID: 17540905]
50. James WP, Astrup A, Finer N, et al. Effect of sibutramine on weight maintenance after weight loss: a randomised trial. *STORM Study Group. Sibutramine Trial of Obesity Reduction and Maintenance. Lancet*. 2000;356:2119-25. [PMID: 11191537]

group. At the end of 3 years, those on orlistat were still 2.4 kg lighter (52).

A meta-analysis of clinical trials on the long-term effect of anti-obesity drugs found that orlistat produced a weighted mean weight loss of 5.70 ± 7.28 kg (12.6 lb) compared with 2.40 ± 6.99 kg (5.3 lb) in the placebo group, giving a net—or placebo-subtracted weighted mean weight loss—of 2.87 kg (CI, 3.21 to 2.53) (6.4 lb) (51).

Generally, clinical trials of orlistat have shown that about 70% of patients achieve greater than 5% weight loss, and 70% of them maintain it at 2 years. Orlistat use has been documented for up to 4 years. One advantage of the drug is its beneficial effect on levels of low-density-lipoprotein cholesterol. Because it blocks fat absorption, the reduction in low-density-lipoprotein cholesterol is about twice that seen with weight loss alone.

Orlistat is poorly absorbed, and all of its side effects are those expected from inhibition of lipase in the intestine. It can produce fecal incontinence, anal leakage, bloating, and borborygmi, but these tend to occur early in treatment and deter very few patients. It can also lower levels of fat-soluble vitamins. A multivitamin taken at a time other than when orlistat is taken can prevent the reduction in vitamin levels.

Sympathomimetic Amines

The FDA has approved 4 sympathomimetic drugs for weight loss. Two of them—phentermine and diethylpropion—are schedule IV drugs, and the other 2—benzphetamine and phendimetrazine—are schedule III drugs. All 4 are approved only for a “few weeks” of use, usually interpreted as up to 12 weeks. These drugs are less expensive than sibutramine and orlistat. Clinicians should obtain written informed consent if phentermine is prescribed for longer than 12 weeks because data on long-term use are

insufficient. Phentermine is not available in Europe.

Off-Label Drugs for Weight Loss and Medications under Evaluation

Several other drugs have been used off-label for the treatment of overweight and obese patients, including fluoxetine, bupropion, topiramate, zonisamide, exenatide, and pramlintide. These should be used with caution, and informed consent from the patient should be obtained before they are prescribed.

New drugs for the treatment of obesity are currently under evaluation and in advanced stages of clinical trials. Four are combinations of single drugs already approved for weight loss. Two are new chemical entities: lorcaserin, (a serotonin-2C agonist) and tesofensine (a combined multi-amine reuptake inhibitor).

Rimonabant, a specific antagonist of the cannabinoid receptor, is approved and marketed in Europe for treatment of obesity but was not approved by the FDA because of increased incidence of psychiatric side-effects, such as depression and anxiety. Cannabinoid receptors respond to endogenous endocannabinoids and are distributed throughout the brain in the areas related to feeding as well as in fat cells and the gastrointestinal tract. Blocking these receptors decreases hunger and leads to weight loss similar to that seen with sibutramine and orlistat.

When should clinicians consider surgical treatment for overweight patients, and what types of surgical interventions are effective in weight reduction?

Clinicians should consider surgical treatment for adult patients if they have a BMI greater than 40 kg/m^2 or a BMI greater than 35 kg/m^2 with serious comorbid conditions, such as sleep apnea, diabetes mellitus, or joint disease (53). Guidelines

51. Rucker D, Padwal R, Li SK, et al. Long term pharmacotherapy for obesity and overweight: updated meta-analysis. *BMJ*. 2007;335:1194-9. [PMID: 18006966]
52. Richelsen B, Tonstad S, Rössner S, et al. Effect of orlistat on weight regain and cardiovascular risk factors following a very-low-energy diet in abdominally obese patients: a 3-year randomized, placebo-controlled study. *Diabetes Care*. 2007;30:27-32. [PMID: 17192328]
53. NIH conference. Gastrointestinal surgery for severe obesity. Consensus Development Conference Panel. *Ann Intern Med*. 1991;115:956-61. [PMID: 1952493]

Surgical Procedures to Treat Obesity

- Gastric bypass
- Gastroplasty
- Pancreaticobiliary bypass
- Laparoscopically placed band around the stomach

from the American College of Physicians set the threshold higher, suggesting that surgery be considered in patients with a BMI greater than 40 kg/m² who have associated disorders (48). Potential candidates must have tried and failed nonsurgical weight-loss treatment, must understand the procedure and its complications, and must be an acceptable surgical risk.

Several surgical procedures have been used to treat obesity, and all of them can be performed laparoscopically (see Box). Gastric bypass was one of the first, and it produces among the largest weight loss. It involves making a small pouch of stomach just below the esophagus that empties into a loop of jejunum. Gastroplasty provides elongation of the stomach with a staple line paralleling the lesser curvature and a ring at the end of this narrowing to delay entry of food into the stomach. Pancreaticobiliary bypass involves forming 2 parallel intestinal limbs, one of which empties the stomach and the other the pancreatic and biliary secretions, which are then brought together near the ileocecal valve. The least invasive is the laparoscopically-placed band around the stomach, which is similar to the gastroplasty in that it narrows the opening between the upper and lower stomach.

Only a few good-quality clinical trials have been performed to evaluate the effect of bariatric surgery on development or remission of diabetes and mortality (54).

In a randomized, controlled trial, 60 patients with diabetes and a BMI between 30 and 40 kg/m² were randomly assigned to either the lap-band operation or a lifestyle program. At 2 years, patients in the lap-band group had lost 20.0% of their body weight compared with 1.4% body weight in patients in the lifestyle group. Remission of diabetes occurred in 73% of those in the surgical group but only 13% of those in the diet-treated group. The relative

risk for remission from diabetes was 5.5 (CI, 2.2 to 14.0) and was related to weight loss (55).

The Swedish Obese Subjects Study found that patients who had bariatric surgery had greater improvements in cardiovascular risk factors than those in the control group during the first 2 years after surgery. Increased weight loss was associated with a decreased incidence of new cases of diabetes at 2 and 10 years. In the patients who lost more than 12% of their body weight and maintained it, there were no new cases of diabetes at 2 years (56). A follow-up study demonstrated a 29% reduction in mortality after 10.9 years in the surgery group compared with the control group (adjusted hazard ratio, 0.71; P = 0.01) (57).

Another study compared long-term mortality over an 8-year period among 9949 patients who had undergone gastric bypass surgery with 9628 severely obese control participants. There was a 40% adjusted reduction in long-term all-cause mortality in the surgery group compared with those in the control group (37.6 vs. 57.1 deaths per 10 000 person-years; P < 0.001) (58).

Liposuction has sometimes been used as a surgical procedure to treat obesity. It was originally developed as a plastic surgical procedure for contouring body fat stores, but with current techniques, several kilograms of fat can be removed. However, rapid removal of too much fat has been associated with fatality. Furthermore, in 1 study in which patients were compared before and after extensive liposuction, there were no significant improvements in metabolic or cardiac risk factors, suggesting that even more than subcutaneous fat must be removed in order to realize metabolic benefits (59).

What are the adverse effects of surgical interventions for obesity?

Clinicians and patients should be aware of the various adverse effects associated with surgical interventions for obesity (Table 4). Patients who undergo bariatric surgery may also develop deficiencies in levels of iron, vitamin B₁₂, folate, and calcium,

54. Maggard MA, Shugarman LR, Suttorp M, et al. Meta-analysis: surgical treatment of obesity. *Ann Intern Med.* 2005;142:547-59. [PMID: 15809466]
55. Dixon JB, O'Brien PE. Changes in comorbidities and improvements in quality of life after LAP-BAND placement. *Am J Surg.* 2002;184:51S-54S. [PMID: 12527352]
56. Swedish Obese Subjects Study Scientific Group. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. *N Engl J Med.* 2004;351:2683-93. [PMID: 15616203]
57. Swedish Obese Subjects Study. Effects of bariatric surgery on mortality in Swedish obese subjects. *N Engl J Med.* 2007;357:741-52. [PMID: 17715408]
58. Adams TD, Gress RE, Smith SC, et al. Long-term mortality after gastric bypass surgery. *N Engl J Med.* 2007;357:753-61. [PMID: 17715409]

Table 4. Adverse Effects Associated with Surgical Interventions for Obesity

Complication	Gastric Bypass	Gastroplasty	Laparoscopic Gastric Bands
Mortality	0%–1%	0%–1%	0%–0.1%
DVT and pulmonary embolus	0%–3%	0%–3%	0%–3%
Anastomotic leak or staple line disruption	0%–5.1%	27%–31%	–
Stomal stenosis or obstruction	6%–20%	20%–33%	2%
Marginal ulcer or band erosion	0.6%–13%	1%–7%	0%–3%
Ventral incisional hernia with reflux	0%–1.8%	8%–21%	–
Revisional surgery	–	–	Up to 40%
Dilatation of GI tract	–	–	Up to 10%
Infection at port site	–	–	0%–9%

DVT = deep venous thrombosis; GI = gastrointestinal. Adapted from (60).

and they should be evaluated for such deficiencies and receive appropriate treatment. Successful pregnancy has been documented after all of these procedures. In general, the infants tend to be smaller than infants born to the same mother before the bariatric operation, but there is no increase in adverse perinatal outcomes.

When should clinicians consider specialty referral for overweight patients?

Clinicians should consider specialist consultation primarily for complications of obesity. Patients with suspected obstructive sleep apnea may require referral for polysomnography and advice on treatment. Those with complicated diabetes mellitus may benefit from consultation with an endocrinologist. Overweight children may benefit from consulting a pediatric endocrinologist, especially if an inherited syndrome is suspected. Patients contemplating a very-low-calorie diet should be followed in a clinic specializing in this treatment. Finally, patients who are candidates for bariatric surgery need referral to a bariatric surgeon, preferably at an institution where these procedures are performed frequently.

What are the best strategies for maintaining weight loss?

Exercise is an important strategy for maintaining weight loss over an extended period of time (60).

In the Nurses' Health Study, women who maintained vigorous levels of physical activity had smaller weight gains over 6 years of follow-up than those who did not (61).

Another important factor for maintaining weight loss is self-monitoring of eating patterns, which can be encouraged by lifestyle-modification advice either by the primary care physician or in a more formal setting (62).

Although all calorie-restricted diets are effective in helping patients lose weight, a particular diet may be easier to follow for a particular patient. It is important for clinicians and patients to discuss the options and consider changing diets if a specific one is not effective.

Smoking may have an effect on weight, and cessation of smoking may increase weight. However, smoking carries its own substantial risks. In the Framingham study, obese female smokers lost 13.3 years of life and obese male smokers lost 13.7 years compared with 7.1 years in nonsmoking women and 5.8 years in nonsmoking men (63). Weight loss should not serve as a rationale for withholding advice about smoking cessation.

Clinicians should always be aware of medications that can cause weight gain and avoid them when possible.

59. Klein S, Fontana L, Young VL, et al. Absence of an effect of liposuction on insulin action and risk factors for coronary heart disease. *N Engl J Med.* 2004;350:2549-57. [PMID: 15201411]
60. Bray GA. *Metabolic Syndrome and Obesity.* Totawa, NJ: Humana Press; 2007.
61. Field AE, Wing RR, Manson JE, et al. Relationship of a large weight loss to long-term weight change among young and middle-aged US women. *Int J Obes Relat Metab Disord.* 2001;25:1113-21. [PMID: 11477495]
62. Wing RR, Phelan S. Long-term weight loss maintenance. *Am J Clin Nutr.* 2005;82:2225-2255. [PMID: 16002825]
63. Peeters A, Barendregt JJ, Willekens F, et al. Obesity in adulthood and its consequences for life expectancy: a life-table analysis. *Ann Intern Med.* 2003;138:24-32. [PMID: 12513041]

Treatment... Clinicians should encourage attainable weight-loss goals and work with patients to achieve them. Treatments for obesity include behavior modification strategies, counseling, reduced food intake, increased physical activity, drug therapy, and bariatric surgery. Clinicians should carefully monitor patients on specific diets and those who undergo bariatric procedures. Specialist referral is recommended for serious complications of obesity, such as complicated diabetes mellitus, cardiovascular disease, and sleep apnea, as well as for bariatric surgery when required.

CLINICAL BOTTOM LINE

Practice Improvement

What do professional organizations recommend with regard to the management of overweight patients?

In 2003, the U.S. Preventive Services Task Force issued a guideline on screening for obesity in adults. It recommended that clinicians screen adults for obesity and offer counseling and behavioral interventions to promote weight loss in obese patients but stated that evidence was insufficient to recommend these measures to promote sustained weight loss in obese and overweight patients (8).

The American College of Physicians published guidelines on pharmacologic and surgical management of obesity in 2005. It recommended counseling for all obese patients on lifestyle and

behavior modifications, such as diet and exercise, to meet their individualized goals; pharmacologic therapy with specific drugs for those who fail to meet those goals, with discussion of the limitations and adverse effects of available drugs; and bariatric surgery in experienced centers for those with a BMI greater than 40 kg/m² who have not maintained weight loss with other measures and present with comorbid conditions related to obesity (48).

In 1998, the National Heart, Lung, and Blood Institute issued extensive guidelines on management of patients with obesity, including detailed evidence tables on diet, physical activity, and combined interventions; behavioral therapy; and pharmacotherapy (9).

in the clinic Tool Kit Obesity

PIER modules

pier.acponline.org

Access the PIER module on obesity. PIER modules provide evidence-based, updated information on current diagnosis and treatment in an electronic format designed for rapid access at the point of care.

Body Mass Index Table and Calculator from the National Heart, Lung and Blood Institute at the NIH

Table: www.nhlbi.nih.gov/guidelines/obesity/bmi_tbl.htm

Calculator: www.nhlbisupport.com/bmi/bmicalc.htm

Easy-to-use tools to facilitate rapid determination of BMI.

Patient Education Resources

www.annals.org/intheclinic

Access the Patient Information material that appears on the following page for duplication and distribution to patients.

www.acponline.org/patients_families/pdfs/health/obesity.pdf

American College of Physicians: 100 Million Adult Americans Are Overweight and at Risk of Serious Disease

www.cdc.gov/nccdphp/dnpa/bmi/index.htm

Centers for Disease Control and Prevention: Healthy Weight: Assessing your Weight

www.cdc.gov/nccdphp/dnpa/obesity/faq.htm

Centers for Disease Control and Prevention: Overweight and Obesity: Frequently Asked Questions (FAQs)

in the clinic

WHAT YOU SHOULD KNOW ABOUT OBESITY

In the Clinic
Annals of Internal Medicine
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Being overweight means that you weigh more than is healthy. Overweight people have medical problems, such as high cholesterol, diabetes, heart disease, arthritis, and breathing problems, as well as shorter lives. Losing weight can be hard, but losing even a little can make you healthier.

How do you know if you are overweight?

Body mass index (BMI) measures how tall you are in meters (m) and how much you weigh in kilograms (kg) to tell you if you weigh too much.

- Normal BMI is under 25 kg/m². You are overweight if your BMI is between 25 kg/m² and 30 kg/m². You are obese if it is over 30 kg/m².

What are the best ways to lose weight?

- To lose weight, you have to eat less and exercise more. Some diets are easier than others for some people.
- Sometimes getting advice or joining self-help groups makes it easier to stay on a diet.
- If diet and exercise are not enough, your doctor may give you medicine to lose weight.
- If you are very obese and have serious medical problems, your doctor may consider surgery on your stomach so that you eat less and lose weight.

Why is losing weight so hard?

- It is hard for your body to change. When you go on a diet, you lose some weight and then stop for a while.



- Set a goal for your new weight that you can reach. Even a few pounds makes a difference.

Web Sites with Good Information on Losing Weight

National Heart, Lung, and Blood Institute:
Aim for a Healthy Weight!

www.nhlbi.nih.gov/health/public/heart/obesity/lose_wt/index.htm

American Heart Association: Healthy Lifestyle
www.americanheart.org/presenter.jhtml?identifier=1200009

Centers for Disease Control and Prevention:
Overweight and Obesity
www.cdc.gov/nccdphp/dnpa/obesity/index.htm

Surgeon General: Physical activity and health: A report of the Surgeon General
www.cdc.gov/nccdphp/sgr/sgr.htm

ACP

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1. A 20-year-old woman presents to your clinic for an initial visit. She has always been heavy, but she has gained almost 13.5 kg (30 lb) since starting college 2 years ago. She has a diet rich in convenience and snack foods. She has several alcoholic beverages on most weekends, but does not consider alcohol to be a problem for her socially. She has never smoked cigarettes. She used to play soccer competitively, but finds little time for regular physical activity. Her father is overweight and has type 2 diabetes mellitus and hypertension. The patient does not have polyuria, polydipsia, blurred vision, changes in her skin or hair, changes in her regular menses, or cold intolerance.

On physical examination, she is 167.5 cm (66 in) tall and weighs 99.5 kg (219 lb); her body mass index (BMI) is 35. Her blood pressure is 148/92 mm Hg.

What would be the most appropriate management of obesity in this young woman?

- Sibutramine, 10 mg/d, plus a protein-rich, carbohydrate-restricted diet
- Orlistat, 120 mg with meals, plus a calorie-restricted diet with a calorie deficit of 500 kcal/d, less than 30% calories from fat, and limited refined sugars
- An exercise prescription for 30 minutes of brisk walking 5 or more times a week, progressing to 45 to 60 minutes of vigorous exercise on most days
- A calorie-restricted diet with a calorie deficit of 500 kcal/d, less than 30% calories from fat, and limited refined sugars, combined with a progressive exercise program
- Base recommendations on the results of laboratory testing, including serum thyroid-stimulating hormone level, fasting lipid panel, and determination of fasting serum glucose level

2. A 56-year-old woman is evaluated during a routine annual visit. The patient would like to lose weight. She works as a teacher and is physically active, walking briskly 2 or 3 times a week for 20 or 30 minutes. She does not smoke and drinks alcohol only on occasion. Her medical history includes hypertension and hyperlipidemia, both well controlled with medications.

On physical examination, the blood pressure is 135/88 mm Hg and the BMI is 36 kg/m². The remainder of the physical examination is normal. Laboratory studies include a fasting plasma glucose level of 105 mg/dL (5.83 mmol/L) and a serum thyroid-stimulating hormone level of 2.5 μ U/mL (2.5 mU/L). A goal is set for a reduction in weight of 5% to 15%.

Which of the following diets should be advised for this patient?

- A balanced low-calorie diet (1200 to 1500 kcal/d)
 - A very-low-calorie diet (<1000 kcal/d)
 - A reduced-fat diet (fat constitutes <30% total caloric intake/d)
 - A low-carbohydrate diet (<35 g carbohydrates/d)
3. A 55-year-old man is evaluated for obesity. The patient has been overweight all his life. He has tried a balanced calorie-restricted diet over the past 6 months and has increased his exercise to include walking for 20 minutes three times weekly. Although he was initially successful in losing weight, he has not been able to maintain the weight loss. He works as a high school teacher and believes that his weight has interfered with his success in being asked to take leadership positions in his field. He does not smoke, and he drinks alcohol occasionally in a social context. His medical history is significant for hyperlipidemia and hypertension, both controlled with medications.

On physical examination, the pulse rate is 65/min, and the blood pressure is

142/88 mm Hg. The BMI is 40 kg/m². Fasting plasma glucose level is 106 mg/dL (5.88 mmol/L), serum low-density lipoprotein cholesterol level is 120 mg/dL (3.1 mmol/L), serum total cholesterol level is 204 mg/dL (5.28 mmol/L), and serum creatinine level is 1.2 mg/dL (106.1 μ mol/L). A chest radiograph shows borderline cardiomegaly, and the electrocardiogram is normal.

Which of the following is supported by the best evidence for sustained weight loss in this patient?

- Sibutramine
- Orlistat
- A low-carbohydrate diet
- A restricted-fat diet
- Gastric bypass surgery

4. A 67-year-old man is evaluated for pain in his knees with ambulation. He smokes 1 pack of cigarettes per day and drinks alcohol occasionally. His medical history includes hypertension controlled with metoprolol, and hyperlipidemia controlled with simvastatin.

On physical examination, the pulse rate is 65/min, respiration rate is 14/min, and blood pressure is 145/92 mm Hg. The BMI is 36 kg/m², and the abdominal circumference is 130 cm (51 in). The musculoskeletal examination reveals crepitus on knee flexion and extension but no synovial joint effusions or signs of inflammation. Laboratory studies indicate a fasting plasma glucose level of 110 mg/dL (6.11 mmol/L).

A moderate weight loss of 5% will be associated with which of the following outcomes in this patient?

- Decreased risk for cardiovascular mortality
- Decreased risk for overall mortality
- Decreased risk for progression to type 2 diabetes mellitus
- Improvement in symptoms of osteoarthritis
- Social and economic benefits from weight loss

Questions are largely from the ACP's Medical Knowledge Self-Assessment Program (MKSAP). Go to www.annals.org/intheclinic/ to obtain up to 1.5 CME credits, to view explanations for correct answers, or to purchase the complete MKSAP program.