In the Clinic

Obesity

Health Consequences  page ITC3-2
Screening and Prevention  page ITC3-3
Diagnosis  page ITC3-4
Treatment  page ITC3-6
Practice Improvement  page ITC3-14
Tool Kit  page ITC3-14
Patient Information  page ITC3-15
CME Questions  page ITC3-16

Physician Writers
Adam Gilden Tsai, MD, MSCE
Thomas A. Wadden, PhD
Deborah Cotton, MD, MPH
Darren Taichman, MD, PhD
Sankey Williams, MD

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 divisions 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, http://www.acponline.org/products_services/mksap/15/?pr31, and other resources referenced in each issue of In the Clinic.

CME Objective: To review current evidence for the health consequences, screening and prevention, diagnosis, treatment, and practice improvement of obesity.

The information contained herein should never be used as a substitute for clinical judgment.

© 2013 American College of Physicians
What health problems are associated with overweight and obesity?

Obesity, particularly severe obesity, affects nearly every organ system of the human body. Most obesity-related medical conditions are caused by the metabolic effects of adipose tissue, but some are caused by the increased body mass itself (see the Box: Obesity-Related Health Problems). Obesity is associated with an overall increase in mortality. The relationship between weight and mortality follows a J-shaped curve, with the lowest mortality traditionally believed to occur with a body mass index (BMI) of 20.0–24.9 kg/m² (i.e., normal weight).

The relationship between obesity and mortality is complex, with BMI accounting for only part of the risk. Other factors that may affect mortality include body fat distribution (i.e., visceral fat vs. subcutaneous fat, not captured by BMI), age, sex, race and ethnicity, smoking, associated health conditions (including unknown existing conditions), and fitness level. Larger studies with longer follow-up periods have been the most likely to show deleterious effects of obesity (beginning at a BMI of 30 kg/m²). Regardless of whether overweight or class I obesity are associated with increased mortality, they are strongly related to development of comorbid conditions, including type 2 diabetes, hypertension, sleep apnea, and other cardiovascular disease (CVD).

What is the evidence that intentional weight loss improves health outcomes?

There is strong evidence that intentional weight loss reduces the burden of obesity-related comorbid disease and improves overall health-related quality of life. For...
example, weight loss of 5–10% of starting weight reduces the risk for type 2 diabetes among at-risk persons (2).

Results from the multicenter randomized Look AHEAD trial (n = 5145) showed that moderate weight loss (8.6% of starting weight after 1 year, 6.15% after 4 years) led to better physical function, decreased sleep apnea, improved sexual function, improved mood, reduced urinary incontinence, improved health-related quality of life, and reduced need for medication for CVD risk factors, compared with a usual care condition.

The Look AHEAD study was stopped in late 2012 because it did not show lower CVD morbidity and mortality in the intervention group than in the usual care group (3). However, the Swedish Obese Subjects (SOS) study showed that patients who had bariatric surgery for severe obesity and who maintained a loss of 15–25% of initial weight 10 years later had a 29% reduction in all-cause mortality, compared with a control group that was matched on 18 characteristics. The major reductions in mortality resulted from decreases in cardiovascular- and cancer-related deaths (4).

Health Consequences... Obesity increases the risk for many chronic medical conditions. Moderate to severe obesity (BMI ≥ 35 kg/m²) clearly increases the risk for mortality. Modest weight loss (5–10% of initial weight) reduces the burden of comorbid disease in overweight or obese patients. Larger weight loss (15–30%) may reduce mortality.

Insulin and certain other antihyperglycemic medications (sulfonylureas, thiazolidenediones) are associated with some weight gain, but in the context of a weight loss intervention (e.g., the Look AHEAD trial) persons receiving insulin can lose nearly as much weight as those not on insulin (6). One randomized trial showed that use of bupropion after smoking cessation reduced weight gain after 1 and 2 years (7).

In adults, obesity prevention behaviors include reading food labels, eating smaller portions, eating 5 servings of fruits and vegetables per day, eating adequate amounts of fiber (25 g/d), and exercising for 45–60 minutes per day. Other behaviors associated with less weight gain include reducing job stress (8), limiting car commuting (9), and getting adequate sleep (6–9 h/night) (10). Most of these results are derived from observational studies.

A study that combined 3 cohorts with a total of 120 877 people followed for 12–20 years each found that weight gain was

**CLINICAL BOTTOM LINE**

**Screening and Prevention**

Should clinicians 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, multicomponent behavioral interventions, or refer patients to programs that offer such interventions (5).

How can patients prevent obesity? Internists can sometimes help their patients prevent weight gain by reviewing concurrent medications. Several medications are associated with weight gain (see the Box: Medications Associated With Weight Gain). The largest increases are associated with glucocorticoids and second-generation antipsychotics, but many commonly used medications also result in weight gain. Smoking cessation also increases body weight by an average of 3–5 kg in the first year. (However, patients should be counseled to prioritize smoking cessation.)

Infections: Greater severity of influenza with morbid obesity, skin and soft tissue infections

Mechanical effects Pulmonary: Obstructive sleep apnea, restrictive lung disease
Musculoskeletal: Osteoarthritis, low back pain

Psychosocial effects Depression and anxiety
Social stigmatization

Obesity-Related Health Problems (continued)
Renal: Nephrolithiasis, proteinuria, chronic kidney disease
Genitourinary: In women, the polycystic ovarian syndrome, infertility, pregnancy complications; in men, benign prostatic hypertrophy, erectile dysfunction
Neurologic: Migraine, pseudotumor cerebri

Diagnosis

How do clinicians diagnose obesity?
Both the National Institutes of Health (NIH) and the World Health Organization (WHO) recommend using BMI to diagnose overweight and obesity. In the general population, BMI correlates well with total adiposity, as well as with morbidity and mortality. The accepted U.S. definitions of overweight and of classes 1, 2, and 3 obesity are 25–29.9 kg/m², 30–34.9 kg/m², 35–39.9 kg/m², and ≥ 40.0 kg/m², respectively (16). Class 3 obesity is also referred to as “extreme” or “severe” obesity, replacing the earlier term “morbid.”

When can BMI be misleading in terms of health risk?
The diagnosis of obesity must be individualized. Risk for diabetes begins to increase at a BMI of 23 kg/m² for East Asian (e.g., Chinese, Japanese) and South Asian patients (e.g., East Indians). The Asia–Oceania criteria for obesity differ from those used by the NIH and the WHO. Specifically, normal weight is defined as a BMI of 18.5–22.9 kg/m², overweight as 23.0–24.9 kg/m², and obese as ≥ 25.0 kg/m². By contrast, disease risk may be lower in African Americans than in whites at the same BMI.

Body fat is normally about 12% higher in women than in men at the same BMI (17). The higher level of body fat in women, along with assessment of waist circumference (discussed later) and metabolic risk, must be taken into account when determining whether obesity is adversely affecting health. BMI may also be misleading in elderly patients. Older persons at a given BMI have a higher risk for obesity–associated conditions.

Screening and Prevention... Clinicians should screen patients for obesity and refer them to intensive interventions for treatment. They should also review their patients’ medication lists to assess whether changing a medication could reduce weight gain. Certain behaviors can prevent weight gain, including several that are not directly related to eating or exercise, such as adequate sleep.

CLINICAL BOTTOM LINE

Medications Associated With Weight Gain
Glucocorticoids (prednisone)
Diabetes medications (insulin, sulfonylureas, thiazolidinediones, meglitinides)
First-generation antipsychotics (thioridazine)
Second generation antipsychotics (risperidone, olanzapine, clozapine, quetiapine)
Neurologic and mood stabilizing agents (carbamazepine, gabapentin, lithium, valproate)
Antihistamines (especially cyproheptadine)
Antidepressants (paroxetine, citalopram, amitriptyline, nortriptyline, imipramine, mirtazapine)
Hormonal agents (especially progestins, e.g., medroxyprogesterone)
Beta-blockers (especially propranolol)
Alpha-blockers (especially terazosin)

most strongly associated with intake of potato chips, potatoes, red meat, and sugar-sweetened beverages and was inversely associated with intake of vegetables, fruits, whole grains, nuts, and yogurt (11).

In a randomized crossover trial, sleep deprivation (5.5 h/night vs. 8.5 h) reduced the amount of weight lost during a calorie-restricted diet and increased both loss of lean body mass and neuroendocrine markers of hunger (12).

Emerging evidence suggests that social and physical environments affect weight. Evidence is mixed on whether proximity to supermarkets improves dietary intake and/or weight. Having a friend or close family member with obesity seems to increase the risk for being obese (13). Offspring of women who have significant weight gain during pregnancy or gestational diabetes are at greater risk for being obese in childhood (14).

In a randomized trial, 4,498 low-income, mostly African American women were assigned to a control group, receipt of a housing voucher, or receipt of a housing voucher that could only be redeemed in a low-poverty area (where <10% of residents were poor). After 12–14 years, the low-poverty voucher group had lower rates of moderate to severe obesity (BMI ≥ 35 kg/m²) than the control group and lower rates of type 2 diabetes than either of the other 2 groups (15).
5- to 10-year intervals), including weight history (at other abnormal physical features. The history of the present illness should include a weight history (at 5- to 10-year intervals), including weight gain. Several rare genetic syndromes can cause obesity in adults, most of which are associated with developmental delay or with other abnormal physical features. The patient’s medication list should also be reviewed, as discussed previously.

The history of the present illness should include a weight history (at 5- to 10-year intervals), including weight events associated with significant weight gain (e.g., pregnancy). Clinicians should inquire about previous weight loss attempts, with a particular focus on successful efforts (i.e., resulting in a loss of \( \geq 5\% \) of body weight), as well as reasons attributed by the patient for recidivism. The medical history and review of systems should focus on the major comorbid conditions listed in the Box. The physical examination can be brief and focused (Table 1).

Is a family history of obesity important? A strong family history of obesity, particularly severe obesity, suggests a genetic component, although genetic polymorphisms are more common than the genetic abnormalities responsible for many of the rare syndromes. Genetics accounts for approximately 40–70% of the variability in BMI, although genetic factors alone are unlikely to explain the explosive increase in obesity and severe obesity in the United States over the past 30 years. Clinicians should help patients understand that obesity and its related diseases are responsive to lifestyle modification even if a genetic predisposition is suspected. The reader is referred elsewhere for secondary causes of obesity should be ruled out but are uncommon in adults. Traumatic brain injury, if accompanied by hypothalamic injury, can cause weight gain. Several rare genetic syndromes can cause obesity in adults, most of which are associated with developmental delay or with other abnormal physical features. The patient’s medication list should also be reviewed, as discussed previously.

The history of the present illness should include a weight history (at 5- to 10-year intervals), including weight loss (18). BMI may also be misleading in elite athletes, whose elevated weight may be attributable to increased lean mass, which does not increase risk.

When and how should clinicians measure waist circumference? Waist circumference provides information on central adiposity beyond that provided by BMI. Central adiposity correlates well with visceral adiposity, which elevates the risk for such obesity-related diseases as diabetes, hypertension, and nonalcoholic fatty liver disease. Clinicians generally should measure waist circumference in patients who are overweight or have class 1 obesity. However, waist measurement does not usually add additional risk information if the BMI is \( < 25 \text{ kg/m}^2 \) or \( \geq 35 \text{ kg/m}^2 \). Waist circumference should be measured over the iliac crests in a horizontal plane after the patient exhales following a normal breath. A waist circumference of \( \geq 35 \text{ inches (88 cm)} \) for women and \( \geq 40 \text{ inches (102 cm)} \) for men is considered elevated.

What elements of the history and physical examination are important in patients with obesity? Secondary causes of obesity should be ruled out but are uncommon in adults. Traumatic brain injury, if accompanied by hypothalamic injury, can cause weight gain. Several rare genetic syndromes can cause obesity in adults, most of which are associated with developmental delay or with other abnormal physical features. The patient’s medication list should also be reviewed, as discussed previously.

The history of the present illness should include a weight history (at 5- to 10-year intervals), including life events associated with significant weight gain (e.g., pregnancy). Clinicians should inquire about previous weight loss attempts, with a particular focus on successful efforts (i.e., resulting in a loss of \( \geq 5\% \) of body weight), as well as reasons attributed by the patient for recidivism. The medical history and review of systems should focus on the major comorbid conditions listed in the Box. The physical examination can be brief and focused (Table 1).

Is a family history of obesity important? A strong family history of obesity, particularly severe obesity, suggests a genetic component, although genetic polymorphisms are more common than the genetic abnormalities responsible for many of the rare syndromes. Genetics accounts for approximately 40–70% of the variability in BMI, although genetic factors alone are unlikely to explain the explosive increase in obesity and severe obesity in the United States over the past 30 years. Clinicians should help patients understand that obesity and its related diseases are responsive to lifestyle modification even if a genetic predisposition is suspected. The reader is referred elsewhere for secondary causes of obesity should be ruled out but are uncommon in adults. Traumatic brain injury, if accompanied by hypothalamic injury, can cause weight gain. Several rare genetic syndromes can cause obesity in adults, most of which are associated with developmental delay or with other abnormal physical features. The patient’s medication list should also be reviewed, as discussed previously.

The history of the present illness should include a weight history (at 5- to 10-year intervals), including life events associated with significant weight gain (e.g., pregnancy). Clinicians should inquire about previous weight loss attempts, with a particular focus on successful efforts (i.e., resulting in a loss of \( \geq 5\% \) of body weight), as well as reasons attributed by the patient for recidivism. The medical history and review of systems should focus on the major comorbid conditions listed in the Box. The physical examination can be brief and focused (Table 1).

Is a family history of obesity important? A strong family history of obesity, particularly severe obesity, suggests a genetic component, although genetic polymorphisms are more common than the genetic abnormalities responsible for many of the rare syndromes. Genetics accounts for approximately 40–70% of the variability in BMI, although genetic factors alone are unlikely to explain the explosive increase in obesity and severe obesity in the United States over the past 30 years. Clinicians should help patients understand that obesity and its related diseases are responsive to lifestyle modification even if a genetic predisposition is suspected. The reader is referred elsewhere for secondary causes of obesity should be ruled out but are uncommon in adults. Traumatic brain injury, if accompanied by hypothalamic injury, can cause weight gain. Several rare genetic syndromes can cause obesity in adults, most of which are associated with developmental delay or with other abnormal physical features. The patient’s medication list should also be reviewed, as discussed previously.

The history of the present illness should include a weight history (at 5- to 10-year intervals), including life events associated with significant weight gain (e.g., pregnancy). Clinicians should inquire about previous weight loss attempts, with a particular focus on successful efforts (i.e., resulting in a loss of \( \geq 5\% \) of body weight), as well as reasons attributed by the patient for recidivism. The medical history and review of systems should focus on the major comorbid conditions listed in the Box. The physical examination can be brief and focused (Table 1).

Is a family history of obesity important? A strong family history of obesity, particularly severe obesity, suggests a genetic component, although genetic polymorphisms are more common than the genetic abnormalities responsible for many of the rare syndromes. Genetics accounts for approximately 40–70% of the variability in BMI, although genetic factors alone are unlikely to explain the explosive increase in obesity and severe obesity in the United States over the past 30 years. Clinicians should help patients understand that obesity and its related diseases are responsive to lifestyle modification even if a genetic predisposition is suspected. The reader is referred elsewhere for

---

### Clinical Findings in Patients With Obesity

<table>
<thead>
<tr>
<th>Organ/Organ System</th>
<th>Physical Finding</th>
<th>Associated Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td>Acne/hirsutism</td>
<td>The polycystic ovary syndrome</td>
</tr>
<tr>
<td>Thyroid</td>
<td>Striae*</td>
<td>Insulin resistance</td>
</tr>
<tr>
<td>Cardiovascular system</td>
<td>Nodules/goiter</td>
<td>The Cushing syndrome</td>
</tr>
<tr>
<td>Abdomen</td>
<td>Blood pressure/pulse</td>
<td>Hypothyroidism</td>
</tr>
<tr>
<td>Eyes</td>
<td>Cardiac rhythm</td>
<td>Hypertension, deconditioning</td>
</tr>
<tr>
<td>Musculoskeletal system</td>
<td>S3/S4 gallop</td>
<td>Atrial fibrillation</td>
</tr>
<tr>
<td></td>
<td>Waist circumference</td>
<td>Congestive heart failure</td>
</tr>
<tr>
<td></td>
<td>Peripher edema</td>
<td>Abdominal obesity</td>
</tr>
<tr>
<td></td>
<td>Papilledema</td>
<td>Venous stasis, pulmonary hypertension</td>
</tr>
<tr>
<td></td>
<td>Proximal muscle weakness</td>
<td>Pseudotumor cerebri</td>
</tr>
</tbody>
</table>

*Striae in the Cushing syndrome are classically purple in color and broad-based.*
more detailed information on the role of genetics (19).

**What laboratory tests or other evaluations should be done in patients with obesity?**

Routine laboratory studies in patients with obesity should include measurement of levels of fasting glucose and/or hemoglobin A₁c, thyroid-stimulating hormone, liver-associated enzymes, and fasting lipids. Optional tests depend on the results of the history, physical examination, and initial blood tests and may include electrocardiography, echocardiography, overnight sleep study, right upper quadrant ultrasound (fatty liver), transvaginal ultrasound (ovarian cysts), or imaging and laboratory tests to assess the hypothalamic–pituitary–adrenal axis for the uncommon patient with suspected hypothalamic obesity.

Beyond measurement of BMI and waist circumference, no additional methods are recommended for routine assessment of body composition or adiposity. Bioelectrical impedance analysis is not substantially more accurate than estimates based on demographic and physical characteristics alone (e.g., age, sex, weight, height). Dual energy x-ray absorptiometry provides a more accurate estimate of body composition. Computed tomography or magnetic resonance imaging can accurately quantify central and visceral adiposity, but both are expensive, and computed tomography exposes the patient to radiation. Assessment of resting metabolic rate, together with level of physical activity, can provide an estimate of total energy requirements, but in a randomized trial (n = 111) did not increase weight loss when added to a behavioral weight loss intervention (20). Energy requirements can be estimated using equations that incorporate information about weight, height, demographic factors, and level of physical activity. Patients and clinicians can easily access the Harris-Benedict equation online.

---

### Treatment

**How should clinicians counsel patients about their weight?**

Excess weight is a sensitive subject for many overweight and obese persons. Studies indicate that patients prefer that clinicians use the terms “weight” or “weight problem,” in lieu of “obesity,” to discuss the topic. Clinicians can start by asking, “Could we talk about your weight today?” The conversation should provide patients an opportunity to discuss their concerns, rather than simply being told that they need to reduce (which most already know). A key challenge for clinicians is to offer patients hope about weight management. This sometimes can be achieved by explaining that a loss of only 5–10% of initial weight may significantly improve comorbid conditions. Patients frequently believe they must lose 25% or more of their starting weight to be successful (21).
The Centers for Medicare & Medicaid Services (CMS), in its 2011 decision to reimburse primary care providers for obesity treatment, recommended using a 5A approach: Assess (weight and risk factors); advise (weight loss, personalize the recommendation to the patient); agree (on a target for behavior change); Assist (with a referral); Arrange (follow-up).

An algorithm developed by the National Heart, Lung, and Blood Institute can assist patients and clinicians in selecting an intervention (Table 2). The algorithm recommends a comprehensive program of lifestyle modification for patients with a BMI ≥25 kg/m² who need to reduce (16). Weight loss medications may be considered with persons with a BMI ≥30 kg/m² (or ≥27 kg/m² with a comorbid condition) who are unable to reduce satisfactorily with lifestyle modification alone. Surgery is an option for persons with a BMI ≥40 kg/m² (or ≥35 kg/m² with a comorbid condition).

What are the lifestyle modifications for obesity?

Comprehensive lifestyle modification programs for obesity have 3 components: diet, physical activity, and behavior modification (Table 3) (22). Behavior modification provides a set of principles and techniques, such as goal-setting and recordkeeping. Obese persons should typically try to achieve an energy deficit of 500–1000 kcal/d to induce a corresponding weight loss of approximately 1–2 pounds (0.5–1 kg) per week. The U.S. Preventive Services Task Force has recommended only high-intensity lifestyle modification programs (defined as 12–26 sessions in the first year [5]) because lower-intensity programs have not shown consistent effectiveness. High-intensity lifestyle modification programs provide weekly individual or group treatment sessions (of 30–60 minutes) for 16–26 weeks (16, 22). High-intensity interventions produce mean weight loss of approximately 6–9 kg (approximately 6–9% of initial weight). For example, the Diabetes Prevention Program produced a mean loss of approximately 7 kg in 6 months (2).

What dietary strategies are used in lifestyle modification?

Calorie restriction is the principal method for inducing weight loss because most patients find it far easier to reduce their food intake by 500–1000 kcal/d than they do to increase their energy expenditure by an equivalent amount. For example, to achieve a 500 kcal/d energy deficit, on a daily basis a patient could either eliminate two 20-ounce sugar-sweetened drinks or walk 5 miles. Moreover, research suggests that in adults, greater weight loss can be achieved via dietary interventions than by

![A Guide to Selecting Treatment*](http://annals.org/)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diet, physical activity, and behavior therapy</td>
<td>25–26.9 kg/m²</td>
</tr>
<tr>
<td>With comorbid conditions</td>
<td>27–29.9 kg/m²</td>
</tr>
<tr>
<td>Pharmacotherapy</td>
<td>30–34.9 kg/m²</td>
</tr>
<tr>
<td>With comorbid conditions</td>
<td>35–39.9 kg/m²</td>
</tr>
<tr>
<td>With comorbid conditions</td>
<td>≥40 kg/m²</td>
</tr>
<tr>
<td>Surgery</td>
<td></td>
</tr>
<tr>
<td>With comorbid conditions</td>
<td></td>
</tr>
</tbody>
</table>

BMI = body mass index.
* From reference 41.

**Table 2. A Guide to Selecting Treatment**
interventions focusing on physical activity. Physical activity, however, is an important component of weight management programs and is particularly important in maintaining weight loss in adults (see below). Clinicians can help overweight and obese persons identify the daily calorie target needed to lose weight by using equations to estimate daily energy expenditure, and then subtracting 500 to 1000 kcal from this value.

This calorie prescription, however, assumes that persons can precisely measure food intake. Studies have shown that overweight and obese persons underestimate caloric intake by approximately 40% per day (23). Because of this finding, men and women who weigh <250 lb (113.6 kg) are commonly prescribed 1200–1499 kcal/d, whereas those ≥250 lb are prescribed 1500–1800 kcal/d (to compensate for underestimation of calorie intake). Greater calorie restriction, as achieved with very-low-calorie diets (<800 kcal/d), produces greater, more rapid initial weight loss but is not recommended for most patients because of the cost of closer medical monitoring and the difficulty in maintaining the greater weight loss.

A variety of diets can be incorporated in lifestyle modification programs. A unifying feature of several diets is consumption of foods that are low in energy density (number of calories per weight of food), such as fruits, vegetables, lean protein, and whole grain carbohydrates that are high in fiber.

Low-fat diets
Fat has 9 calories per gram, compared with 4 calories per gram for carbohydrate and protein. Therefore, if not compensated by increased intake of other calorie sources, restriction of fat intake facilitates caloric restriction, which in turn should lead to greater weight loss.

A recent meta-analysis that included 33 randomized trials (n = 74 000 participants) concluded that participants assigned to low-fat diets (<30% of calories from fat) lost 1.6 kg more than persons assigned to control diets (with 28–43% of calories from fat) (24).

Low-carbohydrate diets
Low-carbohydrate diets typically provide fewer than 50 grams of carbohydrate per day (<10% of total kcal).

---

### Key Components of a Comprehensive Lifestyle Modification Program to Achieve and Maintain a 7–10% Weight Loss at 1 Year or Longer

<table>
<thead>
<tr>
<th>Component</th>
<th>Weight Loss</th>
<th>Maintenance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency, duration, and type of</td>
<td>At least 12–26 visits in person or by telephone in the first y, as recommended by the USPSTF (Internet/e-mail contact yields smaller weight loss); group or individual contact</td>
<td>Contact every other wk for 52 wk (or longer) (monthly contact may be adequate); group or individual contact</td>
</tr>
<tr>
<td>treatment contact</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dietary prescription</td>
<td>Low-calorie diet (1200–1500 kcal for persons &lt;250 lb; 1500–1800 kcal for those ≥250 lb); typical macronutrient composition: &lt;30% fat (&lt;7% saturated fat); 15% protein; remainder from carbohydrates (diet composition may vary based on individual needs or preferences)</td>
<td>Hypocaloric diet to maintain reduced body weight; typical macronutrient composition similar to that for weight loss</td>
</tr>
<tr>
<td>Physical activity prescription</td>
<td>180 min/wk of moderately vigorous aerobic activity (e.g., brisk walking); strength training also desirable</td>
<td>200–300 min/wk of moderately vigorous aerobic activity (e.g., brisk walking); strength training also desirable</td>
</tr>
<tr>
<td>Behavior therapy prescription</td>
<td>Daily monitoring of food intake and physical activity using paper or electronic diaries; weekly weight monitoring; structured curriculum of behavior change (e.g., diabetes prevention program); regular feedback from an interventionist</td>
<td>Occasional to daily monitoring of food intake and physical activity using similar diaries; twice-weekly to daily weight monitoring; curriculum of behavior change, including relapse prevention and individualized problem solving; periodic feedback from an interventionist</td>
</tr>
</tbody>
</table>

---

calories from carbohydrate for a 2000-calorie diet). These diets experienced renewed popularity in the early 2000s after publication of 2 randomized trials showing greater short-term weight loss with an Atkins-type diet (25, 26). However, 2 larger randomized trials, done since those initial studies, showed that results of a low-carbohydrate diet was similar to calorie-restricted versions of a low-fat diet or to a Mediterranean diet (25, 26).

**Meal-replacement diets**

Meal replacements (shakes, meal bars) and portion-controlled entrees are an easy way to count calories and to simplify meal preparation.

A meta-analysis of 6 randomized trials concluded that a partial meal replacement regimen (replacing 2 meals per day with a shake, plus eating fruits and vegetables during the day) led to an additional 2.5–3 kg of weight loss beyond a prescribed diet with the same number of calories from self-selected food (27).

**Which diet is best for long-term weight loss?**

Most evidence suggests that diets that differ in macronutrient content produce similar amounts of weight loss over the long term. Thus, a calorie-deficit diet that follows federal dietary guidelines (50–60% of calories from complex carbohydrate) and that emphasizes foods that are widely considered to be healthy (e.g., vegetables, nuts, fish) should serve as the initial choice for most patients.

A randomized trial (n = 811) assigned patients in a 2 x 2 fashion to diets with average or high-protein content (15% or 25%) and to low-fat or high-fat (20% or 40%), with carbohydrate making up the remainder. After 2 years, weight loss was similar in all 4 groups, and attendance at group sessions correlated more closely with weight loss than treatment group assignment (28).

**What is the role of exercise in weight loss and maintenance?**

Regular exercise is critical for overall health, but in randomized trials contributed only 1–3 kg of weight loss when combined with a structured diet program. Exercise seems to be more important for maintaining lost weight than for initial reduction. Persons who are able to perform 275 minutes per week (about 40 minutes/day) of exercise are significantly more likely to maintain weight loss over time. Aerobic and resistance training exercise combined may have further health benefits beyond either type of exercise alone (29).

**How can clinicians assess readiness for weight loss?**

Relatively little evidence exists to guide clinicians on which patients are most “ready” to participate in high-intensity obesity treatment programs. The consensus among bariatric clinicians is that patients must be committed to monitoring their food intake and physical activity, be free of untreated major depression, and not in the middle of a major life event. A practical approach to screen for readiness to participate in a high-intensity program is to ask patients to monitor their food intake and physical activity for at least 1 week.

**What makes maintaining weight loss so difficult, and what improves long-term results?**

After completing a 6-month program, patients on average regain one third of lost weight in the ensuing year, with continued regain over time. Previously, it was assumed that regression to old behavior patterns explained weight regain. However, a recent study found that 1 year after a substantial weight loss, levels of hormones that stimulate hunger (e.g., ghrelin) remained elevated, and levels of hormones that mediate satiety (e.g., leptin, amylin) remained depressed (30). These results suggest a physiologic basis for weight regain. Some data suggest that obese persons who have lost weight burn fewer calories than persons with the same lean body mass who were

never obese, thus impeding further weight loss (31).

Continued participation in a structured weight management program (that offers at least monthly and preferably twice-monthly treatment sessions) can help patients maintain lost weight. Other behaviors associated with successful maintenance of weight loss include engaging in physical activity ≥ 60 minutes/day most days of the week; monitoring body weight frequently; eating a reduced-calorie diet; and recording food intake periodically (particularly in response to weight regain). These are the behaviors practiced by members of the National Weight Control Registry, all of whom have lost at least 30 lb (13.6 kg) and maintained the loss for 1 year or more (32).

When is pharmacotherapy indicated for treatment of obesity?

Pharmacotherapy is appropriate for patients with a BMI ≥ 30 kg/m² or those with a BMI ≥ 27 kg/m² who have a significant weight-related condition, such as type 2 diabetes or hypertension (16). Patients should be screened carefully for contraindications to weight loss medications. Ideally, patients receiving weight loss medication should pursue a structured program of lifestyle modification and pharmacotherapy for obesity. N Engl J Med. 2005;353:2111-20. [PMID: 16291981]


The FDA approved 2 obesity agents in 2012, phentermine-topiramate and lorcaserin. A third agent, bupropion-naltrexone, was given an “approvable” decision by the FDA in 2012, subject to a long-term randomized trial of cardiovascular safety. Currently approved weight loss agents are shown in Table 4.

Phentermine-topiramate

Phentermine-topiramate (Qsymia, Vivus Inc.) is a fixed-dose combination of these 2 drugs, both prescribed in a lower dose than as monotherapy, with the goal of reducing side effects from either agent alone. (Topiramate is an FDA-approved agent for treatment of seizures and was observed to cause weight loss as a side effect.) Of the currently approved agents, phentermine-topiramate produces the most weight loss (8–11% of initial weight). Common side effects include paresthesias, change in taste (topiramate), dry mouth, constipation, and insomnia (phentermine). Contraindications include nephrolithiasis (topiramate) as well as uncontrolled blood pressure, resting tachycardia, or established CVD (phentermine). Because heart rate increased slightly in clinical trials (0.6–1.6 beats/min), the manufacturer is performing a large, prospective clinical trial to further assess risk. Topiramate is category X in pregnancy; women of...
In the CONQUER trial, 2487 overweight and obese persons with at least 2 risk factors for CVD were randomized to placebo or phentermine-topiramate 7.5/46 mg or phentermine-topiramate 15/92 mg (36). Weight loss at 1 year was 1.2%, 7.8%, and 9.8% of initial weight, respectively. The SEQUEL extension study, which continued with patients from CONQUER in a double-blind fashion, observed weight loss at 2 years of 1.8%, 9.3%, and 10.5%, respectively (37).

Lorcaserin
Lorcaserin (Belviq, Arena Pharmaceuticals) is an agonist of the 5HT2C receptor in the brain, which helps to regulate appetite. The drug was designed to avoid serotonin agonism in the heart, which was the mechanism determined to cause cardiac valve disease in some patients who received dexfenfluramine or “fen-phen” (fenfluramine-phentermine) in the 1990s. (Phentermine was not identified as a cause of valvulopathy [38]). Lorcaserin must be used with caution in patients receiving drugs with serotonergic mechanisms of action, such as selective serotonin reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors.

In the BLOOM trial, 3182 persons were assigned to placebo or lorcaserin (10 mg) twice daily. At 1 year, weight loss was 2.2% and 5.8% of initial weight, respectively (39). In the BLOOM and BLOOM-DM trials, echocardiograms done on 2472 patients at 1 year and 1127 patients at 2 years showed no increased risk for valvular disease.

Orlistat
Orlistat is available both as a prescription medication (120 mg 3 times daily) and as an over-the-counter agent (60 mg 3 times daily). It induces weight loss by reducing absorption of fat from the gastrointestinal tract. The modest weight loss (3–4% greater than placebo, similar to lorcaserin) and side-effect profile (e.g., oily stools, loose stools, flatulence) are similar to those observed with lorcaserin.

---

4. Currently Approved Weight Loss Agents

<table>
<thead>
<tr>
<th>Agent</th>
<th>Mechanism</th>
<th>Dose</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phentermine*</td>
<td>Sympathomimetic</td>
<td>15–37.5 mg/d</td>
<td>Dry mouth, headache, constipation, tachycardia, insomnia</td>
<td>Established cardiovascular disease, uncontrolled hypertension, glaucoma, hyperthyroidism, or active drug abuse</td>
<td>FDA Schedule IV</td>
</tr>
<tr>
<td>Diethylpropion*</td>
<td>Sympathomimetic</td>
<td>25–75 mg/d</td>
<td>Similar to phentermine</td>
<td>Similar to phentermine</td>
<td>FDA Schedule IV</td>
</tr>
<tr>
<td>Benzphetamine*</td>
<td>Sympathomimetic</td>
<td>20–50 mg TID</td>
<td>Similar to phentermine</td>
<td>Similar to phentermine</td>
<td>FDA Schedule IV</td>
</tr>
<tr>
<td>Phendimetrazine*</td>
<td>Sympathomimetic</td>
<td>17.5–35 mg BID to TID (max 70 mg/d)</td>
<td>Similar to phentermine</td>
<td>Similar to phentermine</td>
<td>FDA Schedule IV</td>
</tr>
<tr>
<td>Phentermine-topiramate*</td>
<td>Sympathomimetic (phentermine); appetite reduction/changes in taste of food (topiramate)</td>
<td>3.75/23 mg, 7.5/46 mg, 15/92 mg</td>
<td>Same as phentermine, plus paresthesias, altered taste, dizziness</td>
<td>Same as phentermine, plus pregnant or trying to become pregnant, or recent nephrolithiasis</td>
<td>Monthly birth control tests recommended</td>
</tr>
<tr>
<td>Lorcaserin</td>
<td>Serotonin 5HT2C agonist</td>
<td>10 mg BID</td>
<td>Headache, back pain, dizziness, fatigue, nasopharyngitis, nausea, constipation, dry mouth</td>
<td>Severe depression, established cardiac valvular disease</td>
<td>Caution with serotonergic drugs (e.g., SSRIs, SNRIs)</td>
</tr>
<tr>
<td>Orlistat</td>
<td>Intestinal lipase inhibitor</td>
<td>60 mg TID (OTC) or 120 mg TID (prescription)</td>
<td>Oily stools, fecal discharge, flatulence, fat-soluble vitamin deficiency</td>
<td>Use of immune suppressive medications; caution with concurrent warfarin</td>
<td>Take vitamin supplement 2 h before/after drug</td>
</tr>
</tbody>
</table>

*BID = twice daily; FDA = U.S. Food and Drug Administration; OTC = over-the-counter; SNRI = serotonin-norepinephrine reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor; TID = three times daily.

* Monitor blood pressure and pulse.

frequent prescription. Side effects, however, can be minimized by patients’ adherence to a low-fat diet, and orlistat remains the only over-the-counter weight loss agent that has been proven effective.

A 4-year randomized trial of orlistat (n = 3305) showed that it reduced the incidence of type 2 diabetes by 37% (40), an effect similar to metformin in the Diabetes Prevention Program (2).

Should weight loss medications be taken long-term?

Patients, on average, regain weight after medications are terminated. Trials of both orlistat and lorcaserin showed that patients who lost weight during the first year and were then randomly assigned to remain on medication for a second year maintained significantly greater weight loss at the end of the second year than did persons randomized to placebo (30). Thus, patients should be counseled that long-term pharmacotherapy will probably be needed. Randomized, controlled trials of previous medications found that treatment could be provided approximately every other month, rather than continuously, with no loss of efficacy (41, 42). The plateau in weight loss that occurs after approximately 6–8 months of pharmacologic treatment should not be interpreted to mean that the medication is “no longer working.” The plateau, in part, reflects the hormonal and metabolic adaptations to weight loss described previously.

Patients and clinicians may have concerns about the safety of long-term pharmacotherapy for obesity raised by a history of unexpected problems with these medications. Medications currently approved for chronic use have been subjected to more rigorous safety testing than in previous eras, which ultimately will include trials to examine long-term risk for cardiovascular events.

When is surgery indicated for treatment of obesity?

Bariatric (weight loss) surgery is generally indicated for patients with a body mass index ≥ 40 kg/m² or for those with a BMI ≥ 35 kg/m² with at least 1 serious weight-related comorbidity condition, such as type 2 diabetes, sleep apnea, or disabling joint disease. Laparoscopic gastric banding is also FDA-approved for patients with a BMI ≥ 30 kg/m² and type 2 diabetes. Before having surgery, patients should have made sustained attempts at weight loss with lifestyle modification and/or pharmacotherapy. It is currently standard of care for patients considering bariatric surgery to undergo preoperative psychological evaluation to determine appropriateness for surgery. Patients must also be well informed of the potential risks of surgery and the need for long-term monitoring of their weight and nutritional status.

Types of bariatric surgery

The 3 types of surgeries most commonly done in the United States are adjustable gastric banding, Roux-en-Y gastric bypass, and sleeve gastrectomy. All 3 can be performed laparoscopically. The gastric band involves placing a band around the upper stomach, creating a small proximal stomach pouch through which food must pass before traversing the rest of the stomach and the intestinal tract. The band is adjustable, which allows the clinician to loosen it (e.g., if the patient has postprandial vomiting) or to tighten it if postsurgical results are suboptimal (e.g., slow weight loss, low level of satiety). Weight loss is achieved by restriction of food intake alone.

With gastric bypass, the stomach is transected proximally, and the midjejunum is also transected and connected to the remaining proximal stomach pouch. The remaining distal stomach, duodenum, and proximal jejunum are Anastomosed to form a “blind limb,” which ends proximally in the closed-off stomach and is no

longer a part of the active digestive process. Roux-en-Y gastric bypass causes restricted food intake, partial malabsorption, and changes in appetite-regulating hormones (e.g., ghrelin), all of which contribute to weight loss. In sleeve gastrectomy, approximately 75% of the stomach is removed, but the remainder of the intestinal tract remains intact. Weight loss is achieved principally by food restriction, although the removal of endocrine-rich gastric tissue and an accelerated rate of gastric emptying may contribute to the greater weight loss than with gastric banding.

**Effectiveness of bariatric surgery**
Bariatric surgery is the most efficacious treatment for severe obesity. One meta-analysis of randomized trials concluded that, after 1 year, gastric banding, gastric bypass, and sleeve gastrectomy were associated with reductions in BMI of 2.4 kg/m², 9.0 kg/m², and 10.1 kg/m², respectively (43). A recent cohort study (n = 8847) that used propensity scoring also reported that sleeve gastrectomy was closer in effectiveness to gastric bypass than to gastric banding (weight loss of approximately 17.1%, 29.7%, and 34.8% of initial weight for gastric banding, sleeve gastrectomy, and gastric bypass, respectively) (44).

The dramatic weight loss seen with bariatric surgery often ameliorates comorbid conditions (45). Type 2 diabetes resolves more often with gastric bypass than to gastric banding, which can lead to gastrointestinal reflux; obstruction; and in rare cases, esophageal or gastric perforation. Potential complications of gastric bypass include anastomotic breakdown, stenosis or ulcers near the anastomotic site, and long-term micronutrient deficiencies. Any patient having bariatric surgery is at risk for perioperative complications, including wound infection, venous thromboembolism, and mortality.

In a multicenter cohort study of patients undergoing surgery at bariatric surgical Centers of Excellence in the United States, 4.3% of patients had at least one major adverse outcome (death, venous thromboembolism, need for reintervention, or failure to be discharged from the hospital); 30-day mortality rates were 0% for gastric banding, 0.2% for laparoscopic gastric bypass, and 2.1% for open gastric bypass (46).

**Complications of bariatric surgery**
All 3 procedures reviewed are associated with complications. Potential complications of gastric banding include slippage or erosion of the band, which may contribute to gastrointestinal reflux; obstruction; and in rare cases, esophageal or gastric perforation. Potential complications of gastric bypass include anastomotic breakdown, stenosis or ulcers near the anastomotic site, and long-term micronutrient deficiencies. Any patient having bariatric surgery is at risk for perioperative complications, including wound infection, venous thromboembolism, and mortality.

Data are somewhat conflicting on whether bariatric surgery reduces mortality. The SOS study, the cohort study in which surgical and control participants were matched on 18 characteristics, found that the large weight loss achieved with bariatric surgery resulted in reduced all-cause mortality (4). However, a well-done observational study from U.S. Veterans Administration data, using propensity score adjustment, did not show a mortality benefit from bariatric surgery (46).

**Toward an evidence-based approach to treatment**
Clinicians should discuss weight with patients, using appropriate language. They should recognize that physiologic factors play a role in weight regain after initial weight loss. Clinicians should advise patients that keeping records of food intake and physical activity are the most important tasks for weight loss. A calorie deficit diet, with 50–60% of calories from complex carbohydrates, should be the first choice for most patients. Pharmacotherapy is appropriate for selected patients with obesity, with appropriate monitoring for potential side effects. Bariatric surgery is the most effective and the most high-risk treatment for severe obesity; it has been shown to improve and occasionally cure comorbid conditions and may reduce mortality from excess weight.
What do professional organizations recommend with regard to management of obesity?

The U.S. Preventive Services Task Force updated its recommendation in 2012 for treatment of obesity. The Task Force recommended that clinicians offer or refer patients with a BMI $\geq 30 \text{ kg/m}^2$ to intensive, multicomponent behavioral interventions (5). The ACP published guidelines for pharmacologic and surgical treatment of obesity in 2005 (48). The NIH guidelines for evaluation and treatment of obesity were originally published in 1998 (16), and an updated version of these guidelines is currently underway (expected in 2013/2014). The CMS has recently approved a benefit for intensive behavior therapy of obesity (49). It will pay for 14 visits (15 minutes each) in the first 6 months, and up to 6 additional monthly visits if the patient loses at least 3 kg in the first 6 months. This schedule of visits can be repeated annually, although the visits must be performed in the physical setting of the primary care office. In 2010, the American Diabetes Association officially recommended using hemoglobin A1c to screen for diabetes. Because of this, many more persons have been diagnosed with prediabetes, and greater attention has been focused on the value of moderate weight loss (5–10% of initial weight) in preventing diabetes. For example, the national Diabetes Prevention Program is undergoing dissemination through collaboration between YMCAs and the Centers for Disease Control and Prevention.
WHAT YOU SHOULD KNOW ABOUT OBESITY

Why is obesity a health problem?
- Being overweight means that you weigh more than is healthy.
- People who are overweight 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/m^2. You are overweight if your BMI is between 25 kg/m^2 and 30 kg/m^2. You are obese if it is over 30 kg/m^2.

What the best ways to lose weight?
- 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.
- Set a reachable goal for your new weight. Even a few pounds makes a difference.
- If diet and exercise are not enough, your doctor may give you medication 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's not easy to break the eating habits that lead to weight gain.
- It takes patience. Healthy, long-term weight loss takes time, and the slow results can dampen your motivation.
- It's hard for your body to change. When you go on a diet, you lose some weight and then stop for a while.

For More Information

Information resources from the National Heart, Lung, and Blood Institute’s Aim for a Healthy Weight! Program.

www.heart.org/HEARTORG/GettingHealthy/WeightManagement/WeightManagement_UCM_001081_SubHomePage.jsp
Guidance on losing weight and on physical activity from the American Heart Association.

www.eatright.org/Public/
Information on food and nutrition, from the Academy of Nutrition and Dietetics (formerly the American Dietetic Association).
CME Questions

1. A 42-year-old man is evaluated for obesity. His weight has gradually increased over the past two decades and is currently 168.2 kg (370 lb). Five years ago, he was diagnosed with type 2 diabetes mellitus, hypertension, and hyperlipidemia. Over the past 6 months, he has unsuccessfully tried diet and exercise therapy for his obesity. He tried over-the-counter orlistat but could not tolerate the gastrointestinal side effects. Medications are metformin, lisinopril, and simvastatin. His total weight loss goal is 45.4 kg (100 lb).

On physical examination, temperature is normal, blood pressure is 130/80 mm Hg, pulse rate is 80/min, and respiration rate is 14/min. BMI is 48. Waist circumference is 121.9 cm (48 in). There is no thyromegaly. Heart sounds are normal with no murmur. There is no lower extremity edema.

Results of complete blood count, thyroid studies, and urinalysis are unremarkable.

Which of the following is the most appropriate management of this patient?
A. Bariatric surgery evaluation
B. Prescribe phentermine
C. Reduce caloric intake to below 800 kcal/d
D. Refer to an exercise program

2. A 48-year-old woman is evaluated during a routine examination. She is concerned about her gradual weight gain over the years and requests counseling on how she can most effectively lose weight.

Over 8 years, she has gained approximately 18 kg (40 lb). With several commercial diets, she has lost weight but always gains it back. She has a sedentary job, and often skips breakfast or eats dinner on the run. She states she cannot fit exercise into her busy day. She takes no medications and has no allergies.

On physical examination, temperature is normal, blood pressure is 132/70 mm Hg, pulse rate is 80/min, and respiration rate is 12/min. BMI is 32. There is no thyromegaly. The abdomen is obese, soft, nontender, and without striae. Fasting plasma glucose level is 106 mg/dL (5.9 mmol/L) and thyroid function test results are normal.

Which of the following is the most appropriate next step to help this patient achieve long-term weight reduction?
A. Exercise 15–30 minutes 5 days/wk
B. Laparoscopic adjustable band surgery
C. Orlistat
D. Reduce current caloric intake by 500–1000 kcal/d

3. A 31-year-old woman is evaluated during a postpartum examination 6 months after giving birth to her first child. The patient was obese before becoming pregnant, developed gestational diabetes mellitus during pregnancy, and was able to maintain her weight and glucose level within the target range throughout her pregnancy with diet alone. Her infant weighed 4139 grams (146 ounces) at birth.

This patient’s infant is at increased risk for which of the following disorders?
A. Childhood obesity
B. Maturity-onset diabetes of the young
C. Type 1A diabetes mellitus
D. Type 1B diabetes mellitus

Questions are largely from the ACP’s Medical Knowledge Self-Assessment Program (MKSAP, accessed at http://www.acponline.org/products_services/mksap/15/?pr31). Go to www.annals.org/intheclinic/ to complete the quiz and earn up to 1.5 CME credits, or to purchase the complete MKSAP program.