

# Treating the Obese Patient

## *Suggestions for Primary Care Practice*

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**O**besity is a major health problem in America. Weight loss is associated with improvements in obesity-related health complications, but patients and practitioners are frequently disappointed by the long-term results of weight control efforts. Recent research has yielded new findings concerning the causes of obesity, as well as new goals for obesity treatment. Traditionally, the goal of therapy has been reduction to ideal weight. Several scientific bodies, however, now recommend a more modest 5% to 15% reduction in initial weight. Current options for weight loss include behavioral or pharmacological management provided during primary care visits, self-help and commercial programs, hospital-based interventions, and bariatric surgery. Regardless of the approach selected, long-term care usually is required to facilitate the maintenance of weight loss.

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Obesity is a major public health problem in America. A recent national survey found that 54.9% of US adults are overweight and that 22.3% of US adults are obese.<sup>1</sup> Studies have linked obesity to increased risk of type 2 diabetes mellitus, hypertension, cardiovascular disease, dyslipidemia, and certain types of cancer.<sup>2</sup> In addition, obese persons suffer from marked discrimination in our society.<sup>3</sup> It is no surprise then that Americans spend more than \$30 billion a year on weight control programs and products.<sup>4</sup>

Despite the clear need for weight loss, both patients and practitioners have been disappointed by the results of weight reduction therapy. Some researchers have gone as far as to say that “diets don’t work,”<sup>5</sup> a view that is based on findings that most dieters regain their lost weight within 5 years of completing treatment.<sup>6</sup> There is also some evidence that severe restriction of energy intake may temporarily induce binge eating.<sup>7</sup> Such findings have immobilized many overweight individuals,

despite the evidence of the clear medical benefits of weight loss.

### RECONCEPTUALIZING OBESITY

This article reviews new findings on the causes and treatment of obesity and provides new directions for the management of this disorder. It begins by examining 5 areas in which our conceptualization of obesity has changed substantially in the past decade.

#### Defining Obesity

Obesity is defined in terms of excess body fat. Because precise assessment of body fat is cumbersome and expensive, body weight is often used as an estimate of obesity. The term *overweight* has traditionally referred to weight in excess of some ideal, usually stipulated by actuarial height and weight tables. Unfortunately, the definition of “ideal” weight varies over time and across cultures, thus making it difficult, for example, to compare the prevalence of obesity in 2 nations.

In recent years, investigators have begun to use the body mass index (BMI) as a measure of overweight because it does not

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rely on comparison with an ideal weight. It is calculated as weight in kilograms divided by the square of height in meters:  $\text{weight (kg)} / [\text{height (m)}]^2$ . Both the National Heart, Lung, and Blood Institute and World Health Organization have defined *overweight* as a BMI of 25.0 to 29.9, while *obesity* is a BMI of 30 or greater.<sup>8,9</sup> **Figure 1** converts traditional measures of height and weight into BMI units.<sup>10</sup> The practitioner may wish to calculate his or her own BMI as a means of becoming more famil-

iar with the measure. The easiest method of calculating your precise BMI is to multiply your weight (in pounds) by 703. Divide this number by your height in inches, and then divide by height a second time. Values of BMI of 19.0 to 24.9 fall in the desirable (nonoverweight) range.

### Understanding Obesity

Obesity has long been thought to be a behavioral disorder that resulted from simply eating too much and/or

exercising too little. There is no question that these factors are associated with weight gain. Changes in our national lifestyle, including the increased consumption of high-fat foods, as well as our increasingly sedentary work and leisure habits, undoubtedly contributed to the marked rise in obesity (ie, from 25% to 33% of the population) observed from 1980 to 1994.<sup>11</sup>

Recent studies, however, have suggested that body weight is under substantial genetic control, accounting for approximately one third of the variation in BMI.<sup>12</sup> Genetic influences appear to contribute to differences among individuals in resting metabolic rate,<sup>13</sup> as well as body fat distribution<sup>14</sup> and weight gain in response to overfeeding.<sup>15</sup> Thus, some people appear to come into the world with a predisposition to obesity, which is readily nourished by our high-fat, low-activity lifestyle.

The most exciting development in the genetics of obesity was the discovery in 1994 of the *ob* gene and its protein product, leptin. Leptin is secreted by adipose tissue and acts on central neural networks that regulate ingestive behavior and energy balance.<sup>16</sup> Under normal conditions, leptin decreases food intake by inhibiting neuropeptide Y, a strong stimulant of eating.<sup>16</sup> As an animal's adipose mass increases, leptin secretion increases proportionally, thus reducing food intake and, eventually, body fat. In addition, high leptin levels are associated with increased energy expenditure, as a result of stimulation of  $\beta_3$ -adrenergic receptors in visceral fat deposits.<sup>17</sup> Stimulation of  $\beta_3$ -adrenergic receptors leads to an increase in production of uncoupling protein.<sup>17</sup> Uncoupling protein is a mitochondrial protein that generates heat instead of adenosine triphosphate from the hydrolysis of fatty acids, leading to energy expenditure rather than energy storage.<sup>18</sup>

The *ob/ob* mouse is severely obese, as a result of producing no leptin, and becomes lean when given exogenous leptin. Initial speculation that obesity in humans was caused by leptin deficiency proved to be incorrect.<sup>19</sup> The vast majority of obese humans appear to have high leptin levels, commensurate with their in-

		Height, m (ft, in)																
		1.52 (5'0")	1.55 (5'1")	1.57 (5'2")	1.60 (5'3")	1.63 (5'4")	1.65 (5'5")	1.68 (5'6")	1.70 (5'7")	1.73 (5'8")	1.75 (5'9")	1.78 (5'10")	1.80 (5'11")	1.83 (6'0")	1.85 (6'1")	1.88 (6'2")	1.91 (6'3")	1.93 (6'4")
56.3 (125)		24	24	23	22	21	21	20	20	19	18	18	17	17	16	16	16	15
58.5 (130)		25	25	24	23	22	22	21	20	20	19	19	18	18	17	17	16	16
60.8 (135)		26	26	25	24	23	22	22	21	21	20	19	19	18	18	17	17	16
63.0 (140)		27	26	26	25	24	23	23	22	21	21	20	20	19	18	18	17	17
65.3 (145)		28	27	27	26	25	24	23	23	22	21	21	20	20	19	19	18	18
67.5 (150)		29	28	27	27	26	25	24	23	23	22	22	21	20	20	19	19	18
69.8 (155)		30	29	28	27	27	26	25	24	24	23	22	22	21	20	20	19	19
72.0 (160)		31	30	29	28	27	27	26	25	24	24	23	22	22	21	21	20	19
74.3 (165)		32	31	30	29	28	27	27	26	25	24	24	23	22	22	21	21	20
76.5 (170)		33	32	31	30	29	28	27	27	26	25	24	24	23	22	22	21	21
78.8 (175)		34	33	32	31	30	29	28	27	27	26	25	24	24	23	22	22	21
81.0 (180)		35	34	33	32	31	30	29	28	27	27	26	25	24	24	23	22	22
83.3 (185)		36	35	34	33	32	31	30	29	28	27	27	26	25	24	24	23	23
85.5 (190)		37	36	35	34	33	32	31	30	29	28	27	26	26	25	24	24	23
87.8 (195)		38	37	36	35	33	32	31	31	30	29	28	27	26	26	25	24	24
90.0 (200)		39	38	37	35	34	33	32	31	30	30	29	28	27	26	26	25	24
92.3 (205)		40	39	37	36	35	34	33	32	31	30	29	29	28	27	26	26	25
94.5 (210)		41	40	38	37	36	35	34	33	32	31	30	29	28	28	27	26	26
96.8 (215)		42	41	39	38	37	36	35	34	33	32	31	30	29	28	28	27	26
99.0 (220)		43	42	40	39	38	37	36	34	33	32	32	31	30	29	28	27	27
101.3 (225)		44	43	41	40	39	37	36	35	34	33	32	31	31	30	29	28	27
103.5 (230)		45	43	42	41	39	38	37	36	35	34	33	32	31	30	30	29	28
105.8 (235)		46	44	43	42	40	39	38	37	36	35	34	33	32	31	30	29	29
108.0 (240)		47	45	44	43	41	40	39	38	36	35	34	33	33	32	31	30	29
110.3 (245)		48	46	45	43	42	41	40	38	37	36	35	34	33	32	31	31	30
112.5 (250)		49	47	46	44	43	42	40	39	38	37	36	35	34	33	32	31	30
114.8 (255)		50	48	47	45	44	42	41	40	39	38	37	36	35	34	33	32	31
117.0 (260)		51	49	48	46	45	43	42	41	40	38	37	36	35	34	33	32	32
119.3 (265)		52	50	48	47	45	44	43	42	40	39	38	37	36	35	34	33	32
121.5 (270)		53	51	49	48	46	45	44	42	41	40	39	38	37	36	35	34	33
123.8 (275)		54	52	50	49	47	46	44	43	42	41	39	38	37	36	35	34	33
126.0 (280)		55	53	51	50	48	47	45	44	43	41	40	39	38	37	36	35	34
128.3 (285)		56	54	52	50	49	47	46	45	43	42	41	40	39	38	37	36	35
130.5 (290)		57	55	53	51	50	48	47	45	44	43	42	40	39	38	37	36	35
132.8 (295)		58	56	54	52	51	49	48	46	45	44	42	41	40	39	38	37	36
135.0 (300)		59	57	55	53	51	50	48	47	46	44	43	42	41	40	39	37	37

**Figure 1.** Table for estimating body mass index from height and weight. A body mass index of 25.0 to 29.9 is defined as overweight by the World Health Organization. Boxes with shading (body mass index  $\geq 30$ ) indicate obesity. Adapted with permission from Guidance for Treatment of Adult Obesity.<sup>10</sup>

creased body fat.<sup>20</sup> Thus, investigators have speculated that some obese individuals may be insensitive to leptin, in the same manner that persons with type 2 diabetes mellitus are insensitive to insulin.<sup>21</sup> This possibility has led to clinical trials, currently under way, in which large doses of leptin are administered to obese individuals to induce weight loss.

### Attitudes Toward Obesity

Society is unforgiving of overweight individuals. Stunkard and Sobal<sup>22(p417)</sup> have called disparagement of obese individuals "the last socially acceptable form of prejudice." Historically, the public has believed that weight loss is a matter of willpower. Obese individuals have been considered weak-willed and unmotivated, a view that is compounded by the claims of easy weight loss promised by many diet books. Unfortunately, many obese persons seem to have accepted this view of themselves.<sup>23</sup> Practitioners are not immune to these beliefs. Physicians in 1 study described their obese patients in such negative terms as "weak-willed," "ugly," and "awkward."<sup>23</sup> Rand and MacGregor<sup>24</sup> found that a majority of candidates for gastric bypass surgery reported that they had been treated disrespectfully by the medical profession because of their obesity. Obese women also have been found to delay or avoid medical care because of weight concerns.<sup>25</sup>

Attitudes, however, toward obesity appear to be changing with the recognition that obesity is a complex, multidetermined disorder with a genetic component.<sup>12</sup> Moreover, findings suggest that physiological and genetic factors may limit the amount of weight that an individual can lose and maintain.<sup>26,27</sup> These findings have led to new empathy for overweight individuals, as well as to a change in the goals of obesity treatment.<sup>28</sup>

### Goals of Obesity Treatment

Traditionally, the goal of obesity treatment has been reduction to ideal weight. This goal, however, has changed dramatically in the past several years. Several scientific bodies

now recommend a 5% to 15% reduction in initial body weight. For example, the Institute of Medicine of the National Academy of Science<sup>29</sup> has proposed that

Successful long-term weight control by our definition means losing at least five percent of body weight . . . and keeping it below our definition of successful weight loss for at least one year.<sup>29(p131)</sup>

Similarly, the 1995 Dietary Guidelines for Americans read,

Many people are not sure how much weight they should lose. Weight losses of only 5-10 percent of body weight may improve many of the problems associated with overweight, such as high blood pressure and diabetes. Even a smaller loss can make a difference.<sup>30(p11)</sup>

These new guidelines have been adopted for a number of reasons. First, most obese individuals cannot reduce to ideal weight, despite their most tenacious efforts. Reviews of the literature indicate that most patients typically lose only 10% to 15% of initial body weight, even with state-of-the-art behavioral treatment<sup>31</sup> or pharmacotherapy.<sup>32,33</sup> Second, even for individuals who manage to lose a large amount of weight, the great majority cannot maintain the loss. A recent review found that most patients had regained 35% to 50% of their weight loss 1 year after treatment, regardless of the weight reduction method used.<sup>31</sup>

A third reason for the new, more modest weight loss goals is the finding, noted above, that patients do not need to reduce to ideal weight to improve their health. Small weight losses are associated with improvements in hypertension, hypercholesterolemia, and type 2 diabetes mellitus.<sup>34</sup> Because most patients achieve weight loss by reducing dietary fat and overall energy intake, it is unclear to what extent improvements in health are attributable to weight loss as opposed to changes in dietary intake.<sup>35</sup> However, studies have shown that these health improvements are generally maintained as long as patients maintain their weight loss. Benefits are frequently retained even with partial weight regain.<sup>36</sup>

### Obesity: A Chronic Disorder

In the past, obesity has been treated as an acute disorder. Many patients still appear to believe that 10 to 20 weeks of treatment should be enough to "cure" obesity or at least control it for several years. This view of obesity is often encouraged by the commercial diet industry, which promises miraculous results with little or no effort. The results of such an approach are clear; if treated as an acute disorder, obesity will return. Guy-Grand<sup>37</sup> noted that all obesity treatments to date are palliative, not curative. Practitioners cannot cure obesity any more than they can diabetes or hypertension. Practitioners need to help patients recognize that obesity is a chronic disorder that requires long-term care. Acceptance of this fact alone should help improve the results of treatment.<sup>37,38</sup>

### ASSESSING THE OBESE PATIENT

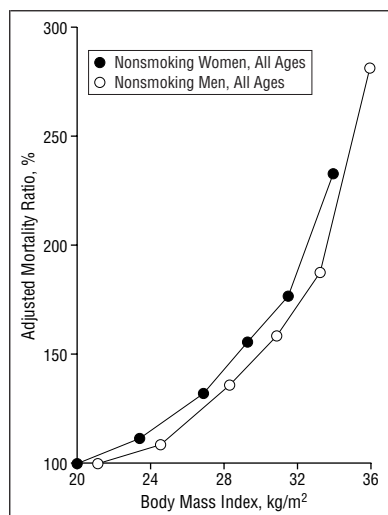
Before prescribing weight loss, the practitioner will want to assess both the patient's need and readiness for treatment. These issues are reviewed at length in the recent report of the National Heart, Lung, and Blood Institute Task Force.<sup>8</sup> We briefly review herein some of the key issues.

#### Health Risk

Some obese patients need to lose weight more than others. Heavier patients usually have more health complications, as shown in **Figure 2**, which plots BMI against mortality risk.<sup>39</sup> The risks of mortality are increased or decreased, depending on a number of other factors. Principal among these are the distribution of body fat and the presence of other risk factors. **Table 1** summarizes the characteristics of persons with an increased (or decreased) need for weight loss.<sup>39</sup>

#### Mood and Behavior

About 25% to 30% of obese patients who seek weight reduction therapy suffer from marked depression or other psychological disturbance.<sup>40</sup> Increased emotional distress are frequently correlated with



**Figure 2.** Adjusted mortality ratios in relation to body mass index of nonsmoking men and women of all ages. The lowest mortality ratio for each relative weight category is assigned a value of 100%. Adapted with permission from Vanitallie and Lew.<sup>39</sup>

binge eating, in which an individual eats a large amount of food in a short period of time and feels out of control while doing so.<sup>41</sup> Practitioners should routinely inquire about the obese patients' mood, sleep, appetite, and enjoyment of activities, as well as their pattern of eating. Obese individuals with marked depression, anxiety, or binge eating may require pharmacotherapy and/or psychotherapy before attempting to lose weight.

### Readiness

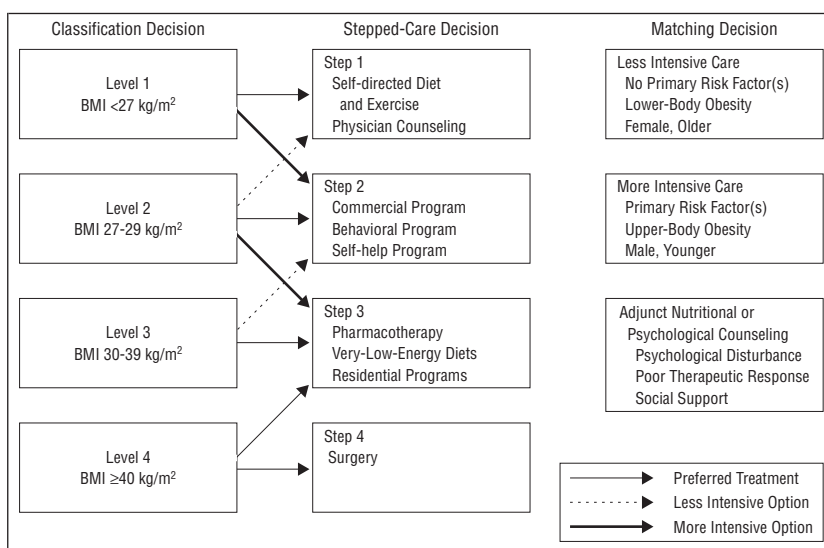
A patient may be severely overweight and have major medical complications but not be ready to make a commitment to weight reduction. Thus, it is important for the practitioner to talk with patients to determine whether they recognize the need for weight loss, instead of implicitly assuming that they do. Discussing findings of the physical examination, history, and laboratory tests can help educate patients about the need for weight reduction.

The practitioner should also determine whether it is a favorable time for the patient to lose weight. Weight loss requires concentration and sustained effort, each of which can be impaired by the occurrence of life stressors such as a job change, financial problems, or a major family illness.<sup>42</sup> If patients

**Table 1. Some Modifiers of Body Mass Index–Associated Morbidity and/or Mortality Risk\***

Abaters	Augmenters
Lower-body (femoral-gluteal) fat distribution pattern	Upper-body (abdominal) fat distribution pattern
Ostensibly good health	Impaired health
Absence of obesity-related risk factors	Presence of $\geq 1$ obesity-related risk factors
Middle-age or elderly	Young adult (20-45 y)
Female	Male
Absence of a family history of obesity-relevant illness	Presence of a family history of obesity-relevant illness
Obesity of brief duration	Obesity of prolonged duration
Membership in a race not known to be vulnerable to obesity-associated health problems	Membership in a race known to be vulnerable to obesity-associated health problems (eg, type 2 diabetes mellitus vulnerability in obese Pima Indians)
Above-normal stature	Below-normal stature

\* Reprinted with permission from Vanitallie and Lew.<sup>39</sup>



**Figure 3.** A conceptual scheme showing a 3-stage process in selecting a treatment for an individual. The first step, the classification decision, divides people into 4 levels on the basis of body mass index (BMI). The level dictates which of 4 steps would be reasonable in the second stage, the stepped-care decision. This indicates that the least intensive, costly, and risky approach will be used from among treatment alternatives. The third stage, the matching decision, is used to make the final selection of a program and is based on an assessment of the patient's need for weight reduction, as judged by the presence of comorbid conditions or other risk factors. In addition, patients with significant psychological problems and/or an eating disorder may require adjunct care. Reprinted with permission of Thomas A. Wadden and Kelly D. Brownell.

feel that they will be unable to make the commitment to treatment, they should wait until their life circumstances improve. In such cases, the immediate goal of treatment is the prevention of further weight gain rather than the induction of weight loss.

### TREATMENT OF THE OBESE PATIENT

There are many options for treating obese individuals (**Figure 3**). The figure suggests that, as a general rule,

more aggressive therapy should be used with persons who are more obese and who have more health complications. The practitioner needs to decide whether he or she will treat the patient's obesity or, instead, will refer the individual to a commercial program or a specialized treatment center. We encourage practitioners to work with patients initially, unless they clearly do not have the staff or time to do so. If the practitioner decides to treat the patient, referrals for other specific services (eg, nutritionist, psychiatrist or psychologist, ex-

ercise specialist) can be made on a case-by-case basis.

## DIET, EXERCISE, AND BEHAVIOR MODIFICATION

All patients, regardless of the specific treatment selected, need help in modifying their diet, eating habits, and physical activity. Both patient and practitioner will find that using a treatment manual, such as the *LEARN Program for Weight Control*,<sup>43</sup> facilitates lifestyle modification. The following are some specific tips for working with patients on behavior change.

### Diet

We encourage patients to eat a diet that they like but to reduce fat and "empty calories," such as alcohol and sweets. A strategy that can be used during office visits is to have patients write down a typical day's breakfast, lunch, dinner, and snacks. Patient and provider can then identify small dietary changes that will reduce energy intake by 2100 kJ/d (500 kcal/d). The Food Guide Pyramid,<sup>44</sup> as well as the Exchange Lists (developed jointly by the American Diabetes Association and the American Dietetic Association),<sup>45</sup> provide guidance for persons who report that they do not know what to eat or do not have a structured meal plan.

Weight loss is facilitated by having patients record their food intake.<sup>42</sup> These records should be reviewed at subsequent visits to assess patients' progress in reducing fat and energy intake. Some studies have shown that consumption of a low-fat diet alone can lead to weight loss, but others have reported that restriction of both fat and energy intake produces larger weight losses. We recommend that patients count calories for at least the first few weeks. Most obese women (BMI >30) will lose about 0.45 kg (1 lb) a week by consuming 5040 to 6300 kJ/d (1200-1500 kcal/d) and men by eating 6300 to 7560 kJ/d (1500-1800 kcal/d).<sup>31</sup> An appropriate reducing diet provides at least 42 kJ (10 kcal) for each 0.45 kg (1 lb) of ideal body weight. Regardless of the target energy

intake level, practitioners should encourage patients to eat a diet that is nutritionally sound, which is difficult if energy intake falls below 5040 kJ/d (1200 kcal/d).

### Eating Habits

In addition to modifying what they eat, many patients need to change when, where, and how they eat. For example, eating while driving or while watching television prevents people from fully attending to their food. Moreover, such events frequently become paired with food and may elicit eating in the absence of hunger. We usually ask patients to identify 3 eating habits they believe contribute to their weight problem. These usually include, in addition to those noted above, snacking throughout the day, consuming too much after dinner, overeating at social events, or eating in response to negative moods. We have them start with the problem they think will be easiest to correct and help them identify coping strategies. At the end of each treatment visit, patients should have a concrete plan for changing 1 problem eating behavior. The plan should describe what they will do and where, when, and how they will do it.

### Exercise

For weight control, any physical activity is better than none. Obese individuals need help in understanding that exercise does not have to be unpleasant or punishing. Most individuals, for example, do not know that they burn approximately the same amount of energy whether they walk a mile or run it. When increasing their activity, patients should develop a specific plan that is grounded in the what-where-when-and-how format described for changing eating habits. The practitioner should follow up at the next appointment to see if patients adhered to their plan. Recommendations for increasing activity should also stress the importance of lifestyle activity. For example, parking further away from the mall entrance and walking a flight of stairs, instead of taking the elevator, add to daily energy expenditure.

Recently, the Centers for Disease Control and Prevention and the

American College of Sports Medicine suggested that all adults should engage in 30 minutes or more of moderately intense physical activity every day or close to every day (this level of activity corresponds to an expenditure of approximately 840 kJ/d [200 kcal/d]).<sup>46</sup> This is an appropriate goal but one that markedly obese individuals will have to build toward gradually. The practitioner's task is to help patients identify where they stand on an activity continuum, ranging from completely sedentary to extremely active, and to have them progress to the next step. For many individuals, this may mean starting with a 5-minute walk at a slow pace.

### Getting the Best Results

Patients are likely to obtain the best results when they are seen frequently. Group behavior modification programs, for example, that are offered in university or hospital clinics usually meet weekly for 16 to 26 weeks and produce average reductions in initial weight of 8% to 10%.<sup>31</sup> Primary care physicians obviously cannot meet with patients weekly. Practitioners, however, could see the patient approximately once every 3 months to assess changes in physical health. A nurse, dietitian, or other staff member could assist the patient with behavior change in monthly office visits. In addition, it may be helpful to set aside a block of time each week (eg, Fridays from 4 to 5:30 PM) to provide 2-minute visits for patients who want to get weighed and quickly review their food and exercise diaries. These brief meetings can provide the necessary level of contact in a cost-effective manner. We have developed a protocol for implementing the 16-week LEARN<sup>43</sup> program in primary care practice. It is available on request.

Practitioners should encourage patients and applaud their success whenever possible. By continuing to praise patients' progress and successful steps toward their goal of weight loss, practitioners can help to keep patients motivated over the long run. This is especially critical when patients have reached a "weight loss plateau."

## SELF-HELP, COMMERCIAL, AND HOSPITAL-BASED PROGRAMS

Practitioners who are unable to provide monthly behavioral visits may wish to refer patients to weight loss programs in the community. These range from self-help approaches, such as Overeaters Anonymous (OA) and Take Off Pounds Sensibly (TOPS), to commercial programs that include Weight Watchers and Jenny Craig, to hospital-based very-low-energy diet programs, including OPTIFAST and Health Management Resources. Similarly, many registered dietitians are skilled in weight management. (You can locate a dietitian in your community by calling [800] 366-1655.) Figure 3 provides guidelines for selecting a commercial program, based on the patient's BMI and severity of health complications.

### Self-help and Commercial Programs

Both OA and TOPS are free of charge and provide valuable group support. Meetings of OA are perhaps most appropriate for individuals who suffer from binge eating or wish to explore emotional issues related to weight and eating.<sup>47</sup> Take Off Pounds Sensibly takes a more skill-based approach to weight control, similar to that described previously.<sup>47</sup> Of the commercial programs, Weight Watchers is by far the most popular. The program is reasonably priced (about \$12 per meeting) and, in addition to social support, provides sound advice on nutrition, exercise, and behavior modification. Group meetings are led by successful program graduates. Most patients lose only modest amounts of weight (ie, perhaps a few kilograms), primarily because they attend fewer than a dozen meetings at any given time they enroll.<sup>48</sup> Programs that require patients to purchase foods or other products can cost as much as \$75 a week. Given that such programs do not disclose their results of treatment (thus potentially justifying their higher costs), we cannot recommend them over the more modestly priced Weight Watchers.

## Hospital-Based Programs

Hospital-based very-low-energy diet programs, providing 3360 kJ/d (800 kcal/d) or less, are appropriate only for persons with a BMI greater than 30 who have failed to reduce their weight by more conventional approaches. These programs are usually provided by a multidisciplinary staff, led by a physician, and induce weight losses of 20% of initial weight in approximately 26 weeks<sup>49-52</sup> at a total cost of about \$2500 to \$3000. Patients typically regain 35% to 50% of their weight loss in the year after treatment,<sup>49,52</sup> although the majority appear to maintain a loss of at least 5% of initial weight for up to 3 years.<sup>53</sup>

## PHARMACOLOGICAL TREATMENT OF OBESITY

On September 15, 1997, Wyeth-Ayerst Laboratories, Philadelphia, Pa, the American distributor of fenfluramine hydrochloride and dexfenfluramine hydrochloride, voluntarily withdrew these medications from the market at the request of the Food and Drug Administration (FDA) because of concerns of increased risks of valvular heart disease.<sup>54</sup> This action muted enthusiasm for the pharmacological treatment of obesity that had begun with Weintraub and coworkers' 1992 reports<sup>55,56</sup> that patients treated by the combination of fenfluramine and phentermine hydrochloride lost 14.3 kg (ie, 16% of initial weight) in 34 weeks and generally maintained this loss for up to 3.5 years, if medication was continued. Investigators are trying to determine the precise occurrence rates of valvular heart disease in persons treated by fenfluramine or dexfenfluramine. Initial surveillance data suggested that the prevalence was as high as one third of persons<sup>57</sup>; a more recent study found the prevalence to be 23%.<sup>58</sup> Additional studies will attempt to identify the specific mechanism responsible for the observed abnormalities.

Withdrawal of these medications clearly represented a temporary setback in the pharmacological treatment of obesity, in much the same way that the perils of amphetamine treatment in the 1950s and

1960s gave all weight loss medication a bad name in the decades that followed. However, on November 24, 1997, the FDA approved a new agent, sibutramine hydrochloride, for "weight loss and the maintenance of weight loss." This action indicates that progress in pharmacological treatment may recover quickly. The current status of weight loss medications is reviewed below.

### Approved Weight Loss Medications

**Table 2** shows prescription weight loss medications currently approved by the FDA.<sup>59</sup> With the exception of sibutramine and orlistat, all are approved for only short-term use (ie, up to 3 months). Before September 1997, phentermine had been the most widely used, having accounted for more than 50% of the weight loss medication market, even when fenfluramine and dexfenfluramine were still available. There have been no reports of valvular heart disease in persons who used phentermine as a monotherapy, but use of this medication has declined substantially since the withdrawal of the fenfluramines.

**Medications Approved for Long-term Use.** At the time of this writing, 1 medication, sibutramine, is approved for long-term use, and another, orlistat, is expected to be approved for long-term use by spring 1999.

Sibutramine and its metabolites inhibit the reuptake of norepinephrine and serotonin (and dopamine to a very limited degree). Sibutramine does not stimulate the release of either of these neurotransmitters, which distinguishes it from the fenfluramines, which are serotonin releasers, and from phentermine, which is a norepinephrine releaser.

Sibutramine reduces food and energy intake in humans, as shown in a recent laboratory study.<sup>61</sup> Its long-term efficacy was shown in a 12-month, double-blind, randomized study. At 12 months, patients who took sibutramine lost 7% to 8% of initial weight, as compared with a loss of only 1% to 2% in patients who received placebo.<sup>62</sup> Maximum

**Table 2. Weight Loss Medications Currently Approved by the Food and Drug Administration\***

Medication Name and Mechanism	DEA Schedule†	Trade Name	Dosage Size, mg	Daily Dose Range, mg
<b>Noradrenergic agents</b>				
Benzphetamine hydrochloride	III	Didrex	25, 50	25-150
Phendimetrazine tartrate	III	Anorex and others	35	70-210
Diethylpropion hydrochloride	IV	Tenuate, Tepanil	25, 75 (slow release)	75
Mazindol	IV	Mazanor, Sanorex	1, 2	1-3
<b>Phentermine</b>				
Resin	IV	Ionamin	15, 30	15-30
Hydrochloride	IV	Adipex-P and others	37.5	18.75-35
Hydrochloride	IV	Fastin and others	30	30
Phenylpropanolamine	Over the counter	Dexatrim and others	25, 75	25-75
<b>Noradrenergic-serotonergic agents</b>				
Sibutramine hydrochloride	IV	Meridia	5, 10, 15	5-15
<b>Other agents</b>				
Orlistat	None	Xenical	120	360

\*All medications except sibutramine and orlistat are approved for short-term use only (ie, 3 months or less). Sibutramine has been approved for long-term use. Orlistat has received an approvable letter from the Food and Drug Administration, with final approval expected by Spring 1999. Adapted from Bray<sup>69</sup> with permission. DEA indicates Drug Enforcement Agency.

†The Controlled Substances Act<sup>60</sup> places all regulated substances into 1 of 5 schedules on the basis of their medical use, potential for abuse, and safety. Schedule I substances have the highest potential for abuse or unsafe use; Schedule V substances, the least.

weight loss was achieved in the first 6 months and was maintained from months 6 to 12.<sup>62</sup>

**Side Effects.** The most common side effects of sibutramine are headache, dry mouth, constipation, and insomnia.<sup>63</sup> Increases in heart rate of 4 to 5 beats per minute and increases in systolic and diastolic blood pressure of 1 to 3 mm Hg have also been reported.<sup>63</sup> For this reason, blood pressure and pulse must be measured before therapy with sibutramine is started, and they should be monitored at regular intervals thereafter.<sup>63</sup> Sibutramine is contraindicated in persons with uncontrolled or poorly controlled hypertension, a history of coronary artery disease, congestive heart failure, arrhythmias, or stroke.<sup>63</sup> Sibutramine is also contraindicated in persons taking monoamine oxidase inhibitors and is not recommended in combination with selective serotonin reuptake inhibitors for depression or migraine headaches. The medication should be used with caution in patients with narrow-angle glaucoma.<sup>63</sup>

The risk of primary pulmonary hypertension, which had been estimated at 23 to 46 cases per million with dexfenfluramine and other anorectic agents,<sup>64</sup> is not known with

sibutramine because of the relatively small number of persons who have used the latter medication. Two preliminary studies found no evidence that sibutramine increased the risk of valvular heart disease.<sup>63</sup> No data are available on the safety or efficacy of sibutramine past 12 months of use.

**Orlistat.** Orlistat has received an approvable letter from the FDA; final approval is expected in spring 1999 for its use in weight loss and the maintenance of weight loss. This agent has no central nervous system effects; it works by inhibiting approximately 30% of intestinal fat absorption.<sup>65,66</sup> The malabsorbed fat is excreted in stool. Patients must consume a diet with a fat content of 30% of energy or less to prevent adverse events that include oily stools, flatulence with discharge, and fecal urgency.<sup>67</sup>

Orlistat produces an average loss of about 8% to 10% of initial weight in 6 to 12 months, with good maintenance of weight loss at 2 years with continued use of medication.<sup>67,68</sup> Use of orlistat has been associated with decreases in serum lipid levels.<sup>67,69</sup> Given its mechanism of action, concerns have been raised that orlistat will reduce the absorption of fat-soluble vitamins A,

D, E, and K. Studies of the short-term effects of orlistat on serum vitamins A and E have been mixed.<sup>65,70</sup> Results of long-term (2-year) studies found that orlistat had minimal effect on serum levels of vitamins A, D, E, and K.<sup>67,68</sup> Generally, the agent lowered serum levels of these vitamins, but the mean values remained within the baseline range.<sup>67,68</sup> In most cases, these effects were reversed with multivitamin supplementation, and patients who take orlistat will be advised to take a multivitamin supplement that includes fat-soluble vitamins.<sup>67</sup>

Orlistat's peripheral mechanism of action suggests that it should not be associated with primary pulmonary hypertension or valvular heart disease. The FDA, however, was informed that this agent was associated in 1 study with an increased incidence of breast cancer,<sup>67</sup> an issue that is being reviewed at the time of this writing.

### Herbal Preparations

With the withdrawal of fenfluramine from the market, several companies began to market a "natural fen-phen" or "herbal fen-phen," usually composed of a combination of St John's wort and the ephedra herb. This combination was chosen because these herbs are thought to have independent effects on appetite, similar to phentermine and fenfluramine. Evidence suggests that St John's wort may be beneficial in the treatment of depression,<sup>71</sup> whereas ephedrine, derived from the ephedra herb (also known as *ma huang*), was shown to be effective in inducing weight loss when combined with caffeine.<sup>72</sup> Studies are under way to determine whether this herbal combination is safe and effective for weight loss. At the time of this writing, however, there are no data to support its use.

### Pharmacotherapy: Patient Selection

The National Task Force on the Prevention and Treatment of Obesity recently reviewed guidelines for the use of weight loss medication.<sup>73</sup> The Task Force noted that most researchers consider a BMI of 27 to be the

minimal acceptable cutoff for using anorectic agents with patients who do not have obesity-related comorbidities. However, the labeling information for sibutramine recommends a cutoff BMI of 30 for patients with no obesity-related comorbidities. As shown in Figure 3, we recommend this more conservative criterion. If, however, the patient has a primary risk factor (see Table 1), a BMI as low as 27 is acceptable. In all cases, patients should be monitored for adverse events.

The decision to use anorectic medication should be based on factors including previous unsuccessful weight loss attempts with behavioral treatment. We believe that, before receiving pharmacotherapy, patients should have tried to lose weight by means of a structured program of diet, exercise, and behavior modification. Weight loss medications are not appropriate for the patient who wishes to lose 5 to 10 kg for cosmetic reasons. Additionally, practitioners must ensure that weight loss medications are not prescribed to persons with eating disorders (eg, anorexia nervosa or bulimia nervosa). Referral to a mental health professional is indicated when the practitioner believes that a patient has an eating disorder.

#### COMBINING BEHAVIORAL AND PHARMACOLOGICAL APPROACHES

Pharmacotherapy helps patients lose weight by modifying internal cues, including hunger and satiety, that regulate food intake<sup>74</sup> (or, as in the case of orlistat, by blocking the absorption of dietary fat). Behavior modification, by contrast, induces weight loss by teaching patients to manage external cues related to eating.<sup>74</sup> Thus, patients are taught to shop from a list at the grocery store, store foods out of sight at home, avoid fast-food restaurants, reduce activities associated with eating (such as watching television), and eat meals in only the kitchen or dining room. In this regard, the mechanisms of action of medication and behavior modification would appear to be quite different but complementary.

A study by Craighead and colleagues<sup>75</sup> showed that the best treatment results can be expected when medication and behavior modification are combined. Patients who were treated with 120 mg of fenfluramine hydrochloride per day, without any behavioral counseling, lost 6.0 kg in 6 months. By contrast, those who received medication and attended 26 weekly group behavior modification sessions lost 15.3 kg, more than double the weight loss with medication alone. Patients treated by group behavior modification lost a significantly smaller 10.9 kg. Thus, the effects of medication and behavior therapy were additive.

Wadden and colleagues<sup>76</sup> recently showed in a pilot study that effective behavioral counseling could be provided by a physician during 15- to 20-minute office visits. All subjects were treated for 1 year with 60 mg of fenfluramine hydrochloride and 15 mg of phentermine hydrochloride (for which we would now substitute sibutramine) per day. In addition, all were asked to read and complete assignments in *The LEARN Program for Weight Control*,<sup>43</sup> as well as *The Weight Maintenance Survival Guide*.<sup>77</sup> Half the patients received behavioral counseling from a physician during 10 brief office visits during the year, whereas the other half attended a total of 32 group behavior modification classes (of 75 minutes each) during this time. Patients in both groups lost approximately 15% of their initial weight and achieved significant reductions in levels of triglycerides and total cholesterol. These findings indicate that physicians can provide effective lifestyle modification (during brief visits) by following a structured approach, as provided by the LEARN Program.

#### SURGERY

For patients who have a BMI of 40 or more (ie, 100% or more overweight), have significant health complications, and have failed to lose weight with more conservative approaches, gastric surgery may be an option.<sup>78,79</sup> Two principal types of procedures are used today: gastric restriction and gastric bypass. Gas-

tric restriction procedures divide the stomach into a small upper pouch and a large lower portion connected by a small stoma. In gastric bypass operations, the majority of the stomach and varying lengths of the duodenum and jejunum are surgically bypassed. Gastric restriction has been regarded by proponents as a more physiological procedure than gastric bypass, in that the latter produces some malabsorption.<sup>80</sup>

Weight losses average 40% to 50% of excess preoperative weight for gastric restriction procedures and 50% to 60% of excess preoperative weight for gastric bypass procedures (usually equal to a 25% to 35% reduction in initial weight).<sup>78,81-83</sup> Weight loss is typically well maintained; Poiries and colleagues<sup>82</sup> found that patients maintained a mean 49% loss of excess body weight for as long as 14 years. Weight loss is associated with major improvements in health-related complications.<sup>78,81,82</sup> In particular, most patients experience substantial improvements in glycemic control, hypertension, sleep apnea, and mobility.<sup>82</sup>

In a large study of complications after bariatric surgery, Mason and colleagues<sup>84</sup> found that 90% of patients had no complications. Only 1% had 2 complications. Risk of the 2 most serious complications (gastrointestinal tract leak and deep venous thrombosis) combined was less than 1%. Operative mortality ranged from less than 1% to 1.5% in centers that specialize in surgery.<sup>82,84,85</sup> Candidates for bariatric surgery should be fully informed of potential complications.

Three months after a gastric bypass operation, most patients can return to their previous diet in terms of variety, but with a marked reduction in volume.<sup>82</sup> Vitamin supplementation, particularly cyanocobalamin, is necessary for these patients as well.<sup>82</sup> Like all interventions for obesity, surgical intervention requires long-term follow-up to help patients adjust to the surgery and adopt healthy eating and activity habits. Long-term monthly support groups that include family members can be useful.<sup>82</sup> The emotional health of these patients should



be considered as well; depression may be a side effect in a significant minority of persons.<sup>82</sup> To ensure long-term success, Brodin<sup>81</sup> recommends that all bariatric surgical patients be examined at least once a year after the second postoperative year.

### TALKING WITH PATIENTS ABOUT WEIGHT CONTROL

#### Need for Empathy

No matter what type of obesity therapy is chosen, the manner in which the practitioner discusses treatment with patients can potentially have a profound effect on outcome. As noted previously, health care professionals may share many of society's negative beliefs about obese individuals; patients appear to be acutely aware of this fact.<sup>24</sup> Obese patients deserve to be treated with the same respect and concern as individuals with other chronic disorders. The more that practitioners communicate that they understand what a challenging and frustrating problem weight control is, the more obese patients will feel supported and understood.

#### Setting Realistic Goals and Treatment Expectations

Before treatment, the physician should examine patients' reasons for and expectations of weight loss. This

includes assessing how much weight patients expect to lose, as well as changes in health or psychological status that they anticipate. Our society overvalues thinness, and dieting in pursuit of cosmetic (rather than medical) changes is perhaps the most common reason people seek weight loss.<sup>86</sup> This emphasis on thinness may lead obese persons to try to achieve a weight that is impossible to maintain, given genetic and physiological factors.<sup>26,27</sup>

In a recent study, Foster and colleagues<sup>86</sup> found that obese women chose a goal weight that required a 32% reduction in initial weight. This is a far greater loss than is produced by even the most successful (non-surgical) weight control programs. Despite losing more weight than they had in any previous efforts, as well as their reporting positive physical and psychosocial effects of weight loss, most patients in Foster and colleagues' study were dissatisfied with their weight loss at the end of treatment. This study highlights the importance of educating patients about what they can realistically expect from obesity treatment and of providing them with criteria to define a successful treatment outcome. In addition to clarifying expectations about treatment, practitioners should outline the prescribed course of treatment, describe the behavioral demands of the program (eg, self-monitoring, decreased energy intake, and increased activity), and discuss

the risks and benefits of the approach selected.

Satisfaction with treatment is dependent on comparing what is obtained with what was expected. From this perspective, patients probably will be more satisfied with their weight loss if the provider first helps them set realistic expectations. For most patients, a realistic goal is to lose 5% to 10% of initial weight.

### IMPROVING THE MAINTENANCE OF WEIGHT LOSS

Nowhere are the needs for empathy and realistic expectations more evident than with the challenge of maintaining weight loss. Weight regain is common after virtually all short-term interventions for obesity. Patients, for example, treated for 16 to 26 weeks by a comprehensive group behavioral program regain approximately one third of their weight loss in the year after treatment, with further regain over time.<sup>31</sup> Results of commercial programs are comparable.<sup>87</sup>

These findings have led to the realization that obesity, like other chronic conditions, requires long-term care. Moreover, weight maintenance requires a different set of skills than weight loss, as shown in **Table 3**.<sup>88</sup> Losing weight is exciting and socially rewarding; maintaining a weight loss requires just as much, if not more, effort than losing weight but brings less gratification. Thus, patients need extra support with weight loss maintenance.

#### Long-term Behavioral Treatment

Two methods, in addition to gastric surgery, reliably improve the maintenance of weight loss: long-term behavioral treatment and, potentially, long-term pharmacotherapy. Several studies have shown that the longer patients remain in behavioral treatment, the longer they maintain their weight losses, even for periods up to 10 years.<sup>38,89,90</sup> Continued treatment visits enhance motivation, provide an opportunity for troubleshooting, and teach patients a new set of skills. The goal of weight loss interventions is to lose a large amount of weight in a rela-

**Table 3. Comparison of Behaviors and Reinforcement Associated With Losing Weight vs Maintaining Weight Loss**

Weight Loss	Maintenance of Weight Loss
The goal of treatment is to lose a large amount of weight, after a prolonged period of weight gain	The goal of treatment is to lose small amounts of weight as small increases in weight occur
The dieter's principal strategy is to avoid eating all foods that have caused the weight problem	The dieter's principal task is to learn to eat troublesome foods in a controlled fashion (mastery) and to eat new foods, low in fat and energy
Treatment is time limited, usually 15 to 25 wk	Treatment is ongoing and lifelong
The dieter receives support from the diet program and from family and friends	The dieter receives little or no support from professionals or family members
Weight loss is highly reinforcing; it is noticeable and pleasing to dieters and their families	Maintenance of weight loss is not very reinforcing; dieters forget about their accomplishments, as do their family members
Dieters do not have to exercise to lose weight	Exercise appears to be critical to maintenance of weight loss

\*Reprinted with permission from Wadden.<sup>88</sup>

tively brief period. By contrast, the goal of weight maintenance programs is to teach patients to reverse small increases in weight, before they become large increases. This is a lifelong process, and one in which increased physical activity plays a critical role. Exercise does not appear to increase short-term weight loss substantially,<sup>91-93</sup> but it has been found to correlate highly with long-term weight maintenance.<sup>94</sup>

Frequent patient-provider contact is associated with the best maintenance of weight loss. As noted earlier, such care could be provided by the physician's support staff during brief office visits or even by telephone contact. Alternatively, patients can be encouraged to use a self-help (ie, OA or TOPS) or commercial (ie, Weight Watchers) program to facilitate weight maintenance (rather than weight loss). Regardless of the option selected, patients should strive to develop the skills that have been reported by successful weight loss maintainers. Such individuals (1) exercise regularly (at least 3 times weekly), (2) monitor their weight frequently (ie, at least once a week to daily), (3) eat a low-fat diet, (4) record their food intake (at least occasionally), and (5) develop effective problem-solving skills.<sup>88</sup>

### Long-term Pharmacotherapy

The study by Weintraub et al<sup>56</sup> of the fenfluramine-phentermine combination initially generated excitement, not because of the size of the weight losses (ie, 16% reduction in initial weight), but because patients maintained the majority of their weight loss at the end of 3.5 years, provided that they continued taking medication.<sup>56</sup> Two additional studies of this combination showed good maintenance of weight loss after 2 years of treatment.<sup>95,96</sup> Similarly, patients treated with sibutramine<sup>62</sup> and orlistat<sup>66,68</sup> generally obtained their maximal weight loss during the first 6 months of treatment and maintained this loss at the end of 1 year (while still receiving medication). These studies suggest that pharmacotherapy's greatest strength, particularly as compared with behav-

ior modification, may reside in maintaining rather than inducing weight loss. This is because long-term pharmacotherapy, as compared with behavior therapy, appears to require less time and effort, from both patient and provider, to facilitate weight maintenance. Studies are needed to compare the long-term effectiveness of these 2 approaches. Clearly, the safety of long-term (ie, >1 year) pharmacotherapy must also be demonstrated before this approach can be advocated.

Provided that safe weight loss medications are found, some investigators have proposed that patients continue taking these agents indefinitely.<sup>97</sup> Long-term weight reduction achieved with pharmacotherapy could eliminate the need for medications used on a long-term basis to control weight-related complications, including hypertension, diabetes, and hyperlipidemia.<sup>98</sup>

Further studies are needed to determine the most appropriate method of using weight-loss medications long term. It may be possible, for example, to maintain weight loss with a smaller dose of medication than was required to induce weight reduction. Similarly, patients may be able to use medications selectively during high-risk periods for weight gain, such as during the winter months. Alternatively, persons who dramatically increase their physical activity may be able to discontinue medication completely but resume taking it in the event of a 5-kg weight gain. Regardless of the approach selected, patient and provider must judge that the benefits of long-term pharmacotherapy (ie, reductions in health complications) outweigh the probable risks associated with the medication's use.

### CONCLUSIONS

A growing body of evidence now shows that relatively modest weight losses can significantly improve physical and psychological health. The high prevalence of obesity in our nation requires that primary care practitioners play a major role in the prevention and management of this disorder. Advances in our under-

standing of this disorder, as well as the availability of new treatments, should improve primary care physicians' ability to help their overweight patients.

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