CLINICAL PRACTICE

Nonsurgical Management of Obesity in Adults

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This Journal *feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the author's clinical recommendations.*

A 44-year-old woman desires weight reduction. Her history is notable for hypertension, snoring, daytime somnolence, and osteoarthritis. Her father was obese and had type 2 diabetes. On physical examination, her weight is 215 lb (98 kg), her body-mass index (BMI) (the weight in kilograms divided by the square of the height in meters) 32.7, her waist circumference 40 in. (102 cm), and her blood pressure 140/92 mm Hg. The stigmata of Cushing's syndrome are not present. The fasting glucose level is 112 mg per deciliter (6.2 mmol per liter). The fasting cholesterol level is 205 mg per deciliter (5.3 mmol per liter), triglyceride level 224 mg per deciliter (2.5 mmol per liter), high-density lipoprotein (HDL) cholesterol level 40 mg per deciliter (1.0 mmol per liter), and low-density lipoprotein (LDL) cholesterol level 120 mg per deciliter (3.1 mmol per liter). The thyrotropin level is normal. What would you advise?

THE CLINICAL PROBLEM

Overweight (BMI ≥25) or obesity (BMI ≥30) now affects almost two thirds of Americans. The National Health and Nutrition Examination Survey, 2003 to 2004, showed prevalences of obesity in U.S. men and women of 31.1% and 33.2%, respectively, with particularly high rates among non-Hispanic black Americans and Mexican Americans.[1] Overweight and obesity are associated with multiple coexisting conditions, including hypertension, glucose intolerance, dyslipidemia, and obstructive sleep apnea. Moreover, obesity is associated with an increased risk of death from cardiovascular disease, diabetes, kidney disease, and obesity-related cancers (colon, breast, esophageal, uterine, ovarian, kidney, and pancreatic).[2]

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STRATEGIES AND EVIDENCE

EVALUATION

The assessment of obese patients should include the history of weight gain, the maximum body weight, consideration of medications that may contribute to weight gain (e.g., corticosteroids, thiazolidinediones, and antipsychotic agents), previous approaches to weight reduction, patterns of food intake (including binge eating), and physical activity. The patient's readiness for weight reduction should also be addressed, since observational data suggest that such readiness may be important in predicting success.[3] The absence of readiness, however, should not preclude communication between provider and patient about the importance of weight reduction.

The environment of the physician's office should be arranged for the care of obese patients (for more information, see Table 1 of the Supplementary Appendix, available with the full text of this article at www.nejm.org).[4] Coexisting conditions

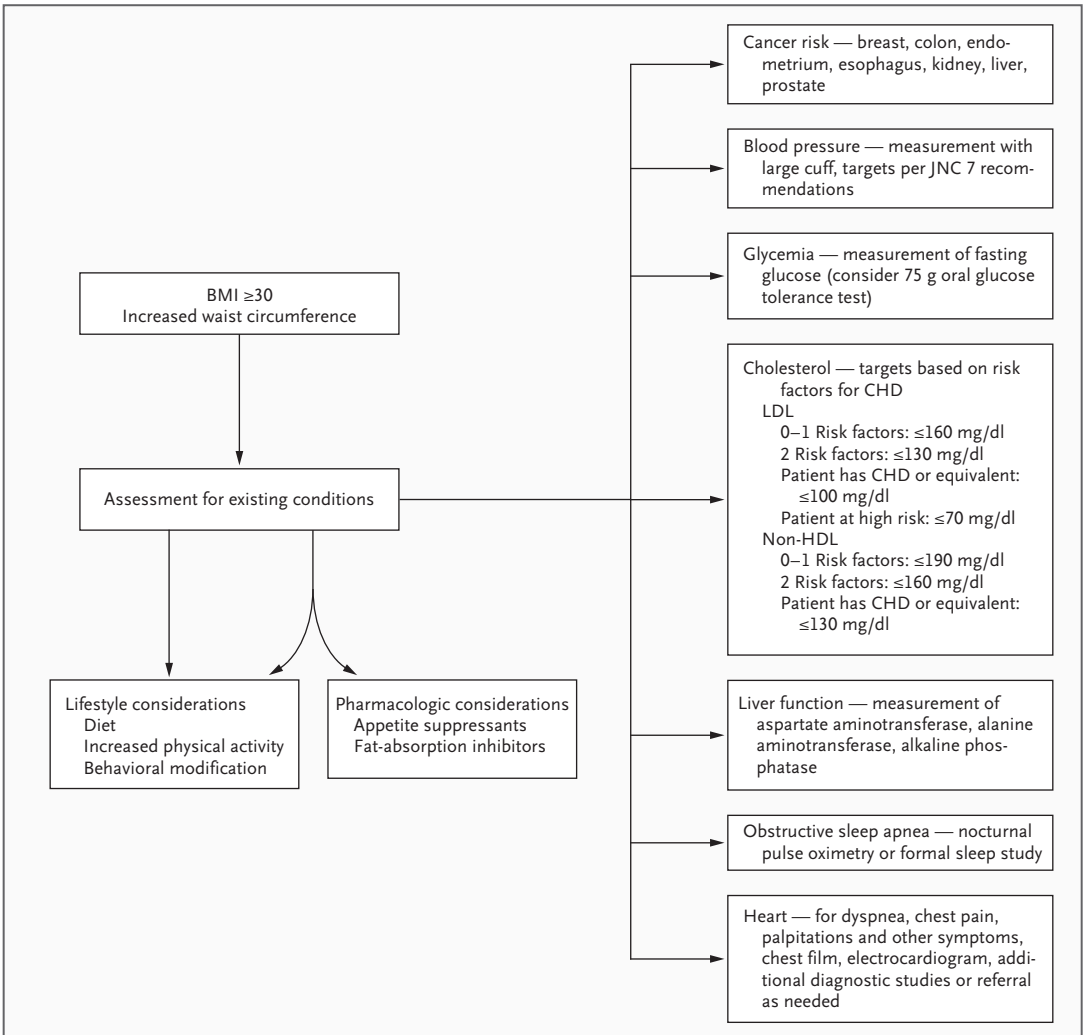

Figure 1. Clinical Evaluation of Obese Adults.

All patients should be assessed for obesity-associated conditions through a history and physical examination. Cancer screening should be performed as recommended by the National Cancer Institute (www.cancer.gov/cancertopics/screening). The Seventh Report of the Joint National Committee (JNC 7) should be used to establish the goals of hypertension treatment (www.nhlbi.nih.gov/guidelines/hypertension). Guidelines from the National Cholesterol Education Program–Adult Treatment Panel III (NCEP–ATP III) should be used to establish acceptable levels of LDL cholesterol and non-HDL cholesterol (www.nhlbi.nih.gov/guidelines/cholesterol/index.htm). Patients at high risk (with a target of ≤70 mg/dl LDL cholesterol) have multiple major risk factors, including the metabolic syndrome, continued cigarette smoking, and, especially, diabetes.[5]

should be assessed by history taking, physical examination, and additional diagnostic studies as needed (Fig. 1).[5]

Most patients with a BMI of 30 or greater, and many with a BMI between 25 and 30, have at least one coexisting condition.[6] Although it is difficult to define the "ideal" body weight, a BMI of 30 or more is associated with increased risks of death from all causes and death from cardiovascular disease. Waist circumference is an independent predictor of these outcomes and should be measured routinely. A reduction in weight as small as 5 to 10% may be sufficient for favorable modification of waist circumference, blood pressure, circulating cytokines, and, variably, fasting levels of glucose, triglycerides, and HDL cholesterol.[7]

The surgical management of obesity was recently reviewed in the *Journal*.[8] This article focuses

on nonsurgical approaches to the treatment of obesity.

LIFESTYLE APPROACHES

Diet

For weight loss to occur, energy intake must be less than energy expenditure. Reduced-calorie diets include those specifying caloric intakes that are very low (less than 800 kcal daily), low (800 to 1500 kcal daily), and moderate (about 500 kcal less than typical daily intake). In the absence of changes in physical activity, consumption of about 500 fewer kcal per day predicts a weight loss of about 1 lb (0.45 kg) per week. Very-low-calorie diets should be used only when more rapid weight loss is needed, and medical monitoring is necessary with such diets. The data are conflicting, however, as to whether a greater caloric deficit at the beginning of a weight-loss program predicts a greater weight loss at 2 years.[9] A detailed discussion of these diets is beyond the scope of this article.

Potential adjuncts to effective dietary management include eating breakfast,[10] adding dietary fiber,[11] and using meal replacements (e.g., Slim-Fast)[12]; of these, only meal replacements have been shown to enhance weight loss in randomized trials. The involvement of dieticians has been shown to improve weight reduction in primary care settings.[13]

A topic of ongoing controversy is how the macronutrient composition of the diet affects weight loss.

Low-Fat Diets

Although substantial epidemiologic and ecologic data have indicated an association between lower fat intake and lower (or at least not greater) body weight,[14] low-fat diets remain controversial.[15] The traditional approach to weight reduction has been to restrict dietary fats to less than 30% of total calories. A very-low-fat diet typically derives no more than 15% of total calories from fat, with about 15% of calories from protein and about 70% from carbohydrates. The Lifestyle Heart Trial, an intensive program of dietary counseling, stress management, and moderate exercise in patients with coronary heart disease, which reduced subjects' fat intake to 7% of calories, resulted in a weight loss of about 24 lb (11 kg) after 1 year, with a lower rate of progression of coronary heart disease at 5 years.[16] However, very-low-fat diets are difficult to maintain on a long-term basis.

Low-Carbohydrate Diets

In recent years, low-carbohydrate diets (less than 60 g of carbohydrates daily) have received increased attention. Many of them (e.g., the Atkins and South Beach diets) start with less than 20 g of carbohydrates daily and gradually increase the quantity. Randomized trials have shown that in the first 6 months, low-carbohydrate diets result in significantly more weight loss than low-fat diets[17,18]; with the exception of one study,[19] however, this difference was no longer significant at 12 months. Diets low in carbohydrates (as compared with those low in fat) result in lower glucose levels in patients with hyperglycemia, lower fasting levels of plasma triglycerides, and higher levels of HDL cholesterol; however, they also tend to increase LDL cholesterol levels.

Low-Glycemic-Index Diets

The glycemic index is a rating system for foods based on the extent to which they raise blood glucose levels 2 hours after their consumption. In randomized trials, reduced-glycemic-index diets have not resulted in increased weight loss beyond that explained by caloric restriction.[20,21] Plasma insulin levels are reduced with such diets, but whether this reduction translates into improved clinical outcomes is not known.

High-Protein Diets

Diets high in protein are usually high in fat. Because protein may enhance satiety, increase meal-induced thermogenesis, protect lean body mass, and decrease energy efficiency,[22] the substitution of protein for carbohydrates during weight loss has been increasingly emphasized. In randomized trials, substitution of protein for carbohydrates in calorie-restricted diets resulted in more weight loss.[23,24]

Specific Commercial Diets

Recent randomized trials have examined the outcomes at 6 months and 12 months when commercial diets are used for weight loss. In two U.S. trials, a total of 471 subjects were randomly assigned to one of four dietary plans: Atkins (carbohydrate restriction), Zone (40% carbohydrates, 30% fat, 30% protein), Weight Watchers or another, similar program (calorie restriction), or Ornish (fat restriction).[19,25] In the first trial, involving men and women 22 to 72 years old with known hypertension, dyslipidemia, or fasting hypergly-

cemia,[25] the mean weight loss at 1 year was similar for all four diets; in the second study (involving healthy women 20 to 50 years old), the Atkins diet resulted in more weight loss than the Zone diet (10.3 lb vs. 3.5 lb [4.7 kg vs. 1.6 kg]), with no other significant differences in weight loss observed among the diets.[19] In general, weight loss was associated with reductions in blood pressure, the ratio of total to HDL cholesterol, and levels of C-reactive protein, glucose, and insulin, with no significant differences among diets; however, reductions in fasting plasma triglyceride levels were significantly greater with the Atkins diet than with the Zone diet.

In a study in the United Kingdom,[26] 293 otherwise healthy overweight or obese adults were randomly assigned to one of four diet plans — Atkins, Slim-Fast, Weight Watchers, or Rosemary Conley — or to a control group. At 6 months, all diets had led to significant, similar losses of body fat (mean, 9.7 lb [4.4 kg]) and weight (mean, 13 lb [5.9 kg]) and to reductions in blood pressure; the diets showed only modest differences in their effects on total cholesterol and fasting glucose levels.

Physical Activity

Increased physical activity alone, without decreased caloric intake, is associated with only modest weight reduction.[27] For example, in one trial, participants who were instructed to jog the equivalent of 20 miles (32.2 km) a week but not to restrict their caloric intake lost only 2.9 kg in 8 months.[28] However, increased physical activity without caloric restriction can reduce abdominal (visceral) adipose tissue and improve insulin resistance.[29] Increases in physical activity combined with caloric restriction result in more weight reduction and more favorable changes in body composition (fat mass vs. lean mass) than diet or physical activity alone[27]; resistance training may be particularly beneficial in modifying body composition. Similarly, increases in plasma HDL cholesterol levels and reductions in triglyceride levels and blood pressure are greater with a combination of dietary restriction and aerobic exercise than with diet alone.[30]

Behavioral Modification

The key features of the standard behavioral-modification program include goal setting, self-monitoring, stimulus control (modification of one's environment to enhance behaviors that will support weight management), cognitive restructuring (increased awareness of perceptions of oneself and one's weight), and prevention of relapse (weight regain).[31] Behavioral treatment, generally provided in individual or small-group sessions weekly for 6 months,[32] has been reported to result in losses of 8 to 10% of body weight at 6 months.[33] However, most studies of behavioral approaches to the treatment of obesity have been carried out in academic medical centers, and the success of these strategies in other treatment settings is less clear.

PHARMACOLOGIC THERAPY

Pharmacologic therapy is appropriate for some patients as an adjunct to lifestyle interventions to facilitate weight loss and prevent weight regain. Current criteria for the use of pharmacologic therapy for obesity are a BMI above 30 or a BMI above 27 in the presence of coexisting conditions.[34] Only four drugs have been approved by the Food and Drug Administration (FDA) for weight reduction (Table 1). In randomized trials of FDA-approved medications combined with changes in lifestyle, as compared with placebo and changes in lifestyle, the reduction in initial weight was 3 to 5% greater with the medications. Reductions in risk factors for cardiovascular disease are generally related to the amount of weight reduction.

Phentermine and diethylpropion are adrenergic stimulants that enhance the release of norepinephrine in certain brain regions and reduce food intake. Efficacy and safety data for these drugs are limited. In the randomized trials of phentermine and diethylpropion that have been reported,[35] weight reduction was 3 to 4% greater in the medication groups than in the placebo groups. Blood pressure must be closely monitored in patients who have prehypertension or are being treated for hypertension. Dependency is an additional concern; these drugs have been classified by the Drug Enforcement Agency as Schedule IV controlled substances, indicating that there is potential for abuse but that it is considered to be low. Limited data suggest that these stimulants may be effective for more than 10 years,[36] but they have been approved only for short-term use.

Sibutramine is a serotonin–norepinephrine reuptake inhibitor that reduces appetite. In several randomized trials, weight loss was about 5% greater for subjects taking sibutramine than for those taking placebo.[35] The combination of sibutramine

Table 1. Drugs Prescribed for Weight Loss.*

Drug	FDA-Approved for Weight Loss	Schedule IV Controlled Substance	Mechanism	Dose	Approximate Weight Loss beyond That with Placebo	Side Effects	Comments
					%		
Diethylpropion (Tenuate, Sanofi-Aventis)	Yes	Yes	Sympathomimetic mechanism	25 mg 3 times a day or 75 mg controlled-release daily	3	Dry mouth, insomnia, dizziness, mild increase in blood pressure and heart rate	Has minimal effect, excreted by kidneys, pregnancy category B, requires monitoring of blood pressure
Orlistat (Xenical, Roche; Alli, GlaxoSmithKline)	Yes	No	Lipase inhibition in gastrointestinal tract	120 mg 3 times a day (Xenical) or 60 mg 3 times a day, available over the counter (Alli)	3	Oily spotting, flatus with discharge, fecal urgency	Side effects decrease with time; may work better when fat remains in diet, but this results in increased side effects; decreases LDL cholesterol, pregnancy category B
Phentermine (e.g., Adipex-P, Gate; Fastin, Hi-Tech; Ionamin, Celltech)	Yes	Yes	Sympathomimetic mechanism	15, 30, or 37.5 mg daily	4	Dry mouth, insomnia, dizziness, mild increase in blood pressure (rarely more severe) and heart rate	Insufficient data from RCTs, increased risk of pulmonary hypertension probably not a concern, pregnancy category C, available as generic, requires monitoring of blood pressure
Sibutramine (Meridia, Abbott)	Yes	No	Inhibition of norepinephrine and serotonin reuptake	5, 10, or 15 mg daily	5	Mild increase in blood pressure and heart rate (rarely more severe), palpitations	Pregnancy category C, requires monitoring of blood pressure
Rimonabant (Acomplia, Sanofi-Aventis)	No	NA	Inhibition of cannabinoid receptor CB1	5 or 20 mg daily	5	Nausea, diarrhea, anxiety, depression	Prototype in a new class of prescription drugs

* LDL cholesterol denotes low-density lipoprotein cholesterol, NA not applicable, and RCTs randomized controlled trials.

and a group program of lifestyle modification resulted in more weight loss at 12 months (12.1 kg) than did use of sibutramine (5.0 kg) or the lifestyle intervention alone (6.7 kg).[37] Successful weight maintenance after reduction was reported to be most likely in subjects who continued to take sibutramine and in those who had the greatest initial weight loss and were most physically active.[38] Common side effects of sibutramine — hypertension and tachycardia — are related to its adrenergic properties.

Orlistat is a triacylglycerol lipase inhibitor that works in the intestinal lumen to reduce dietary fat absorption by about 30%.[39] Although a low-fat diet is recommended for patients taking orlistat, its pharmacologic effect is dependent on the presence of dietary fat. The major side effects — oily spotting, flatus with discharge, and fecal urgency — are typically short-lived. One study showed that orlistat combined with lifestyle changes reduced body weight by about 3% more than lifestyle intervention alone.[40] In one trial (Xenical in the Prevention of Diabetes in Obese Subjects), the use of orlistat for 4 years reduced the incidence of diabetes beyond that achieved with lifestyle changes.[41] In another trial, the combination of orlistat and sibutramine therapy was not superior to the use of either drug alone.[42] Orlistat is now available over the counter at a lower dose (60 mg, three times a day) than that used in the trials; this reduced dose of orlistat, as compared with placebo, has been shown to result in about 2% more weight loss over a period of 4 to 24 months.

The cannabinoid system contributes to the regulation of food intake, energy balance, and body weight.[43] In randomized trials, subjects taking rimonabant (a selective blocker of the cannabinoid receptor CB1) lost about 5% more weight than those taking placebo[44]; the possibility was raised that the drug might have beneficial effects on HDL cholesterol and triglyceride levels that are independent of weight loss, but this remains unproven. Rimonabant is approved for the treatment of obesity in most of Europe and in Mexico and Argentina. It has not been approved for this use by the FDA because of concerns about adverse effects, including depression and anxiety as well as nausea and diarrhea. Patients with neuropsychiatric disorders were excluded from the clinical trials.

MAINTENANCE OF WEIGHT REDUCTION

The long-term maintenance of weight reduction is difficult, as multiple mechanisms exist to modify energy balance to reestablish the original body weight (Fig. 2). Predictors of maintenance of weight loss include eating a low-fat diet, frequent self-monitoring of body weight and food intake, high levels of physical activity,[45-47] and, according to the findings in two randomized trials, long-term patient–provider contact.[48,49] Prospective observational data suggest that physical activity of moderate intensity (brisk walking) for approximately 80 minutes per day or vigorous activity (jogging) for 35 minutes per day, expending about 2500 kcal per week, is protective against weight regain.[50]

AREAS OF UNCERTAINTY

Current therapies for obesity remain inadequate. Although it is recognized that caloric restriction is key to short-term weight loss and that maintenance of weight loss depends on increases in physical activity, it remains uncertain how to facilitate adherence to the lifestyle changes required for sustained success.[51] Translational studies are needed to determine whether the successful weight losses in studies of such interventions as the Diabetes Prevention Program can be achieved in the primary care setting, in commercial programs, or through Internet programs. Large studies involving long-term follow-up of patients after bariatric surgery have suggested significant reductions in the risk of cardiovascular events and death.[52] Although it is logical to assume that weight loss and maintenance achieved through nonsurgical approaches should also reduce these risks, confirmatory data are currently lacking.[53]

More data are needed to better understand the genetic basis of obesity and of responsiveness to lifestyle and pharmacologic interventions.[54] Since the identification of the leptin gene, new hormones and metabolic pathways involved in the regulation of body weight have been discovered (e.g., ghrelin and the melanin-concentrating hor-

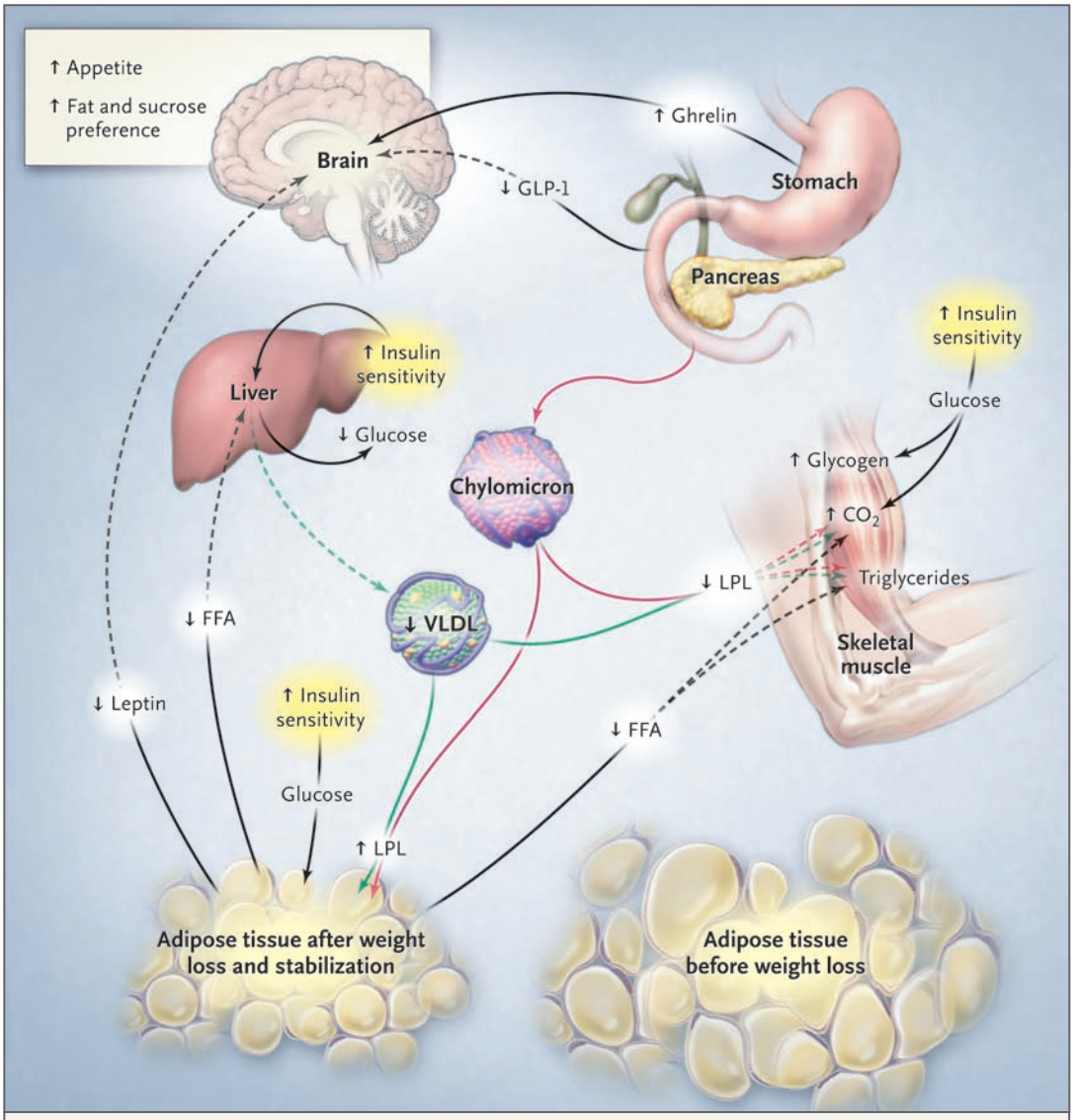

Figure 2. Biologic Mechanisms Protecting Adipose Tissue Mass.

Pathways of metabolic regulation before and after stabilized weight reduction are shown. After stabilized weight reduction, there is a reduction in adipocyte size and in circulating levels of leptin. Increases in ghrelin and reductions in glucagon-like peptide 1 (GLP-1) also stimulate signals in the brain to increase caloric intake. With maintenance of weight reduction, increased insulin sensitivity results in decreased lipolysis of triglyceride stores and free fatty acids (FFAs) in adipose tissue, increased insulin-mediated glucose uptake and storage in adipose tissue and skeletal muscle, and reduced hepatic glucose production. After weight reduction and stabilization, the synthesis and secretion of very-low-density lipoproteins (VLDLs) by the liver are reduced. There is also reduced uptake of FFAs from triglyceride-rich lipoproteins (chylomicrons and VLDLs) in skeletal muscle because of relative decreases in skeletal-muscle lipoprotein lipase (LPL). The increased action of insulin in adipose tissue also results in increased adipose-tissue LPL. Overall, fat calories are more likely to be partitioned in adipose tissue for storage than to be oxidized in skeletal muscle. With close monitoring of caloric intake and energy expenditure, these changes can be overcome, and weight loss sustained.

Table 2. Weight-Loss Treatment Guidelines from the National Heart, Lung, and Blood Institute.*

Treatment	BMI				
	25.0–26.9	27.0–29.9	30.0–34.9	35.0–39.9	>40.0
Diet, physical activity, behavioral therapy, or all three	Yes	Yes	Yes	Yes	Yes
Pharmacotherapy†		In patients with obesity-related disease	Yes	Yes	Yes
Surgery‡				In patients with obesity-related disease	Yes

* Data are from www.nhlbi.nih.gov/guidelines/obesity/ob_home.htm. These guidelines are generally consistent with those from the American Heart Association, the American Medical Association, the American Dietetic Association, the Obesity Society (Practical Guide), the American Diabetes Association, the American Academy of Family Physicians, the American College of Sports Medicine, and the American Cancer Society. BMI denotes body-mass index, calculated as the weight in kilograms divided by the square of the height in meters.

† Pharmacotherapy should be considered only in patients who are not able to achieve adequate weight loss with available conventional lifestyle modifications and who have no absolute contraindications for drug therapy.

‡ Bariatric surgery should be considered only in patients who are unable to lose weight with available conventional therapy and who have no absolute contraindications for surgery.

mone, among others) that may lead to the development of new classes of drugs that can modify energy balance.[55,56]

GUIDELINES FROM PROFESSIONAL SOCIETIES

Recommendations for the management of obesity from the National Heart, Lung, and Blood Institute[8] are shown in Table 2. The recommendations of several other professional organizations (listed in Table 2) and those in this article generally concur with these guidelines. I also recommend the No-Fad Diet from the American Heart Association (www.americanheart.org/presenter.jhtml?identifier=3031890), a user-friendly, evidence-based approach to lifestyle modification, including survey-based personalized recommendations on nutrition, physical activity, and behavior modification.

CONCLUSIONS AND RECOMMENDATIONS

The patient described in the vignette is obese and has several associated conditions, including hypertension, dyslipidemia, impaired fasting glucose, and symptoms suggestive of obstructive sleep apnea. A medical history and additional testing, if indicated, should help to ascertain whether other obesity-associated conditions, such as cardiac disease, are present.

Because the patient's BMI is 32.7, she is not a candidate for surgery. However, weight loss is clearly indicated, with a recommended minimum loss of 5% of her current weight. Caloric restriction in the amount of 500 kcal daily would result in the loss of about 1 lb per week. The recommended weight loss should be an amount that will favorably modify the coexisting conditions associated with obesity. Physical activity should be encouraged, with attention to potential limitations associated with her current level of fitness and obesity-associated conditions; options include walking (use of a pedometer is recommended), joining a gym, and developing a home-centered program with a combination of aerobic and resistance training.

A weight-loss medication is also an option. Given the patient's current blood pressure of 140/92 mm Hg, I would not prescribe phentermine or sibutramine, at least until hypertension is better controlled. Orlistat could be considered; the patient should be informed about side effects of oily spotting, flatus with discharge, and fecal urgency and should be instructed to take a multivitamin daily, given possible malabsorption of fat-soluble vitamins.

The patient should be encouraged to set realistic goals, record her food intake and energy expenditure, and weigh herself at least weekly.[57] Strategies for weight maintenance should be discussed, including continuation of regular physical activity.

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An audio version of this article is available at www.nejm.org.

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