The 2013 American Heart Association/American College of Cardiology/The Obesity Society Guideline for the Management of Overweight and Obesity in Adults
What Is New About Diet, Drugs, and Surgery for Obesity?
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Case Presentation
An obese, 55-year-old man with metabolic syndrome meeting all 5 of the Adult Treatment Plan III National Cholesterol Education Program criteria, including hypertension, type 2 diabetes mellitus, atherogenic dyslipidemia with low high-density lipoprotein cholesterol, elevated triglycerides, and abdominal obesity with a high waist circumference, is having trouble losing weight on his own through lifestyle intervention. He has hired a personal trainer and is working out 3 times a week but has lost no weight. He enjoys eating out with his wife or his business associates 3 to 4 times per week. This is where he reports consuming most of his excess calories in both food and alcohol. He takes 7 medications to control his obesity-related comorbidities. These include: Atenolol 50 mg once per day, valsartan 80 mg once per day, glipizide 5 mg twice per day, pioglitazone 30 mg once per day, metformin 500 mg twice per day, atorvastatin 40 mg once per day, and insulin glargine 20 U nightly. Anthropometrics and laboratory data include a weight of 264 lbs, height 5 feet 10 inches, body mass index (BMI) 38 kg/m², waist circumference 47 inches, blood pressure 150/95 mmHg, hemoglobin A1c 7.2%, fasting blood glucose 150 to 175 mg/dL, total cholesterol 220 mg/dL, triglycerides 300 mg/dL, low-density lipoprotein cholesterol 130 mg/dL, and high-density lipoprotein cholesterol 40 mg/dL.

The 2013 guidelines encourage the provider to help patients lose weight with lifestyle modification. Adding a low-calorie diet to his exercise routine would be an important first step to enhance lifestyle modification. Another important step for the provider would be to evaluate the medical regimen to determine if there are any medications that might exacerbate weight gain, and to consider alternatives.

If diet, exercise, and antiobesity agents do not achieve weight loss and weight maintenance, he is a candidate for bariatric surgery, based on the presence of type 2 diabetes mellitus and BMI 35 to 40 kg/m². The 2013 American Heart Association/American College of Cardiology/The Obesity Society guidelines acknowledge the National Institutes of Health guidelines for bariatric surgery, which recommend a BMI ≥ 40 kg/m² or >35 with at least 1 serious comorbidity, such as type 2 diabetes mellitus, coronary artery disease, sleep apnea, or hypertension.

American Association of Clinical Endocrinologists diabetes management guidelines recommend avoiding hypoglycemia and weight gain while administering diabetes medications to those with prediabetes and type 2 diabetes mellitus and to enhance lifestyle modification. The medications to titrate downward to avoid hypoglycemia while undergoing weight loss with a diet include the antihyperglycemic agents insulin, glipizide, and pioglitazone. These medications should be slowly reduced based on blood glucose, one at a time, using an organized plan.
discussed with the patient. Blood glucose fingersticks should be checked by the patient 3 times per day during this process. As blood glucose declines toward 100 mg/dL, medications should be decreased to prevent hypoglycemia. These changes can be facilitated by consultation with an endocrinologist or obesity medicine specialist. However, an example of a down titration regimen would be either halving or cutting the medication by one-third the dose, 1 medication at a time, until each medication is stopped. The first medication in this patient’s list to decrease would be the insulin, because it is an injectable agent and least appealing to patients.

During down titration, metformin can be maximized to 1000 mg twice a day, and a glugagon-like peptide-1 agonist, like liraglutide or exenatide, could be added, based on American Association of Clinical Endocrinologists guidelines. Canagliflozin or dapagliflozin, sodium-glucose cotransporter-2 inhibitors, can also be considered. All these drugs have been associated with weight loss while ameliorating blood glucose and hemoglobin A1c.

The provider should counsel the patient to continue down titration of antihyperglycemic medications that cause weight gain until most or all have been stopped based on blood glucose values during the weight loss period. In cases where type 2 diabetes mellitus has been present for more than several years, the severity of diabetes mellitus is high, or both occur, it may not be possible to stop all hypoglycemic medications. The blood glucose values will guide the provider and the patient.

This patient should also be weaned off atenolol, if possible, replacing it with another agent, such as a thiazide diuretic, angiotensin-converting enzyme inhibitor, or angiotensin receptor blockers. β-blocking agents may cause weight gain and should not be considered first-line agents for hypertension in the setting of obesity and type 2 diabetes mellitus.

Should weight loss plateau following these changes, obesity pharmacotherapy such as lorcaserin or the phentermine/topiramate combination can be added.

If the patient is placed on phentermine/topiramate combination, blood pressure should be monitored carefully because it is already elevated. Alternatively, lorcaserin can be considered. For those on selective serotonin reuptake inhibitors, lorcaserin is relatively contraindicated owing to the risk of serotonin syndrome. This warning also pertains to the use of serotonin-norepinephrine reuptake inhibitors, monoamine oxidase inhibitors, trip-tans, bupropion, dextromethorphan, and St John’s Wort.

This case is a good starting point to discuss the American Heart Association/American College of Cardiology/The Obesity Society update of the earlier National Institutes of Health/National Heart, Lung, and Blood Institute Obesity guidelines (Obesity 1), recently Food and Drug Administration–approved antiobesity medications, and the newest bariatric surgery option, the sleeve gastrectomy.

First, the new American Heart Association/American College of Cardiology/The Obesity Society guidelines (Obesity 2) were released in 2013 and focus on diets, behavioral approaches, and surgical options for obesity.

There are 5 recommendations (Table 1). The first recommendation helps the provider identify patients who need to lose weight and uses BMI as a first step to assess health risks. The waist circumference should also be measured, because it is a risk factor.

The second recommendation advises the provider to counsel patients who need to lose weight on lifestyle changes and how much weight is needed for health benefit. As little as 3% to 5% weight loss can reap benefits in terms of lowering lipids, hemoglobin A1c, and cardiovascular risk. More weight loss will produce greater benefits.

The third recommendation was developed after an investigation of the literature concerning diets of differing macronutrient content for weight loss.

The conclusion after investigating the literature was that there is no ideal diet for weight loss and that the diet that seems most befitting the patient should be the one to prescribe, whether a low-carbohydrate, low-fat, Mediterranean style, or other low-calorie diet. The evidence is clear that it is the reduction of the caloric content of the diet that matters for weight loss.

The fourth recommendation was based on the literature on behavioral interventions for weight loss, which concluded that a high-intensity intervention of ≥14 sessions over 6 months led by a trained interventionist delivered the best results for weight loss. Interventions should last at least ≥1 year to be successful long term.

The fifth recommendation reiterated the indications for pharmacotherapy for obesity (BMI ≥30 or 27–30 with a comorbidity) from Obesity 1; no other mention was made in Obesity 2 regarding the various pharmacotherapeutic options because there was very little in the literature on the new drugs available at the time.

Based on these 5 recommendations, the first steps in treating our patient would be to provide diet and behavior counseling by a trained interventionist with or without pharmacotherapy. This should last at least 6 months before considering surgery.

Current medications that are Food and Drug Administration approved for obesity prescription as of the end of 2014 (Table 2) include phentermine/topiramate, naltrexone/bupropion, lorcaserin, phentermine (short-term), orlistat, and liraglutide. Orlistat is also available over the counter at half the prescription dose. Initial options include any of these long-term, with the exception of phentermine. Phentermine was approved for use as an antiobesity agent in 1959 for short-term use and, therefore, should be used for only 3 months at a time. Long-term options include phentermine/topiramate, which is dosed initially at 3.75 mg phentermine/23 mg topiramate once per day for 2 weeks, and then escalated to the most commonly used dose of 7.5 mg phentermine/46 mg topiramate once per
Table 1. AHA/ACC/TOS Obesity Guidelines – Summary²

Recommendation 1 grade A (strong)
To identify patients who might be at risk for CVD, type 2 DM, and all-cause mortality: use BMI as a first screening step.

Recommendation 2 grade A
Counsel patients about the benefits of weight loss (3%–5%) which results in improvements in TG, blood glucose, hemoglobin A1c, and DM risk. Greater amounts will improve BP, LDL, and HDL-C.

Recommendation 3 grade A
Prescribe a diet to achieve a reduced caloric intake as part of a comprehensive lifestyle intervention regardless of macronutrient content of the diet.

Recommendation 4 grade A
Patients who need to lose weight should receive a comprehensive program that is at least 6 mo or longer in length. This should include diet, physical activity, and behavior modification and medications are considered appropriate for those with BMI ≥30 or ≥27 with a comorbidity (expert opinion).

Recommendation 5 grade A
Advise your patients with a BMI >35 with a comorbidity or >40 that bariatric surgery may be an appropriate option to improve health and offer referral.

References:
1. AHA/ACC/TOS Obesity Guidelines – Summary
2. AHA/ACC/TOS indicates American Heart Association/American College of Cardiology/The Obesity Society; BMI, body mass index; BP, blood pressure; CVD, cardiovascular disease; DM, diabetes mellitus; HDL-C, high-density lipoprotein cholesterol; LDL, low-density lipoprotein; and TG, triglycerides.

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For this patient, medical treatment has been successful. He has made lifestyle changes that are consistent with those seen in successful weight loss and maintenance patients enrolled in the Weight Loss Registry.16 Patients who keep a ≥10% weight loss for longer than 2 to 5 years as seen in the Weight Loss Registry generally weigh themselves almost every day, eat a low-calorie diet, exercise to expend the equivalent of 3250 kcal/wk, and eat breakfast daily. This patient could also have achieved substantial weight reduction and weight maintenance from the sleeve gastrectomy. The choice between a sleeve gastrectomy and the roux-en-y gastric bypass is a decision that should be made during the discussion between the surgical team and the patient. Obesity 2 guidelines concluded that there was insufficient evidence in the literature to compare weight loss, complications, and other outcomes between the roux-en-y gastric bypass and the sleeve gastrectomy. However, large databases generally confirm that the most weight loss results from the roux-en-y gastric bypass, while the sleeve gastrectomy, with the least weight loss from the laparoscopic adjustable gastric band. The most commonly performed surgical procedures in the United States (the roux-en-y gastric bypass and the sleeve
Table 2. Pharmacotherapy for Obesity in the United States. December 2014

<table>
<thead>
<tr>
<th>Drug (Generic)</th>
<th>Dosage</th>
<th>Mechanism of Action</th>
<th>Weight Loss Above Diet and Lifestyle</th>
<th>Duration of Clinical Studies</th>
<th>FDA Drug Approval Date</th>
<th>Common Side Effects</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Short-term use (3 mo)</strong></td>
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<tr>
<td>Phentermine resin</td>
<td>Adipex P (37.5 mg) 37.5 mg/d</td>
<td>Norepinephrine-releasing agent</td>
<td>3.6 kg (7.9 lb)</td>
<td>1960s</td>
<td>Headache, Elevated BP, Elevated HR, Insomnia, Dry mouth, Constipation, Anxiety, Cardiovascular Palpitation, tachycardia, elevated BP, ischemic events, Central nervous system, Overstimulation, restlessness, dizziness, euphoria, dysphoria, tremor, headache, psychosis</td>
<td>Anxiety disorders (agitated states), History of heart disease, Uncontrolled hypertension, Seizure, MAOIs, Pregnancy and breastfeeding, Hyperthyroidism, Glaucoma, History of drug abuse, Sympathomimetic amines</td>
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<tr>
<td></td>
<td>Ionamin (30 mg) 30–37.5 mg/d</td>
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<td>2–24 wk</td>
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<tr>
<td>Diethylpropion</td>
<td>Tenuate (75 mg) 75 mg/d</td>
<td>Norepinephrine-releasing agents</td>
<td>3.0 kg (6.6 lb)</td>
<td>1960s</td>
<td>Headache</td>
<td>See Phentermine resin for contraindications</td>
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<tr>
<td><strong>Chronic weight management</strong></td>
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<tr>
<td>Liraglutide</td>
<td>3.0 mg injectable</td>
<td>GLP-1 agonist</td>
<td>5.8 kg (12.8 lb)</td>
<td>2014</td>
<td>Nausea</td>
<td>Medullary thyroid cancer history</td>
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<td>1 y&lt;sup&gt;1,2&lt;/sup&gt;</td>
<td></td>
<td>Vomiting</td>
<td>Multiple endocrine neoplasia (MEN) type 2 history</td>
<td></td>
</tr>
<tr>
<td>Lorcaserin (10 mg)</td>
<td>10 mg twice a day</td>
<td>5HT2c receptor agonist</td>
<td>3.6 kg (7.9 lb), 3.6%</td>
<td>2012</td>
<td>Headache</td>
<td>Pregnancy and breastfeeding</td>
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<td>Naltrexone/ bupropion (NB)</td>
<td>32 mg/360 mg</td>
<td>Reuptake inhibitor of dopamine and norepinephrine (B) and opioid antagonist (N)</td>
<td>4.8%</td>
<td>2014</td>
<td>Nausea</td>
<td>Use with caution: SSRI, Dry mouth, Dizziness, SNRI/MAOI, Fatigue, Constipation, Triptans, Bupropion, Dextromethorphan, Uncontrolled hypertension, seizure disorders</td>
<td></td>
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(Continued)
gastrectomy) are successful in producing and maintaining weight losses of ≈25% to 32% of initial body weight chiefly by altering the gut hormone milieu responsible for influencing appetite and satiety at the level of the hypothalamus.17

**Summary and Recommendations**

Patients with obesity and metabolic syndrome on multiple medications for each condition should be managed with intensive behavioral therapy, including changes in diet and physical activity. Evaluate medications to determine if any may exacerbate weight gain and obesity. A dietary and exercise prescription combined with a plan to wean off medications that enhance weight gain is appropriate. Alternative medications should be weight neutral or those that may cause weight loss. A meta-analysis and guidelines on using commonly prescribed medications that cause weight gain and weight loss were published by the Endocrine Society.10 If these initial low-risk steps do not produce weight loss, weight loss medications can be considered. If BMI is >40 kg/m² or >35 with comorbidities, bariatric surgery should be considered and discussed with the patient.

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References

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