TREATMENT OF ADULT OBESITY

by

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ABSTRACT

As rates of obesity have increased this disease has become a common problem that physicians are faced with treating. This paper aims to review the different options for patients and determine the best treatments for obesity. Modalities that are considered include dietary treatment, exercise, pharmacologic treatment, and weight loss surgery. This study compares reduced calorie diets, low fat diets, low glycemic index/load diets, the Mediterranean diet, and low carbohydrate diets. The validity of exercise as an effective prescription for obesity is evaluated and debunked. Pharmacologic treatments that are contrasted include those drug therapies that are currently approved by the United States Food and Drug Administration for the long-term treatment of obesity. Those are orlistat, lorcaserin and phentermine/topiramate. The surgical treatments reviewed include vertical banded gastroplasty, adjustable gastric banding, Roux-en Y gastric bypass, biliopancreatic diversion, and biliopancreatic diversion with duodenal switch. After a comprehensive review of the literature the conclusion reached was that treatment for obesity should begin with the least
invasive options and those that have the least potential for harm. That is, diet should be a first course of action. Among diets a Mediterranean diet or another culturally adapted low glycemic index/load diet is best. However, more studies are needed to determine how to translate the diets for different cultures and individual tastes. When diets are unable to produce enough weight loss, pharmacologic treatments are considered. Among them, lorcaserin and phentermine/topiramate do not have enough long-term studies to warrant a strong recommendation as of the publishing of this paper. The only other option available, orlistat, comes with many uncomfortable gastrointestinal side effects, so it is also not an ideal option. In addition, orlistat does not produce the amount of weight loss that is seen with surgical procedures. Patients and physicians considering surgical treatment for obesity will find that the best option is laparoscopic adjustable gastric banding.
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<td>AGB</td>
<td>adjustable gastric banding</td>
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<tr>
<td>BID</td>
<td>twice daily</td>
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<td>BLOOM</td>
<td>Behavioral Modification and Lorcaserin for Overweight and Obesity Management</td>
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<td>FDA</td>
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<td>HDL</td>
<td>high density lipoprotein</td>
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<td>LSM</td>
<td>least squares mean</td>
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<td>OR</td>
<td>odd ratio</td>
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<td>QD</td>
<td>once daily</td>
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<td>RGB</td>
<td>Roux-en Y gastric banding</td>
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<td>RR</td>
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<td>SOS</td>
<td>Swedish obese subjects</td>
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<td>USDA</td>
<td>United States Department of Agriculture</td>
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INTRODUCTION

Obesity is defined as a metabolic disorder that is diagnosed when a patient has body mass index (BMI) of at least 30 kg/m² (Thompson, Cook, Clark, Bardia, & Levine, 2007). A patient’s BMI describes the patient’s weight in relation to his or her height. It is calculated by dividing the person’s mass in kilograms by height squared in meters squared (Thompson, Cook, Clark, Bardia, & Levine, 2007). The idea of using BMI as a measure of healthy or unhealthy weight has been criticized because it does not account for differences in lean body mass, but that does not seem to be an issue in the obese population (Flegal, Carroll, Ogden, & Curtin, 2010).

Over one third of adults in the United States are obese. The prevalence is similar between men and women, with only about one percent more women with obesity than men. However, prevalence does differ between age groups and ethnic groups for both women and men, with the Hispanic and non-Hispanic black population at greater risk for obesity (Flegal, Carroll, Ogden, & Curtin, 2010).

Obesity is associated with increased mortality rates and increased prevalence of many diseases such as type II diabetes, many cancers, and cardiovascular disease. Furthermore, it is inextricably linked with metabolic syndrome. Metabolic syndrome is a disorder defined by a set of comorbid diseases. It is common among obese patients, and it is associated with
increased risk in development of cardiovascular complications and type II diabetes, although many patients have these prior to developing metabolic syndrome. There are differing accepted definitions of metabolic syndrome. Generally, a patient with diagnosis of metabolic syndrome has waist-to-hip ratio of $> 0.9$ for males or $> 0.85$ for females and/or BMI $\geq 30$, in addition to at least two of the following disorders: decreased high density cholesterol ($< 0.9$ mmol/L for males or $< 1.0$ mmol/L for females), increased triglycerides ($> 1.7$ mmol/L), hypertension ($> 140/90$ mmHg), and/or increased fasting plasma glucose (Eckel, Grundy, & Zimmet, 2005).

The different treatment modalities for obesity, including dietary intervention, increased physical activity, pharmacologic treatment, and bariatric surgery will be discussed. The most respected dietary interventions include calorie restriction, low fat diets, low carbohydrate diets, low glycemic index/load diets, and the Mediterranean diet. Exercise is also often recommended along with changes in diet, but as will be discussed, it is not an effective treatment for obesity. Pharmacologic treatments that will be discussed include all of the United States Food and Drug Administration’s (FDA) currently approved medications for chronic weight management. Those are orlistat (Xenical or Alli), Belviq (lorcaserin), and Qsymia (phentermine/topiramate). Belviq and Qsymia were recently approved in the summer of 2012, and hold much promise. Finally, the controversy of bariatric surgery- to cut or not to cut – will be discussed, including the most popular forms of bariatric surgery in the United States, vertical
banded gastroplasty (also known as stomach stapling or Mason Procedure),
adjustable gastric banding (also known as Lap-Band®, when done laparoscopically), Roux-en-Y gastric bypass, biliopancreatic diversion, and biliopancreatic diversion with duodenal switch.

Finally, the merits of these treatments, interventions, and procedures for obesity will be considered. The best choice of treatment for which patient will be discussed, as will ideas for future research directions.
DIETARY TREATMENT

Kilocalorie Restriction

Simple kilocalorie restriction has been the cornerstone of weight loss recommendations since the different food groups were assigned differing amounts of energy levels. Popular kilocalorie restricting diets include the highly commercialized Weight Watchers diet. A very significant and controversial study published in 2009 in the New England Journal of Medicine comparing weight loss diets with differing macronutrient compositions (fat:protein:carbohydrate) found that there was no significant difference between groups in regards to weight loss, leading them to conclude that weight loss is due solely to the hypocaloric nature of the diet (that is, calories in less than calories out). In the authors’ own terms, “reduced-calorie diets result in clinically meaningful weight loss regardless of which macronutrients they emphasize” (Sacks et al., 2009). This study was highly publicized and sent the message that the only quality of a food that is of importance to a dieter should be its kilocalorie content. This notion made news headlines, but the study had its critics. In an editorial piece in the same issue of the New England Journal of Medicine it was proposed that the data warranted more scrutiny (Katan, 2009). The main criticism was that no difference was found between groups because of an outstanding lack of adherence to the prescribed diets that were supposed to differentiate them. That is, the diets that subjects were actually on were essentially all the same, so one would not expect
to find any difference between groups. The editorial’s author further criticized the lack of blinding in the study (Katan, 2009).

*Low Fat Diet*

The classic weight loss diet that has been popular in the United States (and throughout much of the western world) is the low fat diet. A low fat diet is one that emphasizes decreasing dietary fat while increasing carbohydrates. A typical low fat diet has a macronutrient composition in which 60-70% calories from carbohydrates, 10-20% calories from fat and 10-20% calories from protein. See figure 1 for a graphic representation. Supporters of low fat diets believe that kilocalories from fat are less satisfying and kilocalories from carbohydrates are more satisfying (Clegg & Shafat, 2010). However, this claim has been refuted in many studies (Rolls et al., 1994; Sacks et al., 2009).
The United States Department of Agriculture (USDA) has long recommended a diet low in fat and high in grains (Figure 2). There is much controversy about the reasons underlying the government’s recommendations that include well-founded suspicions that economic interests were weighted more highly than questions of health when the recommendations were formed (Pollan,

![USDA Food Pyramid](image-url)

**Figure 2.** USDA food pyramid used 1992-2005. Adapted from United States Department of Agriculture, Center for Nutrition Policy and Promotion, 1996.
Regardless of the reasons, one thing is clear - this recommended diet has not deterred the American population from obesity.

_Glycemic Index/Load_

The obese individual often has a disturbed blood sugar regulation mechanism. Many obese individuals are pre-diabetic or already have diabetes. Most grain food products in the United States come in a highly processed form that spikes blood sugar levels, adding to the obese individual’s blood sugar deregulation. Furthermore, dietary fat is known to attenuate a potential blood sugar spike. For these reasons researchers drew the conclusion that diets used to help diabetics control their blood sugar might help obese patients lose excess weight. Originally conceptualized by Dr. Jenkins and his colleagues at the University of Toronto as a treatment for diabetes, the Glycemic Index has proven to be an important tool in the battle against obesity (D. J. Jenkins et al., 1981).

The Glycemic Index is a value assigned to a particular food that describes its effect on blood sugar soon after consumption. In theory, the higher the Glycemic Index of a food, the higher one’s blood sugar will spike after it is eaten (Jenkins et al., 1981). It is determined in the following manner. A test subject’s blood glucose level is measured via blood draw or finger prick after a 12 hour fast. The subject is then given a test food portion that has 50 grams of available carbohydrate. Blood glucose levels are measured at 15, 30, 45, 60, 90, and 120 minutes after the first bite of test food is consumed. For comparison, the same
procedure is performed replacing the test food with either glucose or white bread. The curve that is drawn using the measurements is called the glycemic-response curve, and the area under it represents the blood sugar spike produced by the test food as a proportion of the test subject’s response to the glucose or white bread. The percent values shown under the curve are averaged to calculate the glycemic index of the test food, while the glycemic index of glucose or white bread, depending on which one was used, is set to 100 (Wolever, Jenkins, Jenkins, & Josse, 1991).

One of the criticisms of the Glycemic Index model is that some foods have higher carbohydrate density than others. A response to this criticism and addendum to the Glycemic Index is the concept of Glycemic Load, which takes into account the carbohydrate content in a given serving of a particular food. The macronutrient composition of a low glycemic load diet would consist of approximately 40% fat, 40% low-glycemic index carbohydrate and 20% protein, as represented in figure 3 (McMillan-Price, Petocz, & Atkinson, 2006).

![Low Glycemic Load Diet](image)

**Figure 3.** Pie chart indicating the recommended macronutrient composition recommended for a low glycemic load diet.
Many popular diets have presented a form of Glycemic Index and/or Glycemic Load in their approaches. For example, Dr. Sears’ The Zone and Dr. Agatston’s The South Beach Diet were both best selling books that prescribed adherence to a low glycemic index/load diet (Agatston, 2003; Sears, 1995).

**Mediterranean Diet**

Another diet that challenged the supremacy of the low fat diet was the Mediterranean Diet. This nutritional regimen was inspired by the traditional diets of countries along the Mediterranean coast, including Spain, Morocco, Italy, and Greece. It involves consumption of large amounts of olive oil, legumes, fruits, vegetable, and fish (Keys, 1970). The Mediterranean diet is relatively high in fat, but still provides protection from cardiac adverse events and mortality in general (Kris-Etherton, Eckel, Howard, St. Jeor, & Bazzarre, 2001; Menotti, Lanti, Puddu, & Kromhout, 2000). An important study published in 2008 in The New England Journal of Medicine comparing a low carbohydrate diet, a low fat diet, and the Mediterranean diet in both men and women found that the three diets produced similar weight loss effects. Interestingly, when the analysis was done looking only at the female subjects it was found that women on the Mediterranean diet lost an average of 3.8 kg (8.4 lbs.) more weight than on the low carbohydrate diet (Shai et al., 2008). Most recently, in 2011 a meta-analysis of 50 studies was conducted that looked at how the Mediterranean diet effects metabolic syndrome. The meta-analysis found that adherence to the Mediterranean diet
correlated with lowered blood pressure, reduced fasting plasma glucose, and decreased triglycerides (Kastorini et al., 2011).

*Low Carbohydrate Diet*

Given that carbohydrates are the source of a food’s sugar and thus the source of blood sugar spikes, scientists and health care providers have postulated that the simple recommendation of decreasing carbohydrate consumption might be the best dietary approach to treat obesity and its comorbidities.

A low carbohydrate diet is a pattern of nutrition in which calories come mostly from protein and fat, instead of carbohydrates. A typical low carbohydrate diet has a macronutrient composition in which 10-20% calories from carbohydrates, 50-60% calories from fat and 20-30% calories from protein. See figure 4 for a graphic representation of this macronutrient composition.

![Figure 4. Pie chart indicating the recommended macronutrient composition recommended for a low carbohydrate diet.](image)
The quintessential low carbohydrate diet is the Atkins Diet, which was popularized by cardiologist Dr. Robert C. Atkins in his books published in 1973, 1992, and 2002 (Foster et al., 2003). Atkins Nutritionals has created its own food pyramid, shown in figure 5, to represent the tenants of its low carbohydrate Atkins Diet.

![Atkins Diet Food Pyramid](http://www.atkins.com/Science/Atkins-Food-Pyramid.aspx)

Figure 5. Atkins Diet food pyramid.

Figure downloaded from Atkins Nutritionals at http://www.atkins.com/Science/Atkins-Food-Pyramid.aspx.
The base of the pyramid consists of protein rich foods that contain negligible amounts of carbohydrates such as eggs, tofu and animal meats. The second tier from the bottom consists of non-starchy vegetables. Next is a level consisting of fruits, with an emphasis on berries. The second to last tier (from the bottom) consists of foods composed mostly of fats such as nuts, oils and cheese. The top and smallest part of the pyramid consist of whole grains. Refined grains and sugars are absent from the pyramid (Atkins Nutritionals, 2012).

According to a systematic review of the literature before 2003 the evidence showing the safety and efficacy of low carbohydrate diets in the treatment of obesity was insufficient (Bravata et al., 2003). Then in 2003 two groundbreaking studies published in the same issue of The New England Journal of Medicine changed the scientific community's perception of low carbohydrate diets like the Atkins diet. Both studies compared obese subjects on low carbohydrate diets with counterparts on conventional diets defined as low in calories, high in carbohydrates, and low in fats. Low carbohydrate dieters in both studies lost more weight than their conventional diet counterparts. In one study low carbohydrate dieters lost 6.8 ± 5.0 (mean ± standard deviation) % of body weight while conventional dieters lost 2.7 ± 3.7 % of body weight in three months. After six months, weight loss was 7.0 ± 6.5 % of body weight for low carbohydrate dieters and 3.2 ± 5.6 % of body weight for those in the conventional group (Foster et al., 2003). In the second study, after six months, weight change was -5.8 ± 8.6 kg in the low carbohydrate group and -1.9 ± 4.2 kg in the
conventional group (Samaha et al., 2003). Furthermore, markers for cardiovascular health improved more in subjects on the low carbohydrate diets. Increases in high-density lipoprotein (HDL) and decreases in triglycerides were greater in the low carbohydrate groups in both studies (Foster et al., 2003; Samaha et al., 2003). One of the studies additionally found a decrease in diastolic blood pressure and increase in insulin sensitivity in the low carbohydrate group (Foster et al., 2003).

Recently, a study published in Journal of the American Medical Association compared the effects of a low-fat diet, low glycemic load diet (moderate carbohydrate content), and a low carbohydrate diet (Ebbeling et al., 2012). The results indicated that although the low carbohydrate diet resulted in the greatest resting energy expenditure, the glycemic index diet resulted in safer levels of circulating stress factors, indicating that a low glycemic load diet might lead to better long-term outcomes (Ebbeling et al., 2012).
Exercise alone may only facilitate fat loss in men, but not in women. The fat loss in men is due to increased resting metabolic rate produced by increases in muscle mass from exercise. Women lack the testosterone levels necessary for significant muscle mass increases from exercise, and therefore, do not benefit from a higher resting metabolic rate from exercise alone. However, even in men the fat loss from exercise alone is rarely clinically significant. An important, often cited study called “Effects of a 16-Month Randomized Controlled Exercise Trial on Body Weight and Composition in Young, Overweight Men and Women” substantiates these claims (Donnelly et al., 2003). The study followed 17-35 year olds with BMIs between 25.0 and 34.9 kg/m$^2$. Although exercise levels were comparable between men and women, only the exercising men lost weight, lowered BMI and decreased fat mass. Men in the exercising group lost 5.2 ± 4.7 kg in body weight, 1.6 ± 1.4 kg/m$^2$ in BMI, and lost 4.9 ± 4.4 kg in fat mass. Women merely maintained all of those parameters (Donnelly et al., 2003).

The literature indicates that exercise’s effectiveness is maximized when it is paired with another weight loss technique, such as dietary changes, but even then the added benefit seems to be only about 1 kg with modest amounts of exercise added to dietary changes (Bensimhon, Kraus, & Donahue, 2006; Thompson, Cook, Clark, Bardia, & Levine, 2007). Increasing the amount of time spent exercising to 90-120 minutes daily during combined therapy results in a
weight loss of 7-8 kg, versus only 3 kg with shorter duration of exercise during combined therapy versus only 2 kg with exercise alone (Jakicic, Marcus, Gallagher, Napolitano, & Lang, 2003; Thompson, Cook, Clark, Bardia, & Levine, 2007).
PHARMACOLOGIC TREATMENT

Pharmacologic treatment of obesity operates by interfering with absorption of nutrients, suppressing appetite and/or increasing metabolism. Orlistat is an example of a weight loss drug that interferes with absorption of dietary fat in the intestine. Drugs that suppress appetite are often catecholamines or catecholamine-derived compounds. Examples include phentermine and other amphetamine-like stimulants, which also increase metabolism. In addition, mood stabilizers and anti-depressants have been used “off label” to suppress appetite. Examples include bupropion and topiramate. Lorcaserin is a newly approved anorectic drug that works by stimulating a specific type of serotonin receptor. Drugs that block cannabinoid receptors, such as Rimonabant (Acomplia), are another class of anti-obesity medications under investigation.

Orlistat

The most commonly used pharmacologic treatment for obesity, orlistat (also known as, tetrahydrolipstatin, and the trade names Xenical and Alli) is a compound that interferes with the absorption of nutrients. It is produced by the saturation of lipstatin, a natural substance from the Streptomyces toxytricini bacterium (Barbier & Schneider, 1988), and interferes with the action of pancreatic lipases in the intestine. The body is then unable to break down triglycerides into free fatty acids, and thus the ability to absorb fat molecules from
the diet is inhibited. Instead, the fat is eliminated in the fecal matter. Hence, patients taking orlistat experience a reduction in calories obtained from the diet (Mancini & Halpern, 2006).

Orlistat comes in two formulations - prescription strength Xenical and over-the-counter strength Alli. The recommended prescription strength dose is 120 mg taken three times per day (that is, before each meal). The recommended over-the-counter strength dose is 60 mg taken three times per day (that is, before each meal). When patients take the prescription dose about 30% of the fat consumed is blocked from absorption. At the over-the-counter dose the proportion of fat blocked reduces to 25%. Orlistat’s fat absorption blocking effects are not dose dependent beyond the standard prescription dose (Rössner, Sjöström, Noack, Meinders, & Noseda, 2000).

Orlistat has been demonstrated to be effective for weight loss. Meta-analysis of clinical trials for orlistat plus behavioral changes (that is, nutrition and physical activity) showed that by the end of one year, subjects taking orlistat lost 2.0 - 3.0 kg, or 4.4 - 6.6 lbs., more than subjects taking a placebo (Mancini & Halpern, 2006). Another meta-analysis estimated the twelve-month average weight loss of patients taking orlistat to be 2.89 kg (95% confidence interval: 2.27-3.51 kg), relative to placebo (Li et al., 2005). Figure 6 shows a summary of weight loss results for the studies used in that meta-analysis. A deeper look at one of those clinical trials for orlistat revealed that by the end of one year 35.3% - 54.8% of subjects decreased their body mass by greater than or equal to five
percent. Furthermore, 16.4% - 24.8% of the study subjects decreased their body mass by greater than or equal to ten percent. After orlistat treatment was discontinued subjects regained less than 35% of their original weight loss (Davidson et al., 1999).

Figure 6. Summary of clinical trials of orlistat used in meta-analysis: average difference in weight loss between patients on orlistat and those on placebo. Figure taken from Li et al., 2005.
In addition to a promising weight loss profile, orlistat treatment has been demonstrated in the obese population of subjects to show improvements in blood pressure levels and type II diabetes prevention. It is not clear that these improvements were due solely to orlistat administration, as opposed to being secondary to the effects of the weight loss itself, however. After long-term use of orlistat the mean reduction in systolic blood pressure was 2.5 mmHg, and the mean reduction in diastolic blood pressure was 1.9 mmHg (Siebenhofer et al., 2009). One randomized controlled trial showed a 40% decrease in occurrence of type II diabetes among obese subjects on orlistat (Torgerson, Hauptman, Boldrin, & Sjostrom, 2004). Another study showed that over four years the occurrence of type II diabetes among obese subjects on orlistat was 6.2%, while the incidence while on placebo was 9.0% (Torgerson, Hauptman, Boldrin, & Sjostrom, 2004). These data shed a positive light on orlistat as a viable treatment for obesity related disorders.

The major downside of orlistat treatment lies in its embarrassing gastrointestinal side effects. Among those side effects are flatulence, steatorrhea (excess fat in the feces, producing oily stools), frequent/urgent bowel movements, and dissolute fecal matter. Meta-analysis of treatment effects of orlistat for pooled odds ratio (OR), 95% confidence interval (CI), relative risk (RR), and number needed to treat for harm for orlistat’s side effects are shown in Table 1). For diarrhea OR was 54.85, 95% CI was 44.88 - 67.48, RR was 3.40, and number needed to treat for harm was 1.48. For flatulence OR was 3.72,
95% CI was 3.16 – 4.39, RR was 3.10, and number needed to treat for harm was 6.49. For bloating, abdominal pain, and dyspepsia OR was 1.55, 95% CI was 1.18 – 2.06, RR was 1.48, and number needed to treat for harm was 25.80. Other less common side effects included headache, nausea and vomiting, gall bladder problems, and depression and mood change. All data were calculated relative to placebo (Li et al., 2005).

<table>
<thead>
<tr>
<th>Adverse Event by Drug</th>
<th>Pooled OR (95% CI)</th>
<th>Relative Risk</th>
<th>Number Needed To Treat for Harm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orlistat</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>5.485 (4.68–6.48)</td>
<td>3.40</td>
<td>1.48</td>
</tr>
<tr>
<td>Flatulence</td>
<td>3.72 (3.16–4.39)</td>
<td>3.10</td>
<td>6.49</td>
</tr>
<tr>
<td>Bloating, abdominal pain, and dyspepsia</td>
<td>1.55 (1.18–2.06)</td>
<td>1.48</td>
<td>25.80</td>
</tr>
<tr>
<td>Headache</td>
<td>1.18 (0.68–2.05)</td>
<td>Not calculated</td>
<td>Not calculated</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>0.95 (0.46–1.98)</td>
<td>Not calculated</td>
<td>Not calculated</td>
</tr>
<tr>
<td>Gallbladder problems</td>
<td>0.71 (0.27–1.82)</td>
<td>Not calculated</td>
<td>Not calculated</td>
</tr>
<tr>
<td>Depression and mood change</td>
<td>0.33 (0.01–4.15)</td>
<td>Not calculated</td>
<td>Not calculated</td>
</tr>
</tbody>
</table>

Table 1. Adverse events reported in meta-analysis of treatment of obesity with orlistat. Table taken from Li et al., 2005.

Fortunately, many of the gastrointestinal side effects can be somewhat mitigated by behavior change including, for example, avoidance of high fat foods. One study found that flatulence and oily stools could be controlled by limiting dietary fat intake to a maximum of 15 grams per meal (Wyatt, Catenacci, & Hill, 2007). The maker of the over-the-counter version of orlistat, GlaxoSmithKline (London, United Kingdom), describes the gastrointestinal side effects as part of the “aversion therapy” that forms part of the orlistat weight loss plan. That is,
patients learn, via negative reinforcement, to eat a diet that is generally lower in fat and lower in calories (Wyatt, Catenacci, & Hill, 2007).

Other less benign possible physical side effects from orlistat have been reported, including severe acute liver injury and impaired kidney function. Although a much more deleterious adverse effect of the medication than those mentioned earlier, liver injury is also much rarer. However, given the gravity of severe liver injury, the United States Food and Drug Administration (FDA) ordered a revised safety label for orlistat on May 26, 2010 that included these severe side effects (U.S. Food and Drug Administration, 2010). The safety labeling for over the counter strength orlistat, Alli, includes a warning for kidney stones, while prescription strength orlistat, Xenical, indicates a risk for increased urinary oxalate (U.S. Food and Drug Administration, 2012c). One large study showed that acute kidney injury was three times more likely in subjects using orlistat versus placebo (Weir et al., 2011). Still, other studies indicate that although there is a correlative link, a causal link for acute kidney injury may not exist (Beyea, Garg, & Weir, 2012). As with any medication, these physical side effects are a cause for concern, but more data and investigation is needed to make definitive decisions about the risks versus benefits of orlistat.
Lorcaserin

Lorcaserin (also known as ADP-356 and commercially as Belviq) is a new anti-obesity medication. It received FDA approval on June 27, 2012 for the treatment of obesity in adults with a BMI of at least 30, or adults with a BMI of at least 27 who additionally have one or more obesity-related comorbidities including hypercholesterolemia, hypertension, and/or diabetes mellitus (Smith et al., 2009).

The hypothesized mechanism of action by which this drug suppresses appetite is by stimulating the hypothalamus’ 5-HT₂C receptors. Once these serotonergic receptors are stimulated, pro-opiomelanocortin is produced. Pro-opiomelanocortin is thought to be responsible for the eventual anorectic effects of lorcaserin (Smith et al., 2010).

Arena (San Diego, California), the pharmaceutical company responsible for lorcaserin, concluded the required clinical trials to achieve FDA approval on June 27, 2012. Phase two and phase three clinical trials were submitted and considered for the drug’s eventual approval. Until enough time has passed to allow for post-market research this is currently the only data available to evaluate this drug’s safety and efficacy (U.S. Food and Drug Administration, 2012a).

During the phase two clinical trials the only change that patients made in their lives was administration of lorcaserin (that is, subjects were not asked to change nutrition or increase exercise). After twelve weeks of taking 10 mg, 15 mg or 20 mg lorcaserin per day, subjects in the intervention group lost 4.0
pounds, 5.7 pounds and 7.9 pounds, respectively, on average. The average weight loss of the placebo group was 0.7 pounds. All weight was regained in all groups shortly after treatment cessation. Lorcaserin was relatively well tolerated, so phase three clinical trials soon followed (Powell, Apovian, & Aronne, 2011).

Three different phase three clinical trials of lorcaserin were conducted shortly after the positive results of the phase two trials became evident. Each of the randomized placebo-controlled trials lasted at least 52 weeks and investigated populations of overweight and obese adults of ages 18-65 years with BMIs of 27 - 45 kg/m². In all three studies, subjects were counseled on diet and exercise.

In the first of lorcaserin’s phase three clinical trials, called “Behavioral Modification and Lorcaserin for Overweight and Obesity Management” (BLOOM), subjects took either 10 mg lorcaserin twice daily or placebo two times per day. After one year on this regime those subjects on lorcaserin lost 5.8% body weight on average compared to 2.2% body weight lost on placebo. In order to test the effects of lorcaserin on maintenance of weight loss after the initial 52 weeks researchers reassigned those patients who had lost at least five percent of their baseline body weight to either a new placebo group or the lorcaserin treatment group. The result was that 50.3% of subjects on placebo maintained at least a five percent weight loss versus 67.9% of subjects on lorcaserin, a statistically significant difference (P<0.001). See table 2 for a summary of the results in the BLOOM study (Smith et al., 2010).
In the second lorcaserin phase three clinical trial, called "Behavioral Modification and Lorcanerin Second Study for Obesity Management" (BLOSSOM), subjects were randomized to either placebo, 10 mg lorcaserin once
daily or 10 mg twice daily. The least squares mean body weight losses were 2.8% (95% CI: 2.5 - 3.2%) for placebo, 4.7% (95% CI: 4.3 - 5.2%) for lorcaserin once daily and 5.8% (95% CI: 5.5 - 6.2%) for lorcaserin twice daily. Another look at the data shows that 25% of subjects on placebo lost at least five percent of body weight, while 40.2% and 47.2% lost at least five percent on either lorcaserin once daily or lorcaserin twice daily, respectively. Table 2 summarizes these results of the BLOSSOM study (Fidler et al., 2011).

For both the BLOSSOM and BLOOM studies, the most common side effects reported by subjects in the intervention groups were: headache, dizziness, and nausea (Fidler et al., 2011; Smith et al., 2010). With BLOOM and BLOSSOM lorcaserin proved its relative safety and efficacy for treatment of obesity.

The third and final lorcaserin phase three clinical trial called “Behavioral Modification and Lorcaserin for Overweight and Obesity Management in Diabetes Mellitus” (BLOOM-DM) followed a similar protocol as the other two phase three clinical trials, but its subjects had to fulfill the additional inclusion criterion of having type II diabetes (that is, they had 7-10% glycated hemoglobin $A_1c$). Given their diabetic state, the subjects in this study also took metformin and/or sulfonylurea. Over one year subjects were treated with placebo, 10 mg lorcaserin taken once per day or 10 mg lorcaserin taken twice per day. The least squares mean ± standard error of the mean body weight changes were -1.5 ± 0.36% for placebo, -5.0 ± 0.5% for lorcaserin once daily and -4.5 ± 0.35% for
lorcaserin twice daily. The proportions of patients that lost at least five percent of their body weight were 16.1% on placebo, 44.7% on lorcaserin once daily and 37.5% on lorcaserin twice daily. Interestingly, in this study, the lower dose of lorcaserin (10 mg once daily) proved slightly more effective then the higher dose (10 mg twice daily). See Table 2 for a summary of the results of the BLOOM-DM study. Furthermore, markers for diabetes severity improved in the intervention groups more than in the placebo group. HbA1c and fasting plasma glucose, both decreased in the intervention groups. Frequent adverse events included headache, nausea, nasopharyngitis, and back pain (O'Neil et al., 2012).

**Phentermine/topiramate**

Drug intervention is often met with controversy especially when it concerns treatment of obesity, since the long-term efficacy and safety of most pharmacologic treatments is unclear. For example, the one time gold standard of obesity drug therapy, fenfluramine/phentermine, or “fen-phen,” was eventually found to cause cardiac abnormalities. Consequently, it was taken off the market after a number of deaths were attributed to the medication (Wadden et al., 1998). The phentermine half of the fen-phen duo was allowed to remain on the market.

Phentermine, along with phendietrazine and benzphetamine, are appetite suppressing weight-loss drugs similar to amphetamine with its anorectic effects. They are approved for the short-term treatment (up to twelve weeks) of obesity in combination with nutritional changes and increases in exercise (Colman, 2005).
They are not approved for long-term treatment of obesity. Given the lack of long-term data as well as the lack of FDA approval for use of these drugs in the long-term, it is not recommended that patients use them beyond the allotted twelve-week period.

Phentermine works in two ways—by decreasing hunger and by promoting the breakdown of corporal adiposity, but the main weight loss producing action is thought to be due to its anorectic effects. The main adverse effects experienced by users are tachycardia and elevated blood pressure. Some users may also experience trouble sleeping, restlessness and palpitations. Critics of the drug cite that even with short-term use patients will begin to experience tolerance to the drug. In addition, studies show that in the short term a weight loss of 3.5 kg is achievable with phentermine (Haddock, Poston, Dill, Foreyt, & Ericsson, 2002; Thompson, Cook, Clark, Bardia, & Levine, 2007), but most patients gain the weight back after discontinued use of weight-loss drugs (Li et al., 2005). For that reason, many health care providers find little use these appetite suppressants when they are used alone (that is, not in combination with other drugs) (Thompson, Cook, Clark, Bardia, & Levine, 2007).

On July 17, 2012 the FDA announced its approval of the sale and marketing of Qsymia (formerly known as Qnexa), a drug developed by Vivus Pharmaceuticals (Mountain View, California) that is a combination of phentermine and topiramate, for the long-term treatment of obesity (U.S. Food and Drug Administration, 2012b). The topiramate (trade name Topamax) half of
Qsymia is an anticonvulsant used in the management of epilepsy and migraine. Studies show that Topamax is associated with 6% body weight loss after 24 weeks (Li et al., 2005; Thompson, Cook, Clark, Bardia, & Levine, 2007). However, it is not approved as a stand-alone treatment for obesity or overweight (Gadde et al., 2011; Wilding, Gaal, Rissanen, Vercruysse, & Fitchet, 2004).

Three phase three clinical trials were considered for the recent FDA approval of the Qsymia. The first of these blinded, randomized controlled trials, dubbed EQUIP, lasted 56 weeks. It involved severely obese patients on either placebo, 3.75 mg phentermine with 23 mg topiramate controlled release (“3.75/23 mg”), or 15.0 mg phentermine with 92 mg topiramate controlled release (“15.0/92 mg”). Subjects followed a reduced-calorie diet while taking placebo or either medication protocol. The percent body weight lost was 1.6% for placebo and 5.1%, 10.9% respectively for the two treatment regimes. The proportion of subjects losing at least 5% of their body weight was 17.3% for placebo and 44.9%, 66.7% for the 3.75/23 mg and 15.0/92 mg treatments, respectively. Table 3 summarizes the results of the EQUIP study. Common adverse events in this study included constipation, trouble sleeping, paraesthesia, and dry mouth (Allison et al., 2012).

The second randomized control trial, called CONQUER, studied the effects of different doses of Qsymia on overweight and obese subjects who were following a reduced calorie diet. Subjects took either placebo, 7.5 mg phentermine with 46 mg topiramate controlled release (“7.5/46 mg”), or 15.0 mg
phentermine with 92 mg topiramate controlled release ("15.0/92 mg"). The change in body weight at the end of the 56-week trial was -1.4 kg for placebo, -8.1 kg for the 7.5/46 mg treatment, and -10.2 kg for the 15.0/92 mg treatment. The proportion of subjects losing at least 5% of their body weight was 21% for placebo, 62% and 70% for the 7.5/46 mg, 15.0/92 mg treatments, respectively. The proportion of subjects losing at least 10% of their body weight was 7% for placebo and 37% and 48% for the 7.5/46 mg, 15.0/92 mg treatments, respectively. See Table 3 for a summary of the weight loss results of the CONQUER study. Physical adverse events were similar to those in the EQUIP study (Allison et al., 2012; Gadde et al., 2011).

Psychiatric adverse events were an important concern with Qsymia because the topiramate half of Qsymia’s phentermine/topiramate medication duo has been shown to induce psychiatric problems in patients. When used in monotherapy topiramate can produce depression, anxiety, irritability and attention disturbances (Gadde et al., 2011; Wilding, Gaal, Rissanen, Vercruysse, & Fitchet, 2004). The same psychiatric adverse events occurred with statistically significant higher frequencies in the higher dose Qsymia group (15.0/92 mg) compared to placebo. However, frequencies were small enough to bring their clinical significance into question. Anxiety in the 15.0/92 mg group occurred in 4% of subjects versus 2% on placebo. Irritability in the 15.0/92 mg group occurred in 3% of subjects versus less than 1% of subjects on placebo. Attention
disturbances occurred in 4% of the subjects in the 15.0/92 mg group versus less than 1% of those on placebo (Gadde et al., 2011).

<table>
<thead>
<tr>
<th>EQUIP (56 weeks)</th>
<th>Group</th>
<th>Weight change LSM</th>
<th>% Subjects losing ≥ 5% body weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>1.6%</td>
<td>17.3%</td>
<td></td>
</tr>
<tr>
<td>Qsymia 3.75/23 mg</td>
<td>5.1%</td>
<td>44.9%</td>
<td></td>
</tr>
<tr>
<td>Qsymia 15.0/92 mg</td>
<td>10.9%</td>
<td>66.7%</td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CONQUER (56 weeks)</th>
<th>Group</th>
<th>Weight change LSM</th>
<th>95% confidence interval</th>
<th>% Subjects losing ≥ 5% body weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>-1.2%</td>
<td>-1.8 - -0.7%</td>
<td>21%</td>
<td></td>
</tr>
<tr>
<td>Qsymia 7.5/46 mg</td>
<td>-7.8%</td>
<td>-8.5 - -7.1%</td>
<td>62%</td>
<td></td>
</tr>
<tr>
<td>Qsymia 15.0/92 mg</td>
<td>-9.8%</td>
<td>-10.4 - -9.3%</td>
<td>70%</td>
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</tr>
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</table>

<table>
<thead>
<tr>
<th>SEQUEL (additional 52 weeks)</th>
<th>Group</th>
<th>Weight change* LSM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>-1.8%</td>
<td></td>
</tr>
<tr>
<td>Qsymia 7.5/46 mg</td>
<td>-9.3%</td>
<td></td>
</tr>
<tr>
<td>Qsymia 15.0/92 mg</td>
<td>-10.5%</td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Weight loss results of Qsymia’s phase three clinical trials- EQUIP, CONQUER and SEQUEL as reported by Allison 2012, Gadde 2011 and Garvey 2012.

* Weight change since baseline of CONQUER study
The third clinical trial for Qsymia, called SEQUEL, was an extension of the CONQUER study. It continued where CONQUER left off and followed patients for another 52 weeks, so that patients were followed for a total of 108 weeks. Not only did subjects continue to lose more weight on Qsymia compared to placebo, but additionally, rates of adverse events during these last 52 weeks were lower than the rates of adverse events in the first 56 weeks reported in the CONQUER study (Garvey et al., 2012). Table 3 summarizes the results from the SEQUEL study.
WEIGHT LOSS SURGERY

The subject of surgical treatment (that is, bariatric, or gastrointestinal, surgery), like that of pharmacologic treatment of obesity is contentious. Some physicians argue that given the possible effectiveness of other non-invasive treatments for obesity, when the level of patient adherence is sufficient, surgical treatment should not be considered as an option. Others cite the high success rate of bariatric surgery and the high likelihood of patients regaining lost weight after undergoing non-surgical treatments (Robinson, 2009). Most physicians consider bariatric surgery as a viable option only after other non-invasive treatments have failed their patients afflicted with morbid obesity (Bult, van Dalen, & Muller, 2008; Maggard et al., 2005; Robinson, 2009). The National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, has issued its criteria for bariatric surgery. They recommend that a candidate for weight loss surgery have a “BMI of 40 or more [approximately 45 kg overweight for men and 36 kg for women] or BMI between 35 and 39.9 kg/m² and a serious obesity-related health problem such as type II diabetes, heart disease, or severe sleep apnea” (National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, 2004). Further recommendations are summarized as follows.

The patient should:
Understand the operation and the lifestyle changes that will be needed;
Be unlikely to lose weight or maintain weight loss long term with nonsurgical measures;
Be well informed about the surgical procedure and the effects of treatment;
Be motivated to lose weight and improve health;
Be aware of how life may change after the operation (e.g. the need to chew food well and the inability to eat large meals);
Have no psychological contraindications to obesity surgery such as untreated depression or personality disorders;
Be aware of the potential for serious complications, dietary restrictions, and occasional failures;
Be committed to lifelong medical follow-up and vitamin/mineral supplementation;
Realize that no method, including surgery, is guaranteed to produce and maintain weight loss and that success is possible only with long-term commitment to behavioral change and medical follow-up. (Thompson, Cook, Clark, Bardia, & Levine, 2007)

The option of surgery is one that has become more attractive over the years since its inception for many reasons. Most importantly, modern procedures such as gastric bypass, stomach stapling, Lap-Band®, and others, have decreased the rates of obesity-related death. This significantly counterbalances the mortality rate due to bariatric surgery itself, which meta-analysis shows is less than 1% (Maggard et al., 2005).

Once the decision has been made to proceed with surgery, the physician and the patient must then decide which type of bariatric surgery is best suited for that patient. Each surgery comes with its own set of risks and potential rewards which must all be considered carefully. Risks to consider are mortality, perioperative surgical risks, post-surgery complications (both short-term and long-term complications), cost, and psychosocial issues. Benefits include reduced overall mortality, weight loss (but rarely down to normal weight), lifestyle
upgrades, and improvement of most cardio-metabolic risk factors, especially reduced type II diabetes risk (Sjöström et al., 2004).

Weight loss surgeries can be of three types: restrictive, malabsorptive and combination restrictive/malabsorptive. Restrictive type surgeries reduce the volume of food that the body can physically hold, and thus patient food intake is reduced. These procedures usually involve adjustments made to the stomach size. Operations of this type include adjustable gastric banding (AGB) and vertical banded gastroplasty (VBG). Malabsorptive procedures reduce the body’s ability to absorb food nutrients and thus more food energy is eliminated in the waste. These usually involve a resection of the intestines. Purely malabsorptive procedures are no longer performed. Instead, physicians opt to perform combination restrictive/malabsorptive procedures that both limit food intake and food absorption. Surgeries of this type include Roux-en Y gastric bypass (RGB), biliopancreatic diversion (BPD), and biliopancreatic diversion with duodenal switch (BPD/DS).

**Vertical Banded Gastroplasty**

Vertical banded gastroplasty (also known as stomach stapling or Mason Procedure) is a restrictive type surgical procedure that relies on staples and a band in the stomach to create a smaller space for food. The staples block access to the fundus of the stomach. The band makes a smaller entryway to the rest of the stomach (Bult, van Dalen, & Muller, 2008; National Institute of
A large randomized controlled study, called the Swedish Obese Subjects (SOS) Study, followed bariatric surgery patients for ten years. It found that patients that underwent VBG lost 16.5% of their body weight at the ten year mark. This was more than with banding alone, such as is done with adjustable gastric banding, but less than with gastric bypass. Figure 8 compares weight change for subjects in the SOS Study undergoing different surgeries (Sjöström et al., 2004).

In most cases VBG is considered permanent, and it is usually performed as an open procedure. Open procedures, compared to laparoscopic surgeries, have a greater risk for infection, more trauma to tissues, longer operation time, as well as longer hospital stays and recovery. For these reasons, physicians prefer other weight loss surgeries that are performed laparoscopically, such as
Adjustable gastric banding (also known as Lap-Band®, when done laparoscopically) is another restrictive procedure that is commonly performed. The “band” refers to a hollow silicone band that is placed around the upper part
of the stomach in order to shrink its capacity to hold food. A port near the surface of the skin is connected to the silicone band by a tube. Saline can be added or removed via the port to the inside of the hollow silicone band. Adding saline makes the gastric pouch that receives food smaller, and removing saline expands the gastric pouch volume. Thus, the procedure is adjustable after surgery. See figure 9 for an illustration of adjustable gastric banding (Bult, van Dalen, & Muller, 2008; National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, 2004).

The surgical risks with laparoscopically performed adjustable gastric banding are minor, and some consider it to be “the safest bariatric procedure” (Hainer, Toplak, & Mitrakou, 2008). The rate of mortality for this type of procedure is 0.05%, lower than that of any other kind of bariatric surgery (Hainer, Toplak, & Mitrakou, 2008). This procedure also has the added benefit of being reversible (Bult, van Dalen, & Muller, 2008). Obese patients with a BMI greater
than 50 kg/m\(^2\) benefit more from this type of surgery compared with their thinner counterparts. Because the Lap-Band\textsuperscript{®} procedure works as a weight loss aid by restricting food intake it cannot effectively help obese patients who already eat very little before the surgery. These may be obese patients who have confounding medical issues or other metabolic abnormalities who despite continued restriction are no longer able to lose more weight for a significant period of time. (Hainer, Toplak, & Mitrakou, 2008).

The SOS Study (Figure 8) reported a ten-year percent body weight loss of 13.2\% for banding surgeries like AGB (Sjöström et al., 2004).

*Roux-en-Y Gastric Bypass*

Roux-en-Y gastric bypass surgery works to aid in weight-loss of the patient by restricting the stomach’s capacity as well as by creating malabsorption of nutrients. In this procedure, the stomach is stapled to create a smaller pouch that is resected to the distal portion of the small intestine. The proximal

![Figure 10. Roux-en Y gastric bypass. Figure taken from National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, 2004.](image-url)
portion of the small intestine is rejoined in such a way that a Y shape is formed (Bult, van Dalen, & Muller, 2008). Figure 10 illustrates the procedure.

One significant adverse effect observed after Roux-en-Y gastric bypass is reduced calcium absorption resulting in osteopenia (stemming from metabolic bone disease) and secondary hyperparathyroidism. Reduced calcium absorption in patients that have undergone Roux-en-Y gastric bypass surgery is due to the fact that food is diverted from the duodenum where most calcium transporters are located.

The SOS Study (Figure 8) reported a ten-year percent body weight loss of 25.0% for subjects that underwent RGB (Sjöström et al., 2004). Meta-analysis comparing laparoscopic, open or either type of RGB found that on average patients that underwent laparoscopic procedures lost 38 kg, patients that underwent open procedures lost 43 kg and patients that underwent either type of RGB lost 41 kg after 36 months (Maggard et al., 2005).

_Biliopancreatic Diversion_

Biliopancreatic diversion (BPD) is a procedure developed to produce weight loss via malabsorptive mechanisms. See figure 11 for an illustration of the BPD surgery. Most patients that undergo this procedure have problems with malnourishment. The problems have been severe enough to warrant a modification of the procedure. Presently, biliopancreatic diversion as it was
classically performed is no longer in practice. Instead, physicians opt to perform a biliopancreatic diversion with duodenal switch (BPD/DS).

According to meta-analysis 36-month weight loss after BPD averaged 53 kg (Maggard et al., 2005).

_Biliopancreatic Diversion with Duodenal Switch_

In BPD/DS the duodenum and jejunum of the small intestine are bypassed by connecting the end of the small intestine with the stomach. See Figures 11 and 12 to compare BPD with BPD/DS.

Even with the addition of the duodenal switch patients that have undergone the surgery can experience severe nutritional deficiencies. For these patients nutritional supplements of vitamins and minerals are necessary to prevent complications such as anemia and osteopenia, a common complication of malabsorptive procedures.

As with any procedure that results in rapid weight loss, BPD/DS patients are at risk for gallstones. Thus, surgeons will either remove the gall bladder...
during surgery or they will administer medications to prevent gallstones after surgery. In any case, patients will require continued monitoring for years after surgery. Obese patients with a BMI greater than 50 kg/m² benefit more from biliopancreatic diversion compared with their thinner counterparts (Hainer, Toplak, & Mitrakou, 2008).

Figure 12. Biliopancreatic diversion with duodenal switch.

Figure taken from National Institute of Diabetes and Digestive and Kidney Diseases, National
DISCUSSION

The cause and definition of obesity is the excess fat carried by the patient. The goal of any treatment for obesity is to rid the patient of those unhealthy levels of adiposity. The question is which method is best for whom.

The first modalities to consider are those that are the least invasive and pose the least risk that is behavior modifications in diet and exercise. Although exercise should not be discouraged for its other health benefits, the evidence does not support its utility as a weight loss method. For that reason it is omitted from this discussion. Diet, however, is a potentially effective way to lose weight.

The simple “calories in versus calories out” model is not effective because it does not account for the quality of the food consumed. Scientists in support of recommending a hypocaloric diet frequently cite the first law of thermodynamics as support for their claim that this diet is the best nutritional solution for weight loss (Buchholz & Schoeller, 2004). They explain that energy “in” (in the form of kilocalories) must be less than energy “out.” While that statement alone is true, the problem is that it neglects the thermic effect of food. The physiologic effects of poor quality food as well as certain hormonal responses can cause the dieter to over eat (Feinman & Fine, 2004).

Low fat diets can be described as an extension of hypocaloric diets. Fat has nine kilocalories per gram while the other macronutrients, carbohydrates and protein, each have about four kilocalories per gram. Part of the philosophy
behind a low fat diet is that eating a higher fat content results in eating more kilocalories over all. However, as discussed earlier this reasoning is flawed because it ignores the satiating effects of fat.

Diets that focus on carbohydrates (whether quality or quantity) fare better than their low fat and hypocaloric counterparts. The most robust studies show a greater weight loss with low carbohydrate diets. However, given that some studies show elevated stress factors that could lead to heart disease are associated with low carbohydrate diets, this solution might not be ideal for obese patients who are already at a higher risk for developing cardiovascular disease, if they do not already have it (Ebbeling et al., 2012). When diets fail or their results fall short of the weight loss necessary to reduce obesity-related health risks, the next level of treatment options to consider should be pharmaceuticals because despite their side effects, the immediate risks of any surgery are greater (see below). The relevant medications to consider are those approved for long term use, namely, orlistat (Xenical, Alli), lorcaserin (Belviq), and phentermine/topiramate (Qsymia).

Bariatric surgery is the last resort option for treating obesity. Bariatric surgery, although very effective for weight loss, comes with many risks that exceed the risks that are associated with any major surgery. It is a viable consideration, however, when diets and medications have failed. Ninety percent of bariatric surgeries done in the United States are one of three types: laparoscopic Roux-en Y gastric bypass (RGB), the open approach to Roux-en Y
gastric bypass and laparoscopic adjustable gastric banding (AGB) (Robinson, 2009). Laparoscopic procedures come with fewer risks, so for most patients considering weight loss surgery the choice is between laparoscopic RGB and laparoscopic AGB. Laparoscopic RGB produces greater weight loss but it is a much more complicated and riskier surgery. It involves an irreversible resection of the patient’s internal organs. Meanwhile, laparoscopic AGB produces significant weight loss, and it is considered a reversible procedure with less risk for mortality involved. Since the major advantage of laparoscopic RGB over laparoscopic AGB is the potential for greater sustained weight loss with the RGB procedure, an important consideration is the amount of weight that the patient needs to lose in order to make significant improvements in health. That appraised against the safety profile of the procedures are the major considerations.
CONCLUSION

The problem with coming to a conclusion based on the currently available data is that there is a lack of robust studies showing which diet the patient will most likely follow successfully without quitting in a non-clinical setting. Given that the Mediterranean diet is a low glycemic index diet that has been naturally followed for centuries by people in the Mediterranean, it seems like the likely winner. However, this diet is highly culturally specific, and may not translate well to people of different backgrounds. One solution might be to conduct more mechanistic studies of the Mediterranean Diet so that those aspects of the diet that produce the most health enhancing effects can be translated to different cultures. For example, if studies found that it is the polyunsaturated nature of the fats in olive oil that are key, an effort can be made to find and promote sources of polyunsaturated fats from sources familiar to different cultures or encourage the use of olive oil instead of traditional fat sources. Still, studies comparing the diets in a realistic setting must be done to uncover the most effective diet for treatment of obesity.

Given that lorcaserin and phentermine/topiramate were only approved in 2012 it would be wise to wait for post-marketing data to reveal the long-term safety and efficacy of the drugs. Studies running longer than 108 weeks and studies replicating the results of the phase three clinical trials for these
medications are also warranted before the higher recommendation of these
drugs over orlistat.

Finally, studies that consider combined treatment regimes including diet, exercise, pharmaceuticals and surgery might produce better mechanisms for patients to lose weight. The identification of which diet works best with which type of surgery, and which medications are most effective in patients who have undergone bariatric surgery would provide useful information for treating physicians. The key, however, is to tailor treatments to individual patients based on their physiological needs as well as their ability to tolerate and maintain specific medications, diets and surgeries.
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