

# Continuing Education

## Bariatric Surgery: Less is More

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## Learning Objectives

- Describe the four different types of bariatric surgery and the qualifications for surgery
- Summarize expected outcomes of bariatric surgery including perioperative risks
- Discuss how bariatric surgery impacts medications
- Implement strategies to assist patients in adjusting pharmacotherapy after bariatric surgery
- Understand how bariatric surgery can affect other comorbidities

## Introduction

Excess body weight poses one of the most significant public health challenges in modern medicine. According to the World Health Organization, obesity is now recognized as a global epidemic, affecting nearly 300 million individuals with a prevalence that continues to rise.<sup>1,2</sup> With an increased risk of all-cause mortality, the implications of obesity have created a substantial economic burden on healthcare as well.<sup>3</sup> With this comes a responsibility for pharmacists and clinicians to stay informed on current treatment strategies and therapeutic management surrounding patients with obesity. This article will address the impact of obesity on healthcare, the criteria for bariatric surgery, the types of procedures currently utilized, the expectations and outcomes, and the clinical implications associated with life after surgery including its impact on medication administration and dosing.

## The Burden of Obesity

Obesity is defined as abnormal or excessive fat accumulation that may impair health.<sup>4</sup> Body mass index (BMI) is used to screen and diagnose obesity. For adults, the

World Health Organization (WHO) defines obesity as a BMI greater than or equal to 30.<sup>4</sup>

$$\text{BMI} = \frac{\text{weight (kg)}}{\text{height (m}^2\text{)}}$$

Obesity is a multifactorial disease. Only 10% of the obesity in the population is due to a genetic component, while the other 90% is the result of environmental factors. A number of additional hormonal, metabolic, psychological, cultural and behavioral factors promote fat accumulation and weight gain. Table 1 describes these factors. Furthermore, weight gain itself induces a variety of hormonal, metabolic and molecular changes that increase the risk for even greater fat accumulation.<sup>5</sup>

**Table 1. Factors Promoting Fat Accumulation and Weight Gain**

| Factors promoting fat accumulation and weight gain |  |
|--|--|
| • Genetics   | • Stress   |
| • Excessive eating                                 | • Psychological distress   |
| • Sedentary behavior                               | • Medications (certain diabetes medications, various antidepressants and antipsychotics, steroid hormones, etc.) |
| • Chronic sleep loss                               |  |

More than one-third of adults in the United States are considered obese. The prevalence of obesity is highest in middle-aged citizens (40.2%) and women (38.3%). Non-Hispanic white, non-Hispanic black, and Hispanic adults are more likely to be obese than non-Hispanic Asians.<sup>6</sup> Alabama's adult obesity rate is currently 35.7 percent,

which is ranked as the third highest adult obesity rate in the nation, according to *The State of Obesity: Better Policies for a Healthier America* released in August 2017.<sup>7</sup> Figure 1 shows how Alabama's obesity rate compares to other states in the U.S.

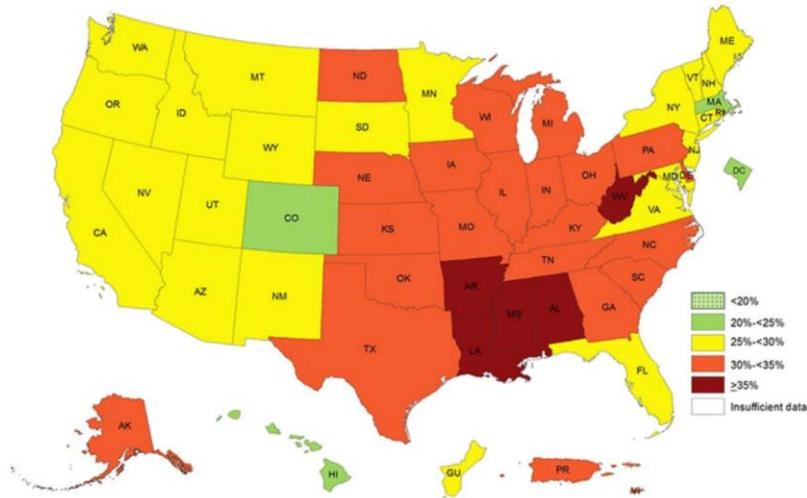


Figure 1. Prevalence of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2016.

Available from:

<https://www.cdc.gov/obesity/data/prevalence-maps.html>

Medical care costs of obesity in the United States are staggering, with the last reliable estimate presented in 2008 at \$147 billion. Severe obesity (most often defined as a BMI  $\geq 35$  with comorbid health conditions or a BMI  $\geq 40$  without conditions) leads to impaired quality of life, substantial morbidity and premature mortality.<sup>8,9</sup> Furthermore, severely obese adults are highly affected by other chronic health conditions, including type 2 diabetes, cardiovascular disease, major depression, coronary heart disease, and osteoarthritis.<sup>10</sup> Figure 2 provides a generalized list of medical complications associated with obesity.

Given obesity's negative impact on health along with its progressive nature, life-long treatment and control is often required. Treatment depends on the severity of obesity as well as the patient's comorbid conditions and may include lifestyle interventions, pharmacotherapy, and bariatric surgical procedures.

Because weight loss through lifestyle changes, such as diet and exercise, is problematic for most patients and

### Medical Complications of Obesity

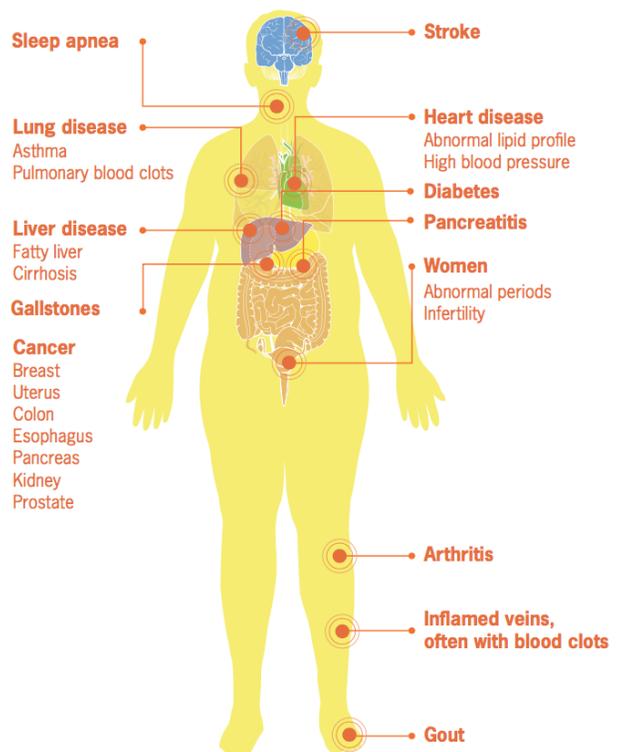


Figure 2. Medical Complications of Obesity. Available from: <https://www.cdc.gov/vitalsigns/pdf/2010-08-vitalsigns.pdf>

with the literature suggesting a tendency for the weight to return, interest in surgical intervention to this issue have surged.<sup>11</sup> A growing body of evidence indicates that bariatric surgery can produce sustained reductions in weight, improve comorbidities, and prolong survival.

### Benefits of Bariatric Surgery

Bariatric surgery is a procedure that helps patients lose weight by making changes to their digestive system, either by changing the anatomy of the gastrointestinal tract or by causing physiologic changes in the body that affect a patient's energy balance and fat metabolism.

When combined with a comprehensive treatment plan, bariatric surgery may offer many benefits, such as<sup>12</sup>:

- **Providing long term weight-loss:** Surgery induces hormonal changes that improve weight loss by maintaining or enhancing energy expenditure.
- **Improvement in overall quality of health:** Improvement in or even resolution of obesity-related comorbidities for many of patients.
- **Reducing a patient's medication burden:** By improving or resolving obesity-related comorbidities, the patient may be able to reduce their medication regimen as well.
- **Improvement in quality of life:** Measures of quality of life that are positively affected may include self-esteem, social interactions, mobility, physical activity, work, and sexual function. Furthermore, depression and anxiety may be reduced.
- **Improved longevity:** Several large population studies find that severely obese individuals who undergo bariatric

surgery have a lower risk of death than individuals affected by obesity who do not have surgery.

### Qualifications for Bariatric Surgery

Consistent with the growing obesity epidemic, the demand for bariatric surgery has increased drastically over the past two decades. Surgery currently remains the most effective and durable intervention for the treatment of obesity.<sup>13</sup> The current clinical practice guideline qualifications for surgical intervention are as follows<sup>14</sup>:

- BMI  $\geq$  40, or more than 100 pounds' overweight
- BMI  $\geq$  35 and at least one or more obesity-related comorbidities such as type 2 diabetes, hypertension, sleep apnea and other respiratory disorders, non-alcoholic fatty liver disease, osteoarthritis, lipid abnormalities, gastrointestinal disorders, and heart disease
- Inability to achieve a healthy weight loss sustained for a period of time with prior weight loss efforts

Additionally, surgery may also be offered to patients with a BMI between 30-34.9 with diabetes or metabolic syndrome but long-term data has yet to demonstrate its overall benefits.<sup>13</sup>

### Types of Bariatric Surgery

Bariatric surgery is a term used to describe surgical procedures that promote weight loss by altering the gastrointestinal tract. The procedures can either be restrictive or malabsorptive.<sup>13,14</sup> Restrictive procedures change the size of the stomach so that it reduces the amount of food a person consumes. Malabsorptive procedures reduce the surface area of the

intestines to limit the time of nutrient absorption. There are four common surgical procedures used in bariatric surgery and they are (1) gastric bypass, (2) sleeve gastrectomy, (3) laparoscopic adjustable gastric band, and (4) biliopancreatic diversion with duodenal switch. According to the American Society for Metabolic and Bariatric Surgery (ASMBS), there were 216,000 total bariatric surgeries performed in 2016.<sup>15</sup> The gastric bypass and the laparoscopic adjustable gastric band surgeries were the two most commonly used in the United States. The average cost of gastric bypass surgery is \$23,000 and the average cost of laparoscopic band surgery is \$14,500.<sup>16</sup> Insurance coverage varies, but more insurance companies are starting to provide coverage for weight loss surgery.

### Gastric Bypass

The Roux-en-Y gastric bypass (RYGB), or gastric bypass, is considered the gold standard of weight loss surgery.<sup>14</sup> It is a combination of a restrictive and malabsorptive procedure.

There are two components of the gastric bypass. First, the top portion of the stomach is divided from the rest of the stomach to create a small stomach pouch. Then, the small intestine is divided into two parts, the top and bottom. The bottom portion of the small intestine is connected to the newly created stomach pouch, whereas the top portion of the small intestine is connected further down the intestine line. This is done so that the stomach acids and digestive enzymes from the bypassed stomach and first portion of small intestine will eventually mix with the food.<sup>14</sup>

The gastric bypass works in several different ways. First, the smaller stomach

pouch allows for smaller meals to fill full which reduces the number of calories consumed. Secondly, with food bypassing parts of the small intestines, there is less absorption of calories. Most importantly, the rerouting of the food stream produces changes in gut hormones that promote satiety, suppresses hunger, and reverses one of the primary mechanisms by which obesity induces type 2 diabetes.<sup>14</sup>

The advantages to a gastric bypass include significant long-term weight loss, restriction of the amount of food consumed, and favorable changes in gut hormones to reduce appetite and promote satiety. Furthermore, patients are typically able to maintain greater than fifty percent excess weight loss. The disadvantages of a gastric bypass are greater risk for complications, longer hospital stay, and long-term vitamin and mineral deficiencies which requires life-long vitamin and mineral supplementation.

### Sleeve Gastrectomy

The laparoscopic sleeve gastrectomy, or “the sleeve”, has been shown to be as effective as the gastric bypass in terms of weight loss and improvement of diabetes.<sup>14</sup> It is considered a restrictive procedure.

The sleeve is performed by removing about eighty percent of the stomach and reconstructing the remaining stomach into a tubular, banana like pouch. It works to reduce weight by reducing the volume of the stomach. This significantly reduces the amount of food and calories that can be consumed. The greatest impact seems to be the reduction of gut hormones which reduces hunger and promotes fullness.

The advantages of the sleeve include restriction of the amount of food the stomach can hold, favorable changes in gut hormones that suppress hunger, reduce appetite, and encourage satiety. Also, this procedure is associated with a relatively short hospital stay.<sup>14</sup> Disadvantages of the sleeve include long term vitamin deficiencies, association with higher early complication rates, and it being a non-reversible procedure.

#### Laparoscopic Adjustable Gastric Band

The adjustable gastric band, or the lap band, involves an inflatable band being placed around the upper portion of the stomach.<sup>14</sup> It is considered a restrictive procedure.

The band is performed by using an inflatable band to create a small stomach pouch above it. This will allow just a small amount of food to satisfy hunger and provide a sense of fullness. The size of the stomach opening can be adjusted by filling the band with sterile saline through a port.<sup>14</sup> Reduction of the stomach opening size is done gradually over time. There is no malabsorption of calories or nutrients. The food is digested and absorbed normally. The clinical implication of the band is its reduction in hunger.

The band induces excess weight loss of approximately forty to fifty percent. Other advantages include it being a reversible and adjustable procedure that requires no cutting of the stomach or re-rerouting the intestines, having the lowest rate of early postoperative complications and mortality, and having the lowest risk of vitamin and mineral deficiency. However, the band results in slower and less early weight loss than other surgical procedures, with a

higher rate of re-operation. Other disadvantages include greater percentage of patients failing to lose at least fifty percent of excess body weight and the potential for mechanical problems.

#### Biliopancreatic Diversion with Duodenal Switch Gastric Bypass

The biliopancreatic diversion with duodenal switch (BPD/DS) is a two component procedure involving the stomach and small intestine. It is considered a combination of a restrictive and malabsorptive procedure.

The BPD/DS is performed by first creating a small, tubular pouch similar to the sleeve. Then, the duodenum is divided just past the outlet of the stomach. A segment of the distal small intestine is then connected to the outlet of the newly created stomach to bypass a large portion of the small intestine. The bypassed small intestine is reconnected to the last portion of the small intestine so that bile and pancreatic enzymes can mix with the food to induce breakdown and absorption of protein and fat. Because of this, there is a significant decrease in the absorption of calories, vitamins, and nutrients leading to weight loss. The BPD/DS procedure does affect gut hormones to have an impact on hunger, satiety, and blood sugar. It is considered the most effective surgery for the treatment of diabetes out of all the bariatric procedures. Similar to the other bariatric procedures, the BPD/DS helps to reduce the amount of food consumed initially; however, the effect lessens and patients are able to consume near normal amount of food.<sup>14</sup>

The advantages of the BPD/DS are it results in the greatest weight loss, allows

patients to eventually eat near normal meals, reduces absorption of fat by seventy percent or more, causes favorable changes in gut hormones to reduce appetite and improve satiety, and is the most effective procedure against diabetes. The disadvantages of the BPD/DS are higher complication rates and risk for mortality, longest hospital stay, greater potential for protein deficiencies and long-term vitamin and mineral deficiencies.<sup>14</sup>

### Comparing Bariatric Surgeries

Evidence has shown that the malabsorptive procedures will generally yield greater and longer lasting weight loss than purely restrictive methods.<sup>13</sup> One prospective randomized study of seventy-two patients was conducted to compare six month and one year outcomes in patients undergoing lap band surgery versus gastric bypass.<sup>17</sup> Thirty six patients were divided into each group and underwent surgery. There was no 30-day mortality and no significant difference in complications rates between the two groups. There was no significant difference in the overall prevalence of comorbidities and nutritional deficiencies. Both bariatric surgeries produced significant reduction in weight and BMI at the 6 month and 1 year follow up. There was no significant difference in BMI reduced of gastric bypass (33.8 kg/m<sup>2</sup>) when compared to lap band (32.8 kg/m<sup>2</sup>). Similarly, there was no statistical significance in the percentage of excess weight loss between gastric bypass (54.4%) and lap band (58.1%) at 6 months or gastric bypass (64.2%) and lap band (67.6%) at 1 year. The results of this study show that both procedures are equally effective and safe in weight reduction.

A randomized clinical trial that included 217 adults with morbid obesity was conducted to assess weight loss between the laparoscopic sleeve procedure and the gastric bypass.<sup>18</sup> The patients were randomized into the two procedure groups with 112 patients undergoing the laparoscopic sleeve procedure and 113 patients undergoing the gastric bypass. The primary endpoint of this study was weight loss, defined as percentage excess BMI loss. Both procedures were shown to have significant reductions in percentage excess BMI loss over the observational period, but there were no statistically significant differences in percentage excess BMI loss for the laparoscopic sleeve (72.4%) compared to the gastric bypass (76.7%) at 1 year.

According to the American Society of Metabolic and Bariatric Surgery (ASMBS), there is no consensus on absolute contraindications to bariatric surgery; however, contraindications do exist for the implantation of a laparoscopic band. The band device should not be used in patients with Crohn's Disease or other inflammatory diseases of the gastrointestinal tract, cirrhosis of the liver, chronic pancreatitis, severe heart disease, and severe lung disease.<sup>19</sup>

All of the discussed bariatric surgeries have been shown to promote significant weight loss. Gastric bypass is considered the gold standard of bariatric surgery because of its proven efficacy in treating obesity. The lap band and sleeve procedures have been shown to be just as effective as the gastric bypass in promoting weight loss. Only the biliopancreatic diversion with duodenal switch has been shown to provide a greater reduction of weight within the

first year, when compared to the gastric bypass, but it is associated with more perioperative risks.<sup>20</sup> Therefore, the advantages and disadvantages of each procedure should be taken into account when deciding which surgery a patient should undergo. Table 2 provides a comparative summary of the advantages and disadvantages of each type of surgery.

**Table 2. Advantages and Disadvantages of the Four Types of Bariatric Surgeries**

|  | <b>Advantages<sup>14</sup></b>  | <b>Disadvantages<sup>14</sup></b>   |
|--|---|---|
| <b>Gastric Bypass</b>  | <ul style="list-style-type: none"> <li>• Significant long-term weight loss</li> <li>• Restriction of the amount of food consumed</li> <li>• Increased energy expenditure</li> <li>• Favorable changes in gut hormones that reduce appetite and enhance satiety</li> <li>• Patients are typically able to maintain &gt;50% excess weight loss</li> </ul>   | <ul style="list-style-type: none"> <li>• Greater risk for complications</li> <li>• Longer hospital stay</li> <li>• Long term vitamin and mineral deficiencies which requires life-long supplementation</li> </ul>   |
| <b>Sleeve Gastrectomy</b>  | <ul style="list-style-type: none"> <li>• Rapid and significant weight loss</li> <li>• Restricts the amount of food the stomach can hold</li> <li>• Requires no placement of foreign objects or re-routing of the food stream</li> <li>• Relatively short hospital stay</li> <li>• Favorable changes in gut hormones that suppress hunger, reduce appetite, and improve satiety</li> </ul>   | <ul style="list-style-type: none"> <li>• Long term vitamin deficiencies</li> <li>• Associated with higher early complication rates</li> <li>• Non-reversible procedure</li> </ul>   |
| <b>Laparoscopic Adjustable Gastric Band</b>                          | <ul style="list-style-type: none"> <li>• Reduction in the amount of food the stomach can hold</li> <li>• Induces excess weight loss of approximately 40-50%</li> <li>• Does not involve cutting of the stomach or re-rerouting the intestines</li> <li>• Shorter hospital stay</li> <li>• Reversible and adjustable</li> <li>• Lowest rate of early postoperative complications and mortality</li> <li>• Lowest risk of vitamin and mineral deficiency</li> </ul> | <ul style="list-style-type: none"> <li>• Slower and less early weight loss than other surgical procedures</li> <li>• Greater percentage of patients failing to lose at least 50 percent of excess body weight</li> <li>• Requires placement of a foreign device</li> <li>• Possible band slippage or erosion</li> <li>• Mechanical problems with the band</li> <li>• Can result in dilation of the esophagus if the patient overeats</li> <li>• Highest rate of re-operation</li> </ul> |
| <b>Biliopancreatic Diversion with Duodenal Switch Gastric Bypass</b> | <ul style="list-style-type: none"> <li>• Results in the greatest weight loss</li> <li>• Allows patients to eventually eat near normal meals</li> <li>• Reduces absorption of fat by <math>\geq 70\%</math></li> <li>• Causes favorable changes in gut hormones to reduce appetite and improve satiety</li> <li>• The most effective against diabetes</li> </ul>   | <ul style="list-style-type: none"> <li>• Higher complication rates and risk for mortality</li> <li>• Longest hospital stay</li> <li>• Greater potential for protein deficiencies and long-term vitamin and mineral deficiencies</li> </ul>  |

### Expected Outcomes of Surgery

Predicted weight loss varies based on the type of procedure and the magnitude of BMI elevation at baseline. This decline is most extensive in the first year and is generally most rapid in the first few months when caloric restriction is at its highest. The rate of weight loss is variable per patient depending on their baseline body weight. The degree of weight loss gradually dwindles overtime with maximal results occurring 12 to 18 months following the procedure.<sup>12</sup> Observed weight loss tends to be greater with gastric bypass and sleeve gastrectomy when compared to gastric banding. The extent of reduction and successful attainment of a BMI below 35 tends to be most substantial in patients undergoing RYGB.<sup>21</sup>

In a meta-analysis assessing weight loss in 161,756 patients across an assortment of surgical interventions, researchers found percent of excess weight loss (%EWL) averaged around 33.8% for gastric banding, 60.6% for sleeve gastrectomy, and 68.3% for gastric bypass in the first year after surgery.<sup>21</sup> These values express weight loss achieved relative to defined goal set individually for each patient. In the Swedish Obese Subjects (SOS) study, which has now reached 20 years of follow-up, reports a comparison of 4,047 patients who either underwent surgical intervention or received conventional treatment for obesity by means of pharmacotherapy and lifestyle modifications.<sup>9</sup> Surgical treatments assessed included gastric banding, vertical banded gastroplasty (VBG), or gastric bypass. Again, gastric bypass served as the most successful method achieving substantial weight loss, followed by VBG and gastric banding. At 20 years, surgical interventions averaged a sustained

reduction in weight of 18% below baseline with conventional treatment of diet and exercise accomplishing a mere 1%.<sup>9</sup>

The reduction in all-cause mortality following bariatric surgery is primarily due to weight loss on improving co-morbid conditions worsened by the disease. This list of co-morbidities includes hypertension, diabetes, dyslipidemia, sleep apnea, asthma and other obesity-related breathing disorders, arthritis, GERD, fatty liver disease, venous stasis, urinary incontinence, and others. The International Diabetes Federation released a statement in 2011 supporting bariatric surgery as a treatment option for select patients with T2DM. This approval was echoed by the updated American Association of Clinical Endocrinologists guidelines for comprehensive diabetes care.<sup>22,23</sup> A review of more than 600 studies found that bariatric surgery resulted in improvement of T2DM in more than 85% of the diabetic population and remission of the disease in a remarkable 78% of subjects.<sup>24</sup> Findings from the SOS study at two years of follow-up indicated that surgical interventions resulted in resolution of diabetes in 72% of patients compared to conventional treatment accomplishing a 21% resolution of the disease.<sup>9</sup> Following this discovery, the American Diabetes Association revised their definition of diabetes remission to include HbA<sub>1c</sub> <6% and fasting plasma glucose <100g/dL in absence of medications for at least one year following bariatric surgery.<sup>23</sup> Although weight loss is undeniably an important factor in the improvement and possible resolution of T2DM, researchers have investigated the possibility that resulting hormonal changes following surgery having an impact on this outcome as well.<sup>25</sup>

A common assumption of bariatric surgery might suggest considerable weight reduction in all patients, however, studies have identified some that fail to observe significant weight loss after surgery.<sup>26</sup> Quantifying failure, however, is difficult due to lack of a set cut-off for "acceptable weight loss" defining successful treatment. Since analysis of suboptimal weight loss is somewhat futile, considerable attention is being paid to identifying factors that reliably predict failure to reach a notable reduction in weight. Attributes that may influence trajectory of weight loss include baseline behavioral and psychological status (mood/anxiety disorders), patient expectations with respect to anticipated weight reductions, and unhealthy eating behaviors (binge eating, emotional eating, nighttime snacking). Presence of these factors will compromise ability to reach individualized target outcomes and emphasis should be placed on lifestyle changes in such event.<sup>27,28</sup>

Early post-operative complications include GI hemorrhage, gastric or bowel perforation, and the risk of pulmonary embolism and infection generally seen with surgical treatment. During the recovery process, patients may experience reflux, dysphagia, nausea, vomiting, diarrhea, and/or constipation.<sup>29</sup> Late complications may include incisional hernia, stenosis at the anastomotic site(s), bowel obstruction, formation of ulcers at the esophageal sphincter, dumping syndrome, and vitamin/mineral deficiencies.<sup>30</sup> Certain adverse events reported are not technically complications of the procedure itself but occur as a result of rapid weight loss. During the first several months following surgery, patients may experience fatigue, cold

intolerance, hair loss, and cholelithiasis, with an expected resolution upon stabilization of weight loss.<sup>30</sup> Mortality rates differ according to procedure used, patient demographics, and surgeon skill, but is generally found to be negligible. In a 2007 meta-analysis conducted on 85,048 patients, an overall mortality rate of 0.28% in the first 30 days was reported<sup>31</sup>, a decline from 0.89% in 1998<sup>32</sup>, with a rate of 0.35% between 31 days and two years<sup>31</sup>. Invasiveness of the procedure resulted in a proportional increase in 30-day mortality, with gastric bypass having the highest risk. Death was seemingly influenced by gender, with men having 3-fold increased risk over women<sup>32</sup>. Physician experience played a likely role in adverse outcomes as well, with a reduction in mortality reported by institutions with a higher case volume.<sup>33</sup> Concerns regarding patient safety and quality of surgical performance prompted partnership between the American College of Surgeons and the American Society of Metabolic and Bariatric Surgery in implementation of an accreditation program for these procedures.<sup>34</sup>

### **Life After Bariatric Surgery**

Arrangements for post-surgical care are integral in equipping the patient for an effective recovery with optimal outcomes. Physical activity is very important for substantial weight loss. Exercise activities should be encouraged shortly after surgery. More invasive procedures equate to a longer healing time before exercise can be resumed again. Patients can generally participate in low impact exercises in the first few weeks after discharge and should be challenged to progress to more vigorous activities with each passing week. Incorporating aerobic, resistance, and flexibility training into the fitness routine

favor optimal results. Weight loss of 1 to 2 pounds per week is considered a safe amount for patients making lifestyle changes.<sup>35</sup>

In addition to the benefits of bariatric procedures, long-term complications should be communicated to patients considering surgery. Malabsorptive processes permanently alter the anatomy of portions within the GI tract, including the stomach and small intestine. Modifying the visceral framework necessitates changes in dietary habits post-operatively and strict adherence to this regimen. Compliance with these changes will help to mitigate risk for nutritional deficiencies, address inadequate serum concentrations of certain medications, and manage intolerance to certain foods, particularly meat products.

Dietary changes tend to be the most significant behavioral modification following bariatric intervention. In light of this, patients will be referred to a dietitian to assist with management. Patients will receive a unique nutrition plan to follow to guide them through progression to consuming solid foods again. Feeding will gradually advance, over a matter of weeks, from a strict liquid diet to pureed foods and eventually to solid, more regularly-textured foods. During the first few months of recovery, maintaining adequate fluid intake is of utmost importance. Dehydration remains the most common cause of hospital readmission.<sup>29,36</sup> Metabolic processes require fluid to convert adipose reservoirs to usable energy. Patients are encouraged to drink 64 fluid ounces of water daily and warned of signs and symptoms in identifying a dehydrated state.<sup>36</sup> Sufficient protein intake is a mainstay both in reducing hunger between

meals and thwarting malnutrition and its associated complications. A daily goal of 60 – 80g is targeted in the majority of patients but requirements may vary depending on response to surgery, type of procedure, and amount of activity.<sup>37</sup> Sugar-rich foods and refined carbohydrates can lead to dumping syndrome and these individuals should therefore be counseled on consuming these foods in moderation or avoiding them altogether.<sup>12,37</sup>

Due to the alterations in the small intestine, particularly in the duodenum and jejunum segments, patients who undergo malabsorptive procedures are at an increased risk of nutritional deficiencies. Restrictive processes, such as sleeve gastrectomy and gastric banding, tend to have minimal effects in the absorption of medications.<sup>38</sup> However, reconfiguration of the viscera seen with gastric bypass and intestinal diversion can have pronounced consequences on the absorption process.<sup>38</sup> Most of the available literature on absorption following bariatric surgeries, and recommended strategies to overcome these effects, are based on a procedure that has since fallen out of favor after being linked to deleterious and even life-threatening complications. The jejunoileal bypass demonstrated dramatic weight loss but the resulting renal and hepatic failure compromised benefit of the procedure.<sup>39</sup>

### **The Role of Pharmacists After Surgery**

Vitamins and minerals absorbed in the duodenum and jejunum include folate, thiamine, riboflavin, niacin, pyridoxine, vitamin C, iron, and copper.<sup>40</sup> Table 3 illustrates micronutrients that have potential for deficiency following bariatric procedures in which appropriate replacement using vitamin supplementation

should be advised. Accepted recommended augmentation for post-op patients regardless of procedure includes a once daily multivitamin (containing vitamin D and calcium), supplemental iron, and a B-complex preparation, with a chewable form being used for at least 12 weeks following

the procedure.<sup>41</sup> Supplementation can be tailored, however, according to expected deficits based on the table below. Failure to maintain adequate intake of select vitamins may precipitate issues pertaining to anemia and osteoporosis.

**Table 3. Altered Absorption of Micronutrients<sup>39,42</sup>**

| Vitamin/Mineral         | Lab Monitoring                        | BPD/DS | RYGB | SG | LAGB |
|-------------------------|---------------------------------------|--------|------|----|------|
| Calcium                 | Bone Density                          | ✓      | ✓    | ✓  | ✓    |
| Iron                    | Fe Panel, Ferritin, TIBC              | ✓      | ✓    | ✓  | ✓    |
| Vitamin B <sub>12</sub> | Vitamin B <sub>12</sub> , MMA         | ✓      | ✓    | ✓  |      |
| Folate                  | RBC Folate                            | ✓      | ✓    |    |      |
| Thiamin                 | Serum Thiamin                         | ✓      | ✓    |    |      |
| Vitamin D               | 25-OH-Vitamin D, Serum PTH            | ✓      | ✓    | ✓  | ✓    |
| Zinc                    | Serum or Plasma Zinc                  | ✓      | ✓    |    |      |
| Copper                  | Serum Copper, Ceruloplasmin           | ✓      | ✓    |    |      |
| Vitamin A, E, and K     | Plasma Retinol, Plasma Tocopherol, PT | ✓      |      |    |      |

There are a modest number of studies that investigated the influence of bariatric interventions on absorption and resulting bioavailability of medications. However, therapeutic implications have yet to be assessed and thus limit the reliability of current recommendations in place for adjustments in therapy. Despite this shortcoming, evidence has ascertained that bariatric procedures do have ramifications on the absorptive process by means of altering drug

solubility and available surface area for absorption.

Medications considered acid soluble will have increased absorptive effects when in an acidic environment.<sup>42</sup> Reduction in gastric acid, which will result to some extent with all bariatric procedures, will decrease bioavailability of medications requiring this type of environment for absorption and distribution. Likewise, malabsorptive procedures altering intestinal anatomy will have the same effect on bioavailability of alkaline-soluble drugs. The modifications to intestinal composition will affect drugs with long absorptive phases, such as extended release or enteric coated formulations, that require extensive housing in the intestine for appreciable delivery to systemic circulation.<sup>42,43</sup>

Absorption is not the only pharmacokinetic parameter to consider in post-operative management of these patients. Reductions in adipose tissue as a result of weight loss affects the distribution of highly lipophilic drugs, such as propofol. The reduction in adipose tissue affects partitioning of these agents by decreasing the amount of fat they can distribute into.<sup>43</sup> Caution should be taken in highly lipophilic agents and medications requiring weight-based dosing as continuing a dose indicated for obesity will have potential for toxic effects. The mechanism behind these changes include:<sup>39</sup>

- Evasion of primary site of absorption in the proximal small intestine
- Changes in drug dissolution as a result of altered gastric emptying, diminished mucosal exposure, and a shift in intestinal pH

- Altered metabolism by intestinal cytochrome P450 enzymes, particularly CYP3A4 and CYP2C19
- Active substrate efflux by P-glycoprotein with increasing expression of transporter in distal regions of the viscera

BPD/DS and RYGB have the greatest risk for nutritional and medication deficits, by and large.<sup>14</sup> These techniques combine restriction in stomach volume with re-routing of the intestinal tract. Tables 4 and Table 5 represent altered drug bioavailabilities observed in post-procedural bariatric population.

**Table 4. Reduced Drug Bioavailability Following Bariatric Surgery**

| Decreased Bioavailability <sup>39</sup> |   |
|---|---|
| Antimicrobials                          | <ul style="list-style-type: none"> <li>• Azithromycin</li> <li>• Moxifloxacin</li> <li>• Nitrofurantoin</li> <li>• Amoxicillin</li> <li>• Penicillin</li> </ul> |
| Immunosuppressants                      | <ul style="list-style-type: none"> <li>• Ciclosporin</li> <li>• Tacrolimus</li> <li>• Sirolimus</li> <li>• Mycophenolic Acid</li> </ul>                         |
| Thyroid Supplement                      | <ul style="list-style-type: none"> <li>• Levothyroxine</li> </ul>   |
| Anti-convulsants                        | <ul style="list-style-type: none"> <li>• Phenytoin</li> <li>• Phenobarbital</li> </ul>  |
| Antidepressants                         | <ul style="list-style-type: none"> <li>• Selective Serotonin Reuptake Inhibitors (SSRIs)</li> <li>• Tricyclic Antidepressants (TCAs)</li> </ul>                 |

**Table 5. Enhanced Drug Bioavailability Following Bariatric Surgery**

| Increased Bioavailability <sup>39</sup>  |
|--|
| <ul style="list-style-type: none"> <li>• Metformin</li> <li>• Digoxin</li> <li>• Nifedipine</li> </ul> |

Early in recovery, administration of larger tablets or capsules may be discouraged as potential for these sizable formulations to become lodged would increase the risk of post-operative complications. Medication classes that recovering gastric bypass patients should be counseled to avoid are

NSAIDs and corticosteroids.<sup>42,43</sup> NSAIDs are linked to marginal ulcers in the GI tract that can perforate and bleed, which has been identified as a common cause of re-operation and, on rare occasion, reversal of gastric bypass. Corticosteroids can also increase this risk but may be necessary. Some prescription medications can induce weight gain and assessment of risk versus benefit may dictate medication selection. Table 6 represents medications that may somewhat compromise the benefits of bariatric surgery.

**Table 6. Medications Inducing Weight Gain<sup>44</sup>**

| Antidiabetics                                   | Psychiatric   | Anticonvulsants   | Steroids/Hormones                           |
|---|---|---|---|
| Insulins<br>Thiazolidinediones<br>Sulfonylureas | Tricyclic Antidepressants<br><br>Selective Serotonin Reuptake Inhibitors<br><br>Lithium<br><br>Antipsychotics | Valproic Acid<br>Carbamazepine<br>Topiramate<br>Lamotrigine<br>Zonisamide | Oral Corticosteroids<br>Oral Contraceptives |

In addition to improvements in health and longevity, surgical weight loss impacts a patient's overall quality of life. Measures of quality of life that are positively affected include ambulation, self-esteem, effort and initiative pertaining to work and other related affairs, social interactions, and sexual function.<sup>45</sup> Furthermore, symptomatic depression and anxiety is significantly reduced following bariatric surgery.<sup>45</sup>

**Conclusion**

Despite the increasing popularity and established health benefits, the approach carries risks in which many pressing questions still remain. Research continues to evaluate the advantages and disadvantages of the varying procedures, how best to select candidates for surgery, and the effects on specific co-morbidities

with regard to therapeutic outcomes. This includes expectations on extent of weight loss, peri-operative risks, and the lasting effects on nutrition and quality of life. Considering the support and acclaim this dynamic approach has received of late, it is crucial that healthcare professionals have a clear understanding of how bariatric surgery fits into caring for these patients.

Bariatric surgery can be a useful tool to help break the vicious weight gain cycle, achieve long term weight loss, and improve overall quality of health and life. Regardless of which bariatric surgery procedure determined to be of highest benefit for the individual patient, it is important to remember that bariatric surgical intervention is only a tool. Overall success is dependent upon the other important factors discussed throughout this article.

## References:

1. Flegal KM, Carroll MD, Ogden CL, Curtin LR. Prevalence and trends in obesity among US adults, 1999–2008. *JAMA*. 2010 Jan 20;303(3):235–41.
2. James PT. Obesity: the worldwide epidemic. *Clin Dermatol*. 2004 Jul;22(4):276–80.
3. Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJ. Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. *Lancet*. 2006 May 27;367(9524):1747–57.
4. WHO: Obesity and Overweight [Internet]. World Health Organization; 2018 [updated 2018 Feb, cited 2018 Mar 6]. Available from: <http://www.who.int/mediacentre/factsheets/fs311/en/>
5. Martin K, Mani M, Mani A. New targets to treat obesity and the metabolic syndrome. *Eur J Pharmacol*. 2015 Sep 15; 763: 64-74
6. CDC: Adult Obesity Facts [Internet]. Atlanta (GA): U.S. Department of Health and Human Services; 2018. [updated 2018 Mar 5, cited 2018 Mar 6]. Available from: <https://www.cdc.gov/obesity/data/adult.html>
7. The State of Obesity: Better Policies for a Healthier America. Washington (DC): Trust for America's Health; 2004-2018 [cited 2018 Mar 6]. Available from: <https://stateofobesity.org/states/al>
8. Must A, Spadano J, Coakley EH, Field AE, Colditz G, Dietz WH. The disease burden associated with overweight and obesity. *JAMA* 1999;282:1523-9.
9. Sjöström L, Narbro K, Sjöström CD, Karason K, Larsson B, et al. Effects of bariatric surgery on mortality in Swedish obese subjects. *N Engl J Med*. 2007;357:741–752.
10. Arterburn DE, Courcoulas AP. Bariatric surgery for obesity and metabolic conditions in adults. *BMJ*. 2014 Aug 27; 349: g3961.
11. Avenell A, Broom J, Brown TJ, et al. Systematic review of the long-term effects and economic consequences of treatments for obesity and implications for health improvement. *Health Technol Assess*. 2004;8(21):1–182.
12. Mechanick JI, Youdim A, Jones DB, et al. Clinical Practice Guidelines for the Perioperative Nutritional, Metabolic, and Nonsurgical Support of the Bariatric Surgery Patient—2013 Update: Cosponsored by American Association of Clinical Endocrinologists, The Obesity Society, and American Society for Metabolic & Bariatric Surgery. *Endocr Pract*. 2013 Mar;19(2):337–72.
13. Sheehan A, Chen JT, Yanovski JA, Calis K. Obesity. In: DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey L. eds. *Pharmacotherapy: A Pathophysiologic Approach*, 10e New York, NY: McGraw-Hill. Accessed 2018 Mar 4. Available from: <http://accesspharmacy.mhmedical.com/content.aspx?bookid=1861&sectionid=133894259>.
14. American Society for Metabolic and Bariatric Surgery. Bariatric Surgery Procedures. 2018. Accessed 2018 Mar 4. Available from: <https://asmbs.org/patients/bariatric-surgery-procedures>
15. American Society for Metabolic and Bariatric Surgery. Estimate of Bariatric Surgery Numbers. Accessed 2018 Mar 5. Available at <http://asmbs.org/resources/estimate-of-bariatric-surgery-numbers>.
16. Obesity Coverage. Weight Loss Surgery Insurance Coverage and Costs. 2017 Oct 3. Accessed 2018 Mar 5. Available from: <https://www.obesitycoverage.com/weight-loss-surgery-insurance-coverage-and-costs/>
17. Paluszkiwicz R, Kalinowski P, Wroblewski T, Bartoszewicz Z, Bialobrzaska-Paluszkiwicz J, Ziarkiewicz-Wroblewska B, et al. Prospective randomized clinical trial of laparoscopic sleeve gastrectomy versus open roux-en-y gastric bypass for the management of patients with morbid obesity. *Wideochir Inne Tech Maloinwazyjne*. 2012 Dec 20;7(4):225-232.

18. Peterli R, Wolnerhanssen BK, Peters T, et al. Effect of laparoscopic sleeve gastrectomy vs laparoscopic roux-en-y gastric bypass on weight loss in patients with morbid obesity: the SM-BOSS randomized clinical trial. *JAMA*. 2018;319(3):255-265.
19. Allergan. LAP-BAND AP Adjustable Gastric Banding System with OMNIFORM Design. Available at [http://www.allergan.com/assets/pdf/lapband\\_dfu.pdf](http://www.allergan.com/assets/pdf/lapband_dfu.pdf).
20. Sovik TT, Taha O, Aasheim ET, Engstrom M, Kristinsson J, Bjorkman S, Schou CF, et al. Randomized clinical trial of laparoscopic gastric bypass versus laparoscopic duodenal switch for superobesity. *Br J Surg*. 2010;97(2):160-166.
21. Buchwald H, Avidor Y, Braunwald E, et al. Bariatric surgery: a systematic review and meta-analysis. *JAMA*. 2004 Oct 13;292(14):1724-37.
22. Handelsman Y, Mechanick JL, Blonde L, et al. AACE Task Force for Developing Diabetes Comprehensive Care Plan. American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for developing a diabetes mellitus comprehensive care plan. *Endocr Pract*. 2011 Apr;17(Suppl 2):1-53.
23. Mechanick JL. Bariatric surgery and the role of the clinical endocrinologist: 2011 update. *Endocr Pract*. 2011 Oct;17(5):788-97.
24. Fanin A, Benetti A, Ceriani V, Pontiroli AE. Bariatric surgery versus medications in the treatment of type 2 diabetes. *Minerva Endocrinol*. 2015 Dec;40(4):297-306.
25. Guidone C, Manco M, Valera-Mora E, et al. Mechanisms of recovery from type 2 diabetes after malabsorptive bariatric surgery. *Diabetes*. 2006 Jul;55(7):2025-31.
26. Dalle Grave R, Calugi S, Molinari E, et al. Weight loss expectations in obese patients and treatment attrition: an observational multicenter study. *Obes Res*. 2005 Nov;13(11):1961-9.
27. Dalle Grave R, Calugi S, Corica F, Di Domizio S, Marchesini G, QUOVADIS Study Group. Psychological variables associated with weight loss in obese patients seeking treatment at medical centers. *J Am Diet Assoc*. 2009 Dec;109(12):2010-6.
28. Odom J, Zalesin KC, Washington TL, et al. Behavioral predictors of weight regain after bariatric surgery. *Obes Surg*. 2010 Mar;20(3):349-56.
29. Maggard MA, Shugarman LR, Suttrop M, et al. Meta-analysis: surgical treatment of obesity. *Ann Intern Med*. 2005 Apr 5;142(7):547-59.
30. Edwards ED, Jacob BP, Gagner M, Pomp A. Presentation and management of common post-weight loss surgery problems in the emergency department. *Ann Emerg Med*. 2006 Feb;47(2):160-6.
31. Buchwald H, Estok R, Fahrenbach K, Banel D, Sledge I. Trends in mortality in bariatric surgery: a systematic review and meta-analysis. *Surgery*. 2007 Oct;142(4):621-35.
32. Zhao Y, Encinosa W. Bariatric surgery utilization and outcomes in 1998 and 2004: HCUP statistical brief #23. Agency for Healthcare Research and Quality. Last accessed March 3, 2018. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK63485/pdf/sb23.pdf>
33. Nguyen NT, Paya M, Stevens CM, Mavandadi S, Zainabadi K, Wilson SE. The relationship between hospital volume and outcome in bariatric surgery at academic medical centers. *Ann Surg*. 2004 Oct;240(4):586-94.
34. Inabnet W, Bour E, Joyce C, et al. Part 4: the American Society for Metabolic and Bariatric Surgery Bariatric Surgery Center of Excellence Bariatric Quality Improvement Program (ASMBS BSCOE/BQIP) – Joint task force recommendations for credentialing of bariatric surgeons. *Surg for Obes Relat Dis*. 2013 Jun;9(5):595-97.
35. U.S. Department of Health and Human Services. Physical Activity Guidelines for Americans. Last accessed March 3, 2018. Available from: <http://www.health.gov/paguidelines/pdf/paguide.pdf>
36. Manchester S, Roye GD. Bariatric Surgery: An overview for dietetics professionals. *Nutr Today*. 2011 Dec;46(6):264-73.

37. Parrott J, Frank L, Rabena R, Craggs-Dino L, Isom KA, Greiman L. ASMBS integrated health nutritional guidelines for the surgical weight loss patient 2016 update: micronutrients. *Surg Obes Relat Dis*. 2017 May;13(5):727–41.
38. Franco JV, Ruiz PA, Palermo M, Gagner M. A review of studies comparing three laparoscopic procedures in bariatric surgery: sleeve gastrectomy, Roux-en-Y gastric bypass and adjustable gastric banding. *Obes Surg*. 2011 Sept;21(9):1458–68.
39. Sawaya RA, Jaffe J, Friedenber L, Friedenber FK. Vitamin, mineral, and drug absorption following bariatric surgery. *Curr Drug Metab*. 2012 Nov;13(9):1345–55.
40. Marinella MA. Anemia following Roux-en-Y surgery for morbid obesity: a review. *South Med J*. 2008 Oct;101(10):1024–31.
41. Aills L, Blankenship J, Buffington C, Furtado M, Parrott J. ASMBS allied health nutritional guidelines for the surgical weight loss patient. *Surg Obes Relat Dis*. 2008 Oct;4(5 Suppl):S73–108.
42. Miller AD, Smith KM. Medication and nutrient administration considerations after bariatric surgery. *Am J Health Syst Pharm*. 2006 Oct;63(19):1852–7.
43. Smith A, Henriksen B, Cohen A. Pharmacokinetic considerations in roux-en-Y gastric bypass patients. *Am J Health Syst Pharm*. 2011 Dec;68(23):2241–7.
44. Obesity Action Coalition. Prescription medications and weight gain – what you need to know. Available from: <http://www.obesityaction.org/educational-resources/resource-articles-2/general-articles/prescription-medications-weight-gain>
45. Batsis JA, Lopez-Jimenez F, Collazo-Clavell ML, Clark MM, Somers VK, Sarr MG. Quality of life after bariatric surgery: a population-based cohort study. *Am J Med*. 2009 Nov;122(11):1055.e1–10.