MICRONUTRIENT DEFICIENCIES AS A RESULT OF BARIATRIC SURGERY

By
Ashlie Lewis

A Senior Project submitted
In partial fulfillment of the requirements for the degree of
Bachelor of Science in Nutrition

Food Science and Nutrition Department
California Polytechnic State University
San Luis Obispo, CA

June 2010
ABSTRACT

The most effective method of sustainable weight loss in obese patients is bariatric surgery. However, micronutrient deficiencies that can result after bariatric surgery can cause health problems that may outweigh its benefits. Micronutrient deficiencies are most common in patients who undergo Roux-en-Y gastric bypass or biliopancreatic diversion with or without duodenal switch. The majority of vitamin B₁₂ and folate deficiencies studies showed significant prevalence rates in their patient populations. Most concluded that routine oral B₁₂ supplementation was ineffective at resolving deficiency; very high oral doses (≥ 350 µg) or intramuscular injections of crystalline B₁₂ were typically required. Studies of iron deficiency after bariatric surgery found high prevalence rates due to inadequate oral supplementation, which can lead to the need for parenteral supplementation. Calcium and vitamin D deficiency studies also showed high prevalence rates of deficiency, which is important to address as deficiency can result in metabolic bone disease. Overall, the need for lifelong supplementation and follow up, early detection of deficiencies, patient education, and more aggressive supplementation regimens were emphasized to increase quality of life in bariatric surgery patients. Future research in bariatric surgery studies should include long-term health outcomes, patient education on required supplementation, and more aggressive supplementation regimens.
Introduction

Throughout the past several decades, prevalence of overweight and obesity in the United States has steadily increased. National Health and Nutrition Examination Survey (NHANES) data from 2007-2008 show an age-adjusted combined prevalence rate of 68% overall in both men and women in the U.S. (Flegal, Carroll, Ogden, & Curtin, 2010). Overweight is defined as a body mass index (BMI) of 25.0-29.9, and obese is classified as a BMI >30.0. Over one-third of the U.S. population is obese, and approximately 15 million Americans have a BMI >40, labeled as morbid obesity (Nagle, 2010). Consequences of overweight and obesity manifest as increased risk for developing chronic health conditions such as coronary heart disease, type 2 diabetes mellitus, hypertension, dyslipidemia, osteoarthritis, some cancers, and other chronic diseases, resulting in important public health concerns (National Heart, Lung and Blood Institute [NHLBI], 1998). Medical costs attributed to obesity are as high as $147 billion annually; obese persons spent on average 42% more on health care than persons of normal weight (Centers for Disease Control and Prevention [CDC], 2009).

The most effective long-term solution for the morbidly obese is bariatric surgery, which has been shown to achieve sustainable and significant weight loss, improve chronic comorbidities, and reduce risk of mortality (Toh, Zarshenas, & Jorgensen, 2009). Bariatric surgery patients achieve weight loss of 30% to 70% of excess body weight, compared to 5% to 10% with non-surgical weight loss approaches (Kushner & Neff, 2010). Bariatric surgeries are growing more popular, as approximately 220,000 bariatric procedures were performed in the U.S. in 2008; however, only 1% of eligible persons undergo the procedure. Eligibility requires a BMI of ≥40 or ≥35 with an obesity-related disease (American Society for Metabolic and Bariatric Surgery [ASBS]). These procedures result in gastrointestinal anatomy and physiologic
changes; altered diet quality and quantity; malabsorption; and can lead to macronutrient and micronutrient deficiencies (Toh et al., 2009). Overall incidence of developing complications after the surgery is low; the most common major complications being gastrointestinal leaks, pulmonary embolus, anastomotic stricture, esophageal ulcer, and hernia (Malinowski, 2006). The purpose of this review is to provide an overview of common bariatric procedures and the micronutrient deficiencies that can result.

**Bariatric Surgery**

Several different bariatric surgeries are performed, each with their own unique procedures and complications. Figure 1 below is a basic diagram of how the stomach and small intestine are altered in each procedure.

**Figure 1.** Four surgical procedures of bariatric surgery (Pories, 2009).
**Gastric Bypass**

*Roux-en-Y gastric bypass.* The standard Roux-en-Y gastric bypass (RYGBP) procedure, the most common bariatric surgery performed in the United States, involves connecting the jejunum to a small pouch, created at the proximal portion of the stomach, with a capacity of 15-30 mL (Nelms, Sucher, & Long, 2007; ASBS, 2005; Federle & Blachar, 2002). The amount of small intestine bypassed in the standard procedure does not cause macronutrient malabsorption. However, the bypassed portion of the small intestine is where most iron and calcium absorption takes place, which can result in long-term complications such as anemia and osteoporosis (ASBS, 2005). In the distal RYGBP procedure, the surgeon modifies the standard RYGBP to cause both volume restriction and macronutrient malabsorption. Weight loss after the distal RYGBP is greater than the standard procedure but results in more severe nutritional deficiencies (ASBS, 2005). Cholelithiasis, formation of cholesterol stones in the gallbladder, is a common complication of RYGBP, due to the rapid weight loss, with reported incidence rates of 50%. Use of ursodiol for six months after RYGBP has been effective in reducing gallstone formation. Some surgeons choose to prophylactically remove the gallbladder at the time of surgery (Malinowski, 2006).

The laparoscopic RYGBP procedure is usually performed through five to six small abdominal incisions of 0.5 to 2.0 cm in length, whereas the open surgical procedure requires larger incisions and abdominal wall retractors for exposure (ASBS, 2005). Most complications are minor, usually consisting of incision drainage, urinary tract infection, nausea, or painful abdominal wall muscle spasms. Major complications occur in less than 1% of patients, and include serious wound infection, intra-abdominal bleeding, infections within the abdomen, and hernias (Duke University Health System, 2007). Laparoscopic RYGBP results in less blood loss,
shorter hospital stays, reduced postoperative pain, less pulmonary complications, faster recovery, and fewer incisional hernias and infections. The open surgery procedure is reserved for patients with an extremely high BMI, multiple previous upper abdominal surgeries, and patients who have previously undergone bariatric surgery (ASBS, 2005).

**Biliopancreatic diversion.** The biliopancreatic diversion (BPD) procedure works through significant malabsorption of nutrients by removing approximately 70% of the stomach and creating a much shorter anastomosis (connection of two hollow organs) into the small intestine than the RYGBP procedure. The post-operation stomach produces significantly less gastric acid. Stomach volume is much greater than the RYGBP pouch, which allows for patients to eat larger volumes of food before experiencing satiety (ASBS, 2005). The amount of excess weight shed by BPD patients has been reported around 70% with weight loss persisting in some patients for up to 18 years. Life-long medical follow-up is required due to the highly malabsorptive nature of the procedure (ASBS, 2005).

**Duodenal switch.** Duodenal switch (DS) is a modification of BPD in which the stomach is fashioned into a small tube, preserving the pylorus. Then a lengthy portion of the duodenum is rerouted to create two separate pathways and one common channel. The digestive loop, the shorter of the two pathways, moves chyme (partially digested food) from the stomach to the common channel. The longer biliopancreatic loop carries bile from the liver to the common channel. The common channel consists of 75 to 150 cm of the small intestine, in which the chyme mixes with the bile before emptying into the colon. This reduces the amount of time the body has to gain energy from the chyme in the small intestine and limits fat absorption. The duodenum is tolerant of gastric acid, and is much less prone to ulceration than the ileum and jejunum (Baltasar et al., 2001; ASBS, 2005). The BPD/DS procedure also prevents dumping
syndrome, a condition that involves rapid gastric emptying into the small intestine before food is digested, resulting in diarrhea, bloating, and other uncomfortable symptoms due to hyperosmolar food (Baltasar et al., 2001; Nelms et al., 2007; ASBS, 2005). However, a skilled surgeon is necessary due to the location of several large blood vessels and the major bile duct next to the duodenum. Injury to these structures can be life-threatening (ASBS, 2005).

**Restrictive Procedures**

*Vertical-banded gastroplasty.* Vertical-banded gastroplasty (VGB) (not shown in Figure 1) combines the creation of a pouch based on the lesser curvature of the stomach and a polypropylene mesh band around the outlet of the pouch (ASBS, 2005). Lack of anastomosis results in a lower risk of contracting infection, and also features low risk of micronutrient deficiencies and mortality (ASBS, 2005). The procedure’s popularity has decreased due to high risk of weight regain and exacerbation of severe heartburn (ASBS, 2005).

*Sleeve gastrectomy.* Sleeve gastrectomy (SG) is a restrictive procedure in which approximately 60% of the stomach is removed laparoscopically so that the stomach takes the shape of a tube, or “sleeve.” This procedure is typically reserved for superobese patients (BMI >50) or high-risk patients, in which performing a malabsorptive or more extreme procedure in the beginning may cause a higher risk of complications. Sleeve gastrectomy is usually performed with the intention of following up with a duodenal switch or Roux-en-Y procedure at a later time, if the patient does not lose enough weight by SG alone (Columbia University Center for Metabolic and Weight Loss Surgery [CUCMWLS]). The combined surgery approach has decreased risk of bariatric surgery for specific groups of patients, even compared to the sum of the risks of the two surgeries. Most patients undergoing sleeve gastrectomy alone can expect to lose 30% to 50% of their excess weight, over a 6- to 12-month period (CUCMWLS). However,
it is also used as a one-stage restrictive long-term procedure and has also been performed on patients who underwent BPD or BPD-DS and failed to achieve adequate weight loss (Frezza, 2007).

Adjustable gastric banding. Laparoscopic adjustable gastric banding (AGB) is the least invasive surgical approach to treat obesity. Instead of cutting the stomach and/or intestine, the gastric band divides the stomach into a small upper pouch above the band and a larger pouch below the band. This restricts the amount of food intake at one given time similar to the restrictive procedures, and no malabsorption is involved (Brown, Korin, Burton & O’Brien, 2009). A unique feature of AGB is that the stoma between the two parts of the stomach can be adjusted after the surgery by altering the amount of saline in the band and is a normal part of follow-up. Because the band can be later adjusted and/or removed and the stomach anatomy is not permanently altered, it is a less drastic option for patients who might not consider other more invasive procedures as viable treatment options. Perioperative death or complication risks are very low, at 0.05% and 2.6%, respectively (Brown, Korin, Burton & O’Brien, 2009). Hospital stays are usually shorter after AGB. Estimated weight loss is approximately 40% to 60% of excess body weight over a two-year span (CUCMWLS). Late complications are usually related to the band becoming displaced, which tend to arise from the patient eating too much food too quickly against a band that is too tight (Brown et al., 2009). Gastric bypass is usually preferred to AGB in the most severely obese patients (Coupaye et al., 2009).

Micronutrient Deficiencies Resulting from Bariatric Surgery

The nutritional and metabolic complications from bariatric surgery can significantly detract from weight loss benefits. In most cases, these complications can be predicted, prevented, and treated. They are to a large degree directly related to the surgically-induced anatomical
changes in the gastrointestinal tract, as well as patient non-compliance with prescribed nutritional supplementation, clinical follow-up visits, and appropriate dietary modifications (Malinowski, 2006). The extent to which nutrients are rendered unavailable to the body is dependent on the type of procedure. Common micronutrient deficiencies that occur in RYGBP and BPD patients include severe malnutrition; vitamin B12, folate, iron, calcium, and fat-soluble vitamin deficiencies (Malinowski, 2006). Figure 2 depicts where macro and micronutrients are absorbed in the gastrointestinal tract.

![Image of absorption sites in the gastrointestinal tract](image)

Figure 2. Absorption sites of the gastrointestinal tract (Bloomberg et al, 2005).
**Vitamin B\textsubscript{12} and Folate Deficiencies**

*Pathophysiology.* Folate is most efficiently absorbed in the jejunum, however, if folate is not continuously supplemented, malabsorption and short bowel problems that result from gastric bypass can quickly result in deficiency (Gropper, Smith & Groff, 2009; Malinowski, 2006). Under normal conditions, vitamin B\textsubscript{12} is released from animal protein sources by hydrochloric acid and pepsin in the stomach. R-binder proteins, secreted by saliva and gastric juices then attach to B\textsubscript{12} are released a second time by pancreatic enzymes in the duodenum. The B\textsubscript{12} molecule then binds to intrinsic factor to form a proteolytic-resistant complex that remains intact until it adheres to specific receptors in the distal ileum prior to absorption (Rhode et al., 1995). After gastric bypass, the pouch does not produce sufficient hydrochloric acid or possibly pepsin to cleave B\textsubscript{12} from ingested protein. Bypass of the duodenum, decreased contact time with the terminal ileum, and intolerance of red meats after bariatric surgery contribute to decreased B\textsubscript{12} bioavailability (Rhode et al., 1995; Malinowski, 2006).

Deficiency of folate and/or B\textsubscript{12} results in megaloblastic macrocytic anemia, a condition in which proerythroblasts and erythrocytes fail to mature and are abnormally large due to dysfunctional DNA synthesis (Gropper et al., 2009). Signs and symptoms are typically of hematologic and neurologic origin; signs include skin pallor, fatigue, palpitations, tingling and numbness in extremities, loss of concentration, disorientation, and dementia (Gropper et al., 2009).

*Diagnosis of deficiency.* Folate status is most often assessed by measuring plasma, serum, or erythrocyte folate concentrations (Gropper et al., 2009). The primary Schilling test measures absorption of B\textsubscript{12} via oral ingestion then intramuscular injection of B\textsubscript{12}. Analysis of a urine sample determines if absorption is sufficient (ADAM Medical Encyclopedia, 2010). Gastric
bypass patients usually show ability to absorb crystalline B\textsubscript{12} by the primary Schilling test (Rhode et al., 1995). Folate deficiency usually consists of a serum level <6.8 ng/mL, while serum B\textsubscript{12} concentrations of <200 pg/mL result in deficiency (Gropper et al., 2009). Measurement of serum methylmalonic acid and homocysteine are more sensitive in diagnosing B\textsubscript{12} deficiency as opposed to measuring serum B\textsubscript{12}. Increased homocysteine concentrations indicate deficiency due to decreased B\textsubscript{12}-dependent enzyme activity (Rhode et al., 1995; Gropper et al., 2009).

**Prevalence of deficiencies after bariatric surgery.** Various studies have been conducted to determine prevalence of folate and B\textsubscript{12} deficiencies after bariatric surgery to establish effectiveness of routine supplementation practices. Table 1 summarizes the characteristics, designs, treatments, results and conclusions of seven studies that measured folate and/or B\textsubscript{12} deficiency prevalence. Limitations of most of these studies include samples of patient populations from a single institution, the majority of subjects being female and of Caucasian descent, and measurement of outcomes after three years or less. The studies also used different values for defining deficiency.

Gasteyger, Suter, Gallard and Giusti (2008) found that at two years post-RYGBP, 80% of the 137 subjects required additional intramuscular B\textsubscript{12} supplementation, and 45% required additional folic acid supplementation, in addition to the standard multivitamin preparation prescribed at their institution (Gasteyger, Suter, Gallard & Giusti, 2008). Patient diet analysis was not included to determine dietary intake of folate and B\textsubscript{12} food sources. The population was divided into two groups based on pre-op BMI and Roux limb length, however B\textsubscript{12} and folate deficiency prevalence and supplementation requirement were not compared between the two groups. The Roux limb length impacts the extent of bile mixing with fats and fat-soluble vitamins, which therefore influences extent of malabsorption and deficiency in RYGBP patients.
(Jin et al., 2009). Addressing any impact of Roux limb length on water-soluble vitamin absorption could provide significant insight on their absorption after RYGBP, which could impact suggested supplementation regimens.

A prospective study of 75 RYGBP patients five or more years after surgery found that 61.8% of their patients were vitamin B₁₂ deficient and 5.5% were folic acid deficient by their last follow-up appointment (Dalcanale et al., 2009). Only one-third of the sample reported reliable adherence to the recommended supplement regimen, which shows a need to place more emphasis on patient education and the importance of supplementation and follow-up compliance (Dalcanale et al., 2009). The authors did not specify whether the RYGBP procedure performed on these patients included long or short-limb modifications. Including Roux-limb length in their analysis would have clarified the extent of malabsorption their patients were expected to experience.

Coupaye et al. (2008) compared gastric bypass and AGB groups, and found lower concentrations of B₁₂ in gastric bypass patients one year after surgery compared to baseline measurement. A low increase in prevalence after gastric bypass was reported, in five patients at baseline compared to six patients at one year. Prevalence in the AGB group increased from 5% of the sample population at baseline to 19% after one year. However, 20 patients began intramuscular supplementation before the one-year mark. Folate deficiency in the AGB group increased from 5% at baseline to 10% after one year, whereas prevalence in the gastric bypass group decreased from 4% at baseline to 0% at one year (Coupaye et al., 2008). Neither the specific method of folate and B₁₂ measurement, nor the specific gastric bypass method, were reported in the literature, and mid-year assessments were not included in the analysis.

Toh et al. (2009) reported an increase in B₁₂ deficiency prevalence from 1% preoperative
to 11% one-year post surgery in their RYGBP group, contrasting a decrease in prevalence from 4% preoperative to 0% at one-year post surgery in their study. Folate deficiency, measured by erythrocyte folate, increased from 1% at baseline to 12% at one-year in the RYGBP group, versus a decrease from 7% to 0% in the sleeve gastrectomy group (Toh et al., 2009). Unfortunately, their sample population experienced a significant loss to follow-up and lack of comprehensive biochemistry results for all patients, which decreases generalization of their results to the general bariatric patient population. Significance of erythrocyte folate has been questioned, because few patients develop megaloblastic anemia (Toh et al., 2009). The study did not disclose the Roux limb length.
<table>
<thead>
<tr>
<th>Author</th>
<th>Design</th>
<th>Treatment</th>
<th>Results</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aasheim et al. (2009)</td>
<td>n=60</td>
<td>Group 1: GBP (23 women, 8 men) Group 2: BPD/DS (19 women, 10 men)</td>
<td>B_{12} concentrations remained stable in BPD/DS patients, and increased in GBP patients.</td>
<td>BPD/DS patients may require different dietary supplements and monitoring than GBP patients.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Duration: 1y post-op Type: Randomized clinical trial</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Daily multivitamin supplement, plus Fe sulfate: 100 mg Ca carbonate: 100 mg Vit D_{3}: 10 µg Folic acid: 200 µg GBP patients received additional B_{12} supplement: 1 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coupaye et al. (2008)</td>
<td>n=70</td>
<td>AGB: 3 men, 18 women GBP: 4 men, 45 women Duration: 1y Type: Prospective study of nutritional parameters</td>
<td>Prevalence of B_{12} deficiency increased in AGB patients from 5% at baseline to 19% after 1y, and in GBP patients from 10% at baseline to 12% after 1y. Folate deficiency in AGB increased from 5% at baseline to 10% at 1y, and decreased from 4% at baseline to 0% at 1y in GBP patients.</td>
<td>Prevalence of deficiencies decreased 1y after GBP in patients taking multivitamin supplements. B_{12} deficits require specific supplementation.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Prevalence of deficiencies decreased 1y after GBP in patients taking multivitamin supplements. B_{12} deficits require specific supplementation.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>GBP: Multivitamin containing B_{1}: 1.6 mg, Folate: 0.8 mg, Vit C: 100mg Vit A: 4,000 IU, Vit E: 15 mg, Vit D_{3}: 500 IU, Ca: 125 mg, Fe: 60mg B_{12} 1,000 µg injections after deficiency observed AGB: None</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dalcanale et al. (2009)</td>
<td>n=8</td>
<td>Duration: &gt;5y after documentation of RYGBP Type: Prospective study of nutritional parameters after open RYGBP &gt;5y prior to study</td>
<td>61.8% of patients exhibited B_{12} deficiency at last follow-up. 5.5% of patients experienced folate acid deficiency at last follow-up. 33.3% reported reliable intake of supplement regimen. Values at two years remained stable until the end of the follow-up period, except for</td>
<td>Priorities should include patient education, more aggressive prescription of and compliance with supplements, and frequent clinical and biochemical follow up.</td>
</tr>
<tr>
<td></td>
<td>67</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study Authors</td>
<td>n=</td>
<td>Total sleeve gastrectomy:</td>
<td>Routine post-op prescription:</td>
<td>B&lt;sub&gt;12&lt;/sub&gt; deficiency treatment:</td>
</tr>
<tr>
<td>-------------------------------------</td>
<td>----</td>
<td>--------------------------</td>
<td>-------------------------------</td>
<td>-------------------------------------</td>
</tr>
<tr>
<td>Gehrer, Kern, Peters, Christoffel-Courtin &amp; Peter (2009)</td>
<td>136</td>
<td>37 women, 13 men</td>
<td>Berocca brand effervescent tablet: 1/: Vit B&lt;sub&gt;1&lt;/sub&gt;: 15 mg Vit B&lt;sub&gt;2&lt;/sub&gt;: 15 mg Vit B&lt;sub&gt;6&lt;/sub&gt;: 10 mg Vit B&lt;sub&gt;12&lt;/sub&gt;: 0.01 mg Vit C: 500 mg Folic acid: 0.4 mg Ca: 100 mg Zn: 10 mg</td>
<td>Vitarubin brand 1 ampulla/1ml; 1,000 µg cyanocobalamin via injection. Folate deficiency treatment: Folvite brand 1mg/d</td>
</tr>
<tr>
<td>Gasteyger, Suter, Gallard, &amp; Guisti (2008)</td>
<td>110</td>
<td>27 men after RYGBP Group 1: n=90; pre-op BMI of ≤48.0</td>
<td>Standardized multivitamin preparation prescribed between first and sixth postoperative months: Vit A: 800 µg Vit B&lt;sub&gt;12&lt;/sub&gt;: 3 µg Vit C: 180 mg Folic acid: 0.6 mg Vit D: 5 µg Zn: 8 mg</td>
<td>Specific substitutions: Vit B&lt;sub&gt;12&lt;/sub&gt;: 1 mg/mo Fe: 80 mg/d Ca: 1000 mg/d Vit D: 0.02 mg/d Folic acid: 1mg/d Zn: 5 mg/d</td>
</tr>
<tr>
<td>Toh, Zarshenas, &amp; Jorgensen (2009)</td>
<td>232</td>
<td>12 men, 35 women</td>
<td>All patients: liquid, effervescent, or chewable multivitamin and mineral supplement/d RYGBP patients: In addition to standard supplement, additional calcium citrate 1500 mg B&lt;sub&gt;12&lt;/sub&gt; 1000 µg injections every 6 mo Fe supplements if deficient</td>
<td>B&lt;sub&gt;12&lt;/sub&gt; deficiency prevalence increased from 1% at baseline to 11% at 1y in RYGBP patients. Prevalence decreased from 4% at baseline to 0% at 1y in SG patients. RBC folate deficiency increased in RYGBP from 1% to 12%, but decreased in SG from 7% to 0%.</td>
</tr>
</tbody>
</table>
Vargas-Ruiz et al. (2007) performed a retrospective analysis of 30 patients at their outpatient clinic who completed a minimum follow-up period of at least two years after RYGBP. They noted a progressive increase in B₁₂ deficiency prevalence from 0% prior to surgery to 3.3%, 6.6%, 16.6%, and 18% at six months, one year, two years, and three years post-procedure, respectively. Overall B₁₂ deficiency prevalence, including cases of combined B₁₂ and iron deficiency, was recognized in 27% of patients at year three. Folate deficiency was not observed in their sample population. Vitamin B₁₂ deficiency was not evident before patients completed at least two years of follow-up appointments (Vargas-Ruiz et al., 2007).

Aasheim et al. (2009) performed a randomized control trial in which patients underwent either laparoscopic RYGBP or BPD/DS, then underwent follow-up at six weeks, six months, and one year after surgery. They reported increased B₁₂ concentrations in the RYGBP group after additional supplementation, and stable concentrations in BPD/DS patients, who did not receive additional B₁₂ supplementation (Aasheim et al., 2009).

Treatment. A clinical trial to determine the most effective therapeutic dose of oral crystalline vitamin B₁₂ found that in 102 patients who underwent RYGBP, isolated RYGBP, or gastroplasty, whose average serum B₁₂ levels were 90 ± 21 pmol/L, that at least 350 µg/d of crystalline B₁₂ was required to maintain serum levels at or above the reference range of ≥ 150.
pmol/L in 95% of the sample population. Homocysteine levels dropped below the cut-off point with the 350 µg/d dosage but did not drop further with larger doses (p >0.40); despite being statistically insignificant, this result is still relevant because it is important to determine appropriate dosage of B₁₂ supplementation for bariatric patients. Continuous therapy was found to be necessary, as serum B₁₂ levels declined rapidly over three months post treatment (Rhode et al., 1995).

Most of the previously cited studies concluded that standard multivitamin supplementation was usually insufficient to prevent folate and B₁₂ deficiencies and B₁₂ supplementation should be patient-specific. Frequent clinical follow-up is necessary (Dalcanale et al., 2009; Vargas-Ruiz, Hernandez-Rivera & Herrera, 2007; Gehrer et al., 2009; Aasheim et al., 2009; Toh., 2009; Coupaye et al., 2008; Gasteyger et al., 2008).

Iron Deficiency

Pathophysiology. Iron deficiency after gastric bypass arises from several characteristics of the procedure. Low red meat tolerance is a common result of bariatric surgery, which results in decreased consumption (Ruz et al., 2009). Greatly reduced stomach capacity strictly limits hydrochloric acid and protease secretion, which are required to hydrolyze heme iron from proteins. Reduction in intestinal absorption surface area after gastric bypass consequently results in less iron absorption capacity, as absorption is highest in the duodenum and initial portions of the jejunum (Gropper et al., 2009; Ruz et al., 2009). Prolonged deficiency ultimately manifests as iron deficiency anemia, which results in skin pallor, fatigue, impaired cognitive performance, decreased work productivity, and decreased resistance to infection (Gropper et al., 2009).

Prevalence of deficiency and treatment recommendations after bariatric surgery.

Overall, iron deficiency after VGB and AGB is considered rare, but is a more common result of
RYGBP and BPD/DS (Malinowski, 2006 & Shah, Simha & Garg, 2010). Table 2 summarizes nine studies of iron deficiency prevalence in patients after bariatric surgery. Many of these studies suffered from the same pitfalls of the previously mentioned B₁₂ and folate studies: they were studies of a patient population of a single institution, the majority of sample populations consisted of premenopausal Caucasian women, measurement of outcomes after three years or less, and the retrospective cohort studies did not include dietary intake data in their analyses. Not all of the studies used a uniform indicator to define deficiency.

Ruz et al. (2007) tested the effectiveness of an “improved” supplement regimen against their institution’s standard multivitamin recommendation after RYGBP. Typical dietary intake was assessed via a 3-day food record and computer analysis; red meat consumption decreased by about half post-op versus pre-op amounts. Anemia prevalence increased from 1.5% prior to surgery to 38.8% at 18 months (Ruz et al., 2007). Vitamin C concentration was reduced from 250 mg/d in the standard group to 100 mg/d in the “improved” group. Analysis did not include the effect of this decrease on iron absorption, as simultaneous vitamin C ingestion with non-heme iron is known to increase absorption (Ruz et al., 2007; Gropper et al., 2009). These authors found that iron absorption from both a standard diet and a typical dose of ferrous iron ascorbate significantly decreased after six months of RYGBP, and an average supplemental iron intake of approximately 20 mg/d was largely insufficient in preventing deficiency. Improved highly available iron formulations or periodic parenteral infusions are likely necessary to prevent deficiency after RYGBP (Ruz et al., 2007).
Table 2. Summary of iron deficiency studies.

<table>
<thead>
<tr>
<th>Author</th>
<th>Design</th>
<th>Supplementation</th>
<th>Results</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ruz et al. (2007)</td>
<td><strong>n = 67 menstruating women after RYGBP</strong>&lt;br&gt;n completed = 51&lt;br&gt;<strong>Duration:</strong> 18 mo&lt;br&gt;<strong>Group A:</strong> Standard vitamin and mineral supplementation&lt;br&gt;<strong>Group B:</strong> “Improved” vitamin and mineral supplementation&lt;br&gt;<strong>Type:</strong> Experimental trial</td>
<td><strong>Standard:</strong>&lt;br&gt;Fe: 0 mg&lt;br&gt;Ca: 640 mg&lt;br&gt;Zn: 7.5 mg&lt;br&gt;Cu: 1000 µg&lt;br&gt;Se: 15 µg&lt;br&gt;Vit C: 250 mg&lt;br&gt;Vit E: 200 mg&lt;br&gt;Folic acid: 0 mg&lt;br&gt;Vit A: 0 µg&lt;br&gt;Vit D: 250 IU</td>
<td>Differences in Fe absorption in A and B were not significant at 6, 12 and 18 mo. Prevalence of anemia increased from 1.5% at baseline to 38.8% at 18 mo Prevalence of Fe-deficiency anemia at 18 mo: 23.9%</td>
<td>Average supplemental Fe intake of ~20 mg/day is insufficient to prevent Fe deficiency after RYGBP.</td>
</tr>
<tr>
<td>Coupaye et al. (2008)</td>
<td><strong>n = 70</strong>&lt;br&gt;AGB: 3 men, 18 women&lt;br&gt;GBP: 4 men, 45 women&lt;br&gt;<strong>Duration:</strong> 1y&lt;br&gt;<strong>Type:</strong> Prospective study of nutritional parameters</td>
<td>GBP: Multivitamin containing B₁: 1.6 mg, Folate: 0.8 mg, Vit C: 100mg, Vit A: 4,000 IU, Vit E: 15 mg, Vit D₃: 500 IU, Ca: 125 mg, Fe: 60mg&lt;br&gt;B₁₂ 1,000 µg injections after deficiency observed&lt;br&gt;AGB: None</td>
<td>Fe deficiency anemia increased from 4% at baseline to 10% after 1y in GBP&lt;br&gt;Fe deficiency anemia prevalence did not change from baseline to 1y after AGB (10%). Overall prevalence considered low.</td>
<td>Prevalence of deficiencies decreased 1y after GBP in patients taking multivitamin supplements. Assessment of transferrin saturation is required to evaluate risk of Fe deficiency in obese patients.</td>
</tr>
<tr>
<td>Dalcanale et al. (2009)</td>
<td><strong>n = 8 men, 67 women</strong>&lt;br&gt;<strong>Duration:</strong> &gt;5y after documentation of RYGBP&lt;br&gt;<strong>Type:</strong> Prospective study of nutritional parameters after open RYGBP ≥5y prior to study</td>
<td>Materna, 1 tablet/d:&lt;br&gt;Retinol: 5,000 IU&lt;br&gt;Cholecalciferol: 400 IU&lt;br&gt;Vit C: 100 mg&lt;br&gt;Folic acid 1 mg&lt;br&gt;Tocopherol acetate: 30 IU&lt;br&gt;Vit B₁₂: 12 µg&lt;br&gt;Ca: 250 mg&lt;br&gt;Fe: 60 mg&lt;br&gt;Cu: 2 mg&lt;br&gt;Zn: 25 mg</td>
<td>Deficiencies in Hgb (50.8%), Fe (29.8%), and ferritin (36.0%) were evident at last follow up. 33.3% reported reliable intake of supplement regimen. Values at two years remained stable until the</td>
<td>Priorities should include patient education, more aggressive prescription of and compliance with supplements, and frequent clinical and biochemical follow up.</td>
</tr>
<tr>
<td>Study</td>
<td>Study Details</td>
<td>Outcome Summary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------</td>
<td>---------------</td>
<td>-----------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gehrer, Kern, Peters, Christoffel-Courtin &amp; Peter (2009)</td>
<td>n= 136 total sleeve gastrectomy: 37 women, 13 men RYGBP: 61 women, 15 men <strong>Duration:</strong> Routine follow up until 36 mo <strong>Type:</strong> Prospective study</td>
<td>Routine post-op prescription: Berocca brand effervescent tablet 1/d: Vit B₁: 15 mg Vit B₂: 15 mg Vit B₆: 10 mg Vit B₁₂: 0.01 mg Vit C: 500 mg Folic acid: 0.4 mg Ca: 100 mg Zn: 10 mg <strong>Treatment of:</strong> Fe deficiency: 100 mg iron II glycine sulphate 1/d or 300-900 mg iron III hydroxide saccharose 1-2/yr</td>
<td>Prevalence in Fe deficiency increased from 3% post-op to 18% after sleeve gastrectomy and 28% after RYGBP at year 3 (P value: NS). Sleeve gastrectomy leads to fewer deficiencies in first 2y than RYGBP. General multivitamin supplements alone do not prevent specific deficiencies</td>
<td></td>
</tr>
<tr>
<td>Hakeam, O’Regan, Salem, Bamerhriz, &amp; Eldali (2009)</td>
<td>n= 31 men and 30 women after sleeve gastrectomy <strong>Duration:</strong> 1y <strong>Type:</strong> Prospective cohort</td>
<td>ADEKs brand Fe-free multivitamin: folic acid: 0.2 mg cyanocobalamin: 12 mcg</td>
<td>Fe deficiency increased from 0% to 3% after 6-mo and 12-mo post-op (Two females and one male). Impact of sleeve gastrectomy on Fe indices was negligible. Fe supplementation is likely unnecessary in non-anemic patients.</td>
<td></td>
</tr>
</tbody>
</table>
| Gasteyger, Suter, Gallard, & Guisti (2008) | n= 110 women, 27 men after RYGBP Group 1: n=90; pre-op BMI of ≤48.0 RYGBP limb: 100 cm Group 2: n=47 BMI >48.0 RYGBP limb: 150 cm **Duration:** minimum 2y follow-up at clinic **Type:** Retrospective | Standardized multivitamin preparation prescribed between first and sixth postoperative months: Vit A: 800 µg Vit B₁₂: 3 µg Vit C: 180 mg Folic acid: 0.6 mg Vit D: 5 µg | Specific substitutions: Vit B₁₂: 1 mg/mo Fe: 80 mg/d Ca: 1000 mg/d Vit D: 0.02 mg/d Folic acid: 1mg/d Zn: 5 mg/d 60% of patients were prescribed additional Fe supplementation at 24 months due to Fe deficiency. Post-operative supplementation with a standardized multivitamin alone is not adequate to prevent nutritional deficiencies after RYGBP.
<table>
<thead>
<tr>
<th>Study</th>
<th>n=</th>
<th>Type</th>
<th>Duration</th>
<th>Treatment</th>
<th>Prevalence of Fe deficiency</th>
<th>Conclusion</th>
</tr>
</thead>
</table>
| Toh, Zarshenas, & Jorgensen (2009)       | 232 | Retrospective cohort        | 1y             | All patients: liquid, effervescent, or chewable multivitamin and mineral supplement/d  
RYGBP patients: In addition to standard supplement, additional calcium citrate 1500 mg  
B$_{12}$ 1000 µg injections every 6 mo Fe supplements if deficient | Prevalence in Fe deficiency increased from 2% pre-op to 21% 1y post-op in RYGBP.  
Prevalence in Fe deficiency at pre-op and 1y post-op remained at 0% in SG patients. | Routine nutrition screening, recommendation of appropriate supplements and adherence monitoring is necessary. |
| Vargas-Ruiz, Hernandez-Rivera & Herrera (2007) | 25 | Retrospective cohort        | Minimum 2y follow-up at clinic | Uniformly-prescribed Centrum vitamin and mineral supplements:  
Dosage: 1 tablet/day  
Contents:  
Fe: 18 mg  
Folic acid: 400 µg  
Cobalamin: 6 µg | Prevalence of Fe deficiency increased from 16.6% at baseline to 23.3% at 2y.  
Five patients diagnosed with isolated Fe deficiency remained deficient after 2y. | Routine practice of vitamin supplementation is not sufficient in preventing Fe deficiency. |
(elemental Fe: 65 mg) 3-4/d  
or ferrous fumarate 324 mg  
(elemental iron 106 mg) 2/d  
Parenteral Fe sucrose complex  
(Venofer, 20mg elemental Fe/ml) | The number of anemia-related hospitalizations and additional therapy was greater for patients who underwent BPD/DS.  
Incidence after AGB was very low (4.76%).  
The median interval between surgery and parenteral Fe replacement was 42.5 months. | Patients who do not respond to oral Fe therapy should be referred early for parental Fe.  
Fe monitoring should continue indefinitely after surgery, especially in premenopausal women. |

Retrospective and prospective cohort studies on iron deficiency largely concluded that routine iron and multivitamin supplementation are inadequate to prevent deficiency after
RYGBP, and life-long supplementation, frequent clinical follow-up and adherence to supplementation are necessary to prevent deficiency (Vargas-Ruiz, Hernandez-Rivera & Herrera, 2007; Gasteyger, Suter, Gallard, & Guisti, 2008; Toh, Zarshenas, & Jorgensen, 2009; Dalcanale et al., 2009; Gehrer, Kern, Peters, Christoffel-Courtin & Peter, 2009; Varma et al., 2008).

Vargas-Ruiz et al. (2007) found an increase in prevalence from 16.6% before RYGBP to 23.3% at year two (Vargas-Ruiz et al., 2007). Neither diet assessment, nor vitamin C intake with the supplement, were included in the analysis, nor were other study limitations included in the discussion. Gasteyger et al. (2008) noted that in their sample population, iron supplementation was second to vitamin B\textsubscript{12} in frequency (60%) by year two (Gasteyger et al., 2008). As seen with the previous study, dietary intake was not included in the analysis. Toh et al. (2009) found that iron deficiency increased from 2% in their RYGBP group to 21% at one year post surgery. Mean ferritin levels dropped significantly in the SG group at one year post surgery, but deficiency never occurred. As previously mentioned in the folate and B\textsubscript{12} analysis of this paper, the significant loss to follow up and lack of biochemistry labs available hindered their attempt at a more comprehensive analysis of their population (Toh et al., 2009).

Varma et al. (2008) studied bariatric patients who received parenteral iron replacement therapy after failure of oral supplementation, and found that hospitalization due to anemia and additional iron replacement after the first treatment were more likely to occur after BPD/DS than RYGBP, and incidence after AGB was very low, at 4.76%. The median interval period between bariatric surgery and date of first parenteral iron replacement therapy was 42.5 months. Premenopausal women experienced a much shorter average interval time than men and postmenopausal women. They also emphasized the need for lifelong follow up and early referral for parenteral iron replacement therapy if patients fail to respond to oral supplementation (Varma
et al., 2008).

In their prospective cohort, Coupaye et al. (2009) noted an increase in iron deficiency from 4% at baseline to 10% after one year of undergoing gastric bypass. The number of reported cases did not change in the AGB group, but overall prevalence of deficiency after both procedures was considered low. Very few patients took additional oral supplements at year one. (Coupaye et al., 2009). The low prevalence may have been due to a routine supplementation practice that contained higher concentrations of iron (60 mg/d) than other typical supplementation regimens. However, the specific gastric bypass procedure was not reported in their study.

Dalcanale et al. (2009) reported deficiencies after RYGBP of 50.8%, 29.8% and 36.0% in hemoglobin, iron and ferritin, respectively, and massive weight loss, frequent vomiting, dumping syndrome, and women of reproductive age were observed as high-risk for developing anemia. As noted previously, only about one-third of patients reported reliable intake of recommended supplementation at year one (Dalcanale et al., 2009). Gehrer et al. (2010) studied SG and RYGBP and observed an increase in iron deficiency prevalence from 3% post surgery to 18% after SG and 28% after RYGBP at 36 months. Patients were regularly consulted by a dietitian to assess diet quality, but food records were not taken and thus not analyzed (Gehrer et al., 2010). A unique feature of this study was the extent of the study length, at three years.

Hakeam, O’Regan, Salem, Bamerhriz, and Eldali (2009) ran a prospective cohort of sleeve gastrectomy on iron indices. They noted a very low increase in prevalence in iron deficiency at one year post surgery, and concluded that supplementation is likely unnecessary in non-anemic patients undergoing the sleeve gastrectomy procedure. However, the patient population was primarily Arab, and management of B₁₂ deficiency was not consistently managed
in the study, which may decrease generalizability to other patient populations and may have skewed the results (Hakeam, O’Regan, Salem, Bamerhriz, & Eldali, 2009).

**Vitamin D and Calcium Deficiency**

*Pathophysiology.* Both vitamin D and calcium are well-known for their role in building strong bones. Vitamin D is usually obtained through the diet, supplementation, or sunlight exposure. With the help of bile, Vitamin D₃ is absorbed most rapidly in the duodenum, but the largest amount is absorbed in the distal small intestine (Gropper et al., 2009). Prevalence of vitamin D deficiency prior to bariatric surgery has been reported at rates of 60% to 80% (Toh et al., 2009). Superobese patients usually must undergo the RYGBP procedure with a longer Roux limb length, which increases malabsorption of vitamin D and other fat-soluble vitamins due to poor mixing of bile salts that are required for its proper absorption (Jin et al., 2009).

Calcium is primarily absorbed in the duodenum and proximal jejunum, which are typically bypassed after RYGBP, which results in decreased absorption (Johnson et al., 2006). Calcium absorption is vitamin D dependent and is involved in parathyroid hormone (PTH) homeostasis, which regulates blood calcium and bone turnover (Gropper et al., 2009).

*Diagnosis of deficiency.* Assessment of vitamin D status involves measuring 25-OH D₃, which should be maintained >30 ng/mL (Gropper et al., 2009). Serum calcium concentrations normally range from approximately 8.5 to 10.5 mg/dL in adults. Serum ionized calcium can reflect alterations in calcium metabolism. Bone density is typically assessed through imaging such as dual-energy X-ray absorptiometry (DEXA) (Gropper et al., 2009).

*Consequences of deficiency.* The major adverse effect of chronic vitamin D and calcium depletions in morbidly obese patients undergoing RYGBP is metabolic bone disease, which manifests as osteopenia, osteoporosis, and ultimately osteomalacia (Johnson et al., 2006).
Metabolic bone disease results from secondary hyperparathyroidism (HPT). An inverse relationship exists between calcium and blood pressure, and is also thought to decrease colorectal cancer risk through its ability to bind carcinogenic bile acids and free fatty acids. (Gropper et al., 2009). Emerging research in vitamin D suggests that it significantly impacts the cardiovascular, neuromuscular and immune systems, and participates in cell proliferation, differentiation, and apoptosis (Carlin, Rao, Yager, Parikh & Kapke, 2008).

Prevalence of deficiency after bariatric surgery. Table 3 summarizes eight vitamin D and calcium studies. Carlin, Rao, Yager, Parikh and Kapke (2009) found that vitamin D deficiency prevalence decreased significantly in patients who received weekly pharmacologic doses of 50,000 IU/week in addition to the standard 800 IU/d versus the control group, who received only the standard supplementation (Carlin et al., 2009). However, secondary HPT persisted in the group receiving the pharmacological dosage. Therefore, additional factors might contribute to persistent HPT after RYGBP, such as calcium malabsorption. Hip bone mineral density (BMD) decreased by one-third in the supplemented group as opposed to the control group (Carlin et al., 2009). Aasheim et al. (2009) observed that BPD/DS might be associated with higher risk of vitamin D deficiency than RYGBP (Aasheim et al., 2009). Toh et al. (2009) noted a decrease in deficiency from more than half prior to surgery to 30% after RYGBP and 42% after GS at one year, however they were unable to account for seasonal variations in preoperative 25-OHD levels, and as previously mentioned the study suffered from a large loss to follow up (Toh et al., 2009). The impact of Roux limb length was not disclosed in their study; including Roux limb length in the analysis would provide additional insight into how it impacted absorption in their sample population. Coupaye et al. (2009) found that better supplement regimen compliance resulted in greater reductions in deficiency (Coupaye et al., 2009). As previously mentioned, the
authors did not disclose the specific gastric bypass procedure, which would have provided additional insight into the expected extent of vitamin D malabsorption and how supplementation impacted expected deficiency.

Gasteyger et al. (2008) observed that 60% of patients required vitamin D and calcium supplementation at two years after gastric bypass, and deficiency risk was higher in patients with a BMI >48.0 who required a longer Roux limb. The proportion of patients who required calcium and vitamin D₃ supplementation post-op was significantly higher in group 2, who required a longer Roux limb, than in group 1, who required a shorter Roux limb (74% compared with 52% respectively; P value=0.02) (Gasteyger et al., 2008).

Johnson, Maher, DeMaria, Downs, Wolfe, & Kellum (2006), in their longitudinal study, observed a similar result to Gastgeyer et al. (2009), in which patients with a Roux limb >100 cm had a significantly lower serum 25-OHD level than patients with a Roux limb <100 cm, and progressive increase in prevalence the longer patients were followed up after the procedure. Average post-op follow-up was longer in the >100 cm group (5.7 ± 2.5 years) when compared to the <100 cm group (3.1 ± 3.6 years) (Johnson et al., 2006). This difference in the extent of follow-up may have skewed the results, as equivalent extent of follow-up in both groups may or may not have revealed increased prevalence of deficiency in the shorter Roux limb group.

A study by Flores et al. (2010) found vitamin D insufficiency and deficiency in 80% of their sample population, which significantly decreased after one year. They were able to observe seasonal variations in serum vitamin D concentrations, however their results may have been affected by the unavailability of calcium citrate at their facility in Spain (Flores et al., 2010).

Jin et al. (2009) identified several independent risk factors for developing vitamin D deficiency after RYGBP: being of African-American descent, having a pre-operation serum 25-
OHD level of <16 ng/mL, and having a Roux limb of ~160 cm. Prevalence of vitamin D deficiency in their study increased from 41% prior to surgery to 42% after one year. By year one, 71% patients who were deficient prior to surgery remained deficient, despite oral vitamin D and calcium supplementation (Jin et al., 2009). The authors did appear to monitor supplement adherence monitoring in their patient sample. Lack of patient accountability weakens their conclusion, as poor adherence would increase risk of deficiency while causing their independent risk factors to be viewed as the main predictors of vitamin D deficiency.

Treatment. No consensus currently exists regarding the amount of supplemental vitamin D required to optimize nutritional status and to prevent potential adverse effects of deficiency in patients after RYGBP (Carlin et al., 2009). A recent randomized control trial found that calcium citrate was superior to calcium carbonate in bioavailability and ability to reduce PTH after RYGBP. Calcium carbonate absorption is dependent on gastric acid secretion, whereas calcium citrate is partially soluble in water, allowing for increased bioavailability (Tondapu et al. 2009). Vitamin D doses as high as 50,000 IU/week have been suggested to treat deficiency. Serum 25-OHD should be checked every six to twelve months to detect deficiency early (Carlin et al., 2009). At most institutions, the common daily recommended amount of vitamin D is 400 I.U. to 800 I.U. However, this regimen is based on requirements of non-obese patients and does not account for malabsorption of vitamin D after gastric bypass surgery (Jin et al., 2009).
<table>
<thead>
<tr>
<th>Author</th>
<th>Design</th>
<th>Supplementation</th>
<th>Results</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aasheim et al. (2009)</td>
<td><strong>n=60</strong> Group 1: GBP (23 women, 8 men) Group 2: BPD/DS (19 women, 10 men)</td>
<td><strong>Duration</strong>: 1y post-op <strong>Type</strong>: Randomized clinical trial Daily multivitamin supplement, plus Fe sulfate: 100 mg Ca carbonate: 100mg Vit D3: 10 µg Folic acid: 200 µg GBP patients received additional B12 supplement: 1 mg</td>
<td>25-OHD concentrations increased in RYGBP patients (P &lt; 0.001) but tended to decrease among BPD/DS patients (P = 0.059). PTH and ionized calcium concentrations did not change significantly after surgery. 1,25 dihydroxyvitamin D concentrations increased during the 1y follow-up (P &lt;0.001).</td>
<td>BPD/DS may be associated with greater risk of vitamin D deficiency the first year after surgery.</td>
</tr>
<tr>
<td>Carlin, Rao, Yager, Parikh, &amp; Kapke (2009)</td>
<td><strong>n=60</strong> morbidly obese, Vit D depleted women <strong>Duration</strong>: 1 yr after RYGBP <strong>Type</strong>: Randomized clinical trial Both groups: Vitamin D: 800 IU/d Calcium: 1500mg/d Group 1: Additional 50,000 IU vitamin D/weekly Group 2: No additional vitamin D supplementation</td>
<td>Group 1 experienced significantly lower vitamin D depletion at 3, 6 and 12 mo post surgery. The magnitude of decline in hip BMD was 33% lower in group 1. HTN resolution was 75% in group 1 vs. 32% in group 2. Bone turnover elevations existed in both groups.</td>
<td>A weekly pharmacologic dose of 50,000 IU of vitamin D appears safe and effective in improving depletion after RYGBP in morbidly obese patients. Secondary HPT persisted in group 1 despite increased serum 25-OHD levels, likely due to calcium malabsorption.</td>
<td></td>
</tr>
<tr>
<td>Coupaye et al. (2008)</td>
<td><strong>n= 70</strong> AGB: 3 men, 18 women GBP: 4 men, 45 women <strong>Duration</strong>: 1y <strong>Type</strong>: Prospective study of nutritional parameters GBP: Multivitamin containing B1: 1.6 mg, Folate: 0.8 mg, Vit C: 100mg, Vit A: 4,000 IU, Vit E: 15 mg, Vit D3: 500 IU, Ca: 125 mg, Fe: 60mg B12: 1,000 µg injections after deficiency observed AGB: None</td>
<td>25OH-D deficiency decreased from 14% at baseline to 5% at 1y after AGB, and from 16% at baseline to 10% at 1y after gastric bypass. Vitamin D was significantly higher in patients with a good index of medication adherence.</td>
<td>Prevalence of deficiencies decreased 1y after GBP in patients taking multivitamin supplements.</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>n</td>
<td>After RYGBP</td>
<td>Duration</td>
<td>Type</td>
</tr>
<tr>
<td>-------</td>
<td>---</td>
<td>-------------</td>
<td>----------</td>
<td>------</td>
</tr>
<tr>
<td>Flores et al. (2010)</td>
<td>n=222</td>
<td>after RYGBP</td>
<td>1y</td>
<td>Prospective cohort</td>
</tr>
<tr>
<td>Johnson, Maher, DeMaria, Downs, Wolfe, &amp; Kellum (2006)</td>
<td>n=243</td>
<td></td>
<td>&gt;5y</td>
<td>Prospective longitudinal cohort</td>
</tr>
<tr>
<td>Gasteyger, Suter, Gallard, &amp; Guisti (2008)</td>
<td>n=110 women, 27 men</td>
<td></td>
<td>minimum 2y follow-up at clinic</td>
<td>Retrospective cohort</td>
</tr>
</tbody>
</table>

**Flores et al. (2010)**

- **n=222** after RYGBP
- **Duration:** 1y
- **Type:** Prospective cohort

  - Elemental calcium carbonate: 1200 mg/d and vitamin D₃: 800 IU as combined chewable tablets
  - Dietetic reinforcement with calcium-rich foods.

  - Baseline insufficiency and deficiency of vitamin D observed in 80% of patients. 25OH-D significantly increased and PTH decreased at 1y compared to preop values.

**Johnson, Maher, DeMaria, Downs, Wolfe, & Kellum (2006)**

- **n=243**
  - Roux >100 cm: 41
  - Roux <100 cm: 202
- **Duration:** >5y
- **Type:** Prospective longitudinal cohort

  - Roux >100 cm had a significantly lower serum D level when compared to those with Roux <100 cm. 88.9% had an elevated PTH, and 42.1% of those with normal vitamin D levels had elevated PTH. Vitamin D levels progressively decreased and PTH levels increased the longer patients were followed up after surgery. Beyond 5 years of follow up, few patients had levels > 30 ng/mL.

**Gasteyger, Suter, Gallard, & Guisti (2008)**

- **n=110 women, 27 men** after RYGBP
  - Group 1: n=90; pre-op BMI of ≤48.0
  - RYGBP limb: 100 cm
  - Group 2: n=47
  - BMI >48.0
  - RYGBP limb: 150 cm
- **Duration:** minimum 2y follow-up at clinic
- **Type:** Retrospective cohort

  - Standardized multivitamin preparation prescribed between first and sixth postoperative months:
    - Vit A: 800 µg
    - Vit B₁₂: 3 µg
    - Vit C: 180 mg
    - Folic acid: 0.6 mg
    - Vit D: 5 µg
    - Zn: 8 mg

  - Specific substitutions:
    - Vit B₁₂: 1 mg/mo
    - Fe: 80 mg/d
    - Ca: 1000 mg/d
    - Vit D: 0.02 mg/d
    - Folic acid: 1 mg/d
    - Zn: 5 mg/d

  - Calcium + vitamin D₃ supplementation was required in 60% of patients by 2y. In group 2, 74% of patients required calcium and D₃ supplementation compared to 52% in group 1. Prevalence of vitamin D and calcium deficiency increases significantly with the length of the RYGBP limb.

  - Post-operative supplementation with a standardized multivitamin alone is not adequate to prevent nutritional deficiencies after RYGBP.
General Prevention and Treatment Recommendations, and Future Research

Prevention and Treatment

Many of the studies mentioned in this review noted poor patient compliance to recommended supplementation regimens, and suggested frequent, life-long follow-up to detect deficiencies early. Patients have many reasons for not complying with supplemental prescriptions. Oral iron supplements are known to cause digestive problems, which discourages...
regular intake (Coupaye et al., 2009). Gesteyger et al. (2008) estimated that two years post
RYGBP, patients would have to spend an average of $35 USD monthly for nutritional
supplements, an amount high enough to impair compliance in a significant proportion of patients
in countries in which health insurance does not cover these costs (Gesteyger et al., 2008).

Other known predictors of poor adherence include depression, treatment of asymptomatic
disease, complexity of taking many supplements, and lack of belief in the benefit of treatment
(Aasheim et al., 2009).

Over-the-counter multivitamin and mineral supplements do not provide adequate
concentrations of certain micronutrients, such as B₁₂, iron, or fat-soluble vitamins, and patients
will require life-long prophylactic supplementation to maintain optimal nutrient status (Shankar,
Boylan, & Sriram, 2010). Development of a single “multi-pill” or injection containing
appropriate doses of vitamin B₁₂, iron, calcium, vitamin D₃, and folic acid would facilitate
compliance and reduce the patient’s cost burden (Gasteyger, 2008). In order to get the most out
of their supplementation regimen, patients should be made aware of foods that can enhance or
inhibit absorption of micronutrients, such as iron being inhibited by tea consumption but
enhanced by vitamin C consumption (Coupaye et al., 2009). A possible learning tool to use in
bariatric surgery counseling for patients is a pyramid in the likeness of the USDA Food Guide
Pyramid, which includes reminders for supplements at its base (Moize, Pi-Sunyer, Mochari &
Vidal, 2010). Figure 3 below depicts the suggested pyramid guide for gastric bypass patients.
Future Research Needs

As previously noted, most of the studies included in this review were limited by short intervals between undergoing bariatric surgery and last follow-up, the longest was up to five years post-surgery (Dalcanale et al., 2009). Further study of long-term health outcomes after bariatric surgery is especially important in regards to deficiencies such as vitamin D and calcium, which can lead to severe bone loss and greater risk of fracture, and iron, which can suppress the immune system and increase susceptibility to life-threatening infections. These long-term studies would ideally be prospective in nature in order to establish time-order relationships and capture and analyze diet, and in the case of vitamin D, sun exposure. Ideally patient populations would be more diverse, as the studies cited in this paper had sample populations who were overwhelmingly Causasian women of reproductive age, which decreases generalizability toward
other ethnicities, ages, and men. Patient education and motivation should also be explored in order to determine the best methods of increasing and encouraging supplementation compliance.
REFERENCES


