Harrington *et al. Metab Target Organ Damage* 2024;4:11
DOI: 10.20517/mtod.2023.46

Metabolism and Target Organ Damage

Review

Open Access

Long-term complications of significant weight loss: lessons learned from bariatric surgery

Sarah Harrington[1], Sydney Kang[2], Lauren Telesca[3], Ricardo V Cohen[4], Carel W Le Roux[5]

[1]Renaissance School of Medicine, Stony Brook University, Stony Brook, NY 11794, USA.
[2]Milken Institute of Public Health, George Washington University, Washington, DC 20052, USA.
[3]Renaissance School of Medicine, Stony Brook University, Stony Brook, NY 11794, USA.
[4]The Center for the Treatment of Obesity and Diabetes, Hospital Oswaldo Cruz, São Paulo 01323-903, Brazil.
[5]Diabetes Complications Research Unit, University College Dublin, Dublin D04 V1W8, Ireland.

Correspondence to: Prof. Carel W Le Roux, Diabetes Complications Research Unit, University College Dublin, Dublin D04 V1W8, Ireland. E-mail: carel.leroux@ucd.ie; Prof. Ricardo V Cohen, The Center for the Treatment of Obesity and Diabetes, Hospital Oswaldo Cruz, Rua 13 de maio, 1815, 1° andar, São Paulo 01323-903, Brazil. E-mail: ricardo.cohen@haoc.com.br

How to cite this article: Harrington S, Kang S, Telesca L, Cohen RV, Roux CWL. Long-term complications of significant weight loss: lessons learned from bariatric surgery. *Metab Target Organ Damage* 2024;4:11. https://dx.doi.org/10.20517/mtod.2023.46

Received: 28 Nov 2023 **First Decision:** 30 Jan 2024 **Revised:** 21 Feb 2024 **Accepted:** 29 Feb 2024 **Published:** 14 Mar 2024

Academic Editor: Wah Yang **Copy Editor:** Yanbing Bai **Production Editor:** Yanbing Bai

Abstract

The increasing prevalence of worldwide obesity calls for a comprehensive understanding of available treatment options. Bariatric surgery remains a very effective obesity treatment, showing substantial effects on obesity-related complications, including type 2 diabetes mellitus and cardiovascular disease, mainly related to significant long-term weight loss. Besides the benefits, weight loss can lead to some deleterious consequences, such as gallstones, constipation, muscle mass loss, bone fractures, vitamin deficiencies, peripheral neural palsy, suicide, eating disorders, alcohol dependency syndrome, and increased divorce. Those consequences may also be seen after long-term effective pharmacotherapy for obesity. Understanding these risks will lead to improved awareness and successful treatment with both surgical and nonsurgical treatments.

Keywords: Bariatric surgery, body composition, eating disorders, gallstones, GLP-1 receptor agonists, psychiatric disorders, vitamin deficiencies, and anti-obesity medications

INTRODUCTION

Obesity is a chronic disease with increasing prevalence worldwide[1]. According to the World Health Organization, there were over 650 million adults with obesity in 2016, representing almost 13% of the world's adult population[2]. The International Federation for the Surgery of Obesity and Metabolic Disorders reports that over 300,000 bariatric surgeries were performed globally in 2022[3]. Internationally, sleeve gastrectomy (SG) is the most common bariatric surgery performed, followed by Roux-en-Y gastric bypass (RYGB)[3]. The safety of bariatric surgery is outstanding, with a reported 90-day mortality of 0.11% following surgery[3]. Bariatric surgery also leads to substantial weight loss and has significant effects on obesity-related complications, including type 2 diabetes, liver fibrosis, cardiovascular events, and cancer[4]. In addition to the benefits of bariatric surgery, it is associated with some unwanted consequences of significant weight loss. This review article will highlight the diverse long-term weight-loss-dependent challenges after bariatric surgery, including increased risk for cholelithiasis[5], constipation[6], decreased bone density and muscle mass[7], vitamin deficiencies[8], peripheral neural palsy[9], suicide[10], disordered eating[11], alcohol dependency syndrome[12], and increased divorce rates[13]. Higher cognizance of these risks will lead to effective management of related issues. It may further aid the recognition and understanding of the long-term side effects of medical weight-loss interventions. New-generation anti-obesity medications have shown more than 10% of overall body weight loss, which is unprecedented compared to previously available pharmacologic agents[14]. Long-term data on the safety and efficacy of these medications, including high-dose Semaglutide, have not yet been established[14]. Understanding the physiology of the long-term risks of bariatric surgery can serve as an indicator of potential risks of newer anti-obesity medications. This study aims to provide a comprehensive review of the longer-term risks of bariatric surgery that are not surgery-related.

GALLSTONES

While obesity is an established risk factor for gallstone disease[15], rapid weight loss, as seen in the case of bariatric surgery, can lead to increased rates of gallstones[5]. Other risk factors for gallstone disease include the female sex, pregnancy, and genetic predisposition[16,17]. While rates vary, most studies report an incidence rate of cholelithiasis around 20%-30% after bariatric surgery[18-20]. Bariatric surgery patients with preoperative asymptomatic gallstones had a 15% chance of developing postoperative symptomatic gallstone disease, revealing a statistically significant increase compared to patients with no prior history[21]. Symptomatic cholelithiasis can lead to abdominal pain, jaundice, acute cholecystitis, biliary colic, and pancreatitis[22,23].

The mechanism of postoperative gallstone formation is not entirely understood but is believed to involve gallbladder hypomotility, cholesterol saturation of bile, decreased bile secretion, and hypersecretion of mucus[22-25]. However, recent studies explore other contributing factors[26]. Guman *et al.* compared the fasting metabolome, fecal microbiome, and liver and adipose transcriptome in preoperative and postoperative patients[26]. They discovered differences in the gut microbiome, revealing an increased abundance of Lactobacilli and Enterobacteriaceae in patients who did not develop gallstones. Transcriptome analysis revealed the suppression of four genes linked to cholesterol and bile acid metabolism in patients who developed postoperative gallstones[26]. These studies reveal a new potential pathological mechanism of post-bariatric surgery gallstones and can help predict which patients are more susceptible, leading to better treatment options.

Treatment for gallstone formation after bariatric surgery has been controversial, as multiple factors influence the incidence of development, including the patient's history of gallstones[21]. Prophylactic ursodeoxycholic acid (UDCA) in the first 6 postoperative months resulted in a significant decrease in post-

bariatric gallstone formation from 22% in the placebo group to 6.5% in the treated group[5]. The trial excluded patients with a previous history of cholelithiasis and/or cholecystectomy[5]. In this study, overall gallstone incidence after surgery was 9.7%, of which 3.8% were symptomatic. Other studies[16] have also revealed a decrease in symptomatic gallstones with prophylactic UDCA, decreasing the need for postoperative cholecystectomy. In a study by Haal *et al.*, the effect of UDCA prophylaxis in patients with preoperative gallstones was negligible[21]. While prophylactic cholecystectomy was previously recommended, the increased rate of complications, hospital stays, and mortality have led to a decline in this practice[22]. Given the risks, concomitant cholecystectomy should be reserved for preoperative symptomatic patients undergoing bariatric surgery[27]. The American Clinical Practice Guidelines for the Perioperative Nutritional, Metabolic, and Nonsurgical Support of Bariatric Surgery patients recommend postoperatively treatment with UDCA during the first 3-6 months[28].

In the future, patients should be educated about their risk and consider suggested treatment options such as prophylactic UDCA and monitoring with ultrasound[17]. Given recent evidence, further studies should be conducted to determine the influence of statins on reducing risk[21]. Data should continue to be collected to guide physicians and patients on surgical and pharmaceutical prevention and treatment.

PANCREATITIS

Acute pancreatitis is a rare complication of bariatric surgery that most commonly presents with sharp abdominal pain in the epigastric region and back, jaundice, nausea, and vomiting. However, pancreatitis can be painless and only present with weight loss and steatorrhea[29]. Due to the concurrent weight loss component of bariatric surgery, pancreatitis can be challenging to detect. This complication is relatively rare compared to other nonsurgical consequences of bariatric surgery. Only 138 of 3,765 patients who underwent a SG developed postoperative pancreatic-biliary complications (3.6%). Of these 138 patients, only 10 (0.27%) developed acute pancreatitis after a 3-year follow-up[30].

Recognized risk factors of acute pancreatitis include gallstones and alcohol abuse, both of which are commonly observed nonsurgical complications of bariatric procedures. In individuals with gallstones or type 2 diabetes, the mortality rate can be as high as 20%[31]. About 20% of patients who undergo bariatric surgery develop gallstones, and 32% of patients can develop alcohol dependence[17,32]. These risk factors also contribute to higher rates of a second acute pancreatitis attack[33]. A related factor for acute pancreatitis is pancreatic exocrine insufficiency (PEI). PEI is a known complication after bariatric and gastric procedures. In a previously conducted study, 31% of observed bariatric patients were diagnosed with PEI over 52 months[34]. Another study revealed that 63.4% of observed bariatric patients had abnormal results from the Pancreatic Exocrine Insufficiency Questionnaire (PEI-Q)[35]. An additional risk factor is the use of medication.

LIVER FAILURE

The rapid weight loss after bariatric surgery may lead patients with decompensated nonalcoholic steatohepatitis and metabolic dysfunction-associated steatohepatitis to experience acute liver failure[36]. In both nonalcoholic steatohepatitis and metabolic dysfunction-associated steatohepatitis, fat deposits in the liver lead to inflammation and fibrosis of the liver tissue[37]. After bariatric surgery, a variety of metabolic changes in the body can increase the release of fat from the liver, which overwhelms the liver's capacity to efficiently process these fats[38]. As a result, liver tissue can become further inflamed, fibrosed, and injured, which may lead to acute liver failure[39].

Factors that may contribute to the process of acute liver failure in patients with nonalcoholic steatohepatitis and metabolic dysfunction associated with steatohepatitis after bariatric surgery include rapid weight loss[40], nutritional deficiencies[41-44], and metabolic changes[41]. In terms of rapid weight loss, there has been no observed consistent relationship between the speed or amount of fat loss and the development of acute liver injury after bariatric surgery[41]. However, one study showed that a weight loss greater than 1.6 kilograms per week was associated with an increase in inflammation and fibrosis of the liver portal system[40]. In addition to this study, one case study suggests that two patients who underwent bariatric surgery and reported a symptom-free postoperative period had no significant weight loss during that period. However, they experienced acute liver injury only directly after a period of significant, unexplained weight loss[45]. Furthermore, weight loss after bariatric surgery is associated with an increase in peripheral insulin sensitivity and a subsequent decrease in endogenously produced insulin from pancreatic islet cells[46]. This, therefore, leads to an increased breakdown of fat stores and the release of fatty acids, which reach the liver through the portal system, overwhelming hepatocytes' ability to metabolize them through mitochondrial beta-oxidization[38]. The substantial increase in beta-oxidization of fatty acids has been linked to the production of reactive oxygen species which has been linked to mitochondrial damage and subsequent release of cytokines, including tumor necrosis factor-alpha and interleukin-6, that may damage the liver[36,47,48]. However, more studies have suggested that in practice, interleukin-6 gene expression may decline in the post-bariatric surgery period. These inconsistencies have been addressed in another paper[49], which prompts further research into the reality of inflammatory cytokine release in post-bariatric patients.

In terms of nutritional deficiencies in post-bariatric patients, protein and amino acid deficiency may play a significant role in the pathogenesis of acute liver injury in patients with nonalcoholic steatohepatitis and metabolic dysfunction-associated steatohepatitis. The amino acids serine, histidine, phenylalanine, lysine, glycine, alanine, methionine, and threonine are among the most significant deficiencies after bariatric surgery. Deficiency of amino acids, especially arginine and threonine, is associated with an increase in hepatocyte triglyceride accumulation, which may make the liver vulnerable to injury[50]. In RYGB, the duodenum and proximal portion of the jejunum are bypassed, which are the locations where methionine and choline are absorbed[51,52]. Deficiencies in methionine may also be associated with a decrease in GI pH, which occurs because of decreased gastric volume. Methionine is absorbed by a pH-dependent carrier transport method, and therefore, a decrease in pH can cause a decrease in methionine uptake[53]. Deficiency of choline may occur because of a change in the gut microbiome after surgery[54], which may cause an accumulation of bacteria that convert choline to trimethylamine[55], therefore decreasing choline bioavailability[56]. In a society that already lacks sufficient choline intake, this leaves patients who undergo bariatric surgery especially at risk[57]. Deficiencies of both methionine and choline together have been linked to a decrease in beta-oxidation and very low-density lipoprotein production. Choline deficiency alone, however, has been linked to decreased liver function as a result of macrovesicular steatosis, oxidative stress, and hepatocyte apoptosis[58,59].

Although developing acute liver failure is rare in patients with nonalcoholic steatohepatitis and metabolic dysfunction-associated steatohepatitis who undergo bariatric surgery, it is important to understand these risks and create a pre- and postoperative plan of care. Providing proper nutrition and ensuring the surgery does not create a disproportionally long alimentary loop can help prevent acute liver failure in patients with existing liver disease[41]. Additional research is needed to find accurate biomarkers of sufficient nutrition.

CONSTIPATION

Changes in bowel habits, including constipation and diarrhea, often occur postoperatively in individuals who have undergone bariatric surgery[6]. Several factors contribute to postoperative bowel habits, including

changes in diet, patient predisposition, and the type of procedure performed[6]. A systematic review evaluating the impact of bariatric surgery on defecatory disorders revealed heterogeneous results in the literature[60]. In a study conducted by Afshar *et al.*, the proportion of patients suffering from constipation after either RYGB or SG increased from 8% to 27%, although this was not statistically significant[61].

Apart from the type of surgical procedure performed, several factors contribute to constipation in the post-bariatric surgery population. One cause could be decreased frequency of bowel movement and increased firmer stools after surgery[61]. Elevating gut hormones, specifically GLP-1 and PYY, may also contribute to slower bowel transit[62]. Another contributing factor in most patients is likely a significant decrease in dietary fiber after surgery[61,63,64]. Patients suffering from constipation postoperatively should consider appropriate dietary advice and fiber supplementation[61]. A study conducted by Shah *et al.* correlated post-bariatric surgery constipation with thiamine deficiency, and the frequency of defecation for these patients improved after properly treating the thiamine deficiency[65].

A thorough pre-surgical history should be taken to address constipation in postoperative patients to identify a predisposition to gastrointestinal issues. Given the considerable patient-to-patient variability, the choice of surgery type should be discussed, and the post-surgical team should involve dietitians and physicians. Patients experiencing long-term constipation after surgery should consider exercise, better hydration, and consuming at least five servings of fruits and vegetables daily[66]. Patients should also be educated about the importance of fiber intake, hydration, and other constipation treatments. If necessary, stool softeners and laxatives should be considered as pharmacologic treatments. Further, well-controlled studies are needed to assess the impact of bariatric surgery on constipation and other defecatory disorders appropriately[60].

BODY COMPOSITION

Muscle mass loss

Muscle mass loss can result in unfavorable health outcomes, including cardiovascular disease, metabolic syndrome, functional disability, decreased quality of life, and mortality[67,68]. Muscle tissue regulates metabolism, thermoregulation, bone health, and functional capacity[69,70]. Extensive and rapid weight loss, as observed in bariatric surgery, leads to both fat and muscle mass loss[7]. Studies have failed to reveal indicators for high-risk individuals, although insulin resistance and low baseline fat-free and skeletal muscle mass may impact post-surgical outcomes[71,72]. In a meta-analysis study conducted by Nuijten *et al.*, average lean body mass loss, defined by total body mass excluding fat mass and bone mineral content, was -8.1 kg[7]. Fat-free mass, consisting of bone tissue, organ tissue, and skeletal muscles, saw an average loss of -8.2 kg, and skeletal muscle mass loss average was 3.2 kg. Most of this loss occurs within the first 3 months postoperatively and continues during the first year[7,73]. Another study by Zhou et al. reported an average mean total body weight loss of 22%, 35% fat mass loss, 43% visceral adipose tissue loss, and 12% lean mass loss[74]. Voican *et al.* reported the prevalence of low skeletal muscle mass at 32% 1-year postoperatively, compared to 8% prior to surgery[75]. An additional report concluded that the loss of fat-free muscle was 21% ± 14% of total weight loss at 2 years follow-up[76].

The balance of muscle mass synthesis and breakdown can be externally influenced by diet and physical activity[68]. The mechanism of postoperative muscle mass loss involves a decrease in protein intake related to the restriction of overall food intake and a decrease in muscle protein synthesis[7]. Given the inability of the body to store protein, a prolonged state of deprivation leads to muscle wasting and proteolysis to provide amino acids necessary for metabolic function[7,74].

The multi-faceted mechanism of post-bariatric muscle wasting allows for multiple therapeutic approaches to minimize this effect. Regarding diet, studies have shown that an increased intake of whey protein aids in reducing muscle loss and preserving myofibrillar protein synthesis[68]. Dietary protein can influence satiety and energy expenditure, impacting lean body mass retention[77]. According to the American Association of Clinical Endocrinologists, along with other obesity-related associations, a protein intake of 1.5 g/kg is recommended for post-bariatric patients. In comparison, most patients report a protein intake of less than 60 g per day at three months post-surgery[78]. Along with a high-protein diet, moderately intensive resistance exercise can reduce muscle loss[68,69,73,78-80]. However, the influence of exercise is controversial, as some studies reveal only an increase in muscle strength[81,82], while others show an attenuation of the loss of fat-free muscle mass[69,83]. Suppression of the ubiquitin-proteosome system and an increase in angiogenesis following exercise could reduce muscle mass loss[69]. Further studies using magnetic resonance imaging to detect fat-free muscle mass should be conducted in the future to help determine the influence of exercise on post-bariatric muscle mass loss[69].

Interventions to limit muscle mass loss should start before or immediately after surgery[7,71]. Fat-free mass loss has been shown to play a role in weight regain due to its role in long-term appetite control[84]. Along with weight regain, sarcopenic obesity, a syndrome characterized by excessive body fat, low muscle mass, and reduced muscle strength, can increase morbidity and mortality[67,72]. Considering the timeline of postoperative muscle mass loss, patients should be informed on the subject and have a team of providers, including those specializing in nutrition and physiotherapy. Taken all this together, it does appear that in most cases, the fat-free mass loss is predominantly a physiological response related to the overall reduction in muscle work required due to total body weight loss. Fat-free-mass loss does not appear pathological as one would expect if purely calorie restriction was used to achieve 30% total body weight loss[67].

Bone fractures

Studies of bone loss in people who underwent significant weight loss are challenging. Dual-energy X-ray absorptiometry technology loses accuracy in persons with obesity, and changes in fat mass introduce artifacts that may compromise accuracy and precision[75]. Thus, it may be challenging to assess bone health and relate it to fractures in a long-term follow-up after surgery.

There is conflicting information regarding the relationship between bone fractures and bariatric surgery, with many results available. The risk of bone fractures increases by up to 2.3 times for individuals who have had bariatric surgery compared to the general population[85]. However, limited and sometimes conflicting information is available, making it challenging to understand the mechanism or direct link between bone fractures and bariatric surgery outcomes.

One randomized controlled trial did not observe increased risk after bariatric surgery[86]. The Swedish Obesity Subjects study compared three techniques with a medical control group with up to 26 years of follow-up[87]. It showed an increased risk of fracture after *RYGB* compared with the control. The gastric banding group and the vertical banded gastroplasty group had less risk of fractures compared to RYGB, but still greater than the control group. RYGB produced more weight loss than the other procedures (not performed anymore), and RYGB patients were mainly postmenopausal women prone to bone mass loss. An increased risk for fractures after surgery may be attributed to osteoporosis, reduction in mechanical unloading, nutritional deficiencies, hormonal changes, and endocrine factors[88].

The mechanical loading of bones directly determines their size, mass, and other biochemical properties. Any change in this load can lead to localized bone remodeling, either increasing or decreasing cortical bone

mass concerning the microstrain range[89]. This process can be observed in populations unrelated to weight loss, such as individuals on extended bedrests[90], demonstrating the fast-acting nature of mechanical loading changes and localized bone remodeling.

Loss in hip bone density has been shown in individuals who lose significantly less weight than individuals after bariatric surgery. In individuals who participated in a 1-year lifestyle intervention to lose weight, there was an 8.6% decrease in bone mineral density[91]. In a short-term study following individuals who underwent a sleeve gastrectomy, bone mineral density decreased for the spine by 1.2%, femoral neck by 7.0%, and total hip by 5.2% after 6 months, affecting a majority of participants[92]. After another six months, the number of participants impacted by bone density loss increased further. In a group of individuals who received RYGB, there was a 10.2% decrease in femoral neck bone mineral density, increasing to 12.9% three years post-operation[93]. Areas of the body that show the highest loss of bone mineral density are high-loading points, such as the hip[94]. A rapid reduction in the amount of weight loss can lead to decreased mechanical loading of the bones, causing localized bone remodeling and increased fracture risk[95].

Another potential mechanism for bone fractures is nutritional deficiencies after bariatric surgery[96]. Many individuals who undergo bariatric surgery experience micronutrient deficiencies due to decreased nutritional intake and, to a lesser degree, malabsorption of nutrients, which can vary based on the type of procedure performed. Common postoperative deficiencies in calcium and vitamin D have been observed in those who undergo any type of bariatric surgery[8], thought to be related to their impaired absorption due to alterations in the jejunum and ileum[97]. These changes are especially notable in RYGB and biliopancreatic diversion procedures[97]. These two deficiencies have explicitly been linked to an increased frequency of bone fractures and the development of osteoporosis[98]. This side effect may be directly related to the anatomical changes after surgery, which medications will not be subject to, but other mechanisms may also be involved. However, long-term use of the new anti-obesity medications may lead to a decreased food intake. This can be a possible cause of micronutrient deficiencies after long-term use of medications.

Different bariatric procedures are associated with varying levels of risk for bone fractures. While multiple studies have shown no increase in bone fracture risk in laparoscopic adjustable gastric banding (LAGB)[99,100], this procedure has been primarily replaced by RYGB, sleeve gastrectomy. To some extent, each of these procedures has been associated with higher risks of bone fractures. Roux-en-Y gastric bypass has been associated with a 43%-70% increased risk of nonvertebral fracture compared to LAGB and nonsurgical control groups[101,102]. It is important to highlight that LAGB was less effective than RYGB of SG and, in many cases, had a complication of being overly restrictive where the physiological mechanisms were overshadowed by non-physiological restriction of calories. Despite the rise in sleeve gastrectomy procedures, a limited number of studies evaluate each surgery method individually. The available information points to sleeve gastrectomies do not correlate with an increased risk of bone fractures[102]. In another study comparing sleeve gastrectomy patients with unoperated patients, those with surgery had a much lower risk of sustaining a humeral fracture when evaluated for 3 years post-operation[103].

More research is needed on bone mineral density changes following different bariatric surgeries, such as prevention methods and bone strengthening. The most widely supported recommendation to combat the possible risk of bone fractures is regular postoperative visits, exercise, and prescribed lifelong calcium and vitamin D supplements[88,97]. The recommended dose of supplements to prevent adverse bone effects after surgery is 1,200-1,500 mg/day of calcium and 3,000 IU/day of vitamin D[88]. The impact that anti-obesity medications may have on bone fracture rates will not be known for several years. Thus, mechanistic studies are needed earlier to pre-empt a potential problem.

VITAMIN DEFICIENCIES

There is a high prevalence of nutritional deficiencies in people with severe and complex obesity. The most common consequences and deficiencies include anemia, ferritin, folate, vitamin B12, and vitamin D. All candidates should have a comprehensive nutritional assessment before bariatric surgery. Nutritional deficiencies should be investigated and corrected as clinically indicated before surgery[104].

Vitamin deficiencies following bariatric surgery can often be attributed to reduced food intake, alteration in digestion and absorption, and patient non-adherence to postoperative nutritional regiments. This commonly occurs and affects several nutrients, including, but not limited to, thiamine (vitamin B1), vitamin B12, vitamin D, and iron levels, and can lead to further health issues[8]. Available information regarding each deficiency is limited, but the rapid loss of adipose tissue affects fat-soluble vitamins like vitamins A and E and changes in nutrient absorption can impact all deficiencies. These deficiencies may be more severe in patients undergoing biliopancreatic diversion than in Roux-en-Y gastric bypass[105]. Table 1 describes various vitamin deficiencies and their symptoms. While there is a high possibility of additional nutrient deficiencies beyond those described, insufficient information is available to make a significant connection between those deficiencies and bariatric surgery. Again, it should be noted that the rearrangement of the intestines may contribute to these deficiencies. However, the significant reduction in calorie intake and the nutrient composition of what is consumed may also become important with the new anti-obesity medications.

Thiamine deficiency can occur in up to 5% of bariatric surgery patients[114] and can cause a multitude of severe health complications if not adequately addressed. These complications include oxidative stress leading to cell death, peripheral neuropathy, cardiomyopathy, and the neuropsychiatric Wernicke-Korsakoff syndrome[106]. Due to thiamine's water-soluble nature, the body cannot produce and store its supply, making individuals dependent on dietary thiamine intake[115]. This property causes individuals who have undergone bariatric surgery to be susceptible to deficiencies due to reduced food intake and nutrient absorption. Additionally, individuals affected by alcoholism are much more likely to have a thiamine deficiency and develop Wernicke-Korsakoff syndrome, given the impact of ethanol metabolism on the gastrointestinal absorption of thiamine[116]. This puts bariatric surgery patients at further risk of deficiencies, given the higher likelihood of developing alcohol dependency syndrome after the procedure. A known side effect of the anti-obesity medications is vomiting, which may also contribute to thiamine deficiency.

Vitamin A deficiency is one of the most common deficiencies after surgery and can lead to further complications such as vision loss, impaired immune system function, and dermatological issues[108]. Vitamin A is a fat-soluble vitamin primarily stored in adipose tissue. Bariatric surgery causes rapid loss of this adipose tissue, depleting previously stored vitamin A. In a retrospective chart review of patients with RYGB, 35% and 18% were found to be vitamin A deficient after 6 weeks and 1 year, respectively[117]. An alternative study reported that 69% of patients who underwent a biliopancreatic diversion (duodenal switch) experienced vitamin A deficiency four years post-operation[118]. These findings highlight the importance of monitoring and addressing vitamin A levels in bariatric surgery patients to prevent potential complications associated with its deficiency. The fat mass loss with the new anti-obesity medications may not be dissimilar to what we currently see after surgery.

Patients must adhere to postoperative dietary changes and take prescribed supplements to ensure that nutrient levels remain stable and that future complications are avoided[96]. After bariatric surgery, lifelong supplementation is recommended as part of postoperative care[119]. Individuals with Roux-en-Y gastric

Table 1. Vitamins and symptoms of their deficiencies. These symptoms can become apparent post-bariatric surgery if not treated

Vitamin	Signs of deficiency
Thiamine (B1)	Cell death, peripheral neuropathy, cardiomyopathy, and Wernicke-Korsakoff syndrome[106]
Vitamin B12	Fatigue, shortness of breath, jaundice, vision problems, dementia, peripheral neuropathy, ataxia, and a loss of proprioception[107]
Vitamin A	Vision loss, loss of immune system function, and dermatological issues[108]
Iron	Anemia, fatigue, hair loss, and restless legs[109]
Vitamin D	Symmetric low back pain, proximal muscle weakness, muscle aches, and osteoporosis[110]
Vitamin K	Excessive bleeding, poor bone development, osteoporosis, and increased risk of cardiovascular disease[111]
Calcium	Muscle cramps, confusion, tingling in the lips and fingers, and osteoporosis[112]
Vitamin E	Neuronal disorders, impaired immune response, hemolytic anemia, and oxidative-based disorders[113]

bypass or a sleeve gastrectomy were followed to measure their adherence to their prescribed calcium-vitamin D, vitamin B12, and iron supplements. 60% of participants had a high adherence rate, and 15% had discontinued their use of prescribed supplements two years post-operation[120]. 30% of individuals who stopped supplements contributed to this being forgetful[119]. Regular post-operation appointments with the prescribing clinician appear necessary for monitoring supplement adherence. Making patients aware of the lifetime commitment to supplements is an important preoperative step and can reduce discontinuation rates[119]. Patients treated with anti-obesity medications are not asked to take nutritional supplements, but this may become necessary in subgroups of patients. In cases of long-term Orlistat treatment, supplementation of fat-soluble vitamins was deemed necessary[121].

PERIPHERAL NEURAL PALSY

Foot drop is an inability to lift the forefoot due to dorsiflexor weakness and can cause an antalgic gait, potentially resulting in a higher likelihood of falls[122]. Foot drops can be directly caused by peripheral neuropathy affecting the peroneal nerve[122]. Individuals with obesity are already at a higher risk of experiencing neuropathy prior to surgery because of concomitant metabolic diseases such as type 2 diabetes[123]. Peripheral neuropathy is a prevalent condition affecting 23% of individuals with diabetes[124] and 33.3% of individuals with obesity[125]. Studies consistently point to obesity and diabetes as the main metabolic factors associated with neuropathy[126-128]. For these individuals, there is a higher risk of developing peripheral neuropathy regardless of undergoing bariatric surgery[129].

Peripheral neuropathy is one of the most common neurological experiences for bariatric patients, with significant weight loss affecting between 16%-60% of patients[130,131]. The large variability in reported numbers is due to the broad criteria used to identify peripheral neuropathy and different postoperative parameters across studies[132]. Most studies focus on general peripheral neuropathy, rather than specific nerves, making it difficult to accurately evaluate the causal link between bariatric surgery and foot drop caused by peripheral neuropathy in the peroneal nerve[133]. Studies that specifically focus on foot drop have a much smaller subject group. In a retrospective study, 7% of patients who had undergone bariatric surgery developed peripheral neuropathy. However, < 1% developed foot drop[133].

In most cases of peripheral neuropathy after bariatric surgery, symptoms do not develop until about 4 years after the operation[9]. Some precipitating factors for foot drop may also include the reduction of protective fat pads where the nerve crosses long bones. Thus, the bone may cause mechanical pressure on the nerve when the fat pad disappears.

Peripheral neuropathy is strongly connected to thiamine levels. Thiamine deficiency has been observed in 5% of bariatric surgery patients and is one of the most common nutritional deficiencies[114]. In a previously studied case report, a patient who developed severe neuropathy after bariatric surgery was then diagnosed with an extreme thiamine deficiency. Once treated for this deficiency, the neuropathy condition improved but was not fully reversed[134]. Monitoring nutritional levels and avoiding deficiencies can effectively prevent severe postoperative neuropathy[135]. Thiamine deficiency numbers reported here mainly include patients with AGB or other operations where patients had an increased number of episodes of vomiting.

The recommendation to combat foot drop after surgery is controlled weight loss. A study compared bariatric patients who developed foot drop and those who did not. Among patients who developed foot drop, there was a mean weight loss of 45 kg over 9 months compared to the control group's mean weight loss of 44 kg over 22 months[136]. Not only is the amount of weight loss significant, but the time also impacts neuropathy outcomes[136,137]. Given the rapid weight loss period following bariatric surgery[138], controlled weight loss is difficult. Weight loss after medication can theoretically be controlled by slowing the dose titration, albeit many patients and clinicians want to achieve maximal weight loss in the shortest period of time. Thus, adjusting expectations and clinical practice may be required when medications become more commonly used in primary care.

MENTAL HEALTH

Suicide

The psychosocial impacts of bariatric surgery must be acknowledged and appropriately addressed. Overall, patients have a substantial improvement in quality of life as measured by SF36, but this is mainly attributed to the functional domain of SF36[139,140]. The mental domain of SF36 improves during the weight loss phase but returns to baseline after a few years. In subpopulations of patients, there may be an increased risk of depression, self-harm, and suicide following bariatric surgery[10,140-145]. Depression after surgery may lead to weight regain, comorbid psychopathology, and reduced quality of life[10]. The initial decline in depressive symptoms in the short term after surgery is also known as the "honeymoon phase," followed by a long-term increase in symptoms comparable to pre-surgical levels of depressive symptoms[10,140,143,144,146,147]. In a meta-analysis conducted by Castaneda *et al.*, the rate of mortality from suicide, thus the number of people who died after a suicide attempt, was 2.7 deaths per 1,000 people in post-bariatric patients, compared to 0.11 deaths per 1,000 people in the general population[143]. Other studies reported post-bariatric suicidal mortality rates ranging from 0.041%-0.3%[142,148,149]. Higher rates of suicidality occur 12 years postoperatively compared to control groups, and health-related quality of life (HRQOL) appears to be an accurate indicator of the risk of suicidal thoughts and behaviors in bariatric patients[140]. The SOS study reported that during long-term follow-up, suicide and self-harm are rare, but more common in the surgical arm, regardless of the technique employed[150].

The increased prevalence of suicide and self-harm in the post-bariatric population has not been linked to a singular, specific mechanism[140,143]. There is a greater level of preoperative depression and psychiatric disease in people with obesity prior to bariatric surgery compared to the general population[140,143,145]. Rates of alcohol and substance use are also increased in subpopulations of patients after bariatric surgery[143]. The potential impact of emotional eating, constituting binge eating in response to emotion despite a lack of physiologic hunger, and neurotic defense mechanisms may also impact suicide risk in post-bariatric patients[151]. Changes in peripheral released peptides after surgery can impact mood, and further studies are needed to understand this impact better[148,152,153]. Psychosocial factors involving disappointment with results, relationship changes, and weight gain can impact patients[140,143,153]. Medical complications of obesity may not always resolve following surgery, which can negatively impact a patient's mindset[148]. Males have an

increased risk of suicide post-surgery compared to females[154]. Van den Eynde *et al.* reported that the most significant predictor for postoperative self-harm was a history of a psychiatric health disorder within 5 years preoperative and, thus, should be an indication for appropriate monitoring[147]. Underlying mental health issues, an increase in substance use, feelings of disappointment, and low self-esteem could potentially contribute to the increased prevalence of suicide in this population, calling for supervision of at-risk patients[140,143,148].

To correctly address the risk of suicide in bariatric patients, action should be taken prior to surgery. The American Society for Metabolic and Bariatric Surgery (ASMBS) released guidelines for psychological consultation before bariatric surgery involving a face-to-face evaluator and follow-up visits after surgery to determine the need for psychotherapy or pharmaceutical intervention[143]. In The Bariatric Surgery and Education study[155], patients with clinically significant depression symptoms at baseline who underwent a 1-year postoperative videoconferencing-based psychoeducational group intervention had lower depressive scores and a significantly better health-related quality of life one year after surgery compared to the control group. HRQOL assessments should be used in the short-term following surgery to help predict the risk of suicidality in the long term[140]. Given the impact of gastric bypass procedures on pharmacokinetics, physicians should be aware of the physiologic changes being made. The altered metabolism of psychiatric medications and substances should be considered, and physicians should make appropriate dosing changes in these patients and provide counseling on the effects of surgery[143]. Additional clinical monitoring before and after bariatric surgery is necessary to address psychiatric concerns appropriately[150,151,156,157]. Mental health professionals should be involved in bariatric teams pre- and postoperatively to assess patients who may fall vulnerable to depression and suicide[10,148]. As early reports emerge regarding patients who have had suicidal ideation after treatment with anti-obesity medications, some thought must be given to how to identify and manage patients who may be more vulnerable to suicide before starting medications to treat the disease of obesity.

Eating disorders

A subpopulation of people seeking bariatric surgery are at high risk for eating disorders, but recent studies suggest that in some rare cases, patients may also be at risk of developing eating disorders in the postoperative period[11]. Eating disorders are associated with high rates of morbidity, mortality[158], and psychological issues[159], and are subsequently a severe potential consequence of bariatric surgery. Therefore, physicians need to consider the possible risks and complications of the procedure, including the development of eating disorders, to provide the appropriate treatment and support for patients in the long-term postoperative period. This section will focus on the prevalence, risk factors, potential mechanisms, and clinical implications of eating disorders among patients after bariatric surgery.

There are limited and conflicting data regarding the prevalence of eating disorders in bariatric patients. Concerning preoperative patients, one recent study shows that up to 42% of such patients have symptoms of binge eating disorder[160,161]. In terms of the postoperative population, another review claims that eating disorders were prevalent in 7.8% of patients. Of these eating disorders, binge eating disorder was the most common, with a rate of 3.8%[162].

Binge eating disorder or loss of control eating disorder (LOC) are eating disorders characterized by objective binge episodes (OBEs). Objective binge episodes occur when a person eats large portions of food and feels out of control. In the short-term postoperative period, this type of eating disorder is not usually possible due to a variety of metabolic changes, but over time can develop[11,163,164]. Additionally, patients in the postoperative period can experience loss of control while eating, even if the portion is not objectively

large. This is a subjective binge-eating episode[165]. Patients who have experienced objective binge episodes or qualified for a binge eating disorder prior to undergoing bariatric procedure are most at risk of developing LOC or binge eating disorder postoperatively[11,166]. By 2 years post-surgery, 10%-39% develop LOC eating regardless of their preoperative history of eating disorders[11,163].

The degree to which we can learn from this information is limited by the variation in data collected on eating disorders. This variation arises from the use of several different guidelines used to diagnose eating disorders, including the DSM (Diagnostic and Statistical Manual of Mental Disorders[162,167] and ICD (International Statistical Classification of Diseases and Related Health Problems)[162,168]. Additionally, the lack of standardization of survey materials contributes to the variability in data. For instance, only one survey was specific to bariatric patients[169]. Furthermore, the timing of the survey administration, whether pre- or post-surgery, is not standardized[162]. Consequently, several factors prevent the retrieval of reliable data on eating disorders in the postoperative period.

Aside from a pre-existing eating disorder, other psychological factors may also influence post-bariatric eating disorders. While more research is needed to confirm the impact of different psychiatric disorders and psychopathological traits on post-surgical outcomes, studies suggest that "greater affective instability" is associated with worse results after bariatric surgery. Emotional dysregulation and psychological issues are significant in weight control and eating behaviors[170]. The postoperative period can be challenging for some individuals as they may struggle to cope with stress and other emotions[171]. After surgery, hormonal changes in the gastrointestinal tract make weight loss a passive process driven by less food intake, which may prevent patients from coping with stress the same way as before the surgery[172]. Therefore, patients with a previous LOC eating pattern may develop a new, restrictive eating disorder, such as bulimia nervosa or anorexia nervosa, in the postoperative period[153,171]. Studies also suggest that patients with disordered eating behaviors display decreased executive function[173]. Additionally, after bariatric surgery, patients may experience a more active reward system and, therefore, be at a higher risk of developing an eating disorder[162,174,175].

Unrealistic expectations regarding bariatric surgery results may lead to body dissatisfaction after surgery. A longitudinal study involving 64 bariatric patients measured their desired post-surgery weight, comparing it against three different surveys, including an Eating Disorder Examination Questionnaire, Beck Depression Inventory, and Body Shape Questionnaire. Results revealed that 81.1% of patients did not achieve their desired weight. Notably, the study found a significant association between higher differences in desired and actual post-surgery weight and increased levels of body image dissatisfaction and eating psychopathology scores[176].

The development of eating disorders in patients after bariatric surgery is a rare but significant complication that requires standardization of assessment measures to intervene and support at-risk patients. Patients need to follow up with providers after surgery to prevent the development of eating disorders in the long term. A multidisciplinary approach to treatment can include mental health and dietary counseling and management of post-surgical expectations[11].

It is possible that the development of new eating disorders after anti-obesity medication can be attenuated by reducing or stopping the medications, but it is another significant effect that is not being considered at the moment.

Alcohol dependency

While substance abuse, particularly alcohol dependency syndrome, is a rare complication of bariatric surgery, it can significantly impact patients' health and quality of life in the long term[12]. One study suggests that substance abuse alone is prevalent in 32% of postoperative bariatric surgery patients[32,177]. Furthermore, alcohol dependence may increase over time following the surgery, with the Roux-en-Y gastric bypass being especially linked to alcohol misuse in the postoperative period[12,177,178]. Moreover, women may be more susceptible to developing alcohol dependence than men in the postoperative period. Further investigation is warranted for potential gender-specific approaches to alcohol recommendations[177].

One risk factor for developing alcohol dependence after bariatric surgery is the alteration of alcohol metabolism that occurs due to changes in gastrointestinal physiology. Although most alcohol metabolism in the body occurs in the liver through hepatic alcohol dehydrogenase, some alcohol is metabolized in the gastric mucosa. After a Roux-en-Y gastric bypass, less alcohol passes through the patient's stomach, and therefore, less alcohol is metabolized, ultimately leading to higher blood alcohol concentration[177,179]. This may cause an increased sensitivity to the effects of alcohol, given its longer-lasting effects[12,179-181]. This would not apply to the new anti-obesity medications.

A change in the brain's reward system after surgery can also play a role in developing alcohol dependence. Similar responses in the brain are triggered by alcohol, drugs, and food[12]. This aligns with the theory of 'addiction transfer' that suggests patients cannot fulfill the behavior of eating and experience its reward as they did before surgery, so it is replaced with a new behavior that achieves a similar reward, like drinking alcohol[12,182]. Patients can also have an increase in sensitivity to the hormone ghrelin after surgery, which may increase the rewarding properties of alcohol quicker and more frequently[12]. Furthermore, alterations in neurotransmitter balance are also associated with an increased risk of alcohol abuse. Patients with RYGB are seen to have a decrease in dopamine D2 receptor availability, specifically in the ventral striatum and caudate nucleus, which are areas of the brain that play an important role in regulating the body's alcohol reward system[12]. Some individuals may be genetically predisposed to reduced dopamine signaling in the alcohol reward system[12,182]. Additionally, psychosocial factors such as depression, anxiety, smoking, and other substance abuse disorders may increase the likelihood of developing alcohol dependence in postoperative bariatric patients[12]. These mechanisms may also apply to the new anti-obesity medications.

Given the significance of alcohol dependence as a potential complication after bariatric surgery, it is crucial to closely monitor patients and provide appropriate preventative measures to improve quality of life and patient outcomes. While alcohol misuse is common after bariatric surgery in the short term, emerging evidence suggests that patients may also be at risk in the long term. As research continues to assess the complex relationship between alcohol dependence and bariatric surgery, the field also needs to consider what may happen with the new anti-obesity medications.

Divorce rates

Increased divorce rates are another rare outcome after bariatric surgery, prompting a need for a better understanding of this relationship. Although research on bariatric surgery's impact on marital relations is limited, several observational, longitudinal, and retrospective studies have tried to explore this. The Swedish Obese Subject study shows that bariatric surgery is associated with an increased incidence of divorce rates and separation in comparison to a control. The surgery group reported a 9.4% divorce/separation rate, whereas the control group reported a 5.5% divorce/separation rate after 4 years[13]. After 10 years, the surgery group reported a 17.1% divorce/separation rate, while the control group reported an 11.6% separation rate[13]. In an additional cohort study using data from the Scandinavian Obesity Surgery Registry (SOReg) of the general population, 14.4% of the surgery group reported divorce, whereas 8.2% of the control

group reported divorce after 4 years[13]. A Danish study also reported divorce rates among bariatric surgery (15%) to be higher than nonsurgical groups (8%)[183,184]. An American study measured the cumulative incidence of divorce after bariatric surgery over five years and presented evidence of an increased separation and divorce rate (8%) among married people who had bariatric surgery in comparison to the general US adult population (3.5%)[183]. These findings are consistent with the Swedish studies' conclusion that an increased divorce rate is associated with bariatric surgery. However, the incidence of divorce after surgery in the US (8%) is about half the incidence of divorce after surgery in the Scandinavian countries (15%).

Multiple studies suggest that poorly functioning relationships in the preoperative period are more likely to result in divorce in the postoperative period[13,185]. Bariatric surgery can add strain to a relationship, and any additional tension added to a poorly functioning relationship is more likely to lead to divorce[13,186]. The SOReg and SOS cohort studies reported that younger age, previous divorce, and shorter time in relationships were associated with an increased divorce rate after bariatric surgery[13,186]. It will also be necessary to understand whether this will be the case after anti-obesity medications.

Although many studies show that psychological factors such as depression and anxiety in patients undergoing bariatric surgery may improve in the short- and medium-term postoperative period[187], it is important to recognize that adjusting to life after surgery can be difficult and have negative psychological consequences[171]. A subset of patients who have undergone bariatric surgery are more likely to attempt suicide and experience alcohol and substance abuse disorders[188]. Additionally, there is an increased risk of divorce among couples in which one or both partners experience mental illness[189]. Moreover, starting psychiatric medication after surgery is associated with an increased divorce rate in the postoperative period[183]. Therefore, as some patients may be more likely to experience mental health issues after surgery, this could increase the risk of divorce in the postoperative period.

On the other hand, patients who experience a positive change in psychosocial factors, such as an increase in self-esteem, autonomy, and self-value, may be more likely to leave an unhealthy relationship[184]. Again, this needs to be understood in the context of anti-obesity medications.

The reason for the association between bariatric surgery and divorce is still unclear. The strength and duration of the relationship prior to surgery, age, mental health status, and medication may all contribute to increased divorce rates in the postoperative period. Additional studies are therefore needed to appropriately address the issues patients may face in their relationships prior to and after bariatric surgery, as well as prior to and after anti-obesity medications.

The design of this narrative review has several limitations. One notable limitation involves restricted access to detailed data, as only summary-level statistics were provided for some studies. Furthermore, specific topics discussed had limited available information, limiting the ability to generalize some research findings. This was often the case when non-randomized cohort studies or real-world data were used to understand the rare complications of surgery. In future studies, improved access to research and new findings will allow a more comprehensive review.

CONCLUSION

Understanding the long-term consequences of significant weight loss after bariatric surgery may help prepare clinicians and patients as the treatment with anti-obesity medications expands. Undoubtedly, the benefits of bariatric surgery include significant control of the disease of obesity and associated complications, including diabetes mellitus, cardiovascular disease, and various cancers[10,147,190].

Due to the varying prevalence of those consequences, different risk factors for each problem, and patient individuality, a thorough assessment of each patient is necessary. Patient phenotyping, which helps to characterize the diverse types of obesity, has not yet been utilized to guide diagnosis and implement treatment strategies[191]. Vitamin supplementation, psychiatric follow-up visits, and awareness of possible risks are integral to preventing developing nonsurgical complications. However, as data on some of the discussed topics remain conflicting and the underlying mechanisms are not fully understood, conducting further long-term studies is crucial to accurately inform patients of their risks and develop appropriate treatment plans should those issues arise.

Considering the increased use of anti-obesity medications and their increasing potency[192], studying the long-term effects of weight loss following bariatric surgery may provide insight into potential future situations with the medications. Ultimately, the goal is to reduce these issues through prevention and awareness and provide a framework for assessing and managing the potential consequences.

DECLARATIONS

Authors' contributions

Performed data acquisition, as well as providing administrative, technical, and material support: Harrington S, Kang S, Telesca L

Conceived the idea and edited the manuscript: Cohen RC, Le Roux CW

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

The authors declared that there are no conflicts of interest, except:

RVC received research grants from Johnson & Johnson Medical Devices Brazil; received honoraria for lectures from Johnson & Johnson Brazil, Medtronic, Janssen Pharmaceutical; and participated in scientific advisory boards for Johnson & Johnson Brazil, Medtronic, GI Dynamics, Novo Nordisk.

ClR reports grants from the Irish Research Council, Science Foundation Ireland, Anabio, and the Health Research Board. He serves on advisory boards and speakers panels of Novo Nordisk, Roche, Herbalife, GI Dynamics, Eli Lilly, Johnson & Johnson, Glia, Irish Life Health, Boehringer Ingelheim, Currax, Zealand Pharma, Keyron, Zealand Pharma, Roche, AstraZeneca, and Rhythm Pharma. ClR is a member of the Irish Society for Nutrition and Metabolism outside the area of work commented on here. He was the chief medical officer and director of the Medical Device Division of Keyron in 2021. Both of these are unremunerated positions. ClR was a previous investor in Keyron, which develops endoscopically implantable medical devices intended to mimic the surgical procedures of sleeve gastrectomy and gastric bypass. No patients have been included in any of Keyron's studies and they are not listed on the stock market. ClR was gifted stock holdings in September 2021 and divested all stock holdings in Keyron in September 2021. He continues to provide scientific advice to Keyron for no remuneration. ClR provides obesity clinical care in the Beyond BMI clinic and is a shareholder in the clinic.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

REFERENCES

1. Risk Factor Collaboration (NCD-RisC). Trends in adult body-mass index in 200 countries from 1975 to 2014: a pooled analysis of 1698 population-based measurement studies with 19.2 million participants. *Lancet* 2016;387:1377-96. DOI PubMed PMC
2. World Health Organization. Obesity and Overweight. Available from: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight [Last accessed on 4 Mar 2024].
3. Brown WA, Shikora S, Liem R, et al. 7th IFSO global registry report. Available from: https://www.ifso.com/pdf/ifso-7th-registry-report-2022.pdf [Last accessed on 4 Mar 2024].
4. Arterburn DE, Telem DA, Kushner RF, Courcoulas AP. Benefits and risks of bariatric surgery in adults: a review. *JAMA* 2020;324:879-87. DOI PubMed
5. Talha A, Abdelbaki T, Farouk A, Hasouna E, Azzam E, Shehata G. Cholelithiasis after bariatric surgery, incidence, and prophylaxis: randomized controlled trial. *Surg Endosc* 2020;34:5331-7. DOI PubMed
6. Potoczna N, Harfmann S, Steffen R, Briggs R, Bieri N, Horber FF. Bowel habits after bariatric surgery. *Obes Surg* 2008;18:1287-96. DOI PubMed
7. Nuijten MAH, Eijsvogels TMH, Monpellier VM, Janssen IMC, Hazebroek EJ, Hopman MTE. The magnitude and progress of lean body mass, fat-free mass, and skeletal muscle mass loss following bariatric surgery: a systematic review and meta-analysis. *Obes Rev* 2022;23:e13370. DOI PubMed PMC
8. Saltzman E, Karl JP. Nutrient deficiencies after gastric bypass surgery. *Annu Rev Nutr* 2013;33:183-203. DOI PubMed
9. Riccò M, Rapacchi C, Romboli A, et al. Peripheral neuropathies after bariatric surgery. Preliminary results from a single-centre prospective study in Northern Italy. *Acta Biomed* 2019;90:259-65. DOI PubMed PMC
10. Müller A, Hase C, Pommnitz M, de Zwaan M. Depression and suicide after bariatric surgery. *Curr Psychiatry Rep* 2019;21:84. DOI PubMed
11. Ivezaj V, Carr MM, Brode C, et al. Disordered eating following bariatric surgery: a review of measurement and conceptual considerations. *Surg Obes Relat Dis* 2021;17:1510-20. DOI PubMed PMC
12. Blackburn AN, Hajnal A, Leggio L. The gut in the brain: the effects of bariatric surgery on alcohol consumption. *Addict Biol* 2017;22:1540-53. DOI PubMed PMC
13. Bruze G, Holmin TE, Peltonen M, et al. Associations of bariatric surgery with changes in interpersonal relationship status: results from 2 Swedish cohort studies. *JAMA Surg* 2018;153:654-61. DOI PubMed PMC
14. Perdomo CM, Cohen RV, Sumithran P, Clément K, Frühbeck G. Contemporary medical, device, and surgical therapies for obesity in adults. *Lancet* 2023;401:1116-30. DOI PubMed
15. Stender S, Nordestgaard BG, Tybjaerg-Hansen A. Elevated body mass index as a causal risk factor for symptomatic gallstone disease: a Mendelian randomization study. *Hepatology* 2013;58:2133-41. DOI PubMed
16. Mulliri A, Menahem B, Alves A, Dupont B. Ursodeoxycholic acid for the prevention of gallstones and subsequent cholecystectomy after bariatric surgery: a meta-analysis of randomized controlled trials. *J Gastroenterol* 2022;57:529-39. DOI PubMed
17. Melmer A, Sturm W, Kuhnert B, et al. Incidence of gallstone formation and cholecystectomy 10 years after bariatric surgery. *Obes Surg* 2015;25:1171-6. DOI PubMed
18. Guzmán HM, Sepúlveda M, Rosso N, San Martin A, Guzmán F, Guzmán HC. Incidence and risk factors for cholelithiasis after bariatric surgery. *Obes Surg* 2019;29:2110-4. DOI PubMed
19. Nagem R, Lázaro-da-Silva A. Cholecystolithiasis after gastric bypass: a clinical, biochemical, and ultrasonographic 3-year follow-up study. *Obes Surg* 2012;22:1594-9. DOI PubMed
20. Amorim-Cruz F, Santos-Sousa H, Ribeiro M, et al; C. Risk and prophylactic management of gallstone disease in bariatric surgery: a systematic review and a Bayesian meta-analysis. *J Gastrointest Surg* 2023;27:433-48. DOI PubMed PMC
21. Haal S, Guman MSS, Bruin S, et al. Risk factors for symptomatic gallstone disease and gallstone formation after bariatric surgery. *Obes Surg* 2022;32:1270-8. DOI PubMed PMC
22. Son SY, Song JH, Shin HJ, Hur H, Han SU. Prevention of gallstones after bariatric surgery using ursodeoxycholic acid: a narrative review of literatures. *J Metab Bariatr Surg* 2022;11:30-8. DOI PubMed PMC
23. Tustumi F, Pinheiro Filho JEL, Stolzemburg LCP, et al. Management of biliary stones in bariatric surgery. *Ther Adv Gastrointest Endosc* 2022;15:26317745221105087. DOI PubMed PMC
24. Weinsier RL, Ullmann DO. Gallstone formation and weight loss. *Obes Res* 1993;1:51-6. DOI
25. Di Ciaula A, Wang DQ, Portincasa P. An update on the pathogenesis of cholesterol gallstone disease. *Curr Opin Gastroenterol* 2018;34:71-80. DOI PubMed PMC
26. Guman MSS, Hoozemans JB, Haal S, et al. Adipose tissue, bile acids, and gut microbiome species associated with gallstones after

bariatric surgery. *J Lipid Res* 2022;63:100280. DOI PubMed PMC

27. Nogueiro J, Santos-Sousa H, Ribeiro M, et al. Incidence of symptomatic gallstones after bariatric surgery: the impact of expectant management. *Langenbecks Arch Surg* 2023;408:160. DOI PubMed PMC
28. Mechanick JI, Youdim A, Jones DB, et al; American Association of Clinical Endocrinologists; Obesity Society; American Society for Metabolic & Bariatric Surgery. 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. *Obesity* 2013;21 Suppl 1:S1-27. DOI PubMed PMC
29. Szatmary P, Grammatikopoulos T, Cai W, et al. Acute pancreatitis: diagnosis and treatment. *Drugs* 2022;82:1251-76. DOI PubMed PMC
30. Sarwal A, Khullar R, Sharma A, Soni V, Baijal M, Chowbey P. Acute pancreatitis as an unusual early post-operative complication following laparoscopic sleeve gastrectomy. *J Minim Access Surg* 2018;14:164-7. DOI PubMed PMC
31. Gapp J, Tariq A, Chandra S. Acute pancreatitis. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482468/ [Last accessed on 4 Mar 2024].
32. Malik S, Mitchell JE, Engel S, Crosby R, Wonderlich S. Psychopathology in bariatric surgery candidates: a review of studies using structured diagnostic interviews. *Compr Psychiatry* 2014;55:248-59. DOI PubMed PMC
33. Mohy-ud-din N, Morrissey S. Pancreatitis. Available from: https://www.ncbi.nlm.nih.gov/books/NBK538337/ [Last accessed on 4 Mar 2024].
34. Borbély Y, Plebani A, Kröll D, Ghisla S, Nett PC. Exocrine pancreatic insufficiency after Roux-en-Y gastric bypass. *Surg Obes Relat Dis* 2016;12:790-4. DOI PubMed
35. Guman MSS, van Olst N, Yaman ZG, et al. Pancreatic exocrine insufficiency after bariatric surgery. *Surg Obes Relat Dis* 2022;18:445-52. DOI
36. Reiniers MJ, van Golen RF, van Gulik TM, Heger M. Reactive oxygen and nitrogen species in steatotic hepatocytes: a molecular perspective on the pathophysiology of ischemia-reperfusion injury in the fatty liver. *Antioxid Redox Signal* 2014;21:1119-42. DOI PubMed PMC
37. Francque SM, Marchesini G, Kautz A, et al. Non-alcoholic fatty liver disease: a patient guideline. *JHEP Rep* 2021;3:100322. DOI PubMed PMC
38. Verna EC, Berk PD. Role of fatty acids in the pathogenesis of obesity and fatty liver: impact of bariatric surgery. *Semin Liver Dis* 2008;28:407-26. DOI
39. Tsai JH, Ferrell LD, Tan V, Yeh MM, Sarkar M, Gill RM. Aggressive non-alcoholic steatohepatitis following rapid weight loss and/or malnutrition. *Mod Pathol* 2017;30:834-42. DOI PubMed PMC
40. Andersen T, Gluud C, Franzmann MB, Christoffersen P. Hepatic effects of dietary weight loss in morbidly obese subjects. *J Hepatol* 1991;12:224-9. DOI
41. van Golen RF, de Waard NE, Moolenaar LR, et al. Acute liver injury and acute liver failure following bariatric surgery. *Case Rep Gastroenterol* 2022;16:240-6. DOI PubMed PMC
42. Lammers WJ, Tilburg AJV, Apers JA, Wiebolt J. Liver failure caused by prolonged state of malnutrition following bariatric surgery. *World J Hepatol* 2018;10:396-9. DOI PubMed PMC
43. Zeisel SH, Da Costa K, Franklin PD, et al. Choline, an essential nutrient for humans. *FASEB J* 1991;5:2093-8. DOI
44. Mazidi M, Katsiki N, Mikhailidis DP, Banach M. Adiposity may moderate the link between choline intake and non-alcoholic fatty liver disease. *J Am Coll Nutr* 2019;38:633-9. DOI
45. Eilenberg M, Langer FB, Beer A, Trauner M, Prager G, Staufer K. Significant liver-related morbidity after bariatric surgery and its reversal-a case series. *Obes Surg* 2018;28:812-9. DOI PubMed PMC
46. Jaworski K, Sarkadi-Nagy E, Duncan RE, Ahmadian M, Sul HS. Regulation of triglyceride metabolism. IV. Hormonal regulation of lipolysis in adipose tissue. *Am J Physiol Gastrointest Liver Physiol* 2007;293:G1-4. DOI PubMed PMC
47. Cardoso AR, Kakimoto PA, Kowaltowski AJ. Diet-sensitive sources of reactive oxygen species in liver mitochondria: role of very long chain acyl-CoA dehydrogenases. *PLoS One* 2013;8:e77088. DOI PubMed PMC
48. Csak T, Ganz M, Pespisa J, Kodys K, Dolganiuc A, Szabo G. Fatty acid and endotoxin activate inflammasomes in mouse hepatocytes that release danger signals to stimulate immune cells. *Hepatology* 2011;54:133-44. DOI PubMed PMC
49. Hafida S, Mirshahi T, Nikolajczyk BS. The impact of bariatric surgery on inflammation: quenching the fire of obesity? *Curr Opin Endocrinol Diabetes Obes* 2016;23:373-8. DOI PubMed PMC
50. Nishi H, Yamanaka D, Kamei H, et al. Importance of serum amino acid profile for induction of hepatic steatosis under protein malnutrition. *Sci Rep* 2018;8:5461. DOI PubMed PMC
51. Mastrototaro L, Sponder G, Saremi B, Aschenbach JR. Gastrointestinal methionine shuttle: Priority handling of precious goods. *IUBMB Life* 2016;68:924-34. DOI PubMed
52. Horie A, Ishida K, Watanabe Y, Shibata K, Hashimoto Y. Membrane transport mechanisms of choline in human intestinal epithelial LS180 cells. *Biopharm Drug Dispos* 2014;35:532-42. DOI PubMed
53. Ulker İ, Yildiran H. The effects of bariatric surgery on gut microbiota in patients with obesity: a review of the literature. *Biosci Microbiota Food Health* 2019;38:3-9. DOI PubMed PMC
54. Shen N, Caixàs A, Ahlers M, et al. Longitudinal changes of microbiome composition and microbial metabolomics after surgical weight loss in individuals with obesity. *Surg Obes Relat Dis* 2019;15:1367-73. DOI PubMed PMC

55. Ciobârcă D, Cătoi AF, Copăescu C, Miere D, Crișan G. Bariatric surgery in obesity: effects on gut microbiota and micronutrient Status. *Nutrients* 2020;12:235. DOI PubMed PMC
56. Romano KA, Vivas EI, Amador-Noguez D, Rey FE. Intestinal microbiota composition modulates choline bioavailability from diet and accumulation of the proatherogenic metabolite trimethylamine-N-oxide. *mBio* 2015;6:e02481. DOI PubMed PMC
57. Wallace TC, Blusztajn JK, Caudill MA, et al. Choline: the underconsumed and underappreciated essential nutrient. *Nutr Today* 2018;53:240-53. DOI PubMed PMC
58. Mehedint MG, Zeisel SH. Choline's role in maintaining liver function: new evidence for epigenetic mechanisms. *Curr Opin Clin Nutr Metab Care* 2013;16:339-45. DOI PubMed PMC
59. Nicoletti CF, Morandi Junqueira-Franco MV, dos Santos JE, Marchini JS, Salgado W Jr, Nonino CB. Protein and amino acid status before and after bariatric surgery: a 12-month follow-up study. *Surg Obes Relat Dis* 2013;9:1008-12. DOI PubMed
60. Poylin V, Serrot FJ, Madoff RD, et al. Obesity and bariatric surgery: a systematic review of associations with defecatory dysfunction. *Colorectal Dis* 2011;13:e92-103. DOI
61. Afshar S, Kelly SB, Seymour K, Woodcock S, Werner AD, Mathers JC. The effects of bariatric procedures on bowel habit. *Obes Surg* 2016;26:2348-54. DOI PubMed PMC
62. Marathe CS, Rayner CK, Jones KL, Horowitz M. Effects of GLP-1 and incretin-based therapies on gastrointestinal motor function. *Exp Diabetes Res* 2011;2011:279530. DOI PubMed PMC
63. Sileri P, Franceschilli L, Cadeddu F, et al. Prevalence of defaecatory disorders in morbidly obese patients before and after bariatric surgery. *J Gastrointest Surg* 2012;16:62-6; discussion 66. DOI
64. Grosse CS, Cope VC. Dietary fibre intake and bowel habits after bariatric surgery: a structured literature review. *Obes Surg* 2019;29:2247-54. DOI PubMed
65. Shah HN, Bal BS, Finelli FC, Koch TR. Constipation in patients with thiamine deficiency after Roux-en-Y gastric bypass surgery. *Digestion* 2013;88:119-24. DOI PubMed
66. Bramante C, Wise E, Chaudhry Z. Care of the patient after metabolic and bariatric surgery. *Ann Intern Med* 2022;175:ITC65-80. DOI PubMed
67. Coral RV, Bigolin AV, Machry MC, et al. Improvement in muscle strength and metabolic parameters despite muscle mass loss in the initial six months after bariatric surgery. *Obes Surg* 2021;31:4485-91. DOI
68. Ho C, Samwil SNM, Kahairudin Z, Jamhuri N, Abd Aziz A. Exercise and pre-habilitation with high whey-protein-based meal replacement therapy promote weight loss and preserve muscle mass before bariatric surgery. *Asian J Surg* 2023;46:3716-21. DOI PubMed
69. Gil S, Kirwan JP, Murai IH, et al. A randomized clinical trial on the effects of exercise on muscle remodelling following bariatric surgery. *J Cachexia Sarcopenia Muscle* 2021;12:1440-55. DOI PubMed PMC
70. Wolfe RR. The underappreciated role of muscle in health and disease. *Am J Clin Nutr* 2006;84:475-82. DOI PubMed
71. Holanda N, Crispim N, Carlos I, Moura T, Nóbrega E, Bandeira F. Musculoskeletal effects of obesity and bariatric surgery - a narrative review. *Arch Endocrinol Metab* 2022;66:621-32. DOI PubMed PMC
72. Molero J, Olbeyra R, Flores L, et al. Prevalence of low skeletal muscle mass following bariatric surgery. *Clin Nutr ESPEN* 2022;49:436-41. DOI
73. Davidson LE, Yu W, Goodpaster BH, et al. Fat-free mass and skeletal muscle mass five years after bariatric surgery. *Obesity* 2018;26:1130-6. DOI PubMed PMC
74. Zhou N, Scoubeau C, Forton K, et al. Lean mass loss and altered muscular aerobic capacity after bariatric surgery. *Obes Facts* 2022;15:248-56. DOI PubMed PMC
75. Voican CS, Lebrun A, Maitre S, et al. Predictive score of sarcopenia occurrence one year after bariatric surgery in severely obese patients. *PLoS One* 2018;13:e0197248. DOI PubMed PMC
76. Martínez MC, Meli EF, Candia FP, et al. The impact of bariatric surgery on the muscle mass in patients with obesity: 2-year follow-up. *Obes Surg* 2022;32:625-33. DOI PubMed PMC
77. Westerterp-Plantenga MS, Lemmens SG, Westerterp KR. Dietary protein - its role in satiety, energetics, weight loss and health. *Br J Nutr* 2012;108 Suppl 2:S105-12. DOI PubMed
78. Morales-Marroquin E, Kohl HW 3rd, Knell G, de la Cruz-Muñoz N, Messiah SE. Resistance training in post-metabolic and bariatric surgery patients: a systematic review. *Obes Surg* 2020;30:4071-80. DOI PubMed
79. Oppert JM, Bellicha A, Roda C, et al. Resistance training and protein supplementation increase strength after bariatric surgery: a randomized controlled trial. *Obesity* 2018;26:1709-20. DOI
80. Huck CJ. Effects of supervised resistance training on fitness and functional strength in patients succeeding bariatric surgery. *J Strength Cond Res* 2015;29:589-95. DOI PubMed
81. Stegen S, Derave W, Calders P, Van Laethem C, Pattyn P. Physical fitness in morbidly obese patients: effect of gastric bypass surgery and exercise training. *Obes Surg* 2011;21:61-70. DOI PubMed
82. Daniels P, Burns RD, Brusseau TA, et al. Effect of a randomised 12-week resistance training programme on muscular strength, cross-sectional area and muscle quality in women having undergone Roux-en-Y gastric bypass. *J Sports Sci* 2018;36:529-35. DOI
83. Herring LY, Stevinson C, Carter P, et al. The effects of supervised exercise training 12-24 months after bariatric surgery on physical function and body composition: a randomised controlled trial. *Int J Obes (Lond)* 2017;41:909-16. DOI PubMed
84. Grannell A, De Vito G, Murphy JC, le Roux CW. The influence of skeletal muscle on appetite regulation. *Expert Rev Endocrinol*

Metab 2019;14:267-82. DOI PubMed
85. Nakamura KM, Haglind EG, Clowes JA, et al. Fracture risk following bariatric surgery: a population-based study. *Osteoporos Int* 2014;25:151-8. DOI PubMed PMC
86. Maghrabi AH, Wolski K, Abood B, et al. Two-year outcomes on bone density and fracture incidence in patients with T2DM randomized to bariatric surgery versus intensive medical therapy. *Obesity* 2015;23:2344-8. DOI PubMed PMC
87. Ahlin S, Peltonen M, Sjöholm K, et al. Fracture risk after three bariatric surgery procedures in Swedish obese subjects: up to 26 years follow-up of a controlled intervention study. *J Intern Med* 2020;287:546-57. DOI PubMed
88. Sayadi Shahraki M, Mahmoudieh M, Kalidari B, et al. Bone health after bariatric surgery: consequences, prevention, and treatment. *Adv Biomed Res* 2022;11:92. DOI PubMed PMC
89. Frost HM. Bone "mass" and the "mechanostat": a proposal. *Anat Rec* 1987;219:1-9. DOI PubMed
90. Zerwekh JE, Ruml LA, Gottschalk F, Pak CY. The effects of twelve weeks of bed rest on bone histology, biochemical markers of bone turnover, and calcium homeostasis in eleven normal subjects. *J Bone Miner Res* 1998;13:1594-601. DOI
91. Schwartz AV, Johnson KC, Kahn SE, et al; Look AHEAD Research Group. Effect of 1 year of an intentional weight loss intervention on bone mineral density in type 2 diabetes: results from the Look AHEAD randomized trial. *J Bone Miner Res* 2012;27:619-27. DOI PubMed PMC
92. Pluskiewicz W, Bužga M, Holéczy P, Bortlík L, Šmajstrla V, Adamczyk P. Bone mineral changes in spine and proximal femur in individual obese women after laparoscopic sleeve gastrectomy: a short-term study. *Obes Surg* 2012;22:1068-76. DOI PubMed PMC
93. Vilarrasa N, San José P, García I, et al. Evaluation of bone mineral density loss in morbidly obese women after gastric bypass: 3-year follow-up. *Obes Surg* 2011;21:465-72. DOI
94. Bergmann G, Deuretzbacher G, Heller M, et al. Hip contact forces and gait patterns from routine activities. *J Biomech* 2001;34:859-71. DOI PubMed
95. Hart DA. Regulation of bone by mechanical loading, sex hormones, and nerves: integration of such regulatory complexity and implications for bone loss during space flight and post-menopausal osteoporosis. *Biomolecules* 2023;13:1136. DOI PubMed PMC
96. Bal BS, Finelli FC, Shope TR, Koch TR. Nutritional deficiencies after bariatric surgery. *Nat Rev Endocrinol* 2012;8:544-56. DOI PubMed
97. Stein EM, Silverberg SJ. Bone loss after bariatric surgery: causes, consequences, and management. *Lancet Diabetes Endocrinol* 2014;2:165-74. DOI PubMed PMC
98. Sunyecz JA. The use of calcium and vitamin D in the management of osteoporosis. *Ther Clin Risk Manag* 2008;4:827-36. DOI PubMed PMC
99. Lalmohamed A, de Vries F, Bazelier MT, et al. Risk of fracture after bariatric surgery in the United Kingdom: population based, retrospective cohort study. *BMJ* 2012;345:e5085. DOI PubMed PMC
100. Douglas IJ, Bhaskaran K, Batterham RL, Smeeth L. Bariatric surgery in the united kingdom: a cohort study of weight loss and clinical outcomes in routine clinical care. *PLoS Med* 2015;12:e1001925. DOI PubMed PMC
101. Yu EW, Lee MP, Landon JE, Lindeman KG, Kim SC. Fracture risk after bariatric surgery: Roux-en-Y gastric bypass versus adjustable gastric banding. *J Bone Miner Res* 2017;32:1229-36. DOI PubMed PMC
102. Paccou J, Martignène N, Lespessailles E, et al. Gastric bypass but not sleeve gastrectomy increases risk of major osteoporotic fracture: french population-based cohort study. *J Bone Miner Res* 2020;35:1415-23. DOI PubMed
103. Khalid SI, Omotosho PA, Spagnoli A, Torquati A. Association of bariatric surgery with risk of fracture in patients with severe obesity. *JAMA Netw Open* 2020;3:e207419. DOI PubMed PMC
104. Parrott J, Frank L, Rabena R, Craggs-Dino L, Isom KA, Greiman L. American society for metabolic and bariatric surgery integrated health nutritional guidelines for the surgical weight loss patient 2016 update: micronutrients. *Surg Obes Relat Dis* 2017;13:727-41. DOI PubMed
105. Sherf-Dagan S, Buch A, Ben-Porat T, Sakran N, Sinai T. Vitamin E status among bariatric surgery patients: a systematic review. *Surg Obes Relat Dis* 2021;17:816-30. DOI PubMed
106. Fattal-valevski A. Thiamine (Vitamin B_1). *J Evid Based Complementary Altern Med* 2011;16:12-20. DOI
107. Novak P, Novak P. Case 80: Vitamin B12 Deficiency. In: Novak P, editor. Autonomic Testing. Oxford University Press; 2019. pp. 403-6.
108. Powers HJ. Vitamin requirements for term infants: considerations for infant formulae. *Nutr Res Rev* 1997;10:1-33. DOI PubMed
109. DeLoughery TG. Iron deficiency anemia. *Med Clin North Am* 2017;101:319-32. DOI PubMed
110. Abbasi E, Vijayashankar SS, Goldman RD. Management of acute supraventricular tachycardia in children. *Can Fam Physician* 2023;69:839-41. DOI PubMed
111. Eden RE, Daley SF, Coviello JM. Vitamin K Deficiency. Available from: https://www.ncbi.nlm.nih.gov/books/NBK536983/ [Last accessed on 5 Mar 2024].
112. Cormick G, Belizán JM. Calcium intake and health. *Nutrients* 2019;11:1606. DOI PubMed PMC
113. Boltshauser E, Weber KP. Laboratory investigations. The Cerebellum: From Embryology to Diagnostic Investigations. Elsevier; 2018. pp. 287-98.
114. Milone M, Di Minno MN, Lupoli R, et al. Wernicke encephalopathy in subjects undergoing restrictive weight loss surgery: a systematic review of literature data. *Eur Eat Disord Rev* 2014;22:223-9. DOI

115. Singleton CK, Martin PR. Molecular mechanisms of thiamine utilization. *Curr Mol Med* 2001;1:197-207. DOI PubMed
116. Agabio R. Thiamine administration in alcohol-dependent patients. *Alcohol Alcohol* 2005;40:155-6. DOI PubMed
117. Zalesin KC, Miller WM, Franklin B, et al. Vitamin a deficiency after gastric bypass surgery: an underreported postoperative complication. *J Obes* 2011;2011:1-4. DOI PubMed PMC
118. Slater GH, Ren CJ, Siegel N, et al. Serum fat-soluble vitamin deficiency and abnormal calcium metabolism after malabsorptive bariatric surgery. *J Gastrointest Surg* 2004;8:48-55; discussion 54. DOI PubMed
119. Smelt HJM, Pouwels S, Smulders JF, Hazebroek EJ. Patient adherence to multivitamin supplementation after bariatric surgery: a narrative review. *J Nutr Sci* 2020;9:e46. DOI PubMed PMC
120. Spetz K, Svedjeholm S, Roos S, Grehn S, Olbers T, Andersson E. Adherence to vitamin and mineral supplementation after bariatric surgery - A two-year cohort study. *Obes Res Clin Pract* 2022;16:407-12. DOI PubMed
121. Heck AM, Yanovski JA, Calis KA. Orlistat, a new lipase inhibitor for the management of obesity. *Pharmacotherapy* 2000;20:270-9. DOI PubMed PMC
122. Nori SL, Stretanski MF. Foot drop. Available from: https://www.ncbi.nlm.nih.gov/books/NBK554393/ [Last accessed on 5 Mar 2024].
123. O'Brien PD, Hinder LM, Callaghan BC, Feldman EL. Neurological consequences of obesity. *Lancet Neurol* 2017;16:465-77. DOI PubMed PMC
124. Callaghan BC, Reynolds E, Banerjee M, Chant E, Villegas-Umana E, Feldman EL. Central obesity is associated with neuropathy in the severely obese. *Mayo Clin Proc* 2020;95:1342-53. DOI PubMed PMC
125. Lim JZM, Burgess J, Ooi CG, et al. The peripheral neuropathy prevalence and characteristics are comparable in people with obesity and long-duration type 1 diabetes. *Adv Ther* 2022;39:4218-29. DOI PubMed PMC
126. Callaghan BC, Xia R, Reynolds E, et al. Association between metabolic syndrome components and polyneuropathy in an obese population. *JAMA Neurol* 2016;73:1468-76. DOI PubMed PMC
127. Andersen ST, Witte DR, Dalsgaard EM, et al. Risk factors for incident diabetic polyneuropathy in a cohort with screen-detected type 2 diabetes followed for 13 years: ADDITION-Denmark. *Diabetes Care* 2018;41:1068-75. DOI
128. Schlesinger S, Herder C, Kannenberg JM, et al. General and abdominal obesity and incident distal sensorimotor polyneuropathy: insights into inflammatory biomarkers as potential mediators in the KORA F4/FF4 cohort. *Diabetes Care* 2019;42:240-7. DOI
129. Bongetta D, Zoia C, Luzzi S, et al. Neurosurgical issues of bariatric surgery: A systematic review of the literature and principles of diagnosis and treatment. *Clin Neurol Neurosurg* 2019;176:34-40. DOI
130. Thaisetthawatkul P, Collazo-Clavell ML, Sarr MG, Norell JE, Dyck PJ. A controlled study of peripheral neuropathy after bariatric surgery. *Neurology* 2004;63:1462-70. DOI PubMed
131. Koffman BM, Greenfield LJ, Ali II, Pirzada NA. Neurologic complications after surgery for obesity. *Muscle Nerve* 2006;33:166-76. DOI PubMed
132. Aluísio S, Dedi Ferreira Alves N, Évelin Pereira da S, et al. Peripheral neuropathies after bariatric surgery: a current review. *Int J Neurol Neurother* 2021;8:107. DOI
133. Thaisetthawatkul P, Collazo-Clavell ML, Sarr MG, Norell JE, Dyck PJ. Good nutritional control may prevent polyneuropathy after bariatric surgery. *Muscle Nerve* 2010;42:709-14. DOI PubMed PMC
134. Aasheim ET, Hofsø D, Hjelmesaeth J, Sandbu R. Peripheral neuropathy and severe malnutrition following duodenal switch. *Obes Surg* 2008;18:1640-3. DOI PubMed
135. Rudnicki SA. Prevention and treatment of peripheral neuropathy after bariatric surgery. *Curr Treat Options Neurol* 2010;12:29-36. DOI PubMed
136. Weyns FJ, Beckers F, Vanormelingen L, Vandersteen M, Niville E. Foot drop as a complication of weight loss after bariatric surgery: is it preventable? *Obes Surg* 2007;17:1209-12. DOI PubMed
137. Reyhani A, Dortcan N. A rare etiology of bilateral foot drop: weight loss. *Euras J Fam Med* 2020;9:251-4. DOI
138. Deledda A, Pintus S, Loviselli A, Fosci M, Fantola G, Velluzzi F. Nutritional management in bariatric surgery patients. *Int J Environ Res Public Health* 2021;18:12049. DOI PubMed PMC
139. Sierżantowicz R, Ładny JR, Lewko J. Quality of life after bariatric surgery-a systematic review. *Int J Environ Res Public Health* 2022;19:9078. DOI PubMed PMC
140. Mabey JG, Kolotkin RL, Crosby RD, Crowell SE, Hunt SC, Davidson LE. Mediators of suicidality 12 years after bariatric surgery relative to a nonsurgery comparison group. *Surg Obes Relat Dis* 2021;17:121-30. DOI PubMed PMC
141. Lagerros YT, Brandt L, Hedberg J, Sundbom M, Bodén R. Suicide, self-harm, and depression after gastric bypass surgery: a nationwide cohort study. *Ann Surg* 2017;265:235-43. DOI PubMed
142. Peterhänsel C, Petroff D, Klinitzke G, Kersting A, Wagner B. Risk of completed suicide after bariatric surgery: a systematic review. *Obes Rev* 2013;14:369-82. DOI PubMed
143. Castaneda D, Popov VB, Wander P, Thompson CC. Risk of suicide and self-harm is increased after bariatric surgery-a systematic review and meta-analysis. *Obes Surg* 2019;29:322-33. DOI PubMed
144. Goueslard K, Jollant F, Petit JM, Quantin C. Self-harm hospitalization following bariatric surgery in adolescents and young adults. *Clin Nutr* 2022;41:238-45. DOI
145. Konttinen H, Sjöholm K, Jacobson P, Svensson PA, Carlsson LMS, Peltonen M. Prediction of suicide and nonfatal self-harm after bariatric surgery: a risk score based on sociodemographic factors, lifestyle behavior, and mental health: a nonrandomized controlled

trial. *Ann Surg* 2021;274:339-45. DOI PubMed PMC

146. Herpertz S, Müller A, Burgmer R, Crosby RD, de Zwaan M, Legenbauer T. Health-related quality of life and psychological functioning 9 years after restrictive surgical treatment for obesity. *Surg Obes Relat Dis* 2015;11:1361-70. DOI PubMed
147. Van den Eynde A, Mertens A, Vangoitsenhoven R, et al. Psychosocial consequences of bariatric surgery: two sides of a coin: a scoping review. *Obes Surg* 2021;31:5409-17. DOI
148. Lim RBC, Zhang MWB, Ho RCM. Prevalence of all-cause mortality and suicide among bariatric surgery cohorts: a meta-analysis. *Int J Environ Res Public Health* 2018;15:1519. DOI PubMed PMC
149. Tindle HA, Omalu B, Courcoulas A, Marcus M, Hammers J, Kuller LH. Risk of suicide after long-term follow-up from bariatric surgery. *Am J Med* 2010;123:1036-42. DOI PubMed PMC
150. Neovius M, Bruze G, Jacobson P, et al. Risk of suicide and non-fatal self-harm after bariatric surgery: results from two matched cohort studies. *Lancet Diabetes Endocrinol* 2018;6:197-207. DOI PubMed PMC
151. Güzel K, Aksu MH, Geniş B, Gürhan N. The effect of defense mechanisms and eating awareness on the probability of suicide after bariatric surgery. *Turk Psikiyatri Derg* 2022;33:180-6. DOI PubMed
152. Brown RM, Guerrero-Hreins E, Brown WA, le Roux CW, Sumithran P. Potential gut-brain mechanisms behind adverse mental health outcomes of bariatric surgery. *Nat Rev Endocrinol* 2021;17:549-59. DOI PubMed
153. Mitchell JE, Crosby R, de Zwaan M, et al. Possible risk factors for increased suicide following bariatric surgery. *Obesity* 2013;21:665-72. DOI PubMed PMC
154. Bhatti JA, Nathens AB, Thiruchelvam D, Grantcharov T, Goldstein BI, Redelmeier DA. Self-harm emergencies after bariatric surgery: a population-based cohort study. *JAMA Surg* 2016;151:226-32. DOI PubMed
155. Wild B, Hünnemeyer K, Sauer H, et al. A 1-year videoconferencing-based psychoeducational group intervention following bariatric surgery: results of a randomized controlled study. *Surg Obes Relat Dis* 2015;11:1349-60. DOI
156. Yen YC, Huang CK, Tai CM. Psychiatric aspects of bariatric surgery. *Curr Opin Psychiatry* 2014;27:374-9. DOI PubMed PMC
157. Roizblatt A, Roizblatt D, Soto-Aguilar B F. [Suicide risk after bariatric surgery]. *Rev Med Chil* 2016;144:1171-6. DOI PubMed
158. Arcelus J, Mitchell AJ, Wales J, Nielsen S. Mortality rates in patients with anorexia nervosa and other eating disorders. A meta-analysis of 36 studies. *Arch Gen Psychiatry* 2011;68:724-31. DOI PubMed
159. Udo T, Grilo CM. Psychiatric and medical correlates of DSM-5 eating disorders in a nationally representative sample of adults in the United States! *Int J Eat Disord* 2019;52:42-50. DOI PubMed
160. Pehlivan MJ, Miskovic-Wheatley J, Le A, et al. Models of care for eating disorders: findings from a rapid review. *J Eat Disord* 2022;10:166. DOI PubMed PMC
161. Opolski M, Chur-Hansen A, Wittert G. The eating-related behaviours, disorders and expectations of candidates for bariatric surgery. *Clin Obes* 2015;5:165-97. DOI PubMed
162. Taba JV, Suzuki MO, Nascimento FSD, et al. The development of feeding and eating disorders after bariatric surgery: a systematic review and meta-analysis. *Nutrients* 2021;13:2396. DOI PubMed PMC
163. Colles SL, Dixon JB, O'Brien PE. Loss of control is central to psychological disturbance associated with binge eating disorder. *Obesity* 2008;16:608-14. DOI PubMed
164. Carter KA, Fodor AA, Balkus JE, et al. Vaginal microbiome metagenome inference accuracy: differential measurement error according to community composition. *mSystems* 2023;8:e0100322. DOI PubMed PMC
165. Conceição EM, Mitchell JE, Pinto-Bastos A, Arrojado F, Brandão I, Machado PPP. Stability of problematic eating behaviors and weight loss trajectories after bariatric surgery: a longitudinal observational study. *Surg Obes Relat Dis* 2017;13:1063-70. DOI PubMed
166. de Zwaan M, Hilbert A, Swan-Kremeier L, et al. Comprehensive interview assessment of eating behavior 18-35 months after gastric bypass surgery for morbid obesity. *Surg Obes Relat Dis* 2010;6:79-85. DOI PubMed
167. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-IV). Available from: https://www.gammaconstruction.mu/sites/default/files/webform/cvs/pdf-diagnostic-and-statistical-manual-of-mental-disorders-dsm-iv-american-psychiatric-association-pdf-download-free-book-9223cc7.pdf [Last accessed on 5 Mar 2024].
168. Kuhn JH, Adachi T, Adhikari NKJ, et al. New filovirus disease classification and nomenclature. *Nat Rev Microbiol* 2019;17:261-3. DOI PubMed PMC
169. PhenX Toolkit. Protocol eating disorders examination bariatric surgery interview. Available from: https://www.phenxtoolkit.org/protocols/view/230103 [Last accessed on 14 Mar 2024]
170. Barbuti M, Carignani G, Weiss F, et al. Eating disorders and emotional dysregulation are associated with insufficient weight loss after bariatric surgery: a 1-year observational follow-up study. *Eat Weight Disord* 2023;28:49. DOI PubMed PMC
171. Busetto L, Dicker D, Azran C, et al. Practical recommendations of the obesity management task force of the european association for the study of obesity for the post-bariatric surgery medical management. *Obes Facts* 2017;10:597-632. DOI PubMed PMC
172. Pucci A, Batterham RL. Mechanisms underlying the weight loss effects of RYGB and SG: similar, yet different. *J Endocrinol Invest* 2019;42:117-28. DOI PubMed PMC
173. Guerrero-Hreins E, Foldi CJ, Oldfield BJ, Stefanidis A, Sumithran P, Brown RM. Gut-brain mechanisms underlying changes in disordered eating behaviour after bariatric surgery: a review. *Rev Endocr Metab Disord* 2022;23:733-51. DOI PubMed
174. Lindgren E, Gray K, Miller G, et al. Food addiction: a common neurobiological mechanism with drug abuse. *Front Biosci* 2018;23:811-36. DOI PubMed

175. Kessler RM, Hutson PH, Herman BK, Potenza MN. The neurobiological basis of binge-eating disorder. *Neurosci Biobehav Rev* 2016;63:223-38. DOI PubMed
176. Conceição EM, de Lourdes M, Moreira L, Pinto-Bastos A, Félix S. Weight loss expectations and weight loss after surgery: the mediating role of body image and weight concerns. *Surg Obes Relat Dis* 2020;16:932-9. DOI PubMed
177. Mellinger JL, Shedden K, Winder GS, et al. Bariatric surgery and the risk of alcohol-related cirrhosis and alcohol misuse. *Liver Int* 2021;41:1012-9. DOI PubMed PMC
178. Sogg S. Comment on: Alcohol and other substance use after bariatric surgery: prospective evidence from a us multicenter cohort study. *Surg Obes Relat Dis* 2017;13:1402-4. DOI PubMed
179. Woodard GA, Downey J, Hernandez-Boussard T, Morton JM. Impaired alcohol metabolism after gastric bypass surgery: a case-crossover trial. *J Am Coll Surg* 2011;212:209-14. DOI
180. Hagedorn JC, Encarnacion B, Brat GA, Morton JM. Does gastric bypass alter alcohol metabolism? *Surg Obes Relat Dis* 2007;3:543-8; discussion 548. DOI PubMed
181. Holt PR. Changes in alcohol metabolism after gastric bypass surgery. *Lancet* 2011;378:767-8. DOI PubMed
182. Blum K, Chen AL, Oscar-Berman M, et al. Generational association studies of dopaminergic genes in reward deficiency syndrome (RDS) subjects: selecting appropriate phenotypes for reward dependence behaviors. *Int J Environ Res Public Health* 2011;8:4425-59. DOI PubMed PMC
183. King WC, Hinerman AS, White GE. Changes in marital status following Roux-en-Y gastric bypass and sleeve gastrectomy: a US multicenter prospective cohort study. *Ann Surg Open* 2022;3:e182. DOI PubMed PMC
184. Bramming M, Hviid SS, Becker U, et al. Changes in relationship status following bariatric surgery. *Int J Obes* 2021;45:1599-606. DOI
185. Rand CSW, Kuldau JM, Robbins L. Surgery for obesity and marriage quality. *JAMA* 1982;247:1419. DOI
186. Neill JR, Marshall JR, Yale CE. Marital changes after intestinal bypass surgery. *JAMA* 1978;240:447. DOI PubMed
187. White MA, Kalarchian MA, Levine MD, Masheb RM, Marcus MD, Grilo CM. Prognostic significance of depressive symptoms on weight loss and psychosocial outcomes following gastric bypass surgery: a prospective 24-month follow-up study. *Obes Surg* 2015;25:1909-16. DOI PubMed PMC
188. Backman O, Stockeld D, Rasmussen F, Näslund E, Marsk R. Alcohol and substance abuse, depression and suicide attempts after Roux-en-Y gastric bypass surgery. *Br J Surg* 2016;103:1336-42. DOI PubMed
189. Idstad M, Torvik FA, Borren I, Rognmo K, Røysamb E, Tambs K. Mental distress predicts divorce over 16 years: the HUNT study. *BMC Public Health* 2015;15:320. DOI PubMed PMC
190. Liao J, Yin Y, Zhong J, et al. Bariatric surgery and health outcomes: An umbrella analysis. *Front Endocrinol* 2022;13:1016613. DOI PubMed PMC
191. Portincasa P, Frühbeck G. Phenotyping the obesities: reality or utopia? *Rev Endocr Metab Disord* 2023;24:767-73. DOI PubMed PMC
192. Drucker DJ. GLP-1 physiology informs the pharmacotherapy of obesity. *Mol Metab* 2022;57:101351. DOI PubMed PMC