### **Psychiatric Comorbidities and Weight Loss Recommendations** in Bariatric Surgery Patients

KRISTY DALRYMPLE, PhD; CRISTINA TOBA, MD

#### **ABSTRACT**

Metabolic and bariatric surgery is increasingly utilized as a treatment for obesity worldwide. Despite significant weight loss, weight regain can occur long-term with bariatric surgery, with factors related to weight regain including the presence of comorbid psychiatric conditions. Psychiatric comorbidity in bariatric surgery candidates is common; although these comorbidities sometimes improve in the short-term, they may worsen in the longterm or new problems may emerge post-surgically. Many patients may continue to take psychotropic medications after surgery to maintain behavioral health, yet some medications are associated with weight gain or may pose certain risks due to changes in pharmacokinetics following surgery. The research on psychiatric comorbidity in bariatric surgery patients is presented, along with a review of psychotropic medications that may pose risks of weight gain post-surgically. Clinical recommendations are provided based on existing evidence with respect to managing psychiatric comorbidity in patients in ways that can optimize behavioral health outcomes while also ensuring positive outcomes with bariatric surgery.

**KEYWORDS:** Psychiatric Comorbidity, Medication, Psychotherapy, Bariatric Surgery

#### INTRODUCTION

Metabolic and bariatric surgery is increasingly utilized as a treatment for obesity worldwide,1 with the most common procedures being Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG). Maximum weight loss is achieved in the first one-two years post-surgery,2 with additional long-term benefits.<sup>3</sup> Despite significant weight loss, weight regain can occur long-term with bariatric surgery, with factors related to weight regain including the presence of comorbid psychiatric conditions and challenges in adjusting to the new social demands after weight loss surgery.<sup>4,5</sup> The following review will focus on psychiatric comorbidity in bariatric surgery patients, its impacts on surgical outcomes, and evidence-based clinical recommendations for managing this comorbidity pattern in bariatric surgery candidates.

#### **OBESITY-PSYCHIATRIC COMORBIDITY** IN BARIATRIC SURGERY CANDIDATES

Psychiatric comorbidity in bariatric surgery candidates tends to be higher compared to the general population and those experiencing obesity but who are non-treatment seeking.6 Individuals seeking medical interventions for obesity are more likely to have medical comorbidities, including diabetes, obstructive sleep apnea, and cardiovascular disease, and these severe medical conditions are associated with high levels of psychiatric conditions such as depression.<sup>7</sup>

As many as 81% of bariatric surgery patients have met criteria for at least one lifetime psychiatric disorder at the pre-surgical evaluation, with mood and anxiety disorders being the most common.8 The most common lifetime disorders are affective disorders (e.g., major depression), while the most common current disorders are anxiety disorders.<sup>6</sup> One study of over 1,000 bariatric surgery candidates found that specific phobia was the most prevalent current disorder (9.0%), followed by social anxiety disorder (7.9%). However, some studies have found that eating disorders were the most common current diagnosis, and other studies have demonstrated a high prevalence of posttraumatic stress disorder (PTSD) in bariatric surgery candidates. Even in the absence of PTSD, rates of childhood trauma (particularly childhood sexual traumal tend to be higher in this population. In addition to being associated with PTSD, childhood trauma is associated with problematic eating behaviors and obesity.6

Rates of substance use disorders are low in presurgical candidates relative to other disorders (e.g., 7.6% in the Longitudinal Assessment of Bariatric Surgery [LABS-2] study], 10 yet overall use of substances pre-surgically may be high and may confer certain risks after surgery. Alcohol use has been as high as nearly 75% in bariatric surgery patients, with high-risk drinking in 17% of pre-surgical candidates.<sup>11</sup> Although alcohol use decreases following surgery, a percentage of patients experience the emergence of new-onset alcohol use problems or disorder post-surgically, particularly for those receiving the RYGB procedure. 11 Similar findings have occurred with other substances.12



## IMPACT OF PSYCHIATRIC COMORBIDITY AND CORRELATES ON SURGICAL OUTCOMES

Psychiatric comorbidities tend to improve in the short-term, particularly one-two years post-surgery.<sup>8</sup> However, results from longer-term follow-up studies indicate that a decline in behavioral health tends to occur as many as 10 years after surgery.<sup>13,14</sup> A nine-year follow-up study showed there was a 32% increase in mood and eating disorders over the follow-up period compared to the pre-surgery period, with peak prevalence occurring at 72–96 months post-surgery.<sup>8</sup>

Findings are mixed as to whether psychiatric disorders are related to insufficient weight loss or weight regain after bariatric surgery. For example, mood, anxiety, and binge-eating disorders are associated with poorer weight loss outcomes up to 50 months after surgery. Conversely, seven years after surgery there is an inconsistent relationship between the presence of presurgical psychiatric disorders and weight loss outcomes. Although one recent study showed that the prevalence of psychiatric disorders increased over the post-surgical period, they also found that psychiatric disorders were not associated with percent excess weight loss over the post-surgical period.

These mixed findings could be due to the variability in how psychiatric disorders were assessed. When using semi-structured diagnostic interviews, different types of instruments can be used, and prevalence rates may differ based on the assessment instrument. Other studies have used unstructured clinical interviews, which often underdiagnose psychiatric conditions. The degree to which the assessment process was independent of the presurgical approval process may also impact prevalence rates. When the assessment is a formal part of the surgical clearance process, symptoms may be underreported by patients due to fears of not being cleared. Furthermore, mixed findings could be due to the range of disorders that are assessed; some studies have examined only single disorders, while other studies have assessed a range of psychiatric disorders.

One correlate of psychiatric conditions, emotional eating, has been found to affect surgical outcomes. Emotional eating is defined as eating with the intended function of reducing stress or emotional upset. It has been shown to occur in 24–40% of bariatric surgery candidates, even in those with no lifetime psychiatric disorder. Pre-surgical emotional eating severity is significantly associated with poorer weight loss following RYGB, laparoscopic adjustable gastric band, and biliopancreatic diversion, lathough one study found that it was associated with increased odds of postsurgical weight loss success. If it is also significantly associated with higher levels of anxiety and depression in bariatric surgery candidates. If 200

Perhaps psychiatric conditions have an indirect, rather than direct, effect on weight loss outcomes. Psychological factors such as mindfulness (e.g., nonjudgmental stance towards emotions and thoughts) have mediated the relationship

between depression symptoms and emotional eating presurgically, such that higher levels of depression symptoms were associated with greater emotional eating through higher levels of judgment towards thoughts and feelings.<sup>21</sup> Other studies showed that higher levels of mindfulness skills were associated with lower engagement in problematic eating behaviors, including emotional eating.<sup>22</sup> Emotion regulation skills may also be an important psychological factor to address, as it has been associated with problematic eating behaviors such as emotional eating in bariatric surgery candidates.<sup>23</sup>

## WEIGHT GAIN AND PSYCHOTROPIC MEDICATIONS

In the LABS study,<sup>24</sup> 40% of 4500 presurgical candidates were taking an antidepressant medication (AD). ADs are the most prescribed psychotropic medications and are often continued during the post-surgical period, unlike medications for medical comorbidities. Overall, 65% of patients taking ADs report a side effect of weight gain, with 21% having a higher risk of greater than 5% weight gain compared to those not taking ADs. Across all ADs, tricyclics, MAOIs, and mirtazapine have the highest risk for weight gain.<sup>25</sup>

A recent review<sup>25</sup> showed that within selective serotonin reuptake inhibitors (SSRIs), paroxetine and citalogram have the highest risk of weight gain, while fluoxetine and sertraline are generally weight-neutral but may cause weight gain with long-term use. Compared with sertraline, escitalopram, paroxetine, and citalopram were associated with greater weight gain at six months, while fluoxetine was weight-neutral and bupropion was associated with weight loss. Serotonin norepinephrine uptake inhibitors (SNRIs) can cause weight gain, but the effect is less pronounced than with some other AD classes. Short-term studies show weight neutrality or even slight weight loss with SNRIs, but weight gain risk becomes higher with longer-term use. The risk of weight gain with SNRIs is lower than with tricyclic antidepressants or mirtazapine, but higher than with bupropion.25 Tricyclic antidepressants (TCAs) can cause significant weight gain, with amitriptyline being the most potent TCA for inducing weight gain. The Endocrine Society recommends that clinicians consider the risk of weight gain when selecting AD therapy, especially for patients at risk for obesity or metabolic complications.<sup>26</sup>

For mood stabilizers, lithium, valproic acid derivatives, and gabapentin are associated with significant weight gain, while carbamazepine has a low risk of weight gain. Lamotrigine and topiramate are associated with weight loss or are weight-neutral. A systematic review showed that valproate is associated with weight gain in up to 50% of users, often detectable within two–three months of initiation, while carbamazepine carries a lower but present risk. 5

Second-generation antipsychotics are associated with



significant weight gain and other metabolic side effects (e.g., glucose dysregulation). Clozapine and olanzapine have the highest risk for weight gain among atypical antipsychotic medications, followed by quetiapine, risperidone, and paliperidone. The lowest risk for weight gain in antipsychotic medications is with aripiprazole and ziprasidone. This pattern is consistent across adult and pediatric populations, and the risk is particularly pronounced in antipsychotic-naive patients. Newer antipsychotic medications lurasidone and cariprazine are associated with some weight gain, but the magnitude is generally lower than many other second-generation antipsychotics. Both drugs are considered to have a favorable metabolic profile regarding weight gain, but monitoring is still recommended as part of standard care for all atypical antipsychotics.<sup>27</sup>

# EARLY SURGICAL RISKS OF PSYCHOTROPIC MEDICATIONS AND IMPACTS ON SURGICAL OUTCOMES

Some research suggests that a possible risk with lithium is lithium toxicity immediately following surgery. For the SSRIs, some research has shown that they are associated with upper GI bleeding. Due to disruptions in taking medications immediately post-surgery, or due to early changes in pharmacokinetics, problems such as SSRI discontinuation syndrome or withdrawal symptoms may occur. There may be a higher risk with this related to venlafaxine because of its short half-life.<sup>25</sup>

Research on changes in pharmacokinetics has been more well-established for RYGB than for sleeve gastrectomy, due to changes in the surface area of the small intestine that impacts medication absorption, changes in pH levels, changes in gastric emptying times, changes in gastric motility, and changes in drug metabolism. Sertraline exposure was 40% of that in non-surgical matched controls, and maximal plasma concentration was lower than matched controls one year after RYGB.<sup>28</sup> Duloxetine exposure was approximately 60% of that in non-surgical matched controls, and there was a shorter time to maximal plasma concentration compared to matched controls.29 However, there was no difference in pharmacokinetics related to lisdexamfetamine compared to matched non-surgical controls.<sup>30</sup> Other studies have found reduced bioavailability for various SSRIs and SNRIs at one month post-surgery,31 reduced serum concentrations post-RYGB with escitalopram,32 and reduced drug absorption post-RYGB for haloperidol, lithium, risperidone, valproate, lurasidone, and paliperidone long-acting injection.<sup>25</sup> For the treatment of addictive disorders, changes in methadone or buprenorphine absorption may occur, which could lead to issues such as respiratory depression or opioid use disorder relapse.25

Some individuals treated with ADs after surgery have experienced worsened outcomes one year post-surgery.

However, there have been mixed findings with the association between AD use and weight loss outcomes in bariatric surgery. Some studies have indicated lower percent total weight loss in those taking ADs 24 months after RYGB surgery, compared to those not taking ADs.<sup>33</sup> Other studies have shown no association between AD use and weight loss outcomes in bariatric surgery.<sup>34</sup>

## TREATMENT APPROACHES FOR MITIGATING MEDICATION-RELATED WEIGHT GAIN

#### **Medication Approaches**

Because of the prevalent use of psychotropic medications in this population, it is important to optimize psychiatric outcomes and minimize weight gain that can occur from these medications to facilitate surgical success. For patients who need to continue with psychotropic medications after surgery, it is recommended to consider decreasing the dose to the lowest therapeutic level possible while monitoring symptoms, or switching to medications with more weightneutral properties. Add-on medications could be considered, when appropriate, that would assist in reducing weight gain with these medications. Such medications may include topiramate, metformin, or liraglutide.<sup>35,36</sup>

Metformin is the most evidence-based adjunct for both prevention and treatment of psychotropic-induced weight gain and is recommended as first-line adjunctive therapy when lifestyle interventions are insufficient and switching agents is not feasible. Metformin may be co-commenced with psychotropic drugs that have weight gain liability (e.g., olanzapine: OLZ-MET) if an alternative agent with lower weight gain liability is not an option.<sup>37</sup> OLZ-MET has been shown to decrease weight gain in both obese and nonobese populations. Olanzapine-samidorphan (OLZ-SAM) is a newly approved option for the treatment of schizophrenia and bipolar I disorder, which has demonstrated reduced weight gain in a non-obese population.<sup>38</sup> GLP-1 receptor agonists, although less studied than Metformin, have shown promise in mitigating psychotropic-induced weight gain. The overall weight loss attributed to GLP-1 receptor agonists is significantly greater than any other class of bariatric medicine, although long-term safety and efficacy data are still accruing.37

Topiramate is an off-label option for managing psychotropic-induced weight gain, particularly when first-line strategies are inadequate, but requires individualized risk-benefit assessment and monitoring for adverse effects. Cognitive dysfunction, paresthesia, and fatigue are dose-dependent and may lead to discontinuation in a subset of patients; careful monitoring is recommended.<sup>35</sup> For lithium, levels should be closely monitored before and after surgery; for other medications with defined therapeutic ranges, serum concentration levels should be closely monitored. For medications with short half-lives, it is important to provide education on SSRI



discontinuation symptoms that may occur post-surgery due to changes in pharmacokinetics. Should these symptoms occur, a possible recommendation is to increase the AD dose after surgery to address these symptoms. For patients who are stable on medication type and dosage pre-surgery but there is a concern of relapse, trough serum levels could be obtained to allow for comparison with post-surgery levels to monitor symptoms.<sup>25</sup> Overall, it is recommended that measurement-based care be used to monitor symptoms pre- and post-surgery, to allow for efficient adjustments in the treatment plan. Furthermore, collaboration between the surgical team, the pharmacotherapy specialist, and primary care provider is essential in maintaining stability of comorbid psychiatric conditions and ensuring surgical success.

#### **Psychosocial Approaches**

As a first step, it is of critical importance to conduct a comprehensive pre-surgical behavioral health evaluation. This has now become the standard of care and is recommended as part of the multidisciplinary screening process prior to bariatric surgery.<sup>39</sup> Such evaluations should include the use of semi-structured interviews and psychometric testing as a part of evidence-based evaluation.<sup>39</sup> In addition to identifying the presence of psychiatric conditions and correlates that could negatively impact surgical outcomes, these evaluations provide other benefits such as enhancing readiness for surgery, increasing knowledge about post-operative recommendations, addressing possible barriers to surgical success, and providing a positive connection with a behavioral health specialist to support treatment engagement in the future should the patient need it.<sup>39</sup>

Presurgical psychosocial interventions can provide an important opportunity to strengthen coping skills and healthy habits to ensure post-surgical success. Cognitive behavioral therapy (CBT) is recommended as a first-line psychosocial treatment to address depression, anxiety, and eating disorders. Studies have found that CBT provided pre-surgically resulted in improvements in dysfunctional eating/binge eating, depression, and anxiety post-intervention, 40 and significant weight loss at six and 12 months post-surgery. 41 Post-surgical psychosocial interventions and support groups also have resulted in greater weight loss, 42 and can improve problematic eating behaviors, depression, and weight outcomes in those who have experienced weight regain following RYGB. 43,44

#### CONCLUSION

Psychiatric comorbidity is prevalent in bariatric surgery candidates. Findings thus far have been mixed concerning the impact of these comorbidities on surgical outcomes, but many individuals continue to experience psychiatric comorbidities post-surgery or develop new ones post-surgically. For those who continue to experience psychiatric

comorbidities, it is important to consider ongoing management of these conditions post-surgically in ways that reduce the risk of weight gain (e.g., weight-neutral medications and psychosocial interventions). Other correlates are present even in the absence of psychiatric conditions that can negatively affect surgical outcomes, such as problematic eating behaviors. Comprehensive pre-surgical behavioral health assessments are crucial to identifying psychiatric conditions or correlates to determine appropriate treatment plans to ensure that patients receive adequate care and positive bariatric surgical outcomes.

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#### **Authors**

- Kristy Dalrymple, PhD, Brown Health Medical Group, Department of Psychiatry; Alpert Medical School of Brown University, Department of Psychiatry and Human Behavior, Providence, RI.
- Cristina Toba, MD, Brown Health Medical Group, Department of Psychiatry; Alpert Medical School of Brown University, Department of Psychiatry and Human Behavior, Providence, RI.

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#### Correspondence

Kristy Dalrymple, PhD 146 West River Street, Suite 11B, Providence, RI 02904 401-444-7095 Fax 401-444-7109 kdalrymple@brownhealth.org

