# The Role of Mental Health in Obesity Management

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## KEY MESSAGES FOR HEALTHCARE PROVIDERS

- Be aware of the links between mental illness and obesity, and ensure you manage the weight gain side-effects of medications used in the treatment of mental illness.

- Be aware that mental illness can impact obesity management efforts, and screen patients for potential mental illnesses that need to be addressed.

- Off-indication use of antipsychotics should be avoided, as significant metabolic adverse effects can occur even when these medications are prescribed at lower doses.

- For patients with severe mental illness who gain weight on antipsychotic treatments, glucagon-like-1-peptides (GLP-1) have the most safety and efficacy evidence among medications indicated for chronic obesity management in Canada. Cost may be a barrier for individuals trying to access this class of medications.

- When initiating antipsychotic treatment for the first time, avoid medications with higher metabolic risk, as individuals in their first episode respond well regardless of which medication is prescribed (and are at greatest risk for weight gain).

- Consider switching strategies to a lower metabolic liability antipsychotic in individuals with severe mental illness who gain weight on an antipsychotic treatment.

- For patients with severe mental illness who gain weight on antipsychotic treatments, metformin can be used in conjunction with behavioural obesity management interventions.

- Behavioural obesity management therapy, ideally as part of a multi-modal treatment approach, can be effective in managing weight in individuals with co-occurring mental illness. The intensity of the behavioural intervention will need to increase for individuals with more severe psychopathology in the context of obesity.

- Individuals undergoing bariatric surgery should undergo a pre-surgical mental health screen by a qualified bariatric clinician with experience in mental health to identify early risk factors for poor weight-loss outcomes or mental health deterioration.

- Following pre-surgical screening, individuals should receive ongoing monitoring by a healthcare provider for psychiatric symptoms, eating psychopathology and substance use disorders, and for suicidal ideation or self-harm after bariatric surgery. For those individuals continuing psychiatric medications after surgery, monitoring of therapeutic effect is critical to maintaining psychiatric stability.

- For individuals regaining weight after bariatric surgery, psychosocial interventions should be used to address comorbid psychiatric symptoms interfering with obesity management, such as depression and eating psychopathology, and to support behavioural change long-term.

- For individuals with binge eating disorder and obesity or overweight, lisdexamfetamine is indicated to reduce eating pathology. Off-label use of topiramate has also been shown to help.

- Given the prevalence of mental health issues in individuals with obesity, screening for mental illness (with a focus on depression, binge eating disorder and attention deficit hyperactivity disorder) is appropriate in all patients seeking obesity treatment.

- Patients with obesity and a mental health diagnosis should be assessed for comorbidities.

- Physicians should be aware of the weight gain and cardiometabolic risks associated with off-label antipsychotic use (absence of approval by regulatory bodies).

- The current approved obesity medications can be helpful in patients with a mental illness and should be used based on clinical appropriateness.

- In people living with overweight or obesity with Binge Eating Disorder, the following medications are effective to reduce eating pathology and weight: lisdexamfetamine, topiramate, and second-generation antidepressants SSRIs duloxetine and bupropion. These medications are effective in reducing eating pathology, but their effect on weight loss is less certain.

- Patients with comorbid mental illness should be supported with behavioural therapy, preferably as part of a multi-modal intervention, to manage weight.

- Referral for more intense (i.e., long-term) and behavioural interventions, such as cognitive behavioural therapy, should be considered for individuals with significant binge eating and depressive symptoms in the context of obesity.

- Patients seeking bariatric surgery should be screened for mental health comorbidities. The presence of an active psychiatric disorder does not exclude patients from bariatric surgery but warrants further assessment of potential impact on long-term weight loss.

- Patients should be monitored for alcohol and substance use changes, as well as self-harm/suicidal ideation, after bariatric surgery. They should be informed about altered alcohol metabolism following Roux-en-Y gastric bypass surgery.

- Post-bariatric surgery patients should be monitored for emergence of early postoperative psychiatric symptoms, self-harm and suicidal ideation and eating pathology (given their impact on weight loss outcomes.

- Patients should undergo pre-bariatric surgery psychosocial assessment by an experienced bariatric clinician. Assessment should continue following surgery and can include the use of either clinician-administered or patient self-report measures.

- We recommend psychiatric medication monitoring following bariatric surgery due to potential changes in drug absorption and therapeutic effect, especially with malabsorptive surgical procedures. For psychiatric medications with narrow therapeutic index, use of available protocols to manage perioperative levels is warranted.

- Post-bariatric surgery behavioural and psychological interventions to support maintenance of weight loss and to prevent significant weight regain may be useful.

- Bariatric surgery teams should focus on strategies to improve patient engagement during the post-surgery follow-up period, specifically for high-risk patient groups.

## RECOMMENDATIONS

1. We recommend regular monitoring of weight, glucose and lipid profile in people with a mental health diagnosis who are taking medications associated with weight gain (Level 3, Grade C).[1,2]

2. Healthcare providers can consider both efficacy and effects on body weight when choosing psychiatric medications (Level 2a, Grade B).[3–15]

3. Metformin and psychological treatment such as cognitive behavioural therapy should be considered for prevention of weight gain in people with severe mental illness who are treated with antipsychotic medications associated with weight gain (Level 1a, Grade A).[16,17]

4. Healthcare providers should consider lisdexamfetamine and topiramate as an adjunct to psychological treatment to reduce eating pathology and weight in people with overweight or obesity and binge-eating disorder (Level 1a, Grade A).[18–20]

## Introduction

Much like trying to untangle the etiology of obesity, trying to understand the association between weight gain and mental illness is currently beyond our ability.[21] We are aware of vulnerabilities that increase risk, both of weight gain in those with mental illness and, conversely, mental health issues in those with weight issues, and we know the end result is that the presence of one illness can impact the other.[22,23] We also know the unconscious bias, a factor that those with weight issues and mental illness often face, is compounded when the conditions co-occur and can be especially damaging in medical settings.[24] This has profound effects on patient care, medical outcomes and, from a broader systems perspective, on healthcare costs and access to care.[25]

This chapter's evidenced-based recommendations are meant to serve as a guideline to ensure healthcare practitioners are evidence-informed and can provide the best care to an often complicated and marginalized patient group.

The mechanisms underlying the association between mental illness and early onset and sustained weight gain are multifaceted and involve both biological and psychological factors superimposed on the background of social health determinants, and medication and metabolic side effects.[21] This association is supported by clinical and epidemiological research reporting prevalence rates of overweight and obesity of 25%–60% for bipolar disorder, 30%–70% for schizophrenia and 20%–50% for depression.[26,27] Links have also been made between overweight and obesity and binge eating disorder (BED), attention deficit disorder (ADHD) and post-traumatic stress disorder (PTSD).[21,28] Given the high prevalence of mental health issues in those struggling with obesity, it is not surprising that mental illness is more prevalent in those presenting with weight-related comorbidities and those seeking weight management treatment. It is critical, therefore, that healthcare practitioners involved in the care of those with obesity prioritize clients' mental health needs as well.[29]

Being aware of the association between mental illness and obesity is not simply an academic exercise. Individuals with mental illness have increased morbidity and mortality, in some cases with a risk of premature death of up to 15 years, because of medical comorbidities, many of which are linked to weight gain.[30] It can be challenging to address both the physical and mental health needs of this population, but given the interaction between the two conditions it should be considered a priority, both at an individual and a health systems level. Research has indicated that individuals with mental health issues often fall through the cracks; this outcome can be prevented with a standardized screening approach.[31] There is a clear and irrefutable link between psychiatric medications and weight gain. While this association has been most clearly studied and documented with respect to antipsychotics,[10] medications used in the treatment of bipolar disorder, major depressive disorder (MDD) and anxiety have all been shown to be associated with significant weight gain.[7] While it is important that medication efficacy be the first priority, it is also important that tolerability be considered. There is significant premature mortality secondary to physical health problems documented in those with mental health problems. Also, weight gain secondary to medication use is a common cause of medication discontinuation in patients requiring psychotropic medications.[32] It is therefore important that healthcare practitioners be aware of the side-effect profile associated with different psychiatric medications, and consider

both efficacy and tolerability in deciding on appropriate short-term and long-term psychopharmacology.

Second-generation antipsychotics are approved by the US Food and Drug Administration for the treatment of schizophrenia, bipolar disorder, and depression under drug-specific circumstances. While second generation antipsychotics have been argued to have a lower propensity for causing extrapyramidal side effects as compared to their "first generation" counterparts when used "on-label", they are indisputably associated with significant metabolic sequelae, including weight gain, glucose dysregulation, and dyslipidemia.[33]

## Off-label use of antipsychotic medications: what are the safety and efficacy implications for metabolic comorbidity?

In Canada, prescription of antipsychotic medications doubled, exceeding seven million prescriptions annually, between 2005–2012.[34] Concerningly, the most rapid increases in prescription patterns were attributed to use in off-label indications for which clinical evidence is less certain, including: ADHD, anxiety, dementia, eating disorders, insomnia, obsessive-compulsive disorder, personality disorders, PTSD, substance use disorders and Tourette syndrome. A meta-analysis and several individual studies reported significant occurrence of metabolic adverse effects in the context of off-label antipsychotic use, including increased appetite and weight gain, increased triglyceride abnormalities, and increased risk of precipitating diabetes.[35,36] In elderly patients with dementia, use of antipsychotics has been associated with increased risk of mortality and cardiovascular events.[37–39]

## Pharmacological interventions in mental illness and comorbid overweight or obesity

While behavioural interventions are first-line approaches for addressing metabolic comorbidities, these often are not sufficient on their own, and pharmacological interventions must be considered. Pharmacological interventions approved for treatment of obesity in the general population likely have a place in the management of obesity in patients with mental illness, keeping in mind population-specific considerations of efficacy and safety. For example, the combination bupropion-naltrexone may not be the first-line choice for patients with bipolar disorder due to the risk of mania induction.[40] In addition, because mechanisms driving obesity may be different in patients with severe mental illness compared with the general population (i.e., psychotropic medications impact neurotransmitters associated with metabolic homeostasis), treatments not approved by licensing bodies for obesity treatment have been studied off-label in this population. Because antipsychotics, as well as antidepressants and mood stabilizers, carry a differential weight-gain risk, lower-liability medications can also be considered as a strategy to target metabolic comorbidity in this population. While switching strategies have a place in clinical practice, the decision to switch antipsychotic drugs must be considered on a case-by-case basis in the context of efficacy, tolerability and patient choice.[41,42]

## How effective are pharmacological interventions for obesity in patients with mental illness?

Agents currently approved for treatment of obesity in Canada include liraglutide (Saxenda®), a glucagon-like peptide–receptor agonist (GLP1 RA); bupropion-naltrexone (Contrave®), and orlistat (Xenical®), an inhibitor of intestinal fat absorption. In the United States, locaserin, a selective agonist of 5-hydroxytryptamine receptor 2C and phentermine-topiramate controlled release are also approved by the FDA and available for treatment of obesity. For more information on obesity management pharmacotherapy refer to the Pharmacotherapy in Obesity Management chapter.

Three randomized controlled trials have examined GLP-1 RAs (liraglutide or exenatide) in people living with overweight or obesity with schizophrenia spectrum disorders taking antipsychotic medications.[43–45] Data from these trials were recently analyzed in a participant-level data meta-analysis (n=141 participants). Endpoint weight for GLP-1 RAs was 3.61 kg lower than for controls. Body mass index (BMI), HbA1C, fasting glucose and visceral adiposity were all lower for the GLP-1 RA group. Weight loss in the GLP-1 RA group appeared to be greater for participants on clozapine or olanzapine, and for longer study endpoints. GLP-1 RAs were well tolerated, with no safety concerns aside from more common reports of nausea in the treatment group.[46]

Naltrexone-bupropion was examined in males with obesity and schizophrenia who were smokers and showed no differences in weight change or smoking cessation rates as compared to placebo.[47] In patients with schizophrenia on olanzapine, naltrexone alone (a component of naltrexone-bupropion), when compared to placebo in a small double-blind randomized clinical trial, did not find differences in BMI over a 12-week treatment period.[48] In women with obesity and MDD, naltrexone-bupropion was found to modestly reduce both weight and depression scores.[49] Orlistat was examined in a double-blinded randomized clinical trial in patients with schizophrenia spectrum or bipolar disorder taking antipsychotics.[50] The data did not show a significant difference in body weight between groups.

A wide spectrum of medications, including antihyperglycemic agents (metformin, rosiglitazone, intranasal insulin), antiepileptic medications (topiramate), stimulants (dextroamphetamine, atomoxetine, modafinil), antidepressants (fluoxetine, reboxetine, sibutramine), histaminergic antagonists (famotidine, nizatidine), dopaminergic agents (aripiprazole- an antipsychotic drug with partial agonism of dopaminergic (D)-2 receptor; amantadine), melatonin receptor agonists (ramelteon) and nutritive supplements (dill, celery, green tea) have been investigated in the treatment or prevention of antipsychotic-associated weight gain and obesity in patients with severe mental illness.

Across several published meta-analyses of randomized control trials in patients with schizophrenia spectrum disorders, metformin consistently emerges as an effective and safe intervention resulting in modest weight loss as compared to placebo (average of 3.5 kg), as well as improvements in lipid and insulin sensitivity parameters.[16,17,51,52] A meta-analysis which included patients with mood disorders receiving mood stabilizers found similar beneficial

effects of metformin over placebo.[53] Similar findings have been reported in two meta-analyses that assessed all randomized control trials investigating metformin for antipsychotic induced weight gain.[17,54] The effect of metformin may be greater in first-episode patients as compared with chronically ill populations, although this could also be driven by ethnicity, as all the first-episode studies have been conducted in Chinese populations.[17,54]

Topiramate, approved in Canada for epilepsy and migraines, represents a component of the topiramate-phentermine combination approved in the United States by the FDA for obesity treatment. A recent meta-analysis of randomized control trials examined the use of topiramate in patients with schizophrenia spectrum disorders and reported superiority of topiramate as compared to placebo on weight (3.76 kg) and BMI (1.62 kg/m$^2$) reduction.[55] Overall, the side-effect profile was comparable to control groups, with the exception of paresthesia, which was more common in topiramate-treated patients. The topiramate group also had small improvements in psychopathology. Similarly, a meta-analysis examining randomized control trials conducted in mixed populations of schizophrenia spectrum and mood disorders (bipolar disorder) found topiramate to be associated with weight loss as compared to placebo (3.95 kg), with no safety concerns reported.[53] Although cognitive disturbances have been linked with topiramate use (particularly in epilepsy populations),[56] these have not been sufficiently studied in schizophrenia spectrum disorders[55] but are clearly an issue to be aware of in assessing tolerability. An open-label trial in patients with anxiety disorders who experienced weight gain with selective serotonin reuptake inhibitors (SSRIs) also found topiramate to be associated with weight loss and reported no safety concerns.[57] In summary, adjunctive off-label use of topiramate appears to be modestly effective to mitigate weight gain in the context of schizophrenia spectrum illnesses.[16,52,53,55] However, larger studies of extended treatment, and more detailed examination of potential adverse effects on cognition are required prior to advocating for routine use in the management of obesity in severe mental illness.

Other off-label weight loss interventions that may be effective in the treatment of antipsychotic-associated weight gain and obesity include aripiprazole and H2 agonists, such as nizatidine. However, the quality of the evidence for these interventions is low, making the effects uncertain.[16,51,52] A published meta-analysis investigating H2 receptor agonists in antipsychotic-induced weight gain failed to find differences in weight reduction as compared to placebo.[58] Recommendations about the use of most pharmacological agents are limited by the small number of studies utilizing the agents, variability in the studies testing the same agent, and variable intensity and duration of the studies using the same interventional agent. Making a consensus statement on these treatments is currently challenging.

## How effective are behavioural interventions for obesity in patients with mental illness?

In patients with comorbid depression and obesity, behavioural weight-loss therapy has been studied alone and in combination with other treatments. Two randomized controlled trials comparing behavioural weight-loss therapy in combination with an additional psychological treatment, namely a behavioural intervention or CBT, resulted in comparable weight loss between groups and showed no advantage of combination treatment.[62,63] The addition of depression-specific interventions, such as behavioural therapy, to a behavioural intervention may provide additional benefit than treatment with a behavioural intervention alone for reducing depressive symptoms in patients with obesity.[59]

Significant research exists on the efficacy of behavioural treatments for obesity in individuals with severe mental illness, including patients with psychotic illness and severe mood disorders. Interventions focused primarily on physical activity have shown inconclusive results related to weight loss in two meta-analyses.[61,62] A comprehensive meta-analysis, conducted by Caemmerer et al., evaluated the effectiveness of non-pharmacological interventions for obesity management in patients with severe mental illness across 17 included studies.[63] This review consisted of CBT, psychoeducational interventions and nutrition and exercise interventions, with treatments lasting a mean of 19.6 weeks. The review demonstrated a mean difference in weight of -3.12 kg and a BMI reduction of -0.94 kg/m$^2$ overall across studies, with some studies showing sustained benefits at eight- to 52-week follow-up post-intervention.[63] CBT had a smaller effect than nutrition and/or exercise programs. Analysis of moderating variables showed no difference between prevention versus treatment studies, studies with interventions greater or less than three months duration, and individual versus group treatments. A second meta-analysis also confirmed the above results related to overall weight loss. However, it showed that prevention trials were slightly more effective than treatment interventions for obesity in severe mental illness.[64]

An additional meta-analysis focusing on pharmacological and behavioural interventions to improve cardiovascular risk factors in adults with severe mental illness analyzed 10 studies using behavioural interventions, which included either lifestyle interventions or CBT.[65] Behavioural interventions resulted in a mean difference of -3.13 kg. A more recent meta-analysis involving 17 studies using a lifestyle intervention for weight loss in people living with overweight or obesity with severe mental illness showed that interventions of < six months and > 12-months duration led to comparable weight loss.[66] For these long-term lifestyle interventions (> 12-months), patients had more than 60% greater odds of achieving clinically significant weight loss (> 5% weight loss) compared to controls. Bruins et al. also evaluated the efficacy of lifestyle interventions for individuals with obesity and severe mental illness in a meta-analysis and showed improvements in specific cardiometabolic risk factors, namely waist circumference, triglycerides, fasting glucose and insulin.[67] No effects were observed for blood pressure and cholesterol levels.

In summary, the results of these meta-analyses suggest that behavioural interventions, including lifestyle, nutrition and physical activity changes, results in an average weight loss of 3 kg and a BMI reduction of 0.9 to 1 kg/m$^2$. Research is needed to further elucidate the optimal duration and intensity of behavioural

interventions for weight loss in patients with severe mental illness. Negative results for weight loss from the STEPWISE study, which used group psychoeducation, behavior-focused sessions, suggest that more intense and multi-modal interventions may be needed for long-term weight loss, especially for individuals with schizophrenia spectrum disorders.[68]

## How effective are pharmacological treatments for obesity in binge eating disorders?

Several studies have explored the effectiveness of various pharmacological interventions (antidepressants, appetite suppressants, stimulants and anticonvulsants) in patients with BED. A recent meta-analysis of placebo-controlled randomized control trials reported a significantly greater reduction in binge eating and related psychopathology for second generation antidepressants (bupropion, SSRIs and duloxetine), lisdexamfetamine (a central nervous system stimulant originally marketed for ADHD) and topiramate (an anticonvulsant). Antidepressants were analyzed as a class due to lack of replication studies for individual agents (bupropion n=1 study), SSRIs (fluoxetine n=2; citalopram, n=1; escitalopram n=1; fluvoxamine n=1, sertraline n=1), serotonin-norepinephrine reuptake inhibitors (SNRIs; duloxetine n=1). Only topiramate and lisdexamfetamine (but not antidepressants) reduced weight compared to placebo in patients. A systematic review and network meta-analysis was subsequently published to review comparative effectiveness, suggesting that lisdexamfetamine was better at increasing binge abstinence as compared with second generation antidepressants. Weight as an outcome was not compared.[19]

An issue with this work is that the studies predominantly included middle-aged females of white ethnicity living with overweight or obesity. Questions of generalizability beyond this population, and data on how long an individual might need to remain on treatment, remain unanswered. Of these interventions, lisdexamfetamine (Vyvanse®) is approved for treatment of binge eating disorder in Canada. However, lisdexamfetamine is a central nervous system stimulant. Thus, efficacy and safety may not be generalizable to patients with a history of substance use disorders, suicidal attempts, bipolar disorder and psychosis, as these populations could be more susceptible to abuse or mental deterioration.

Given the high prevalence of psychiatric disorders in patients with obesity,[69] several studies have explored the impact of the bi-directional relationship of obesity and mental illness on the efficacy of behavioural interventions for weight loss and improvement in metabolic outcomes. Given that the most highly prevalent psychiatric disorders in obesity include MDD and BED, several studies have focused on the impact of behavioural and related psychosocial interventions. In addition, there has been increasing focus on the role of behavioural interventions to address the high prevalence of obesity in individuals with severe mental illness, related to both the illness and treatment with antipsychotics. The result has been growing evidence in this area, which is summarized below.

## How effective are behavioural interventions for obesity in patients with comorbid binge eating disorder?

Several studies have explored the effectiveness of behavioural interventions in patients with BED and obesity. However, a meta-analysis by Peat and colleagues was limited to a qualitative analysis of study trials due to heterogeneity in treatment outcome measures.[19] Nonetheless, this review reported a significantly greater reduction in BMI with behavioural weight loss therapy compared to therapist-led cognitive behavioural therapy, although this benefit was only found at end of treatment, and the difference in BMI disappeared at follow-up.[30] Moreover, behavioural weight loss therapy had inconclusive and inferior results in comparison to CBT in terms of abstinence from binge eating and improvement in binge eating frequency, respectively. The dose of behavioural therapy may also influence the effectiveness of therapy in reducing binge eating severity in obesity, with current evidence indicating that high-moderate doses, consisting of 16 to 24 sessions, may be needed to adequately address binge eating.[70]

## What is the impact of food addiction on obesity?

Evidence from animal models suggests that ingredients from highly processed foods can result in addictive-like biological and behavioural responses,[71–73] such as food craving.[74,75] In human studies, the symptoms of food addiction have mirrored the Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5) diagnostic criteria for substance use disorder, which has led to the use of the Yale Food Addiction Scale as a measure of food addiction.[74,76,77] Although DSM-5 has not recognized food addiction as an official diagnosis, the Yale Food Addiction Scale has continued to be a primary tool to define the construct of food addiction. However, there remains controversy about the influence of obesity and binge eating disorder on the prevalence of food addiction,[78] and researchers have cautioned equating obesity with food addiction.[75] Given the need for greater clarity and research regarding the diagnosis of food addiction, there is limited evidence on effective treatments for food addiction symptoms in the context of obesity. Moreover, authors have highlighted the need to better understand the impact of the food addiction label for patients living with obesity in terms of stigma, ethics and health policy issues.[79]

## How does mental illness affect bariatric surgery outcomes?

Studies have demonstrated high lifetime rates of psychiatric illness in bariatric surgery patients, with rates approximating 70% when using structured psychiatric interviews.[69,80] According to the Ontario Bariatric Network registry, rates of a current psychiatric diagnosis were found to be 51%.[84] In a meta-analysis of 52 studies reporting prevalence data, rates of any current mood disorder, BED and anxiety were 23%, 17% and 12%, respectively.[85] Social phobia has been linked to body image disturbance in patients with obesity, and rates of a current diagnosis of social phobia have approximated 3% in studies.[69]

Following bariatric surgery, data from the Longitudinal Assessment of Bariatric Surgery Research Consortium has shown a significant reduction in any axis I psychiatric disorder (as per DSM IV-TR) at year two (16.8%) and year three (18.4%) post-surgery, as compared to pre-surgery rates (30.2%).[83] Moreover, bariatric surgery can result in improvements in cognition, most commonly memory and attention/executive function.[84] Only post-surgery eating disorder symptoms have been associated with less weight loss after bariatric surgery in multiple studies.[83,85]

Increases in suicide and self-harm have been noted post-bariatric surgery.[86–87] A meta-analysis identified a pooled prevalence of 0.3% of suicide, compared with 1.8% for the pooled prevalence of all-cause mortality post-bariatric surgery.[88] A Canadian population-based study examining self-harm emergencies three years before and after bariatric surgery showed an increase in self-harm emergencies post-surgery (3.63 versus 2.33 per 1000 patient-years), with intentional overdose being the most common method.[86] Risk factors for self-harm included individuals 35 years or older, lower income status and living in rural areas.

Studies have also identified an association between substance use disorders[86] post-bariatric surgery. Rates of a lifetime substance use disorder in bariatric surgery candidates are 35.7%, with alcohol use disorder being observed in 33.2% of bariatric surgery candidates.[69] In a systematic review, the proportion of new-onset substance use post-surgery among bariatric patients ranged from 34.3% to 89.5%.[89] In this review, the most reliable predictor of postoperative substance use was a preoperative history of substance use.

Cigarette smoking and alcohol use disorders are common in bariatric surgery candidates. Cigarette smoking is problematic post-surgery due to risks of post-surgical ulcers. Although studies suggest that 28.6% of patients who were smoking before surgery quit after surgery, approximately 12% of patients were new onset cigarette smokers after surgery.[89] In contrast, several studies have demonstrated an increased prevalence of new onset alcohol use disorder after bariatric surgery. Rates of new onset alcohol use disorder following Roux-en-Y gastric bypass surgery, for example, approximate 7%–8% at two-years post-surgery.[90,91] Roux-en-Y gastric bypass is associated with a higher risk of alcohol use disorder post-surgery, which was confirmed in a study comparing the procedure and laparoscopic adjustable gastric banding (. This study showed an adjusted hazard ratio (AHR) of 2.08 for incident alcohol use disorder, and an AHR of 1.76 for incident illicit drug use after surgery.[92] It has been suggested that increased alcohol use disorders may be related to altered alcohol pharmacokinetics after Roux-en-Y gastric bypass surgery versus other bariatric surgeries.[93]

Limited data is available on opioid use disorders related to bariatric surgery; however, preliminary data suggest that 4% of patients could become chronic opioid users after bariatric surgery.[97,98] Risk factors for chronic post-surgery opioid use are higher pre-surgery total days of opioid use, pre-surgery non-analgesics, anti-anxiety medications and tobacco use.[94,95] Further research is needed to clearly elucidate rates and predictors of opioid use in bariatric surgery populations.

## How do psychiatric symptoms affect weight loss after bariatric surgery?

Several studies have attempted to assess mental health and eating psychopathological predictors of bariatric surgery outcomes. A meta-analysis did not find an association between pre-surgery psychiatric disorders and weight-loss outcomes after bariatric surgery.[82] Moreover, a review suggests that pre-surgery psychosocial variables, such as cognitive impairment, and personality variables (e.g. high neuroticism) may be associated with reduced weight loss after bariatric surgery, although the latter may be more closely linked to eating pathology than weight loss directly.[96] Depressive symptoms after bariatric surgery have also been associated with reduced weight loss post-surgery. However, results from additional studies have shown conflicting results.[97–99] In addition, conflicting results suggest that pre-surgical complex psychiatric illness is not clearly associated with poor weight loss outcomes post-bariatric surgery.[96,100] Therefore, there is limited data on clear pre-surgery psychosocial predictors of weight loss outcomes related to bariatric surgery.

Further, studies have identified preliminary evidence suggesting that early adaptation to the eating changes required with bariatric surgery may be an early indicator of weight loss. This is reinforced by three-year data from a large multi-site study demonstrating that, although overall eating pathology declines post-surgery, those patients that had higher eating pathology post-surgery experienced less weight loss after bariatric surgery.[101] These findings were replicated in a postoperative cohort study in Canada that showed that binge eating symptoms at one-year post-bariatric surgery were a predictor of reduced total percent weight loss at two-years post-surgery.[85] Additional longitudinal studies are needed, but existing data suggests that bariatric surgery programs should continue with ongoing monitoring of eating-related symptoms after surgery.

## What tools can assist with assessment of pschiatric conditions before bariatric surgery and post-surgery monitoring?

Pre-bariatric surgery assessment of psychiatric stability is recommended by bariatric behavioural health clinicians with experience and specialized knowledge of the assessment and care of psychosocial issues before and after surgery.[20] Moreover, ongoing psychosocial monitoring is recommended given the influence of post-bariatric surgery psychopathology on weight loss and psychiatric outcomes. Recent guidelines recommend a comprehensive psychosocial assessment before bariatric surgery to identify risk factors and proactive identification of potential postoperative challenges that could be problematic post-surgery.[20] Psychosocial assessment should be conducted using clinical interview and can be guided by such resources as the Boston Interview for Gastric Bypass assessment.[102] In addition, an interprofessional risk assessment tool called the Toronto Bariatric Interprofessional Psychosocial Assessment Suitability Scale (BIPASS) can provide a standardized approach to pre-surgery psychosocial assessment and can inform risk stratification pre-bariatric surgery.[103]

Patient self-reporting tools can be used to assist with pre- and post-surgery assessment of psychiatric symptoms. Currently, there is no single robust assessment tool that assesses all psychosocial domains during the pre-bariatric surgery assessment.[104] In a 2015 systematic review, the Master Questionnaire, a 56-item true/false questionnaire, was identified as the only tool that assessed patients on multiple eating behaviour domains in patients with obesity.[104] In this same review, the binge eating scale was identified as having the most support for assessing binge eating symptoms in patients undergoing bariatric surgery. A second review of patient self-report measures recommended the use of the binge eating scale, The Night Eating Questionnaire (NEQ)and the Eating Disorder Examination Questionnaire (EDE-Q) to assess eating psychopathology in patients undergoing bariatric surgery.[105] The PHQ-9 (Patient Health Questionnaire-9) and the Alcohol Use Disorders Identification Test (AUDIT) are recommended for assessing depressive symptoms and alcohol use in bariatric surgery candidates, respectively.[105,106] However, further research is needed to fully establish self-report patient measures with robust psychometric properties in assessing eating psychopathology in bariatric surgery patient populations, especially in the unique post-surgery context.[107]

## How are psychiatric medications affected by bariatric surgery?

Antidepressants are the most commonly prescribed psychotropic medication in bariatric surgery candidates, with accounts of up to 35% of a cohort of 2146 patients in the LABS-2 study.[108] Bariatric surgery procedures, whether restrictive or malabsorptive can have an impact on drug absorption, distribution metabolism or excretion.[109]

The literature is far from robust; however, antidepressants are the most studied class of psychotropic medications in the bariatric population. Despite small sample sizes, studies have demonstrated evidence of reduced bioavailability post-bariatric surgery, specifically with malabsorptive procedures, such as the Roux-en-Y gastric bypass. Antidepressants, such as sertraline and duloxetine, have shown reduced antidepressant plasma concentration following bariatric surgery compared to controls.[110] Therefore, clinicians have to be vigilant to make sure bariatric patients do not exhibit discontinuation symptoms or worsening of depressive symptoms, especially in the course of at least the first postoperative year.[111]

The impact of psychiatric medications on patient outcomes varies with the type of psychiatric medication and the therapeutic index of the medication. Anecdotal reports indicate that patients may be at risk of antidepressant discontinuation syndrome due to drops in therapeutic levels of antidepressant early on after surgery. These symptoms are significant, as they may be mistaken as dumping syndrome and should be assessed in the early postoperative phase in patients.[112]

In addition, mood stabilizers require special attention due to the frequent comorbidity of obesity and mood disorders and significant risk of acute relapse with subtherapeutic levels. Due to its narrow therapeutic index, lithium management could be challenging in the bariatric surgery population due to unpredictable absorption, preoperative liquid diets, possible fluid and salt shifts and postoperative limited oral intake. Cases of lithium toxicity as well as subtherapeutic levels have been described in the literature and, as a result, perioperative bariatric surgery lithium protocols have been developed to improve clinician management of lithium.[113]

Data regarding the use of antipsychotics in the bariatric population are limited to case reports. However, it is important for clinicians to be aware of possible pharmacokinetic changes due to bariatric surgery procedures as well as the metabolic adverse effects of these medications. For example, patients taking ziprasidone or lurasidone may have inconsistent absorption due to low-calorie intake in the perioperative period.[114] Clinicians should work collaboratively with patients' existing mental health providers to ensure that alternative antipsychotic options have been explored when preparing for bariatric surgery.

## What is the evidence for psychosocial interventions to support weight loss after bariatric surgery?

There are some contrasting results regarding the impact of psychological interventions on weight loss post-bariatric surgery. While studies have examined the effectiveness of pre-surgery behavioural and structured psychological interventions on weight-loss outcomes, results have been inconclusive in the pre-surgery phase. For example, psychological support focused on behaviour change and modifying cognitions pre- and post-bariatric surgery had no impact on weight loss as measured by BMI.[115] In a systematic review, behavioural interventions delivered with bariatric surgery improved weight loss outcomes, and, although the number of studies were limited, the data suggest that postoperative psychological interventions had a greater effect.[116] Moreover, a meta-analysis of five studies also showed greater weight loss post-bariatric surgery when surgery was combined with postoperative behavioural interventions.[117] Therefore, the optimal time to initiate adjunctive behavioural interventions is after bariatric surgery, but before significant weight regain has occurred.[118]

Specific psychological treatment modalities have been examined within bariatric surgery patient populations. These interventions include cognitive behavioural therapy (in-person or remotely delivered via telephone),[119,120] acceptance commitment therapy,[121] mindfulness-based therapies,[122] and other psychological modalities, which have improved eating pathology and psychological distress post-bariatric surgery short-term. Despite these symptom benefits, these psychological treatments have not translated to long-term post-surgery improvements in weight loss outcomes.

## What factors impact adherence and engagement in bariatric surgery after care?

Poor adherence to post-surgical after care continues to challenge surgical practices. Regular postoperative follow-up for bariatric patients

is important to detect nutritional deficiencies and post-surgery eating difficulties, and to optimize weight loss.[123,124] Despite high rates of attrition from bariatric aftercare programs, only a few studies have explored the reasons for non-attendance. Studies report high follow-up loss rates ranging from 10%–80%, with estimates approximating 50% in the first postoperative year and only 41% attending year-two follow-up appointments.[125–127] Possible factors associated with poor postoperative appointment attendance include higher preoperative weight, younger age, family-related problems, work problems or unemployment, lack of insurance coverage, avoidant attachment (relationship) style and longer distance to travel.[123,126–129]

Although there is no consensus regarding the reasons for patient non-adherence to recommended follow-up after bariatric surgery, a qualitative study exploring factors influencing patients' decisions to attend post-bariatric surgery after care identified several variables. Patients who stopped attending post-surgery follow-up appointments:

1. Had greater confidence in their primary care physician's ability to manage their bariatric surgery care;

2. Had challenges with travel distance in terms of time and financial implications;

3. Felt that they failed to achieve weight loss goals; and

4. Perceived that follow-up had limited utility to their current care.[130]

Additional studies are needed to further identify potential factors contributing to follow-up attrition.

Difficulties with patients' adherence to behavioural changes and the post-bariatric surgery regimen have also been studied in the literature. Poor dietary adherence has been associated with baseline depressive symptoms and the presence of binge eating disorder.[131] Moreover, higher attachment (relationship) anxiety and younger age (i.e., adolescents) has also been associated with poor adherence to postoperative vitamins.[129,131] Interventions to improve patient engagement and adherence to bariatric surgery follow-up recommendations have not been well studied.

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