





The Role of Mental Health in Obesity Management

Valerie H Taylor MD PhDi, Sanjeev Sockalingam MD MHPEi, Raed Hawa MDii, Margaret Hahn MD PhDiv

- i) Department of Psychiatry, University of Calgary
- ii) Department of Psychiatry, University of Toronto; Centre for Addiction and Mental Health; University Health Network
- iii) Centre for Mental Health, University Health Network; Department of Psychiatry, University of Toronto
- iv) Centre for Addiction and Mental Health, Complex Illnesses

Cite this Chapter

Taylor VH, Sockalingam S, Hawa R, Hahn M. Canadian Adult Obesity Clinical Practice Guidelines: The Role of Mental Health in Obesity Management. Available from: https://obesitycanada.ca/guidelines/mentalhealth. Accessed [date].

Update History

Version 1, August 4, 2020. Adult Obesity Clinical Practice Guidelines are a living document, with only the latest chapters posted at obesitycanada.ca/guidelines.

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 anti-psychotics 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 anti-psychotic treatments, glucagon-like peptide 1 (GLP-1) has 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 anti-psychotic 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 anti-psychotic in individuals with severe mental illness who gain weight on an anti-psychotic treatment.
- For patients with severe mental illness who gain weight on anti-psychotic 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 anti-psychotic 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 anti-depressants 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 post-operative 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 anti-psychotic 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}

KEY MESSAGES FOR PEOPLE LIVING WITH OBESITY

- There are clear links between mental illness and weight. Please ensure your healthcare provider is aware of the treatments you are taking for your mental health issues.
- Individuals with co-occurring mental illness should receive behavioural therapy in combination with a multi-modal treatment approach to manage obesity.
- Early emergence of psychiatric symptoms and eating difficulties after bariatric surgery could negatively influence post-surgical weight loss. Individuals should undergo mental health screening before bariatric surgery and have an interprofessional team identify and manage psychiatric symptoms and eating difficulties arising after surgery.
- Given the potential risk for relapse of psychiatric symptoms, increased risk of substance use problems (such as alcohol) and potential risk of suicide, individuals undergoing bariatric surgery should be aware of changes in how alcohol can affect you, psychiatric medication absorption and the importance of mental health monitoring after bariatric surgery.

- Anti-psychotics medications should not routinely be prescribed (especially on a long-term basis) for issues like sleep and anxiety.
- If you are gaining or have gained weight when taking an anti-psychotic medication and changes in behaviour have not been sufficient, metformin can be used to help prevent further weight gain and/or reduce weight.
- Early studies suggest that, among medications approved for long-term obesity management in Canada, liraglutide has the most evidence to support its use to help reduce weight gained from anti-psychotic medications.
- If you have gained weight from an anti-psychotic medication, you can ask your physician if there might be another antipsychotic with a lower weight gain risk. This should be a decision made together with your doctor, taking into careful consideration other potential side effects/tolerability and risk of mental health worsening.
- If you have binge eating disorder, two medications (lisdexamfetamine and topiramate) can be helpful to reduce both binge episodes and weight.

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 that unconscious bias, a factor that those with obesity 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 multi-faceted 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 obesity 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 anti-psychotics,7 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 shortterm and long-term psychopharmacology.

Second-generation anti-psychotics are approved by the U.S. Food and Drug Administration (FDA) for the treatment of schizophrenia, bipolar disorder and depression under drug-specific circumstances. While second-generation anti-psychotics 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 anti-psychotic medications: what are the safety and efficacy implications for metabolic comorbidity?

In Canada, prescription of anti-psychotic 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 anti-psychotic 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 anti-psychotics 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 naltrexone/bupropion 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 anti-psychotics, as well as anti-depressants 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 has a place in clinical practice, the decision to switch anti-psychotic 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 1 receptor agonist (GLP-1 RA); naltrexone/bupropion (Contrave®); and orlistat (Xenical®), an inhibitor of intestinal fat absorption. In the United States, lorcaserin, 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 anti-psychotic 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 using 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-blind randomized clinical trial in patients with schizophrenia spectrum or bipolar disorder taking anti-psychotics. ⁵⁰ The data did not show a significant difference in body weight between groups.

A wide spectrum of medications, including anti-hyperglycemic agents (metformin, rosiglitazone, intranasal insulin), anti-epileptic medications (topiramate), stimulants (dextroamphetamine, atomoxetine, modafinil), anti-depressants (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 anti-psychotic-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 anti-psychotic-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/m²) 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 disorders⁵⁵ 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 obesity interventions that may be effective in the treatment of anti-psychotic-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 anti-psychotic-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 obesity therapy has been studied alone and in combination with

other treatments. Two randomized controlled trials comparing behavioural obesity 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. ^{59,60} 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/m² 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 behavioural 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 behavioural 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 behavioural 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/m². 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 and behaviour-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 (anti-depressants, appetite suppressants, stimulants and anti-convulsants) 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 anti-depressants (bupropion, SSRIs and duloxetine), lisdexamfetamine (a central nervous system stimulant originally marketed for ADHD) and topiramate (an anti-convulsant). Anti-depressants 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) and serotonin-norepinephrine reuptake inhibitors (SNRIs; duloxetine n = 1). Only topiramate and lisdexamfetamine (but not anti-depressants) 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 anti-depressants. 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 anti-psychotics. 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 obesity 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.¹⁹ Moreover, behavioural obesity 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.74-76 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.74,77,78 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,75 and researchers have cautioned equating obesity with food addiction.76 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%.⁸¹ 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.⁸² 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 disorders⁸⁶ 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 post-operative substance use was a pre-operative 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. 94,95 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 post-operative 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 post-operative 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. 104 A second review of patient self-report measures recommended the use of the binge eating scale, The Night Eating Questionnaire and the Eating Disorder Examination Questionnaire to assess eating psychopathology in patients undergoing bariatric surgery. 105 The PHQ-9 (Patient Health Questionnaire-9) and the Alcohol Use Disorders Identification Test 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?

Anti-depressants 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, anti-depressants 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. Anti-depressants, such as sertraline and duloxetine, have shown reduced anti-depressant plasma concentration following bariatric surgery compared to controls. 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 post-operative year.

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 anti-depressant discontinuation syndrome due to drops in therapeutic levels of anti-depressant early on after surgery. These symptoms are significant, as they may be mistaken as dumping syndrome and should be assessed in the early post-operative 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, pre-operative liquid diets, possible fluid and salt shifts and post-operative 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 anti-psychotics 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 anti-psychotic 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 weightloss 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 was 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 post-operative 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 that have improved eating pathology and psychological distress post-bariatric surgery in the 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 post-operative 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 after care 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 post-operative year and only 41% attending year-two follow-up appointments. 125–127 Possible factors associated with poor post-operative appointment attendance include higher pre-operative 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 post-operative vitamins.^{129,131} Interventions to improve patient engagement and adherence to bariatric surgery follow-up recommendations have not been well studied.

Downloaded from: https://obesitycanada.ca/guidelines/mentalhealth.

This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License (CC BY-NC-ND 4.0)

The summary of the Canadian Adult Obesity Clinical Practice Guideline is published in the Canadian Medical Association Journal, and contains information on the full methodology, management of authors' competing interests, a brief overview of all recommendations and other details. More detailed guideline chapters are published on the Obesity Canada website at www.obesitycanada.ca/guidelines.

Correspondence:

guidelines@obesitynetwork.ca

References

- Morin AK. Off-label use of atypical antipsychotic agents for treatment of insomnia. Ment Heal Clin. 2014;4(2):65-72. doi:10.9740/mhc.n190091
- Ludwick JJ, Oosthuizen PP. Screening for and monitoring of cardio-metabolic risk factors in outpatients with severe mental illness in a primary care setting. African J Psychiatry (South Africa). 2009;12:287-292. doi:10.4314/ajpsy. v12i4.49047
- Arterburn D, Sofer T, Boudreau D, et al. Long-Term Weight Change after Initiating Second-Generation Antidepressants. J Clin Med. 2016;5(4):48. doi:10.3390/jcm5040048
- Correll CU, Detraux J, De Lepeleire J, De Hert M. Effects of antipsychotics, antidepressants and mood stabilizers on risk for physical diseases in people with schizophrenia, depression and bipolar disorder. World Psychiatry. 2015;14(2):119-136. doi:10.1002/wps.20204
- Thompson A, Hetrick SE, Álvarez-Jiménez M, et al. Targeted intervention to improve monitoring of antipsychotic-induced weight gain and metabolic disturbance in first episode psychosis. Aust N Z J Psychiatry. 2011;45(9):740-748. doi:10.3109/00048674.2011.595370
- Patten SB, Williams JVA, Lavorato DH, Khaled S, Bulloch AGM. Weight gain in relation to major depression and antidepressant medication use. J Affect Disord. 2011;134(1-3):288-293. doi:10.1016/j.jad.2011.06.027

- Chouinard VA, Pingali SM, Chouinard G, et al. Factors associated with overweight and obesity in schizophrenia, schizoaffective and bipolar disorders. Psychiatry Res. 2016;237:304-310. doi:10.1016/j.psychres.2016.01.024
- Fjukstad KK, Engum A, Lydersen S, et al. Metabolic Abnormalities Related to Treatment with Selective Serotonin Reuptake Inhibitors in Patients with Schizophrenia or Bipolar Disorder. J Clin Psychopharmacol. 2016;36(6):615-620. doi:10.1097/JCP.00000000000000582
- Smits J, Rosenfield D, Mather A, Tart C, Henriksen C, Sareen J. Psychotropic medication use mediates the relationship between mood and anxiety disorders and obesity: Findings from a nationally representative sample. J Psychiatr Res. 2010;44(15):1010-1016. doi:10.1038/jid.2014.371
- Bak M, Fransen A, Janssen J, Van Os J, Drukker M. Almost all antipsychotics result in weight gain: A meta-analysis. PLoS One. 2014;9(4):e94112. doi:10.1371/ journal.pone.0094112
- Strassnig M, Kotov R, Cornaccio D, Fochtmann L, Harvey P, Bromet E. Twenty-year progression of body mass index in a county-wide cohort of people with schizophrenia and bipolar disorder identified at their first episode of psychosis. Bipolar Disord. 2017;19(5):336-343. doi:10.1016/j.physbeh.2017.03.040
- Arterburn D, Wood GC, Theis MK, et al. Antipsychotic medications and extreme weight gain in two health systems. Obes Res Clin Pract. 2016;10(4):408-423. doi:10.1016/j.orcp.2015.08.012

- Vandenberghe F, Gholam-Rezaee M, Saigí-Morgui N, Delacrétaz A, Choong E, Solida-Tozzi A. Importance of early weight changes to predict long-term weight gain during psychotropic drug treatment. J Clin Psychiatry. 2015;76:e1417-1423. doi:10.1002/j.1875-9114.2012.01120
- Correll CU, Robinson DG, Schooler NR, et al. Cardiometabolic risk in patients with first-episode schizophrenia spectrum disorders baseline results from the RAISE-ETP study. JAMA Psychiatry. 2014;71(12):1350-1363. doi:10.1001/jamapsychiatry.2014.1314
- Boudreau D, Arterburn D, Bogart A, Haneuse S, Theis M, Westbrook E. Influence of body mass index on the choice of therapy for depression and follow-up care. Obesity. 2013;21(3):E303-313. doi:10.1016/j.physbeh.2017.03.040
- Mizuno Y, Suzuki T, Nakagawa A, et al. Pharmacological strategies to counteract antipsychotic-induced weight gain and metabolic adverse effects in schizophrenia: A systematic review and meta-analysis. Schizophr Bull. 2014;40(6):1385-1403. doi:10.1093/schbul/sbu030
- Zheng W, Li X Bin, Tang YL, Xiang YQ, Wang CY, De Leon J. Metformin for Weight Gain and Metabolic Abnormalities Associated with Antipsychotic Treatment: Meta-Analysis of Randomized Placebo-Controlled Trials. J Clin Psychopharmacol. 2015;35(5):499-509. doi:10.1097/JCP.0000000000000392
- Berkman ND, Brownley KA, Peat CM, et al. Management and Outcomes of Binge- Eating Disorder [Internet]. 2015.
- Peat CM, Berkman ND, Lohr KN, et al. Comparative Effectiveness of Treatments for Binge-Eating Disorder: Systematic Review and Network Meta-Analysis. Eur Eat Disord Rev. 2017;25(5):317-328. doi:10.1002/erv.2517
- Sogg S, Lauretti J, West-Smith L. Recommendations for the presurgical psychosocial evaluation of bariatric surgery patients. Surg Obes Relat Dis. 2016;12(4):731-749. doi:10.1016/j.soard.2016.02.008
- Taylor VH, McIntyre RS, Remington G, Levitan RD, Stonehocker B, Sharma AM. Beyond pharmacotherapy: Understanding the links between obesity and chronic mental illness. Can J Psychiatry. 2012;57(1):5-12. doi:10.1177/070674371205700103
- Calkin C, Van De Velde C, Růžičková M, et al. Can body mass index help predict outcome in patients with bipolar disorder? Bipolar Disord. 2009;11(6):650-656. doi:10.1111/j.1399-5618.2009.00730.x
- Kloiber S, Ising M, Reppermund S, et al. Overweight and Obesity Affect Treatment Response in Major Depression. Biol Psychiatry. 2007;62(4):321-326. doi:10.1016/j.biopsych.2006.10.001
- 24. Pearl RL, Puhl RM. Weight bias internalization and health: A systematic review. Obes Rev. 2018;19(8):1141-1163. doi:10.1111/obr.12701
- Mulligan K, McBain H, Lamontagne-Godwin F, et al. Barriers to effective diabetes management a survey of people with severe mental illness. BMC Psychiatry. 2018;20:1020-1030. doi:10.1186/s12888-018-1744-5
- Goldstein BI, Liu SM, Schaffer A, Sala R, Blanco C. Obesity and the three-year longitudinal course of bipolar disorder. Bipolar Disord. 2013;15(3):284-293. doi:10.1111/bdi.12035
- Avila C, Holloway AC, Hahn MK, et al. An Overview of Links Between Obesity and Mental Health. Curr Obes Rep. 2015;4(3):303-310. doi:10.1007/s13679-015-0164-9
- Kivimäki M, Batty GD, Singh-Manoux A, et al. Association between common mental disorder and obesity over the adult life course. Br J Psychiatry. 2009;195(2):149-155. doi:10.1192/bjp.bp.108.057299
- Hasnain M, Vieweg WVR, Hollett B. Weight gain and glucose dysregulation with second-generation antipsychotics and antidepressants: A review for primary care physicians. Postgrad Med. 2012;124(4):154-167. doi:10.3810/ pgm.2012.07.2577
- Bradshaw T, Mairs H. Obesity and Serious Mental III Health: A Critical Review of the Literature. Healthcare. 2014;2(2):166-182. doi:10.3390/healthcare2020166

- Hensel JM, Taylor VH, Fung K, Vigod SN. Rates of mental illness and addiction among high-cost users of medical services in Ontario. Can J Psychiatry. 2016;61(6):358-366. doi:10.1177/0706743716644764
- 32. Wong MMC, Chen EYH, Lui SSY, Tso S. Medication adherence and subjective weight perception in patients with first-episode psychotic disorder. Clin Schizophr Relat Psychoses. 2011;5(3):135-141. doi:10.3371/CSRP.5.3.3
- 33. Thorpe J, Saeed S, Moodie EEM, Klein MB. Antiretroviral treatment interruption leads to progression of liver fibrosis in HIV-hepatitis C virus co-infection. Aids. 2011;25(7):967-975. doi:10.1097/QAD.0b013e3283455e4b
- Pringsheim T, Gardner DM. Dispensed prescriptions for quetiapine and other second-generation antipsychotics in Canada from 2005 to 2012: a descriptive study. C Open. 2014;2(4):E225-E232. doi:10.9778/cmajo.20140009
- Maglione M, Maher A, Hu J, Wang Z, Shanman R, Shekelle P. Comparative Effectiveness Review Off-Label Use of Atypical Antipsychotics: An Update Evidence-based Practice Center Director. Agency Healthc Res Qual. 2011;43.
- Katzman MA, Brawman-Mintzer O, Reyes EB, Olausson B, Liu S, Eriksson H. Extended release quetiapine fumarate (quetiapine XR) monotherapy as maintenance treatment for generalized anxiety disorder: A long-term, randomized, placebo-controlled trial. Int Clin Psychopharmacol. 2011;26(1):11-24. doi:10.1097/YIC.0b013e32833e34d9
- Ray WA, Chung CP, Murray KT, Hall K, Stein CM. Atypical antipsychotic drugs and the risk of sudden cardiac death. N Engl J Med. 2009;360(3):225-235. doi:10.1056/NEJMoa0806994
- Gill SS, Bronskill SE, Normand SLT, et al. Antipsychotic drug use and mortality in older adults with dementia. Ann Intern Med. 2007;146(11):775-786. doi:10.7326/0003-4819-146-11-200706050-00006
- Schneider LS, Dagerman K, Insel PS. Efficacy and adverse effects of atypical antipsychotics for dementia: Meta-analysis of randomized, placebo-controlled trials. Am J Geriatr Psychiatry. 2006;14(3):191-210. doi:10.1097/01. JGP.0000200589.01396.6d
- Tek C. Naltrexone HCI/bupropion HCI for chronic weight management in obese adults: Patient selection and perspectives. Patient Prefer Adherence. 2016;10:751-759. doi:10.2147/PPA.S84778
- Marteene W, Winckel K, Hollingworth S, et al. Strategies to counter antipsychotic-associated weight gain in patients with schizophrenia. Expert Opin Drug Saf. 2019;18(12):1150-1160. doi:10.1080/14740338.2019.1674809
- Stroup TS, McEvoy JP, Ring KD, et al. A randomized trial examining the effectiveness of switching from olanzapine, quetiapine, or risperidone to aripiprazole to reduce metabolic risk: Comparison of Antipsychotics for Metabolic Problems (CAMP). Am J Psychiatry. 2011;168(9):947-956. doi:10.1176/appi.ajp.2011.10111609
- Larsen JR, Vedtofte L, Jakobsen MSL, et al. Effect of liraglutide treatment on prediabetes and overweight or obesity in clozapine- or olanzapine-treated patients with schizophrenia spectrum disorder: A randomized clinical trial. JAMA Psychiatry. 2017;74(7):719-728. doi:10.1001/jamapsychiatry.2017.1220
- Siskind DJ, Russell AW, Gamble C, et al. Treatment of clozapine-associated obesity and diabetes with exenatide in adults with schizophrenia: A randomized controlled trial (CODEX). Diabetes, Obes Metab. 2018;20(4):1050-1055. doi:10.1111/dom.13167
- 45. Ishøy PL, Knop FK, Broberg B V., et al. Effect of GLP-1 receptor agonist treatment on body weight in obese antipsychotic-treated patients with schizophrenia: a randomized, placebo-controlled trial. Diabetes, Obes Metab. 2017;19(2):162-171. doi:10.1111/dom.12795
- 46. Siskind D, Hahn M, Correll CU, et al. Glucagon-like peptide-1 receptor agonists for antipsychotic-associated cardio-metabolic risk factors: A systematic review and individual participant data meta-analysis. Diabetes, Obes Metab. 2019;21(2):293-302. doi:10.1111/dom.13522
- Lyu X, Du J, Zhan G, et al. Naltrexone and Bupropion combination treatment for smoking cessation and weight loss in patients with schizophrenia. Front Pharmacol. 2018;9:181. doi:10.3389/fphar.2018.00181

- Taveira TH, Wu WC, Tschibelu E, et al. The effect of naltrexone on body fat mass in olanzapine-treated schizophrenic or schizoaffective patients: A randomized double-blind placebo-controlled pilot study. J Psychopharmacol. 2014;28(4):395-400. doi:10.1177/0269881113509904
- Guerdjikova AI, Walsh B, Shan K, Halseth AE, Dunayevich E, McElroy SL. Concurrent Improvement in Both Binge Eating and Depressive Symptoms with Naltrexone/Bupropion Therapy in Overweight or Obese Subjects with Major Depressive Disorder in an Open-Label, Uncontrolled Study. Adv Ther. 2017;34(10):2307-2315. doi:10.1007/s12325-017-0613-9
- Joffe G, Takala P, Tchoukhine E, et al. Orlistat in clozapine- or olanzapine-treated patients with overweight or obesity: A 16-week randomized, double-blind, placebo-controlled trial. J Clin Psychiatry. 2008;69(5):706-711. doi:10.4088/JCP.v69n0503
- Maayan L, Vakhrusheva J, Correll CU. Effectiveness of medications used to attenuate antipsychotic-related weight gain and metabolic abnormalities: A systematic review and meta-analysis. Neuropsychopharmacology. 2010;35(7):1520-1530. doi:10.1038/npp.2010.21
- Choi YJ. Efficacy of adjunctive treatments added to olanzapine or clozapine for weight control in patients with schizophrenia: A systematic review and meta-analysis. Sci World J. 2015. doi:10.1155/2015/970730
- Fiedorowicz J, Miller, D R, Bishop J A, Calarge C L, Ellingrod V G, W H. Systematic Review and Meta-analysis of Pharmacological Interventions for Weight Gain from Antipsychotics and Mood Stabilizers. Curr Psychiatry Rev. 2012;8(1):25-36. doi:10.2174/157340012798994867. Systematic
- Silva VA De, Suraweera C, Ratnatunga SS, Dayabandara M. Metformin in prevention and treatment of antipsychotic induced weight gain: a systematic review and meta-analysis. BMC Psychiatry. 2016;16(1):341. doi:10.1186/s12888-016-1049-5
- Goh KK, Chen CH, Lu ML. Topiramate mitigates weight gain in antipsychotic-treated patients with schizophrenia: meta-analysis of randomised controlled trials. Int J Psychiatry Clin Pract. 2019;23(1):14-32. doi:10.1080/13651501.2018.1449864
- Lee S, Sziklas V, Andermann F, Farnham S, Risse G, Gustafson M. The effects of adjunctive topiramate on cognitive function in patients with epilepsy. Epilepsia. 2003;44(3):339-347. doi:10.1046/j.1528-1157.2003.27402.x
- Van Ameringen M, Mancini C, Pipe B, Campbell M, Oakman J. Topiramate treatment for SSRI-induced weight gain in anxiety disorders. J Clin Psychiatry. 2002;63(11):981-984. doi:10.4088/JCP.v63n1104
- Kishi T, Iwata N. Efficacy and tolerability of histamine-2 receptor antagonist adjunction of antipsychotic treatment in schizophrenia: A meta-analysis of randomized placebo-controlled trials. Pharmacopsychiatry. 2015;48(1):30-36. doi:10.1055/s-0034-1390478
- Pagoto S, Schneider K, Whited M, et al. Randomized controlled trial of behavioral treatment for comorbid obesity and depression in women: The Be Active Trial. Int J Obes. 2013;37(11):1427-1434. doi:10.1038/ijo.2013.25.Randomized
- Linde J, Simon G, Ludman E, Ichikawa L, Operskalski B, D A. A randomized controlled trial of behavioral weight loss treatment versus combined weight loss/depression treatment among women with comorbid obesity and depression.
 Ann Behav Med. 2011;41(1):119-130. doi:10.1007/s12160-010-9232-2.A
- Firth J, Cotter J, Elliott R, French P, Yung AR. A systematic review and meta-analysis of exercise interventions in schizophrenia patients. Psychol Med. 2015;45:1343-1361. doi:10.1017/S0033291714003110
- Pearsall R, Smith DJ, Pelosi A, Geddes J. Exercise therapy in adults with serious mental illness: a systematic review and meta-analysis. BMC Psychiatry. 2014;14(1):117. doi:10.1186/1471-244X-14-117
- Caemmerer J, Correll CU, Maayan L. Acute and maintenance effects of non-pharmacologic interventions for antipsychotic associated weight gain and metabolic abnormalities: A meta-analytic comparison of randomized controlled trials. Schizophr Res. 2012;140(1-3):159-168. doi:10.1016/j.schres.2012.03.017
- Bonfioli E, Berti L, Goss C, Muraro F, Burti L. Health promotion lifestyle interventions for weight management in psychosis: a systematic review and meta-analysis of randomised controlled trials. BMC Psychiatry. 2012;12:78. doi:10.1186/1471-244X-12-78

- Gierisch J, Nieuwsma J, Bradford D, Wilder C, Mann-Wrobel M, McBroom A. Pharmacologic and behavioral interventions to improve cardiovascular risk factors in adults with serious mental illness: A systematic review and meta-analysis. J Clin Psychiatry. 2014;75(5):e424-440. doi:10.4088/JCP.13r08558
- Naslund JA, Whiteman KL, Mchugo GJ, et al. Lifestyle interventions for weight loss among overweight and obese adults with serious mental illness: A systematic review and meta-analysis. Gen Hosp Psychiatry. 2017;47:83-102. doi:10.1016/j.genhosppsych.2017.04.003.Lifestyle
- 67. Bruins J, Jörg F, Bruggeman R, Slooff C, Corpeleijn E, Pijnenborg M. The Effects of Lifestyle Interventions on (Long-Term) Weight Management, Cardiometabolic Risk and Depressive Symptoms in People with Psychotic Disorders: A Meta-Analysis. PLoS One. 2014;9:e112276. doi:10.1371/journal.pone.0112276
- Holt RIG, Gossage-worrall R, Hind D, et al. Structured lifestyle education for people with schizophrenia, schizoaffective disorder and first-episode psychosis (STEPWISE): randomised controlled trial. Br J Psychiatry. 2019;214:63-73. doi:10.1192/bjp.2018.167
- Mitchell J, Selzer F, Kalarchian M, Devlin M, Strain G, Elder K. Psychopathology before surgery in the Longitudinal Assessment of Bariatric Surgery-3 (LABS-3) Psychosocial Study. Surg Obes Relat Dis. 2012;8(5):533-541. doi:10.1016/j. soard.2012.07.001.Psychopathology
- Ariel A, Perri M. Effect of dose of behavioral treatment for obesity on binge eating severity. Eat Behav. 2016;22:55-61. doi:10.1016/j.eatbeh.2016.03.032.Effect
- 71. Schulte EM, Avena NM, Gearhardt AN. Which Foods May Be Addictive? The Roles of Processing, Fat Content, and Glycemic Load. PLoS One. 2015;10:e0117959. doi:10.1371/journal.pone.0117959
- Curtis C, Davis C. A Qualitative Study of Binge Eating and Obesity From an Addiction Perspective. Eat Disord. 2014;22(1):19-32. doi:10.1080/10640266.2014.857515
- 73. Gilhooly CH, Das SK, Golden JK, et al. Food cravings and energy regulation: The characteristics of craved foods and their relationship with eating behaviors and weight change during 6 months of dietary energy restriction. Int J Obes. 2007;31(12):1849-1858. doi:10.1038/sj.ijo.0803672
- 74. Gearhardt A, White M, Masheb R, Morgan P, Crosby R, Grilo C. An examination of the food addiction construct in obese patients with binge eating disorder. Int J Eat Disord. 2012;45(5):657-663. doi:10.1002/eat.20957.
- 75. Davis C. A commentary on the associations among 'food addiction', binge eating disorder, and obesity: Overlapping conditions with idiosyncratic clinical features. Appetite. 2017;155:3-8. doi:10.1016/j.appet.2016.11.001
- American Journal of Psychiatry. Available from: http://ajp.psychiatryonline. org/article.aspx?articleID=158714%5Cnhttp://scholar.google.com/scholar?hl=en&btnG=Search&q=intitle:DSM-5#0.
- 77. Gearhardt AN, Corbin WR, Brownell KD. Preliminary validation of the Yale Food Addiction Scale. Appetite. 2009;52:430-436. doi:10.1016/j.appet.2008.12.003
- Penzenstadler L, Soares C, Karila L, Khazaal Y. Systematic Review of Food Addiction as Measured with the Yale Food Addiction Scale: Implications for the Food Addiction Construct. Curr Neuropharmacol. 2018;17:526-538. doi:10.2174/1570159X16666181108093520
- Cassin SE, Buchman DZ, Leung SE, et al. Ethical, Stigma, and Policy Implications of Food Addiction: A Scoping Review. Nutrients. 2019;11:710. doi:10.3390/ nu11040710
- 80. Mühlhans B, Horbach T, Zwaan M De. Psychiatric disorders in bariatric surgery candidates: a review of the literature and results of a German prebariatric surgery sample. Gen Hosp Psychiatry. 2009;31(5):414-421. doi:10.1016/j.genhosppsych.2009.05.004
- 81. Taylor VH, Hensel J. Multimorbidity: A Review of the Complexity of Mental Health Issues in Bariatric Surgery Candidates Informed by Canadian Data. Can J Diabetes. 2017;41(4):448-452. doi:10.1016/j.jcjd.2017.04.004
- Dawes AJ, Maggard-gibbons M, Maher AR, et al. Mental Health Conditions Among Patients Seeking and Undergoing Bariatric Surgery A Meta-analysis. JAMA - J Am Med Assoc. 2016;315(2):150-163. doi:10.1001/jama.2015.18118

- Kalarchian M, King W, Devlin M, Marcus M, Garcia L, Chen J. Psychiatric disorders and weight change in a prospective study of bariatric surgery patients:
 A 3-year follow-up. Psychosom Med. 2017;78(3):373-381. doi:10.1097/PSY.0000000000000277.Psychiatric
- Thiara G, Cigliobianco M, Muravsky A, et al. Evidence for Neurocognitive Improvement After Bariatric Surgery: A Systematic Review. Psychosomatics. 2017;58(3):217-227. doi:10.1016/j.psym.2017.02.004
- 85. Nasirzadeh Y, Kantarovich K, Wnuk S, Okrainec A, Cassin SE. Binge Eating, Loss of Control over Eating, Emotional Eating, and Night Eating After Bariatric Surgery: Results from the Toronto Bari-PSYCH Cohort Study. Obes Surg. 2018;28:2032-2039. doi:10.1007/s11695-018-3137-8
- Bhatti J, Nathens A, Thiruchelvam D, Grantcharov T, Goldstein B, Redelmeier D. Self-harm Emergencies After Bariatric Surgery: A Population- Based Cohort Study. JAMA Surg. 2016;151(226-32). doi:10.1001/jamasurg.2015.3414.Self-harm
- 87. Peterhänsel C, Petroff D, Klinitzke G, Kersting A, Wagner B. Risk of completed suicide after bariatric surgery: A systematic review. Obes Rev. 2013;14:369-382. doi:10.1111/obr.12014
- 88. Lim RBC, Zhang MWB, Ho RCM. Prevalence of All-Cause Mortality and Suicide among Bariatric Surgery Cohorts: A Meta-Analysis. Int J Env Res Public Heal. 2018;15:1519. doi:10.3390/ijerph15071519
- Li L, Wu L. Substance use after bariatric surgery: A review. J Psychiatr Res. 2016;76:16-29. doi:10.1016/j.jpsychires.2016.01.009.Substance
- King W, Chen J, Mitchell J, Kalarchian M, Steffen K, Engel S. Prevalence of alcohol use disorders before and after bariatric surgery. JAMA - J Am Med Assoc. 2012;307(23):2516-2525. doi:10.1001/jama.2012.6147.Prevalence
- 91. Mitchell J, Steffen K, Engel S, King W, Chen J, Winters K. Addictive disorders after Roux-en-Y gastric bypass. Surg Obes Relat Dis. 2015;11(4):897-905. doi:10.1016/j.soard.2014.10.026.Addictive
- 92. King WC, Chen J, Courcoulas AP, et al. Alcohol and other substance use after bariatric surgery: prospective evidence from a U.S. multicenter cohort study. Surg Obes Relat Dis. 2017;13(8):1392-1402. doi:10.1016/j.soard.2017.03.021.Alcohol
- 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;212:209-214. doi:10.1016/j.jamcollsurg.2010.09.020
- Raebel MA, Newcomer SR, Bayliss EA, et al. Chronic opioid use emerging after bariatric surgery. Pharmacoepidemiol Drug Saf. 2014;23:1247-1257. doi:10.1002/pds
- Raebel MA, Newcomer SR, Reifler LM, et al. Chronic Use of Opioid Medications Before and After Bariatric Surgery. JAMA - J Am Med Assoc. 2013;310(13):1369-1376. doi:10.1001/jama.2013.278344
- Wimmelmann CL, Dela F, Mortensen EL. Psychological predictors of weight loss after bariatric surgery: A review of the recent research. Obes Res Clin Pract. 2014;8(4):e299-e313. doi:10.1016/j.orcp.2013.09.003
- Sheets CS, Peat CM, Berg KC, et al. Post-operative Psychosocial Predictors of Outcome in Bariatric Surgery. Obes Surg. 2015;25(2):330-345. doi:10.1007/ s11695-014-1490-9.Post-Operative
- Zwaan M De, Enderle J, Wagner S, et al. Anxiety and depression in bariatric surgery patients: A prospective, follow-up study using structured clinical interviews. J Affect Disord. 2011;133(1-2):61-68. doi:10.1016/j.jad.2011.03.025
- Sockalingam S, Hawa R, Wnuk S, et al. Psychosocial predictors of quality of life and weight loss two years after bariatric surgery: Results from the Toronto Bari-PSYCH study. Gen Hosp Psychiatry. 2017;47:7-13. doi:10.1016/j.genhosppsych.2017.04.005
- 100. Thomson L, Sheehan KA, Meaney C, Wnuk S, Hawa R, Sockalingam S. Prospective study of psychiatric illness as a predictor of weight loss and health related quality of life one year after bariatric surgery. J Psychosom Res. 2016;86:7-12. doi:10.1016/j.jpsychores.2016.04.008
- 101. Devlin MJ, King WC, Kalarchian MA, et al. Eating pathology and experience and weight loss in a prospective study of bariatric surgery patients: 3-year follow-up. Int J Eat Disord. 2016;49(12):1058-1067. doi:10.1002/eat.22578.Eating

- 102. Sogg S, Mori DL. Psychosocial Evaluation for Bariatric Surgery: The Boston Interview and Opportunities for Intervention. Obes Surg. 2009;19:369-377. doi:10.1007/s11695-008-9676-7
- 103. Thiara G, Yanofksy R, Abdul-Kader S, Santiago V, Cassin S, Okrainec A. Toronto Bariatric Interprofessional Psychosocial Assessment Suitability Scale: Evaluating A New Clinical Assessment Tool for Bariatric Surgery Candidates. Psychosomatics. 2016;57(2):165-173. doi:10.1016/j.psym.2015.12.003
- 104. Barclay KS, Rushton PW, Forwell SJ. Measurement Properties of Eating Behavior Self-Assessment Tools in Adult Bariatric Surgery Populations: a Systematic Review. Obes Surg. 2015;25:720-737. doi:10.1007/s11695-015-1593-y
- Marek RJ, Heinberg LJ, Lavery M, Merrell Rish J, Ashton K. A review of psychological assessment instruments for use in bariatric surgery evaluations. Psychol Assess. 2016;28(9):1142-1157. doi:10.1037/pas0000286
- 106. Cassin S, Sockalingam S, Hawa R, Wnuk S, Royal S, Taube-Schiff M. Psychometric Properties of the Patient Health Questionnaire Surgery Candidates. Psychosomatics. 2013;54(4):352-358. doi:10.1016/j.psym.2012.08.010
- 107. Parker K, O'Brien P, Brennan L. Measurement of Disordered Eating Following Bariatric Surgery: a Systematic Review of the Literature. Obes Surg. 2014;24:945-953. doi:10.1007/s11695-014-1248-4
- 108. Mitchell J, King W, Chen J, Devlin M, Flum D, L G. Course of depressive symptoms and treatment in the longitudinal assessment of bariatric surgery (LABS-2) study. Obesity. 2014;22(8):1799-1806. doi:10.1002/oby.20738.
- Padwal R, Brocks D, Sharma AM. A systematic review of drug absorption following bariatric surgery and its theoretical implications. Obes Rev. 2010;11(1):41-50. doi:10.1111/j.1467-789X.2009.00614.x
- 110. Roerig JL, Steffen K. Psychopharmacology and Bariatric Surgery. Eur Eat Disord Rev. 2015;23:463-469. doi:10.1002/erv.2396
- 111. Hamad G, Helsel J, Perel J, Kozak G, McShea M, Hughes C. The effect of gastric bypass on the pharmacokinetics of serotonin reuptake inhibitors. Am J Psychiatry. 2012;169(3):256-263. doi:10.1176/appi.ajp.2011.11050719.The
- 112. Bingham K, Hawa R, Sockalingam S. SSRI Discontinuation Syndrome Following Bariatric Surgery: A Case Report and Focused Literature Review. Psychosomatics. 2014;55(6):692-697. doi:10.1016/j.psym.2014.07.003
- 113. Bingham KS, Thoma J, Hawa R, Sockalingam S. Perioperative Lithium Use in Bariatric Surgery: A Case Series and Literature Review. Psychosomatics. 2016;57(6):638-644. doi:10.1016/j.psym.2016.07.001
- 114. Bingham KS, Yanofsky R. Psychopharmacology in Bariatric Surgery Patients. Psychiatr Care Sev Obes. 2017:313-333. doi:10.1007/978-3-319-42536-8_23
- 115. Ogden J, Hollywood A, Pring C. The Impact of Psychological Support on Weight Loss Post Weight Loss Surgery: a Randomised Control Trial. Obes Surg. 2015;25:500-505. doi:10.1007/s11695-014-1428-2
- 116. Stewart F, Avenell A. Behavioural Interventions for Severe Obesity Before and / or After Bariatric Surgery: a Systematic Review and Meta-analysis. Obes Surg. 2016;26:1203-1214. doi:10.1007/s11695-015-1873-6
- 117. Rudolph A, Hilbert A. Post-operative behavioural management in bariatric surgery: A systematic review and meta-analysis of randomized controlled trials. Obes Rev. 2013;14:292-302. doi:10.1111/obr.12013
- 118. Kalarchian MA, Marcus MD. Psychosocial Interventions Pre and Post Bariatric Surgery. Eur Eat Disord Rev. 2015;23:457-462. doi:10.1002/erv.2392
- 119. Sockalingam S, Cassin S, Wnuk S, Du C, Jackson T, Hawa R. A Pilot Study on Telephone Cognitive Behavioral Therapy for Patients Six-Months Post-Bariatric Surgery. Obes Surg. 2017;27(3):670-675. doi:10.1007/s11695-016-2322-x.A
- Paul L, Van Der Heiden C, Hoek HW. Cognitive behavioral therapy and predictors of weight loss in bariatric surgery patients. Curr Opin Psychiatry. 2017;30(6):474-479. doi:10.1097/YCO.000000000000359
- 121. Bradley LE, Forman EM, Kerrigan SG, et al. A Pilot Study of an Acceptance-Based Behavioral Intervention for Weight Regain After Bariatric Surgery. Obes Surg. 2016;26:2433-2441. doi:10.1007/s11695-016-2125-0

- 122. Wnuk SM, Du CT, Van Exan J, et al. Mindfulness-Based Eating and Awareness Training for Post-Bariatric Surgery Patients: a Feasibility Pilot Study. Mindfulness (N Y). 2018;9(3):949-960. doi:10.1007/s12671-017-0834-7
- 123. Vidal P, Ramón JM, Goday A, et al. Lack of Adherence to Follow-Up Visits After Bariatric Surgery: Reasons and Outcome. Obes Surg. 2014;24:179-183. doi:10.1007/s11695-013-1094-9
- 124. Kim HJ, Madan A, Fenton-lee D. Does Patient Compliance with Follow-up Influence Weight Loss After Gastric Bypass Surgery ? A Systematic Review and Meta-Analysis. Obes Surg. 2014;24:647-651. doi:10.1007/s11695-014-1178-1
- 125. Goode R, Ye L, Sereika S, Zheng Y, Mattos M, Acharya S. Socio-demographic, anthropometric, and psychosocial predictors of attrition across behavioral weightloss trials. Eat Behav. 2016;20:27-33. doi:10.1016/j.eatbeh.2015.11.009.Socio-demographic
- 126. Moroshko I, Brennan L, Brien PO. Predictors of dropout in weight loss interventions: A systematic review of the literature. Obes Rev. 2011;12:912-934. doi:10.1111/j.1467-789X.2011.00915.x
- Larjani S, Spivak I, Hao GM, Aliarzadeh B, Wang W, Robinson S. Preoperative predictors of adherence to multidisciplinary follow-up care postbariatric surgery. Surg Obes Relat Dis. 2016;12(2):350-356. doi:10.1016/j.soard.2015.11.007
- 128. Sockalingam S, Cassin S, Hawa R, et al. Predictors of Post-bariatric Surgery Appointment Attendance: the Role of Relationship Style. Obes Surg. 2013;23:2026-2032. doi:10.1007/s11695-013-1009-9
- Hood MM, Corsica J, Bradley L, Wilson R, Chirinos DA, Vivo A. Managing severe obesity: understanding and improving treatment adherence in bariatric surgery. J Behav Med. 2016;39(6):1092-1103. doi:10.1007/s10865-016-9772-4
- 130. Aarts MA, Sivapalan N, Nikzad SE, Serodio K, Sockalingam S, Conn LG. Optimizing Bariatric Surgery Multidisciplinary Follow-up: a Focus on Patient-Centered Care. Obes Surg. 2017;27(3):730-736. doi:10.1007/s11695-016-2354-2
- Sunil S, Santiago VA, Gougeon L, et al. Predictors of Vitamin Adherence After Bariatric Surgery. Obes Surg. 2017;27(2):416-423. doi:10.1007/s11695-016-2306-x