Clinical Practice GUIDELINE for the Management of Obesity in Adults in Ireland

The Role of Mental Health in Obesity Management

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KEY MESSAGES FOR HEALTHCARE POLICY MAKERS

- **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.**
- **Physicians should be aware of the weight gain and cardiometabolic risks associated with off-label anti-psychotics use (absence of approval by regulatory bodies), even when these medications are prescribed at lower doses.**
- **When initiating anti-psychotic treatment for the first time, medications with higher metabolic risk, such as olanzapine, should be avoided.** Individuals in their first episode usually respond well to therapeutic doses, 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 mental illness who gain weight on an anti-psychotic treatment, if clinically appropriate.**
- **Behavioural therapy, ideally as part of a multi-disciplinary treatment approach, can be effective in helping to manage obesity in individuals with co-occurring mental illness.** The type and intensity of the behavioural intervention will need to be personalised to the needs of individuals with more severe psychopathology in the context of obesity.
- **Given the prevalence of mental health issues in individuals with obesity, screening for mental illness is recommended, as undetected mental health difficulties may have a negative impact on obesity management.**

KEY MESSAGES FOR HEALTHCARE PROFESSIONALS - Continued

- **For patients with severe mental illness who gain weight on anti-psychotic treatments, the option of trialling weight management medications in conjunction with behavioural obesity management interventions should be explored.** Glucagon-like peptide 1 (GLP-1) agonists are licenced in Ireland for weight management and have the greatest supporting evidence of both safety and efficacy in chronic obesity management of all licensed preparations.

- **However, off-label use of metformin is also an effective and more commonly used intervention that has been studied extensively in patients with mental illness and anti-psychotic-induced weight gain.** Metformin is likely to be more effective when initiated at earlier stages of anti-psychotic treatment and should be considered as a first-line management option prior to GLP-1 agonists. Cost may be a barrier for individuals trying to access GLP-1 agonists. See Table 1 for prescribing information for these medications.

- **For individuals regaining weight after bariatric surgery, biopsychosocial/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 (BED) 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 is recommended, given the potential negative impact that undetected mental health difficulties may have of management and recovery for obesity.** Screening for conditions such as depression, anxiety, BED, attention deficit hyperactivity disorder (ADHD) and trauma should be considered in patients seeking obesity treatment.

- **The current approved obesity medications can be helpful in patients with a mental illness and should be used based on clinical appropriateness and cost considerations.** GLP-1 agonists have the greatest supporting evidence of efficacy in chronic obesity management and indirect evidence demonstrates their superior efficacy compared to alternative options. These options include orlistat and the combination tablet naltrexone/bupropion. The latter is contraindicated amongst those with a history of bipolar disorder due to risk of mania induction. See Chapter 11 Pharmacotherapy in Obesity Management for further information.

- **For people with overweight or obesity and BED, evidence highlights that the following medications, lisdexamfetamine, topiramate and second-generation anti-depressants, including serotonin reuptake inhibitors, duloxetine, and bupropion, can be effective in reducing eating pathology.** However, all are off-label pharmacological interventions in Ireland. While these medications are effective in reducing eating pathology, their effect on weight loss is less certain.

- **Referral for more intense (i.e., longer term) psychological and behavioural interventions, such as cognitive behavioural therapy, interpersonal therapy and acceptance and commitment therapy should be considered for individuals with significant binge eating and depressive symptoms in the context of obesity, in an effort to address comorbid mental health issues that may contribute significantly to their obesity management and outcomes.**

- **If a patient is actively attending a mental health service, such as their local community mental health team, clear communication and liaison with their treating team should take place during the weight-management interventions to optimise positive outcomes.**

- **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 the potential impact on long-term weight loss and consideration of the impact that surgical intervention may have on mental health stability.

- **A stepped care model should be utilised to organise provision of mental health services.** The level of care is "stepped up" to more intensive or specialist services as required and, depending on the level of patient distress, senior liaison psychiatry input should form part of the multi-disciplinary team.

- **Individuals undergoing bariatric surgery should undergo a pre-surgical mental health screen by a specialist mental health clinician to identify early risk factors for poor outcomes or mental health deterioration.**

- **Assessment and monitoring of an individual's mental health should continue following surgery and can include the use of either clinician-administered or patient self-report measures, where appropriate.**

- **Individuals with mental health difficulties should receive ongoing monitoring by a healthcare professional for mental health symptomatology, including eating psychopathology, substance misuse and risk behaviours, such as suicidal ideation or self-harm, after bariatric surgery.**

- **Patients should be monitored for alcohol- and substance-use changes, after bariatric surgery and informed about the possibility of altered alcohol metabolism following surgery.**

- **For individuals regaining weight after bariatric surgery, biopsychosocial interventions should be used to address comorbid psychiatric symptoms complicating obesity management.**

- **Patients should undergo pre-bariatric surgery psychosocial and mental health assessments by an experienced mental health 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 thus therapeutic effect, especially with malabsorptive surgical procedures.** Furthermore, for individuals with existing mental illness, continuing psychiatric medications after surgery, and monitoring of therapeutic effect, is critical to maintaining mental health stability in the post-surgical period and longer term.

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

- **Multi-disciplinary bariatric surgery teams should focus on evidence-based strategies to improve patient engagement during the post-surgery follow-up period, specifically for high-risk patient groups, to optimise patient recovery and good outcomes.** Such strategies should include close communication with other specialities, such as mental health and primary care.

RECOMMENDATIONS

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

2. Healthcare professionals (HCPs) can consider both efficacy and effects on body weight when choosing psychotropic medications (Level 2a, Grade B)[4-16].

3. Pharmacological treatment, such as 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)[17,18].

4. HCPs should be aware that both lisdexamfetamine and topiramate have been shown to reduce eating pathology and weight in people with overweight or obesity and in binge eating disorders (Level 1a, Grade A)[19-21]. However, neither medication is licensed in Ireland for this indication currently, and specialist opinion should be sought before considering such treatment options in conjunction with psychological interventions (Level 4, Grade D, consensus).

KEY MESSAGES FOR PEOPLE LIVING WITH OBESITY

- **There are clear links between mental illness and weight. Healthcare professionals should be aware of all treatments that patients are taking for their mental health.**

- **Individuals with co-occurring mental illness should be offered biopsychosocial interventions, including behavioural therapy to help manage obesity.**

- **Individuals with co-occurring mental illness should receive psychoeducation about the potential impact of bariatric surgery on their mental state and the potential effects on the efficacy of their psychotropic medications.**

- **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 a specialised multi-disciplinary team to identify and manage psychiatric symptoms and eating difficulties arising after surgery.

KEY MESSAGES FOR PEOPLE LIVING WITH OBESITY - Continued

- **Given the potential risk for relapse of psychiatric symptoms, individuals undergoing bariatric surgery should be made aware of the potential changes in the absorption and metabolism of their psychotropic medications post-bariatric surgery and should be advised to discuss this with their treating team.**

- **Given the potential increased risk of substance-use problems (such as alcohol), individuals undergoing bariatric surgery should be made aware of the potential changes in absorption and metabolism of these substances following bariatric surgery, and they should be advised to seek help as needed.**

- **The importance of monitoring mental health in the post-operative period should be emphasised, to ensure that individuals access appropriate supports.**

- **Anti-psychotic medications should not routinely be prescribed (especially on a long-term basis) for issues like sleep and anxiety.** Psychological interventions, such as cognitive behavioural therapy, should be recommended in the first instance, where appropriate.

- **If a patient has started an anti-psychotic recently and has gained weight, or there is concern about future weight gain, and behavioural interventions have not or are unlikely to be sufficient in addressing this concern, metformin can be used to prevent further weight gain.** Metformin may also help to reduce some weight already gained. However, it's main benefit is in preventing future weight gain from anti-psychotics.

- **Where anti-psychotics have caused a significant amount of weight gain, metformin treatment may not be sufficient to reverse this.** Early studies suggest that, amongst medications approved for long-term weight management in Ireland and overseas, glucagon-like peptide 1 (GLP-1) receptor agonists have the most evidence to support their use in reversing weight gained from anti-psychotics.

- **No medication is licensed in Ireland for preventing or treating weight gain caused by anti-psychotics.** GLP-1 receptor agonists also currently come at significant cost to patients. Individuals should discuss with their doctor or pharmacist what options might be suitable and affordable for them.

- **If an individual has gained weight from an anti-psychotic medication, they should be advised to ask their doctor or pharmacist if there might be another anti-psychotic with a lower weight-gain risk.** This should be a collaborative decision, taking into careful consideration other potential side effects/tolerability and risk of deterioration in mental health.

- **For patients with binge eating disorder, two medications (lisdexamfetamine and topiramate) can be helpful to reduce both binge episodes and weight.** These medications are currently not licenced in Ireland for these indications but have shown benefits for some patients.

Introduction

Much like trying to untangle the aetiology of obesity, trying to understand the association between weight gain and mental illness is complicated[22]. We are aware of vulnerabilities that increase risk, both of weight gain in those with mental illness and, conversely, mental health issues in those living with obesity, and we know the end result is that the presence of one illness can impact the other[23,24]. We also know that unconscious bias, a factor that those living with obesity and mental illness often face, is compounded when the conditions co-occur, and can be especially damaging in medical settings[25]. This has profound effects on patient care, medical outcomes and, from a broader systems perspective, on healthcare costs and access to care[26].

In Ireland, approximately 60% of the population has a body mass index (BMI) > 25kg/m^2. Furthermore, evidence highlights that certain vulnerable patient cohorts are more at risk, including patients with major mental illness and other psychological conditions. The exact rate of overweight or obesity amongst this patient cohort in this country is not clearly defined; however, research in the UK has previously highlighted that approximately 85% of patients with a major mental illness had a BMI > 25 kg/m^2.[27] Moreover, patients living with severe obesity in Ireland have significantly reduced self-rated health and psychological wellbeing[28]. Improving psychological wellbeing and self-rated health through targeted interventions including social support may, in turn, help to promote improved health in this group, highlighting the importance of a biopsychosocial model of care in the overall management of this complex patient cohort[28].

This chapter's evidenced-based recommendations are meant to serve as a guideline to ensure healthcare professionals (HCPs) are informed and can provide the best care to an often complex and marginalised patient group with challenging presentations secondary to their comorbidities.

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 determinants of health, and medication and metabolic side effects[22]. This association is supported by clinical and epidemiological research reporting prevalence rates of overweight and obesity of 25% – 60% for bipolar affective disorder (BPAD), 30% – 70% for schizophrenia and 20% – 50% for depression[29,30]. Links have also been made between overweight and obesity and binge eating disorder (BED), attention deficit disorder (ADHD), post-traumatic stress disorder (PTSD) and, specifically, childhood trauma[22,31,32]. Given the high prevalence of mental health issues in those living with obesity, it is not surprising that mental illness is more prevalent in those presenting with weight-related comorbidities and those seeking obesity treatment. It is critical, therefore, that HCPs involved in the care of those with obesity prioritise patients' mental health needs as well[33].

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[34]. 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 standardised screening approach[35].

There is a clear and irrefutable link between psychotropic medications and weight gain. While this association has been most clearly studied and documented with respect to anti-psychotics[8], medications used in the treatment of BPAD, major depressive disorder (MDD) and anxiety disorders, such as anti-depressants and mood stabilisers, have also been shown to be associated with significant weight gain[8].

While it is important that medication efficacy is prioritised, 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[36]. It is therefore important that HCPs be aware of the side-effect profile associated with different psychotropic medications and consider both efficacy and tolerability in deciding on appropriate short-term and long-term psychopharmacology.

Second-generation anti-psychotics are approved by the U.S. Food and Drug Administration (FDA), and here in Ireland by the Health Products Regulatory Authority (HPRA), for the treatment of schizophrenia, BPAD and depression under drug-specific circumstances. While second-generation anti-psychotics have been argued to have a lower propensity for causing extrapyramidal side effects compared to their first-generation counterparts when used on-label, they are indisputably associated with significant metabolic sequelae, including weight gain, glucose dysregulation and dyslipidaemia [37].

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

A recent European review, conducted in 2017 in multiple countries including Ireland, found high rates of off-label use of anti-psychotics and mood stabilisers, where the reported prevalence varied from 30% – 48% of adult psychiatric prescriptions and 29% – 66% of the patients reviewed[38]. A meta-analysis conducted in 2011 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[39,40]. In elderly patients with dementia and behavioural and psychological symptoms of dementia (BPSD), off-label use of anti-psychotics has been associated with increased risk of mortality and cardiovascular events[41-43].

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 also be considered, either in conjunction with behavioural interventions, or as an alternative first-line approach. 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 BPAD due to the risk of manic relapse[44]. 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. As anti-psychotics, as well as anti-depressants and mood stabilisers, carry a differential weight-gain risk, use of lower-liability medications can also be considered as a strategy to target metabolic comorbidity in this population.

Anti-psychotics typically come with the highest risk of weight gain amongst psychotropic medication. However, it should be noted that in the case of many anti-psychotics, efficacy of switching medications to influence weight has largely been demonstrated in preventing further weight gain, rather than reversing previous weight gained, or has not been adequately studied. A recent meta-analysis of randomised controlled trials and uncontrolled before-and-after studies found switching to aripiprazole only to be associated with significant average reductions in weight of –5.52 kg in randomised controlled trials and –2 kg in before-and-after studies. No worsening of psychotic symptoms was observed amongst those included studies; however, the average study duration was 26.3 weeks, and this may limit the power of these studies to detect significant changes in psychiatric symptoms[45].

It is likely that in the case of many anti-psychotic switches, particularly when moving from high-risk agents (e.g., olanzapine), one of the primary benefits of switching is inducing a plateau of further weight gain. The largest benefits to be gained is when switching is undertaken early in anti-psychotic treatment. Whilst still a meaningful outcome for many, efficacy of the current medication regimen, success of previous medication trials, potential side effects of the new anti-psychotic and patient preference, must all be considered, against the likely effect of switching medication on weight.

Where weight loss is the goal, additional interventions, including pharmacological treatments, will likely be needed alongside switching of psychotropic medications. For examples of lower risk medications that also have demonstrated efficacy in managing the underlying mental health condition, specialist psychiatric resources, such as the Maudsley Prescribing Guidelines, should be referenced. Also Table 9 in Chapter 6 Clinical Assessment of People Living with Obesity provides more information on this in an Irish context. Close collaboration with a patient's treating mental health team is essential to ensure that any changes in medications are clinically appropriate and response to treatments monitored closely.

Dose reduction of anti-psychotics has also not been sufficiently shown to be effective in reversing anti-psychotic-induced weight gain and is accompanied by a significant risk of deterioration of mental health. Dose reduction should not be used as a method to reverse or attenuate anti-psychotic-induced weight gain[46-48].

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

Agents currently approved for treatment of obesity in Ireland include liraglutide (Saxenda®), a glucagon-like peptide 1 receptor agonist (GLP-1 RA), naltrexone/bupropion (Mysimba®) and orlistat (Xenical®), an inhibitor of intestinal fat absorption. An additional GLP-1 RA, semaglutide 2.4 mg (Wegovy®) has also been licensed for use throughout the European Union in 2022.

No agent is licensed in Ireland specifically for the management of weight gain induced by psychotropic medication. The above three medications are approved for chronic obesity management amongst those with a BMI of ≥ 30 kg/m² or ≥ 27 kg/m² to < 30 kg/m² in the presence of at least one weight-related comorbidity, such as dysglycaemia (prediabetes or type 2 diabetes), hypertension, dyslipidaemia or obstructive sleep apnoea, in addition to increased physical activity and a reduced-energy diet. Given the multiple causes of the significantly higher rates of overweight and obesity amongst those with a severe mental illness, there is also a potential role for these medications in this cohort.

For more information on obesity-management pharmacotherapy refer to Chapter 11 Pharmacotherapy in Obesity Management. Medications studied specifically in the prevention and treatment of weight gain induced by psychotropic medications is summarised below.

A wide spectrum of medications, including anti-hyperglycaemic agents (metformin, rosiglitazone, intranasal insulin, GLP-1 RA), anti-epileptic medications (topiramate), stimulants (dextro-amphetamine, atomoxetine, modafinil, d-fenfluramine), anti-depressants (fluoxetine, reboxetine, sibutramine), histaminergic antagonists (famotidine, nizatidine), dopaminergic agents (aripiprazole, an anti-psychotic drug with partial agonism of dopaminergic (D)-2 receptor, amantadine), melatonin receptor agonists (ramelteon), NMDA receptor antagonists (memantine) and nutritive supplements (dill, celery, green tea) have been investigated in the treatment or prevention of anti-psychotic-induced weight gain and obesity in patients with severe mental illness. The following is a summary of the evidence supporting those interventions associated with the most consistent and significant results as demonstrated in randomised controlled trials. Most interventions have been associated with small to medium effect sizes[49].

Metformin

Adjunctive treatment with metformin is the most frequently studied pharmacological intervention in both the prevention and treatment of anti-psychotic-induced weight gain. Across several published meta-analyses of randomised 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[17,18,50,51]. A meta-analysis which included patients with mood disorders receiving mood stabilisers found similar beneficial effects of metformin over placebo[52]. Similar findings have been reported in two meta-analyses that assessed all randomised control trials investigating metformin for anti-psychotic-induced weight gain[18,53]. The effect of metformin is greater in first-episode patients (average 5.94 kg) as compared with chronically ill populations, where the greater weight loss can be largely accounted for via significantly more weight gain in the placebo group of the first-episode patients compared to those with chronic psychosis[18,53]. This difference reflects one of the most significant benefits to be obtained via metformin use early in anti-psychotic treatment — the induction of a plateau of weight gain. Without intervention, this has been cited as taking months to years to occur in the case of olanzapine and clozapine, respectively, and in the case of many anti-psychotics, is unknown[54,55].

Guidelines have recently been published outlining the optimised use of metformin to manage anti-psychotic-induced weight gain within the Irish setting[56]. Table 1 of this guideline gives an overview of optimised prescribing of metformin for this indication. The most common side effects associated with metformin treatment are related to the gastrointestinal tract. A dosing strategy using a starting dose of 500 mg once daily to twice daily (OD-BD) and titrated upwards by 500 mg OD at weekly intervals until 1000 mg BD is reached should be employed to reduce the occurrence of these side effects. Extended time between dosing intervals and prescribing the extended-release preparation should be employed in the case of distressing gastrointestinal side effects before trying alternative preparations, as there is a significant cost difference between metformin and other interventions used in managing psychotropic-induced weight gain. Metformin does not require blood glucose

monitoring when used for this indication, unless used alongside other medications known to cause hypoglycaemia. Use should be continued as long as clinical benefit is being obtained. Limited evidence shows reversal of weight loss following cessation of metformin when used to manage anti-psychotic-induced weight gain[57].

GLP-1 agonists (liraglutide, exenatide, semaglutide)

Three randomised 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[58-60]. Data from these trials were recently analysed in a participant-level data meta-analysis (n = 141 participants). Endpoint weight for GLP-1 RAs was 3.61 kg lower than for controls. BMI, glycated hemoglobin (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[61]. However, the relatively small number of participants and short duration of treatment limit the power of these studies to detect more serious but uncommon or rare side effects that have been associated with the use of GLP-1 RA in the general population. Chapter 11 Pharmacotherapy in Obesity Management should be consulted for more information on potential risks associated with GLP-1 RA. Of note, GLP-1 RA have not been associated with neuropsychiatric side effects in any population[62]. In Ireland, their practical use is currently limited by their high cost to patients.

Given superior weight-loss outcomes associated with the once weekly semaglutide 2.4 mg preparation when compared to all other available GLP-1 RA when used at weight-management doses, it is likely that use of this preparation will replace liraglutide as the first-line GLP-1 RA in chronic weight management[63,64]. Prescribers should consider using the most effective GLP-1 agonist available at the time of prescribing and licensed for chronic weight management. Safety outcomes are similar across all GLP-1 agonists[65]. Semaglutide is a once-weekly preparation which may improve compliance when compared to once-daily liraglutide or exenatide.

Naltrexone/bupropion (Mysimba®)

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[66]. In patients with schizophrenia using olanzapine, naltrexone alone (a component of naltrexone/bupropion), when compared to placebo in a small double-blind randomised clinical trial, did not find differences in BMI over a 12-week treatment period[50]. In women with obesity and MDD, naltrexone/bupropion was found to modestly reduce both weight and depression scores. The use of naltrexone/bupropion combination is contraindicated amongst those with a history of BPAD due to concerns over the potential of bupropion to induce hypomanic or manic episodes amongst this cohort[51]. The combination has also been associated with suicide-related events (including suicidal ideation) in post-marketing studies when used in the general population for obesity management. These concerns, and lack of comparative efficacy with more commonly studied alternatives e.g., metformin, limit the use of this combination amongst those with a severe mental illness.

Orlistat

Orlistat was examined in a double-blind randomised clinical trial in patients with schizophrenia spectrum or bipolar disorder taking anti-psychotics[67]. The data did not show a significant difference in body weight between groups.

Topiramate

Topiramate is approved in Ireland for epilepsy and migraine management. A recent meta-analysis of randomised controlled 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[68]. Overall, the side-effect profile was comparable to control groups, with the exception of paraesthesia, which was more common in topiramate-treated patients. The topiramate group also had small improvements in psychopathology. Similarly, a meta-analysis examining randomised controlled trials conducted in mixed populations with 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[52]. Although cognitive disturbances have been linked with topiramate use (particularly in epilepsy populations)[69], these have not been sufficiently studied in schizophrenia spectrum disorders[68] 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[70]. In summary, adjunctive off-label use of topiramate appears to be modestly effective to mitigate weight gain in the context of schizophrenia spectrum illnesses[17,52,68,71]. 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. It should also be noted that use of topiramate in females of child-bearing age without highly effective contraception is contraindicated due to associated teratogenicity[72].

Other options

Other off-label obesity interventions that have demonstrated efficacy in the treatment of anti-psychotic-associated weight gain and obesity include aripiprazole in treating weight gain associated with clozapine and olanzapine, H2 agonists such as nizatidine, as well as the dopaminergic agent, amantadine. However, the quality of the evidence for these interventions is low, making the effects uncertain[17,53,71]. 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[73]. Recommendations about the use of most pharmacological agents are limited by the small number of studies utilising 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. Preference should be given to the use of the other options outlined above with demonstratable efficacy and safety for this indication, namely metformin and GLP-1 RA.

Many options licensed in Ireland for obesity management are not reimbursed by national drug schemes, thus the cost to the patient can be significant. Cost of different products should be discussed with patients at the time of prescribing and at frequent intervals thereafter, as this is recognised as a significant barrier to effective, continued treatment.

Table 1: **Summary of Prescribing Particulars of Medications Indicated in Preventing and Managing Overweight and Obesity Amongst Those with a Severe Mental Illness**

	Metformin[49,74,75]	Liraglutide[58,76]	Semaglutide[63,77]
Role(s) amongst SMI population	Prevention of future/ further anti-psychotic-induced weight gain. Treatment of weight gain associated with anti-psychotics and mood stabilisers.	Treatment of anti-psychotic-induced weight gain and prediabetes. Chronic overweight and obesity management as an adjunct to a reduced-energy diet and increased physical activity for weight management in adult patients with an initial BMI ≥ 30 kg/m² or ≥ 27 kg/m² to < 30 kg/m² in the presence of at least one weight-related complication, such as dysglycaemia, hypertension, dyslipidaemia or obstructive sleep apnoea.	Not yet studied in the management of psychotropic-induced weight gain. Chronic overweight and obesity management adjunct to a reduced-energy diet and increased physical activity for weight management, including weight loss and weight maintenance, in adults with an initial BMI of ≥ 30 kg/m2 or ≥ 27 kg/m2 to < 30 kg/m2 in the presence of at least one weight-related complication.
Mode of administration	Oral	Subcutaneous	Subcutaneous
Optimal dose	1000 mg BD	*1.8 mg OD studied in management of anti-psychotic-induced weight gain. 3 mg OD studied in chronic overweight and obesity management.	2.4 mg once weekly[$]
Effect on weight (kg), placebo subtracted	-5.94 (95% CI -6.75 to –5.12) amongst those with first-episode psychosis at mean 24 weeks[74]. -3.27 kg (95% CI –4.49 to –2.06) amongst those with chronic psychosis[75].	-5.3 (95% CI -7.0 to –3.7) amongst those with schizophrenia spectrum disorder treated with olanzapine or clozapine at 16 weeks[49].	-12.44 (95% CI -13.37 to –11.51) at 68 weeks[77].
Significant effect(s) on other cardiometabolic parameters	-0.38 (95% CI 0.69 to –0.07) reduction in HbA1c measurement. -0.51 (95% CI –0.81 to –0.2) reduction in total cholesterol. 0.45 (95% CI 0.00 to 0.9) increase in HDL-C measurement. -0.28 (95% CI –0.45 to –0.11) reduction in triglycerides.	9.2% (95% CI 2.6 to 32.7%) reversal in prediabetic status. -0.2% (95% CI –0.3 to –0.1%) reduction in glycated haemoglobin. -19.3 mg/dl (95% CI –30.9 to –7.7) reduction in total cholesterol[49].	11.2 (95% CI 8.9 to 14.2) odds ratio of losing 5% or more of baseline body weight[77]. -9.42 cm (95% CI –10.30 to –8.53) reduction in waist circumference[77]. -5.10 mmHg (96% CI –6.34 to –3.87) reduction in blood pressure[77]
Monitoring	Baseline renal function (dose adjustment required eGFR < 45 ml/ min). Repeat eGFR + Vitamin B_{12} every 6-12 months.	Monitor for signs and symptoms congruent with gallbladder dysfunction or pancreatitis throughout treatment.	Monitor for signs and symptoms congruent with gallbladder dysfunction or pancreatitis throughout treatment.
Cost for 1 month supply of maintenance dose**	€3.27	€257.53	Awaiting official costing.

	Metformin[49,74,75]	Liraglutide[58,76]	Semaglutide[63,77]
Contraindications	History of metabolic acidosis. Severe renal failure (eGFR < 30 ml/min). Acute conditions with potential to alter renal function e.g., dehydration, severe infection. Hypoxic conditions (including heart failure, respiratory failure, recent myocardial infarction, shock). Hepatic insufficiency. Alcoholism.	Hypersensitivity to the active substance or excipients.	Hypersensitivity to the active substance or excipients.
Common side effects	Nausea, vomiting, abdominal pain, diarrhoea.	Nausea, constipation, diarrhoea, vomiting.	Nausea, constipation, diarrhoea, vomiting.
Rare side effects	Vitamin B_{12} deficiency, lactic acidosis.	Pancreatitis, cholelithiasis.	Pancreatitis, cholelithiasis.
Drug interactions	Verapamil, rifampicin, cimetidine, trimethoprim, crizotinib, olaparib, doluetgravir, ranolazine.	May affect absorption of medications due to slowing of gastric emptying. No formal recommendations for dose adjustment of concomitant medications. Monitor for lack of sustained therapeutic response of concomitant medications. Increased monitoring of International Normalised Ratio (INR) recommended amongst those on warfarin.	May affect absorption of medications due to slowing of gastric emptying. No formal recommendations for dose adjustment of concomitant medications. Monitor for lack of sustained therapeutic response of concomitant medications.
Deprescribing	Treatment should be discontinued after 24 weeks on the 1000 mg BD dose if patients have not lost at least 5% of their initial body weight, where weight loss is the intention. Continue treatment if prediabetic or improvement in other cardiometabolic parameters seen. Where prevention of future weight gain is the intended goal, treatment should continue as long as weight-inducing medication is prescribed.	Treatment should be discontinued after 12 weeks at maintenance dosing if patients have been unable to lose at least 5% of the body weight as measured at the start of therapy. Note liraglutide is also used in the general population to maintain weight loss induced by other methods e.g., diet and lifestyle interventions.	No deprescribing advice specified.

* Liraglutide 3 mg OD recommended by some sources for management of anti-psychotic-induced weight gain due to greater evidence of appetite suppression at higher doses in the general population.
**Cost in Ireland as of November 2021. This represents product cost. Cost to patient may be greater. Non-oral products will also be charged VAT at 23%. No GLP-1 RA is reimbursable under community drug schemes at the time of guideline writing.
$ At the time of CPG publication this dose is not available in Ireland.

BD: twice daily; BMI: Body Mass Index; CI: Confidence Interval; eGFR: estimated Glomerular Filtration Rate; OD: Once Daily; SMI: Serious Mental Illness.

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 randomised controlled trials comparing behavioural obesity therapy in combination with an additional psychological treatment, namely a behavioural intervention or cognitive behavioural therapy (CBT), resulted in comparable weight loss between groups and showed no advantage of combination treatment[78,79]. 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[78].

However, in Ireland, practice-based evidence indicates that introducing behavioural interventions prior to addressing underlying

issues could be counterproductive if the patient cannot engage in behavioural therapy while a range of psychological treatment modalities e.g., acceptance and commitment therapy (ACT)[80], are utilised to treat the underlying issue.

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[81,82]. 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[83]. 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[83]. CBT had a smaller effect than nutrition and/or exercise programmes. 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[84].

An additional meta-analysis focusing on pharmacological and behavioural interventions to improve cardiovascular risk factors in adults with severe mental illness analysed 10 studies using behavioural interventions, which included either lifestyle interventions or CBT[85]. 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[86]. 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[87]. 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, result 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 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[88]. Furthermore, practice-based evidence from the Irish context supports the argument for multi-modal interventions; however, for certain patient cohorts, such as patients with comorbid psychosis, negative symptoms of schizophrenia, for example, can limit efficacy of any such programmes[89].

In the Irish context, it is important to first outline the national Health Service Executive (HSE) care model. The HSE Model of Care for the Management of Overweight and Obesity[90] outlines the following levels of service provision in Ireland: level 0 refers to people living well with overweight and obesity, level 1 refers to people presenting at GPs and Primary Care Services; level 2 refers to Community Specialist Ambulatory Care; level 3 refers to Acute Specialist Ambulatory Care, i.e., Specialist Obesity Multidisciplinary Team (MDT); and level 4 refers to Specialist Hospital Care, i.e., bariatric surgery and inpatient care.

The commentary in this chapter draws from clinical practice at the publicly funded weight-management service for complicated obesity which is a level 3 and level 4 service. In this service, clinical practice indicates that for patients with obesity who have a comorbid mental health diagnosis (such as depression, anxiety, PTSD, BED or personality disorder), individualisation of treatment approach is key. Practice-based evidence indicates it is important to treat these comorbid diagnoses as these can be barriers to effective engagement in behavioural interventions. A range of therapeutic models including Compassion Focused Therapy (CFT) and Insight-Oriented Psychotherapy are currently offered to patients in level 3 services.

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 randomised controlled 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 analysed 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 were 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[20].

An issue with this research is that the studies predominantly included middle-aged females of white ethnicity, living with overweight or

obesity. Questions of generalisability beyond this population, and data on how long an individual might need to remain on treatment, remain unanswered.

In Ireland, no medication is licensed for binge eating disorder. However, preparations of lisdexamfetamine are licensed within other countries, including Canada and the US, for this indication. Use of similar products within Ireland is considered off-label. It should be noted that lisdexamfetamine is a central nervous system stimulant. Thus, efficacy and safety may not be generalisable to patients with a history of substance-use disorders, suicidal attempts, BPAD and psychosis, as these populations could be more susceptible to abuse or deterioration in their mental state. Use of lisdexamfetamine may be limited by its considerable patient cost. Regarding topiramate, its use is restricted in Ireland for females of childbearing potential. It is only available to this cohort in limited clinical circumstances, with concomitant prescription of highly effective contraception, due to risk of teratogenicity in offspring, exposed to topiramate in utero[91]. Due to licensing and risk considerations, prescription of topiramate and lisdexamfetamine should be restricted to specialists with experience in managing eating disorders.

Given the high prevalence of psychiatric disorders in patients with obesity[92] several studies have explored the impact of a bi-directional relationship of obesity and mental illness on the efficacy of behavioural interventions on 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 summarised 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[20]. Nonetheless, this review reported a significantly greater reduction in BMI with behavioural obesity therapy compared to therapist-led CBT, although this benefit was only found at end of treatment, and the difference in BMI disappeared at follow-up[20]. 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 number of sessions of behavioural therapy may also influence the effectiveness of therapy in reducing binge eating severity in obesity, with current evidence indicating that 16 to 24 sessions may be needed to adequately address binge eating[93].

However, in the Irish context, as mentioned above, individualisation of psychological therapy to a patient's presenting needs is key. When binge eating is a coping mechanism to manage other conditions (as determined by clinical assessment), such as depression, anxiety, PTSD, there are a variety of evidence-based therapies, such as eye movement desensitisation and reprocessing (EMDR) for PTSD, a first-choice treatment alternative to CBT[94], have been found to be equally effective[95].

Current level 3 and 4 practice involves clinical application of the Fairburn model[96] to stabilise eating pattern, followed by trauma-informed psychotherapy (e.g., EMDR, CFT, emotion-focused therapy, comprehensive resource model or insight-oriented psychotherapy, psychoanalytic approach, ACT) rather than 16 to 24 sessions of behaviour therapy[80].

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[97-99], such as food craving[100-102]. 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[100,103,104].

Although DSM-5 has not recognised 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[101], and researchers have cautioned equating obesity with food addiction[102]. 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[105].

A significant number of patients in level 3 and 4 report previous alcohol misuse or alcohol misuse following bariatric surgery and this "addiction transfer" also fits the addiction model[106]. However, food addiction is not currently assessed or used as a clinical construct in the Irish publicly funded level 3 and 4 services, and as mentioned above, warrants further research.

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[92,107]. For example, in Canada, according to the Ontario Bariatric Network registry, rates of a current psychiatric diagnosis were found to be 51%[108]. 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[109]. 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[92].

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%)[110]. Moreover, bariatric surgery can result in improvements in cognition, most commonly memory and attention/executive function[111]. Only post-surgery eating disorder symptoms have been associated with less weight loss after bariatric surgery in multiple studies[110,112].

Increases in suicide and self-harm have been noted post-bariatric surgery[113,114]. 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[115]. 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 1,000 patient-years), with intentional overdose being the most common method[113]. 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 and bariatric surgery[113]. 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[92].

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[116]. 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[117,118]. 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[119]. 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[120].

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[121,122]. 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[121,122]. Further research is needed to clearly elucidate rates and predictors of opioid use in bariatric surgery populations.

There is no Irish data on post-surgery rates of mental illness. Post-surgery alcohol-use disorder is noted as a significant problem clinically and appears to be associated with childhood trauma, current anxiety or mood disorder and/or a history of high alcohol intake (AUDIT = >8)[123], but no national data is available.

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[109]. 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[124]. Depressive symptoms after bariatric surgery have also been associated with reduced weight loss post-surgery. However, results from additional studies have shown conflicting results[125-127]. In addition, conflicting results suggest that pre-surgical complex psychiatric illness is not clearly associated with poor weight loss outcomes post-bariatric surgery[124,128]. 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[129]. 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[112]. Additional longitudinal studies are needed, but existing data suggests that bariatric surgery programmes should continue with ongoing monitoring of eating-related symptoms after surgery. In Ireland, there is currently no liaison psychiatry input to the MDTs in obesity services; however, addition of this specialist input is recommended.

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

It is recommended that mental health clinicians with experience and specialised knowledge undertake assessments, underpinned by the biopsychosocial model of care to identify psychosocial issues or mental health comorbidities before and after surgery that may impact a patient's treatment care plan and recovery pathway[21].

Moreover, ongoing monitoring of a patient's mental health is recommended given the influence of post-bariatric surgery psychopathology on health and psychiatric outcomes.

Recent guidelines recommend a comprehensive biopsychosocial mental health assessment is undertaken before bariatric surgery to identify risk factors and proactive identification of potential post-operative challenges that could be problematic post-surgery[21]. Along with completion of a comprehensive assessment, a number of tools, such as the Boston Interview for Gastric Bypass assessment[130] and the Toronto Bariatric Interprofessional Psychosocial Assessment Suitability Scale (BIPASS), can provide a standardised approach to pre-surgery assessment and can inform risk stratification pre-bariatric surgery[131].

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 biopsychosocial domains during the pre-bariatric surgery assessment[132]. 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[132]. 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[132]. 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[133]. 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[133,134]. 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[135]. A stepped care model[136] should be utilised, where patients presenting with more severe distress or psychiatric disorders have access to senior liaison psychiatry input as part of the MDT throughout their surgical intervention and recovery pathways.

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 2,146 patients in the LABS-2 study[137]. Bariatric surgery procedures, whether restrictive or malabsorptive, can have an impact on drug absorption, distribution metabolism or excretion[138].

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[139]. 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[140].

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[141].

In addition, mood stabilisers 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 sub-therapeutic levels have been described in the literature and, as a result, peri-operative bariatric surgery lithium protocols have been developed to improve clinician management of lithium[142].

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-energy intake in the peri-operative period[143]. Olanzapine and quetiapine are primarily absorbed from the stomach, and duodenum in the case of olanzapine. Patients established on these medications prior to surgery will be at increased risk of relapse post-surgery. Increased monitoring for loss of response and rapid development of withdrawal symptoms should be undertaken. Potential for increased risk of adverse effects and associated risk-reduction measures should also be considered; for example, malabsorptive states may increase risk of QTc prolongation associated with anti-psychotics. Clinicians should work collaboratively with patients' existing mental health providers to ensure that alternative anti-psychotic options, including alternative delivery formulations, have been explored when preparing for bariatric surgery and after surgery to optimise medication choice. Anti-psychotics associated with high risk of weight gain should be reviewed if already prescribed and avoided where possible in those with a history of bariatric surgery[144].

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[145]. 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 post-operative psychological interventions had a greater effect[146]. Moreover, a meta-analysis of five studies also showed greater weight loss post-bariatric surgery when surgery was combined with post-operative behavioural interventions[147]. Therefore, the optimal time to initiate adjunctive behavioural interventions may be after bariatric surgery, but before significant weight regain has occurred[148].

Specific psychological treatment modalities have been examined within bariatric surgery patient populations. These interventions include CBT (in-person or remotely delivered via telephone)[149,150], ACT[151], mindfulness-based therapies[152] 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.

Practice in Ireland's publicly funded level 4 services is that patients are invited to participate in psychologist-led group interventions or individual psychological support post-surgery, depending on patient choice and suitability. Travel can impact uptake and attrition to these groups, as distances to a treatment centre can be an issue in Ireland due to lack of regional services.

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

Regular post-operative follow-up for bariatric patients is important, to detect nutritional deficiencies and post-surgery eating difficulties, and to optimise outcomes[153,154]. Despite high rates of attrition from bariatric aftercare programmes, 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[155-157]. Research has highlighted that possible factor 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[153,156-159]. Specifically in the case of patients with pre-existing mental health difficulties, the likelihood of non-attendance with follow up care can be higher and there is a need to focus on this vulnerable group to ensure adequate MDT follow-up to optimise patient outcomes.

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 aftercare 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[160].

Additional studies are needed to further identify potential factors contributing to follow-up attrition. However, it may suggest that liaison between bariatric teams, primary care and mental health specialists in the post-operative period may help to ensure that appropriate follow-up care is delivered to this patient cohort. Further research is required to clarify.

Difficulties with adjustment to the post-bariatric surgery regimen have also been studied in the literature. Difficulties with dietary adherence has been associated with base- line depressive symptoms and the presence of binge eating disorder[161]. Moreover, higher attachment (relationship) anxiety and younger age (i.e., adolescents) has also been associated with poor adherence to post-operative vitamins[159,161]. Interventions to improve patient engagement and adherence to bariatric surgery follow-up recommendations have not been well studied. Interventions to optimise communication and collaborative engagement between specialities and primary care may help to address these issues.

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