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CHILD AND ADOLESCENT DISORDERS (T BENTON, SECTION EDITOR)

Obesity in Adolescents with Psychiatric Disorders

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Abstract

Purpose of Review This narrative review synthesized recent research related to obesity in adolescents with psychiatric disorders, with a focus on epidemiology, mechanisms, and weight management approaches. The paper reviews literature on depressive and anxiety disorders, bipolar disorder, and schizophrenia spectrum and other psychotic disorders.

Recent Findings Depression has a bidirectional relationship with obesity. Bipolar disorder and schizophrenia spectrum disorders, and their treatments, increase the risk of developing obesity. Mechanisms underlying this weight gain include lifestyle and environmental factors and psychiatric medications, though emerging evidence has also suggested the role of genetic and neuroendocrine processes. Evidence about the most effective treatments for obesity in adolescents with psychiatric disorders remains limited.

Summary Adolescents with psychiatric disorders are at high risk for obesity. Close monitoring for increases in weight and cardiometabolic risk factors with use of antipsychotic and mood-stabilizing medications is recommended. Clinical trials are needed that test the efficacy of weight management strategies for this population.

Keywords Adolescence · Obesity · Psychiatric disorders · Depression · Bipolar disorder · Schizophrenia

Introduction

Individuals with psychiatric disorders have a life expectancy 10 years less than the general population [1]. Approximately half of deaths can be attributed to natural causes [1], most notably cardiometabolic diseases [2, 3]. Obesity in adults is defined as a body mass index (BMI) $\geq$ 30 kg/m^2 (body weight in kg divided by height in meters squared) and is one of the strongest modifiable risk factors for cardiometabolic diseases [4]. The prevalence of obesity is nearly twice as high in adults with psychiatric disorders relative to those without a psychiatric disorder [5, 6].

Adolescence is a critical time associated with the development of obesity. The prevalence of adolescent obesity, defined as a BMI $\geq$ 95th percentile of the sex-specific BMI for age, is 20.5% in the USA [7]. Pediatric growth charts of BMI for age and gender are available through the Centers for Disease Control [8]. About 80% of adolescents with obesity will continue to have this condition as an adult [9]. Obesity during adolescence is associated with a number of short- and long-term illnesses including hypertension, type 2 diabetes, hyperlipidemia, obstructive sleep apnea, psychosocial distress, and future cardiovascular disease [10–14].

Adolescents with psychiatric disorders are a particularly vulnerable group at risk for developing obesity. In adolescents with psychiatric disorders, excess weight may add to disease burden, increase stigmatization, decrease self-esteem and social function, and reduce self-management behaviors such as adherence to medication regimens [15]. Understanding the epidemiology, mechanisms, and treatment of obesity among adolescents with psychiatric disorders is important to improve health outcomes in these patients.

This narrative review provides an overview of the relationship between obesity and psychiatric disorders in adolescence. The aims are to (1) examine the concurrent and longitudinal associations between adolescent obesity and psychiatric disorders, (2) describe potential mechanisms underlying the

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relationships between obesity and psychiatric disorders in adolescence, including the role of psychiatric medications, and (3) discuss management of obesity in adolescents with psychiatric disorders. The review focused on the most current literature from 2013 to 2018 and the most common psychiatric disorders that have been associated with adolescent obesity: depressive and anxiety disorders, schizophrenia spectrum and other psychotic disorders, and bipolar and related disorders.

Epidemiology and Course of Obesity and Psychiatric Disorders in Adolescence

Depressive and Anxiety Disorders In a community-based sample of youth from the Minnesota Twin Family Study ($N = 1512$), the prevalence of comorbid major depressive disorder and obesity for ages 11 to 24 years was 7.8% for males and 11.9% for females [16]. The relationship between depression and obesity is likely bidirectional. A meta-analysis of 18 observational studies showed that youth with obesity were 1.3 times more likely to have depression compared to those who are of normal weight [17••]. Compared to youth of normal weight, those with obesity had more severe depressive symptoms [17••]. The association between depression leading to obesity appears to be stronger than obesity leading to depression. A meta-analysis of 13 longitudinal studies found that relative to adolescents without depression, adolescents with depression had a 70% increased risk of being obese [18••]. Adolescents with obesity had a 40% increased risk of being depressed compared to those of normal weight. The relationship between depression and obesity was stronger among females than males [16]. Adolescents with obesity report 1.3 greater odds of suicidal ideation relative to adolescents with normal weight [19]. In the Nurses' Health Study II, compared to women with a BMI of 18.5 to 21.9 kg/m^2 at age 18, women with a body mass index $\geq$ 25 kg/m^2 at age 18 had a 2.3 greater risk of premature death by suicide [20].

Few studies have been conducted assessing the relationship between anxiety disorders and obesity among adolescents. In a multi-wave study of adolescents, cross-sectional analyses showed that the presence of an anxiety disorder was associated with a 46% increased odds of obesity [21]. However, in that study, anxiety disorder did not increase risk for obesity, and weight status did not increase risk of anxiety disorder after 1 year [21].

Schizophrenia Spectrum and Bipolar Disorders

Most studies in adolescents have shown that psychotropic-naïve adolescents in a first episode of psychosis (FEP) have a similar prevalence of obesity as those without psychosis. In a cross-sectional study, BMI z scores did not differ between antipsychotic-naïve youths, aged 12–17 years with FEP, and healthy controls (who were matched on sex, age, and parental education). The 18.6% of patients with FEP with obesity did not differ significantly from the 11.7% of controls [22]. In a multisite, prospective study of individuals ages 7 to 35 years in Spain, patients with a FEP had a similar BMI as healthy, age, gender, and parental socioeconomic status-matched controls [23•]. Both groups had a BMI of 23.5 kg/m^2 at baseline. In the control group, 6.6% met criteria for obesity compared to 8% in the FEP group. However, after 2 years, the FEP group showed significant increases in body weight and BMI. Compared to an average BMI of 23.7 kg/m^2 in the control group, in which 4.3% of participants met criteria for obesity, the BMI in the FEP group was 26.1 kg/m^2, with 20.4% meeting criteria for obesity. A total of 55.1% of the FEP patients gained > 7% of body weight during the 2 years of follow-up [23•]. Weight gain after 2 years did not differ among participants who were or were not treated with antipsychotics. However, 81.3% of participants who received antidepressant treatment had a weight gain > 7%, which was significantly more than the 54.7% of participants who were not treated with antidepressants.

Adults with bipolar disorder are over 60% more likely to have obesity than those without this disorder. There is also suggestion that obesity is correlated with increased bipolar disorder severity [24, 25]. Although limited, available findings demonstrate that this weight gain often begins in adolescence. Data from the National Comorbidity Survey-Adolescent Supplement showed no significant difference in the prevalence of obesity between adolescents (13–17 years) with bipolar disorder (17.1%) and those without a mood disorder (15.1%) [26•]. Though adolescents with and without bipolar disorder have a similar prevalence of obesity, excessive weight gain begins early and accrues over time. In a longitudinal cohort study of people with bipolar depression after their first episode of mania (14–35 years of age), patients with bipolar disorder had a higher trajectory of estimated BMI increase over 3 years of follow-up compared to healthy controls [27]. Obesity was significantly associated with illness severity including suicide attempt and self-injurious behavior [28].

Mechanisms

Lifestyle and Environmental Factors

Relative to adolescents without psychiatric disorders, those with psychiatric disorders tend to report unhealthier dietary

and physical activity behaviors. For example, adolescents with higher depressive symptoms report higher total energy intake [29] and higher intake of energy-dense and processed foods than those with lower depressive symptoms [30]. Females with high depressive symptoms are two times more likely than adolescents with no or low depressive symptoms to develop overeating and binge eating [31]. Compared to controls, adolescents with bipolar disorder report worse nutrition and eating habits [32]. Several studies have shown an association between depression and lower levels of physical activity [33] and higher sedentary behaviors [34]. Total screen time is related to higher depressive symptoms in adolescents with overweight and obesity [35]. Thus, adolescents with psychiatric disorders have more difficulty with unhealthy eating, physical activity, and screen time—all of which may lead to increases in obesity rates.

Stigma, Teasing, and Bullying Both obesity and psychiatric illness are independently associated with stigma, teasing, and bullying [36, 37]. Compared to their peers, adolescents with obesity report more internalized weight stigma, body dissatisfaction, and lower self-esteem, which may lead to or worsen psychological distress and depressive symptoms [36, 38]. Weight-related teasing and bullying are also associated with psychological symptoms and higher depressive symptoms [39, 40]. Stigma related to psychiatric disorders or obesity can contribute to suboptimal healthcare and less engagement with health behaviors [41, 42]. Adolescents with both obesity and a psychiatric illness may have additive risks, which may worsen both the mental illness and obesity.

Psychiatric Medications

Antipsychotic Drugs Antipsychotic drugs are commonly used to treat adolescents with major psychiatric disorders including bipolar and schizophrenia spectrum disorders. Psychiatric medications can cause weight gain [43]. In youth, most antipsychotics are associated with greater weight gain relative to placebo or to not taking antipsychotics (Table 1) [44••]. In particular, second-generation antipsychotics can cause significant and rapid weight gain. Compared to first-generation antipsychotics, second-generation antipsychotics result in a mean increase of 2.6 kg and in BMI of 1.6 kg/m^2 over 6–12 weeks [44••]. Antipsychotic-induced weight gain is associated with patients discontinuing their medications [45]. Earlier use of antipsychotics results in a longer lifetime exposure to their adverse effects. Relative to adults, youth seem to be at higher risk for antipsychotic-induced weight gain [46]. Rate of weight gain is highest in the first 3 to 6 months after beginning an antipsychotic (mean increase of 3.8–8 kg), and weight gain continues throughout the course of treatment, progressing to 12 kg over the first 2 years and 18 kg over 4 years [47].

Antipsychotic drugs have different weight gain propensities. In a meta-analysis of 22 studies that assessed the relative harm from olanzapine compared to placebo in youth, olanzapine resulted in a weight increase of 4.1 kg, compared with gains of 0.9 kg for aripiprazole, 1.3 kg for quetiapine, and 1.9 kg for risperidone. Most of the studies included were of short term (6–12 weeks) [48••]. Clozapine, which is often effective for treatment-resistant schizophrenia [45], also has an adverse weight gain potential [49, 50]. Ziprasidone appears to cause the least amount of weight gain [50, 51]. In a network meta-analysis of randomized studies in youth with schizophrenia, olanzapine, quetiapine, clozapine, paliperidone, risperidone, asenapine, and aripiprazole produced significantly more weight gain than placebo [52•]. Molindone and ziprasidone produced less weight gain. Molindone is a first-generation, typical antipsychotic medication, which may place patients at greater risk of developing tardive dyskinesia compared to the atypical antipsychotics and is, thus, prescribed less often [53]. Lurasidone, a relatively newer second-generation antipsychotic drug, produced the lowest weight gain [52•].

Antipsychotic-Induced Weight Gain and Therapeutic Benefit Evidence suggests a correlation between antipsychotic-induced weight gain and therapeutic benefit for psychiatric illness. Some studies of adults have demonstrated a relationship between improved therapeutic outcomes in adults with schizophrenia and antipsychotic-induced weight gain [54]. For example, the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study included 1493 adults with schizophrenia who were randomized to olanzapine, perphenazine, quetiapine, or risperidone for up to 18 months. Time to discontinuation of treatment was significantly longer among those in the olanzapine group relative to the quetiapine and risperidone groups, but olanzapine was associated with greater discontinuation for weight gain or metabolic effects [45]. In adults, studies have demonstrated a consistent association between antipsychotic-induced weight gain and clinical improvement with olanzapine and clozapine [43]. In adolescents (ages 13–17 years) with schizophrenia enrolled in a 6-week, double-blind placebo-controlled trial comparing olanzapine and placebo, weight gain was associated with greater reductions on the Brief Psychiatric Rating Scale for Children among olanzapine-treated subjects. However, olanzapine-related weight gain was not independently associated with symptomatic outcome when controlling for treatment duration [55]. Weight gain $\geq$ 7% was not significantly associated with response or remission. Among individuals ages 16–45 years with schizophrenia spectrum disorders who were in the first 5 years since psychosis onset, there was a significant worsening in the prevalence of obesity soon after the onset of psychotic symptoms [56]. Investigators have hypothesized that the neurotransmitters such as histamine H1 (H1), serotonin 2A/2C

Table 1 Select psychiatric medications and their effect on weight in adolescence

Medication	Medication type	Potential indication	Weight gain potential
Antipsychotics			
Asenapine	SGA	Bipolar disorder*	Low
Aripiprazole	SGA	Bipolar disorder*; schizophrenia*	Low
Chlorpromazine	FGA	Bipolar disorder; schizophrenia	Moderate
Clozapine	SGA	Schizophrenia	High
Haloperidol	FGA	Bipolar disorder; schizophrenia	Low
Iloperidone	SGA	Schizophrenia	Moderate
Loxapine	FGA	Bipolar disorder; schizophrenia	Low
Lurasidone	SGA	Bipolar disorder*; schizophrenia*	Low
Molindone	FGA	Schizophrenia	Low
Olanzapine	SGA	Schizophrenia*; bipolar disorder*; depression	High
Paliperidone	SGA	Schizophrenia*	Moderate
Perphanazine	FGA	Schizophrenia	Moderate
Quetiapine	SGA	Bipolar disorder*; schizophrenia*	Moderate
Risperidone	SGA	Bipolar disorder*; schizophrenia*	Moderate
Ziprasidone	SGA	Bipolar disorder; schizophrenia	Low
Mood stabilizers			
Carbamazepine	Anticonvulsant	Bipolar disorder; schizophrenia	Low
Lamotrigine	Anticonvulsant	Bipolar disorder	Low
Lithium		Bipolar disorder; adjunctive treatment for unipolar depression	Moderate
Valproic acid	Anticonvulsant	Bipolar disorder	Moderate
Antidepressants			
Amitriptyline	TCA	Depression*	High
Bupropion	Atypical	Depression	Low
Citalopram	SSRI	Depression	Low
Desvenlafaxine	SNRI	Depression	Moderate
Doxepine	TCA	Anxiety; depression	Moderate
Duloxetine	SNRI	Anxiety*; depression	Low
Escitalopram	SSRI	Depression*	Low
Fluoxetine	SSRI	Depression*	Low
Fluvoxamine	SSRI	Anxiety	Moderate
Imipramine	TCA	Depression	Moderate
Mirtazapine	Atypical	Depression	High
Nortriptyline	TCA	Depression	Moderate
Paroxetine	SSRI	Anxiety; depression	Moderate
Phenelzine	MAOI	Depression	High
Sertraline	SSRI	Anxiety; depression	Low
Venlafaxine	SNRI	Anxiety; depression	Low

Only indications marked with an asterisk have an FDA pediatric label for adolescents as of September 7, 2018 (https://www.accessdata.fda.gov/scripts/sda/sdNavigation.cfm?sd=labelingdatabase). Use in other conditions would be considered off-label. Potential indications listed are not exhaustive and only include bipolar disorder, depression, schizophrenia, and anxiety. The table does not include other uses for the medication. Weight gain propensities are from adolescent studies where possible but due to the limited literature may have been extrapolated from adult studies

FGA first-generation antipsychotic, *SGA* second-generation antipsychotic, *TCA* tricyclic antidepressant, *SSRI* selective serotonin reuptake inhibitor, *SNRI* serotonin and norepinephrine reuptake inhibitor, *MAOI* monoamine oxidase inhibitor

(5-HT2A/C), and dopamine D1/D2/D3 receptors, which are implicated in the therapeutic actions of antipsychotics, overlap with those of weight regulation [43]. Future studies are necessary to examine if antipsychotic-induced weight gain and therapeutic benefit operate independently and to examine potential mechanisms underlying this relationship.

There is large variability in the amount of weight gain with antipsychotics. Clinical and pharmacogenomic predictors of antipsychotic-induced weight gain have begun to be explored. A meta-analysis of 72 studies of single nucleotide polymorphisms (SNPs), with prospectively assessed antipsychotic-related weight or BMI changes, found that 13 SNPs from 9 genes were significantly associated with antipsychotic-related weight gain [57]. The pathophysiology and mechanisms for weight gain of these SNPs have yet to be described.

Mood Stabilizers Mood stabilizers are frequently used to treat bipolar disorder and schizoaffective disorder, and lithium is sometimes used to augment treatment in unipolar depression. Compared to youth who were not treated with mood stabilizers, treatment with lithium, carbamazepine, or valproic acid derivatives was associated with a 1.9 greater odds of incident obesity or excessive weight gain (Table 1) [58]. In short-term trials of $\leq$ 12 weeks, weight gain with combined mood stabilizers and antipsychotics was 5.5 kg, which was significantly more than the 1.2-kg gain among those treated with one mood stabilizer and the 2.1-kg gain among those treated with two mood stabilizers [59]. In an 8-week trial, youth with bipolar disorder who were randomly assigned to risperidone gained 3.3 kg (mean BMI increase of 1.4) which was significantly greater than the 1.4-kg gain of those assigned to lithium (mean BMI increase of 0.37) [60].

Antidepressants While findings from adult studies have suggested that selective serotonin reuptake inhibitors (SSRIs) are weight neutral and may have favorable effects on weight in the short term, evidence is more inconsistent among adolescents. SSRIs are generally the first-line medication for depression in adolescents. Some studies have demonstrated that in adolescents, SSRIs do not seem to cause weight gain [61–63]. However, a recent population-based study using electronic health record data from youth ages 8 to 18 years showed that depression diagnosis and antidepressant use (of any class) were independently associated with BMI trajectory [64]. Compared to youth who did not receive antidepressants, those who received 12 or more months of antidepressants had a modest gain of 2.1 kg at 18 years of age. SSRI use was significantly associated with weight gain. Those with a longer duration of diagnosis and treatment had greater weight gain. In a study that examined electronic health records of adolescents who were overweight, those who were prescribed SSRIs had significant increases in age- and sex-standardized BMI over time [65]. Prospective, randomized controlled trials are needed to fully assess these relationships. In adults, tricyclic antidepressants (TCAs) and some atypical antidepressants are associated with modest weight gain [66, 67]. Since atypical antidepressants and TCAs are used less frequently in adolescents, the relationship between these medications and weight gain in this population is not clear.

Biological

Several shared biological mechanisms link psychiatric disorders and obesity, though the majority of studies have been conducted using adult samples. Potential mechanisms include overlapping genetic susceptibility between obesity and mental disorders. About 12% of the genetic component of depression is shared with obesity [68]. Several genes have been identified that are shared between mental disorders and obesity including *FTO*, *POMC*, *ITIH4*, *TLR4*, *BDNF*, and *CREB1* [69]. Research is also examining the role of symptom profiles, given the heterogeneity of mental disorders such as depression. For example, data from the Psychiatric Genomics Consortium demonstrated that participants with major depressive disorder who reported increased appetite/weight during a depressive episode carried higher genetic risk for elevated BMI, C-reactive protein, and leptin, an endocrine biomarker commonly associated with obesity [70]. Other proposed biological mechanisms underlying mental disorders and obesity include altered circadian rhythms [71], dysregulated function of the hypothalamic-pituitary-adrenocortical axis, inflammatory processes, and imbalanced hormones [72] and neurotransmitters [73].

Management of Obesity in Adolescents with Psychiatric Disorders

Despite the importance of minimizing weight gain and managing obesity in adolescents with psychiatric disorders, few randomized controlled trials have assessed the efficacy of obesity prevention and intervention strategies in this population. Guidance on weight management in youth with psychiatric disorders has been published from Canada [74], the UK [75••, 76], the American Academy of Child and Adolescent Psychiatry [77], and the American Diabetes Association/American Psychiatric Association/American Association of Clinical Endocrinologists/and North American Association for the Study of Obesity [78].

Screening

Early recognition and intervention among adolescents who are overweight and those experiencing rapid weight gain are crucial to weight management (Fig. 1). Measurement of weight and height and calculation of age-for-sex BMI percentile is indicated for all youth with psychiatric disorders. Guidelines suggest that weight should be measured at baseline, monthly for the first 3 months, and then at least every 3 months [46]. Monitoring rate of weight change is especially important when initiating psychopharmacological treatments. The National Institute for Health and Care Excellence guidelines recommend that for youth starting antipsychotics, weight

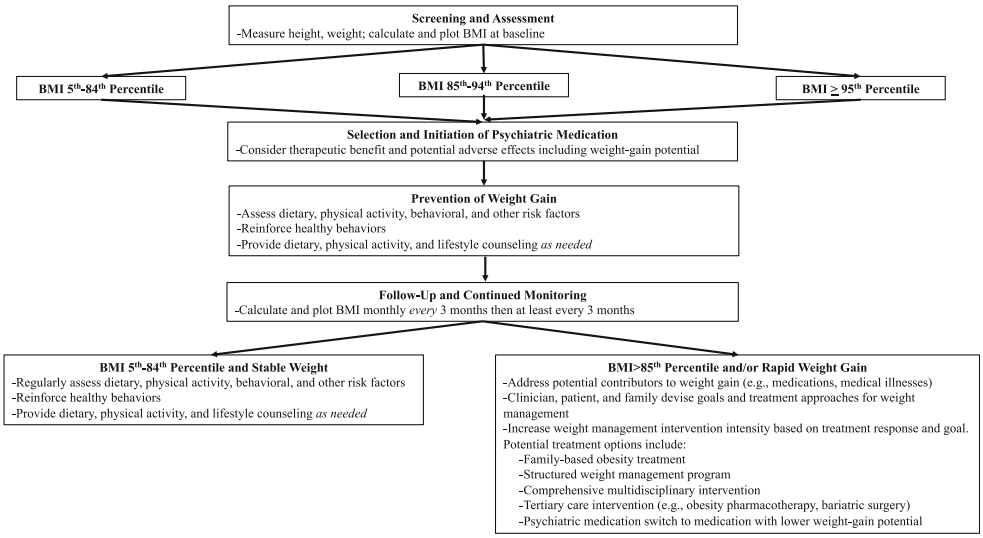

Fig. 1 Conceptual algorithm for weight management in adolescents beginning a psychiatric medication. Algorithm focuses on weight and does not include other cardiometabolic parameters that also should be monitored regularly. This is a conceptual algorithm and research is needed to assess the efficacy of these approaches

should be measured before initiation of the antipsychotic, weekly for the first 6 weeks, at 12 weeks, and then every 6 months thereafter and height before initiation of the antipsychotic and every 6 months [75••]. Weight should be plotted on a growth chart. In cases of rapid weight gain, potential contributors to weight change, such as other medications or new medical illnesses, also should be considered and addressed if needed [79]. In addition, other cardiovascular risk factors should be monitored at baseline and regularly thereafter (i.e., every 6 months) including blood pressure, lipids, and glucose [78]. This practice will alert the provider to possible development of hypertension, lipid disorders, and hyperglycemia. Consultation with primary care and specialty providers is recommended if these conditions develop.

Family-Based Behavioral Obesity Treatment

We recommend a proactive approach to encourage healthy behaviors and suggest giving age-appropriate lifestyle advice at diagnosis of a psychiatric disorder and at least annually thereafter. Patients who are started on second-generation antipsychotic medication should receive nutrition, exercise, and behavioral counseling at the initiation of therapy, regardless of baseline BMI [46]. Family-based obesity interventions are effective in adolescents without psychiatric disorders [80, 81] but have not been well tested in adolescents with psychiatric illness. Research is needed about how to best tailor obesity treatment programs for adolescents with psychiatric disorders. Nutritional and behavioral interventions significantly reduce weight, compared to control conditions, in adults with both new onset of a psychiatric diagnosis as well as among those with an established diagnosis [82, 83]. A small study of a 12-week dietician-delivered nutrition intervention for 15–25-year-olds with FEP, who were initiating antipsychotic medication, demonstrated that there were significant pre-to-post-treatment changes in daily energy intake, as well as increased vegetable intake and reduced sodium intake [84•]. The intervention group had a mean weight gain of 1.1 kg, which was significantly less than a 7.8-kg weight gain in the control group.

Psychiatric Medications

Initial selection of a psychiatric medication should balance the efficacy of the medication with the risks, including weight gain. Reviews have been conducted previously about the efficacy of pharmacological treatments for treatment of adolescents with depression [85], anxiety [86], schizophrenia [87], or bipolar disorder [88]. Some medications such as clozapine, risperidone, and olanzapine have demonstrated a dose-response relationship with greater weight gain; thus, it is important to consider if the lowest dose is being used [50, 89]. In patients with severe weight gain after the first 3 months of beginning medication, lifestyle intervention should be attempted. For those who are not successful, consideration should be given to the benefits and risks of discontinuing the medication and to reassessing the patient's need for another antipsychotic with a lower propensity for weight gain (such as ziprasidone or lurasidone if clinically appropriate). Discontinuation of a medication can result in weight improvement [90]; however, discontinuation must be balanced with the clinician's assessment of the patient's psychiatric status and need for continued medication treatment.

Medication switches should be considered as soon as a trajectory of rapid weight gain is detected (i.e., within a few weeks of initiating treatment). Medications may require a direct, complete switch in which a current medication is discontinued and a new one is initiated or may require a cross-taper in which a new medication is gradually titrated up as the current medication is gradually withdrawn to help reduce symptom exacerbation. The beneficial effects of switching to a second-generation antipsychotic with high-weight gain potential (e.g., olanzapine,

quetiapine) to one with a lower liability (e.g., ziprasidone, lurasidone) are effective in mitigating weight gain and promoting weight loss in adults [79]. The switch should be evidence-based to minimize potential relapse of patients' psychiatric illness and other potential complications such as withdrawal, drug-drug interactions, and adverse effects [79]. For example, for a patient with psychosis or bipolar disorder (or both) who has had more than one episode, most likely ongoing treatment with psychiatric medications will be needed. There are also patients who have gained weight after being treated with clozapine for treatment-resistant schizophrenia who are doing significantly better clinically, and discontinuation of this medication cannot be recommended; weight management for these patients can be clinically challenging and more research is needed to develop better weight loss interventions. Close monitoring of clinical status is needed when switching medications, as patients may need to be placed back on the medication initially used because of better therapeutic response to the psychiatric illness.

Weight Loss Medications

Five medications have been approved by the US Food and Drug Administration (FDA) for chronic weight management in adults: orlistat, liraglutide, lorcaserin, naltrexone-bupropion, and phentermine-topiramate. Orlistat is the only FDA-approved medication for obesity treatment in adolescents (without psychiatric illnesses) [91]. Orlistat is a gastric lipase inhibitor that reduces the amount of fat absorbed in the intestine. Studies assessing the efficacy of orlistat for weight management have not yet been conducted in youth with psychiatric disorders. In adolescents without psychiatric disorders, those who received orlistat, in combination with lifestyle modification, had a reduction in BMI of 0.6 kg/m^2, which was significantly greater than the 0.3-kg/m^2 BMI increase among placebo-treated individuals ($p = 0.001$). More adolescents taking orlistat attained a $\geq$ 5% decrease in BMI (26.5%) compared to the placebo group (15.7%; $p = 0.005$) [92]. The other weight loss medications have not yet been studied in randomized controlled trials, so the use of these weight medications cannot be recommended at this time. Any use in adolescents with psychiatric disorders would be considered off-label prescribing. We hope that such studies will be conducted in youth with obesity, including patients with psychiatric illness.

Metformin is FDA-approved for the treatment of type 2 diabetes in youth $\geq$ 12 years of age but is not approved for weight loss in either children or adults. Meta-analyses have shown that metformin, prescribed as 1000 to 2000 mg/day, facilitated the loss of 3.3 kg in adults who took antipsychotics [93]. Metformin has been tested in some small trials in youth taking antipsychotic medications and has demonstrated a modest benefit in stabilizing weight [94•]. There currently is an ongoing prospective, pragmatic, randomized trial of the use of metformin and lifestyle intervention versus lifestyle alone in youth with bipolar spectrum disorder treated with second-generation antipsychotics [95]. Results from this trial are not yet available as the study is ongoing.

Bariatric Surgery

Evidence is emerging about the benefits and risks of bariatric surgery among adolescents with severe obesity (BMI $\geq$ 35 kg/m^2 with serious comorbidities (e.g., type 2 diabetes, severe steatohepatitis, obstructive sleep apnea) or a BMI $\geq$ 40 kg/m^2 with minor comorbidities (e.g., hypertension, dyslipidemia) [96]. Recommendations suggest that significant psychiatric disorders including severe or unstable psychosis and major depressive disorder should be contraindications to bariatric surgery, though few studies have assessed the influence of psychiatric disorders on outcomes after bariatric surgery among adolescents [97, 98]. A recent study found that 71% of adolescents who completed a presurgical psychological evaluation for laparoscopic sleeve gastrectomy qualified for a psychiatric disorder with the most common diagnoses being depression (42%) and anxiety (26%) [99]. None of the psychiatric diagnoses predicted percent excess weight loss at 12 months post-surgery. Future studies are needed to investigate bariatric surgery in adolescents with psychiatric disorders.

Potential Obesity Treatment Care Models

Little is known about care models that may be effective for obesity treatment in adolescents with mental disorders, and there is a clear need for research that addresses this topic. Approaches that have been proposed and tested for the general integration of pediatric physical and mental health may be effective. Collaborative care for weight management could be delivered in the primary medical home or mental health practice, and the extent of integration could be on a continuum from consultative, coordinated, colocated, or fully integrated [100, 101]. Future work is needed to examine the feasibility and effectiveness of these care models are needed. Both mental health and pediatric healthcare providers may have had limited training in providing weight management, thus training may be necessary.

Conclusions

Adolescents with psychiatric disorders continue to be vulnerable to excess weight gain and obesity, as well as worsening of cardiometabolic risk factors. Weight management in adolescents with psychiatric disorders is complex and research is urgently needed about the best way to prevent and treat obesity among this population. While our knowledge regarding the epidemiology, mechanisms, and treatment strategies pertaining to obesity in adolescents with psychiatric disorders is increasing, much work is needed to improve the care of these individuals. Treatment with antipsychotic and mood-stabilizing medications

may be associated with significant increases in weight and BMI, as well as cardiometabolic risks. Close monitoring of BMI changes and associated risk factors is recommended when these medications are used and switching to an alternative medication when possible is recommended when excessive weight gain becomes problematic. A healthy lifestyle including a balanced nutritional intake, physical activity, and reduced screen time is also recommended.

Studies are needed to further examine longitudinal trends and mechanisms underlying the relationship between psychiatric disorders and obesity, which can help to better tailor treatment. Few studies have examined weight change using sex- and age-adjusted BMI *z* scores or percentiles and most studies are of short duration. Lastly, studies on different treatment approaches and strategies are urgently needed for adolescents with psychiatric disorders and obesity. Use of integrated care models that help coordinate mental health and primary care may be a promising approach.

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Compliance with Ethical Standards

Conflict of Interest Ariana M. Chao reports grants and personal fees from Shire Pharmaceuticals, outside the submitted work.

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- • Of importance
- •• Of major importance

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