

Medical Management of Obesity Associated With Mental Disorders

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Obesity and mental disorders are major public health problems that co-occur to a significant degree. They also significantly overlap in phenomenology and response to medications. However, many psychotropic agents have adverse effects on appetite, binge eating, and weight. In this review, we aim to improve understanding of the relationship between obesity and mental illness and provide practical clinical guidelines for the management of obesity associated with mental disorders.

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Obesity is common among patients with certain mental disorders,^{1–16} particularly schizophrenia,^{1–7} bipolar disorder,^{8–10} and binge-eating disorder,^{11–16} and weight gain is a common side effect of many frequently used psychotropics.^{2–4,6–10,17–31} However, little is known about the medical management of obesity in patients with mental disorders.^{31–33} Antiobesity agents as a class have rarely been studied in obese mentally ill patients, as have those psychotropics associated with therapeutic changes in appetite, eating behavior, or weight. In this article, we briefly review the relationship between obesity and some mental disorders; the effects of commonly used psychotropics on appetite, weight, binge eating, and primary obesity; and the effects of anti-obesity agents on binge eating and mood disorder. We conclude by presenting preliminary guidelines for the medical management of obesity associated with psychotic, mood, and binge-eating disorders.

BRIEF OVERVIEW OF OBESITY

Obesity is the condition of having an abnormally high proportion of body fat. It is most commonly operationally defined as a body mass index (BMI) (weight in kilograms divided by height in meters squared) of 30 or greater.^{31–34} Abdominal obesity reflects fat that is centrally distributed between the thorax and pelvis as opposed to lower body obesity, which reflects fat that is distributed around the hips, thighs, and buttocks. Abdominal obesity is often operationally defined by the waist circumference or the waist-to-hip ratio. In contrast to lower body obesity, abdominal obesity is particularly associated with

type 2 diabetes mellitus, dyslipidemia, hypertension, coronary heart disease, stroke, and early mortality.^{33,35}

Although the pathogenesis of obesity is unknown, it is often viewed as a polygenic, heterogeneous metabolic disorder due to consuming more calories than are expended as energy.^{31–34} Factors etiologically associated with obesity are family history of obesity, overeating, and physical inactivity. Low resting metabolic rate is not thought to play a major role in causing or maintaining most obesity.³¹ Of theoretical note, dysfunction in neurotransmitter and neuropeptide systems hypothesized to underlie various mental disorders³⁶ has also been hypothesized to be involved in obesity.^{35,37} Implicated shared neurotransmitter systems have included serotonin, dopamine, and norepinephrine; implicated neuropeptides have included corticotropin-releasing factor and neuropeptide Y.^{35–37}

BRIEF OVERVIEW OF PSYCHOPATHOLOGY IN OBESITY

Numerous studies of psychopathology in persons with obesity have been conducted over the past 50 years.^{33,34,38–50} The results of these studies have been inconsistent, with some concluding that obesity and psychopathology are not related,³⁴ some concluding that obesity and psychopathology are inversely related,^{34,41,50} and others concluding that obesity may be related to mood, eating, or other disorders.^{34,45} Many of these studies, however, have significant methodological limitations.³⁹ Few studies assessed the presence of psychiatric symptoms or disorders using standardized rating instruments, operationalized diagnostic criteria, or structured clinical interviews; some studies examined weight gain or overweight rather than obesity; and many studies that used clinical samples did not have control groups.³⁹

Modern studies addressing the above methodological limitations have included community studies using standardized definitions of obesity and structured instruments to assess psychopathology^{40,41,47–50} and clinical studies of obese patients using control groups.^{42–45,46} In general, these studies have suggested that there may be an association between obesity and both mood and binge-eating symptomatology and disorders in both clinical and community populations, although the relationship is clearly

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stronger in clinical populations. These studies further suggest that the relationship between obesity and mood symptomatology may be stronger for females than males for total body obesity (as measured by BMI),⁵⁰ but similar for females and males for abdominal obesity (as measured by waist-to-hip ratio).^{40,41,47,49} The relationship between obesity and binge-eating symptomatology appears similar for males and females.^{16,44} Moreover, among obese persons seeking treatment, numerous studies suggest a relationship between binge eating and depressive symptoms, as well as degree of binge eating and severity of obesity.^{13,45}

STUDIES OF OBESITY IN PSYCHOTIC DISORDERS

There are no community studies of obesity in persons with psychotic disorders. Uncontrolled studies^{1-5,7} of obesity in patients with schizophrenia and other chronic mental disorders who are receiving treatment with antipsychotic (and often other psychotropic) medications have reported prevalence rates ranging from 26%⁵ to 62%.³ In the only controlled study, Allison et al.⁶ compared data from 80,130 nonschizophrenic and 150 self-reported schizophrenic individuals from the mental health supplement of the 1989 National Health Interview Study (NHIS), 420 noninstitutionalized individuals with DSM-IV-defined psychotic disorders (schizophrenia or schizoaffective disorder) from a Pfizer Inc-supported ziprasidone trial, and 17,689 nonschizophrenic individuals from the National Health and Nutrition Examination Survey III (NHANES III). In the NHIS data set, men with schizophrenia had a mean BMI similar to that of men without schizophrenia (26.1 vs. 25.6, respectively), whereas women with schizophrenia had a significantly higher mean BMI than did women without schizophrenia (27.4 vs. 24.5, respectively; $p < .001$). In the ziprasidone and NHANES III data sets, men and women with schizophrenia each had mean BMIs similar to those of men and women without schizophrenia (26.8 vs. 26.5 for men and 27.3 and 27.4 for women, respectively). The authors concluded that individuals with schizophrenia were, on the whole, as obese or more obese than individuals without schizophrenia.

STUDIES OF OBESITY IN MOOD DISORDERS

Although numerous clinical and community studies have shown that a subset of persons with depression report hyperphagia, weight gain, and reduced activity,^{51,52} there have been no community studies of obesity in persons with mood disorders. Nonetheless, certain subtypes of depression have been delineated because of their association with features that have also been associated with obesity. These include atypical depression (characterized by hyperphagia, hypersomnia, leaden paralysis, mood reactivity, and rejection sensitivity)⁵³ and somatic depression (characterized by fatigue, appetite disturbance, and sleep disturbance).⁵⁴ Moreover, in a recent prospective study of body weight in mood disorder, childhood depression was associated with overweight in adulthood. Pine et al.⁵⁵ followed 2 groups of children 6 to 17 years old with major depression ($N = 90$) or no

psychiatric disorder ($N = 87$) for 10 to 15 years with standardized psychiatric interviews. The authors found that childhood depression was positively associated with BMI during adulthood: subjects with childhood depression were, on average, 1.9 ± 4.7 larger in BMI than were subjects who had been healthy in childhood ($p < .01$). This association was not explained by age, gender, cigarette or alcohol use, or medication history. However, duration of depression between childhood and adulthood predicted adult BMI.

Although there were no associations or interactions with gender in Pine and colleagues' findings,⁵⁵ many studies comparing depressive symptoms in females and males have found that females with depression are more likely than their male counterparts to report hyperphagia and weight gain.⁵⁶⁻⁵⁸ In addition, atypical and somatic depression are more common in females than males.^{53,54}

The prevalence of obesity has been examined to a limited degree in patients treated for mood disorders. In 1 uncontrolled study of tricyclic-associated weight gain in patients with depressive disorders, the rate of obesity was 25%.¹⁹ In uncontrolled studies of lithium-associated weight gain in patients with bipolar disorder, rates of obesity have been reported to be 12% to 19%.⁸ In the only controlled study of obesity in bipolar disorder, Elmslie et al.^{9,10} found that both total-body obesity (measured by BMI) and abdominal obesity (measured by waist-to-hip ratio) were significantly more prevalent in 89 euthymic patients with DSM-IV bipolar disorder compared with matched reference subjects from a general population sample. Female patients were more often overweight and obese than female reference subjects, whereas male patients were similarly overweight but more often obese than male reference subjects. Hypothyroidism was significantly more common in men, but not women, who were overweight or obese. Moreover, obesity was significantly associated with treatment with antipsychotic drugs, but not with lithium treatment.

STUDIES OF OBESITY IN EATING DISORDERS

There have been relatively few studies of obesity in persons with eating disorders. The few community studies that have been done have found associations with obesity for both bulimia nervosa and binge-eating disorder.^{11,12,14,16,59} A growing number of clinical studies have found that patients with binge-eating disorder presenting for psychological or psychopharmacologic treatment are often overweight or obese.^{13,15,60,61}

EFFECTS OF PSYCHOTROPICS ON APPETITE AND WEIGHT

Psychotropics have varied effects on appetite and weight. It is well known that certain psychotropics may increase appetite and/or induce weight gain,^{2-4,6-10,17-31} whereas some have little or no effect on appetite and weight, and others may decrease appetite and/or induce weight loss (Table 1).⁶²⁻⁷⁸ The mechanism(s) by which psychotropic drugs exert these effects are not well

understood, but are presumed to involve increased energy intake (e.g., overeating), decreased energy expenditure (e.g., reduced resting metabolic rate, reduced physical activity, or reduced diet-induced thermogenesis), or a combination of the two.^{31,79–82}

Psychotropics that stimulate appetite or cause weight gain include tricyclic antidepressants (tertiary amines more so than secondary amines); the novel antidepressant mirtazapine; the mood stabilizers lithium, valproate, and to a lesser extent carbamazepine; both typical and atypical antipsychotics; and the anxiolytic gabapentin (see Table 1).^{2–4,6–10,17–31} The appetite-stimulating/weight-gaining effects of tricyclics, mirtazapine, and antipsychotics have been attributed in part to their antagonism of histamine, serotonin, and (for antipsychotics) dopamine receptors (especially histamine-1, serotonin-2C, and dopamine-2 receptors).^{79–82} The mechanism(s) of weight gain from valproate, carbamazepine, and gabapentin are unknown.

Pharmacologic manipulation of receptor systems affected by medications that cause weight gain may offer therapeutic approaches to managing psychotropic-induced appetite stimulation and/or weight gain. For example, the histamine-2 antagonist cimetidine has been shown to be superior to placebo in reducing weight in patients with primary obesity in 1 of 2 controlled trials.^{83–85} More recently, cotreatment with the histamine-2 antagonist nizatidine (at 300 mg/day but not 150 mg/day) was shown to be superior to placebo in reducing weight gain in a study of patients with schizophrenia and related disorders who were receiving olanzapine.⁸⁶ Similarly, the dopamine agonist amantadine has been reported in 2 open trials to be useful in inducing weight loss in antipsychotic-treated patients with schizophrenia without worsening of psychiatric symptoms.^{87,88}

Psychotropics associated with reduced appetite or weight loss include most psychostimulants, some antidepressants, 2 novel antiepileptics (topiramate, zonisamide) with putative thymoleptic properties, and opiate antagonists.^{62–78} Virtually all psychostimulants (including those indicated for narcolepsy and attention-deficit/hyperactivity disorder, with the possible exception of the novel antinarcolepsy agent modafinil) are associated with appetite suppression and weight loss.⁶² Indeed, some of these agents (phentermine, diethylpropion, mazindol, and phenylpropranolamine) have U.S. Food and Drug Administration (FDA) approval for the short-term treatment of obesity.^{32,89,90} The appetite suppressant and weight loss effects of these drugs have been attributed to their enhancement of brain catecholamine function, which includes promotion of dopamine and norepinephrine release and blockade of dopamine and norepinephrine reuptake.^{89,90}

Antidepressants associated with appetite suppression or weight loss, at least over the short term, include serotonin selective reuptake inhibitors (SSRIs), the norepinephrine selective reuptake inhibitor bupropion, and the serotonin-norepinephrine selective reuptake inhibitor venlafaxine.^{63–69} Over the long term, controlled data indicate that this weight loss may not be sustained (at least for SSRIs), but there is no weight gain above baseline weight.⁶⁶ The precise mechanism(s) of appetite suppression and weight loss of these agents are unknown, but they enhance sero-

Table 1. Estimated Relative Risk of Weight Change, Effectiveness in Binge Eating, and Effectiveness in Obesity of Various Psychotropic Drugs^a

Drug	Estimated Risk of Weight Change ^b	Effectiveness in Binge Eating ^c	Effectiveness in Obesity ^d
Antidepressants			
Tertiary amine TCAs	3	+++	NA
Secondary amine TCAs	2	+++	NA
SSRIs	-1 to 0	+++	+++
Nonselective MAOIs	2 to 3	+++	NA
Bupropion	-1 to 0	++	++
Venlafaxine	-1 to 0	NA	NA
Mirtazapine	3	NA	NA
Mood stabilizers			
Lithium	2 to 3	+/-	NA
Valproate	3	+/- ^e , ↑	NA
Carbamazepine	0 to 1	- ^e	NA
Topiramate	-2 to 1	+	+
Lamotrigine	0	NA	NA
Zonisamide	-1 to 0	NA	NA
Anxiolytics			
Benzodiazepines	0 to 1	NA	NA
Gabapentin	1 to 2	NA	NA
Antipsychotics			
Haloperidol	1	NA	NA
Phenothiazines	2 to 4	NA	NA
Clozapine	4	NA	NA
Olanzapine	3 to 4	NA	NA
Risperidone	2 to 3	NA	NA
Quetiapine	2 to 3	NA	NA
Ziprasidone	0	NA	NA
Molindone	-1 to 0	NA	NA
Pimozide	0	NA	NA
Opiate antagonist			
Naltrexone	-1 to 0	+/-	-
Psychostimulants			
	-2 to 1	+	+++

^aTable shows summarized findings based on the authors' review of literature references 2–4, 6–10, 17–31, and 62–78). Abbreviations:

MAOI = monoamine oxidase inhibitor, NA = not assessed, SSRI = selective serotonin reuptake inhibitor, TCA = tricyclic antidepressant. Symbols:

+ = significant effectiveness suggested by open-label studies and/or case reports, ++ = superior to placebo in at least 1 controlled study, +++ = superior to placebo in at least 2 controlled studies, +/- = inconsistent data, - = negative placebo-controlled data, ↑ = reports of agent increasing binge eating.

^bAuthors' judgment, based on literature reviewed, of relative risk of weight change on a scale from -2 to 4, where -2 = highest risk of weight loss, 0 = no effect on weight, and 4 = highest risk of weight gain.

^cAuthors' judgment of effectiveness in binge eating (in bulimia nervosa or binge-eating disorder) based on literature reviewed.

^dAuthors' judgment of effectiveness in obesity (not due to psychotropic medication or binge eating) based on literature reviewed.

^ePatients with binge eating and comorbid bipolar disorder or mood instability who responded to treatment have been reported.

tonergic or noradrenergic function without antagonizing serotonin, histamine, and/or dopamine receptors. (Of note, the anti-obesity agent sibutramine is also a serotonin-norepinephrine selective reuptake inhibitor.)

Topiramate and zonisamide are novel antiepileptics reported clinically to have antimanic and, for topiramate, mood-stabilizing properties in bipolar disorder.^{70–76} Each drug has been associated with anorexia and weight loss in controlled studies in patients with epilepsy.^{70,71} For topiramate, the weight loss was more common in heavier subjects, was dose related, and peaked after 12 to 18 months of treatment.^{70,71} Less has been reported about the weight loss associated with zonisamide. Topiramate has been used

successfully to treat weight gain in patients with treatment-resistant bipolar disorder receiving mood stabilizers and antipsychotics,⁷²⁻⁷⁴ in patients with treatment-resistant major depression who are receiving antidepressants,^{91,92} and in patients with schizophrenia who are receiving antipsychotics.⁹³ The mechanism(s) of the anorectic and weight loss effects of topiramate and zonisamide are unknown, but the mechanism of topiramate may be related to its antiglutamatergic action.^{92,94}

Naloxone and naltrexone are opiate antagonists used in alcohol and opioid use disorders that have been reported to have anorectic and weight loss properties in healthy controls and with substance use disorder patients.^{77,78} The anorectic and weight loss properties of these drugs have been hypothesized to be due to their effects on the endogenous opioid system.

EFFECTS OF PSYCHOTROPICS ON BINGE EATING

An increasing number of psychotropics have been reported effective in the treatment of binge eating (see Table 1). These include antidepressants, mood stabilizers, antiepileptics, psychostimulants, and opiate antagonists.⁹⁴⁻¹⁰⁴ Agents that have been found superior to placebo in treating binge eating associated with bulimia nervosa, binge-eating disorder, or both in controlled trials include the antidepressants fluoxetine, fluvoxamine, imipramine, desipramine, bupropion, phenelzine, and nomifensine.^{95,96} Of note, fluoxetine is approved by the FDA for the treatment of bulimia nervosa; in the pivotal clinical trials, 60 mg/day, but not 20 mg/day, was superior to placebo in reducing binge-eating and vomiting episodes. Other drugs reported effective in reducing binge eating in open trials and/or case reports of bulimia nervosa or binge-eating disorder include carbamazepine, lithium, phenytoin, valproate, naltrexone, methylphenidate, and most recently, topiramate.^{94,95,97-104} Controlled studies of lithium⁹⁹ and carbamazepine⁹⁸ in bulimia nervosa were negative but had methodological limitations. Our group has been particularly impressed with the apparent effectiveness of topiramate in the binge-eating symptoms of binge-eating disorder and bulimia nervosa, both as monotherapy and adjunctively with antidepressants.^{94,100} Medications reported to be effective in reducing weight in patients with binge eating and obesity have included SSRIs and topiramate.

EFFECTS OF PSYCHOTROPICS ON PRIMARY OBESITY

Psychotropic agents (besides psychostimulants) that have been studied in the treatment of primary obesity include SSRIs, bupropion, and the opiate antagonist naltrexone.¹⁰⁵⁻¹¹² Fluvoxamine, fluoxetine, and sertraline have been shown in placebo-controlled trials¹⁰⁵⁻¹⁰⁸ to have modest short-term (e.g., 6- to 28-week) weight-loss effects in obese patients in doses effective in bulimia nervosa (e.g., 60 mg/day for fluoxetine). However, significant regain of weight occurred after the first 6 months of treatment despite continued drug therapy. Of note, in all treatment studies of antiobesity agents that were 1 year in duration (which involved dexfenfluramine, sibutramine, and orlistat), the

majority of the weight loss occurred in the first 6 months of treatment with a plateau or actual increase in weight in the following 6 months.³²

Regarding other nonstimulant psychotropics studied in primary obesity, bupropion has been shown superior to placebo in an 8-week controlled study¹⁰⁹ in inducing weight loss and reducing minor depressive symptoms in obese women without major depression or bulimia nervosa. By contrast, several placebo-controlled studies of naltrexone in primary obesity have been negative.¹¹⁰⁻¹¹²

EFFECTS OF ANTI-OBESITY DRUGS ON EATING AND MOOD DISORDERS

Centrally active antiobesity drugs (psychostimulants, the serotonin-releasing agents fenfluramine and dexfenfluramine, and the serotonin-norepinephrine reuptake inhibitor sibutramine) have received relatively little systematic study in the treatment of eating or mood disorders. Nonetheless, the psychostimulant methylphenidate has been reported to reduce binge eating in patients with bulimia nervosa, including patients resistant to antidepressants.^{101,102} Also, numerous clinical studies support the use of various psychostimulants as sole agents in depression associated with medical illness and as augmenting agents of standard antidepressants in treatment-resistant depression.⁶² Fenfluramine has been shown to be superior to placebo in treating binge eating associated with binge-eating disorder.¹¹³ It has also been reported to improve mood in premenstrual¹¹⁴ and bipolar¹¹⁵ depression. Moreover, the presumed mechanism of action (norepinephrine and serotonin reuptake inhibition)^{89,90} and preclinical profile¹¹⁶ of sibutramine suggest that it may have antidepressant properties.

Of note, to our knowledge, there has been no study of the effects of peripherally acting antiobesity agents (e.g., lipase inhibitors) on appetite, eating behavior, mood, or other psychological parameters in subjects with eating or mood disorders. However, we have observed obese patients with binge-eating disorder misuse orlistat to compensate for their binge-eating behavior.¹¹⁷

ANTI-OBESITY DRUGS IN OBESE MENTALLY ILL PATIENTS

There are surprisingly few studies of antiobesity drugs in mentally ill patients with obesity. However, mental disorder is usually an exclusion criterion for treatment with antiobesity drugs,³² and there have in fact been a number of reports of patients developing psychoses with manic and/or schizophrenic features while taking psychostimulants, fenfluramine, or sibutramine.¹¹⁸⁻¹²³ Nonetheless, we located 3 studies¹²⁴⁻¹²⁶ of antiobesity agents in obese mentally ill patients. In the first study¹²⁴ (the only study of a psychostimulant in obese mentally ill patients we were able to find), 30 chronically mentally ill, chlorpromazine-treated female patients received chlorphentermine or phenmetrazine for 6 weeks, followed by the other drug for another 6

weeks after a 1-week washout under double-blind conditions. Patients showed no changes in weight with either medication. In the second study,¹²⁵ 4 obese patients receiving X for X were treated with fenfluramine; 2 lost weight. In the third study,¹²⁶ fenfluramine was found to be superior to placebo in reducing weight in 16 obese patients with schizophrenia who were stable on treatment with antipsychotic medication. In all 3 studies, patients receiving active medication showed no worsening of their psychiatric symptoms. The latter observation suggests that patients with psychotic disorders may be given centrally active antiobesity agents without adverse sequelae as long as their disorders are properly treated.

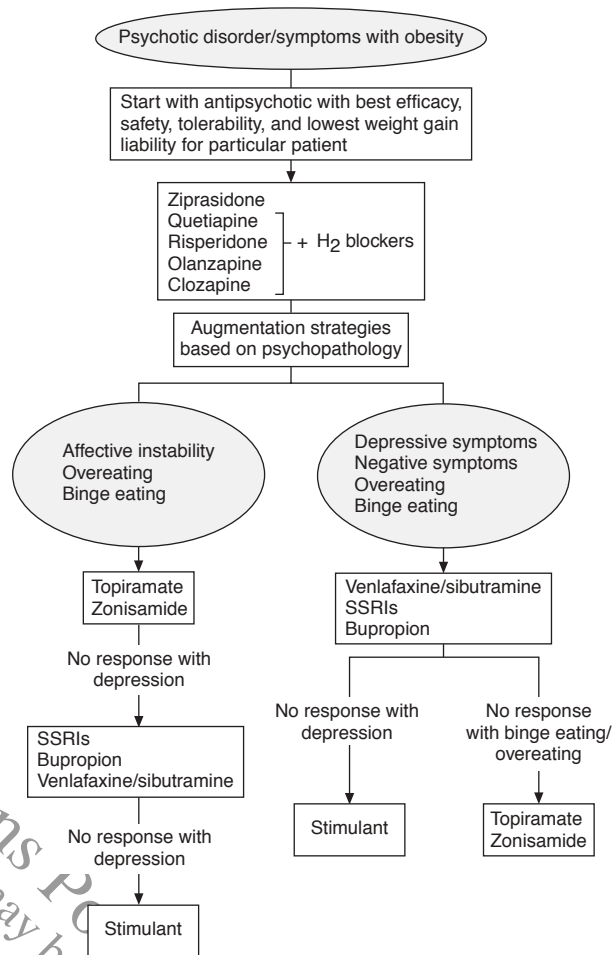
CONCLUSION

Obesity and mental disorders are both serious public health problems that may overlap to a clinically significant degree. Many psychotropic medications have adverse as well as therapeutic effects on appetite, weight, binge eating, and even primary obesity. Conversely, some antiobesity agents may have effects on binge eating and mood.

A thorough understanding of the relationship among obesity, psychopathology, and the effects of psychotropic and antiobesity agents on appetite, eating behavior, weight, mood, and psychopathology should enable optimal treatment of obese mentally ill patients' psychopathology while maximizing weight loss (or minimizing weight gain). Thus, for mentally ill patients with obesity, optimal first-line treatments would include psychotropics with maximal efficacy for their primary mental disorder that also possess appetite suppressant, weight loss, or anti-binge-eating properties as well as optimal tolerability and safety. If such a drug is not available for a patient's particular psychopathology, drugs that are weight neutral followed by drugs that have lower weight gain liabilities could be chosen, provided that the drugs have comparable efficacy, tolerability, and safety.

When treating psychotic disorders associated with obesity, ziprasidone might be chosen before risperidone or quetiapine, which might be chosen before olanzapine or clozapine (Figure 1). Alternatively, olanzapine could be started with a histamine-2 antagonist. For treating depressive disorders associated with obesity, venlafaxine, bupropion, and SSRIs (alone and in combination) might be used before agents that cause weight gain such as tricyclics, monoamine oxidase inhibitors, or mirtazapine (Figure 2). For treating bipolar disorders associated with obesity, topiramate or zonisamide might be used adjunctively with standard mood stabilizers (lithium, valproate, olanzapine) for patients with more severe forms (bipolar I disorder; schizoaffective disorder, bipolar type) and as monotherapy or in combination for patients with mild forms (e.g., bipolar II disorder, cyclothymia) (Figure 3). For binge-eating disorder, venlafaxine, an SSRI, or bupropion (as long as there is no associated purging) might be considered, particularly if the patient has associated depressive symptoms or a comorbid depressive disorder. Topiramate might be considered if the patient has a comorbid bipolar

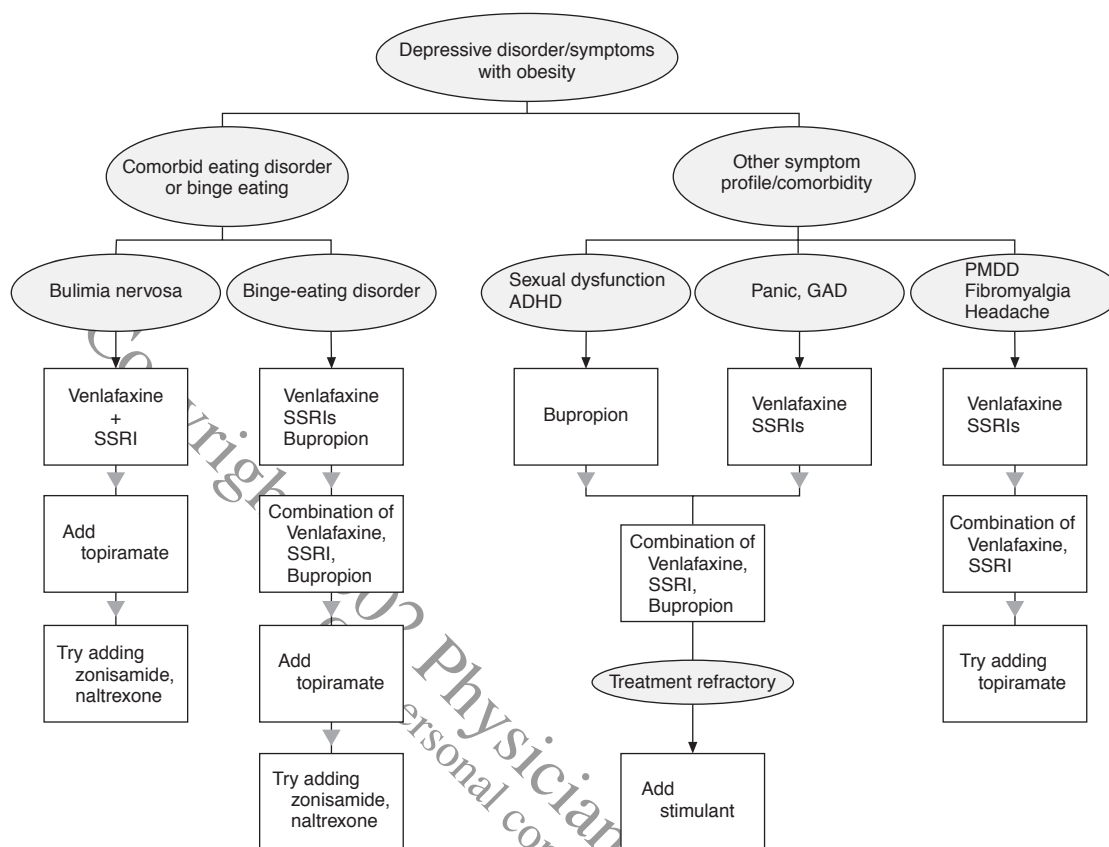
Figure 1. Treatment Algorithm for Psychotic Disorder With Obesity^a



^aAbbreviations: H₂ = histamine-2, SSRI = selective serotonin reuptake inhibitor.

disorder, associated affective instability or hypomanic symptoms, or is inadequately responsive to antidepressant treatment. Zonisamide might be considered as an alternative or adjunct for patients who are inadequately responsive or are unable to tolerate topiramate.

However, sometimes a drug with weight-gaining liability must be used because it is the most efficacious, the best tolerated, or the safest. In such cases, psychotropic-associated weight gain can be managed using adjunctive treatment with psychotropics with appetite suppressant, weight loss, or anti-bingeing properties, or centrally or peripherally acting antiobesity agents, depending on the patient's particular clinical situation. Thus, topiramate may be added to the treatment regimen of an obese patient with a psychotic, mood, or eating disorder when there is associated appetite stimulation, overeating, binge eating, mood instability, and/or hypomanic, manic, or mixed symptoms. Venlafaxine, SSRIs, or bupropion may be added when there are associated depressive or binge-eating symptoms. Psychostimulants may be added for associated depressive and/or binge-eating

Figure 2. Treatment Algorithm for Depressive Disorder/Symptoms With Obesity^a

^aAbbreviations: ADHD = attention-deficit/hyperactivity disorder, GAD = generalized anxiety disorder, PMDD = premenstrual dysphoric disorder, SSRI = selective serotonin reuptake inhibitor. Symbol: ▼ = no response/partial response.

symptoms if the patient is already receiving an antidepressant, particularly if the patient has prominent fatigue or a medical disorder contributing to his or her depressive symptoms. Histamine-2 antagonists and amantadine may be considered with appetite stimulation associated with histamine (olanzapine, clozapine, mirtazapine) or dopamine (typical or atypical antipsychotics) receptor blockade, respectively. Orlistat may be considered in patients who are overeating, but should probably be avoided for those who are binge eating.

In short, a thorough understanding of the relationships among obesity; psychopathology; the adverse and therapeutic effects of psychotropics on appetite, binge eating, and weight; and the effects of antiobesity agents on eating behavior, mood, and psychopathology should enable optimal medical treatment of the obese mentally ill patient's psychopathology while minimizing weight gain or, ideally, promoting weight loss.

Drug names: amantadine (Symmetrel and others), bupropion (Wellbutrin and others), carbamazepine (Tegretol and others), chlorpromazine (Thorazine and others), cimetidine (Tagamet and others), clozapine (Clozaril and others), desipramine (Norpramin and others), diethylpropion (Tenuate and others), fluoxetine (Prozac and others), fluvoxamine (Luvox and others), gabapentin (Neurontin), haloperidol (Haldol and others), lamotrigine (Lamictal), mazindol (Sanorex, Mazanor), methylphenidate (Ritalin and others), mirtazapine (Remeron), modafinil (Provigil), molindone (Moban), naloxone (Narcan and others),

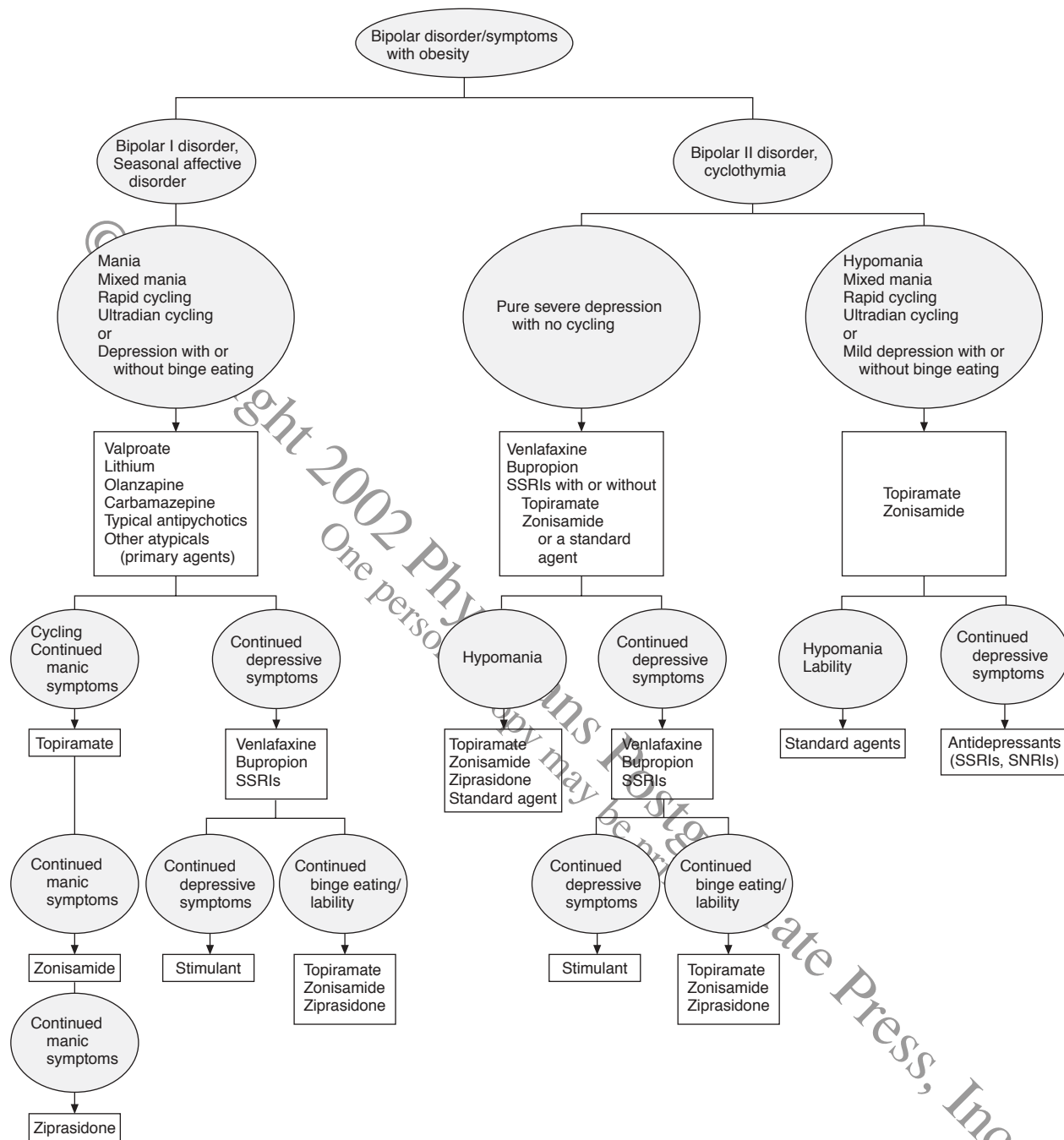
naltrexone (ReVia), nizatidine (Axid), olanzapine (Zyprexa), orlistat (Xenical), phenelzine (Nardil), phentermine (Adipex-P, Fastin), phenylpropranolamine (Ornade and others), phenytoin (Dilantin and others), pimozide (Orap), quetiapine (Seroquel), risperidone (Risperdal), sertraline (Zoloft), sibutramine (Meridia), tacrine (Cognex), topiramate (Topamax), venlafaxine (Effexor), ziprasidone (Geodon), zonisamide (Zonegran).

Disclosure of off-label usage: The authors have determined that, to the best of their knowledge, amantadine, bupropion, cimetidine, fluoxetine, and naloxone have not been approved by the U.S. Food and Drug Administration for the treatment of obesity; carbamazepine, lamotrigine, and zonisamide for the treatment of bipolar disorder; desipramine, fenfluramine, imipramine, methylphenidate, naloxone, naltrexone, nomifensine, and sertraline for the treatment of binge eating; fluoxetine, fluvoxamine, topiramate, venlafaxine, and zonisamide for the treatment of binge eating disorder; methylphenidate for the treatment of depression; naltrexone and nizatidine for the treatment of obesity; and topiramate and venlafaxine for the treatment of weight loss.

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Figure 3. Treatment Algorithm for Bipolar Disorder/Symptoms With Obesity^a



^aAbbreviations: SSRI = selective serotonin reuptake inhibitor, SNRI = serotonin-norepinephrine reuptake inhibitor.

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