



Caring for the Patient with Obesity and Psychiatric Illness

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Disclosures

Speaker Bureau: Novo Nordisk

46-year-old female with an 18-year history of bipolar disorder who has been on many mood stabilizers and antipsychotic medications over time that caused her to gain weight. Two years ago, she was stabilized on 200 mg lamotrigine and achieved a 40 lb weight loss with lifestyle interventions. Olanzapine 15 mg was added 6 mo ago after a manic episode triggered by insomnia. Attempts to reduce olanzapine have resulted in return of insomnia. She has regained 20 pounds in the last 6 months without change in diet or activity.

Which of the following does olanzapine treatment place her at risk for?

- A Hyperlipidemia
- B Diabetes
- C. Sleep related eating disorder
- D. All of the above



A 25-year-old female presents concerned about slow weight gain with a weight of 172 lb and BMI 28.7 kg/m².

During the clinical interview she states she hasn't eaten breakfast since she was a teen. She reports that she has recently received a promotion which has been stressful and makes for a hectic workday, but she is good about packing and eating a small late lunch. Dinner is most often eaten at home with her roommates. Her roommates have commented that some of her eating and sleeping behaviors are strange. She had never thought them out of the ordinary as they were normal in her home growing up.

You suspect her slow weight gain is associated with which eating disorder?

- A Bulimia Nervosa
- B Binge Eating Disorder
- C Night Eating Syndrome
- D Sleep Related Eating Disorder



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During the clinical interview she states she hasn't eaten breakfast since she was a teen. She reports that she has recently received a promotion which has been stressful and makes for a hectic workday, but she is good about packing and eating a small late lunch. Dinner is most often eaten at home with her roommates. Her roommates have commented that some of her eating and sleeping behaviors are strange. She had never thought them out of the ordinary as they were normal in her home growing up.

Which medication is the most studied in this eating disorder?

- A. lisdexamfetamine
- B. sertraline
- C. fluoxetine
- D. zolpidem

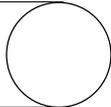


Objectives

- Identify the associations between obesity, psychiatric illness, and psychiatric treatment
- Diagnose and manage eating behavior disorders (binge-eating disorder, night eating syndrome, bulimia nervosa, and sleep-related eating disorder) that may exist concomitantly with obesity and other psychiatric illnesses
- Formulate pharmacological and nonpharmacological treatment approaches for patients with obesity, psychiatric disease, and weight gain from psychiatric medications

Mental Health and Obesity

MENTAL ILLNESS IN THE U.S.



1 in 5

Adults live with
Mental Illness
22.8 %



57.8

Million People

5.5%

Adults experience
Serious Mental
Illness

1 in 3

Adults are
Overweight
30.7%



Overweight/
Obesity

2 in 5

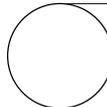
Adults are
Obese
42.4%



Severe
Obesity

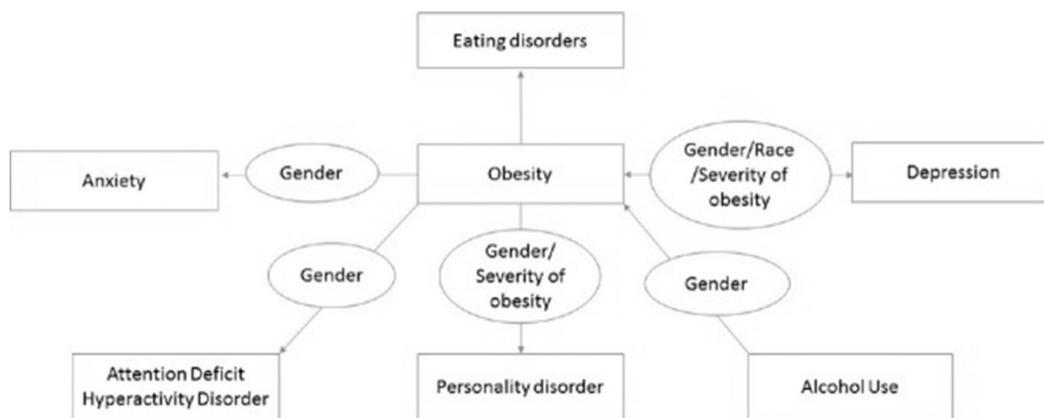
1 in 11

Adults have
Severe Obesity



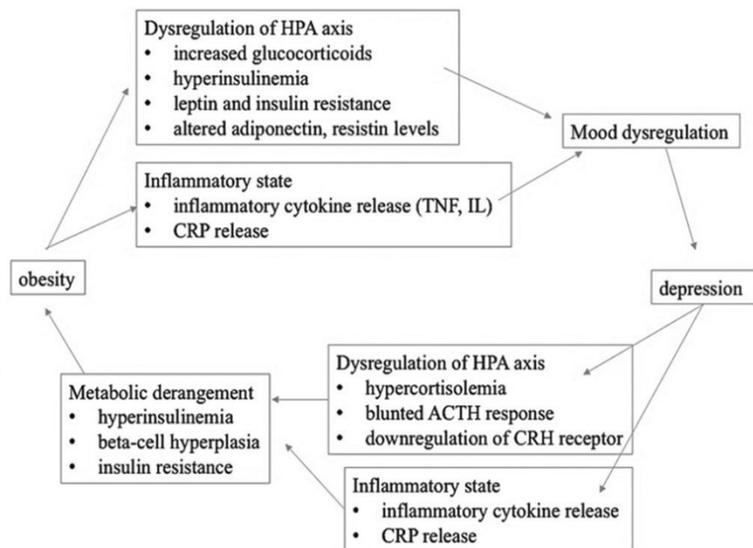
OBESITY IN THE U.S.

Associations: Psychiatric Disorders & Obesity



OFTEN BIDIRECTIONAL

Shared Pathogenic Pathways



Pathoetiological connection between obesity and depression. ACTH-Adrenocorticotrophic hormone; CRH-Corticotropin-releasing hormone; CRP-C-reactive protein; HPA-Hypothalamic-pituitary-adrenal; IL-Interleukin; TNF-Tumour necrosis factor

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Depression + Obesity

Bidirectional

- Obesity – 55% increased risk for MDD
- MDD – 58% increased risk for obesity
- Strongest association in teens (70%)

Gender

- Protective effect in men
- Predicted obesity in women

Severity of Obesity

- Modest link between severity of obesity and severity of depression



Bipolar Disorder + Obesity

Bidirectional

- 2.8% prevalence in BMI ≥ 30 vs 1.9% in BMI < 30

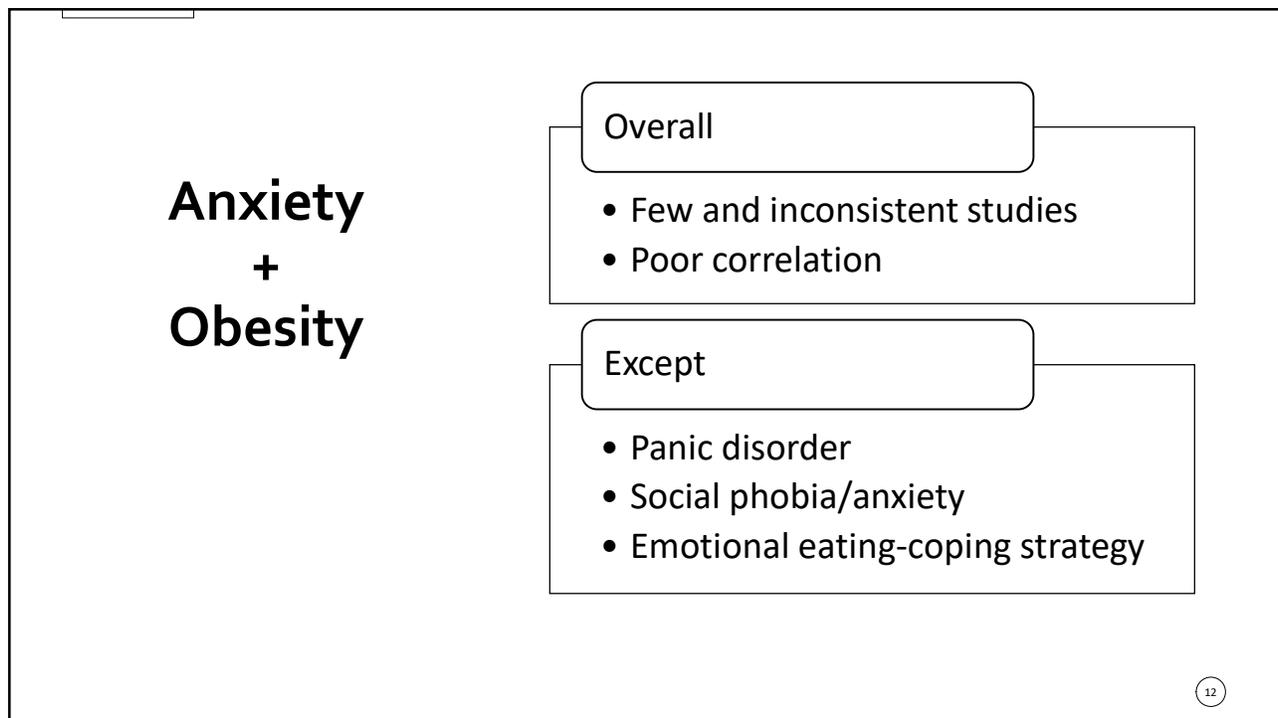
Worsened Prognosis

- Obesogenic medications
- Obesity more difficult to treat
- Higher frequency of mood episodes with shorter euthymic periods

Commonly accompanied by eating disorders

- Binge Eating Disorder
- Increased severity of obesity





ADHD + Obesity

Bidirectional

- ADHD Prevalence ≈27% in BMI ≥ 30 vs. 3-4% in general population
- Increased risk of developing of obesity: 70% - adults, 40% children

Shared abnormalities

- Brain reward pathway dysfunction
- Emotion regulation process dysfunction
- Executive function disruption
- Short sleep duration

Additional considerations

- Female>Male
- Childhood treatment reduces risk of adult obesity
- ADHD major cause of treatment failure in adults with severe obesity

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Personality Disorder (PD) + Obesity

Greater odds of any PD in people with Obesity

- Risk proportional to severity of obesity (24% in Class III obesity)
- Female > Male

Most Common

- Avoidant PD
- Antisocial PD



Alcohol Use Disorder (AUD) + Obesity

Obesity not a clear risk factor for AUD

AUD predicted obesity in women only.

Bariatric Surgery increases risk of AUD

- > 2 years post surgery
- > in Gastric Bypass





Metabolic Impact of Psychiatric Treatment

Key Considerations

Unique Response to Treatments

- Psychotropic effect
- Metabolic side effects
- Change in medication for the sole purpose of improvement in body weight should be approached with caution

Weight Change: Disease Process or Treatment

- Assess weight gain/loss associated with uncontrolled psychiatric condition.
- Expect normalization of weight with treatment
- Monitor weight at each visit
- Act early to mitigate/treat weight gain

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Antidepressant Impact on Weight

Side effects of antidepressant medications^[1-7]

Drug	Anticholinergic	Drowsiness	Insomnia/agitation	Orthostatic hypotension	QTc prolongation*	Gastrointestinal toxicity	Weight gain	Sexual dysfunction
Selective serotonin reuptake inhibitors¹								
Citalopram	0	0	1+	1+	3+ ⁵	1+ ¹	1+	3+
Escitalopram	0	0	1+	1+	2+	1+ ¹	1+	3+
Fluoxetine	0	0	2+	1+	1+	1+ ¹	0	3+
Fluvoxamine	0	1+	1+	1+	1+	1+ ¹	1+	3+
Paroxetine	1+	1+	1+	2+	0 to 1+	1+ ¹	2+	4+
Sertraline	0	0	2+	1+	1 to 2+	2+ ¹	1+	3+
Atypical agents								
Agomelatine ⁸ (not available in United States)	0	1+	1+	0	0	1+	0	0 to 1+
Bupropion	0	0	2+ (immediate release) 1+ (sustained release)	0	1+	1+	0	0
Mirtazapine	1+	4+	0	0	1+	0	4+	1+
Serotonin-norepinephrine reuptake inhibitors^{1,9}								
Desvenlafaxine ⁹	0	0	1+	0	0	2+	Unknown	1+
Duloxetine	0	0	1+	0	0	2+ ¹	0 to 1+	1+
Levomilnacipran ¹	0 ⁷	0	0 to 1+	0 to 1+	0	2+ ¹	0	1+
Milnacipran ¹	0	1+	0	0	0	2+ ¹	0	1+
Venlafaxine ⁷	0	1+	1+	0	1 to 2+	2+	0 to 1+	3+
Serotonin modulators								
Nefazodone ¹⁰	1+	2+	0	1+	0	2+	0	0
Trazodone	0	4+	0	1+ (hypnotic dose) 3+ (antidepressant dose)	1 to 2+	1+ (hypnotic dose) 3+ (antidepressant dose)	0 (hypnotic dose) 1+ (antidepressant dose)	1+ ¹¹
Vilazodone	0	0	2+	0	0	4+ ¹²	0	2+
Vortioxetine	0	0	0	0	0	3+	0	1+
Tricyclic and tetracyclic antidepressants								
Amitriptyline	4+	4+	0	3+	1 to 2+	1+ ¹³	4+	3 to 4+
Imipramine	2+	2+	2+	2+	1+	0 ¹⁴	2+	ND
Clomipramine	4+	4+	1+	2+	3+	1+ ¹⁵	4+	4+
Desipramine	1+	2+	1+	2+	1 to 2+	0 ¹⁶	1+	ND
Doxepin	3+	3+	0	2+	3+	0 ¹⁷	4+	3+
Imipramine	3+	3+	1+	4+	3+	1+ ¹⁸	4+	3+
Nortriptyline	2+	3+	0	2+	1+	0 ¹⁹	2+	ND
Nortriptyline	2+	2+	0	1+	1 to 2+	0 ²⁰	1+	ND
Protriptyline	2+	1+	1+	2+	1+	1+ ²¹	1+	3 to 4+
Trimipramine	4+	4+	1+	3+	1+	0 ²²	4+	ND
Monoamine oxidase inhibitors								
Isocarboxazid	1+	1+	2+	2+	0	1+	1+	4+
Phenelzine	1+	2+	1+	3+	0	1+	2+	4+
Safegiline	1+	0	1+	1+	0	0	0	0
Tranylcypromine	1+	1+	2+	2+	0	1+	1+	4+

Scales: 0 = none; 1+ = slight; 2+ = low; 3+ = moderate; 4+ = high; ND = inadequate data.

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Antidepressant Impact on Weight

Side effects of antidepressant medications^[1-7]

Drug	Anticholinergic	Drowsiness	Insomnia/agitation	Orthostatic hypotension	QTc prolongation*	Gastrointestinal toxicity	Weight gain	Sexual dysfunction
Selective serotonin reuptake inhibitors¹								
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Fluoxetine	0	0	2+	1+	1+	1+ [†]	0	3+
Fluvoxamine	0	1+	1+	1+	1+	1+ [†]	1+	3+
Paroxetine	1+	1+	1+	2+	0 to 1+	1+ [†]	2+	4+
Sertraline	0	0	2+	1+	1 to 2+	2+ ^{†◊}	1+	3+
Atypical agents								

Scale: 0 = none; 1+ = slight; 2+ = low; 3+ = moderate; 4+ = high; ND = inadequate data.

Antidepressant Impact on Weight

0 Weight Gain

- Bupropion
- Fluoxetine
- SNRI's (0 to 1+)
- Serotonin Modulators (0 to 1+)

2+ Weight Gain

- Paroxetine

4+ Weight Gain

- Mirtazapine
- Amitriptyline
- Doxepin
- Clomipramine
- Imipramine
- Trimipramine

Metabolic Impact of Antipsychotics

Heat map of antipsychotic drugs ranked according to associated degree of alteration

	Weight	Body-mass index	Glucose	LDL cholesterol	Total cholesterol	HDL cholesterol	Triglycerides
Haloperidol	0.10	0.08	0.59		0.59		0.63
Ziprasidone	0.10		0.42	0.12	0.25	0.24	0.33
Aripiprazole	0.26	0.11	0.55	0.48	0.50	0.26	0.33
Lurasidone	0.32	0.37	0.09	0.27	0.27	0.45	0.26
Cariprazine	0.37		0.70	0.07	0.16	0.47	0.28
Fluphenazine	0.38						
Amisulpride	0.41		0.14		0.64	0.83	0.42
Brexipiprazole	0.45		0.40	0.66	0.52	0.18	0.23
Flupenthixol	0.44						
Asenapine	0.56		0.22				
Risperidone and Paliperidone	0.58	0.56	0.46	0.54	0.55	0.51	0.39
Quetiapine	0.65	0.68	0.47	0.91	0.82	0.59	0.71
Iloperidone	0.70		0.73		0.19		0.63
Sertindole	0.81	0.72	0.36		0.26		0.29
Zotepine	0.88		0.94				0.94
Clozapine	0.90	0.85	0.97		0.97		0.97
Olanzapine	0.92	0.93	0.67	0.96	0.91	0.76	0.83



[https://doi.org/10.1016/S2215-0366\(19\)30416-X](https://doi.org/10.1016/S2215-0366(19)30416-X)

Metabolic Impact of Antipsychotics

Worst

- Clozapine
- Olanzapine

- Quetiapine
- Risperidone

Best

- Aripiprazole
- Brexpiprazole
- Cariprazine
- Lurasidone
- Ziprasidone

Other Common Medications Used in Mental Health Treatment that Impact Weight

Mood Stabilizers

May Increase Body Weight:

- Gabapentin
- Divalproex
- Lithium
- Valproate
- Vigabatrin
- Cariprazine
- Carbamazepine

Variable/Neutral Effects on Body Weight:

- Lamotrigine (sometimes reported to decrease body weight)
- Oxcarbazepine

Hypnotics

May Increase Body Weight:

- Diphenhydramine
- Zolpidem (may increase risk of sleep-related eating disorder)

May Have Limited Effects on Body Weight:

- Benzodiazepines
- Melatonergic hypnotics
- Trazodone

OMA Obesity Algorithm 2023

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**Eating Behavior Disorders
+
Obesity**

Bulimia Nervosa: DSM-5 Diagnostic Criteria

- Consuming an unusually large amount of food in a short duration while experiencing a loss of control over one's eating behavior during this time.
- Recurrent inappropriate compensatory behaviors in order to prevent weight gain such as self-induced vomiting; misuse of laxatives, diuretics, or other medications; fasting or excessive exercise.
- Self-evaluation is unjustifiably influenced by body shape and weight.
- The disturbance does not occur exclusively during episodes of anorexia nervosa.
- The binge eating and inappropriate compensatory behaviors occur, on average, at least once a week for 3 months.

Bulimia Nervosa

Diagnosis:

Clinic Interview; EAT-26, EDI

Obesity Related Factors:

- 33% with bulimia nervosa experience obesity at sometime in life.

Treatment:

- CBT-E
- HAPIFED
- SSRI
 - High dose fluoxetine
- Topiramate

Avoid: bupropion

Binge Eating Disorder (BED): DSM-5 Diagnostic Criteria

Consuming an unusually large amount of food in a short duration while experiencing a loss of control over one's eating behavior during this time.

3 of the following:

- Consuming food more rapidly than normal
- Eating food until uncomfortably full
- Consuming large amounts of food when not hungry
- Consuming food alone to avoid embarrassment
- Feeling disgusted, depressed, or guilty after eating event

PLUS:

- Associated distress
- Occurs at least 1x/wk x 3 mo
- Not isolated to episode of bulimia/anorexia nervosa

Diagnosis:

- Clinic Interview
- BEDS-7

Binge Eating Disorder (BED)

Prevalence:

- 1-3% general population
- Female > Male
- Typical age of onset 15-28 years
- Average duration 4-8 years

Comorbidities:

- 80% w/another DSM disorder
- Independent risk for physical health comorbidities
 - Diabetes/metabolic syndrome
 - Hypertension
 - Chronic pain disorders

Obesity Related Factors:

- 3-6x more likely to be obese
- Earlier onset of obesity
- Higher among those seeking bariatric surgery
- Increases drop out rate in weight management programs

Red Flags:

- Negative talk about weight/eating from family members
- Body shape concerns
- Weight cycling

Binge Eating Disorder (BED)

Psychopathology:

Restraint model · Affect regulation · Escape theory

Psychotherapy Treatment:

- CBT/CBT-E (1st line)
 - Pros: overall efficacy, rapid response
 - Cons: weight loss
- Interpersonal Therapy (ITP)
 - Pros: long term recovery rate
 - Cons: lower initial response
- Dialectal Behavioral Therapy (DBT)
- Behavioral Weight Loss (BWL)
 - Pros: weight loss
 - Cons: less durable effect on BED symptoms

Pharmacotherapy Treatment:

- Lisdexamfetamine (FDA indicated)
 - Pros: weight loss
 - Cons: mild effect on abstinence
- SSRI
 - Pros: reduction in depression
 - Cons: minimal weight loss
- Topiramate
 - Pros: weight loss
 - Cons: side effects, pregnancy risk

Night Eating Syndrome (NES) : Diagnosis

Recurrent episodes of night eating:
Excessive food consumption in the evening or eating after awakening from sleep (25%+ daily caloric intake)

Must include:

- Awareness of eating episodes
- Significant distress or impairment in function
- Not better explained by external factors or another disorder

Plus 3:

- Morning anorexia
- Strong urge to eat between dinner & sleep or during the night
- Insomnia (onset or maintenance)
- Frequent depressed mood or worsened mood in the evening
- Belief that one cannot get to sleep without eating

Diagnosis: Clinic Interview; NEQ

Night Eating Syndrome (NES)

Prevalence

- 1.5 % in general population
- Long lasting; Remission /Relapse associated to life stressors
- Onset early adulthood
- Male = Female

Comorbidities

- Another eating disorder (BED)
- Insomnia
- Metabolic syndrome/diabetes

Obesity Related Factors:

- 2.5-2.8x greater with obesity
- Development of obesity over time
- Symptoms present in up to 55% seeking bariatric surgery

Night Eating Syndrome (NES)

Psychopathology

- Genetic
- Neurobiological-Circadian rhythm disruption
- Psychological processes

NES Treatment → Weight Loss

Treatment:

- Psychotherapy
 - CBT
 - BWL
 - Regulation of eating pattern
- Pharmacotherapy
 - SSRI- sertraline
 - Topiramate
- Progressive muscle relaxation
- Photo therapy

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Sleep Related Eating Disorder (SRED)

Dysfunctional eating behaviors that occur after an arousal during the main sleep period.

Partial or complete loss of awareness during eating episode and impaired recall of the episode.

Not linked to daytime eating disturbances (bulimia nervosa, anorexia nervosa, BED)

At least one:

- Consumption of peculiar forms/combinations of foods
- Ingestion of toxic or non-food items
- Sleep related injuries or risk of injury while in pursuit of food
- Adverse health consequences from recurrent nocturnal eating (ex weight gain)

Sleep Related Eating Disorder (SRED)

Parasomnia

Diagnosis: Clinic Interview

Prevalence:

- Up to 5%
- Young adult females

Treatment

- Address trigger
- Topiramate

Assess for precipitating factors:

- Medications
 - Psychotropic (anticholinergics, lithium, antipsychotics); Sedative-hypnotic agents
 - High dose
 - Drug-drug interactions
- Physical
 - Sleep deprivation; recovery from
 - Fever, menses, internal stimuli (bladder distention)
- Comorbid sleep disorders
 - Obstructive sleep apnea, restless leg syndrome, sleep walking
- External stimuli

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Differentiate BED/NES/SRED



BED

Larger quantity of food eaten per episode
 Concern for shape or weight
 Emotional coping
 Absence of compensatory behaviors



NES

Smaller quantity of food per episode
 Motivation to achieve sleep
 Aware of eating episode



SRED

Composition of food choice during episode
 Not psychologically triggered
 Reduced awareness of eating episode



**Treatment Plan:
Psychiatric
+
Obesity**

Mitigate/Treat Weight Gain: Lifestyle Interventions

Weight loss in people with obesity has been shown to improve mood

Nutrition

- A variety of diet strategies are effective
- Patient adherence is the most important factor
- Consider psychiatric disorders in choosing dietary strategy

Physical Activity

- Priority: Decrease physical inactivity
- Increase in exercise time (Aerobic, Resistive Strength Training, Combination)
- Leisure time activity; Non-Exercise Activity Time (NEAT)

Mitigate/Treat Weight Gain: Lifestyle Interventions

Behavior Treatment

- Treat psychiatric illness in particular eating disorders (CBT)
- Gain insight into eating and physical inactivity behaviors and progress toward behavior change
- Elements for success include
 - Doable
 - Measurable/Accountable
 - Efficacious
 - Self-ownership
 - Frequent Encounters

Pharmacological Interventions: Metformin

- $\geq 5\%$ weight loss in about half of patients
- Greater efficacy in
 - Antipsychotic naive patients
 - Higher BMI
 - Greater severity of insulin resistance
- Start 500 mg; increase weekly or slower to target dose of 1000 mg twice daily (some studies dose 2550 mg/day IR)
- Extended-Release formulation tolerated better, improved if taken with food
- Gastrointestinal side effects (diarrhea, bloating and stomach pain) often resolve with time



Adequate dose
Adequate time

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Pharmacological Interventions: Topiramate

- $\geq 6\%$ expected weight loss
- Caution in women of childbearing age:
 - Cleft palate birth defect risk
 - Reduced efficacy of OCP (dose dependent)
- Start 25 mg; increase to by 25 mg weekly to effective dose; 50-200 mg (up to 400 mg in some ED studies)
- Common side effects are paresthesia, changes in taste, hypoesthesia, concentration/memory impairment, somnolence
 - Monitor mood
 - Serious adverse effects rare



Greatest effect at higher doses and longer treatment duration

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Pharmacological Interventions : GLP-1 Receptor Agonists

- AGA preferential choice for obesity treatment
- Potential for greater comorbidity improvement (CV, fatty liver disease)
- Potential direct benefit on psychopathology
- Warning for worsening depression/suicidal ideation
- Limitations for use
 - Gastrointestinal side effects; often transient
 - Cost/access
 - Subcutaneous injection

Pharmacological Interventions : GLP-1 Receptor Agonists

- Liraglutide
 - Start 0.6 mg daily; increase weekly to 1.8 or 3.0 mg
- Semaglutide
 - Start 0.25 mg weekly; increase Q4 weeks to 2.0 or 2.4 mg
- Tirzepatide
 - 2.5 mg weekly; increase Q4 weeks to 15 mg



Mitigate side effects with:
Slow titration
Least effective dose
Food volume/choice

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Pharmacological Interventions: Anti-Obesity Medications

FDA Indications for use

Adjunct to nutritional, physical activity,
and behavioral therapies

Patients with obesity (BMI ≥ 30 kg/m²)

Patients with overweight (BMI ≥ 27
kg/m²) with presence of weight related
complications (e.g. Type 2 diabetes
mellitus, hypertension, dyslipidemia)

Phentermine

Diethylpropion

Phendimetrazine

Orlistat

Phentermine/Topiramate

Naltrexone/ Bupropion

Liraglutide

Semaglutide

Tirzepatide

Nonsystemic Oral
Hydrogel

Setmelanotide

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Summary

Mental illness and obesity are very prevalent in the US

There is a bidirectional association between mental illness and obesity

Psychotropic medications often impact weight regulation

Eating behavior disorders and obesity often co-occur

Mitigate psychotropic related weight gain early and with adequate treatment dose and duration to provide clinically meaningful results

Treatment for weight gain resulting from psychotropic medication should include lifestyle modifications and may include add-on pharmacotherapy

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Questions

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