



The Intersection of Obesity and Mental Health Treatment

KARON POTTER PA-C, RD, CSOWM, CDE

Disclosures

Speaker Bureau: Novo Nordisk

Objectives

- Discuss the relationship between obesity and psychiatric disease.
- Identify Eating Behavior Disorders (Binges Eating Disorder, Night Eating Syndrome, Bulimia Nervosa, and Sleep Related Eating Disorder) that may exist concomitantly with obesity and other psychiatric illnesses.
- Recognize the impact that common psychiatric medications may have on an individual's weight regulation
- Formulate pharmacological and nonpharmacological treatment approaches for patients with obesity, psychiatric disease, and weight gain from psychiatric medications

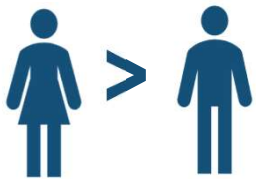
Mental Health and Obesity

MENTAL ILLNESS IN THE U.S.



1 in 5

Adults live with
Mental Illness
22.8 %



57.8

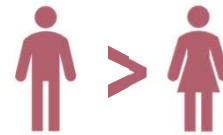
Million People

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%

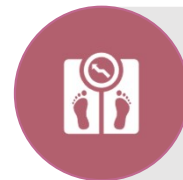


Severe
Obesity

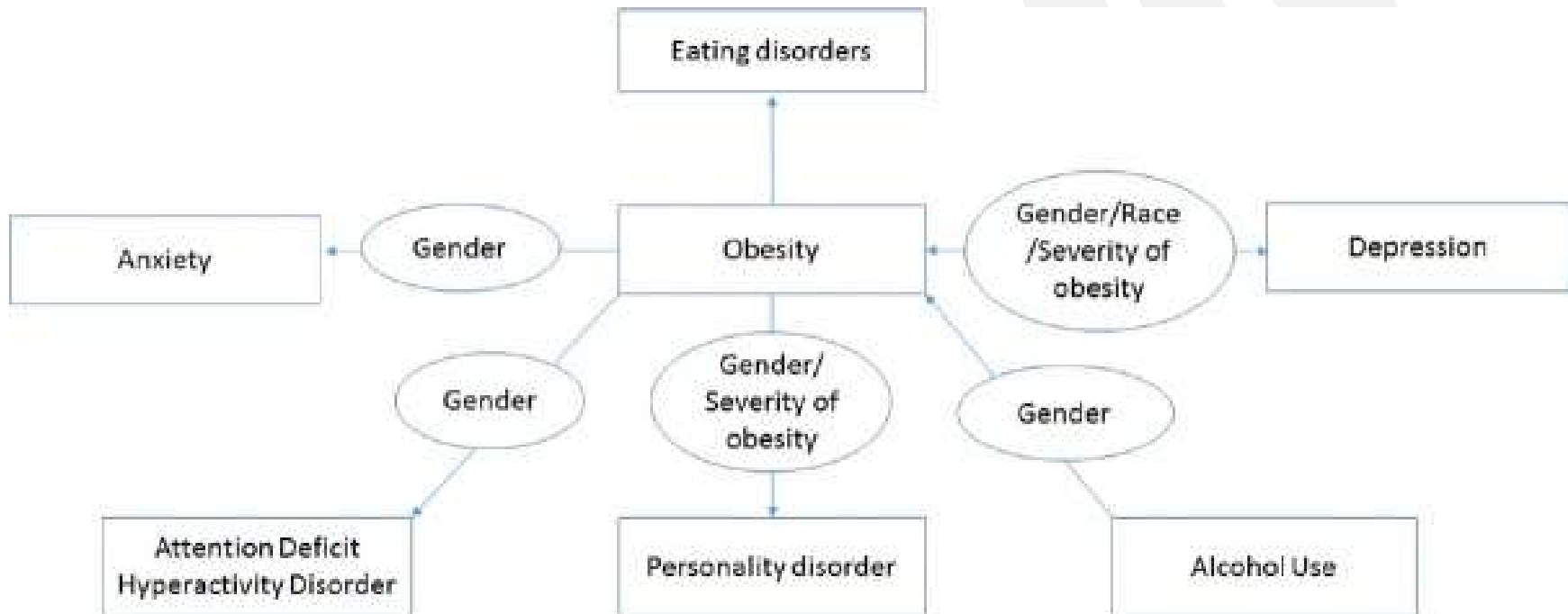
1 in 11

Adults have
Severe Obesity

OBESITY IN THE U.S.



Associations: Psychiatric Disorders & Obesity



Associations: Depression + Obesity

Bidirectional

- Obesity is a risk factor for the development of depression
- Depression is a risk factor for the development of obesity
- Strongest association in teens

Gender

- Protective effect in men
- Predicted obesity in women

Race

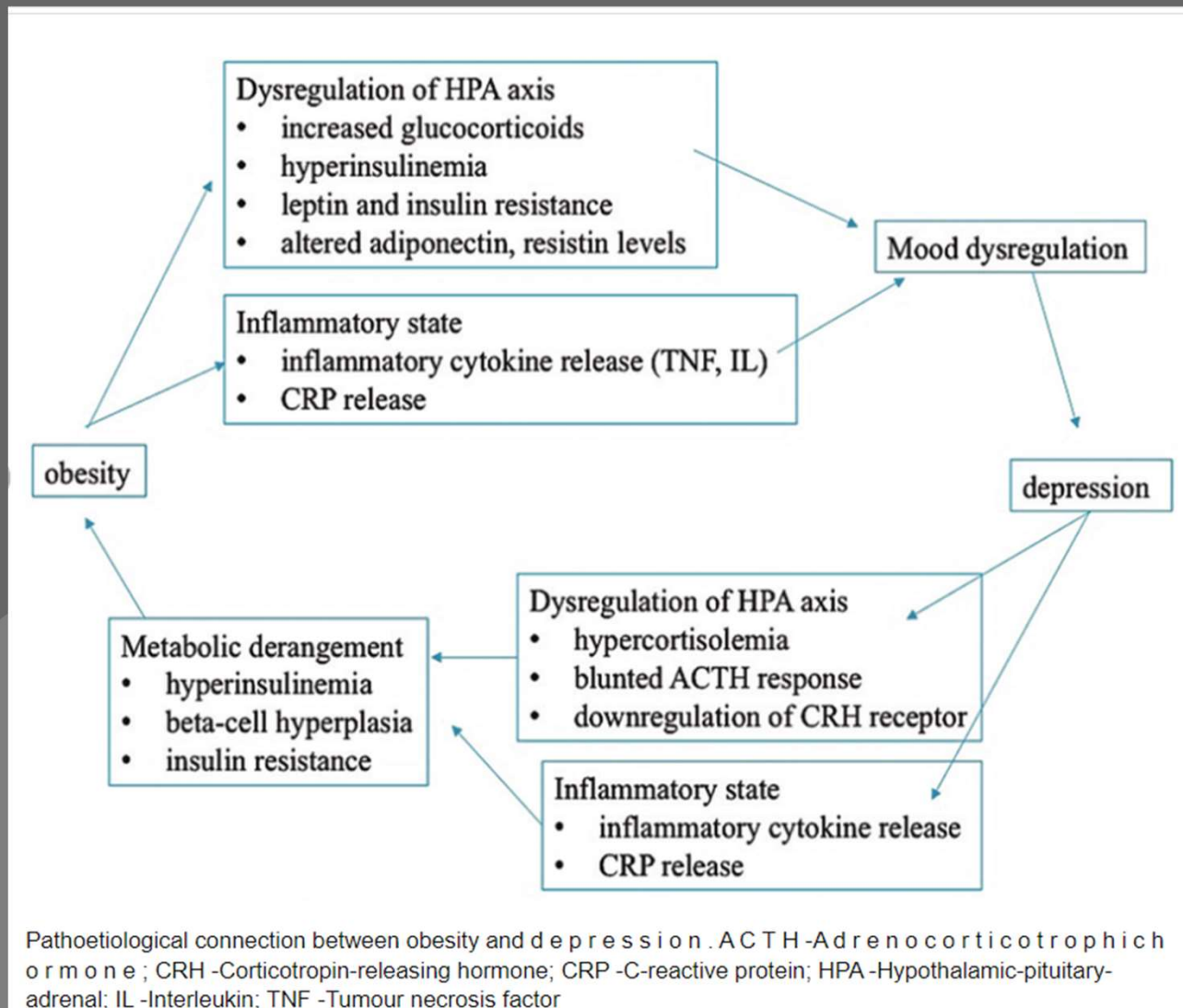
- White women

Severity of Obesity

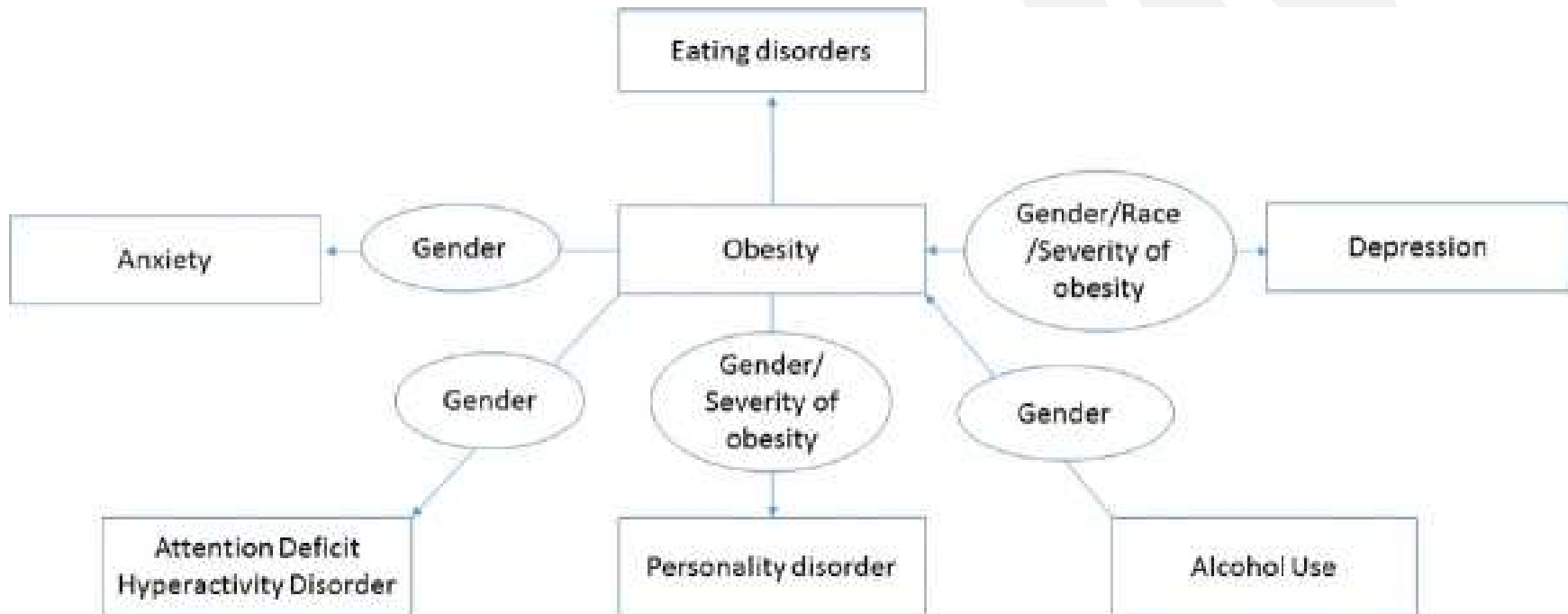
- Modest link between severity of obesity and severity of depression



Shared Pathogenic Pathways



Associations: Psychiatric Disorders & Obesity



Associations:

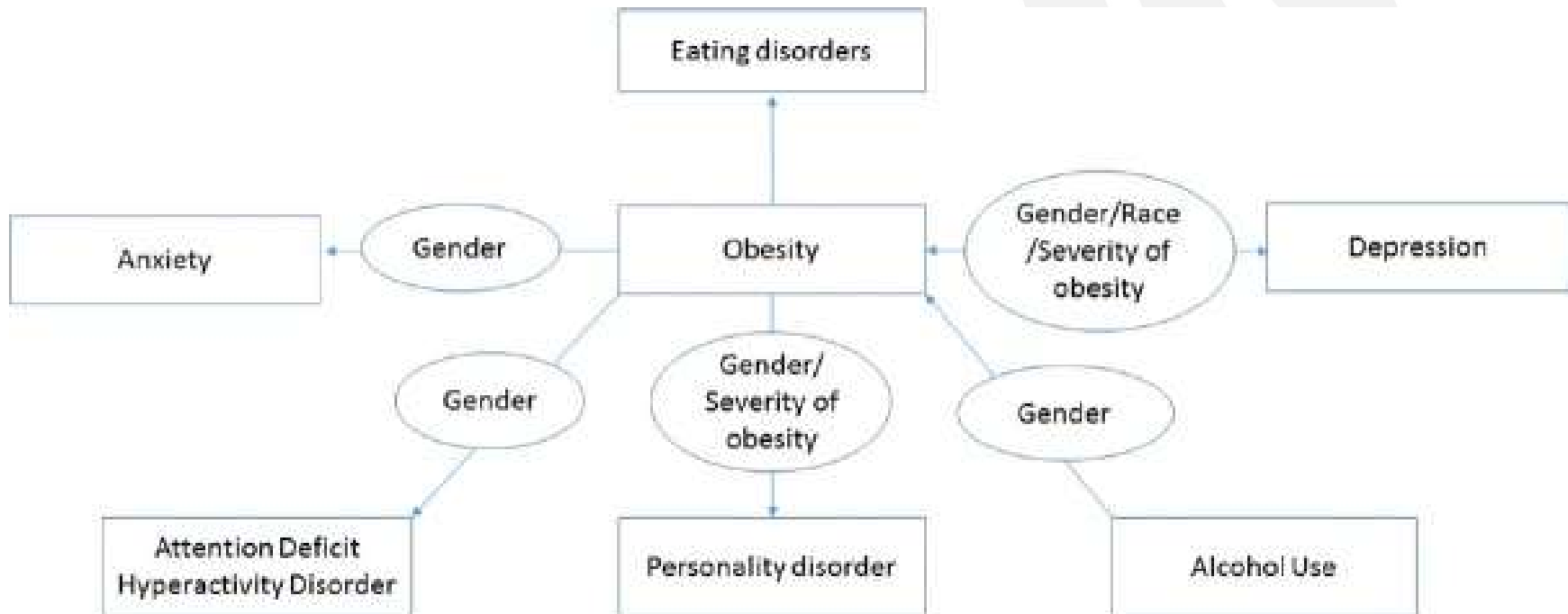
Anxiety + Obesity

- Greater risk for Panic Disorder
- Greater risk for Social Anxiety
- Studies inconsistent

ADHD + Obesity

- 3 categories of ADHD
 - Remitted, persisting, lifetime
 - Correlated with obesity in women for all three categories
- Persisting ADHD correlated with obesity in men and women

Associations: Psychiatric Disorders & Obesity



Associations:

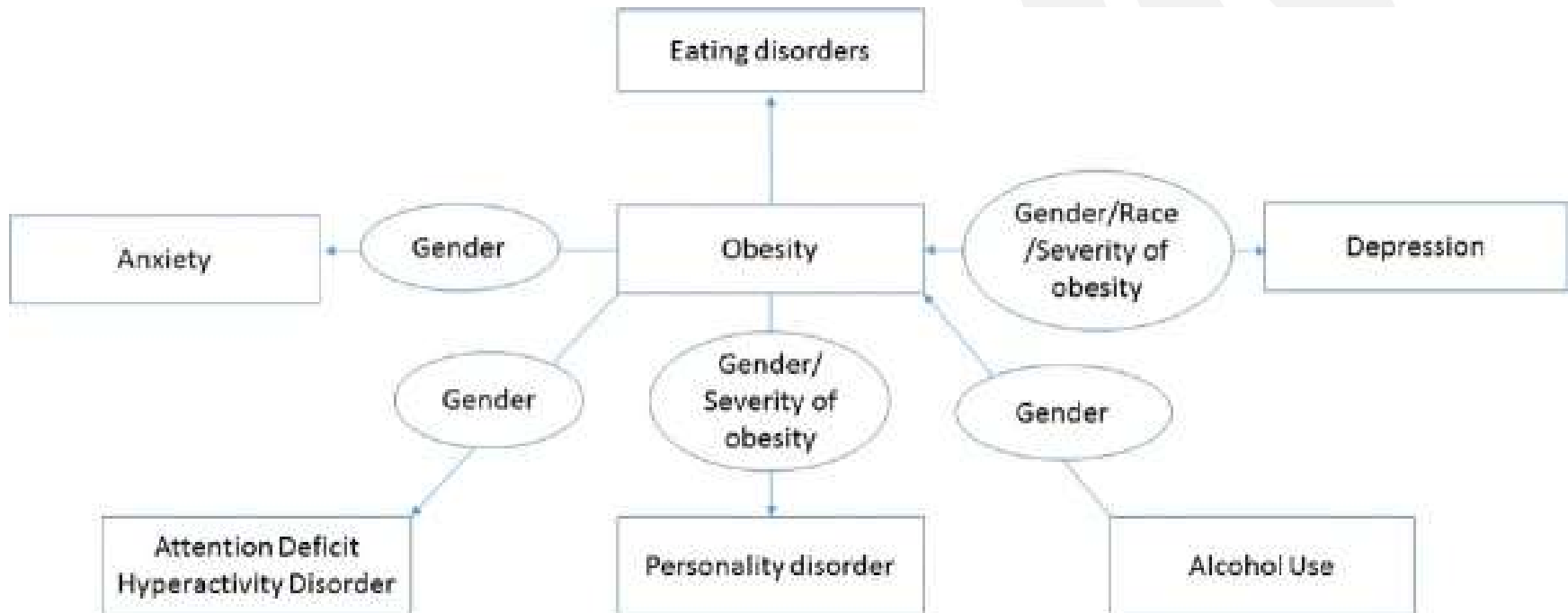
Personality Disorder + Obesity

- Greater risk of personality disorder in people with obesity
- Risk proportional to severity of obesity
- Higher risk in women
- Avoidant and Antisocial most common

Alcohol Use + Obesity

- Obesity not a clear risk factor for alcohol use
- Alcohol use disorders predicted obesity in women only.

Associations: Psychiatric Disorders & Obesity



Eating Behavior Disorders in Obesity :

Bulimia Nervosa

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.

Diagnosis: Clinic Interview; EAT-26. EDI

Obesity Related Factors:

- 33% with Bulimia Nervosa had obesity at sometime in life.

Unmet need: Integrated treatments for obesity and bulimia nervosa

Eating Behavior Disorders in Obesity :

Binge Eating Disorder (BED)

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 must also be present

- 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

Obesity Related Factors:

- 3-6x more likely to be obese
- Earlier onset of obesity
- Higher among those seeking bariatric surgery

Red Flags: Negative talk about weight/eating from family members, body shape concerns, weight cycling.

Eating Behavior Disorders in Obesity :

Night Eating Syndrome (NES)

Recurrent episodes of night eating, as manifested by eating after awakening from sleep or by excessive food consumption after the evening meal. (25%+)

- Awareness of recall of the eating.
- Not better explained by external influences such as changes in the individual's sleep-wake cycle or by local social norms.
- Causes significant distress and/or impairment in functioning.
- Not better explained by binge-eating disorder and or another mental disorder, including substance use, and is not attributable to another medical disorder or to an effect of medication.

Diagnosis: Clinic Interview; NEQ

Important Considerations:

- Prevalence 2.5-2.8x greater with obesity
- Long lasting; Remission /Relapse associated to life stressors
- Potential genetic link
- Differentiate from BED/SRED
- NED may contribute to development of obesity over time.
- Increased risk for metabolic syndrome/diabetes

Eating Behavior Disorders in Obesity :

Sleep Related Eating Disorder (SRED)

Parasomnia

Characterized by dysfunctional eating behaviors that occur after an arousal during the main sleep period.

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)

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)

Diagnosis: Clinic Interview

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
- External Stimuli



Metabolic Impact of Psychiatric Medications

Mitigation and Treatment
of Negative Metabolic
Effects

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

Antidepressant Impact on Weight

Side effects of antidepressant medications^[1-7]

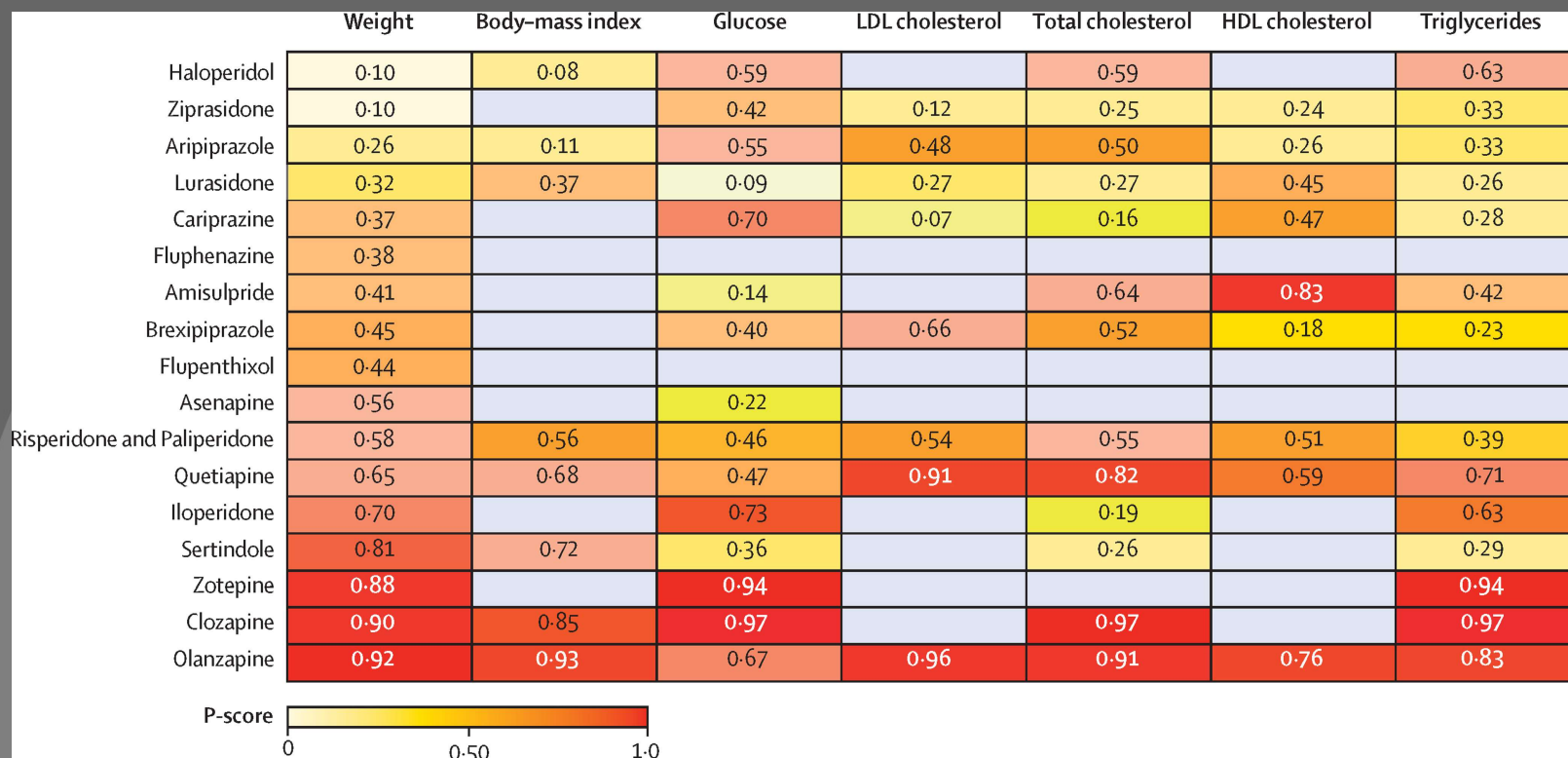
Drug	Anticholinergic	Drowsiness	Insomnia/agitation	Orthostatic hypotension	QTc prolongation*	Gastrointestinal toxicity	Weight gain	Sexual dysfunction
Selective serotonin reuptake inhibitors¹								
Citalopram	0	0	1+	1+	3+ ^Δ	1+ [§]	1+	3+
Escitalopram	0	0	1+	1+	2+	1+ [§]	1+	3+
Fluoxetine	0	0	2+	1+	1+	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								
Agomelatine ⁵ (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,¶}								
Desvenlafaxine ⁷	0	0	1+	0	0	2+	Unknown	1+
Duloxetine	0	0	1+	0	0	2+ [§]	0 to 1+	1+
Levominlacipran ²	0 ⁷	0	0 to 1+	0 to 1+	0	2+ [§]	0	1+
Milnacipran ²	0	1+	0	0	0	2+ [§]	0	1+
Venlafaxine ²	0	1+	1+	0	1 to 2+	2+	0 to 1+	3+
Serotonin modulators								
Nefazodone ^{8,9}	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+ [¶]
Vilazodone	0	0	2+	0	0	4+ ^{ΔΔ}	0	2+
Vortioxetine	0	0	0	0	0	3+	0	1+
Tricyclic and tetracyclic antidepressants								
Amitriptyline	4+	4+	0	3+	1 to 2+	1+ ^{○○}	4+	3 to 4+
Amoxapine	2+	2+	2+	2+	1+	0 ^{○○}	2+	ND
Clomipramine	4+	4+	1+	2+	3+	1+ ^{○○}	4+	4+
Desipramine	1+	2+	1+	2+	1 to 2+	0 ^{○○}	1+	ND
Doxepin	3+	3+	0	2+	3+	0 ^{○○}	4+	3+
Imipramine	3+	3+	1+	4+	3+	1+ ^{○○}	4+	3+
Maprotiline	2+	3+	0	2+	1+	0 ^{○○}	2+	ND
Nortriptyline	2+	2+	0	1+	1 to 2+	0 ^{○○}	1+	ND
Protriptyline	2+	1+	1+	2+	1+	1+ ^{○○}	1+	3 to 4+
Trimipramine	4+	4+	1+	3+	1+	0 ^{○○}	4+	ND
Monoamine oxidase inhibitors								
Isocarboxazid	1+	1+	2+	2+	0	1+	1+	4+
Phenelzine	1+	2+	1+	3+	0	1+	2+	4+
Selegiline	1+	0	1+	1+	0	0	0	0
Tranylcypromine	1+	1+	2+	2+	0	1+	1+	4+

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

References:
 1. Kessler D, et al. (2011) Antidepressant use and the risk of weight gain. *Arch Gen Psychiatry* 68(12): 1288-1295.
 2. Mulsant BR, et al. (2004) Weight gain associated with second-generation antidepressants in patients with major depressive disorder: Results from a systematic review with relevant meta-analysis. *Drug Saf* 27(4): 27-38.
 3. Mulsant BR. A weight risk assessment of citalopram in the treatment of major depression. *Drug Saf* 20(1): 39-50.
 4. Lexicon-Drugs. Copyright © 1979-2011 Lexicon, Inc. All Rights Reserved.
 5. Nelson DL, Christy L, Hines L, et al. The safety and tolerability of agomelatine: Analysis of data from randomized placebo-controlled trials and open-label extension studies. *J Psychiatr Res* 2010; 44(2): 123-132.
 6. Group Evaluation of 2-D,3-D,4-D,5-Hydroxytryptamine and 2-Aminoindane Receptor for Non-antidepressant Drug - Quindin and Anand. *Journal of Psychiatry and Drug Administration*, June 2011; Available at: <http://www.fda.gov/oc/ohrt/2-D,3-D,4-D,5-Hydroxytryptamine%20and%202-Aminoindane%20Receptor%20for%20Non-antidepressant%20Drug%20Quindin%20and%20Anand.pdf>
 7. The American Psychiatric Association. *Textbook of Psychopharmacology*. 4th ed. Washington DC: American Psychiatric Association Publishing; 2011.

Metabolic Impact of Antipsychotics

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



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

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
- Adequate food intake (protein) early in the day if NES

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

Mitigate/Treat Weight Gain: Pharmacological Interventions

Metformin

- ≥ 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 2550mg/day)
- Extended-Release formulation tolerated better, improved if taken with food
- Gastrointestinal side effects (diarrhea, bloating and stomach pain) often resolve with time



Mitigate/Treat Weight Gain: Pharmacological Interventions

Topiramate

- Effective to control weight gain in a variety of populations including schizophrenia and bipolar disorder
- Reduced weight and symptoms in BED, NED, SRED and Bulimia Nervosa + Obesity
- Weight effect greater with higher dose and longer duration of treatment (28+ weeks)
- 6x greater chance to achieve $\geq 5\%$ weight loss than placebo
- Caution in women of childbearing age: Cleft palate birth defect risk. Reduces efficacy of oral contraceptives (dose dependent)
- Start 25 mg; increase to by 25 mg weekly to effective dose; 50-200 mg (some eating disorder studies use doses up to 400 mg)
- Common side effects are paresthesia, changes in taste, hypoesthesia, concentration/memory impairment, somnolence
 - Monitor mood
 - Serious adverse effects rare

Mitigate/Treat Weight Gain: Pharmacological Interventions

Liraglutide 1.8 mg

- Improvement in body weight and glucose control in patients taking antipsychotic medication;
- Improved function in patients with obesity and depression
- Reduced binge eating behavior, BMI and weight in subclinical binge eating
- Dosing
 - Start 0.6 mg increase weekly to dose of 1.8 mg (3.0 mg – obesity)
 - Gastrointestinal side effects such as heartburn, nausea, vomiting and constipation are common and often resolve with continued use or slower titration

Semaglutide

- Ongoing studies

Mitigate/Treat Weight Gain: 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 increased adiposopathic complications (e.g. Type 2 diabetes mellitus, hypertension, dyslipidemia)

- Phentermine
- Diethylpropion
- Phendimetrazine
- Orlistat
- Phentermine/Topiramate
- Naltrexone/ Bupropion
- Liraglutide
- Semaglutide
- Nonsystemic Oral Hydrogel
- Setmelanotide

Summary

Mental illness and obesity are very prevalent in the US

There is a bidirectional association between mental illness and obesity

Eating behavior disorders and obesity often co-occur

Psychotropic medications often impact weight regulation

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 medications should include lifestyle modifications and may include add-on pharmacotherapy

References

Bays HE, McCarthy W, Burrige K, Tondt J, Karjoo S, Christensen S, Ng J, Golden A, Davisson L, Richardson L. Obesity Algorithm eBook, presented by the Obesity Medicine Association. www.obesityalgorithm.org. 2023. <https://obesitymedicine.org/obesity-algorithm/> (Accessed 3/24/22)

Camkurt MA, Lavagnino L, Zhang XY, Teixeira AL. Liraglutide for psychiatric disorders: clinical evidence and challenges. *Horm Mol Biol Clin Investig*. 2018 Jul 18;36(2):/j/hmbci.2018.36.issue-2/hmbci-2018-0031/hmbci-2018-0031.xml. doi: 10.1515/hmbci-2018-0031. PMID: 30020885.

da Luz FQ, Hay P, Touyz S, Sainsbury A. Obesity with Comorbid Eating Disorders: Associated Health Risks and Treatment Approaches. *Nutrients*. 2018 Jun 27;10(7):829. doi: 10.3390/nu10070829. PMID: 29954056; PMCID: PMC6073367.

de Silva VA, Suraweera C, Ratnatunga SS, Dayabandara M, Wanniarachchi N, Hanwella R. Metformin in prevention and treatment of antipsychotic induced weight gain: a systematic review and meta-analysis. *BMC Psychiatry*. 2016 Oct 3;16(1):341. doi: 10.1186/s12888-016-1049-5. PMID: 27716110; PMCID: PMC5048618.

Garg, Rajat & Saxena, SachinKumar & Bashir, Sabreen. (2019). Is obesity a risk to depression? A cross-sectional study. *Industrial Psychiatry Journal*. 28. 130. 10.4103/ipj.ipj_59_19.

Garvey WT, Mechanick JI, Brett EM, Garber AJ, Hurley DL, Jastreboff AM, Nadolsky K, Pessah-Pollack R, Plodkowski R; Reviewers of the AACE/ACE Obesity Clinical Practice Guidelines. AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND AMERICAN COLLEGE OF ENDOCRINOLOGY COMPREHENSIVE CLINICAL PRACTICE GUIDELINES FOR MEDICAL CARE OF PATIENTS WITH OBESITY. *Endocr Pract*. 2016 Jul;22 Suppl 3:1-203. doi: 10.4158/EP161365.GL. Epub 2016 May 24. PMID: 27219496.

Kramer CK, Leitão CB, Pinto LC, Canani LH, Azevedo MJ, Gross JL. Efficacy and safety of topiramate on weight loss: a meta-analysis of randomized controlled trials. *Obes Rev*. 2011 May;12(5):e338-47. doi: 10.1111/j.1467-789X.2010.00846.x. Epub 2011 Mar 28. PMID: 21438989.

Leombruni P, Lavagnino L, Fassino S. Treatment of obese patients with binge eating disorder using topiramate: a review. *Neuropsychiatr Dis Treat*. 2009;5:385-92. doi: 10.2147/ndt.s3420. PMID: 19649212; PMCID: PMC2714287.

References

McCuen-Wurst C, Ruggieri M, Allison KC. Disordered eating and obesity: associations between binge-eating disorder, night-eating syndrome, and weight-related comorbidities. *Ann N Y Acad Sci.* 2018 Jan;1411(1):96-105. doi: 10.1111/nyas.13467. Epub 2017 Oct 16. PMID: 29044551; PMCID: PMC5788730.

Merino D, Gérard AO, Van Obberghen EK, Ben Othman N, Ettore E, Giordana B, Viard D, Rocher F, Destere A, Benoit M, Drici MD. Medications as a Trigger of Sleep-Related Eating Disorder: A Disproportionality Analysis. *J Clin Med.* 2022 Jul 4;11(13):3890. doi: 10.3390/jcm11133890. PMID: 35807172; PMCID: PMC9267629.

Pillinger T, McCutcheon RA, Vano L, Mizuno Y, Arumuham A, Hindley G, Beck K, Natesan S, Efthimiou O, Cipriani A, Howes OD. Comparative effects of 18 antipsychotics on metabolic function in patients with schizophrenia, predictors of metabolic dysregulation, and association with psychopathology: a systematic review and network meta-analysis. *Lancet Psychiatry.* 2020 Jan;7(1):64-77. doi: 10.1016/S2215-0366(19)30416-X. Epub 2019 Dec 17. PMID: 31860457; PMCID: PMC7029416.

Rajan TM, Menon V. Psychiatric disorders and obesity: A review of association studies. *J Postgrad Med.* 2017 Jul-Sep;63(3):182-190. doi: 10.4103/jpgm.JPGM_712_16. PMID: 28695871; PMCID: PMC5525483.

Seifarth C, Schehler B, Schneider HJ. Effectiveness of metformin on weight loss in non-diabetic individuals with obesity. *Exp Clin Endocrinol Diabetes.* 2013 Jan;121(1):27-31. doi: 10.1055/s-0032-1327734. Epub 2012 Nov 12. PMID: 23147210.

Zhuo C, Xu Y, Liu S, Li J, Zheng Q, Gao X, Li S, Jing R, Song X, Yue W, Zhou C, Uptegrove R. Topiramate and Metformin Are Effective Add-On Treatments in Controlling Antipsychotic-Induced Weight Gain: A Systematic Review and Network Meta-Analysis. *Front Pharmacol.* 2018 Nov 28;9:1393. doi: 10.3389/fphar.2018.01393. PMID: 30546312; PMCID: PMC6280187.

<https://www.nimh.nih.gov/health/statistics/mental-illness>

<https://www.niddk.nih.gov/health-information/health-statistics/overweight-obesity>