MAKING WEIGHT:

Wrestling with the Challenges of Obesity

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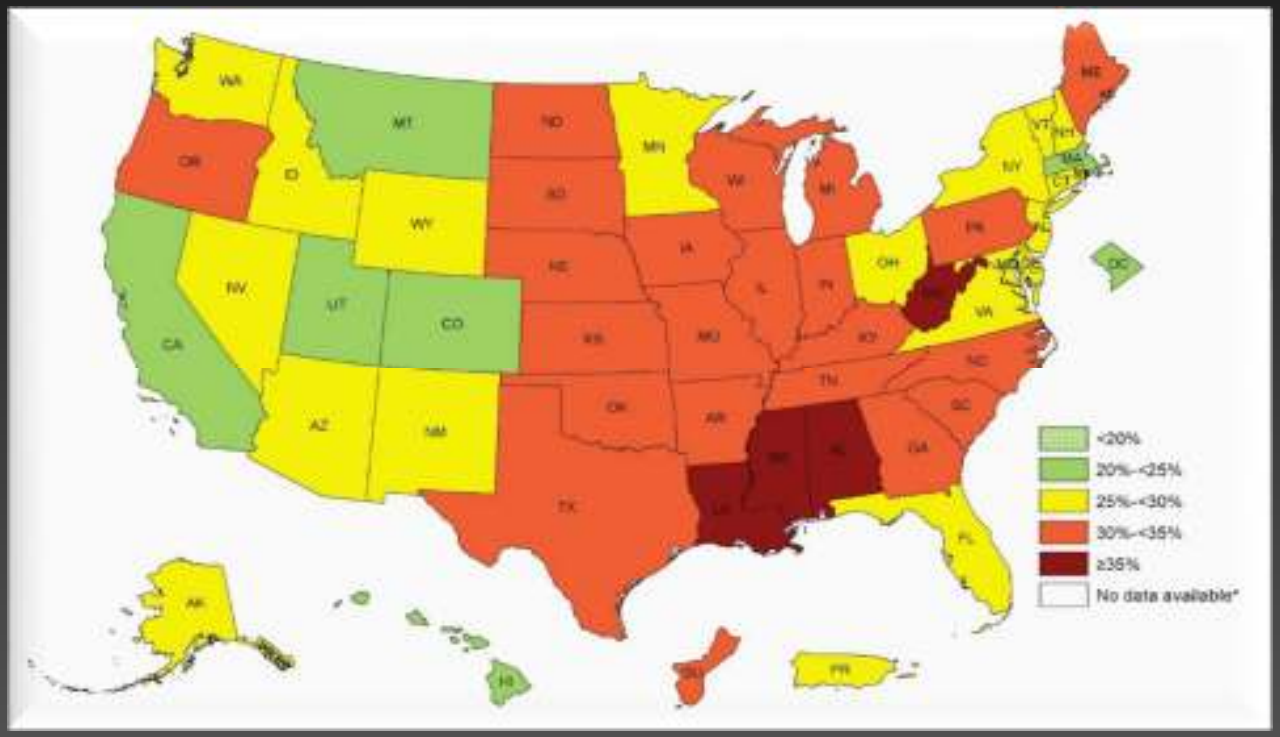
Faculty Disclosures

- Shannon Hillier, DO, MPH
  - No financial support or personal connections to disclose that could be perceived to bias this work
- Kelly Murray, PharmD, BCACP
  - No financial support or personal connections to disclose that could be perceived to bias this work

Objectives

- As a result of participating in this activity, learners will be able to:
  - Discuss the epidemiology of obesity and Oklahoma's role in the epidemic.
  - Understand different classifications for obesity.
  - Recall neurobiological mechanism of obesity.
  - List specific treatment strategies for obesity, with a focus pharmacotherapy options.
  - Address specific challenges associated with patients with obesity within the primary care setting.

Obesity: Epidemiology



- No state has a prevalence of obesity less than 20%.
- 6 states and the District of Columbia have a prevalence of obesity between 20% and 25%.
- 19 states and Puerto Rico have a prevalence of obesity between 25% and 30%.
- 21 states and Guam have a prevalence of obesity between 30% and 35%.
- 4 states (Alabama, Louisiana, Mississippi, and West Virginia) have a prevalence of obesity of 35% or greater.

Prevalence reflects Behavioral Risk Factor Surveillance System (BRFSS) methodological changes started in 2011, and these estimates should not be compared to those before 2011. Centers for Disease Control and Prevention. Obesity Prevalence Maps. https://www.cdc.gov/obesity/data/prevalence-maps.html. 2015 Obesity Prevalence map. Accessed September 12, 2016. National Vital Statistics System Mortality https://www.cdc.gov/nchs/nvss/deaths.htm accessed Aug 2018.

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Obesity: Epidemiology

References:

- Centers for Disease Control
- Trust for America's Health
- Obesity Action Coalition

OAC
Obesity Action Coalition
www.ObesityAction.org

Obesity Action Coalition; www.obesityaction.org Accessed Aug 2018

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Obesity: Classical Definition

Body Mass Index (BMI)	18.5-24.9 kg/m²	25.0-29.9 kg/m²	≥30 kg/m²
Percent Body Fat	Male: <25% Female: <32%		Male: >25% Female: >32%
Waist Circumference	Male: <40 in. Female: <35 in.		Male: >40 in. Female: >35 in.

Weight Categories	BMI, kg/m²
Underweight	<18.5
Healthy Weight	>18.5 and <25
Overweight	>25 and <30
Obesity Class I	>30 and <35
Obesity Class II	>35 and <40
Obesity Class III	>40

World Health Organization. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. *World Health Organ Tech Rep Ser. 2000:894 1-253.*

Obesity: Is Not Simple

- Major Driver:
  - Over consumption of food
  - Energy dense meals
  - In greater excess than is needed by the body
- FOOD CONSUMPTION IS NOT SIMPLY A BIOLOGICAL BEHAVIOR TO MEET BODY ENERGY NEEDS:
  - Cognitive, emotional, sensory, economic and environmental factors influence motivation to eat

Obesity: Disease Definition

"Obesity is defined as a chronic, relapsing, multi-factorial, neurobehavioral disease, wherein an increase in body fat promotes adipose tissue dysfunction and abnormal fat mass physical forces, resulting in adverse metabolic, biomechanical, and psychosocial health consequences."

The adverse health consequences of increased body fat are not simply "co-morbidities" or "associated risk factors"

Bays HE, Seger JC, Primack C, McCarthy W, Long J, Schmidt SL, Daniel S, Wendt J, Horn DB, Westman EC: Obesity Algorithm 2017, presented by the American Society of Bariatric Physicians. 2016 - 2017. www.obesityalgorithm.org ; Obesity Algorithm®. ©2017-2018 Obesity Medicine Association.

Obesity: Recognized as a Disease

"…obesity is a serious chronic disease with extensive and well-defined pathologies, including illness and death"

"Recognizing obesity as a disease will help change the way the medical community tackles this complex issue that affects approximately one in three Americans" [2] *- 2015*

"Obesity is a chronic disease, prevalent in both developed and developing countries, and affecting children as well as adults" [3]

"Obesity is a complex, multifactorial condition characterized by excess body fat. It must be viewed as a chronic disorder that essentially requires perpetual care, support, and followup. Obesity causes many other diseases, and it warrants recognition by health-care providers and payers." [1]

1. Mechanick JI et al. *Endocr Pract.* 2012;18:642–648. **2.** AMA position statement. At: http://www.ama-assn.org. Accessed Oct 2014. **3.** WHO. Obesity and overweight. At: http://www.who.int/dietphysicalactivity/media/en/gsfs_obesity.pdf. Accessed Aug 2018. **4.** US Food and Drug Administration. Federal Register. 2000;65(4):1000-1050.

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Obesity: Recognized as a Disease

"Obesity is a complex, multifactorial disease that develops from the interaction between genotype and the environment. Our understanding of how and why obesity occurs is incomplete; however, it involves the integration of social, behavioral, cultural, and physiological, metabolic, and genetic factors"- 1998

"Overweight and obesity are chronic diseases with behavioral origins that can be traced back to childhood"- 2013

"E66.9 Overweight or Obesity … conditions that my be a focus of clinical attention, affect the diagnosis, course, prognosis, or treatment of a patient's mental disorder" - 2013

Diagnostic And Statistical Manual Of Mental Disorders, Fifth Edition (2013);
Diagnostic and Statistical Manual of Mental Disorders, 4th Edition TR (2000)

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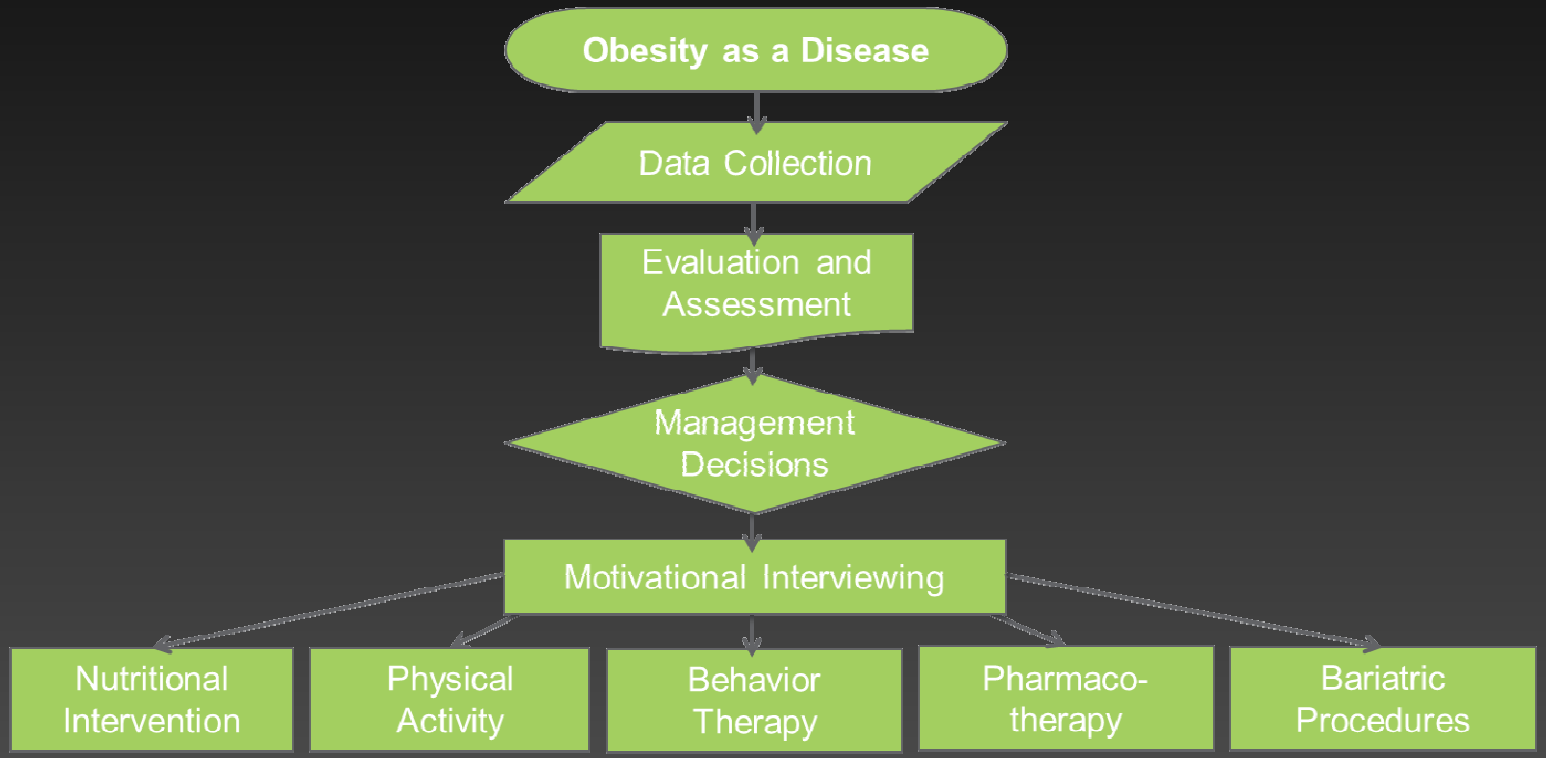
Obesity: Algorithm



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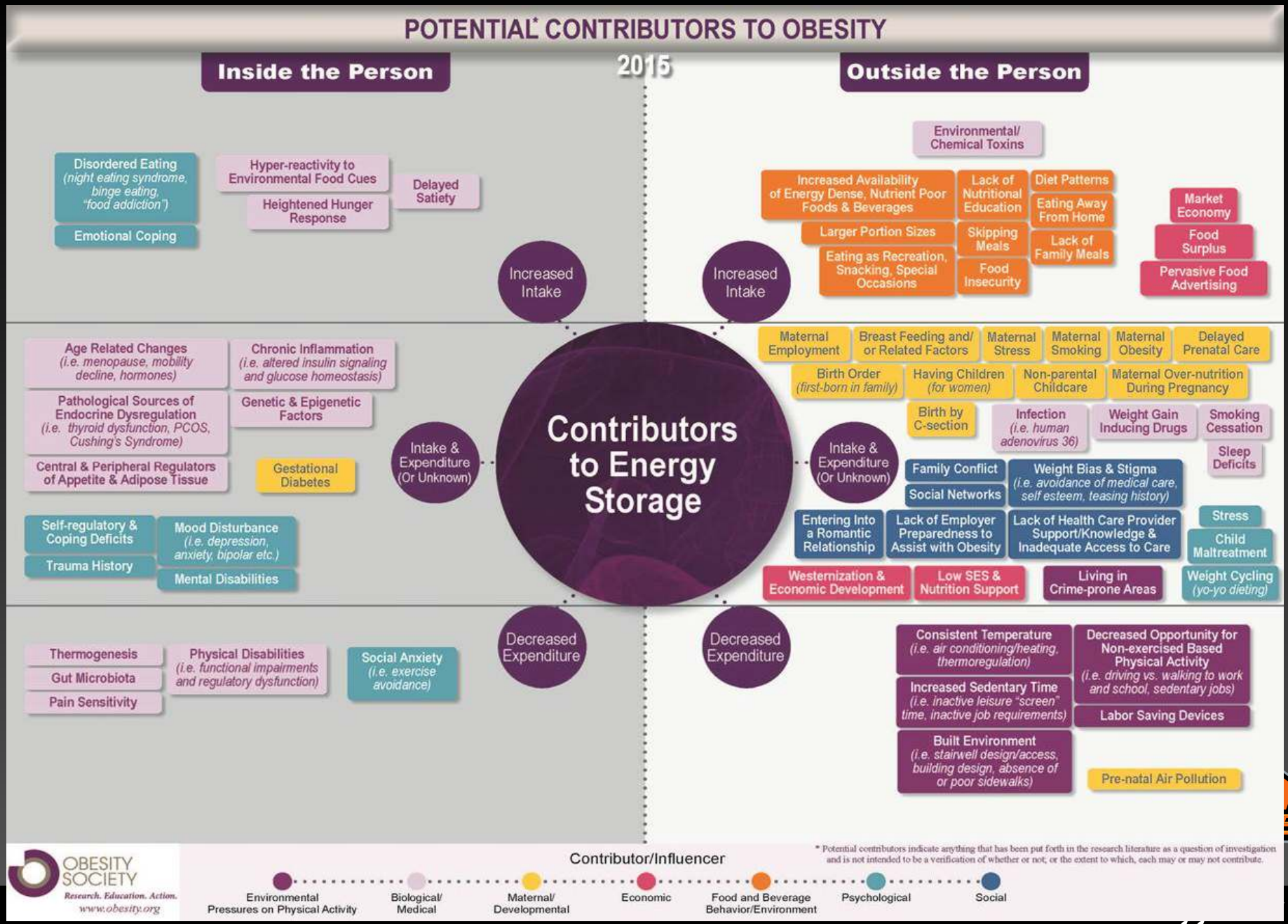
Obesity: Evaluation and Assessment

Comprehensive Evaluation of the Patient with Overweight/Obesity	
History	Weight history, past medical history, family history, social history, screening for weight-promoting medications, food intake, activity, review of systems
Physical Examination	Height, weight, blood pressure, body composition analysis, waist measurement, complete physical examination
Laboratory Tests*	Complete blood count, electrolytes, liver function, kidney function, fasting lipid profile, thyroid tests, hemoglobin A1c, uric acid, vitamin D
Diagnostic Testing*	EKG, echocardiogram, exercise stress test, sleep study, barium swallow or esophagoduodenoscopy
Psychiatric Examination	Rule out impulse control disorders, eating disorders, depression, anxiety etc.

Reference/s: [1]



http://tosconnect.obesity.org/obesity/resources/facts-about-obesity Accessed AUG 2018

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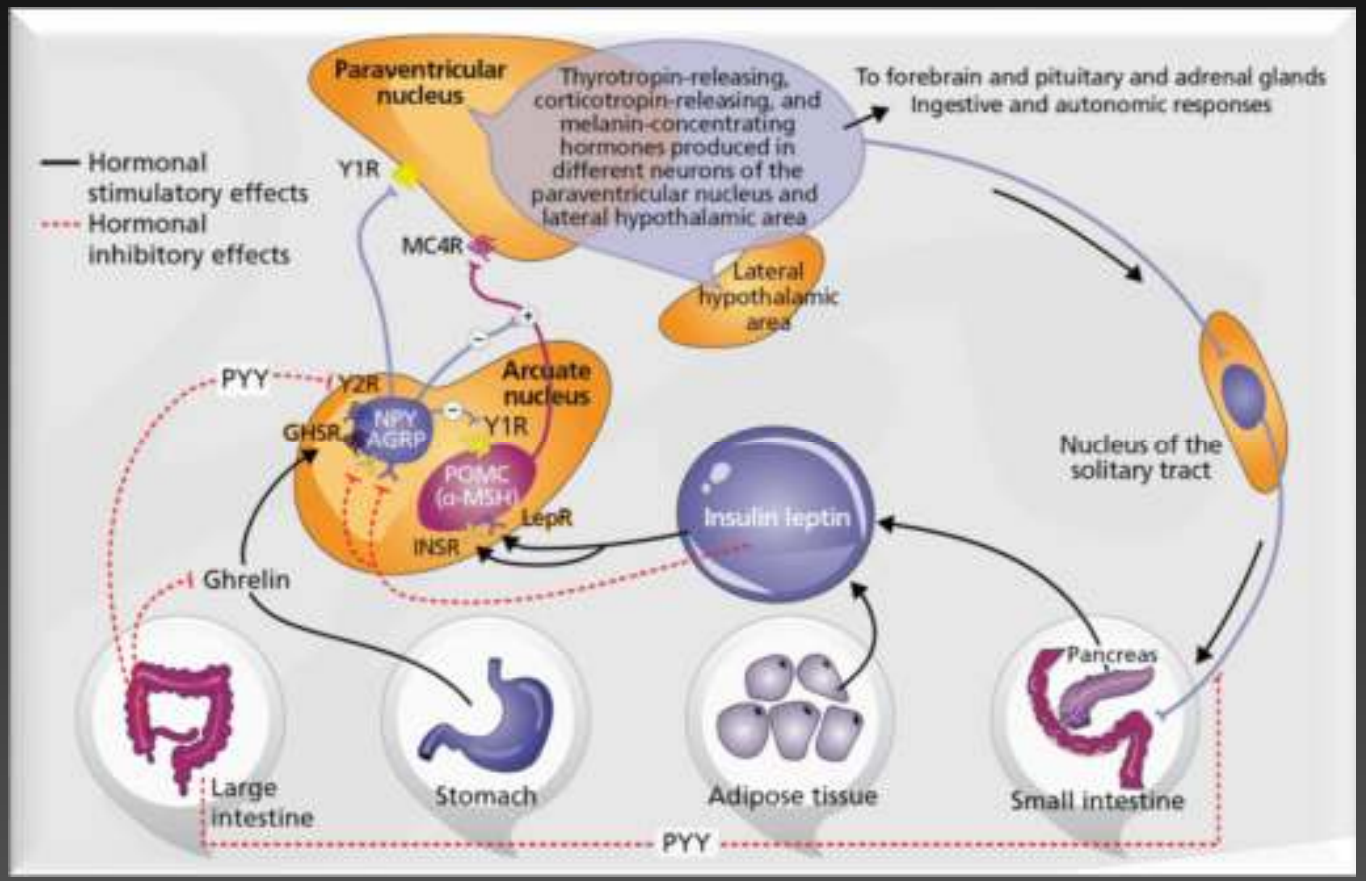
Obesity: Appetite Complexities



AGRP: agouti-related peptide; α-MSH: α-melanocyte-stimulating hormone; GHSR: growth hormone secretagogue receptor; INSR: insulin receptor; LepR: leptin receptor; MC4R: melanocortin-4 receptor; NPY: neuropeptide Y; POMC: proopiomelanocortin; PYY: peptide YY; Y1R; neuropeptide Y1 receptor; Y2R: neuropeptide Y2 receptor. Apovian CM, Aronne LJ, Bessesen D et al. *J Clin Endocrinol Metab*. 2015;100:342-362.

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Obesity: Neurobiology

- **I'm Satisfied** ☺
- LEPTIN
- CHOLECYSTOKININ
- PANCREATIC POLYPEPTIDE
- PP
- PEPTIDE TYROSINE-TYROSINE
- PYY
- OXYNTOMODULIN
- OXM
- GLP-1
- CCK

I'M HANGRY!

GHRELIN

OREXIN

Subramaniapillai M, McIntyre R: A review of the Neurobiology of Obesity and the Available Pharmacotherapies. CNS Spectrums (2017).

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I'M HANGRY!

- Low blood glucose levels (or other signals) excite the ARCUATE NUCLEUS in the hypothalamus

↑ **OREXIN** ↑ **GHRELIN**

- Stimulates hunger / food consumption behaviors / fat storage
- Decreases fat oxidation / energy expenditure
- Elevates DA in VTA / nucleus accumbens

Subramaniapillai M, McIntyre R: A review of the Neurobiology of Obesity and the Available Pharmacotherapies. CNS Spectrums (2017).

I'm Satisfied ☺

via my hypothalamus

- ADIPOSE tissues produce **LEPTIN** which signals the ARCUATE NUCLEUS in the hypothalamus

- **ADIPOSE**

LEPTIN

- Reduces hunger / food intake
- Increases fat oxidation / energy expenditure
- Decreases 35% DA in VTA /nucleus accumbens
  - Reduced amount and duration of food intake

Subramaniapillai M, McIntyre R: A review of the Neurobiology of Obesity and the Available Pharmacotherapies. CNS Spectrums (2017).

I'm Satisfied ☺

via my brainstem

- Food in the GI track triggers enteroendocrine cells to produce **CHOLECYSTOKININ (CCK)**
- Afferent VAGAL NERVES innervating the stomach and duodenum signal NUCLEUS TRACTUS SOLITARIUS (NTS) in the brainstem

- Aids in digestion
- Increases the sensation of fullness DURING a meal

Subramaniapillai M, McIntyre R: A review of the Neurobiology of Obesity and the Available Pharmacotherapies. CNS Spectrums (2017).

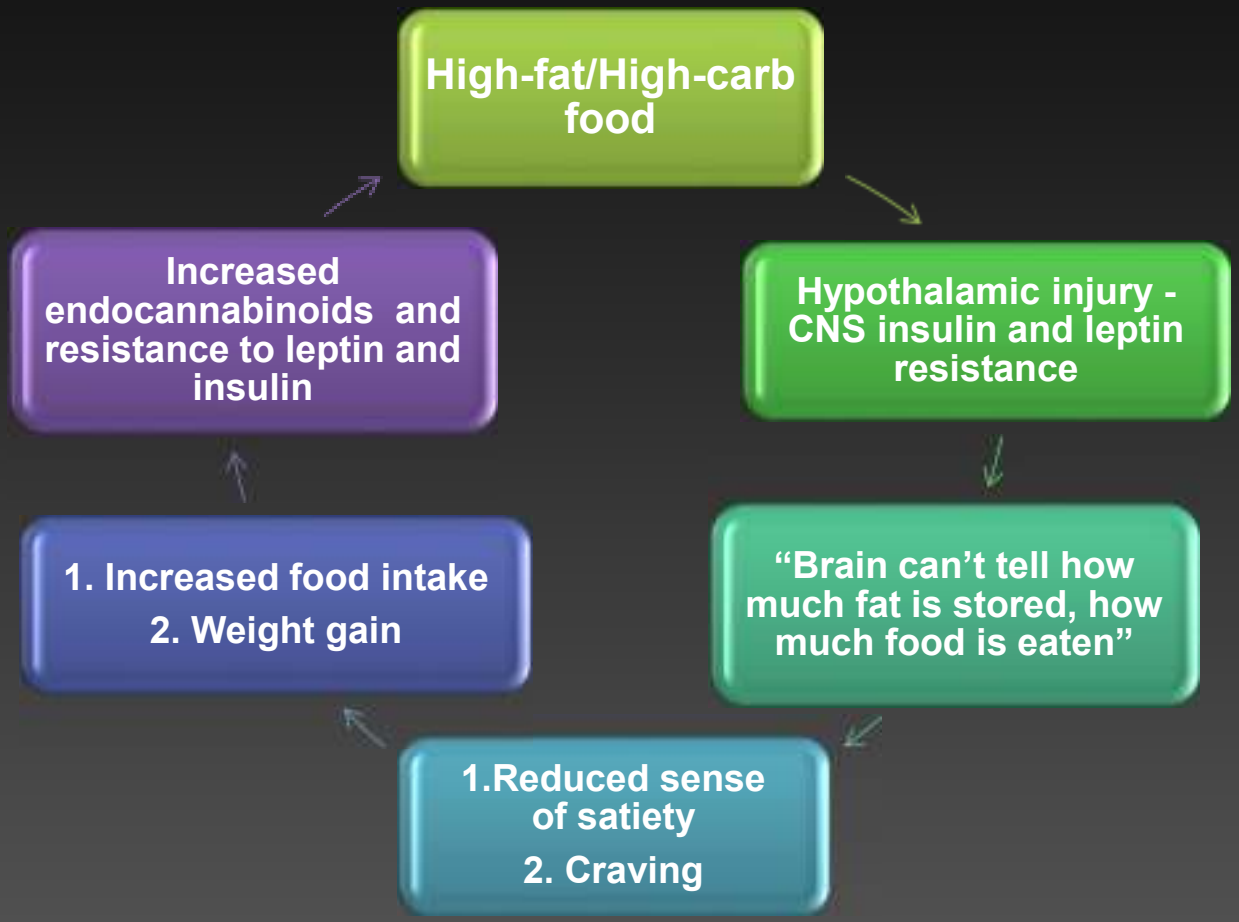
I'm Satisfied ☺

via my brainstem

- After a meal, **GLUCAGON-LIKE PEPTIDE-1 (GLP-1)** produced by enteroendocrine cells (intestine) and by the NTS (brainstem), which then encourages the release of INSULIN (pancreas)
- increases the feeling of fullness during and between meals by acting on appetite centers in the brain and by slowing the emptying of the stomach

Subramaniapillai M, McIntyre R: A review of the Neurobiology of Obesity and the Available Pharmacotherapies. CNS Spectrums (2017).

Obesity: Positive Feedback



Slide courtesy of Louis J. Aronne, MD. Wang J, Diabetes, 2001
DiMarzo V pers comm; Ozcan L, et al, *Cell Metabolism*; 2009

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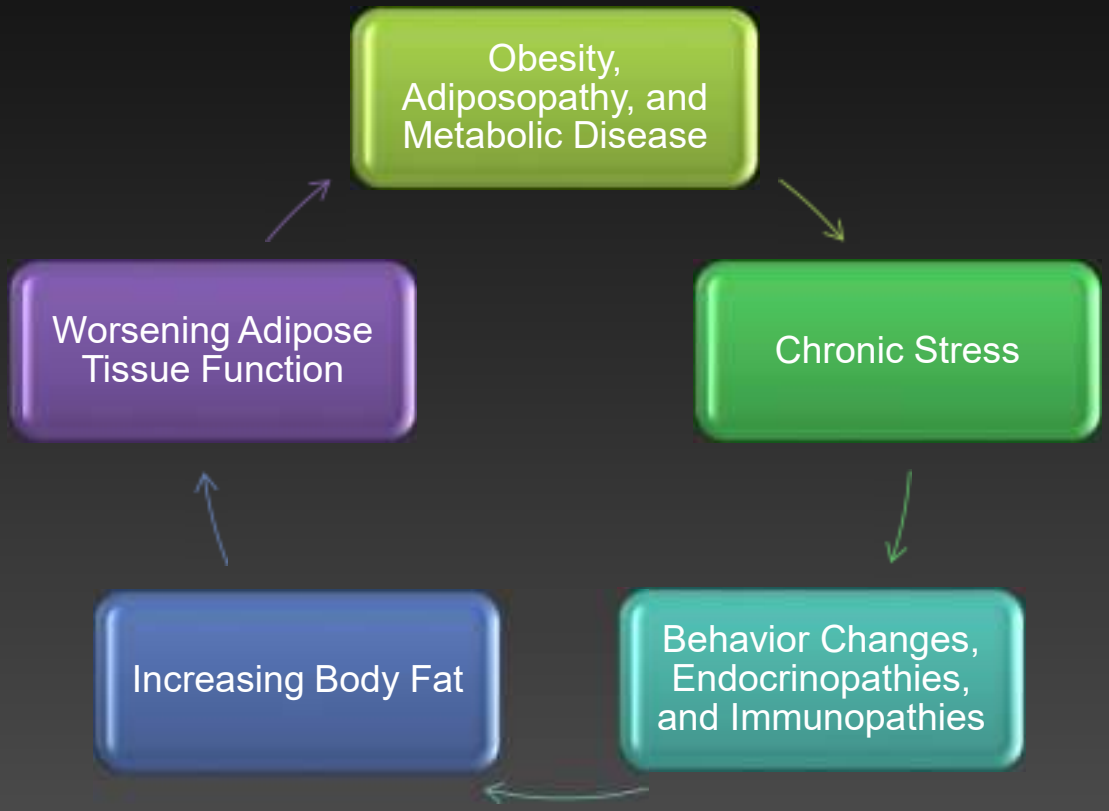
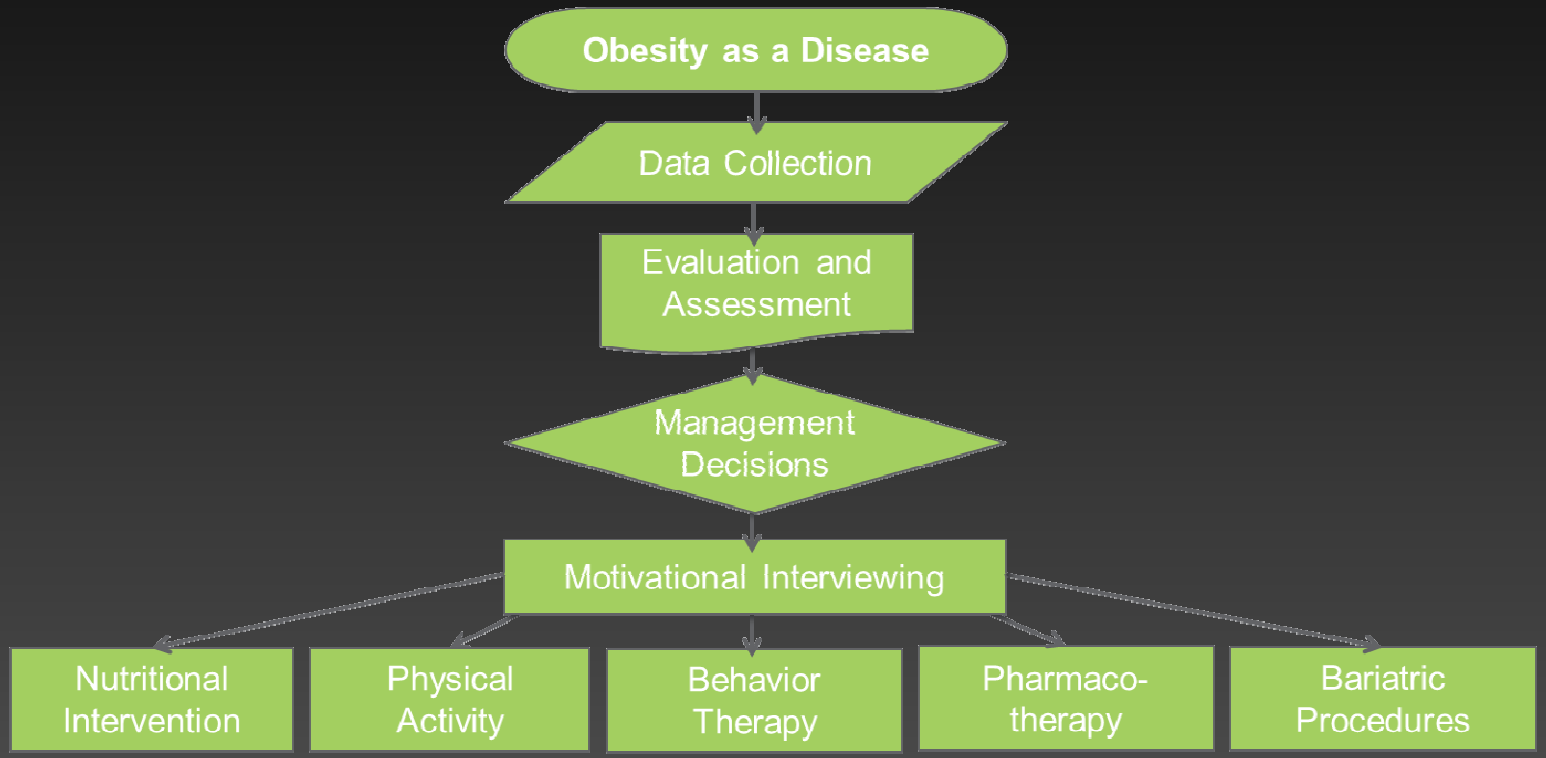
Obesity: Stress Cycle



Reference/s: [1]

Obesity: Algorithm



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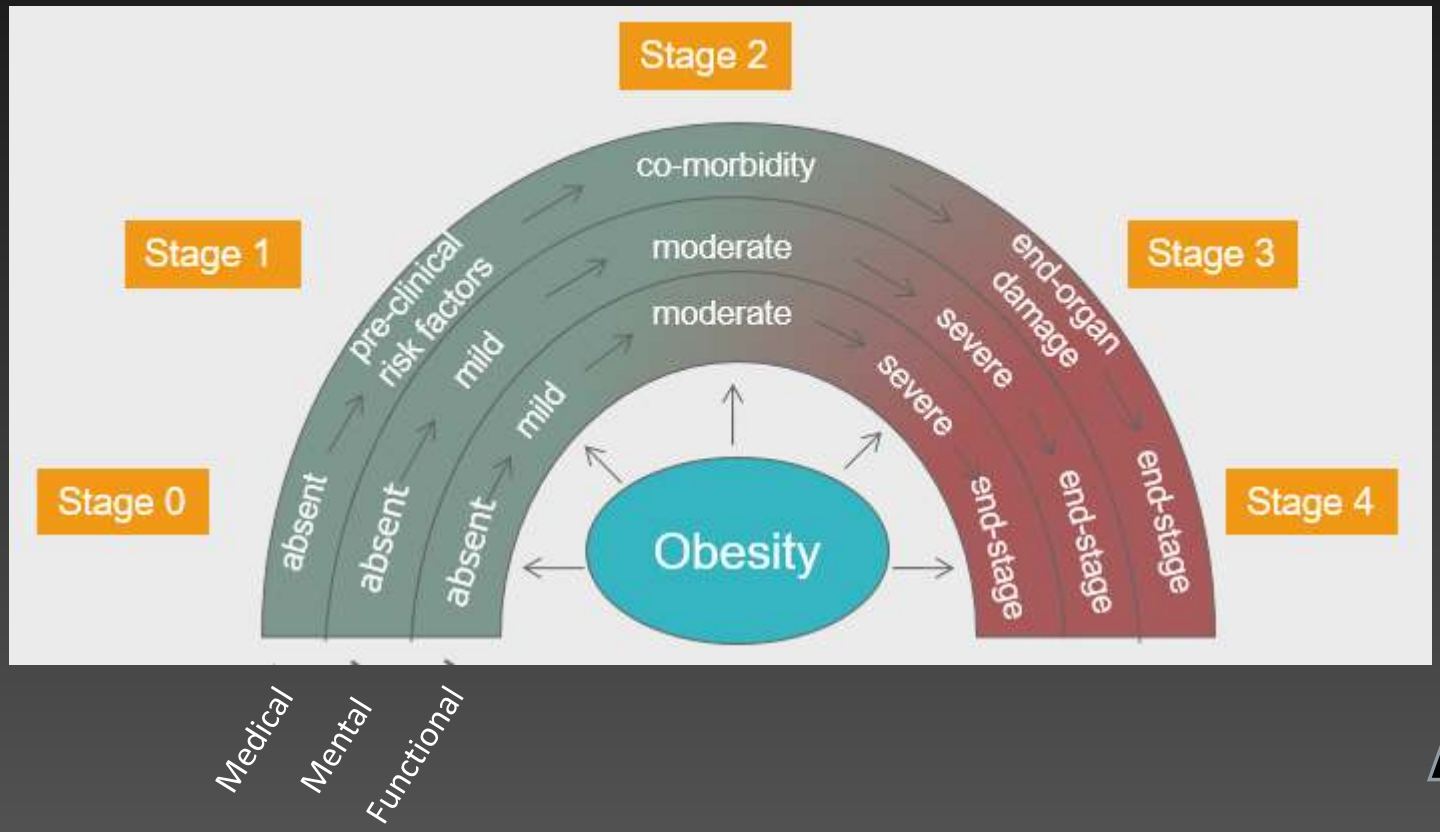
Obesity: Assessing RISK

Edmonton Obesity Staging System (EOSS)



Sharma AM et al. Int J Obes. 2009

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Obesity: Assessing RISK

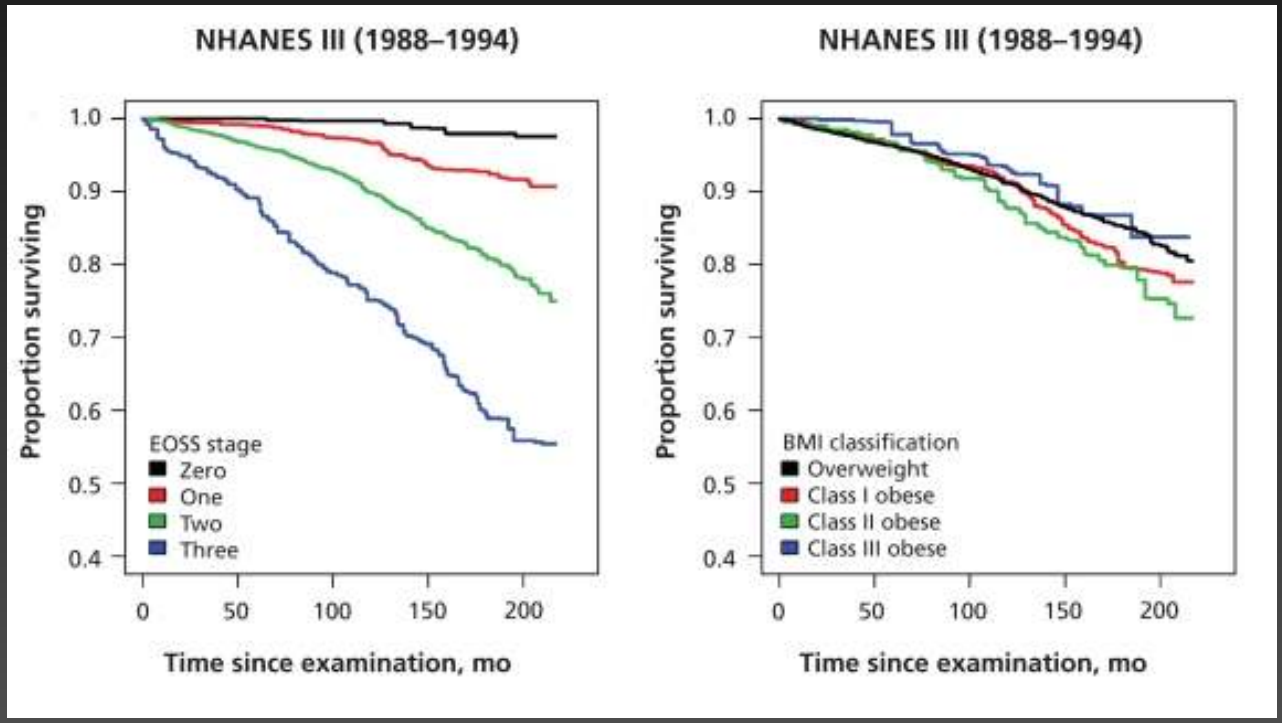
- Edmonton Obesity Staging System

0	No apparent risk factors (e.g., blood pressure, serum lipid and fasting glucose levels within normal range), physical symptoms, psychopathology, functional limitations and/or impairment of well-being related to obesity
1	Presence of obesity-related subclinical risk factors (e.g., borderline hypertension, impaired fasting glucose levels, elevated levels of liver enzymes), mild physical symptoms (e.g. dyspnea on moderate exertion, occasional aches and pains, fatigue), mild psychopathology, mild functional limitations and/or mild impairment of well-being
2	Presence of established obesity-related chronic disease (e.g., hypertension, type 2 diabetes, sleep apnea, osteoarthritis), moderate limitations in activities of daily living and/or well-being
3	Established end-organ damage such as myocardial infarction, heart failure, stroke, significant psychopathology, significant functional limitations and/or impairment of well-being
4	Severe (potentially end-stage) disabilities from obesity-related chronic diseases, severe disabling psychopathology, severe functional limitations and/or severe impairment of well-being

Sharma AM et al. Int J Obes. 2009

Obesity: Assessing RISK

- Edmonton Obesity Staging System



Sharma AM et al. Int J Obes. 2009

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Obesity: Comprehensive Treatment

Nutrition

Physical Activity

Behavior

Medication

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Obesity: Comprehensive Treatment

Body Mass Index (BMI)	18.5-24.9 kg/m²	25.0-29.9 kg/m²	≥30 kg/m²
Percent Body Fat	Male: <25% Female: <32%		Male: >25% Female: >32%
Waist Circumference	Male: <40 in. Female: <35 in.		Male: >40 in. Female: >35 in.
Edmonton Obesity Staging System	Stage 0, 1, 2, 3, 4		
No Obesity	**Overweight**	**Obesity** Class I: BMI 30.0-34.9 Class II: BMI 35-39.9 Class III: BMI ≥ 40.0	
Prevention	Primary care provider or dietitian		
	If treatment is ineffective, refer to an obesity medicine specialist.	Consider referring to an obesity medicine specialist.	

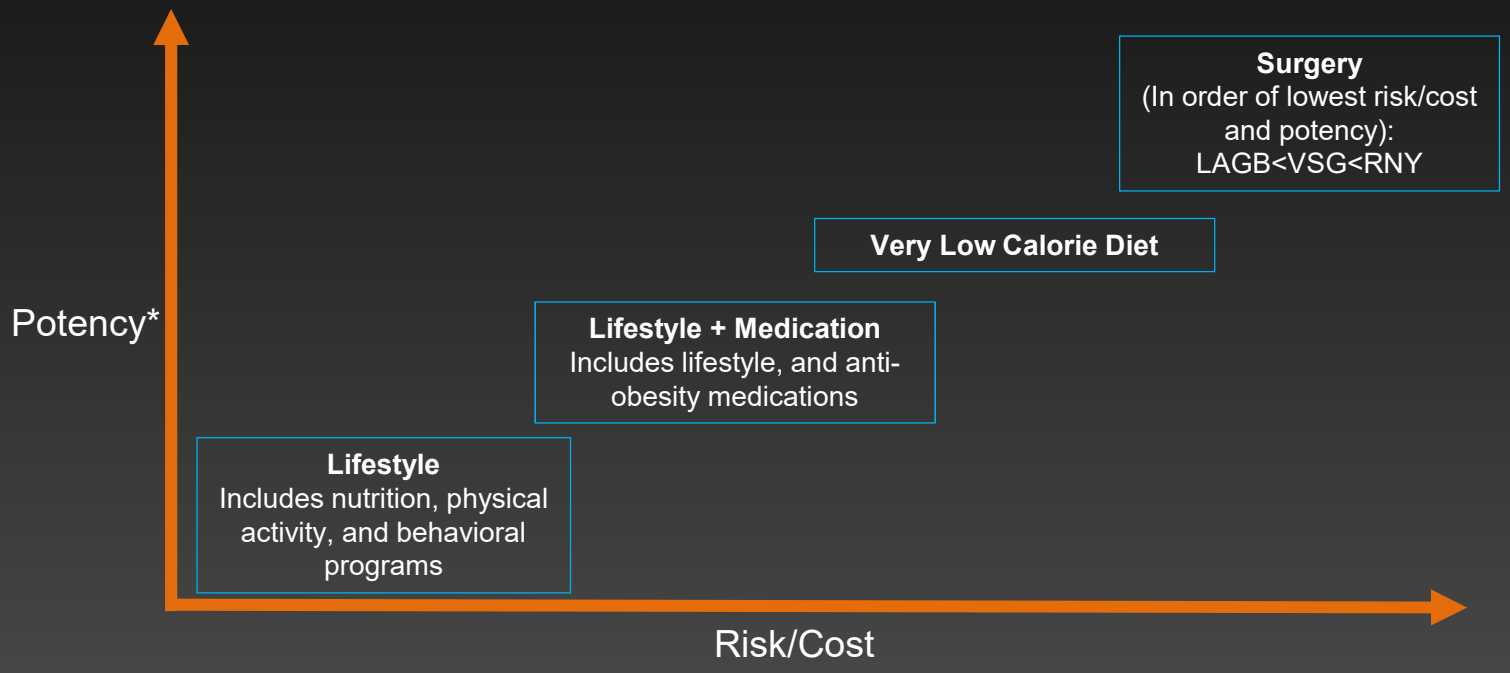
*If ineffective, consider referral to a metabolic and bariatric surgeon. Optimal pre- and post-operative care includes an obesity medicine specialist.

Obesity medicine specialists, certified by the American Board of Obesity Medicine, dedicate a portion or all of their practice to the treatment of obesity. They perform a medical evaluation (history, physical, laboratory, body composition) and provide medical supervision for lifestyle change (nutrition, activity, behavior change), medications, or very low-calorie diets. Obesity is a chronic medical disease and often requires lifelong treatment.

*lab and diagnostic testing should be individualized

Individualized Treatment Plans*	
Diet	Use calorie restriction, carbohydrate restriction, food journaling, very low-calorie diet programs
Activity	Give exercise prescription, use pedometers, limit TV and computer time, decrease sedentary time, initial goal of 150 minutes per week of moderate-intensity physical activity
Counseling	Eliminate provider bias and stigma, identify self-sabotage, develop strong support, address stress management, sleep optimization, other psychological support as needed
Pharmacotherapy	Use pharmacotherapy as part of a comprehensive program
Referral	Consider referral to an obesity medicine specialist

Obesity: Current Treatment

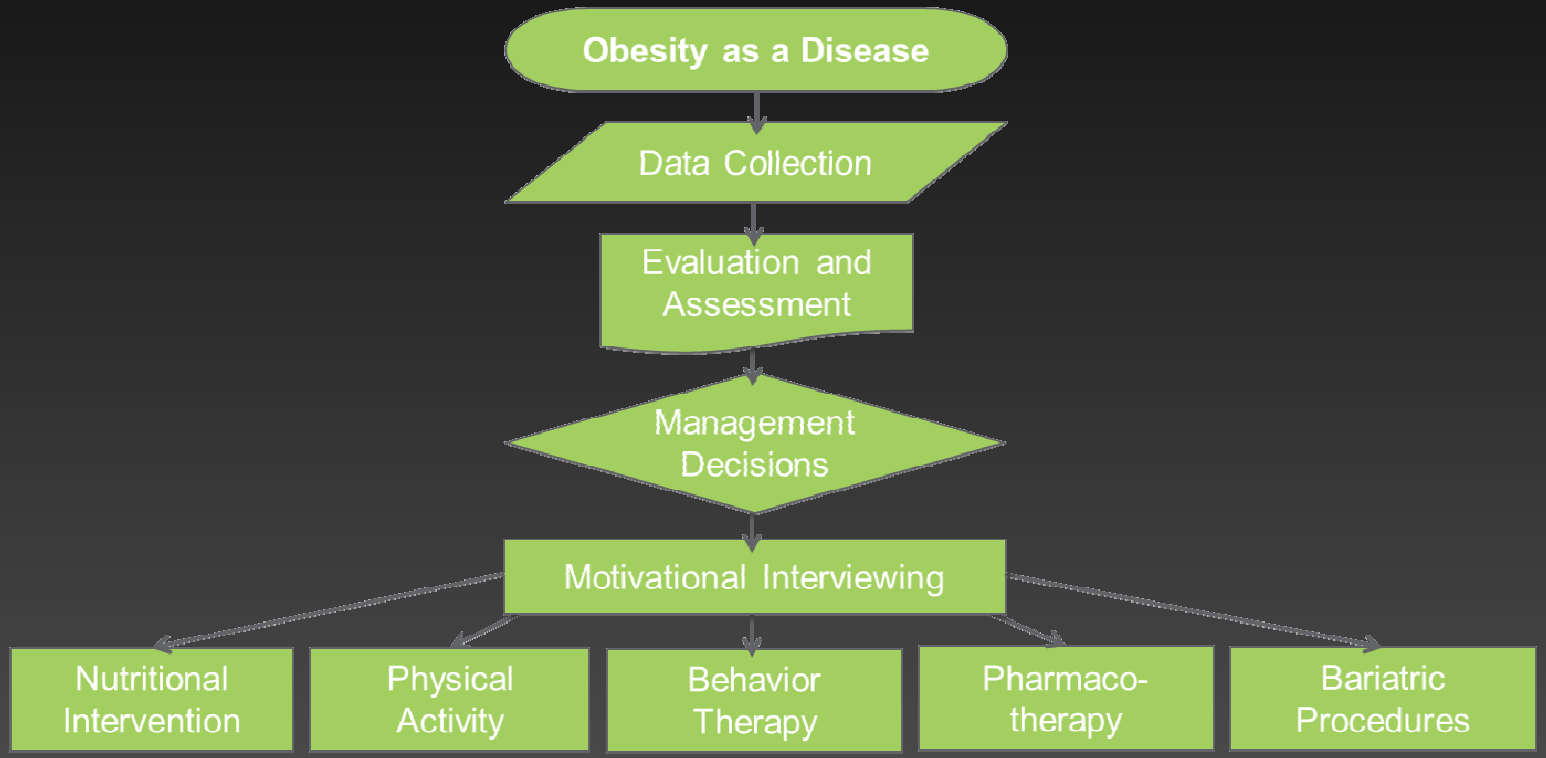


*Potency includes many factors, such as the amount, rate, and sustainability of weight loss, and the long-term resolution of adiposopathy and fat mass disease. Potency varies greatly for each individual (i.e., long-term adherence to a lifestyle program can be as potent as gastric bypass surgery).

Reference/s: [1]

Oklahoma State University Center for Health Sciences

Obesity: Algorithm



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Motivational Interviewing: Stages

Reference/s: [204] [205]

MI: Principles

- Express empathy
- Avoid argumentation
- Develop discrepancy
- Resolve ambivalence
- Support self-efficacy

MI Techniques: 5A's

Ask	• Ask for permission to discuss body weight. • Explore readiness for change.
Assess	• Assess BMI, waist circumference, and obesity stage. • Explore drivers and complications of excess weight.
Advise	• Advise the patient about the health risks of obesity, the benefits of modest weight loss (i.e., 5-10 percent), the need for long-term strategy, and treatment options.
Agree	• Agree on realistic weight-loss expectations, targets, behavioral changes, and specific details of the treatment plan.
Arrange/Assist	• Assist in identifying and addressing barriers; provide resources; assist in finding and consulting with appropriate providers; arrange regular follow up.

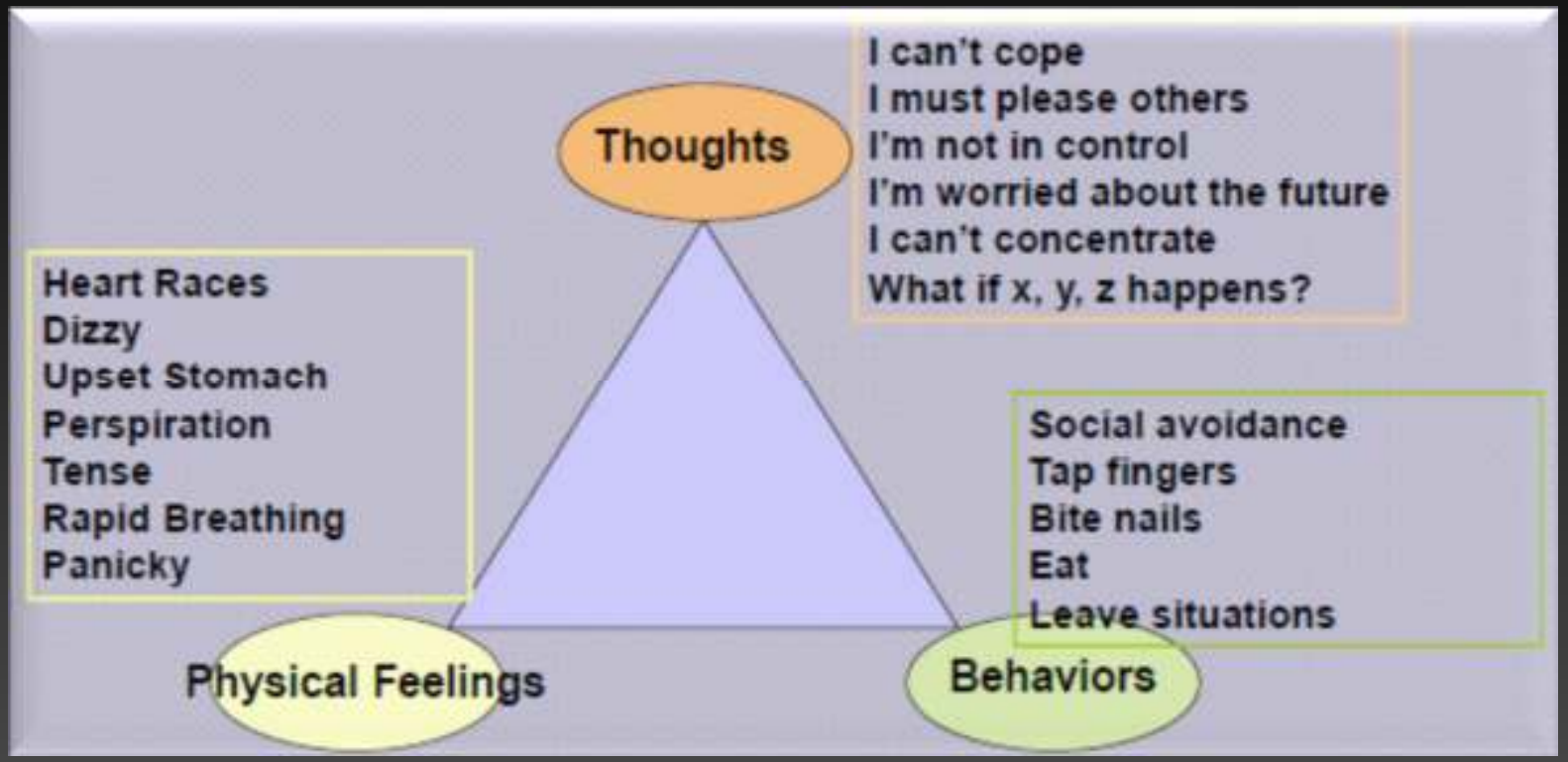
Reference/s: [226] [227]

MI Techniques: FRAMES

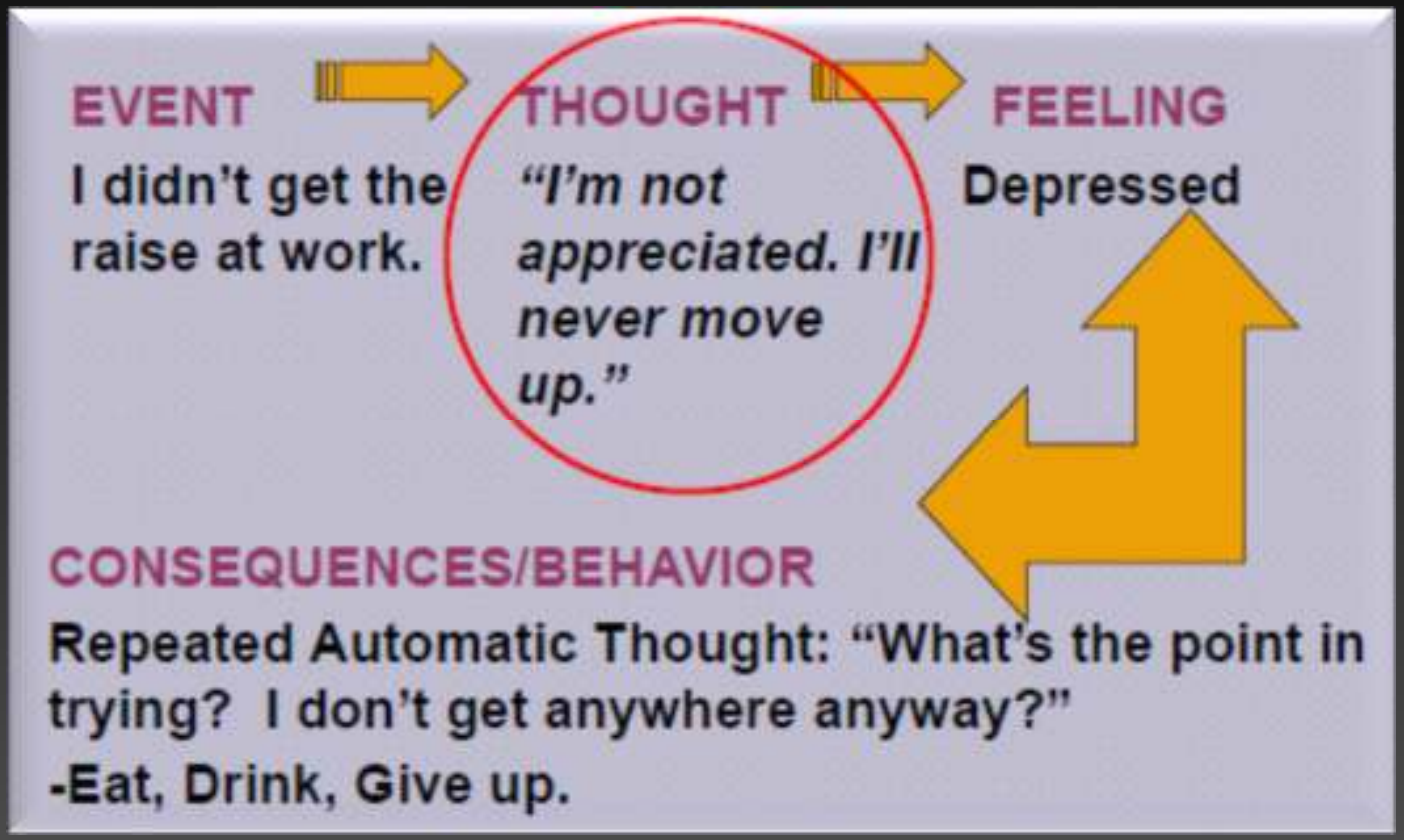
- Feedback about Personal Risk
- Responsibility of Patient
- Advice to Change
- Menu of Strategies
- Empathetic Style
- Self-efficacy

Reference/s: [228] [229]

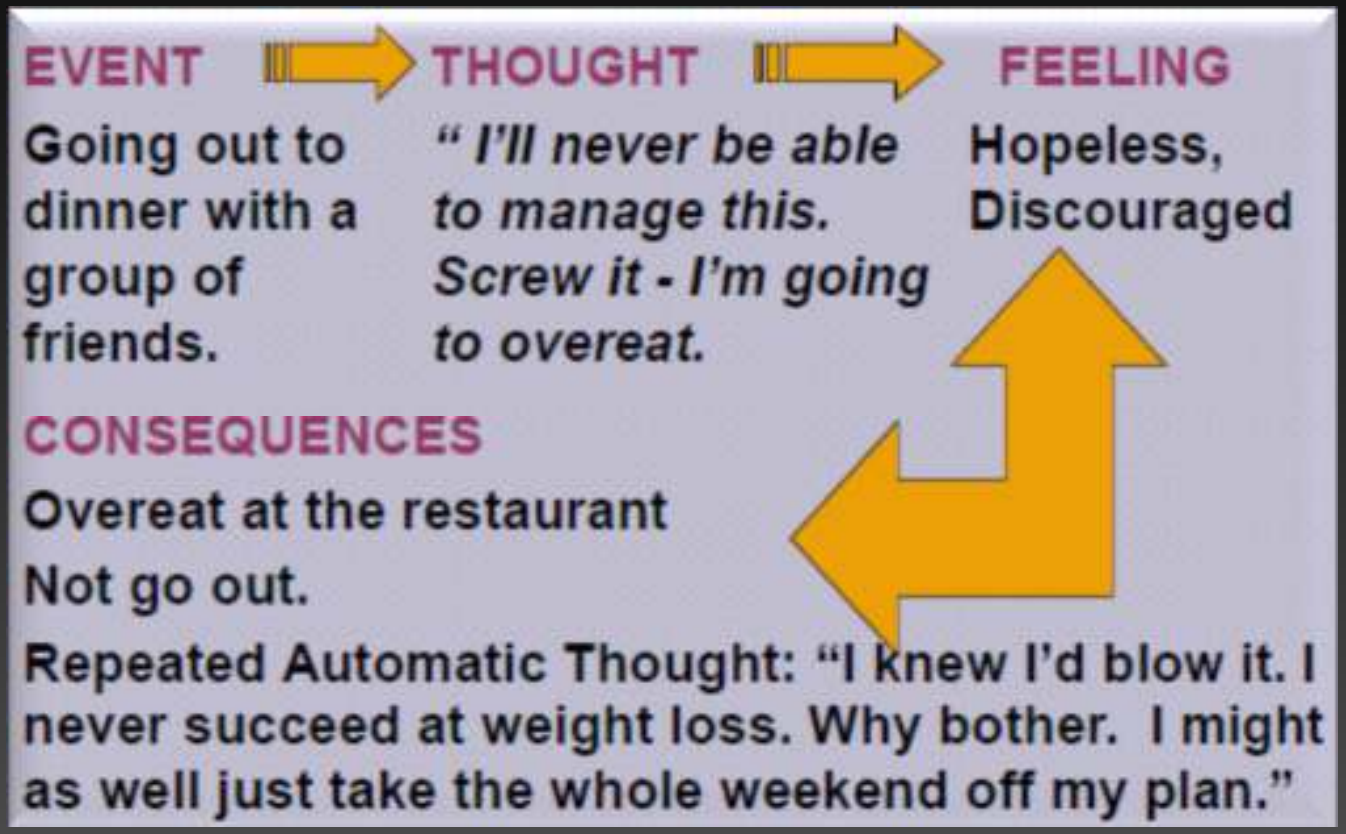
Obesity: Behavioral Modification



Obesity: Behavioral Modification



Obesity: Behavioral Modification



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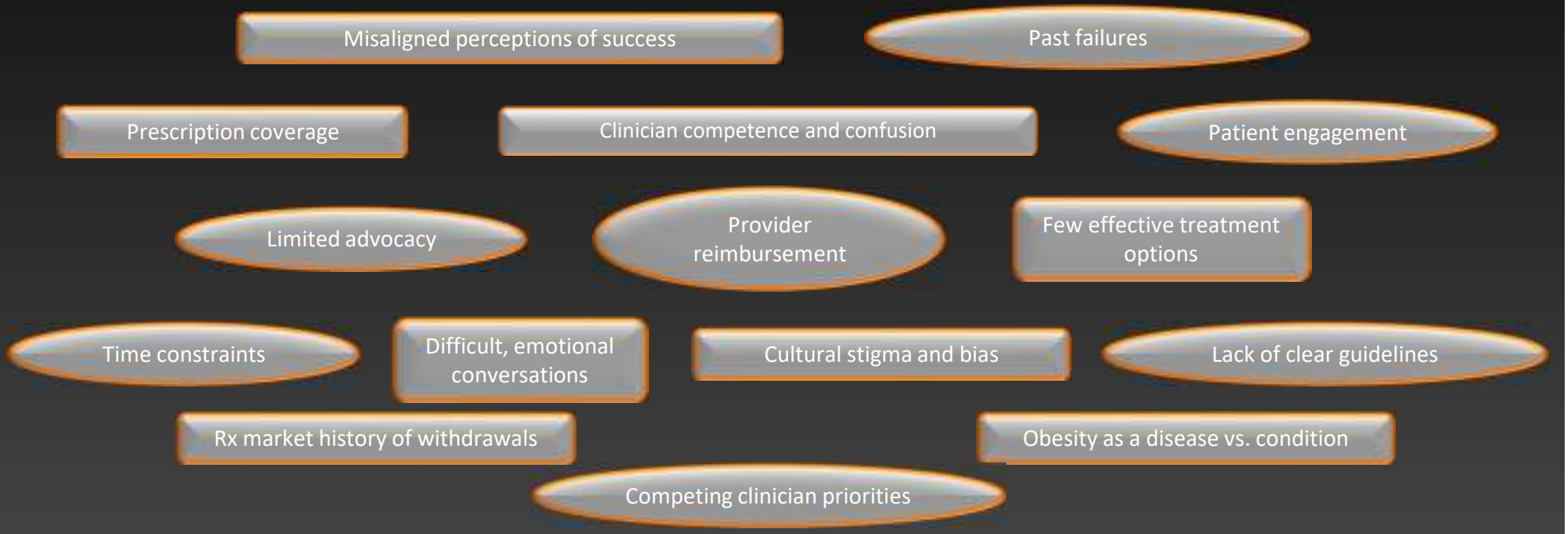
Obesity: Behavioral Modification

Challenging Cognitive Distortions:

1. What evidence supports this thought?
2. What evidence is against this thought?
3. What other thoughts, feelings, and behaviors does this thought provoke?
4. What kind of automatic thought is this?
5. Can you think of a more rationale thought?

Obesity: Barriers to Care



STOP Obesity Alliance. Available at: www.stopobesityalliance.org/wp-content/assets/2010/03/STOP-Obesity-Alliance-Primary-Care-Paper-FINAL.pdf. Forman-Hoffman V et al. *BMC Family Practice*. 2006;7:35.

Oklahoma State University

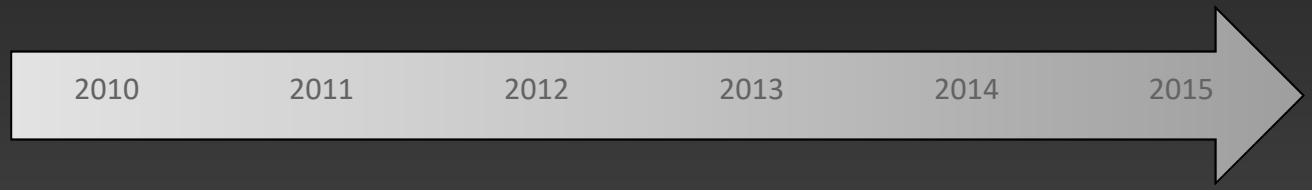
Center for Health Sciences

Obesity: Evolution of Reimbursement

Prior to 2012:
Behavioral therapy often outright excluded by most payers, as well as most other services. Bariatric surgery intermittently covered.

As of 2012:
Medicare and most private payers cover USPSTF-recommended screening and behavioral counseling when delivered by a primary care provider (not a specialist)

Going Forward:
Affordable Care Act (ACA) mandates coverage of screening and counseling. Coverage remains inconsistent in terms of number of visits and insurer guidelines.



Centers for Disease Control and Prevention. http://www.cdc.gov; Department of Health and Human Services Centers for Medicare and Medicaid. IBT for obesity. ICN 907800. January 2014.

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Endocrine Society: Indications for Medication

1. Patients with obesity (e.g., BMI ≥ 30kg/m2)

2. Patients who are overweight (e.g., BMI ≥ 27kg/m2) with presence of increased adiposity complications (e.g., type 2 diabetes mellitus, hypertension, dyslipidemia)

If no clinical improvement (≥5% loss) after 12 weeks with one anti-obesity medication, consider alternative anti-obesity medication or increasing anti-obesity medication dose (if applicable).

Apovian CM, et al. Pharmacological management of obesity: An Endocrine Society Clinical Practice Guidelines. J Clin Endocrinol Metab 2015;100(2):342-362.

Medication Therapy Options

Older options (≤1999):

- Phentermine (‘59)
- Diethylpropion (‘59)
- Benzphetamine (‘60)
- Phendimetrazine (‘76)
- Orlistat (‘99)

Newer options (≥2007):

- Orlistat OTC (‘07)
- Lorcaserin (‘12)
- Phentermine / topiramate ER (‘12)
- Naltrexone / bupropion ER (‘14)
- Liraglutide (‘14)

Bays HE, Seger, J, Primack C, Long J, Shah NN, Clark TW, McCarthy W. Obesity Algorithm, presented by the Obesity Medicine Association. www.obesityalgorithm.org. 2017-2018. www.obesityalgorithm.org (Accessed = 18 July 2018).

FDA Approvals

Medication	Short term weight loss (adults)	Obesity mgmt (adults)	Obesity mgmt (peds)
Phentermine (and others)	x		
Orlistat		x	x
Lorcaserin		x	
Phentermine/topiramate ER		x	
Naltrexone/bupropion ER		x	
Liraglutide		x	

Lexicomp, Inc. Accessed at http://www.uptodate.com on 7/2018.

Sympathomimetic Amines

- Phentermine, diethylpropion, phendimetrazine, benzphetamine
  - MOA: Sympathomimetic; stimulate the release of norepinephrine; reduce food intake causing early satiety; anorexiant
  - FDA Approved for SHORT TERM treatment of obesity (12 weeks)
- Efficacy (Phentermine): average loss is 6.4 - 7.4 kg
- Safety:
  - Palpitation, tachycardia, HTN, overstimulation, tremor, dizziness, insomnia, dysphoria, headache, dry mouth, dysgeusia, diarrhea, constipation, preg category X
  - DEA schedule: CIII or CIV

Lexicomp, Inc. Accessed at http://www.uptodate.com on 7/2018.
Bays HE, et al. Obesity Algorithm, presented by the Obesity Medicine Association. 2017-2018. (Accessed = 18 July 2018).
Hurren KM, Dunham MW. Obesity and Metabolic Syndrome. In: Dong BJ, Elliott DP, eds. Ambulatory Care Self-Assessment Program, 2014 Book 1. Endocrinology/Rheumatology. Lenexa, KS: American College of Clinical Pharmacy, 2014:72-84.

Orlistat

- Orlistat (Alli, Xenical) or Cetilistat (Phase 2 in US)
  - MOA: reversible inhibitor of gastric and pancreatic lipases; fat is not completely hydrolyzed and fecal fat excretion is increased; inhibits absorption by 30%
  - FDA approved for obesity management in adults AND children ≥ 12

- Efficacy: Absolute reduction = 3 kg after 1 year, 3.26 kg after 2 years

Lexicomp, Inc. Accessed at http://www.uptodate.com on 7/2018.
Bays HE, et al. Obesity Algorithm, presented by the Obesity Medicine Association. 2017-2018. (Accessed = 18 July 2018).
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Orlistat

- Safety
  - CI: pregnancy, chronic malabsorption syndrome, cholestasis
  - AE:
    - GI in 15-30% (intestinal borborygmi and cramps, flatus, fecal incontinence, oily spotting, flatus with discharge)
      - Avoid high-fat diets (no more than 30% fat)
    - Reduced absorption of vitamins A, D, E, K and beta-carotene
      - Give vitamin supplements to patients on orlistat
      - Separate dose by at least 2 hours from vitamins
    - Severe liver injury
    - Oxalate-induced kidney injury

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Lorcaserin

- Belviq, Belviq XR
  - MOA: Activates the 5-HT_{2C} receptors, stimulating POMC neurons, leading to increased alpha-melanocortin stimulating hormone release at melanocortin-4 receptors and resulting in satiety and reduced food intake
- Efficacy: 4.7-5.0 kg loss
  - Other benefits: improves TC, triglycerides, A1c
  - BLOOM and BLOSSOM studies
- Safety:
  - CI: pregnancy (category X)
  - AE: HA, URI, nasopharyngitis, dizziness, nausea, hypoglycemia (in DM pts); serotonin syndrome risk
  - DEA Schedule IV

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Phentermine / Topiramate ER

- Qsymia
  - MOA: sympathomimetic amine + appetite suppression/satiety
- Efficacy
  - ≥ 1 year = 10.2 kg (also improves TC, BP, LDL, TG, HDL, A1c)
- Safety
  - CI: pts with CVD, pregnancy, glaucoma, hyperthyroidism, MAO-I
  - AE (>10%): dry mouth, constipation, paresthesia, psych/cognitive AE, tachycardia, renal calculi, HA, insomnia, dysgeusia, dizziness
  - Drug Interactions: Oral contraceptives (irreg. bleeding), CNS depressants, non-potassium sparing diuretics (hypokalemia)
  - DEA Schedule IV

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Naltrexone / Bupropion ER

- Contrave 8mg/90mg (titrate up)
  - MOA: unknown; opioid antagonist + dopamine/norepinephrine reuptake inhibitor
  - Efficacious for patients with food addictions
- Efficacy: 4-5% weight loss (6.1 kg)
- Safety:
  - CI: chronic opioid use, uncontrolled HTN, SZ, bulimia/anorexia, MAO-I, linezolid, methylene blue, pregnancy
  - AE: HA, sleep disorder, nausea, vomiting, constipation, dry mouth, cardiovascular events (tachycardia, HTN), liver dysfunction, neuro/psych events
  - Pregnancy Category: X
  - Do not administer with a high-fat meal (increased levels)

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Liraglutide

- Saxenda: SubQ; D/C if <4% loss at 16 weeks
  - MOA: glucagon-like peptide-1 receptor agonist, delays gastric emptying, promotes satiety
- Efficacy: 2 – 4 kg (DM) and 4.8 – 8 kg (weight loss)
- Safety:
  - CI: pregnancy, thyroid tumor (hx or FH)
  - AE: nausea (37-47%), vomiting (12-16%), diarrhea, low blood sugar, anorexia, pancreatitis, gallbladder disease, renal impairment, suicidal thoughts, thyroid tumors
  - Delayed absorption of drugs requiring rapid absorption (i.e. pain meds, oral contraceptives)

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Hurren KM, Dunham MW. Obesity and Metabolic Syndrome. In: Dong BJ, Elliott DP, eds. Ambulatory Care Self-Assessment Program, 2014 Book 1. Endocrinology/Rheumatology. Lenexa, KS: American College of Clinical Pharmacy, 2014:72-84.

Efficacy and Safety

Less Weight Loss (2-3%)	Greater Weight Loss (>3-5%)	Robust Weight Loss (>5%)
Orlistat	Phentermine	Topiramate/ phentermine
	Naltrexone/ bupropion	

- Discontinuation of therapy leads to weight re-gain
- Long-term data (1-2 years)
  - Topiramate/phentermine
  - Lorcaserin
  - Orlistat
  - Naltrexone/bupropion
  - Liraglutide
- All are pregnancy category X

Apovian CM, et al. Pharmacological management of obesity: An Endocrine Society Clinical Practice Guidelines. J Clin Endocrinol Metab 2015;100(2):342-362.
Igel LI, et al. Practical use of pharmacotherapy for obesity. Gastroenterology 2017;152:1765-1779.

Patient Selection

- Phentermine:
  - Good Candidate: need appetite suppression
  - Poor Candidate: uncontrolled HTN, CAD, hyperthyroidism, glaucoma, anxiety, insomnia, sensitive to stimulants, drug abuse, on MAO-Is
- Orlistat:
  - Good Candidate: patients able to comply with low fat diets, hypercholesterolemia, constipation
  - Poor Candidate: malabsorption, GI upset/diarrhea, unable to modify fat content of diet
- Lorcaserin:
  - Good Candidate: patients who describe inadequate meal satiety
  - Poor Candidate: on concomitant serotonin modulating medications, known cardiac valvular disease

Igel LI, et al. Practical use of pharmacotherapy for obesity. Gastroenterology 2017;152:1765-1779.

Patient Selection

- Phentermine/topiramate:
  - Good Candidates: patients who would benefit from appetite suppression without cardiovascular history
  - Poor Candidates: uncontrolled HTN, CAD, hyperthyroidism, glaucoma, anxiety, insomnia, sensitive to stimulants, drug abuse, on MAO-Is, hx of nephrolithiasis
- Naltrexone/bupropion:
  - Good Candidate: concomitant depression, tobacco/alcohol use, food cravings
  - Poor Candidate: uncontrolled HTN, uncontrolled pain, recent MAO-I use, hx of seizures/predisposition to seizures
- Liraglutide:
  - Good Candidate: inadequate meal satiety and/or have Type 2 DM, prediabetes, or impaired glucose tolerance, psych patients
  - Poor Candidate: aversion to needles, hx of pancreatitis, hx or FH of medullary thyroid carcinoma, or multiple endocrine neoplasia syndrome type 2

Igel LI, et al. Practical use of pharmacotherapy for obesity. Gastroenterology 2017;152:1765-1779.

Therapeutic Challenge:

COST OF MEDICATIONS

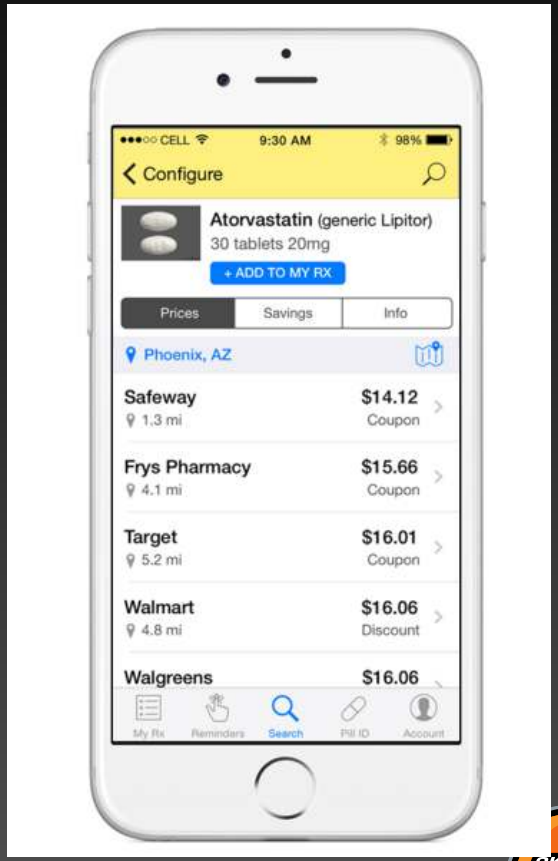
Brand or Generic?

Medication Name	Available as:
Phentermine	Brand and Generic, Rx
Orlistat	Brand only, Rx and OTC
Lorcaserin	Brand only, Rx only
Phentermine/topiramate ★	Brand only, Rx only
★ Naltrexone/bupropion ER ★	Brand only, Rx only
Liraglutide	Brand only, Rx only
Topiramate	Generic, Rx only
Bupropion ER	Generic, Rx only
Naltrexone	Generic, Rx only

Lexicomp, Inc. Accessed at http://www.uptodate.com on 7/2018.

Prescription Resources

- Medication discount cards and apps
  - GoodRx
- Patient Assistance Programs
  - http://www.needymeds.org
- Rx for Oklahoma
  - 1-800-879-6552



OKLAHOMA STATE UNIVERSITY
CENTER FOR HEALTH SCIENCES

Therapeutic Challenge:

WEIGHT EFFECTS OF MEDICATIONS

Antihyperglycemics

Weight Gain	Weight Loss/Neutral
Insulin	Metformin
Sulfonylureas	SGLT-2 inhibitors
Thiazolidinediones	GLP-1 receptor agonists
Meglitinides	Alpha-glucosidase inhibitors
	Amylin analogs
	DPP-4 inhibitors

MOST

LEAST

MOST

LEAST

If insulin is started in a patient with Type 2 DM, a weight loss/neutral medication should be added to mitigate weight gain.

Nathan DM, et al. Diabetes Care 2009; 32:193-203.
Apovian CM, et al. Pharmacological management of obesity: An Endocrine Society Clinical Practice Guidelines. J Clin Endocrinol Metab 2015;100(2):342-362.

Glucocorticoids

- Mechanisms
  - Cause increased appetite
  - Reduce leptin-modulated suppression of food intake through HPA axis and metabolism regulation
  - Dose related effects on glucose, protein and lipid metabolism

- How to minimize gain =
  - Use lowest dose for shortest time
  - Consider alternate day steroid therapy for those in need of long term treatment

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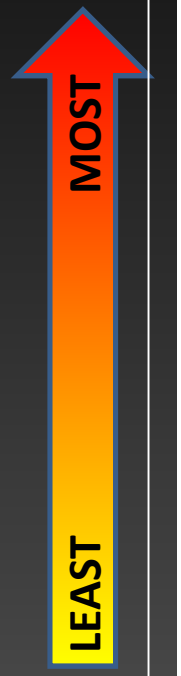
Antipsychotics

- Exact pathophysiology unknown
- Likely due to multiple neurotransmitters:
  - 5-HT_{2a}, 5-$HT_{2c,}$ Histamine H1, α1 and α2 adrenergic receptors
- Significant increase in appetite for nutrient dense foods
  - Potential impact on central feedback system
- Potential hyperprolactinemia induced weight gain

Weight gain:

Olanzapine
clozapine
quetiapine
risperidone
iloperidone
aripiprazole
ziprasidone



Bray GA, Ryan DH. Medical therapy for the patient with obesity. Circulation 2012; 125:1695.

Antidepressants

High Gain	Medium Gain	Low Gain/Neutral	Loss
Mirtazapine	Nortriptyline	Citalopram	Fluoxetine
Amitriptyline	Imipramine	Escitalopram	Bupropion
Doxepin	Clomipramine	Sertraline	
Trimipramine	Paroxetine	Fluvoxamine	
		Vortioxetine	
		Tranylcypromine	

Not enough information: venlafaxine, duloxetine

Himmerich H, et al. Endocr Metab Immune Disord Drug Targets 2015;15:252-260.
Gartlehner G, et al. Rockville, MD: Agency for Healthcare Research and Quality; 2011.
Fava M, et al. J Clin Psychiatry 2000;61(11):863-7.

Antiepileptic Drugs (AEDs)

Effect on Weight	Drugs
Gain 	Valproate, Gabapentin, Pregabalin, Carbamazepine
Neutral 	Lamotrigine, Levetiracetam, Phenytoin
Loss 	Felbamate, Topiramate, Zonisamide

Antihistamines

- Most weight gain with first generation
  - Diphenhydramine, chlorpheniramine, doxylamine
- MOA: Potentially due to reduced energy expenditure secondary to mild sedative effect, increased appetite
- Alternatives for:
  - Motion sickness: scopolamine
  - N/V: meclizine
  - Allergies: montelukast, nasal corticosteroids
  - Insomnia: melatonin, zolpidem

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Bray GA, Ryan DH. Medical therapy for the patient with obesity. Circulation 2012; 125:1695.

Hormonal Therapies

- Oral Contraceptives
  - No difference in weight gain vs. placebo
    - Gain: 0.5 kg
  - Systematic Review ruled out potential for higher degree of weight gain (small amount of gain not ruled out)
  - Risk of VTE increased in obese patient taking OCPs
- Others: Progestin, megestrol acetate

Reubinoff BE. Fertil Steril. 1995;63(3):516.
Maveda ER. J Womens Health (Larchmt) 2014;23(1):38–43.
Gallo MF. Cochrane Database Syst Rev. 2014.
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Abdollahi M, et. al. Thromb Haemost. 2003;89(3):493.

Other Medication Effects

Weight Gain Potential

- Lithium
- Beta-blockers
- Alpha-blockers
- Cannabinoids
- Antiretroviral therapy

Weight Loss Potential

- Levothyroxine
- Stimulants
- Testosterone

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Surgery

- Indicated as adjunct in patients with:

  1. BMI ≥ 35 kg/m2 with comorbidity or

  2. BMI > 40 kg/m2

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Pharmacotherapy Summary

- Pharmacotherapy should always be used as an adjunct to nutritional, behavioral, and exercise therapy
- Be cognizant of weight effects of medications.
  - Consider therapy modification if patient is obese.
- Discontinuation of therapy will result in weight regain
- Early response to medications is predictive of overall response.

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