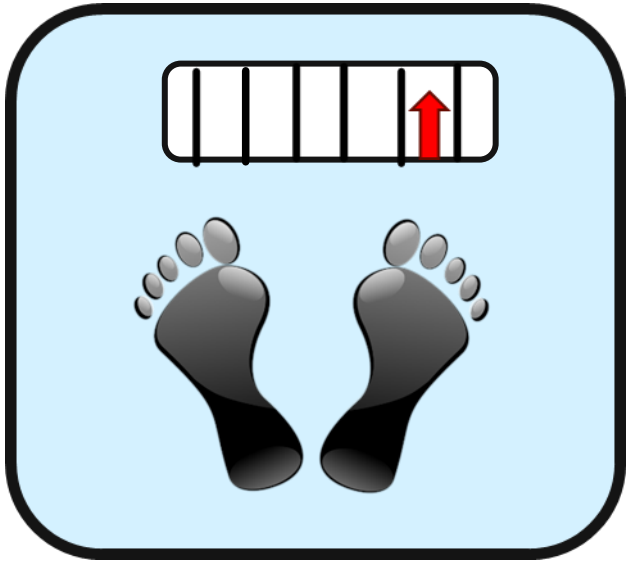
The ABCDs of Adiposity-Based Chronic Disease Management



Christine Kessler MN, ACCNS, ANP-BC, BC-ADM, FAANP
Metabolic Medicine Associates
Journey's Weight Loss

Class Objectives

1. **Accurately screen and appropriately apply differential diagnosis for earlier diagnosis and timely intervention of obesity and comorbidities.**

2. **Effectively assess and manage obesity as a chronic, serious, and progressive disease warranting early intervention and long-term care to minimize related comorbidities (e.g., like diabetes and cardiovascular disease)**

3. **Comprehensively manage obesity with both behavior and lifestyle modifications as well as the inclusion of pharmacotherapy, highlighting the safety and efficacy of available pharmacotherapy.**

- **A**pproach obesity & pre-obesity as a serious, progressive, metabolic disease *without bias*
- **B**ase adiposity management on a correct understanding of its complex, underlying etiology and pathophysiology
- **C**linical evaluation of adiposity must encompass behavior and biology
- **D**rugs and life-style interventions should be individualized and *begun as early as possible*

Approach obesity & pre-obesity as a serious, progressive metabolic disease without bias

What you NEED to know about Obesity & Pre-obesity (Overweight) before treating it

"Overeating does NOT cause obesity; Obesity causes overeating!." -- Lee Kaplan, MD

Obesity is *a chronic, progressive, relapsing* & treatable multi-factorial, neurobehavioral, *(inflammatory)* disease:

Delayed intervention causes biological and anatomical abnormalities at both *organ* and *cellular* levels, *leading to metabolic disease, morbidities, reduced quality of life, and early mortality*

Obesity is the 5th leading cause of death in this country

There is no cure!

N Engl J Med. 2017;376(15):1492

What you NEED to know about Obesity & Pre-obesity (Overweight)

Before treating it

Obesity & pre-obesity are NOT due to a character flaw

Adiposity is not simply about willpower
or
A psychological / moral failing
or
Merely a lifestyle choice

Such beliefs create *bias* (medical, social, personal; *intentional or unintentional*)— that can cause **medical inertia & impede prompt and effective treatment**
(HCP bias leads to worse patient outcomes)

The disease of Obesity **(adiposity)** is not simply about numbers on a scale!

FYI: Weight bias is the fourth most common discrimination (behind race, gender, age)

Y Puhl M et al. Clin Diabetes 2016;34:44–50

The Incidence of Obesity & Pre-obesity

The MOST Common Chronic Disease in America

Change in Obesity Rates in adults:

Pixaby.com

Current State of American's Weight

Over 75% adults have unhealthy excess weight (obesity & pre-obesity)

Obesity:

Highest in women: non-Hispanic blacks (49.6%) & Hispanics (44.8%)

1 in 6 children clinically obese (19.3%)

Prevalence higher in the South & Mid-West

Those with obesity were three times likely to develop T2DM vs without obesity compared (20% vs. 7.3%, respectively).

It is estimated that by 2030 > 50% of the adult population will be obese

The obesity phenotype is NOT going away!

Folks, this is the REAL pandemic

http://stateofobesity.org/rates (accessed 5/2/2023

https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf. (Accessed 3/18/2023)

What is the etiology of Obesity (adiposity)?

- **It is caused by genetic, epigenetic/environmental, behavioral influences**
- Primarily *polygenetic influence* vs monogenetic

- **Environmental & epigenetic influences include;**
  - **Endocrine disrupting chemicals** (EDCs)
  - **Impaired sleep** *(hypercortisolism)*
  - **Stress**, *(emotional, physical, environmental, intrauterine)*
  - **Evening chronotype** *(an **"owl"** vs a "**lark**")*
  - **Poor diet** *(calorie-dense, ultra-processed, food insecurity, eating disorders)*
  - **Obesogenic drugs** (selected BB, SSRIs, SSNRI, psychotropic, antihistamines etc)
  - ***All the above can cause microbiome dysbiosis***

This can result in increased & dysfunctional fat mass that the body defends.

Fall et al. Gastroenterology 2017;152(7):1695–706
N Engl J Med. 2017;376(15):1492: J Am Coll Cardio, 2018:71, 69-84 ; o
OMA: obesitymedicine.org

Base adiposity management on a correct understanding of its underlying, complex etiology and pathophysiology

What is the underlying pathogenesis of obesity?

A *dysfunction* within the Brain that leads to:

- **Impaired appetite regulation within the brain.** (Think of this as a *brain disease*)

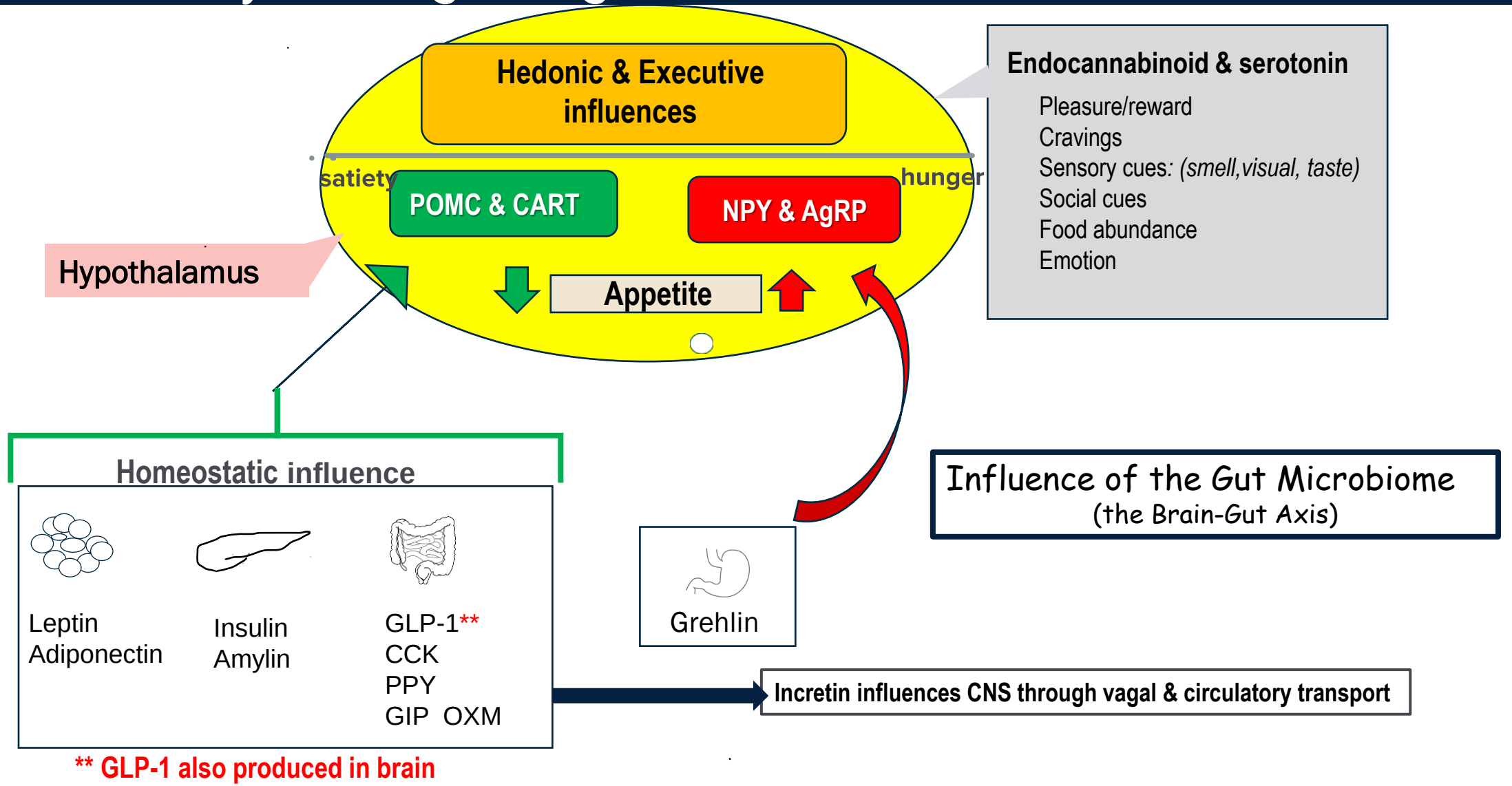
The brain controls eating behaviors (caloric/energy intake)

Homeostatic eating (eating for necessary energy--hunger)
Hedonic eating (eating for pleasure)
Executive eating (deciding to eat)

- **Abnormal growth, capacity, and function of adipose tissue**
  - **Fat mass stores energy– and has immunologic & endocrine function**

N Engl J Med. 2017;376(15):1492

Satiety & hunger regulation in the brain



Kessler C. Nurs Clin North Am. 2021 Dec;56(4):465-478; J Am Assoc Nurse Pract. 2017;29:S15-S29

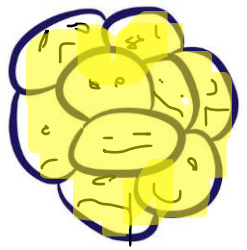
What goes wrong with fat mass?

In a person with increased adiposity risk:

- *Impaired* appetite regulation (with increased caloric consumption)
- *Overwhelmed* subcutaneous fat storage (SAT) capacity (no more room for energy storage)
- *Overflow* energy storage in peripheral adipose tissue (with adipogenesis/ hyperplasia)
- Energy overflow into ectopic, intra- & peri-organ fat tissue deposition (VAT) (with adipocyte hypertrophy …highly inflammatory adipose tissue)

Visceral fat (abdominal organs, liver, pancreas, heart, kidney, muscle, perivascular, etc)

Dysfunctional Fat



Adiposopathy (Sick fat): leads to metabolic disorders

Due to ***hypertrophic, pathogenic adipocytes*** (VAT, *ectopic fat*) leading to inflammation and increased free fatty acids (causing insulin resistance & beta cell failure ➡ T2DM & CVD)

Fat Mass Disease (FMD): leads to high mechanical forces

Due to ***increased weight*** or fat mass effect, (i.e, osteoarthritis, GERD, etc.)

Both lead to~230 complications & mortality risk

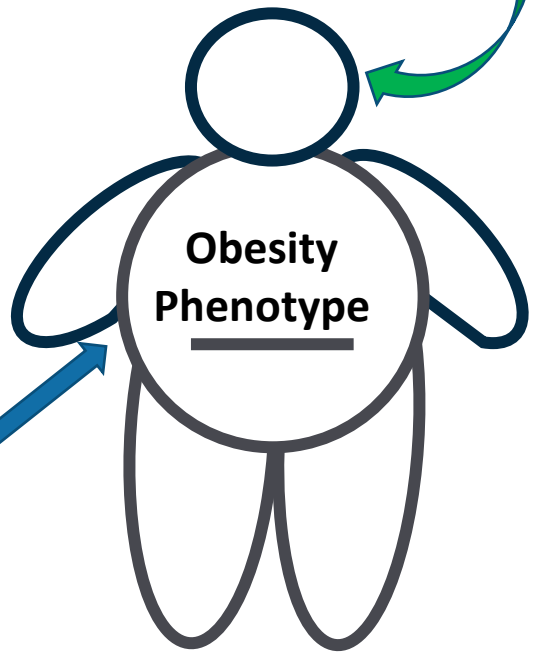
Kessler C. Nurs Clin North Am. 2021 Dec;56(4):465-478

OBESITY RISK → FAT MASS DYSFUNCTION → ADIPOSITY-BASED COMPLICATIONS

Environmental Influences

Diet
Sleep
Physical activity
Circadian rhythm
Endocrine Disrupting Chemicals (EDCs)
Drugs
Stress
Infection (adenovirus)
Intrauterine impact

Epigenetic changes



Inherited Obesity Risk Genes (Genotype)

Cardio-metabolic
-High blood pressure
-Dyslipidemia
-Heart attack
-Heart failure
-Insulin resistance
-Type 2 diabetes
-Hypothyroidism
CKD

Neuro-psychological
-Early dementia
-Pseudotumor cerebri
-Stroke
-Depression, Anxiety
-Eating Disorders

Pulmonary
-Obstructive sleep apnea
-Hypoventilation syndrome
-Asthma

Reproductive
-Infertility, PCOS
-Erectile dysfunction

Vascular
-Ankle swelling

Gastrointestinal
-Fatty liver disease
-Cirrhosis
-Gallstones
-Reflux disease

Musculoskeletal
Osteoarthritis
Joint and back pain

Cancer
-Breast -Kidney
-Uterine -Prostate
-Cervix -Thyroid
-Colon -Esophagus
-Pancreas -Stomach
-Bladder -Lymphoma

Many others…

Kessler C. Nurs Clin North Am. 2021 Dec;56(4):465-478.

Does the location of increased fat mass matter?

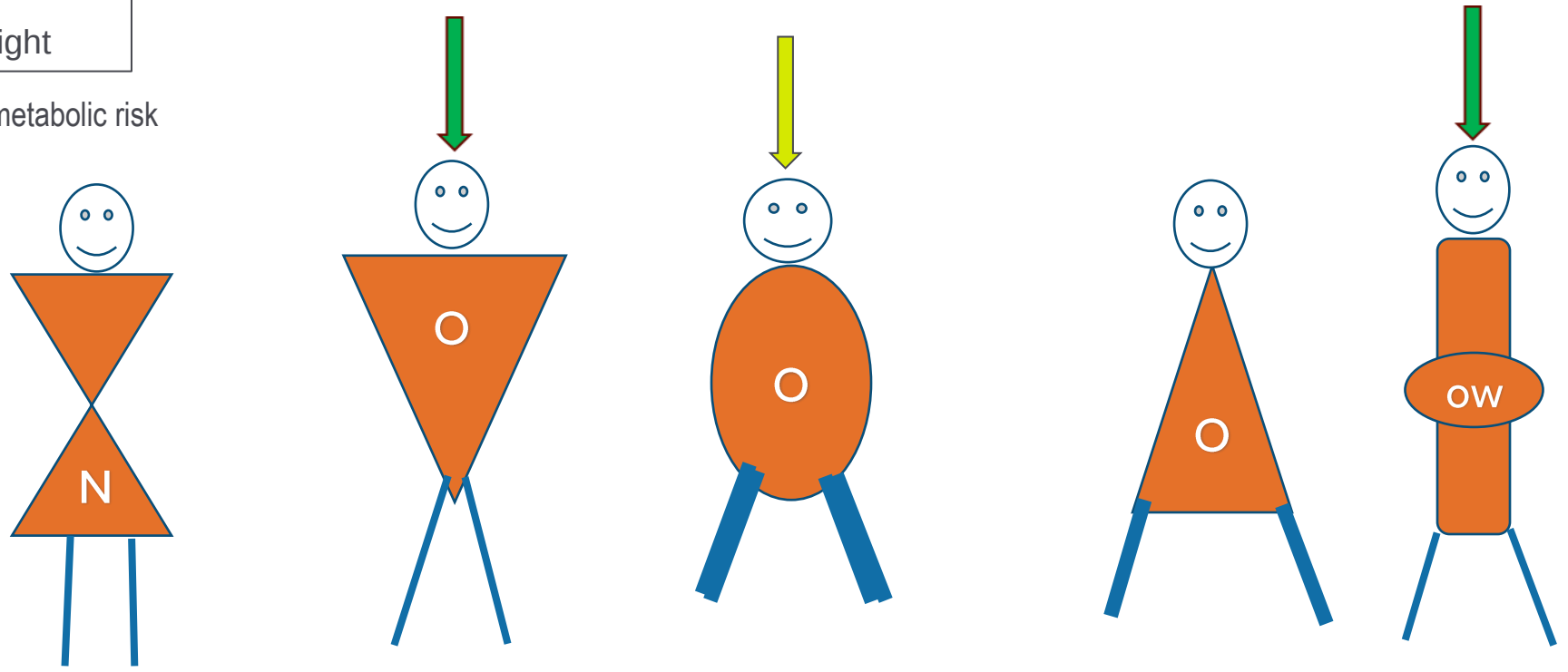
(SAT vs Ectopic/Visceral adipose tissue)

SAT is hyperplasia growth, not inflammatory, does not promote IR

VAT is hypertrophic growth, inflammatory, increases IR, and morbidities

N – Normal weight
O – Obese
OW- Overweight

Higher metabolic risk



What about metabolically healthy obesity (MHO) & health risks?

What about sarcopenic obesity?

JNCI: Journal of the National Cancer Institute, Volume 115, Issue 4, April 2023, Pages 456–467; *Front Nutr.* 2022 Feb 15;9:804719.

(copyrighted: Image created by C. Kessler)

Clinical evaluation of adiposity should encompass behavior and biology

Weight Loss Assessment priorities

HISTORY

Weight gain/loss trends (i.e., yo-yo…)
Dietary trends: what, how much, when
SLEEP* & *Stressors
Medications (weight-inducing drugs *and birth control pills!*)

Activity levels

Related morbidities

- Sleep quality, sleep apnea
- **CV risk (HTN, high lipids)**
- **NAFLD (MASLD)**
- **T2 diabetes**
- Depression
- Hypothyroidism
- infertility

AGE

LAB & PHYSICAL BIOMARKERS

Labs

- CBC, Chemistry, (note **GFR, UCAR & LFTs**)
- Lipids (esp **triglycerides**), (assess insulin resistance?)
- **TSH**
- **A1C**
- Vitamin D
- Uric acid????

Exam

- BMI
- Waist circumference for patients w/ BMI >25
  - >35 inches for women & >40 inches for men
- Blood pressure (and other CV risk factors)

Endocr Pract 2016;22 Suppl 3:1-203

Body Mass Index (BMI): a "Vital Sign," *not* Diagnostic

Important screening too of patient's level of obesity

$$BMI = \frac{\text{weight (kg)}}{\text{height (m}^2\text{)}}$$

Limitation:

- Represents excess weight and body size *regardless of fat: muscle:fat ratio or gender*
- More accurate measurements across populations than individuals

Classification	BMI (kg/m^2)	
	International classification[1]	Asian/Arab/ European population
Underweight	<18.5	
Normal range	≥18.5 and <25	≥18 and <23
Pre-obesity*	≥25 and <30	≥23 and <25
Obesity	≥30	>25

FYI: there is a 30% increase in mortality is associated with **every 5 BMI point increase** above a BMI of 25

Weir CB, Jan A. BMI Classification Percentile And Cut Off Points. [Updated 2023 Jun 26]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023

Obesity classification*

Waist circumference (WC) measures central obesity predicting visceral fat content and metabolic risk independent of BMI. Both BMI and WC should be evaluated

Found to be better identifying cardiometabolic risk than BMI

The threshold for WC depends on race and ethnicity

Classification	BMI (kg/m^2)	Disease risk relative to normal weight[3]	
		Men ≤40 in Women ≤35 in	Men >40 in Women >35 in
Pre-obesity*	≥25 and <30	Increased	High
Obesity	>30	High	High
Obesity class I	≥30 and <35	High	Very high
Obesity class II	≥35 and <40	Very high	Very high
Obesity class III	≥40	Extremely high	Extremely high

*These values are based for Caucasian individuals; other thresholds are recommended for non-Caucasian individuals.

What about a WAIST – CALF measurement?

Weir CB, Jan A. BMI Classification Percentile And Cut Off Points. [Updated 2023 Jun 26]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023

Obesity Management Guidelines

Obesity Medicine Association (OMA)

The Obesity Society (TOS)

The American College of Cardiology (ACC)

American Heart Association (AHA)

The American Association of Clinical Endocrinology (AACE)

American College of Endocrinology (ACE)

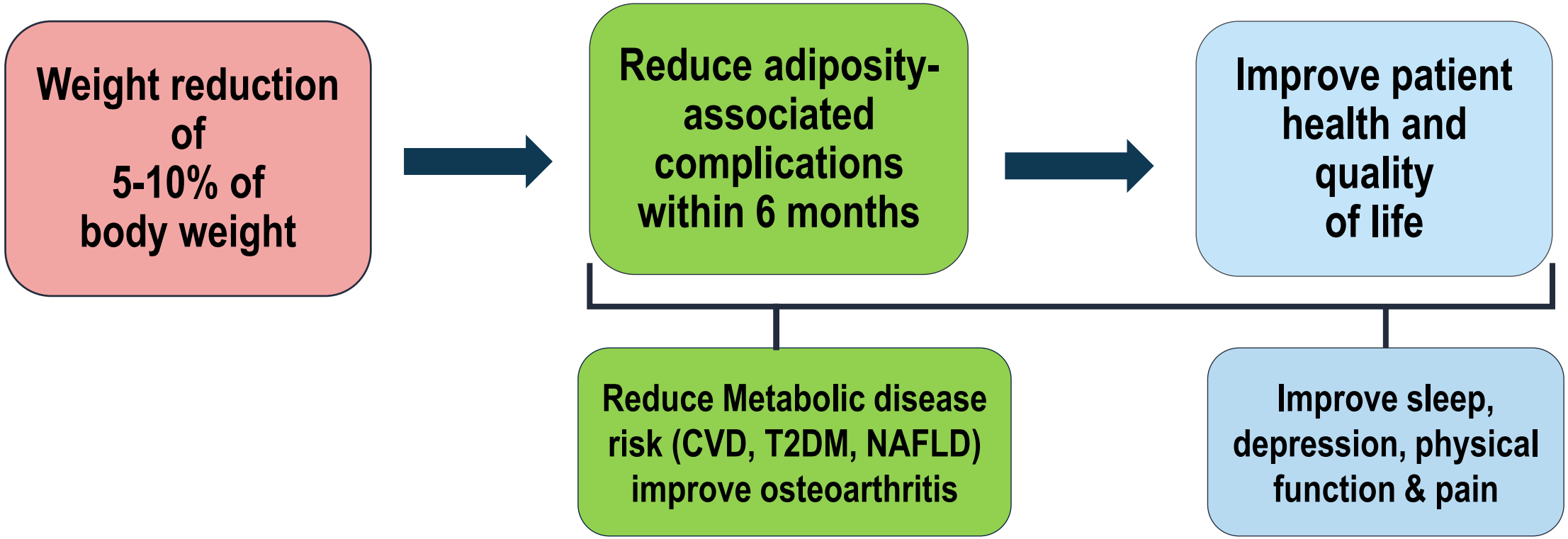
The Canadian Adult Obesity Clinical Practice Guidelines

Obesitymedicine.org

Obesity, diabetes mellitus, and cardiometabolic risk: An Obesity Medicine Association (OMA) Clinical Practice Statement (CPS) 2023https://doi.org/10.1016/j.obpill.2023.100056

Treatment goals: *reduce adiposity*

MEANINGFUL WEIGHT LOSS!!



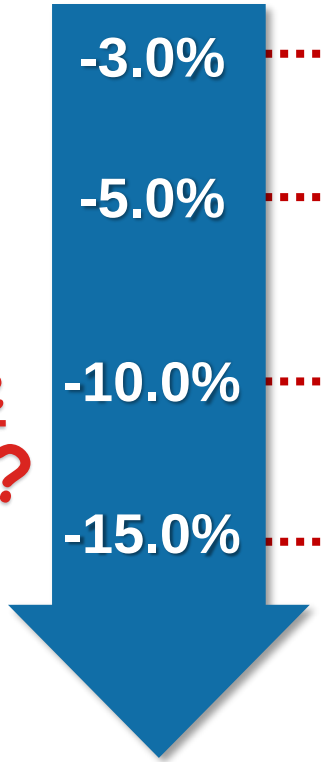
CVD, cardiovascular disease; T2DM, type 2 diabetes mellitus.

Jensen MD, et al. *Circulation*. 2014;129:S102-S138. Garvey WT, et al. *Endocr Pract.* 2016;22 Suppl 3:1-203. Yanovski SZ, et al. *JAMA.* 2014;311:74-86. Apovian CM, et al. *J Clin Endocrinol Metab.* 2015;100(2):342-362.

Set Realistic Goals with *Meaningful* Weight Loss

Look at underlying morbidities

How much weight loss helps reduce complications?



- **-3.0%** — Improved glycemic control: reduce risk for developing diabetes
- **-5.0%** — Improved glycemic control; Reduced BP & triglycerides, increased HDL, reduced NAFLD
- **-10.0%** — Greater improvements in above parameters; Reduced Knee/hip/spinal arthritis pain, reduces NASH, reduces sleep apnea 50%, reduced cancer risk; Reduces IR 50-60%
- **-15.0%** — Even greater improvements in above parameters, reduce CVD risk, and improve a variety of inflammatory conditions; Reduces IR

Remember to cut back on BP meds and/or hypoglycemic drugs (insulin/sulfonylureas) as weight drops

Jensen MD, et al. *J Am Coll Cardiol*. 2014;63(25 Pt B):2985-3023; Newman CB et al J Clin Endocrinol Metab 2020;105(12): .

Drugs and life-style interventions must be individualized and begun as early as possible

Treating obesity & pre-obesity

Medication | **Gastric & endoscopic Tx** | **Surgery**

Weight loss interventions

Lifestyle interventions

Targeted diets and eating plans

- Increased physical activity
- Psychotherapy---behavior changes

Anti-obesity medications (AOMs)

- **Phentermine**
- **Orlistat**
- **Naltrexone HCL-Buproprion HCL (*Contrave*)**
- **Phentermine-topiramate ER (*Qsymia*)**
- **Liraglutide 3 mg (*Saxenda*)**
- **Semaglutide 2.4 mg (*Wegovy*)**
- **Tirzepatide 15 mg (*Zebound*)**

Gastric & Endoscopic interventions

Hydrogels (Plenity)
Intragastic balloons
Endoscopic sleeve gastroplasty
(Refer to GI for this)

Metabolic & Bariatric surgery (MBS)

Adjustable Gastric Band
Sleeve Gastrectomy
Gastric bypass (RYGB)
Duodenal switch
(Refer to bariatric surgeon)

FYI: < 5% of patients who should be on AOMs are prescribed them

Kabiri M, Sexton Wa A, Ramasamy A, et al The Societal Value of Broader Access to Antiobesity Medications. Obesity 2020 Feb;28(2):429-436

Stop obesogenic drugs or change to weight-neutral alternatives (if possible)

Medication type	Weight-promoting	Weight neutral/less weight gain (alternatives)
Antihypertensives	β-adrenergic blockers (*propranolol, atenolol, metoprolol, nadolol*), α-adrenergic blockers	ACE inhibitors, ARBs, β-adrenergic blockers (*carvedilol, nebivolol*), calcium channel blockers, thiazides
Antidiabetics	Insulin, sulfonylureas, thiazolidinediones (*pioglitazone)*, meglitinides (*nateglinide, repaglinide*)	DPP-4 inhibitors, α-glucosidase inhibitors, bromocriptine, colesevelam HCL
Antidepressants	SSRIs (paroxetine), SRNIs, tricyclic antidepressants (amitriptyline, doxepin, imipramine, nortriptyline), lithium, MAOIs, mirtazapine,	SSRIs (fluoxetine, sertraline)
Antipsychotics	Risperidone, clozapine, olanzapine, quetiapine,	Aripiprazole, lurasidone, ziprasidone
Anti-epileptics	gabapentin, pregabalin, valproic acid, carbamazepine,	Lamotrigine, levetiracetam, phenytoin
Antihistamines	First-generation antihistamines (*chlorphenamine, doxylamine*)	Second- & third-generation antihistamines (*diphenhydramine, cetirizine*)
Anti-inflammatories	Glucocorticoids* (*prednisone, hydrocortisone, etc.)*	Inhaled steroids, topical steroids, NSAIDs, DMARDs
Anti-neoplastic	Steroid-based chemotherapy (tamoxifen, arimidex)	

* Cetrizine more likely to cause modest weight gain compared to

**Glucocorticoids (at super-physiologic doses for extended periods) are a major cause for central adiposity--with *increased* risk to cardiometabolic & bone health.

Adapted from: https://obesitymedicine.org/medications-that-cause-weight-gain (accessed 3/13/2023) & J Fam Pract 2016; 65(11):780–88;

Dietary points

Adherence is key no matter the diet & portion **control**Phenotype matters (yep—it's in your DNA)****

The faster you start to lose weight the greater the adherence to treatment regimen

The BEST diet is safe, effective, and one to which the patient will adhere.

Drink plenty of water premeal
Use meal replacements (high fiber/protein)

- **Common dietary plans**
  - Low carb (keto, paleo)
  - Low fat (DASH)
  - Mediterranean
  - Whole Food/Plant Based
  - Energy Focused
    - LCD
    - VLCD
  - Fasting (intermittent or timed)

FYI---studies show that people underestimate their caloric load by 1000 calories a day

Am. J. Clin. Nutr. 2015;101:1320–1329; Diabetes Obes. Metab. 2018;20:858–871.

Core considerations for nutrition intervention in weight loss management

Minimize intake of highly processed (& fast) foods
(nitrates, phosphates & potassium bromate)

Encourage consumption of high-fiber, complex carbohydrates

Add protein to meals (recommended: 1-1.2gm/kg/day)
(Helps maintain lean body mass– greater energy to metabolize)

Avoid eating late at night (when melatonin high)
(late night eating of high fats/carbs= **insulin resistance**)

Should read labels AND beware of marketing claims

Physical Activity Points

Ensure cardiovascular-pulmonary safety for activity

(So pre-exercise evaluation important)

- **Exercise only accounts for 10% of weight loss! Wait…what?! WHY?**
  - *Duration of exercises no longer believed to be as important.*
- Best time to do **aerobic exercise** (esp. men with metabolic syndrome) is in the morning; **weight lifting** best in late afternoon *(to maintain muscle)*
- When walk—start small with intention and increase time involved (even 5 mins)
  - *Recommend walk 2 miles 3 to 4 x a week (each in under an hour)*
- After you eat walk/move for 10 minutes (vs 30 mins/day)

Verboven K, Hansen D. Critical reappraisal of the role and importance of exercise intervention in the treatment of obesity in adults. Sports Med. 2021;51(3):379–389
Paley, C.A., Johnson, M.I. Abdominal obesity and metabolic syndrome: exercise as medicine?. BMC Sports Sci Med Rehabil 10, 7 (2018).

More Exercise Pointers

- **Endurance** training (adjust intensity as needed and tolerated)
  - *OKAY—2 to10 min bouts throughout the day. JUST MOVE with intention!!!*
- **Resistance training** (isometric, weights) **good in older patients**
- **Flexibility training** (stretching, modified yoga, Tai Chi) EXCELLENT
- **Stand more, move more** (and include isotonic exercise more)
  - *Improves cardiopulmonary oxygen utilization*
  - *Improves insulin sensitivity (helps hyperglycemia & fatty liver!)*
  - ***Improves microbiome***
- **JUST MOVE !!**

Verboven K, Hansen D. Critical reappraisal of the role and importance of exercise intervention in the treatment of obesity in adults. Sports Med. 2021;51(3):379–389
http://sciencedrivennutrition.com/dieting-and-metabolism/ (accessed 5/14/2021;
Paley, C.A., Johnson, M.I. Abdominal obesity and metabolic syndrome: exercise as medicine?. BMC Sports Sci Med Rehabil 10, 7 (2018).

Pointers on using Anti-obesity Medications (AOM)

- **They are for life-long therapy—USE WITH LIFESTYLE INTERVENTION…*lose ave. of 5-20+% (responders); Start with monthly perscriptions and FOLLOW UP!!***
- Is the patient ready for intervention **and confident** of success?
- **The 5 C's**
  - **C**autions & contraindications for each AOM (consider age, underlying health status*); OTC meds?*
  - **C**o-morbidities (how can these drugs mitigate some of these beyond weight loss)
  - **C**ues (consider patient described appetite control/habits, mode of delivery, side-effects)
  - **C**ombination (consider combining meaningful lifestyle change with AOMs & surgical options)
  - **C**ost (consider AOM cost, insurance coverage, and access to the drug; Medicare doesn't cover)

- Not used in pregnancy/ breastfeeding! On Birth control? **Stop AOMs if pursuing pregnancy.**
- *Ask about other AOM use as well as OTC weight-loss meds & chart that*
- **Weight loss increases risk of gallbladder disease (which can increase pancreatitis risk)**

Horn, Almandoz, & Look (2022) Postgraduate Medicine, 134:4, 359-375,

FDA Eligibility Criteria for Use of AOMs

Adult

- BMI > 30
- BMI >/= 27 with one complication

Asian adults:

- BMI > 27
- BMI > 23 with one complication

Children:

- > 95% on growth chart

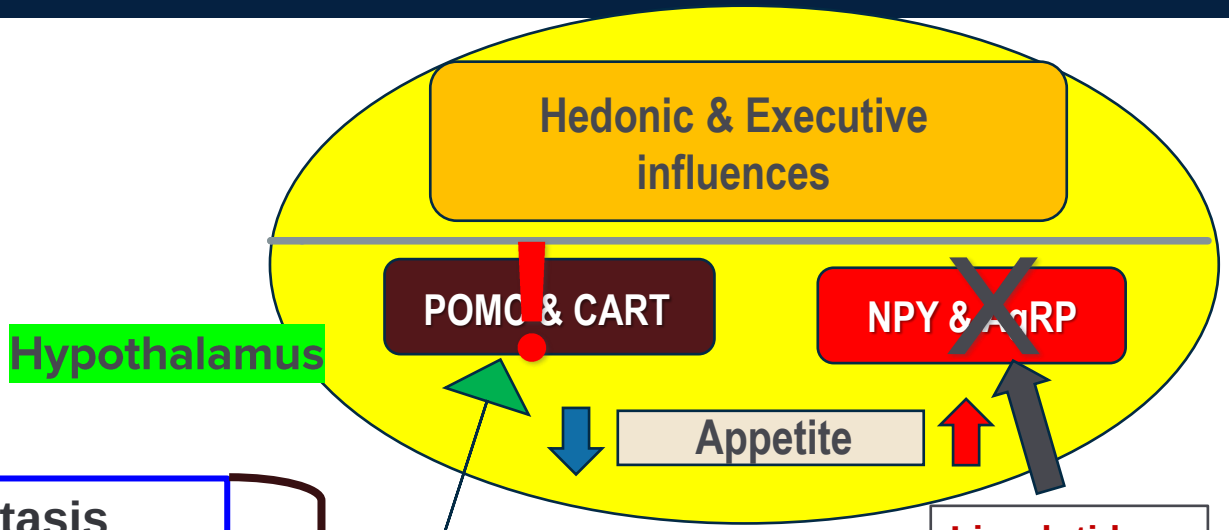
Same adult eligibility criteria for Gastric & Endoscopic devices:

- Hydrogels (Plenity)
  - *3 capsules taken1/2 hr before lunch & dinner with 16 oz of water*
- Intra-gastric balloons
- Endoscopic sleeve gastroplasty

A word about off-label use

FYI: Many patients are excluded in FDA drug indications, as they are not represented in clinical trials: pediatrics, elderly, pregnancy, mental illness, and some minority populations.

How AOM's affect appetite regulation



Hedonic

Opioid (Naltrexone)
Norepinephrine (Bupropion)
GABA (Topiramate)
Dopamine (Bupropion) & (Phentermine)

GLP-1Ra:
(Liraglutide, semaglutide)
Tirzepatide*

Endocannabinoid & serotonin

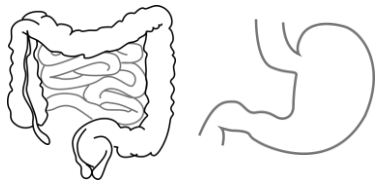
Homeostasis

GLP-1Ra:
Liraglutide
Semaglutide
Tirzepatide*

Bupropion

Phentermine
Setmelanotide

Liraglutide
Semaglutide



Orlistat

Influence of the Gut Microbiome
Restful sleep

Executive influences helped by behavioral therapy

*Tirzepatide not yet FDA approved for weight loss

Kessler C. Nurs Clin North Am. 2021 Dec;56(4):465-478:; J Am Assoc Nurse Pract. 2017;29:S15-S29

Liraglutide (Saxenda) **Semaglitide (Wegovy)**	Starts at 0.6mg and escalates to 3.0mg 12+ yrs Starts at 0.25 mg and escalates to 2.4 mg 12 yrs	~ 8% ~ 15%	Medullary thyroid cancer history, MEN type 2 history, pregnancy and breastfeeding, history of pancreatitis (CAUTION only, not contraindication—depends on cause.) Care with gallbladder disease, retinopathy, gastroparesis, (?) suicidal ideation, acute kidney injure	Nausea, vomiting, diarrhea, constipation, hypoglycemia in patients with T2DM, increased lipase, increased heart rate, pancreatitis	Injectable, GLP1 receptor agonist which helps with feeling full and may impact food cravings. Beneficial for diabetes, prediabetes or insulin resistance. Approximately $1400 cash. https://www.saxenda.com/ Htt[s://www.wegoby.com/
Naltrexone-bupropion ER (Contrave)	Each tablet has 8mg naltrexone and 90 mg bupropion that escalates over time to two tablets twice a day	~ 6%	Uncontrolled HTN, seizure disorder, anorexia or bulimia, drug or alcohol withdrawal, chronic opioid use, MAO inhibitors use, pregnancy and breastfeeding,	Nausea, constipation, HA, dizziness, increased absorption with high fat meals	Opioid receptor antagonist combine with an antidepressant. Decreases hunger and helps with Food cravings. May benefit with treatment of depression. $98/month cash. https://contrave.com/
Orlistat	60 mg over the counter 120 mg 3 times a day within 1 hour of fat-containing meal *12 yrs*	~ 6%	Chronic malabsorption syndrome, pregnancy and breastfeeding, cholestasis, some medications (ex. warfarin, antiepileptic, levothyroxine)	Decreased absorption of fat-soluble vitamins, steatorrhea, flatulence, fecal incontinence	Pancreatic lipase inhibitor, decreases the amount of fat absorbed from food https://reference.medscape.com/drug/alli-xenical-orlistat-342068
Phentermine	8 mg tablets that can be used two or three times a day. *17 or 16 yrs & up*	~ 5%	Anxiety disorder, CV disease, MAO inhibitors, pregnancy and breastfeeding, hyperthyroidism, hx of drug abuse, glaucoma	HA, increased BP and HR, insomnia, constipation, anxiety, palpitations, changes in libido	Sympathomimetic, decreases hunger https://lomaira.com/
Phentermine-topiramate ER (Qsymia)	Initiate treatment at 3.75 mg/23 mg table that can escalate up to 15 mg/92 mg 12 yrs	~ 10 %	hyperthyroidism, glaucoma, some medications (ex MAOI, sympathomimetic), pregnancy and breastfeeding,	Insomnia, constipation, dizziness, paresthesia, dysgeusia, dry mouth	Sympathomimetic combined with an antiseizure medication, decreases hunger. May benefit migraine headache prophylaxis. https://qsymia.com/
Plenity	3 capsules ½ hour before lunch and dinner with 16 ounces of water.	~ 5%	Allergy to any component. Avoid use in with GI conditions like esophageal anatomic anomalies, suspected strictures, or complications from prior gastrointestinal surgery that could affect GI transit and motility	Abdominal distention, bloating, constipation or diarrhea, belching, GERD	Oral hydrogel Is not absorbed from stomach or small intestine. Labeled use for BMI $\geq$ 25 kg/m^2. https://www.myplenity.com/
Tirzepitide (Zebound)	2.5 to 15 mg weekly (titrate in 2.5 increments monthly)	~ 20 %	Medullary thyroid cancer history, multiple endocrine neoplasia type 2 history, suicidal behavior and ideation, pregnancy, breastfeeding, acute gallbladder disease, diabetic acute kidney injury	Nausea, vomiting, diarrhea, constipation, hypoglycemia in patients with T2DM, increased lipase, increased heart rate, pancreatitis	Injectable, GLP1 ra & GIP which help with feeling full and may impact food cravings. Beneficial for diabetes, prediabetes or insulin resistance. Approximately $1400 cash https://www.zepbound.lilly.com/

What about using compounded Semaglutide?

- The FDA **has not approved** or regulated the use of **compounded** semaglutide *or other peptides*

- Their efficacy, purity or safety have not been studied.

- **If prescribed, they should be legally produced**:
  - By source companies whose identities are readily disclosed
  - Who have documented manufacturing processes compliant (GMP) with oversight by applicable regulatory agencies.

- ***Some malpractice insurance brokers are now advising that the new policies have exclusions for compounded peptides.***

- OMA has issued a position statement against their use.

https://www.sciencedirect.com/science/article/pii/S2667368123000074

Focus Points on Some AOMs

- **Phentermine** *(Adipex-P, Suprenza, Lomaira)*
  - Short term use (3 months)…really?; Use short-acting version—avoid late in day (can use with 16 or 17 yrs)
  - **Avoid use in CAD, HTN, tachy-dysrhythmias, glaucoma, hyperthyroidism**

- **Phentermine-topiramate ER (low dose)** *(Qsymia)*
  - Because low doses—can use at 12 yrs+ ; Need to titrate off the drug
  - **Avoid in CAD, HTN, Tachy; causes paresthesia; teratogenic**

- **Orlistat** *(Xenical)* *(use with 12+ yrs)*
  - Limit fat intake with it.
  - **May block absorption of 160 meds; Major GI upset**

- **Naltrexone-bupropion** *(Contrave)*
- (may help carb addiction)
  - Caution if eat high fat with drug, can cause **increased** IContrave blood levels!!
  - **Risk seizures; avoid in suicidality or binge-eating disorder;**

JAMA. 2022;328(4):322; Anti-obesity drug discovery:advances and challenges. at Rev Drug Discov , 2022 (21) 201–223

Focus Points on Some AOMs

- **Liraglutide *3mg* *(Saxenda) daily***
- (also reduces blood glucose)
  - Great for severe hunger; most studied
  - **Avoid in thyroid medullary CA & pancreatitis; GI side effects.**

- **Semaglutide 1.8mg/2.4mg *(Wegovy) weekly***
- (also reduces blood glucose)
  - Great with tandem T2DM; found to helpful in HFpEF, & is pleotropic in CA arteries, liver & within the CNS. HELP WITH ADDICTIONS
  - **GI side effects (esp. nausea, diarrhea or constipation). Avoid in medullary thyroid CA & pancreatitis. (*found increase in retinopathy?*)**

- **Tirzepatide *(Zebound) Weekly***
- (also used in DM as Mounjaro)
  - Newest AOM; GLP-1ra & GIP combo
    - **SAME drug as Mounjaro!!**
  - Greater potential weight loss; likely same CVD benefits
  - **Avoid in thyroid medullary CA & pancreatitis; GI side effects.**

Focused concerns:
Ileus & hypoglycemia

Consider starting AOMs when weight plateaus

JAMA. 2022;328(4):322; Anti-obesity drug discovery: advances and challenges. Nat Rev JAMA. 2022;328(4):322; Anti-obesity drug discovery: advances and challenges. Nat Rev Drug Discov, 2022 (21,)201–223.

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What about off-label drugs not FDA approved for obesity management?

Semaglutide (Ozempic) 1.0 mg & 2.0 mg (monthly titration) (ok for ages 12 yrs+)
GLP-1 agonist used for T2DM (Wegovy 2.4 now approved for patients with BOTH T2DM & obesity)
Good MACE. Help mitigate NAFLD (see Wegovy comments)

FYI: Monjaro is the same drug & dose as Zebound, but order for DM!?

Metformin (2-4% weight loss) (can take if 10 yrs & older) (recommended when starting psychotropic drugs)

- Uncertain HOW it works but know it affects the biomarkers of cardio-met-disease
- Decreases hepatic gluconeogenesis & lipogenesis & increases insulin & antioxidant sensitivity, (& reduce LV hypertrophy?)
- Helps longevity and Slows aging: can use in Pre-diabetes
- Decreases cancer (in T2DM), cognitive decline, stroke & more;
- Believed to work on the gut Microbiome *(also decreases gut glucose absorption)*

Supplements (*usually stimulants*)

JAMA. 2022;328(4):322; **Anti-obesity drug discovery: advances and challenges.** ***Nat Rev Drug Discov*** **21, 201–223 (2022).**

When to consider Metabolic & Bariatric Surgery (MBS)

New criteria for MBS candidates:

- BMI >35 kg/m2, regardless of presence, absence, or severity of co-morbidities.
- ***Considered for individuals with metabolic disease and BMI of 30-34.9 kg/m2.***
- Adjusted BMI in Asian population:
  - BMI >25 kg/m2 suggests clinical obesity,
  - BMI >27.5 kg/m2 should be offered MBS.

Long-term results of MBS consistently demonstrate *safety and efficacy (esp with glycemic control).*

Appropriately selected children and adolescents (13ya+) should be considered for MBS. (*Although currently recommend for patients 19-65 years old)*

The dominant (90%) MBS procedures done: *sleeve gastrectomy and Roux-en-Y gastric bypass (RYGB)*

Other procedures include:

- adjustable gastric banding (AGB),
- biliopancreatic diversion with duodenal switch
- one-anastomosis gastric bypass

American Society of Metabolic and Bariatric Surgery (ASMBS) and International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) Indications for Metabolic and Bariatric Surgery. Obes Surg. 2023 Jan;33(1):3-14

Contraindications to MBS?

There are no **absolute** contraindications:

Relative contraindications do exist:

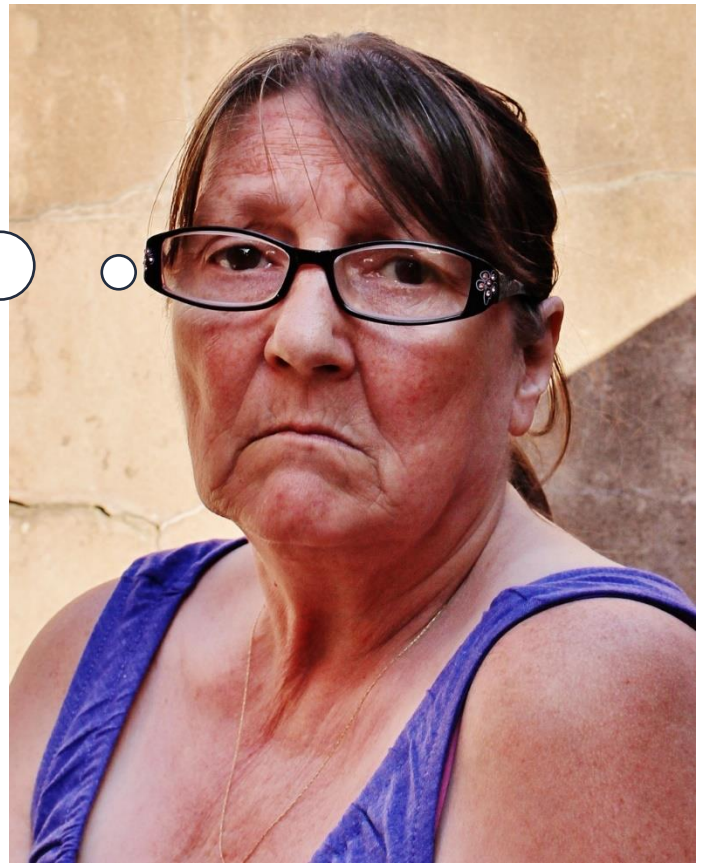
- Severe heart failure
- Unstable coronary artery disease
- End-stage lung disease
- Active cancer treatment
- Portal hypertension
- Drug/alcohol dependency
- Impaired intellectual capacity
- Severe, untreated depression or anxiety
- **Age?**

Stahl JM, Malhotra S. Obesity Surgery Indications and Contraindications. [Updated 2023 Jul 24]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK513285/ (accessed 6/12/2023

Regaining the weight

I LOST the weight…

But it FOUND me again…WHY??!!.

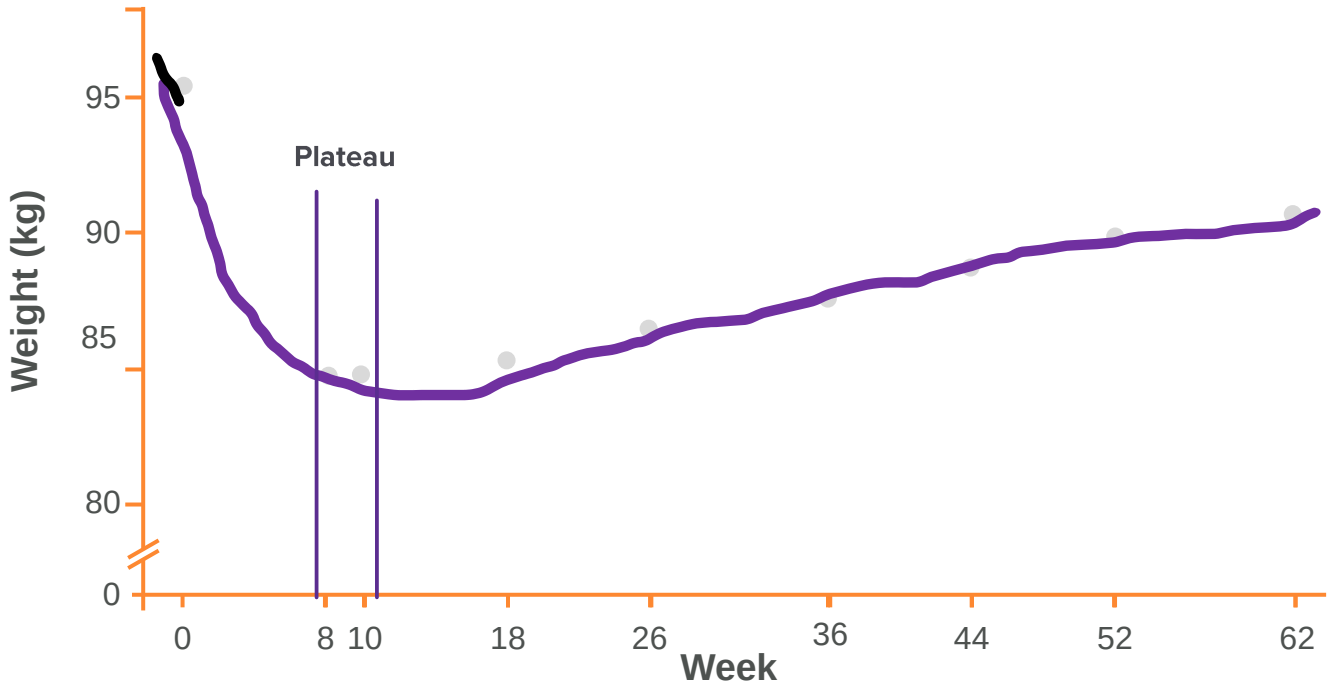


Pixabay.com

Metabolic Adaptation

(A genetic fat mass set-point)

Pixaby.com



The body will defend the fat mass

- **Hunger hormones** *(want to eat more)*
- **Satiety hormones** *(greater hunger)*
- **Resting metabolic rate** *(drops approx. 15% YIKES)*

Adapted from Sumithran P et al. *N Engl J Med.* 2011;365(17):1597-1604.
Busetto L, Bettini S, et al. Mechanisms of weight regain. Eur J Intern Med. 2021;93:3–7.;
Garvey et al. Endocrine Practice. 2016;22:1-203

Weight regain!

Weight regain typically occurs when within 1 to 4 years (& if AOMs are stopped) 1

Successful weight maintenance includes:[2]

- Self-monitoring & followup
- Weight loss of >2kg in 4 weeks
- **Frequent/regular access to weight loss program or with provider**
- Self-belief that weight can be controlled

Here's a tip:

Start AOMs when the weight starts to go back up again after successful Lifestyle Interventions

1. Apovian CM, et al. *J Clin Endocrinol Metab* 2015;100:342-62.2. 2. Thomas JG, et al. *Am J Prev Med*. 2014;46(1):17-23

Case 1: Sarah

37 y/o Caucasian woman

Obesity since age 16—worse with birth of children, starting at 26

Modest weight loss with multiple diet programs, *but always regains her weight*

VS: 5'4" 203# 142/88 HR 78 RR 16 pOx 98

BMI: 34.84 kg/m^2

Waist circumference: 42inches

PMH

HTN (stable), HLD (with TGs 223, sleep apnea, hypothyroidism (treated), NAFLD

NO diabetes (A1C 5.5) or reported depression/anxiety

Poor sleep (not regular use of c-pap)

FMHx: *obesity, T2DM, &CV disease*

Social History: one glass of wine "muscato" nightly, *no use of illicit drugs.*

Craves carbs…sweets; HS snacking, no binging

IS SHE ON BCP?

So which drugs are okay for Sarah?

phentermine

orlistat

phentermine-topiramate (Qsymia)

naltrexone-bupropion (Contrave)

liraglutide 3mg (Saxenda)/semaglutide (Wegovy) 1.7-2.4 mg

semaglutide 1 or 2 mg (Ozempic)

liraglutide 1.6 mg (Victoza)

tirzepatide 15 mg (Zebound)

Metformin

Any other medication?

What about bariatric surgery?

Sarah is concerned about her son, Tristan

Tristan has "always been a bit chubby"– was successfully treated for a sarcoma at the age of 6.

BMI of 36- 72 Kg; > 95%

Elevated BP and TGs (164 g/dl); *A1C 6.1*

Elevated liver enzymes, NAFLD

He says he feels hungry all of the time—even an hour after eating; he has a varied palate. Stays away from sweets but likes "crunchy snacks" like Cheetos. Has a stable family; he's very motivated. He is very active.

Sarah wants to know what, along with lifestyle, can be done for Tristan

So which drugs are reasonable for Tristan?

phentermine

orlistat

phentermine-topiramate (Qsymia)

naltrexone-bupropion (Contrave)

liraglutide 3mg **(Saxenda)/semaglutide (Wegovy)** 1.7-2.4 mg

semaglutide 1 or 2 mg **(Ozempic)**

liraglutide 1.6 mg **(Victoza)**

tirzepatide 15 mg **(Zebound)**

Metformin

Any other medication?

What about bariatric surgery?

Barriers to Weight Loss Treatment

Sad realities about cost and access

- **Disparities**
  - Communities of color, under resourced, or marginalized people experience greater disparities in mental & metabolic health, (e.g., obesity, T2DM, CVD

- **Age > 65**
  - Poor CMS coverage of care
  - Incidence of Sarcopenia is high in this population

- **Pediatrics**
  - More AOMs now available (4)
  - Need extended growth charts for assessment
  - Safe surgical options (MBS) slowly opening for children 13 years +

So final points.....

- Obesity is a chronic, progressive, relapsing but TREATABLE disease
- Obesity is not caused by overeating—obesity causes overeating
- The meaningful goal of obesity treatment is NOT simply about lowering numbers on a scale– but attaining better metabolic health!
- Risks for obesity should be identified early and treated (pre-obesity & adiposity)
- DON’T DELAY TREATMENT
- Supportive HCP engagement can double weight loss efficacy
- Time to stop the shame, blame & bias surrounding this disease state and it’s sufferers.

Still, we CAN win the BATTLE of the BULGE!

Pixabay.com

Thanks!

ckessler@maranatha.net

http://stateofobesity.org/rates (accessed 5/2/2023

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Reference slides!!

Can you get paid?

99215 (*time - <u>with patient for 25 minutes and 20 minutes spent in education and counseling</u> – be sure the documentation tells what you did for counseling*

- **E66.8 Obesity**, other Stage 2 A/E by BMI 36 and ORC
- **I10 Hypertension** A/E by BP of 140/88, changing medication from beta blocker (obesigenic) to ACDE-I, and treating obesity
- **E 78.2** Mixed hyperlipidemia A/E by labwork – will monitor while treating obesity for improvement – goal 5-10% weight loss
- **K 76.9** NALFD A/E by labwork with obesity – will monitor while treating obesity for improvement – likely requiring 20% weight loss

(Shared by Angie Golden DNP)

Example charting

Plan:

- Patient here today for obesity appointment
- Education completed on different eating plans, mindful eating and increasing physical activity
- Reviewed patient food tracking and types of food eating. Patient has SMART goal of reducing fast food by 50% - and moving towards decreasing carbohydrates to under 100 grams
- Patient to be seen again in two weeks.

Time: patient appointment 2:00-2:25pm, Charting 6:00-6:20pm Prescribing 5:55-6:00pm Total time 50 minutes

Shared by Angie Golden DNP