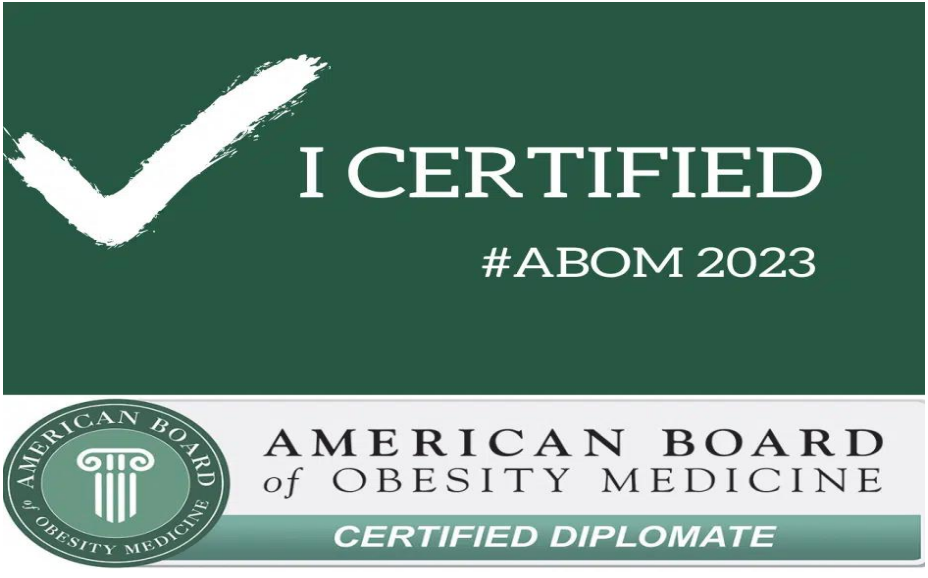
Pediatric Obesity- Introduction and Management

Mahesh Shrestha MD, FAAP, DABOM
Assistant Professor
Western Michigan University Homer Stryker School of Medicine
Kalamazoo, Michigan, USA

About myself

- MD-NAMS 6th batch
- MD-Brooklyn hospital, USA



Western Michigan University
Homer Stryker M.D.
SCHOOL OF MEDICINE

A girl with severe obesity

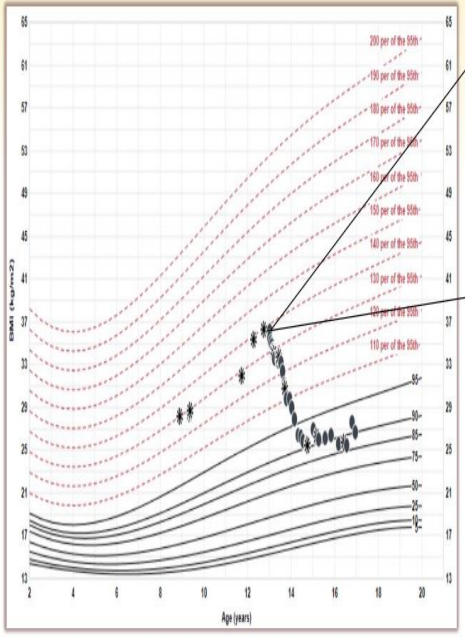
13 yo girl, BMI 36 kg/m^2

- HPI:
  - Otherwise normal development
  - Started to get "heavy" in 3rd-4th grade
- PMH: none
- Meds: none
- FH: mom had bariatric surgery and doing well after 15+ years
- SH:
  - lives with parents and 2 sibs
  - 8th grade, good student

Picture for reference

13 yo girl, BMI 36 kg/m^2

- PE
  - 227 lbs, 5'6", BMI 36.1 (1.39 x 95th percentile)
  - 120/64, P 70
  - Normal exam, no acanthosis nigricans, T5
- Labs
  - TC 139, HDL 33, LDL 95, TG 55
  - HbA1c 6.2%, Glucose 123
  - AST 13, ALT 26



Started flex meal plan

Down 8lbs in 2 mos; very difficult so started topiramate 75 mg qd

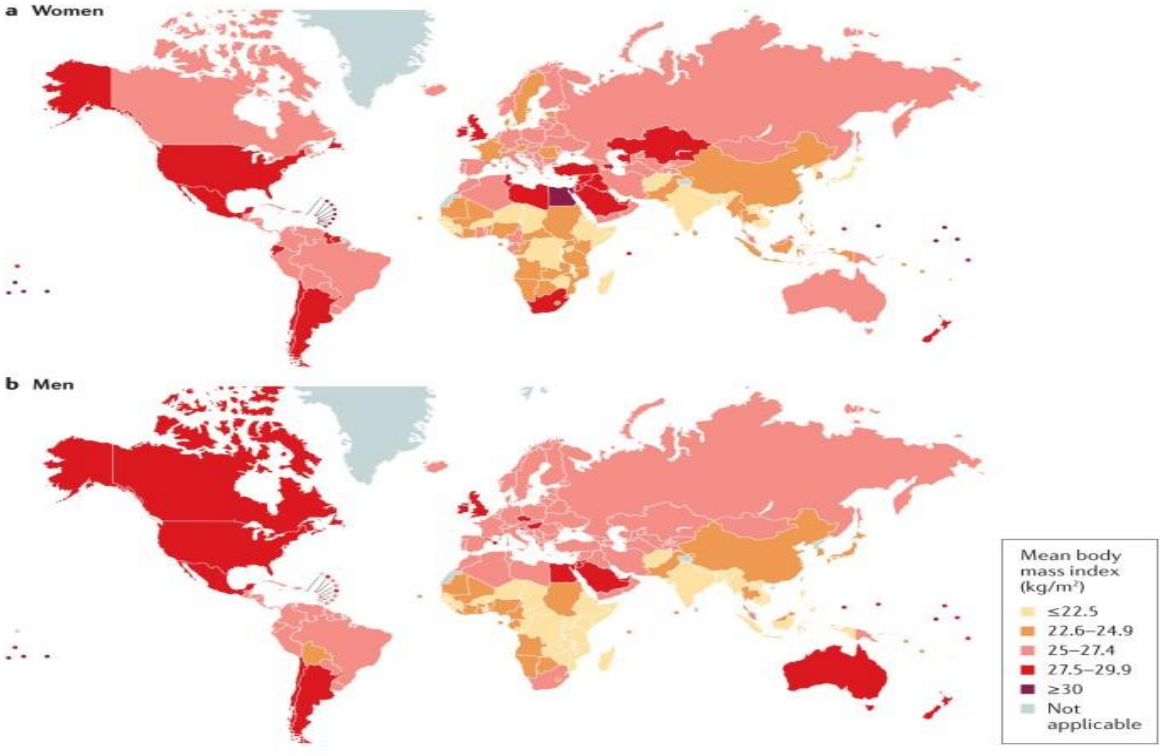
To be continued..

The Obesity Medicine Association's Definition of Obesity

"Obesity is defined as a chronic, progressive, relapsing, and treatable 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."

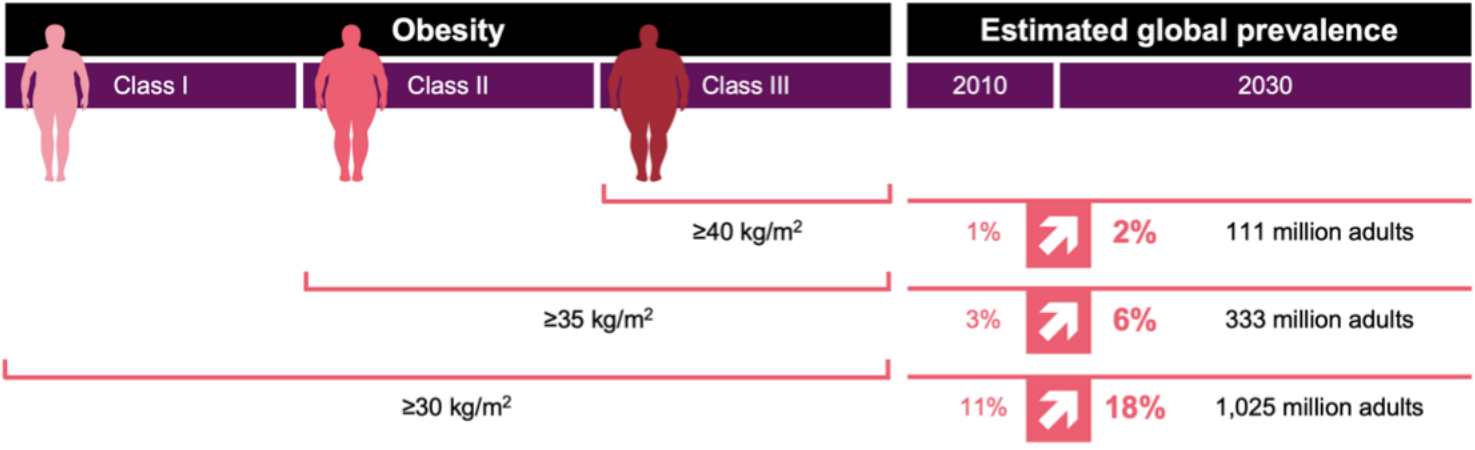
Why is it important to understand that obesity is a disease?

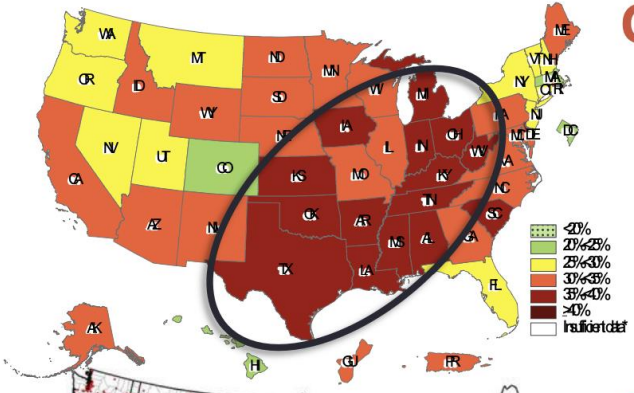
The obesity pandemic



Nature Reviews | Disease Primers

Obesity is a major part of the problem…..
….and a global pandemic in slow motion





Obesity

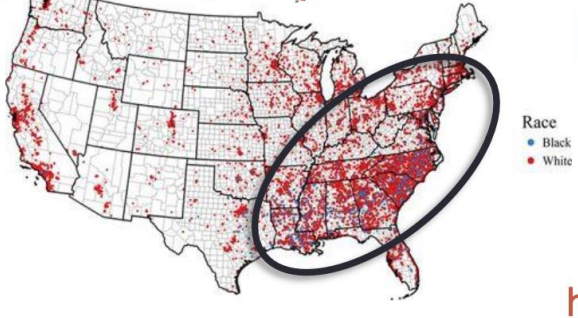
93.3 million US adults, 2015-16

31.1% Overweight

42.5% Obesity

9.0% Severe Obesity

https://www.cdc.gov/obesity/data/prevalence-maps.html



Diabetes, 2015

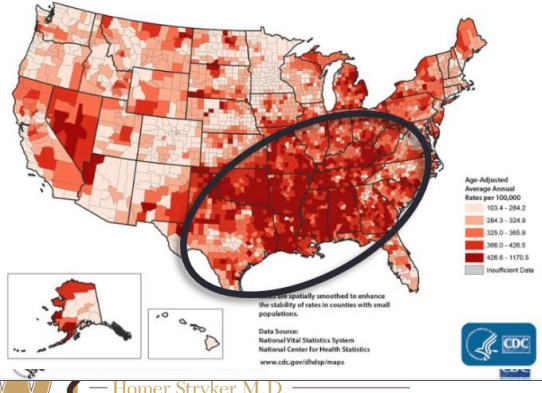
30.3 million people (9.4%)

>29 million projected by 2050

https://www.ahajournals.org/doi/10.1161/circoutcomes.116.003350

Matthew Shane Loop. Circulation: Cardiovascular Quality and Outcomes. Heat Maps of Hypertension, Diabetes Mellitus, and Smoking in the Continental United States, Volume: 10, Issue: 1, DOI: (10.1161/CIRCOUTCOMES.116.003350)

https://nccd.cdc.gov/DHDSPAtlas/?state=State



Heart Disease, 2014-16

92.1 million people

Leading cause of death

https://healthmetrics.heart.org/wp-content/uploads/2018/02/

https://www.cdc.gov/dhdsp/data_statistics/fact_sheets/fs_heart_disease.htm

At-A-Glance-Heart-Disease-and-Stroke-Statistics-2018.pdf

Obesity is a major part of the problem….and a deadly disease:
2.8 million people dying each year as a result of being overweight or obese.

Obesity as a Disease

Endocrine/Immune Response

↓

Adiposopathy
- Impaired fasting glucose
- Metabolic Syndrome
- Hypertension
- Menstrual Dysfunction (girls)
- Early Puberty (girls)
- Delayed Puberty (boys)
- NAFLD
- Dyslipidemia
- Insulin Resistance
- Type 2 DM
- Increased uric acid, microalbuminuria
- Gynecomastia
- Cholecystitis

Physical Response

↓

Fat Mass Disease
- Asthma
- Immobility
- Lipomastia
- Tissue Compression (sleep apnea, GERD, HTN)
- Tissue Friction (intertrigo)
- Stress on weight-bearing joints
- Slipped capital femoral epiphysis, Blount's disease, scoliosis, osteoarthritis)

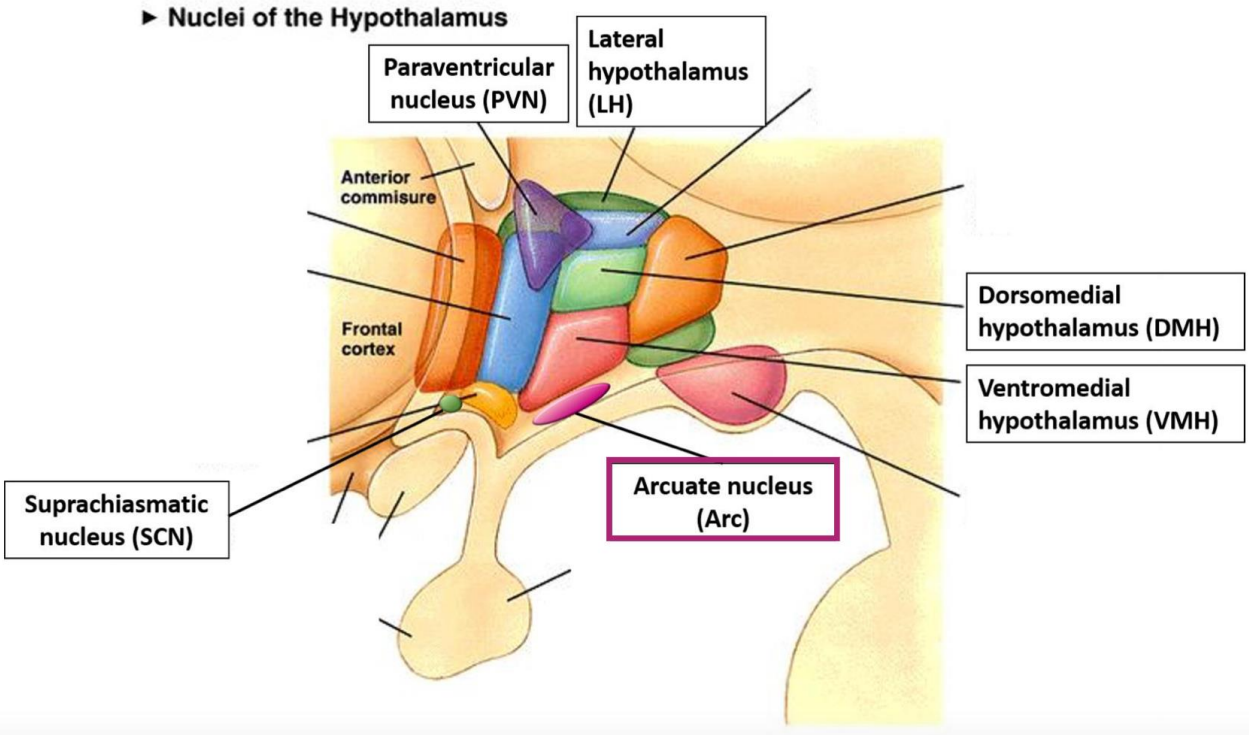
Psychological Response

↓

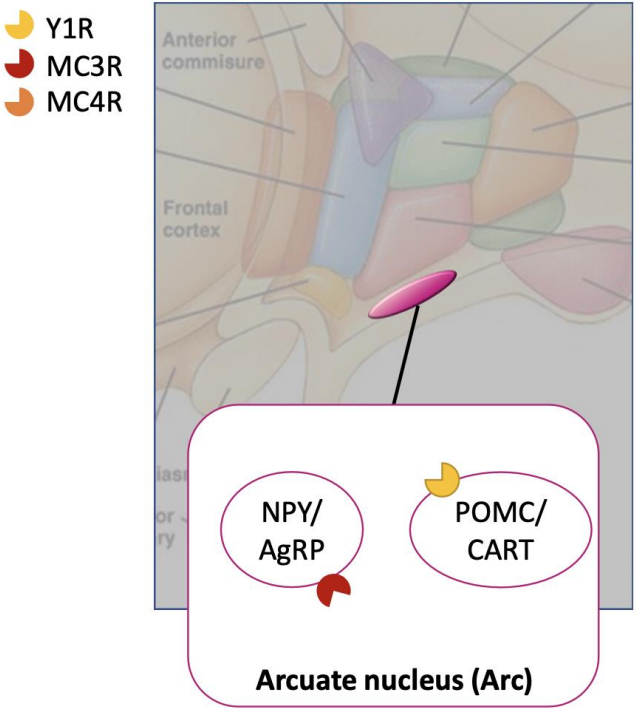
Quality of Life
- Isolation from peers
- Decrease in ability to participate in normal childhood activities
- Subject to bullying
- Lack of social/age appropriate relationships
- Anxiety/depression
- Binge eating disorder
- Night eating disorder
- Bulimia

Understanding hunger pathways

The arcuate nucleus (Arc) in the hypothalamus controls homeostatic signals of feeding



Arc contains **AgRP/NPY and POMC/CART** neurons that stimulate or inhibit food intake

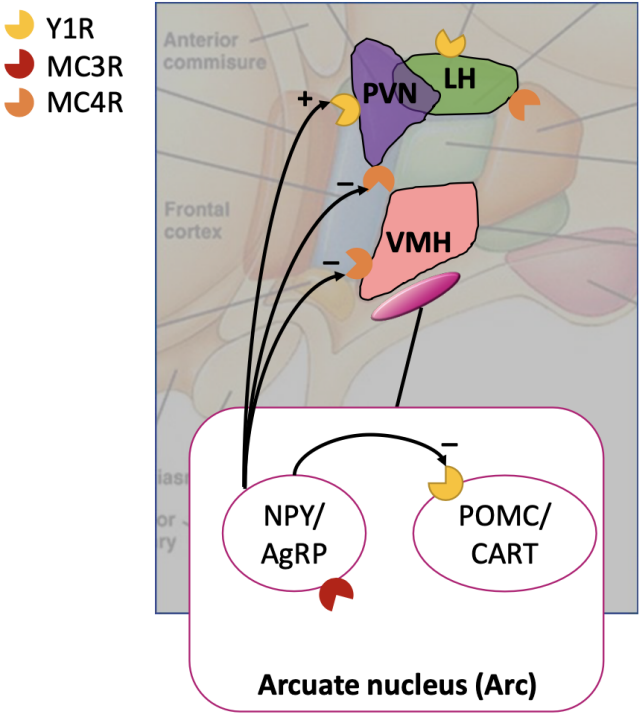


Agouti-related peptide (AgRP) and neuropeptide Y (NPY) are **orexigenic**

Pro-opiomelanocortin (POMC) and cocaine and amphetamine-regulated transcript (CART) are **anorexigenic**

Image: Barsch & Schwartz 2002 (adapted)

“I am hungry”

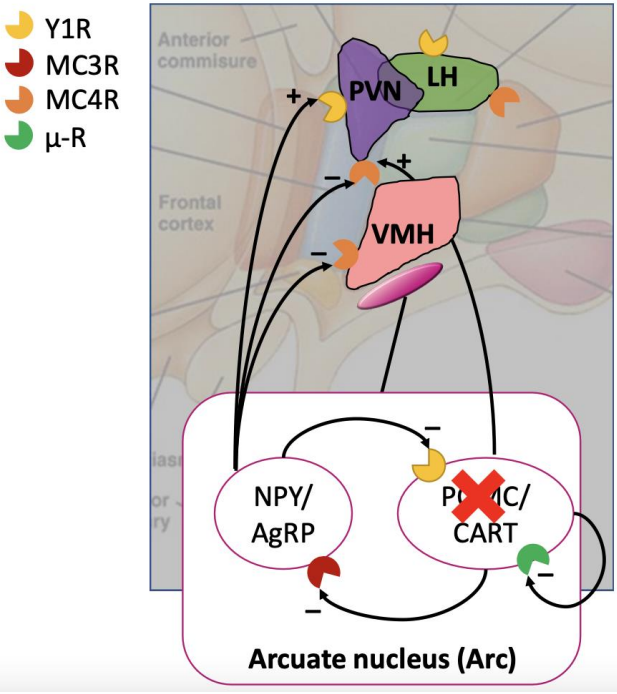


AgRP binds to melanocortin-4-receptor (MC4R) and as an inverse agonist

NPY binds to NPY-1 receptor (Y1R) and activates it

Farooqi et al. 2003; Krude & Gruters 2000; Krude et al 1998

POMC Deficiency



- Adrenal insufficiency
- Hypopigmentation

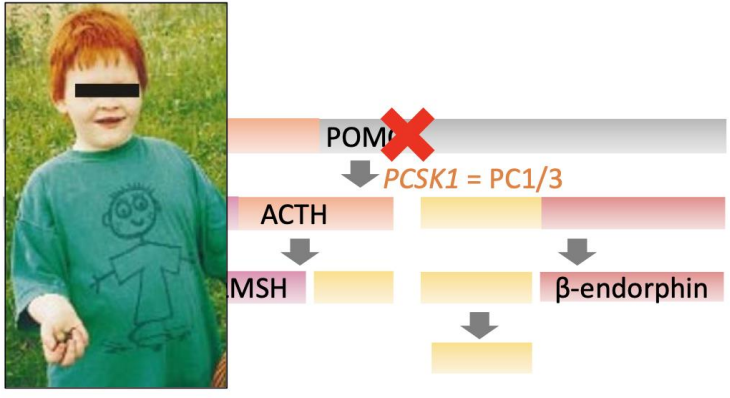
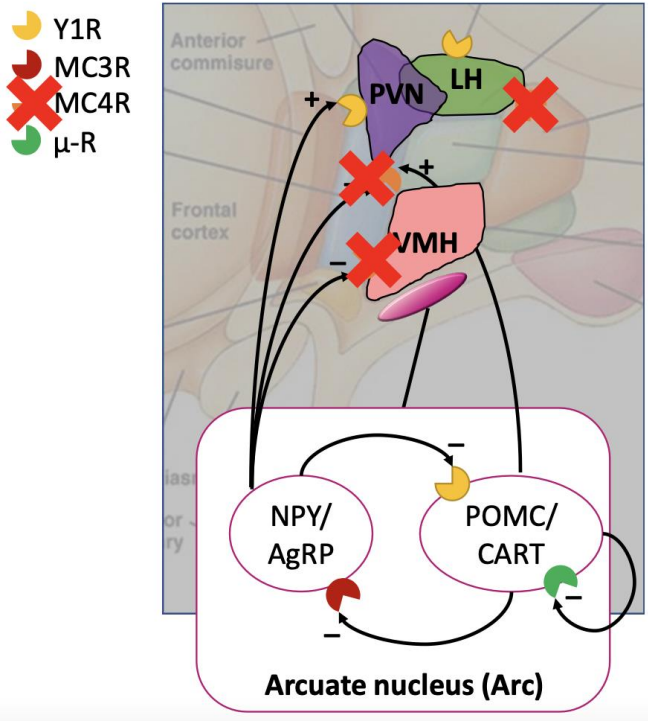


Image: Barsch & Schwartz 2002 (adapted)

MC4R Deficiency



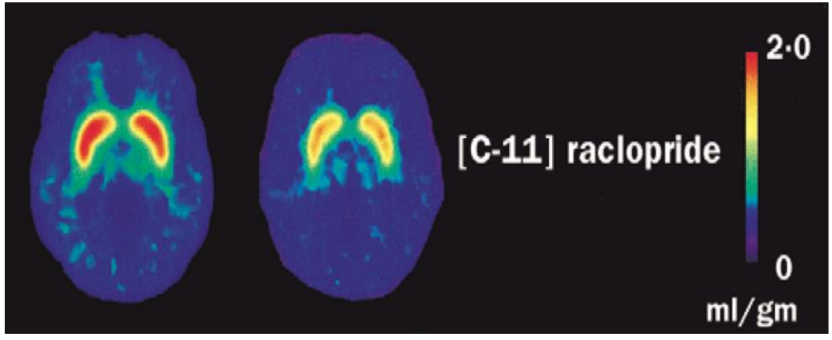
- Most common monogenic obesity
- ↑ lean and fat mass
- Tall
- Normal puberty

Farooqi et al. 2003;348(12):1085-1095.

Syndromes associated with obesity			
Disease	**Gene/Inheritance**	**Defect**	**Presentation**
Prader-Willi	15q partial deletion on paternal chromosome or uniparental imprinting	Elevated ghrelin	Cognitive impairment, short stature, hypotonia, hyperphagia
Bardet-Biedl (aka. Laurence-Moon-B-B)	BBS genes (14)	Impaired cilia	Cognitive impairment, retinitis pigmentosa, polydactyly, hypogonadism, short stature, deafness
Albright Hereditary Osteodystrophy (AHO) (aka. Pseudohypoparathyroidism type 1a)	Maternal transmission of epigenetic methylation defect of GNAS protein	Impaired *GNAS* intracellular signaling for multiple hormones	Pseudohypoparathyroidism, precocious puberty, short stature, short 4th and 5th metacarpals, cataracts
Cohen (aka. Norio, Pepper)	Chrom 8 *COH1/VPS13B* gene mutation / autosomal recessive	Impaired Golgi apparatus Accelerated adipogenesis	Psychomotor retardation; hypotonia, prominent incisors, microcephaly Truncal adiposity but maybe normal BMI
Beckwith-Wiedemann	Chromosome 11 / varied inheritance and mutation pattern	Excess IGF-2	Macroglossia, omphalocele, port-wine stain, nephroblastoma, hepatoblastoma, childhood cancers
Fragile X	CGG trinucleotide repeat on *FMR1* gene on X chromosome	FMR1 important for synapse development	Cognitive impairment, large ears, large testes, long and narrow face
Alstrom (Alstrom-Hallgren)	*ALMS1* mutation / autosomal recessive	(Function of ALMS1 is unknown)	Dilated cardiomyopathy, hepatic and renal failure, neurosensory deficit, male hypogonadism, short stature
Acrocephalopolysyndactyly type II (aka. Carpenter)	*RAB23* / autosomal recessive	Impaired vesicle trafficking	Intellectual disability, craniosynostosis, facial dysplasias, polydactyly, cryptorchidism, hypotonia and failure to thrive in infancy, prominent central incisors, cardiac failure

Omim.org; https://ghr.nlm.nih.gov/; https://rarediseases.info.nih.gov/; Kaur et al. 2017; Obesity: Genetic contribution and pathophysiology/ UptoDate. 2021

Dopamine reward system is abnormal obesity



Control Obesity

Fewer dopamine receptor-2 in striatum in obesity

↓ dopamine receptors also observed in users of cocaine, alcohol, heroin, and methamphetamines

Unclear if it is a cause or an effect of obesity

Wang et al. 2001; Karlsson et al 2015; Volkow et al. 2001; Volkow Nat Rev Neurosci 2017;18: 741-752

Why is it so difficult to lose and maintain weight loss?

fat mass –
our body's defense
against starvations

brain/body defends the
fat mass set point

fat mass set point is
regulated by the **brain**

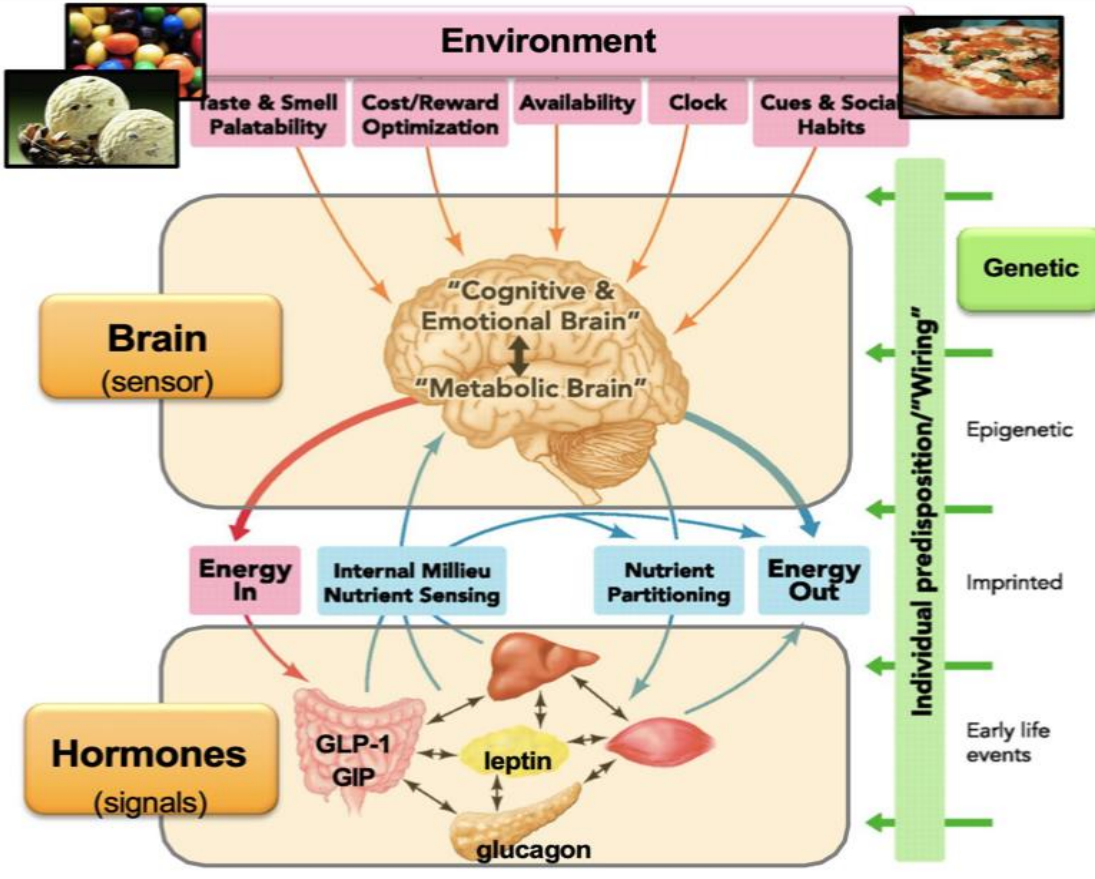


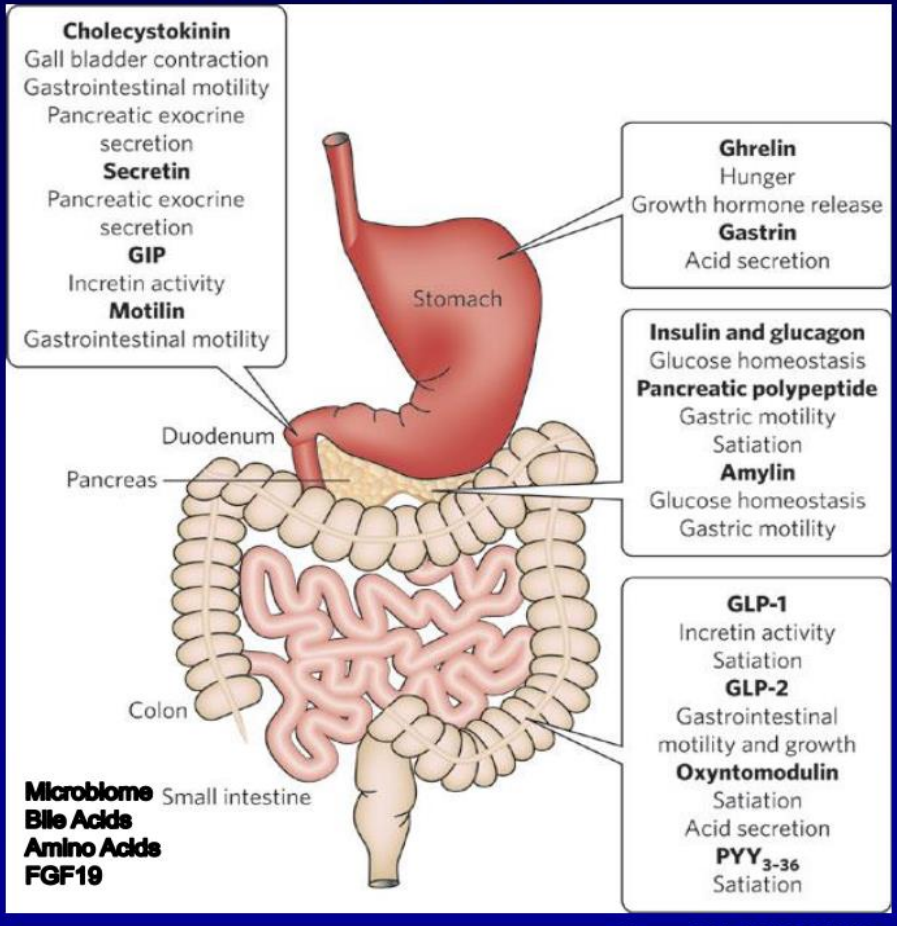
Figure Adapted from Zheng & Berthoud et al. *Physiology*. 2008;23 75-83.

Yale SCHOOL OF MEDICINE

Western Michigan University
Homer Stryker M.D.
SCHOOL OF MEDICINE

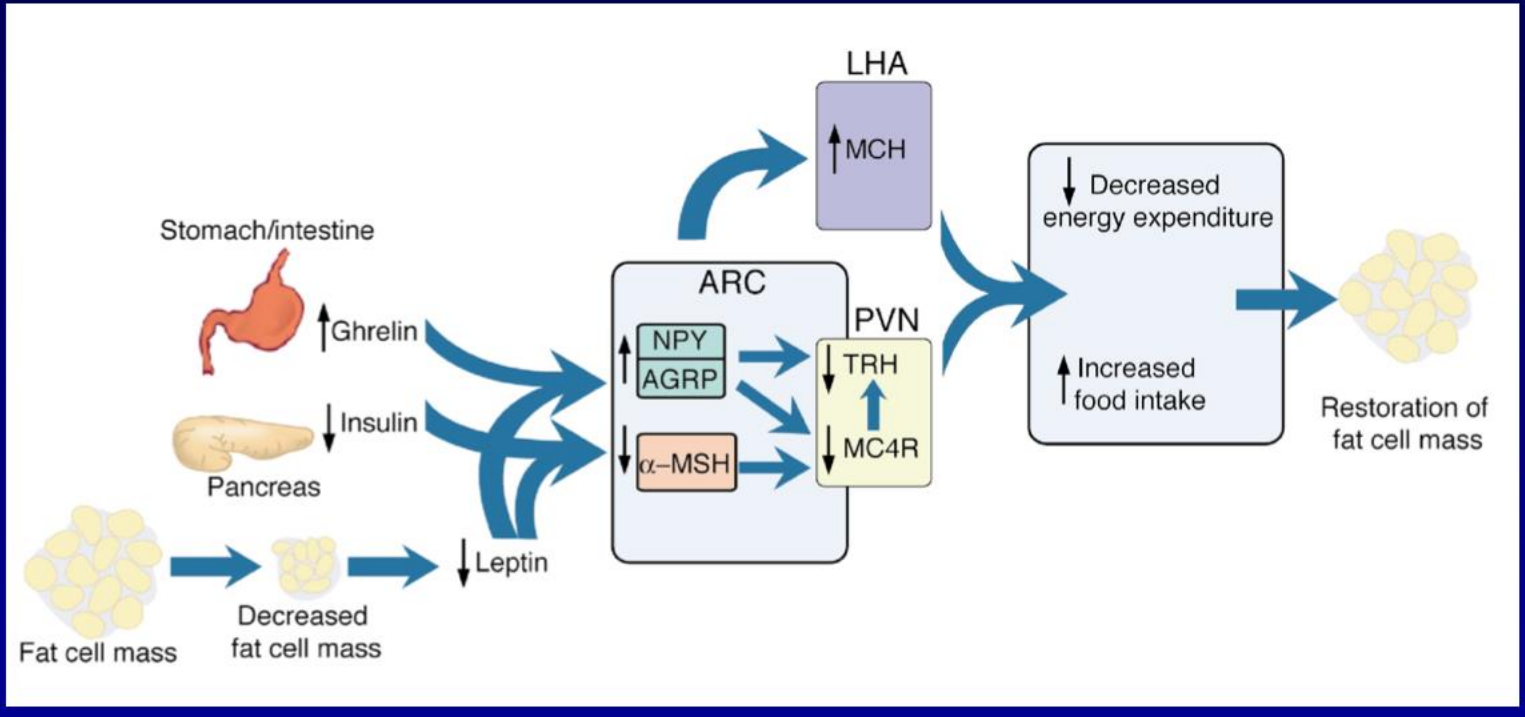
Gut Hormones

- Hunger
- Satiety
- Meal Size
- Meal Frequency
- Insulin Sensitivity
- Insulin Secretion



Nature **444**, 854-859(14 December 2006)

Neurohormonal Changes Associated with Weight Loss



Korner & Aronne, J Clin Invest 111:565-570 (2003)

GHRELIN - a "hunger" hormone

- Ghrelin is produced mainly in the stomach (gastric fundus)
- Ghrelin enhances appetite and food intake, and decreases insulin sensitivity
- Plasma levels of ghrelin are suppressed after a meal
- Plasma levels of ghrelin increase after diet-induced weight loss
- Increases levels of counterregulatory hormones: GH, cortisol and epinephrine

Peptide YY (PYY) - a "satiety" hormone

- PYY is produced in the ileum and colon and is secreted postprandially in proportion to the calorie content of a meal

- Cleavage of PYY(1-36) produces PYY(3-36)

- Increases satiety
- Delays gastric emptying
- Improves insulin sensitivity
- May decrease ghrelin secretion

GLP-1 Modulates Numerous Functions in Humans

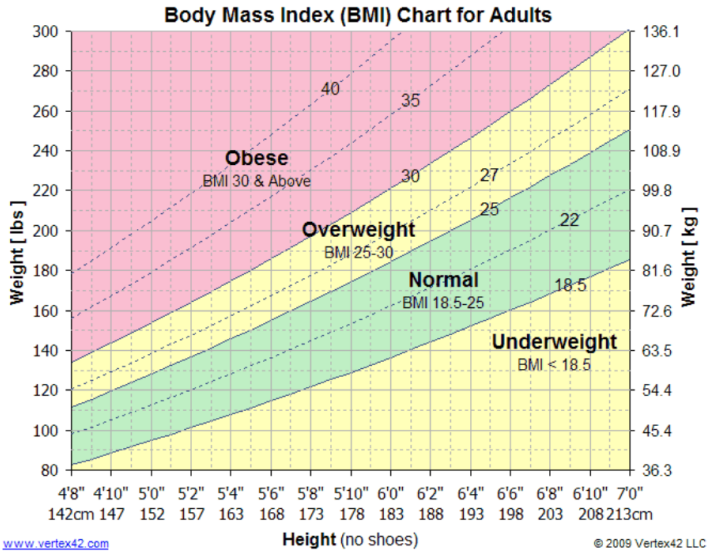
Data from Flint A, et al. *J Clin Invest*. 1998;101:515-520; Data from Larsson H, et al. *Acta Physiol Scand*. 1997;160:413-422
Data from Nauck MA, et al. *Diabetologia*. 1996;39:1546-1553; Data from Drucker DJ. *Diabetes*. 1998;47:159-169

Summary: GI Peptides

	MOA	Source	Site of action	Fed	Fast	Obesity	s/p RYGB
Ghrelin	Orexigenic	Fundus	Hippocampus, hypothalamus	↓	↑	Less suppressed after a meal	↔↑
CCK	Anorexigenic. Promotes satiation, not satiety; slows gastric emptying	I-cells in duodenum and jejunum; release is stimulated by fat and protein	GI, vagus n., hypothalamus	↑	↓	Unclear	↔
GIP	Anorexigenic in conjunction with GLP-1. Stimulates POMC. Incretin. Slows gastric emptying	K-cells in duodenum and jejunum; release is stimulated by glucose and fat	stimulates insulin release and lipoprotein lipase	↑	↓	↑ post-prandial	↑↓
GLP-1	Anorexigenic. Incretin. Inhibits NPY, stimulates POMC, delays gastric emptying, increases insulin release	L-cells in ileum; cleavage product of preproglucagon	Pancreas, gut, brain	↑	↓	Less suppressed after a meal	↑
PYY	Anorexigenic. Stimulates POMC. Promotes satiety, not satiation	L-cells in colon and rectum	Vagus n., hypothalamus	↑	↓	Less suppressed after a meal	↑
Amylin	Anorexigenic, decreases glucagon, enhances CCK satiation effect	Pancreas β-cells	CNS, area postrema	↑	↓	↑	↓
Oxyntomodulin	Anorexigenic	L cells; cleavage product of preproglucagon	Stomach, CNS, binds to GLP1R	↑	↓	Unknown	↑
Insulin	Anorexigenic, increases EE, anabolic	Pancreas β-cells	Hypothalamus	↑	↓	↑ post-prandial	↑ post-prandial
Glucagon	Anorexigenic. Glycogenolysis, Gluconeogenesis	Pancreas α-cells; cleavage product of preproglucagon	Stimulates insulin release and lipoprotein lipase	↓	↑	Unclear	↑

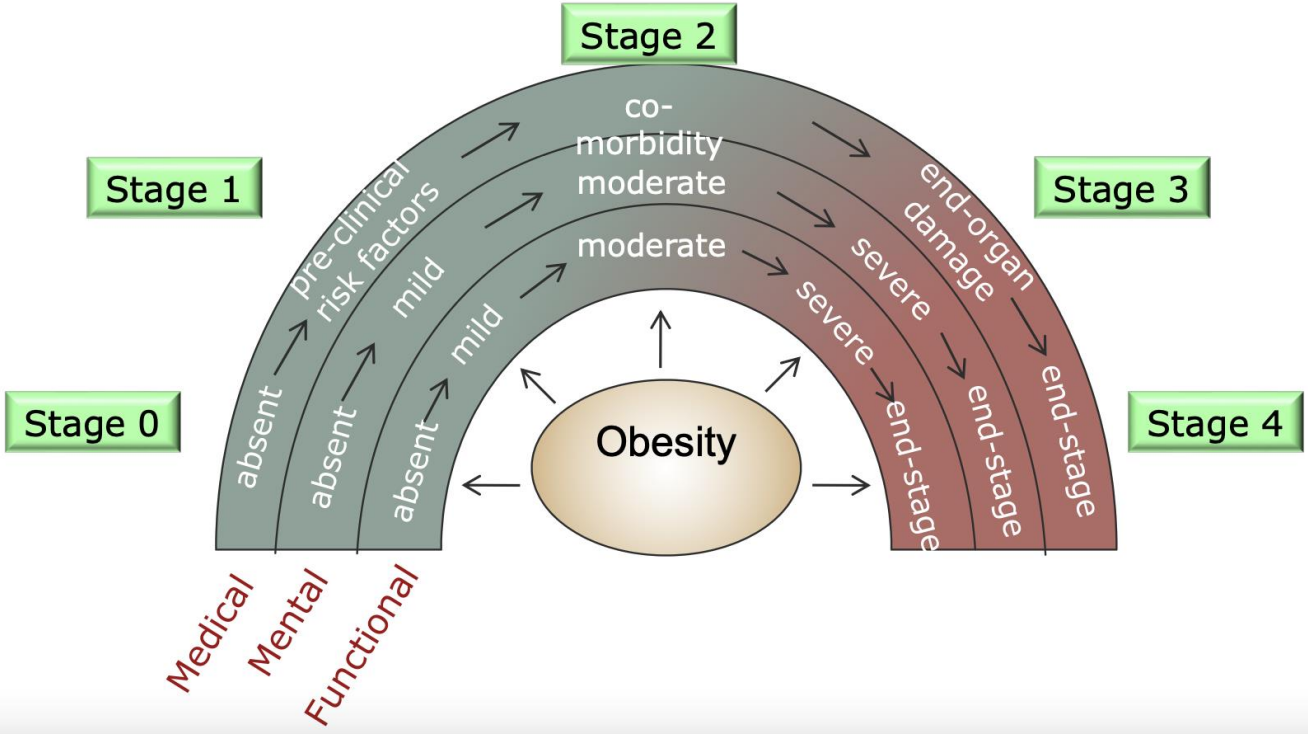
Murphy & Bloom 2006; Buhmann et al. 2014; Namkoong et al 2017

Obesity classification in adults



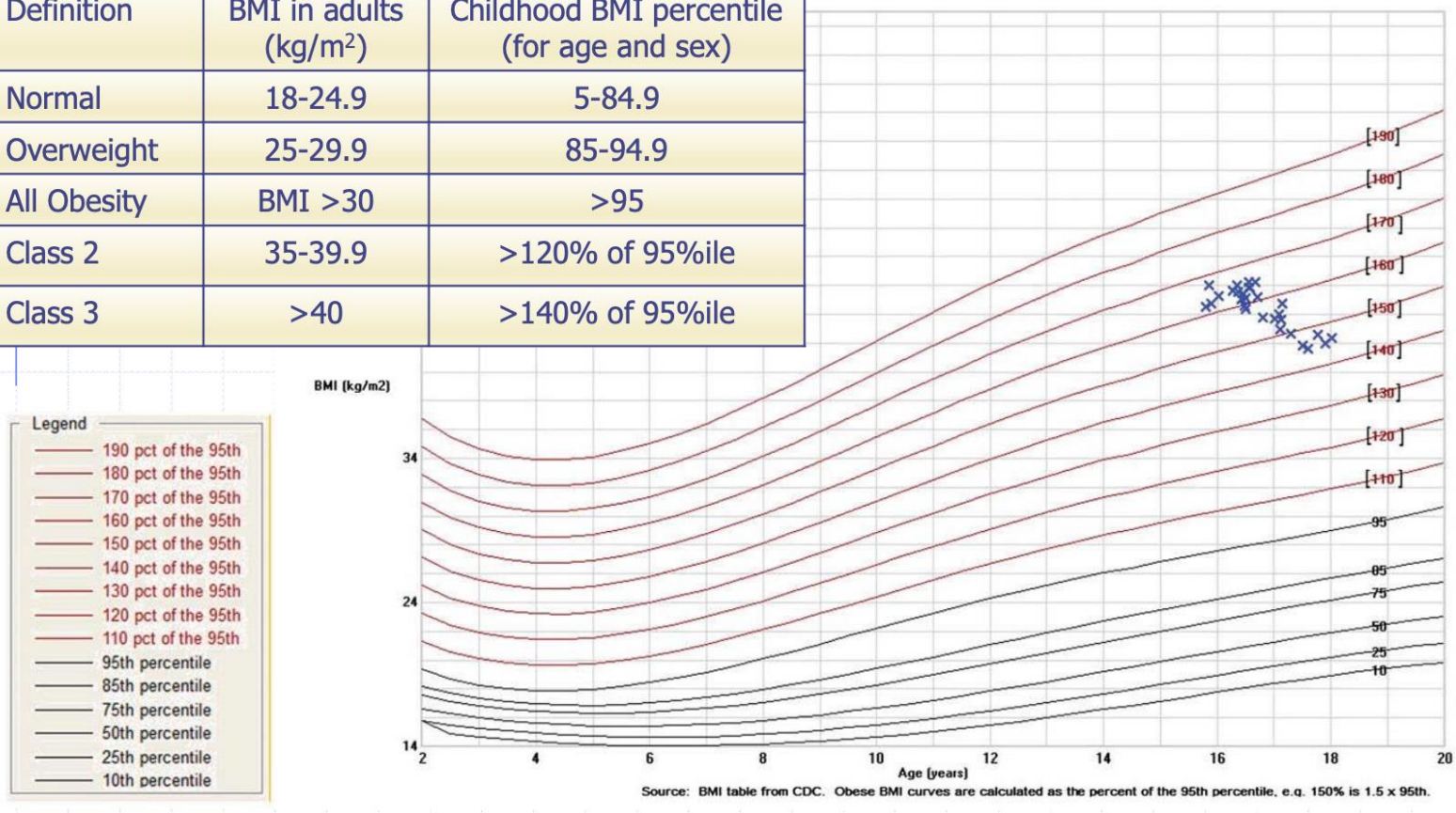
Classes of BMI	
Weight status	**BMI (kg/m^2)**
Underweight	<18.5
Normal weight	18.5-24.9
Overweight	25.0-29.9
Obesity, class I	30.0-34.9
Obesity, class II	35.0-39.9
Obesity, class III	≥ 40.0

Edmonton Obesity Staging System (EOSS)



Definitions of pediatric obesity

Definition	BMI in adults (kg/m^2)	Childhood BMI percentile (for age and sex)
Normal	18-24.9	5-84.9
Overweight	25-29.9	85-94.9
All Obesity	BMI >30	>95
Class 2	35-39.9	>120% of 95%ile
Class 3	>40	>140% of 95%ile



Kelly AS. Circulation. 2013;128:1689-1712; Gulati A. Pediatrics 2012;130:1136-40

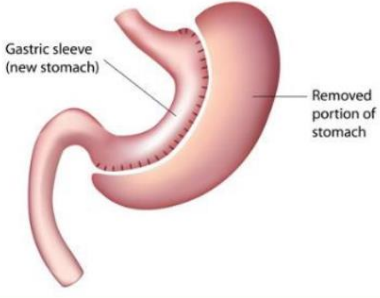
How Do We Treat Obesity?

diet

physical activity

behavioral modifications

medications



surgery

devices

Obesity is a **Multisystem Disease** associated with many complications (>100!) Doesn't it make sense to treat obesity to treat them all?

CNS
Migraine, pseudotumor cerebri, depression, anxiety social stigmatisation, stroke

Cardiovascular
Hypertension, CAD, stroke, congestive HF, atrial fibrillation, venous stasis, pulmonary embolism

Genitourinary
Women: urinary stress incontinence, PCOS, infertility, pregnancy complications
Men: benign prostatic hypertrophy, hypogonadism

Pulmonary
Obstructive sleep apnea, OHS, pulmonary hypertension, restrictive lung disease, respiratory failure

Renal
Nephrolithiasis, proteinuria, CKD

Gastrointestinal
Gastro-oesophageal reflux, cholelithiasis, NAFLD, NASH, hepatic steatosis

Endocrine: prediabetes, T2D, dyslipidaemia

Cancer: colorectal, postmenopausal breast, endometrial, gastrointestinal, liver

Infections: sensitivity to influenza, skin and soft-tissue infections

Others: osteoarthritis, thromboembolism

CAD = coronary artery disease; CKD = chronic kidney disease; HF = heart failure; NAFLD = nonalcoholic fatty liver disease; NASH = nonalcoholic steatohepatitis; OHS = obesity hypoventilation syndrome; PCOS = polycystic ovary syndrome; T2D = type 2 diabetes.

1. Tsai AG, Bessesen DH. *Ann Intern Med*. 2019;170(5):ITC33-ITC48. 2. Sarma S, Sockalingam S, Dash S. *Diabetes Obes Metab*. 2021;23(suppl 1):3-16.

Lifestyle Modification Therapy

US Preventive Services Task Force

Clinical Review & Education

JAMA | US Preventive Services Task Force | RECOMMENDATION STATEMENT

Screening for Obesity in Children and Adolescents
US Preventive Services Task Force
Recommendation Statement

US Preventive Services Task Force

IMPORTANCE Based on year 2000 Centers for Disease Control and Prevention growth charts, approximately 17% of children and adolescents aged 2 to 19 years in the United States have obesity, and almost 32% of children and adolescents are overweight or have obesity. Obesity in children and adolescents is associated with morbidity such as mental health and psychological issues, asthma, obstructive sleep apnea, orthopedic problems, and adverse cardiovascular and metabolic outcomes (eg, high blood pressure, abnormal lipid levels, and insulin resistance). Children and adolescents may also experience teasing and bullying behaviors based on their weight. Obesity in childhood and adolescence may continue into adulthood and lead to adverse cardiovascular outcomes or other obesity-related morbidity, such as type 2 diabetes.

SUBPOPULATION CONSIDERATIONS Although the overall rate of child and adolescent obesity has stabilized over the last decade after increasing steadily for 3 decades, obesity rates continue to increase in certain populations, such as African American girls and Hispanic boys. These racial/ethnic differences in obesity prevalence are likely a result of both genetic and nongenetic factors (eg, socioeconomic status, intake of sugar-sweetened beverages and fast food, and having a television in the bedroom).

OBJECTIVE To update the 2010 US Preventive Services Task Force (USPSTF) recommendation on screening for obesity in children 6 years and older.

EVIDENCE REVIEW The USPSTF reviewed the evidence on screening for obesity in children and adolescents and the benefits and harms of weight management interventions.

FINDINGS Comprehensive, intensive behavioral interventions (>26 contact hours) in children and adolescents 6 years and older who have obesity can result in improvements in weight status for up to 12 months, there is inadequate evidence regarding the effectiveness of less intensive interventions. The harms of behavioral interventions can be bounded as small to none, and the harms of screening are minimal. Therefore, the USPSTF concluded with moderate certainty that screening for obesity in children and adolescents 6 years and older is of moderate net benefit.

CONCLUSIONS AND RECOMMENDATION The USPSTF recommends that clinicians screen for obesity in children and adolescents 6 years and older and offer or refer them to comprehensive, intensive behavioral interventions to promote improvements in weight status. (B recommendation)

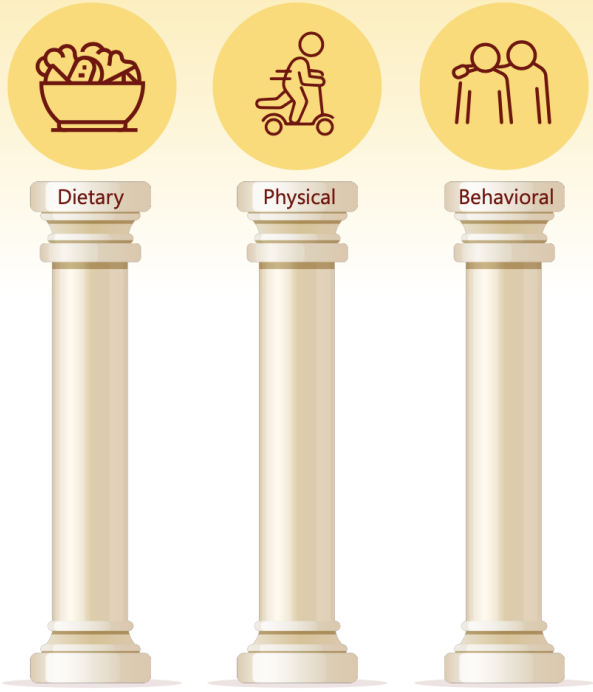
Editorial page 2378
Author Audio Interview
Related article page 2427 and JAMA Patient Page page 2460
CME Quiz at jamanetwork.com/learning
Related articles at jamapediatrics.com jamainternalmedicine.com

Author/Group Information: The US Preventive Services Task Force (USPSTF) members are listed at the end of this article.
Corresponding Author: David C. Grossman, MD, MPH (chair@uspstf.net).

JAMA. 2017;317(23):2417-2426. doi:10.1001/jama.2017.6803

"The USPSTF recommends that clinicians screen for obesity in children and adolescents 6 years and older and offer or refer them to comprehensive, intensive behavioral interventions to promote improvements in weight status."

"The USPSTF found that comprehensive, intensive behavioral interventions with a total of 26 contact hours or more over a period of 2 to 12 months resulted in weight loss. Behavioral interventions with a total of ***52 contact hours or more*** *demonstrated greater weight loss and some improvements in cardiovascular and metabolic risk factors."*



O'Connor et al. *JAMA* 2017.

Center for Pediatric Obesity Medicine

Western Michigan University
Homer Stryker M.D.
School of Medicine

Treatment of the child with obesity

Intensive Health Behavior and Lifestyle Treatment (IHBLT)

WHO:	WHEN:	WHAT:	WHERE:	DOSAGE:	FORMAT:	CHANNEL:
Patient and family in partnership with a multidisciplinary treatment team*	Promptly for child or adolescent with overweight or obesity	Health education and skill building on multiple topics Behavior modification and counseling	Healthcare setting Community-based setting with linkage to medical home	Longitudinal treatment across 3-12 months with ideally ≥ 26 contact hours	Group, Individual, or Both	Face-to-face (strongest evidence) Virtual (growing evidence)

* PCPs and/or PHCPs with training in obesity as well as other professionals trained in behavior and lifestyle fields such as dietitians, exercise specialists and behavioral health practitioners

FIGURE 3
Intensive health behavior and lifestyle treatment.

American Academy of Pediatrics *Clinical Practice Guideline for the Evaluation and Treatment of Children and Adolescents With Obesity.* *Pediatrics* (2023) 151 (2): e2022060640. https://doi.org/10.1542/peds.2022-060640

AAP Clinical Practice Guidelines

TREATMENT

P&PHCPs *should* treat overweight/obesity & comorbidities concurrently (KAS 4) following the principles of the **medical home** and the **chronic care model,** using a **family-centered** and **non-stigmatizing** approach that acknowledges obesity's **biologic, social, and structural drivers.**(KAS 9)

Components of Comprehensive Treatment	Overweight			Obesity		
	<6y	6 to <12y	≥12y	<6y	6 to <12y	≥12y
Motivational Interviewing[f] (KAS 10)	✓	✓	✓	✓	✓	✓
Intensive Health Behavior and Lifestyle Treatment[g] (KAS 11)	⚖	✓	✓	⚖	✓	✓
Weight Loss Pharmacotherapy[h] (KAS 12)						✓
Offer referral to Comprehensive Pediatric Metabolic & Bariatric Surgery programs[i] (KAS 13)						✓[i]

KAS12. Pediatricians and other PHCPs should offer adolescents 12 y and older with obesity weight loss pharmacotherapy, according to medication indications, risks, and benefits, as an adjunct to health behavior and lifestyle treatment. Grade B

Hampl SE, et al. Pediatrics. 2023

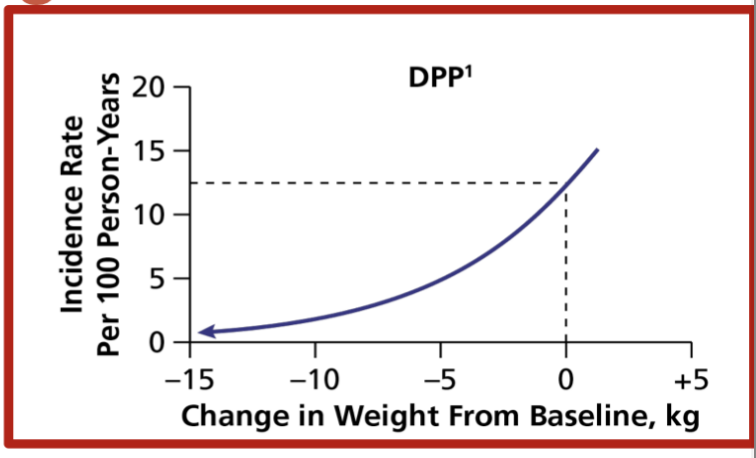
Center for Pediatric Obesity Medicine

Western Michigan University Homer Stryker M.D. School of Medicine

Why Was 5%-10% Weight Loss the Goal of Treatment?

Modest weight loss (5%-10%) can:

- Prevent T2DM[1]
- Improve glycemic control in T2DM
- Reduce need for antidiabetic agents
- Reduce blood pressure
- Reduce triglycerides
- Increase HDL-C
- Reduce CRP
- Improve symptoms of sleep apnea
- Improve markers of NAFLD



5%Weight Loss =
-50% Incidence T2DM

CRP: C-reactive protein; DPP: Diabetes Prevention Program; HDL-C: high-density lipoprotein cholesterol; NAFLD: nonalcoholic fatty liver disease.

1. Hamman RF et al. *Diabetes Care*. 2006;29:2102-2107.
2. http://www.lookaheadtrial.org/public/bibliography.pdf. Accessed September 17, 2014.

The Chronic Care Model for Obesity

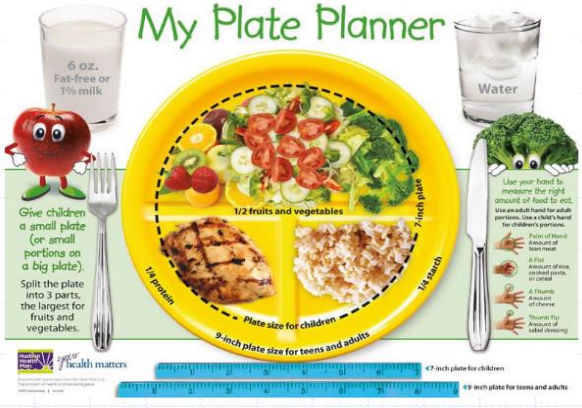
Environment:
- Family
- School
- Work site
- Community

-Genetics

→ **Patient/family self-management** → **Improved health outcomes**

← Medical system:
- Decision supports
- Self-management supports
- Delivery system design
- Information systems

- Decision supports—who is overweight/obese
- Patient self-management support—plate planner
- Delivery system design—provider reimbursement
- Information systems—linking providers to community resources



Dietz W. Health Affairs. 2007;26(2):430-440

Approach to obesity prevention through the life cycle must be specific to child's age

- Pre-gestational and gestational period (epigenetic risk)
  - Kral et al showed that bariatric surgery reduced obesity risk in half for children born after surgery
  - Antibiotic use during pregnancy and birth by C-section increase likelihood of offspring obesity
  - Metformin use in PCOS pregnancies increases risk of offspring higher BMI at 4 yrs old
- Birth to 3 years (toddler) period
  - Time when eating habits develop
  - Time when children's eating (and everything) demands become stronger
  - Time to teach parents about healthy eating and growth and picky eating
- Preschool and Elementary school age period
  - Can prevent and break BMI increase without weight loss
  - Obese children at 7y who normalized BMI by 13y had no higher risk of diabetes at 30y at non-obese
- Middle school and adolescence period
  - Children have control over what they eat
  - Weight loss becomes necessary to achieve healthy BMI
  - Obesity becomes very difficult to treat

Kral J. Pediatr.2006:e1644-9; Oken E. Am J Obstet Gynecol.2007;196:322.e1-8; Engen Hanem L. J Clin Endoc Metab.2018;103:1612-21; Bjerregaard LG, NEJM. 2018;378:1302-12

Effective counseling for preschool families: assess current practices*

- Nutrition:
  - Eating outside of home/school per week
  - Intake of juice and milk daily
  - Eating breakfast per week
  - Snacks vs junk?
- Activity:
  - TV/screen time per week:
  - Regular exercise per week:

*Based on the "15 min obesity prevention protocol" from Davis M. Pediatrics. 2007:120:S245

Intervention: Assessment motivation, develop a joint plan (modified MI)

- Assess concern (scale of 1-10)
  - Importance to change
  - Confidence in being successful
- Develop 3 targets for change
  - 2 Dietary targets
    - Family choose from eating habits discussion
    - Try for 1 positive (start eating breakfast) and one negative (cut down to 1 glass of juice, fast food 2 times per months), be specific
  - 1 Physical activity issues (Screen time, walking to school, playing in park, sports)
- Provide positive feedback
- Agree on a follow-up time (3 months)

Adapted from: Barlow S. Pediatrics. 2007;120 Suppl 4:S164-92

Dietary Targets

Macronutrient	% of energy (calories)	Food Grouping
Carbohydrate *	35-45%	**GO...** Eat plenty
* Foods categorized by glycemic index and glycemic load		**BE CAREFUL...** Control portions
		STOP AND THINK... Limit (or eliminate)
Fat	35-45%	**Fat**
Protein	20%	**Protein**

Carbohydrate

Low-Glycemic

GO...
Eat plenty

Digest slowly and gradually release glucose into the bloodstream

non-starchy vegetables, whole fruits, legumes (beans)

Moderate-Glycemic

BE CAREFUL...
Control portions

Digest and release glucose into the bloodstream at a moderate rate

starchy vegetables, dried fruits, tropical fruits, minimally processed whole grains

High-Glycemic

STOP AND THINK...
Limit (or eliminate)

Digest quickly and rapidly release glucose into the bloodstream

potato products, juices and sugary beverages, most breads and breakfast cereals, white rice

Katherine H. Saunders, MD; Leon I. Igel, MD, FACP, DABOM; Alpana P. Shukla, MD, MRCP; Louis J. Aronne, MD, FACP, DABOM, FTOS
Weill Cornell Medicine, New York, NY

kph2001@med.cornell.edu

Drs. Saunders, Igel, and Shukla reported no potential conflict of interest relevant to this article.

Drug-induced weight gain: Rethinking our choices

Weight gain secondary to medications is a potentially modifiable risk. Here's how to optimize drug choices for patients with several common conditions.

TABLE 3

Weighing in on antidepressants[3]

Weight gain	Weight neutral	Weight loss
TCAs (amitriptyline, doxepin, imipramine, nortriptyline) MAOIs Mirtazapine SSRI (paroxetine)	SSRIs (fluoxetine, sertraline)	Bupropion

MAOIs, monoamine oxidase inhibitors; SSRIs, selective serotonin reuptake inhibitors, TCAs, tricyclic antidepressants.

Saunders KH et al. *J Fam Pract*. 2016;65(11):780-788.

TABLE 1

How these antidiabetic drugs affect weight[3]

Weight gain	Weight neutral	Weight loss
Insulin	Alpha-glucosidase inhibitors	GLP-1 agonists
Meglitinides	Bromocriptine	Metformin
Sulfonylureas	Colesevelam	Pramlintide
Thiazolidinediones	DPP-4 inhibitors	SGLT2 inhibitors

DPP-4, dipeptidyl peptidase-4; GLP-1, glucagon-like peptide-1; SGLT2, sodium-glucose co-transporter 2.

TABLE 2

Antihypertensives and weight[3]

Weight gain	Weight neutral
Alpha-adrenergic blockers	ACE inhibitors
Beta-adrenergic blockers (atenolol, metoprolol, nadolol, propranolol)	Angiotensin receptor blockers
	Beta-adrenergic blockers (carvedilol, nebivolol)
	CCBs
	Thiazides

ACE, angiotensin-converting enzyme; CCBs, calcium channel blockers.

Saunders KH et al. *J Fam Pract*. 2016;65(11):780-788.

Drug-Induced Weight Gain

- Choose **weight-losing and weight-neutral** meds for diabetes
- **Avoid β-blockers** for blood pressure
- Follow a **shared decision-making process** for antidepressants, antipsychotics and antiepileptics
- **Oral** over injectable **contraceptives**
- **Avoid steroids** for inflammatory diseases
- Choose **antihistamines** with less **less sedation**

- **When a weight-promoting medication can't be avoided, use the lowest effective dose for the shortest duration and/or consider adding antiobesity pharmacotherapy**

Apovian CM et al. *J Clin Endocrinol Metab*. 2015;100:342-362.

When Should You Consider Antiobesity Medications?

	BMI ≥ 25 kg/m²	BMI ≥ 27 kg/m² with comorbidity or BMI ≥ 30 kg/m²	BMI ≥ 35 kg/m² with comorbidity or BMI ≥ 40 kg/m²
Diet, exercise, and behavioral modification for all patients with overweight and obesity	Diet, exercise, behavioral modification	Diet, exercise, behavioral modification	Diet, exercise, behavioral modification
Consider pharmacotherapy for patients **unable to lose** weight and maintain weight loss with lifestyle interventions alone		Pharmacotherapy	Pharmacotherapy
	Hydrogel devices	Some devices	Some devices Bariatric surgery

Medications should not be prescribed in the absence of **behavioral counseling**

2023 AAP Guidelines

APPENDIX 1 Algorithm for Screening, Diagnosis, Evaluation, and Treatment of Children and Adolescents with Obesity

SCREENING

P&PHCPs *should* measure height & weight, calculate BMI, and **assess BMI percentile** using age- and sex-specific CDC growth charts or severe obesity growth charts **for all children 2-18 years** (KAS 1)

BMI ≥85th percentile?

- No → Repeat at least annually
- Yes ↓

DIAGNOSIS

Overweight	Obesity	Severe Obesity
BMI ≥85th to <95th percentile	BMI ≥95th percentile	BMI ≥120% of the 95th percentile

EVALUATION

Components of Comprehensive Evaluation	Overweight <10y	Overweight ≥10y	Obesity <10y	Obesity ≥10y
Comprehensive history, MBH screening, SDOH evaluation, physical examination, & diagnostic studies (KAS 2)	✓	✓	✓	✓
Blood pressure (KAS 8)	✓[a]	✓	✓[a]	✓
Fasting lipid panel (KAS 3, 3.1, 5)		✓	⚖	✓
FPG, OGTT, or HgbA1C (KAS 3, 3.1, 6) & **ALT** (KAS 3, 3.1, 7)		⚖[b]		✓

Elevated BP?[c]

- Yes → Refer to **AAP High BP CPG[d]**
- No → Repeat at every visit

Abnormal labs?[e]

- Yes → Refer to **Appendix 4**
- No → *May* repeat testing in 2 years or sooner if changes in exam/risk

TREATMENT

P&PHCPs *should* treat overweight/obesity & comorbidities concurrently (KAS 4) following the principles of the **medical home** and the **chronic care model,** using a **family-centered** and **non-stigmatizing** approach that acknowledges obesity's **biologic, social, and structural drivers.**(KAS 9)

Components of Comprehensive Treatment	Overweight <6y	Overweight 6 to <12y	Overweight ≥12y	Obesity <6y	Obesity 6 to <12y	Obesity ≥12y
Motivational Interviewing[f] (KAS 10)	✓	✓	✓	✓	✓	✓
Intensive Health Behavior and Lifestyle Treatment[g] (KAS 11)	⚖	✓	✓	⚖	✓	✓
Weight Loss Pharmacotherapy[h] (KAS 12)						✓
Offer referral to Comprehensive Pediatric Metabolic & Bariatric Surgery programs[i] (KAS 13)						✓[i]

Approved Anti-Obesity Medications For Pediatric Obesity

Phentermine approved for ≥16 years

Orlistat approved for ≥12 years

Liraglutide 3 mg approved for ≥12 years

Phentermine/topiramate approved for ≥12 years

Semaglutide 2.4 mg approved for ≥12 years

Setmelanotide approved for ≥6 years

Liraglutide 3 mg approved for ≥12 years

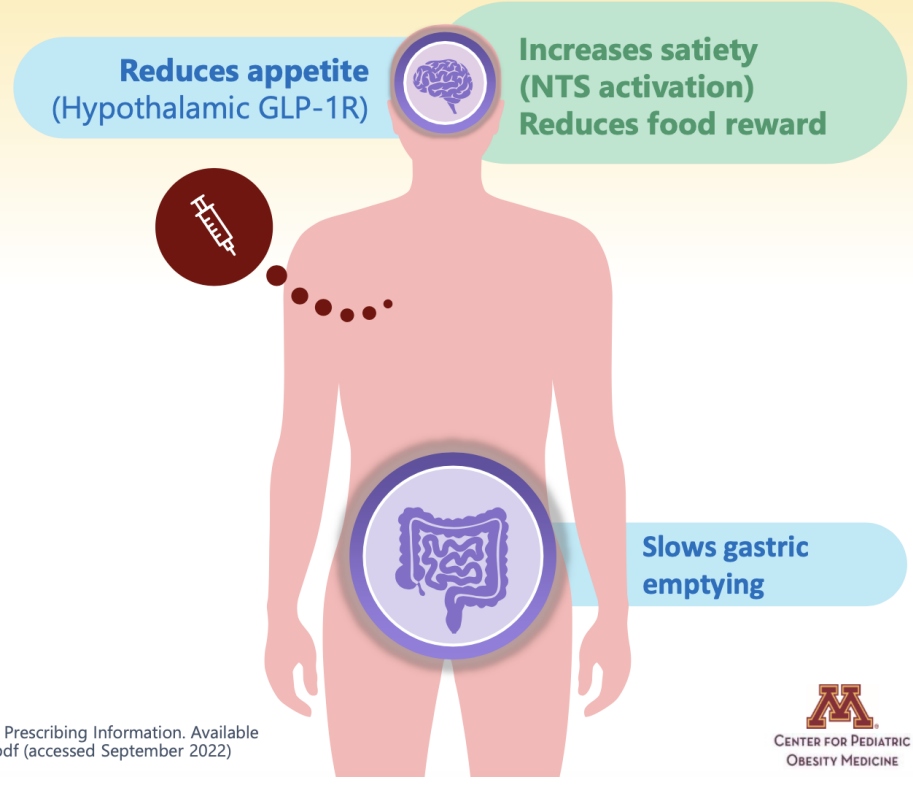
1. Suprenza (phentermine) Prescribing Information. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/202088s005lbl.pdf (accessed September 2022);
2. Xenical (orlistat) Prescribing Information. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/020766s029lbl.pdf (accessed September 2022);
3. Saxenda (liraglutide) Prescribing Information. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2014/206321Orig1s000lbl.pdf (accessed September 2022);
4. Qsymia (phentermine/topiramate) Prescribing Information. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/022580s021lbl.pdf (accessed September 2022);
5. Wegovy (semaglutide 2.4 mg) Prescribing Information. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/215256s000lbl.pdf (accessed September 2022);
6. Saxenda (liraglutide) Summary of product characteristics. Available at: https://www.ema.europa.eu/en/documents/product-information/saxenda-epar-product-information_en.pdf (accessed September 2022);
7. Wegovy (semaglutide 2.4 mg) Summary of product characteristics. Available at: https://www.ema.europa.eu/en/documents/product-information/wegovy-epar-product-information_en.pdf (accessed September 2022).

Center for Pediatric Obesity Medicine

Western Michigan University
Homer Stryker M.D.
School of Medicine

Liraglutide 3 mg

- Glucagon-like peptide-1 receptor agonist
- Originally developed as treatment for type 2 diabetes (increases postprandial insulin secretion, reduces glucagon)
- Administered subcutaneously once per day
- Mechanisms of action: reduces appetite (hypothalamic GLP-1 receptors), increases satiety (NTS activation, gastric emptying), reduces food reward



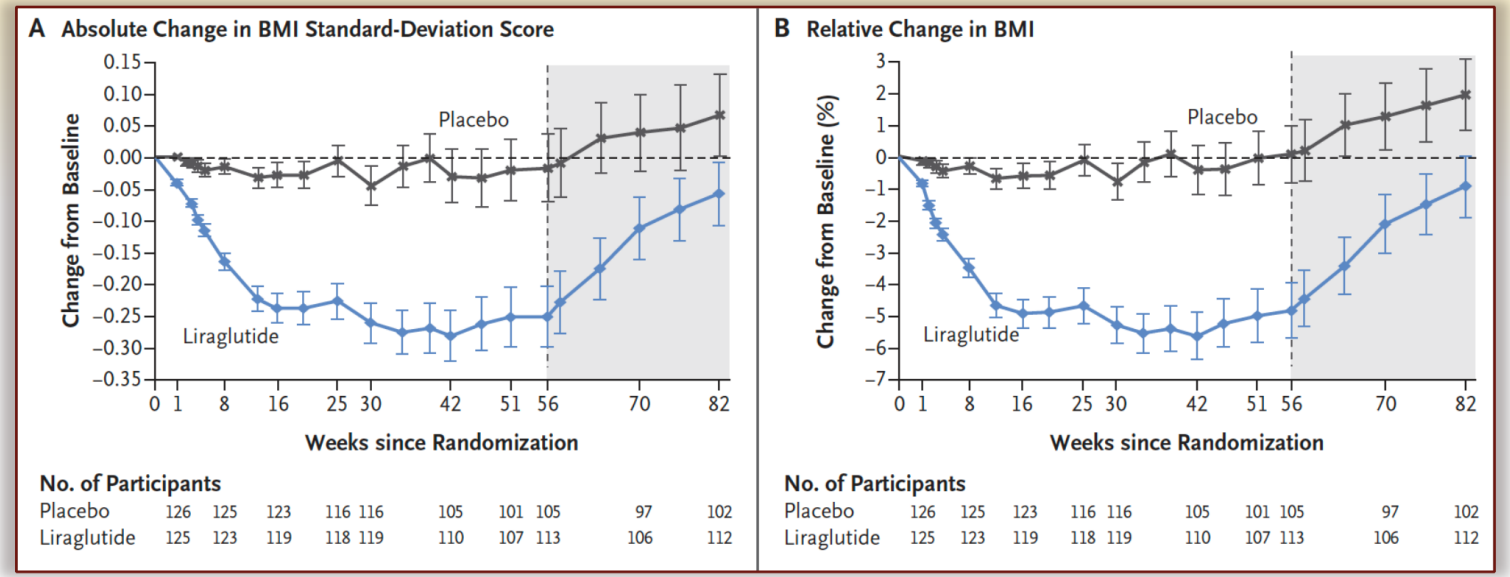
1. Kelly et al. *N Engl J Med* 2020; doi:10.1056/NEJMoa1916038; 2. Saxenda (liraglutide) Prescribing Information. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2014/206321Orig1s000lbl.pdf (accessed September 2022)

Center for Pediatric Obesity Medicine

Western Michigan University
Homer Stryker M.D.
School of Medicine

Liraglutide 3 mg Adolescent RCT

Mean BMI Change By Group



Kelly et al. *NEJM* 2020.

Center for Pediatric Obesity Medicine

Western Michigan University
Homer Stryker M.D.
School of Medicine

Saxenda 3mg

Liraglutide Clinical Pearls

1. Most common side effects: nausea, vomiting, diarrhea, injection site reactions
   - Counsel on the importance of eating small portions and eating slowly to minimize GI side effects
   - Ensure good hydration with V/D
2. Use demo pen to increase acceptability
   - Injections can be done with or without food and at any time of day
3. Start liraglutide 0.6 mg SC daily x 7 days,

   then 1.2 mg SC daily x 7 days,

   then 1.8 mg SC daily x 7 days (Victoza max dose)

   then 2.4 mg SC daily x 7 days,

   then 3 mg SC daily

Semaglutide 2.4 mg

Brand name: **Wegovy**

Approved in 2021 for chronic weight management (Ozempic = 1 mg weekly, approved in 2017 for diabetes and 2020 for cardiovascular risk reduction)

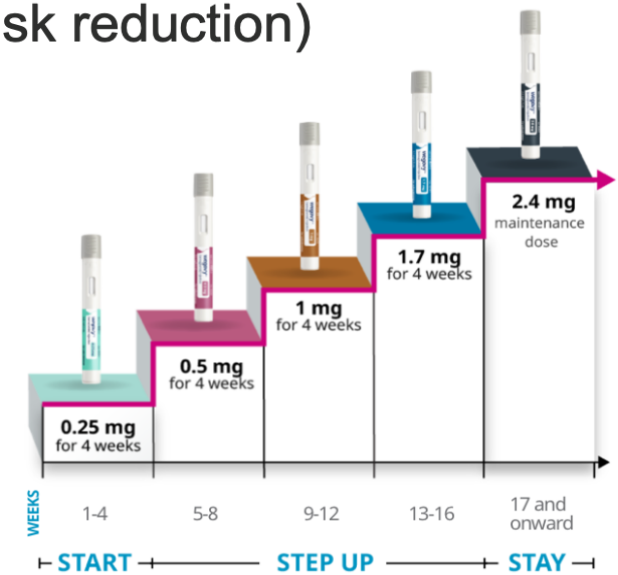
GLP-1 receptor agonist

0.25 – 2.4 mg subcutaneous injection once weekly

<u>Weight loss at 68 weeks</u>

14.9% = 2.4 mg weekly

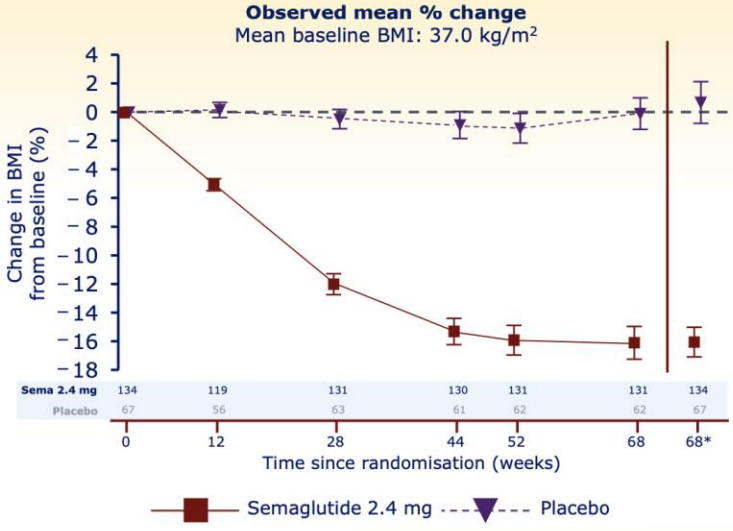
2.4% = lifestyle alone

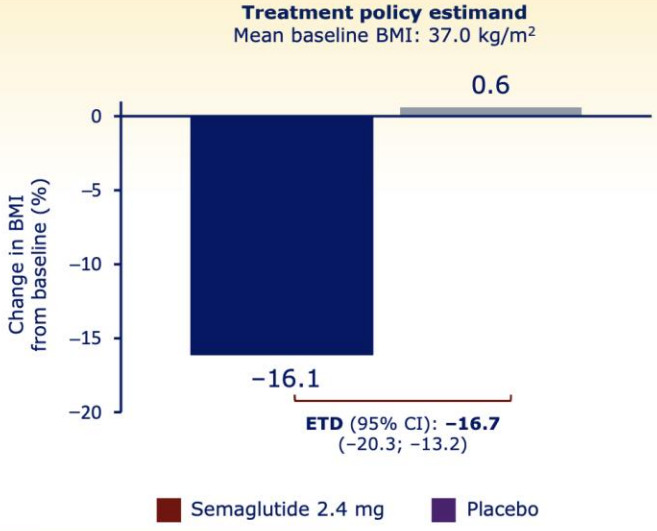


Wilding JPH, et al. N Engl J Med. 2021; 18;384(11):989.

Primary Endpoint: Change in BMI (%)

Estimated means – treatment policy estimand





Analysis at week 68	ETD	95% CI	P-value
Semaglutide 2.4 mg vs placebo	−16.7 %-points	−20.3; −13.2	<0.0001

Weghuber D, et al. NEJM 2022

Center for Pediatric

Western Michigan University
Homer Stryker M.D.
SCHOOL OF MEDICINE

Semaglutide 2.4 mg

Side effects: nausea, vomiting, diarrhea, constipation, dyspepsia, abdominal pain

Caution: pregnancy, gastroparesis, pancreatitis, medullary thyroid carcinoma, multiple endocrine neoplasia syndrome type 2

Special considerations: type 2 diabetes, prediabetes, impaired glucose tolerance, concomitant psychiatric medications, cardiovascular risk

Phentermine

Brand names: **Adipex-P, Lomaira**

Approved in 1959 for short-term use (3 months)

Norepinephrine-releasing agent

Dosing: 8, 15, 37.5 mg

<u>Weight loss at 28 weeks</u>

30 mg = 6.1%

15 mg = 5.5%

Lifestyle alone = 1.7%

Aronne LJ, et al. Obesity (Silver Spring). 2013;21(11):2163-71.

Phentermine

Schedule IV controlled substance

<u>Side effects</u>

- increased heart rate
- headache
- insomnia
- dry mouth

Caution:

- pregnancy
- cardiovascular disease
- hyperthyroidism
- glaucoma

Orlistat

Brand names: **Alli** (OTC) **Xenical** (Rx)

60 mg TID 120 mg TID

Approved in 1999, lipase inhibitor

<u>Side effects</u>: abdominal discomfort, steatorrhea, fecal urgency, fecal incontinence

<u>Special considerations</u>: constipation; psyllium fiber

<u>Decreases absorption</u>:

- vitamins A, D, E, K → take multivitamin
- meds → cyclosporine, levothyroxine, warfarin, antiepileptics

Yanovski SZ, et al. JAMA. 2014;311(1):74-86.

Phentermine/topiramate ER

Brand name: **Qsymia**

Approved in 2012

Phentermine = norepinephrine-releasing agent

Topiramate = neurostabilizer, approved for epilepsy (1996), migraines (2004)

<u>Weight loss at 56 weeks</u>

9.8% - 15/92 mg daily

7.8% - 7.5/46 mg daily

1.2% - lifestyle alone

Gadde KM, et al. Lancet 2011;377(9774):1341–52.

Phentermine/topiramate ER

Schedule IV controlled substance

Side effects: increased heart rate, headache, insomnia, paresthesia

Special considerations: migraines

Caution: cardiovascular disease, hyperthyroidism, glaucoma, nephrolithiasis, pregnancy

Risk Evaluation and Mitigation Strategy (REMS)

A Risk Evaluation and Mitigation Strategy (REMS) is a strategy to manage known or potential serious risks associated with a drug product and is required by the Food and Drug Administration (FDA) to ensure that the benefits of a drug outweigh its risks. The FDA has required a REMS for Qsymia.

The purpose of the Qsymia REMS is to inform prescribers and females of reproductive potential about the:

- Increased risk of congenital malformation, specifically orofacial clefts, in infants exposed to Qsymia during the first trimester of pregnancy
- Importance of pregnancy prevention for females of reproductive potential receiving Qsymia
- Need to discontinue Qsymia immediately if pregnancy occurs

http://www.qsymiarems.com

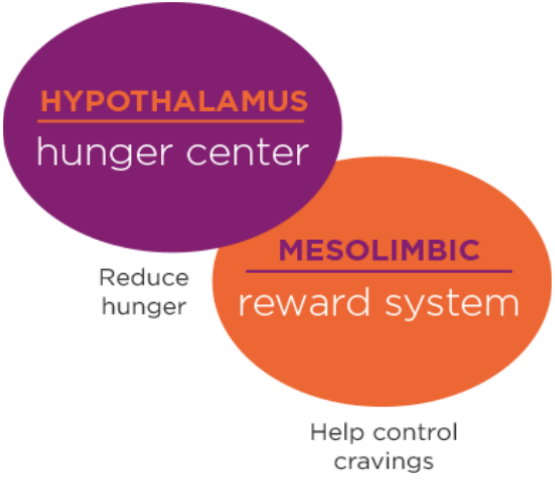
Naltrexone SR/bupropion SR

Brand name: **Contrave**

Approved in 2014

Naltrexone = opioid receptor antagonist

- opioid dependency (1984)
- alcohol addiction (1994)



Bupropion = dopamine and norepinephrine reuptake inhibitor

- depression (1985)
- smoking cessation (1997)

8/90 mg (1 tablet) daily to 16/180 mg (2 tablets) BID

Naltrexone SR/bupropion SR

<u>Weight loss at 56 weeks</u>

6.1% = 16/180 mg (2 tablets) BID

1.3% = lifestyle alone

<u>Side effects</u>: headache, nausea, vomiting, constipation

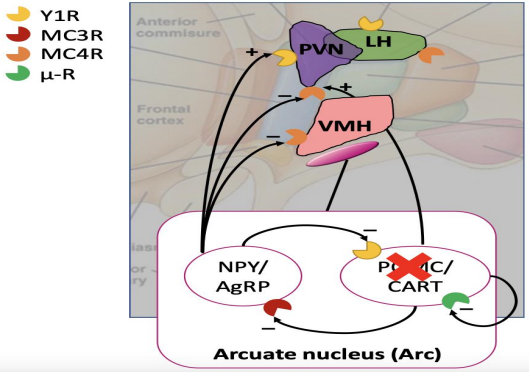
<u>Caution</u>: pregnancy, pain, opioid use, seizures, uncontrolled hypertension

<u>Special considerations</u>: food cravings, addictive food behaviors, depression, desire to quit smoking or reduce alcohol consumption

Greenway FL, et al. Lancet. 2010;376(9741):595–605.

Setmelanotide 2.4 mg > 6 year old

POMC Deficiency



- Adrenal insufficiency
- Hypopigmentation

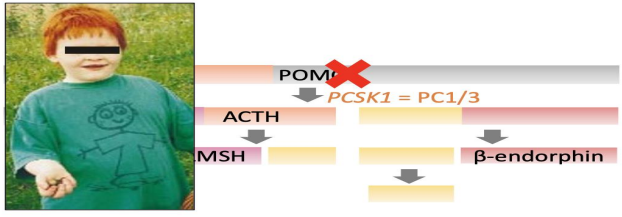
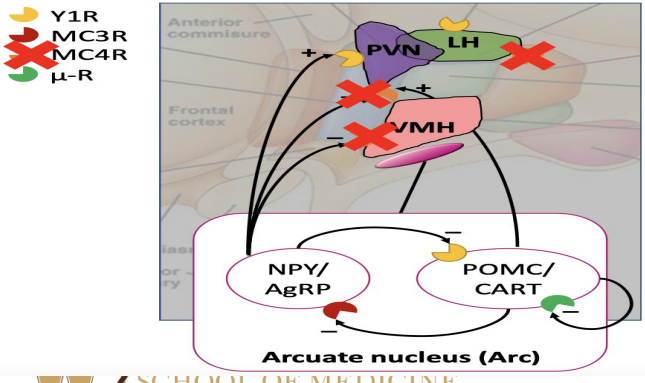


Image: Barsch & Schwartz 2002 (adapted)

MC4R Deficiency



- Most common monogenic obesity
- ↑ lean and fat mass
- Tall
- Normal puberty

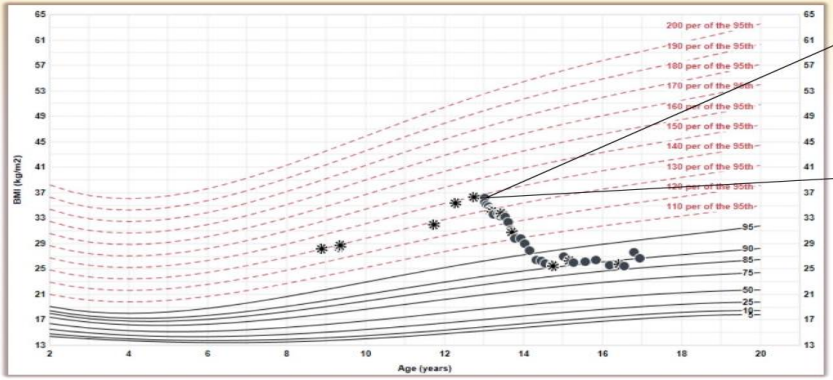
Farooqi et al. 2003;348(12):1085-1095.

Case of severe infantile obesity

- This boy was born after a regular pregnancy from consanguineous parents of Turkish origin with birth parameters in the normal range (weight 3.295 kg; height 50 cm; head circumference 36.5 cm).
- At birth, the boy was rapidly admitted in the local neonatology department for bilateral pneumothorax with a favorable evolution after 1 week. During his stay, several instances of asymptomatic hypoglycemia were noticed, and he received maltodextrin supplementation.
- He rapidly developed cholestasis and the diagnosis of adrenocorticotrophin hormone (ACTH) deficiency was made at day 5 (cortisol < 3 nmol/L [<8.3 µg/L] [range 110-520 nmol/L]; ACTH < 1 pmol/L [< 5 pg/mL]).
- No other hypothalamic-pituitary deficiency or anatomical lesion were found as a newborn or later. Treatment by hydrocortisone was started at day 6 with the usual dose of 20 mg/m^2/day.
- During the first year of life, he developed a severe obesity phenotype (body mass index [BMI] > 97 percentile at the age of 6 months) without adiposity rebound (Fig. 1). The parents described severe hyperphagia and necessity to feed their child every 2 hours after the age of 6 months

Western Michigan University
Homer Stryker M.D.
SCHOOL OF MEDICINE

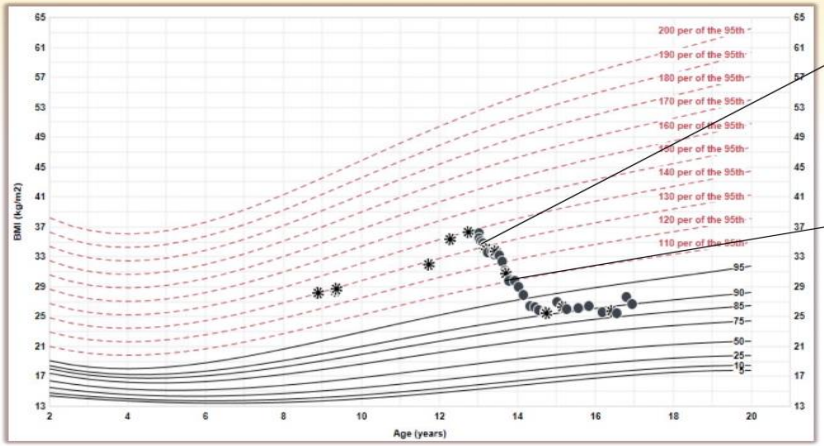
JCEM Case Reports, Volume 1, Issue 3, May 2023, luad041, https://doi.org/10.1210/jcemcr/luad041



Started flex meal plan

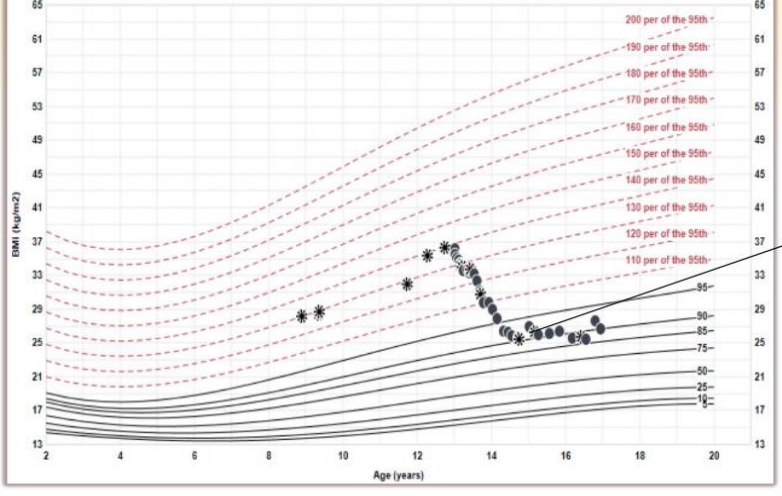
Down 8lbs in 2 mos; very difficult so started topiramate 75 mg qd

13 yo girl, BMI 36 kg/m²

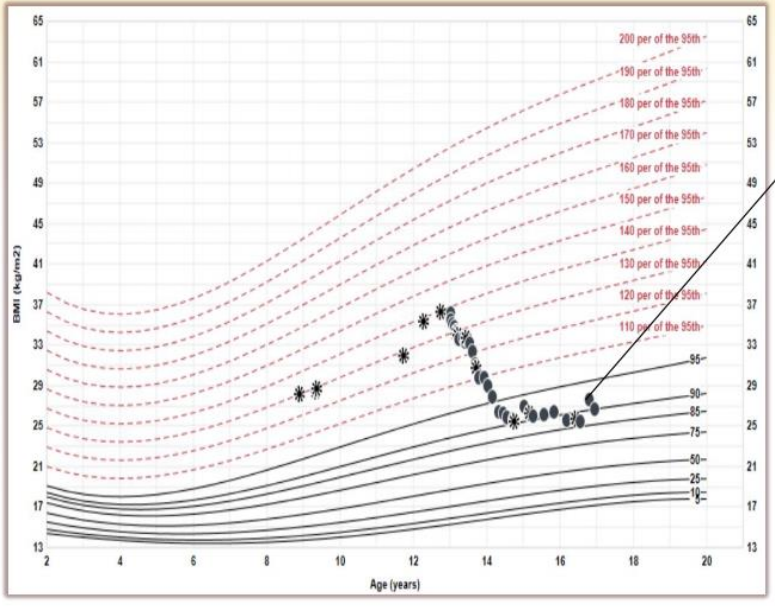


Down 7 lbs in 4 mos. Added phentermine 15 mg qd

Down 21 lbs in next 5 mos; continues with topiramate 75 mg+phentermine 15 mg qd

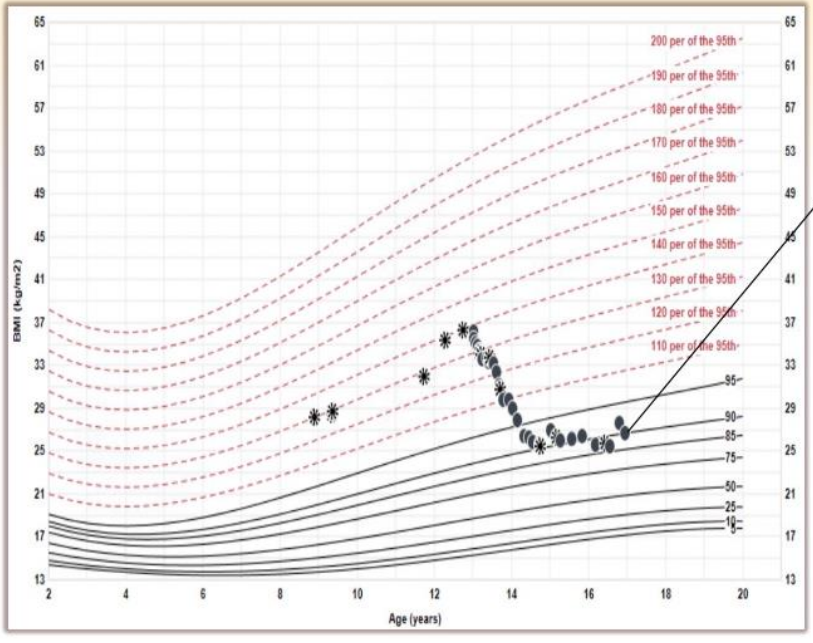


Tried every other day dosing of phentermine but pt felt increase in desire to eat



Gained 14 lbs in past 3 mos; “voracious” appetite; felt that medications were no longer helpful; added liraglutide 1.8 mg qd

13 yo girl, BMI 36 kg/m^2



Down 6 lbs in 2 mos; appetite much better; continued liraglutide 1.8 mg, topiramate 75 mg and phentermine 15 mg

Newer medications

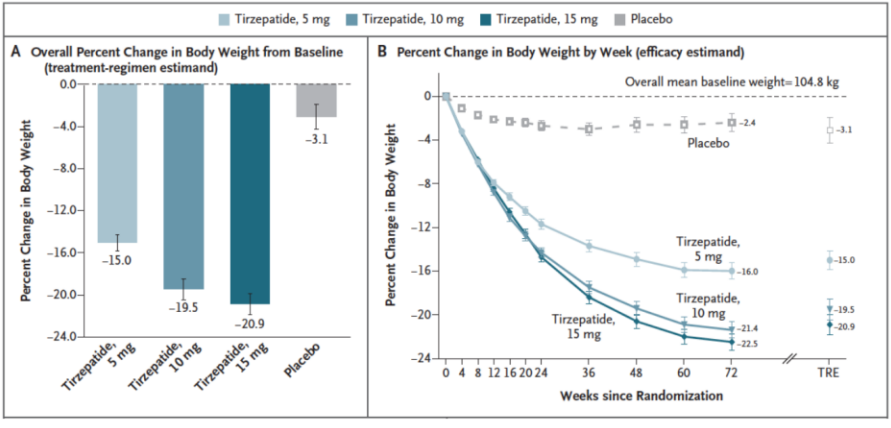
Tirzepatide: Combination GLP1/GIP receptor agonist for the treatment of obesity (currently approved for T2DM)

Glucose-dependent insulinotropic polypeptide (GIP) mechanism of action

- incretin hormone
- Promotes storage of dietary lipid; reduces ectopic fat accumulation
- Activates hypothalamic neurons to reduce food intake
- May enhance GLP-1 mediated weight loss by attenuating aversive response

Tirzepatide (dual GLP1/GIP Receptor agonist)

- Start at 2.5 mg SC weekly and increase dose q4 weeks based on efficacy and tolerability, up to 15mg SC weekly
- Mean 20% weight loss at 1 year on 15 mg dose
- AEs: nausea, vomiting, abd pain, diarrhea, constipation
- Trials underway for antiobesity indication



Which Medication? Consider These Questions

1) **Are there side effects, contraindications or drug-drug interactions?**

- phentermine → anxiety
- bupropion/naltrexone → history of seizure, opioid use

2) **Could any of the medications improve another symptom or condition?**

- phentermine/topiramate → migraines
- liraglutide, semaglutide → elevated blood sugar

Which Medication? Consider These Questions

3) **How effective is the medication?**

- semaglutide → 12.4%*
- orlistat → 3%*

4) **What is the patient's preference re: administration/timing?**

- bupropion/naltrexone → oral, twice daily
- semaglutide → subcutaneous injection, once weekly

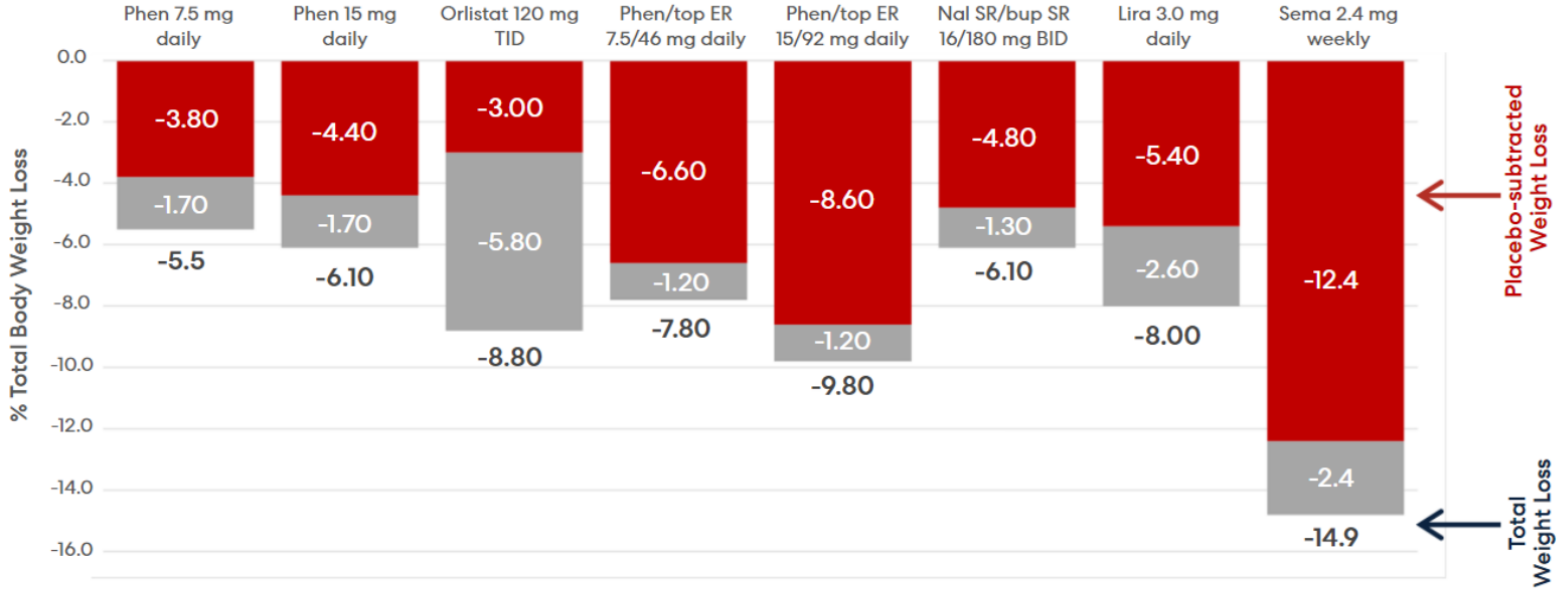
5) **How expensive is the medication? Is it covered?**

- phentermine → $11-50
- liraglutide, semaglutide → >$1,000

*placebo-subtracted weight loss

Gadde KM, et al. Lancet 2011;377(9774):1341–52.
Davidson MH, et al. JAMA. 1999;281(3):235-42.
https://www.GoodRx.com/ (April, 2020)

How Effective are the Meds?



ITT analysis

Phentermine: 28 week study
Semaglutide: 68 week study
All other studies: 52-56 weeks

Western Michigan University
Homer Stryker M.D.
SCHOOL OF MEDICINE

Practical Tips for Treatment

- Medications should not be prescribed in the absence of behavioral counseling on **diet, physical activity and lifestyle interventions**
- Assess **effectiveness and safety** of meds at least monthly x 3 months then at least every 3 months
- Continue med if safe and effective (**≥ 5% at 3 months**)
- Stop med if ineffective or safety/tolerability concerns; **consider alternative** medication or treatment approach

Apovian CM et al. *J Clin Endocrinol Metab*. 2015;100:342-362.

Bariatric Surgery

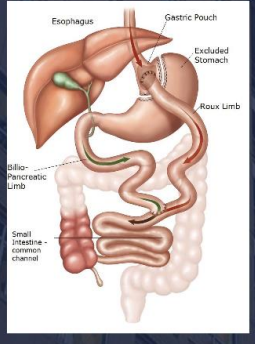
- Metabolic/Bariatric surgery
  - Offered to children ages 12 and above with: class 2 severe obesity with co morbidities or class 3 severe obesity (co morbidities need not be present)

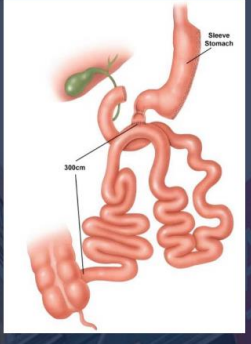
TABLE 20 Criteria for Pediatric Metabolic and Bariatric Surgery[733]

Weight Criteria	Criteria for Comorbid Conditions
Class 2 obesity, BMI $\geq$ 35 kg/m^2 or 120% of the 95th percentile for age and sex, whichever is lower	Clinically significant disease; examples include but are not limited to T2DM, IIH, NASH, Blount disease, SCFE, GERD, obstructive sleep apnea (AHI >5), cardiovascular disease risks (HTN, hyperlipidemia, insulin resistance), depressed health-related quality of life.
Class 3 obesity, BMI $\geq$ 40 kg/m^2 or 140% of the 95th percentile for age and sex, whichever is lower	Not required but commonly present.

AHI, apnea-hypopnea index.

Most Common Surgical Options

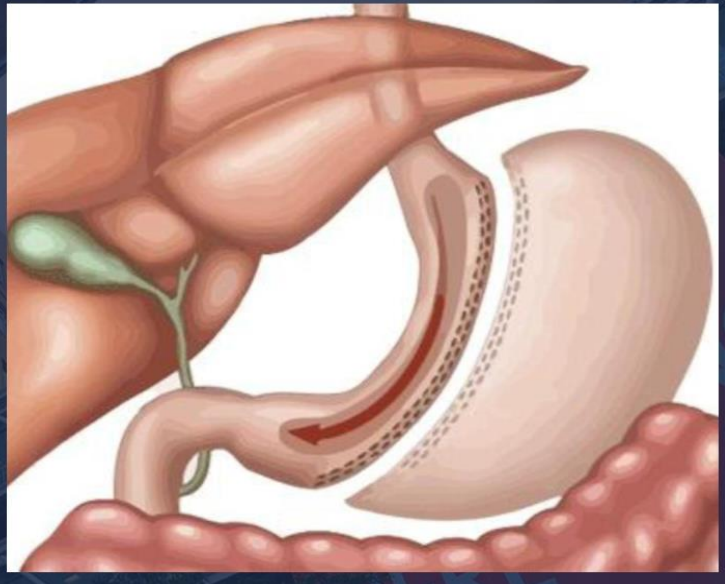




Sleeve Gastrectomy	Gastric Bypass	Duodenal Switch	Gastric Band

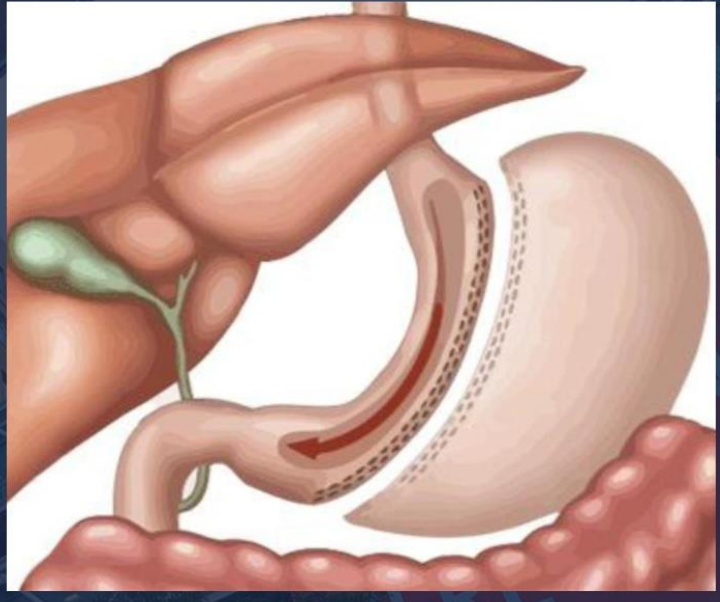
Sleeve Gastrectomy

- Most popular bariatric surgery in world
- Surgery takes < 1 hour.
- 1-2 night hospital stay
  Outpatient surgery?
- Simple
- Expected weight loss 55-60%
- Effective at reducing comorbidities
- Mechanism: restriction + hormone change



Sleeve Complications

- Leak < 1%
- PE
- **Reflux**
- **Barrett's esophagus**
- Narrowing of sleeve
- Bleeding
- Splenic vein thrombosis 0.3-0.7%
- Limited data on long term complications/results



Roux-en-Y Gastric Bypass

Extensive worldwide experience

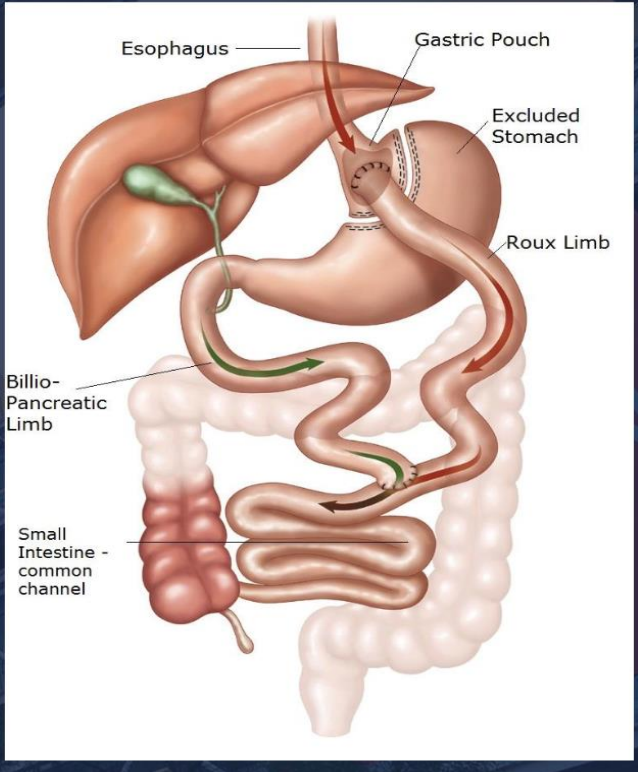
Surgery takes about 1-2 hours

1-2 night postop stay

Expected excess weight loss 52-68%

Restriction, hormonal changes, Malabsorbtion (mainly if distal bypass)

Particularly effective for GERD and diabetes



RYGB risks

- Leak < 1%
- Stricture 5%
- PE < 1%
- Marginal ulcer 5%
- Internal hernia (2-5%)
- Vitamin deficiencies
- Osteoporosis
- Dumping syndrome

- **Diabetes**:
  - complete remission SG 61% and RYGB 67% at 5 years (not clinically significant, underpowered)

- **GERD**:
  - RYGB 66% improved, worse 6%
  - SG 34% improved, 31% worse
  - new onset GERD: SG 31%, RYGB 10% (p =0.01)
  - 9/101 patients required conversion to bypass due to GERD

- both groups had a significant improvement of QOL

- incidence of micronutrient deficiency similar in both groups (SG 28, RYGB 27)
  - vitD, B12, Fe, folic acid, zinc

1. Peterli et al. Effect of Laparoscopic Sleeve Gastrectomy vs Laparoscopic Roux-en-Y Gastric Bypass on Weight Loss in Patients With Morbid Obesity (JAMA, 2018)

What Comes to Mind??

We Make Assumptions Based on Appearance

What is Weight Bias?

Making (negative) assumptions or judgments (consciously or unconsciously) based on the appearance of excess weight

Weight Bias in Healthcare: Individual Examples

I asked a gynecologist for help with low libido. His response: ***"Lose weight so your husband is interested. That will solve your problem."***
I changed doctors after that! And I've told everyone I know to stay away from that doctor.

I became very frustrated when a provider disregarded what I was telling him because he had already made up his mind that ***obesity was at the root of all my problems.***

You could walk in with an ax sticking out of your head and they would tell you your head hurts ***because you are fat.***

“7 A’s” To Address Weight Bias in Healthcare

- **A**ppreciate the complexity of obesity
- **A**wareness of implicit assumptions and beliefs
- **A**ttention to what’s in our control
- **A**ppreciate that shaming doesn’t motivate
- Support patients’ **A**utonomy
- **A**ddress consequences of stigma
- **A**dvocate and Educate

Obesity Terminology

"People-first" language recognizes the potential hazards of referring to or labeling individuals by their disease. Thus, **"patient who is overweight or has obesity" or "patient with overweight or obesity"** are preferred over "obese patient." This is similar to the standard with other diseases, such as diabetes mellitus, wherein "patient with diabetes" is preferred over "diabetic patient."

Encouraged Terms

- Weight
- Unhealthy weight
- Overweight
- Body mass index
- Excessive energy stores
- Affected by obesity

Discouraged Terms

- Morbidly obese
- Obese
- Fat
- Heaviness
- Large size

Attention To What's In Our Control

Attention to What's in Our Control

- Provide wide-based, higher weight capacity chairs
- Consider specialized bariatric chairs, when possible
- Offer large (or thigh-sized) blood pressure cuffs
- Neutral waiting room literature
- Offer extra-large gowns
- Higher capacity scale (ideally >500 lbs), in a private area
- Pedestal rather than wall-mounted toilets, if possible
- Educate your staff about obesity and weight bias

Kahan S, 2015.

Concluding thoughts

- Obesity is a chronic **treatable** disease
- Share the **story of obesity pathophysiology** with your patients
- Provide your patients with the knowledge and understanding that having obesity is **not their fault**
- Long-term goal is to **target treatment to pathophysiology**, as is the case with any disease
- Approach patient in a confident, supportive and **non-judgmental** way
- **Compassion** is paramount
- Be supportive, be persistent, be there for the patient

Treat obesity as you would treat any other disease

References

- 2023 Columbia University obesity conference lectures.
- 2022 Blackburn course of obesity
- Pediatric obesity algorithm 2022. OMA
- Adult obesity algorithm 2021. OMA