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Clinical Practice Guideline for the Evaluation and Treatment of Children and Adolescents with Obesity

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Disclosures

- I have the following financial relationships with the manufacturer(s) of any commercial product(s) and/or provider of commercial services discussed in this CME activity:
 - Research Support: Dexcom, Inc.
 - Consulting: Rhythm Pharmaceuticals, Hippo Medical Education, Guide point
- I intend to discuss unapproved use of commercial products in my presentation

Stigma



Objectives



Review epidemiology of pediatric obesity



Discuss risk factors related to childhood obesity



Describe evaluation of obesity related comorbidities in youth



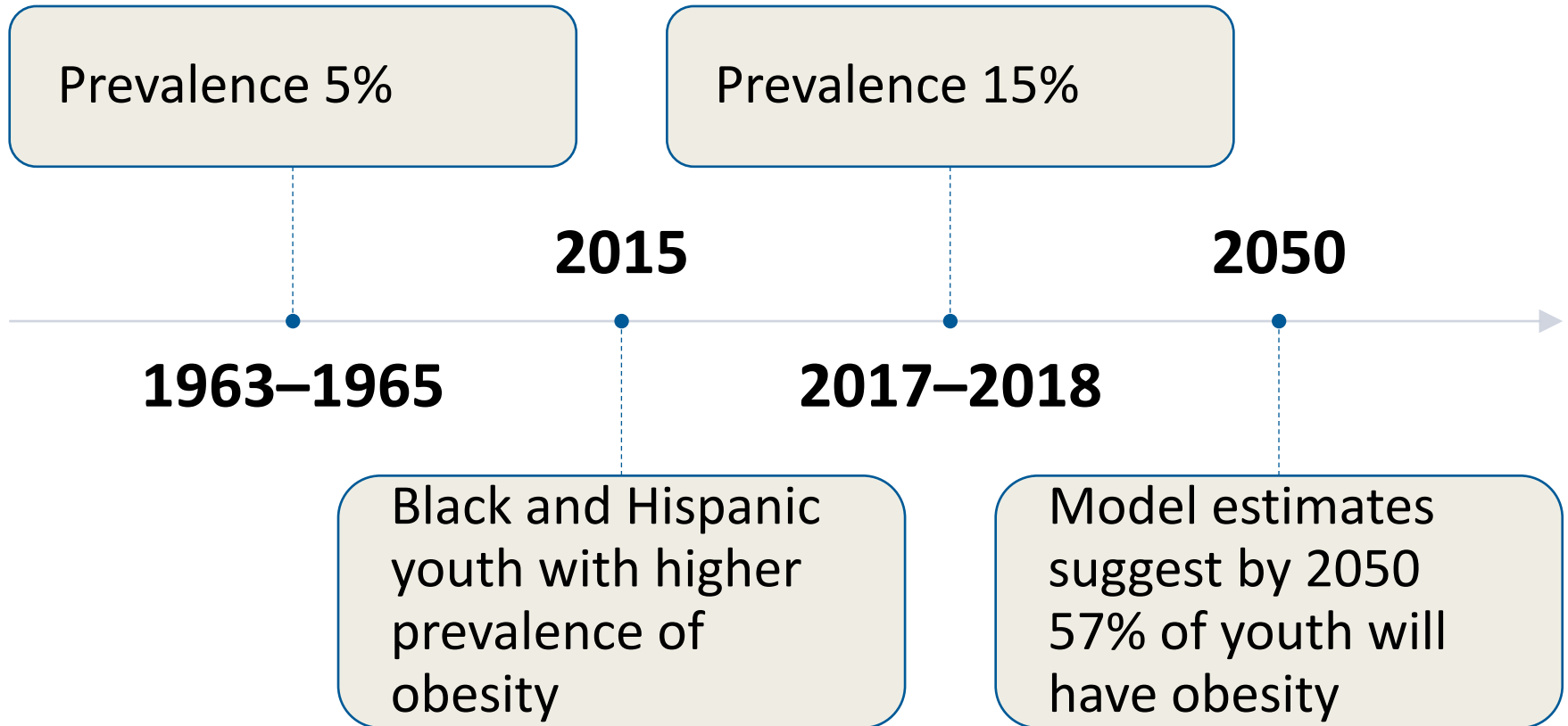
Summarize comprehensive obesity treatment paradigm

Introduction

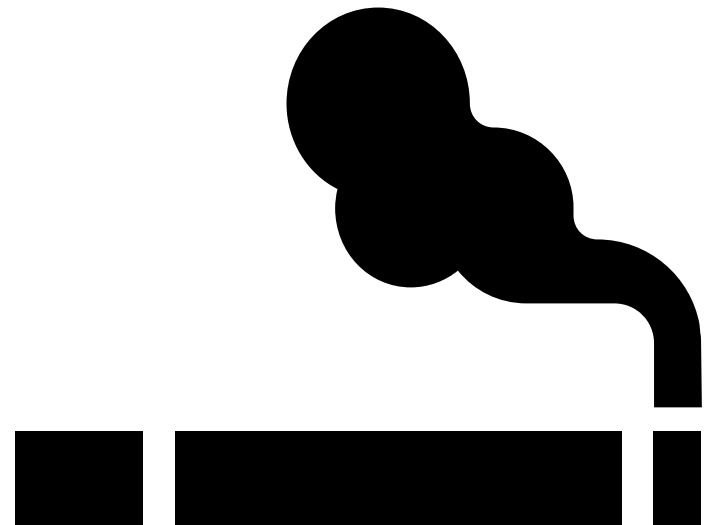
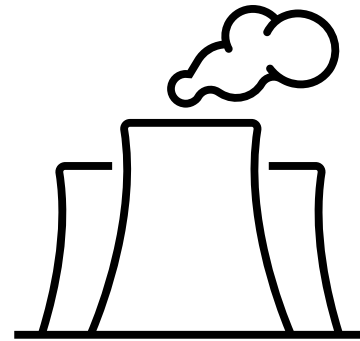


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Prevalence of Childhood Obesity



Pediatric obesity as chronic disease



Diagnosis and Measurement

Definition of Obesity

Class 1

≥95th percentile to <120% of the 95th percentile
or a BMI ≥ 30 kg/m² to <35 kg/m²

Class 2

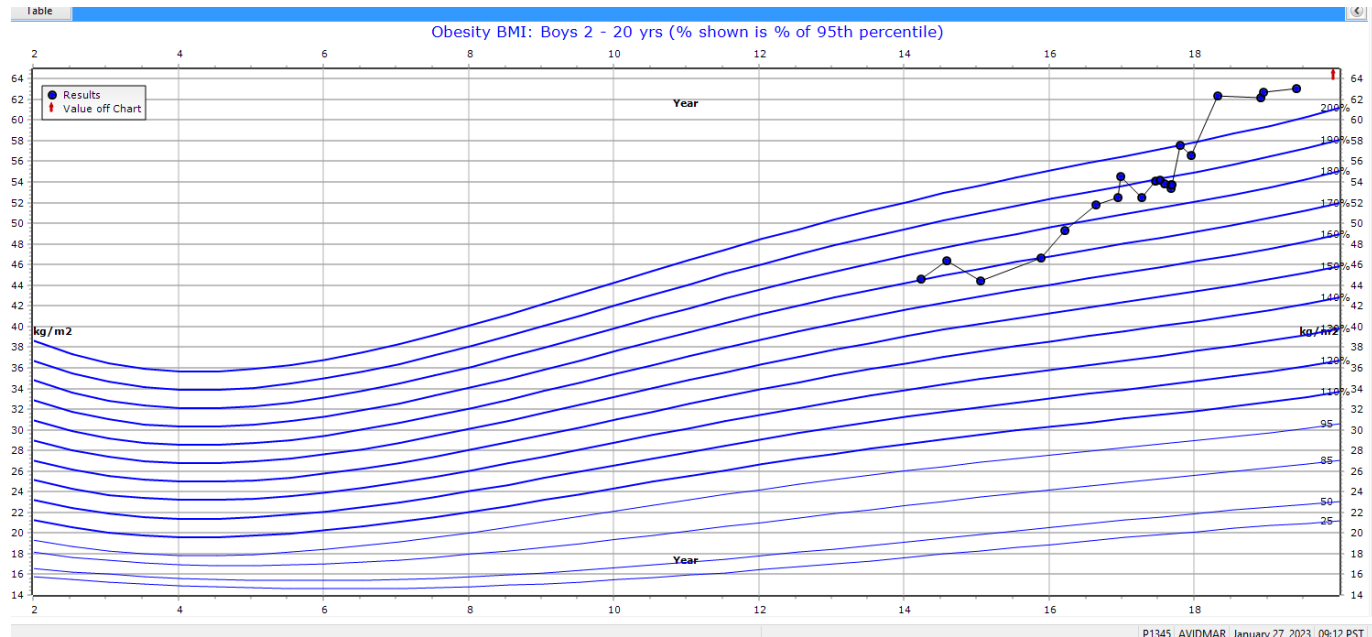
≥120% to <140% of the 95th percentile or a BMI ≥
35 kg/m² to <39 kg/m²

Class 3

≥140% of the 95th percentile or BMI ≥ 40 kg/m²

Alternative Metrics

- $\%BMI_{p95}$: Weight in excess of the 95th percentile



Communication of Weight Status



BMI must be communicated to the patient and family

Conversations can facilitate effective treatment

Avoidance leads to delays and obesity stigma

Weight Bias and Stigma Considerations

Associated with a negative impact on mental health

May adversely affect quality of care

Prevent patients from seeking medical care

Contribute to worsened morbidity and mortality

Health Equity Considerations

Disparity vs. inequity

Embedded in the socioecological and environmental fabric of children's lives

Danger of stigmatizing children with obesity and their families based on race and ethnicity, age, and gender

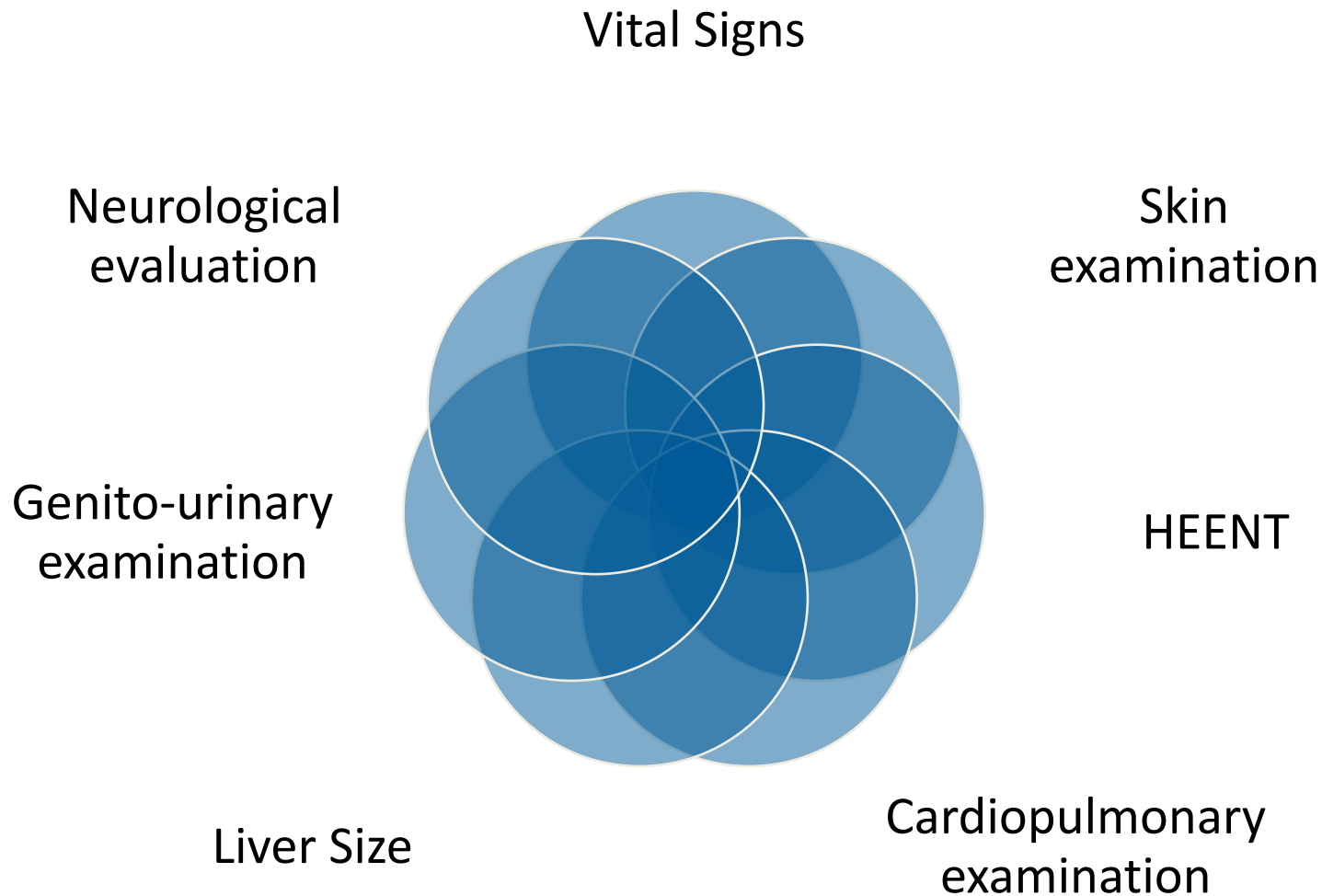
They represent neighborhood-, community-, and population-level factors that can be changed

Evaluation of Pediatric Patient with Overweight or Obesity

Visit

- Medical History
- Family History
- Nutrition and Physical Activity History
 - Eating outside the home
 - Consumption of sweet drinks
 - Portion size
 - Meal habits
 - Snack Habits
 - Fruits and Vegetable consumption
- Review of Systems

Physical Exam



Assessments for Behavioral Health and Disordered Eating Concerns

Depression:

- Pediatric Symptom Checklist's parent or teen versions

Anxiety:

- General Anxiety Disorder assessment
- The Screen for Child Anxiety Related Disorders

ADHD:

- Vanderbilt ADHD Rating Scales

Weight-based bullying

- Child Adolescent Bullying Scale

Disordered eating behaviors

- Binge Eating Disorder Screener 7

Lab Screening

Children < 10 Years with Obesity

- Annual Fasting Lipid Panel, HbA1c, Fasting Blood Glucose, Liver Enzyme

Children 2-9 Years with Obesity and Children > 10 Years with overweight

- Lipid Panel annually
- HbA1c, Fasting Blood Glucose and ALT based on risk factors

Comprehensive Obesity Treatment

Comprehensive Obesity Treatment

Providing	intensive, longitudinal treatment in the medical home
Evaluating	for obesity-related medical and psychological comorbidities
Identifying	social drivers of health
Using	non stigmatizing approaches to clinical treatment
Harnessing	motivational interviewing
Setting	collaborative treatment goals not limited to BMI stabilization or reduction
Integrating	intensive behavior and lifestyle treatment, with pharmacotherapy and surgery

Intensive Health and Behavioral Lifestyle Treatment

Intensive health behavior and lifestyle treatment (IHBLT)

Educates families in nutrition and physical activity changes

Most often effective when it occurs face-to-face

Engages the whole family

Delivers at least 26 hours of lessons over 3 to 12 months.

Should continue longitudinally.

Provided in conjunction with pharmacotherapy and surgery

When IHBLT is not available: Do What you Can!

Reduction of sugar-sweetened beverages

Choose My Plate

60 minute daily of moderate to vigorous physical activity

Reduction in sedentary behavior

Traffic Light Diet

Use of screen based physical activity

Appropriate amount of sleep

Pharmacotherapy

AAP Consensus Recommendation

Pediatricians and other pediatric health care providers:

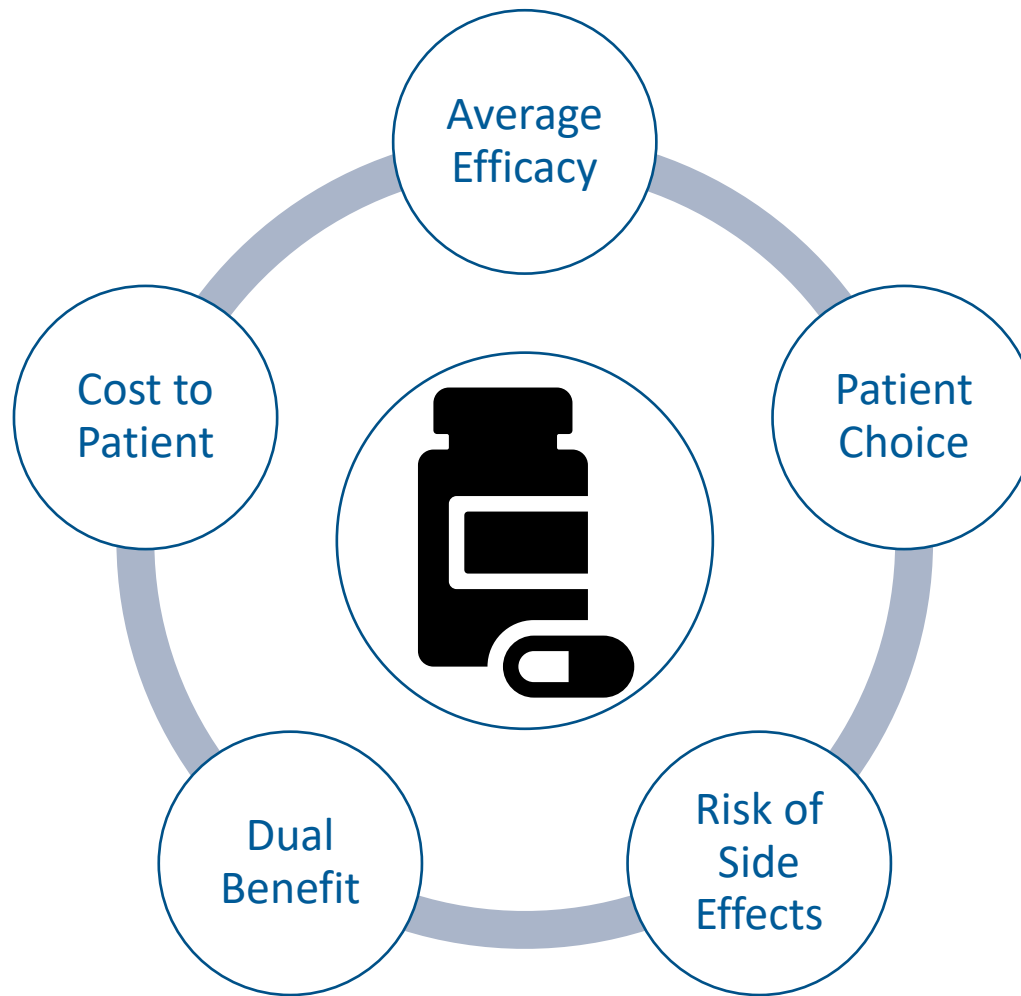
- **SHOULD** offer adolescents 12 y and older with obesity weight loss pharmacotherapy, according to medication indications, risks, and benefits, as an adjunct to health behavior and lifestyle treatment
- **MAY** offer children ages 8 through 11 years of age with obesity weight loss pharmacotherapy, according to medication indications, risks, and benefits, as an adjunct to health behavior and lifestyle treatment

Real-Life Practice

The above PLUS

- Consider for youth 4 and up
- Off-label use as appropriate and available
- As an adjunct to the best available lifestyle treatment, you can offer even if its not comprehensive

How do we choose?



Ideal World: Medication Considerations

Insulin Resistance

- Metformin
- GLP-1 Agonist
- Dual GLP-1/GIP

PCOS

- Metformin

NAFLD

- GLP-1 Agonist

Binge Eating and Emotional Eating

- Vyvanse
- Topiramate

Depression/Anxiety

- Bupropion
- Bupropion/Naltrexone

Hungry Brain

- Phentermine
- Topiramate

Hungry Gut

- GLP-1 agonist

Eating in response to emotions

- Bupropion/Naltrexone

Slow burn

- Phentermine

The Reality of Choosing



- Side Effect Profile
- Average Efficacy
- Dual Benefit

How long to treat?

No cure for pediatric obesity

Tool to manage pathophysiology

Goal is risk reduction and prevention of life-limiting conditions

Trials off medication appropriate in collaboration with patient and family

How to monitor treatment

Ideal state vs. real-life

Mirror chronic disease management

Quarterly visits

Bi-annual lab assessments

Injectable Agents





GLP-1 Agonist

GLP-1 Agonists

Mechanism of Action	<ul style="list-style-type: none">• Stimulates post-prandial insulin secretion• Reduces glucagon secretion• Delays gastric emptying• Reduces hunger and food intake• Increases satiety
Side Effect Profile	<ul style="list-style-type: none">• GI symptoms• Hypoglycemia• Fatigue• Headache• Mood changes
Considerations	<ul style="list-style-type: none">• High Cost (\$1200-2800/mo)• Access challenges• Supply concerns
Reduction in weight from baseline at 1 yr	<ul style="list-style-type: none">• 10 to 20%

Available GLP-1 Agonists in Youth

Liraglutide
(daily
preparation)

Victoza (1.8
mg/daily)

Saxenda (3.0
mg/daily)

FDA approved for
obesity in 12+ (2020)

Semaglutide
(weekly
preparation)

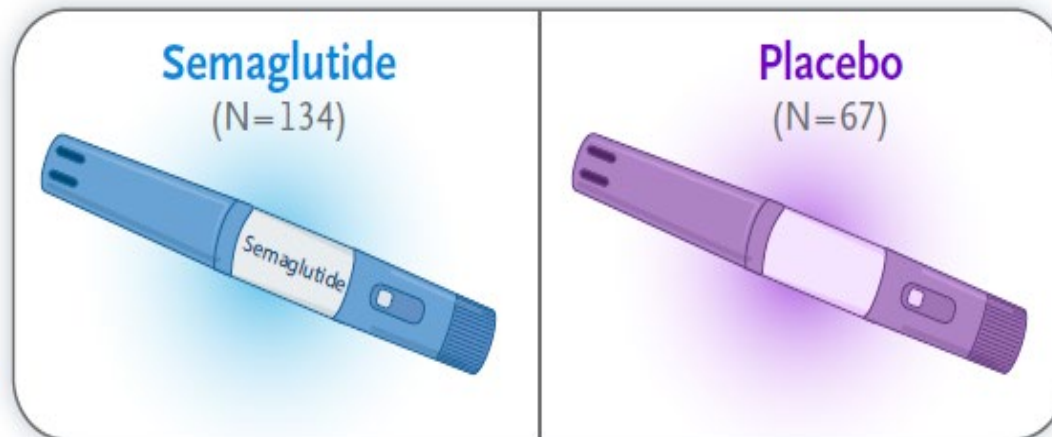
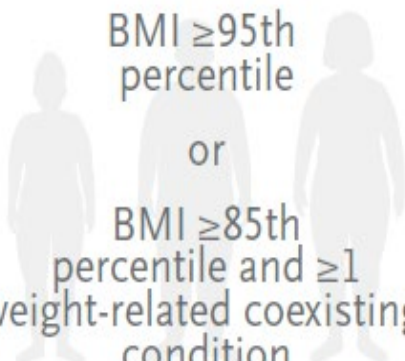
Ozempic (1 mg
weekly)

Wegovy (2.4 mg
weekly)

FDA approved for
obesity in 12+ (2023)

Once-Weekly Semaglutide in Adolescents with Obesity

Adolescents
BMI \geq 95th percentile
or
BMI \geq 85th percentile and \geq 1 weight-related coexisting condition

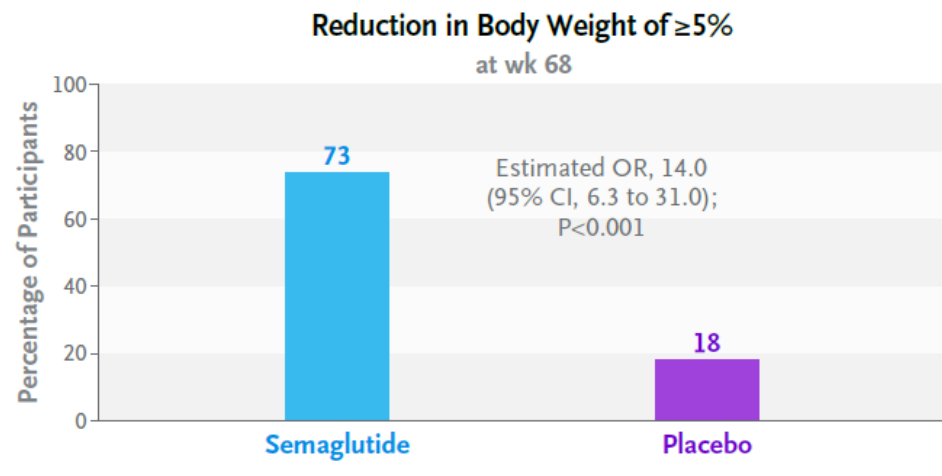
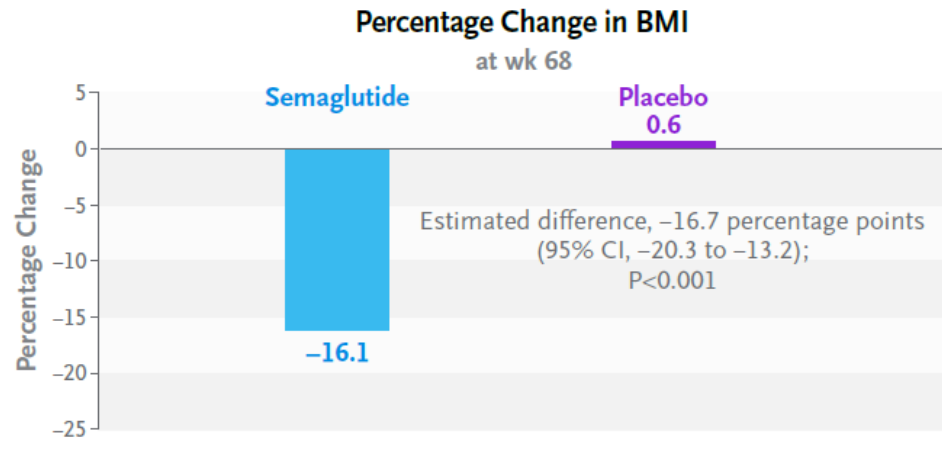


Double-blind,
parallel group,
randomized,
placebo-controlled
trial

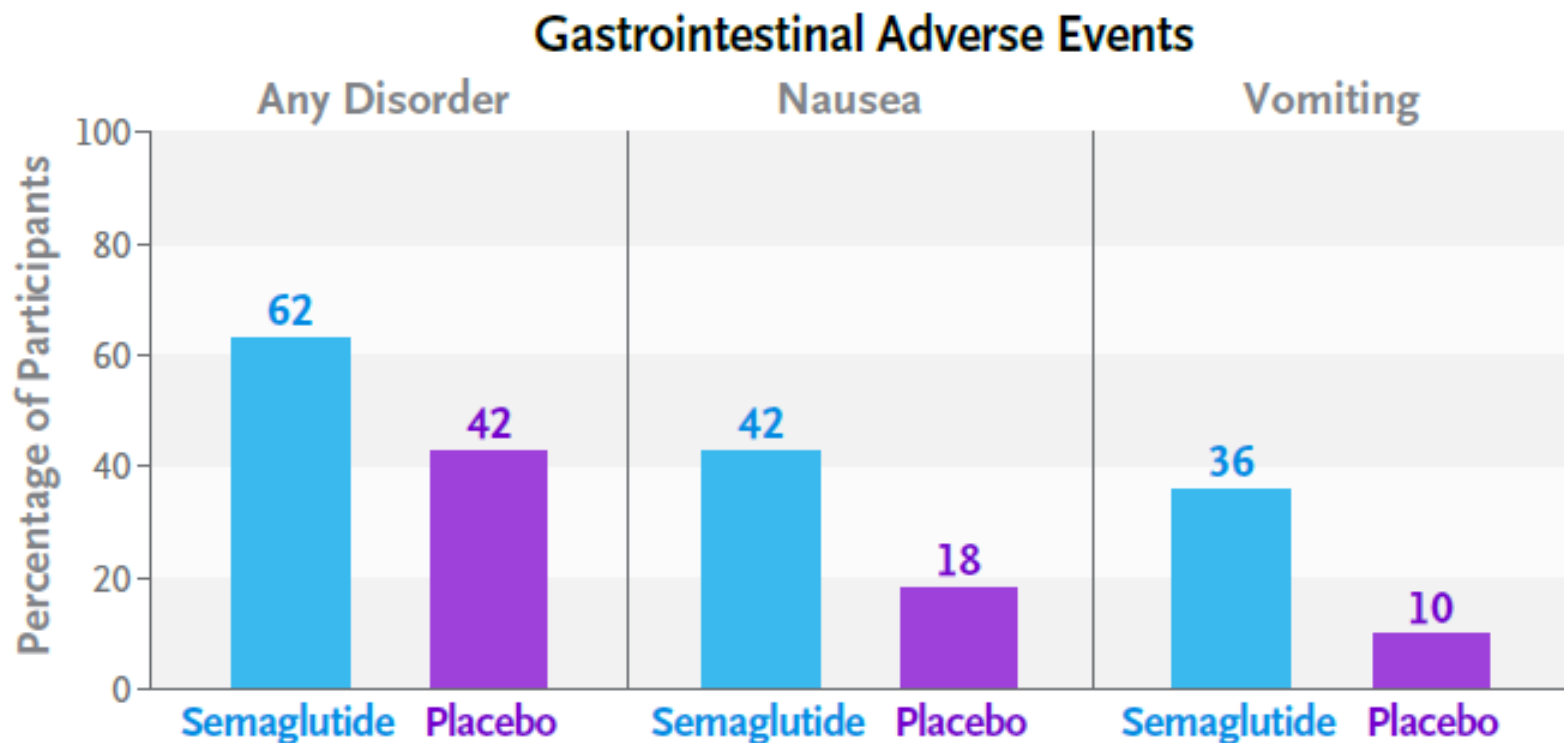
Primary end point:
percentage change
in BMI from
baseline to week 68

Secondary end
point: weight loss of
at least 5% at week
68

Once-Weekly Semaglutide in Adolescents with Obesity



Once-Weekly Semaglutide in Adolescents with Obesity



Mitigating GLP-1 GI Effects In Youth

Eat smaller meals and eat slower

Eat about half of what you usually eat

Take about 15 – 20 minutes to eat your meal

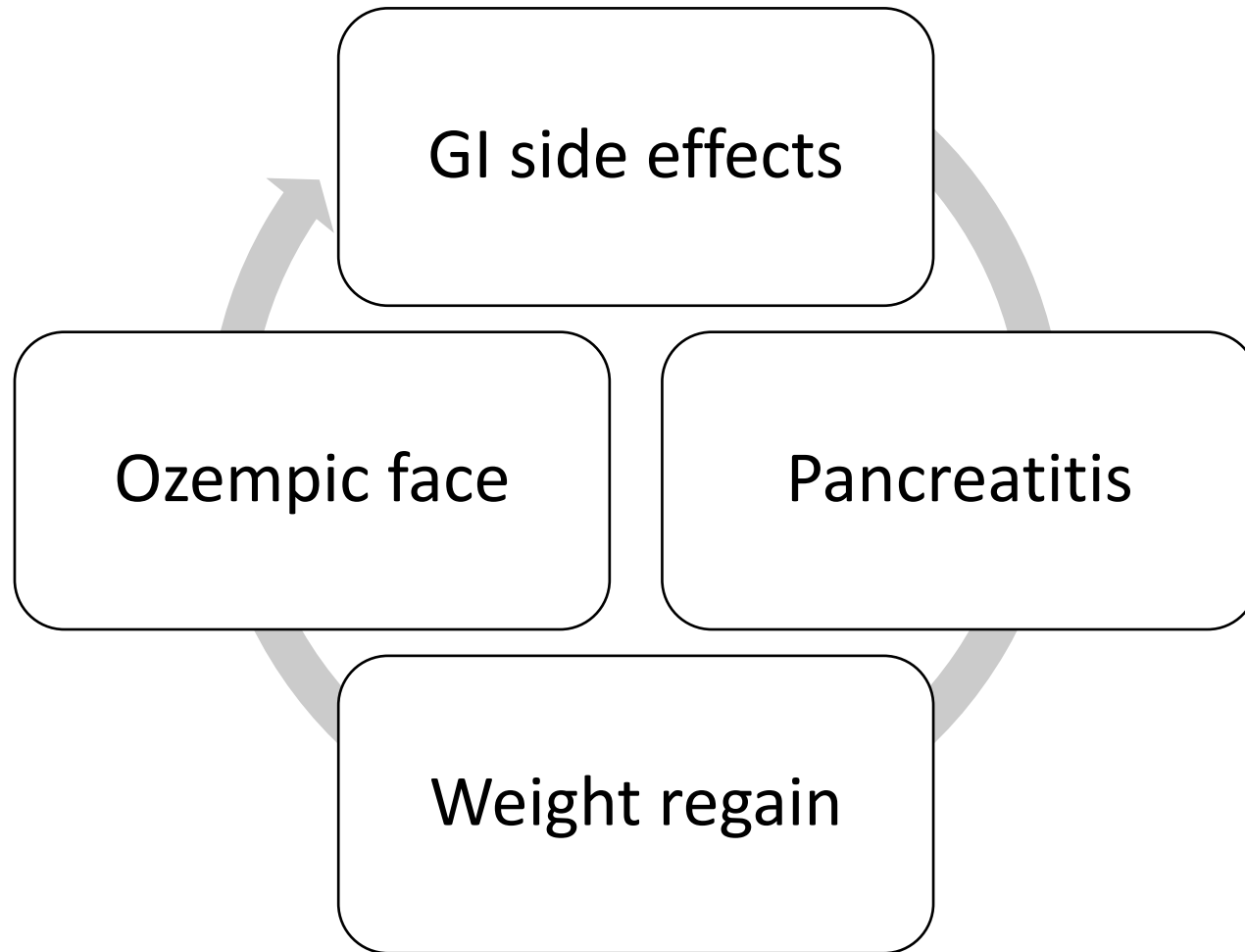
Take with with food

Add fruits, vegetables, whole grains and lean proteins to meals

Limit foods that are spicy, greasy or fried

Drink water instead of sweet drinks

What are we afraid of?



GLP-1/GIP Dual Agonist: Tirzepatide

Mechanism of Action

- GLP-1 MOA +
- GIP: regulates energy balance through cell-surface signaling in the brain and adipose tissue and enhances the GLP-1 effect

Side Effect Profile

- Similar to GLP-1 Agonists
- GI symptoms
- Hypoglycemia
- Cholelithiasis
- Injection site reaction

Efficacy:

- 12 to 20% weight loss compared to placebo

Pediatric trials in process

Setmelanotide

Mechanism of Action	<ul style="list-style-type: none">• MC4R receptor agonist, reduced hunger
Side Effect Profile	<ul style="list-style-type: none">• Hyperpigmentation• GI symptoms• Mood changes• Dizziness, fatigue, headache, insomnia, vertigo, spontaneous penile erections
FDA indication	<ul style="list-style-type: none">• >6 yo with POMC, PCSK1, LEPR deficiency or BBS
Dose	<ul style="list-style-type: none">• 1-3 mg subcutaneously once per day
Cost	<ul style="list-style-type: none">• \$330/mg
Reduction in weight from baseline at 1 yr	<ul style="list-style-type: none">• LEPR: 9.7%• POMC or PCSKI: 23.1%• BBS: 9.5%



Oral
Agents

Phentermine

Topiramate

Phentermine/Topiramate

Vyvanse

Metformin

Orlistat

Naltrexone/Bupropion

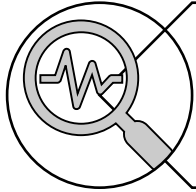
Phentermine

Mechanism of Action	<ul style="list-style-type: none">• Increases catecholamine release in the hypothalamus• Inhibition of norepinephrine reuptake• Potentiates POMC neuronal activity leading to appetite suppression
Side Effect Profile	<ul style="list-style-type: none">• Anxiety, tremors, mild increase in BP/HR, palpitations, insomnia
Contraindications:	<ul style="list-style-type: none">• Cardiac valve disease (in combination with fenfluramine or dexfenfluramine), pregnancy, MAOi use, glaucoma, history of drug abuse
FDA indication	<ul style="list-style-type: none">• Obesity in 16 years and older
Dose	<ul style="list-style-type: none">• 15-37.5 mg once daily in the AM• 8 mg 2-3 times per day
Efficacy	<ul style="list-style-type: none">• 4-8%
Cost	<ul style="list-style-type: none">• \$5/mo [Not covered by insurance]

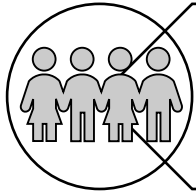
Topiramate

Mechanism of Action	<ul style="list-style-type: none">• Appetite suppression, satiety enhancement, control of food cravings• Enhancement of GABA A activity, antagonizing AMPA glutamate receptors, and inhibition of carbonic anhydrase
Side Effect Profile	<ul style="list-style-type: none">• Paresthesia, cognitive disruption, dizziness, dysgeusia, dry mouth, kidney stones, suicidal ideation, teratogenic
Contraindications:	<ul style="list-style-type: none">• Glaucoma, suicidal ideation, pregnancy
FDA indication	<ul style="list-style-type: none">• Epilepsy 2+ and Migraines 12+
Dose	<ul style="list-style-type: none">• 100-200 mg nightly
Efficacy	<ul style="list-style-type: none">• 2-5%
Cost	<ul style="list-style-type: none">• \$5-11/mo [covered by most insurances]

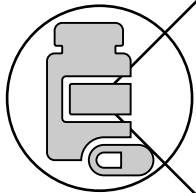
Phentermine/Topiramate Trial



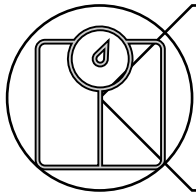
Double-blind, parallel group, randomized, placebo-controlled trial



223 youth, ages 12-17 with obesity

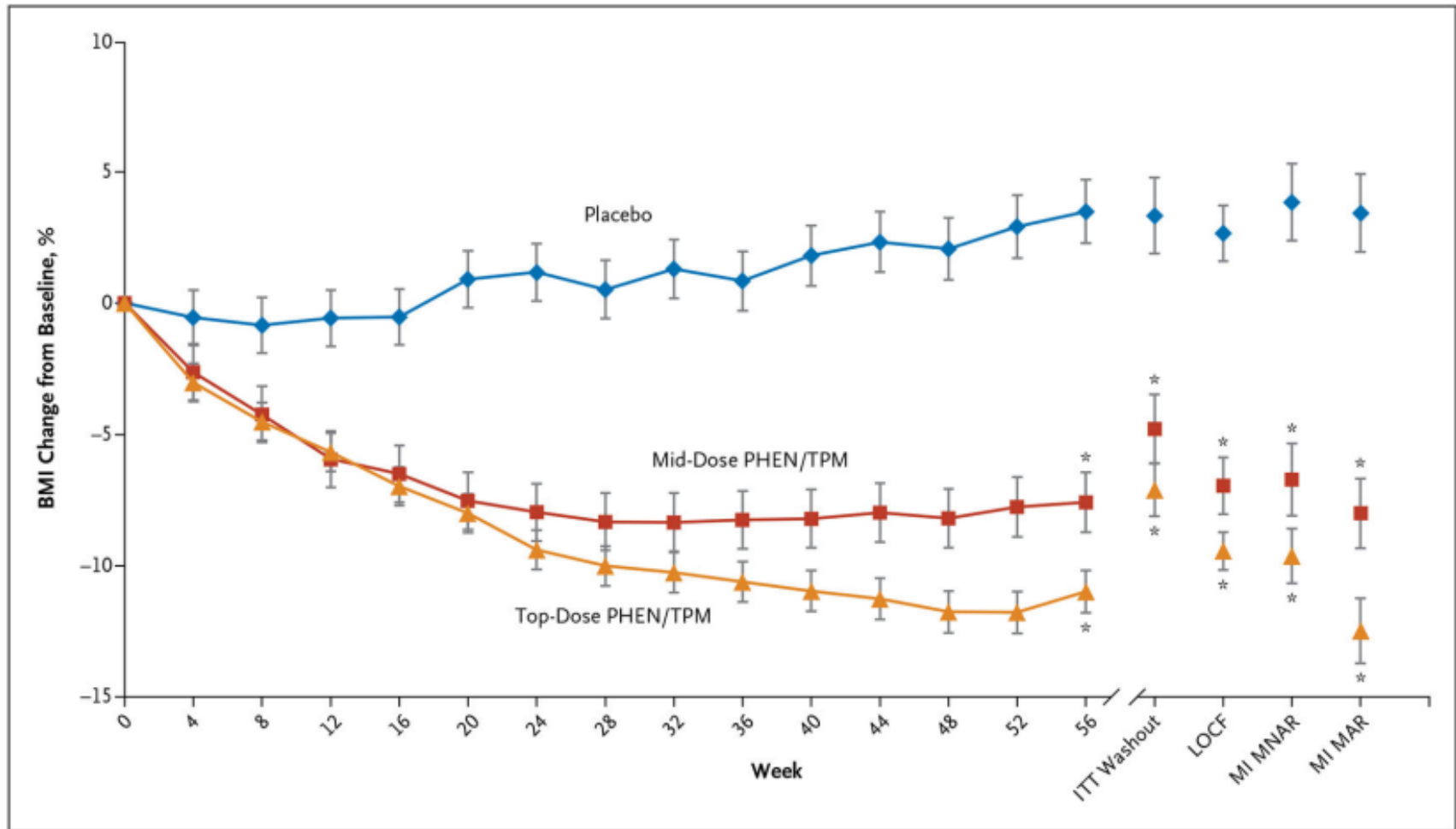


Intervention: Daily Phentermine/Topiramate 7.5/46 mg or 15/92 mg or placebo, plus lifestyle intervention

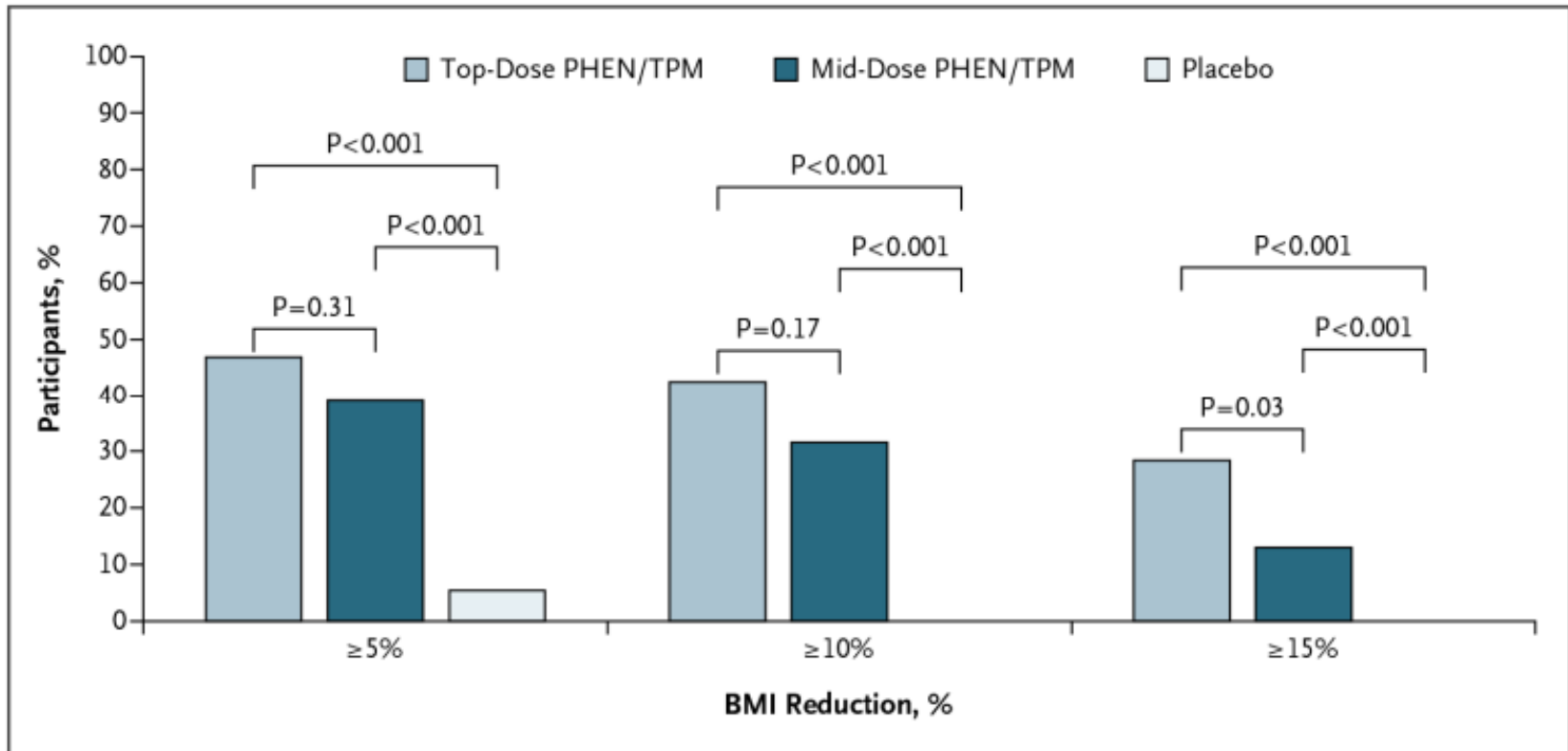


Primary end point: percentage change in BMI from baseline to week 56

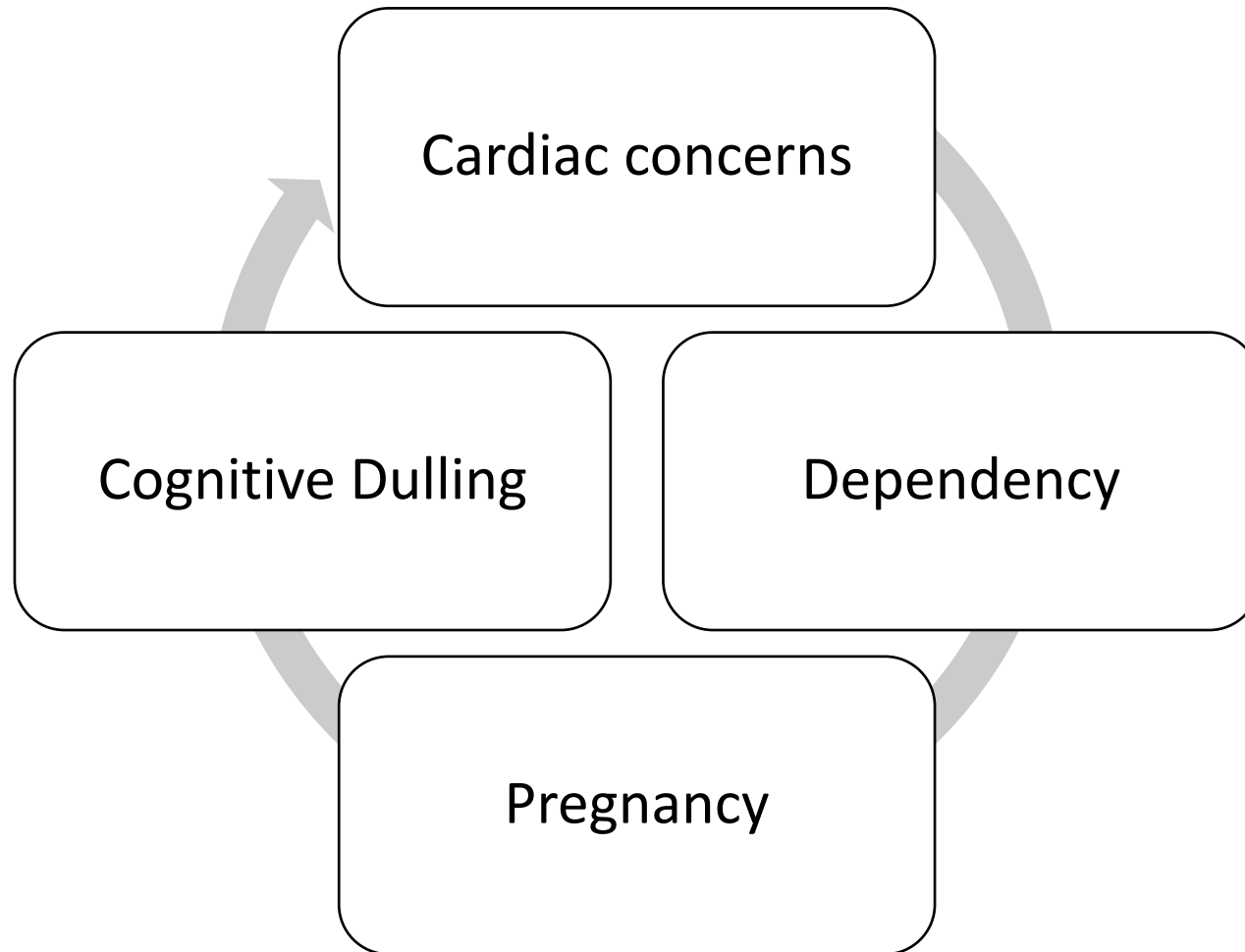
Percent BMI Change Over Time



Percentage of Participants Achieving Various BMI Reduction Benchmarks



What are we afraid of?



Life Hacks

Phentermine

- Unlikely to be covered by insurance
- Controlled substance
- Could consider another stimulant (Vyvanse)
- GoodRx coupon

Topiramate

- Covered by most insurances
- Low cost

Create Script:

- Indication: Pediatric Obesity, Appetite Suppression
- Family consented to treatment
- Okay to pay out of pocket
- Utilize Good rx coupon for purchase

Metformin

Mechanism of Action	<ul style="list-style-type: none">• Activation of AMP-activated protein kinase
Side Effect Profile	<ul style="list-style-type: none">• GI side effects, Vitamin B 12 deficiency, Lactic acidosis (rare)
Contraindications	<ul style="list-style-type: none">• Severe renal dysfunction, acute or chronic metabolic acidosis
FDA indication	<ul style="list-style-type: none">• T2D 10+
Obesity Indication	<ul style="list-style-type: none">• Insulin resistance, PCOS, concurrent use of atypical anti-psychotic agents
Dose	<ul style="list-style-type: none">• Administered orally (500 mg-2000 mg) in twice per day (pediatric use) and once per day (XR)
Cost	<ul style="list-style-type: none">• \$4/mo [Covered by insurance]

Jacobs TF. Metformin. StatPearls. Treasure island (FL). 2022.

Jarskog LF, et al. Am J Psychiatr 2013

Yerevanian A et al. Curr Obes Rep 2019

Correll CU, et al. World Psychiatr 2020

Orlistat

Mechanism of Action

- Blocks dietary fat absorption via inhibition of gastric and pancreatic lipases

Side Effect Profile

- Oily rectal leakage, abdominal
- Pain, flatulence with discharge, bowel urgency, and steatorrhea

Contraindications

- Pregnancy, breast-feeding, cholestasis, malabsorption syndrome

FDA indication

- Obesity 12+

Dose

- 60-120 mg PO TID with meals

Cost

- \$30-50/mo

Naltrexone/Bupropion

Mechanism of Action	<ul style="list-style-type: none">• Bupropion: reuptake inhibitor of norepinephrine and dopamine• Naltrexone: opioid antagonist
Side Effect Profile	<ul style="list-style-type: none">• GI symptoms, headache, dizziness, worsening of depression, suicidal ideation
Contraindications	<ul style="list-style-type: none">• hypertension, seizure disorders, drug or alcohol withdrawal, MAOI usage
FDA indication	<ul style="list-style-type: none">• Obesity in >18 yo
Dose	<ul style="list-style-type: none">• 8mg/90 mg: titrate to 2 tablets twice daily
Efficacy	<ul style="list-style-type: none">• 4-6%

Pediatric Metabolic and Bariatric Surgery

Criteria for Surgery

Weight Criteria	Criteria for Comorbid Conditions
<p>Class 2 obesity BMI >35 kg/m² %BMI_{p95} >120% of the 95th percentile for age and sex</p> <p>Whichever is lower</p>	<p>Clinically significant disease T2DM, IIH, NASH, Blount disease, SCFE, GERD, obstructive sleep apnea, HTN, hyperlipidemia, insulin resistance, depressed health-related quality of life</p>
<p>Class 3 obesity BMI > 40 kg/m² %BMI_{p95} > 140% of the 95th percentile for age and sex</p> <p>Whichever is lower</p>	<p>Not required but commonly present</p>

Take Away Points

Pediatric obesity is a chronic disease

Obesity pharmacotherapies are an appropriate treatment in youth

Agent selection is multifactorial and often based on availability and patient preference

It is appropriate to combine with whatever level of lifestyle modification you can offer

Acknowledgements



Patients and their families living in larger bodies

The Weight Management Team at CHLA: Emily Sousa, Anet Piridzhanyan, Elizabeth Campbell, Rene Melgar, Patty Castillo, Juan Espinoza, Priya Patel, and Brenda Manzanarez

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QUESTIONS?

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