



Lifestyle and Other Strategies in Management of Obesity in Down Syndrome

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California Down Syndrome Conference 2025

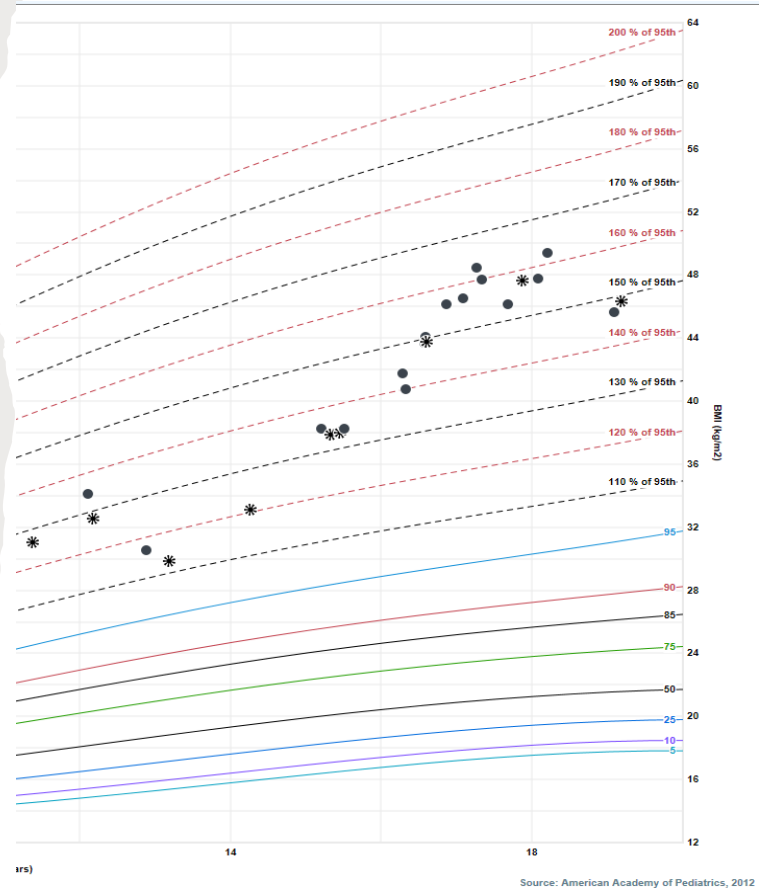


Disclosures

- Speaker for Pri-Med
- Site PI for Eli Lilly Study
- I will be discussing some “off – label” use of medications

Real Life Situation

- RH is a 17-year-old female with Trisomy 21, stable CHD, hypothyroidism, and weight struggles
- Increasing BMI especially since puberty
- Family history of T2D and obesity



Questions?

- Could this be **prevented** or delayed?
- Is this also **possible in DS**?
- What are the **long-term complications** if this weight struggle goes unchecked?
- How can we **manage** this?

Objectives

1. Discuss the unique aspects of obesity in individuals with Down Syndrome
2. Discuss some strategies to maintain healthy lifestyle and “optimal weight”
3. Explore some of the commonly used anti-obesity medications



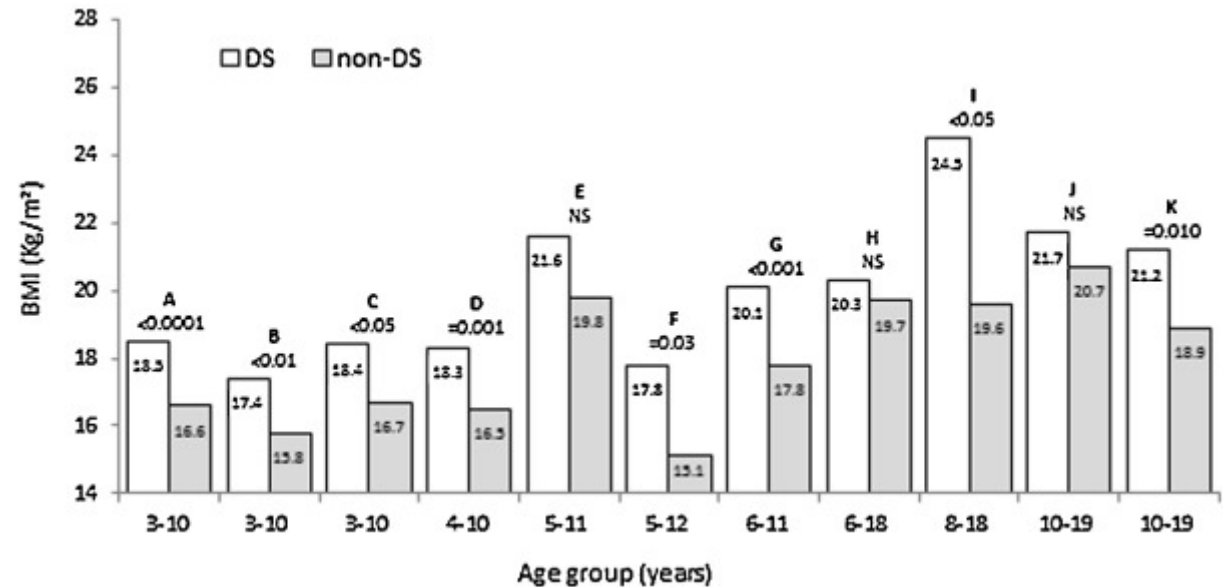
Epidemiology of Obesity in Neuro-atypical Adolescents

IDD Adolescents are 1.5x more likely to be diagnosed with obesity

Down Syndrome

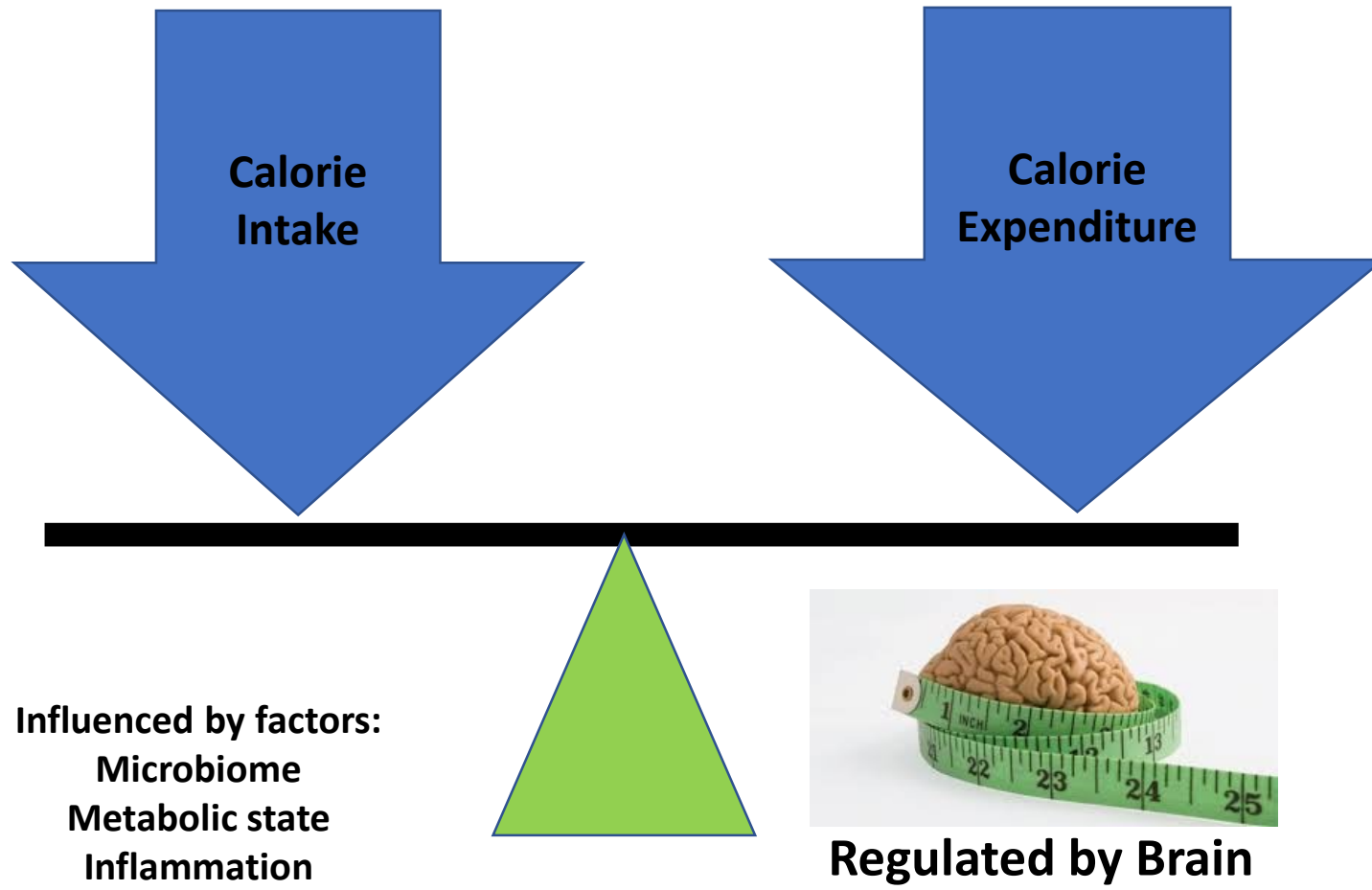
- Higher rates of overweight/obesity in children and adults with DS as compared with non-DS
- Females have higher rates than males

Review of 45 original research articles published between 1988 and 2015



Comparisons of body mass index (BMI) between youth with and without Down syndrome (DS and non-DS, respectively).

Pathophysiology of Obesity – Caloric Imbalance +++



calories

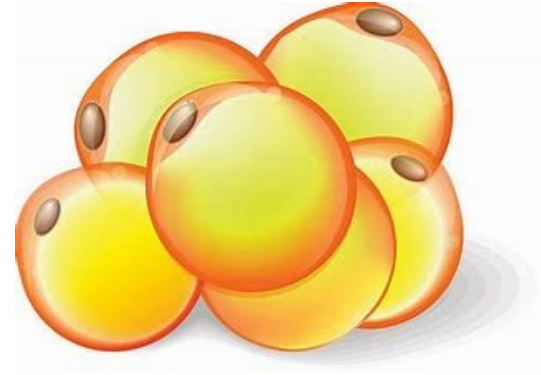
Tiny creatures that live in your closet and sew your clothes a little bit tighter every night.

Weight and Energy Balance

- Regulated by brain
- Body strives to maintain constant adipose tissue

Examples:

- ❖ To maintain adult body weight within 20 lbs, you can only consume one extra potato chip a day. Many adults maintain body weight within 20 lbs – so the fat mass regulation works
 - ❖ Weight lost during acute illness is regained
- Fat mass is not regulated in obesity



Control of Food Intake and Appetite

- **Homeostatic**

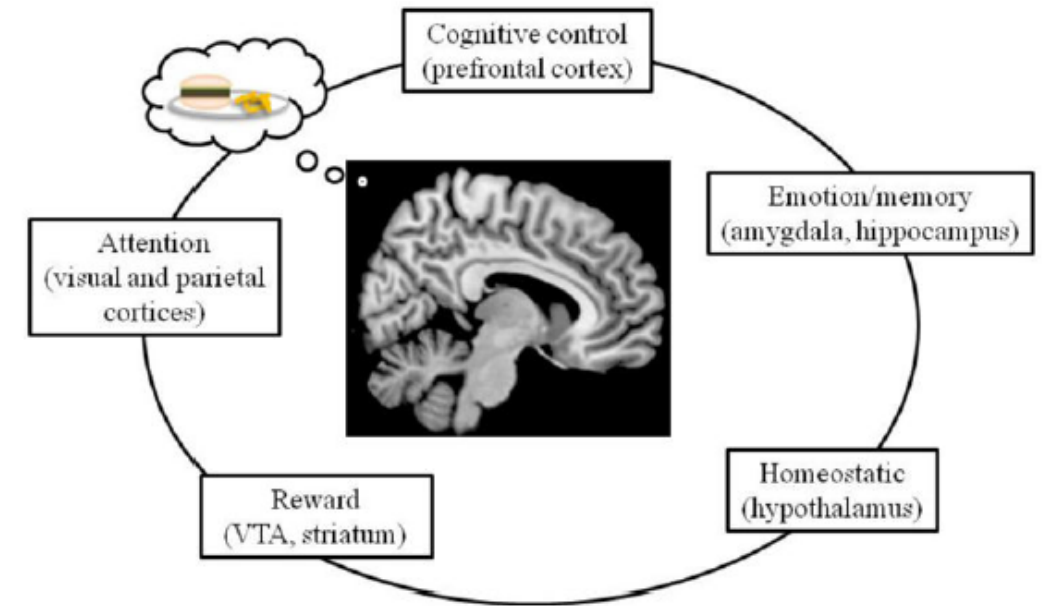
- Response to Energy Requirement
- Mainly under hypothalamic control
- The system is very sensitive to negative energy balance but comparatively tolerant of positive energy balance

- **Hedonic**

- Role of Pleasure in Eating/ Reward
- Corticolimbic Pathways

- **Cognitive**

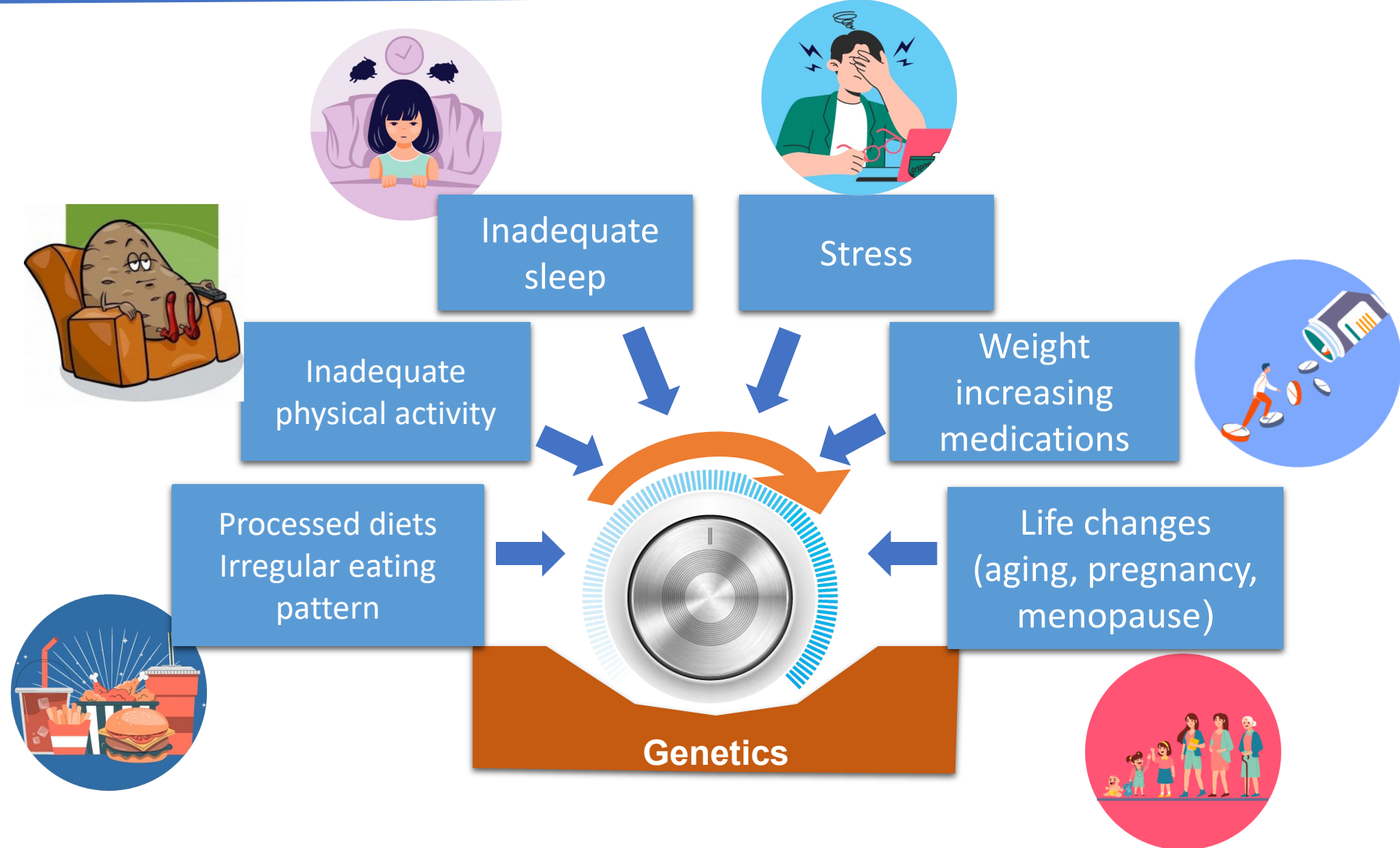
- Prefrontal Cortex



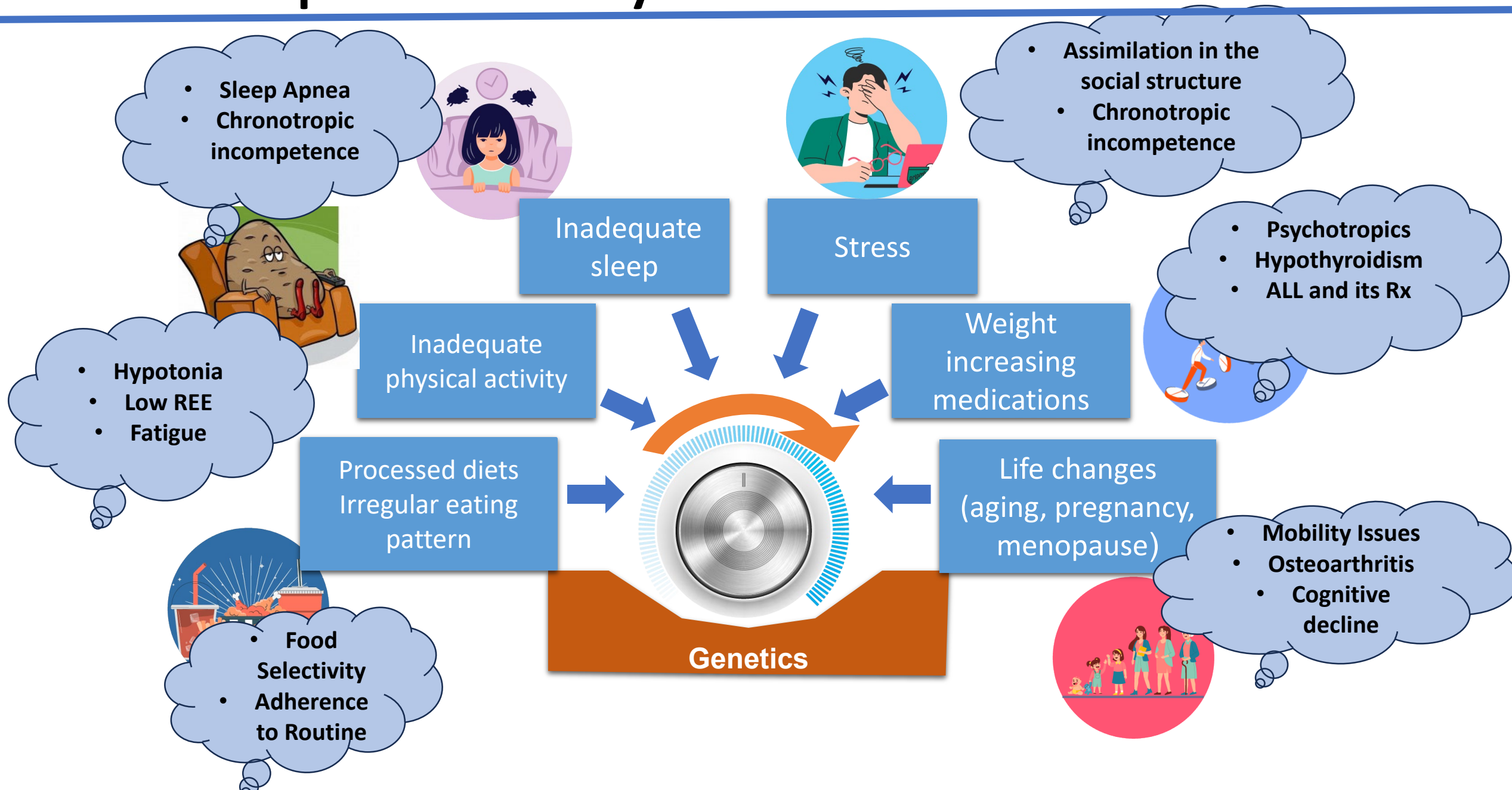
In a food replete modern world, cognitive and emotional factors can overpower energy balance regulation



Factors Attributing to Increased Weight Gain

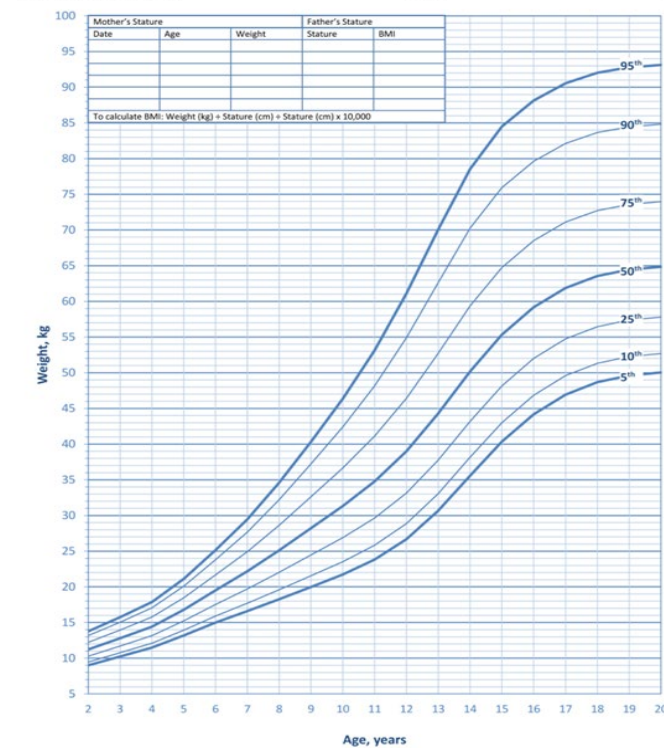


Factors Unique to Down Syndrome

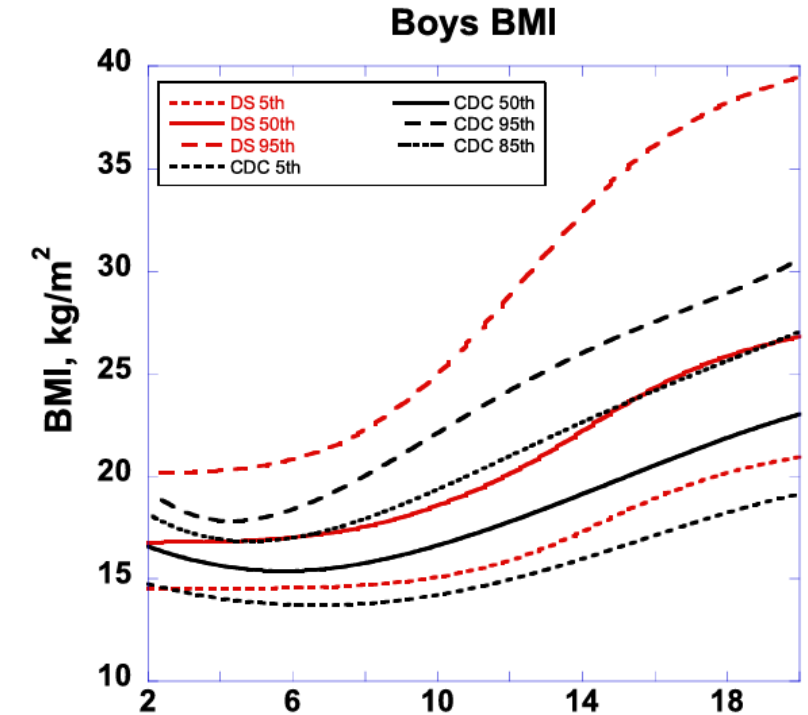
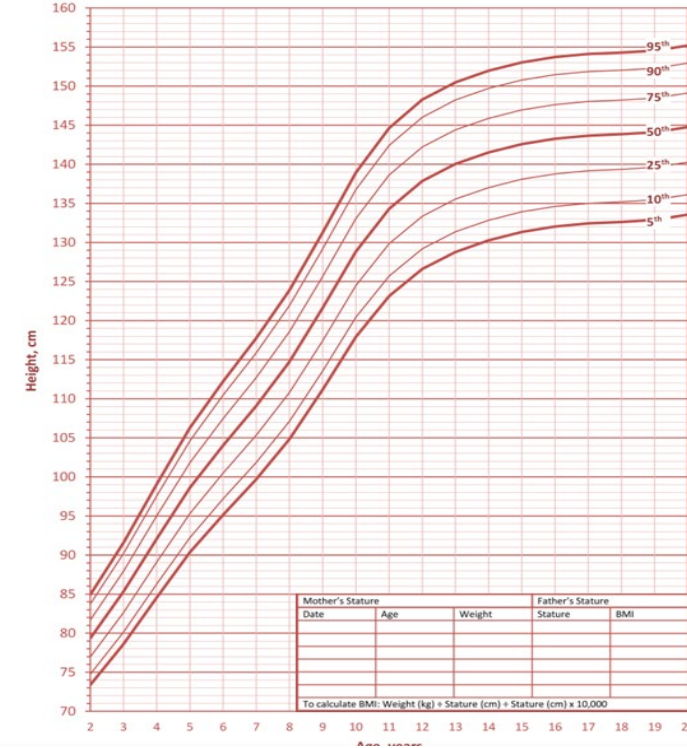


How do we diagnose obesity? - Using Growth charts in Children

Growth Charts for Children with Down Syndrome
2 to 20 years: Boys
Weight-for-age percentiles



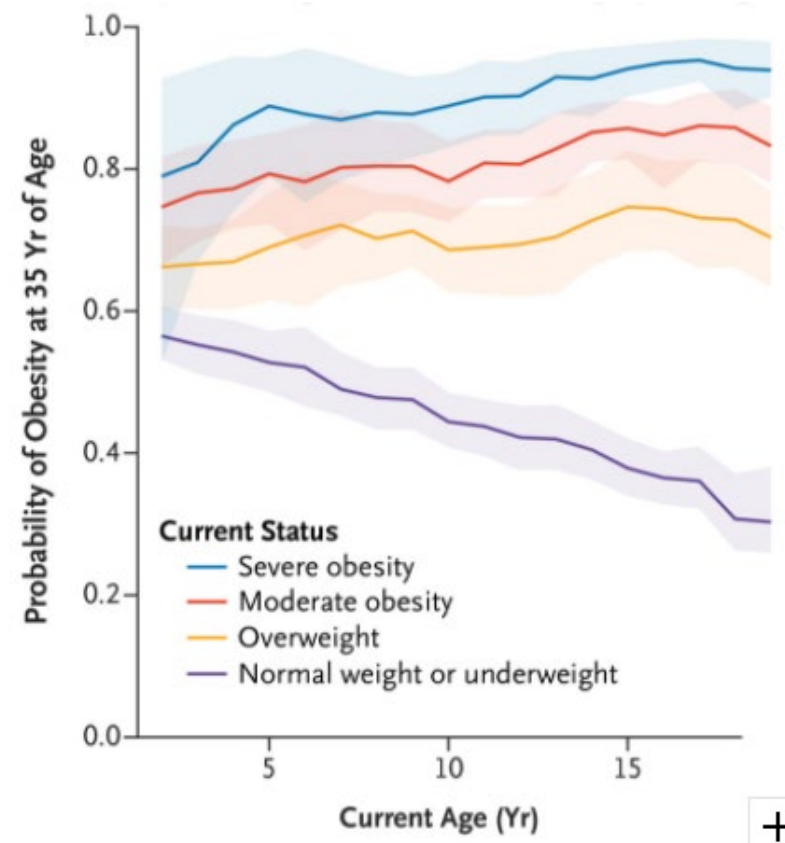
Growth Charts for Children with Down Syndrome
2 to 20 years: Girls
Height-for-age percentiles



- For children and adolescents with DS, the 85th percentile on the CDC BMI growth charts is a better indicator of excess adiposity than the 85th percentile on the DS-specific BMI growth charts
- DS-specific charts are an excellent method to compare patients with DS to their DS peers
- CDC BMI charts should be the preferred method for the early identification obesity in children with DS

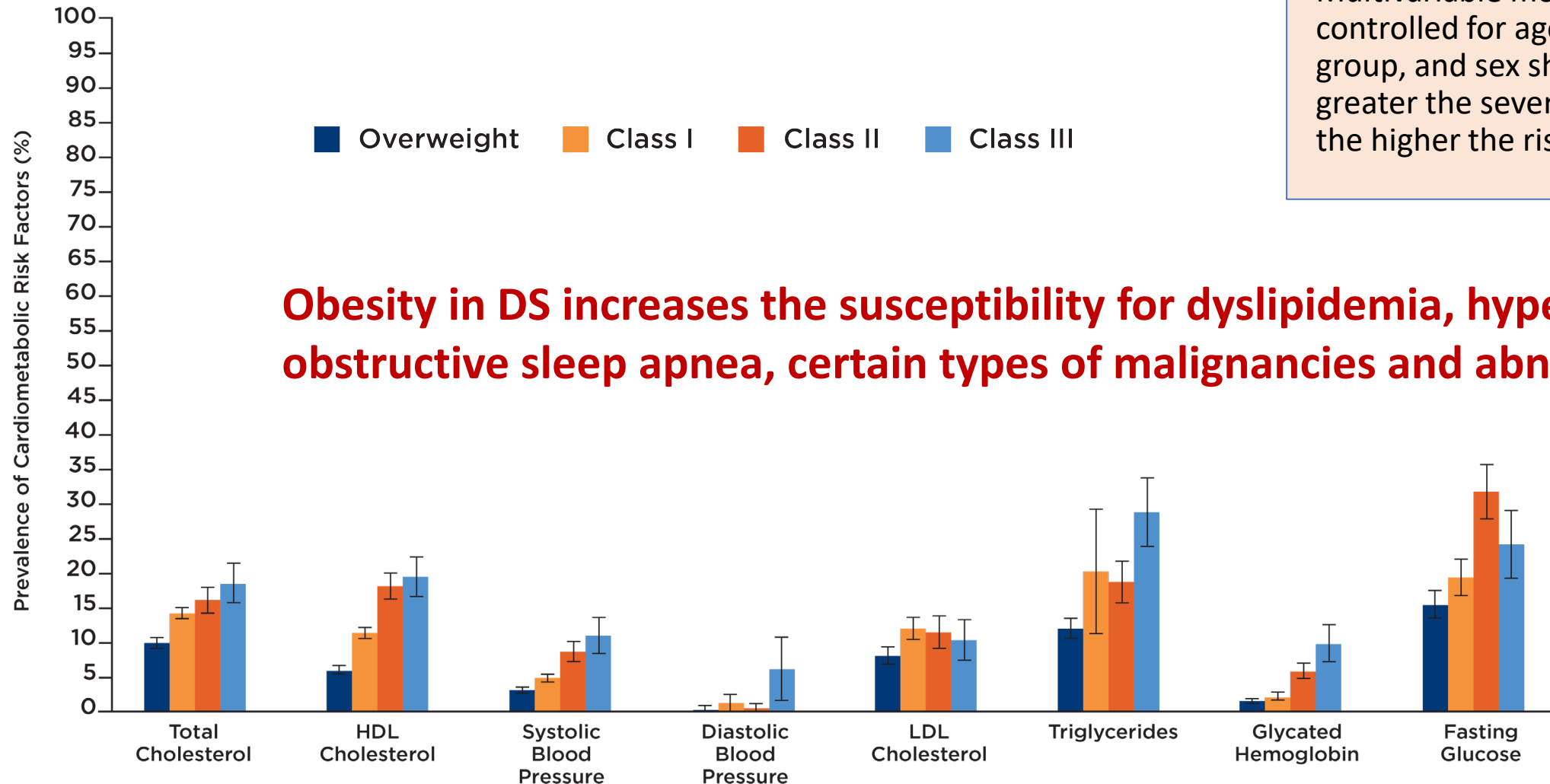
Adult Obesity starts in Childhood

Childhood Obesity Tracks into Adulthood





Prevalence of Cardiometabolic Risk Factors by Weight Status in Children and Adults



Multivariable models that controlled for age, race or ethnic group, and sex showed that the greater the severity of obesity, the higher the risks.

Obesity in DS increases the susceptibility for dyslipidemia, hyperinsulinemia, obstructive sleep apnea, certain types of malignancies and abnormal gait

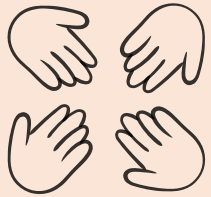
Objectives

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AAP Recommendations - Intensive Health Behavior and Lifestyle Treatment (IHBLT)

Intensive Health Behavior and Lifestyle Treatment (IHBLT)

WHO:



Patient and family in partnership with a multidisciplinary treatment team*

WHEN:



Promptly for child or adolescent with overweight or obesity

WHAT:



Health education and skill building on multiple topics



Behavior modification and counseling

WHERE:

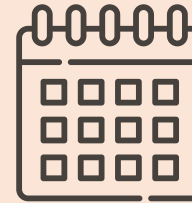


Healthcare setting



Community-based setting with linkage to medical home

DOSAGE:



Longitudinal treatment across 3-12 months with ideally ≥ 26 contact hours

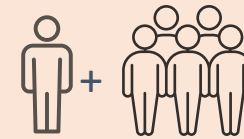
FORMAT:



Group,



Individual, or



Both

CHANNEL:



Face-to-face (strongest evidence)



Virtual (growing evidence)

Healthy Lifestyle: 5-2-1-0 rule applies to all children



No screen time for children younger than 2 years.

HEALTHY EATING FOR A HEALTHY BODY



Eat Mindfully.

- Turn off the TV or phone
- Eat slowly and chew your food well
- Take a sip of water in-between bites
- Notice colors, smells, textures and flavors
- Use MyPlate to practice portion control



Healthy Choices When Out to Eat

- Choose a zero-calorie beverage
- Choose fruits or veggies as a side
- Ask for a to-go box for leftovers
- Plan ahead: look at the menu before to find healthy options



Use:

Non-food based reward systems
Daily routines (setting the table, grocery shopping, snack prep)
Goal charts (see the back)

Keys to Success



- Eat from at least 3 food groups at each meal
- Help with grocery shopping and meal prep
- Drink more water: try a fun water bottle or zero-sugar flavoring



For Parents & Caregivers



- Keep it positive and encouraging
- Include family meals: be a healthy role model
- Offer a variety of healthy choices
- Get support from a nutrition expert



You've Got This!

Start small and stay motivated!



CALORIC DENSITY

low-nutrient, high-calorie foods vs. high-nutrient, low-calorie foods

one
of
these

2 lbs. hamburger

OR

2.5 lbs. chicken

OR

1 lb. Oreos

low-nutrient, high-calorie

or
all
of
these

1 lb. bananas

1 lb. apples

1 lb. mangoes

1 lb. kale

1 lb. spinach

1 lb. carrots

1 lb. cucumbers

1 lb. tomatoes

1 lb. sweet potatoes

AND

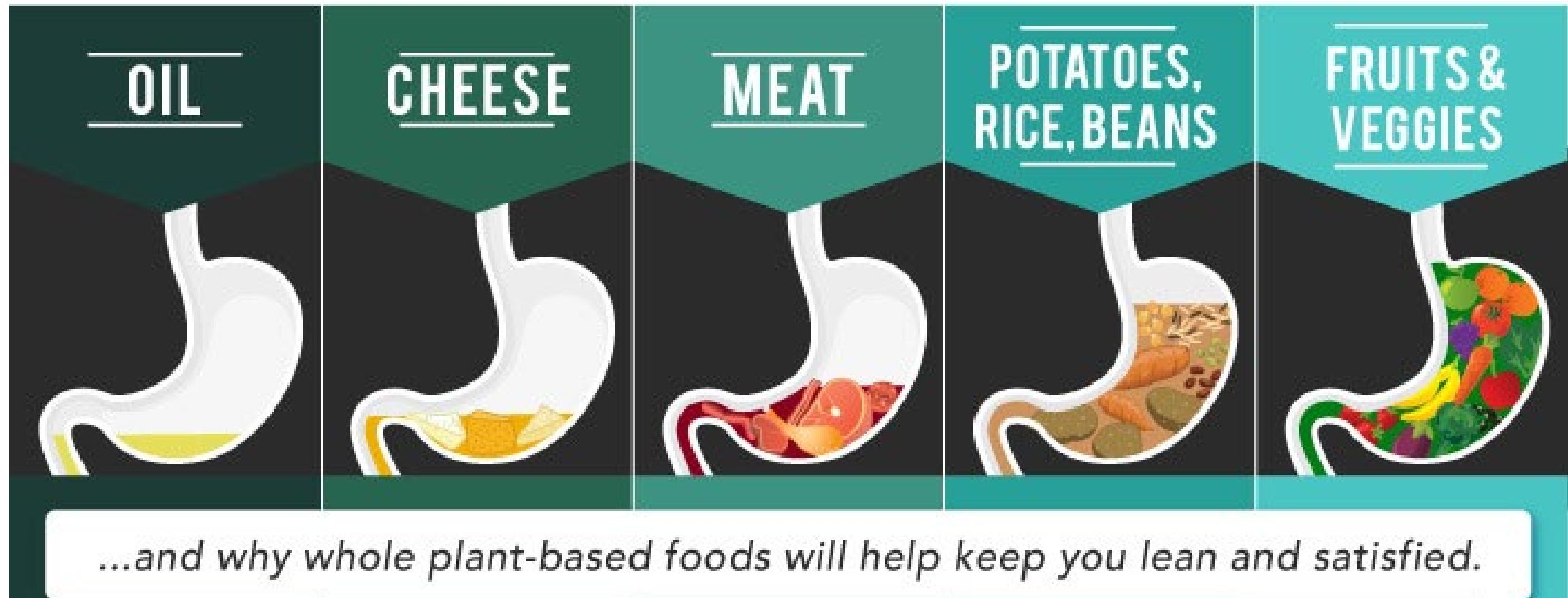
1 lb. celery

high-nutrient, low-calorie

©life.unlabeled.

CALORIE DENSITY

WHAT 500 CALORIES LOOK LIKE

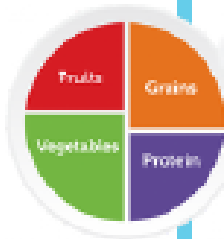


DSMIG- Lifestyle Working Group



Eat Mindfully

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- Notice colors, smells, textures and flavors
- Use MyPlate to practice portion control



Healthy Choices When Out to Eat

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WRITING OUT MY GOALS HELPS ME STAY ON TRACK!

My Nutrition Goal

My goal: _____

Why is this goal important to me?

What steps do I need to take to reach my goal?
1. _____
2. _____
3. _____
4. _____
5. _____

How will I know when I have reached my goal?
_____ ✓

My Exercise Goal

My goal: _____

Why is this goal important to me?

What steps do I need to take to reach my goal?
1. _____
2. _____
3. _____
4. _____
5. _____

How will I know when I have reached my goal?
_____ ✓

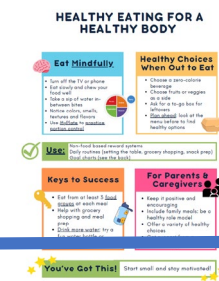
Keeping Track of My Goal

S M T W T F S
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DSMIG- Lifestyle Working Group



Keys to Success



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- Help with grocery shopping and meal prep
- Drink more water: try a fun water bottle or zero-sugar flavoring



For Parents & Caregivers



- Keep it positive and encouraging
- Include family meals: be a healthy role model
- Offer a variety of healthy choices
- Get support from a nutrition expert



Use:

Non-food based reward systems
Daily routines (setting the table, grocery shopping, snack prep)
Goal charts (see the back)

Lets' Get Moving



Why move?

- The more you move, the better you feel!
- All movement counts!
- Goal: 30 minutes activity per day, at moderate intensity
- Balance and strength exercises are extra important! Try to do these 2-3 times a week
- Start slow, make it a success!



Getting started

- What can you do **today** to get moving?
- Change 1 thing in your daily routine.
- Choose something fun!
- Write your goals on the back
- Put it on your calendar
- Make it a routine, a little bit every day!



Use:

Supportive exercise shoes
Calendars and timers to make it part of your routine
Reward systems and goal trackers (see the back)



Lets' Get Moving

What to do

- Take short movement breaks throughout the day
- Exercising with a friend or family member
- Help with groceries/cooking
- Dancing
- Online exercise videos
- Walking
- Simple workouts



For Parents & Caregivers



- Start small!
- Keep it positive and successful
- Start safely: check your doctor before starting
- Find a great team/trainer/buddy/physical therapist
- Use local parks and trails
- Build daily routines

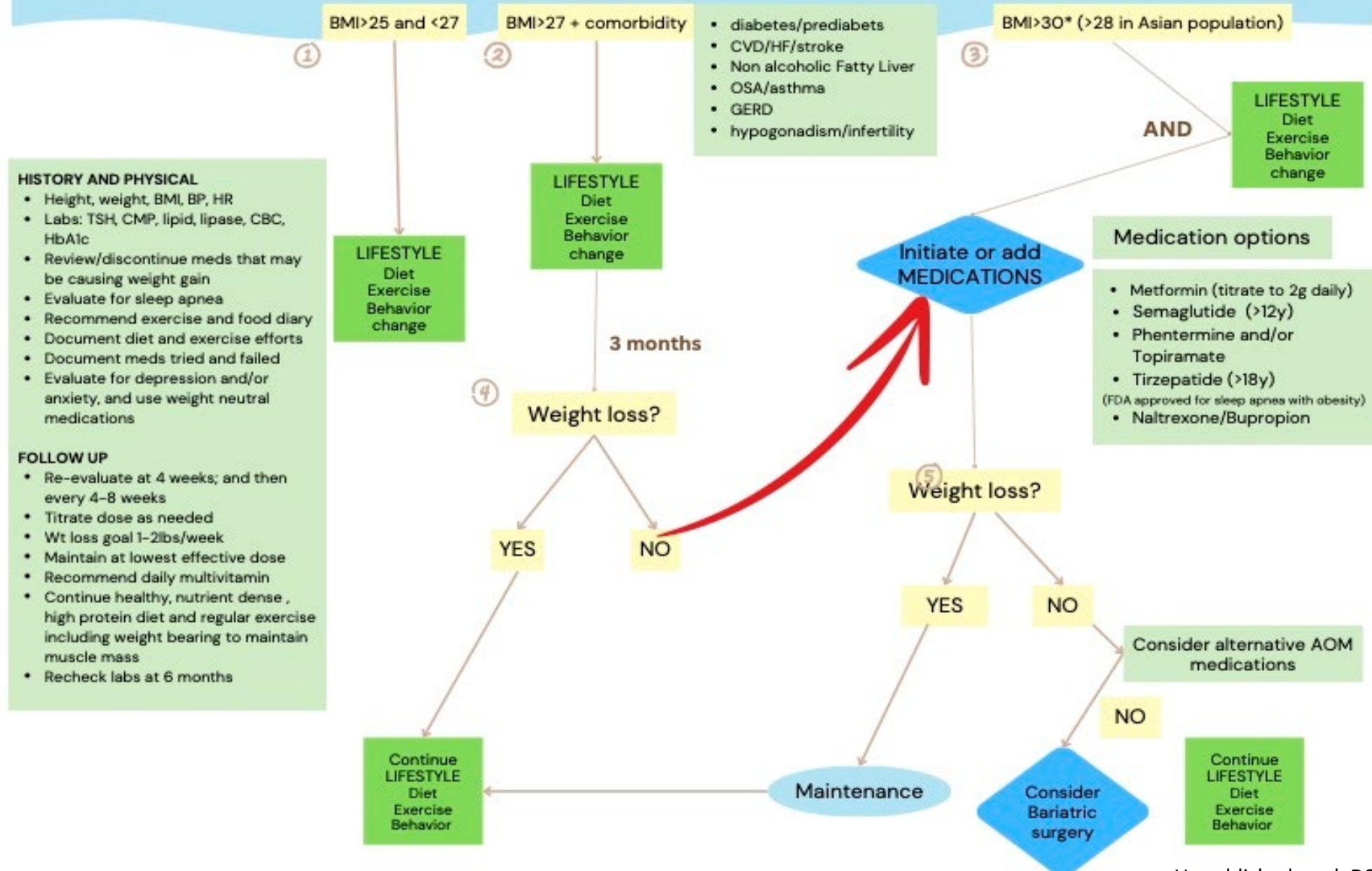
You've Got This!

Every step counts! Let's make it fun and part of your day!

Easier to Eat
Healthier Than
Exercising ALL
THE TIME

	2 slices Little Caesars pepperoni pizza 560 calories	=		65 minutes of moderate cycling
	28 tortilla chips 560 calories	=		57 minutes of Zumba
	1 can of Coca-Cola 140 calories	=		23 minutes of walking (4 mph)
	10 pigs in a blanket 490 calories	=		59 minutes of Bikram Yoga
	4 Double Stuffed Oreos 280 calories	=		1.3 hours of weight lifting
	4 cans of Miller Light 384 calories	=		32 minutes of running (6 mph)
	1 cup Chex Mix 240 calories	=		29 minutes of high impact aerobics

Algorithm for Obesity Management



Real Life Situation

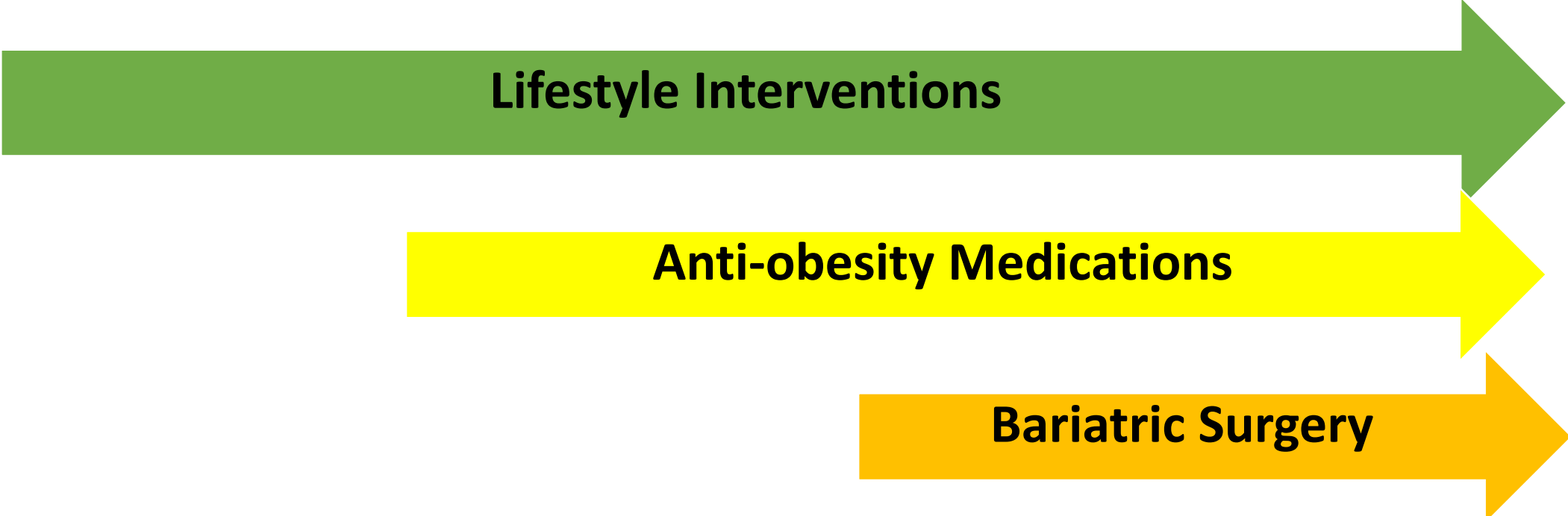
- Trying hard
- Dancing every day as a family
- Mom cooking at home and monitoring her food
- Still no weight loss
- Sleep apnea is a concern – does not keep the mask on- mom states that she has not slept a full night in years



Objectives

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Multimodal Obesity Treatment Approach



Lifestyle Interventions

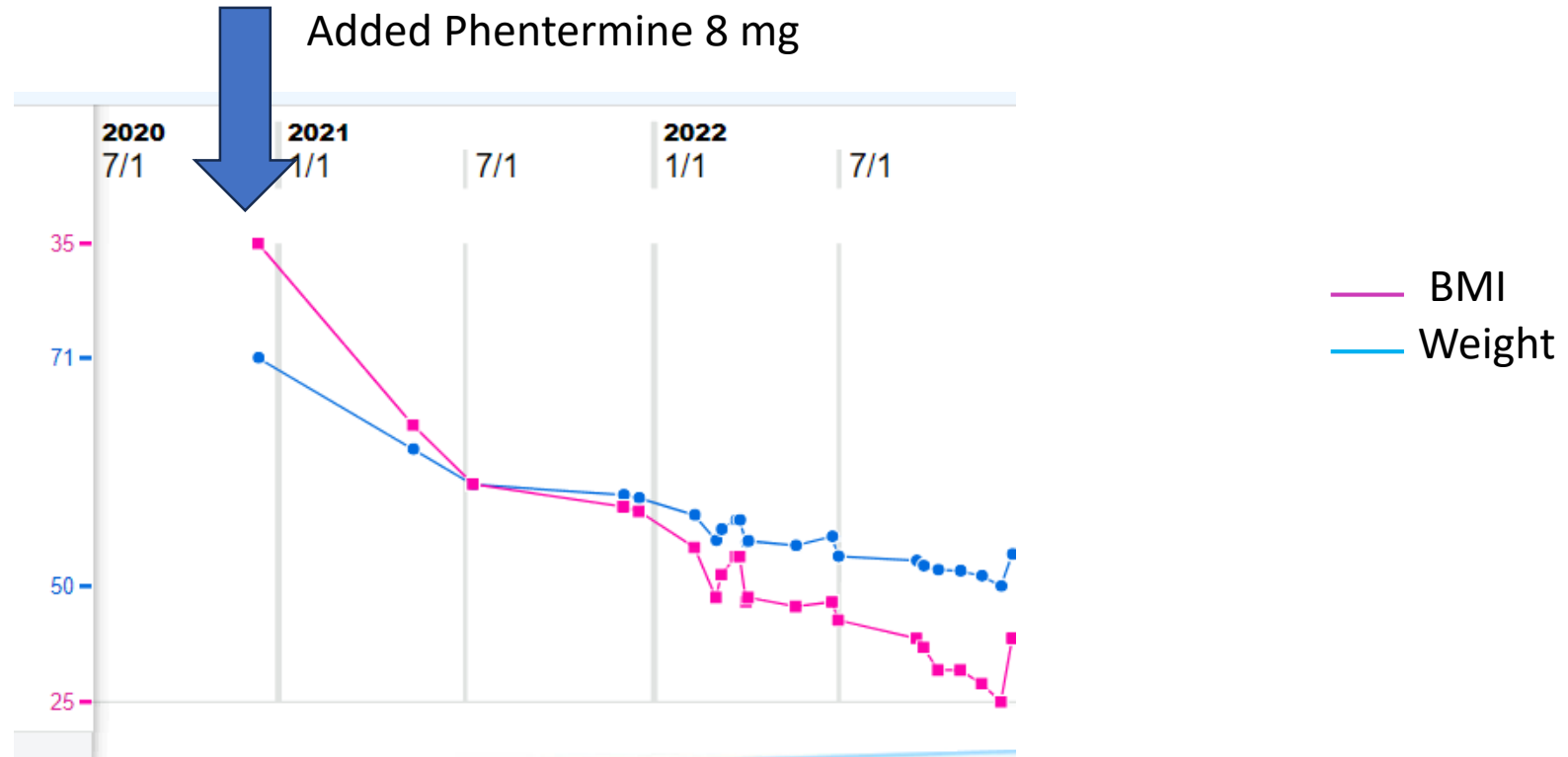
Anti-obesity Medications

Bariatric Surgery

Another Real Life Example - AP

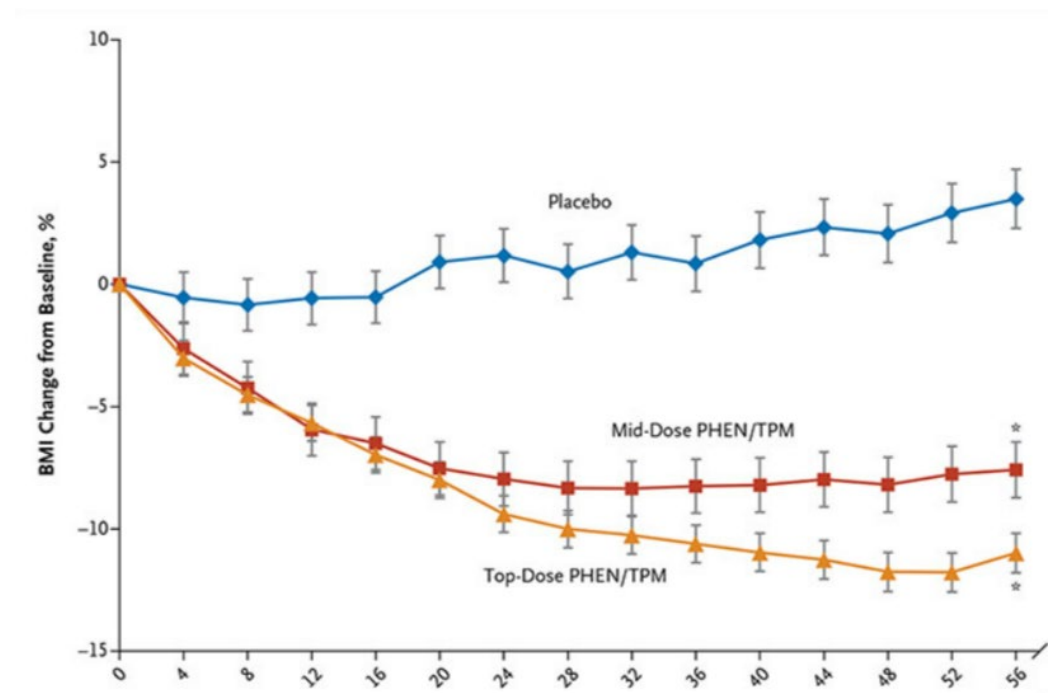
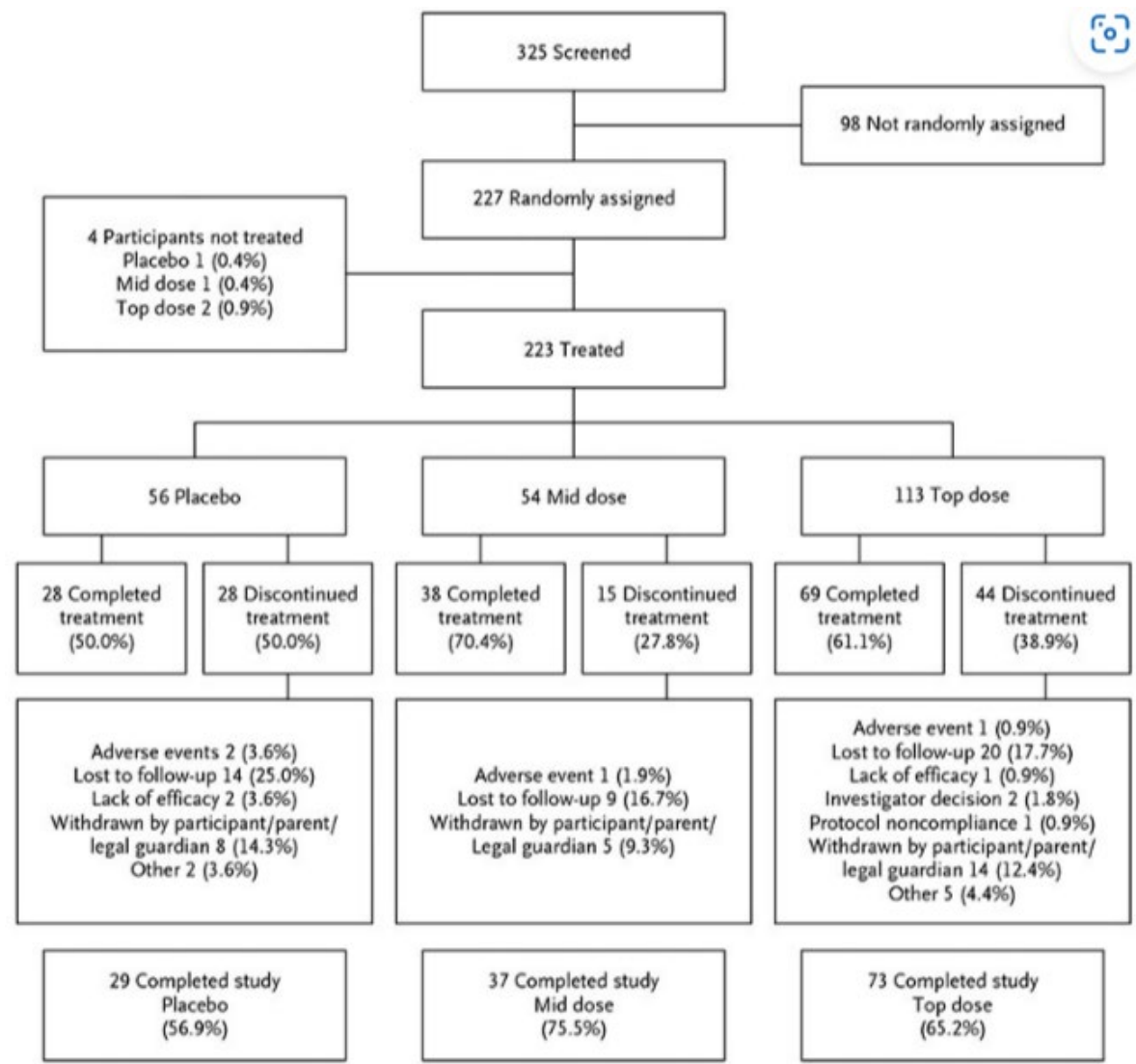
23 y/o young lady with Down syndrome, S/P DVT and pulmonary embolism, sleep apnea (managed with CPAP), anxiety and obesity

Following a healthy lifestyle to the best of her families' abilities
Added Phentermine 8 mg



Anti Obesity Medication: Qsymia

56-week, randomized, double-blind trial enrolled adolescents 12 to less than 17 years of age with obesity

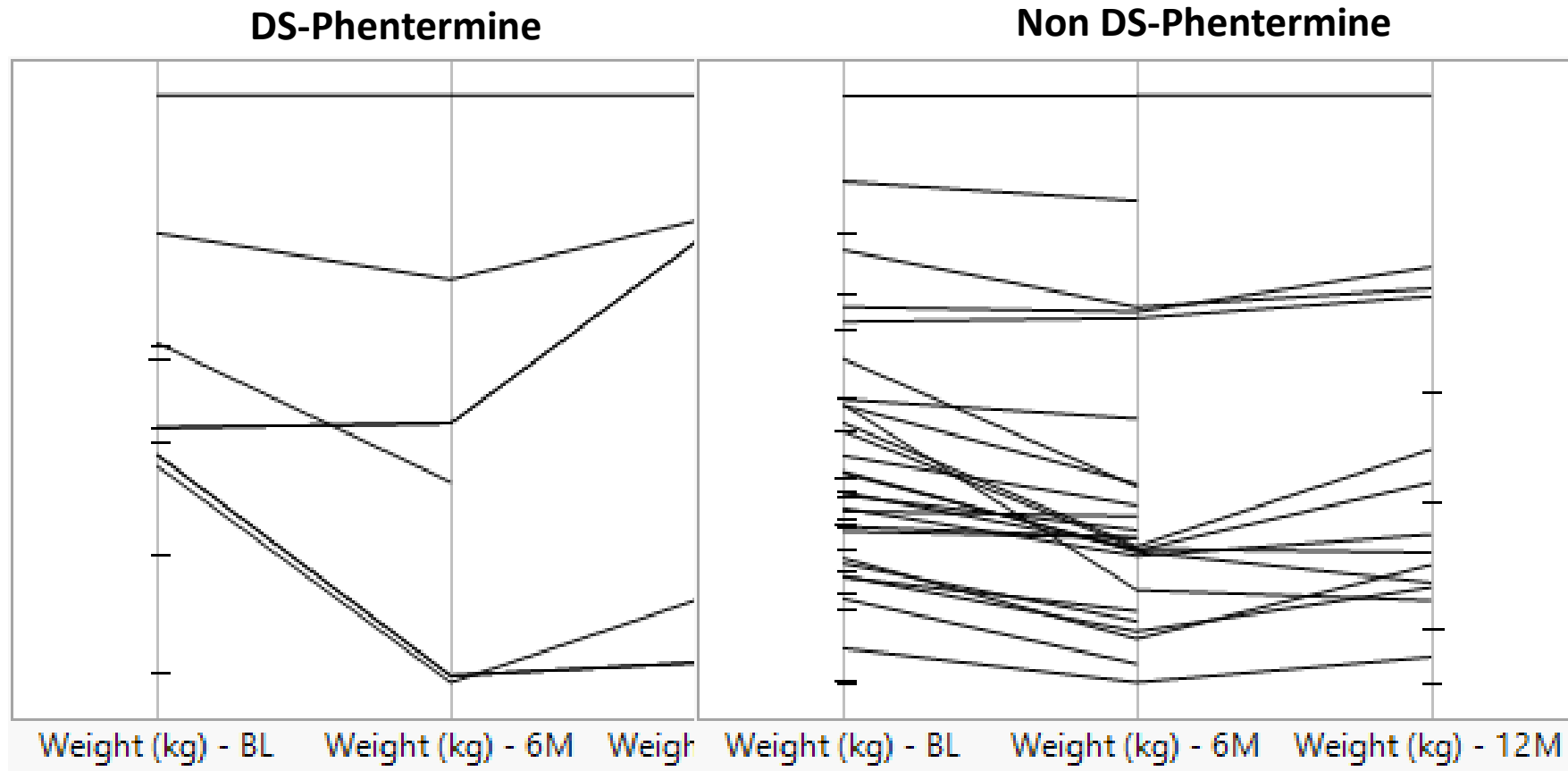


Efficacy of Phentermine in DS as compared with non-DS

Single center Electronic Chart review of 95 Individuals with and without who have obesity between 2015-2021

	DS-GLP1 (n=37)	DS-Phen (n=14)	Non DS-Phen (n=44)
Age (years)	38.0 (25.0-43.0)	27.0 (22.8-41.5)	24.5 (23.0-26.0)
Female n (%)	24.0 (64.9%)	9.0 (64.3%)	35.0 (79.5%)
Weight (kg)	92.2 (76.5-104.4)	77.7 (74.6-86.2)	105.5 (94.0-122.0)
Height (cm)	149 (145.3-154.9)	149.2 (142.9-154.3)	165.1 (160.0-170.2)
BMI (kg/m ²)	40.1 (35.5-44.1)	34.5 (32.6-42.7)	40.0 (35.8-43.8)
A1c (%)	5.3 (5.0-6.0)	5.1 (4.7-5.6)	

Efficacy of Phentermine in DS as compared with non-DS



Mean weight loss of 10.28 (+/- 3.98) kg

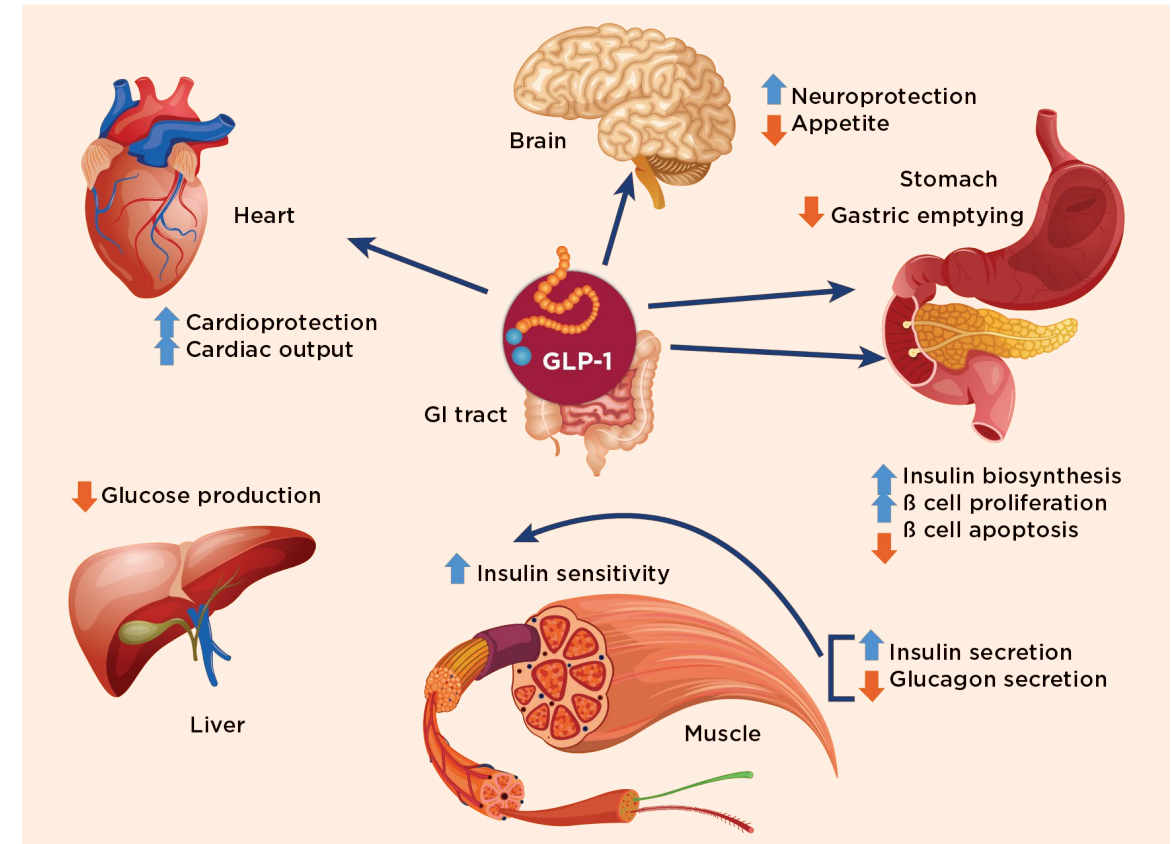
Mean weight loss of 14.4 (+/- 2.98) kg

P=0.39 between groups

Unpublished Data

Anti-Obesity Medication – Glucagon Like Peptide-1 Analogs

- Mechanism of action:
 - Reduces hunger
 - Increases satiety
 - Decreases gastric emptying
 - Central effect on hypothalamus
- FDA approved in children after 12 years for obesity and after 10 years for T2D
- Side effects:
 - Nausea/Vomiting
 - Headaches
 - Pancreatitis
- Thyroid C-cell tumors in rodents
(Contraindication if personal/family history of MEN)



Efficacy of Liraglutide – RCT in Adolescents With Obesity

RCT with 56-wk treatment and a 26-wk follow-up

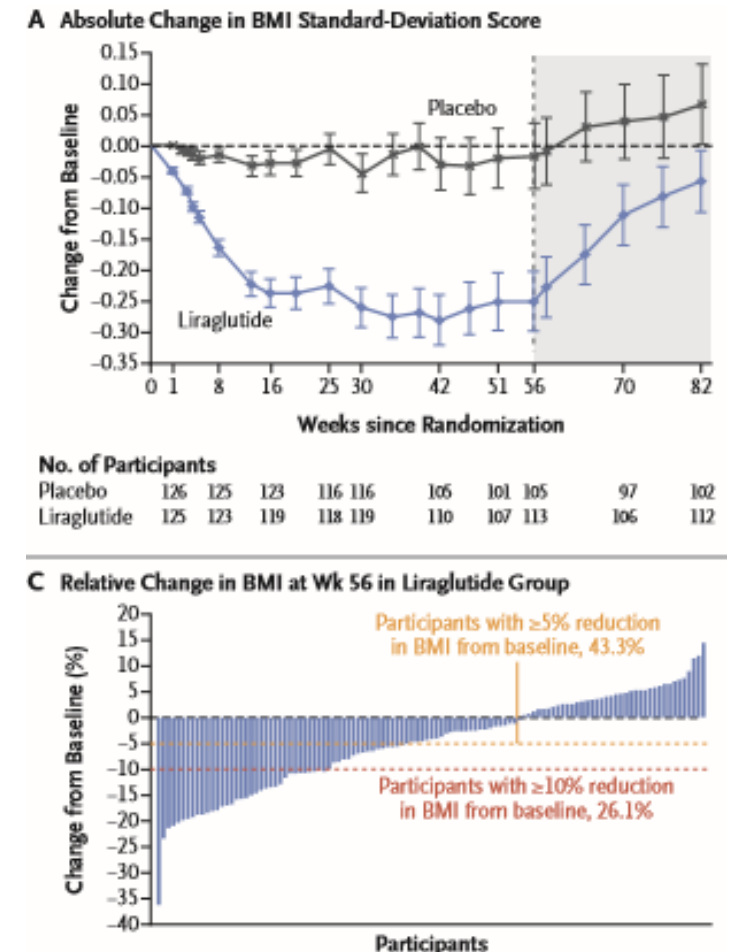
Adolescents (12 to <18 yrs) with obesity and a poor response to lifestyle therapy alone

Randomly assigned (1:1) to either liraglutide (3.0 mg) or placebo subcutaneously once daily in addition to lifestyle

125 liraglutide/ 126 placebo

Reduction in BMI of at least 5% - 51/113 liraglutide and 20/105 placebo

Reduction in BMI of at least 10% - 33/113 liraglutide and 9/105 placebo



Efficacy of Semaglutide – RCT in Adolescents With Obesity

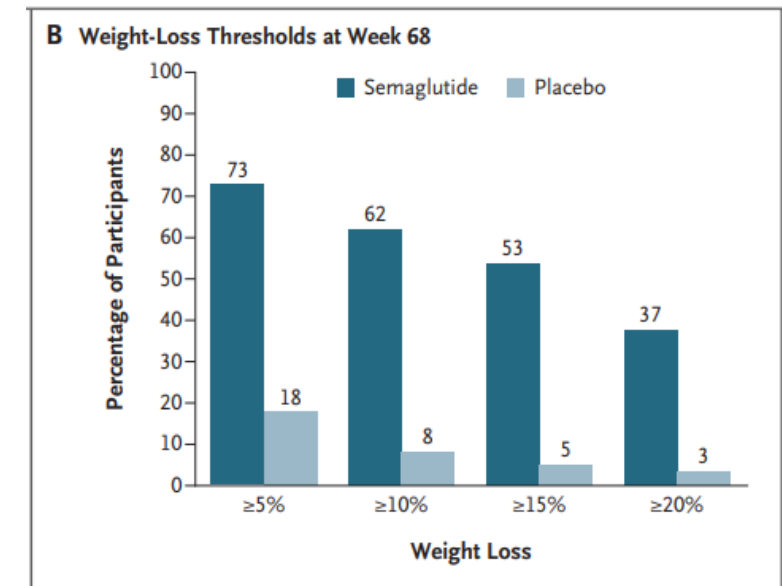
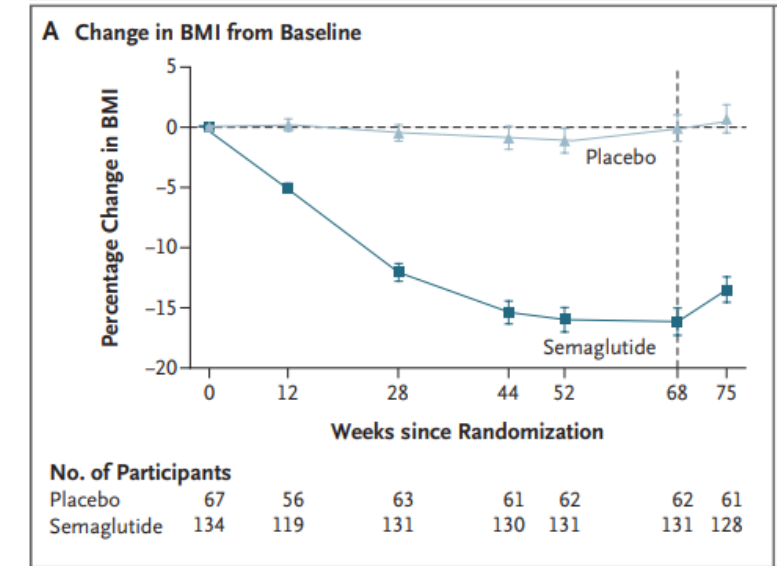
RCT with 68-wk treatment and a 26-wk follow-up

Adolescents (12 to <18 yrs) with obesity and a poor response to lifestyle therapy alone

Randomly assigned (2:1) to either Semaglutide (dose escalation- 0.25, 0.5, 1, 1.7 and 2.4 mg) or placebo subcutaneously once daily in addition to lifestyle

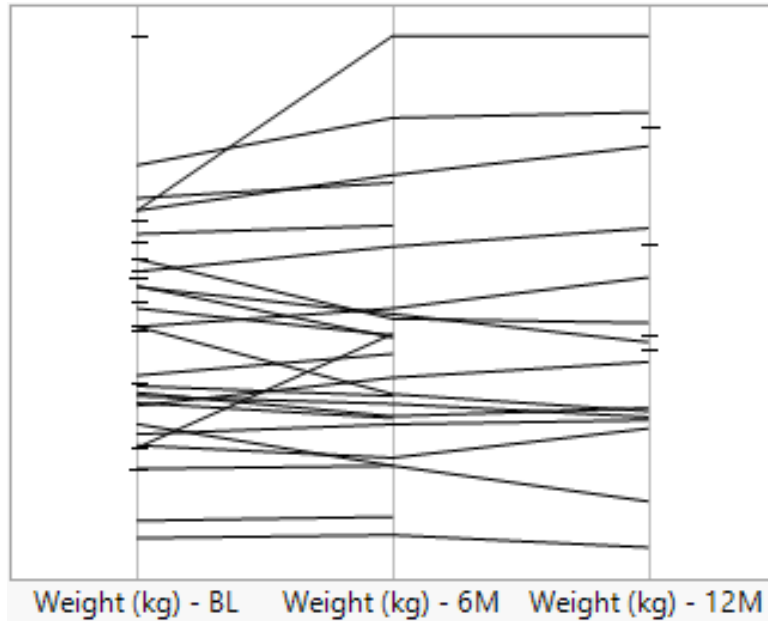
201 randomized- 180 completed the study (90%)

Mean initial BMI: $37 \pm 6 \text{ kg/m}^2$



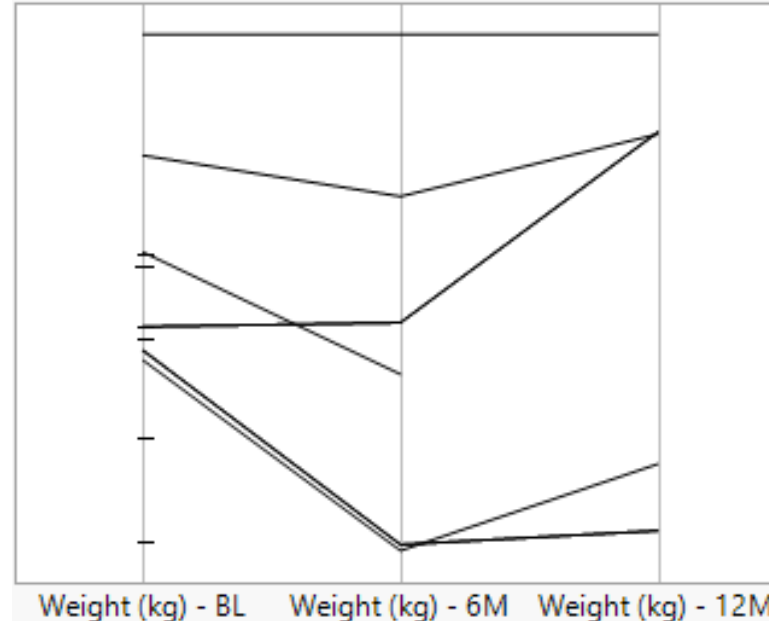
Efficacy of Phentermine in DS as compared with non-DS

DS- GLP-1



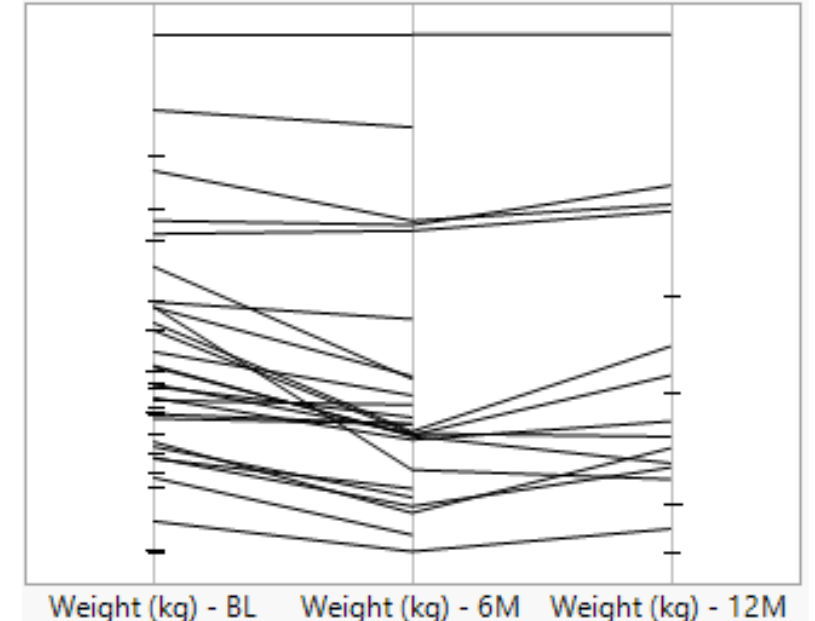
Mean weight loss of
3.84 (+/- 2.42) kg

DS-Phentermine



Mean weight loss of
10.28 (+/- 3.98) kg

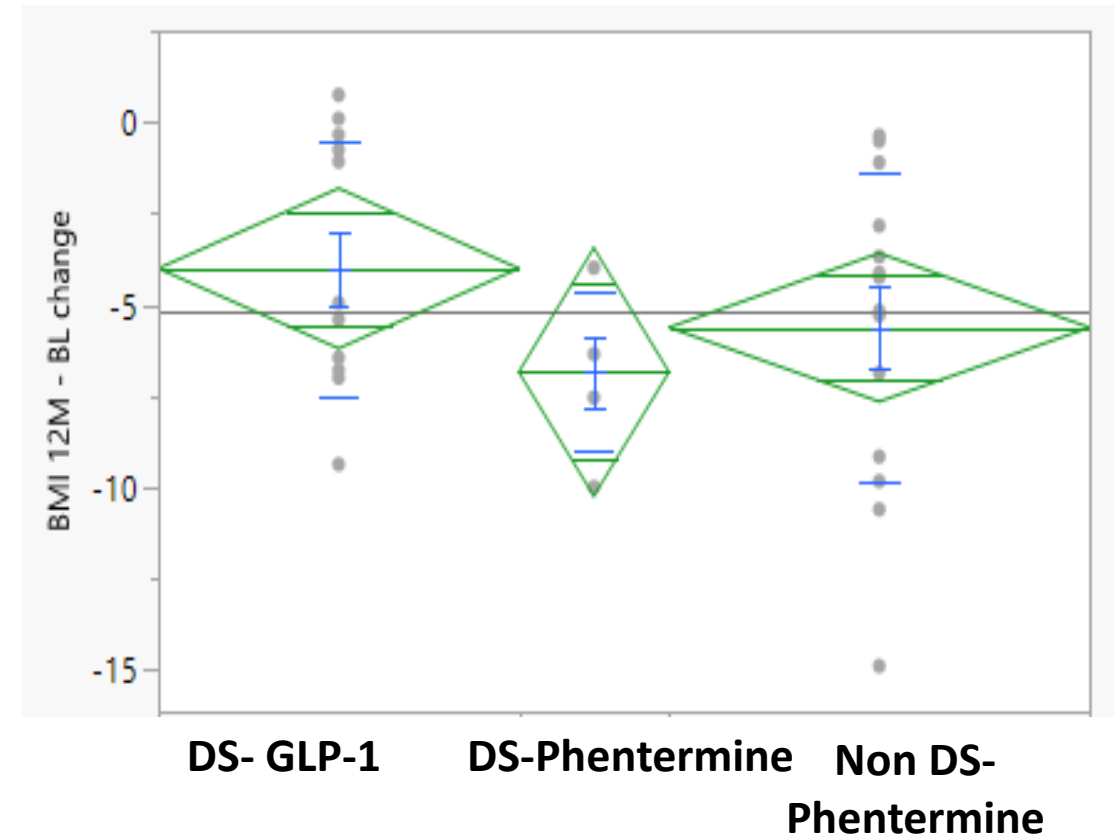
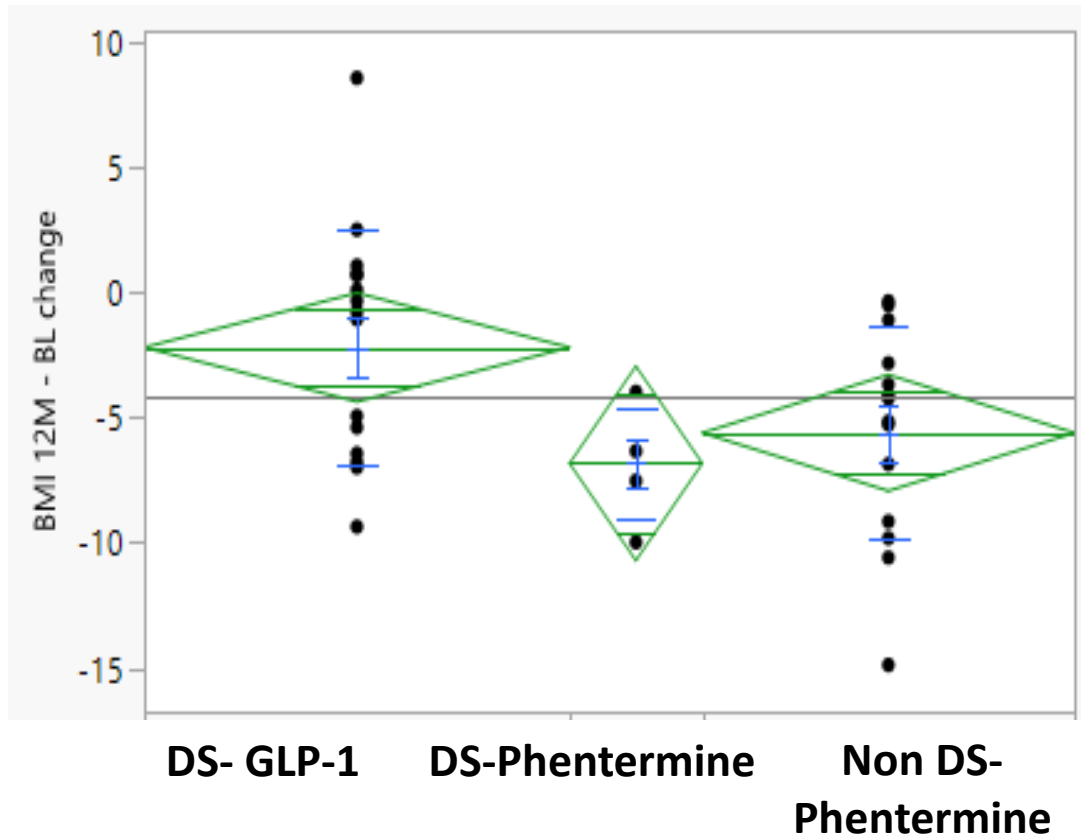
Non DS-Phentermine



Mean weight loss of
14.4 (+/- 2.98) kg

P=0.39 between groups

Efficacy of GLP-1 and Phentermine in DS



Anti Obesity Medication: Metformin

- Mechanism: activation of AMP protein kinase; decreased gluconeogenesis
- FDA approved ≥ 10 y/o for diabetes
- Efficacy: 3.3 kg placebo-subtracted weight loss
- Preferred if:
 1. Antipsychotic induced weight gain
 2. Associated PCOS
 3. Prediabetes
- Adverse effects :
 1. GI including bloating, diarrhea (slow titration with meals)
 2. Lactic acidosis is very rare
 3. Monitor Vitamin B12 levels after prolonged use

Metformin in Antipsychotic induced Weight Gain

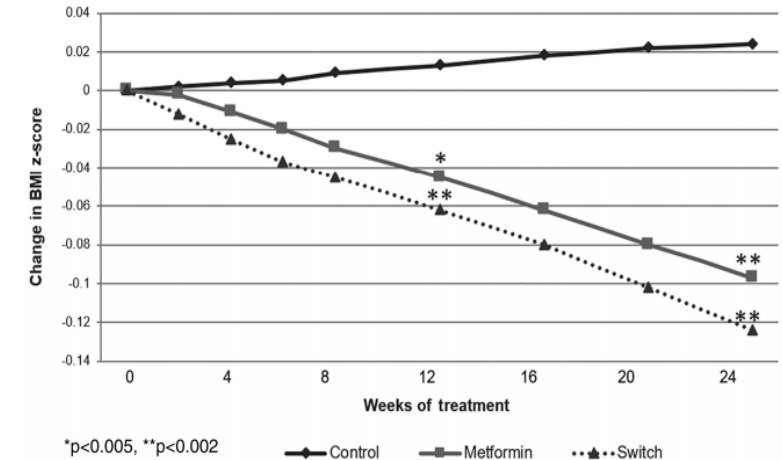
Improving Metabolic Parameters in Antipsychotic Child Treatment (IMPACT): Randomized 24-week clinical trial

- Youth aged 8-19 years with overweight/obesity psychiatrically stable
- DSM-IV diagnosis of severe mental illness (schizophrenia spectrum disorder, bipolar spectrum disorder or psychotic depression)
- Developed substantial weight gain following treatment with a second-generation antipsychotic

Randomized to

1. metformin (MET) n= 49
2. antipsychotic switch (aripiprazole) or, if already exposed to that drug, perphenazine or molindone; SWITCH n=31
3. Continued baseline antipsychotic (CONTROL) n=47

All participants received healthy lifestyle education



BMI z-score decreased significantly with MET (-0.09 ± 0.03 , $p=0.002$) and SWITCH (-0.11 ± 0.04 , $p=0.003$), while it increased in CONTROL (week 24: $+0.04 \pm 0.03$)

MBS – Types and Indications

INDICATIONS:

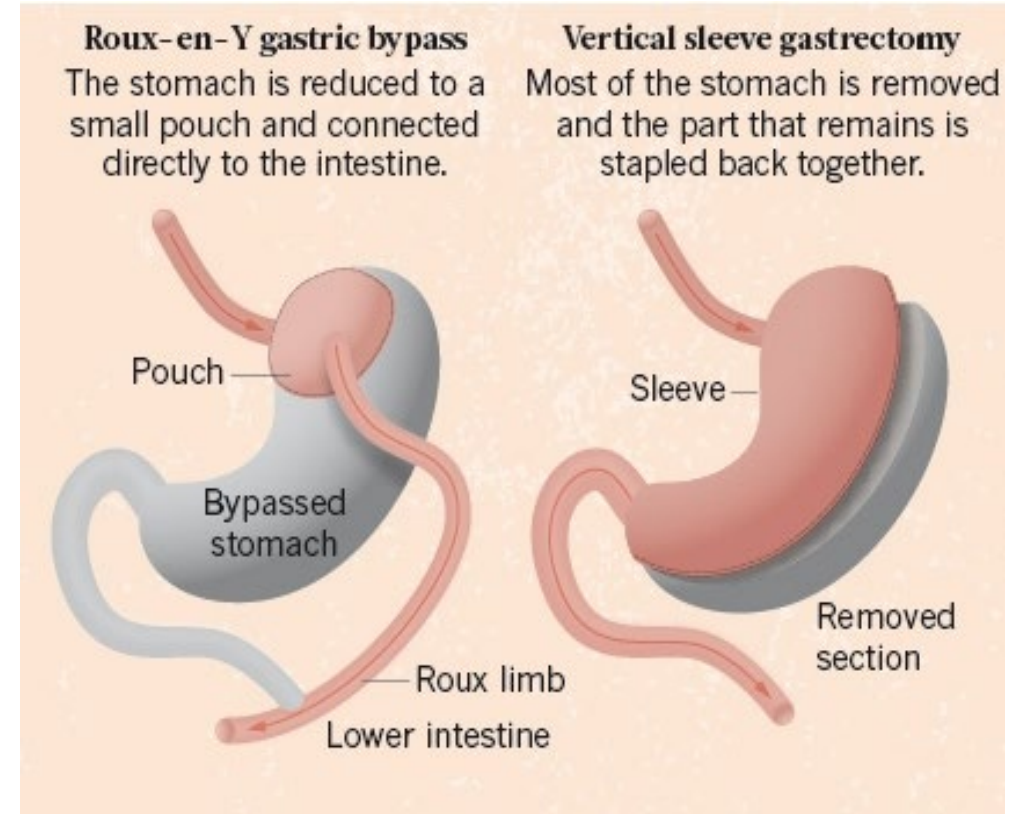
1. BMI ≥ 35 kg/m² or $\geq 120\%$ of the 95th %ile with one comorbid condition

- OSA (AHI > 5 events/h)
- Type 2 diabetes
- NASH
- HTN (on medications)
- PCOS

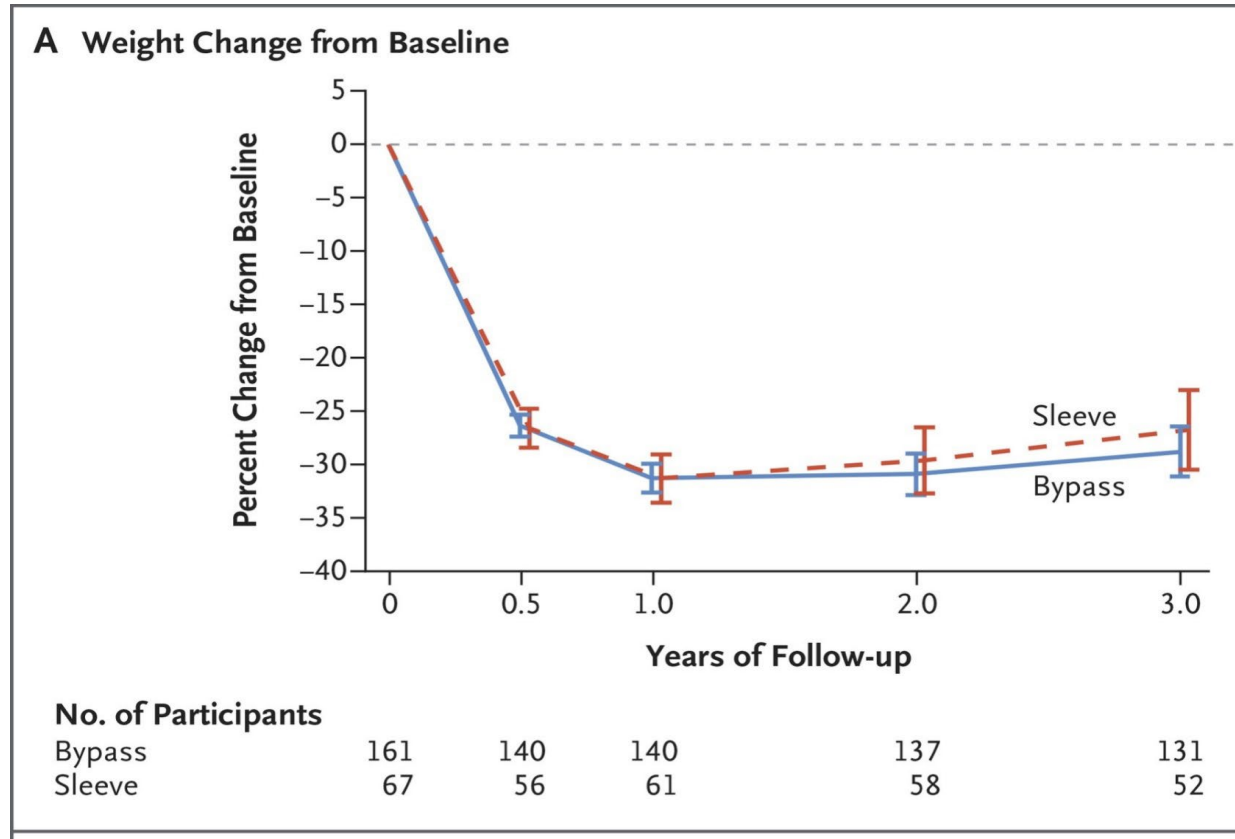
2. BMI ≥ 40 kg/m² or $\geq 140\%$ of the 95th %ile

CONTRAINDICATIONS:

- Pregnant or breast-feeding adolescents
- Unresolved substance abuse, eating disorder
- Untreated psychiatric disorder
- Suicidal attempt in the last year



Weight Loss at 3 Years After Surgery- TEEN Labs



At 3 years:

- 26% of the participants no longer had obesity
- 85-90% of participants had a 10% or greater reduction in BMI



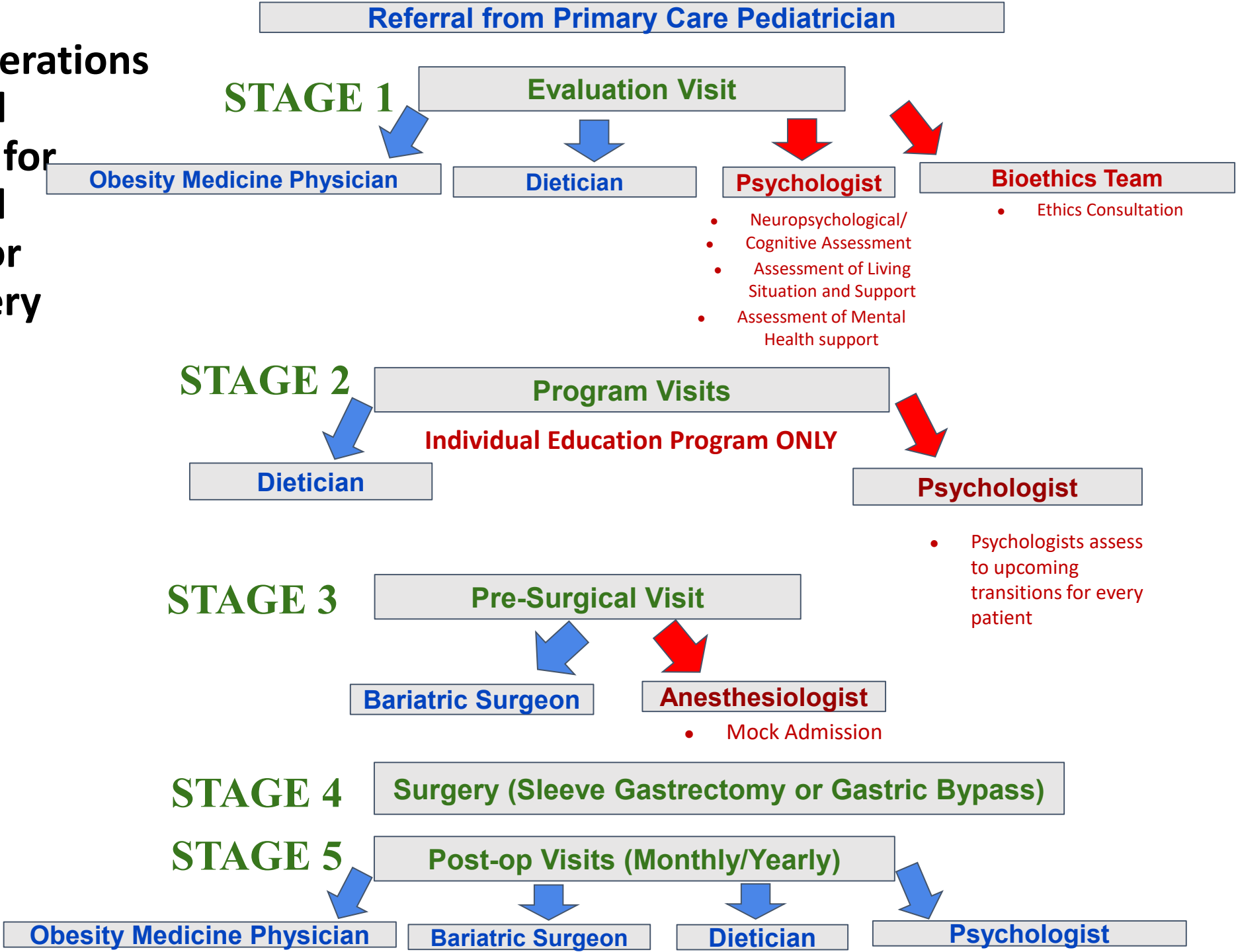
Case Series

Clinical Findings of Three Neuro-atypical Adolescents with Severe Obesity Who Underwent Bariatric Surgery

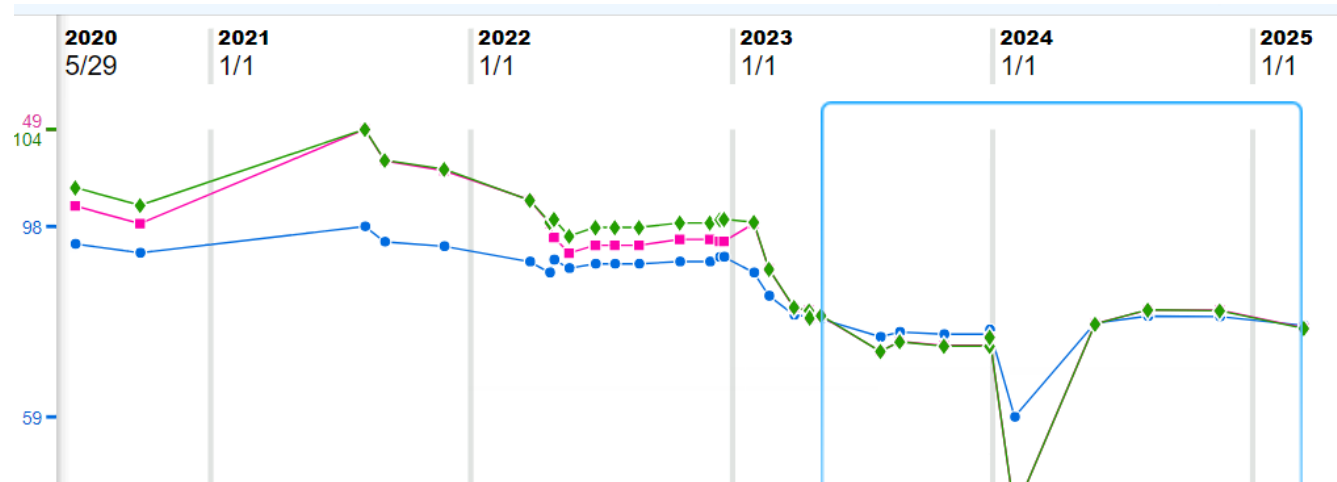
Age/Sex	Race	Neuroatypical Diagnosis	Level of Function	Comorbid condition(s)	Initial Weight/BMI (lbs)/(kg/m ²)
14/F	African American	Autism	Severely Impaired	Polycystic Ovarian Syndrome Prediabetes	306/52.8
18/F	African American	Autism and Trisomy 21	Severely Impaired	Obstructive Sleep Apnea Back Pain	270.5 /61
21/F	Asian	Trisomy 21	Mild-moderate impairment	Obstructive Sleep Apnea Prediabetes Hypertriglyceridemia Hyperinsulinemia	216.1/48.43



Special Considerations and Additional Requirements for Neuro-atypical Adolescents for Bariatric Surgery

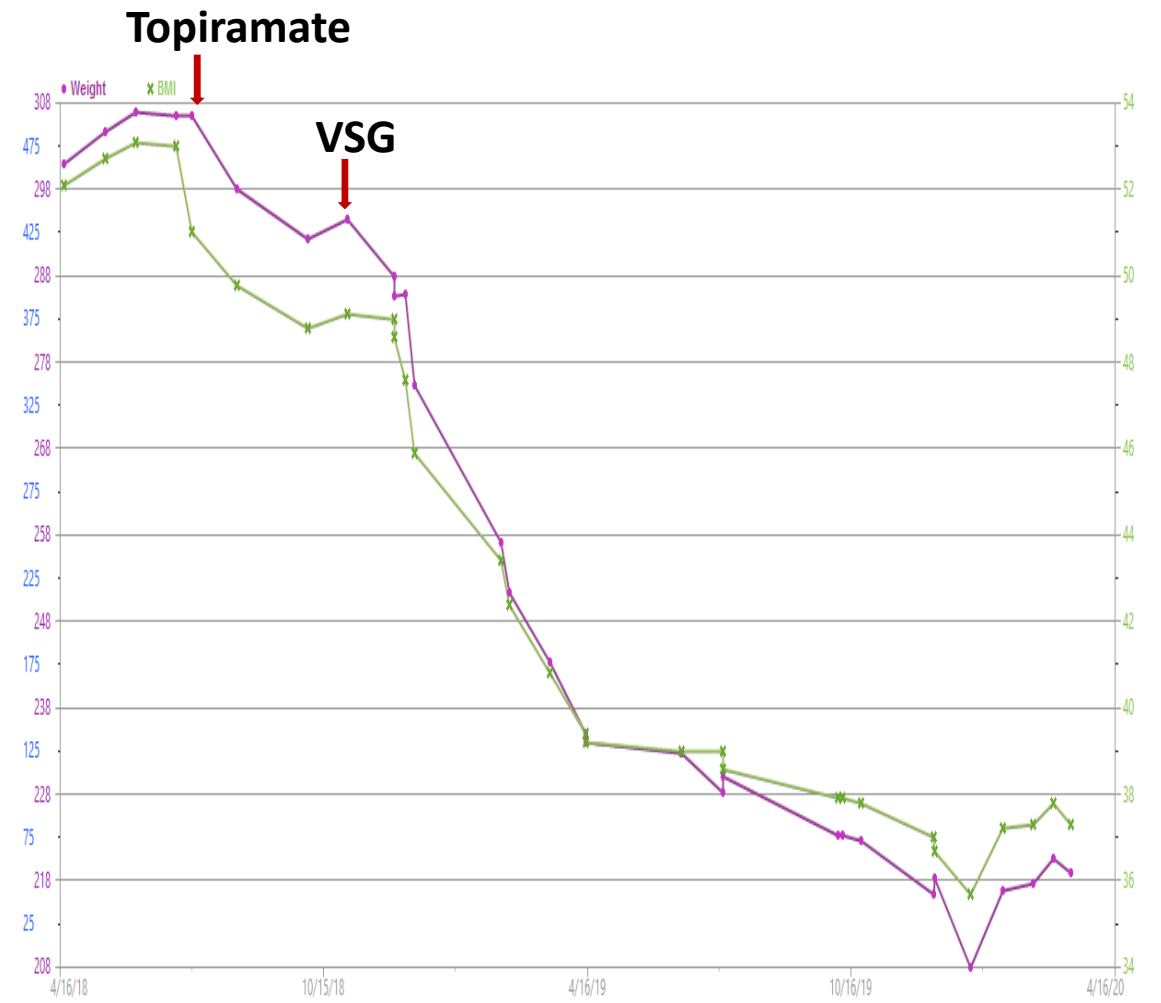


Metabolic and Bariatric Surgery as an Option



Preop Wt – 202 Lb
Post Op Wt – 172 lb
% TBW Loss about 18%

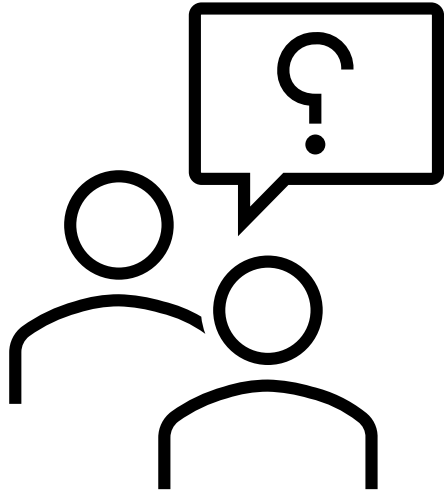




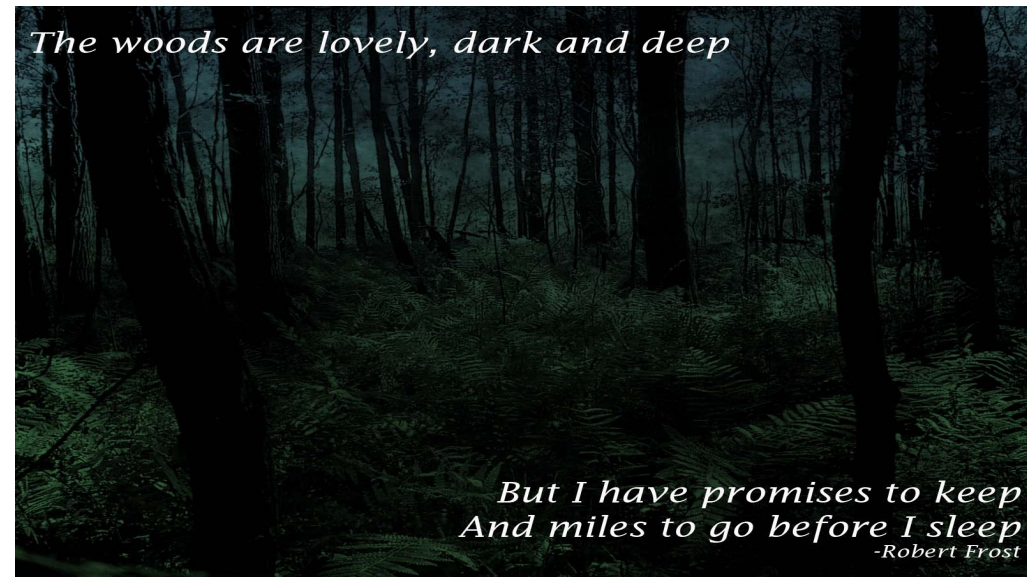
Summarize: Considerations in Individuals with Down syndrome

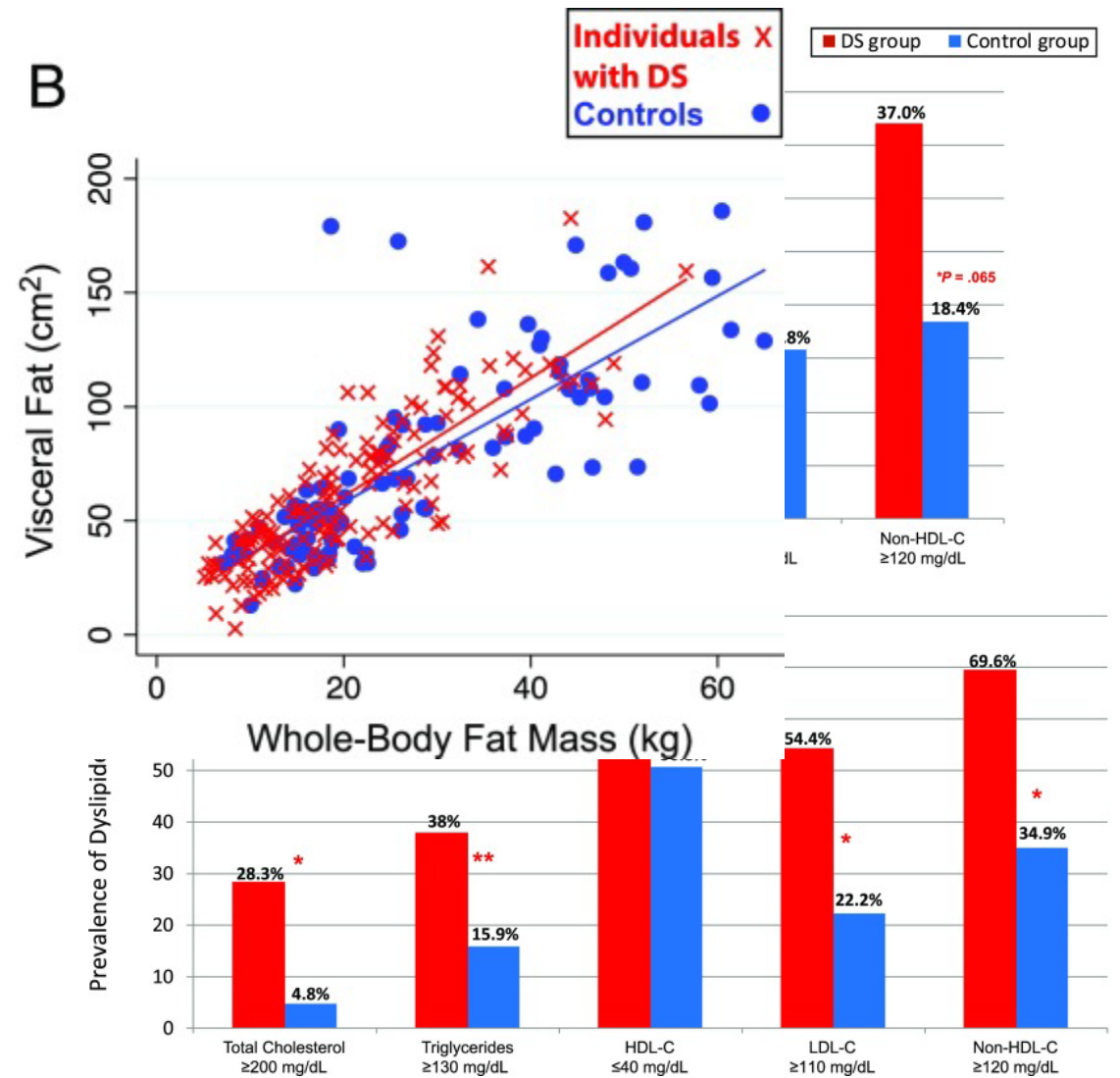
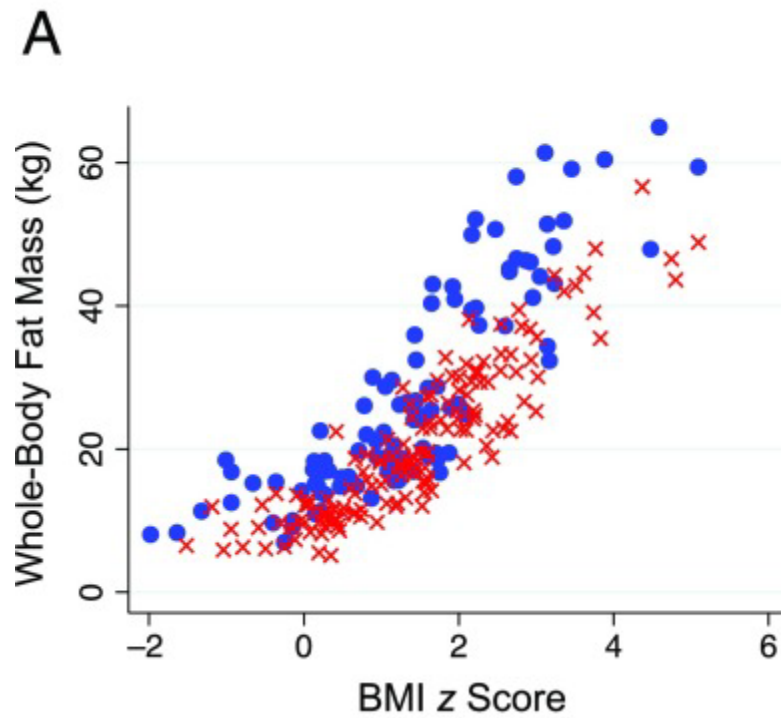
- Rates of Obesity are high and associated with complications
- CDC BMI growth charts are preferred for early detection of obesity
- Special considerations for weight gain – lower REE, associated health conditions and behavioral uniqueness
- Start monitoring weight early and make changes as a family
- No data on the effectiveness and side effects of AOMs in DS population
- MBS may be effective in DS
- We need clinical trials to evaluate the efficacy and safety of weight loss medications and/or surgery in individuals with Down syndrome

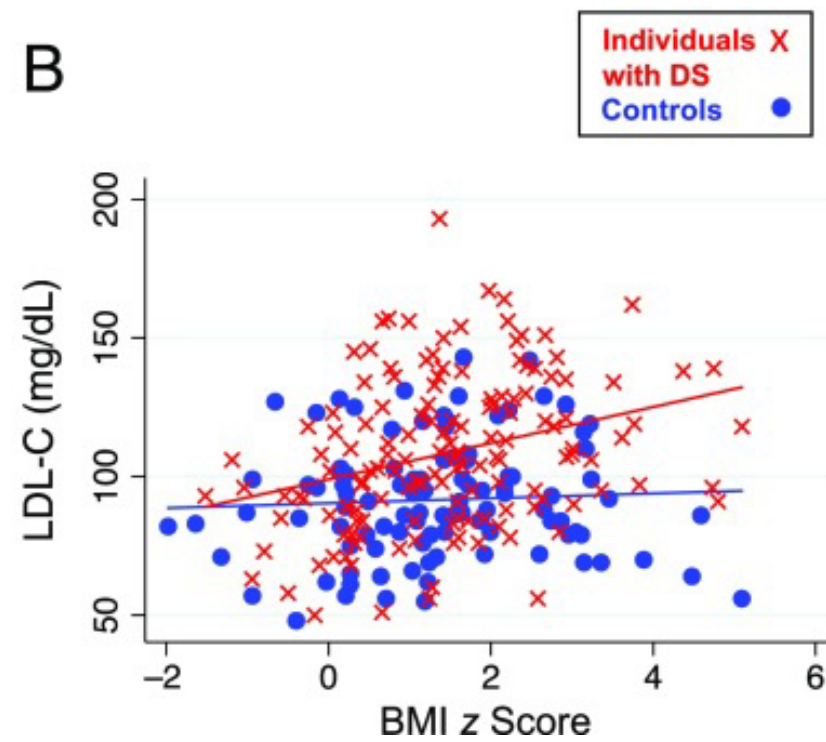
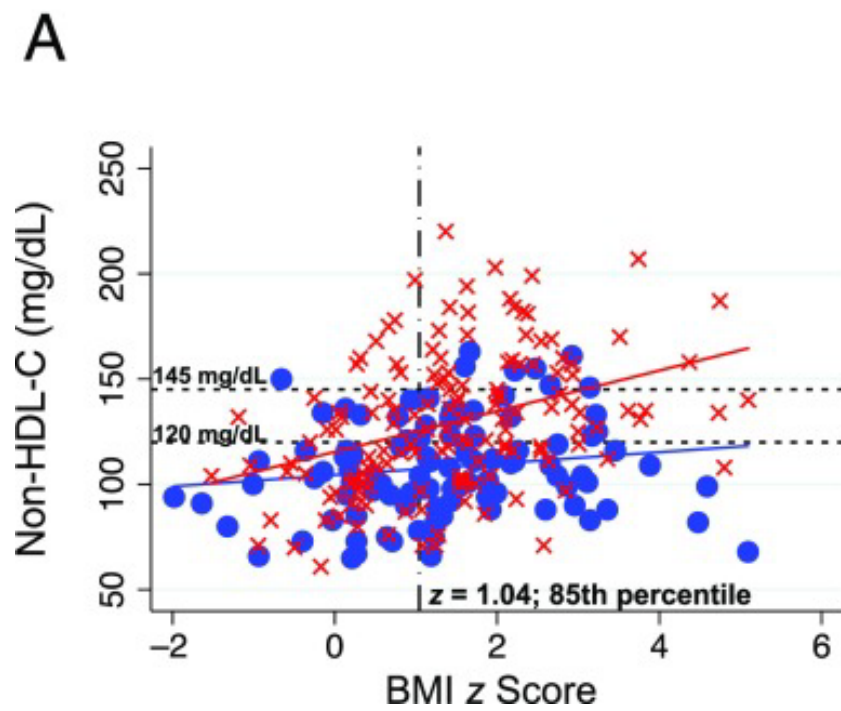
Thank you for your attention!



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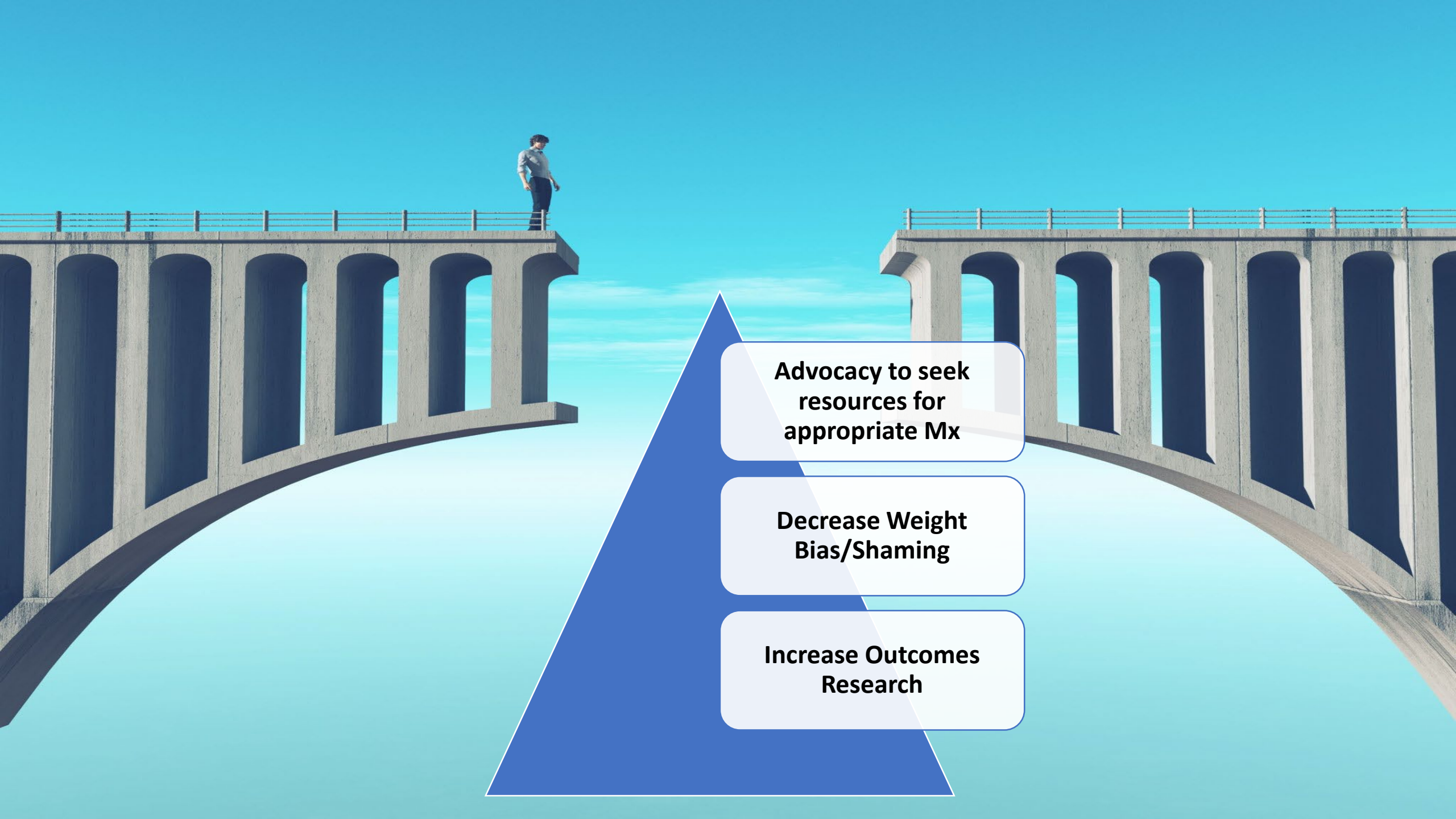






Anti Obesity Medication: General Principles

- Assess Readiness (provider and family)
- Discuss the need for escalating treatment for health purposes (multidisciplinary team)
- Evaluate for complications and any high-risk situations
- FDA approval : above 12 years and with obesity (any severity), overweight with complications. Document off-label use and consent for treatment
- Discuss the need for long term treatment
- Discuss the need for ongoing healthy lifestyle
- Set realistic expectations (keeping in mind insurance coverage)



**Advocacy to seek
resources for
appropriate Mx**

**Decrease Weight
Bias/Shaming**

**Increase Outcomes
Research**