Pediatric Obesity: An Update and Overview

2021 Obesity and Weight Management Symposium: Battle of the Bayou Bulge Part 3

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Disclosures

I conduct clinical trials for a variety of different sponsors whereby my institution is paid via contracts

I do not have any relevant financial disclosures related to this presentation

Outline

- Scope of the problem
- Pathophysiology
- Diagnosis/Evaluation
- Treatment

Definitions

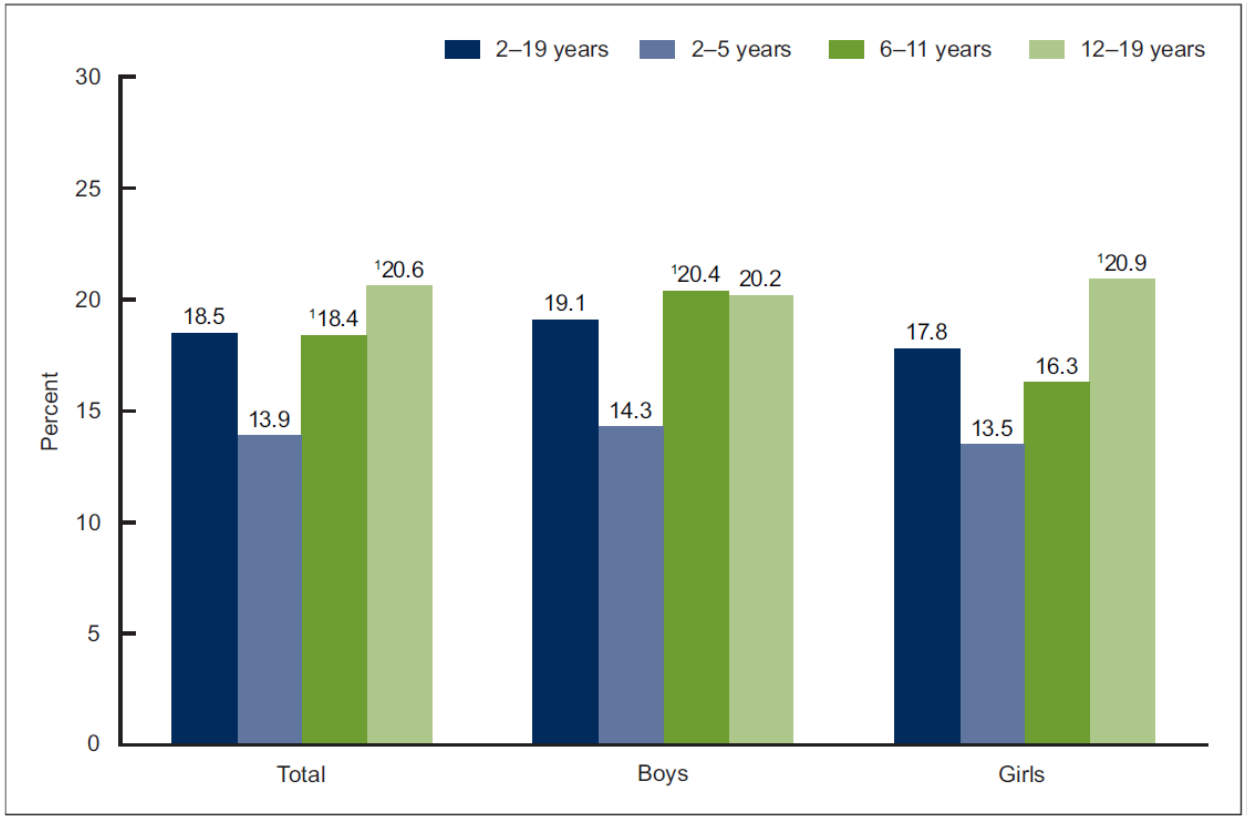
- Body Mass Index (BMI) is a reasonable estimate of adiposity
- BMI may slightly overestimate fatness in children who are short or who have relatively high muscle mass
- BMI may underestimate adiposity in those with reduced muscle mass
- As a result of normal growth and development, the norms for the absolute level of BMI in children vary with age and sex

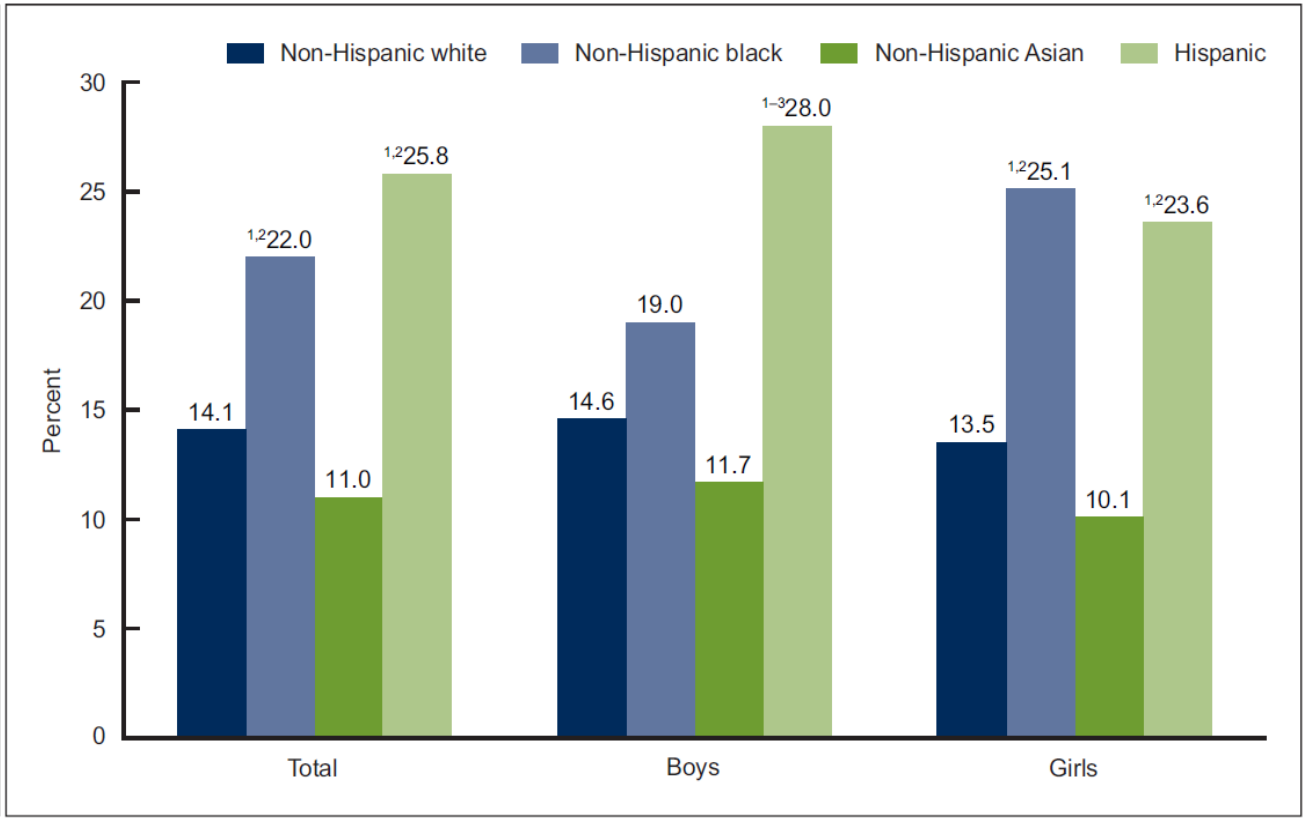
Definitions

- For children and adolescents between 2 and 20 years of age:
- Overweight: BMI ≥ 85th to < 95th percentile for age and sex
- Obesity: BMI ≥ 95th percentile for age and sex
- Severe obesity: BMI ≥ 120% of the 95th percentile or absolute BMI ≥ 35 kg/m^2 (whichever is lower) (~99th percentile)
- Some experts recommend classifying obesity in 3 classes:
  - class I obesity (BMI ≥ 95th percentile to < 120% of the 95th percentile)
  - class II (BMI ≥ 120% to < 140% of the 95th percentile, or BMI ≥ 35 kg/m^2)
  - class III (BMI ≥ 140% of the 95th percentile, or BMI ≥ 40 kg/m^2)

Scope of the Problem

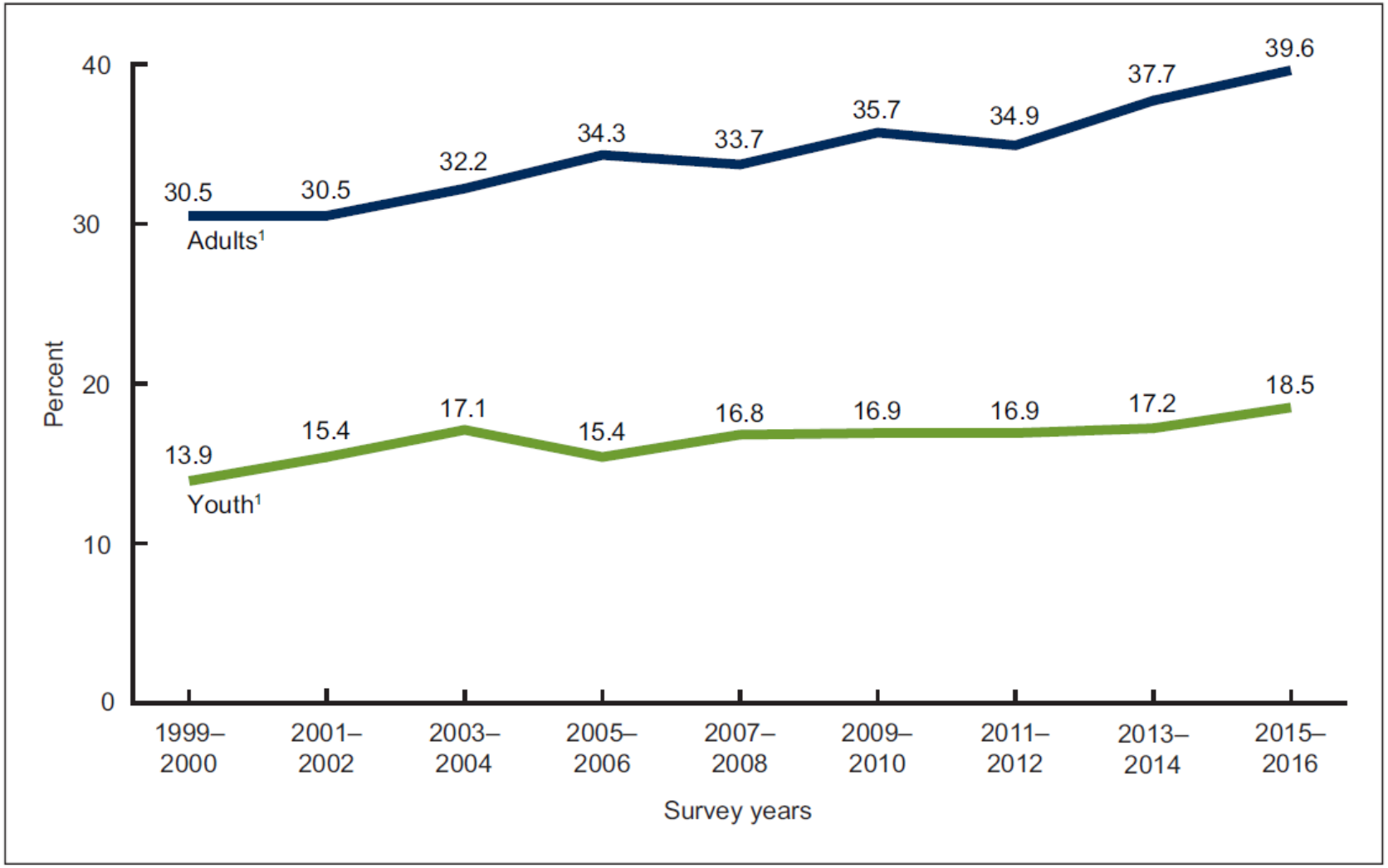
Prevalence of obesity among youth age 2-19 years in the U.S., 2015-2016





Hales CM, et al. Prevalence of Obesity Among Adults and Youth: United States, 2015-2016. NCHS Data Brief. 2017 Oct;(288):1-8.

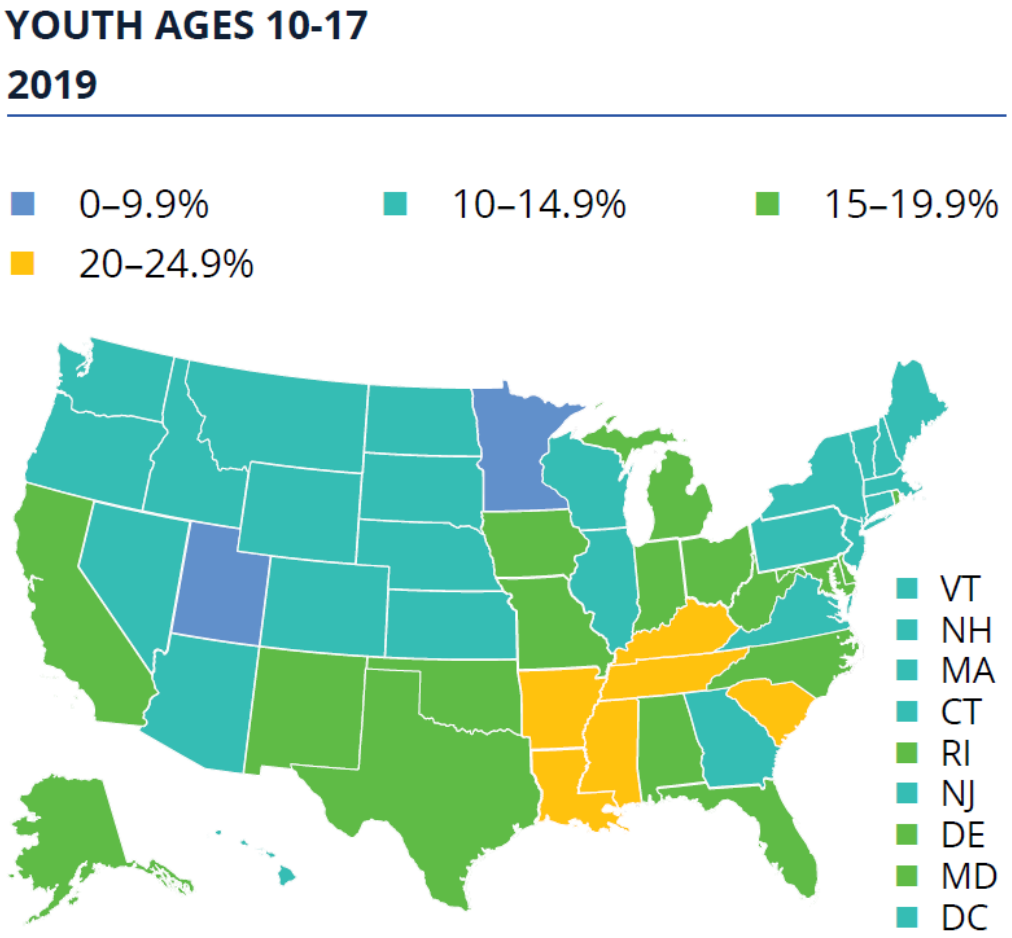
Scope of the Problem



Hales CM, et al. Prevalence of Obesity Among Adults and Youth: United States, 2015-2016. NCHS Data Brief. 2017 Oct;(288):1-8.

What about Louisiana?

- 20.1% of youth ages 10 to 17 had obesity in 2018-2019
- Ranks 6th in the nation for childhood obesity
- Kentucky had the highest overall prevalence of obesity (23.8%) while Utah had the lowest (9.6%)



Tracking of Childhood Obesity Into Adulthood

- Tracking of obesity into adulthood is affected by age of the child, severity of obesity, and presence of parental obesity
- Older age is associated with persistence of obesity into adulthood
  - In one study, 71% of adolescents with severe obesity continued to have severe obesity in adulthood compared to 8% of adolescents with non-severe obesity
- Parental obesity increases the risk of adult obesity by more than 2-fold in children younger than 10 years

Etiology

- Childhood obesity results from the interaction of a complex set of factors related to:
  - Environment
  - Genetics
  - Ecological effects such as the family, community, and school

TABLE 1. Secondary Causes of Pediatric Obesity

Monogenic disorders	**Endocrine**
Melanocortin 4 receptor haploinsufficiency	Hypothyroidism
Leptin deficiency	Glucocorticoid excess (Cushing syndrome)
Leptin receptor deficiency	Growth hormone deficiency
Proopiomelanocortin deficiency	Pseudohypoparathyroidism
Proprotein convertase 1	**Psychological**
Syndromes	Depression
Prader-Willi	Eating disorders (binge eating disorder and night eating disorder)
Bardet-Biedl	**Drug induced**
Cohen	Tricyclic antidepressants
Alström	Glucocorticoids
Albright hereditary osteodystrophy	Antipsychotic drugs
Beckwith-Wiedemann	Antiepileptic drugs
Carpenter	Sulfonylureas
Neurologic	**Hypothalamic causes**
Brain injury	Tumor
Brain tumor	After brain surgery/radiation (craniopharyngioma)
After cranial irradiation	ROHHAD/ROHHADNET syndrome
Hypothalamic obesity	

ROHHAD = rapid-onset obesity with hypothalamic dysfunction, hypoventilation, and autonomic dysregulation; ROHHADNET = rapid-onset obesity with hypothalamic dysfunction, hypoventilation, and autonomic dysregulation with neural crest tumors.

Kumar S, Kelly AS. Review of Childhood Obesity: From Epidemiology, Etiology, and Comorbidities to Clinical Assessment and Treatment. Mayo Clin Proc. 2017 Feb;92(2):251-265.

Etiology-Environment

- Increased caloric consumption
  - Larger portion sizes
  - Excess fat in fast foods
  - Sugar-sweetened beverages
- Reduced levels of physical activity
- Increased time spent in sedentary activities
  - Screen time

Etiology-Genetics

- Inherited factors appear to be responsible for 30% to 50% of the variation in adiposity
- Single gene defects and syndromes account for < 1% of childhood obesity cases
- Prader-Willi syndrome is the most common syndrome associated with obesity
- Mutations in the melanocortin 4 receptor is the most common single gene defect in childhood obesity

Etiology-Ecological Effects

- Psychosocial and emotional distress contribute to excess weight gain
  - Eating to suppress negative emotions
  - Appetite up-regulation
  - Low-grade inflammation
- Parental feeding styles, stress, and depression can affect eating behaviors in children
- Other factors such as birth weight, catch-up growth, antibiotic use, chemical exposure, and microbiota have been proposed

Diagnosis and Evaluation

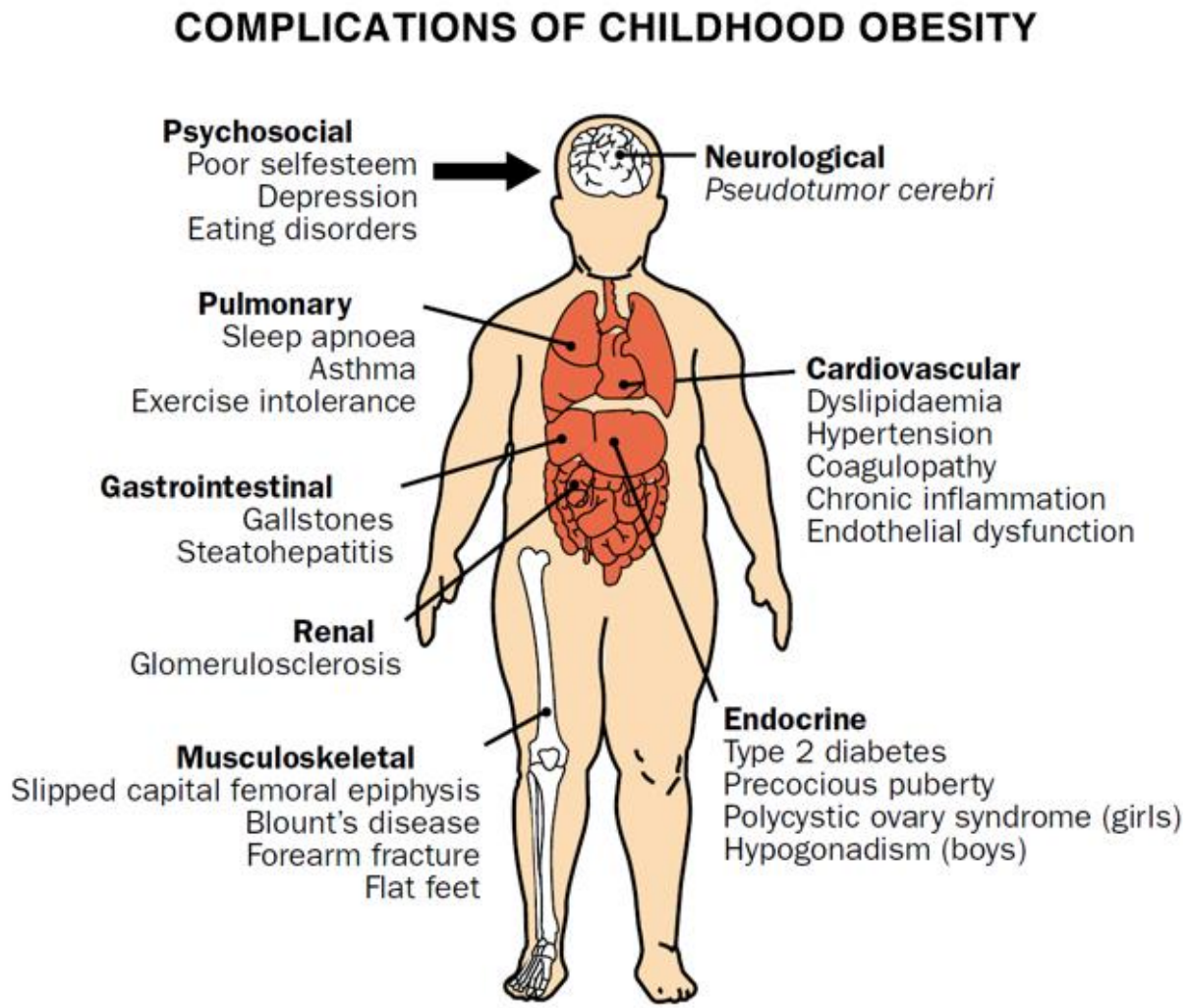
- Complete history and physical exam
  - Dietary history (frequency, content, and location of meals and snacks)
  - Physical activity assessment (P.E., screen time, sports, etc.)
  - Medications that may cause weight gain
  - Evaluation of developmental delay
  - Review of systems to help screen for co-morbidities
  - Family history of obesity is a predictor of obesity persistence
  - Psychosocial screening including depression, peer relationships, and disordered eating
- Most children with exogenous obesity are tall; whereas, children with genetic and endocrine causes of obesity tend to have short stature

Diagnosis / Evaluation

- Lack of standardization and consensus on screening labs for children with obesity
  - Fasting lipid profile is recommended for all children with BMI ≥ 95th percentile even in the absence of risk factors and should be repeated every 2 years
  - Transaminases and fasting blood glucose or HbA1c are recommended for all children with BMI ≥ 95th percentile starting at 10 years of age
  - Other specific testing may be required based on signs and symptoms

Screening for Co-Morbidities

- Co-morbidities can affect nearly every organ system
- Used to be considered “adult” diseases
- Severity increases with the severity of obesity



http://ltipfitness.blogspot.com/2014/06/children-and-obesity-growing-epidemic.html

Staged Approach to Weight Management

- Stage 1 (Prevention Plus)
  - Can be implemented in a primary care office setting
  - 5 or more servings of fruits and vegetables per day
  - Minimize or eliminate consumption of sugar-containing beverages
  - < 2 hours of screen time
  - > 1 hour of physical activity per day
- Stage 2 (Structured Weight Management)
  - Can be implemented in a primary care office with a dietitian
  - Includes stage 1 guidelines plus increased structure of meals and snacks with attention to energy density of foods
  - 1 hour or less of screen time per day
  - Self-monitoring through food and physical activity recording

Staged Approach to Weight Management

- Stage 3 (Comprehensive Multidisciplinary Intervention)
  - Can be implemented in a primary care office with a multidisciplinary team and outside facilities for structured physical activity
  - Includes stage 2 guidelines plus increased structured physical activity and dietary program
  - Weekly visits for the first 8-12 weeks followed by monthly contact
  - Moderate to strong parental involvement is recommended for children < 12 years
- Stage 4 (Tertiary Care Intervention)
  - Ideally implemented in a pediatric weight management center with a multidisciplinary team with expertise in pediatric obesity
  - In addition to stage 3 recommendations, includes medications, extremely structured dietary regimens, or bariatric surgery

Treatment

- Weight loss goals are determined by the child's age, severity of obesity, and the presence of co-morbidities.
- Weight maintenance for children with mild obesity vs weight loss for those with severe obesity
- Weight loss of 1 lb/mo is safe in children between 2 and 11 years of age; whereas, weight loss of up to 2 lb/wk is safe in adolescents with severe obesity

Behavioral Treatment Strategies

Dietary approaches

1. Encourage intake of ≥5 servings of fruits and vegetables daily
2. Decrease intake of calorie-dense foods such as saturated fats, salty snacks, and high glycemic foods such as candy
3. Minimize intake of sugar-containing beverages
4. Minimize eating outside home and fast food in particular
5. Eat breakfast daily
6. Avoid skipping meals

Physical activity

1. Decrease sedentary behavior such as watching television, surfing the Internet, and playing video games to <2 h/d
2. Engage in fun and age-specific exercise that is appropriate to the individual's abilities
3. Increase intensity, frequency, and duration of exercise gradually as tolerated
4. More than 1 h of physical activity daily

Kumar S, Kelly AS. Review of Childhood Obesity: From Epidemiology, Etiology, and Comorbidities to Clinical Assessment and Treatment. Mayo Clin Proc. 2017 Feb;92(2):251-265.

Treatment

- Recommend family-based behavioral approaches that include the child's parents or caregivers
- Assess barriers to healthy eating and physical activity
- Self-monitoring of food intake and physical activity
- Appropriate goals for healthy behavior should be "SMART": specific, measurable, attainable, realistic, and timely

Treatment

- No consensus on what is the best structured dietary strategy for children
- Children 6 years or older should participate in ≥60 minutes of physical activity per day
- Toddlers should be allowed 60 to 90 minutes of moderate to vigorous-intensity activity per day
- Preschoolers should be allowed 90 to 120 minutes of physical activity per day.

Treatment

- “Screen time” be limited to < 2 h/d for children older than 2 years of age
- Optimize sleep hygiene and adequate amount of sleep (10-13 hours a night for preschoolers and 8-10 hours a night for teenagers)
- Moderate or high intensity interventions (26-75 or >75 hours of provider contact, respectively) are effective for short term weight reduction (up to 12 months)
- Weight loss and BMI reductions with lifestyle interventions are modest, ranging from BMI of 1 to 3 kg/m^2

Considerations for Pharmacotherapy

- The cause of obesity varies among individuals
- Side effects need to be weighed against benefits
- Not all patients will benefit from pharmacotherapy
- No weight loss medication has shown decreased CV morbidity/mortality

Pharmacotherapy

- Per Endocrine Society guidelines, suggest pharmacotherapy:
  - If a formal lifestyle modification program fails to limit weight gain or to ameliorate comorbidities
  - That is FDA-approved and prescribed by experienced clinicians
  - Be discontinued if > 4% BMI/BMI z score reduction is not achieved after 12 weeks

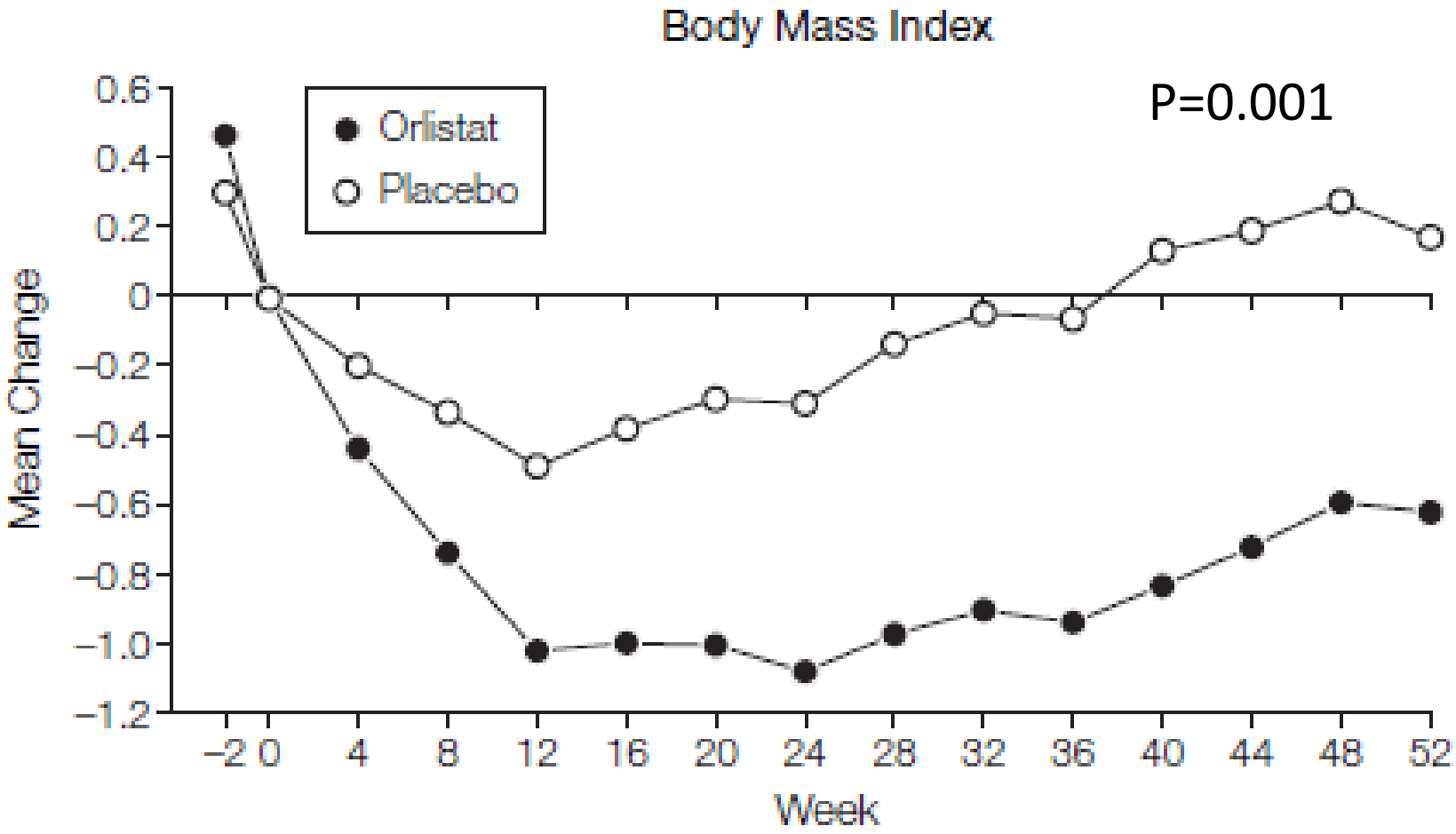
Pharmacotherapy

- Orlistat and Liraglutide are the **only** FDA-approved weight loss medications for long-term use in adolescents ≥12 yrs of age
- Phentermine can be used short-term (≤12 weeks) in individuals 17 yrs or older
- Setmelanotide was approved for patients age 6 yrs and older with pro-opiomelanocortin (POMC) deficiency, proprotein subtilisin/kexin type 1 (PCSK1) deficiency, and leptin receptor (LEPR) deficiency confirmed by genetic testing

Orlistat (Adolescents)

- Approved in 1999 (2003)
- Usual dose is 120 mg TID with meals
- Reduces fat absorption by ~30% by inhibiting gastrointestinal lipases
  - Decreases fat-soluble vitamin absorption
- BMI reduction of ~0.7 to 1.7 kg/m^2
- Fecal urgency/incontinence; fatty/oily stools
- Limited clinical use in adolescents

Orlistat (Adolescents)



- **~35% did not complete the study**
- ~27% of the Orlistat group had a ≥5% BMI decrease
- >50% of the Orlistat group had fatty/oily stools

Chanoine JP, Hampl S, Jensen C, Boldrin M, Hauptman J. Effect of orlistat on weight and body composition in obese adolescents: a randomized controlled trial. JAMA. 2005 Jun 15;293(23):2873-83.

Phentermine

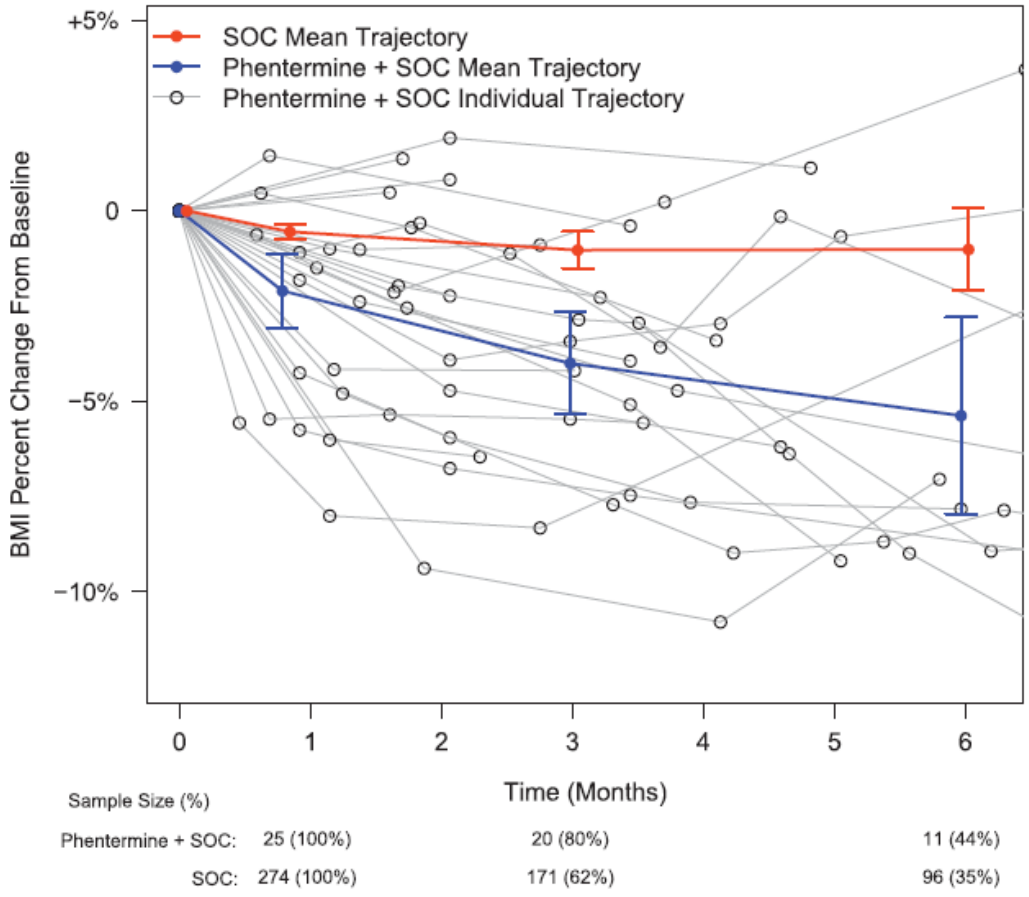
- Amphetamine analog first approved in 1959
- Dosing from 15 to 37.5 mg daily
- Increases catecholamines and serotonin activity in the CNS
- Leads to appetite suppression
- Side effects may include increased BP and HR

Phentermine (Adolescents)

Period	On Long-acting D-amphetamine		On Phentermine		On Placebo	
	No. Losing Weight	Average Loss (kg.)	No. Losing Weight	Average Loss (kg.)	No. Losing Weight	Average Loss (kg.)
First month	22/22	3·4	23/24	2·2	21/22	2·1
Second month.. ..	21/24	1·3	23/24	1·6	13/20	0·5
Third month	18/22	1·7	18/20	1·4	12/26	0·0

Lorber, J. Arch Dis Child. **1966**

- Very limited safety and efficacy data in adolescents



Ryder JR et al. IJO 2017

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Setmelanotide

- MC4R receptor agonist approved on 11/27/2020
- Melanocortin signaling in the hypothalamus leads to decreased food intake and increased energy expenditure
- Dosing from 1-3 mg SC daily
- Weight loss of 12-25%
- Injection site reaction, rash, and nausea are most common side effects

Led to an FDA Label Change on 12/4/2020 to include adolescents 12-17 years old with obesity

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Randomized, Controlled Trial of Liraglutide for Adolescents with Obesity

Aaron S. Kelly, Ph.D., Pernille Auerbach, M.D., Ph.D., Margarita Barrientos-Perez, M.D., Inge Gies, M.D., Ph.D., Paula M. Hale, M.D., Claude Marcus, M.D., Ph.D., Lucy D. Mastrandrea, M.D., Ph.D., Nandana Prabhu, M.Sc., and Silva Arslanian, M.D., for the NN8022-4180 Trial Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

Liraglutide for Adolescents with Obesity

MULTICENTER, RANDOMIZED, DOUBLE-BLIND TRIAL

251
Adolescents with obesity and poor response to lifestyle therapy alone

Liraglutide (3.0 mg) + Lifestyle Therapy
N=125

Placebo + Lifestyle Therapy
N=126

Subcutaneous injection daily

Change in BMI standard-deviation score at 56 wk	−0.23±0.05	−0.00±0.05

Estimated treatment difference, −0.22; 95% CI, −0.37 to −0.08; P=0.002 in favor of liraglutide

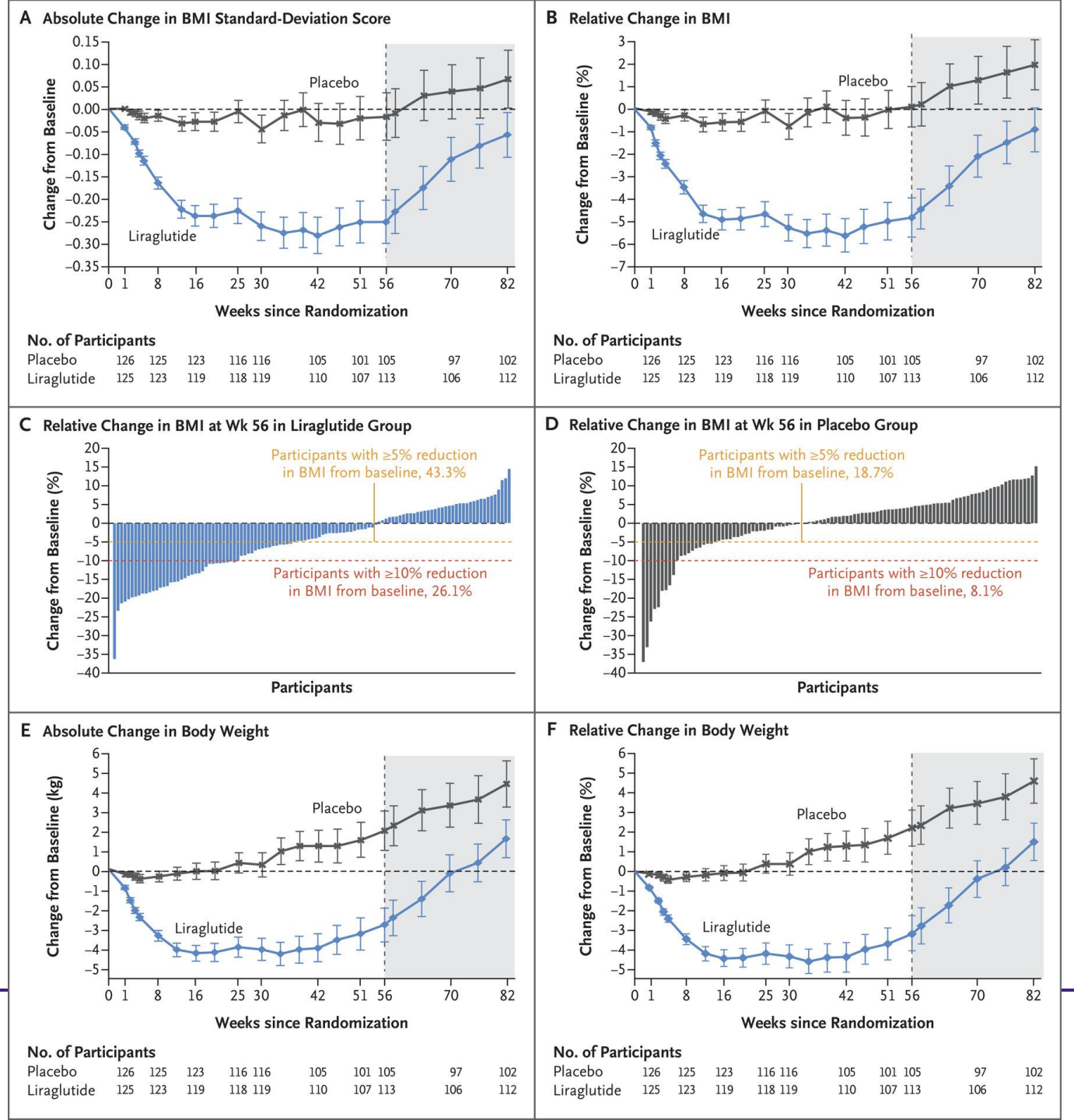
Gastrointestinal side effects	64.8%	36.5%

P<0.001

A.S. Kelly et al. 10.1056/NEJMoa1916038

Results

- Liraglutide was superior to placebo
- BMI reduction of at least 5% seen in 43.3% in the liraglutide group and 18.7% in the placebo group
- BMI reduction of at least 10% seen in 26.1% in the liraglutide group and 8.1% in the placebo group



Kelly AS, NN8022-4180 Trial Investigators, et al. A Randomized, Controlled Trial of Liraglutide for Adolescents with Obesity. N Engl J Med. 2020 May 28;382(22):2117-2128.

Results

- More participants in the liraglutide group vs. the placebo group had GI adverse events (64.8% vs. 36.5%)
- More participants in the liraglutide group vs. the placebo group had adverse events that led to discontinuation of the trial treatment (10.4% vs 0%)

Table 3. Adverse Events during the Treatment Period.*

Event	Liraglutide (N=125)			Placebo (N=126)			P Value
	no. of participants (%)	*no. of events*	*events/1000 exposure-yr*	*no. of participants (%)*	*no. of events*	*events/1000 exposure-yr*	
Any adverse events	111 (88.8)	777	6187.8	107 (84.9)	627	5018.5	0.07†
Gastrointestinal adverse events	81 (64.8)	319	2540.4	46 (36.5)	121	968.5	0.001†
Serious adverse events‡	3 (2.4)	3	23.9	5 (4.0)	6	48.0	0.72§
Adverse events that led to treatment discontinuation	13 (10.4)	19	151.3	0	0	0	<0.001§
Adverse events that occurred in ≥5% of participants							
Nasopharyngitis	34 (27.2)	68	541.5	38 (30.2)	80	640.3	0.60¶
Nausea	53 (42.4)	101	804.3	18 (14.3)	25	200.1	<0.001¶
Headache	29 (23.2)	43	342.4	35 (27.8)	53	424.2	0.41¶
Vomiting	43 (34.4)	85	676.9	5 (4.0)	8	64.0	<0.001¶
Diarrhea	28 (22.4)	44	350.4	18 (14.3)	29	232.1	0.10¶
Upper abdominal pain	17 (13.6)	25	199.1	17 (13.5)	23	184.1	0.98¶
Oropharyngeal pain	11 (8.8)	11	87.6	15 (11.9)	18	144.1	0.42¶
Influenza	11 (8.8)	11	87.6	12 (9.5)	12	96.0	0.84¶
Gastroenteritis	16 (12.8)	22	175.2	6 (4.8)	9	72.0	0.02¶
Upper respiratory tract infection	11 (8.8)	14	111.5	11 (8.7)	16	128.1	0.98¶
Abdominal pain	10 (8.0)	15	119.5	11 (8.7)	15	120.1	0.83¶
Pyrexia	10 (8.0)	11	87.6	9 (7.1)	11	88.0	0.80¶
Dizziness	13 (10.4)	15	119.5	4 (3.2)	5	40.0	0.02¶
Dysmenorrhea	4 (3.2)	5	39.8	8 (6.3)	16	128.1	0.38§
Arthralgia	3 (2.4)	3	23.9	8 (6.3)	8	64.0	0.22§
Pharyngitis	4 (3.2)	5	39.8	7 (5.6)	7	56.0	0.54§

* Adverse events and serious adverse events that occurred from week 0 through week 56 among adolescents in the safety population are included in the table and presented with their preferred terms. Events were included if the date of onset was between the first day the trial drug was administered and 14 days after the last day the trial drug was administered, at the follow-up visit, or at the last trial visit.
† The P value was calculated with a negative binomial model. The number of events was analyzed with a negative binomial model with log-link function and the logarithm of the exposure time (1000 years) for which an adverse event is considered to be reported during the treatment period as an offset. The model included treatment, sex, region, baseline glycemic category, stratification factor for Tanner stage, and interaction between baseline glycemic category and stratification factor for Tanner stage as fixed effects.
‡ The following serious adverse events were reported in one participant each: postprocedural hemorrhage, myositis, and completed suicide in the liraglutide group; and appendicitis, pneumonia, acute cholecystitis, cholelithiasis, and thrombophlebitis in the placebo group.
§ The P value was calculated by means of Fisher's exact test on the basis of the number of participants.
¶ The P value was calculated by means of Pearson's chi-square test on the basis of the number of participants.

Kelly AS, NN8022-4180 Trial Investigators, et al. A Randomized, Controlled Trial of Liraglutide for Adolescents with Obesity. N Engl J Med. 2020 May 28;382(22):2117-2128. PMID: 32233338.

Bariatric Surgery

Indications and contraindications for adolescent metabolic and bariatric surgery (MBS)

Indications for adolescent MBS include

- BMI ≥35 kg/m^2 or 120% of the 95th percentile with clinically significant co-morbid conditions such as obstructive sleep apnea (AHI >5), T2D, IIH, NASH, Blount's disease, SCFE, GERD, or hypertension; or BMI ≥40 kg/m^2 or 140% of the 95th percentile (whichever is lower).
- A multidisciplinary team must also consider whether the patient and family have the ability and motivation to adhere to recommended treatments pre- and postoperatively, including consistent use of micronutrient supplements.

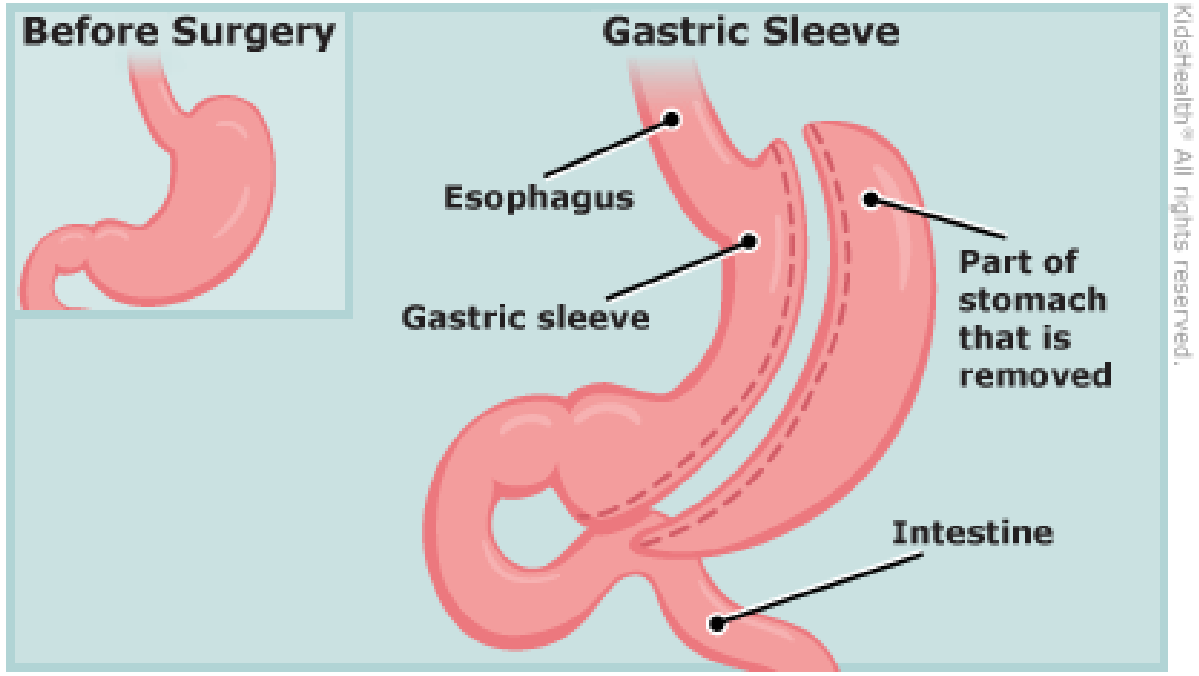
Contraindications for adolescent MBS include

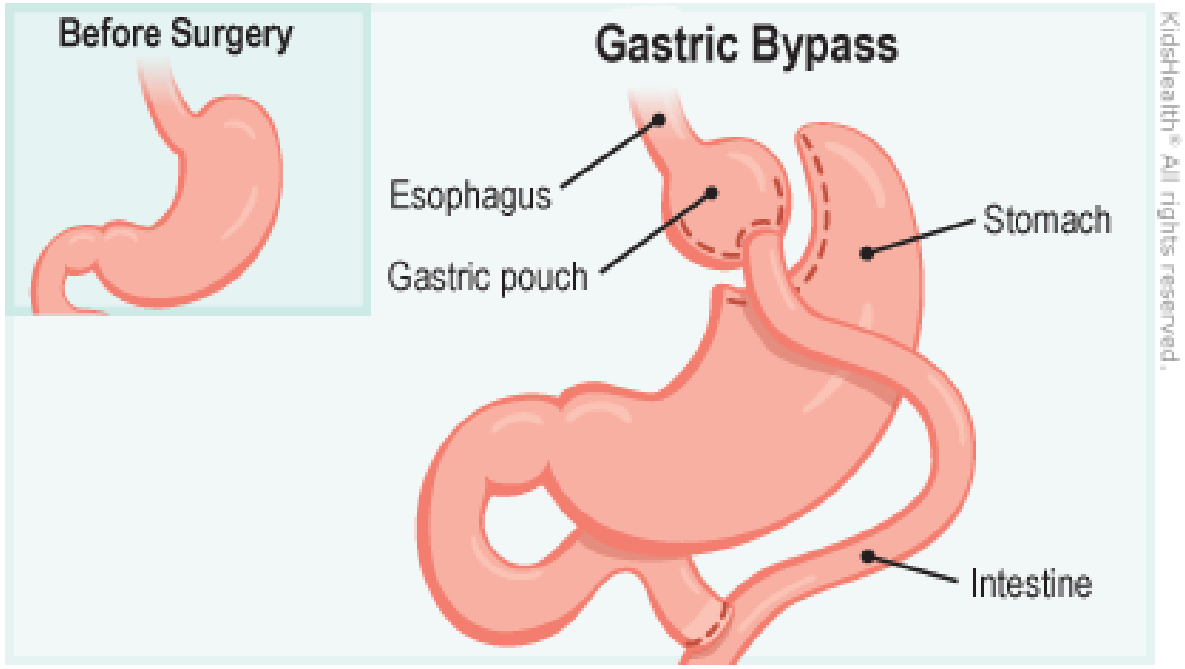
- A medically correctable cause of obesity
- An ongoing substance abuse problem (within the preceding yr)
- A medical, psychiatric, psychosocial, or cognitive condition that prevents adherence to postoperative dietary and medication regimens.
- Current or planned pregnancy within 12 to 18 mo of the procedure

BMI = body mass index; AHI = apnea-hypopnia index; T2D = type 2 diabetes; IIH = idiopathic intracranial hypertension; NASH = nonalcoholic steatohepatitis; SCFE = slipped capital femoral epiphysis; GERD = gastroesophageal reflux disease.

Pratt JSA, Browne A, Browne NT, Bruzoni M, Cohen M, Desai A, Inge T, Linden BC, Mattar SG, Michalsky M, Podkameni D, Reichard KW, Stanford FC, Zeller MH, Zitsman J. ASMBS pediatric metabolic and bariatric surgery guidelines, 2018. Surg Obes Relat Dis. 2018 Jul;14(7):882-901.

Bariatric Surgery-Procedures





Bariatric Surgery-Outcomes

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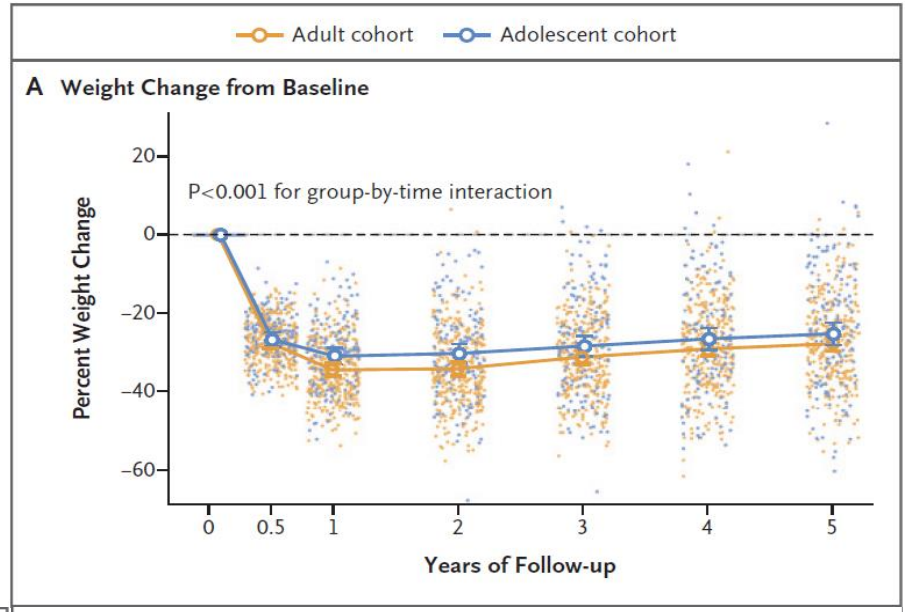
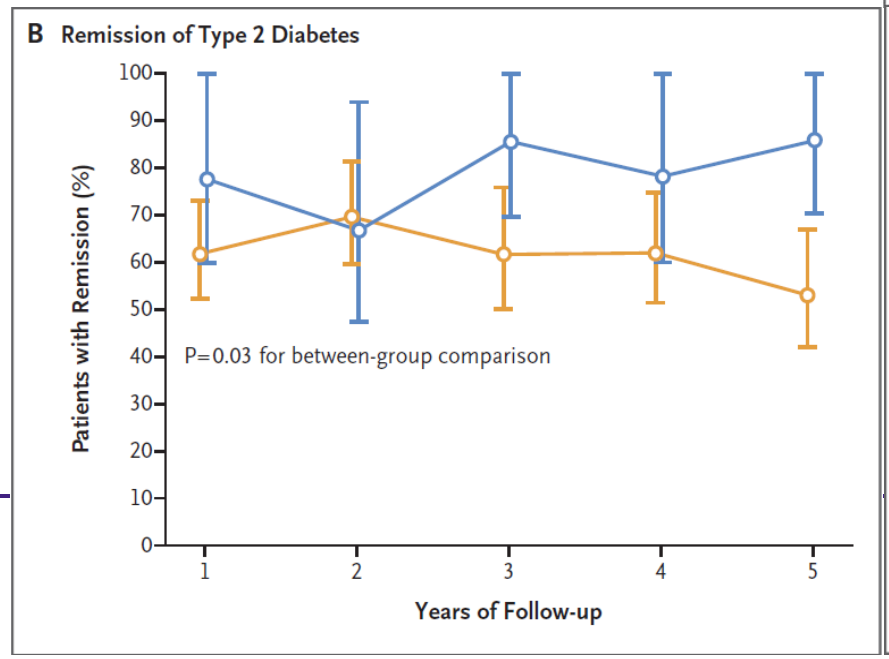
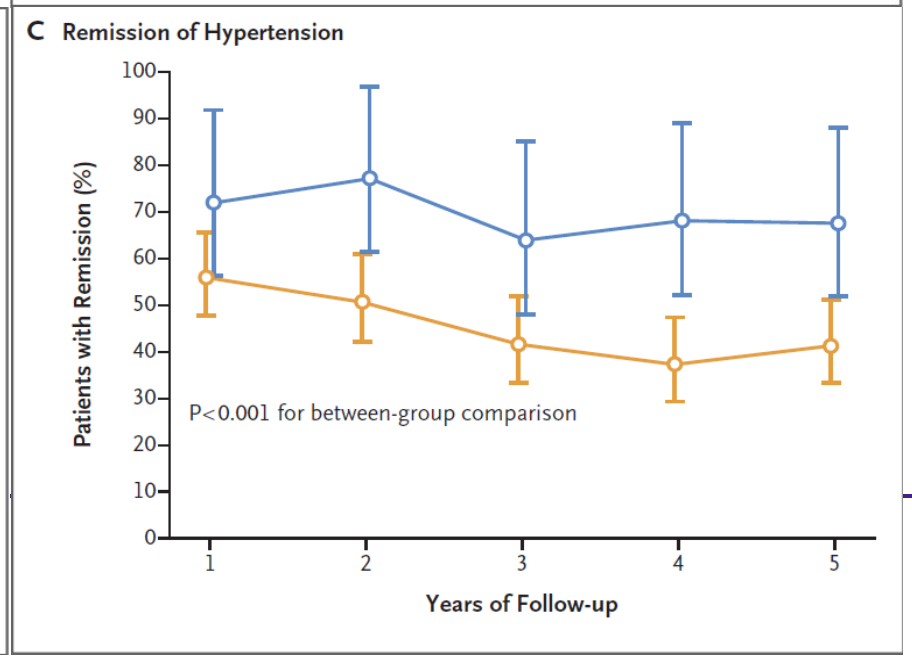
ORIGINAL ARTICLE

Five-Year Outcomes of Gastric Bypass in Adolescents as Compared with Adults

Thomas H. Inge, M.D., Ph.D., Anita P. Courcoulas, M.D., Todd M. Jenkins, Ph.D., Marc P. Michalsky, M.D., Mary L. Brandt, M.D., Stavra A. Xanthakos, M.D., John B. Dixon, Ph.D., M.B., B.S., Carroll M. Harmon, M.D., Ph.D., Mike K. Chen, M.D., Changchun Xie, Ph.D., Mary E. Evans, Ph.D., and Michael A. Helmrath, M.D., for the Teen–LABS Consortium







Summary

- Childhood obesity continues to be one of the most pressing medical and public health problems of our time
- Etiology of childhood obesity is complex and multi-factorial
- Serious co-morbidities can develop in childhood leading to increased risk for morbidity and mortality
- A staged approach has been recommended and pharmacotherapy and/or bariatric surgery should be considered in those who don’t respond to structured weight management

Childhood Obesity and COVID-19

- Effect on dietary habits
  - Lockdowns and stress eating
  - Financial constraints
- Effect on physical activity
  - School closures led to absence of PE
  - Lack of space in the home for physical activity
- Screen time
  - Increased “virtual learning”
  - Increased snacking in front of screens
  - Increase of ~5 hours/day compared to pre-COVID-19

https://www.sciencenewsforstudents.org/article/junk-foods-can-harm-teen-brains
https://www.toledoblade.com/opinion/editorials/2020/03/27/get-outside-safely-coronavirus-metroparks-social-distancing-toledo/stories/20200330007
https://www.baltimoresun.com/opinion/readers-respond/bs-ed-rr-complexities-online-learning-letter-20200723-w2obdahxnbfgdaha4se7e22dou-story.html

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