

Obesity Management: Medications & Surgical Interventions

Does It Cut the Fat?

Ashley Vorenkamp, MD
Assistant Professor General Internal Medicine
University of Alabama at Birmingham
Nathalie Malcolm, MD
Assistant Professor Internal Medicine-Pediatrics
Medical University of South Carolina

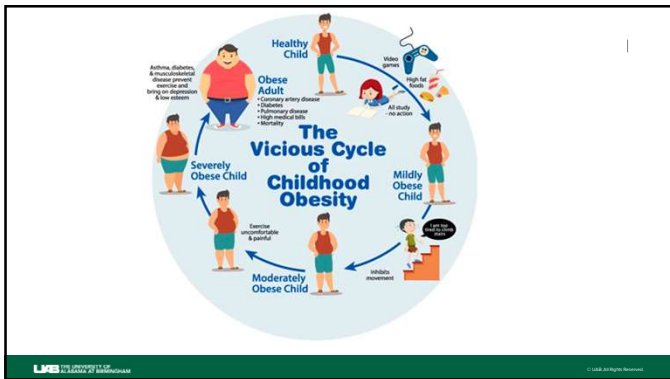
1

Disclosures

We have no potential conflict of interest to report regarding this presentation.

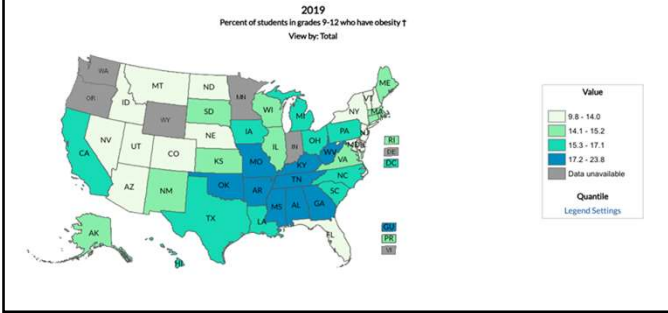
UAB THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

2



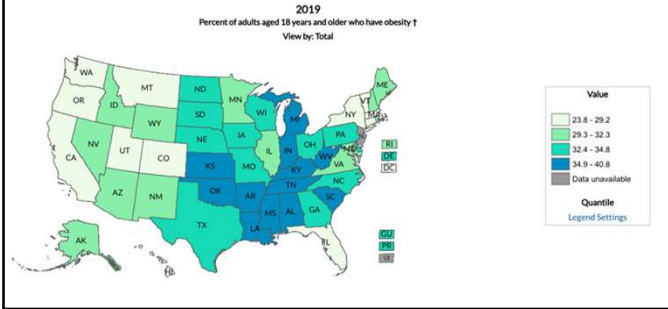
3

National Trends: Why Do We Care?



4

National Trends: Why Do We Care?



5

Objectives

1. Define pediatric obesity and expanded definition of severe obesity
2. Discuss risk factors for the development of pediatric obesity, impact of social determinants of health, and briefly highlight the health outcomes of disease chronicity
3. Review available pharmacotherapy, bariatric surgery, and evidenced based lifestyle recommendations
4. Distinguish what the literature describes regarding liraglutide and semaglutide in youth
5. Share tips on counseling patients and families about FDA approved weight loss medications from personal experience

6

UAB THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

MUSC Health
Medical University of South Carolina

OUTLINE

- Pharmacology/Mechanism of Action
- Clinical Trial Information
- Practical Considerations
- Tips/Tricks for Utilization
- Bariatric Surgery Considerations

7

Definition of Pediatric Obesity

Table 1 Defining Pediatric Obesity

| Organization | Definition of Childhood Obesity |
|---------------------------|---|
| World Health Organization | Birth to age 5 years Overweight: weight for height >2 standard deviations above WHO Child Growth Standards median Obesity: weight for height >3 standard deviations above the WHO Child Growth Standards median |
| | Ages 5-19 years Overweight: BMI for age >1 standard deviation above the WHO Growth Reference median Obesity: BMI for age >2 standard deviations above the WHO Growth Reference median |
| CDC | Ages 2-19 years Overweight: BMI for age 85th percentile to less than 95th percentile Obesity: BMI for age 95th percentile or greater Severe obesity: BMI for age 120% of 95th percentile or greater OR 35 kg/m ² or greater |

WHO: World Health Organization. Sources: References 2, 4, 5.

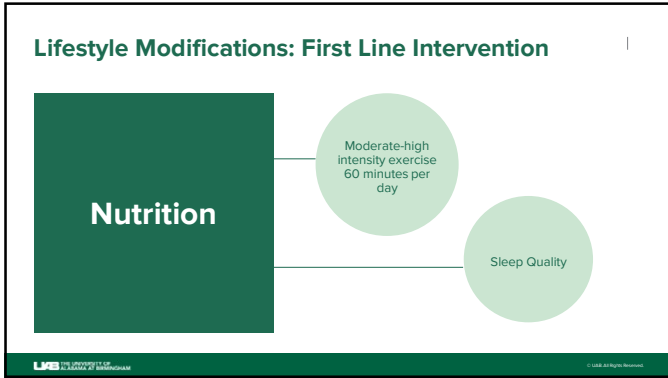
8

Severe Childhood Obesity Expanded

“ An expanded definition of severe obesity is used by the American Academy of Pediatrics (AAP):

- Class 2 Obesity: BMI ≥120% to <140% of the 95th percentile or BMI ≥ 35 to < 40 kg/m²
- Class 3 Obesity: BMI ≥140% of the 95th percentile or BMI ≥ 40 kg/m²”

9



10

What is the recommended amount of sleep needed in a 24 hour period for ages 13-18?

- A. 5 - 7 hours
- B. 6 - 8 hours
- C. 8 - 10 hours
- D. None of the above

UAB THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

11

In the US: 70% adults are obese or overweight

- Eli Lilly makes Mounjaro/Zepbound (tirzepatide)
- Novo Nordisk makes Ozempic/Wegovy (semaglutide) and Victoza/Saxenda (liraglutide)
 - Ozempic/Mounjaro/Victoza branded for Diabetes
 - Wegovy/Zepbound/Saxenda branded for Obesity/Weight Loss

12

Medications Approved for Obesity Treatment

- GLP-1 → Liraglutide (Saxenda) and Semaglutide (Wegovy) [≥ 12 yo]
- Orlistat [≥ 12 yo]
- Phentermine (short course 3 months) [≥16 yo]

13

Mechanism of Action: “incretin effect”

Zepbound --- (Dual Agonist - synergistic effect)

Wegovy/Saxenda

Glucose-dependent insulinotropic polypeptide (GIP) receptor and glucagon-like peptide-1 (GLP-1) receptor agonist

Glucagon-like peptide-1 (GLP-1) receptor agonist

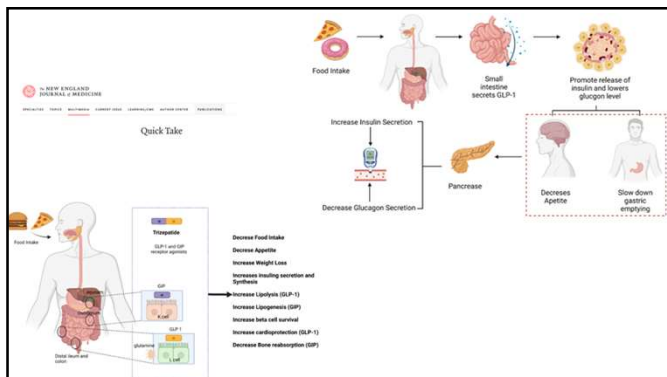
- Increases glucose-dependent insulin secretion
- Decreases inappropriate glucagon secretion
- Slows gastric emptying
- Acts in areas of the brain involved in regulation of appetite and caloric intake (hypothalamus)

- Increases glucose-dependent insulin secretion
- Decreases inappropriate glucagon secretion
- Slows gastric emptying
- Acts in areas of the brain involved in regulation of appetite and caloric intake (hypothalamus)

GIP = increase bone formation/osteoblastic formation (receptors bone, fat cells, tongue)

GIP = increase glucagon secretion during hypoglycemia

14



15

What are contraindications to initiating GLP-1's?

- A. Gastroparesis
- B. Pancreatitis
- C. Personal or Family History of Medullary Thyroid Carcinoma or MEN 2A/2B
- D. Pregnancy
- E. All of the above

16

GLP-1's in the Literature

| 17

- Findings from adult studies demonstrate that semaglutide results in significantly greater weight loss vs liraglutide.
- No current studies are examining superiority between the GLP-1 receptor agonists in the pediatric population.
- Exenatide has also been shown to reduce BMI in the adolescent population, but exenatide is not FDA approved for this group.

Let's review two of the main randomized controlled trials.

17

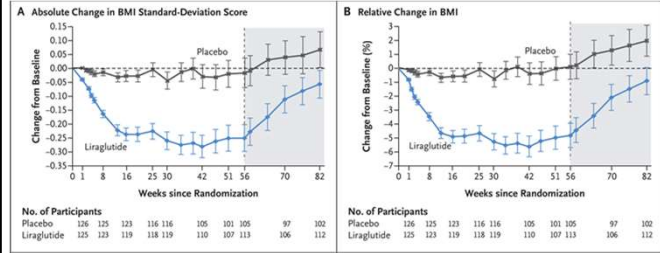
A Randomized, Controlled Trial of Liraglutide for Adolescents with Obesity

Aaron S. Kelly, Ph.D., Penelope Auerbach, M.D., Ph.D., Margarita Samartino-Perez, M.D., Tigran Ghem, M.D., Ph.D., Paula M. Hales, M.D., Claude Marcus, M.D., Ph.D., Lucy D. Macfarlane, M.D., Ph.D., Roshana Paulino, M.Sc., and Silvia Anjosman, M.D. for the NOD32-488 Trial Investigators*

| Methods | Results | Conclusions |
|---|---|---|
| <p>Duration: Treatment 56 weeks + 26 week follow-up period</p> <p>Design: Double-blind, randomized, placebo-controlled trial</p> <p>Participants: 251 patients, ages 12 to <18 years old with BMI of 95th percentile or higher</p> <p>Intervention: Received daily liraglutide 3.0 mg or placebo + lifestyle changes</p> | <p>By week 56:</p> <p>BMI reduction of at least 5%: 43.3% (Liraglutide) vs 18.7% (Placebo)</p> <p>Estimated body weight reduction difference between groups: -4.50kg (absolute) and -5.01% (relative)</p> <p>Follow-up period results</p> | <p>Liraglutide + lifestyle intervention resulted in a greater reduction in BMI standard deviation score than lifestyle intervention alone</p> |

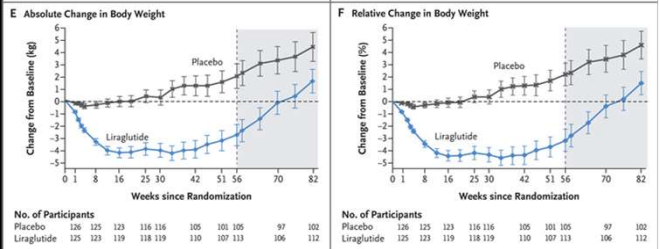
18

Absolute and Relative Change in BMI Standard Deviation



19

Absolute and Relative Change in Body Weight Considering Growth



20

Which of these practices should be avoided to reduce some of the common adverse effects of semaglutide?

- A. Laxative use
- B. Lying down immediately after eating
- C. Consuming fiber
- D. Consuming meals within 30 minutes

21

GLP-1: Side Effects

| Event | Semaglutide (N=134) | | Placebo (N=61) | |
|---|---------------------|---------|---------------------|----------|
| | No. of patients (%) | 95% CI | No. of patients (%) | 95% CI |
| All adverse events | 102 (76) | (70-94) | 58 (95) | (83-100) |
| Serious adverse events | 13 (10) | (5-16) | 4 (7) | (3-13) |
| Adverse events leading to discontinuation | 4 (3) | (1-7) | 2 (3) | (0-7) |
| Discontinuation due to adverse events | 8 (6) | (3-11) | 3 (5) | (1-10) |
| Discontinuation due to other causes | 16 (12) | (8-17) | 11 (18) | (12-24) |
| Discontinuation due to unknown causes | 11 (8) | (4-13) | 11 (18) | (12-24) |
| Discontinuation due to death | 0 (0) | (0-0) | 0 (0) | (0-0) |
| Discontinuation due to withdrawal | 0 (0) | (0-0) | 0 (0) | (0-0) |
| Discontinuation due to other reasons | 0 (0) | (0-0) | 0 (0) | (0-0) |
| Discontinuation due to unknown reasons | 0 (0) | (0-0) | 0 (0) | (0-0) |
| Discontinuation due to death | 0 (0) | (0-0) | 0 (0) | (0-0) |
| Discontinuation due to withdrawal | 0 (0) | (0-0) | 0 (0) | (0-0) |
| Discontinuation due to other reasons | 0 (0) | (0-0) | 0 (0) | (0-0) |
| Discontinuation due to unknown reasons | 0 (0) | (0-0) | 0 (0) | (0-0) |
| Discontinuation due to death | 0 (0) | (0-0) | 0 (0) | (0-0) |
| Discontinuation due to withdrawal | 0 (0) | (0-0) | 0 (0) | (0-0) |
| Discontinuation due to other reasons | 0 (0) | (0-0) | 0 (0) | (0-0) |
| Discontinuation due to unknown reasons | 0 (0) | (0-0) | 0 (0) | (0-0) |
| Discontinuation due to death | 0 (0) | (0-0) | 0 (0) | (0-0) |
| Discontinuation due to withdrawal | 0 (0) | (0-0) | 0 (0) | (0-0) |
| Discontinuation due to other reasons | 0 (0) | (0-0) | 0 (0) | (0-0) |
| Discontinuation due to unknown reasons | 0 (0) | (0-0) | 0 (0) | (0-0) |

Nausea Vomiting Diarrhea Headache Injection-site reactions

22

Once-Weekly Semaglutide in Adolescents with Obesity

Weghuber D et al. DOI: 10.1056/NEJMoa2208661

Methods

Duration: 68 weeks

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

Participants: 201 patients, ages 12 to <18 years old with BMI of 85th percentile or higher

Intervention: Received 2.4 mg weekly semaglutide or placebo + lifestyle changes

Results

By week 68: Mean change in BMI from baseline was -16.1% with semaglutide and 0.8% with placebo (95% confidence interval: -20.3 to -13.2, P <0.001)

73% in the semaglutide group had a weight loss of 5% or more compared to 18% in the placebo group (estimated odds ratio: 14.0; 95% CI: 6.3 to 31.0; P <0.001)

Conclusions

Semaglutide + lifestyle intervention resulted in a greater reduction in BMI than lifestyle intervention alone

23

Semaglutide Primary and Secondary Endpoints

A Change in BMI from Baseline

| Weeks since Randomization | Placebo (n) | Semaglutide (n) |
|---------------------------|-------------|-----------------|
| 0 | 67 | 134 |
| 12 | 56 | 119 |
| 28 | 63 | 131 |
| 44 | 61 | 130 |
| 60 | 62 | 131 |
| 75 | 61 | 128 |

B Weight-Loss Thresholds at Week 68

| Weight Loss Threshold | Semaglutide (%) | Placebo (%) |
|-----------------------|-----------------|-------------|
| ≥5% | 73 | 18 |
| ≥10% | 62 | 8 |
| ≥15% | 53 | 5 |
| ≥20% | 37 | 3 |

24

Supply Shortage Issues

Social media publicity and advertisement dramatically lead to increased utilization



UAB UNIVERSITY HOSPITAL UNIVERSITY OF URBANA

© UAB All Rights Reserved

25

Practical Acquisition of the Medication

Insurance Coverage:

- Zepbound just became FDA approved
- NO coverage currently for Obesity/Weight Loss
- Wegovy (in my experience) only being covered by Viva UAB/Health

Out of Pocket Cost:

- Zepbound monthly: \$1000
- Wegovy monthly: \$1600

Insurance Coverage:

- Zepbound monthly: \$30-\$75
- Wegovy monthly: \$30-\$75

26

Practical Acquisition of the Medication

Compounding Pharmacies!!!

Weight Loss Medicine Clinics

Wellness and Aesthetics Clinics

Roughly \$50-\$100 per injection

| Tirzepatide Plus | | |
|------------------|----------------|-----------|
| PRICE CHART | | |
| DOSE | PRICE PER SHOT | SCHEDULE |
| 2.5 MG | \$75 | WEEK 1-4 |
| 5.0 MG | \$100 | WEEK 5-8 |
| 7.5 MG | \$125 | WEEK 9-12 |

27

Ozempic, Wegovy maker begins legal proceedings against certain med spas, clinics, compounding pharmacies

By Katherine Obregon, CNN
Updated 3:10 PM EDT, Wed, June 21, 2023

NEWS Novo Nordisk sues clinics allegedly selling copycat versions of Ozempic and Wegovy

Some wellness clinics and medical spas are offering what they claim is semaglutide – the active ingredient in both weight loss drugs – but the compound is still under patent.

"Our priority is to ensure that patients have a safe and positive experience with our FDA-approved semaglutide medicines, and these actions are a direct reflection of that focus," Doug Langa, executive vice president of North America operations and president of Novo Nordisk, said in the press release announcing the lawsuit.

28

Which of the following statements is a contraindication to adolescent bariatric surgery?

- A. A cause of obesity that cannot be medically corrected
- B. A substance abuse problem more than 36 months previously
- C. Current or planned pregnancy within 12 to 18 months of the procedure
- D. All of the above

UAB THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

29

Per AAP: Qualifications and Considerations for Bariatric Surgery

Teens 13 years and older

- o BMI greater than 35 kg/m² of the 95th percentile with a co-morbidity OR
- o BMI >40 kg/m² or 140% of the 95th percentile without a co-morbidity (whichever is less)

There is no specific age or cutoff for surgery, but we have the most scientific data in ages 13+

Roux-en-Y Gastric Bypass (RYGB)

Vertical Sleeve Gastrectomy

UAB THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

30

Benefits of Bariatric Surgery

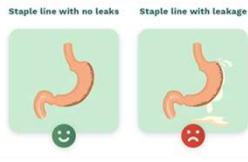
Results can vary from patient to patient, but research shows there is evidence for:

- Better lifestyle choices
- Blood pressure reduction
- Greater physical activity
- Improved self-confidence
- Lipid balance improvement
- Control achieved in patients with type 2 diabetes or prevention of diagnosis

31

Potential Surgical Risks

- Most common short term risks:
 - a. Bleeding and leakage risk
 - b. Infection at the surgical site
- Most common long-term risks:
 - a. Nutritional deficiency concerns
 - b. Weight regain
 - c. "Dumping" syndrome

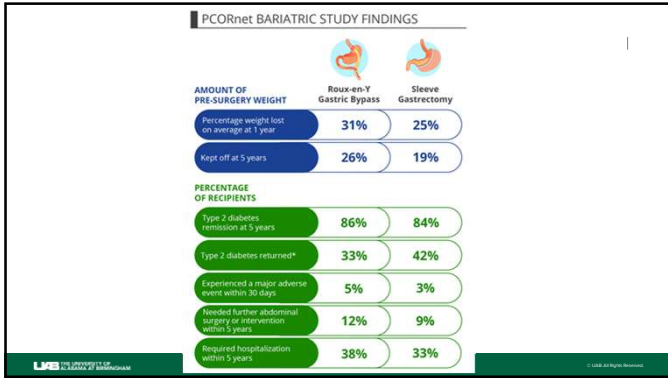


32

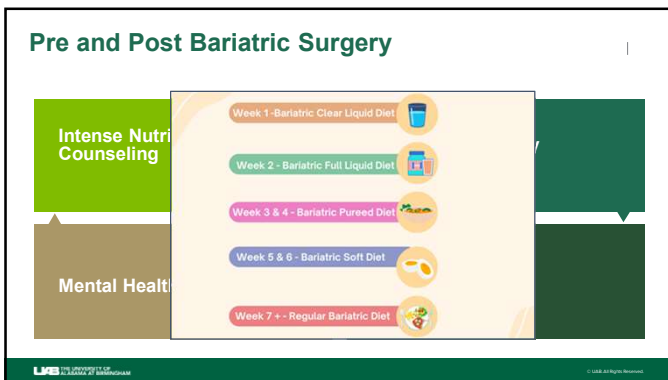
Comparative effectiveness of bariatric procedures among adolescents: The PCORnet bariatric study



33



34



35

With respect to pediatric behavioral patterns around food intake on a daily basis, who is able to affect the most change?

- A. The pediatrician
- B. Legal guardians or parents
- C. Peers
- D. Social Media/Influencers

LMB THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

36

Personal Experience with Counseling Families

Hesitancy
Education provided

Skepticism
Understanding and partnership

Research
Ongoing clinical trials

37

Take Home Messages

- If you are considering medication management in this population, dietary efforts and aerobic exercise should be used in conjunction.
- Reframe how we treat obesity with medication management like any other chronic medical comorbidity.
- Familiarize ourselves with the community and institutional resources to assist our patients and their families with early intervention.
- Although bariatric surgery and pharmacotherapy for weight loss are not as commonly utilized in the pediatric population, these interventions should be considered in at risk youth.

38

REFERENCES

- <https://www.cdc.gov/obesity/data/childhood.html>
- https://nccd.cdc.gov/dnpao_dtm/rdrPage.aspx?rdrReport=DNPAAO_DTM.ExploreByTopic&isClass=OW&isTopic=&go=GO
- <https://www.uchealth.org/today/what-is-mounjaro-and-how-does-it-work-for-weight-loss/>
- <https://www.cdc.gov/healthyschools/nutritionfacts.htm>
- <https://www.cdc.gov/healthyschools/sleep.htm>
- Inge TH, Coley RY, Bazzano LA, Xenithakis SA, McTigue K, Arterburn D, Williams N, Wellman R, Coleman KJ, Courcoulas A, Desai NK, Arihu J, Parolee R, Yoh S, Jarzong C, Cook A, Sturtevant J, Horgan C, Zebreck AJ, Michalsky M, PCORnet Bariatric Study Collaborative. Comparative effectiveness of bariatric procedures among adolescents: the PCORnet bariatric study. *Burg Obes Relat Dis.* 2018 Sep;14(9):1374-1388. doi: 10.1016/j.sobd.2018.04.002. Epub 2018 Apr 17. PMID: 30783877. PMCID: PMC6186084
- Inge TH, Jenkins TM, Xenithakis SA, Dixon JB, Daniels SR, Zeller MH, Helmuth MA. Long-term outcomes of bariatric surgery in adolescents with severe obesity (FABS-5): a prospective follow-up analysis. *Lancet Diabetes Endocrinol.* 2017 Mar;3(3):165-173. doi: 10.1016/S2213-8587(16)30315-1. Epub 2017 Jan 6. PMID: 28065736. PMCID: PMC6282411
- Kelly AS, Auerbach P, Barrantes-Perez M, Gies I, Hale PM, Marcus C, Mastrandrea LD, Prabhu N, Arslanian S. NN8022-4180 Trial Investigators. A Randomized, Controlled Trial of Liraglutide for Adolescents with Obesity. *N Engl J Med.* 2020 May 28;382(22):2117-2128. doi: 10.1056/NEJMoa1916038. Epub 2020 Mar 31. PMID: 32233338
- Malozowski S. Once-Weekly Semaglutide in Adolescents with Obesity. *N Engl J Med.* 2023 Mar 23;388(12):1145-1146. doi: 10.1056/NEJMc2300510. PMID: 36947475
- Page LC, Freemark M. Role of GLP-1 Receptor Agonists in Pediatric Obesity: Benefits, Risks, and Approaches to Patient Selection. *Curr Obes Rep.* 2020 Dec;4(4):391-401. doi: 10.1007/s13679-020-00409-7. Epub 2020 Oct 21. PMID: 33085056
- Shurney D, Gustafson PA. Lifestyle Medicine in Children. *Am J Lifestyle Med.* 2019 Nov 3;14(11):54-56. doi: 10.1177/1559827619879090. PMID: 31903083. PMCID: PMC6933568

39
