



Research Updates in Obesity Medicine

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CENTER FOR PEDIATRIC
OBESITY MEDICINE

Disclosures

- Dr. Kelly engages in unpaid consulting and educational activities for Novo Nordisk, Vivus, Eli Lilly, and Boehringer Ingelheim
- Receives donated drug/placebo from Vivus and Novo Nordisk for National Institute of Diabetes and Digestive and Kidney Diseases-funded clinical trials



Presentation Highlights

A peek over the horizon – what does the AOM pipeline look like

The most compelling unanswered questions in pediatric obesity medicine

The Crystal Ball

Approved Anti-Obesity Medications (AOMs) 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



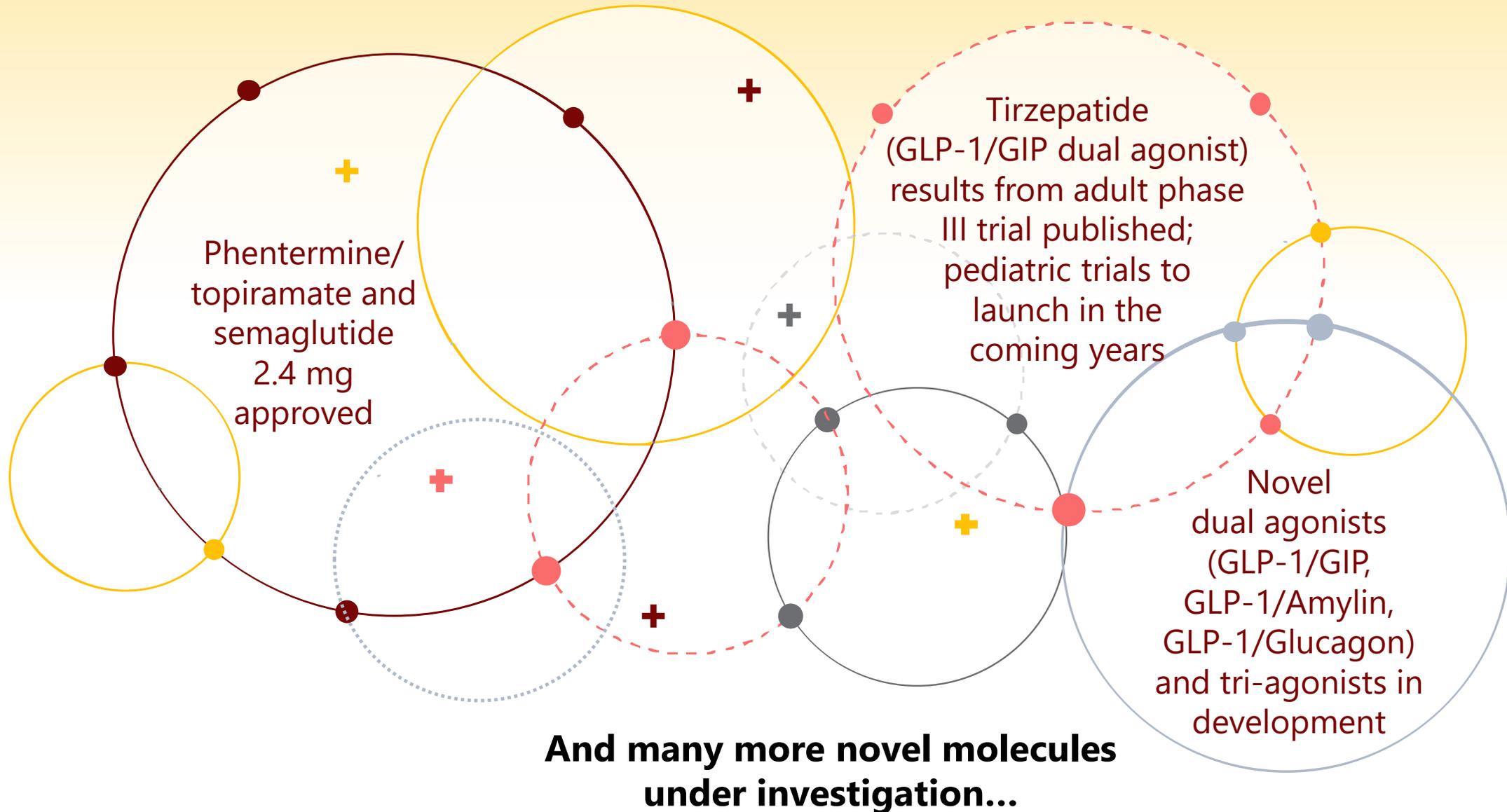
Liraglutide 3 mg approved for ≥ 12 years

Semaglutide 2.4 mg approved for ≥ 12 years

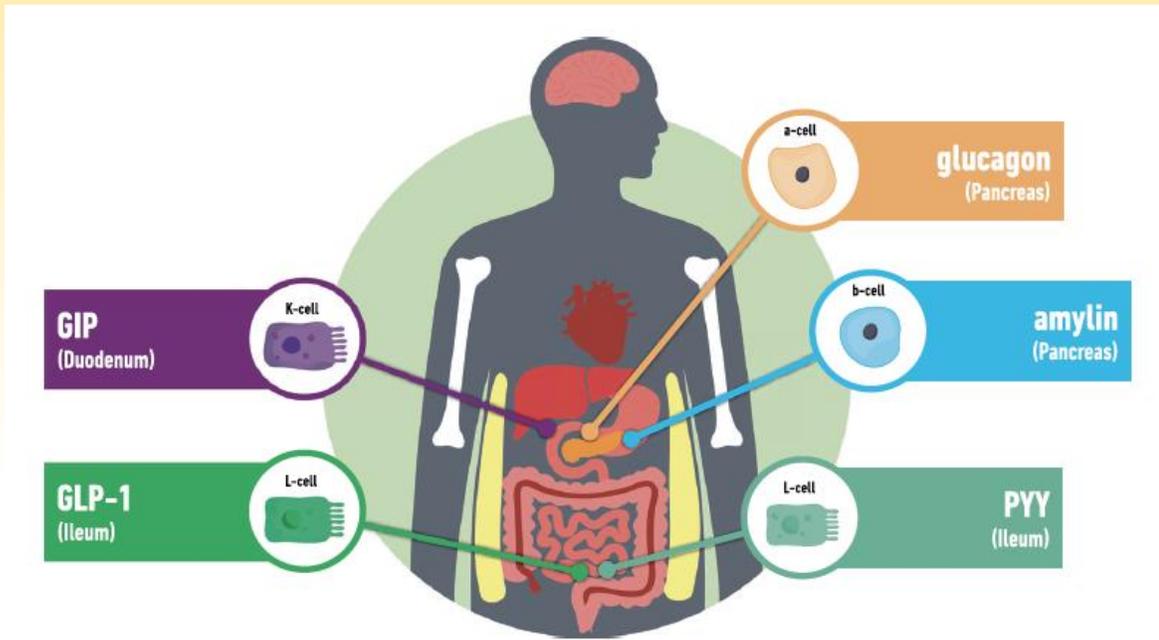
1. Suprenza (phentermine) Prescribing Information. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/202088s005lbl.pdf (accessed September 2022);
2. Xenical (orlistat) Prescribing Information. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/020766s029lbl.pdf (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).



Pediatric Pipeline & Expected Timelines



Gut Hormones in the AOM Pipeline



GLP-1

| | | |
|--|-----------------------------|--------------|
| | ↓ appetite ↓ food intake | ↑ nausea |
| | ↑ insulin, | ↓ glucagon |
| | ↓ gastric emptying | |
| | ↑ lipolysis | |
| | ↑ cardioprotection | ↑ heart rate |

GIP

| | | |
|--|--------------------------|---------------|
| | ↓ appetite* | ↓ nausea |
| | ↑ insulin | ↑ glucagon |
| | ↓ gastric acid secretion | |
| | ↑ lipid deposition | ↑ lipogenesis |
| | ↓ bone resorption | |

Amylin

| | | |
|--|-----------------------|-----------------------|
| | ↓ appetite | ↓ food intake |
| | ↓ glucagon | |
| | ↑ energy expenditure* | |
| | ↓ gastric emptying | |
| | ↓ osteoclast activity | ↑ osteoblast activity |

PYY

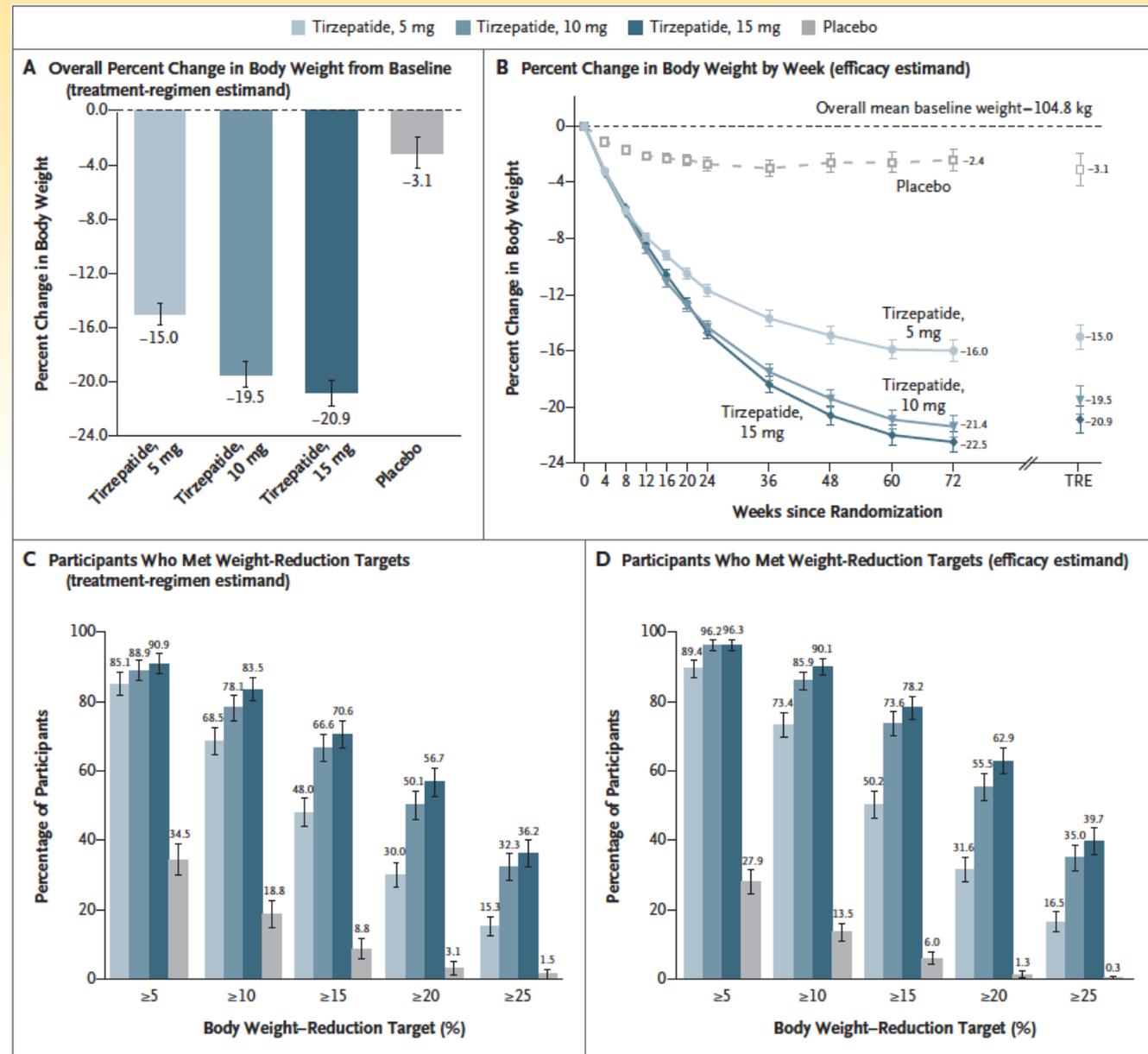
| | | |
|--|-----------------------------|----------|
| | ↓ appetite ↓ food intake | ↑ nausea |
| | ↓ gastric emptying | |
| | ↑ energy expenditure* | |

Glucagon

| | | |
|--|------------------------------|--|
| | ↓ appetite ↓ food intake | ↑ nausea |
| | ↑ insulin | |
| | ↑ hepatic glucose production | ↑ lipid oxidation ↓ hepatic lipid synthesis |
| | ↓ gastric emptying | |
| | ↑ energy expenditure | |
| | ↑ heart rate | |

Tirzepatide

- Dual GLP-1/GIP co-agonist
- Once weekly doses of 5 mg, 10 mg, and 15 mg
- Adolescent trial initiated



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Tirzepatide Once Weekly for the Treatment of Obesity

Ania M. Jastreboff, M.D., Ph.D., Louis J. Aronne, M.D., Nadia N. Ahmad, M.D., M.P.H., Sean Wharton, M.D., Pharm.D., Lisa Connery, M.D., Breno Alves, M.D., Arihiro Kiyosue, M.D., Ph.D., Shuyu Zhang, M.S., Bing Liu, Ph.D., Mathijs C. Bunck, M.D., Ph.D., and Adam Stefanski, M.D., Ph.D., for the SURMOUNT-1 Investigators*



Retatrutide

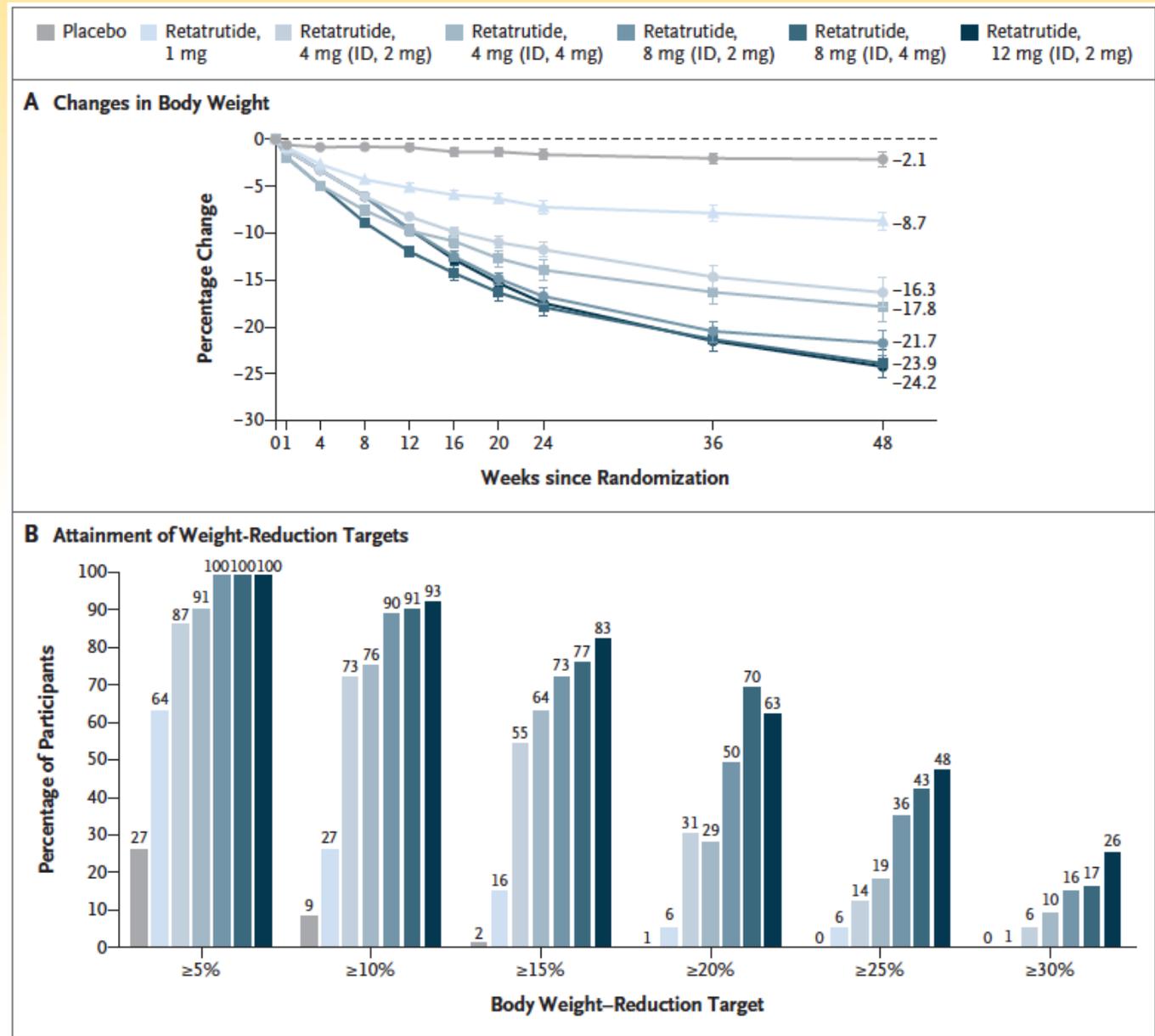
- GLP-1/GIP/Glucagon tri-agonist
- Once weekly doses ranging from 1 mg to 12 mg in phase II trial
- Pediatric plans being discussed

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ORIGINAL ARTICLE

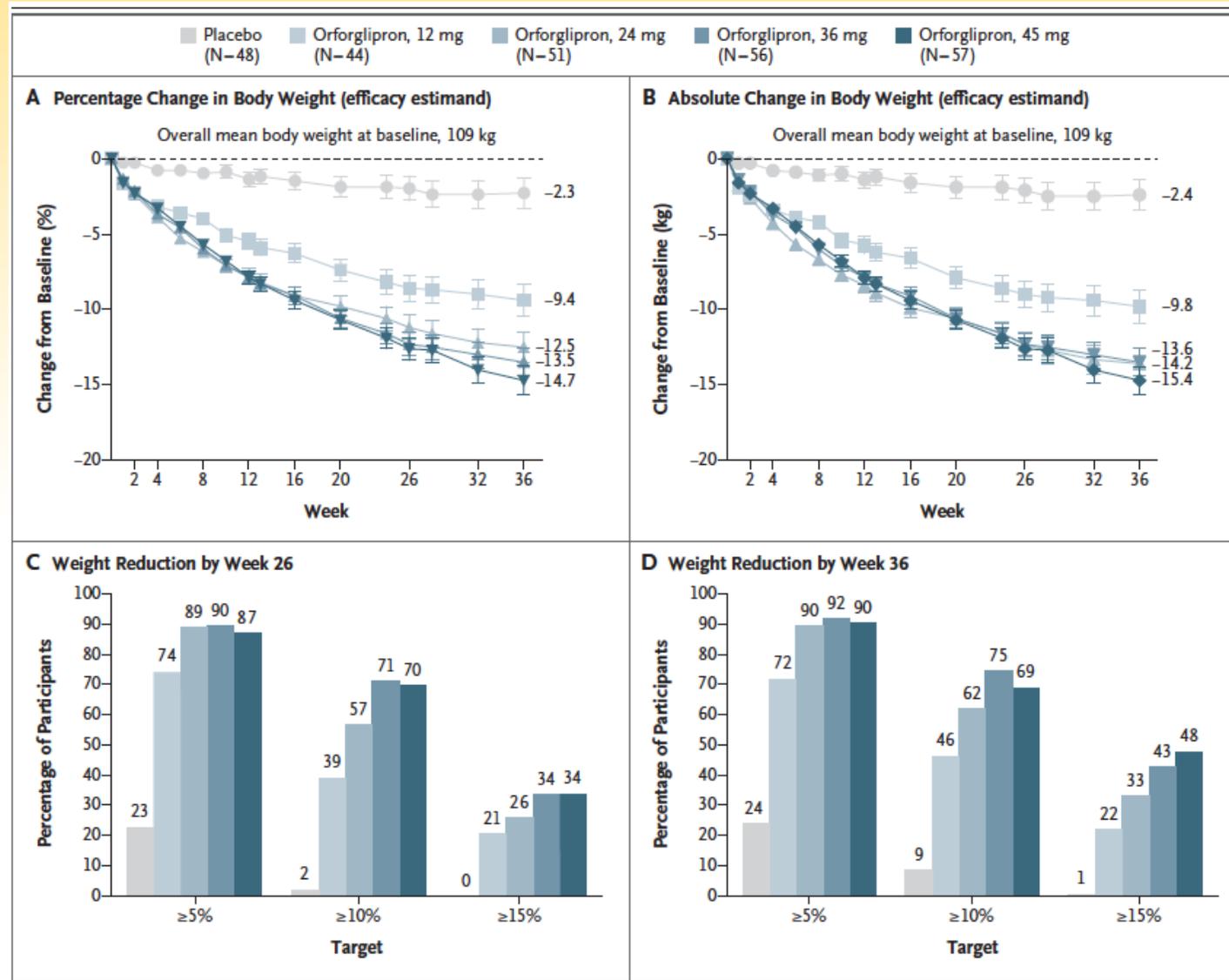
Triple-Hormone-Receptor Agonist Retatrutide for Obesity — A Phase 2 Trial

Ania M. Jastreboff, M.D., Ph.D., Lee M. Kaplan, M.D., Ph.D., Juan P. Frías, M.D., Qiwei Wu, Ph.D., Yu Du, Ph.D., Sirel Gurbuz, M.D., Tamer Coskun, M.D., Ph.D., Axel Haupt, M.D., Ph.D., Zvonko Milicevic, M.D., and Mark L. Hartman, M.D., for the Retatrutide Phase 2 Obesity Trial Investigators*



Orforglipron

- Small molecule, non-peptide GLP-1 receptor agonist
- Once daily oral doses ranging from 12 mg to 45 mg in phase II trial
- Pediatric plans being discussed

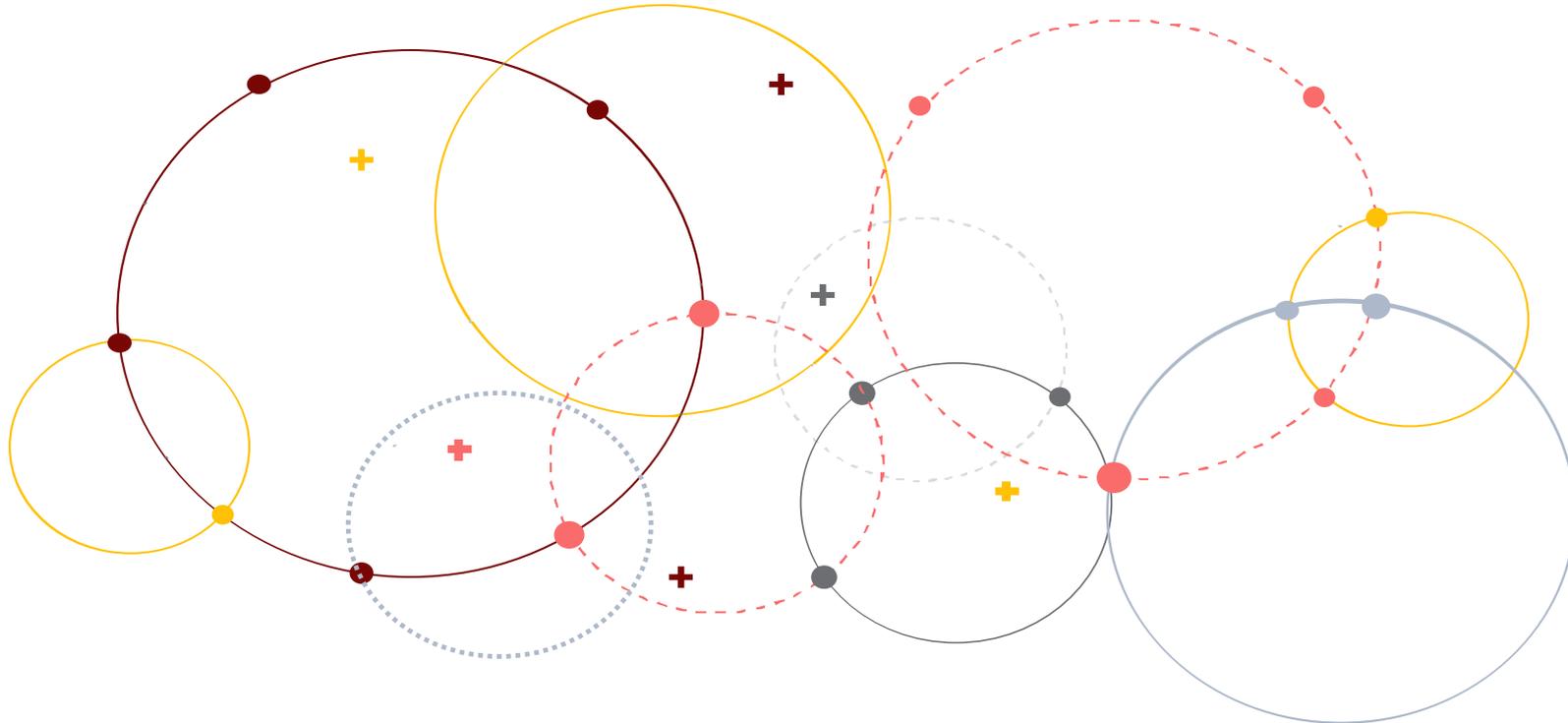


Daily Oral GLP-1 Receptor Agonist Orforglipron for Adults with Obesity

Sean Wharton, M.D., Thomas Blevins, M.D., Lisa Connery, M.D., Julio Rosenstock, M.D., Sohini Raha, Ph.D., Rong Liu, Ph.D., Xiaosu Ma, Ph.D., Kieren J. Mather, M.D., Axel Haupt, M.D., Deborah Robins, M.S., Edward Pratt, M.D., Christof Kazda, M.D., and Manige Konig, M.D., Ph.D., for the GZGI Investigators*

Other AOMs in Development

- Cagrilintide/Semaglutide (GLP-1/Amylin co-agonist) in phase II adult trials
- Survodutide (GLP-1/Glucagon co-agonist) in phase II adult trials
- Bimagrumab (Monoclonal Antibody, Activin Type II Receptor Blocker)
- And many, many others...



Critical Unanswered Questions

Hybrid Meeting

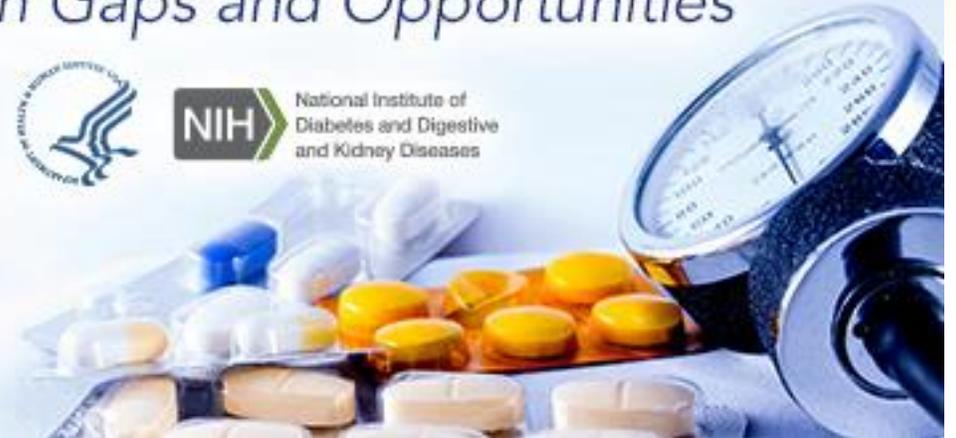
Pharmacotherapy for Obesity in Children and Adolescents:
State of the Science, Research Gaps and Opportunities

November 28–29, 2023

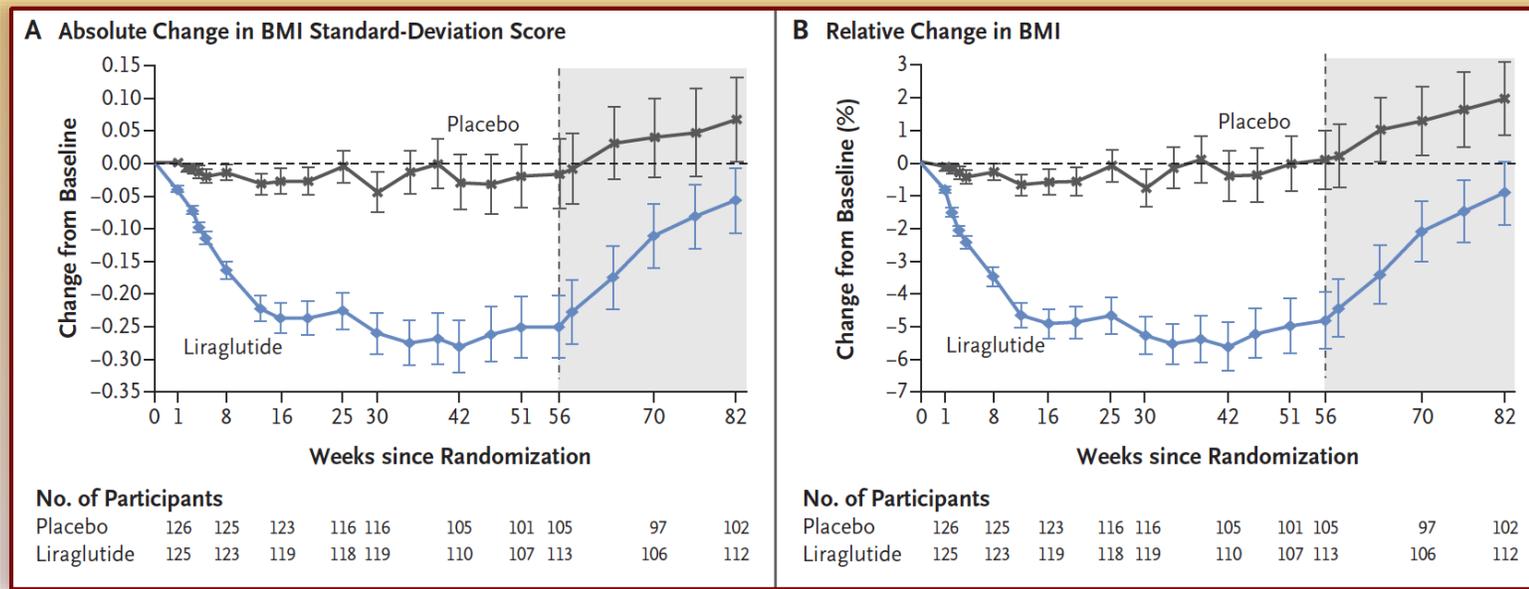


NIH

National Institute of
Diabetes and Digestive
and Kidney Diseases



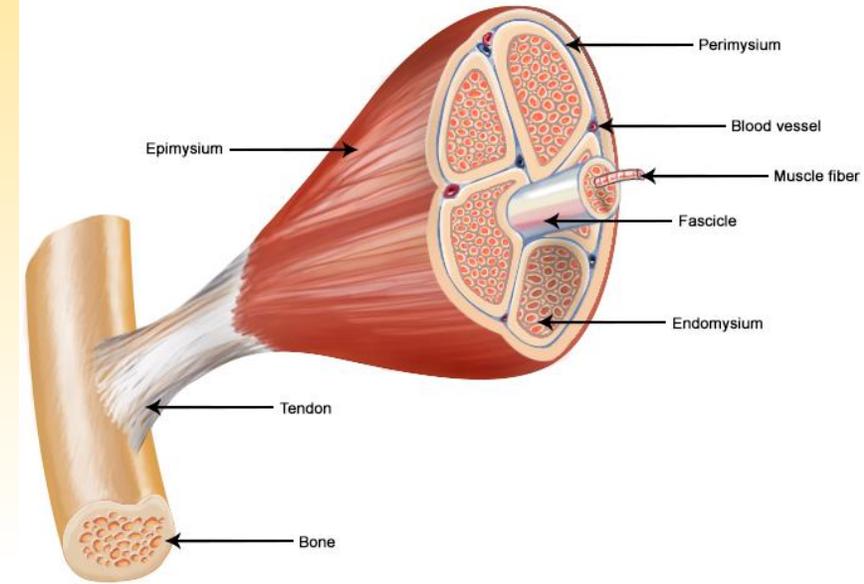
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Timing of pharmacotherapy

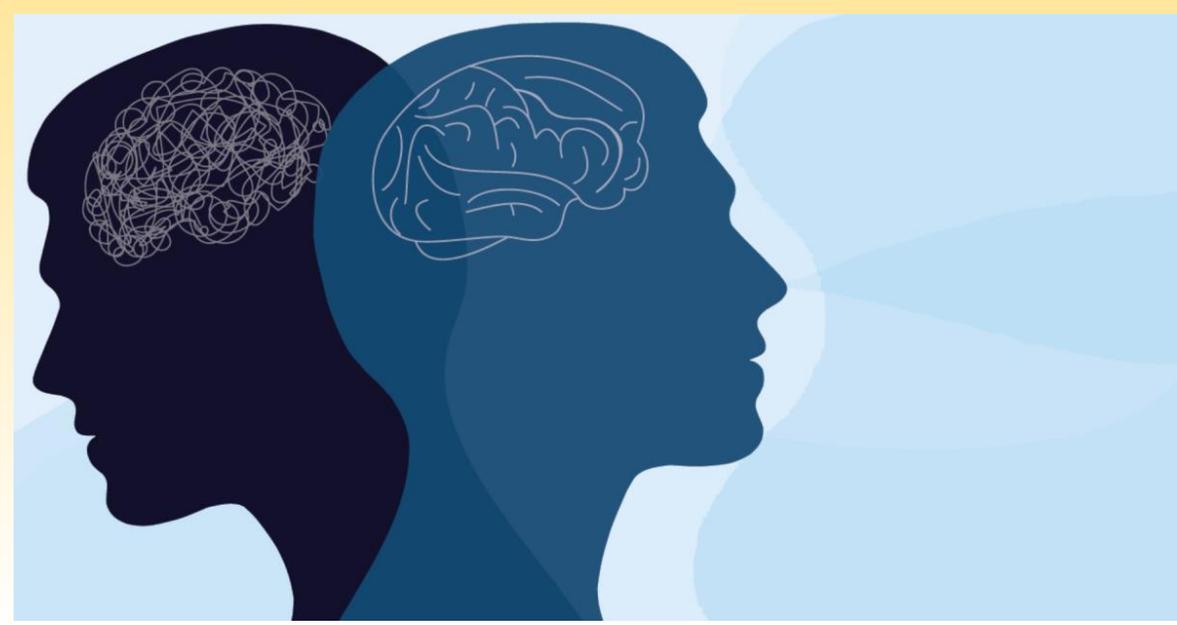
When to initiate, optimal duration of treatment, long-term effectiveness and safety, when to add, when to down-titrate, etc.

Structure of a Skeletal Muscle



Preservation of muscle and bone mass with AOM therapy



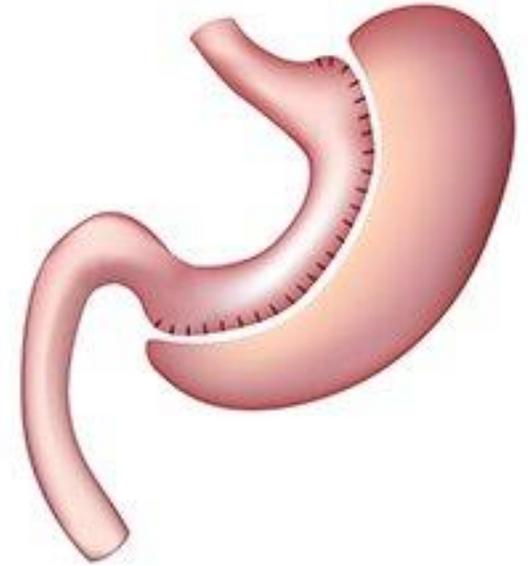


Psychosocial outcomes of AOM therapy

Role of “lifestyle modification therapy” with AOMs



Vertical Sleeve Gastrectomy



Role of AOMs with metabolic and bariatric surgery





Role of telehealth in pediatric obesity care delivery



What is “treating to target?”



Consensus:
obesity is a
disease and not a
social construct



Like mental health, obesity will be de-stigmatized



Diagnosis of obesity will be refined and standardized



Consensus:
"maximum
tolerated dose"
of LMT is
ineffective



First-line therapy
will include the
physiological
treatment of
obesity



AOM costs will drop significantly, and insurances will pay for them



PCPs will become comfortable prescribing AOMs and referring to MBS

Summary & Key Points

The AOM pipeline is strong and growing

Many critical unanswered questions

The future of pediatric obesity medicine is bright

Thank you!

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