Brigham and Women's Hospital
Founding Member, Mass General Brigham

What's new in obesity medications, devices, and procedures

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DISCLOSURES

Eli Lilly, Novo Nordisk, Madrigal, Corcept

- **speakers bureau**

Boehringer Ingelheim

- **consultant**

OBJECTIVES

Describe current new and emerging obesity pharmacologic therapies and navigating clinical scenarios

Discuss new device-based and procedural obesity therapy options

Review a practical, stepwise approach to escalating obesity treatment in the primary care setting

CASE

Pt is a 45 y/o M with a PMH of living with HTN, HLD, T2DM presenting for weight management

- **BMI:** 34 kg/m²
- **Medications:** Metformin, atorvastatin, lisinopril
- **hbA1c:** 7.8%
- **Lifestyle:** intermittent attempts at diet/exercise with limited success

He expresses strong motivation to lose weight, particularly to improve his diabetes and reduce medication burden. However, he states *“I’ve heard about these weight loss shots, but I’m really afraid of needles. Are there any effective pills instead?”*

GLP1s provided a needed treatment option

Role of obesity pharmacotherapy

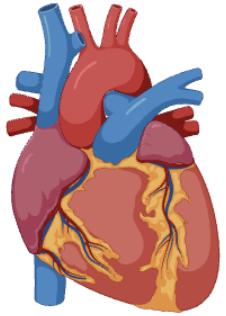
- Obesity is a chronic disease
- Diet and exercise are not always sufficient alone to treat obesity, pharmacotherapy is an important tool
- Now treating weight first rather than last
- Weight is difficult to maintain in the long term

Game changer for obesity medicine

GLP-1 Receptor Agonists (GLP1-RAs)

- FDA first approved for obesity treatment in 2021
- Clinical trials found patients can lose 15%-20% of their body weight
- Reduce risk of heart disease, diabetes and other related conditions

GLP1,GIP: Roles in Metabolic Regulation



Cardiovascular System
↓ Vascular Inflammation

Glucagon-like Peptide-1 Receptor Agonism

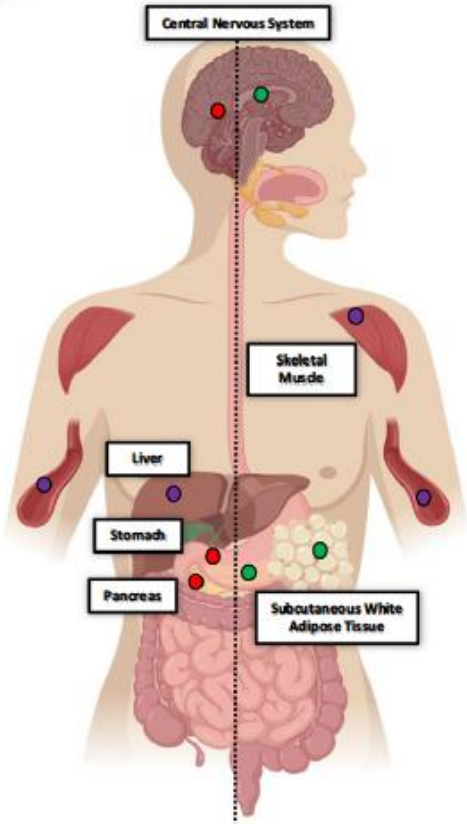
Central Nervous System
- ↑ Satiety
- ↓ Food Intake
- ↑ Nausea
- ↓ Body Weight

Pancreas
- ↑ Insulin
- ↓ Glucagon

Stomach
- ↓ Gastric Emptying

Systemic
- ↓ Hyperglycemia

Liver
- ↑ Insulin Sensitivity
- ↓ Hepatic Glucose Production
- ↓ Ectopic Lipid Accumulation



Glucose-dependent Insulinotropic Polypeptide Receptor Agonism

Central Nervous System
- ↓ Food Intake
- ↓ Nausea
- ↓ Body Weight

Pancreas
- ↑ Insulin
- ↑ Glucagon

Subcutaneous White Adipose Tissue
- ↑ Insulin Sensitivity
- ↑ Lipid Buffering Capacity
- ↑ Blood Flow
- ↑ Storage Capacity
- ↓ Proinflammatory Immune Cell Infiltration

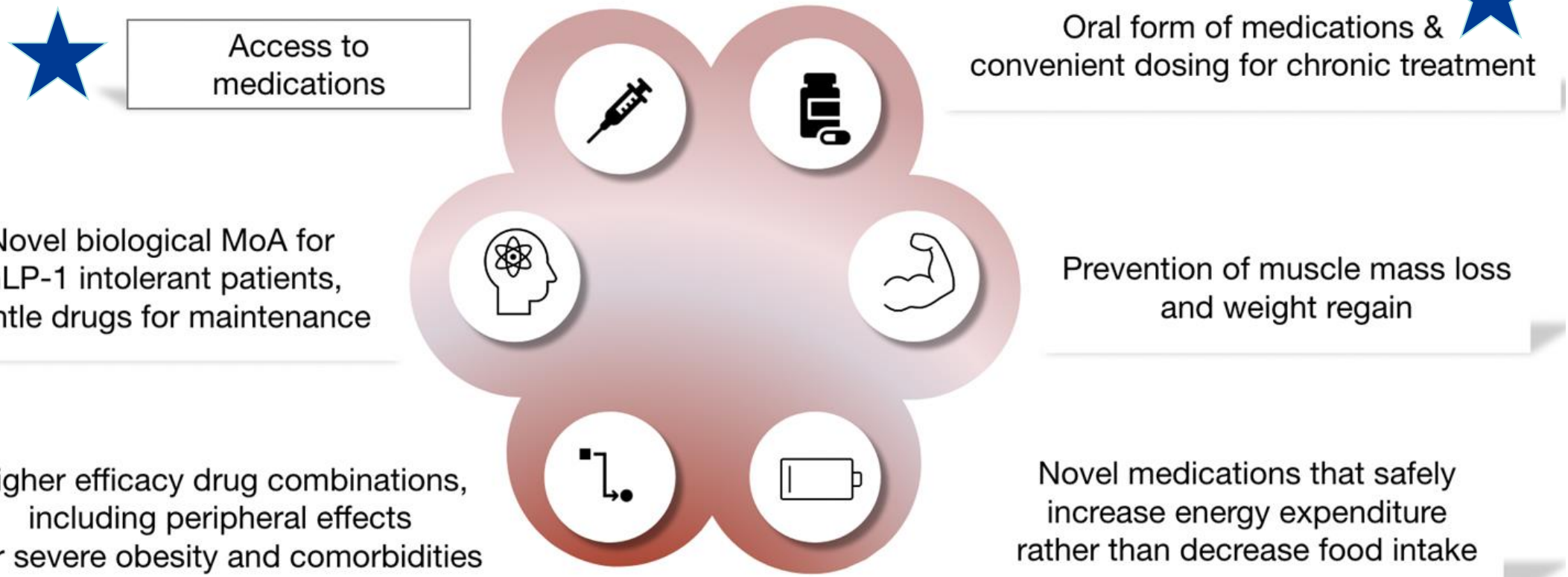
Systemic
- ↓ Hyperglycemia
- ↓ Dietary Triglyceride

Skeletal Muscle
- ↑ Insulin Sensitivity
- ↑ Metabolic Flexibility
- ↓ Ectopic Lipid Accumulation

Glucose-dependent Insulinotropic Polypeptide Receptor Agonism
Glucagon-like Peptide 1 Receptor Agonism
Indirect Action

Samms et al., Trends Endocrinol Metab., 2020
Muller et al., Mol Metab, 2025

Unmet needs of current incretin therapies



MoA: mechanism of action

Pens vs pills

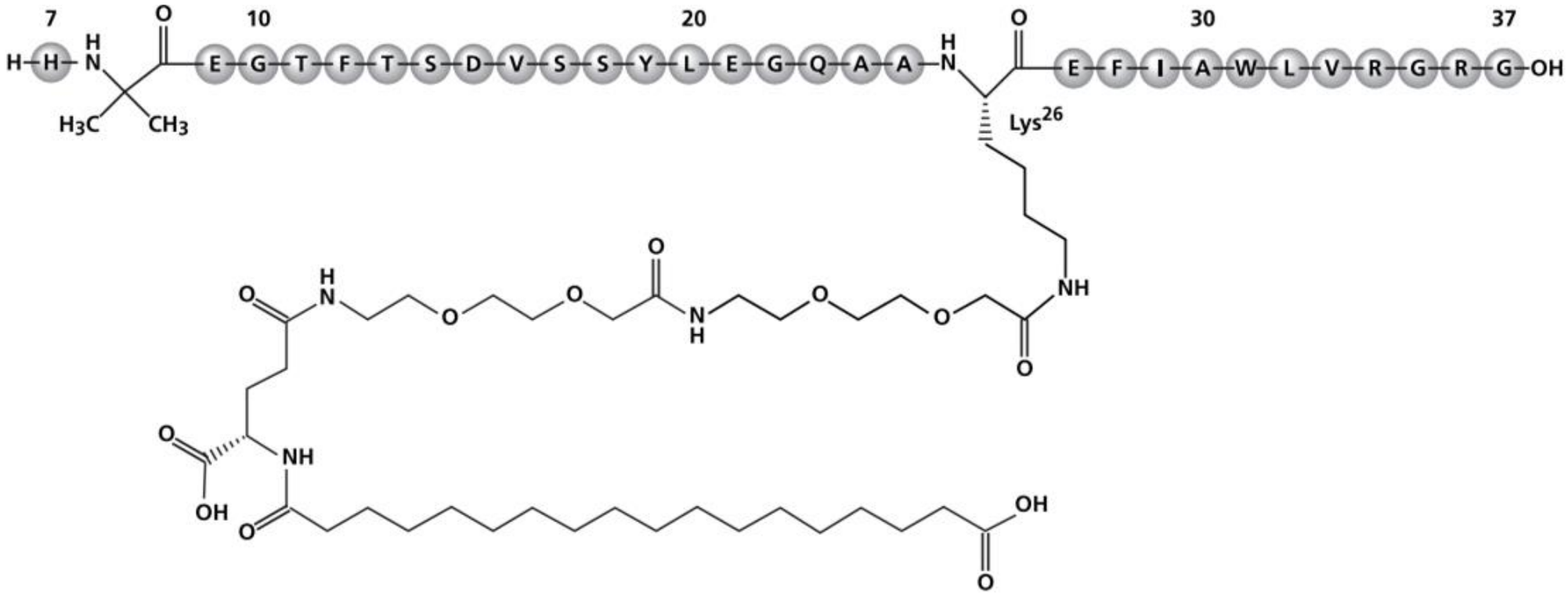
Pros and cons

- Convenient for patients
- Weight/bias and stigma
- Could improve adherence
- People taking oral formulations lost less weight in clinical trials

Pill formulations of GLP1s

- Rybelsus
- Oral semglutide (Ozempic)
- Oral semaglutide (Wegovy) 
- Orforglipron 

Oral semaglutide (wegovy)



Oral semaglutide (wegovy)

Doses:

1.5 mg qdaily

4 mg qdaily

9 mg qdaily

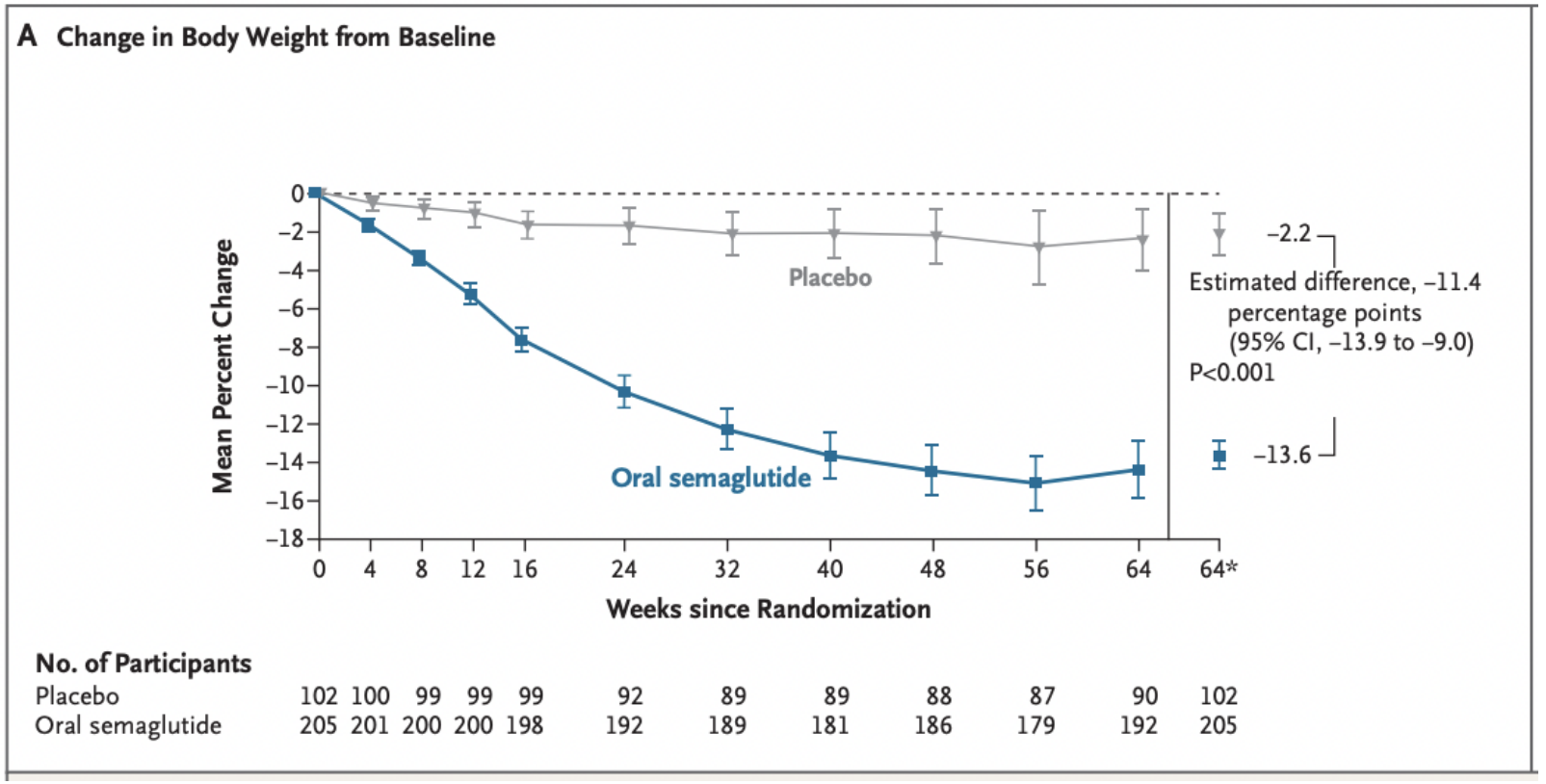
25 mg qdaily

Indications: In combination with a reduced calorie diet and increased physical activity:

• To reduce the risk of major adverse CV events (CV death, non-fatal myocardial infarction, or non-fatal stroke) in adults with established CV disease and either obesity or overweight.

• To reduce excess body weight and maintain weight reduction long term in adults with obesity, or in adults with overweight in the presence of at least one weight-related comorbid condition.

Oral semaglutide (wegovy) OASIS 4



Wharton, Sean, et al. “Oral Semaglutide at a Dose of 25 Mg in Adults with Overweight or Obesity.” *The New England Journal of Medicine.*, vol. 393, no. 11, 2025, pp. 1077–87, https://doi.org/10.1056/NEJMoa2500969.

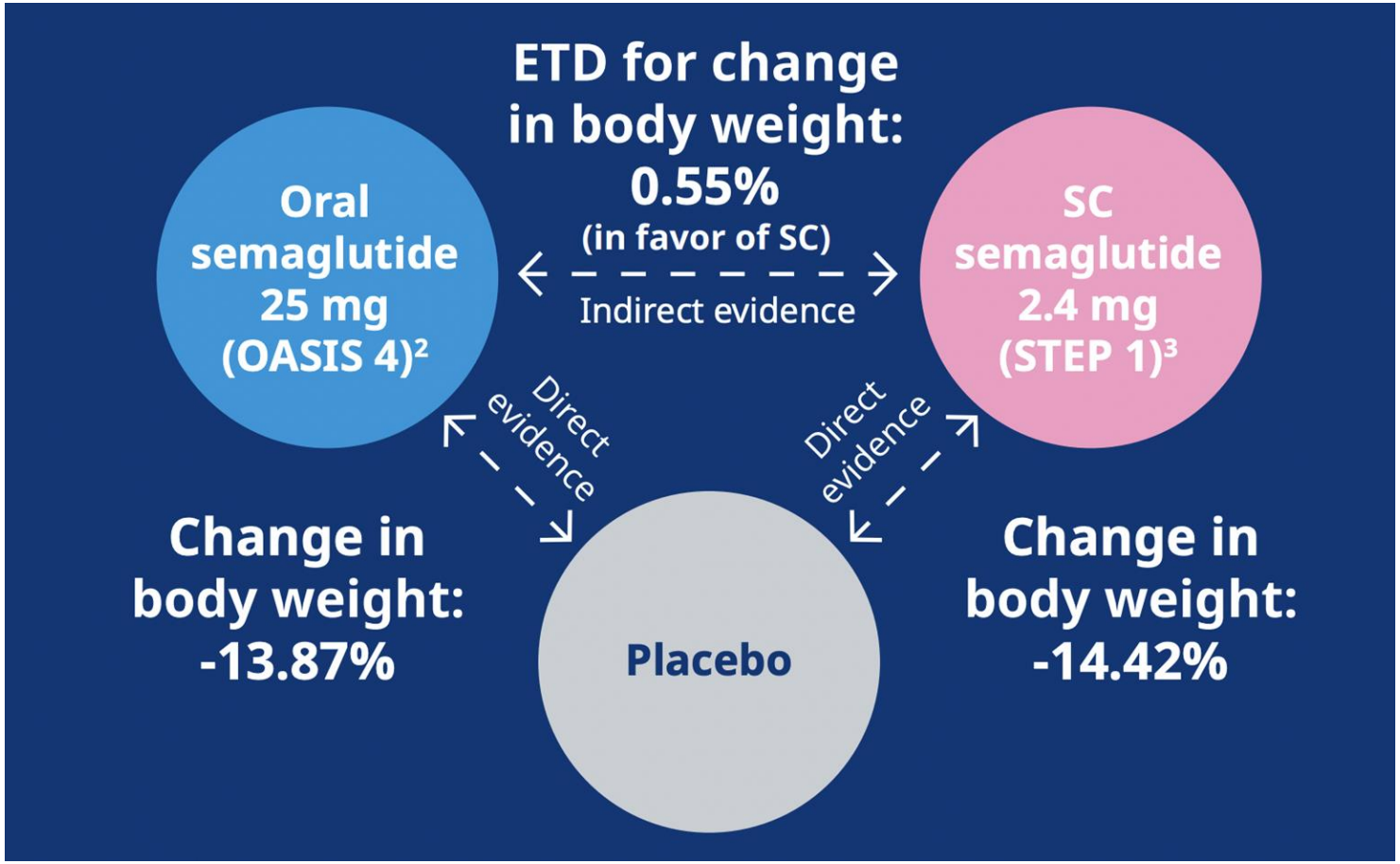
Starting, escalation, maintenance

	Days	Once Daily Tablet Dosage
Starting Dosage	1 through 30	1.5 mg
Dosage Escalation	31 through 60	4 mg
	61 through 90	9 mg
Maintenance Dosage	91 and onward	25 mg

Clinical question:

Patient asks you “are oral semaglutide and the injectable semaglutide are comparable?”

GLP1s provided a needed treatment option

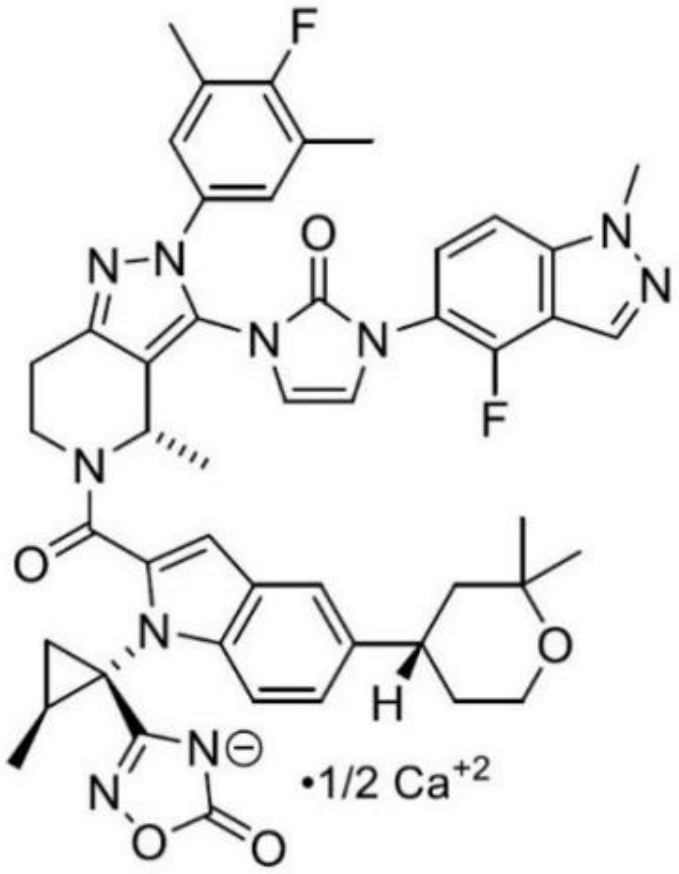


Oral vs Injectable Semaglutide: An Indirect Treatment Comparison of Weight Loss Molly Plotkin, MSc1 ; Milana Ivkovic, MSc2 ; Inger Smith, MSc3 ; Naveen Rathor MD2 ; Rohan Chowdhury, PhD4 ; Alexander Hodkinson, PhD4. (n.d.).

Clinical question:

Patient asks you “I heard there is tirzepatide in a pill which just came out. Can you tell me about that?”

Orforglipron (Foundayo): oral GLP1 receptor agonist



Orforglipron

Doses:

- 0.8 mg qdaily
- 2.5 mg qdaily
- 5.5 mg qdaily
- 9 mg qdaily
- 14.5 mg qdaily
- 17.2 mg qdaily

Indication: GLP-1 receptor agonist indicated in combination with a reduced-calorie diet and increased physical activity to reduce excess body weight and maintain weight reduction long term in adults with obesity or adults with overweight in the presence of at least one weight-related comorbid condition

Starting, escalation, maintenance

Start with 0.8 mg once daily	Initial dosage initiation
After 30 days, can increase to 2.5 mg once daily	First dosage adjustment
After 30 days on 2.5 mg, can increase to 5.5 mg once daily	Second dosage adjustment
After 30 days on 5.5 mg, can increase to 9 mg, 14.5 mg, or 17.2 mg once daily depending on tolerability and reponse	Potential further increases
Maximum dosage is 17.2 mg once daily	Upper limit of dosage

Orforglipron drug interactions

Strong CYP3A4 Inhibitors	
Intervention	The maximum dosage of FOUNDAYO is 9 mg once daily when used concomitantly with a strong CYP3A4 inhibitor. Avoid concomitant use of FOUNDAYO with strong CYP3A4 inhibitors that also inhibit OATP1B (e.g., ritonavir) *[see Dosage and Administration (2.2)]*.
Clinical Impact	CYP3A4 inhibitors increase FOUNDAYO exposure *[see Clinical Pharmacology (12.3)]*, which may increase the risk of FOUNDAYO-associated adverse reactions. Strong CYP3A4 inhibitors that also clinically inhibit OATP1B are expected to significantly increase plasma concentrations of FOUNDAYO, which may increase the risk of FOUNDAYO-associated adverse reactions *[see Warnings and Precautions (5.3), Adverse Reactions (6.1)]*.
Strong CYP3A4 Inducers	
Intervention	Avoid concomitant use of FOUNDAYO with strong CYP3A4 inducers.
Clinical Impact	Induction of CYP3A4 decreases FOUNDAYO exposure *[see Clinical Pharmacology (12.3)]*, which may reduce the effectiveness of FOUNDAYO.
Moderate CYP3A4 Inducers	
Intervention	Monitor FOUNDAYO effectiveness and escalate dosage as needed when used concomitantly with moderate CYP3A4 inducers *[see Dosage and Administration (2.1)]*.
Clinical Impact	Induction of CYP3A4 decreases FOUNDAYO exposure *[see Clinical Pharmacology (12.3)]*, which may reduce the effectiveness of FOUNDAYO.

Orforglipron (Foundayo)

ATTAIN clinical trial program

HTN in people living with overweight or obesity

OSA in people living with overweight or obesity

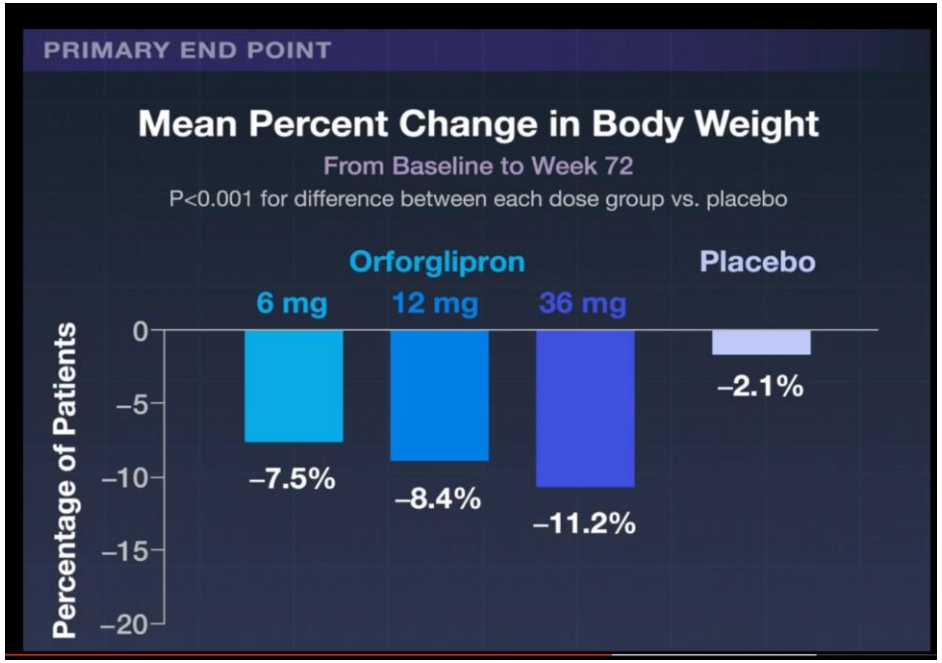
OA in in people living with overweight or obesity

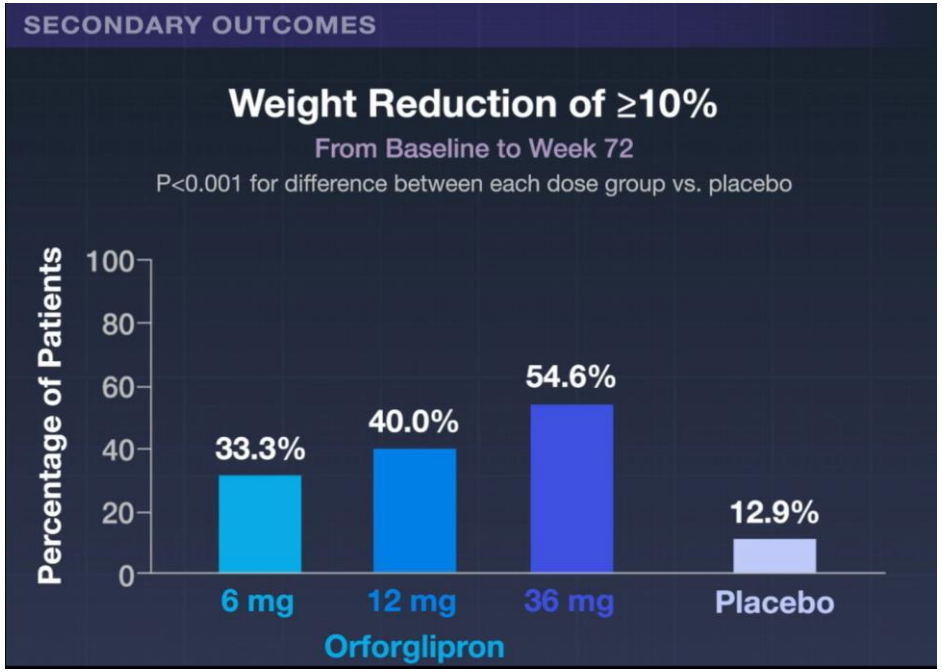
Stress Urinary Incontinence in females living with obesity or overweight

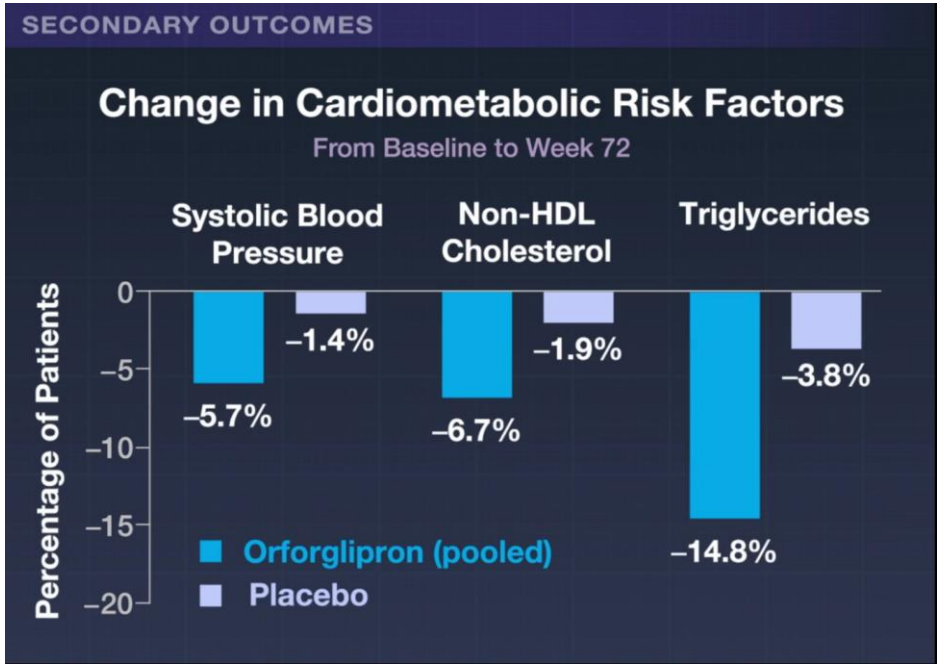
PAD

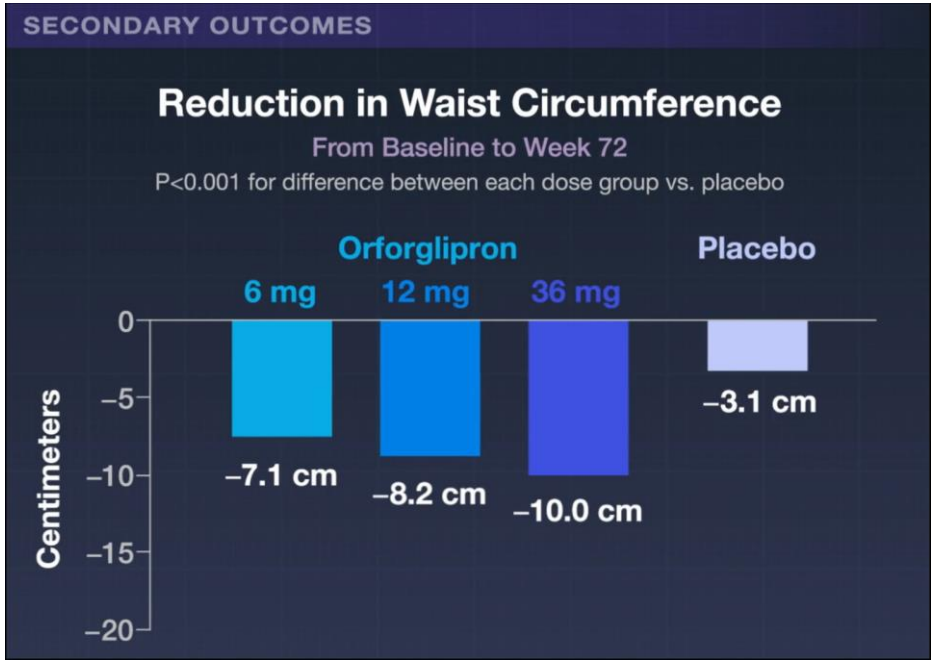
ASCVD and/or CKD

ATTAIN MAINTAIN









Wharton S. Orforglipron, an oral small-molecule GLP-1 receptor agonist for obesity treatment | New England Journal of Medicine. Orforglipron, an Oral Small-Molecule GLP-1 Receptor Agonist for Obesity Treatment. 2025. Accessed May 3, 2026. https://www.nejm.org/doi/full/10.1056/NEJMoa2511774.

NEWS

Press release

8:00 AM April 2 2026

Announcement.pdf

Wegovy® pill demonstrated greater weight loss than orforglipron and lower odds of stopping medication due to side effects in a new indirect comparison to be presented at Obesity Medicine Association 2026

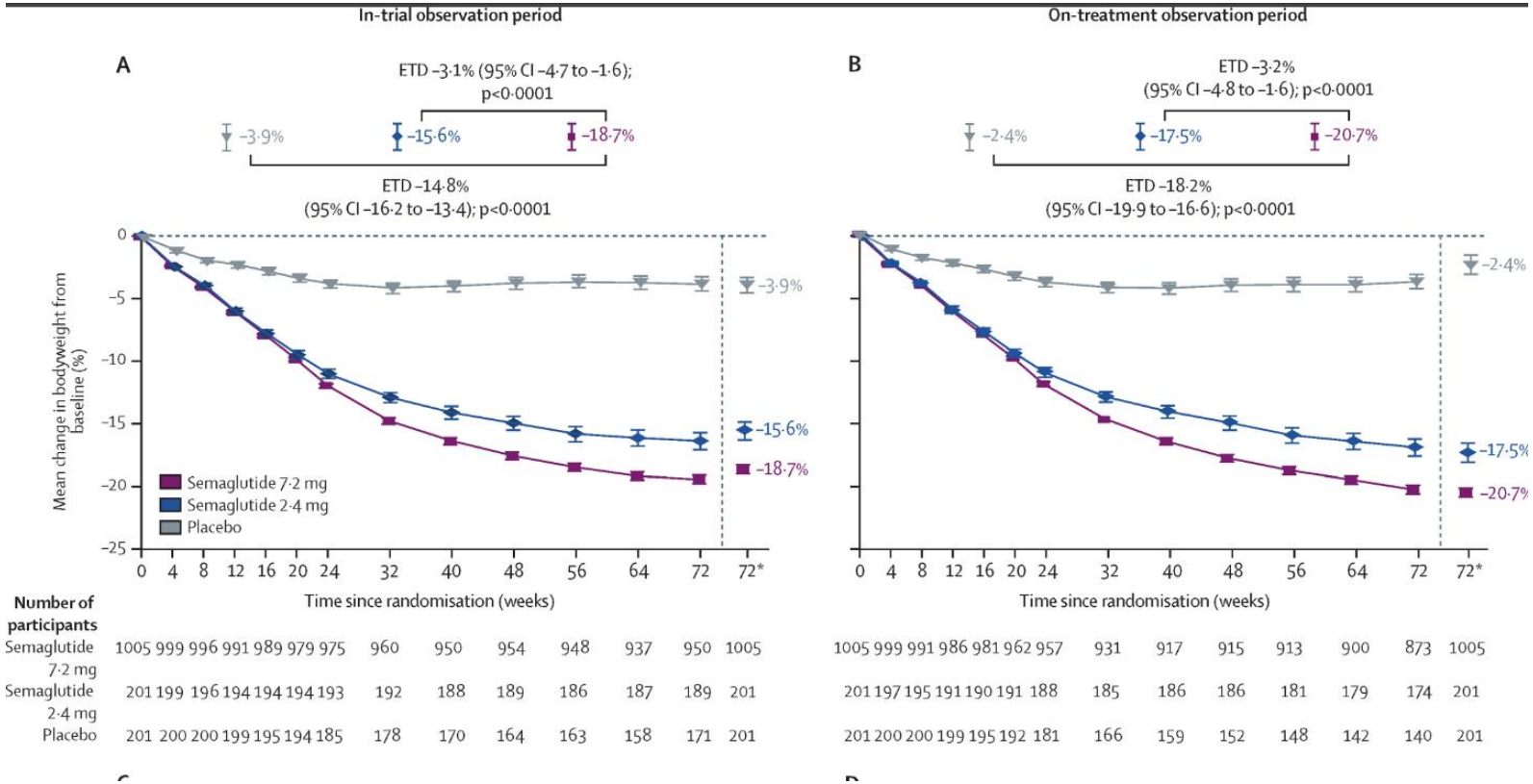
Oral Peptide vs Small Molecule GLP-1 RAs

Category	Oral Peptide GLP1-RA (Semaglutide)	Oral Non-peptide, small molecule (Orforglipron)
Half life	7 days	~48 hours
Storage	stable at room temperature	stable at room temperature
Dosing	Daily	Daily
Administration	Food and water restrictions	No food or water restrictions

Clinical question:

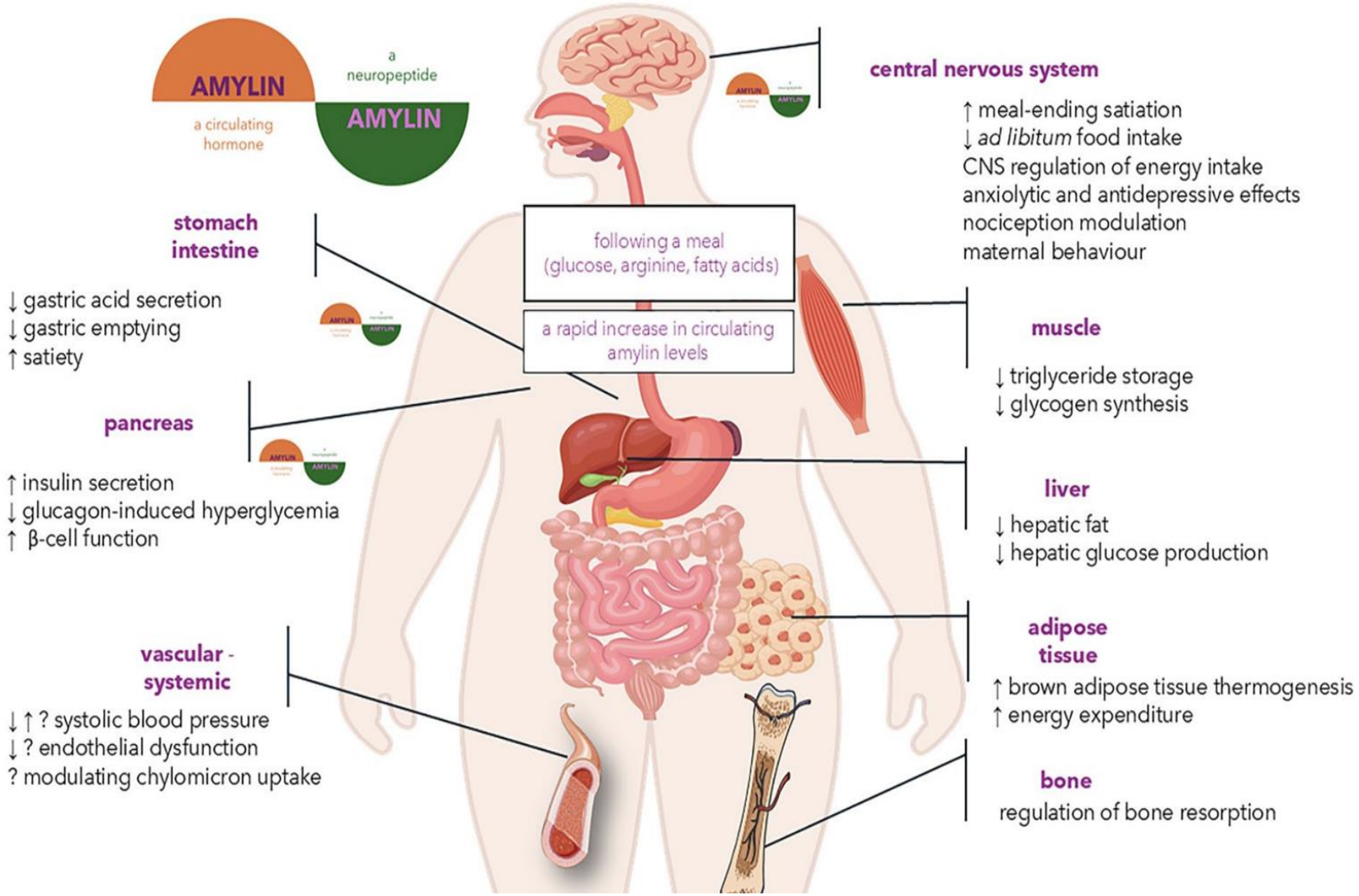
Patient asks you “which oral GLP1 shows greater weight loss?”

Semaglutide 7.2 mg qweekly
STEP UP



Wharton Once-weekly semaglutide 7·2 mg in adults with obesity (STEP UP): a randomised, controlled, phase 3b trial, The Lancet Diabetes & Endocrinology, Volume 13, Issue 11, 2025, Pages 949-963, ISSN 2213-8587, https://doi.org/10.1016/S2213-8587(25)00226-8.

Amylin



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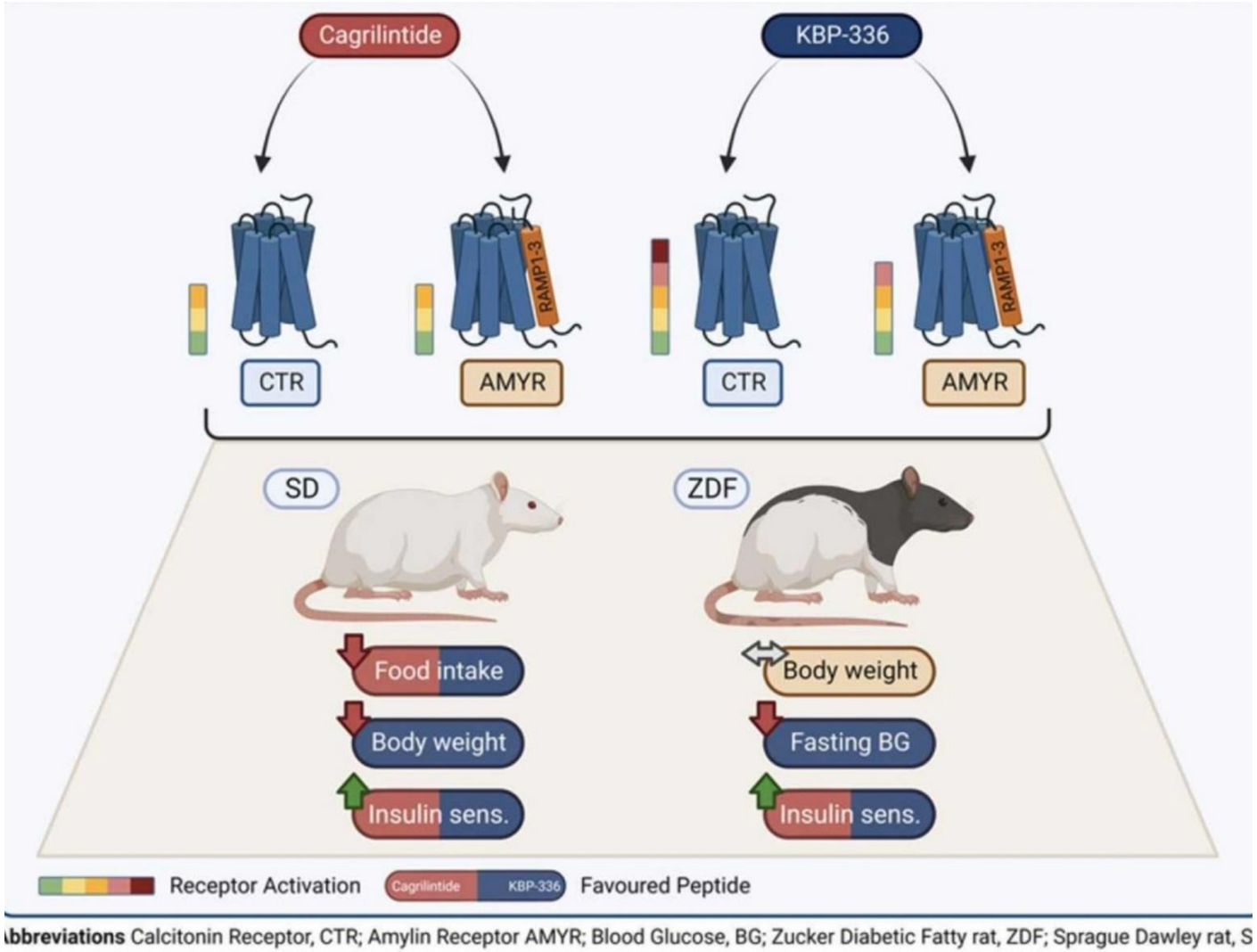
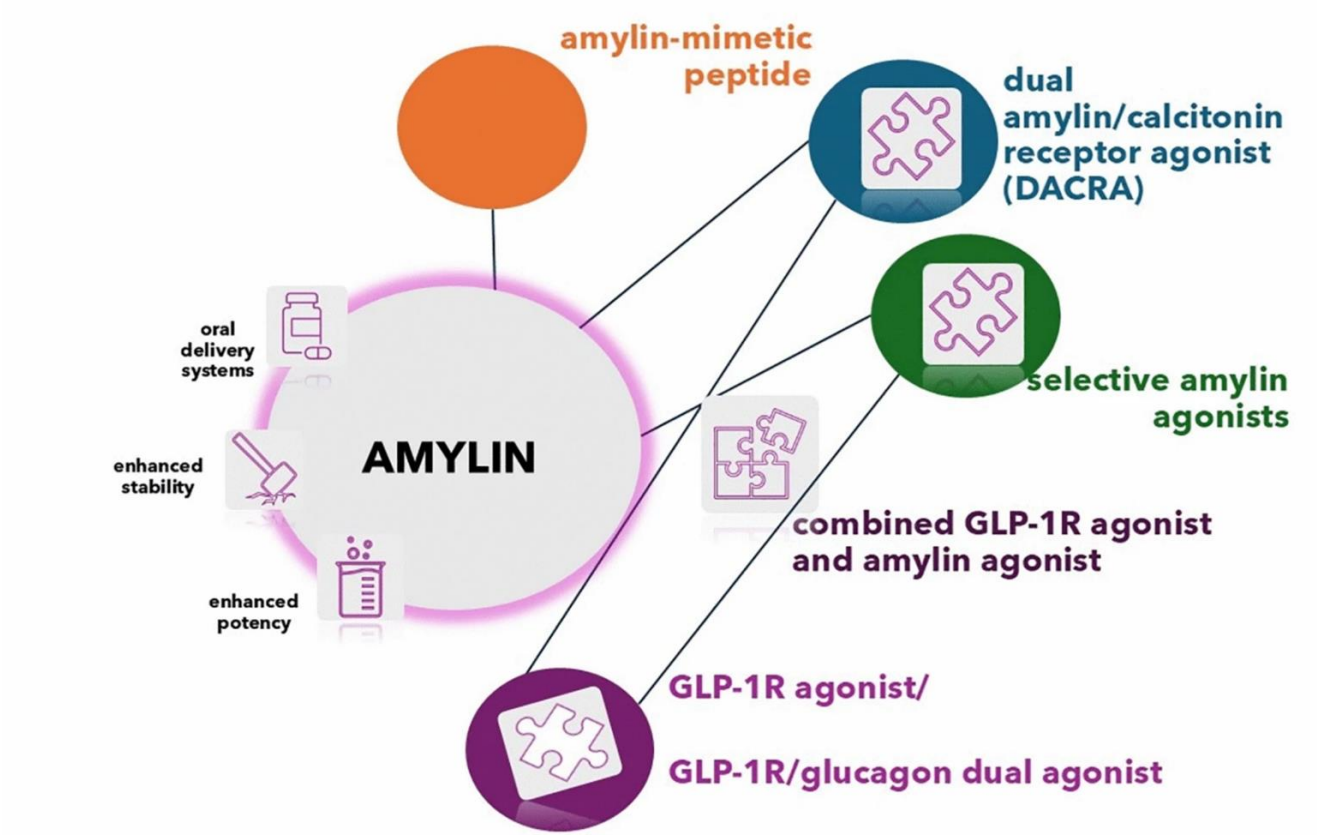


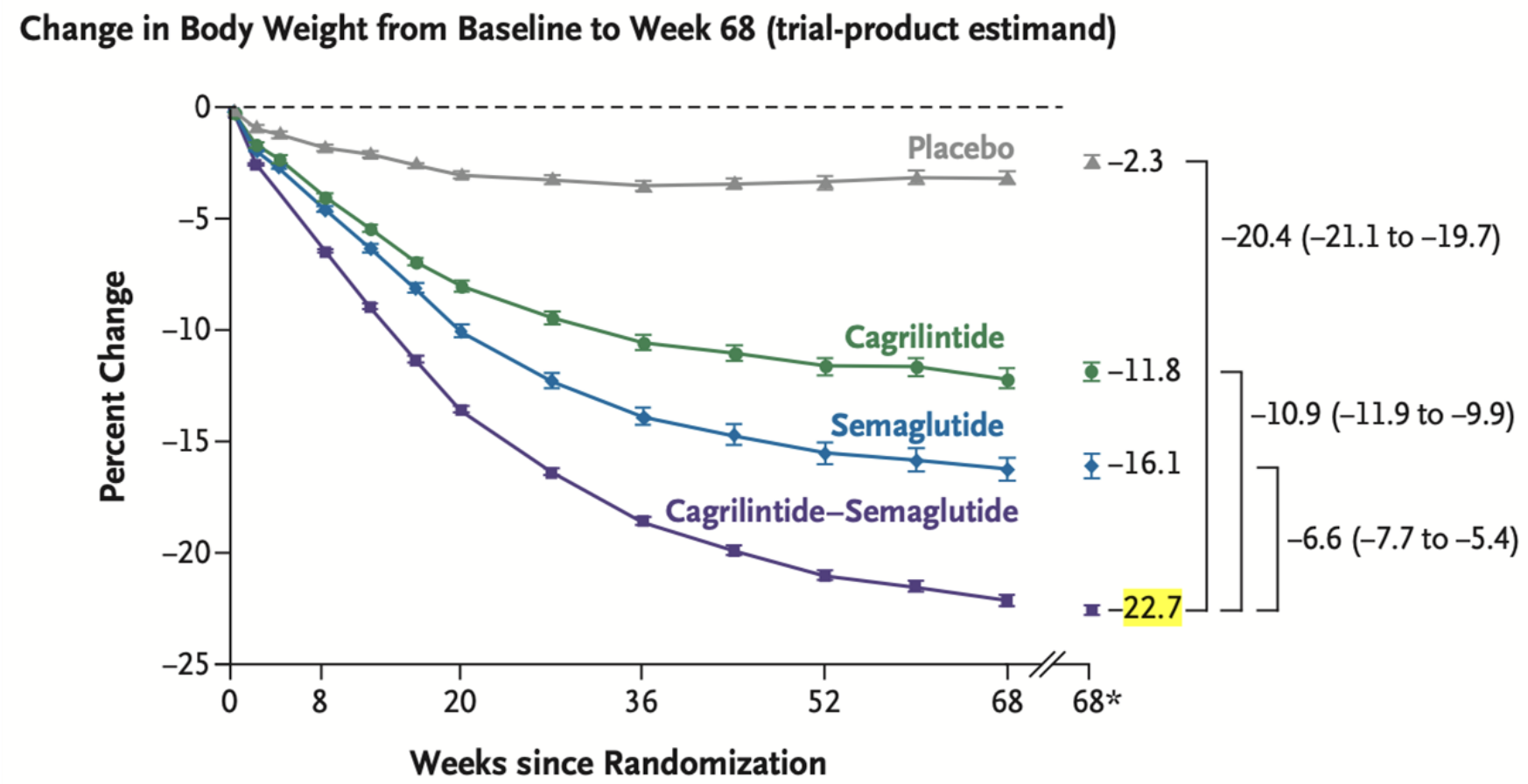
A.T. Larsen Does receptor balance matter? – Comparing the efficacies of the dual amylin and calcitonin receptor agonists cagrilintide and KBP-336 on metabolic parameters in preclinical models, Biomedicine & Pharmacotherapy, Volume 156,
2022, 113842, ISSN 0753-3322

Amylin agonists



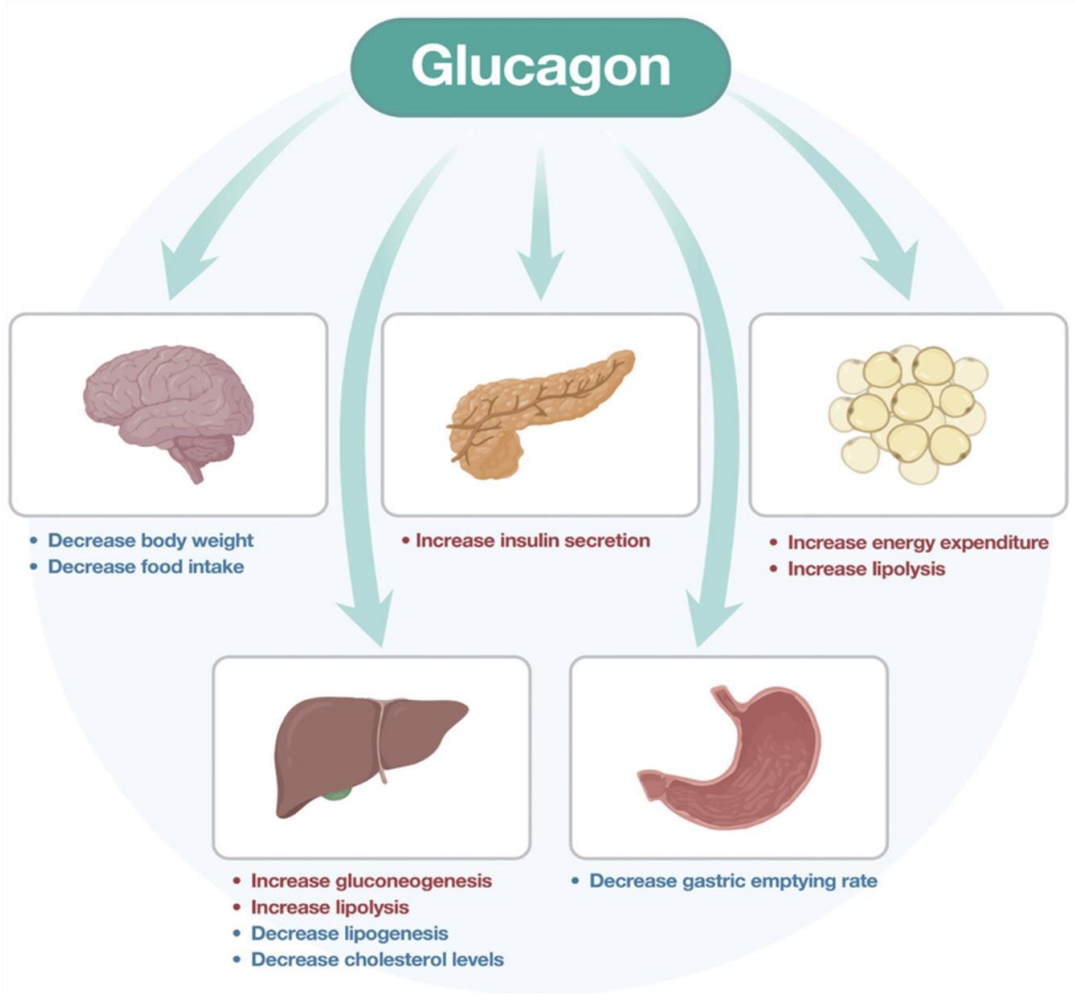
Volčanšek, Š., Koceva, A., Jensterle, M. *et al.* Amylin: From Mode of Action to Future Clinical Potential in Diabetes and Obesity. *Diabetes Ther* **16**, 1207–1227 (2025). https://doi.org/10.1007/s13300-025-01733-8

Cagrilintide



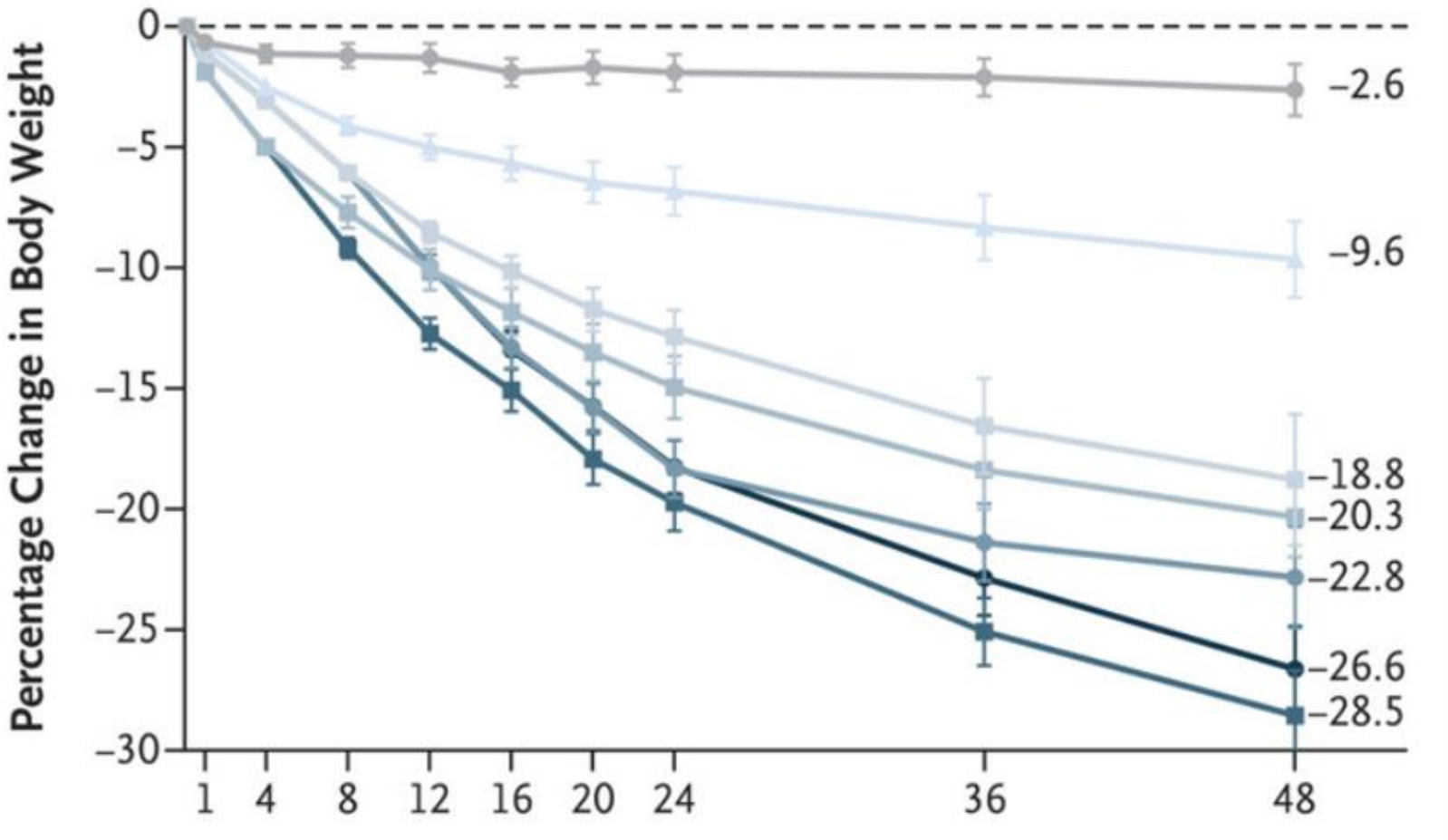
Garvey et al., NEJM, 2025

Glucagon



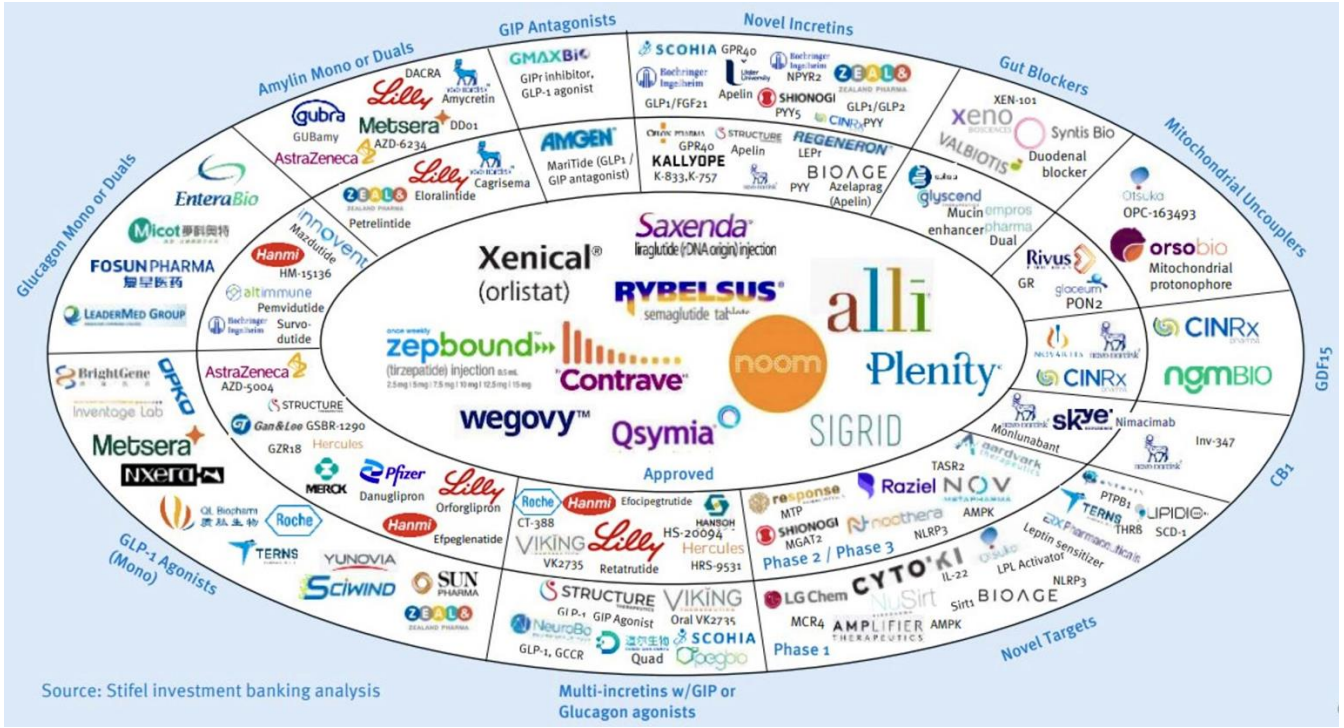
Jakubowska et al.,Endocrinol Metab., 2024

Retatrutide



Jastreboff et al.,NEJM., 2023

Future Pipeline



ÇETİN, ECESU; PEDERSEN, BRIAN; and BURAK, MEHMET FURKAN (2025) "Paradigm shift in obesity treatment: an extensive review of current pipeline agents," Turkish Journal of Medical Sciences: Vol. 55: No. 1, Article 2. https://doi.org/10.55730/1300-0144.5938

Phase 3 Clinical Trial	Retatrutide (LY3437943)	GIP/GLP-1/Glucagon Agonist
Phase 3 Clinical Trial	Survodutide (BI 456906)	GLP-1/Glucagon Agonist
Phase 3 Clinical Trial	Mazdutide	GLP-1/Glucagon Agonist
Phase 3 Clinical Trial	Cagrilintide	Long-acting Amylin Analog
Phase 3 Clinical Trial	Orforglipron	GLP-1 Agonist
Phase 3 Clinical Trial	Taldefgrobep alfa (BHV-2000)	Myostatin Inhibitor
Phase 2 Clinical Trial	Bimagrumab	ActRII Inhibitor
Phase 2 Clinical Trial	Trevogrumab (REGN 1033)	Selective Myostatin Inhibitor
Phase 2 Clinical Trial	Garetosmab	Activin A Inhibitor
Phase 2 Clinical Trial	Pemvidutide	GLP-1/Glucagon Agonist
Phase 2 Clinical Trial	Petrelintide	Long-acting Amylin Analog
Phase 2 Clinical Trial	Dapiglutide	GLP-1/GLP-2 Agonist
Phase 2 Clinical Trial	MariTide	GLP-1 Agonist/GIP Antagonist
Phase 2 Clinical Trial	HU6	Controlled Metabolic Accelerator
Phase 2 Clinical Trial	NT-0796	NLRP3 Inhibitor
Phase 2 Clinical Trial	S-309309	MGAT2 Inhibitor
Phase 2 Clinical Trial	GSBR-1290	GLP-1 Agonist
Phase 2 Clinical Trial	VK2735	GLP-1/GIP Agonist
Phase 1 Clinical Trial	Amycretin (NNC0487-0111)	GLP-1/Amylin Agonist
Phase 1 Clinical Trial	TLC-6740	Liver-targeted Mitochondrial Protonophore
Phase 1 Clinical Trial	KER-065	Selective ActRII Ligand Trap
Phase 1 Clinical Trial	CT-996	GLP-1 Agonist
Phase 1 Clinical Trial	NT-0249	NLRP3 Inhibitor
Preclinical Study	RKER-034	ActRII Ligand Trap
Preclinical Study	SRK-439	Selective Myostatin Inhibitor
Preclinical Study	Anti-GPR75	Gene Silencing
Preclinical Study	WVE-007	Gene Silencing
Preclinical Study	ARO-INHBE	Gene Silencing
Preclinical Study	ARO-ALK7	Gene Silencing

Combinations

Metabolic surgery

TREATMENT GAP

Anti obesity pharmacotherapy
2nd generation, 3rd generation

Lifestyle
(professionally directed)

Lifestyle (self directed)

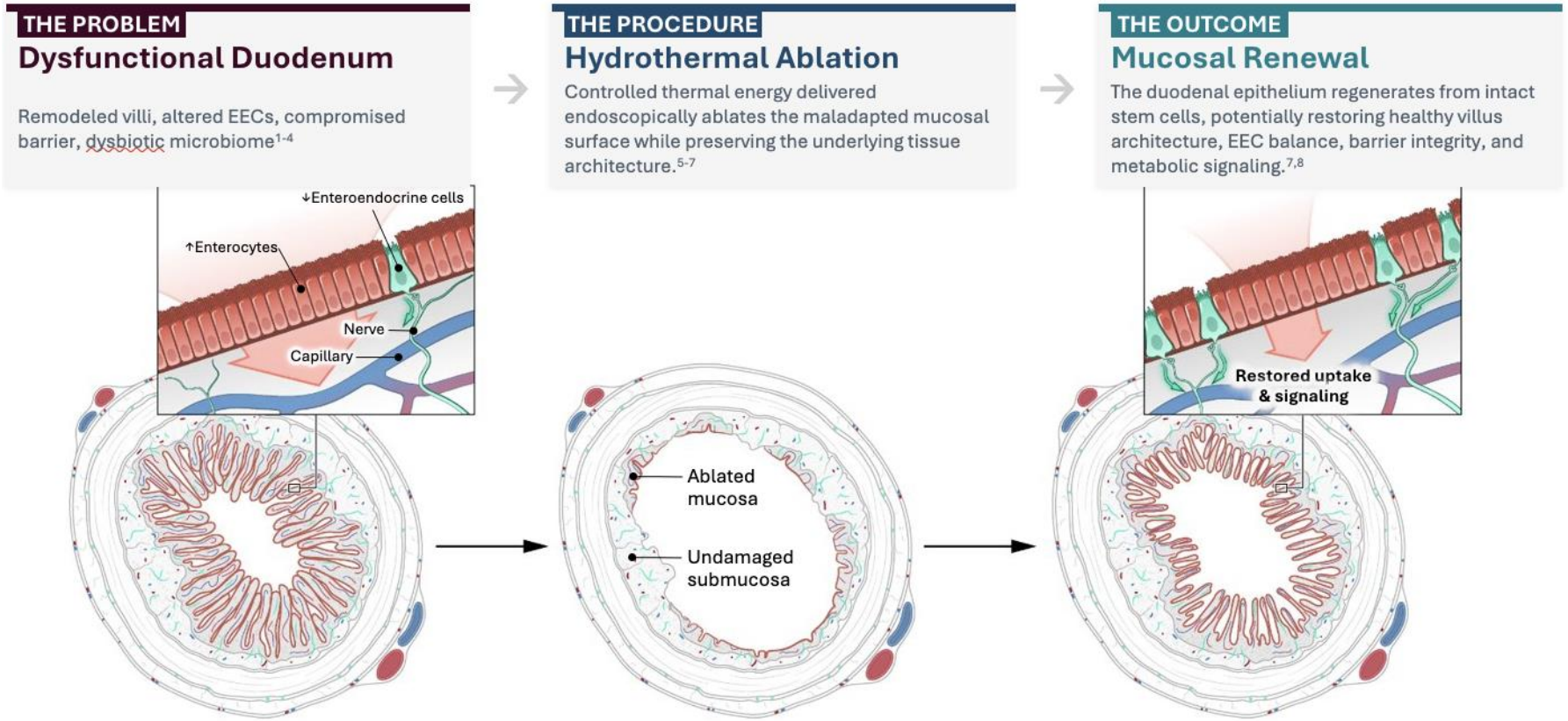
OBESITY IS a DISEASE. Accessed April 6, 2024.
https://medical.lilly.com/us/diseases/assets/vaultpdf/en/8a320555ce59e2bbb378ed2e79cfb078ba89a7c0202a543e6f8888c1b144f76e/obesity-is-a-disease-infographic

Endoscopic Bariatric Therapies

-Intragastic balloons

-Endoscopic sleeve gastroplasty

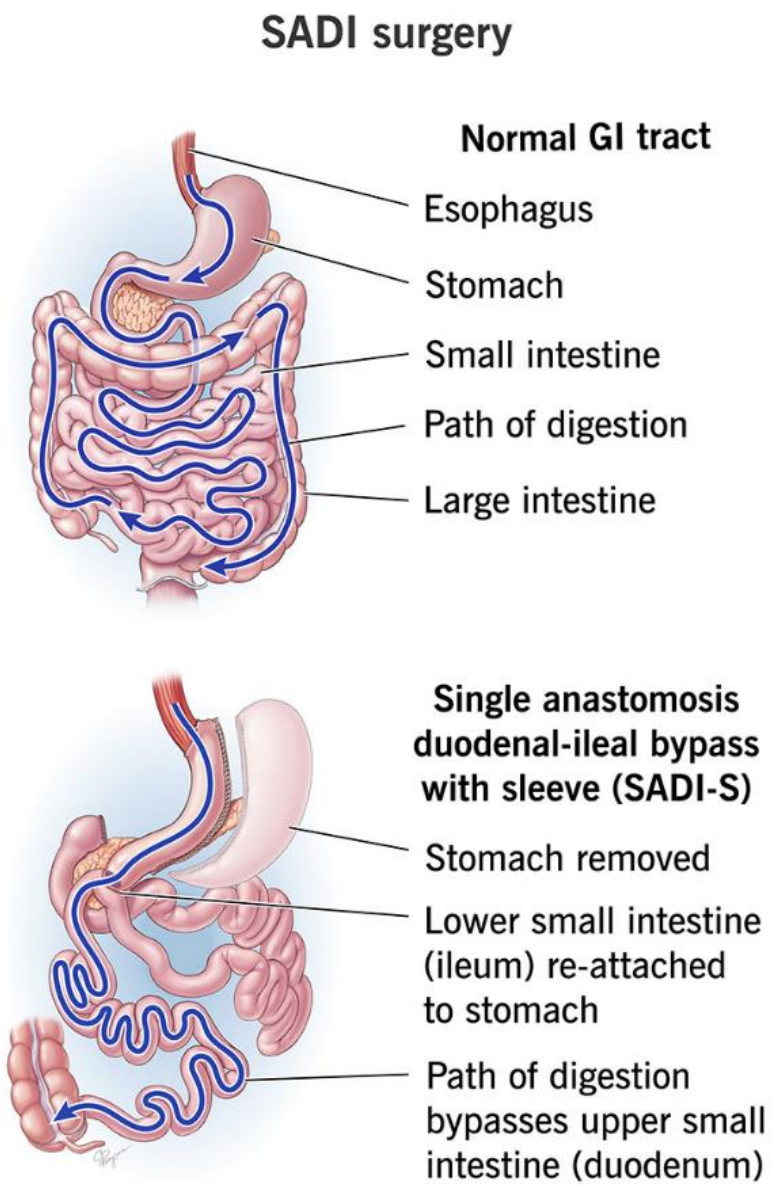
Emerging/Novel Devices



Metabolic surgery

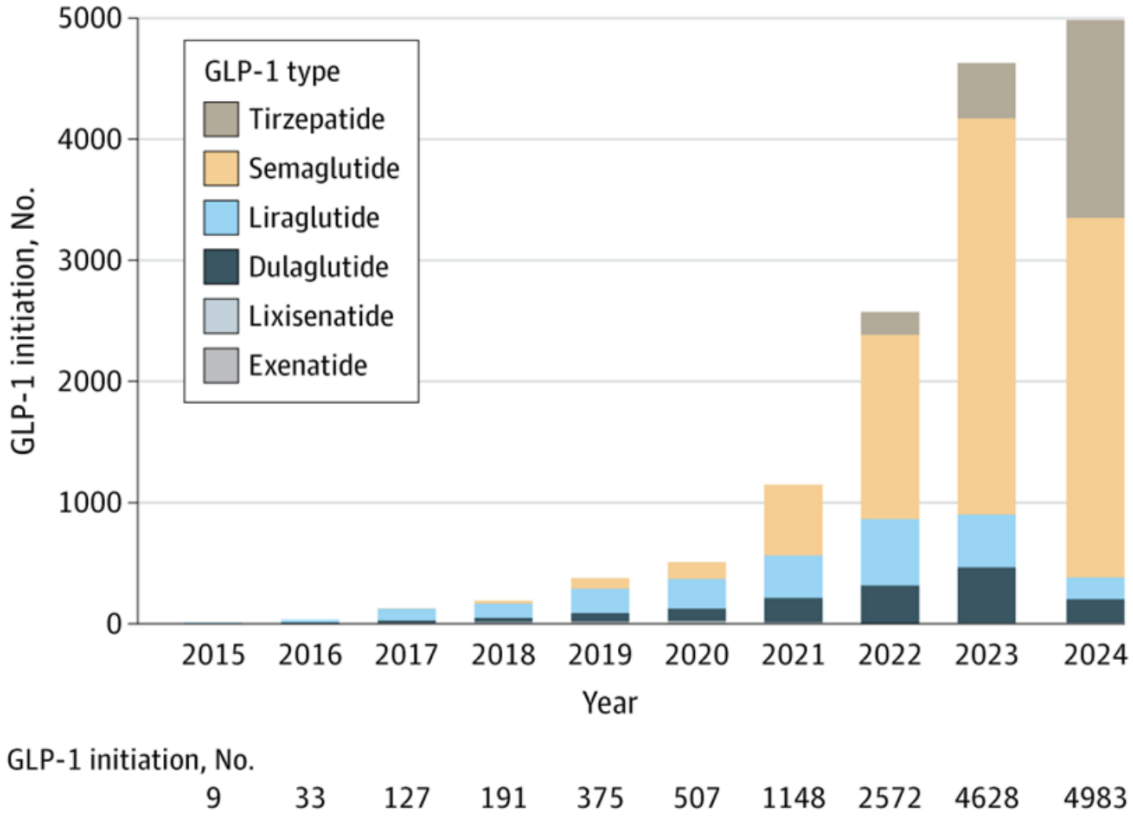
Sleeve gastrectomy

Rou-en-Y gastric bypass



Combination therapies

Figure 3. Trends in Glucagon-Like Peptide-1 Receptor Agonist (GLP-1) Initiation Post-Bariatric Surgery, Stratified by Types of GLP-1s



The number of GLP-1 initiations in 2025 is not presented because data are only available for 5 months. From January to May 2025, a total of 1176 initiations were observed.

Kim M, Schweitzer MA, Kim JS, Alexander GC, Mehta HB. Use of Glucagon-Like Peptide-1 Agonists Among Individuals Undergoing Bariatric Surgery in the US. *JAMA Surg.* 2025;160(10):1058–1066. doi:10.1001/jamasurg.2025.3089

Conclusions

- Advancements in incretin therapies are bridging the gap between medication and surgical therapies
- With increasing efficacy and hormonal targets, the key will be the right therapy for the right patient
- Obesity care has shifted to a multimodal strategy where medications, devices and procedures can and are complementary

THANK YOU

Linked In: Priya Jaisinghani, MD, DABOM

X: @doctorjny

Instagram: @doctorjny

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- Muller et al., Mol Metab, 2025
- Oral vs Injectable Semaglutide: An Indirect Treatment Comparison of Weight Loss Molly Plotkin, MSc1 ; Milana Ivkovic, MSc2 ; Inger Smith, MSc3 ; Naveen Rathor MD2 ; Rohan Chowdhury, PhD4 ; Alexander Hodkinson, PhD4. (n.d.).
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