

Emerging Opportunities

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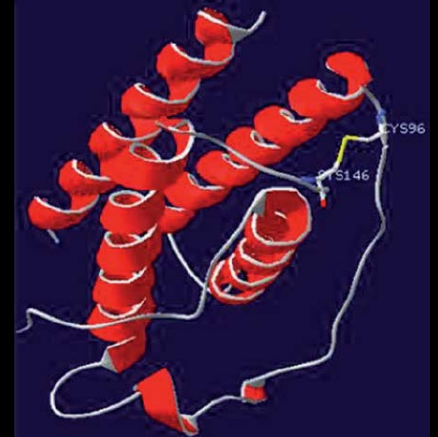
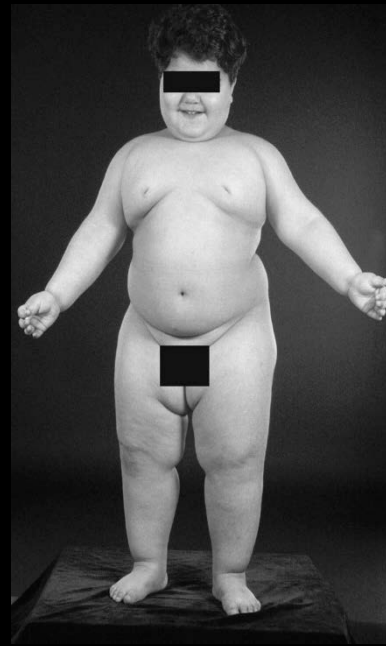
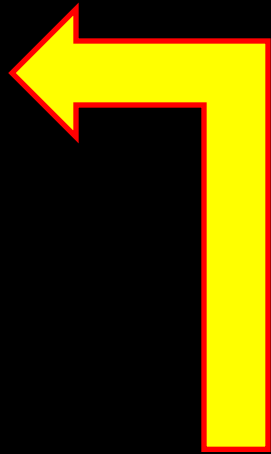
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Disclosures

- **Medical Advisory Board Medifast**
- **Medical Advisory Board Tanita Corp.**

%Fat \propto BMI



= Genes + Epigenes + Environment



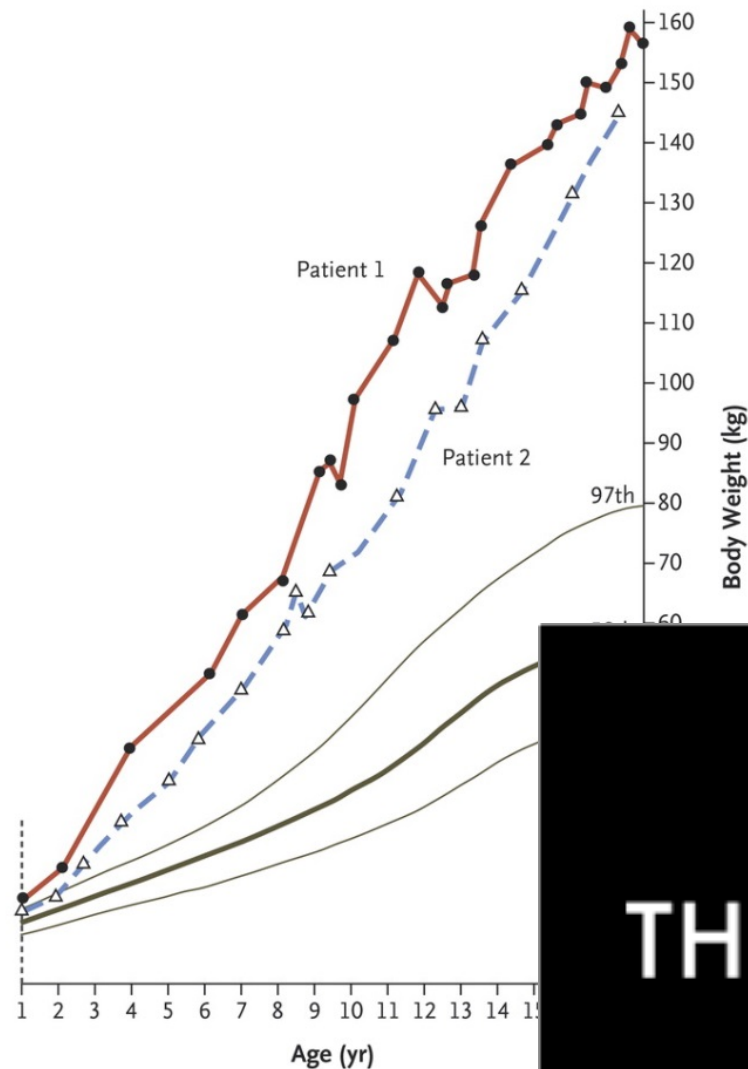
+ G x Epig + G x Environ + Epig x Environ

Leptin Mutations: Targeted Pharmacotherapy

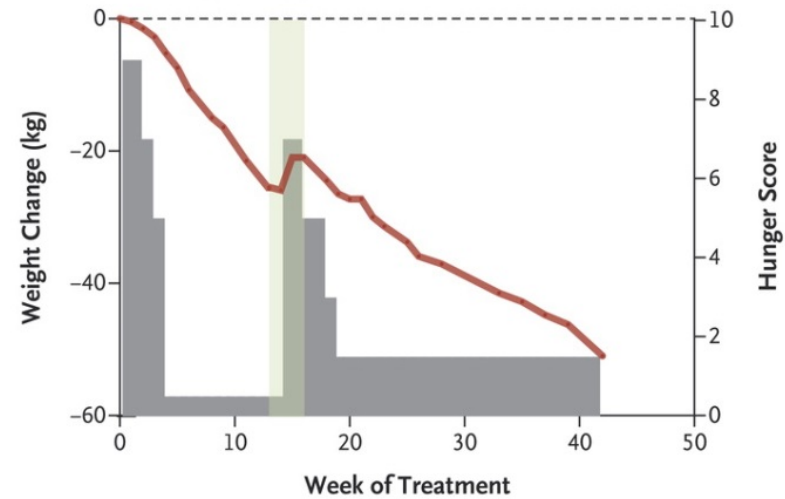


MC4R Mutations: 2 - 5% of Severe Obesity

A Pretherapy Weight of the Two Patients



B Patient 1 during Therapy



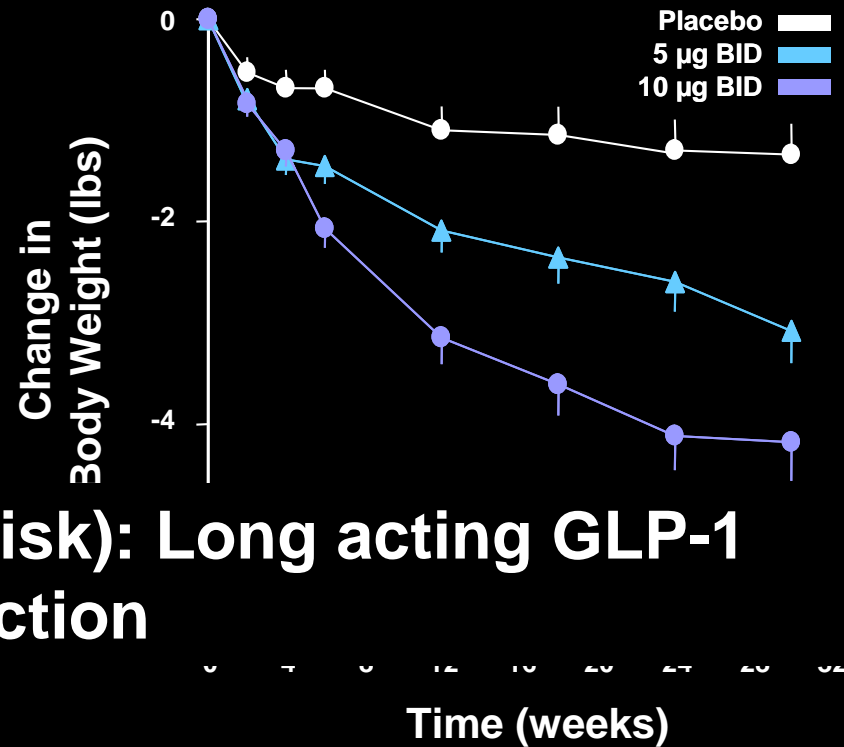
C Patient 2 during Therapy



Peptide Therapeutics



Semaglutide (Novo Nordisk): Long acting GLP-1 agonist for 1X/Week injection



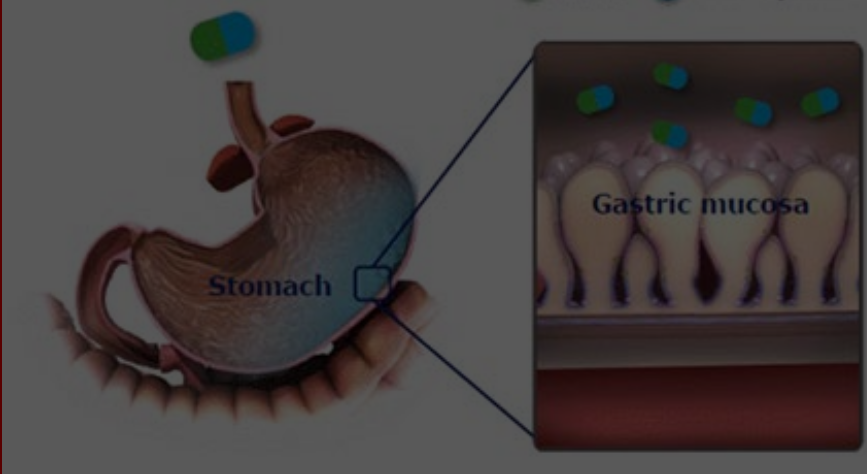
GLP-1: Glucagon-Like Peptide 1



Challenges of Oral Peptide Delivery

Challenges	Solutions
1. Breakdown of drug in the stomach/gastrointestinal tract	1. Stabilisation of peptide backbone and side chain
2. Passage across the gut barrier into the circulation	2. Tablet formulation including carrier and/or coating

Oral version of semaglutide co-formulated with absorption enhancer SNAC which causes localized pH increase leading to higher solubility and protection from enzymatic degradation

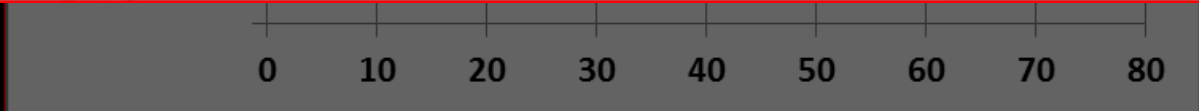
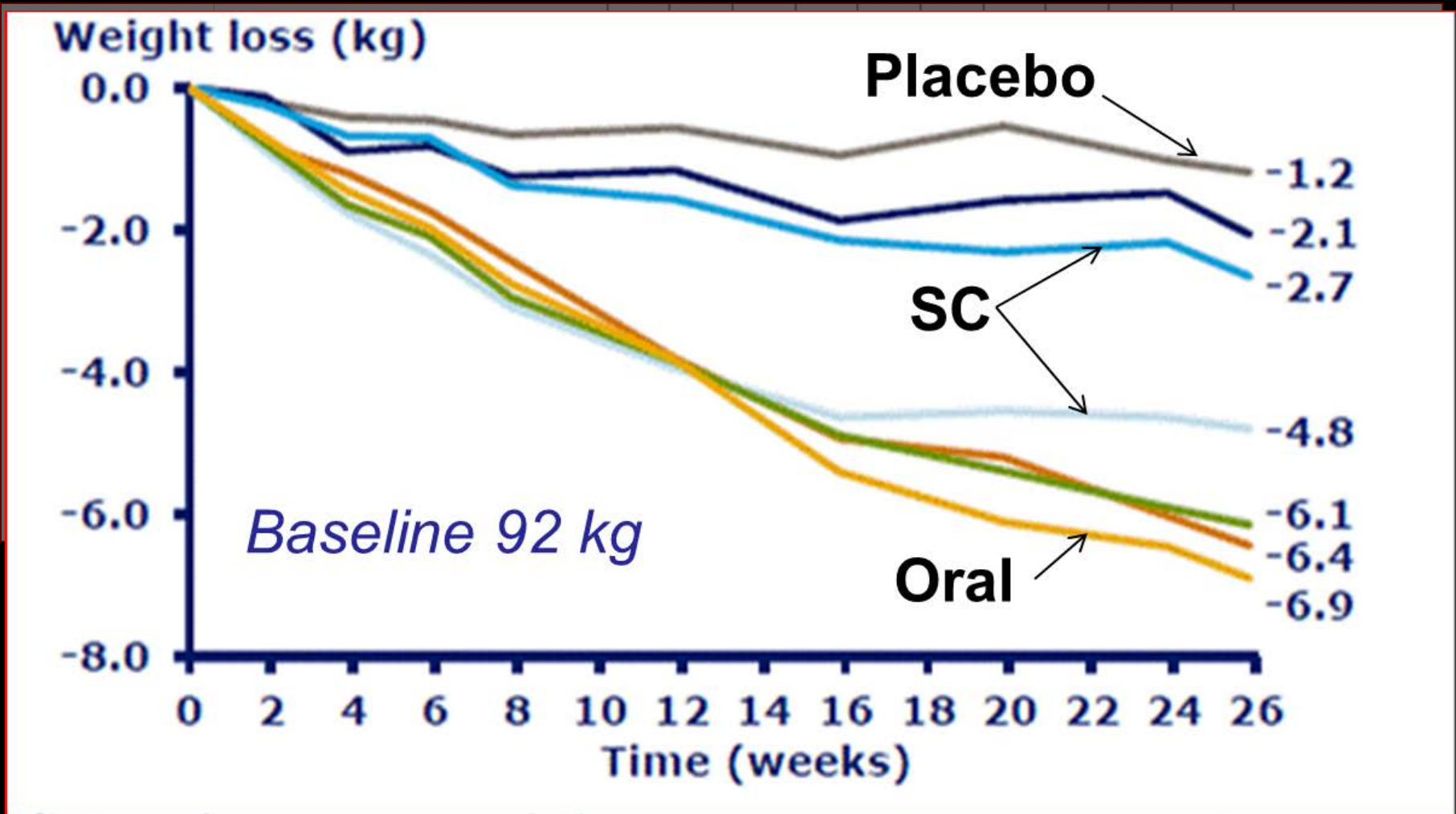


The diagram illustrates the stomach and a cross-section of the gastric mucosa. On the left, a 3D anatomical model of the stomach is shown with a blue and green capsule. A box highlights a section of the stomach wall, which is magnified on the right. This magnified view shows the gastric mucosa with several blue and green capsules (SNAC) positioned near the surface. Below the mucosa, a layer of red liquid is visible, representing the underlying tissue or blood supply.

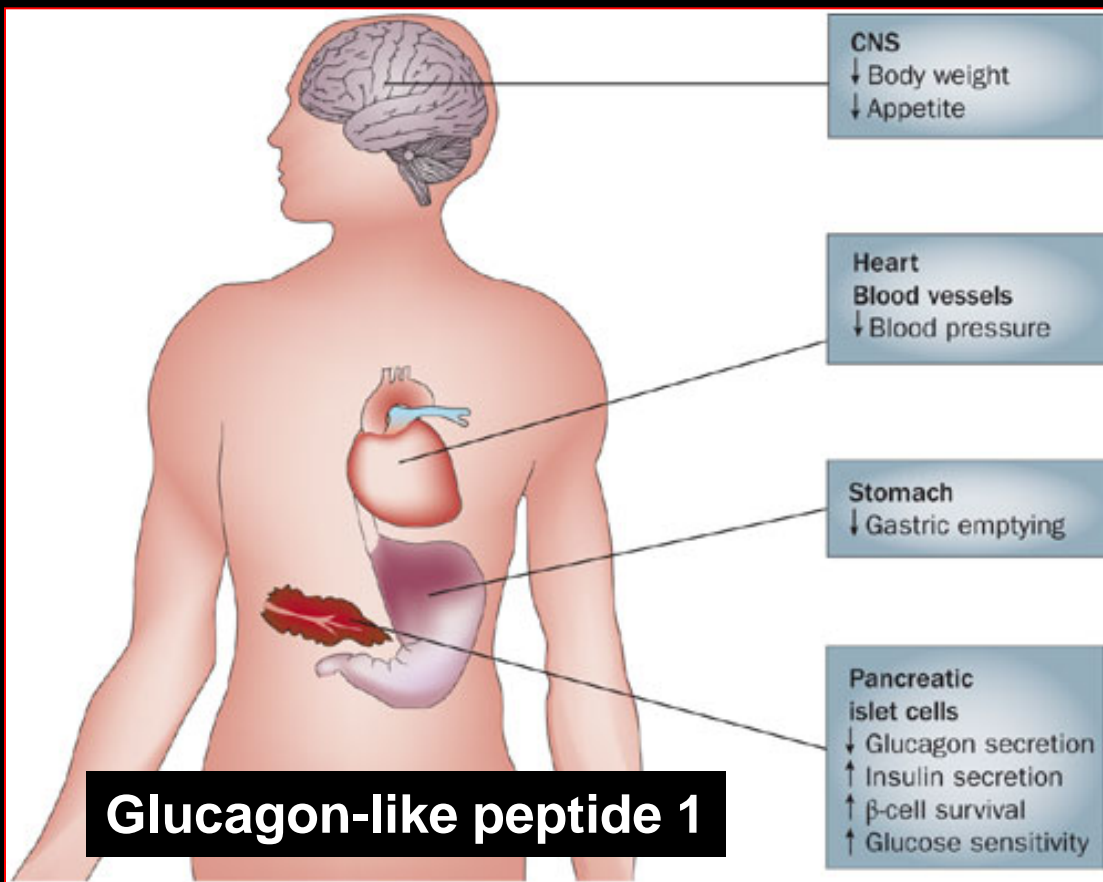
Physical proximity of SNAC and semaglutide

- SNAC facilitates local increase of pH leading to higher solubility
- SNAC interacts with cell membrane facilitating absorption within 30 minutes
- SNAC effect is size-dependent and fully reversible

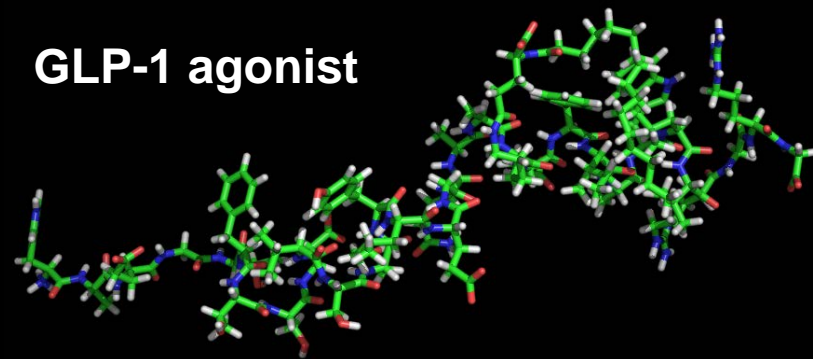
Oral Peptides: Semaglutide



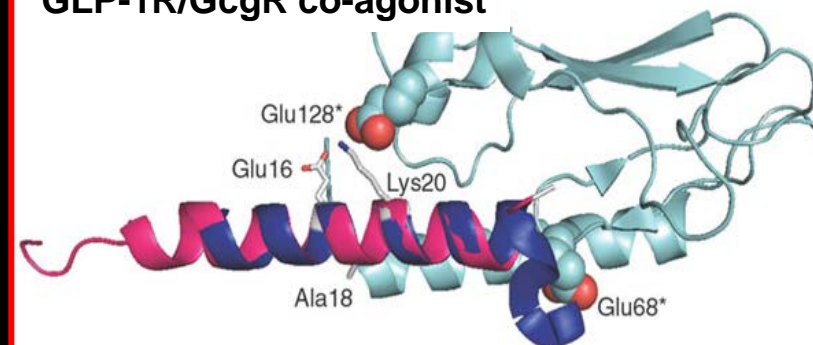
Combination Peptides



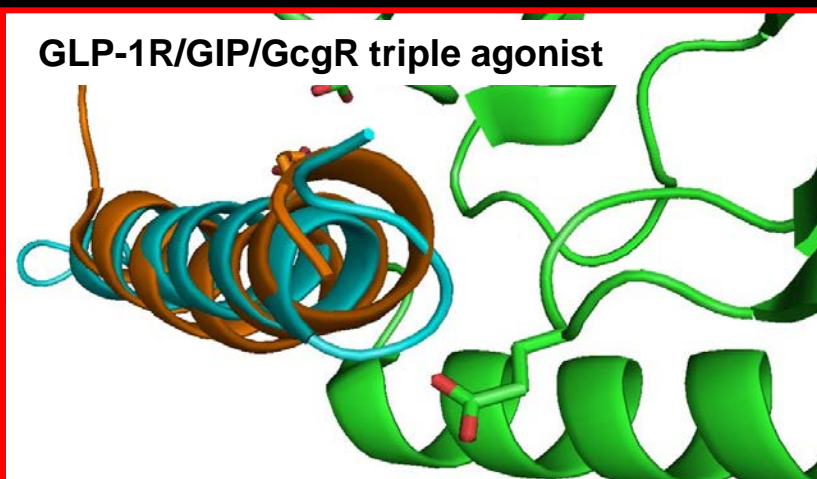
GLP-1 agonist



GLP-1R/GcgR co-agonist



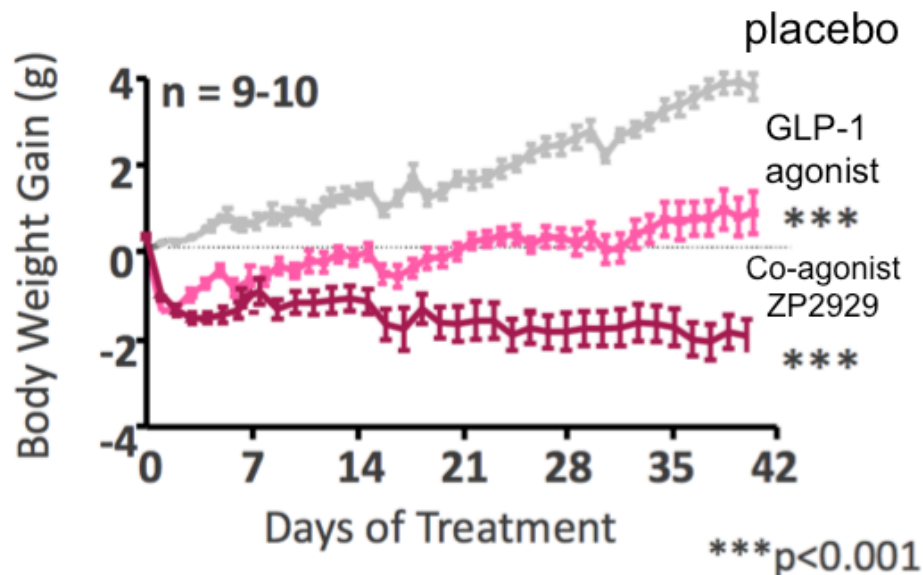
GLP-1R/GIP/GcgR triple agonist



Peptides in Development

- 23+ GLP-1 peptides in development:
 - Oxyntomodulin (GLP-1/glucagon co-agonist peptide)
 - GLP-1-Fc-FGF21; also FGF21 alone
 - GLP-1-GIP
 - With glucagon analog
 - Long-acting preparations

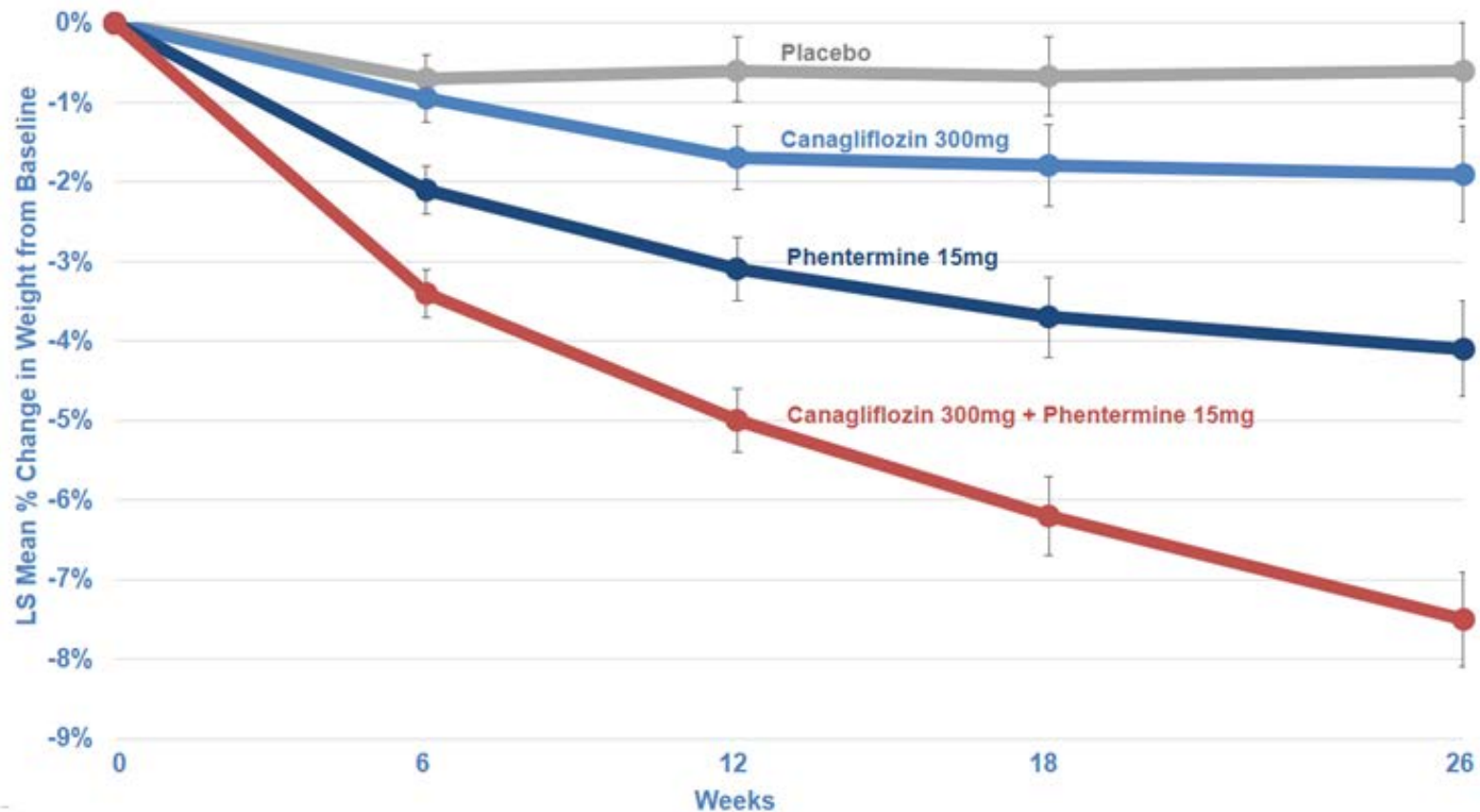
Diet-Induced Obesity Model



New Oral Medication Combinations

- 4

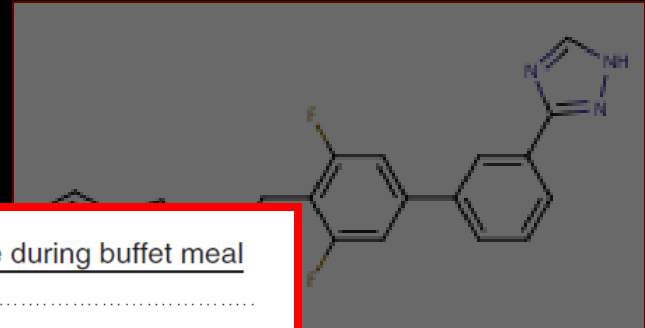
Phase II Weight Loss Efficacy Canagliflozin/Phentermine Combination



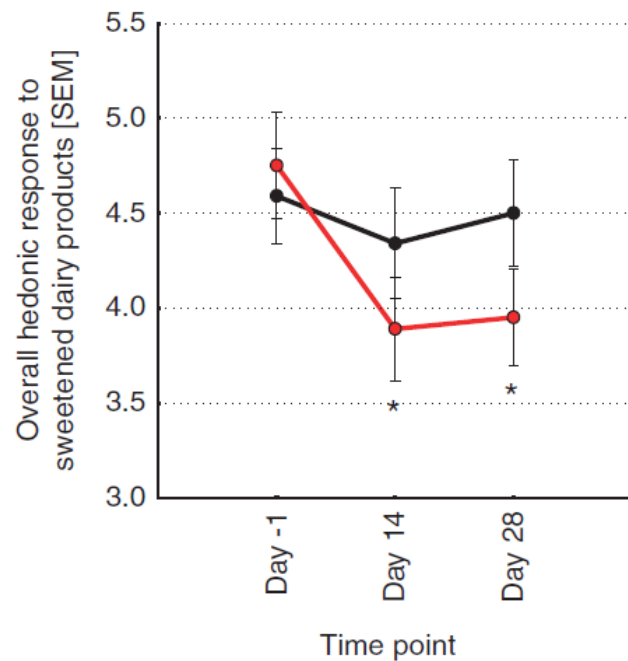
Hollander et al, 2016.06.12, ADA 76th Scientific Sessions, abstract 319-LB

Targeting Hedonic Mechanisms

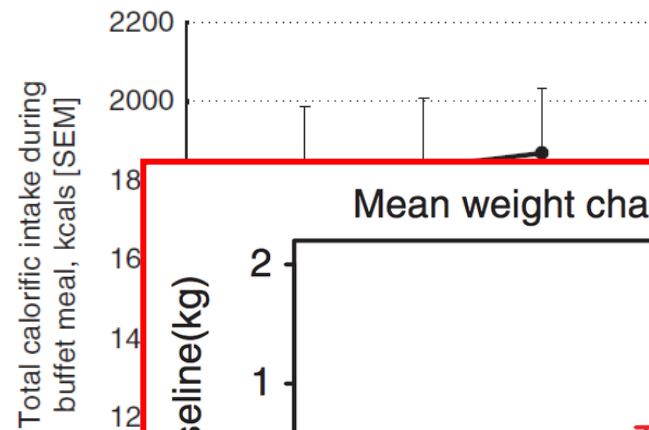
μ -opioid receptor inverse agonist



Hedonic responses to sweetened dairy products

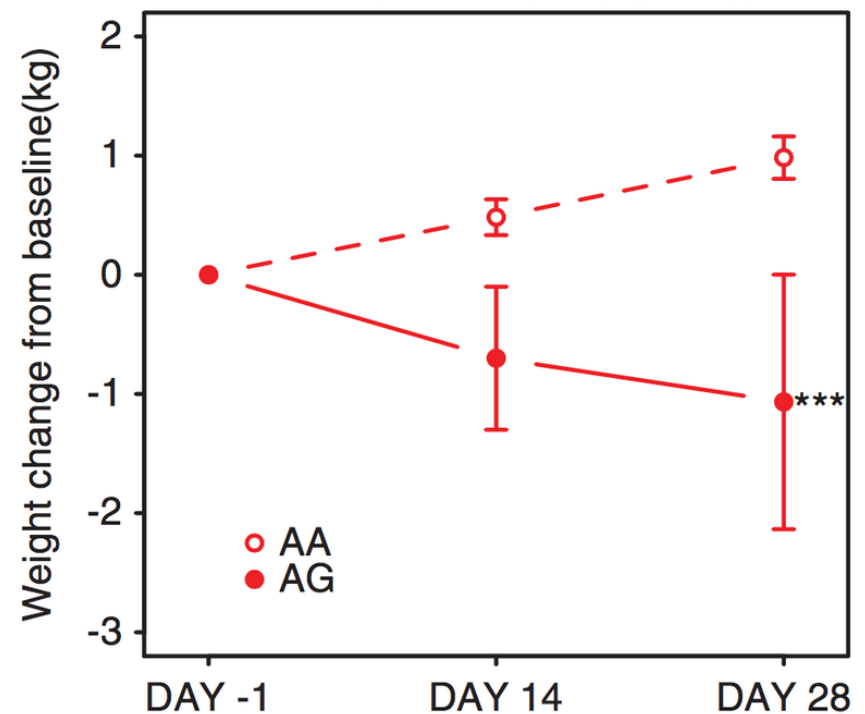


Total calorific intake during buffet meal

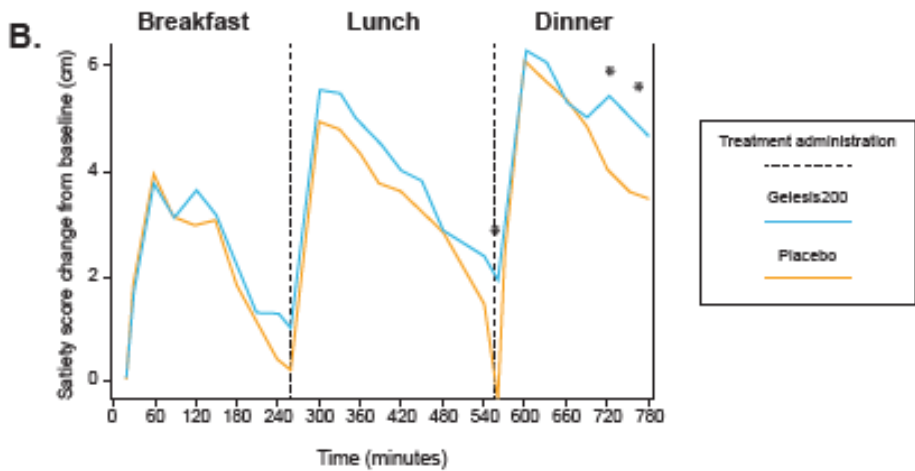
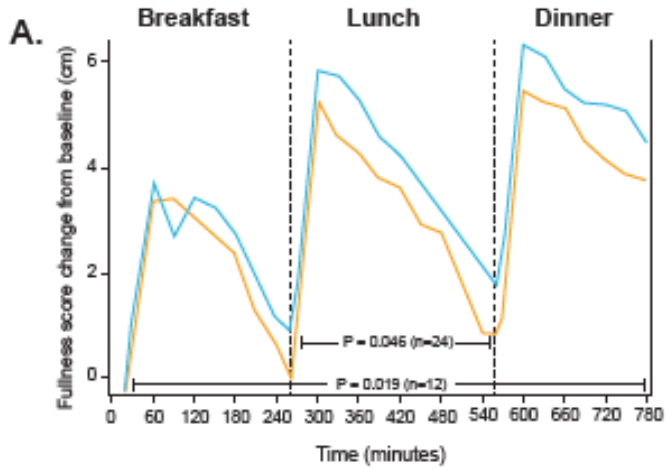


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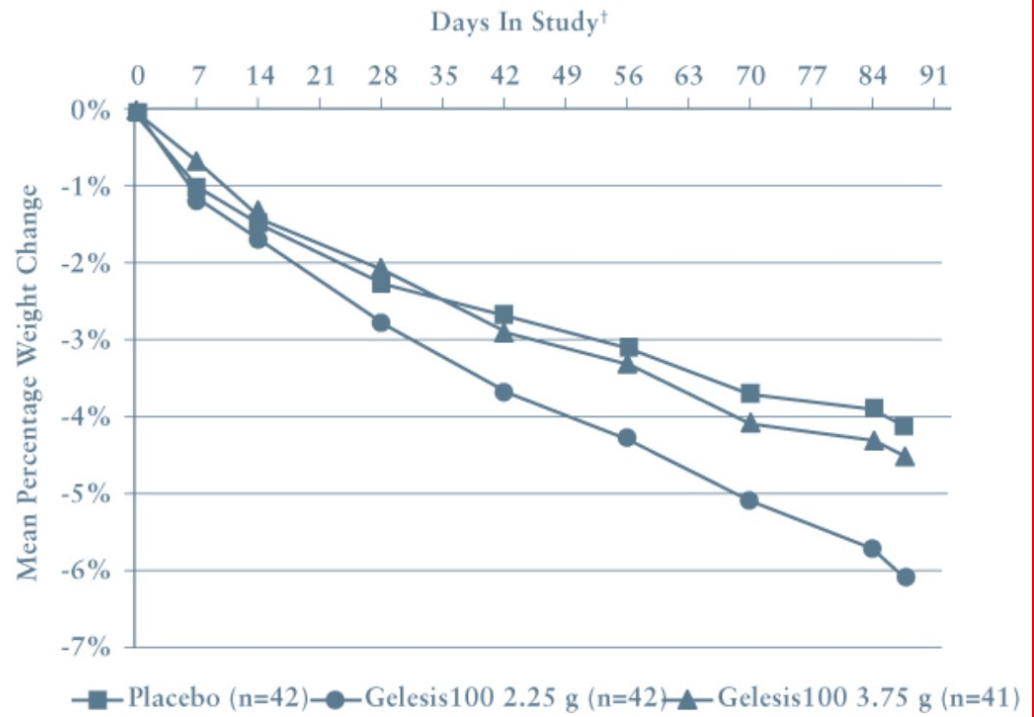
Mean weight change by genotype



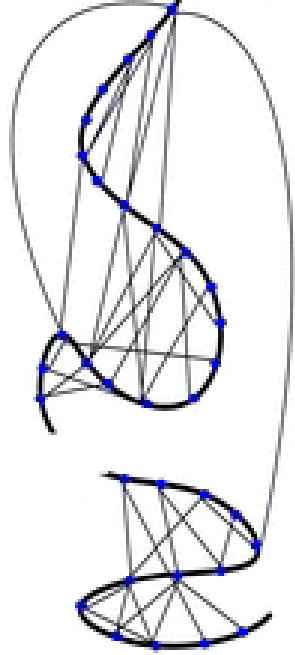
Combine with bupropion



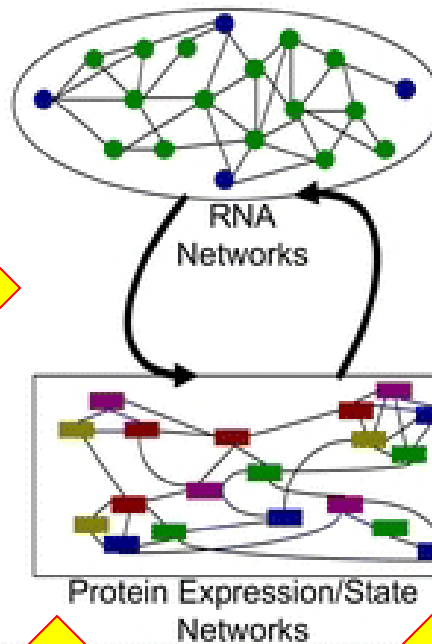
Mean Percentage Weight Change Progression in ITT Population



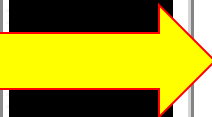
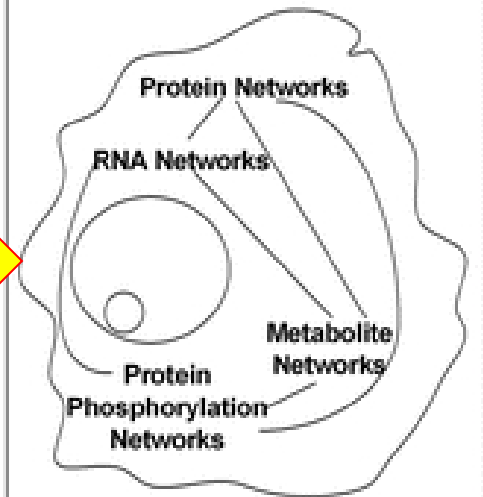
Genomics/Genetics Networks



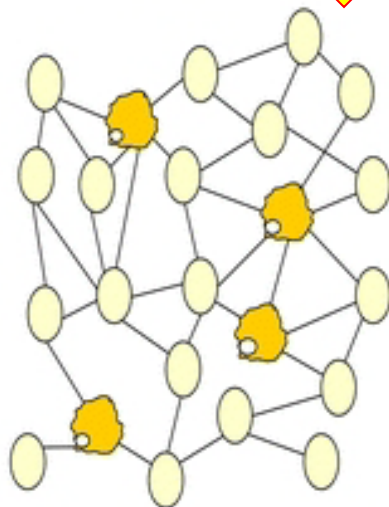
Molecular Networks



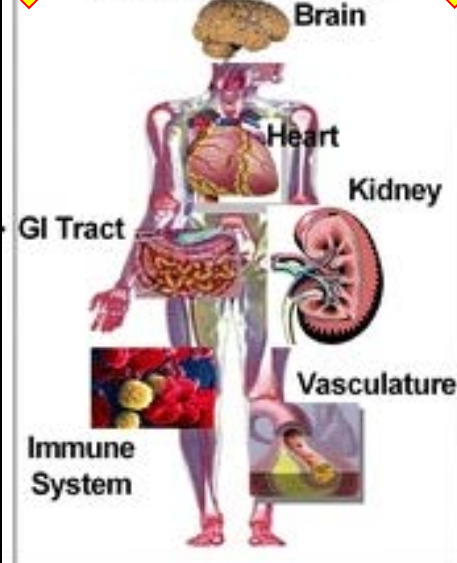
Cellular Networks



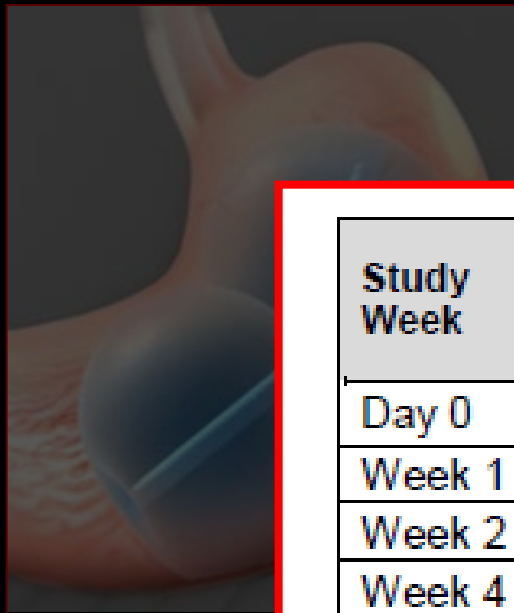
Tissue Networks



Organism Networks



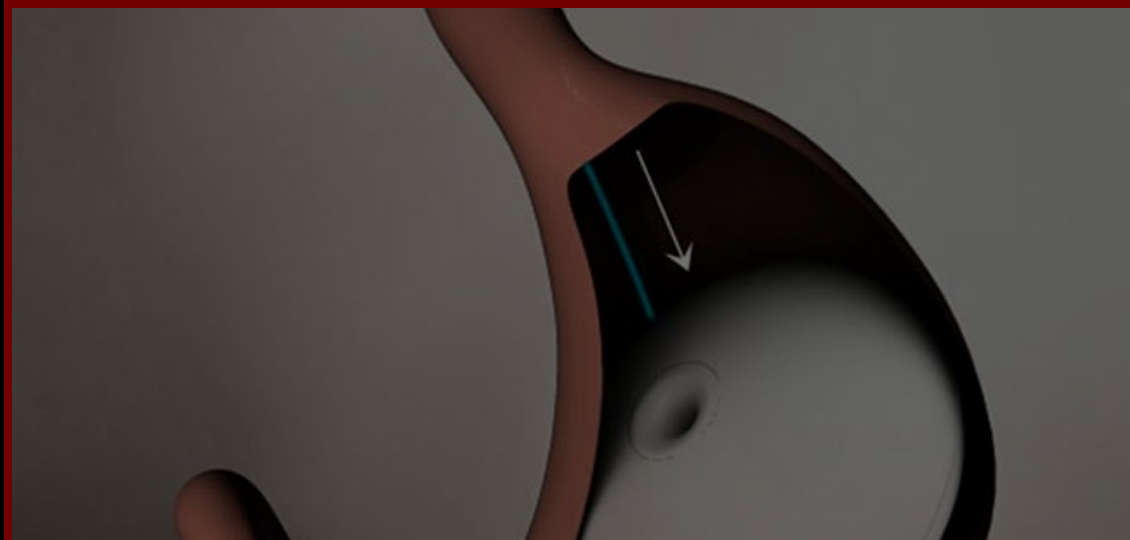
Devices: Gastric Balloon Systems



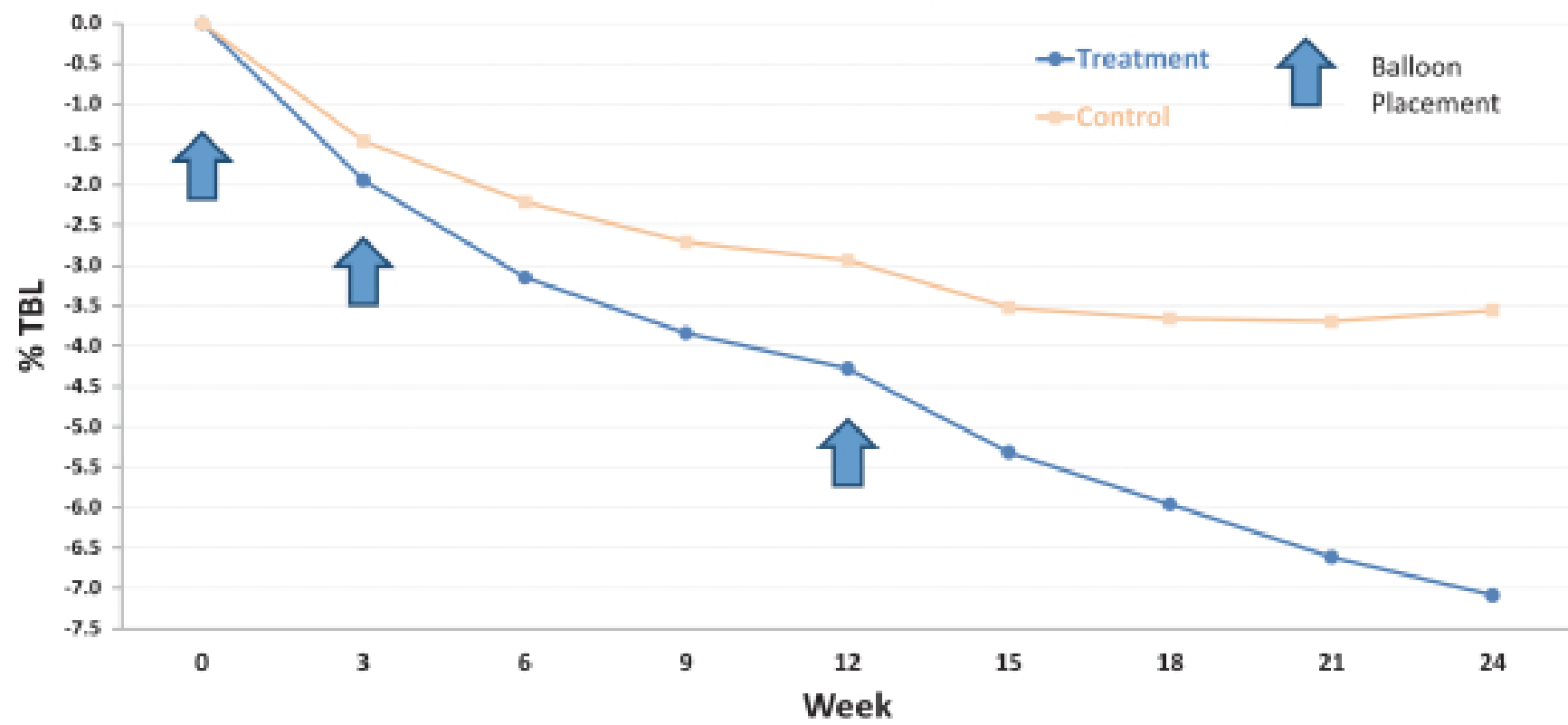
Study Week	ORBERA™ %TBWL	95% CI	Control %TBWL	95% CI
Day 0	0.9%	0.7-1.2	0%	-0.2-0.2
Week 1	3.5%	3.1-3.8	0.9%	0.5-1.2
Week 2	4.1%	3.8-4.5	1.4%	1.1-1.8
Week 4	5.5%	5.1-6.0	2.1%	1.5-2.7
Week 8	7.0%	6.4-7.6	2.6%	2.1-3.2
Week 12	7.9%	7.2-8.7	3.1%	2.5-3.8
Week 16	8.4%	7.5-9.3	3.3%	2.5-4.0
Week 20	8.8%	7.8-9.8	3.4%	2.6-4.2
Week 24	9.1%	8.1-10.2	3.3%	2.5-4.2
Week 26	10.2%	9.0-11.4	3.3%	2.4-4.2
Week 39	9.1%	7.9-10.3	3.4%	2.4-4.3
Week 52	7.6%	6.2-8.9	3.1%	2.0-4.1

ReShape D

Primary Effect	
Primary Endpoint #1 %EWL at 24 Weeks	Re
Intent-to-Treat Population	25. (21.95, 28.21%) (7.61, 14.98%) 18.67%



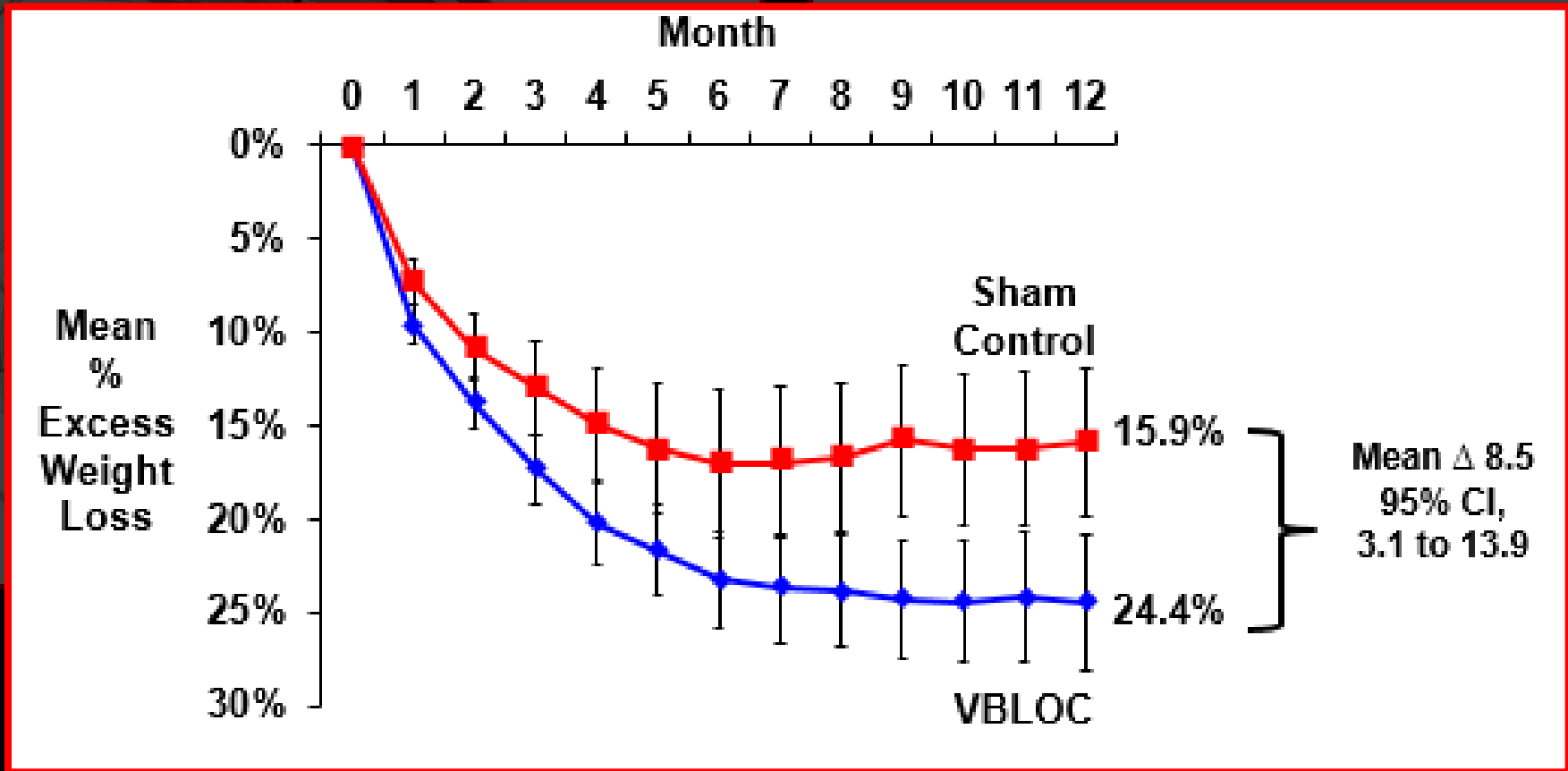
Percent Total Body Loss

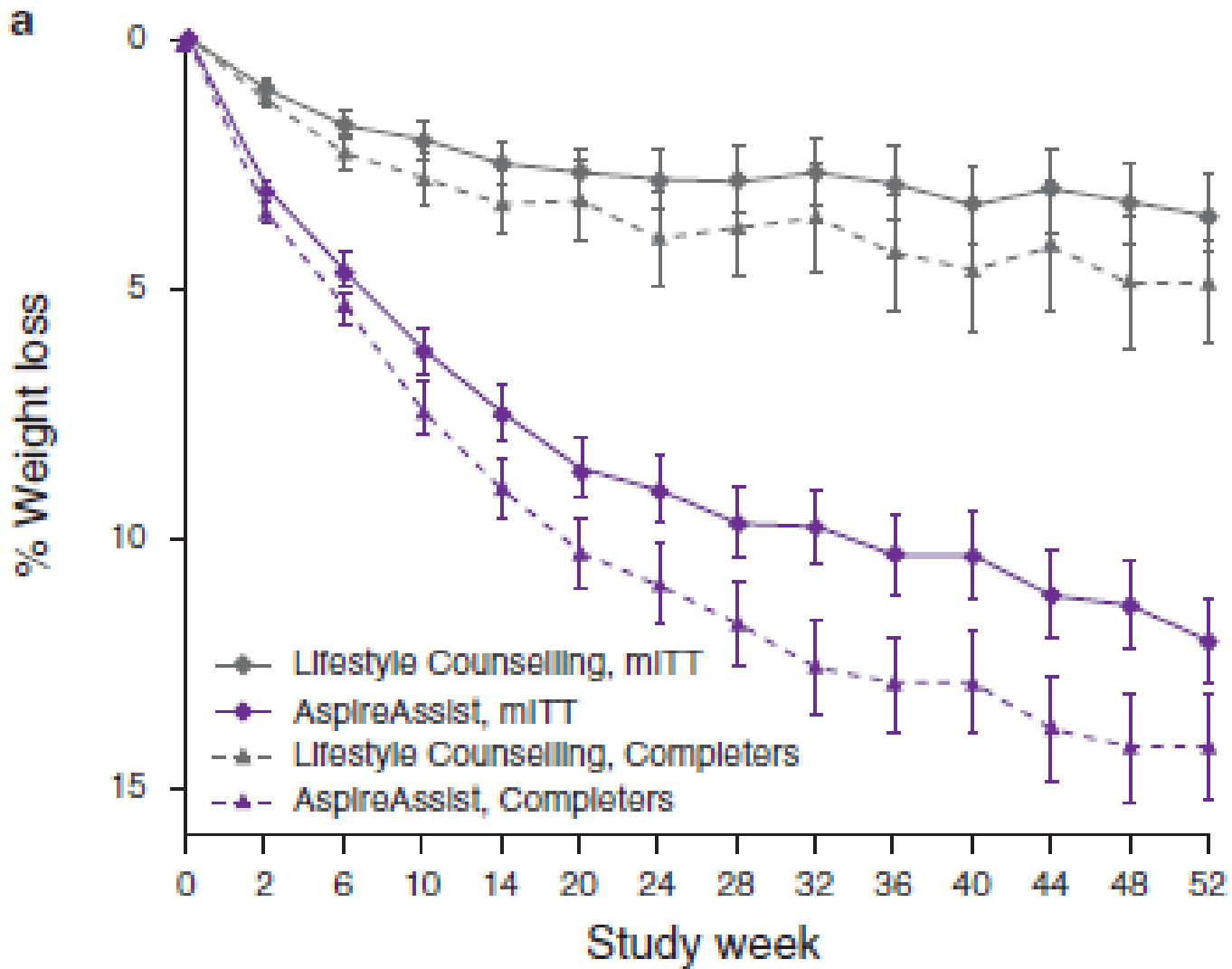


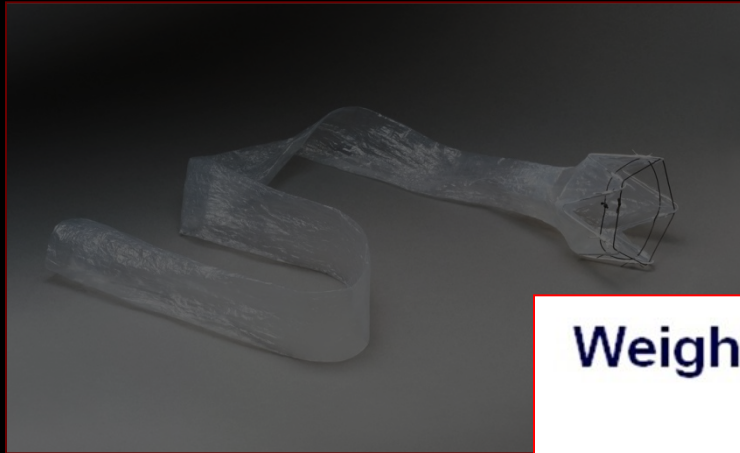
Anterior Vagus Nerve
Trunk with Electrode

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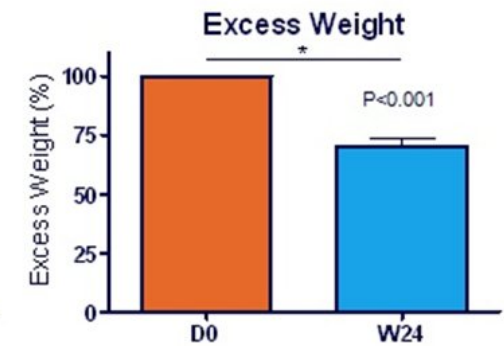
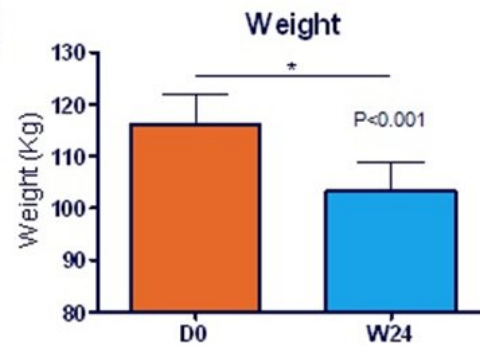




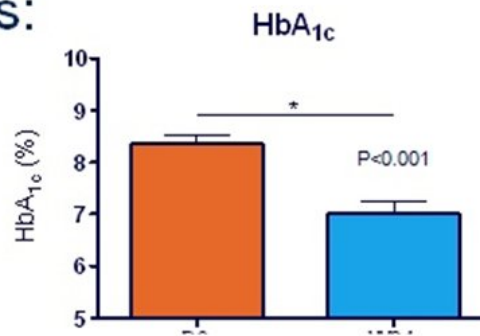
Endobarrier

Weight loss and diabetic improvement

Weight:



Diabetes:



Reduction of anti-diabetic medication in 16/17 patients

ABC Model of Behavioral Obesity Management

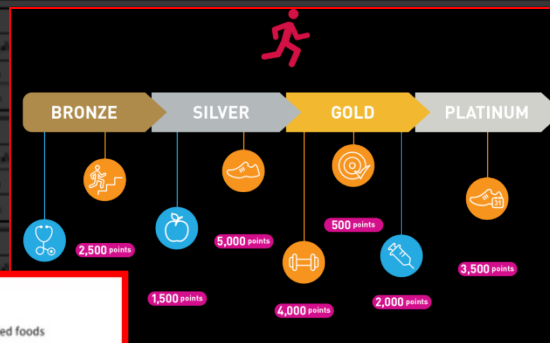


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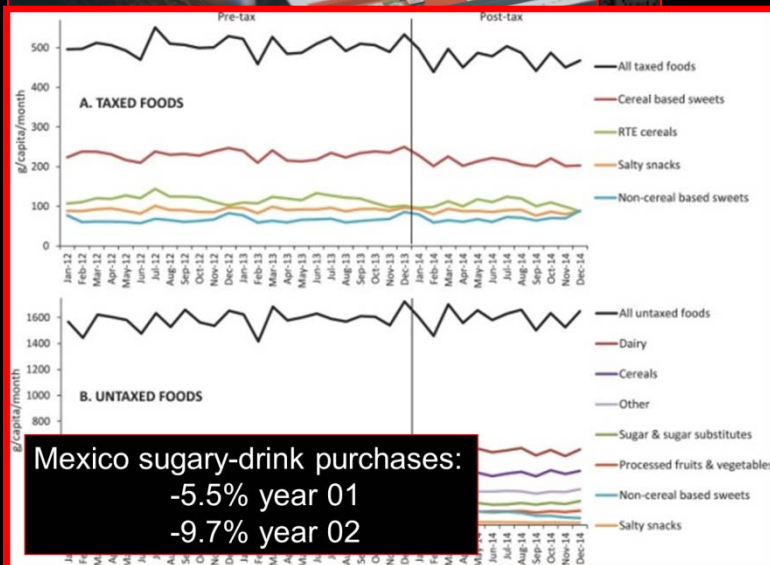
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We help employers and health plans tackle *chronic disease* in the most engaging, effective, and scalable way possible.

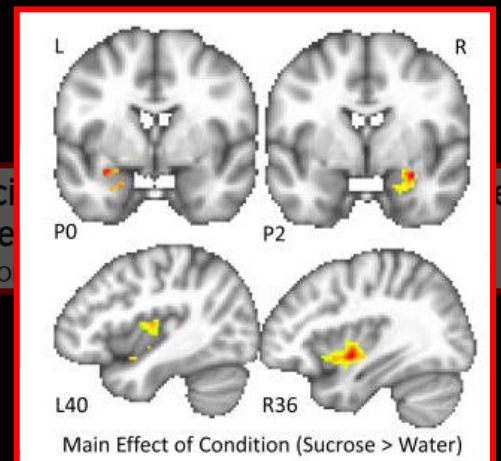
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HOURS OF SLEEP	BODY MASS INDEX	LEPTIN	GHRELIN
8			increases 14.9%
5	increases 3.6%	decreases 15.5%	



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