

# LIFESTYLE MEDICINE & GLP-1-RA MEDICATIONS FOR WEIGHT LOSS

EVIDENCE • RISKS • BENEFITS • BEST PRACTICES



**Jonathan Bonnet**  
MD, MPH, DipABLM, DipABOM



**Mahima Gulati**  
MD, DipABLM, FACLM, FACE



February 9, 2024 | 12-1pm EST  
Moderated by David L. Katz, MD, MPH



# My Patient population



ACLM Story Project: Remission of Type 2 Diabetes

His type 2 diabetes went into remission thanks to lifestyle medicine.

An ACLM Story Project

Watch on YouTube

AMERICAN COLLEGE OF Lifestyle medicine

Share

# My Patient population

- Palo Alto VA
  - Central & Northern California
  - La Vegas & Reno
  - Pacific Islands
- Demographics:
  - 80% white men, >50 yo
  - Increasing percentages of younger, women, black, and Hispanic veterans

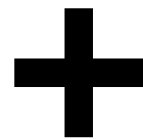
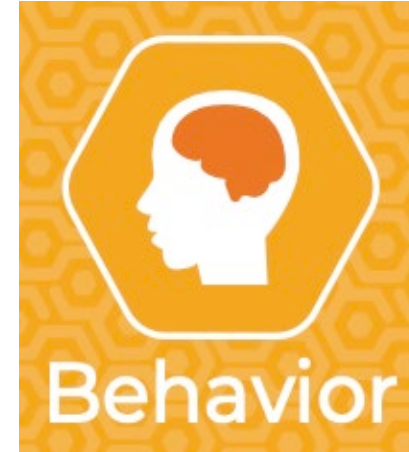


**VA**



U.S. Department  
of Veterans Affairs

# Our treatment approach combines obesity and lifestyle medicine treatments



U.S. Department  
of Veterans Affairs

# Oral weight loss medications

Medication	Study Duration	Mean Weight Loss %	Placebo Mean Weight Loss %	Average US Cost/Month	Estimated Minimum Price
Orlistat	52 weeks	8.8%	5.7%	\$100	\$7
Naltrexone-Bupropion	56 weeks	6.4%	1.9%	\$326	\$54
Topiramate-Phentermine	56 weeks	9.8%	1.2%	\$199	\$1-5
Semaglutide	26 weeks	5.3%	1.3%	\$578	?

\*Estimated Minimum Pricing: were calculated per 30-day course and include costs of active ingredients, excipients, formulation, 27% taxation, and a 10% profit margin

# Injection weight loss medications

Medication	Study Duration	Mean Weight Loss %	Placebo Mean Weight Loss %	Average US Cost/Month	Estimated Minimum Price
Liraglutide	56 weeks	8.0%	2.8%	\$1,418	\$50
Semaglutide	68 weeks	14.9%	2.4%	\$804	\$40
Tirzepatide	72 weeks	20.9%	3.1%	\$1,101	?

\*Estimated Minimum Pricing: were calculated per 30-day course and include costs of active ingredients, excipients, formulation, 27% taxation, and a 10% profit margin

## Obesity

# Cost-effectiveness of endoscopic, surgical and pharmacological obesity therapies: a microsimulation and threshold analyses

Monica Saumoy<sup>1</sup>, Devika Gandhi<sup>2</sup>, Seth Buller<sup>3</sup>, Shae Patel<sup>3</sup>, Yechezkel Schneider<sup>4</sup>, Gregory Cote<sup>5</sup>, Michael L Kochman<sup>6, 7</sup>,  Nikhil R Thiruvengadam<sup>2</sup>,  Reem Z Sharaiha<sup>8</sup>

Correspondence to Dr Reem Z Sharaiha, Gastroenterology & Hepatology, Weill Cornell Medical College, New York, New York, USA; [rzs9001@med.cornell.edu](mailto:rzs9001@med.cornell.edu)

- Authors developed a semi-Markov microsimulation model to compare the effectiveness of sleeve gastrectomy, endoscopic sleeve gastroplasty, semaglutide and lifestyle interventions for weight loss in 40 years old with class I/II/III obesity.
- Semaglutide was not cost-effective compared with lifestyle interventions for class I/II/III obesity ( incremental cost-effectiveness ratios or ICER US\$508 414/QALY, US\$420 483/QALY and US\$350 637/QALY). QALY= Quality Adjusted Life Year
- For semaglutide to be cost-effective compared with lifestyle intervention, it would have to cost less than US\$7462 (class III), US\$5847 (class II) or US\$5149 (class I) annually.
- For semaglutide to be cost-effective when compared with endoscopic bariatric procedure e.g. sleeve gastroplasty, it would have to cost less than US\$1879 (class III), US\$1204 (class II) or US\$297 (class I) annually.

# ARE THESE THESE DRUGS A COST EFFECTIVE SOLUTION?

WSJ Print Edition

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## Employers Cut Off Insurance Coverage For Obesity Drugs

BY PETER LOFTUS

So many people have turned to drugs used for weight loss that some employers are cutting off insurance coverage to head off climbing bills.

Spending on the popular drugs, which belong to the class including Ozempic and

After its costs for the drugs more than tripled over the past 18 months to about \$5 million a month, the University of Texas System said it would end insurance coverage of Novo Nordisk's Wegovy and Saxenda for its employees and others covered by its health plans effective Sept. 1.

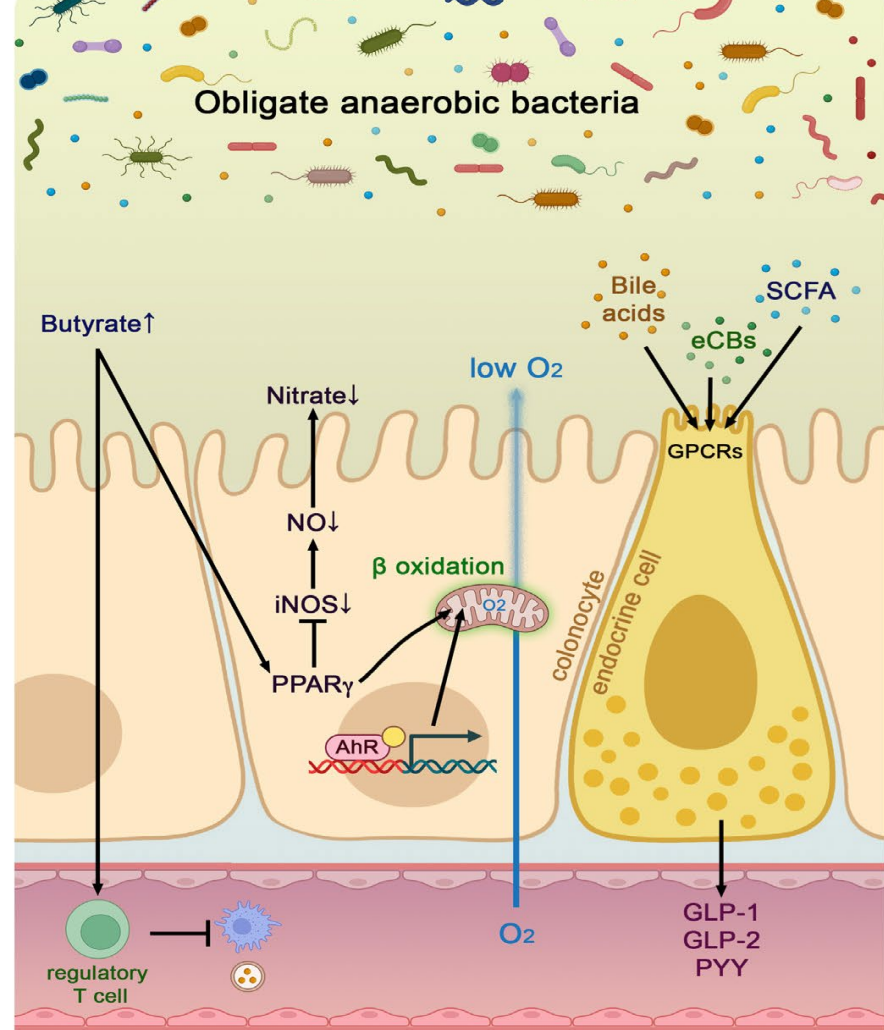


# Annual pharmaceutical spending on all drugs vs. semaglutide for adults with obesity

\$576.9 billion  
*All* drugs

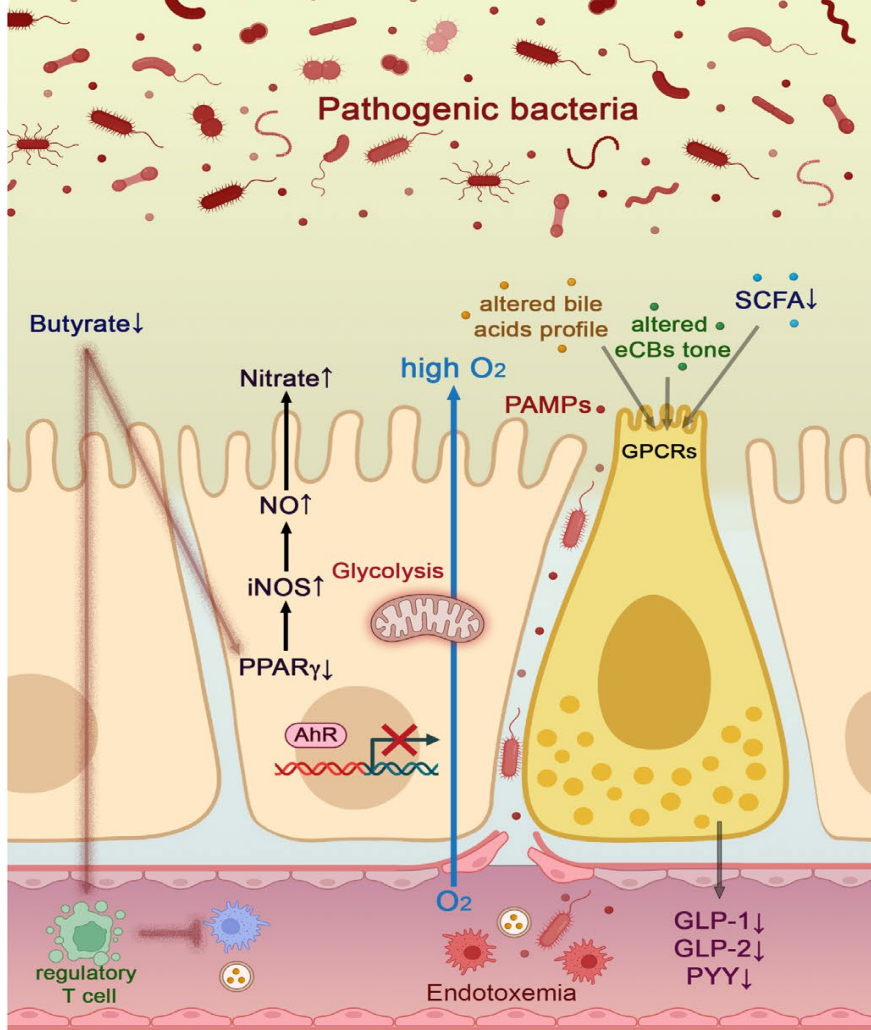


\$1.7 trillion /yr



**Healthy gut**  
“normal gut barrier”

- Glycemia ↓
- Insulin resistance ↓
- inflammation ↓
- Hepatic steatosis ↓
- Food intake ↓
- plasma lipids ↓



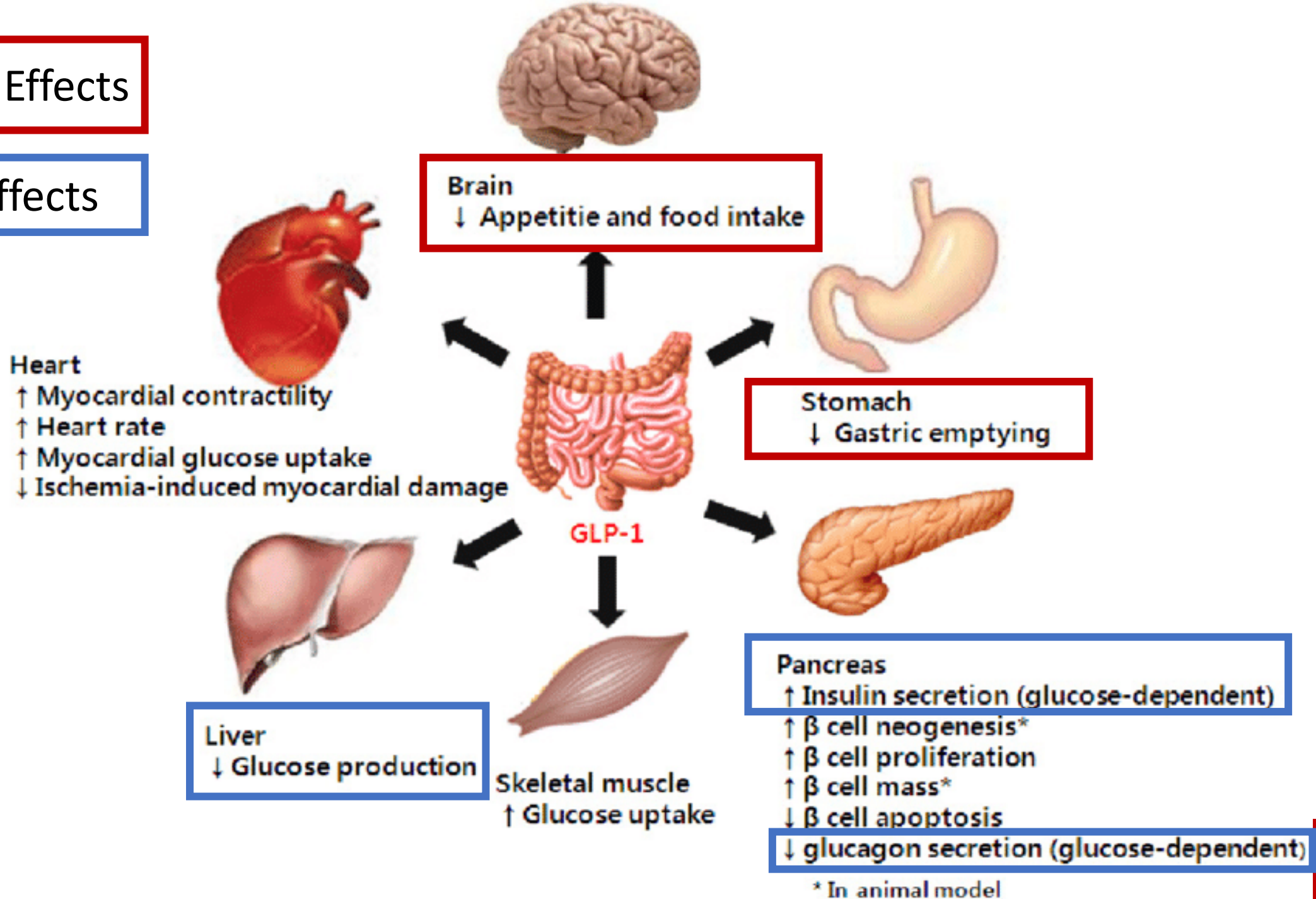
**Leaky gut**  
“impaired gut barrier”

- |                       |                       |                       |                       |
|-----------------------|-----------------------|-----------------------|-----------------------|
|                       |                       |                       |                       |
| ↑ Inflammation        | ↑ Fat mass            | ↑ Inflammation        | ↑ Inflammation        |
| ↓ Insulin sensitivity | ↑ Inflammation        | ↓ Insulin sensitivity | ↓ Insulin sensitivity |
| ↑ Oxidative stress    | ↓ Insulin sensitivity |                       | ↑ Food intake         |
| ↑ Steatosis           | ↑ Oxidative stress    |                       |                       |

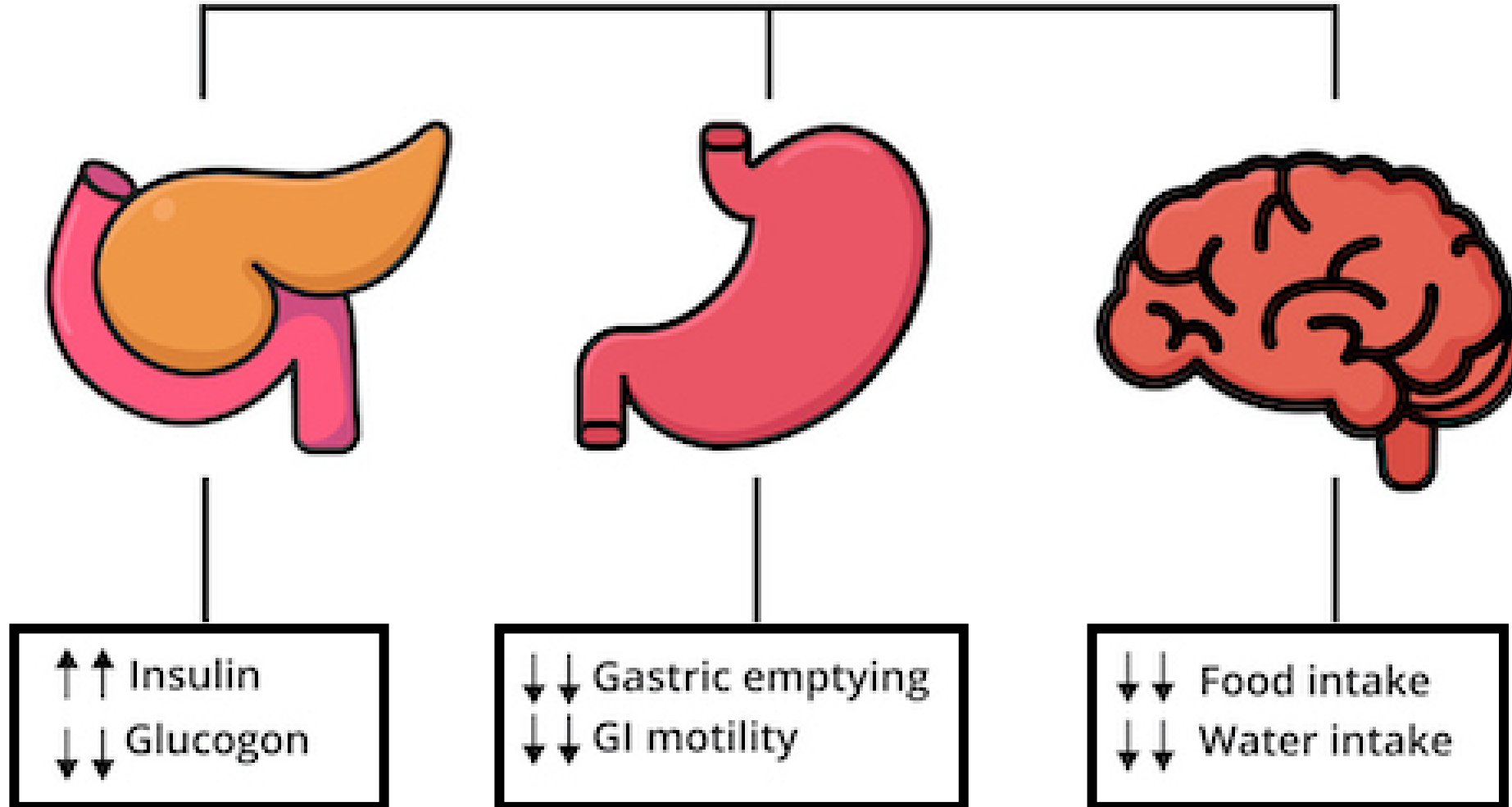
de Vos WM, Tilg H, Van Hul M, et al. *Gut* 2022;**71**:1020–1032.

## Weight Loss Effects

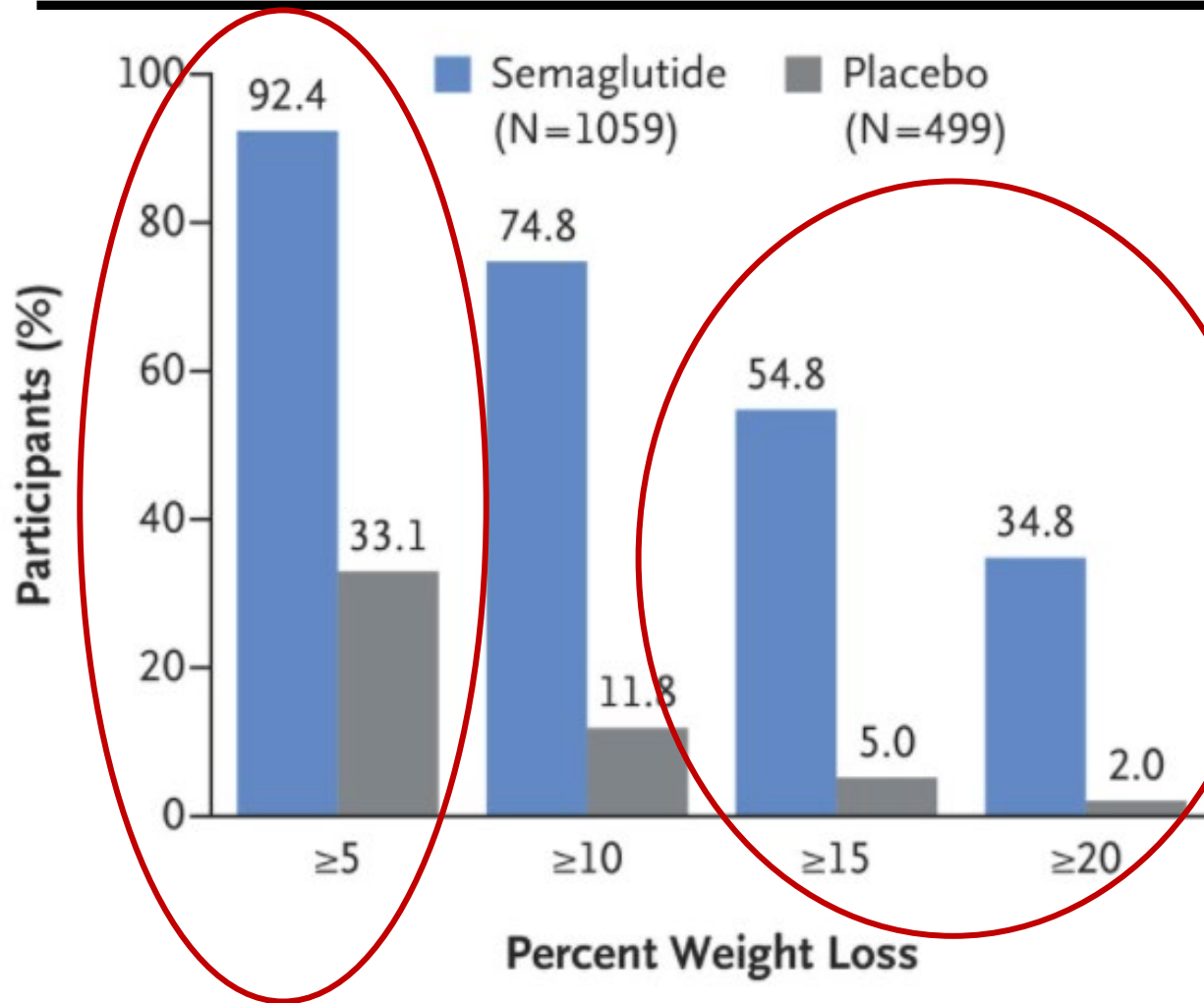
## Diabetes Effects



# GLP-1 has widespread effects, but primarily intestines, pancreas, stomach, & brain



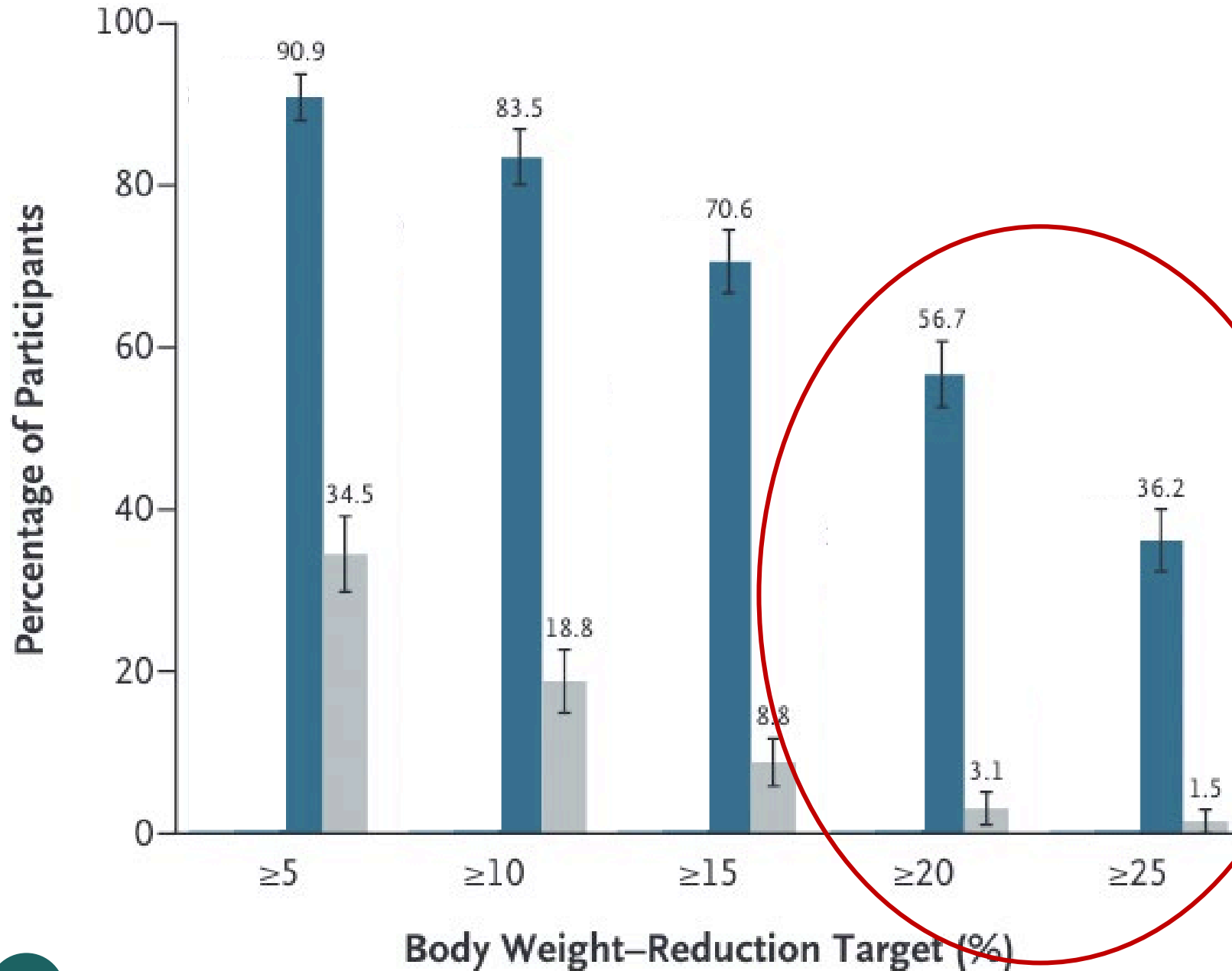
# Average weight loss on Semaglutide is 10-16%, but...



Some people lose more:

- **55%** lose  $\geq 15\%$  of body weight
- **35%** lose  $\geq 20\%$  of body weight

# Tirzepatide Weight Loss



Avg weight  
loss **20.9%**

Shifted one weight category  
← to the right

# Health benefits of weight loss vary based on percentage of body weight lost

Condition	2.5%	5-10%	10%+
Prediabetes Progression	Yes	Yes	-
Type 2 Diabetes Improvement	Yes	Yes	Yes
Triglyceride Improvement	Yes	Yes	Yes
HDL-Cholesterol Increase	-	Yes	Yes
Obstructive Sleep Apnea	-	-	Yes
Knee Pain	-	Yes	-
Fatty Liver	-	Yes	Yes
Quality of Life	-	Yes	Yes
Depression	-	Yes	-
PCOS	Yes	Yes	-
Mortality	-	-	Yes
Health Care Costs	-	Yes	-

# OR10-01 Discordance Between Body Mass Index and Dual-energy X-ray Absorptiometry Based Adiposity Measures Among United States Adults

Aayush Visaria, MD, MPH, Trisha Sindhu, BS, Tina Dharamdasani, MS

*Journal of the Endocrine Society*, Volume 7, Issue Supplement\_1, October-November 2023, bvad114.007, <https://doi.org/10.1210/jendso/bvad114.007>

**Published:** 05 October 2023

- The authors identified non-pregnant U.S. adults 20-59 years from the 2011-2018 National Health and Nutrition Examination Survey (NHANES) with whole body DEXA scan data.
- BMI was categorized into ethnicity-specific (non-Asian: underweight<18.5, normal=18.5-24.9, overweight=25-29.9, obese $\geq$ 30 kg/m<sup>2</sup>, Asian: <18.5, 18.5-22.9, 23-27.4, 27.5+) categories.
- DEXA scans were performed using Hologic Discovery densitometers, analyzed by Hologic software (APEX v4.0), and verified by expert reviewers.
- Total body fat % (BF%) was calculated.



# RESULTS:

- Among 9,784 participants (mean age 39y [SD, 11], 61% NHW, 49% female), 36% had BMI $\geq$ 30 and 74% had obesity per BF%.
- Among normal BMI adults, 44% of NHW, 27% of NHB, 49% of Hispanic, and 49% of Asians had obesity as per BF% ( $p<0.001$ ).
- These suggest that BMI alone may not be sufficient to detect metabolically unhealthy adiposity, especially in Asian Americans and Hispanics.

# SURMOUNT-1 TRIAL NEJM 2022

**Table 1. Demographic and Clinical Characteristics of the Participants at Baseline.\***

Characteristic	Tirzepatide, 5 mg (N=630)	Tirzepatide, 10 mg (N=636)	Tirzepatide, 15 mg (N=630)	Placebo (N=643)	Total (N=2539)
Age — yr	45.6±12.7	44.7±12.4	44.9±12.3	44.4±12.5	44.9±12.5
Female sex — no. (%)	426 (67.6)	427 (67.1)	425 (67.5)	436 (67.8)	1714 (67.5)
Race or ethnic group — no. (%)†					
American Indian or Alaska Native	56 (8.9)	58 (9.1)	59 (9.4)	58 (9.0)	231 (9.1)
Asian	68 (10.8)	71 (11.2)	66 (10.5)	71 (11.0)	276 (10.9)
Black or African American	48 (7.6)	47 (7.4)	51 (8.1)	55 (8.6)	201 (7.9)
White	447 (71.0)	452 (71.1)	443 (70.3)	450 (70.0)	1792 (70.6)
Native Hawaiian or other Pacific Islander	2 (0.3)	2 (0.3)	3 (0.5)	2 (0.3)	9 (0.4)
Multiple	9 (1.4)	6 (0.9)	8 (1.3)	7 (1.1)	30 (1.2)

# STEP-1 TRIAL (SEMAGLUTIDE) NEJM 2021

**Table 1. Demographic and Clinical Characteristics of the Participants at Baseline.\***

Characteristic	Semaglutide (N=1306)	Placebo (N=655)
Age — yr	46±13	47±12
Female sex — no. (%)	955 (73.1)	498 (76.0)
Race or ethnic group — no. (%)†		
White	973 (74.5)	499 (76.2)
Asian	181 (13.9)	80 (12.2)
Black or African American	72 (5.5)	39 (6.0)
Other	80 (6.1)	37 (5.6)
Hispanic or Latino ethnic group — no. (%)†	150 (11.5)	86 (13.1)

	Placebo N = 1261 %	WEGOVY N = 2116 %
Nausea	16	44
Diarrhea	16	30
Vomiting	6	24
Constipation	11	24
Abdominal Pain	10	20
Headache	10	14
Fatigue	5	11
Dyspepsia	3	9
Dizziness	4	8
Abdominal Distension	5	7
Eructation	<1	7
Hypoglycemia in T2DM	2	6
Flatulence	4	6
Gastroenteritis	4	6
GERD	3	5

# Semaglutide Side Effects



# Update on FDA's ongoing evaluation of reports of suicidal thoughts or actions in patients taking a certain type of medicines approved for type 2 diabetes and obesity

*Preliminary evaluation does not suggest a causal link*

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01-11-2024 FDA Drug Safety Communication

# One concern was loss of lean body mass

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	Average Body Weight Loss	Fat Mass Loss	Lean Mass Loss
Traditional Weight Loss	5-10%	75%	25%
New Injection Medications	15-24%	60% (10.4 kg)	40% (6.9 kg)



# BLACK BOX WARNING

## **WARNING: RISK OF THYROID C-CELL TUMORS**

*See full prescribing information for complete boxed warning.*

- **In rodents, semaglutide causes thyroid C-cell tumors at clinically relevant exposures. It is unknown whether WEGOVY causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans as the human relevance of semaglutide-induced rodent thyroid C-cell tumors has not been determined (5.1, 13.1).**
- **WEGOVY is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Counsel patients regarding the potential risk of MTC and symptoms of thyroid tumors (4, 5.1).**

## Has FDA found illegally marketed semaglutide online?

Yes. FDA vigilantly monitors the internet for fraudulent or unapproved products and has issued [warning letters](#) to stop the distribution of illegally marketed semaglutide. These drugs may be counterfeit, which means they could contain the wrong ingredients, contain too little, too much or no active ingredient at all, or contain other harmful ingredients.

## Has FDA found counterfeit Ozempic in the U.S.?

FDA is aware and is investigating reports of counterfeit Ozempic being marketed in the U.S. The agency investigates any report of suspect [counterfeit](#) drugs to determine the public health risks and the appropriate regulatory response, and remains vigilant in protecting the U.S. drug supply from these threats.

## How should patients protect themselves?



(SEMAGLUTIDE)

Safety-related Labeling Changes Approved by FDA Center for Drug Evaluation and Research (CDER)

[Download Data](#)

[Collapse All](#)

09/22/2023 (SUPPL-20)

Approved Drug Label (PDF)

#### 6 Adverse Reactions

##### 6.3 Postmarketing Experience

*Additions and/or revisions underlined:*

The following adverse reactions have been reported during post-approval use of semaglutide, the active ingredient of OZEMPIC. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

*Gastrointestinal Disorders: Ileus*

*Hypersensitivity:* anaphylaxis, angioedema, rash, urticaria.

*Hepatobiliary:* cholecystitis, cholecystectomy

## OTHER LESS COMMON SIDE EFFECTS:

- **Diabetic Retinopathy Complications** in Patients with Type 2 Diabetes: Has been reported in trials with semaglutide. Patients with a history of diabetic retinopathy should be monitored
- **Acute Kidney Injury:** Has occurred. Monitor renal function when initiating or escalating doses of WEGOVY® in patients reporting severe adverse gastrointestinal reactions or in those with renal impairment reporting severe adverse gastrointestinal reactions
- **Acute Pancreatitis/ Pancreatic malignancy:** Has occurred in clinical trials. Discontinue promptly if pancreatitis is suspected. Do not restart if pancreatitis is confirmed
- **Gastroparesis** (next slide)

Research Letter

October 5, 2023

### Risk of Gastrointestinal Adverse Events Associated With Glucagon-Like Peptide-1 Receptor Agonists for Weight Loss

Mohit Sodhi, MSc<sup>1</sup>; Ramin Rezaeianzadeh, BSc<sup>1</sup>; Abbas Kezouh, PhD<sup>2</sup>; et al

Author Affiliations | Article Information

<sup>1</sup>Faculty of Medicine, University of British Columbia, Vancouver, British Columbia, Canada

<sup>2</sup>StatExpert Ltd, Laval, Quebec, Canada

<sup>3</sup>Department of Ophthalmology and Visual Sciences and Medicine, University of British Columbia, Vancouver, Canada

JAMA. 2023;330(18):1795-1797. doi:10.1001/jama.2023.19574

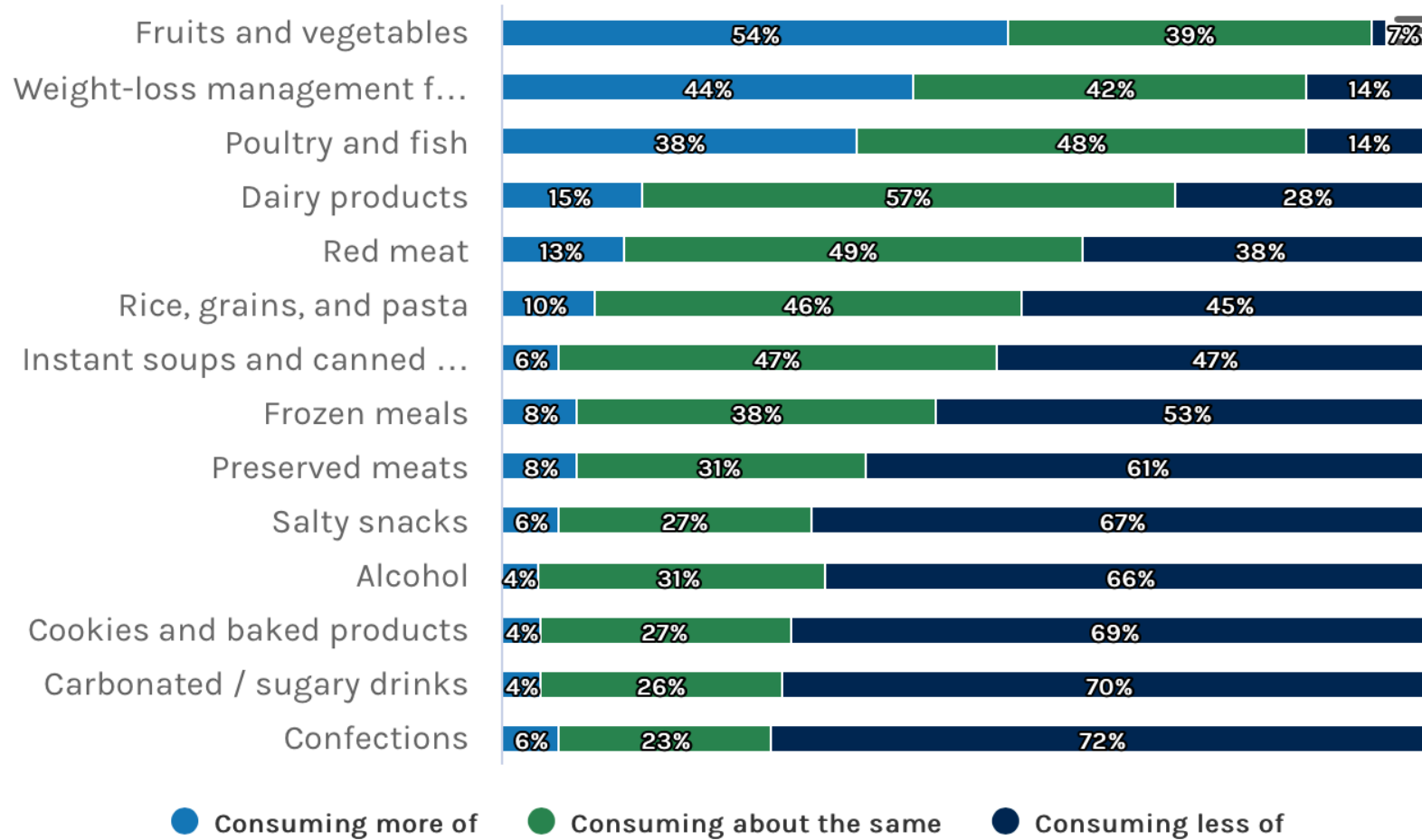
Table 1. Characteristics of Semaglutide, Liraglutide, and Bupropion-Naltrexone Users

	Semaglutide	Liraglutide	Bupropion-naltrexone
No.	613	4144	654
Age, mean (SD), y	53.5 (11.9)	51.3 (12.2)	45.2 (11.1)
Sex, %			
Male	55.8	61.0	82.4
Female	44.2	39.0	17.6
Follow-up, median (IQR), y	0.6 (0.2-1.1)	1.7 (0.8-3.1)	1.7 (0.7-2.9)
Covariates, %			
Alcohol <sup>a</sup>	2.9	0.4	0.6
Smoking <sup>a</sup>	8.7	12.5	9.9
Hyperlipidemia <sup>b</sup>	55.6	22.8	11.5
Abdominal surgery <sup>c</sup>	0	0.12	0
US region			
Northeast	18.3	25.8	18.3
Southeast	34.6	26.1	34.6
Midwest	33.1	30.3	33.1
Southwest	0.2	2.6	0.3
West	13.9	15.3	12.4
Incidence (No.) <sup>d</sup>			
Biliary disease	11.7 (5)	18.6 (162)	12.6 (16)
Pancreatitis	4.6 (2)	7.9 (71)	1.0 (1)
Bowel obstruction	0	8.1 (73)	1.7 (2)
Gastroparesis	9.1 (4)	7.3 (66)	3.1 (3)

# Could Obesity Drugs Take a Bite Out of the Food Industry?

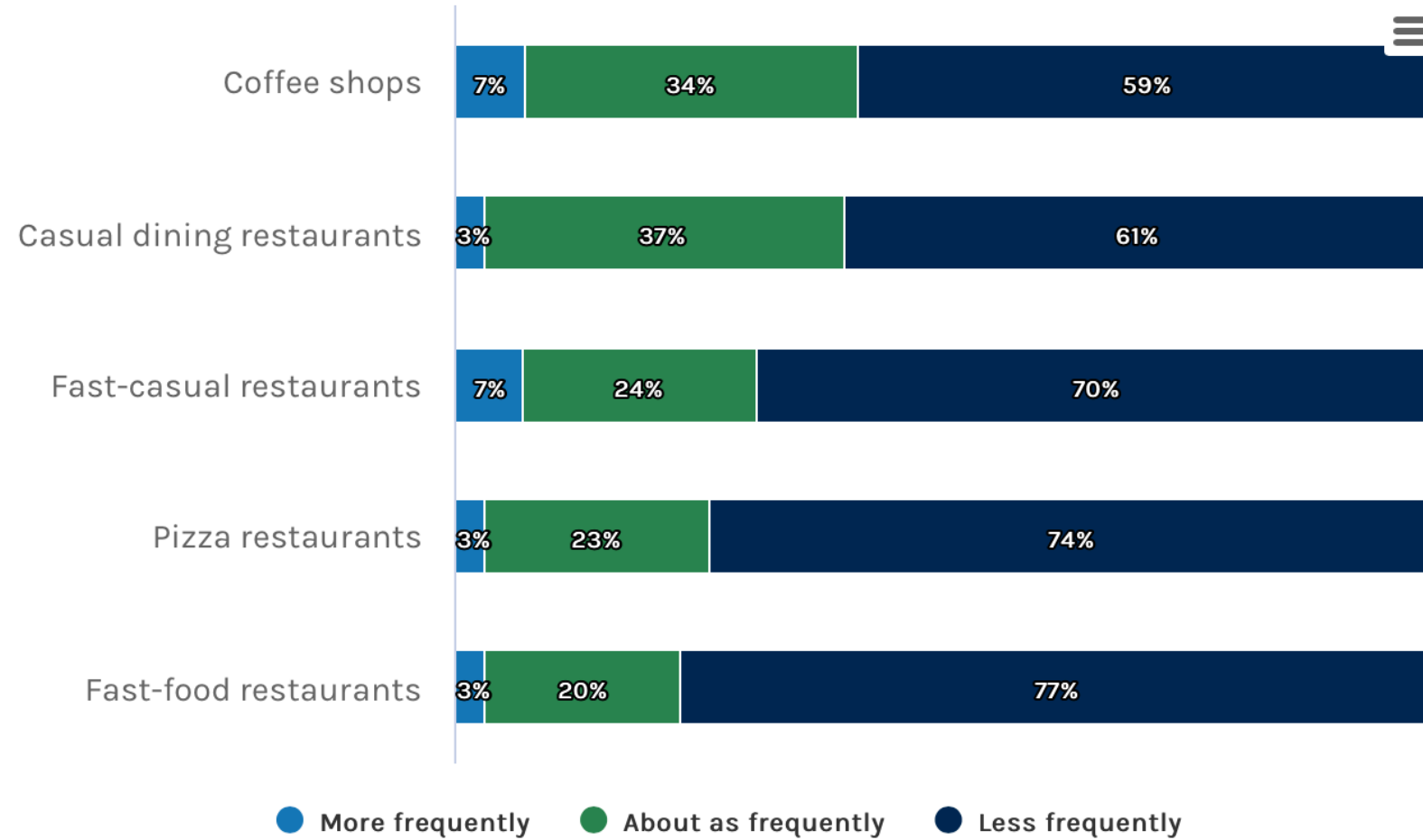
With the use of obesity medicines accelerating, millions of people could be eating less food overall and shunning unhealthy fare. This could have long-term impacts across food-related industries.

## Exhibit 10: Healthier categories see a boost in consumption by patients after starting on AOM



Source: Morgan Stanley Research (including estimates)

## Exhibit 11: Patients report the most significant changes to fast food and pizza restaurant trips



Source: Morgan Stanley Research (including estimates)

# More transformation

- Boom in telehealth and use of digital health apps
- Use of AI (Artificial Intelligence) for nutrition coaching, especially for use by employers
- But my concern is that this is NOT enough, especially in populations where chronic illness burden is the highest (high SDOH)

**FACTORS  
CONTRIBUTING  
TO OBESITY**

**Genetics**

**Biology**

(hormonal &  
metabolic responses)

**Behaviors**

(physical activity,  
food intake, sleep habits)

**Psycho-social**

(quality of life,  
societal bias/stigma)

**Social Determinants  
of Health**

(education, income stabi  
health care access/quali  
built environment/  
neighborhood, social/  
community context)

*Courtesy of Northeast Business Group on Health*





Obesity stems from a complex interplay of micro- and macro-environment in the context of a holobiont

- Thus, a multifaceted problem needs a multidimensional solutions approach (“all of society, all of community, all pillars, all hands-on deck”)


# A vital systems biology concept:

- **Lifestyle changes** (addressing the root cause of the problem) aka “whole systems pathway therapy” will effect global change in the holobiont (whole organism) through multiple molecular pathways (oxidative stress, inflammatory cascades, epigenetic changes, mitochondrial function, microbiome changes, metabolomic (glycation/ cell membrane instability) etc.)
- Whereas specific **drugs** (“single/ dual/ triple agonist/ pathway drugs”) can only address a specific molecular pathway i.e. GLP1/GIP/ Glucagon is only addressing one component of the obesity matrix

### Food Frequency Questionnaire

	Servings per day	OR	Servings per week
Leafy Green Vegetables: 1 cup raw, 1/2 cup cooked			
Cruciferous Vegetables: (Kale, Broccoli, Cauliflower, etc.): 1/2 cup chopped			
Other Vegetables: 1/2 cup chopped (raw or cooked)			
Berries: 1/2 cup fresh or frozen, 1/4 cup dried			
Other Fruit: 1 medium fruit, 1 cup chopped fruit, 1/4 cup dried			4
Legumes (Beans): 1/2 cup cooked beans, 1 cup fresh peas, 1/4 cup hummus or bean dip			
Nuts and Seeds: 1/4 cup nuts or seeds, 2 TBS nut or seed butter			1-2
Whole Grains: 1/2 cup hot cereal (oatmeal), cooked grains, pasta or corn kernels, 1 cup cold cereal, 1 slice bread or tortilla, 1/2 bagel, 3 cups popped corn			2
Ground Flax Seeds: 1 TBS			
Mushrooms: 1 cup fresh, 1/4 cup dried			
Spices			7
Meat: 2-3 ounces	2		
Processed Meat/Deli Meat: 2 slices of bacon, 1.5-2 ounces of deli meat			5
Poultry: 2-3 ounces			2
Fish: 2-3 ounces			
Dairy: 1 cup milk or yogurt, 1.5-2 ounces cheese	2		
Eggs: 1 egg			2
Processed Snack Foods			15
Fried Foods			10
Meal Replacement products (shakes, bars, etc)			2
Foods with artificial sweeteners			7
Unsweetened beverages (water, tea, coffee): 12 ounces			7
Sweetened beverages (soda, sweet tea, energy drinks, etc): 12 ounces			
Alcoholic beverages: wine (5 ounces), beer (12 ounces), spirits (1.5 ounces)			

How much exercise per day/week? *3-4 days*

 American College of Lifestyle Medicine ©2018 American College of Lifestyle Medicine

# Lifestyle Endocrinology Program at Middlesex Health

- Shared Medical Appointments (“SMA”) format.
- Any patient of our practice is welcome to attend these SMAs, which are run by me with my Certified Diabetes Educator.
- TAILORED CURRICULUM FOR EACH SMA, “Delta plus” debriefing model.
- Curated resources from American College of Lifestyle Medicine, VA Whole health, Loma Linda University, MGH, etc.

# The program is multicomponent: and involves all 6 pillars of the ACLM

1. Regular visits with Certified Diabetes Educator;
2. education about digital apps etc. for calorie counting/ macronutrient tracking etc.;
3. physician-guided DM2 medication management/ (de-escalation as indicated);
4. cooking videos & demos
5. emphasis on **community resources**: we have referral resources in place for exercise (PT); Sleep medicine; Smoking cessation counseling program; mindfulness and compassion center for MBSR (Mindfulness based stress reduction); behavioral health; integrative medicine etc.

## 2 Very Important Distinctions:

Prevention of  
obesity vs  
treatment of  
obesity

Individual health  
vs population  
health

# VA offers MOVE! weight management program and our clinic adds medical piece

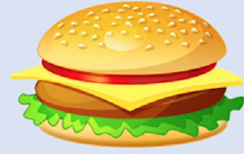
- Individual and group appointments
- All 6 pillars are explored during individual sessions
- SMA sessions:
  1. **Physical Activity:** including PT led exercise demonstration
  2. **Behavioral Medicine:** behavioral psychologist led mindful eating exercise
  3. **Diet:** RD led content including calorie density gameOptional Maintenance Groups

VA



U.S. Department  
of Veterans Affairs

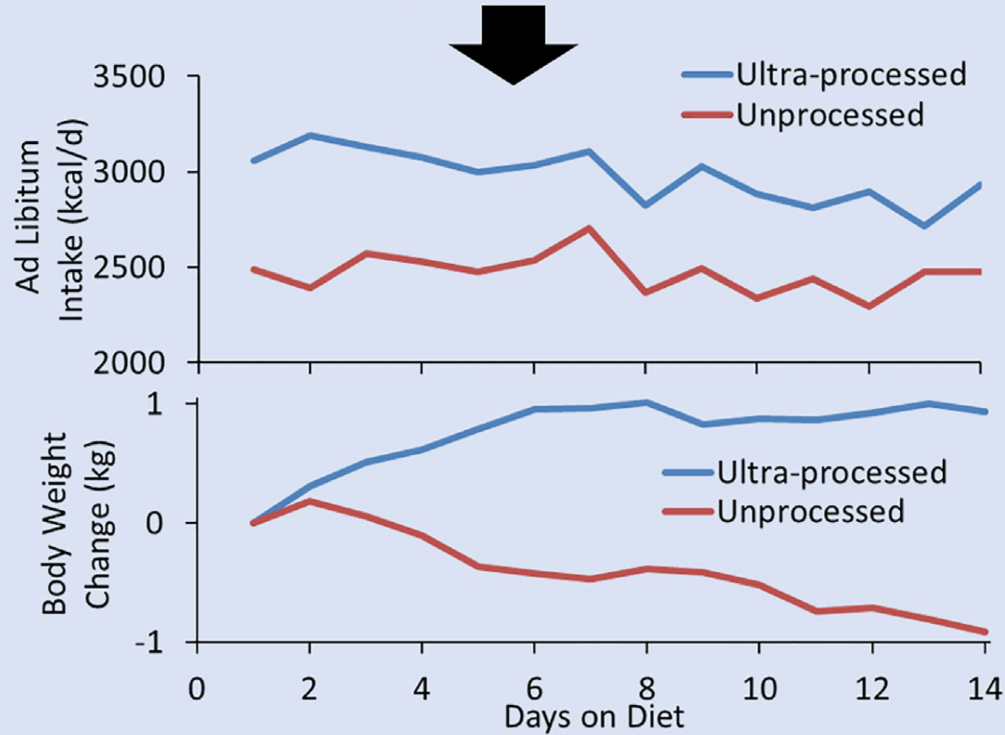
### Ultra-processed Diet



### Unprocessed Diet



Diets were presented in random order and matched for provided calories, sugar, fat, fiber, and macronutrients



Hall KD, *Cell Metab.* 2019;30(1):67-77.e3.

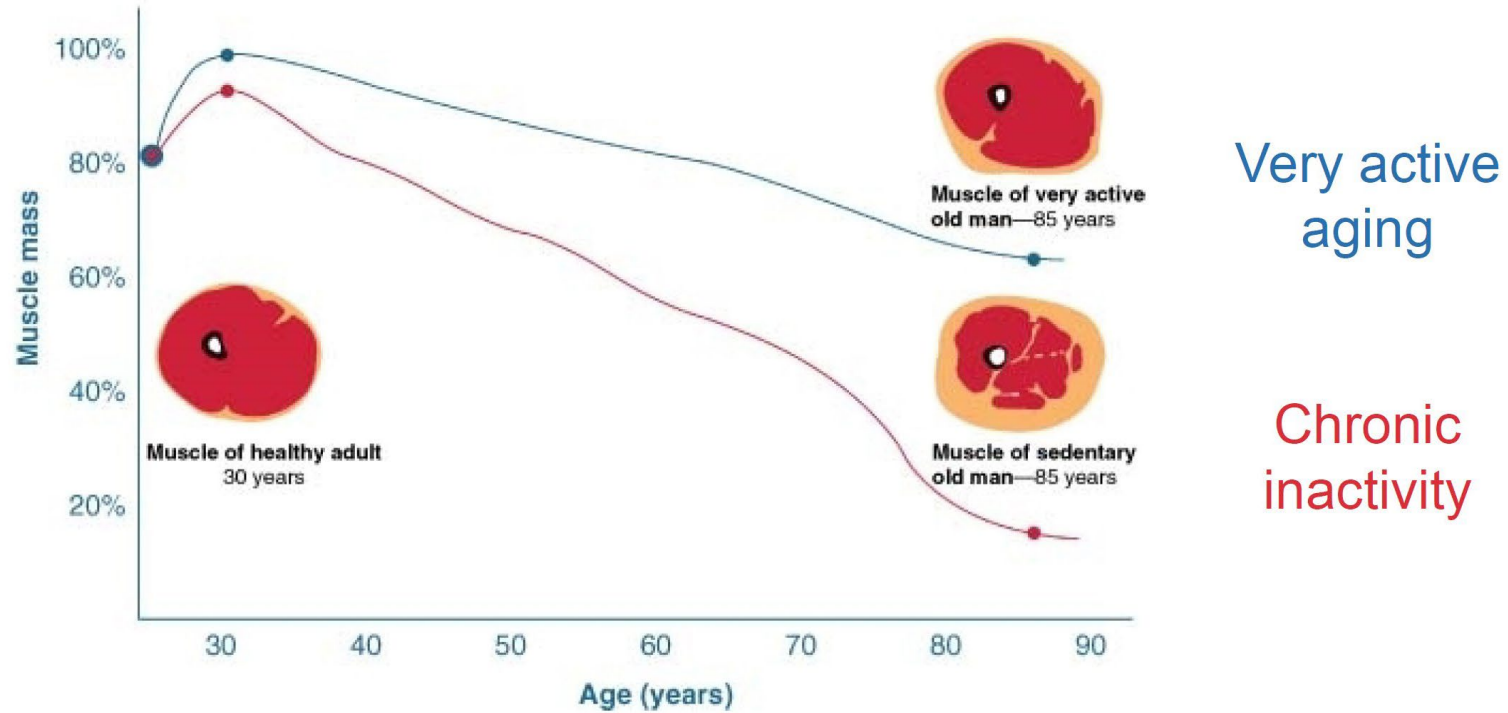




# MY CONCLUSION FROM THIS STUDY:

Quality of food, determines  
quantity of food

# Your lifestyle make a difference

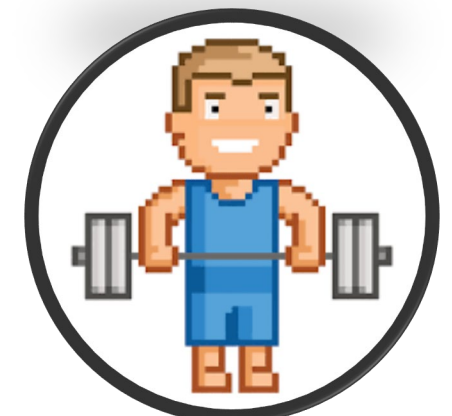
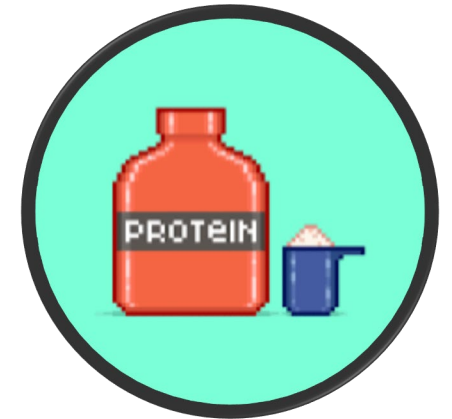


Major Reference Works, Pages: 1281-1304, First published: 19 September 2019, DOI: (10.1002/cphy.c190002)

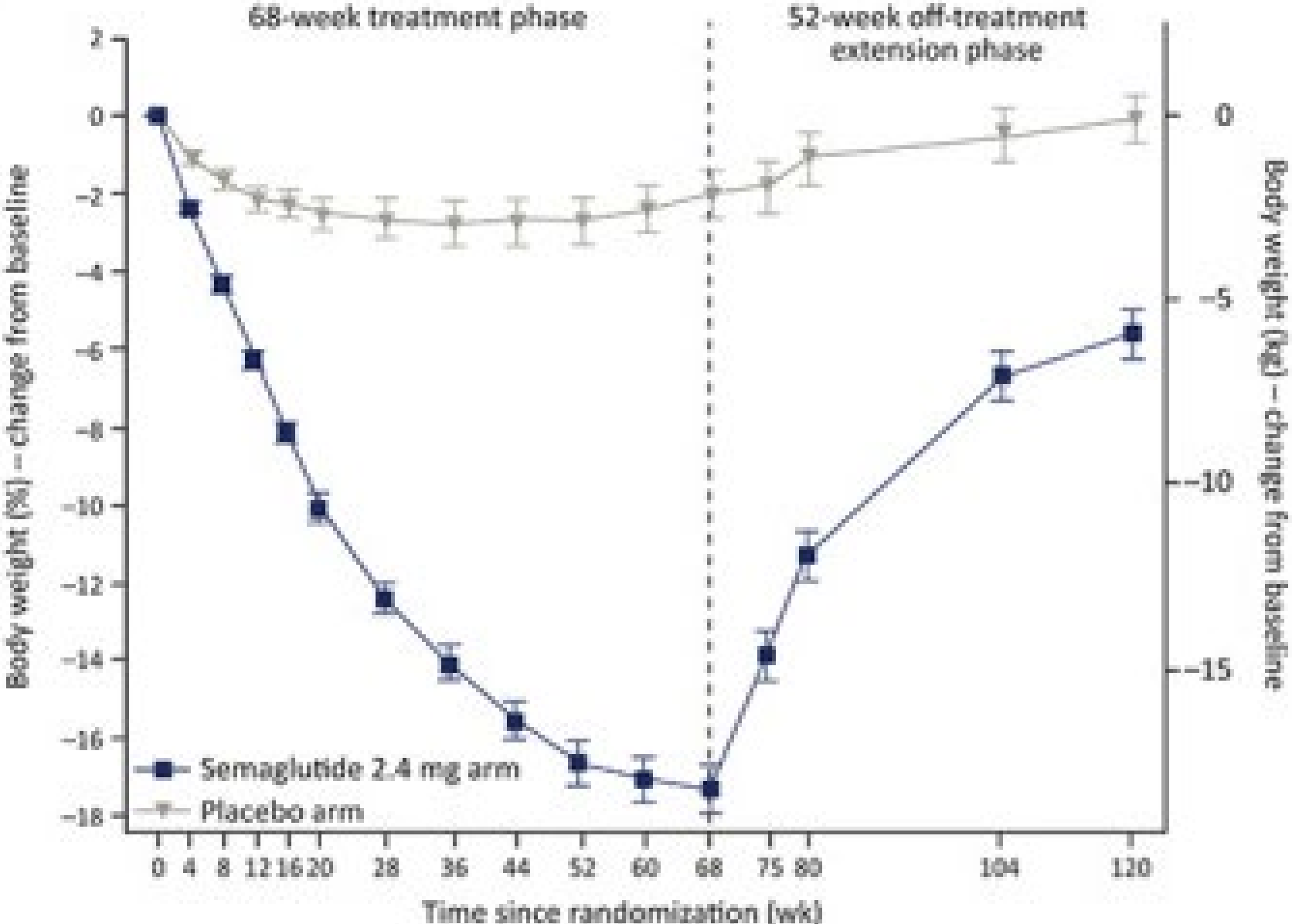
# Mitigating lean mass loss is possible with lower body weight losses

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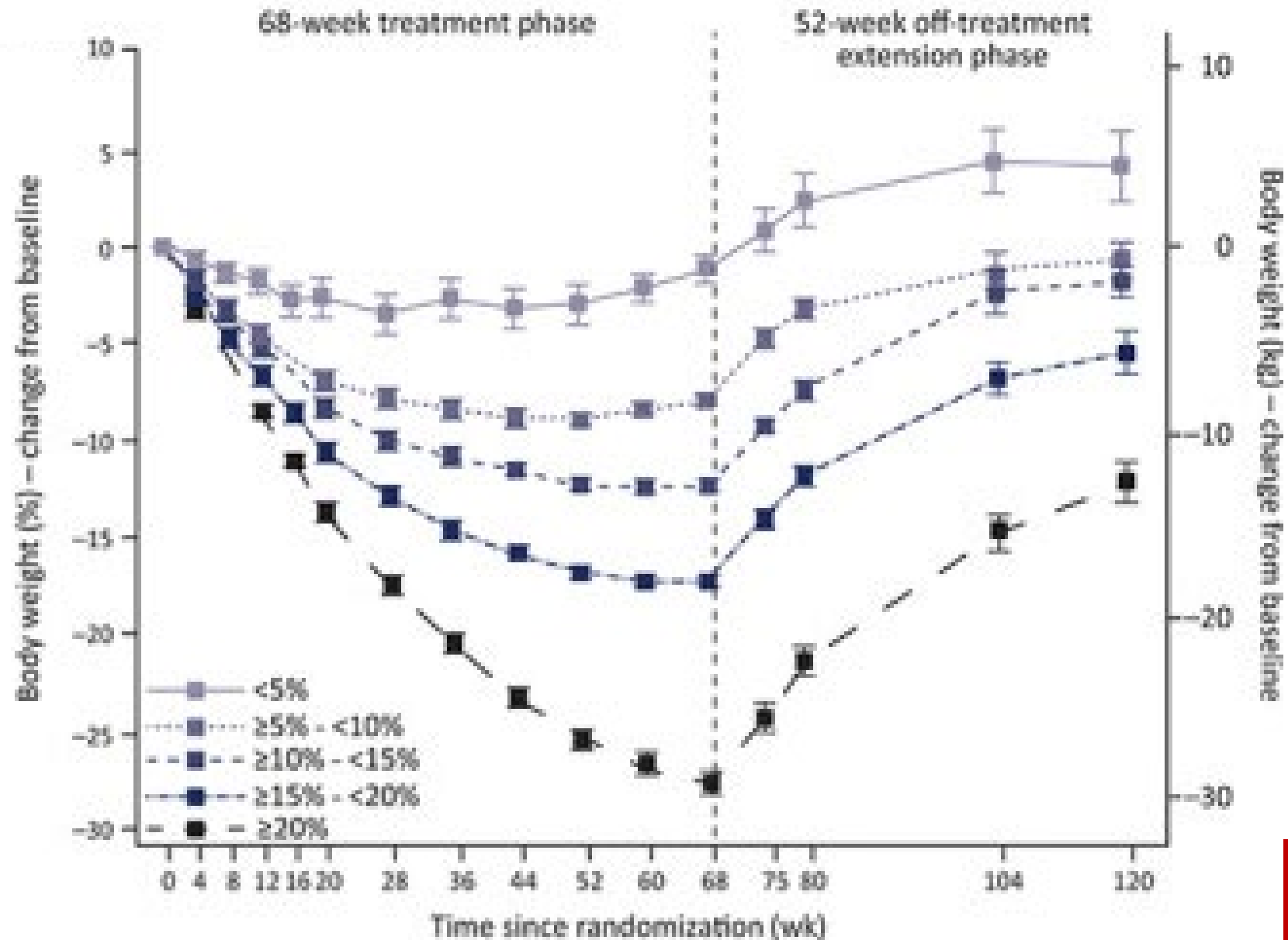
- ❖ Protein and resistance training need to be prioritized on weight loss medications:
  - ✓ At least **1.3 g/kg/day** of protein
  - ✓ Ideally **3** resistance training sessions per week
- ❖ Patients likely need formal guidance



# After stopping Semaglutide 2/3 of weight was regained in 1 year



...but this was only because of subjects who lost  $\geq 15\%$  BW



# Behaviors associated with losing weight and keeping it off include

---



Catching slip-ups



~1 hr/day



Eat Breakfast



Self-Monitor Weight



Eat Low Cal/  
Low Fat Diet



Consistent  
Eating Pattern

Thank you for attending!

Q & A

A photograph of a sunflower field under a clear blue sky. In the foreground, a large, vibrant yellow sunflower is in full bloom, facing right. To its left, another sunflower head is shown, but it is dark brown and appears to be dead or withered. The background is filled with many more sunflowers, some in bloom and some not, stretching towards a horizon line. The overall scene is bright and sunny.

“When a flower doesn’t bloom, you fix the environment in which it grows, not the flower.”

- Alexander Den Heijer