

# Understanding the New Landscape of Anti-Obesity Medications: Evidence to Applied Practice



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**Professional Disclosure:**  
**Consultant, Wondr Health, Inc.**  
**IDEAL Strategy and Consulting**

**Personal Disclosure:**  
**Obesity Treatment Advocate**



*Living with obesity  
isn't easy*

*Treating obesity  
isn't easy*





one size fits  
**NONE**

*Person-Centered*

*Not*

*Method-Centered*



# Objectives

To understand the application and effectiveness of contemporary anti-obesity medications.

Provide an overview of indications, medical management, side-effects, and comprehensive obesity care strategy.

To understand contemporary approaches for inclusion of, and effectiveness of, **physical activity** within the context of contemporary anti-obesity medications.



Renee J. Rogers, PhD • You

Bio-behavioral healthy lifestyle strategist | Engagement + adher...

1mo • Edited •

PSA for [#fitnessprofessionals](#) regarding [#antiobesity](#) medications...



**STOP:** Calling anti-obesity medications, “weight loss” drugs.

**STOP:** Calling all anti-obesity medications, “Ozempic”

**STOP:** Making claims that resistance training and exercise programs will “stop lean mass and muscle mass loss”



**DO:** Read more ([evidence](#)) about what we do and do not know about the role of physical activity...



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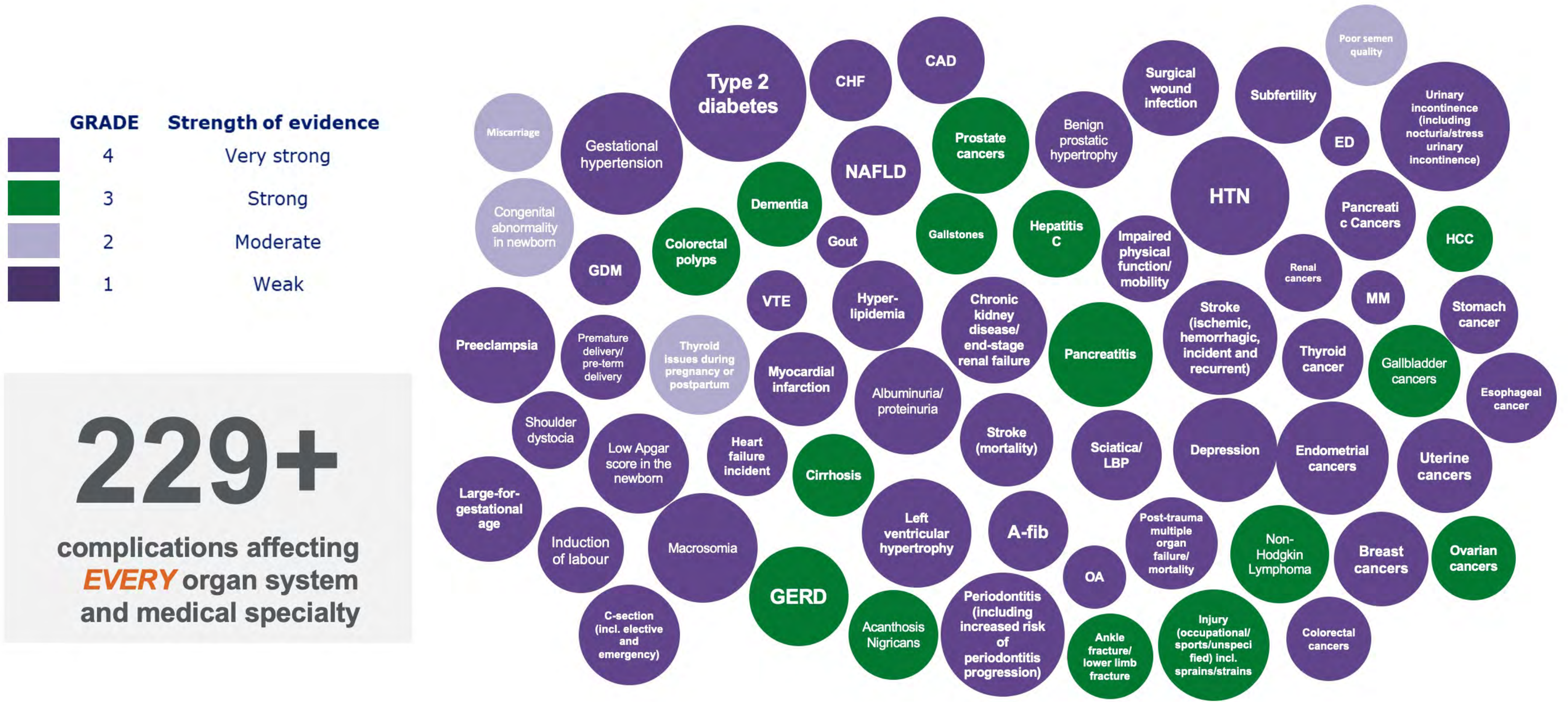
**STOP:** Calling anti-obesity medications, “weight loss” drugs.

These medications are FDA approved for the  
treatment of **obesity\***

Obesity is a chronic disease  
*American Medical Association, 2013*

These medications are **not** for modest weight loss







# Objectives

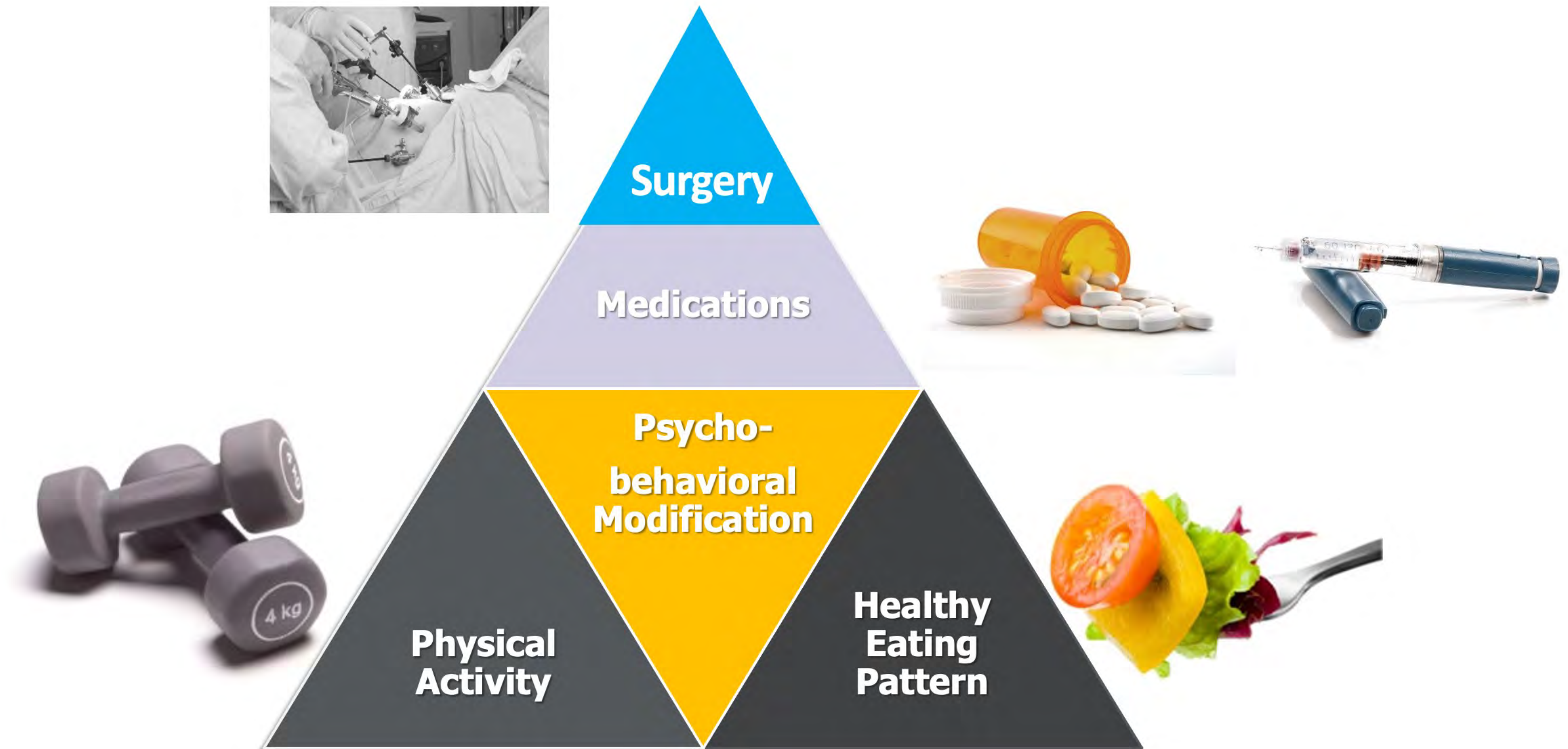


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# Components of an Effective Obesity Management Program



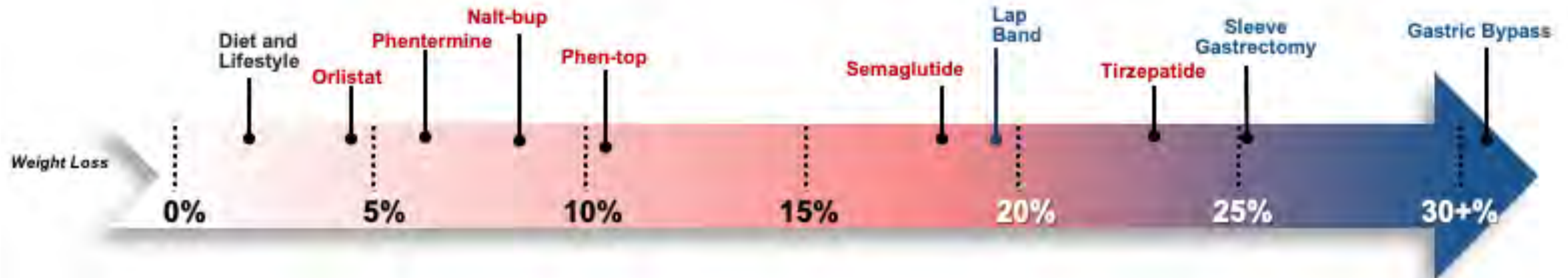
Slide Image credit: Dr. Robert Kushner



## Diet

## Antiobesity Medications

## Devices and Bariatric Surgery



**Bariatric surgery  
currently provides the best results  
– newer drugs are catching up**



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PSA for [#fitnessprofessionals](#) regarding [#antiobesity](#) medications...



**STOP:** Calling all anti-obesity medications, “Ozempic”



# WHAT'S IN A NAME?

- Not all “Ozempic”
  - 2nd or 3rd Generation Medications
  - Incretin-based Hormone Agonists
  - Nutrient Stimulated Hormone (NuSH) Therapies
- GLP-1 agonist receptor therapies have been around
  - Lirglutide (“Victoza/Saxenda”)
  - Dulaglutide (“Trulicity”)

SEMAGLUTIDE

“OZEMPIC”  
TYPE 2 DIABETES

“WEGOVY”  
OBESITY

FDA APPROVAL  
2021

TIRZEPATIDE

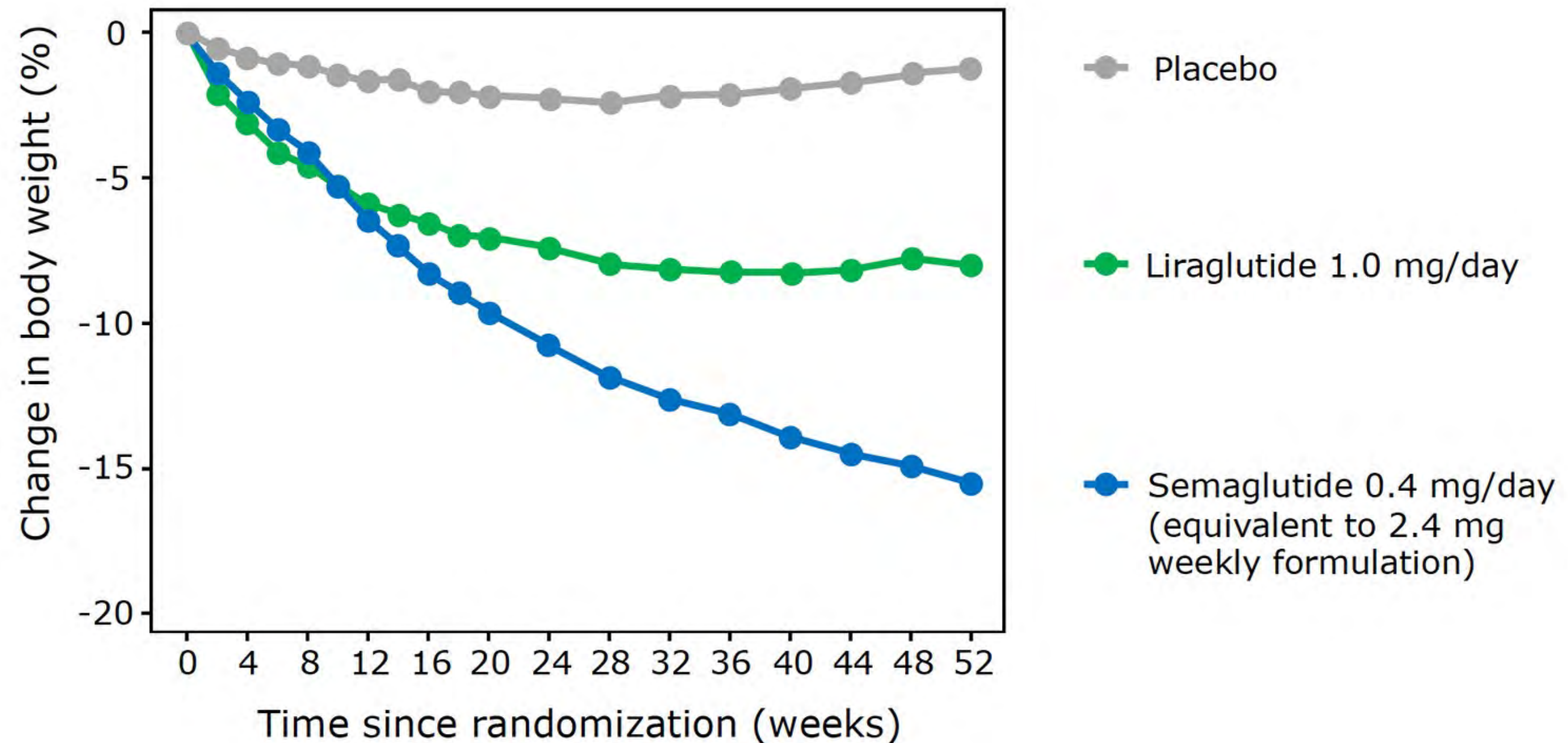
“MOUNJARO”  
TYPE 2 DIABETES

“ZEPBOUND”  
OBESITY

FDA APPROVAL  
2023

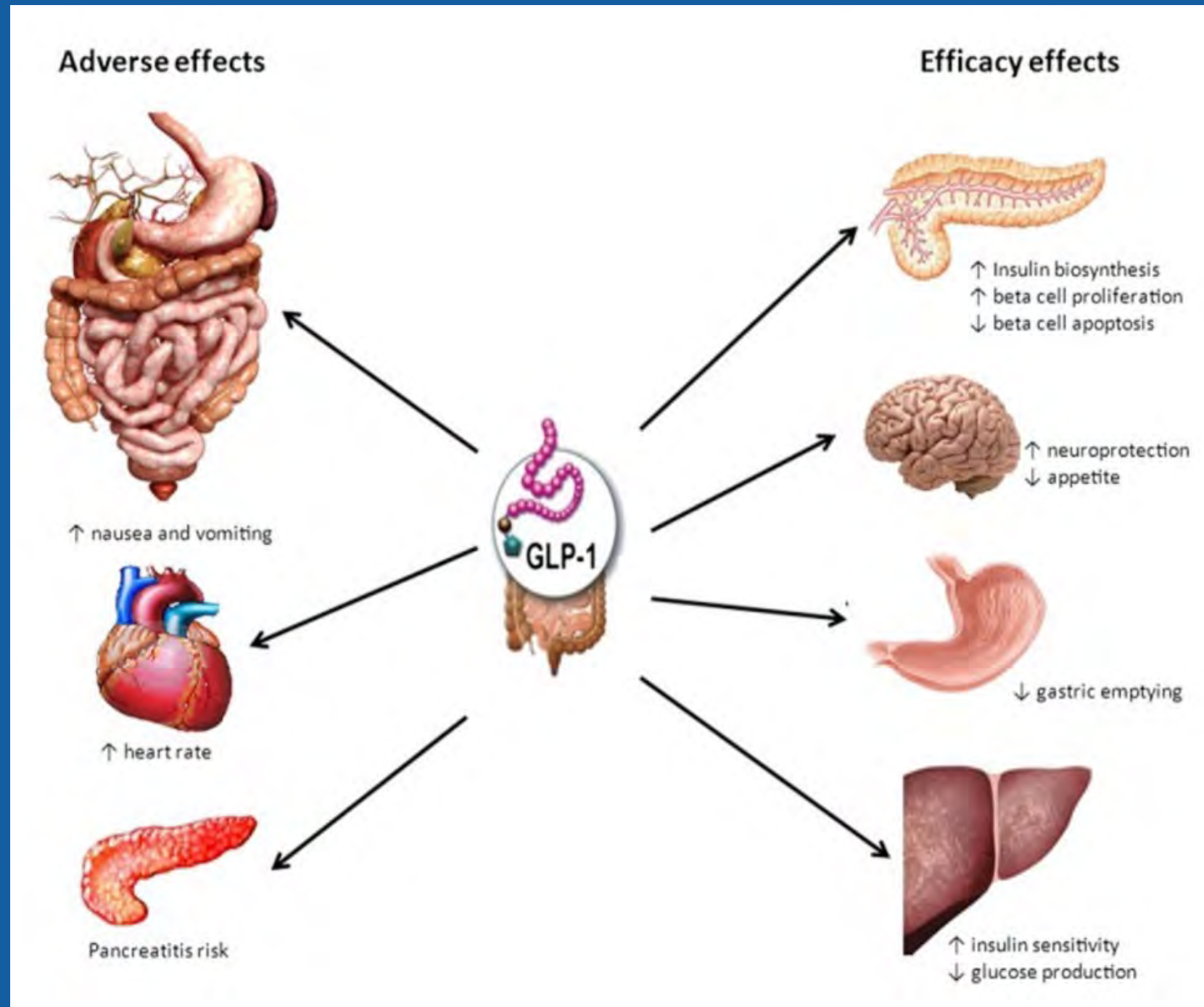


# GLP-1 receptor agonists have widely varying effects on obesity



# SEMAGLUTIDE

GLP-1



## Glucagon-like peptide 1 (GLP-1)

- GLP-1<sub>(7-37)</sub> is a 31-amino acid peptide
- Secreted predominantly from L-cells in the gut
- Also secreted by CNS neurons (hindbrain nucleus tractus solitarius)
- Signals through widely distributed G-protein-coupled receptor



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SLIDES ADAPTED: KAPLAN, LM 2023  
BOSTON COURSE ON OBESITY TREATMENT



**QUESTION** In adults with overweight or obesity without diabetes, what effect does once-weekly subcutaneous semaglutide, 2.4 mg, have on body weight when added to intensive behavioral therapy with an initial low-calorie diet?

**CONCLUSION** When used as an adjunct to intensive behavioral therapy and initial low-calorie diet, once-weekly subcutaneous semaglutide produced significantly greater weight loss than placebo during 68 weeks in adults with overweight or obesity.

## POPULATION

495 Women  
116 Men



Adults with overweight (BMI  $\geq 27$ ) plus 1 comorbidity or obesity (BMI  $\geq 30$ ) without diabetes

Mean age: 46 years

## LOCATIONS

41  
Sites in the US



## INTERVENTION



407

### Semaglutide

Semaglutide, 2.4 mg, once weekly subcutaneously, plus low-calorie diet (for initial 8 weeks) and intensive behavioral therapy for 68 weeks

611 Patients randomized

204

### Placebo

Placebo once weekly subcutaneously, plus low-calorie diet (for initial 8 weeks) and intensive behavioral therapy for 68 weeks

## CO-PRIMARY OUTCOMES

Percentage change in body weight and loss of  $\geq 5\%$  of baseline weight at week 68

## FINDINGS

Weight change by week 68

### Semaglutide

Weight change: **-16.0%**

**86.6%** lost  $\geq 5\%$  of baseline weight

### Placebo

Weight change: **-5.7%**

**47.6%** lost  $\geq 5\%$  of baseline weight

Between-group difference was significant for weight change:

**-10.3 percentage points**

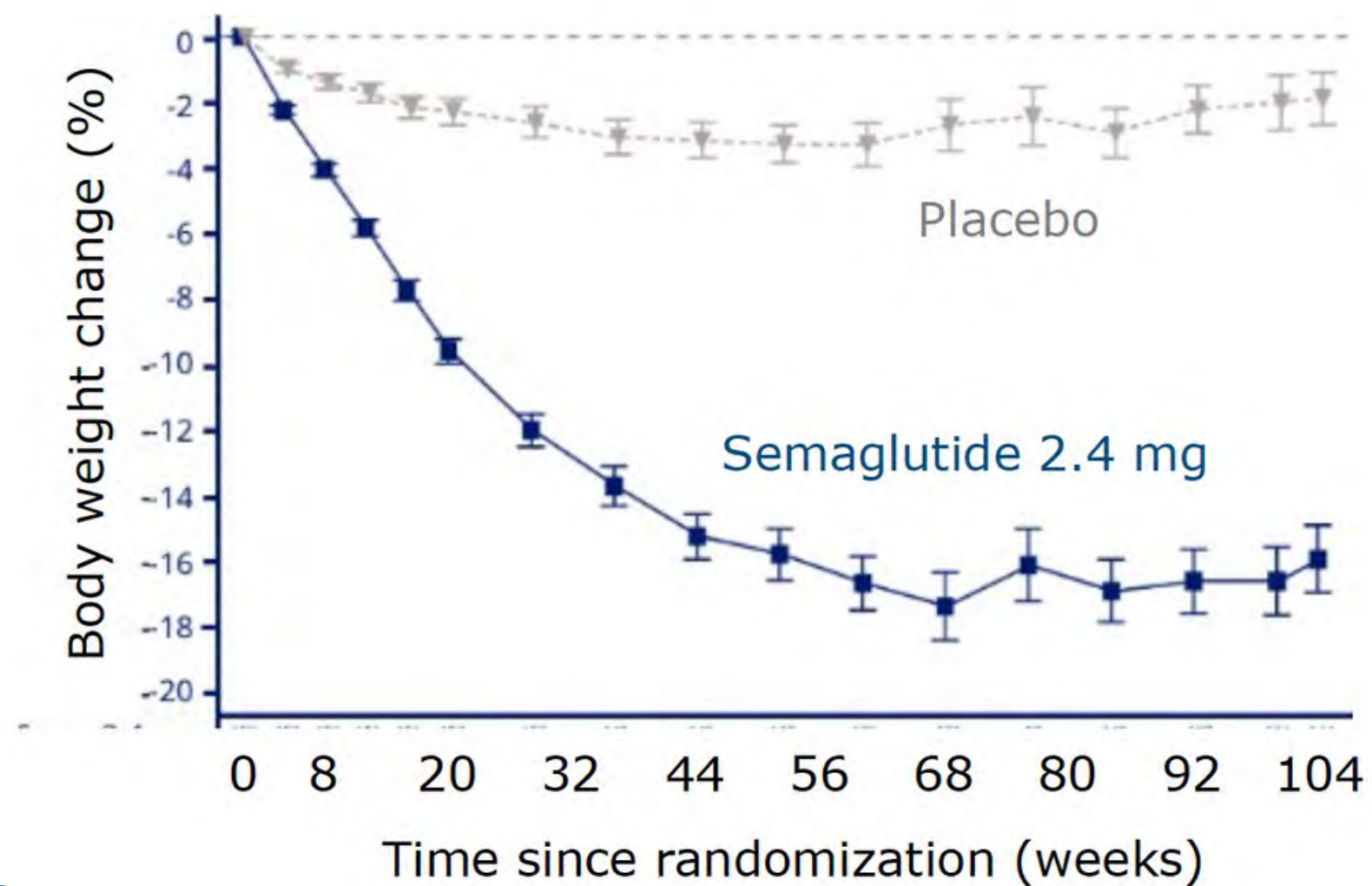
(95% CI, -12.0 to -8.6);  $P < .001$

and for losing  $\geq 5\%$  of baseline weight:  $P < .001$



# Maintenance of semaglutide-induced weight loss at two years

## STEP 5 Trial Subjects without Diabetes



# TIRZEPATIDE

GLP-1 / GIP

## Tirzepatide – a dual GLP-1 + GIP agonist

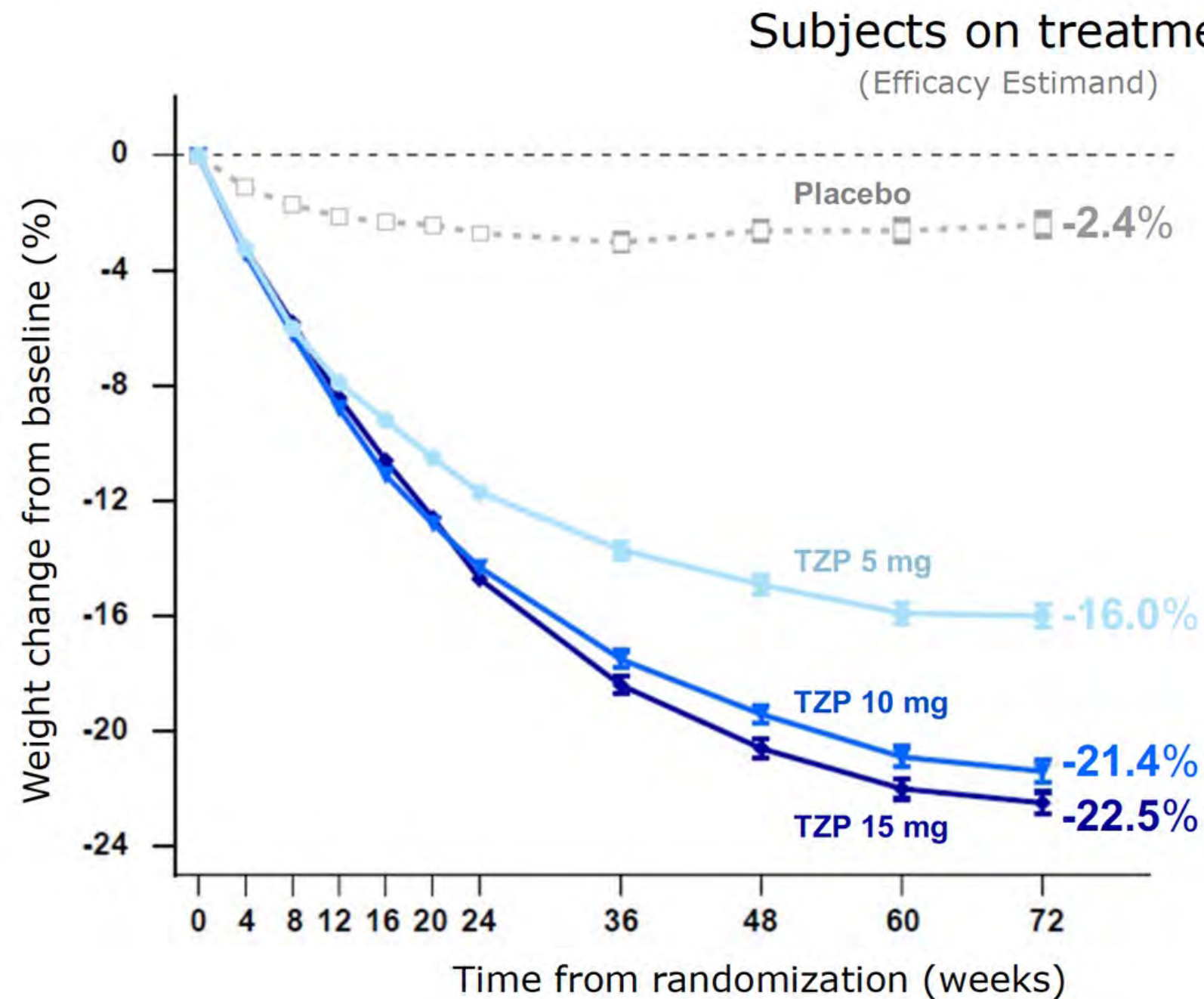
- **GLP-1 and GIP are the two known incretins** - peptides secreted from enteroendocrine cells in the gut mucosa in response to food ingestion
- **Incretins stimulate insulin and amylin secretion from pancreatic  $\beta$ -cells** under conditions of normal or elevated blood glucose
- **GLP-1 in the brain** decreases appetitive drive and induces fat metabolism and weight loss
- **The role of GIP** on appetite, fat metabolism and energy balance **is less clear**
- **Tirzepatide** is a single synthetic peptide that **stimulates both GLP-1 and GIP receptors**

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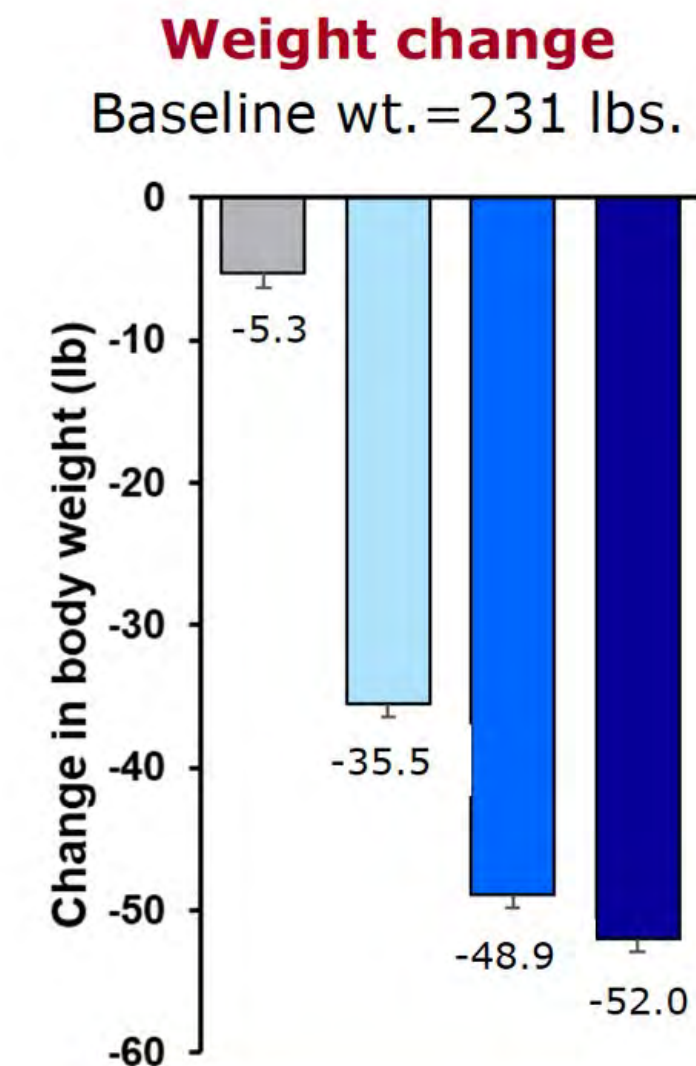
SLIDES ADAPTED: KAPLAN, LM 2023  
BOSTON COURSE ON OBESITY TREATMENT



# Weight reduction on tirzepatide – subjects without diabetes

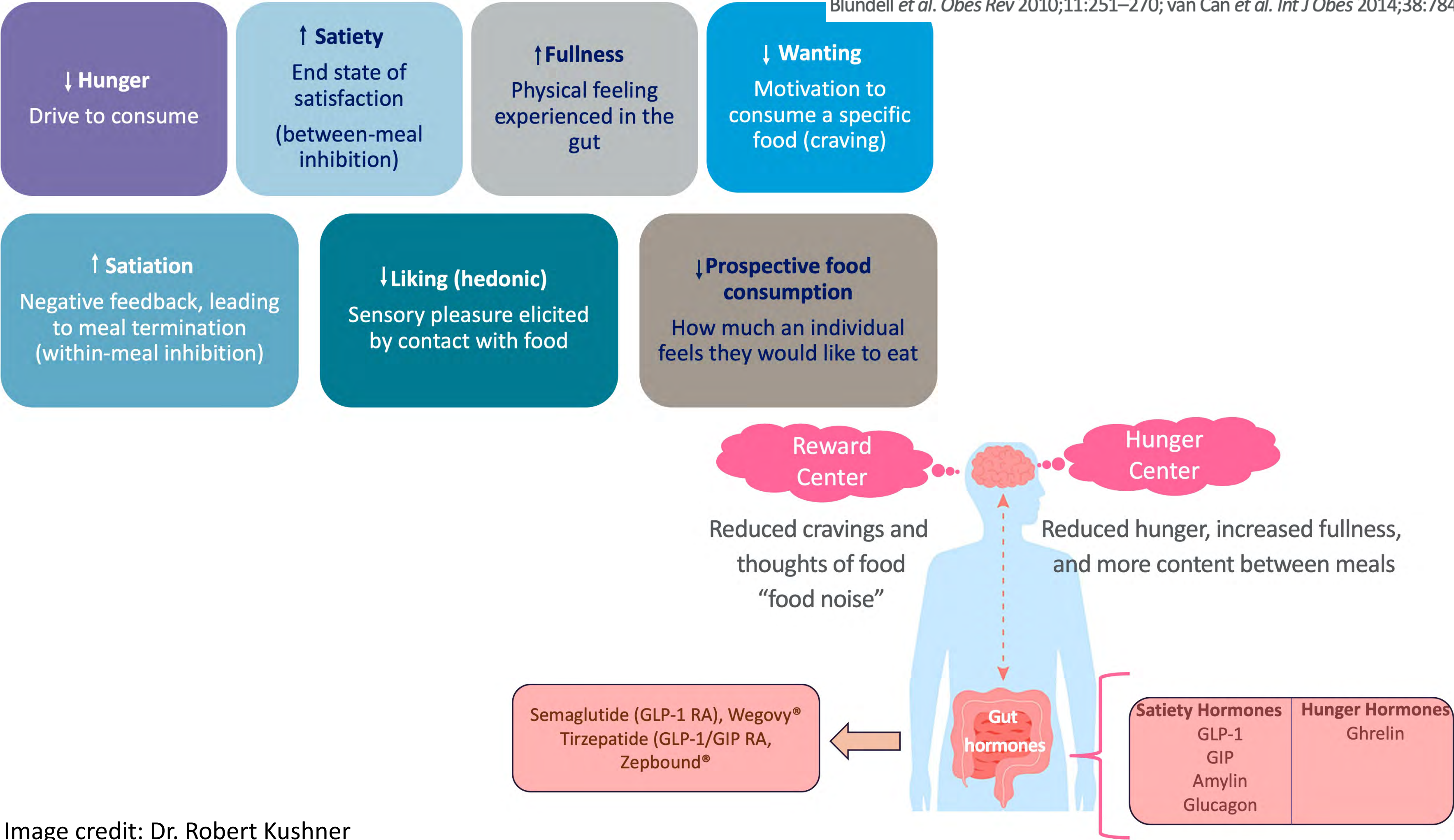


Jastreboff AM *et al*, NEJM 2022



**Average  
weight reduction  
35-52 lbs.**





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# Medical Management



- Indications
- Evaluation
- Administration
- Dosing – Escalation/De-Escalation
- Side Effects
- Dietary changes + increased Physical Activity





100+

AGENTS IN DEVELOPMENT





# Novel nutrient-stimulated hormone-based therapies in the pipeline for obesity treatment – injectable and oral

## GLP-1 receptor agonists approved for obesity treatment

Semaglutide	Weekly SC	STEP trials
Liraglutide	Daily SC	SCALE trials

## MONOTHERAPY

### ENDO-PANCREATIC receptor agonists

Cagrilintide	AMY RA	Phase II	Novo Nordisk	NCT03856047
ZP8396	AMY RA	Phase I	Zealand Pharma	NCT05096598
Amylin agonist LA	AMY RA	Phase I	Eli Lilly	Not available
DACRA QW II	AMY/CAL RA	Phase I	Eli Lilly	Not available

## ORAL MONOTHERAPY

### ORAL GLP-1 receptor agonists

Semaglutide	GLP-1 RA	Phase III	Novo Nordisk	NCT05035095
Danuglipron	sm GLP-1 RA	Phase II	Pfizer	NCT04707313
LY3502970	GLP-1R NPA	Phase II	Eli Lilly	NCT05051579

## DUAL RA combinations

### ENTERO-ENDOCRINE receptor agonists/antagonists

Tirzepatide	GIP/GLP-1 dual RA	Phase III	Eli Lilly	NCT04184622
CT388	GIP/GLP-1 dual RA	Phase I	Carmot Therapeutics	NCT04838405
Dapiglutide	GIP/GLP-2 dual RA	Phase I	Zealand Pharma	NCT04838405
AMG133	GIP Receptor Antagonist/GLP-1 RA	Phase I	Amgen	NCT04478708

## DUAL RA combinations

### PANCREATIC-ENTERO-ENDOCRINE receptor agonists

Cagri-Sema	AMY/GLP-1 dual RA	Phase III	Novo Nordisk	NCT03600480
Pemvidutide	GCG/GLP-1 dual RA	Phase II	Altimune	NCT05295875
BI456906	GCG/GLP-1 dual RA	Phase II	Boehringer Ingelheim	NCT04667377
NN9277	GCG/GLP-1 dual RA	Phase I	Novo Nordisk	NCT03308721

## TRIPLE RA combinations

### PANCREATIC-ENTERO-ENDOCRINE receptor

Retatrutide	GIP/GCG/GLP-1 triple RA	Phase II	Eli Lilly	NCT04881760
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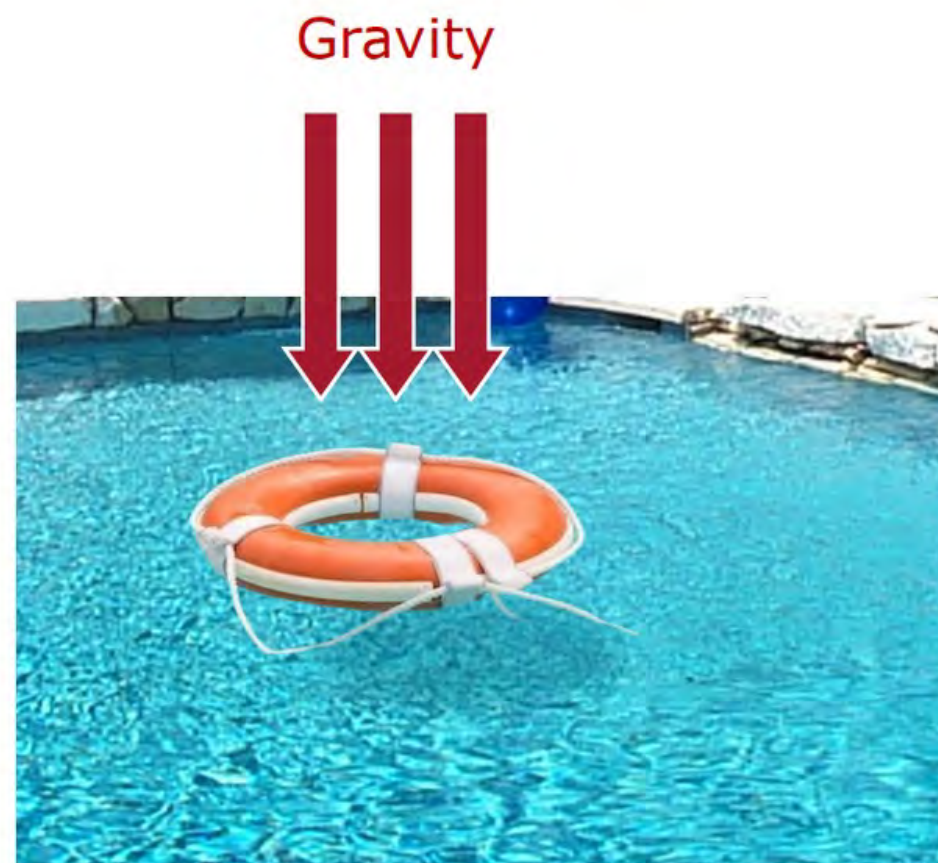


WHY IS THIS  
DIFFERENT FROM  
LIFESTYLE?

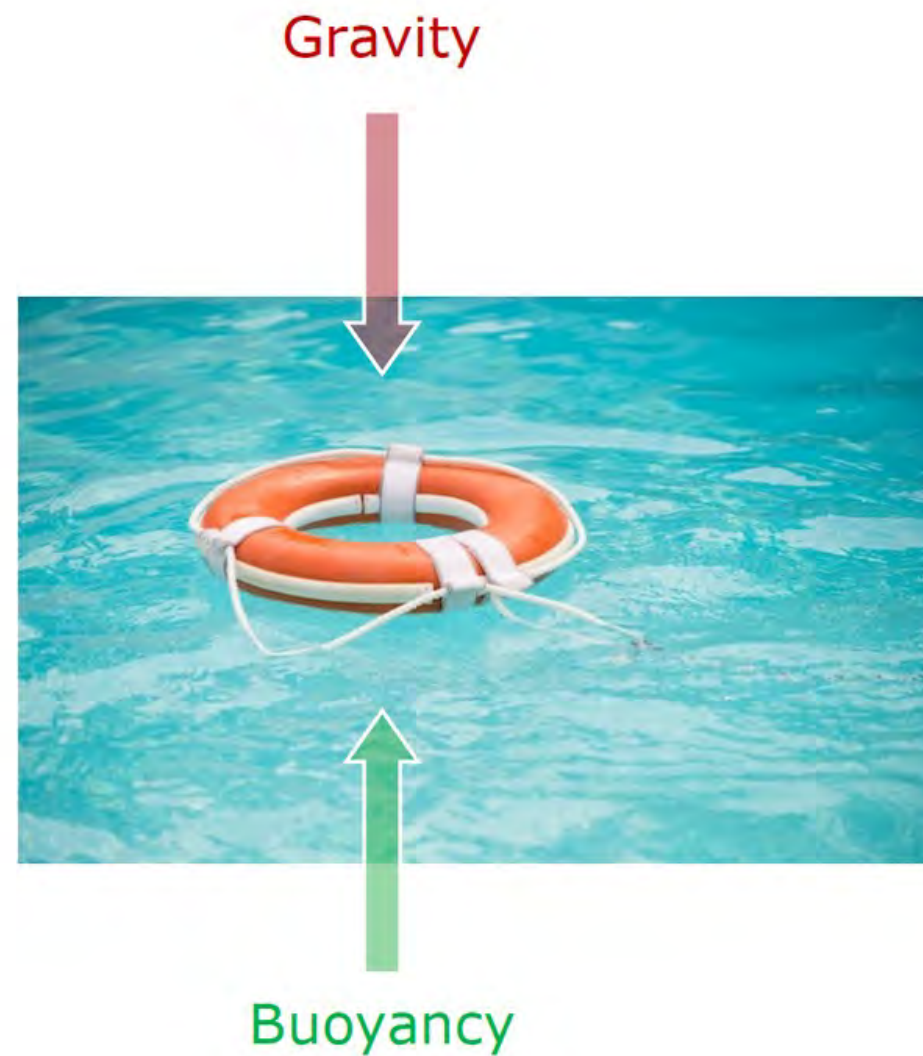


# Defense of set point

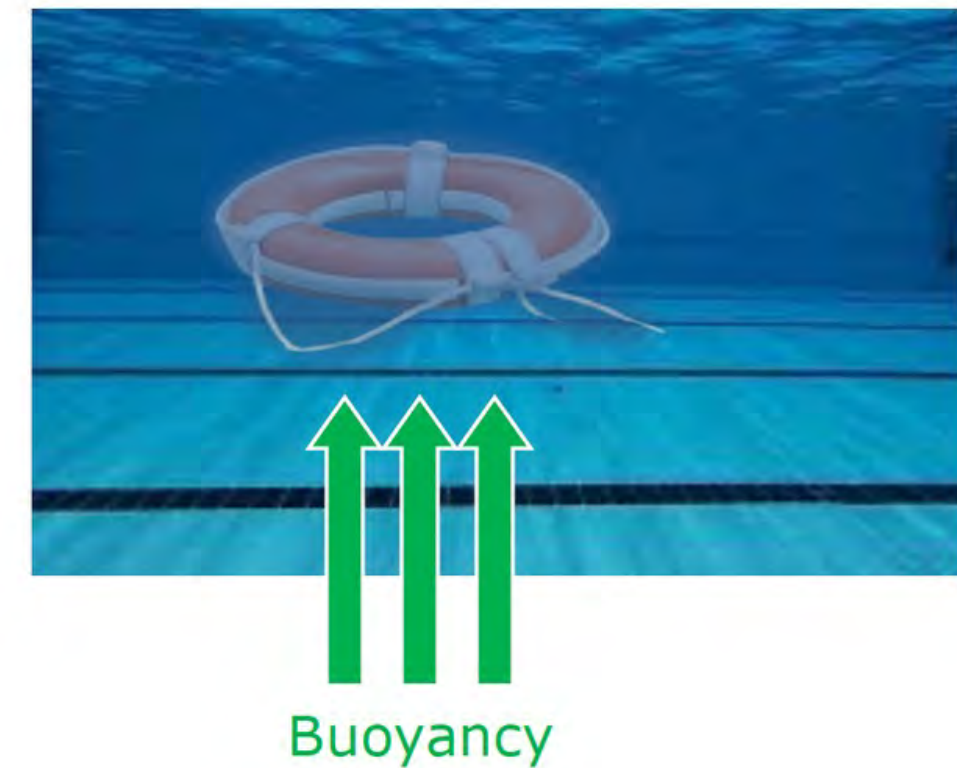
Above set point



At set point



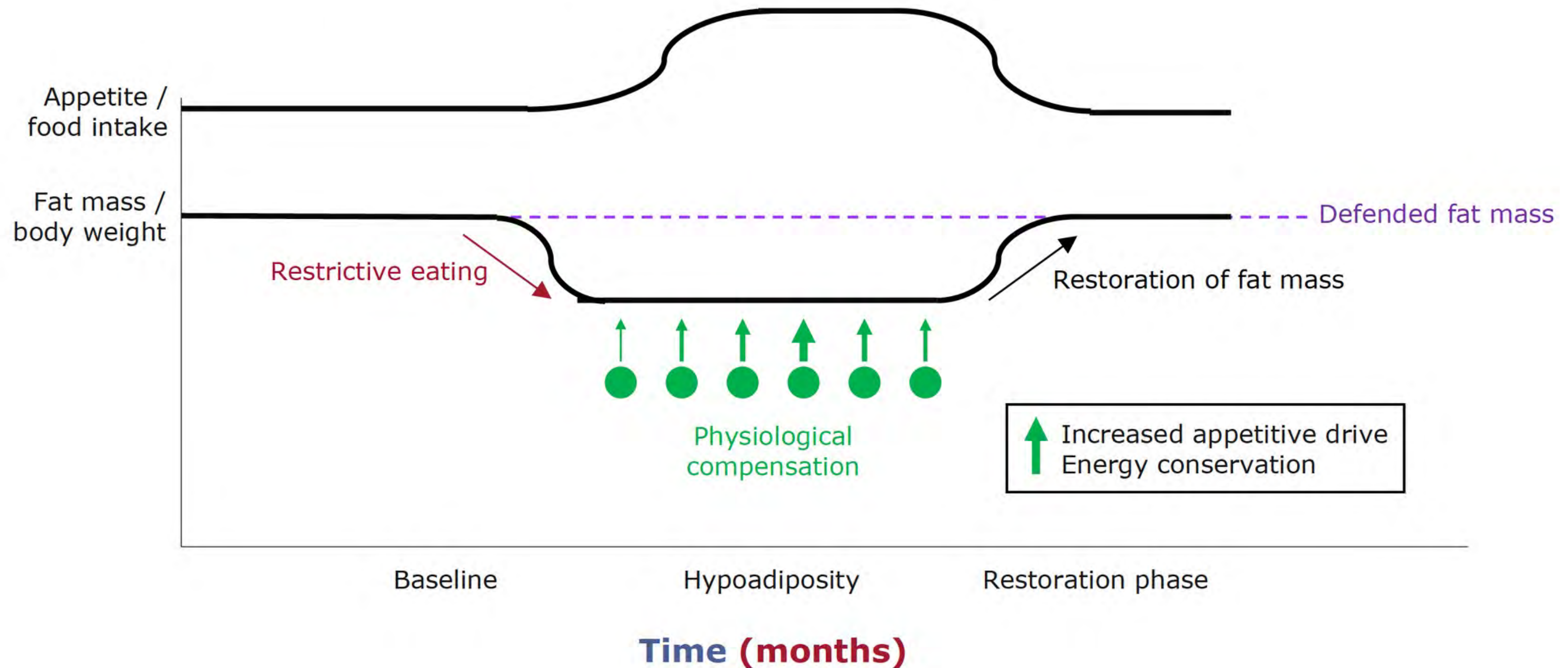
Below set point



How could you **stably** change the vertical position of the ring?



# Metabolic compensatory mechanisms – calorie reduction



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HT AOM

ACSM HOT TOPIC

## A Perspective on Anti-Obesity Medications



## The Challenges:

On these agents, patients:

- Will lose significant weight without engaging in activity,
- Will improve many health parameters without engaging in activity, and
- May not see the value of activity specifically for weight loss.

Despite these challenges, this may open the door for new physical activity opportunities.

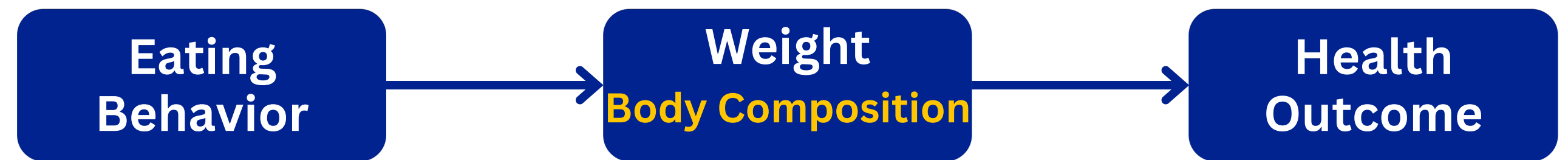
# HOWEVER...

## MORE RESEARCH IS NEEDED



**STOP:** Making claims that resistance training and exercise programs will “stop lean mass and muscle mass loss”

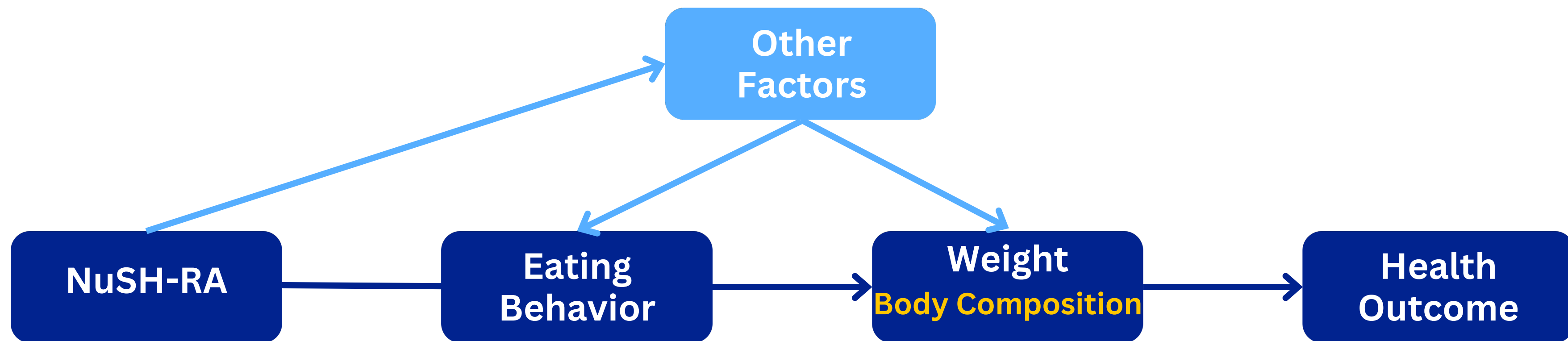




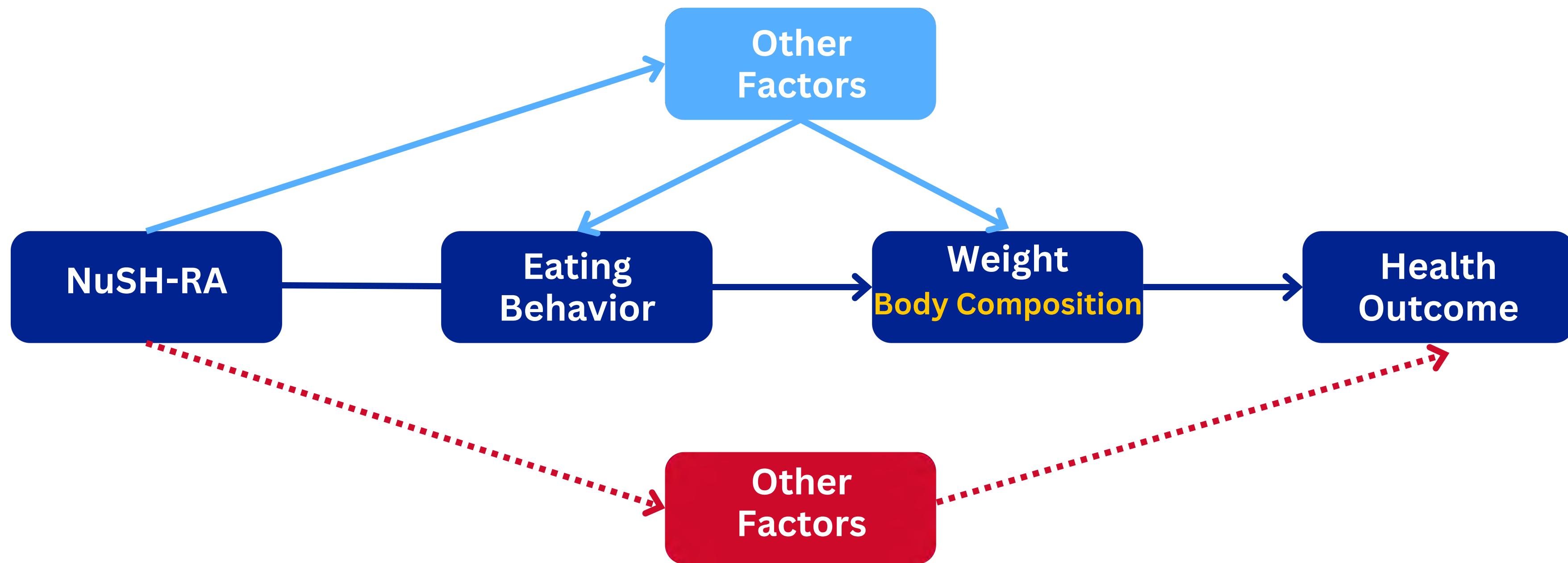


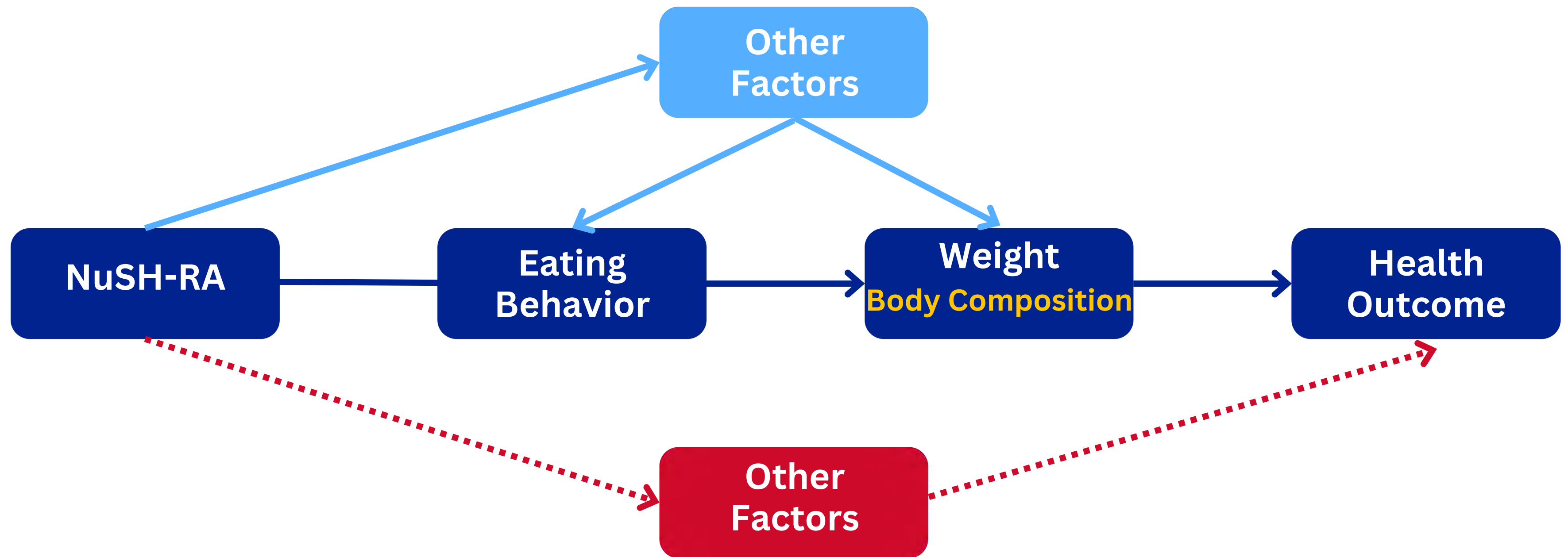












**WHAT IS THE ROLE OF EXERCISE / PHYSICAL ACTIVITY?**





## Contemporary Treatments for Obesity: Physical Activity in the Context of Antiobesity Medications

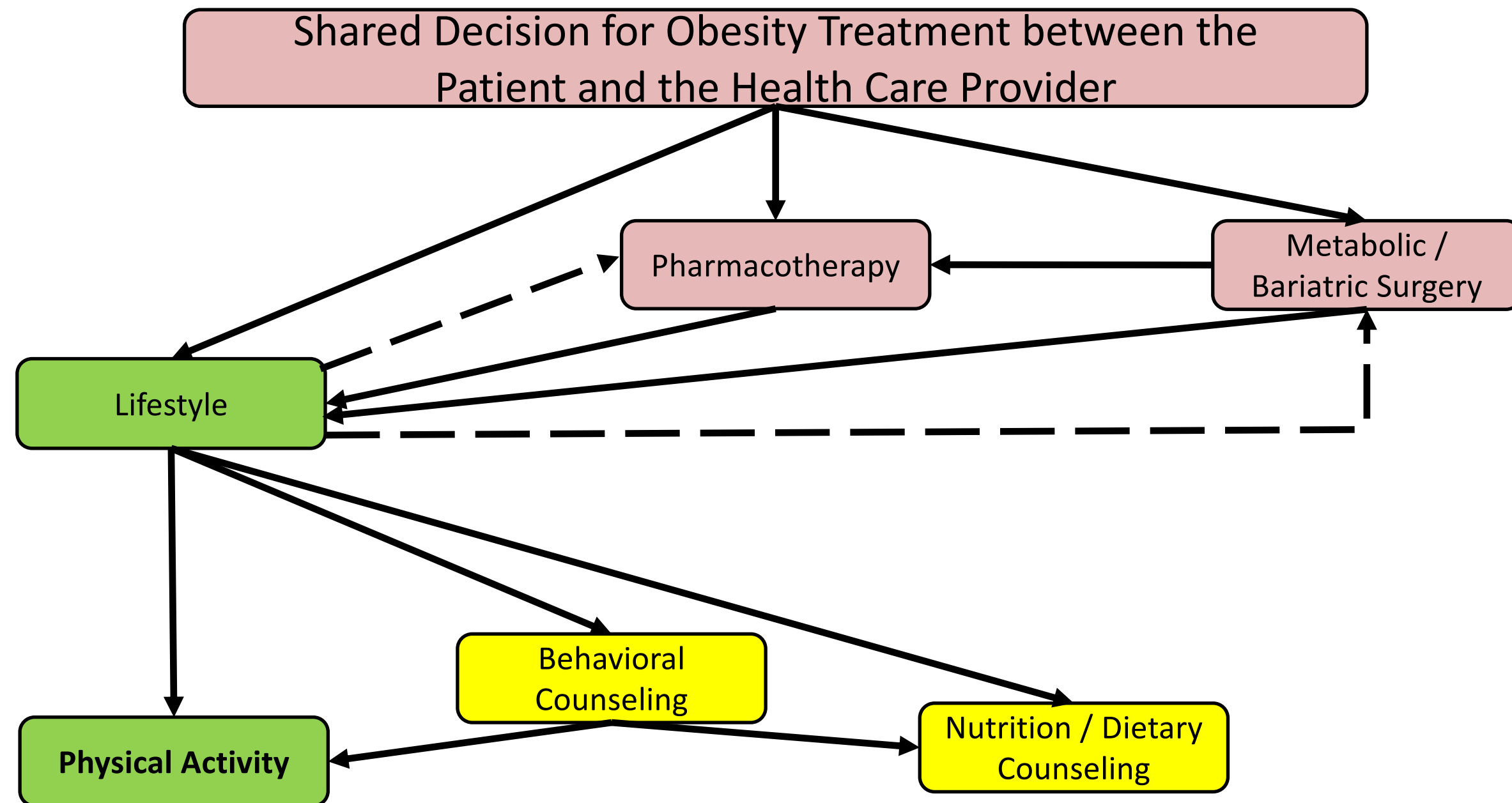
Jakicic, John M.<sup>1</sup>; Rogers, Renee J.<sup>1</sup>; Apovian, Caroline M.<sup>2</sup>

[Author Information](#) 

*Translational Journal of the ACSM* 9(2):e000253, Spring 2024. | DOI:

10.1249/TJX.00000000000000253







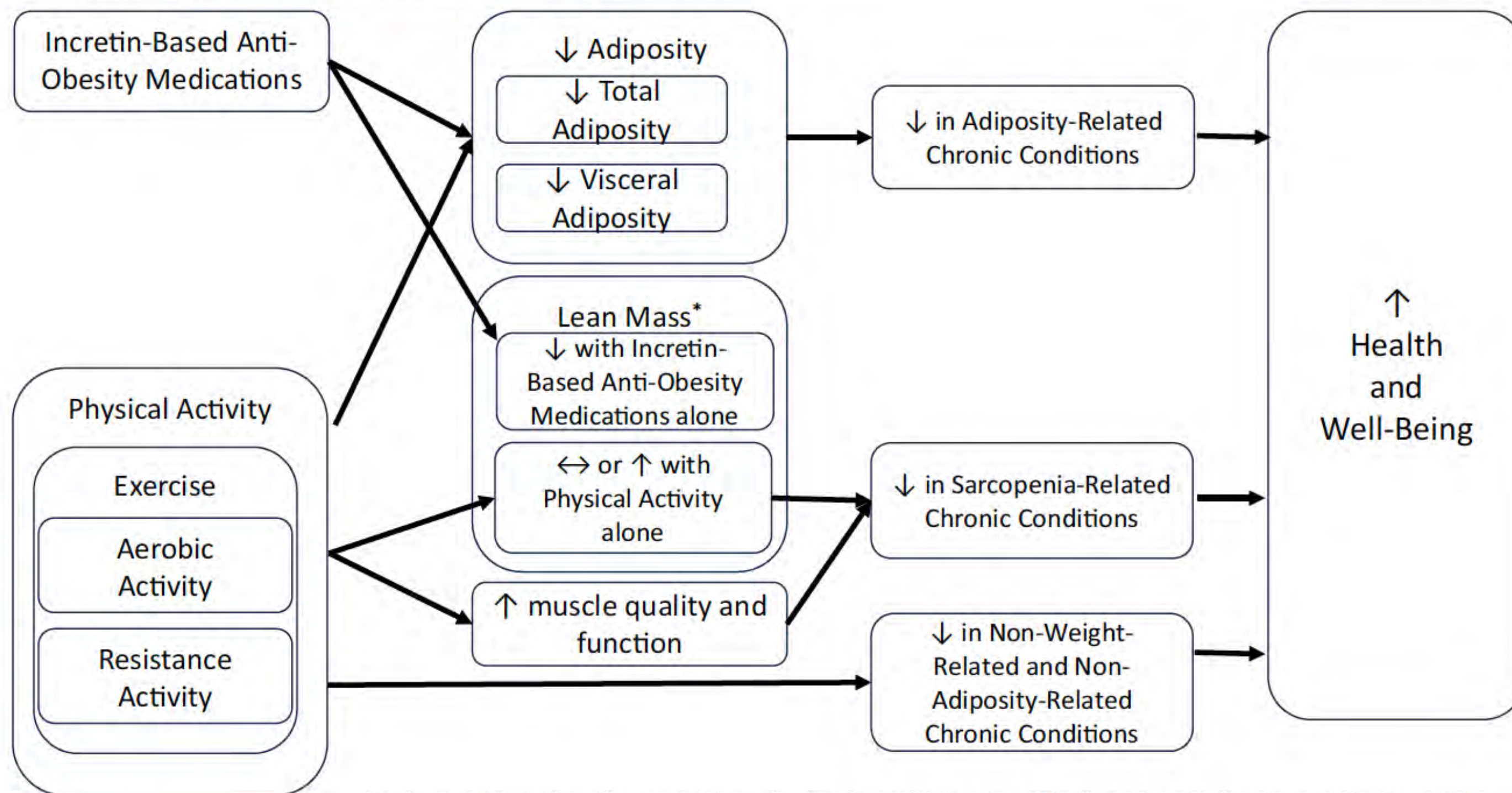
PERSPECTIVE

## Physical activity in the new era of antiobesity medications

John M. Jakicic✉, Renee J. Rogers, Timothy S. Church

First published: 17 October 2023 | <https://doi.org/10.1002/oby.23930>





\*Indicates limited evidence of the effects of combining incretin-based anti-obesity medications with physical activity on the change in lean mass.

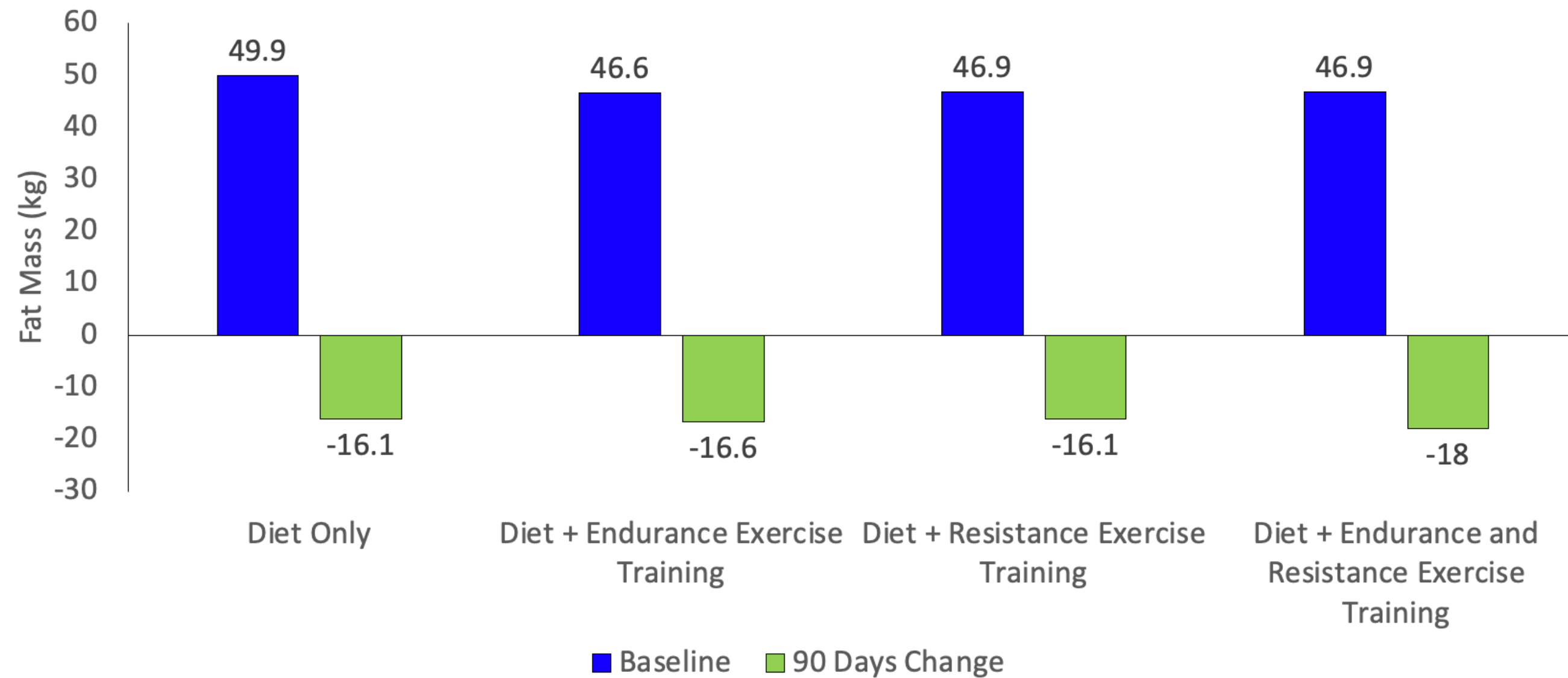
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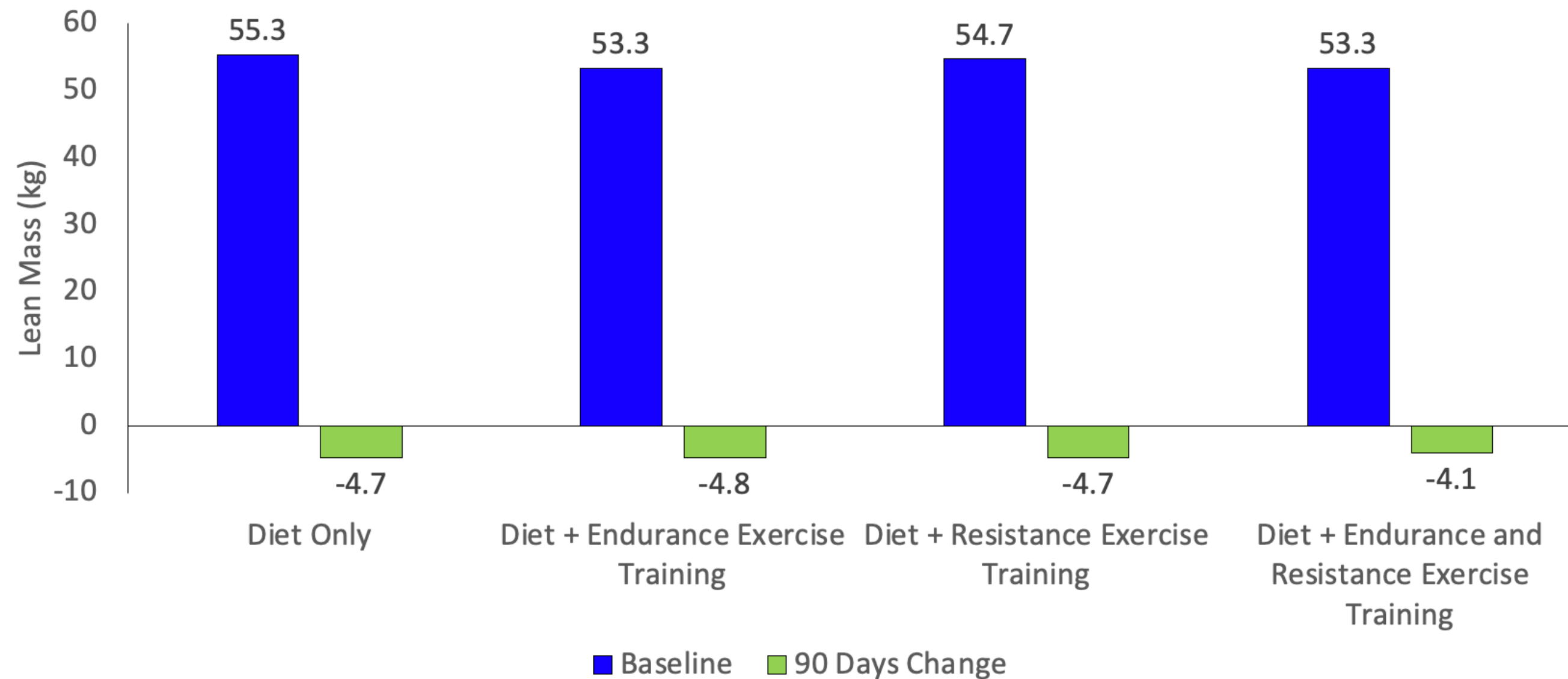
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# Change in Fat Mass



# Change in Lean Mass

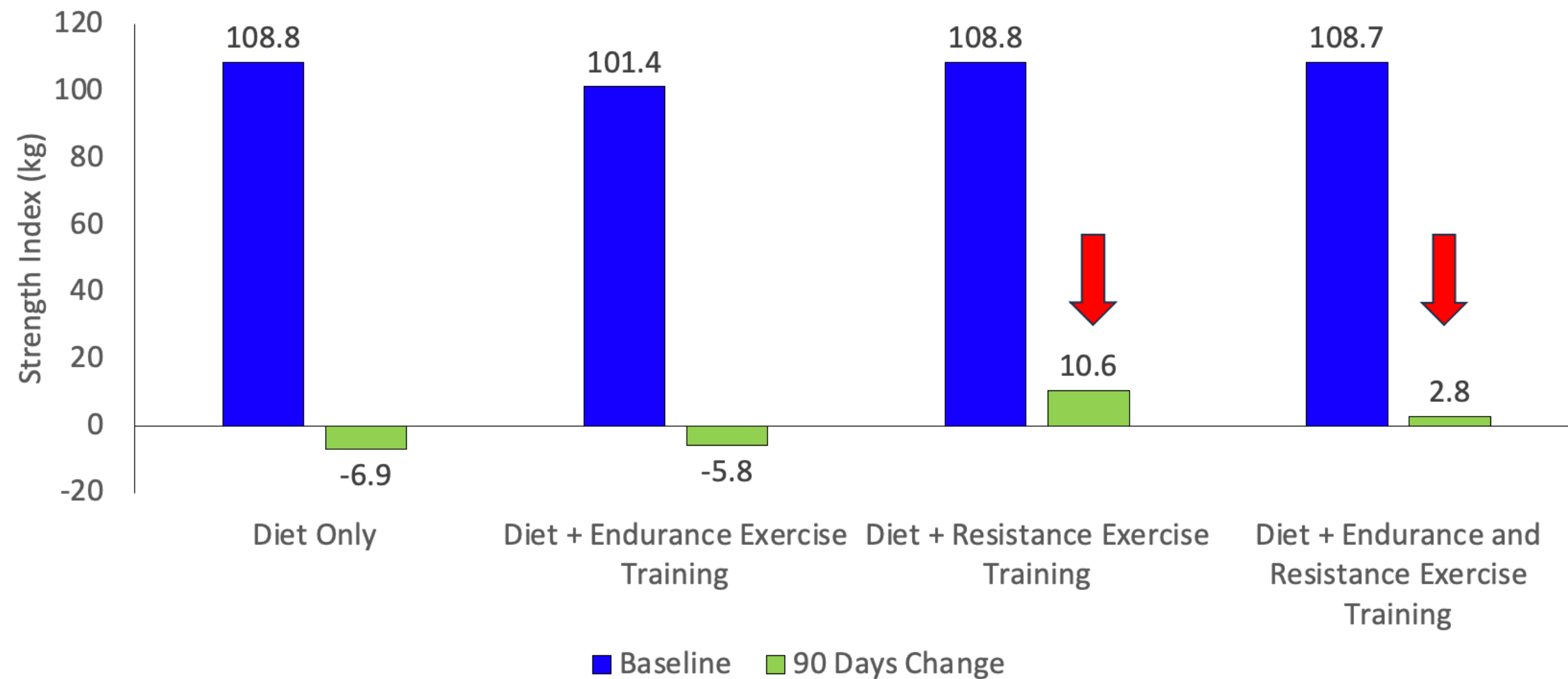






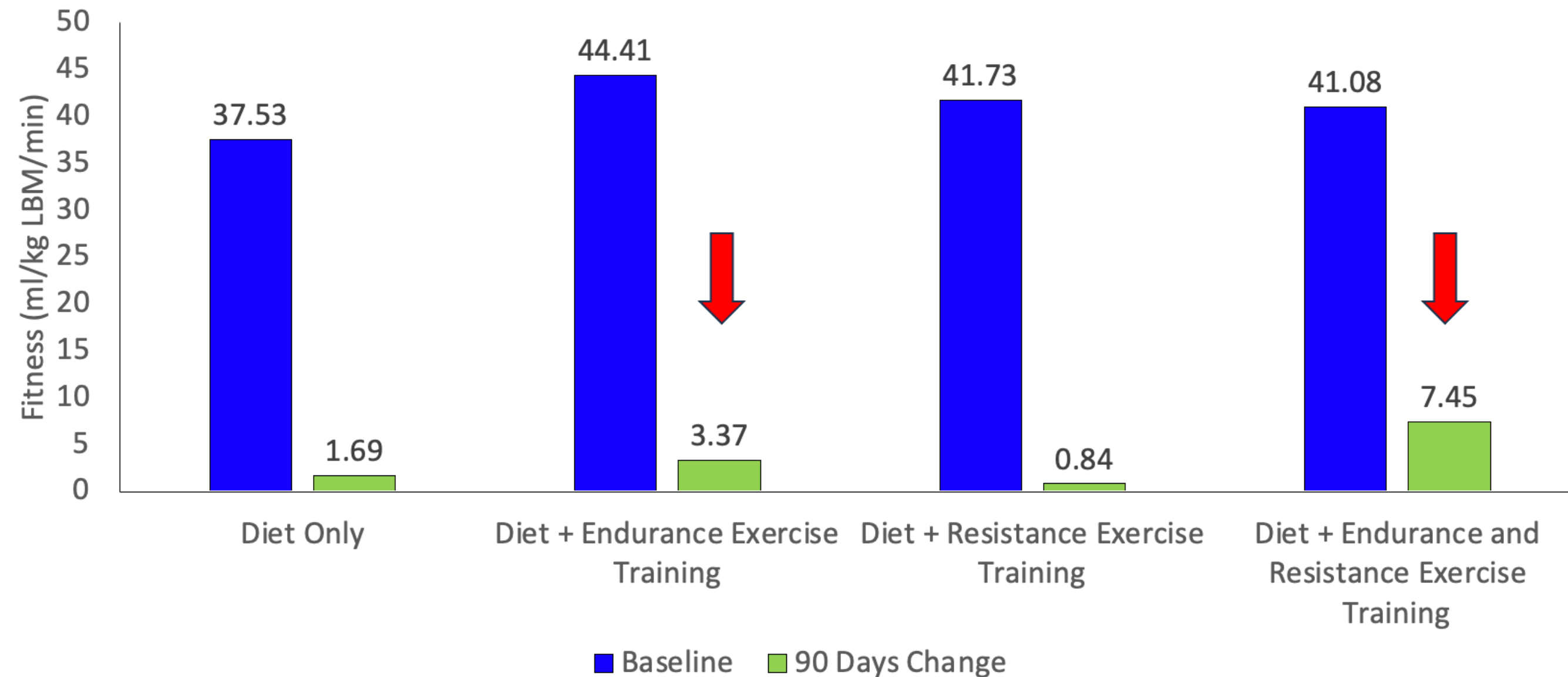
**IS THAT THE  
ENTIRE  
STORY?**

# Change in Strength Index









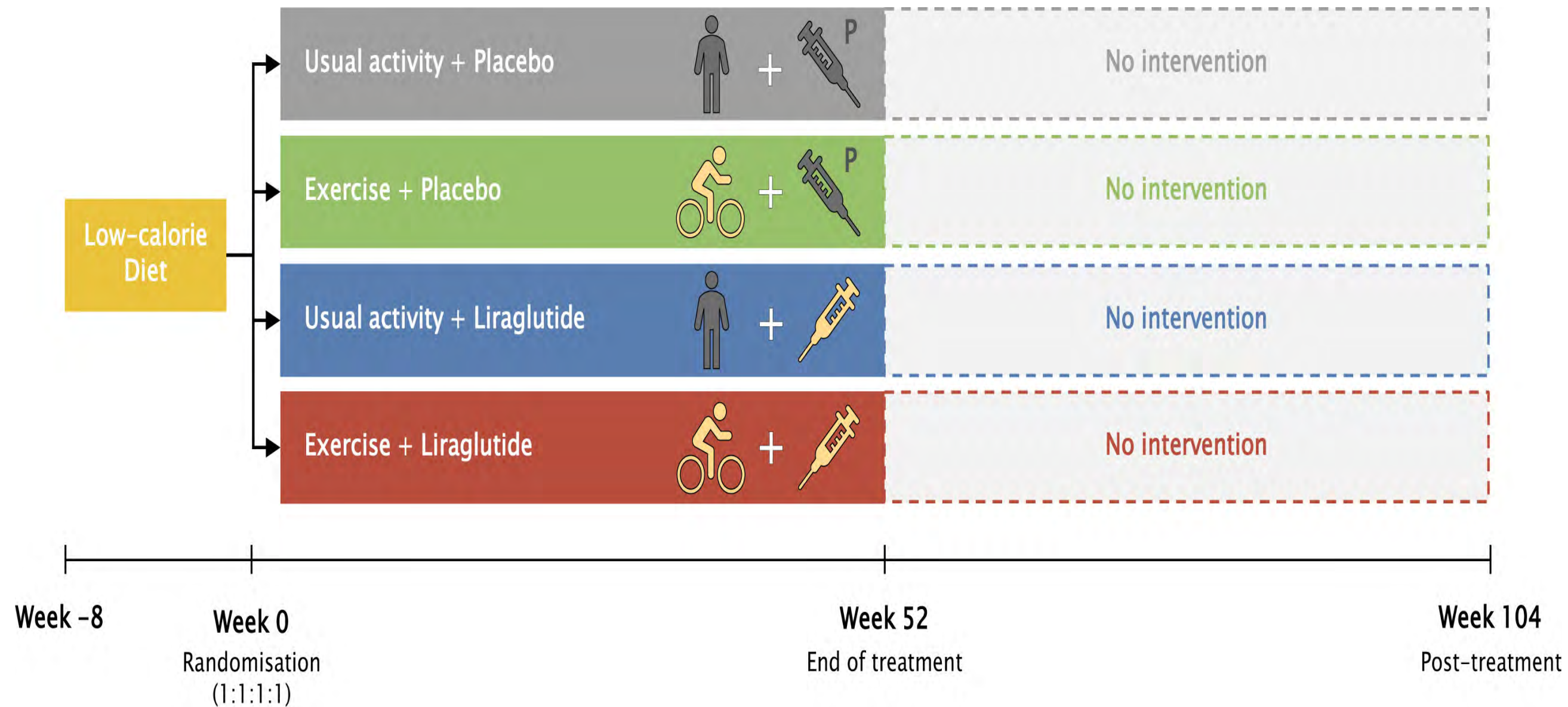
# Change in Cardiorespiratory Fitness



## What do we know about Contemporary AOMs?

Weight Loss	
Better Control of Type 2 Diabetes	
Reductions in Cardiometabolic Risk	
Reductions in Adiposity	
Reductions in Lean Mass  ~25-40%	
Reductions in Muscle Mass	





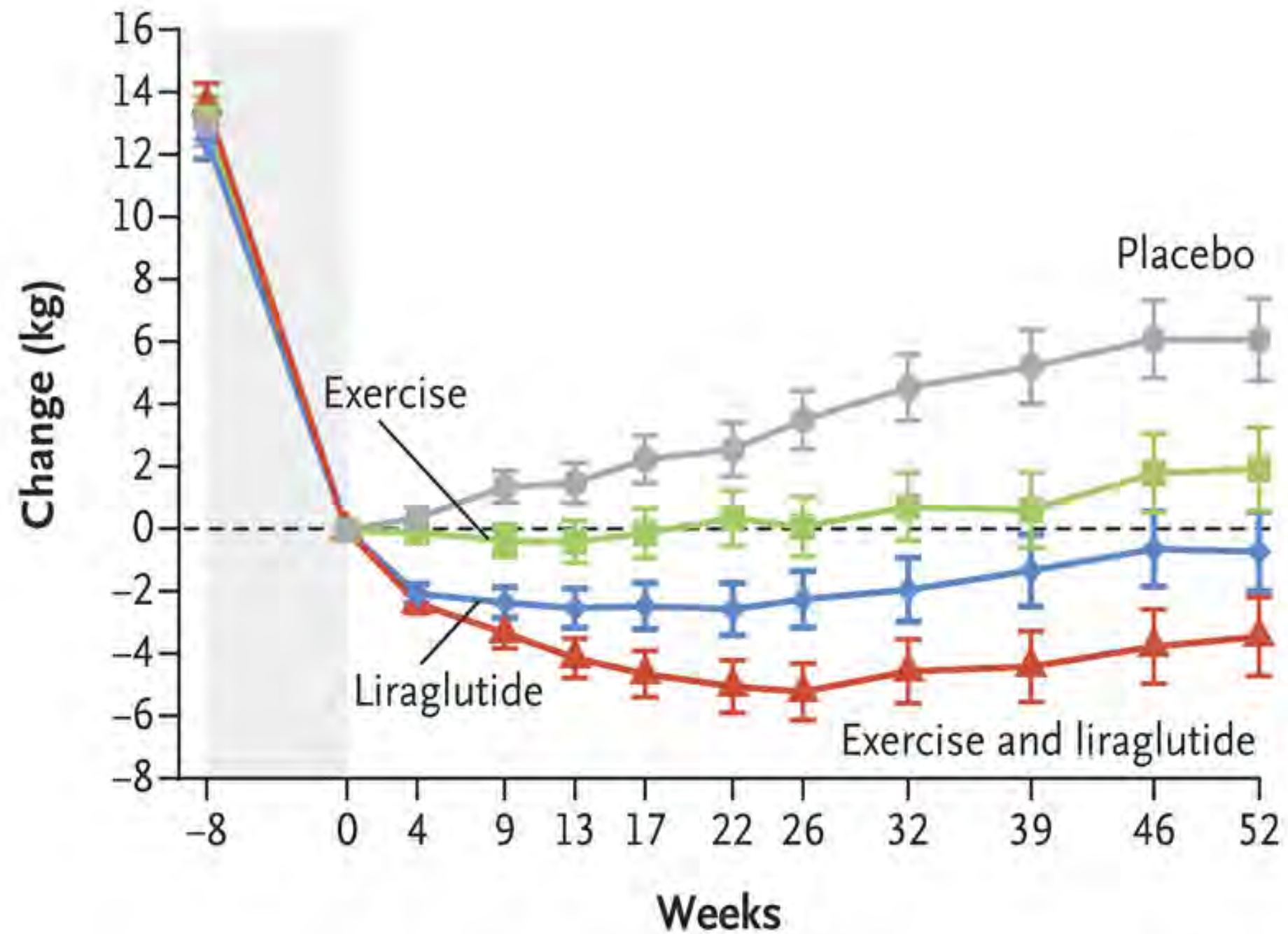
## Healthy weight loss maintenance with exercise, GLP-1 receptor agonist, or both combined followed by one year without treatment: a post-treatment analysis of a randomised placebo-controlled trial

Simon Birk Kjær Jensen,<sup>a</sup> Martin Bæk Blond,<sup>b</sup> Rasmus Michael Sandsdal,<sup>a</sup> Lisa Møller Olsen,<sup>a</sup> Christian Rimer Juhl,<sup>a</sup> Julie Rehné Lundgren,<sup>a</sup> Charlotte Janus,<sup>a</sup> Bente Merete Stallknecht,<sup>a</sup> Jens Juul Holst,<sup>a,c</sup> Sten Madsbad,<sup>d</sup> and Signe Sørensen Torekov<sup>a,\*</sup>

eClinicalMedicine  
2024;■: 102475

Published Online XXX

<https://doi.org/10.1016/j.edinm.2024.102475>



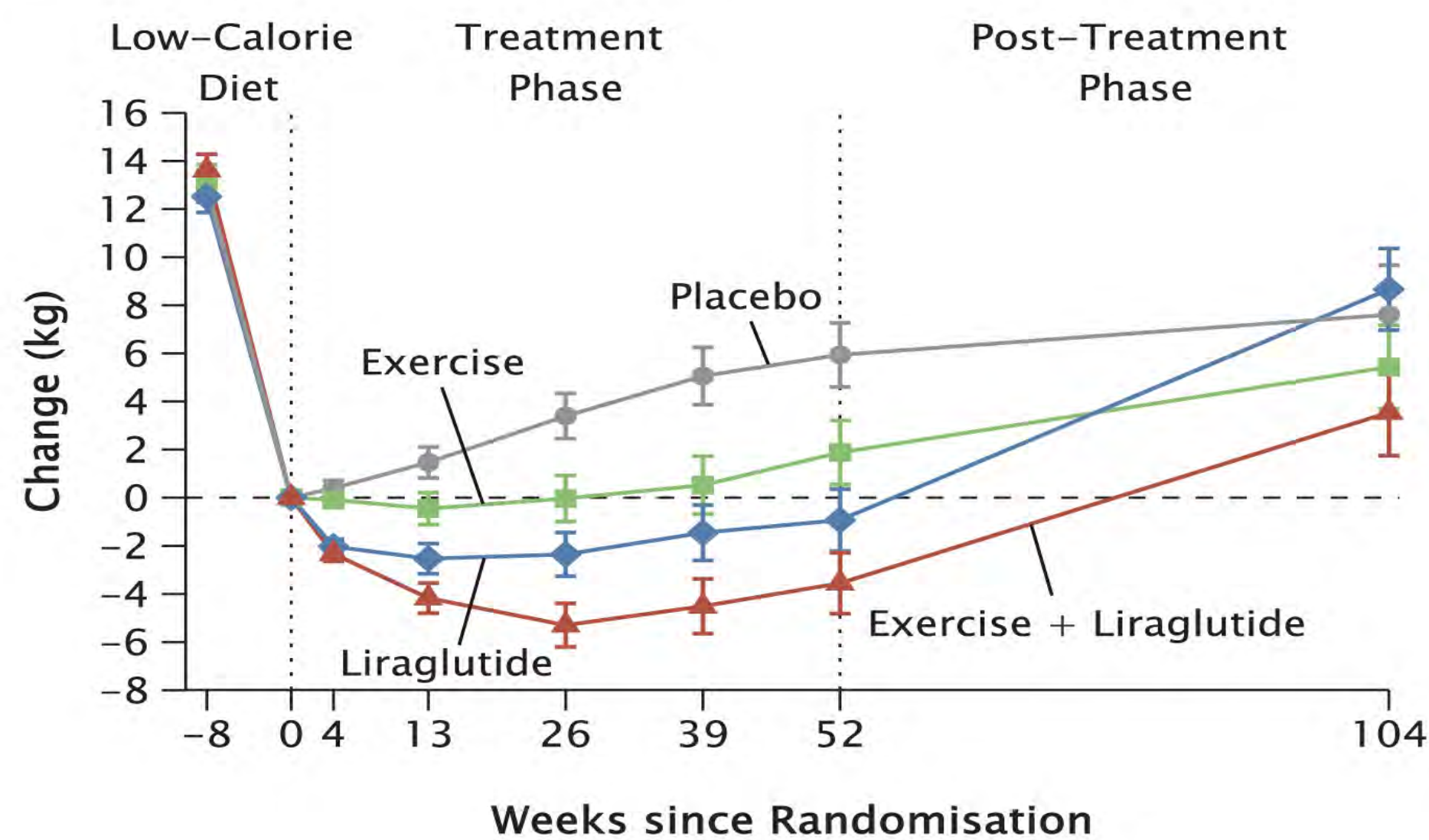
ORIGINAL ARTICLE

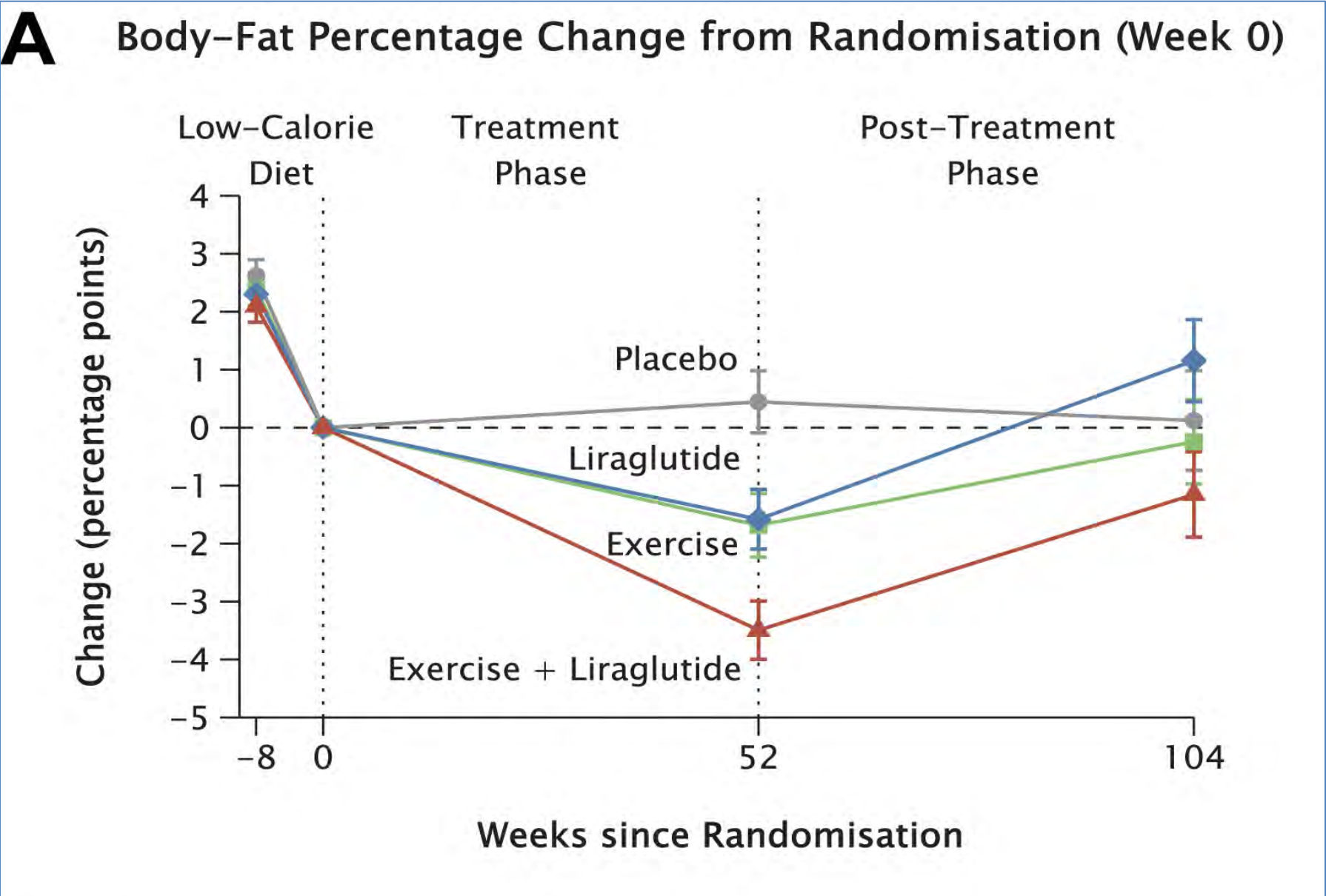
## Healthy Weight Loss Maintenance with Exercise, Liraglutide, or Both Combined

Julie R. Lundgren, M.D., Ph.D., Charlotte Janus, Ph.D., Simon B.K. Jensen, M.Sc., Christian R. Juhl, M.D., Lisa M. Olsen, M.Sc., Rasmus M. Christensen, B.Sc.Med., Maria S. Svane, M.D., Ph.D., Thomas Bandholm, Ph.D., Kirstine N. Bojsen-Møller, M.D., Ph.D., Martin B. Blønd, M.D., Ph.D., Jens-Erik B. Jensen, M.D., Ph.D., Bente M. Stallknecht, M.D., D.M.Sc., *et al.*

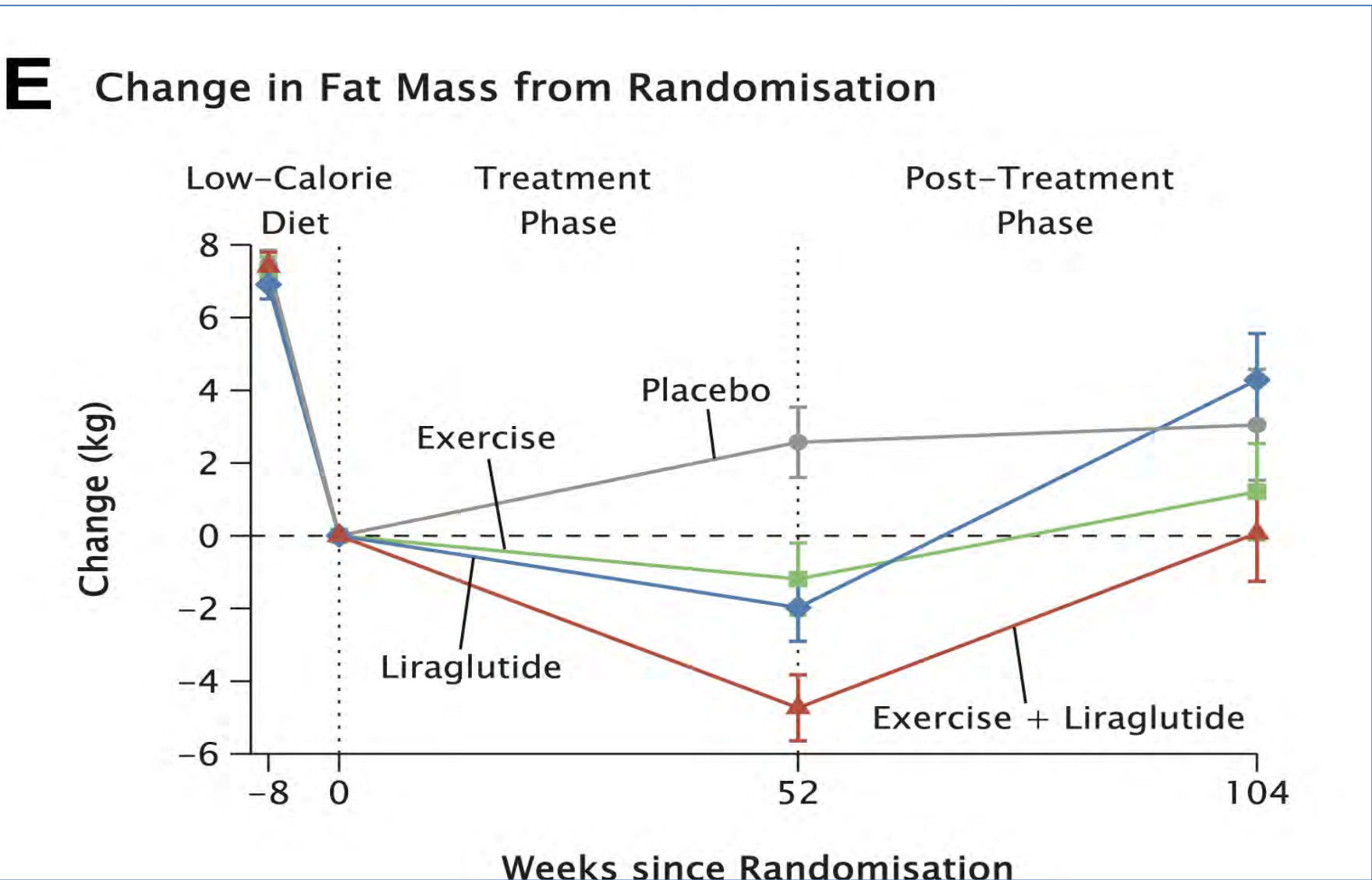


Body Weight Change from Randomisation (Week 0)



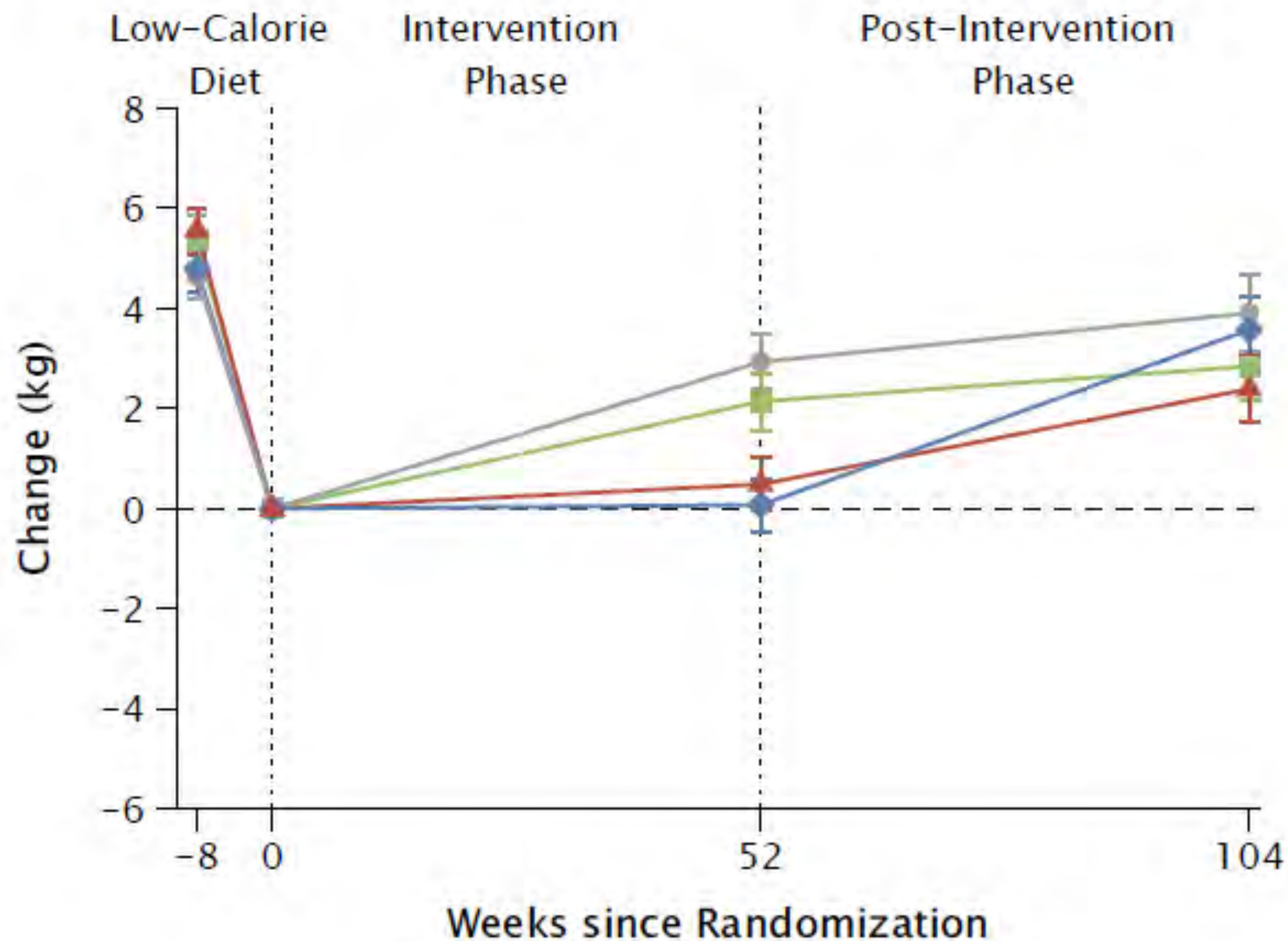


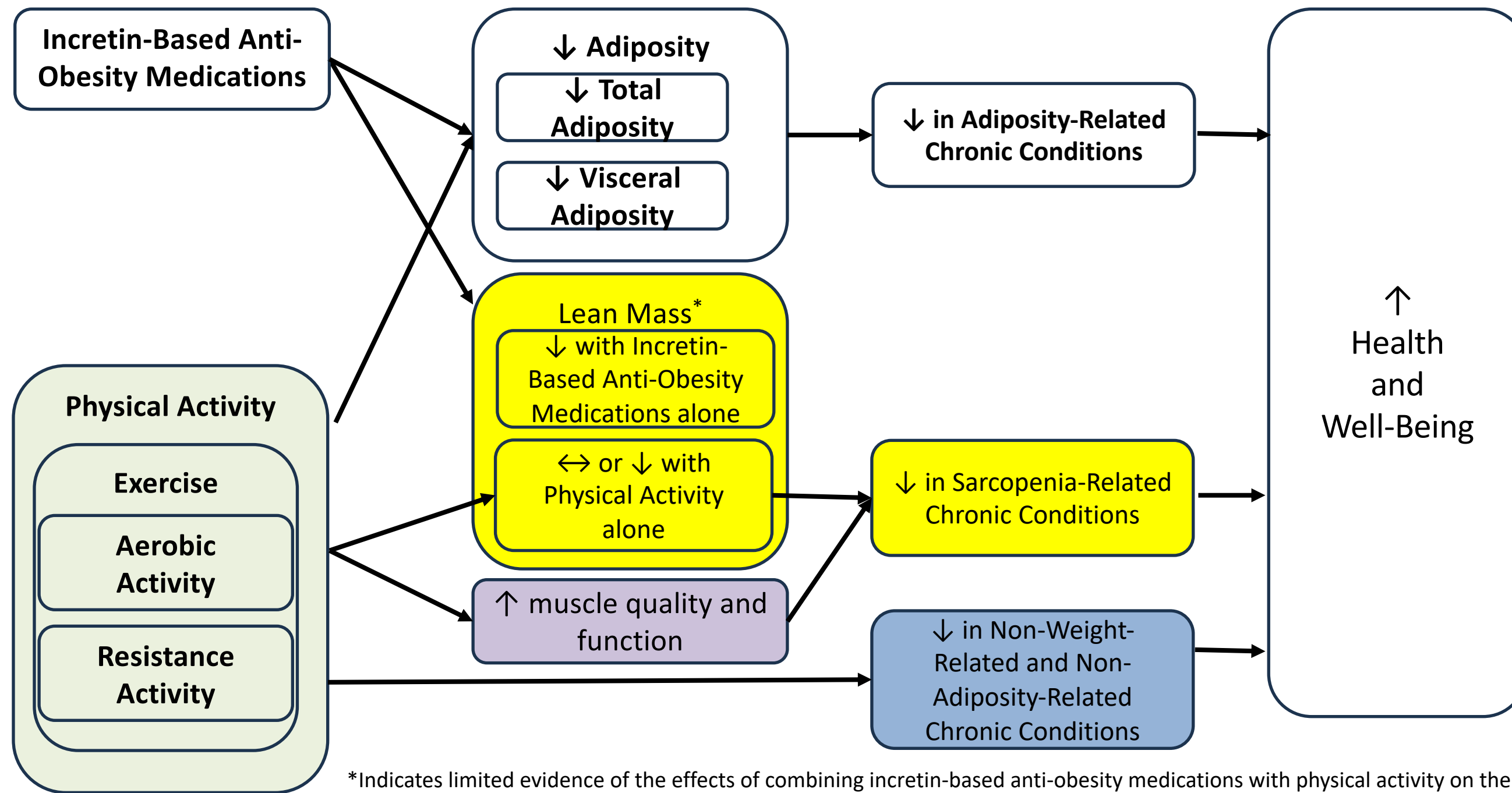
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Published Online XXX  
<https://doi.org/10.1016/j.edinm.2024.102475>





## A Change in Lean Mass







**Move Away from: Exercise to...**

**“Preserve Muscle”**

**“Slow or Stop Muscle Loss”**

**Move to: Exercise for...**

**“Muscle Health”**

**“Quality of Life”**

**“Physical Function”**

## The Challenges:

On these agents, patients:

- Will lose significant weight without engaging in activity,
- Will improve many health parameters without engaging in activity, and
- May not see the value of activity specifically for weight loss.

Despite these challenges, this may open the door for new physical activity opportunities.

## The Opportunities:

We can now:

- Pivot from doses and intensities of physical activity for weight loss and prescribe based on improving health in patients using AOMs,
- Target physical activity for the independent health benefits not realized with weight loss alone, and
- Support patients on their holistic weight loss journey as a part of an integrated team of healthcare professionals.



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**DOSE**



**HEALTH**



**SUPPORT  
TEAM**

**NEXT WEBINAR:**

**EXRX**

**CURRENT BIO-BEHAVIORAL**

**RESEARCH**

**RECOMMENDATIONS**

**BUSINESS CONSIDERATIONS**





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1mo • Edited •

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**DO:** Read more ([evidence](#)) about what we do and do not know about the role of physical activity...





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# Thank You!



**Renee J. Rogers, PhD, FACSM**

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