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# GLP-1 Receptor Agonists for Weight Management

## Update on Trials and Guidelines

# Disclosures

Financial Conflicts of Interest:
None

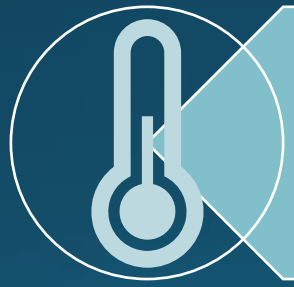
# Learning Objective

- By the end of this session, participants will be able to apply key updates from **recent trials and guidelines on GLP-1–based medications** for weight management, including identifying appropriate patients and recognizing potential health benefits relevant to internal medicine practice.

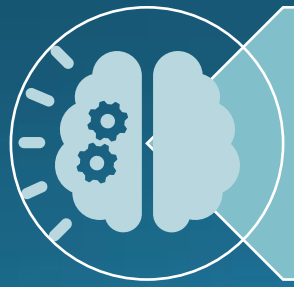
# Background Principles

Obesity is a chronic, often progressive disease

Neurohormonal factors act on brain feeding centers to control body mass

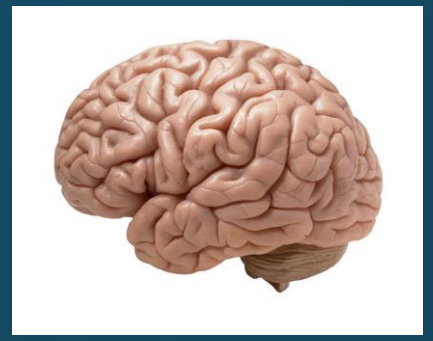


Dysregulated physiology leads to increased adiposity & weight regain

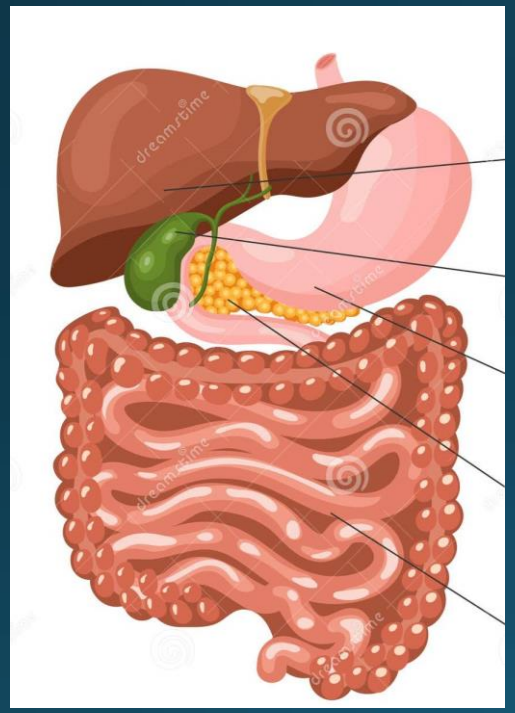


Weight loss medications target the dysregulated hormonal systems

# Terminology



Satiety Signals

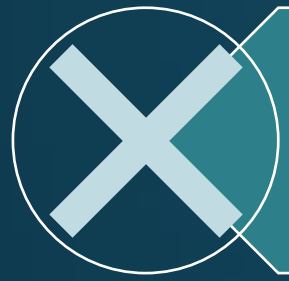


Nutrient-stimulated hormones

- NuSH
  - GLP-1
    - Semaglutide
    - Liraglutide
  - GLP-1 + GIP
    - Tirzepatide
  - Others

GLP-1: Glucagon-like peptide-1
GIP: Glucose –dependent insulinotropic polypeptide

# Weight Stigma & Bias



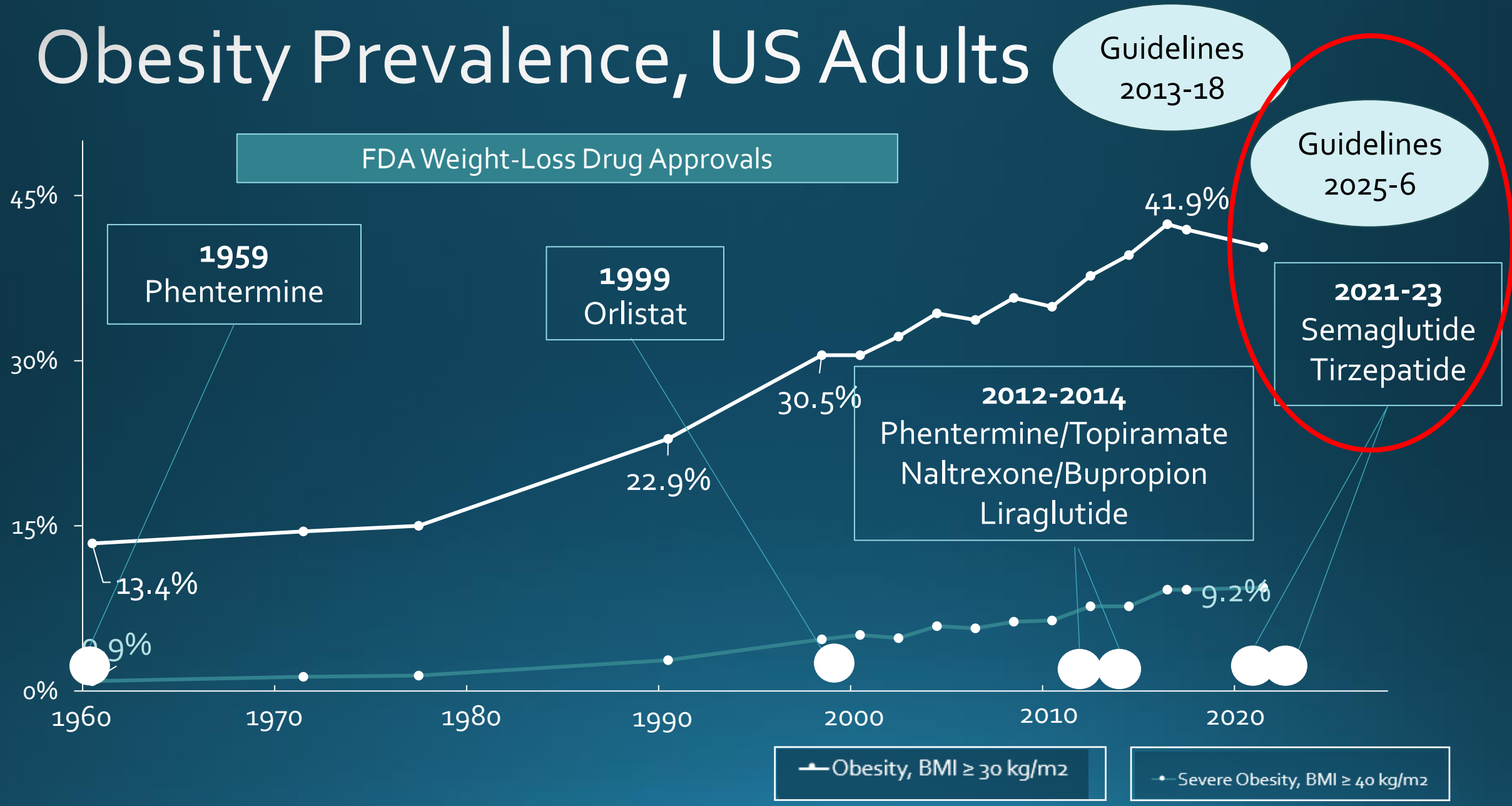
Avoid oversimplifying etiology of obesity

Acknowledge difficulties of persons with obesity

Use first person language ("person with obesity")

Albury *Lancet Diabetes Endocrinol* 2020

# Obesity Prevalence, US Adults




US NHANES data (Fryar 2020, Stierman 2021; Emmerich 2024)

JAMA | Special Communication | CURRENT TOPICS IN OBESITY

*JAMA* December 2025

# World Health Organization Guideline on the Use and Indications of Glucagon-Like Peptide-1 Therapies for the Treatment of Obesity in Adults

Francesca Celletti, MD, PhD; Jeremy Farrar, MD, PhD; Luz De Regil, PhD

AACE Clinical Guidance

*Endocrine Practice* Sept 2025

# American Association of Clinical Endocrinology Consensus Statement: Algorithm for the Evaluation and Treatment of Adults with Obesity/Adiposity-Based Chronic Disease — 2025 Update

# Pharmacologic Treatment of Obesity in Adults: Standards of Care in Overweig

*American Diabetes Association Professional Practice Commit*

*Diabetes, Obesity, and Cardiometabolic CARE 2026;1:5–36* | https://doi.or

CONCISE CLINICAL GUIDANCE

*JACC* June 2025.

# 2025 Concise Clinical Guidance: An ACC Expert Consensus Statement on Medical Weight Management for Optimization of Cardiovascular Health

A Report of the American College of Cardiology Solution Set Oversight Committee

# Joint TOS/OMA/OAC Expert Guidance St Pharmacological Management of United Overweight or Obesity Using the GRADE Approach

Lydia Alexander[1] | Jonathan Q. Purnell[2] | Karlijn Burridge[3] | Marc-André Cornier[4] | Angela Golden[5] | Deborah Bade[6] | Michelle Look[7] | Joe Nadglowski[8] | Camila Ávila-Oliver[9,10] | Francisco Novillo[10,11] | Ana María Rojas-Gómez[10] | Brad Hussey[12] | Ximena Ramos Salas[12]

Recommended

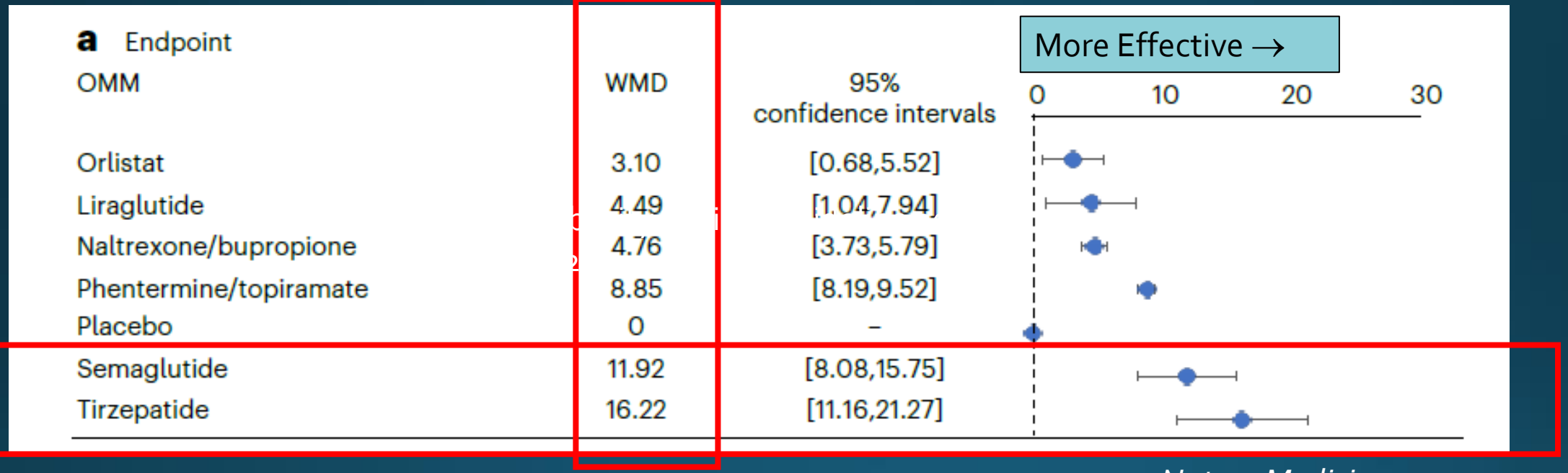
# Treat obesity in adults with weight loss medications

| WHO | TOS/OMA/OAC | ADA Obesity Society |
|---|---|---|
| GLP1 Therapies<br><br>• **Conditional recommend-ation for;** moderate certainty evidence | Tirzepatide<br>Semaglutide<br><br>Bupropion-naltrexone<br>• **Strong recommendation for;** moderate certainty of the evidence<br><br>Orlistat<br>Phentermine<br>Phentermine-topiramate<br>Liraglutide<br>• **Conditional recommendation for;** low certainty of the evidence | Consider obesity medications as part of the treatment plan to promote weight reduction, prevent further weight gain, and reduce the risk of developing obesity-related diseases and complications **A**, **C**<br><br>Offered as part of initial treatment for obesity to adults with or at high risk of obesity-related diseases or complications **A**. |

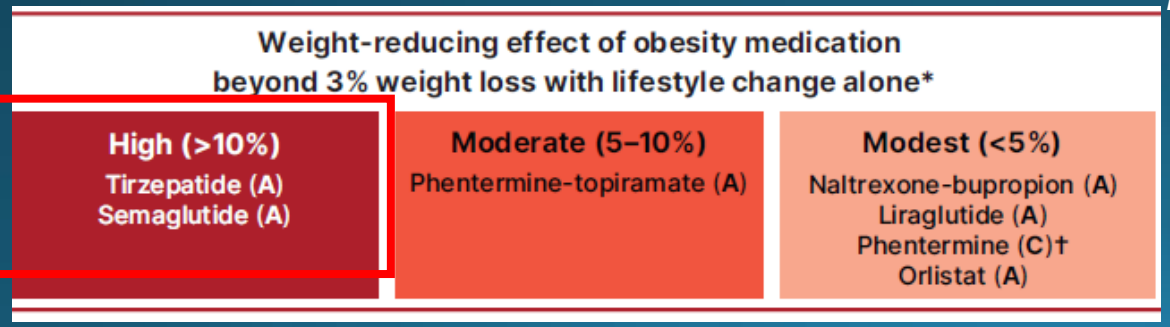
*JAMA*. 2026; 335(5): 434-438.
*Obesity* 2026; 0: 1-20.
*Diabetes Obes Cardio Metab CARE* 2026; 1(1)): 5–36.

# Meta-Analysis of RCTs
# % Weight Loss (IG-CG)

IG=Intervention group
CG=Control group

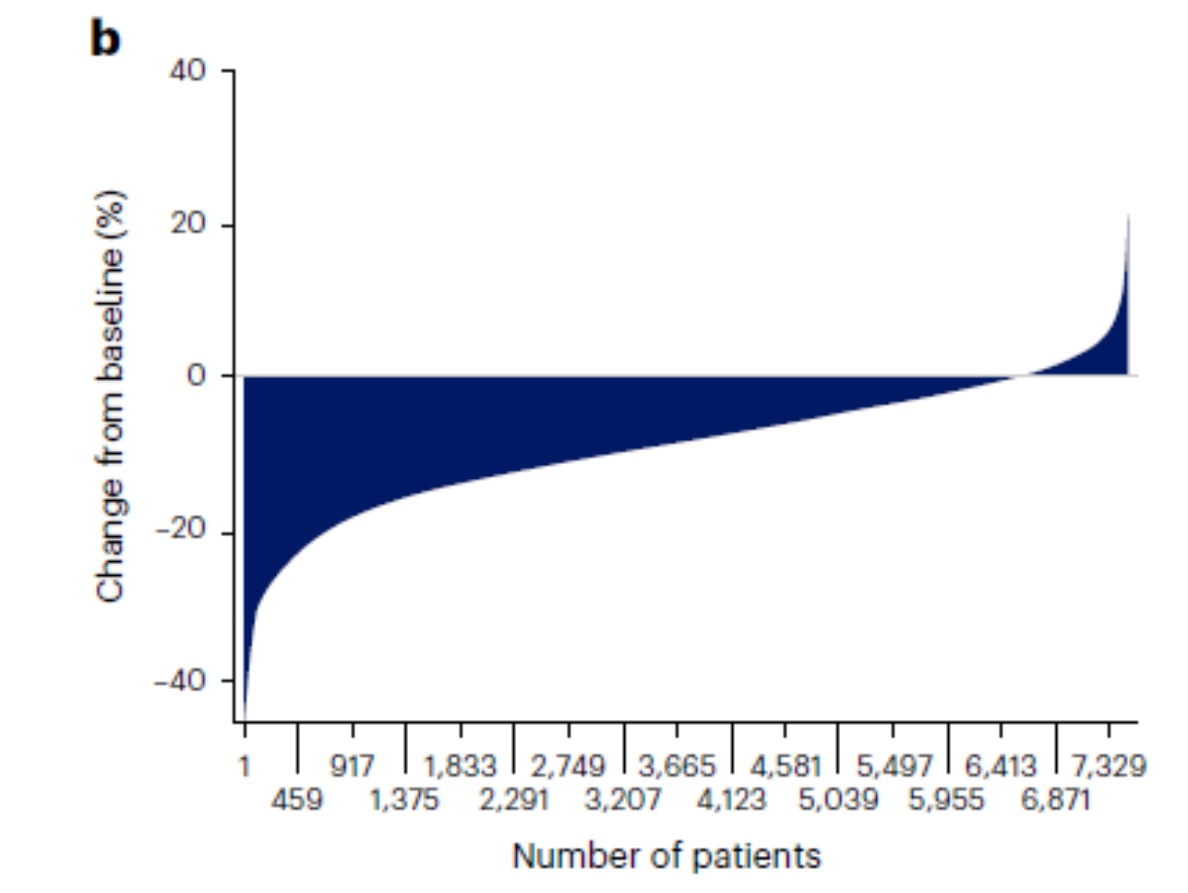



*Nature Medicine*. 2025 ; 31: 3317-3329.




*Diabetes Obes Cardio Metab CARE* 2026; 1(1): 5–36.

# Variation in Response to Medications

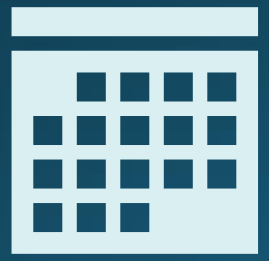



- Participants in SELECT trial (Semaglutide vs Placebo)

*Nature Medicine.* 2024;30(7):2049–2057

Recommended

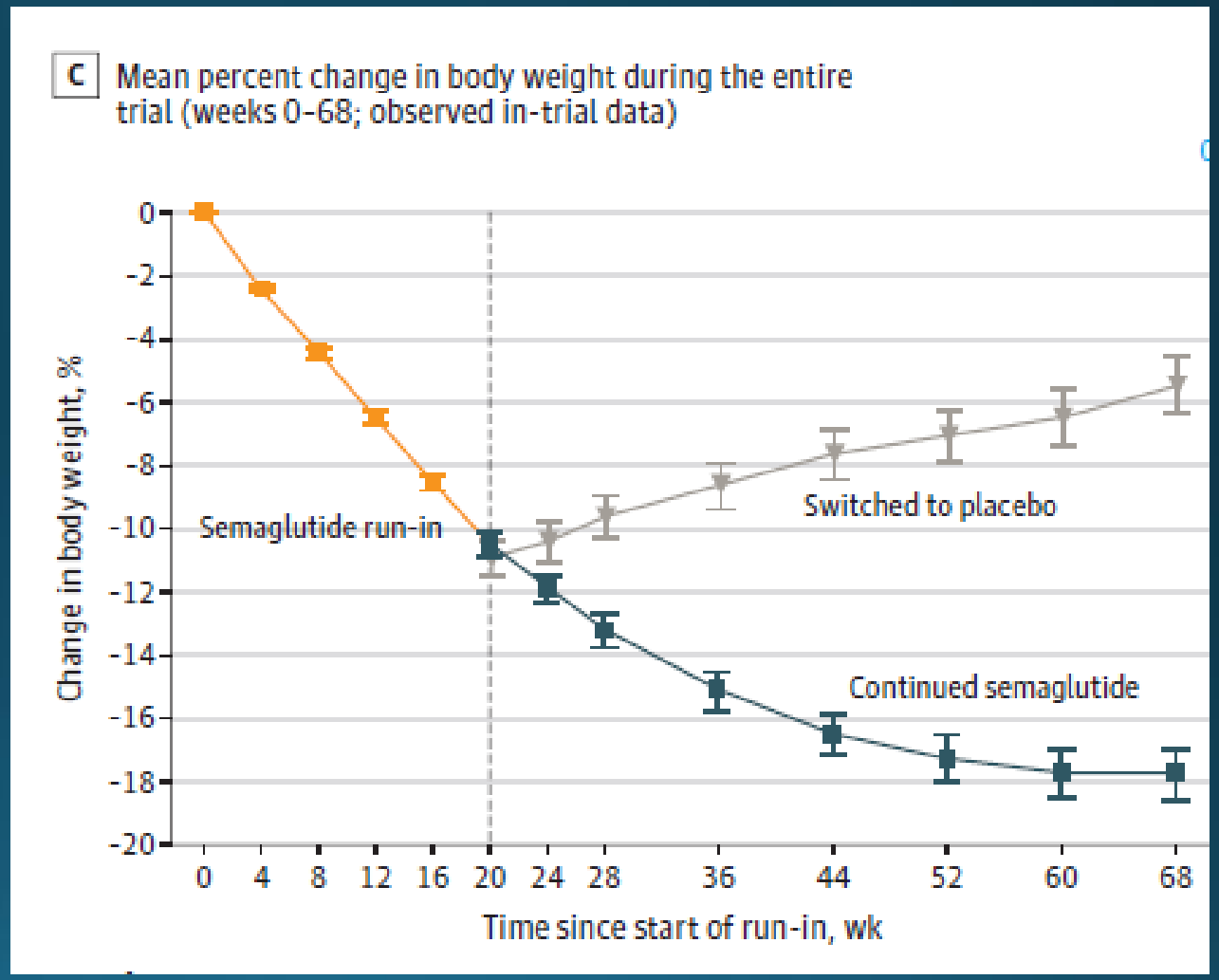
# Continue medication for long-term during maintenance



| WHO | TOS/OMA/OAC | ADA Obesity Society |
|---|---|---|
| **Conditional recommendation for,** moderate certainty evidence | **Strong recommendation for**; moderate certainty of the evidence | **Recommended**<br><br>A |

*JAMA*. 2026; 335(5): 434-438.
*Obesity* 2026; 0: 1-20.
*Diabetes Obes Cardio Metab CARE* 2026; 1(1)): 5–36.

# Effect of Stopping GLP1 Medications




*JAMA*. 2021;325(14):1414–1425.

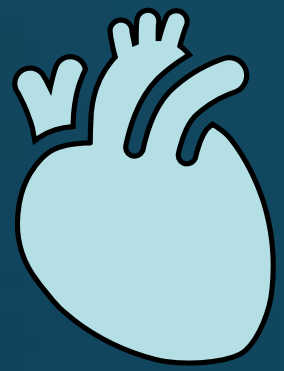
# Lifestyle Recommendations

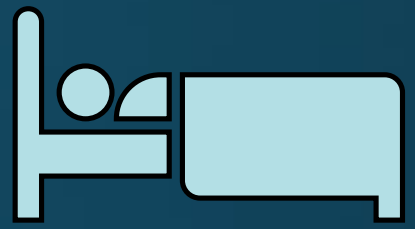


| | WHO | TOS/OMA/OAC | ADA Obesity Society |
|---|---|---|---|
| **Healthy lifestyle** | Medication should be used in conjunction with a healthy lifestyle. Recommended | | Nutrition, physical activity, and behavioral therapy should be used in combination with obesity medications to achieve health goals **A.** |

*JAMA*. 2026; 335(5): 434-438. *Obesity* 2026; 0: 1-20. *Diabetes Obes Cardio Metab CARE* 2026; 1(1)): 5–36.

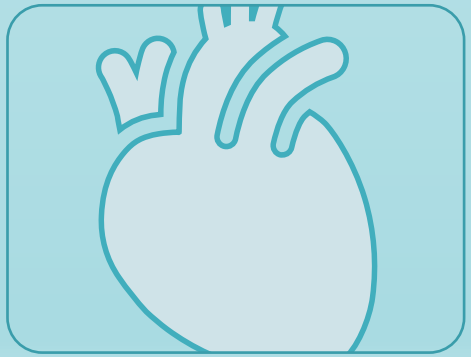
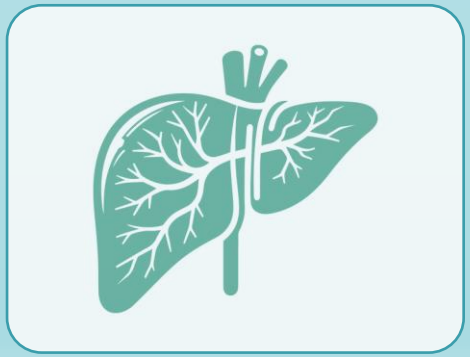
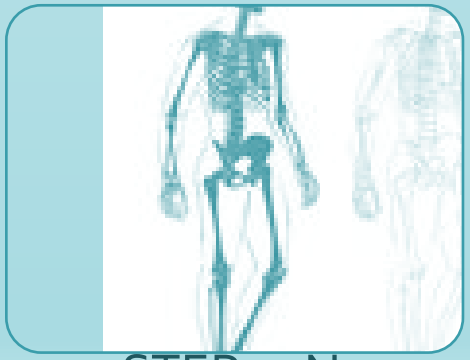
# GLP1 Medications to Treat Specific Diseases





# RCTs Semaglutide in Pts w/ Obesity-Related Diseases*

*AND BMI ≥30 or BMI ≥27; most excluding pts w/diabetes

| | SELECT; N=17,604 | STEP-HFpEF; N=529 | ESSENCE; N=1,197 | STEP 9; N= 407 |
|---|---|---|---|---|
| |  |  |  |  |
| Inclusion criteria* | CVD (MI, stroke, PAD) | HFpEF | MASH** (F2-3 fibrosis) | Knee OA Mod Severity |
| Health Outcomes | • CVD Composite<br>• CVD Mortality<br>• HF Composite<br>• All Cause Mort | • HF Symptoms<br>• 6 min walk<br>• HF Composite (ACM, HF events, symptom score, 6 min wak) | • Resolution steatohep-atitis<br>• Reduction in liver fibrosis | • Pain score<br>• Physical function score |
| Benefits shown | *NEJM* 2023; 389 (24):2221-2232 | *NEJM* 2023; 389: 1069-1084. | *NEJM* 2025; 392 (21):2089–2099. | *NEJM* 2024; 391 (17):1573–1583. |

- **56% had DMT2, 3% lean BMI

# SELECT: Semaglutide 2.4 mg Secondary CVD Prevention

N= 17,604; 104 wks; 96.9% completed

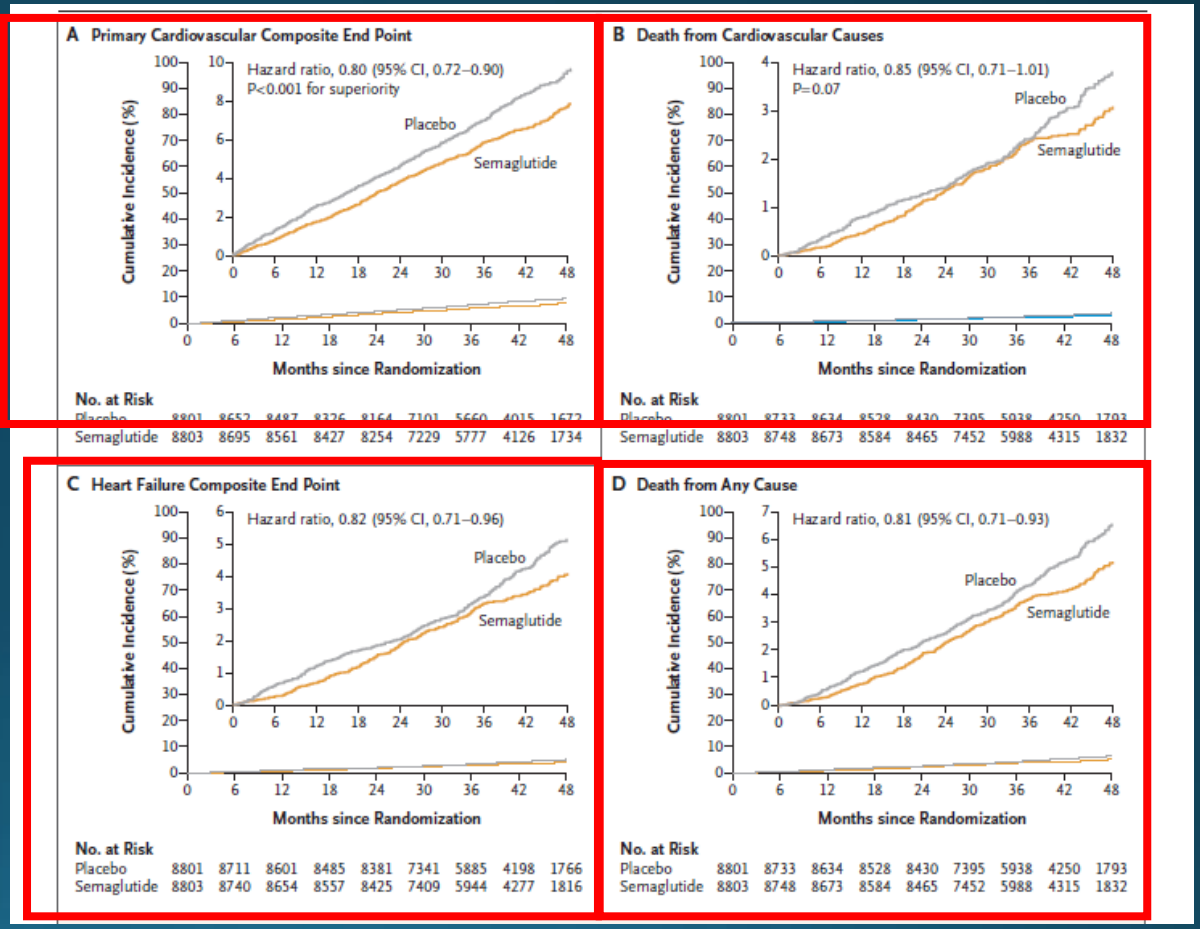
All had hx of MI, Stroke, or PAD; no DM
(Ave Age 62 yrs)

A. CVD Composite:
6.5% IG vs 8.0% CG
(HR 0.80, 0.72 - 0.90)

B. CVD death ns

C. HF composite:
HR 0.82 (0.71 - 0.96)

D. All Cause Mortality:
HR 0.81 (0.71 - 0.93)




*NEJM* 2023; 389 (24):2221-2232.

%Wt loss: IG: -9.39% vs CG: -0.88% , Δ: -8.51 (-8.75 to -8.27); No Lifestyle component to intervention

# RCTs Tirzepatide in Patients w/ Obesity-Related Diseases*

*& BMI ≥30 or ≥27

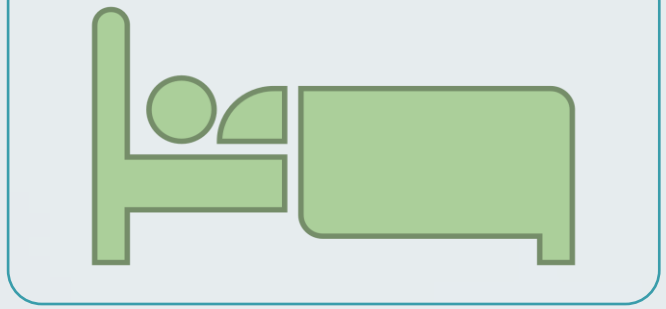
Inclusion criteria*

Health Outcomes

Benefits shown

SURMOUNT OSA
N= 234 +235

SUMMIT
N= 731



## OSA

- Mod-Severe OSA (AHI ≥ 15 /hr)
  - Trial 1: No CPAP
  - Trial 2: On CPAP
- Improved AHI

## HFpEF

- HF & CVD death composite
- 6 min walk
- HF Symptom score

*NEJM* 2024; 391(13): 1193-1205.

*NEJM* 2025; 392 (5):427-437

# Weight Loss Goals

| | |
|---|---|
| ≥5% | • For all adults treated with obesity medications, which may achieve some clinically meaningful health benefits **A.** |
| ≥10% | • to manage many obesity-related diseases or complications (MASLD, HFpEF, Knee OA) **A** |
| ≥15% | • to achieve greater therapeutic benefit (OSA, CVD mortality) **B** |

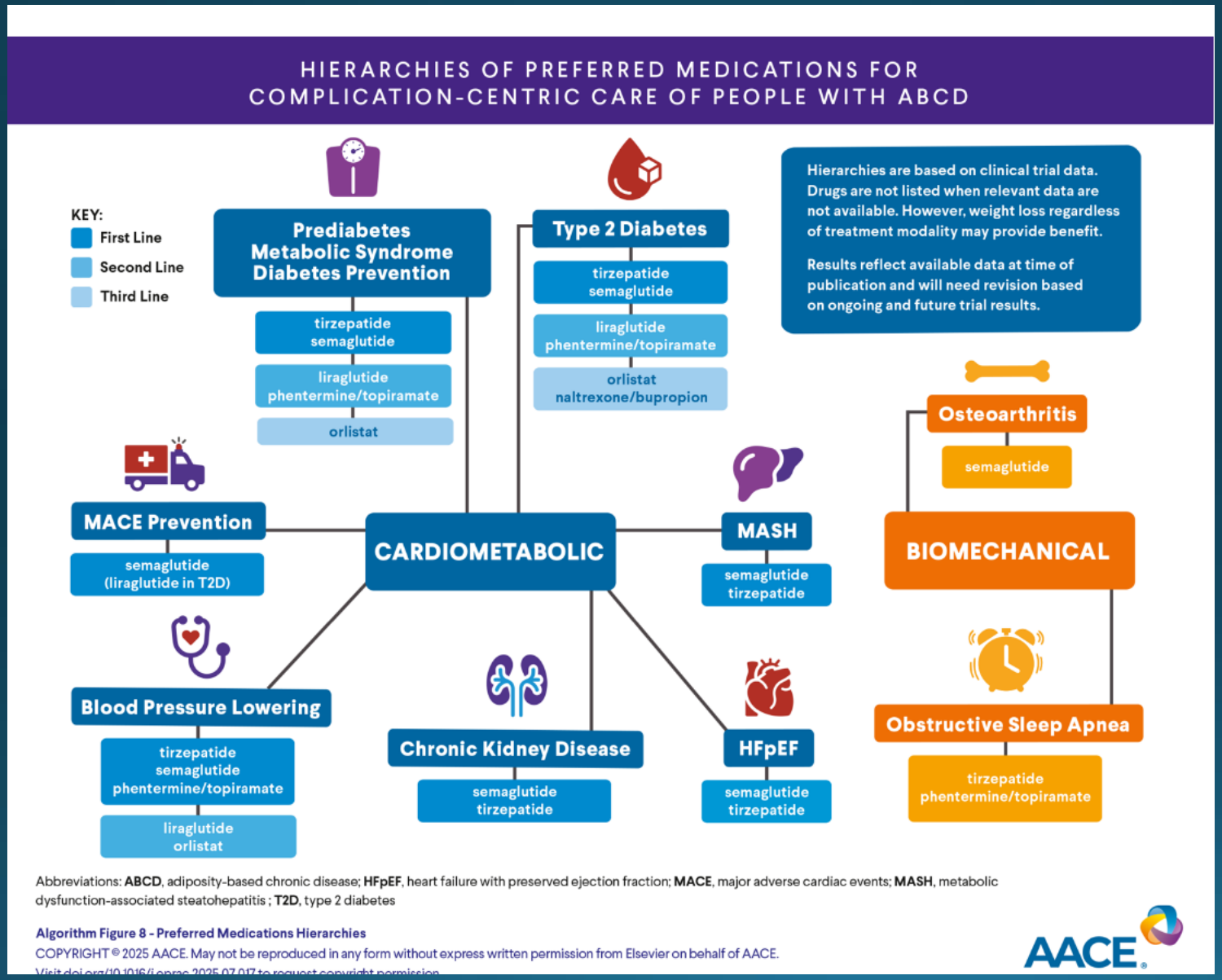
Incremental

Individualized

Based on severity of obesity, & obesity-related diseases; individuals' needs, life circumstances & preferences

(Expert opinion)

Diabetes, Obes, Cardiomet CARE 2026; 1(1)): 5–36.
JACC. 2025; 86 (7): 536-555.




Abbreviations: **ABCD**, adiposity-based chronic disease; **HFpEF**, heart failure with preserved ejection fraction; **MACE**, major adverse cardiac events; **MASH**, metabolic dysfunction-associated steatohepatitis ; **T2D**, type 2 diabetes

**Algorithm Figure 8 - Preferred Medications Hierarchies**



AACE

*Endocrine Practice*. 2025;31(9):1351–1394.

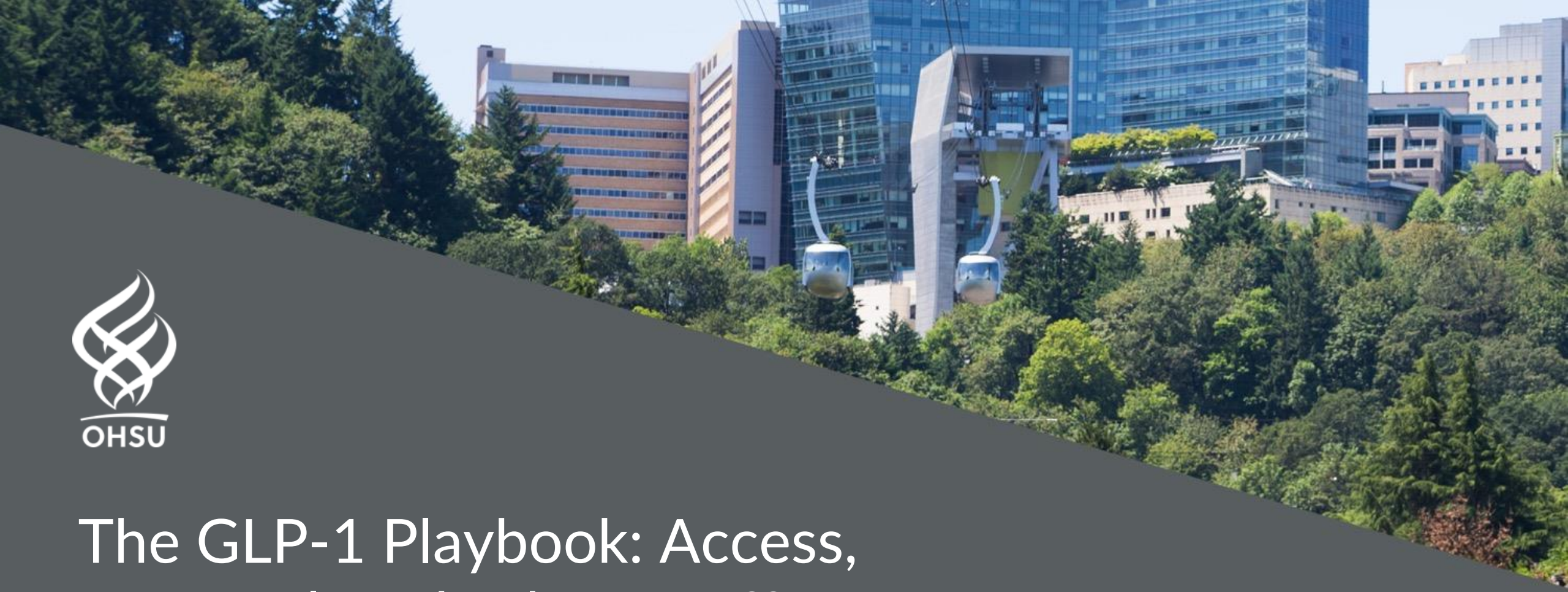
# Evidence Limitations

- Long-term data beyond 4 yrs on durability of weight loss, safety, health outcomes, function, & mortality
- Head-to-head trials comparing newer agents with each other and lower-cost therapies
- Data on  titration, maintenance and discontinuation
- Policy/Systems Context:  High current cost of GLP-1 therapies, lack of health insurance coverage, inadequate health system preparedness, and equity implications.

# Summary

- Data from recent trials and guidelines support treating obesity with FDA-approved weight loss medications as part of initial management along side healthy lifestyle and behavioral therapies.
- Newer GLP-1-based therapies are highly effective and lead to >10% weight loss above lifestyle treatment alone on average.
- Guidelines recommend continuing weight loss medication for long-term maintenance treatment.
- GLP-1- based treatments are demonstrated to improve multiple health outcomes in patients with obesity-related diseases, including
  - Cardiovascular disease, all cause mortality, heart failure symptoms, metabolic associated steatohepatitis, obstructive sleep apnea, osteoarthritis knee pain
- Affordable access to medications remains a major barrier to care.

# Thank you!



# The GLP-1 Playbook: Access, Approval, and Adverse Effect Management

DATE: May 15, 2026

PRESENTED BY: Ashley Beylon, PharmD, BCACP
WOW (Weight Optimization and Wellness) Program, Oregon Health and Science University
Bariatric and Metabolic Surgery

# Disclosure Statement

- I have no relevant financial relationships or conflicts of interest to disclose. The content of this presentation is based on current knowledge and professional experience and is intended for educational purposes only.



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# Learning Objectives

- Identify prevention strategies for common GLP-1 associated side effects.
- Apply practical pharmacologic and non-pharmacologic interventions to manage GLP-1 related adverse effects and improve treatment tolerability and adherence.
- Utilize effective insurance coverage strategies, including leveraging FDA-approved indications and documentation best practices, to optimize patient access to GLP-1 therapies.



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# Side Effect Prevention



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GLP-1
Side Effects
NAUSEA
VOMITING
DIARRHEA
CONSTIPATION
ACID REFLUX
ABDOMINAL PAIN
INJECTION SITE REACTIONS



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# Managing Common GLP-1 Side Effects

Side effects often occur in the first few weeks after initiation or dose escalation

Common effects include nausea, vomiting, diarrhea, constipation, acid reflux, and abdominal pain

Poor tolerability can drive discontinuation and limit long-term benefit



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# Side Effect Prevention

## Provider Interventions

- Start with low dose
- Increase dose slowly to help patient build tolerance

## Patient Interventions

- Eat smaller portions and more frequent meals
- Avoid lying down after meals
- Eat a small meal before injection
- Trial of different injection sites



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# Side Effect Prevention

## Diet Changes

- Avoid greasy, oily, fatty and spicy foods
- Increase fiber intake to prevent constipation
- Protein first to meet daily protein goals
- Hydration!
  - 64 oz of water daily



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# Preserving Lean Muscle Mass

- Consume protein-rich foods first in a meal
  - Minimum 60 grams of protein daily
- Ensure adequate intake and absorption of high-quality protein and micronutrients
  - Oral supplements may be necessary if reduced appetite limits dietary intake



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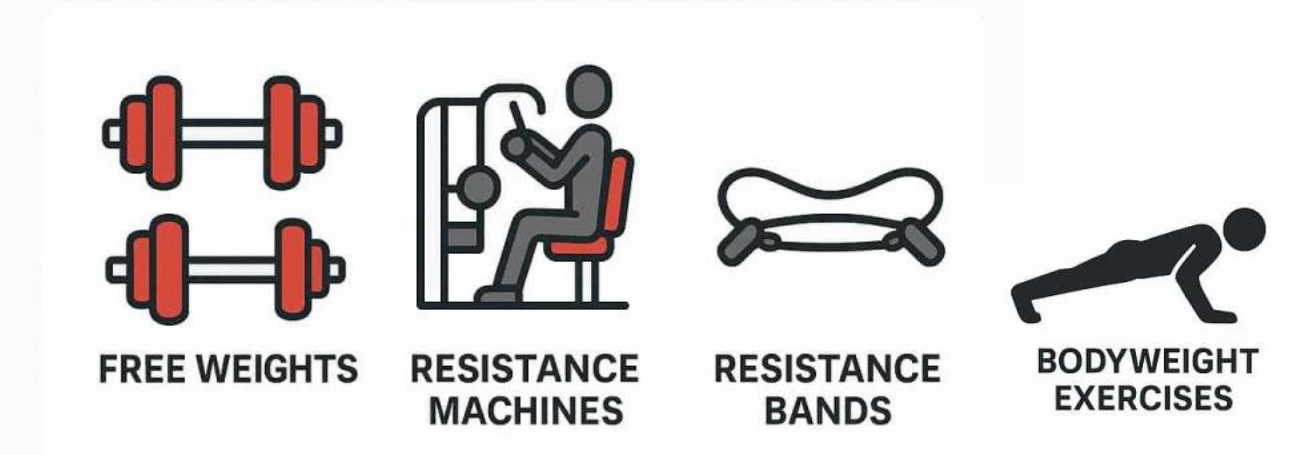
# Preserving Muscle Mass

- Increased protein intake alone is not sufficient to preserve lean muscle mass
- Resistance/ strength training is essential



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# Side Effect Management



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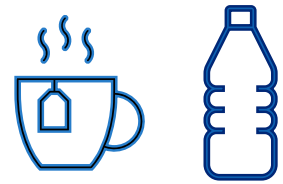
# Nausea/ Vomiting

## Non-Pharmacological Interventions

- Eat bland foods that minimize symptoms (ex: crackers, broth)
- Ginger or peppermint products
- Changes to diet or portion sizes
- Keep a food journal to identify triggering foods
- Prioritize hydration



## Pharmacological Interventions

- Anti-nausea medications as needed (Zofran, Reglan)
- Decrease dose if side effects do not resolve or are intolerable



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# Constipation

## Non-Pharmacological Interventions

- Increase fiber intake (20-35 grams/day)
- Increase hydration

## Pharmacological Interventions

- Fiber supplements (Psyllium)
- Stool softeners (docusate) for dry/ hard stools or straining
- Laxatives
  - Start with osmotic laxatives PEG 3350 (Miralax)
  - Trial of stimulant laxatives if not responding to other products (Senna, Dulcolax)



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# Diarrhea

- Ensure adequate hydration
  - 64 ounces of fluids daily
  - May add rehydration salts or electrolyte drinks
- Short term antidiarrheals
  - Loperamide or bismuth subsalicylate



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# Acid Reflux

## Non-Pharmacological Interventions

- Avoid acidic, fatty and spicy foods
- Avoid lying down 30-60 minutes after eating
- Avoid eating 3 hours before bedtime

## Pharmacological Interventions

- Antacids (Tums)
- H2 blockers (Pepcid)
- Proton pump inhibitors (omeprazole)



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# Injection Site Reaction

- Rotate injections sites
- Apply cold compress after injection
- Over the counter products to reduce discomfort
  - Topical products (hydrocortisone cream) for itching
  - Oral antihistamines (loratadine, cetirizine) for itching
  - Acetaminophen or ibuprofen for pain



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# Insurance Coverage Tips


Most insurance companies DO NOT offer coverage for weight management

# General Tips and Tricks

To increase likelihood of approval:

1. Identify applicable FDA-approved indications (Type 2 Diabetes (T2DM), Obstructive Sleep Apnea (OSA), Metabolic Dysfunction-Associated Steatohepatitis (MASH) with fibrosis (F2 or F3), cardiovascular risk reduction)

2. Complete required labs and diagnostic evaluations prior to prior authorization submission.



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# Obstructive Sleep Apnea

1. Sleep study with an apnea hypopnea index (AHI) ≥ 15 indicating moderate to severe sleep apnea
2. CPAP compliance report (typically 90-day requirement)
3. Patient is enrolled in a weight management program (including diet and exercise) for at least 3 months

* GLP-1 RA's typically not covered for OSA if patient has Type 2 Diabetes

# Type 2 Diabetes

Most variable coverage criteria depending on insurance

1. A1c > 7%
2. May require other medication trial
    1. Metformin, SGLT-2, DPP-4, pioglitazone, or insulin
    2. Some only cover specific GLP-1 (ex: Victoza vs Ozempic)



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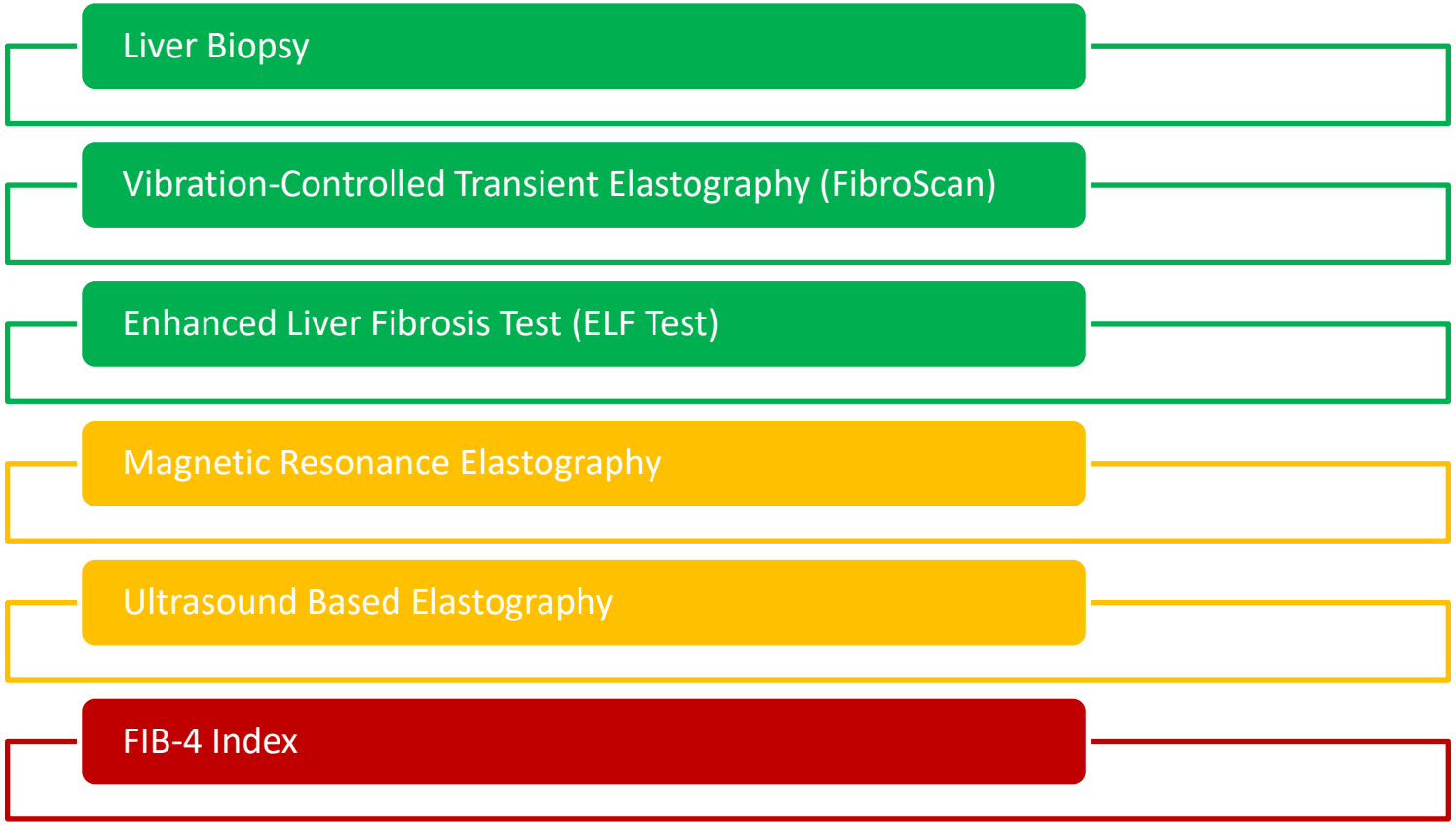
# Metabolic Dysfunction-Associated Steatohepatitis

1. Documentation showing stage F2 or F3  fibrosis
2. Documentation of lifestyle modification including reduced-calorie diet and increased physical activity
3. Documentation that MASH is not caused significant alcohol use
4. May require prescribing in conjunction with hepatology, gastroenterology or endocrinology specialists

# Fibrosis Staging



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# Cardiovascular Risk Reduction

1. Documented history of myocardial infarction, stroke, or symptomatic peripheral artery disease (PAD) with a history of revascularization procedure
2. May require documentation that patient is taking standard of care treatment
    a) antiplatelets, antihypertensive therapy, lipid-lowering therapy

# Appeals

- Don’t feel discouraged if the medication is denied
- Even if patients meet all the criteria, ~ 20% are still denied and may require an appeal
  - Create appeal templates for specific indications
  - Use AI sources to help write your appeals quickly



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# Cash Pay Options

| Ozempic | Wegovy | Oral Wegovy | Zepbound | Foundayo |
|---|---|---|---|---|
| • $199-$499 per month | • $199-$399 per month | • $149-$299 per month | • $299-$449 per month<br>• Vials and Kwikpens available | • $149-$299 per month |

*Starting prices may be offered for limited time



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# Thank You

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- Mozaffarian D, Agarwal M, Aggarwal M, et al. Nutritional priorities to support GLP-1 therapy for obesity: a joint Advisory from the American College of Lifestyle Medicine, the American Society for Nutrition, the Obesity Medicine Association, and The Obesity Society and The American Journal of Clinical Nutrition, 2025; 122, 344-367
- Resistance training. Accessed May 3, 2026. https://wellfitinsider.com/workout-tips/resistance-training/




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# OHSU Internal Medicine Review

## Muscle Loss in Obesity-Medicine Induced Weight Loss: A Safety Issue in Older Patients?

DATE: May 2026

PRESENTED BY:

Jonathan Q. Purnell, MD, FTOS, DABOM
Professor, Knight Cardiovascular Institute
Division of Endocrinology, Diabetes, Clinical Nutr
Oregon Health & Science University
Portland, Oregon

# Disclosures

Society Member:
- The Obesity Society (VP)
- American Diabetes Association
- Endocrine Society

Research:
- NIH

Consulting / Steering Committee:
- Boehringer Ingelheim
- Novo Nordisk
- Zealand Pharmaceuticals

Clinical Trial (PI)
- Novartis
- Amgen



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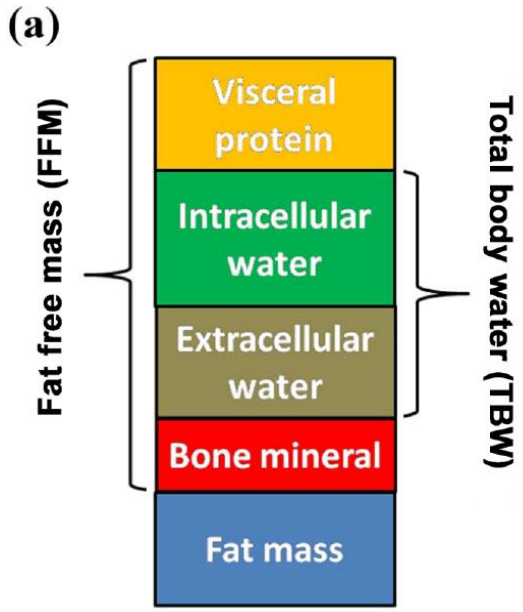
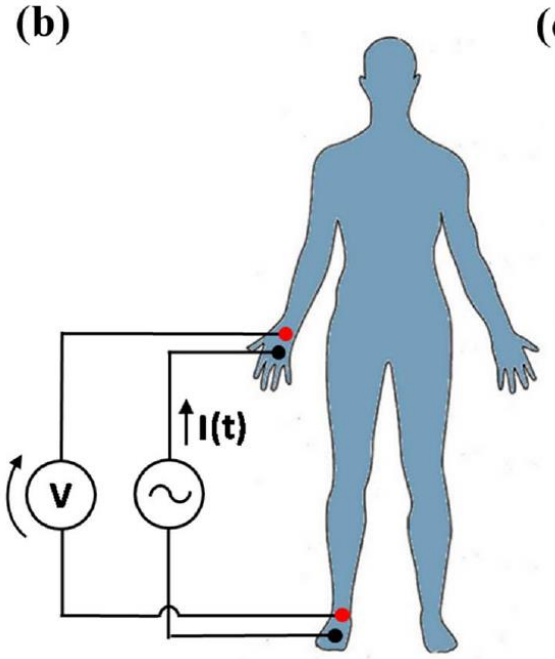
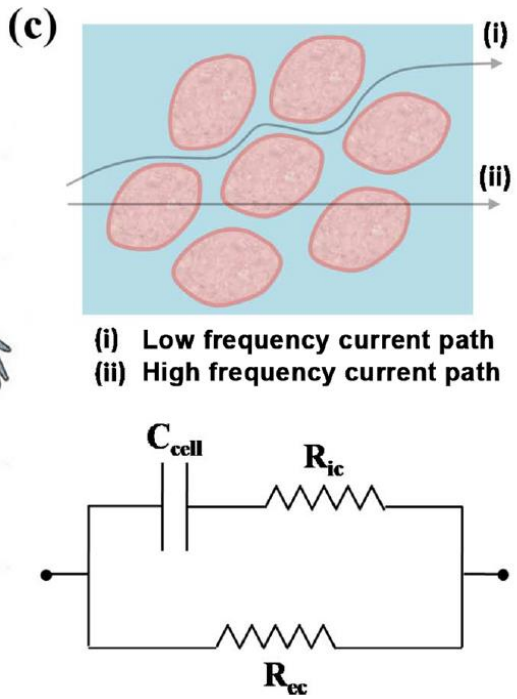
# Body Composition Methods: Bioimpedance Analysis (BIA)

Measures:

- Fat mass
- Non-fat mass:
  - Water
  - Lean mass:
    - Organ mass
    - Muscle mass
    - Bone mass






Grossi and Ricco. J. Sens. Sens. Syst., 6, 303–325, 2017.

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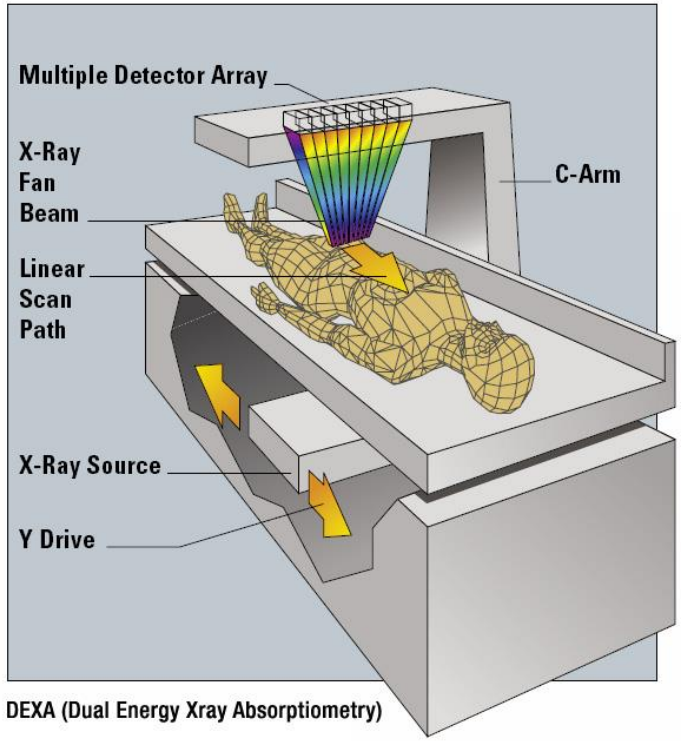
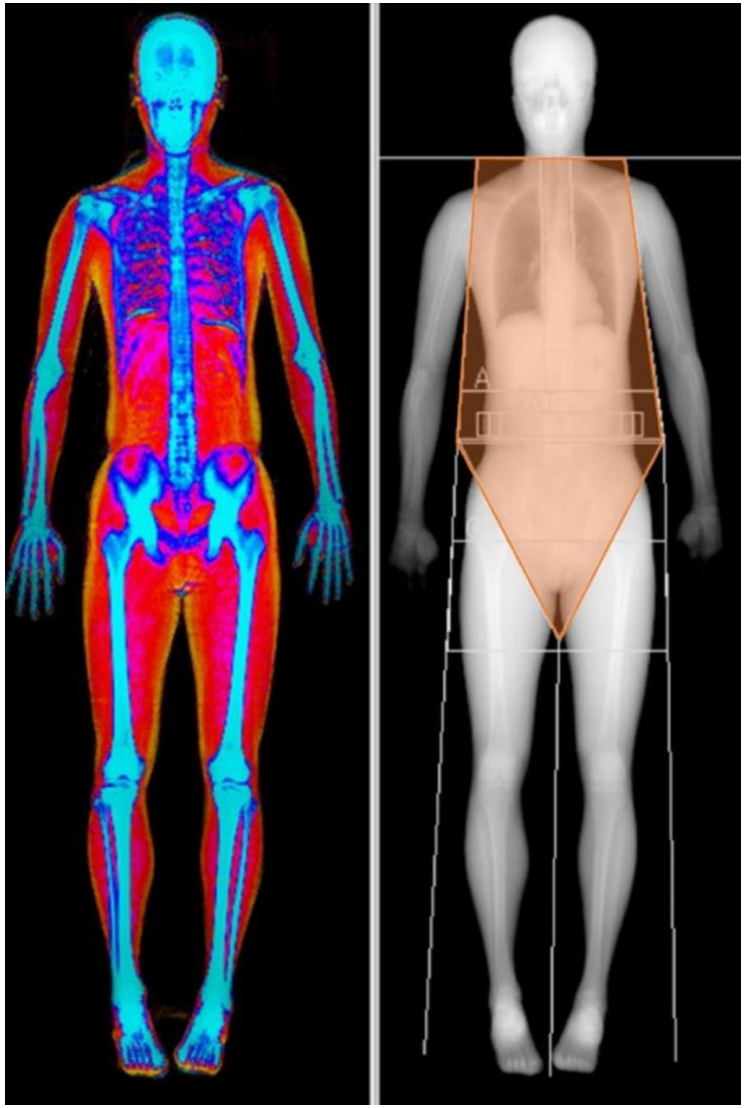
# Body Composition Methods: Dual Energy X-ray Absorptiometry (DEXA)

Measures:

- Fat mass
- Non-fat mass:
  - Water
  - Lean mass:
    - Organ mass
    - Muscle mass
    - Bone mass



DEXA (Dual Energy Xray Absorptiometry)





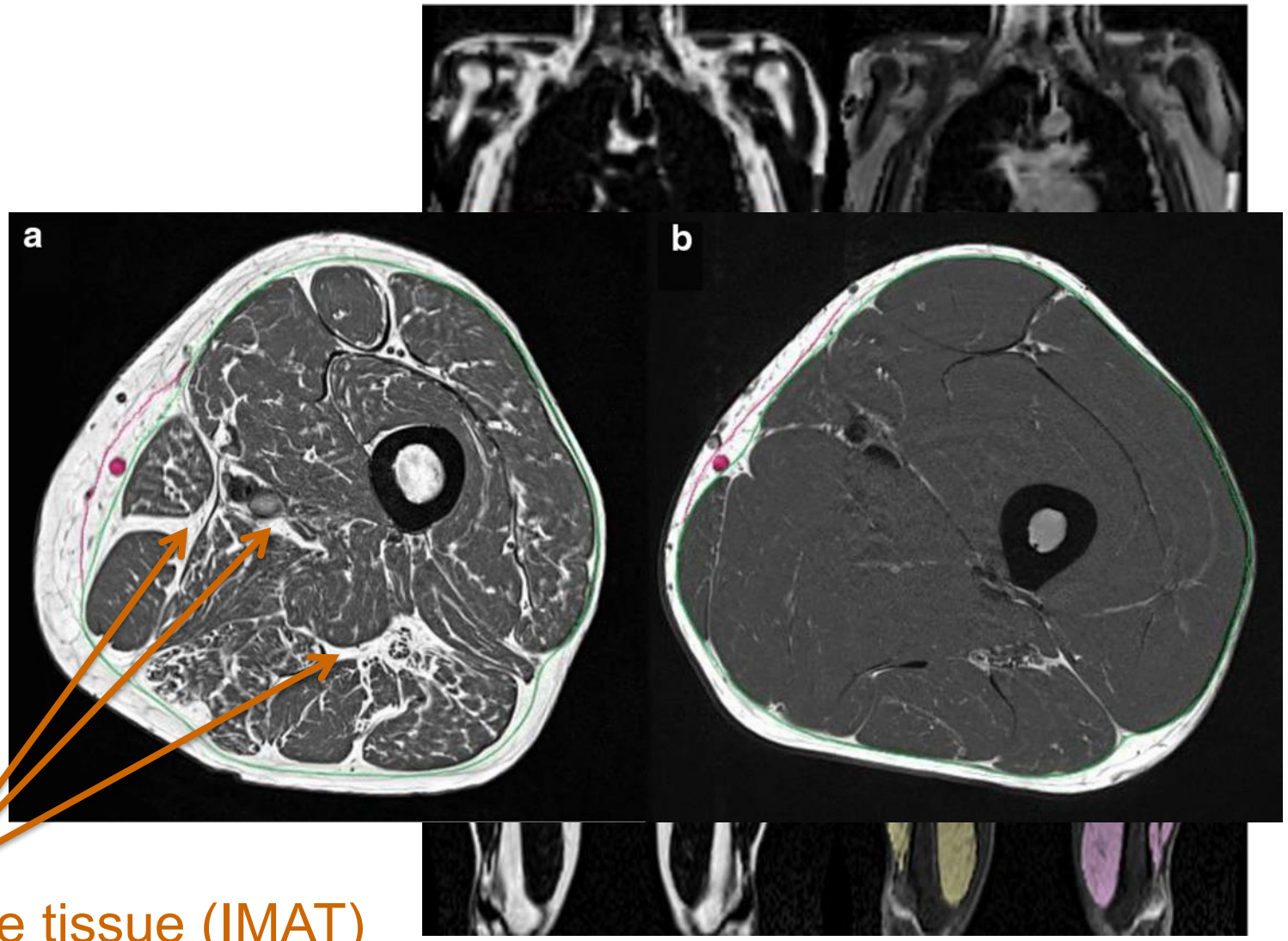
Borga M, et al. J Investig Med. 2018 Jun;66(5):1-9.

# Body Composition Methods

Magnetic Resonance Imaging (MRI)

Measures:

- Fat mass
- Non-fat mass:
  - Water
  - Lean mass:
    - Organ mass
    - Muscle mass
    - Bone mass




Intramuscular adipose tissue (IMAT)


Chaves, et al. Radiol Bras. 2022 55:305–311. Chaudry O, et al. Mag Res Mater Physics Bio Med. 2021. 34:367–376.

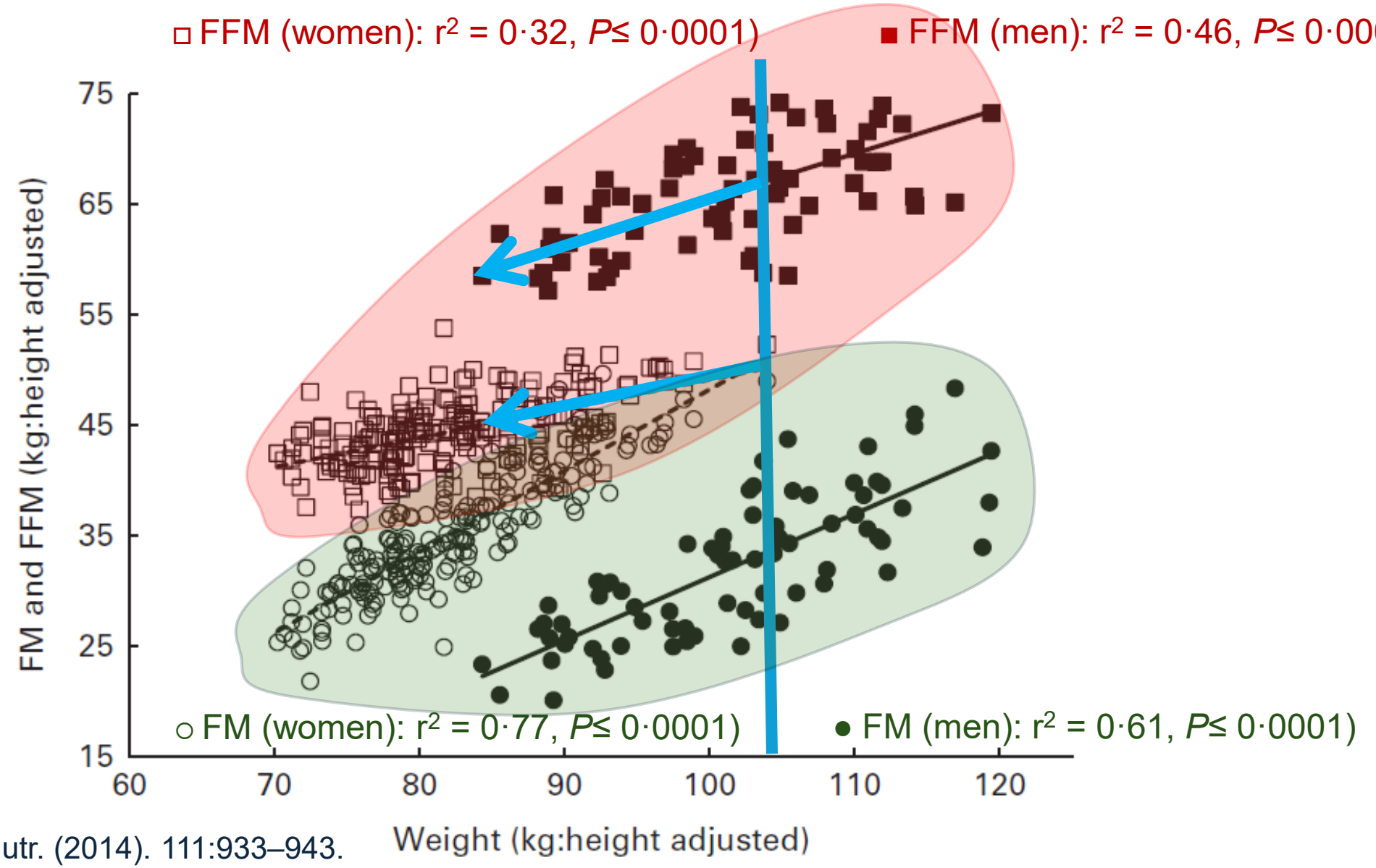
# Questions:

- What is muscle mass in patient with obesity prior to weight loss?
- What happens to muscle mass and function with weight loss?
  - Starvation = “dieting”
  - Metabolic-bariatric surgery
  - Obesity medications (GLP-1(+) RA’s)
- What’s to be done?

# Questions:

- What is muscle mass in patient with obesity prior to weight loss?

# Fat Mass and Fat-Free Mass Increase in Obesity

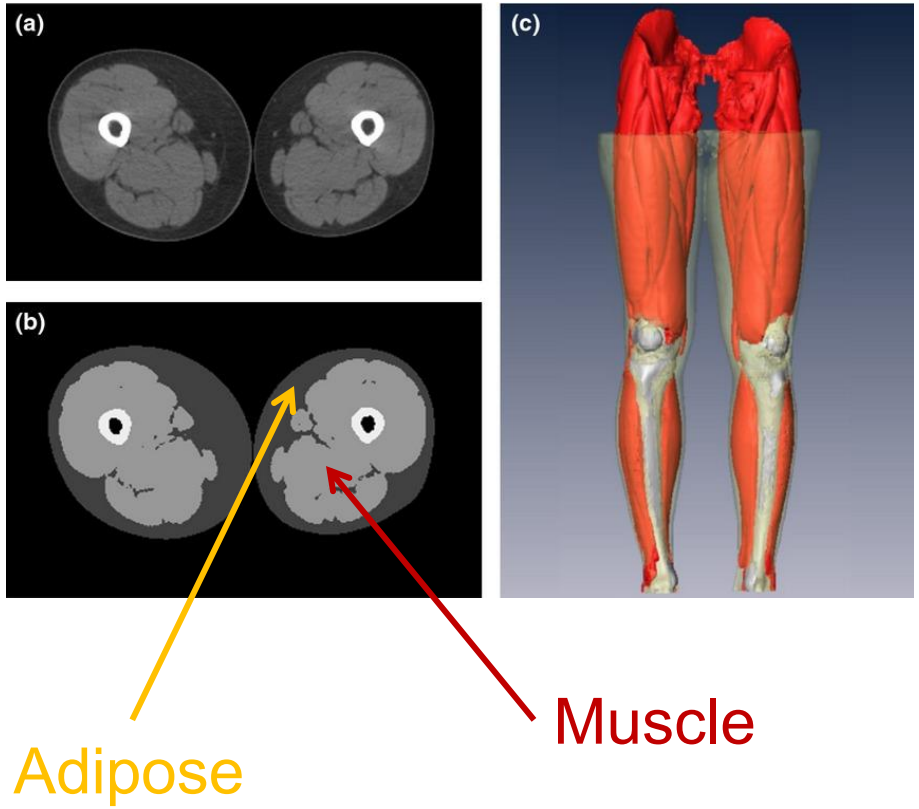



Millward DJ, et al. Br J Nutr. (2014). 111:933–943.

# Muscle Composition and Adiposity

Clin Physiol Funct Imag. 2014. 34:47-55.

n=18 women, 21 men
CT scans of LE




↑ adiposity ($P$<0.001) ∝
↑ Muscle volume ($P$<0.001)
↓ Muscle attenuation (HU) ($P$=0.023)
(↑ IMAT)

Weight loss? (↓ IMAT ?)

# Questions:

- What is muscle mass in patient with obesity prior to weight loss?
  ↑ adiposity ∝ ↑FFM (↑ muscle volume, ↑ muscle lipids/IMAT)
- What happens to muscle mass with weight loss?
  - “Diet”: either low-calorie or △ macronutrient (“carbs,” “fat,” protein”)
    - Normal weight
    - Overweight / Obesity
- Metabolic-bariatric surgery
- Obesity Medications (GLP-1(+) RA)

# Caloric Restriction (Starvation) in NL Wt Adults

Med Sci Sports Exer. 1994. 26:235-40.

-62% FM
-38% total FFM → Reduced dynamic strength of large muscle groups.

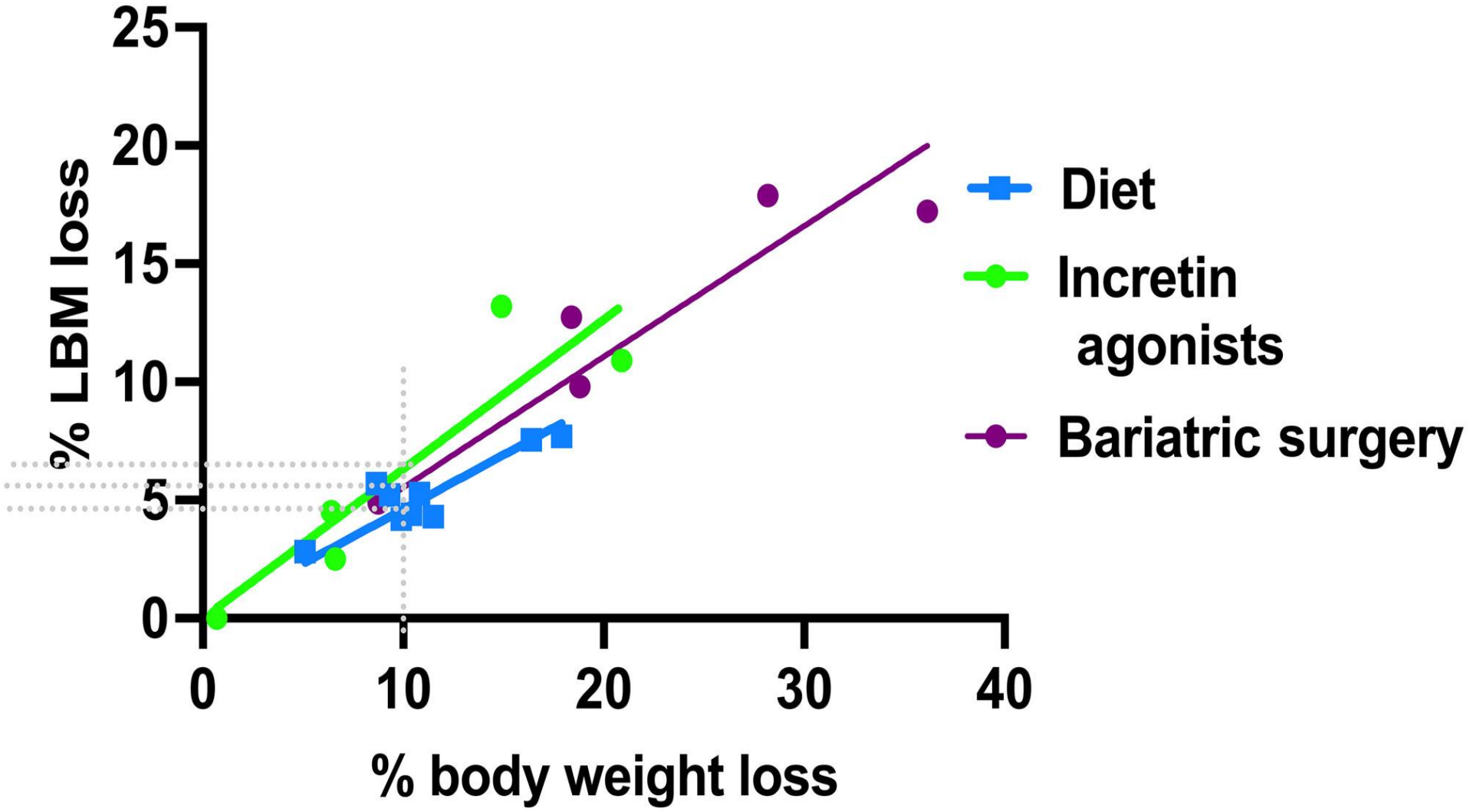
TABLE 1. Mean (±SD) values of body composition and physical performance measurements

| Variable | Baseline | 8 wk | Change | Paired *t*-Test |
|---|---|---|---|---|
| Body wt (kg) | 75.9 ± 9.0 | 63.8 ± 6.7 | −12.1 ± 3.4 | $P < 0.01$ |
| FFM (kg)* | 64.6 ± 6.4 | 60.0 ± 5.8 | −4.6 ± 2.6 | $P < 0.01$ |
| $Clean_{stm}$ (kg) | 77.4 ± 9.6 | 58.7 ± 8.9 | −18.7 ± 8.3 | $P < 0.01$ |
| $GS_{max}$ (N) | 530 ± 57 | 529 ± 63 | −0.5 ± 51 | NS |
| Hold time (s) | 66.2 ± 14.1 | 66.3 ± 16.7 | −0.2 ± 17.8 | NS |

* FFM calculated from % body fat by dual-energy x-ray absorptiometry.

-16% total WL

# Changes in Lean Body Mass Following Weight Loss




Diabetes Obesity Metabolism, Volume: 26, Issue: S4, Pages: 16-27, First published: 27 June 2024, DOI: (10.1111/dom.15728)

# Questions:

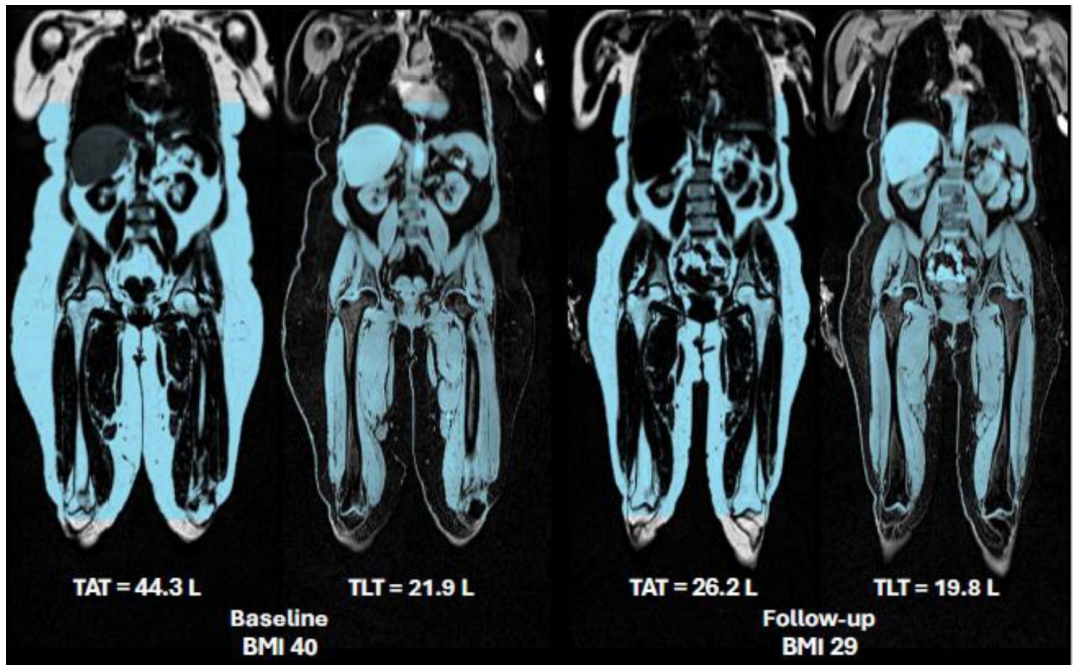
- What is muscle mass in patient with obesity prior to weight loss?
  ↑ adiposity ∝ ↑FFM (↑ muscle volume, ↑ muscle lipids)
- What happens to muscle mass with weight loss?
  - “Diet”: either low-calorie or △ macronutrient (“carbs,” “fat,” protein”)
    - Normal weight — ↓ 38% FFM (reduced muscle function)
    - Overweight / Obesity
    - Metabolic-bariatric surgery
    - Obesity Medications (GLP-1(+) RA)

    } ↓ 25%-29% FFM (? change muscle function)
- What’s to be done?

# Effect of semaglutide on body composition and proximal muscle strength: The STEP UP trial

**Jøran Hjelmesæth**[1,2], Suhas Bhat[3], W. Timothy Garvey[4], Kristoffer Jensen Kolnes[5], Ildiko Lingvay[6], Niklas Kahr Rasmussen[5], Julio Rosenstock[7], Sean Wharton[8]

## Randomized, double-blind, placebo- and active-controlled, multicenter phase 3b trial: 7.2 mg vs. 2.4 mg vs. PBO




**Population (N=1407)**

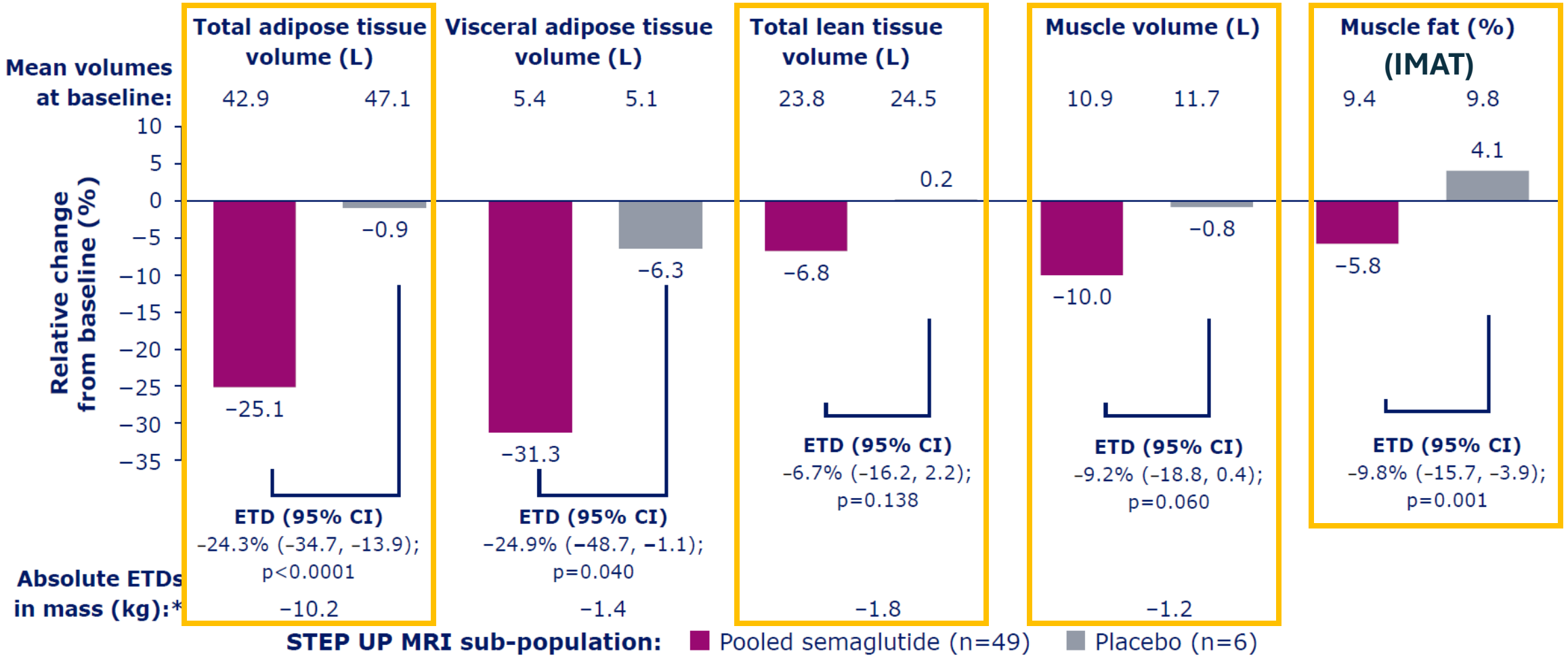
- Adults (≥18 years)
- BMI ≥30 kg/m$^2$
- ≥1 self-reported unsuccessful dietary effort to lose weight
- Without T2D ($HbA_{1c}$ <6.5%)

**MRI sub-population (n=55)**

- Body weight <149 kg at screening
- No metal implants (e.g. pacemaker, intracranial clips, cochlear implant, infusion pump or neurostimulators)
- Suitable for MRI at the investigator's discretion (e.g. no claustrophobia)

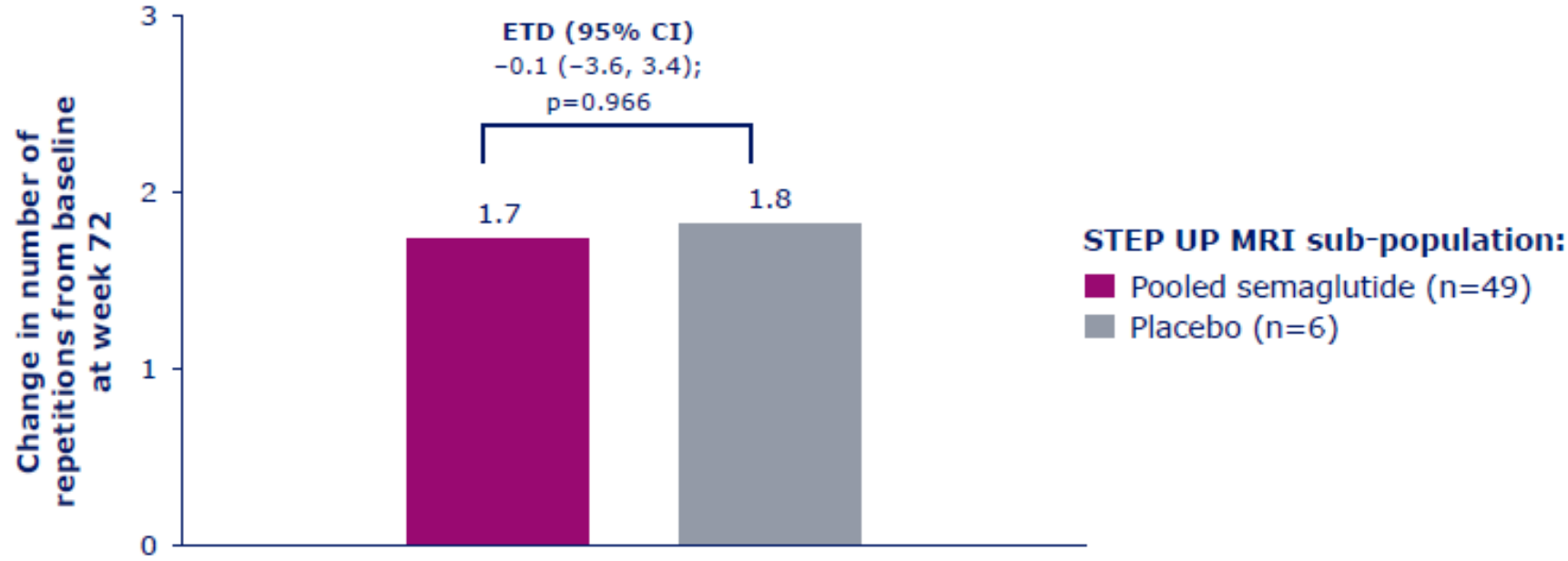
*Hjelmesæth J et al*. Presented at the European Association for the Study of Diabetes (EASD) 61st Annual Meeting, 15–19 September 2025; Vienna, Austria.

# Relative change in different tissue volumes (%) from baseline to week 72



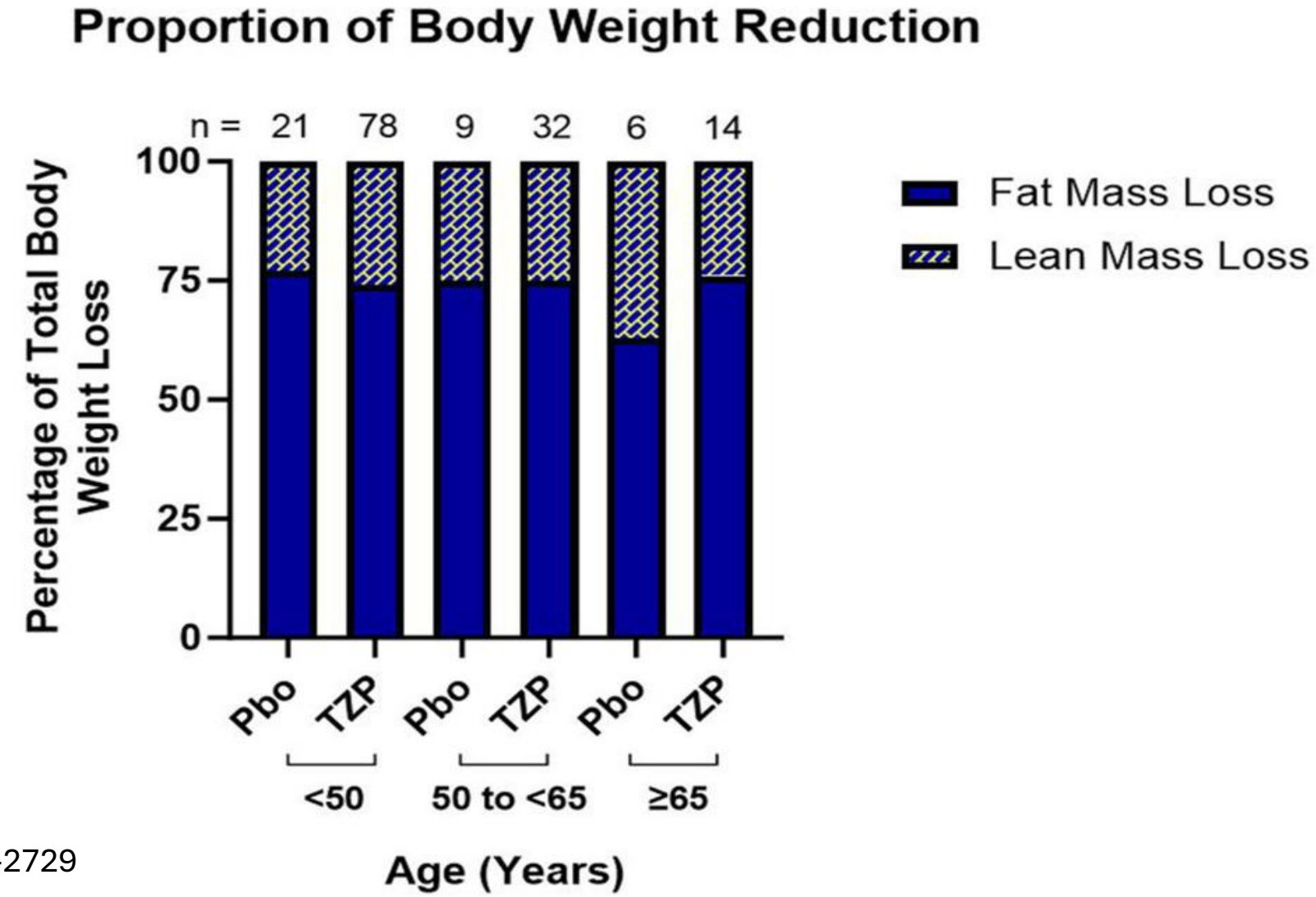
# Change in number of sit-to-stand repetitions from baseline to week 72

| Number of sit-to-stand repetitions | Pooled semaglutide (n=49) | Placebo (n=6) |
|---|---|---|
| Baseline | 13 (4) | 13 (2) |
| Week 72 | 15 (4) | 15 (1) |



# Body Composition By DEXA After One Year of Weight Loss With Tirzepatide: Subset Analysis of SURMOUNT-1 by Age

n=160 of 2539 underwent DEXA,
73.1% female
Mean age: 46.2 years
~20% total weight loss at 1 year




Diabetes Obesity Metabolism. 2025. 27: 2720-2729

# Questions:

- What is muscle mass in patient with obesity prior to weight loss?
  ↑ adiposity ∝ ↑FFM (↑ muscle volume, ↑ muscle lipids)
- What happens to muscle mass with weight loss?
  - “Diet”: either low-calorie or △ macronutrient (“carbs,” “fat,” protein”)
    - Normal weight
    - Overweight / Obesity
    - Metabolic-bariatric surgery
    - Obesity Medications (GLP-1(+) RA)

    ↓ 38% FFM (reduced muscle function)

    ↓ 25%-29% FFM (No Δ muscle function)
- What’s to be done?

# Joint TOS/OMA/OAC Expert Guidance Statement on the Pharmacological Management of United States Adults With Overweight or Obesity Using the GRADE Approach

Lydia Alexander[1] | Jonathan Q. Purnell[2] | Karlijn Burridge[3] | Marc-André Cornier[4] | Angela Golden[5] | Deborah Bade Horn[6] | Michelle Look[7] | Joe Nadglowski[8] | Camila Ávila-Oliver[9,10] | Francisco Novillo[10,11] | Ana María Rojas-Gómez[10] | Brad Hussey[12] | Ximena Ramos Salas[12]

[1]Enara Health, Inc., San Mateo, California, USA | [2]Oregon Health & Science University, Portland, Oregon, USA | [3]Healthy4Life, Naperville, Illinois, USA | [4]Medical University of South Carolina, Charleston, South Carolina, USA | [5]The Obesity Society, Rockville, Maryland, USA | [6]Obesity Medicine Association, Centennial, Colorado, USA | [7]San Diego Sports Medicine Weight and Wellness, San Diego, California, USA | [8]Obesity Action Coalition, Tampa, Florida, USA | [9]Facultad de Medicina Clínica Alemana, Universidad del Desarrollo, Santiago, Chile | [10]Epistemonikos Foundation, Santiago, Chile | [11]School of Dentistry, Faculty of Health and Dentistry, Universidad Diego Portales, Santiago, Chile | [12]Replica Communications, Hamilton, Ontario, Canada

**Correspondence:** Jonathan Q. Purnell (purnellj@ohsu.edu)

**Received:** 13 October 2025 | **Revised:** 27 January 2026 | **Accepted:** 27 January 2026

…for *protein intake-guided nutritional interventions compared with unguided intake* intended to minimize loss of lean mass relative to fat mass during obesity pharmacotherapy interventions, no direct evidence was identified …



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# What's To Be Done?

AACE/TOS/ASMBS/OMA/ASA 2019 Guidelines

**CLINICAL PRACTICE GUIDELINES FOR THE PERIOPERATIVE NUTRITION, METABOLIC, AND NONSURGICAL SUPPORT OF PATIENTS UNDERGOING BARIATRIC PROCEDURES – 2019 UPDATE: COSPONSORED BY AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS/AMERICAN COLLEGE OF ENDOCRINOLOGY, THE OBESITY SOCIETY, AMERICAN SOCIETY FOR METABOLIC & BARIATRIC SURGERY, OBESITY MEDICINE ASSOCIATION, AND AMERICAN SOCIETY OF ANESTHESIOLOGISTS***

- Specialty nutrition advice *during* weight loss:
  - A minimal protein intake of 60 g/d and up to 1.5 g/kg ideal body weight per day should be adequate.
  - Higher amounts of protein intake—up to 2.1 g/kg ideal body weight per day—need to be assessed on an individualized basis (Grade D).
- Go low (dose). Go slow (titration).
- Good preventive recommendations:
  - Incorporate resistance training and aerobics and balance training.

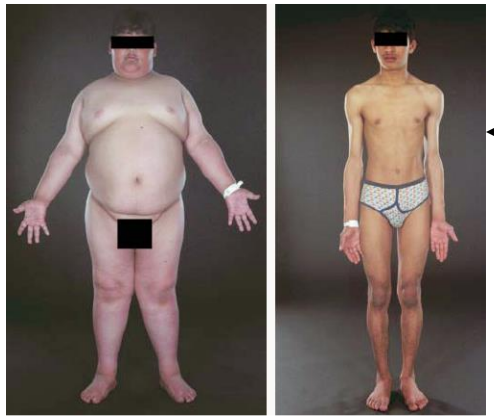
Bariatric Surgery Guidelines, Endocr Pract. 2019;25(No. 12) 3


# Thank You

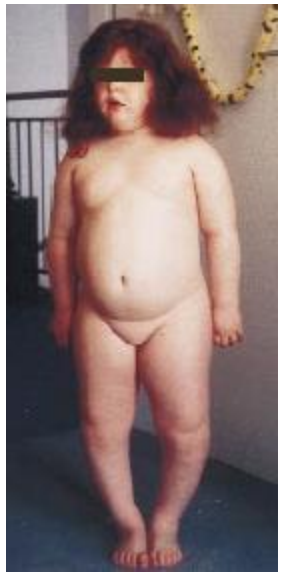
Is there reason to think that the effect of obesity medication-induced weight loss on body composition is different from “dieting”-induced weight loss?

# Higher Order Neurons Transmit Signals Controlling Energy Metabolism

Barsh and Schwartz. Nat Rev Gen. 3:589-600, 2002

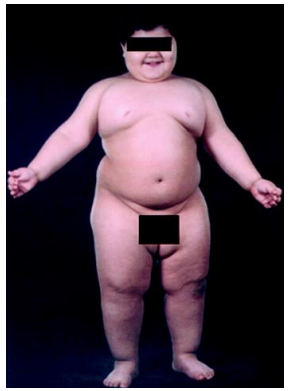


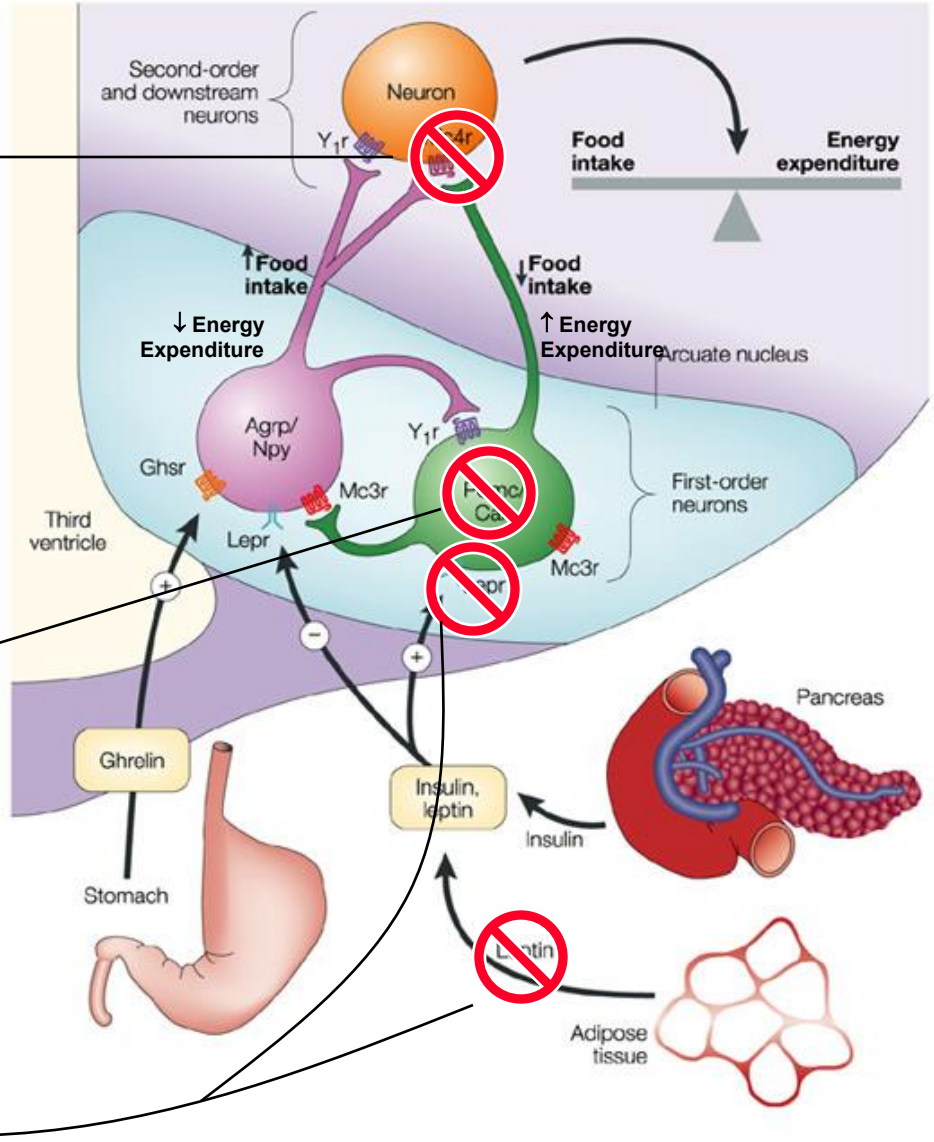
NEJM 2003



Nature 1998

JCI 2002



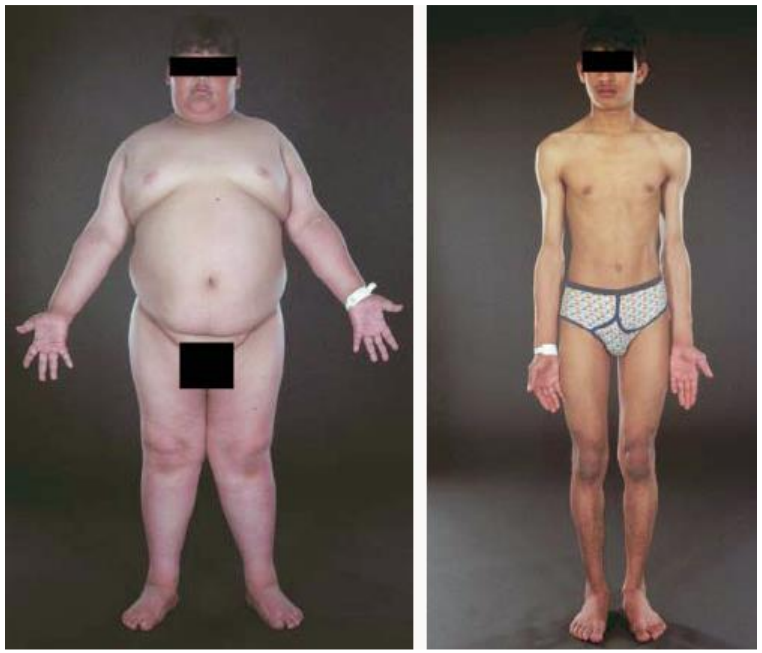


The NEW ENGLAND JOURNAL of MEDICINE

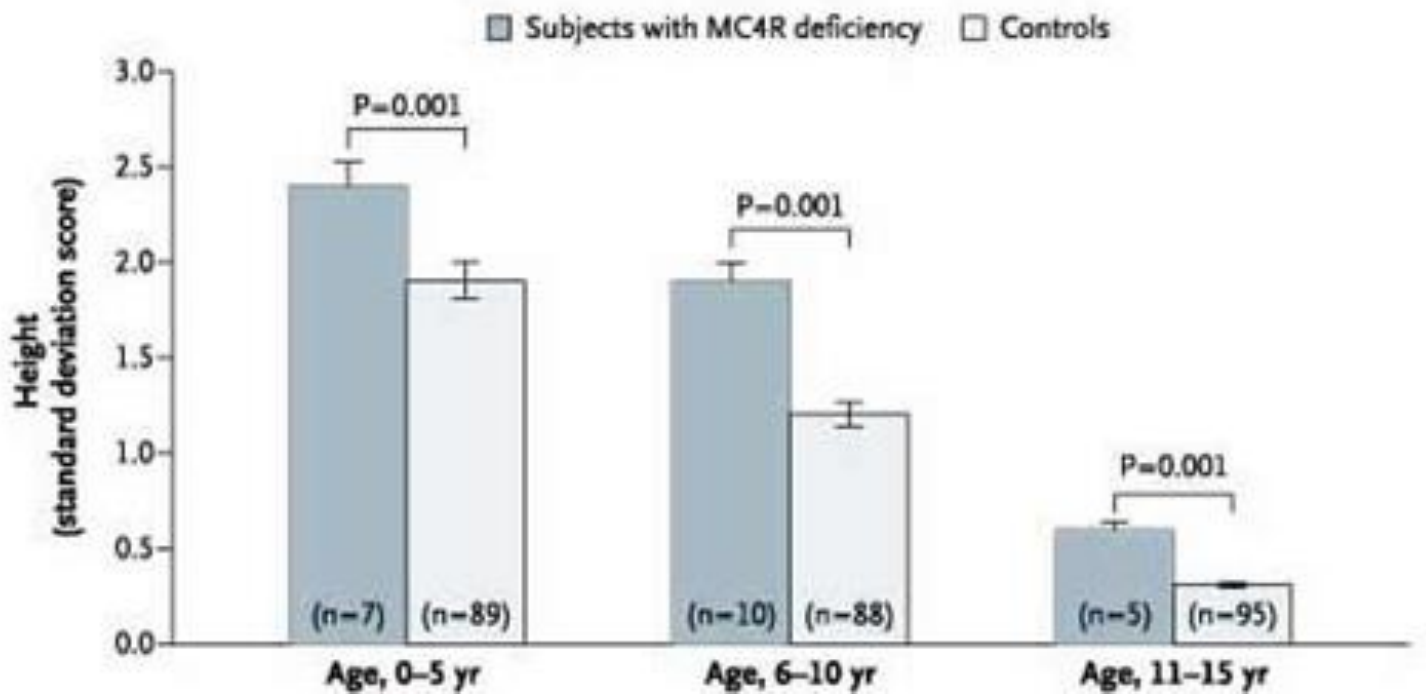
ESTABLISHED IN 1812 MARCH 20, 2003 VOL. 348 NO. 12

# Clinical Spectrum of Obesity and Mutations in the Melanocortin 4 Receptor Gene

I. Sadaf Farooqi, M.D., Ph.D., Julia M. Keogh, B.Sc., Giles S.H. Yeo, Ph.D., Emma J. Lank, B.Sc., Tim Cheetham, M.D., and Stephen O'Rahilly, M.D.







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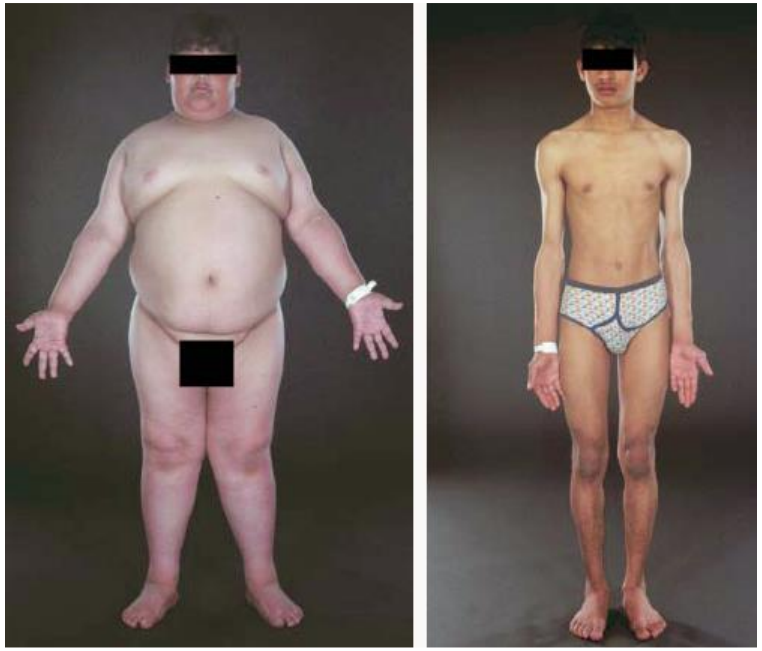


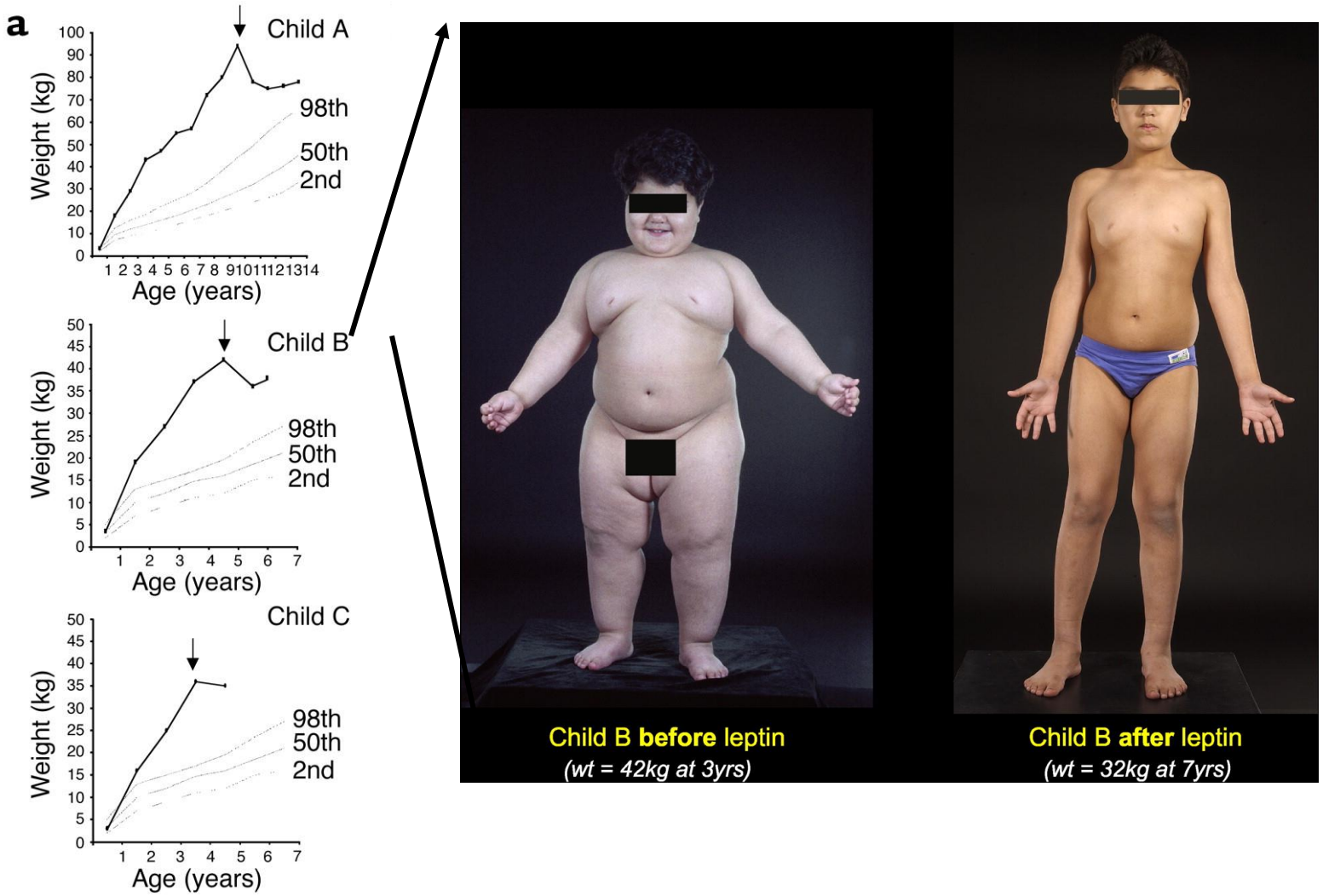
**Table 2. Correlations between Genotype and Phenotype in Children with Melanocortin 4 Receptor (MC4R) Deficiency.***

| Characteristic | Heterozygotes | | Homozygotes | |
|---|---|---|---|---|
| | Inactive MC4R (N=14) | Partially Active MC4R (N=10) | Inactive MC4R (N=3) | Partially Active MC4R (N=4) |
| Body-mass index standard-deviation score | 3.9±0.5† | 2.3±0.3 | 6.2±1.5† | 4.1±0.8 |
| Height standard-deviation score | 1.9±0.4† | 0.4±0.1 | 3.1±0.4† | 2.5±0.2 |
| Bone mineral density z score | 1.9±0.5† | 1.3±0.6 | — | 2.9±0.4 |
| Energy intake (kcal/kg of lean mass) | 44.0±5.1† | 20.3±1.9 | 35.2±1.7† | 20.3±1.3 |
| Plasma insulin (μU/ml) | 27±4.4 | 25±3.8 | 31±3.1 | 28±4.0 |

* Plus–minus values are means ±SD.
† P≤0.05 for the comparison with partially active MC4R.

# Effect of Leptin Treatment in Children with Leptin Deficiency

Farooqi, et al. JCI.110:1093-1103, 2002.




Leptin Treatment:

- ↓ calorie intake 45%-85% of baseline.
- 98% of lost weight from FM.
- Maintained NL somatic growth.

No stunting!