Obesity medicine before and after surgery? When, why, and how

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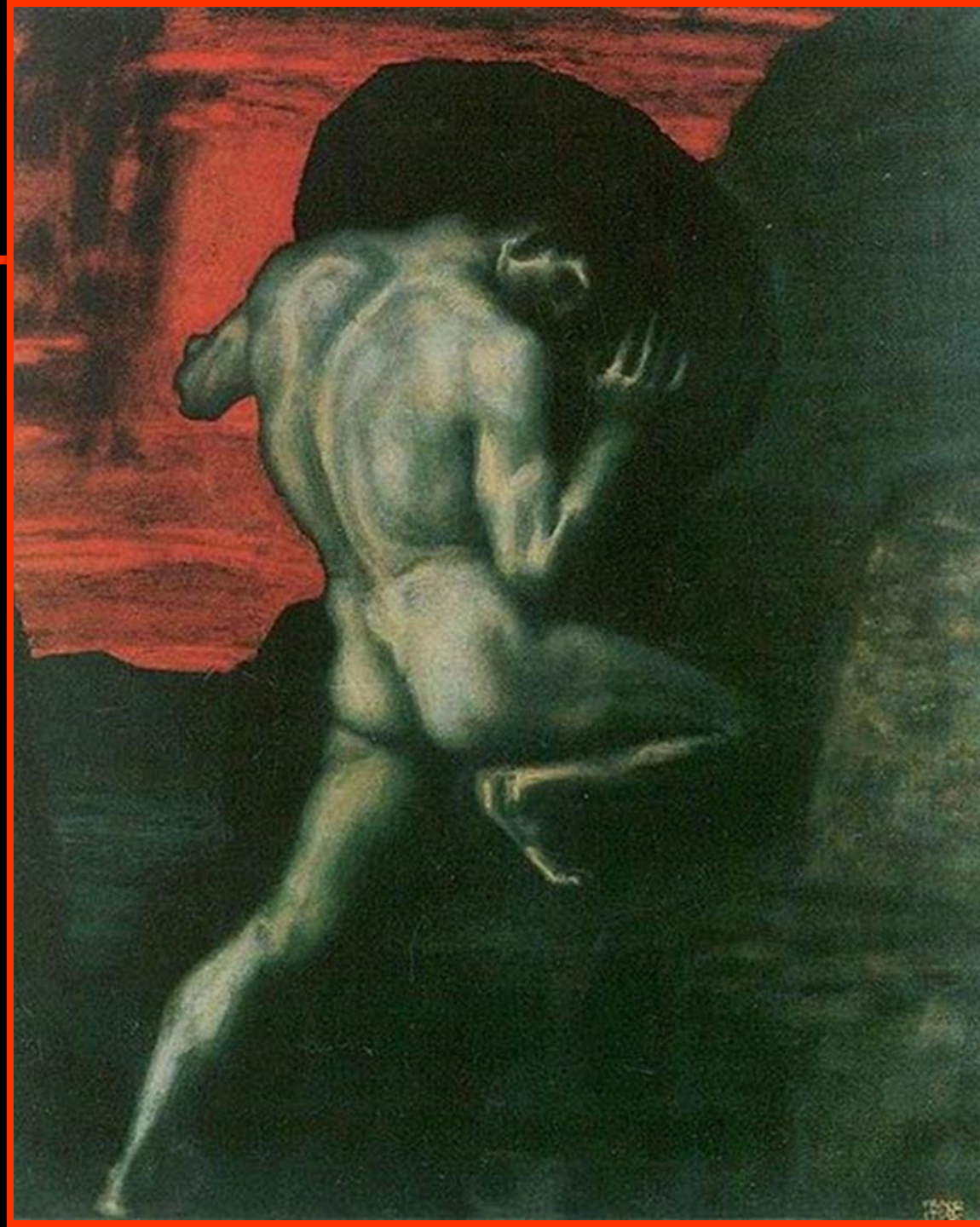
The Gladiator Joseph Wright of Derby, Private collection, 1765

Conflicts of interest

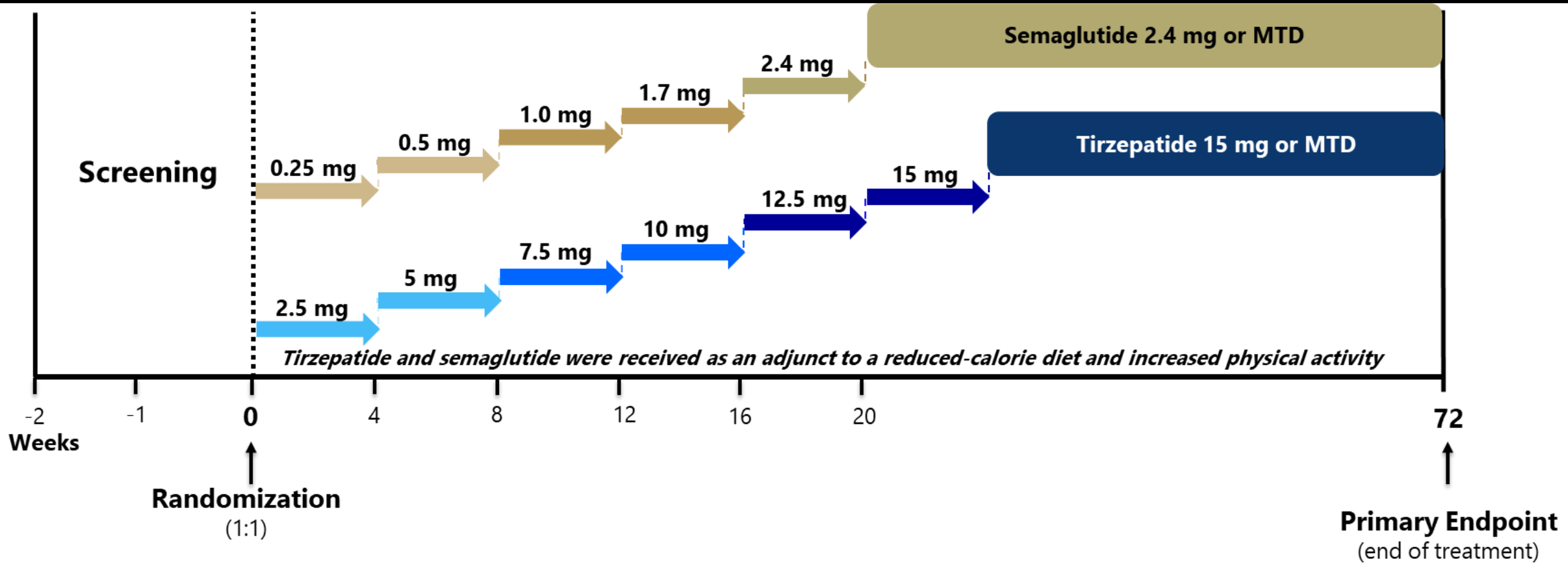
- Consilient Health
- Novo Nordisk
- Herbalife
- Johnson & Johnson
- Covidien
- Fractyl
- GI Dynamics
- Lilly
- Boehringer Ingelheim
- Keyron
- Amgen
- Arrowhead
- Roche
- AstraZeneca



SURMOUNT-5: Study Design in People with Obesity

A Phase 3b, 72-Week, Multicenter, Randomized, Controlled, Parallel-Arm, Open-Label Trial.

- Stratification factors: prediabetes status at randomization, sex, and BMI <35 vs ≥35 kg/m^2
- US only to limit risk to semaglutide supply; US semaglutide label update July 2023, 1.7mg added as maintenance dose



MTD=maximum tolerated dose.

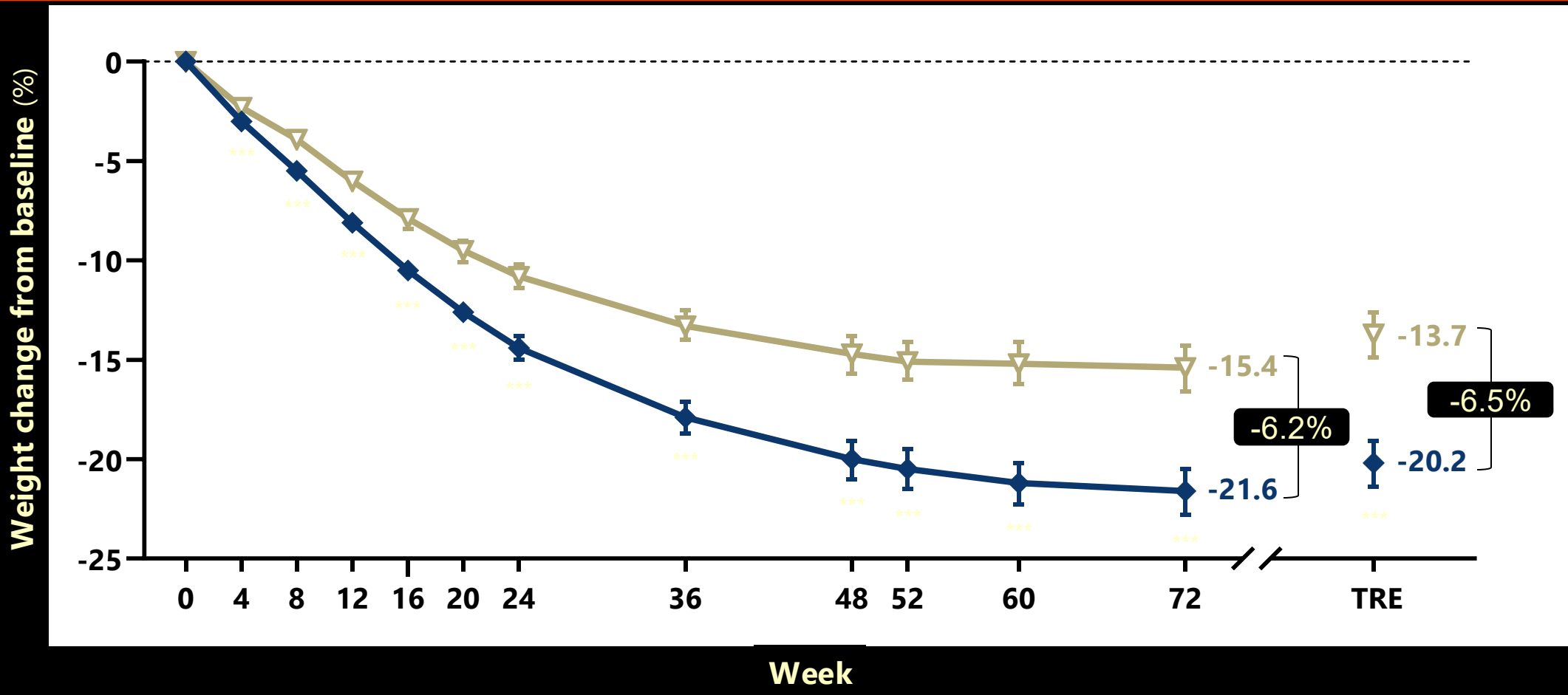
Data from Aronne LJ, et al. N Engl J Med 2025.

Weight Reduction from Baseline to Week 72: percent change

Overall mean baseline weight = 113.2 kg BMI 39.4 kg/m²

On Treatment *Efficacy Estimand*

In Trial *Modified Treatment-Regimen Estimand*



***p<0.001 vs semaglutide. Data are LSM ± 95% CI. Week 4 through Week 60 data were not controlled for multiplicity.

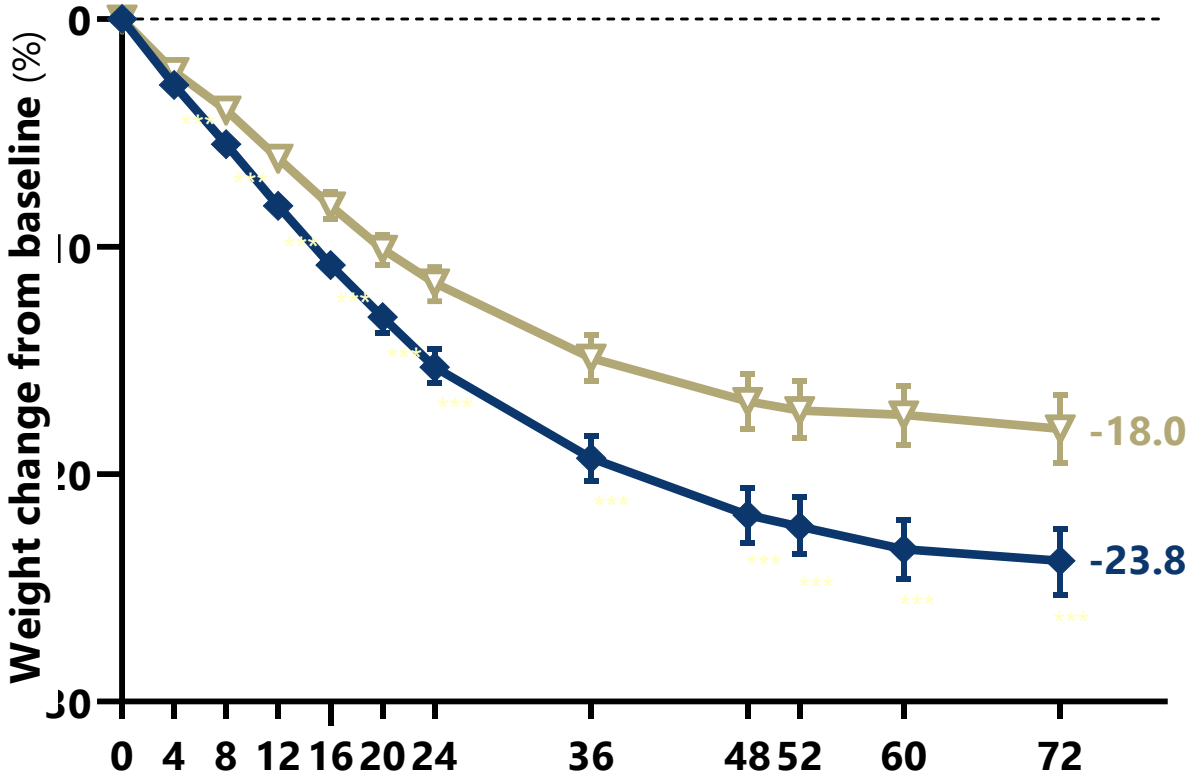
Data from Aronne LJ, et al. N Engl J Med 2025; *in press.*

Weight Reduction from Baseline to Week 72: by sex

On Treatment
Efficacy Estimand

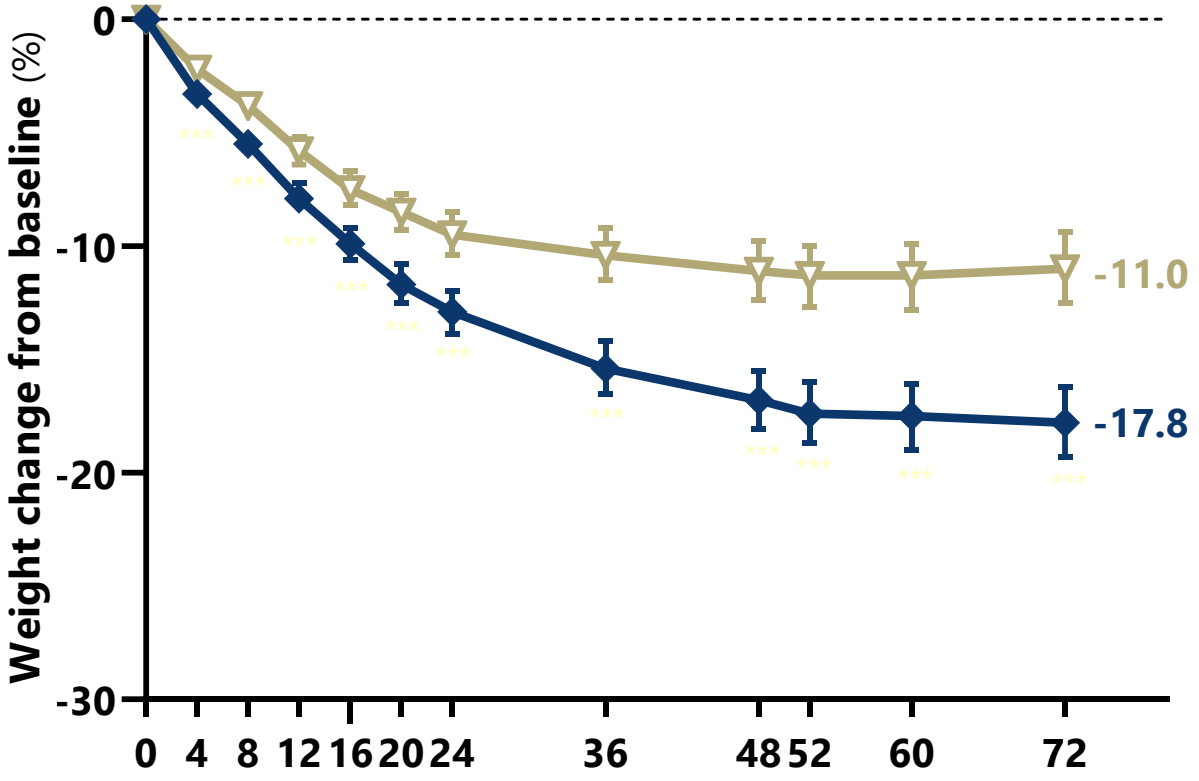
Female

Overall mean baseline weight = 105.7 kg



Male

Overall mean baseline weight = 126.9 kg



Semaglutide 2.4 mg or MTD
Tirzepatide 15 mg or MTD

Week

Week

***p<0.001 vs semaglutide. Data are LSM ± 95% CI. Weight reduction by sex was not controlled for multiplicity.
Data from Aronne LJ, et al. N Engl J Med 2025; *in press*.

Treatment Emergent Adverse Events *With ≥5% Frequency in Any Treatment Group*

Parameter	Semaglutide MTD (N=376)	Tirzepatide MTD (N=374)	Total (N=750)
Nausea	167 (44.4)	163 (43.6)	330 (44.0)
Constipation	107 (28.5)	101 (27.0)	208 (27.7)
Diarrhea	88 (23.4)	88 (23.5)	176 (23.5)
Vomiting	80 (21.3)	56 (15.0)	136 (18.1)
COVID-19	47 (12.5)	51 (13.6)	98 (13.1)
Fatigue	46 (12.2)	39 (10.4)	85 (11.3)
Eructation	29 (7.7)	37 (9.9)	66 (8.8)
Injection site reaction	1 (0.3)	32 (8.6)	33 (4.4)
Upper respiratory tract infection	43 (11.4)	32 (8.6)	75 (10.0)
Alopecia	23 (6.1)	31 (8.3)	54 (7.2)

Data are number of participants (%).
Data from Aronne LJ, et al. N Engl J Med 2025;

Adverse Events of Special Interest

Parameter	Semaglutide MTD (N=376)	Tirzepatide MTD (N=374)	Total (N=750)
Pancreatitis, adjudication-confirmed	1 (0.3)	0	1 (0.1)
Severe or serious gastrointestinal adverse events	14 (3.7)	17 (4.5)	31 (4.1)
Severe or serious gallbladder diseases	5 (1.3)	4 (1.1)	9 (1.2)
Severe or serious hepatic disorders	0	1 (0.3)	1 (0.1)
Severe or serious arrhythmias and cardiac conductive disorders	1 (0.3)	3 (0.8)	4 (0.5)
Hypoglycemia, blood glucose level <54 mg/dl	1 (0.3)	0	1 (0.1)
Severe or serious acute renal events	0	1 (0.3)	1 (0.1)

In SURMOUNT-5, there were <u>no</u> incidences of:

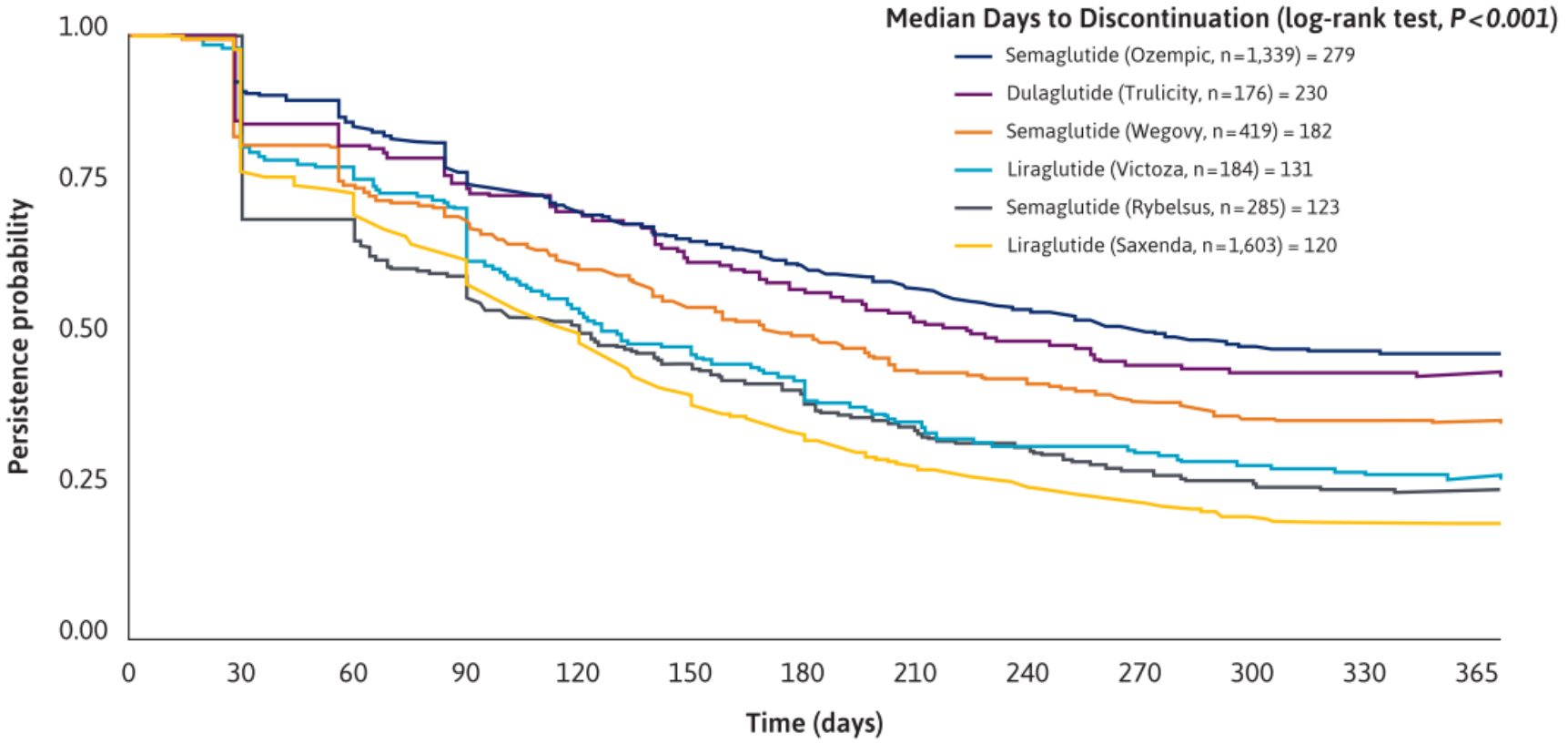
- Death
- Adjudicated MACE
- Hypoglycemia level 3
- Thyroid malignancies and C-cell hyperplasia
- Severe or serious hypersensitivity events
- Severe or serious injection site reactions
- Severe or serious major depressive disorder, suicidal ideation, or suicidal behaviors

Data are number of participants (%).
Data from Aronne LJ, et al. N Engl J Med 2025; *in press*.

1-year discontinuation rates for GLP-1 agonists remain high

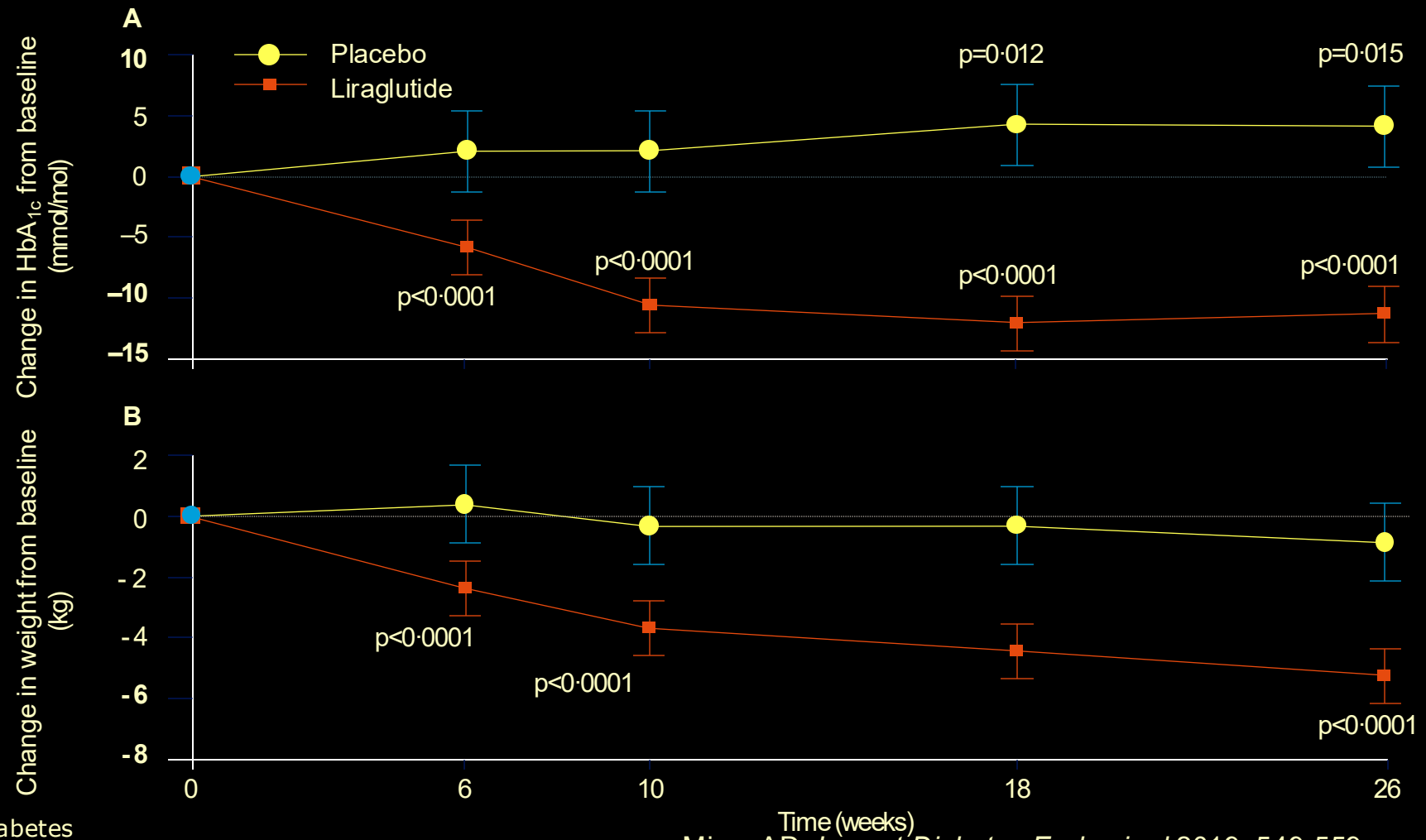
Gleason PP, et al. *J Manag Care Spec Pharm*. 2024; 30(8):860-867

FIGURE 1 Glucagon-Like Peptide-1 Agonists: Kaplan-Meier 1 Year Therapy Persistence (n = 4,066)



Kaplan-Meier curve represents 4,066 obese commercially insured adults without diabetes initiating a GLP-1 product during calendar year 2021. All persistency and adherence measurements were conducted at the GLP-1 product level. Members were considered persistent if they did not have a 60-day gap in therapy and were censored at the end of the 365-day period.

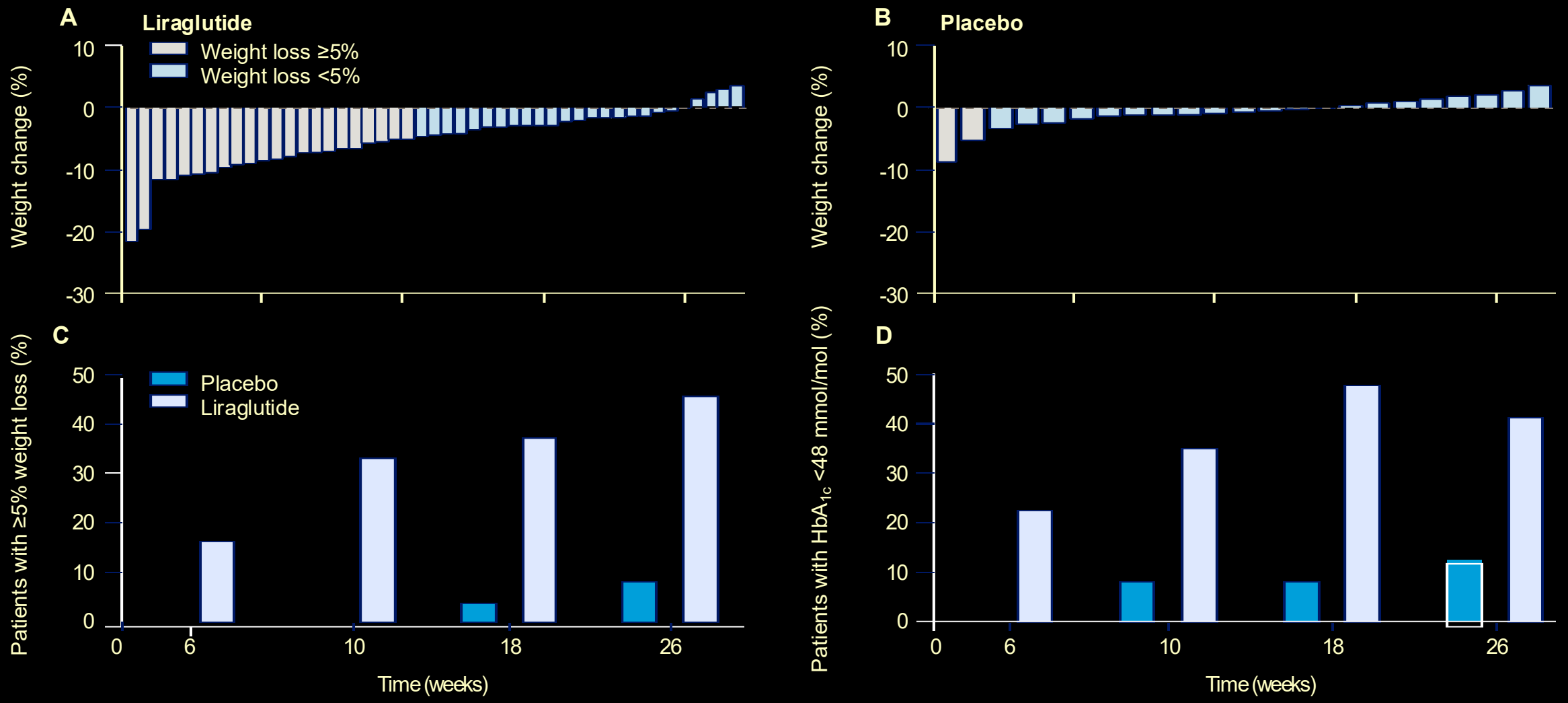
Adjunctive liraglutide treatment in patients with persistent or recurrent T2D after metabolic surgery



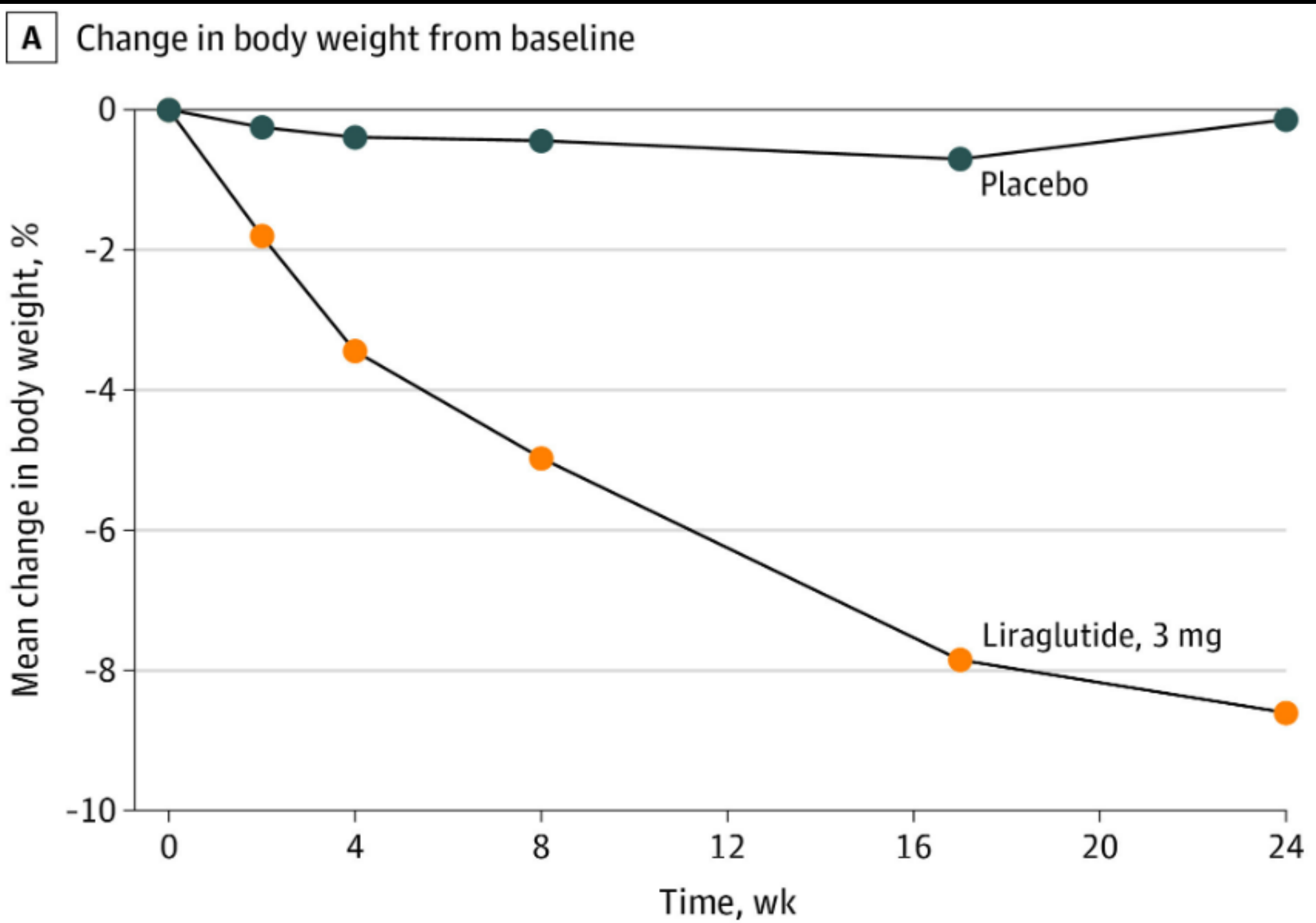
T2D, type 2 diabetes

Miras AD, *Lancet Diabetes Endocrinol* 2019; 549-559

Weight loss and glycaemic improvement responses in participants who completed the trial



Miras AD, *Lancet Diabetes Endocrinol* 2019; 549-559



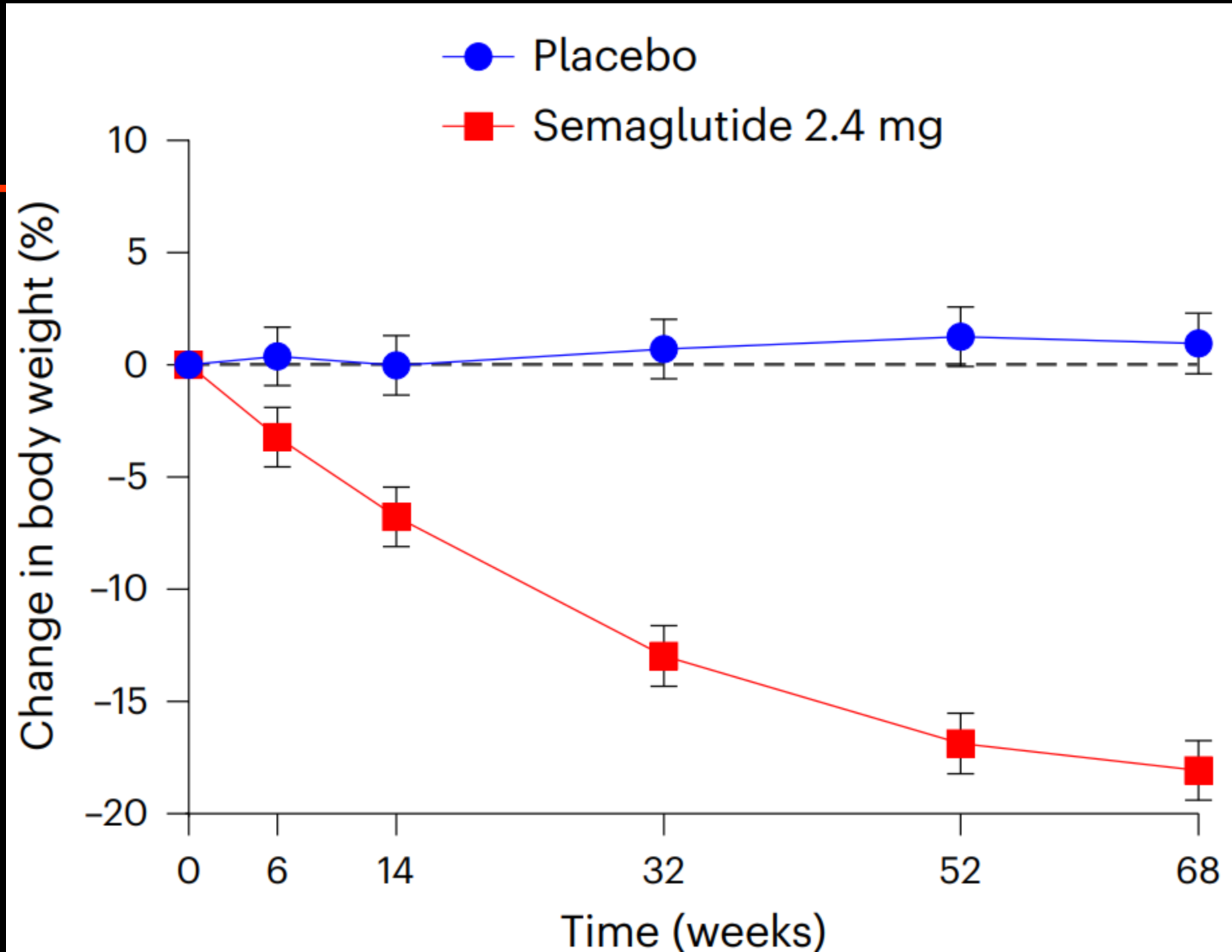
Bari-optimise

Patients with suboptimal response after surgery

Batterham et al JAMA Surgery 2023

BariSTEP Semaglutide after bariatric surgery

Stanley et al Nature Medicine 2026



Received: 12 July 2017 | Revised: 22 September 2017 | Accepted: 14 October 2017
DOI: 10.1111/dom.13131

WILEY

BRIEF REPORT

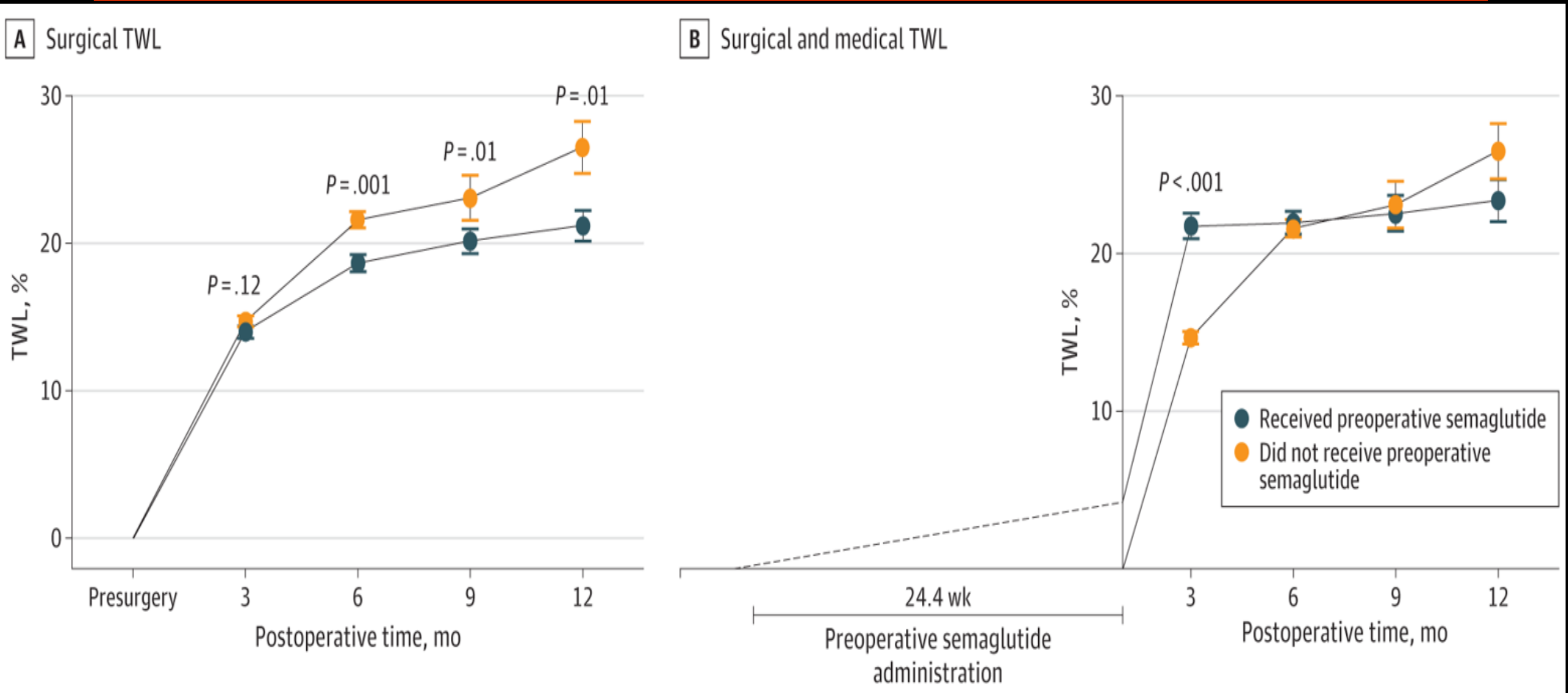
Preoperative weight loss with glucagon-like peptide-1 receptor agonist treatment predicts greater weight loss achieved by the combination of medical weight management and bariatric surgery in patients with type 2 diabetes: A longitudinal analysis

Tien Tang BSc[1†] | Sally Abbott BSc[2†] | Carel W. le Roux MBChB[3] | Violet Wilson RGN[4] | Rishi Singhal FRCS[2] | Srikanth Bellary MD[1,4,5‡] | Abd A. Tahrani MD[4,5,6‡]

GLP-1RA-induced weight change did not predict the weight loss induced by the surgical component alone. Surgery still produced significant weight loss regardless of response to preoperative intervention. Failure to lose weight after GLP-1RA treatment should not be considered a barrier to undergoing bariatric surgery.

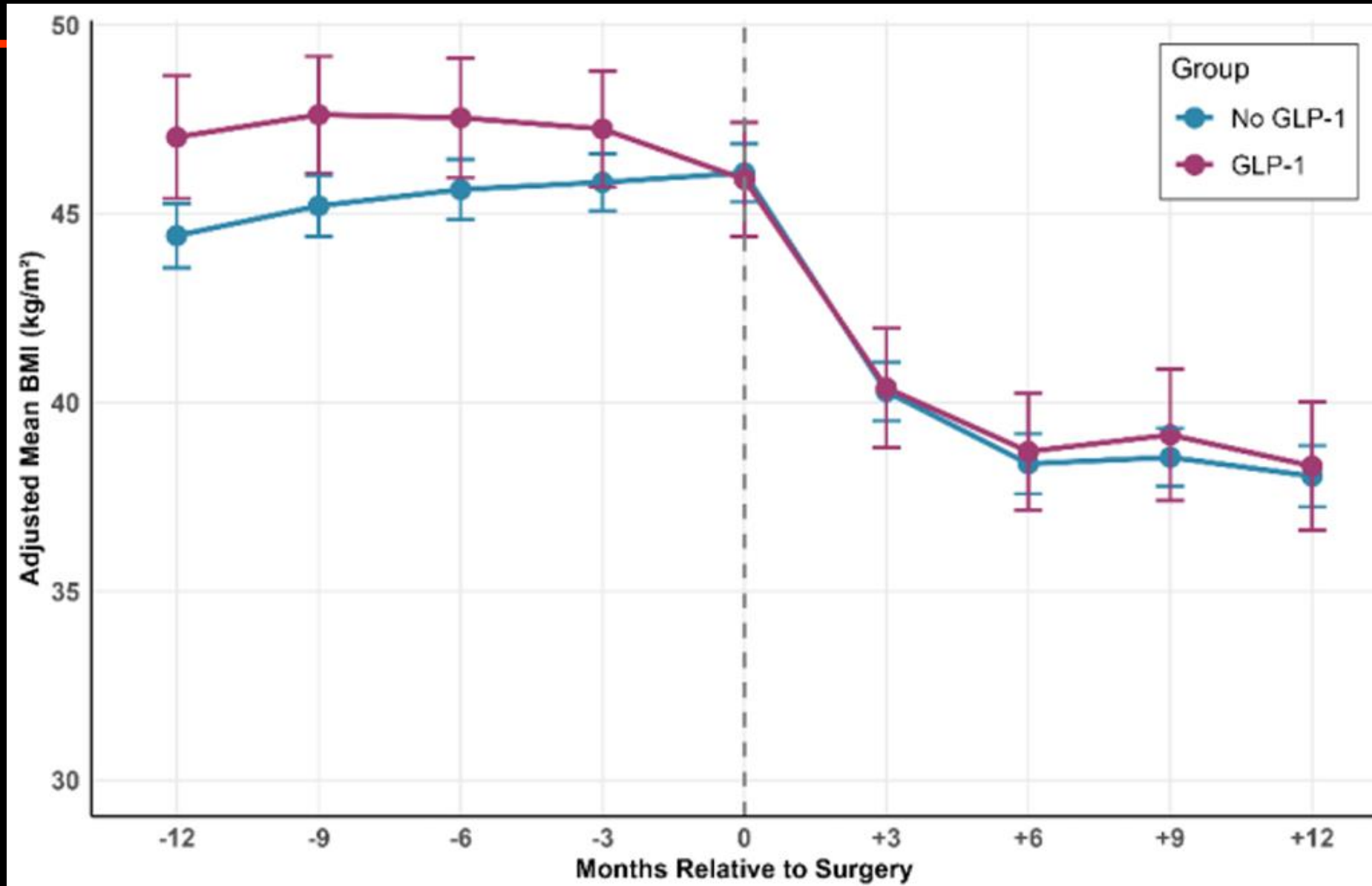
Responses to semaglutide and surgery were not associated.

Mathur V, JAMA Surgery 2025



Preoperative GLP-1 not associated with postoperative weight loss.

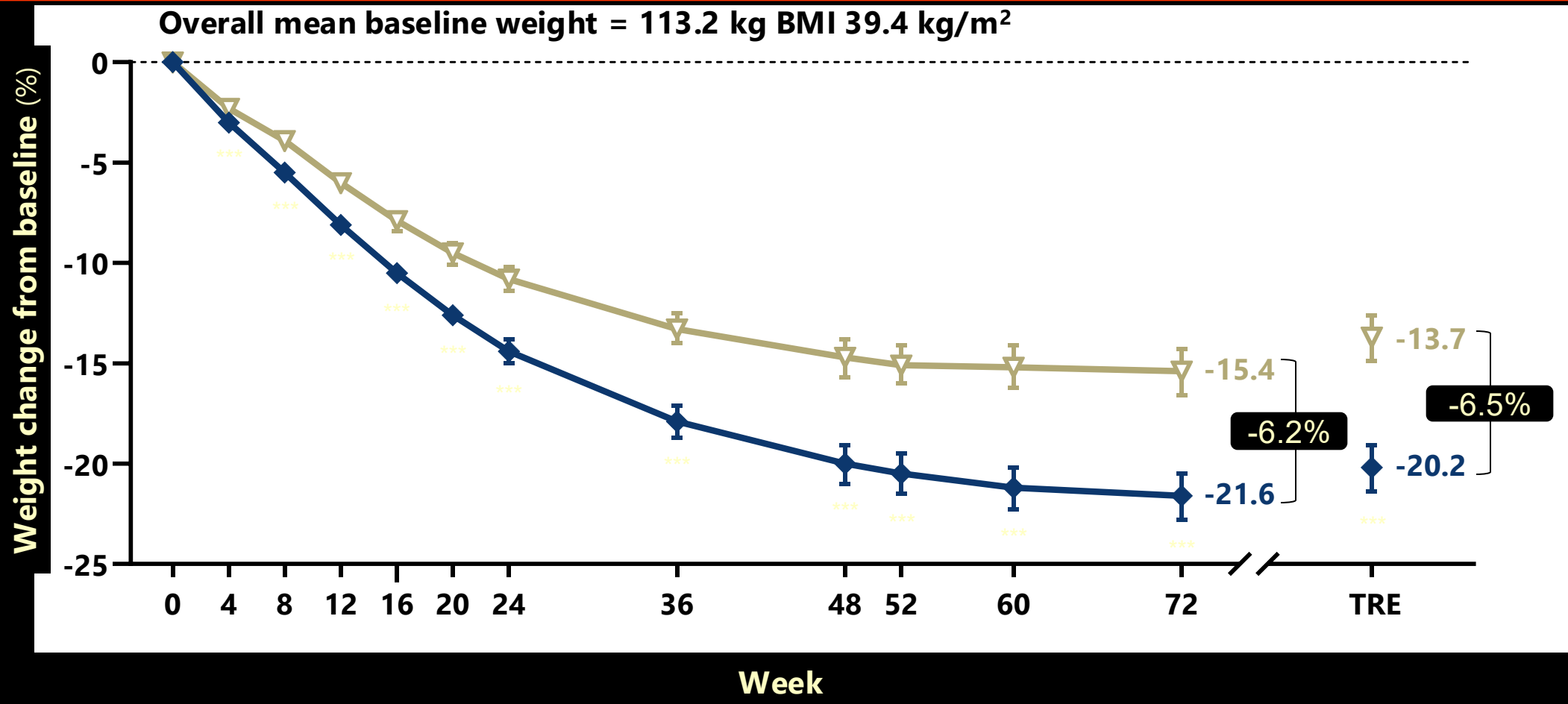
Holler E et al. Annals of Surgery 2026



Tirzepatide compared with Semaglutide for the Treatment of Obesity: The SURMOUNT-5 Trial

Efficacy and Safety

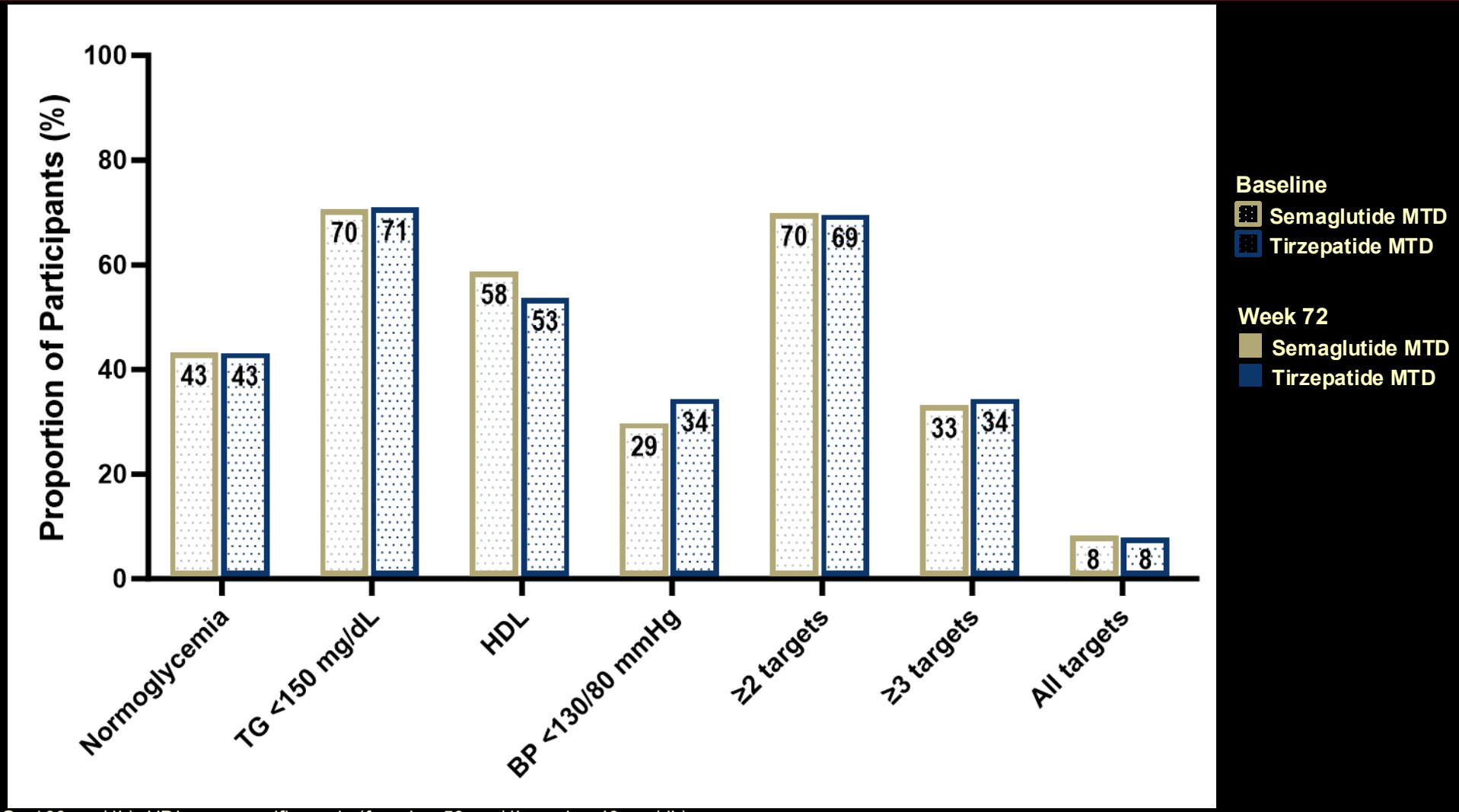
Weight Reduction from Baseline to Week 72: percent change



***p<0.001 vs semaglutide. Data are LSM ± 95% CI. Week 4 through Week 60 data were not controlled for multiplicity.
Data from Aronne LJ, et al. N Engl J Med 2025; *in press.*

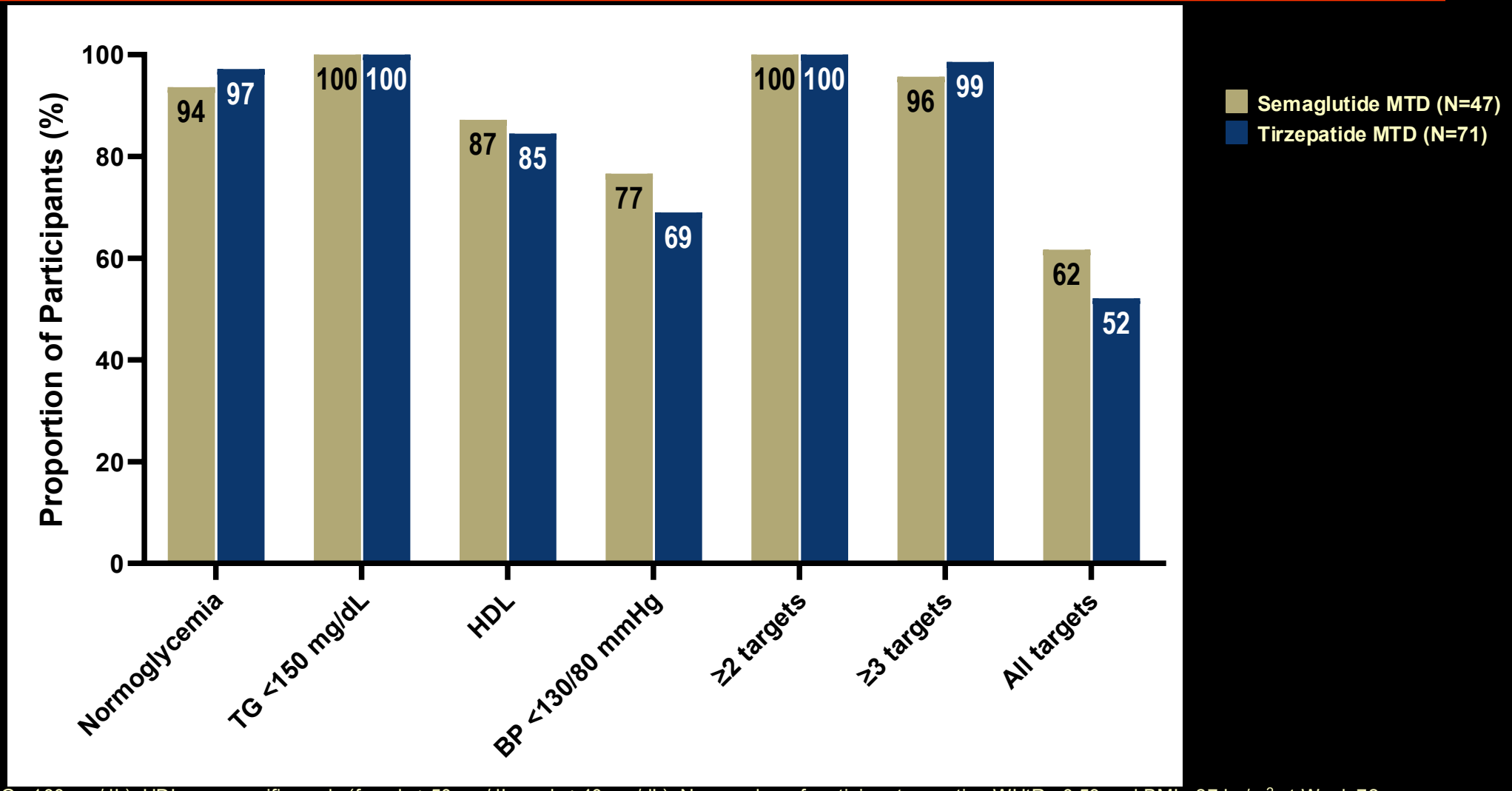
Percent of Participants with Normalization of Cardiometabolic Parameters

Week 72



Normoglycemia (HbA1c <5.7% and FSG <100 mg/dL). HDL sex-specific goals (female ≥50 mg/dL, male ≥40 mg/dL).
Data are means based on observed data at Week 72 or LOCF for participants who completed treatment.

Normalization of Cardiometabolic Parameters in Participants Reaching WHtR <0.53 & BMI <27 at Week 72

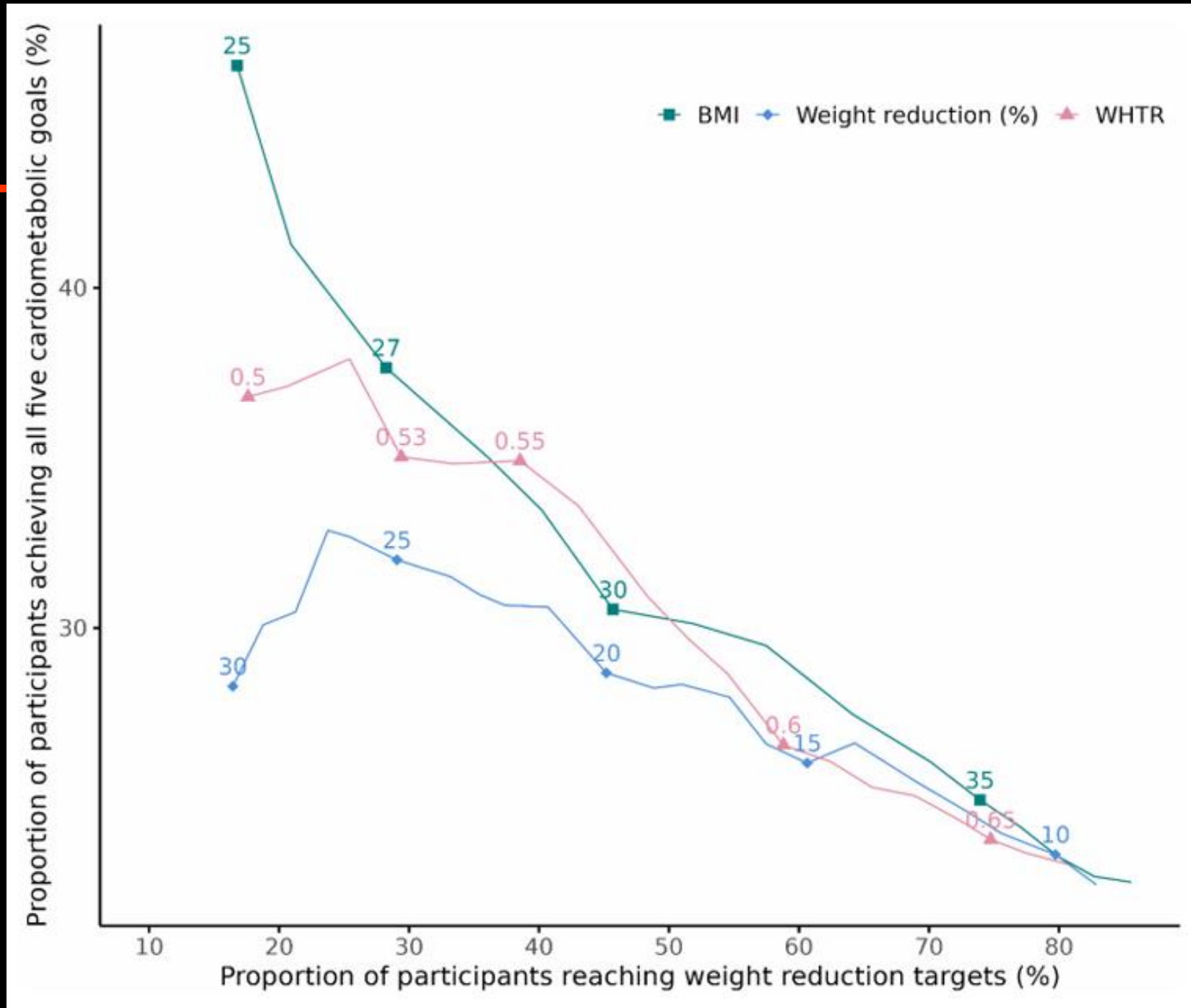


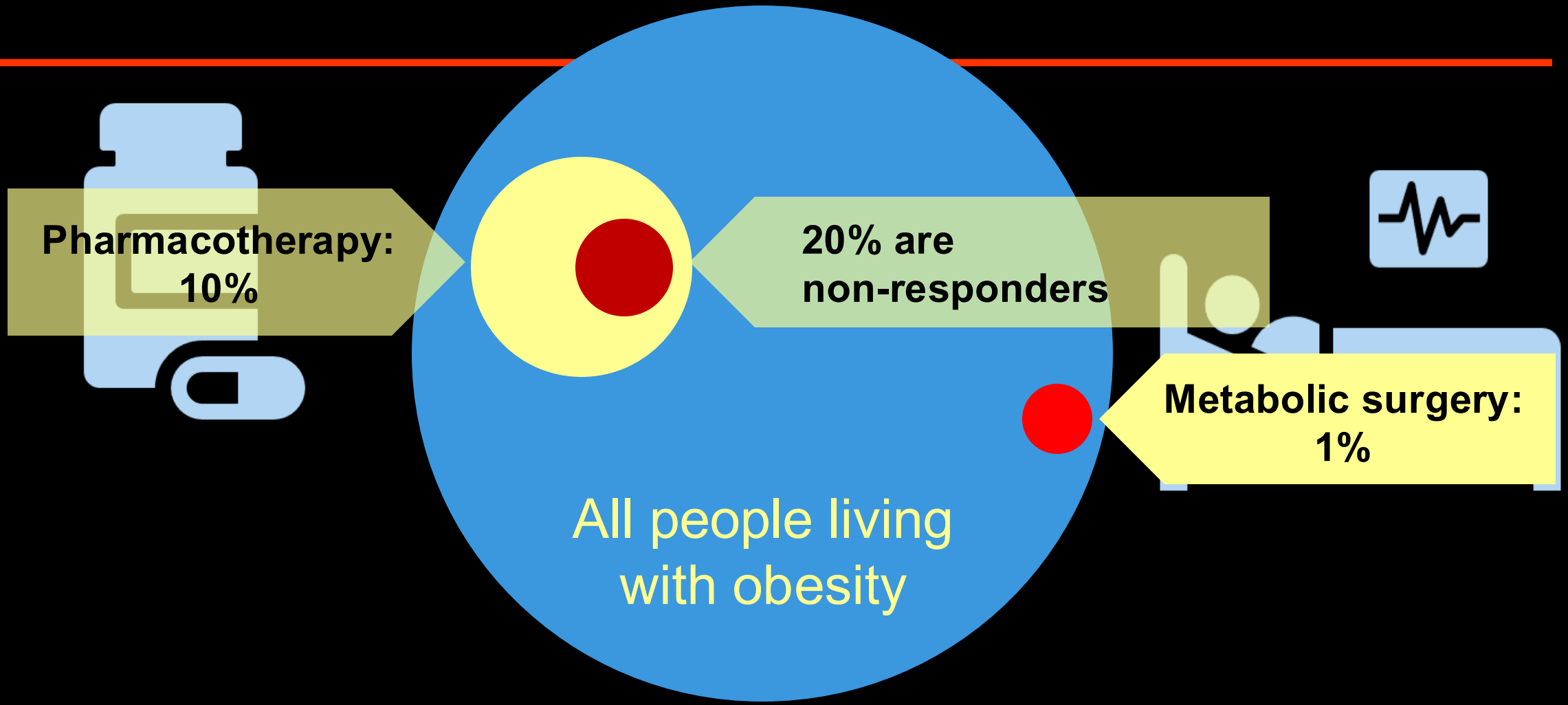
Normoglycemia (HbA1c <5.7% and FSG <100 mg/dL). HDL sex-specific goals (female ≥50 mg/dL, male ≥40 mg/dL). N = number of participants meeting WHtR <0.53 and BMI <27 kg/m^2 at Week 72.
Data are means based on observed data at Week 72 or LOCF for participants who completed treatment.

SURMOUNT-5 Treatment to target outcomes

le Roux et al Diab Obes Metab 2025

le Roux et al DOM 2026




Pharmacotherapy:
10%
20% are
non-responders
Metabolic surgery:
1%
All people living
with obesity

Conclusions

- Response to obesity medication
  - Biological determined and variable
  - Does not predict weight loss after metabolic bariatric surgery
  - Complement and not compete with bariatric surgery
  - Presents an opportunity to increase surgical numbers


METABOLIC
MEDICINE
HEROES

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Florida State University

- Alan Spector

Oswaldo Hospital, São Paulo

- Ricardo Cohen

Catholic University of Chile

- Camilo Boza

Saudi Arabia

- Al-Qahtani, Ghalia Abdeen

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"In the present case it is similarly necessary to renounce a freedom that does not exist and to recognise a dependence of which we are not personally conscious."