Obesity medications in the hands of surgeons

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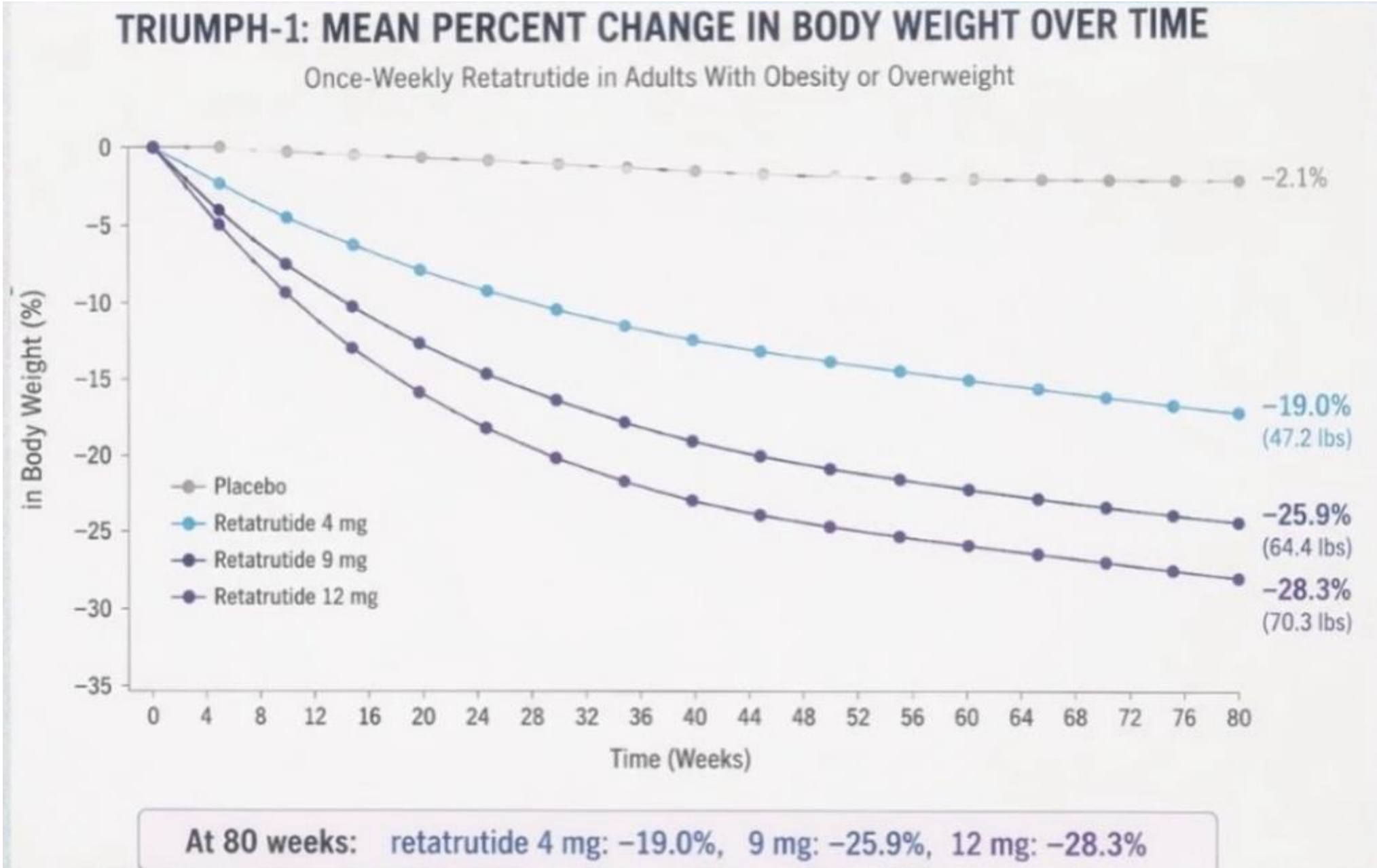
Erysichthon sells his daughter – Jan Havicksz Steen 1650

Conflicts of interest

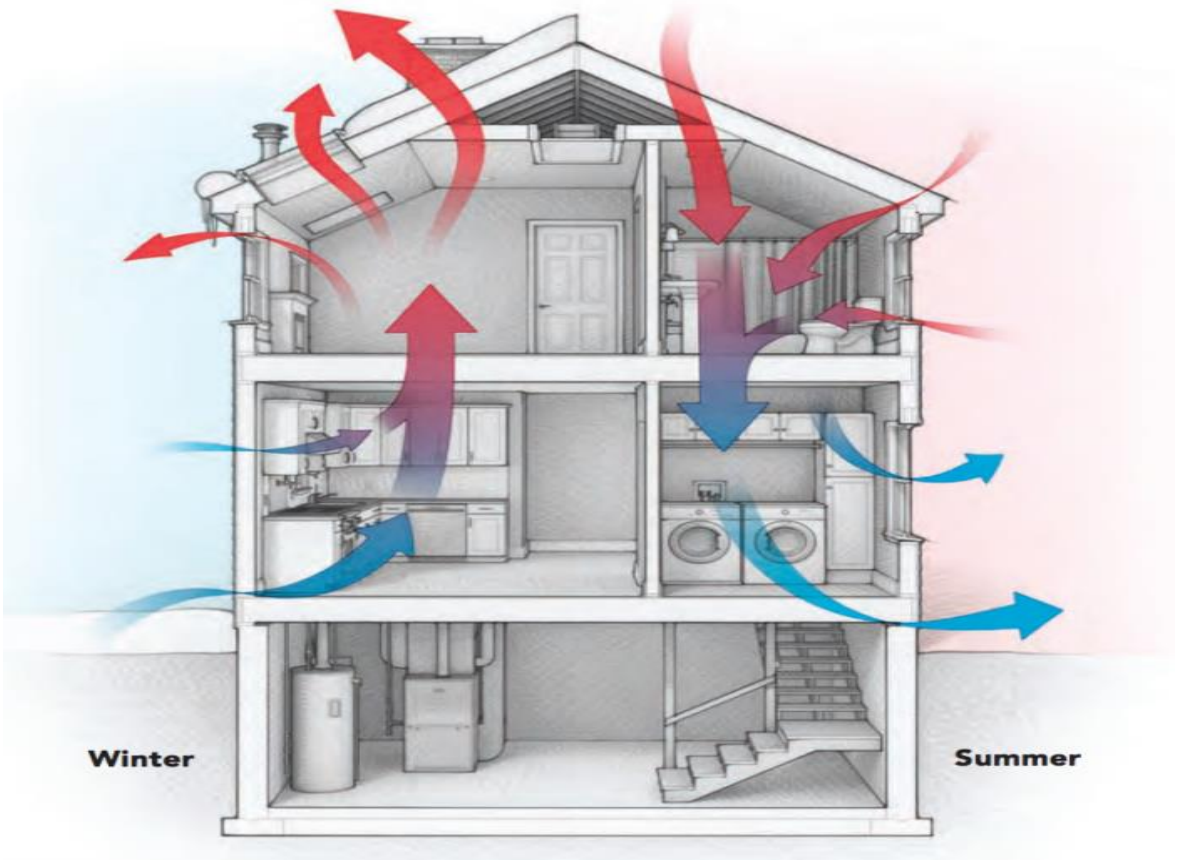
- Consilient Health
- Novo Nordisk
- Herbalife
- Johnson & Johnson
- Covidien
- Fractyl
- GI Dynamics
- Olympus
- Lilly
- Boehringer Ingelheim
- Keyron
- Astra Zeneca
- Roche
- Arrowhead
- Amgen

TRIUMPH 1

Retatrutide data presented at ADA2026



Body Fat Mass Is Actively Regulated by Biological Systems

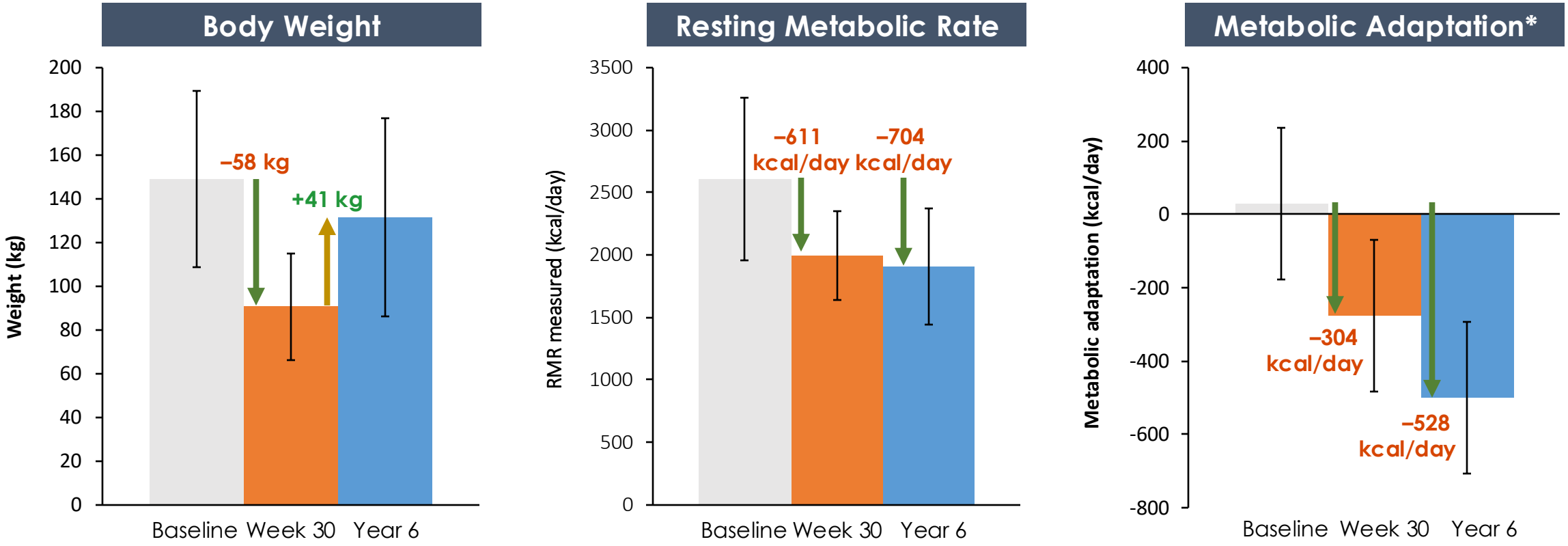


Like temperature regulation in a house, the body continuously adjusts energy intake and expenditure to defend a biologically regulated level of body fat mass

Purnell JQ, le Roux CW. *Diabetes Obes Metab*. 2024;26 Suppl 2:3-12.

The Body Continues to Defend Fat Mass Long After Weight Loss

In participants from a 30-week "The Biggest Loser" weight-loss competition:

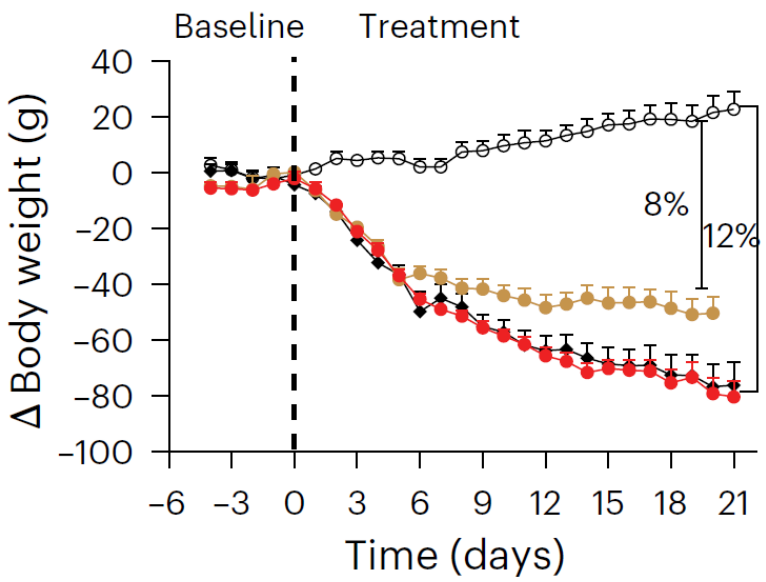


Weight loss results in persistent metabolic adaptation, helping explain why maintaining weight loss remains challenging

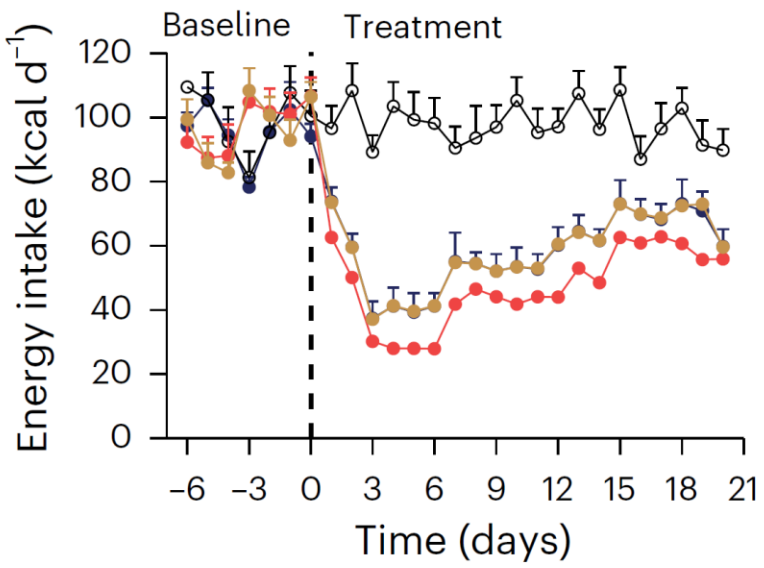
Based on 14 of 16 participants.
Error bars represent standard deviation.
*Defined as the residual resting metabolic rate adjusted for changes in body composition and age.
Fothergill E, et al. *Obesity (Silver Spring)*. 2016;24:1612-1619.

Blunting Metabolic Adaptation Can Alter the Physiological Response to Weight Loss

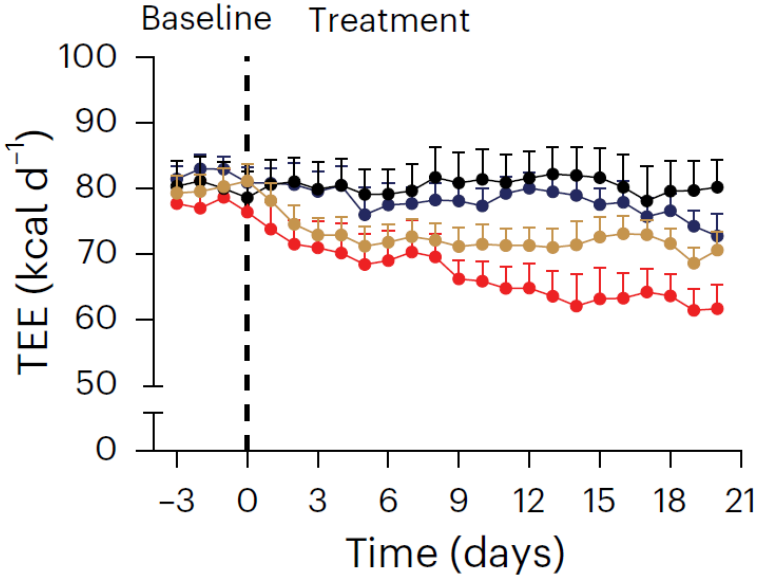
Change in Weight



Change in Energy Intake



Change in Energy Expenditure



Vehicle — CagriSema — Pair-fed — Weight matched

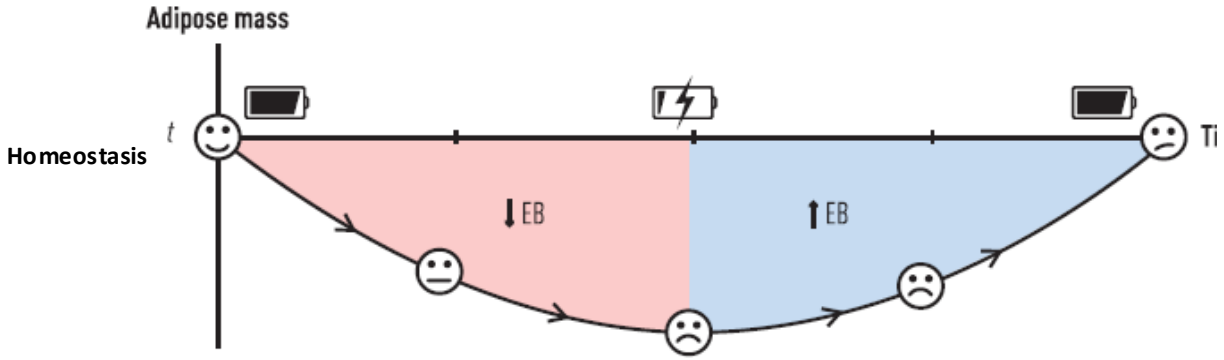
In a preclinical model, blunting metabolic adaptation was associated with coordinated changes in body weight, energy expenditure, and energy intake

*Preclinical study of 41 male diet-induced obese sprague dawley rats evenly distributed into 4 study groups: vehicle (*ad libitum* feeding), CagriSema (*ad libitum* feeding), pair-fed (vehicle with pair-feeding matched to the caloric intake of the CagriSema group), or weight-matched (caloric restriction matched to the weight of the CagriSema group). Rats received once-daily subcutaneous injections of CagriSema (0.5 + 0.5 nmol/kg on day 1, 1 + 1 nmol/kg on day 2, and then 2 + 2 nmol/kg/day from Day 3–21) or vehicle. Body weight, energy intake, and total energy expenditure were assessed over 21 days.

Jacobsen JM, et al. *Nat Metab*. 2025;7:1322-1329.

Effective Obesity Treatment Helps Establish a New, Lower Adiposity Homeostasis

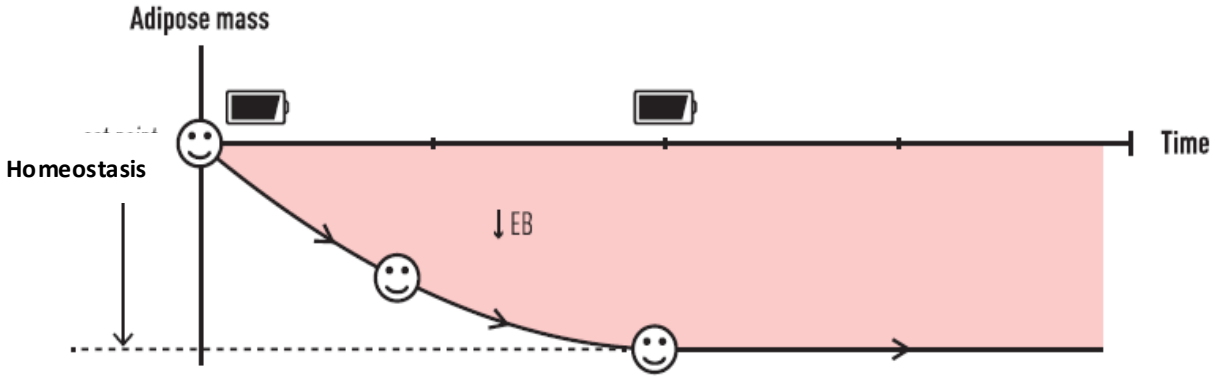
Low-Calorie Diet–Induced Weight Loss



Satiety hormone*	↔	↓	↔
Ghrelin*	↔	↑	↔
Leptin	↔	↓	↔
Energy expenditure	↔	↓	↔
Fat oxidation	↓	↓	↓

Compensatory physiological adaptations favor restoration of the original adiposity homeostasis

Obesity-Medicine–Induced Weight Loss



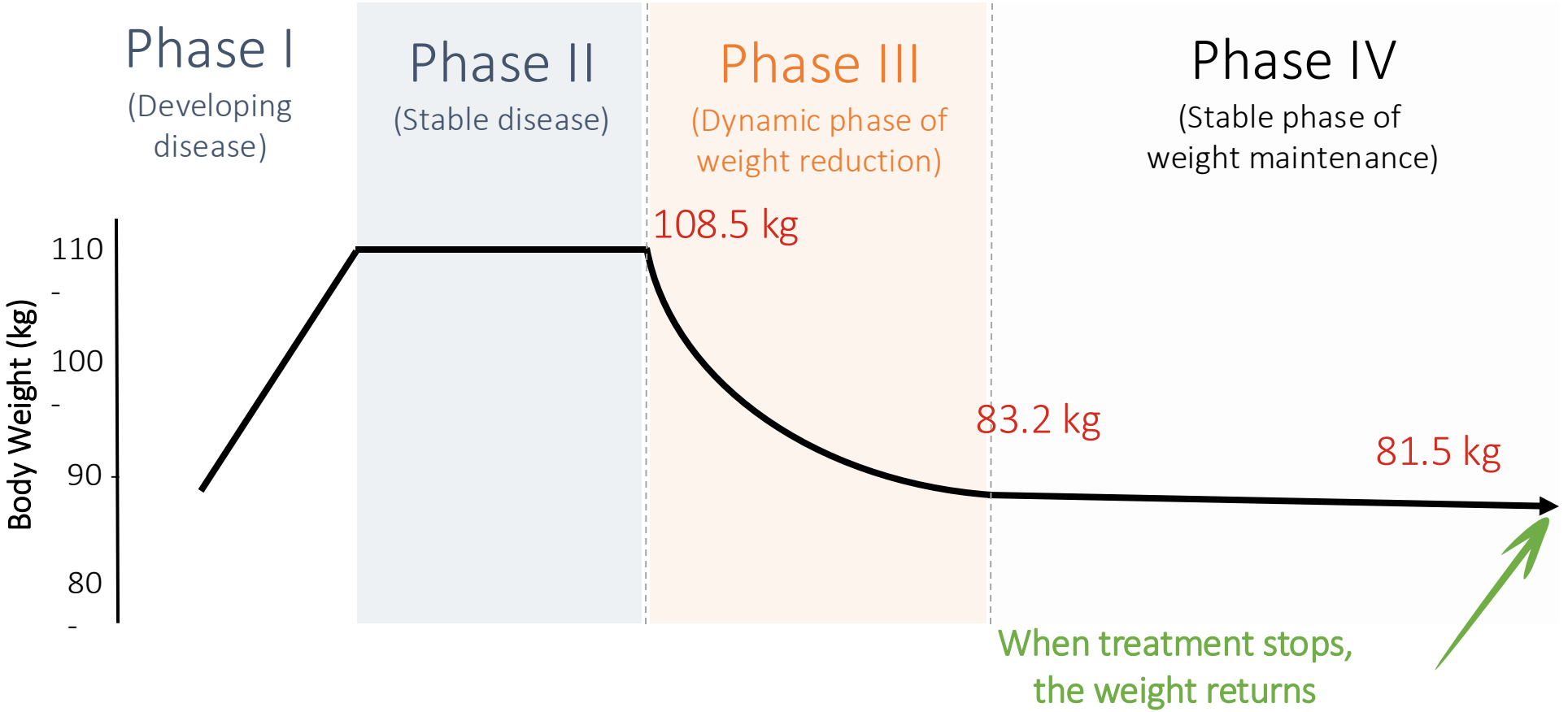
Satiety hormone*	↔	↓
Ghrelin*	↔	↑
Leptin	↔	↓
Energy expenditure	↔	↓
Fat oxidation	↓	↓

Effective obesity treatment supports establishment of a new, lower adiposity homeostasis

Understanding these adaptations helps clinicians set expectations for changes in appetitive behavior, enabling more informed discussions with patients and supporting long-term treatment success

*Fasting + meal-stimulated.
EB = energy balance.
Purnell JQ, Le Roux CW. *J Intern Med*. 2026;299:66-78.

Long-Term Obesity Management Is Needed to Achieve and Maintain Clinically Meaningful Benefits[1,2]



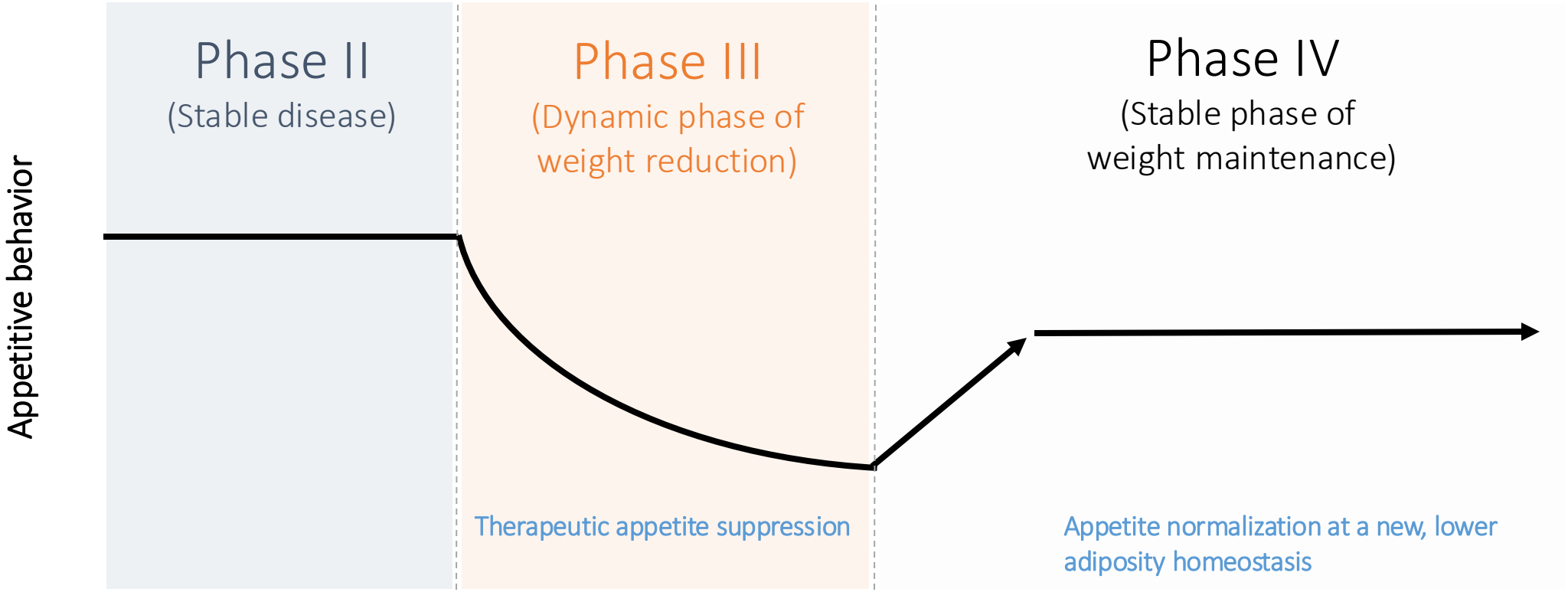
Benefits of sustained weight loss[1,4]

- Reduce **diabetes risk**[3]
- Improve markers of **cardiovascular risk and CVD**
- Improve **other obesity complications**
- Reduce **functional impairment**[4]
- Improve **quality of life**[4]

CVD = cardiovascular disease.

1. Sharma AM. *J Obes Metab Syndr.* 2023;32:285-288. **2.** Jastreboff AM, et al. *N Engl J Med.* 2025;392958-971. **3.** Wadden TA, et al. *Circulation.* 2012;125:1157-1170. **4.** Villareal DT, et al. *Am J Clin Nutr.* 2005;82:923-934.

Appetitive Behavior May Normalize as a New Lower Adiposity Homeostasis Is Established



1. Sharma AM. *J Obes Metab Syndr*. 2023;32:285-288. **2.** Purnell JQ, Le Roux CW. *J Intern Med*. 2026;299:66-78.

Obesus:

Pinguis quasi ob edendum factus (made fat as a result of eating)

The Roman Writer Aulus Gellius 130 AD

Lewis & Short. https://alatius.com/. Accessed July 8, 2026.

Summary

Our understanding of obesity has evolved to recognizing it as a chronic disease of dysregulated biological systems[1,2]

The coordinated biological responses actively defend adiposity, helping explain the challenges of sustaining weight loss and reinforcing the need for chronic disease management[3,4]

Recognizing the biological heterogeneity of obesity provides a rationale for therapies targeting complementary biological pathways[5]

1. Gómez-Ambrosi J, et al. *Int J Obes (Lond)*. 2025;49:168-176. **2.** Koskinas KC, et al. *Eur J Prev Cardiol*. 2024;45:4063-4098. **3.** Purnell JQ, le Roux CW. *Diabetes Obes Metab*. 2024;26 Suppl 2:3-12. **4.** Sharma AM. *J Obes Metab Syndr.* 2023;32:285-288. **5.** Müller TD, et al. *Nat Rev Drug Discov*. 2022;21:201-223.