The Calculus of Calories: Quantifying Body Weight Regulation in Humans

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Intramural Research Program
Our Research Changes Lives

one program
many people
infinite possibilities

Disclosures

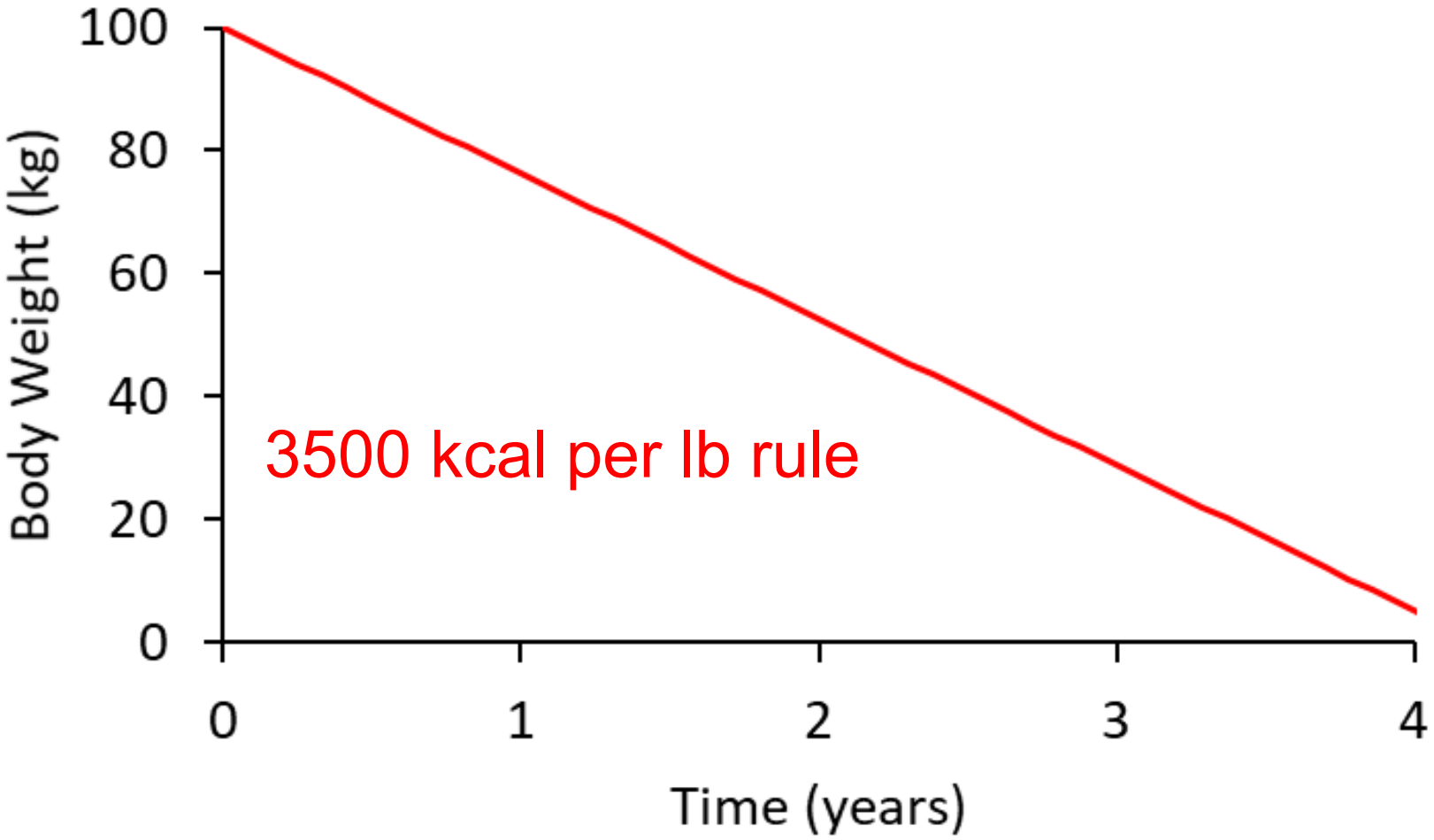
- Nothing to Disclose

*all relevant financial relationships have been mitigated

Learning Objectives

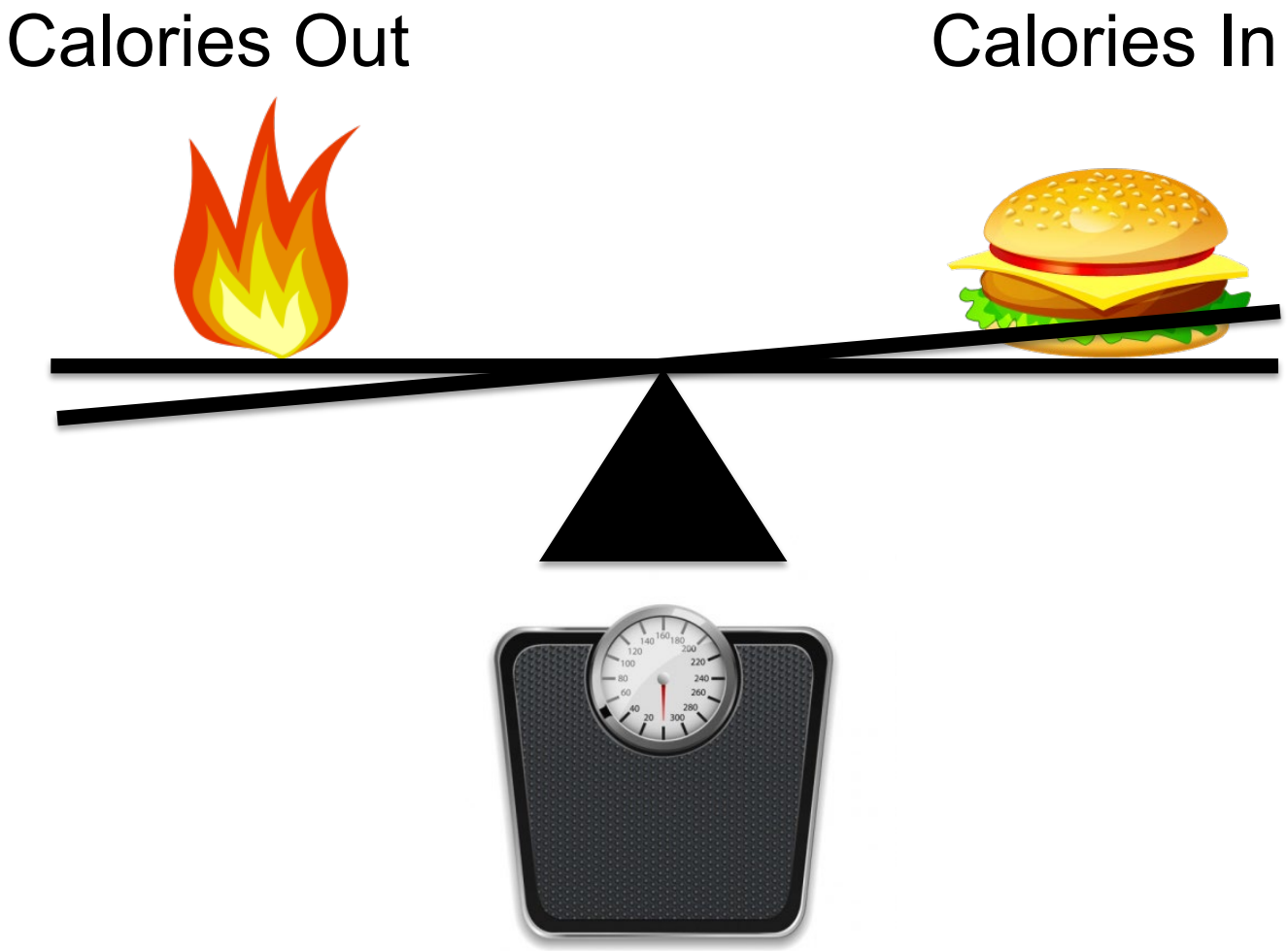
1. Identify how body weight is regulated as part of a negative feedback control system
2. Describe how the body responds to diets with wide variation in their ratio of carbohydrate to fat
3. Describe how the body responds to diets varying in quality as determined by their amount of ultra-processed foods

Erroneous Weight Loss Projections

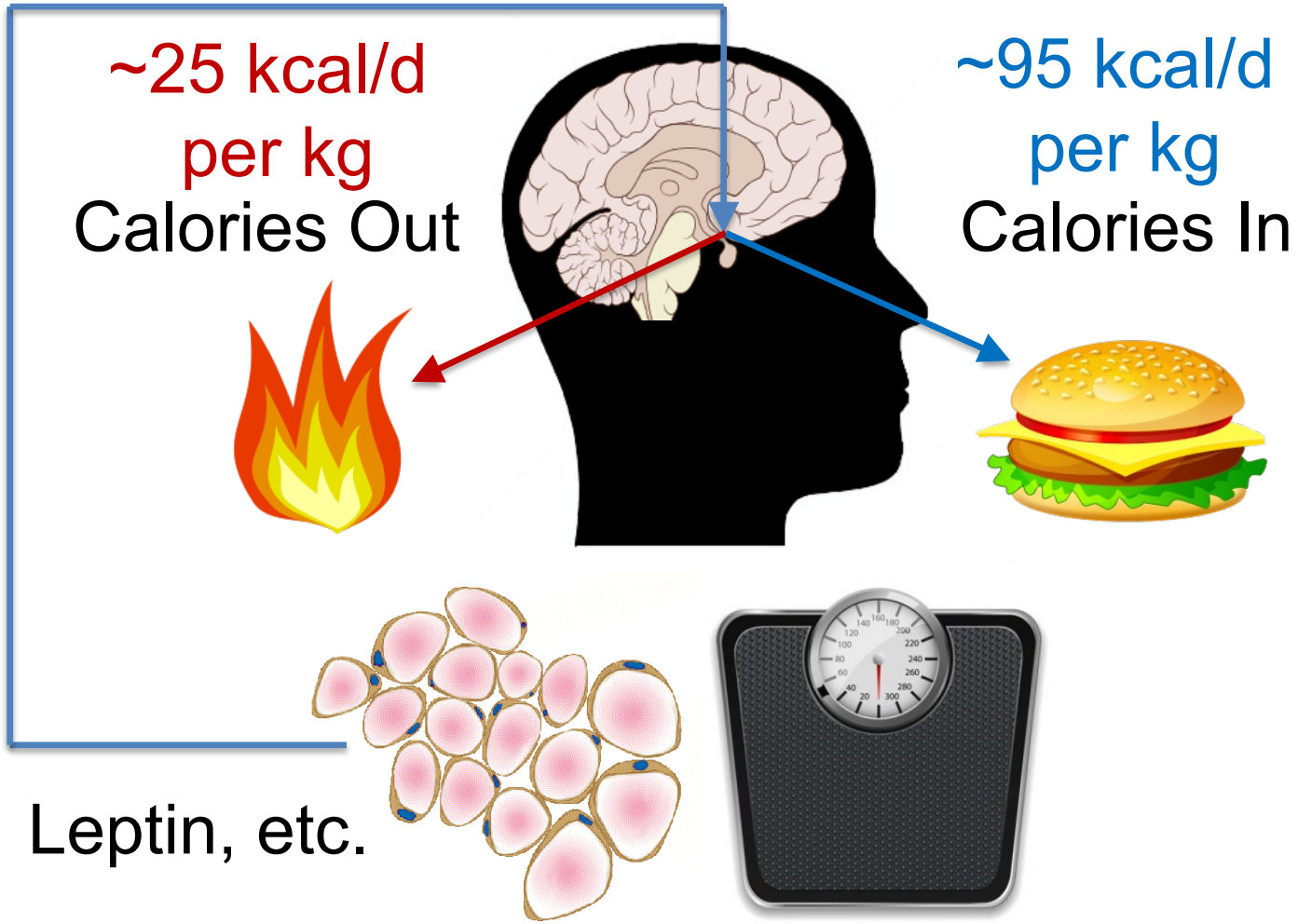


K.D. Hall et al. *Lancet, 738*:826-37 (2011)

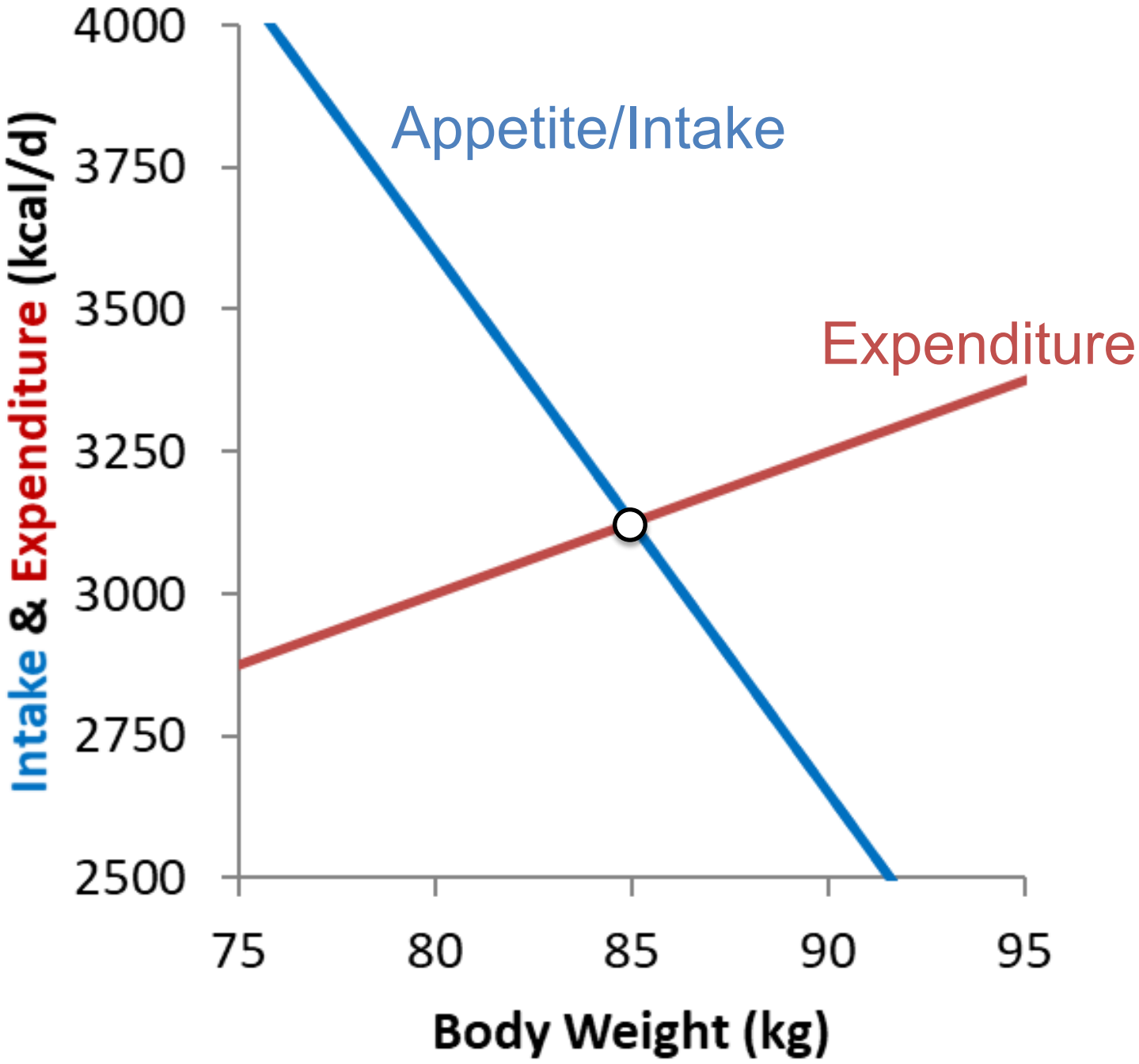
Calories In & Out are NOT Independent

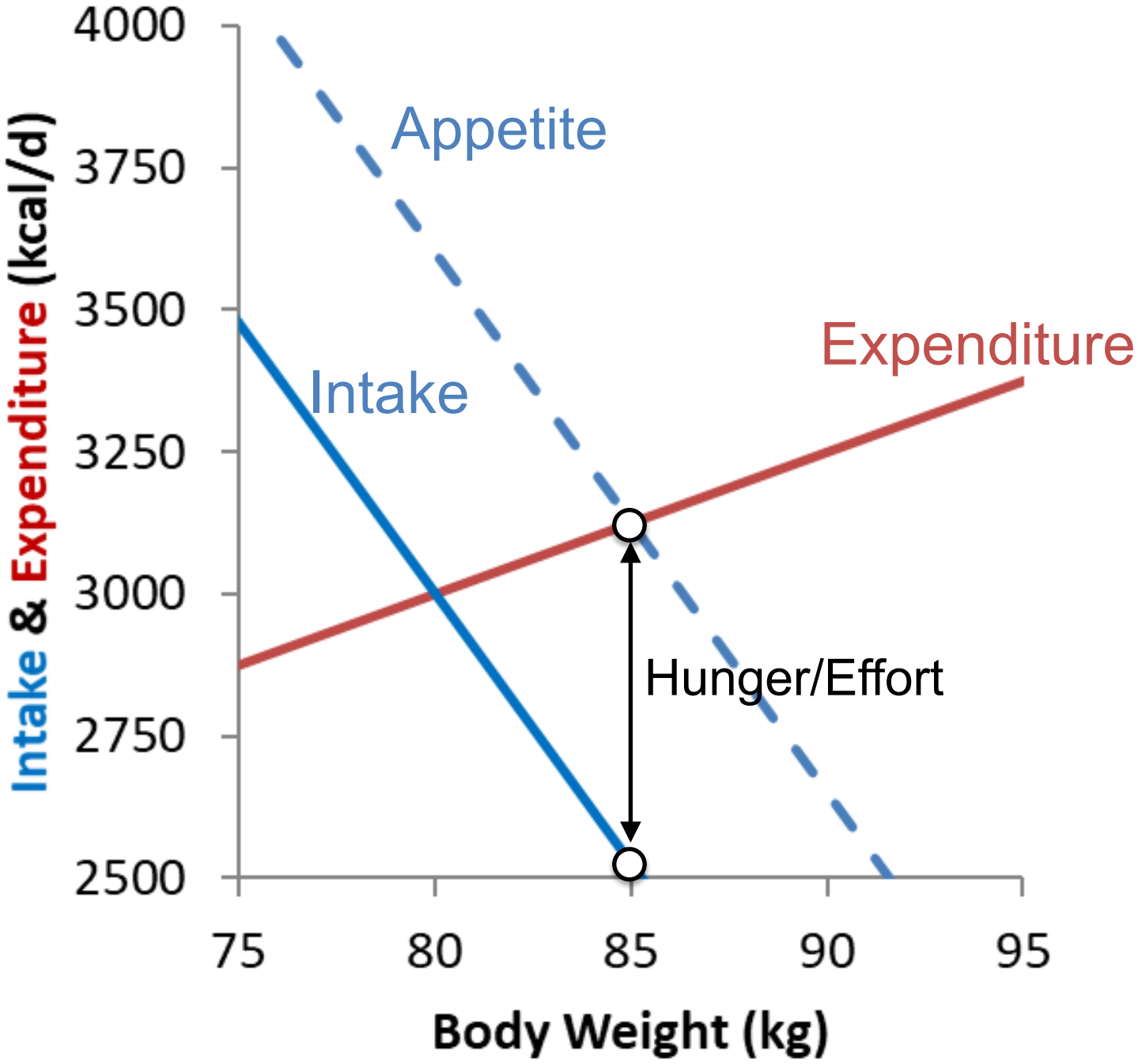


Feedback Regulation of Body Weight

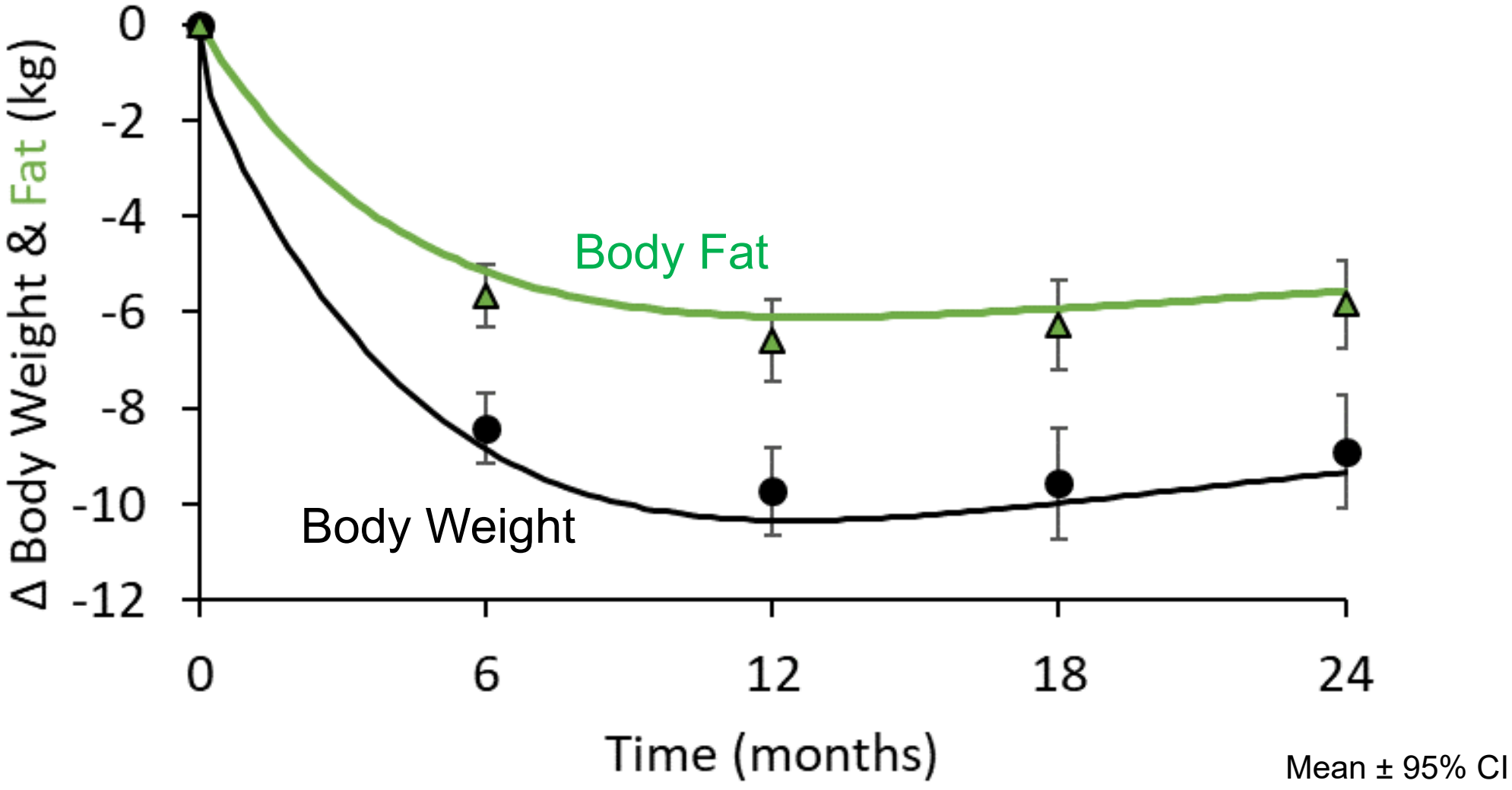


D. Polidori, A. Sanghvi, R. Seeley, K.D. Hall. *Obesity,* 24:2289 (2016)


Appetite/Intake
Expenditure
Intake & Expenditure (kcal/d)
4000
3750
3500
3250
3000
2750
2500
75
80
85
90
95
Body Weight (kg)


4000
3750
3500
3250
3000
2750
2500
Intake & Expenditure (kcal/d)
Appetite
Intake
Expenditure
Hunger/Effort
75
80
85
90
95
Body Weight (kg)

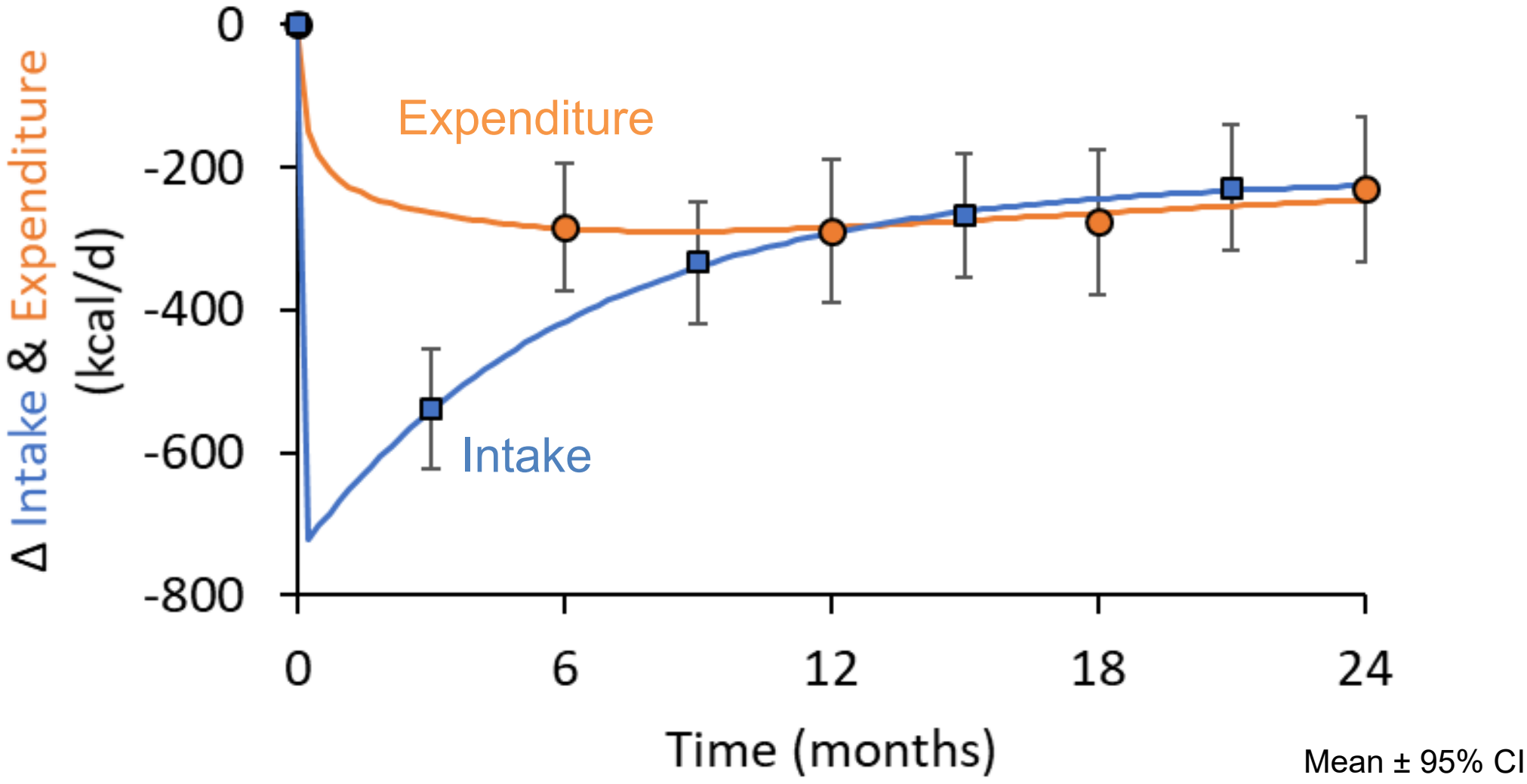
Effects of a 25% Calorie Restriction Intervention



Mean ± 95% CI

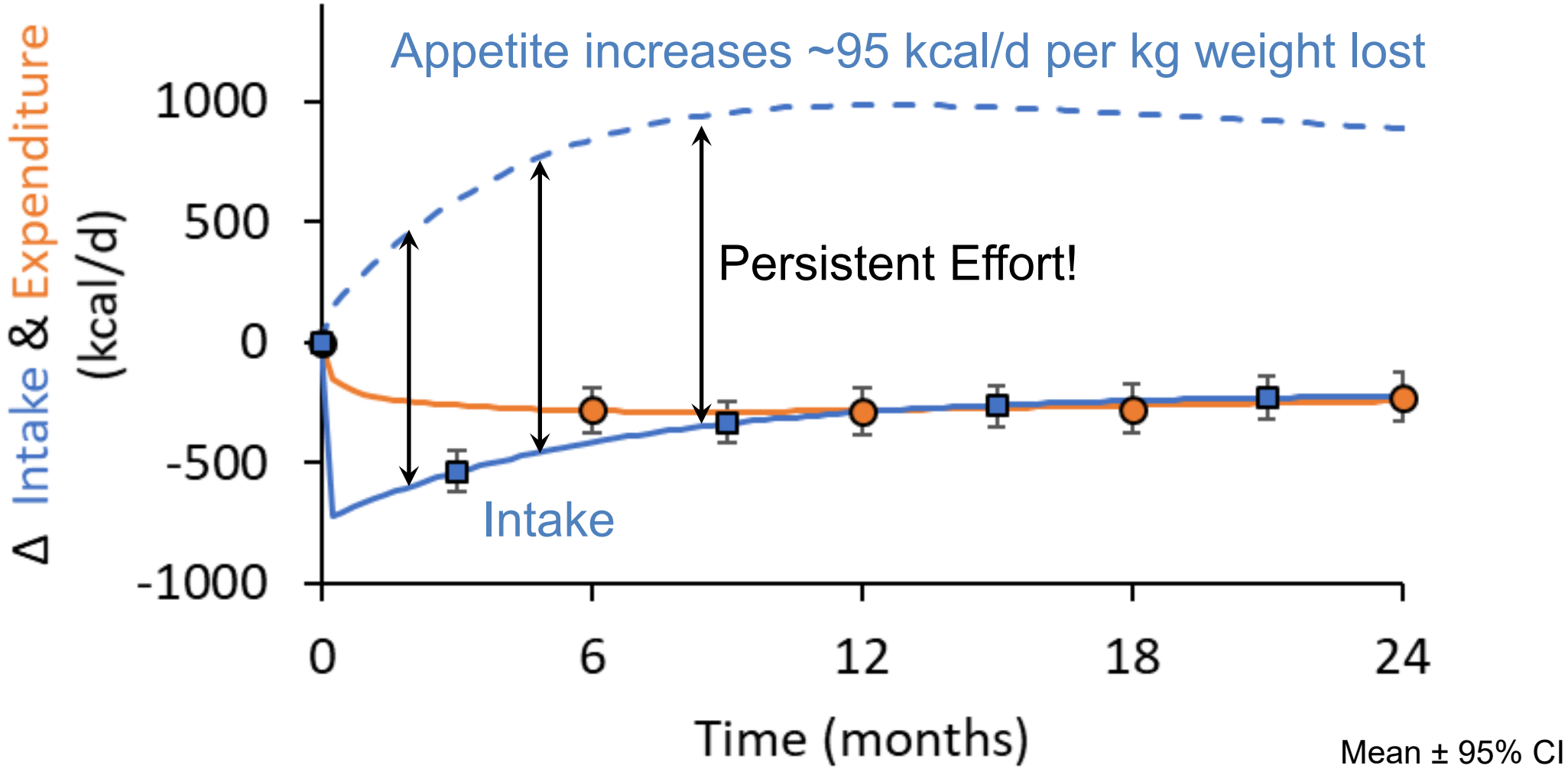
J Guo et al. *Am J Clin Nutr* 107:558–65 (2018).

Effects of a 25% Calorie Restriction Intervention



J Guo et al. *Am J Clin Nutr* 107:558–65 (2018).

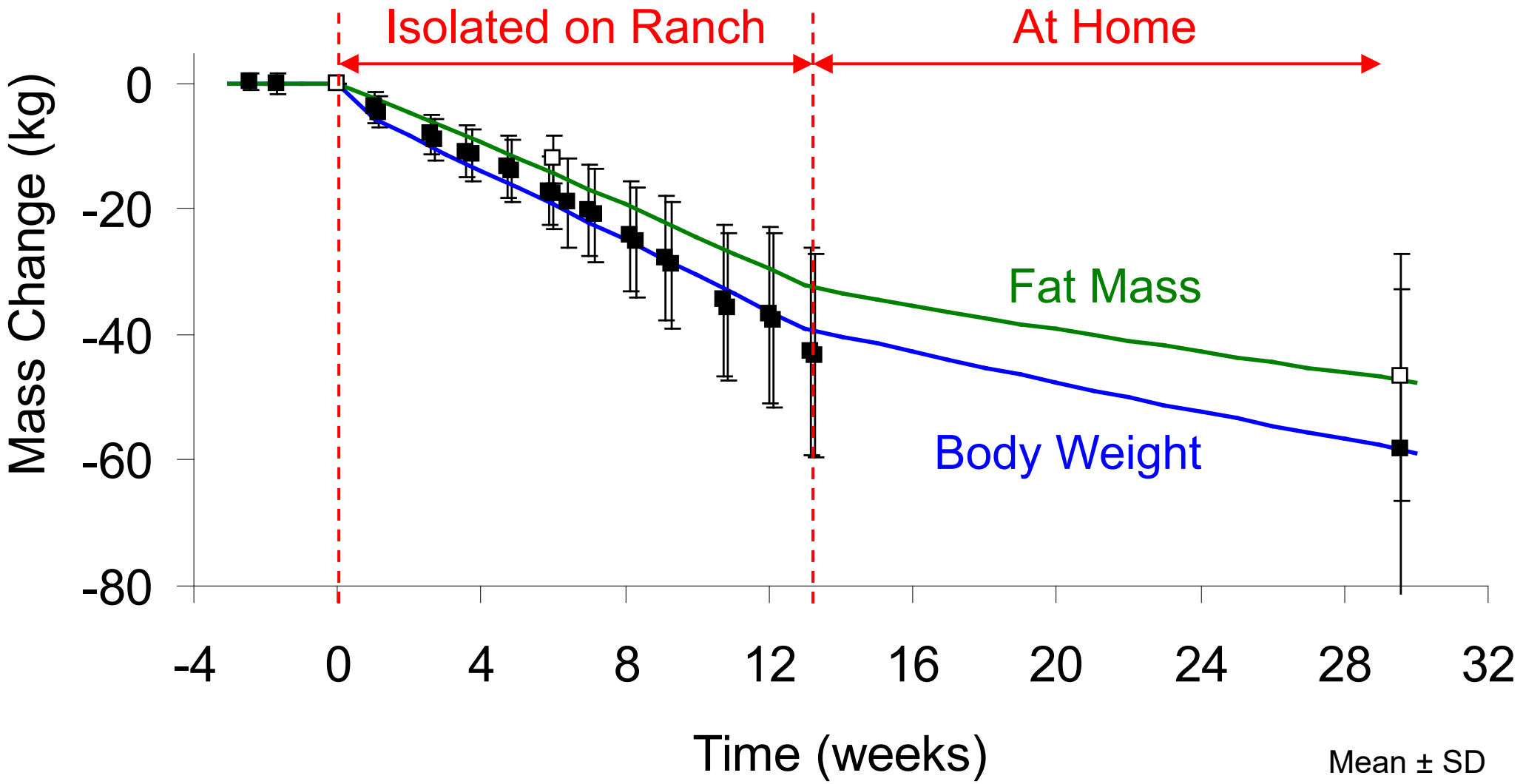
Challenges of Long-term Maintenance of Weight Loss



Aronne et al. *Obesity* 29:S9-24 (2021).

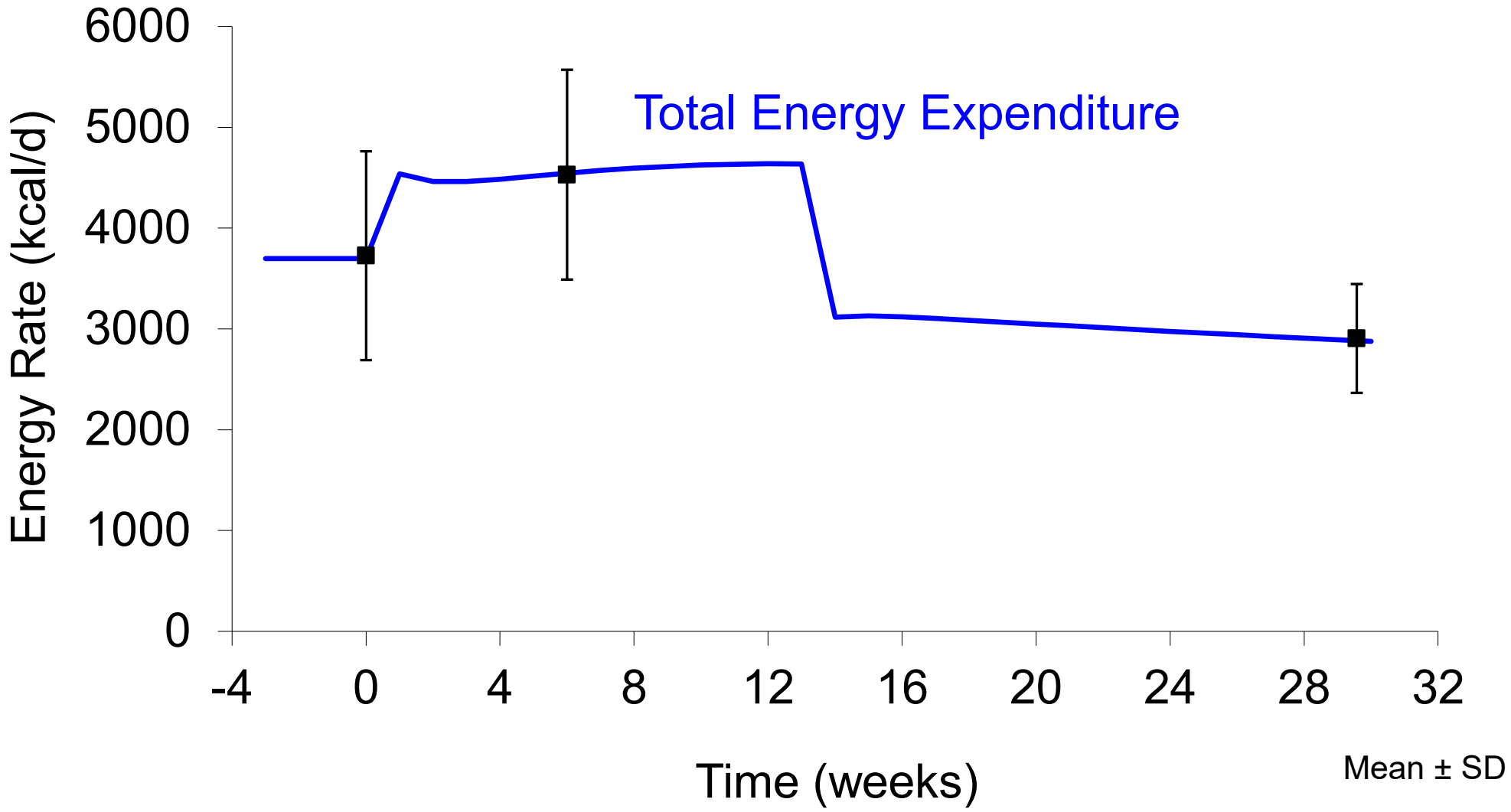
What about Exercise?

Biggest Loser Body Weight and Fat Loss



KD Hall. *Obesity* 21(5):957-9 (2013)

Biggest Loser Energy Balance Dynamics



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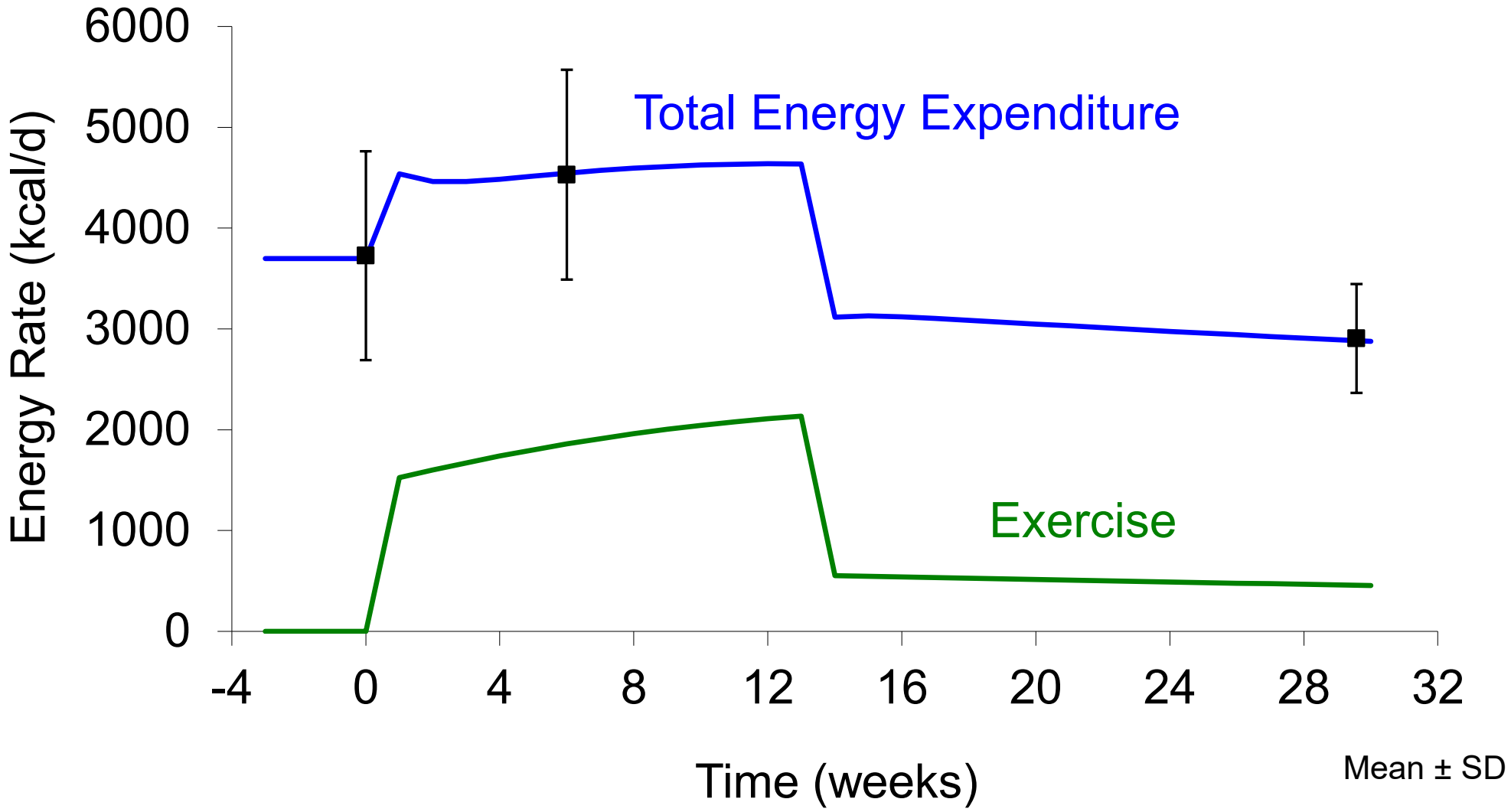
Biggest Loser Energy Balance Dynamics



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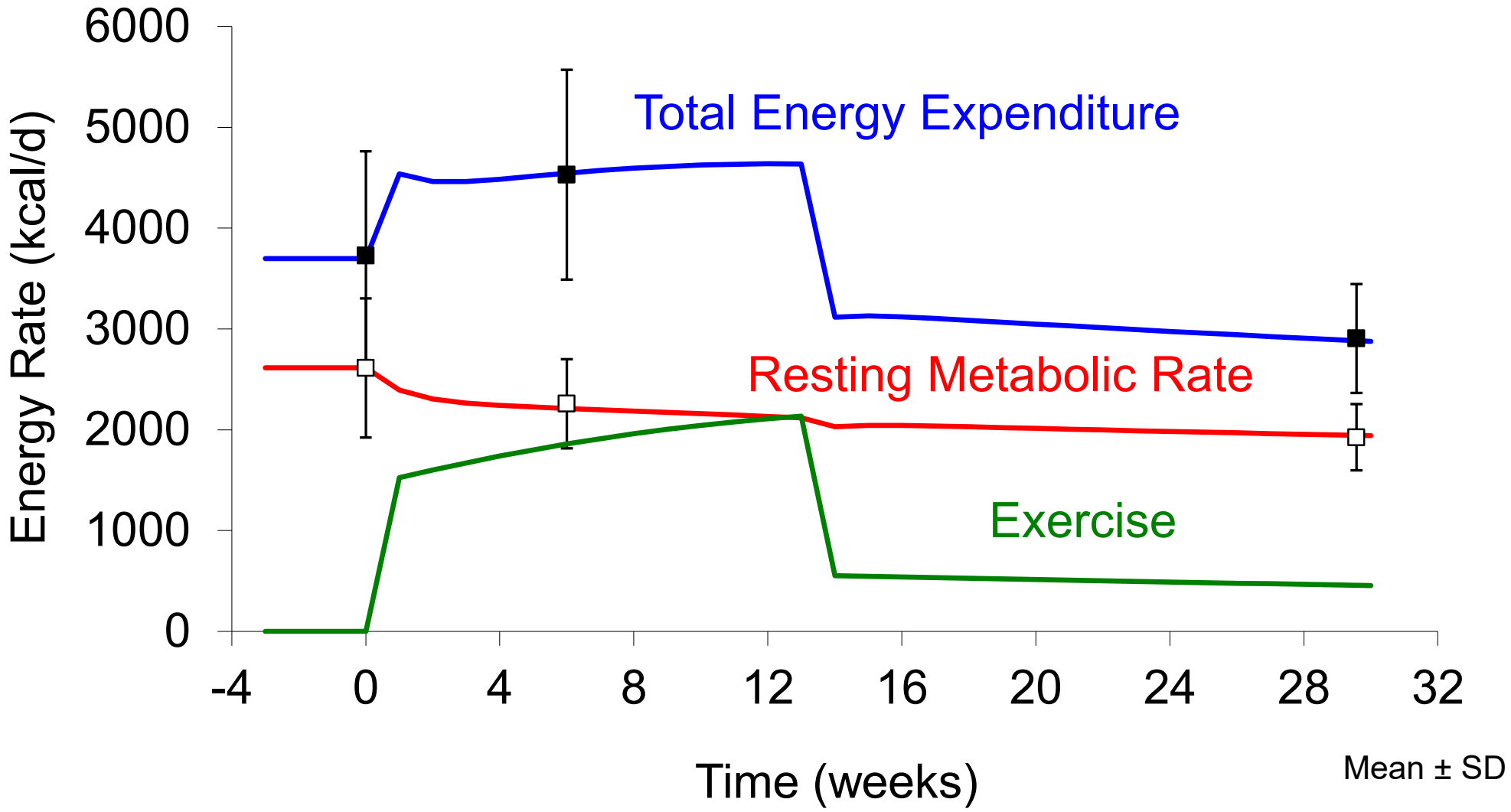

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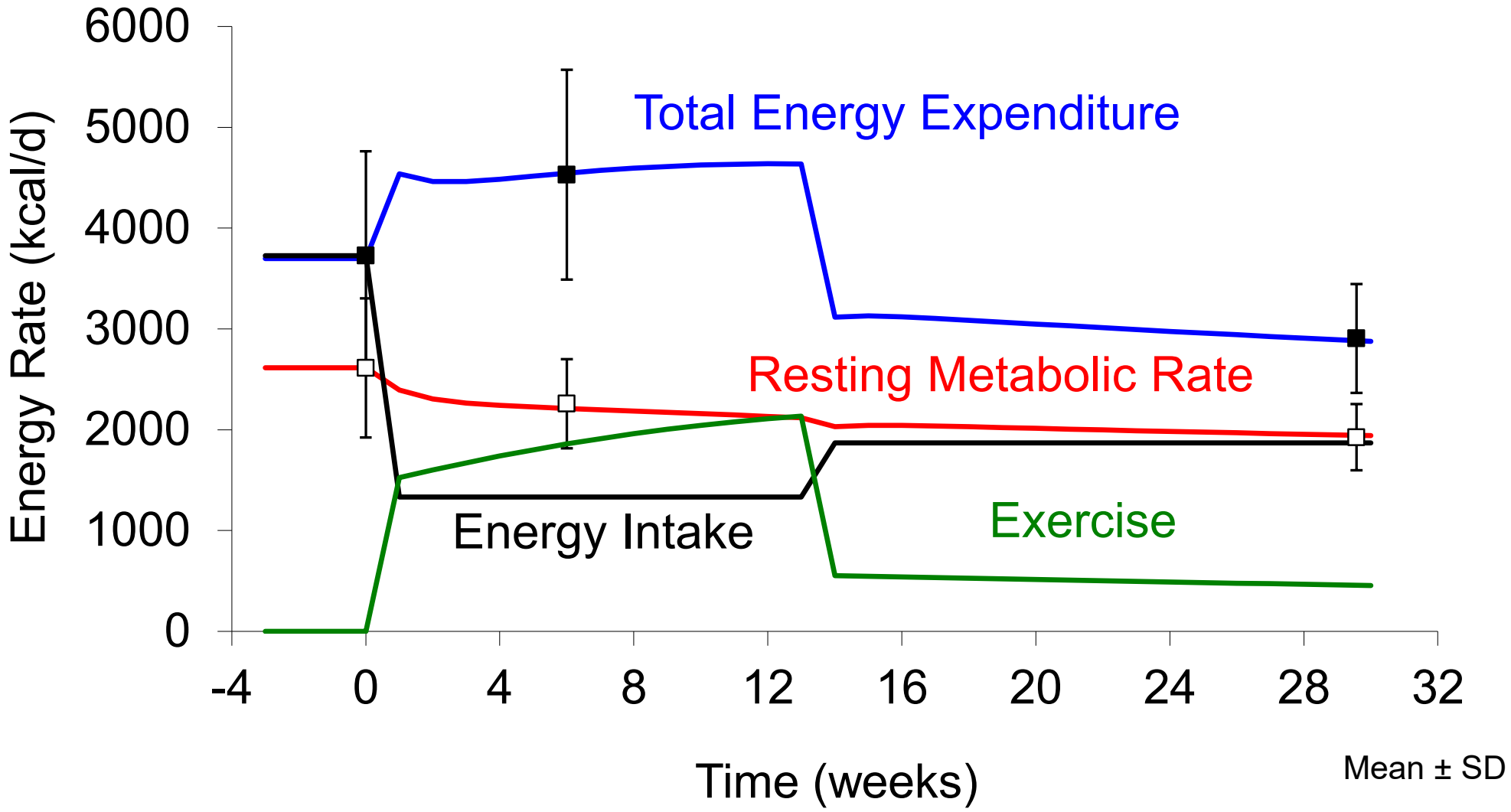
Biggest Loser Energy Balance Dynamics



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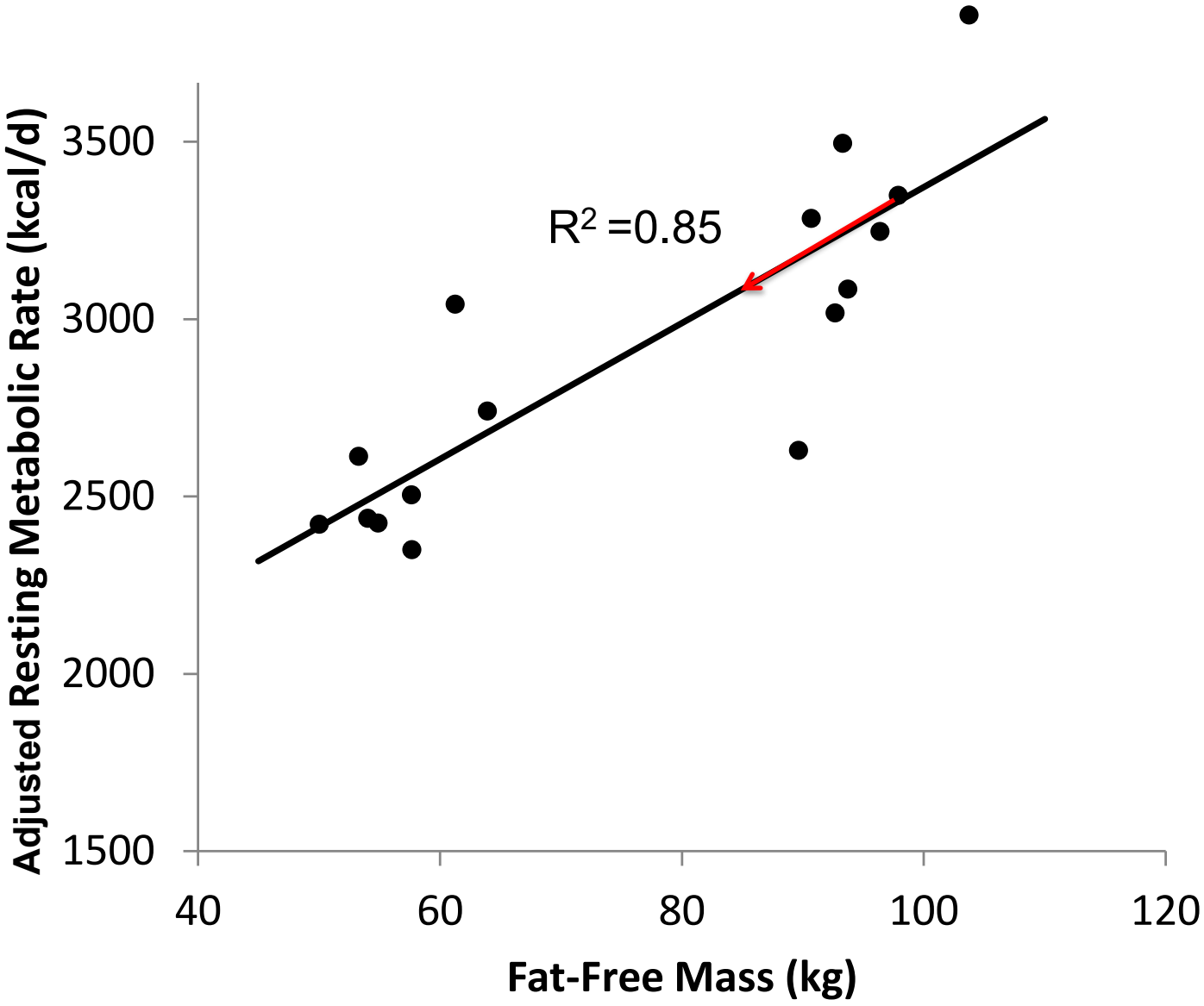
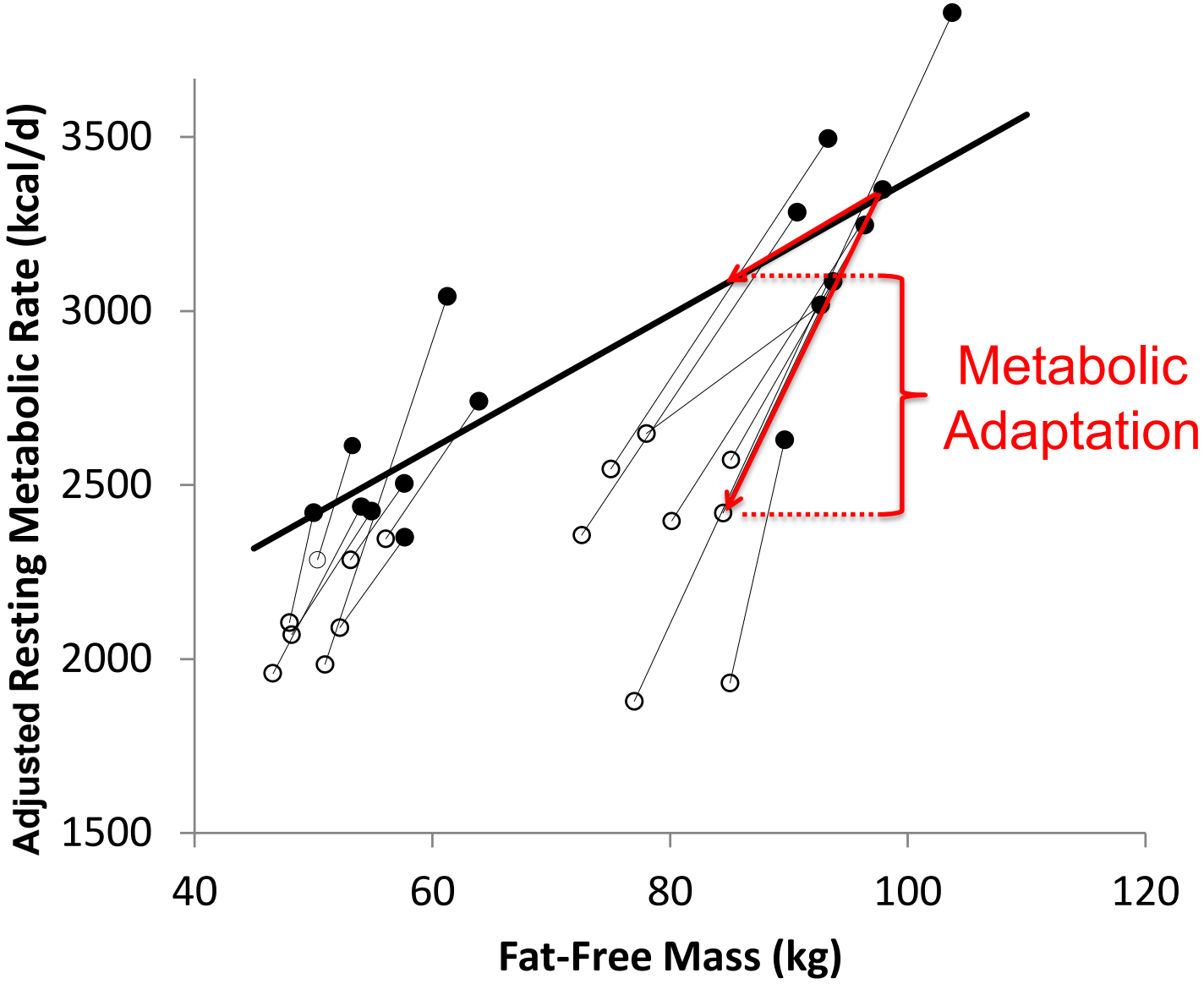
Resting Metabolic Rate before the Biggest Loser



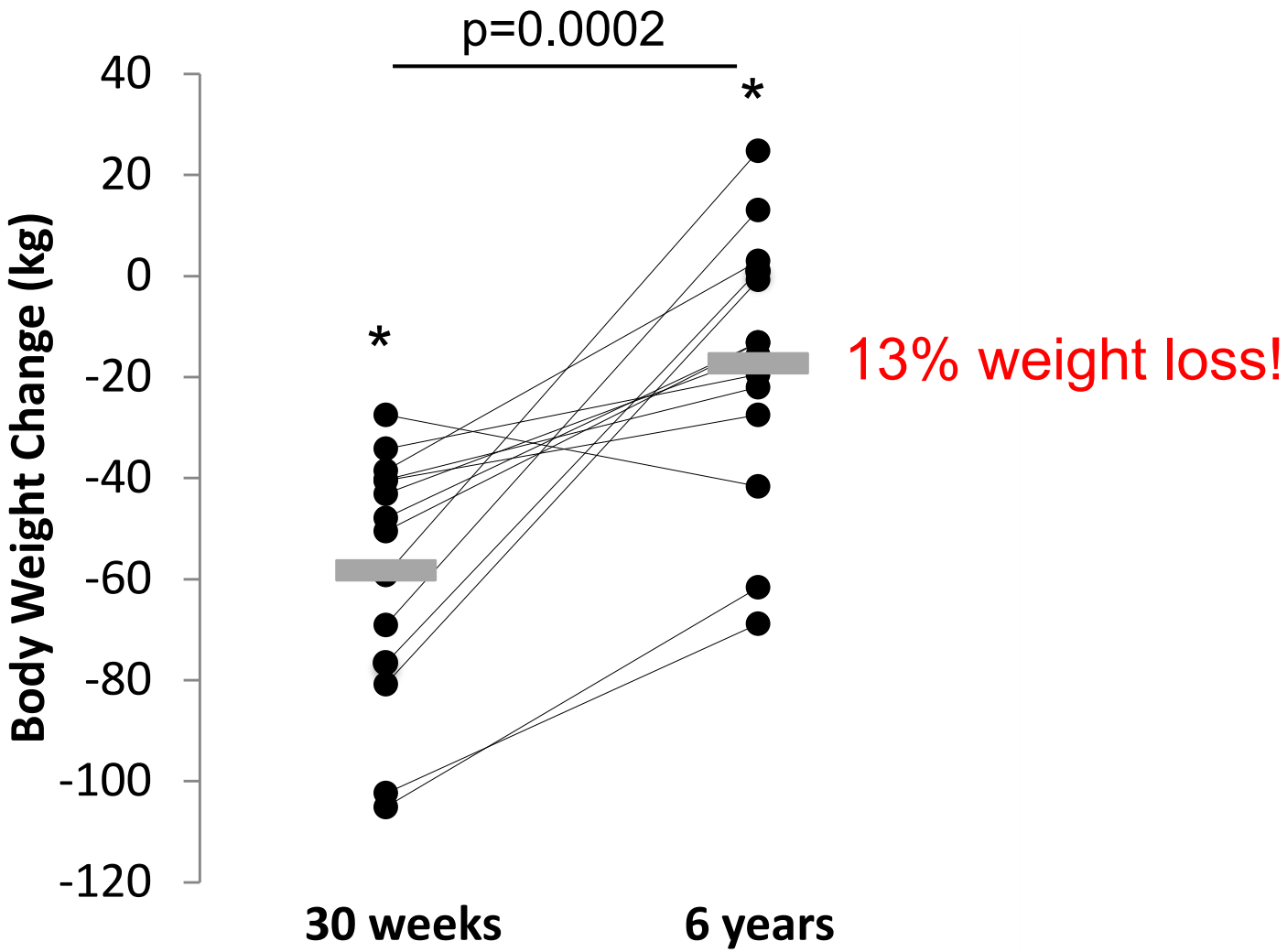
DL Johannsen et al. *JCEM* 97(7):2489–2496 (2012)

Resting Metabolic Rate after the Biggest Loser



DL Johannsen et al. *JCEM* 97(7):2489–2496 (2012)

Two Thirds of the Lost Weight was Regained 6 Years Later

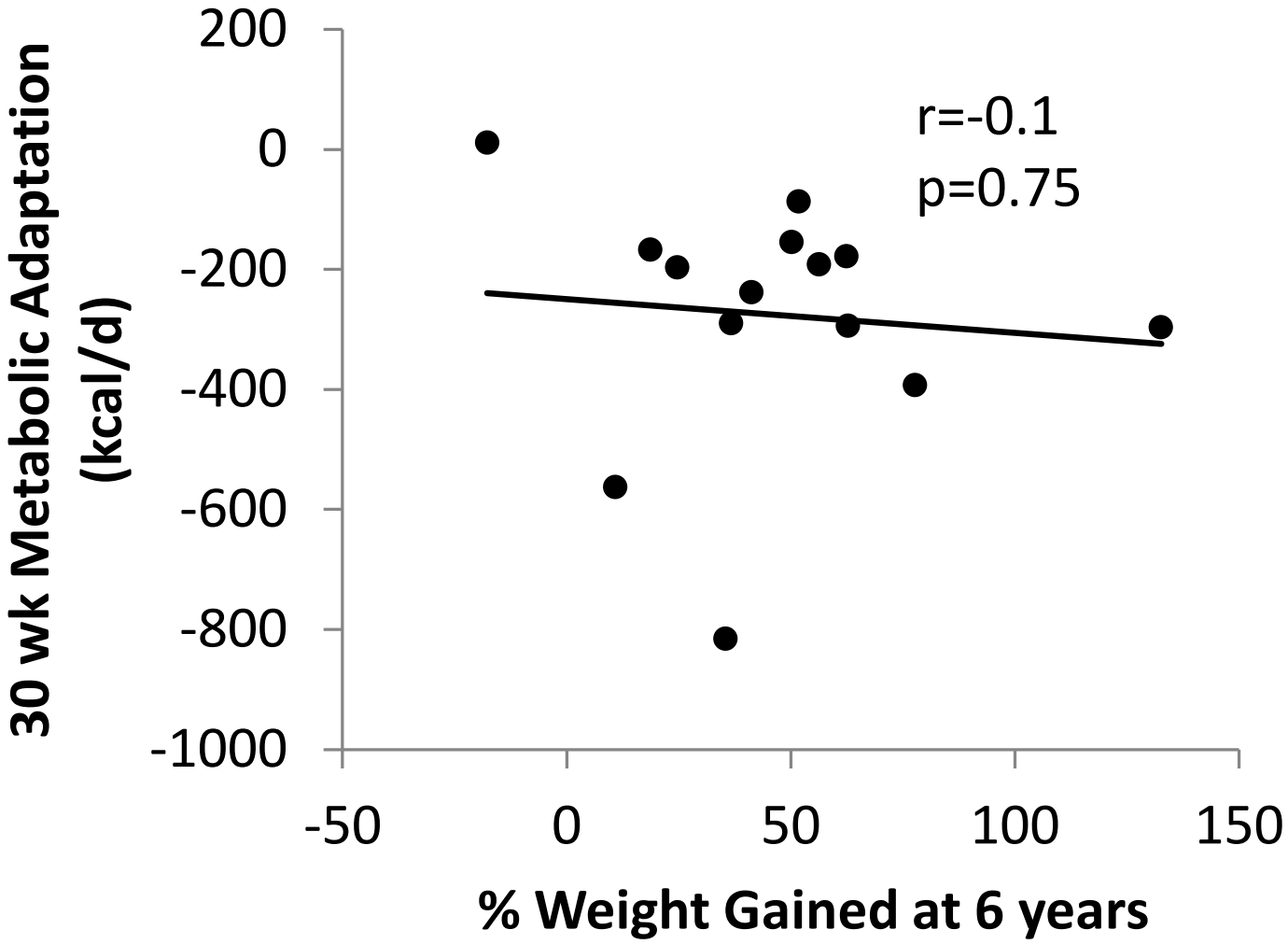


13% weight loss!

*p <0.05 vs. baseline

E Fothergill et al. *Obesity* 24:1612-1619 (2016)

Weight Regain was *Unrelated* to Metabolic Adaptation at the End of the Competition



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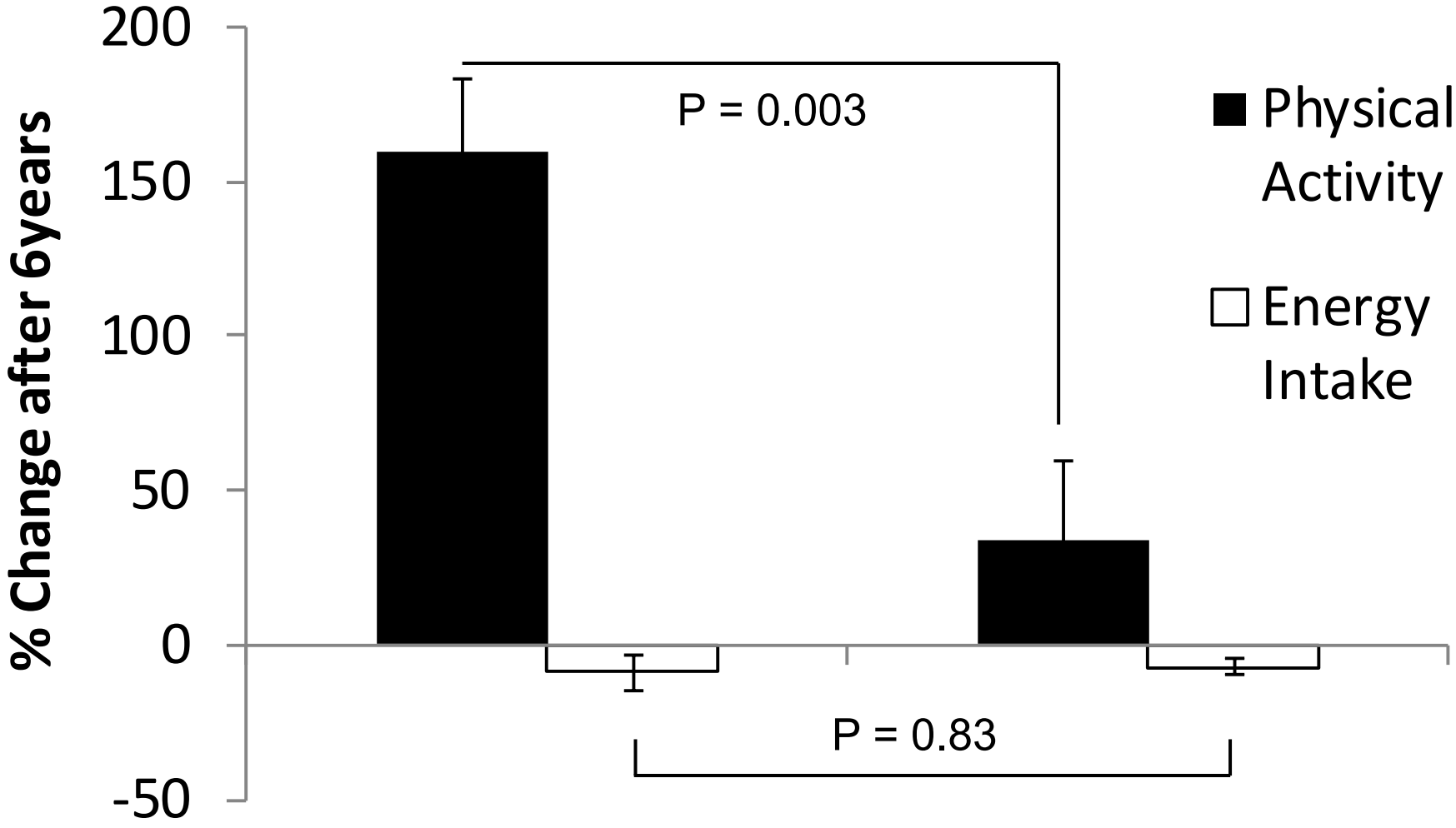
What Explains the Weight Regain?



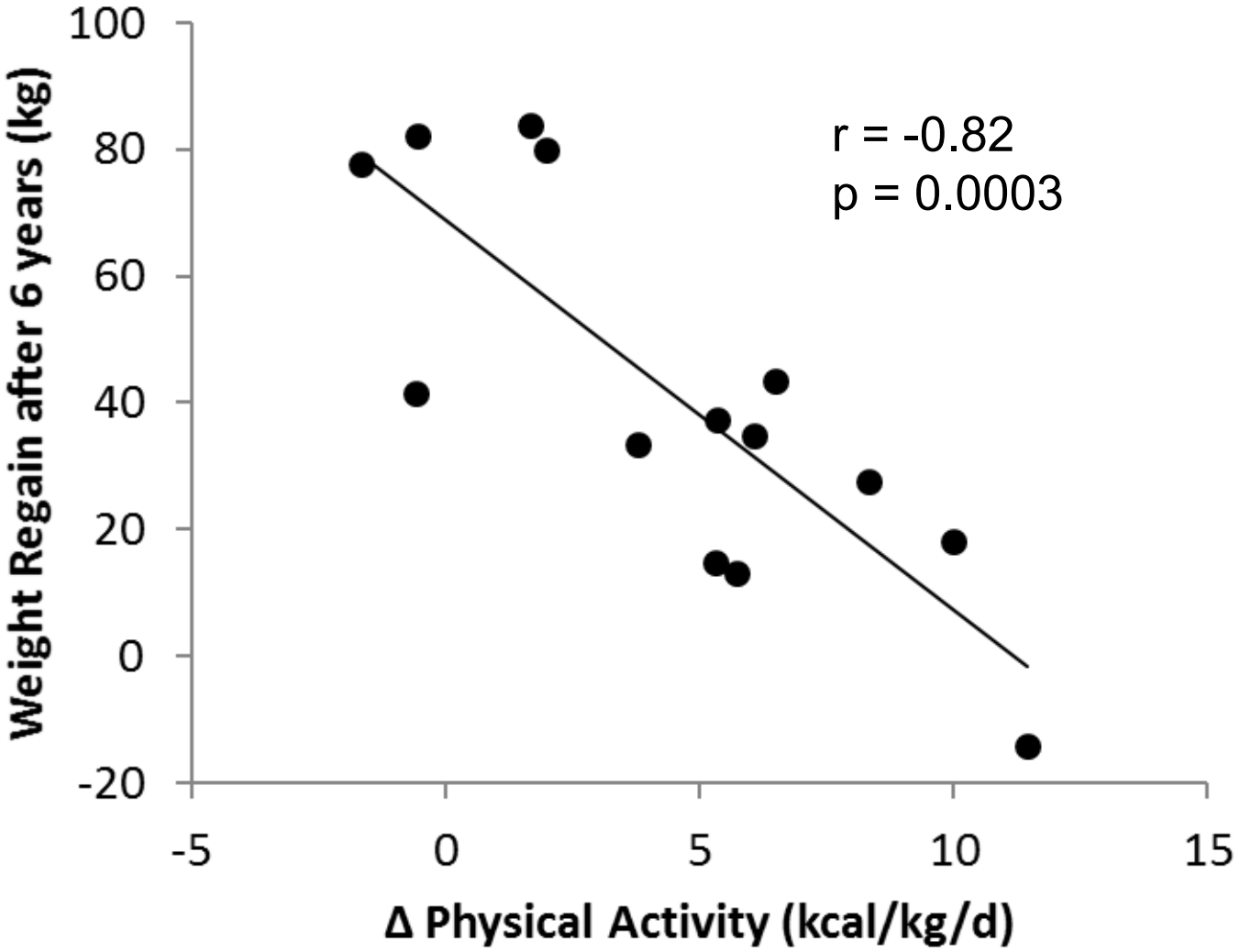
> 13% Weight Loss (-24.9% ± 3.8%)

< 13% Weight Loss (+1.1% ± 4.0%)

Mean ± SE

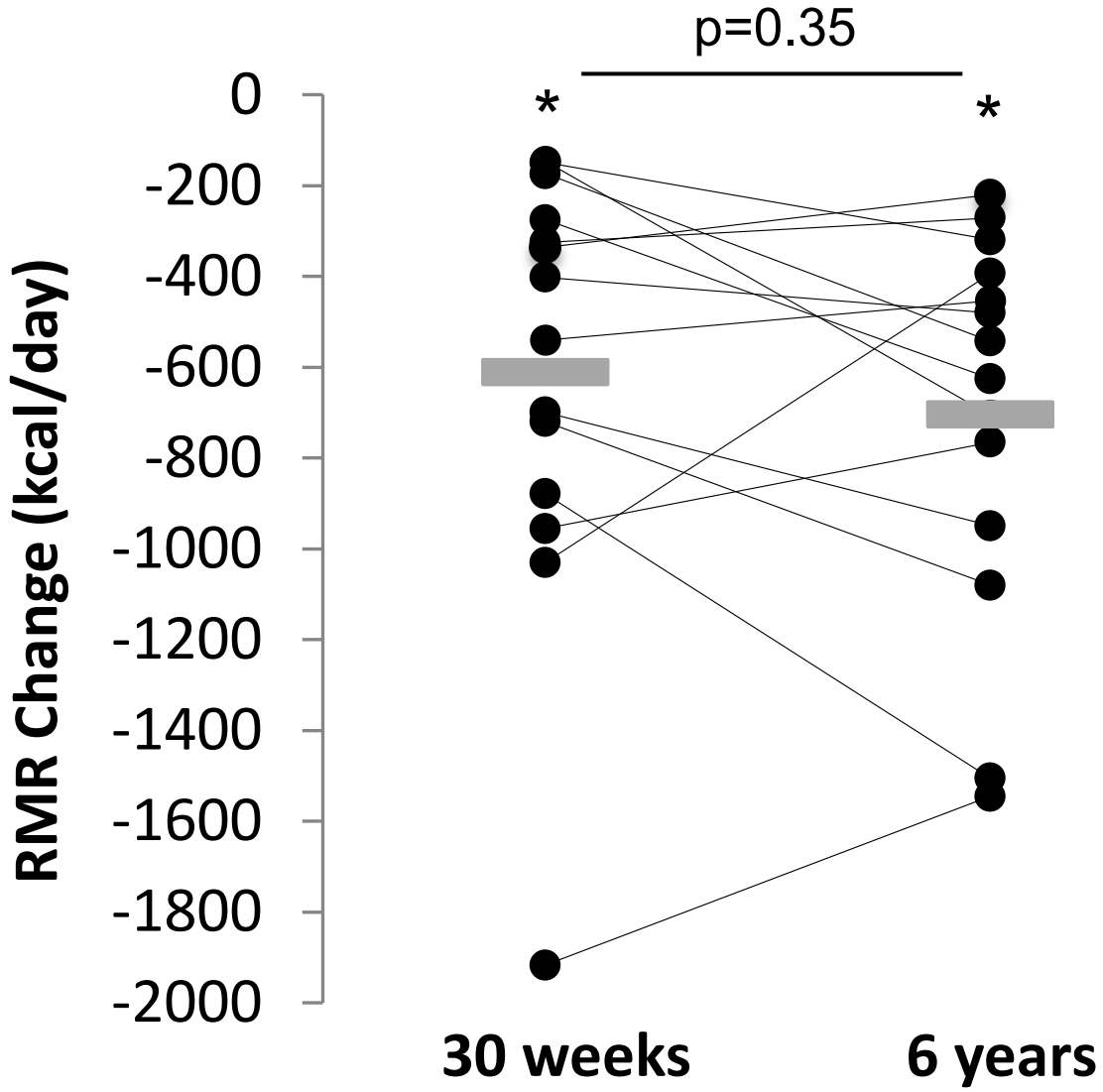
J Kerns et al. *Obesity* 25(11):1838-1843 (2017)

Increased Physical Activity was Associated with the Least Weight Regain



J Kerns et al. *Obesity* 25(11):1838-1843 (2017)

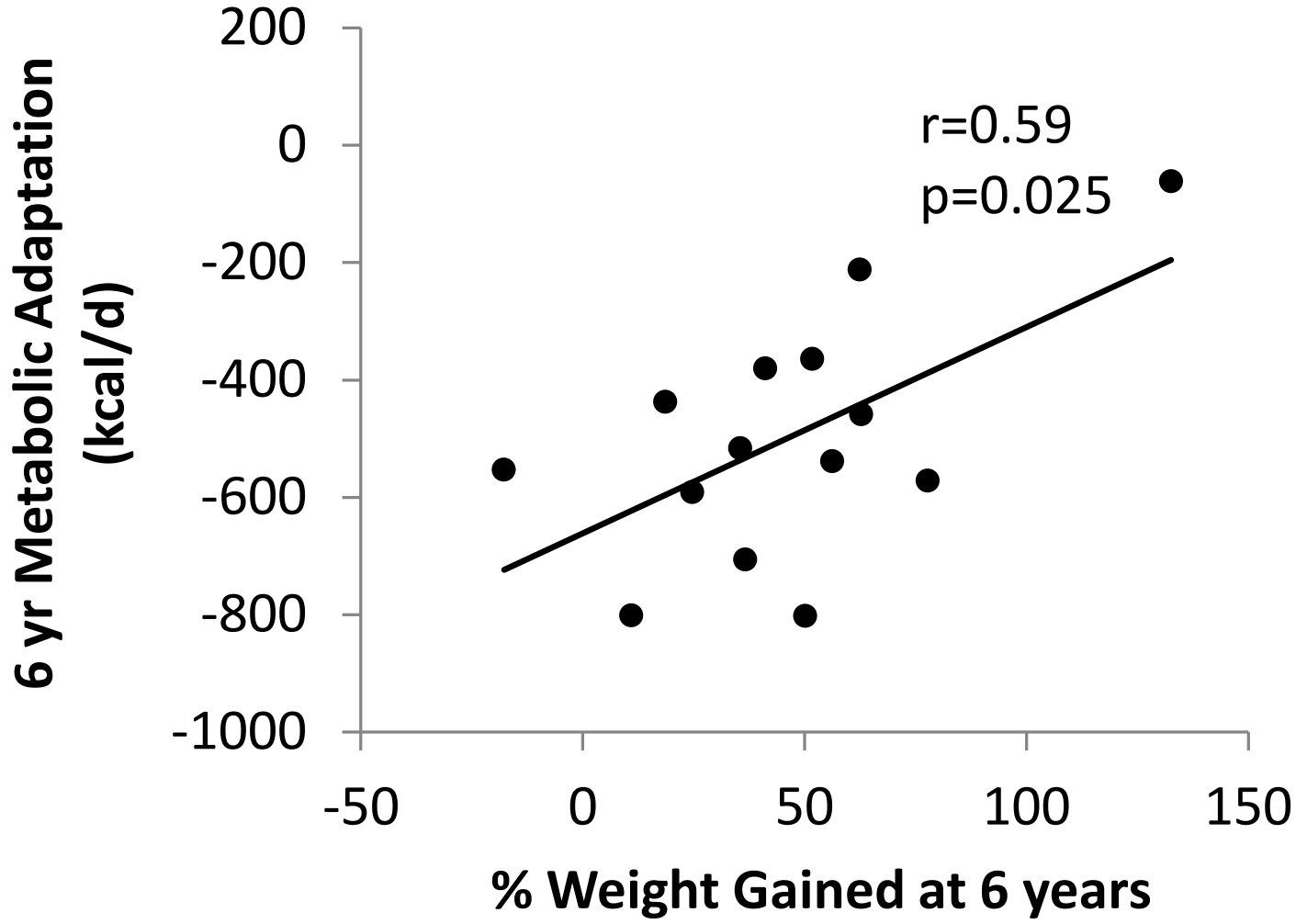
Resting Metabolic Rate Remained Low 6 Years Later



*p <0.05 vs. baseline

E Fothergill et al. *Obesity* 24:1612-1619 (2016)

Less Weight was Regained in those with the *Greatest* Metabolic Adaptation at 6 Years



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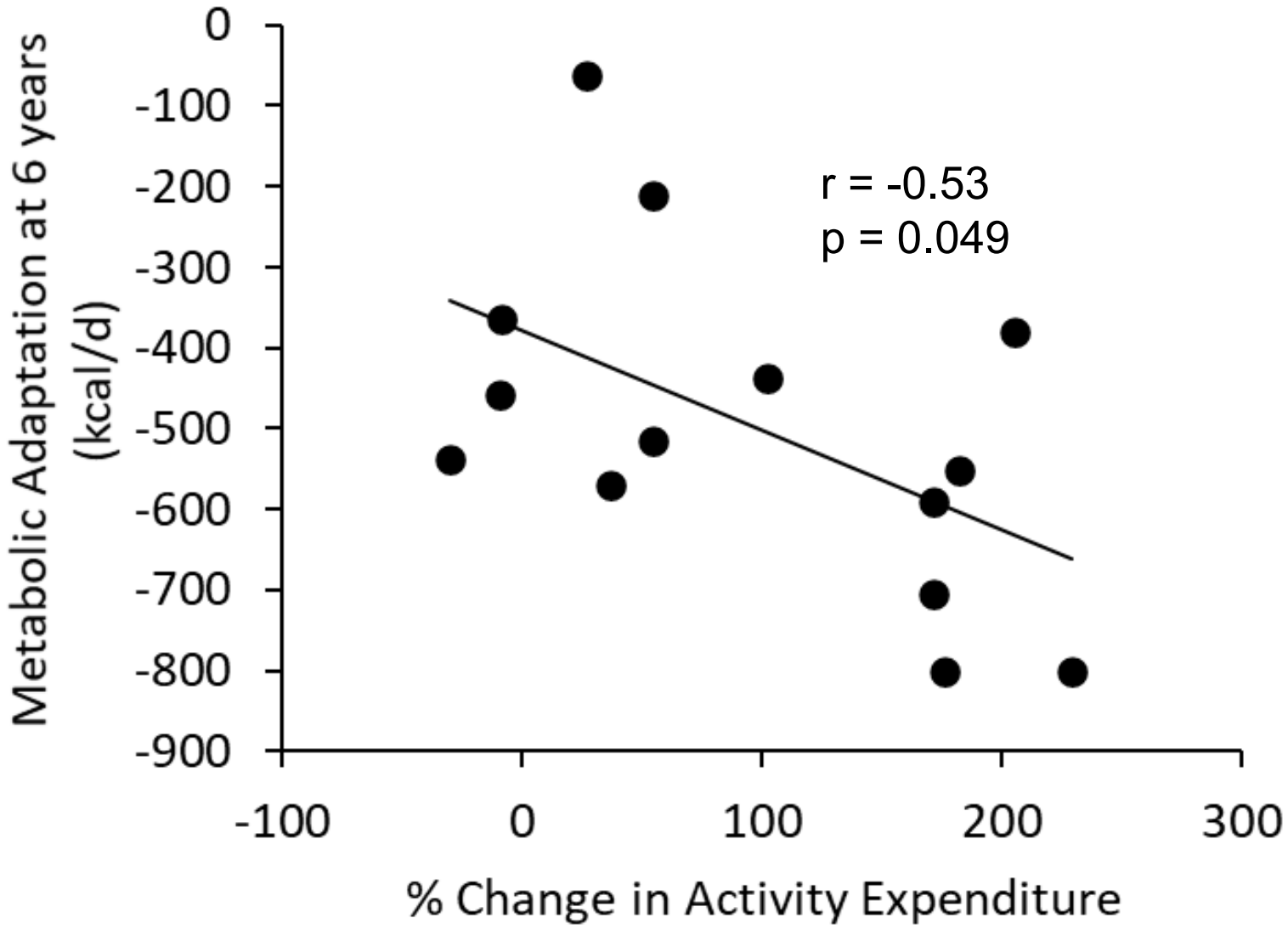
Does Chronic Increased Activity Slow Down Metabolism?



KD Hall. *Obesity* 30(1):11-13 (2022)

Spring Model of Metabolic Adaptation

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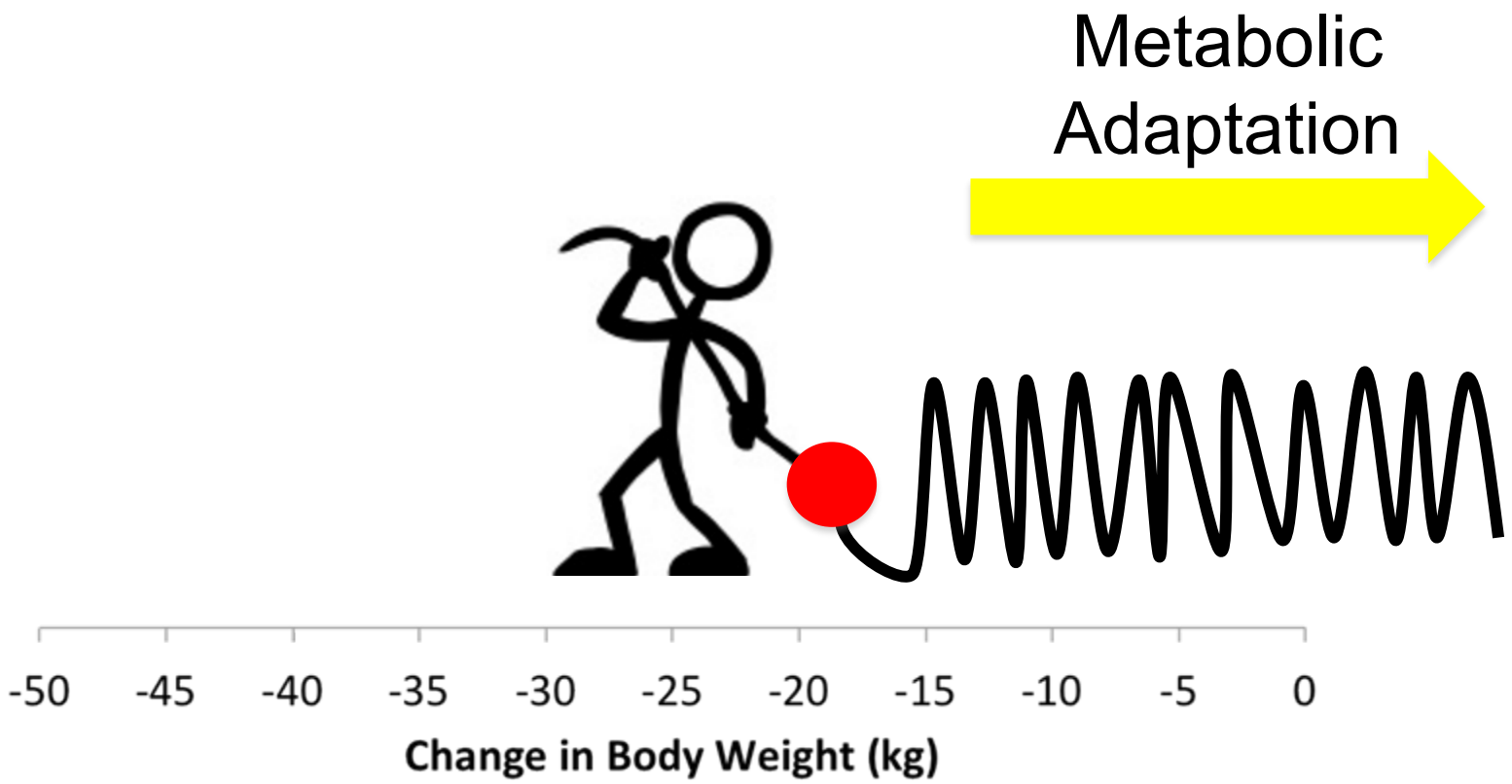
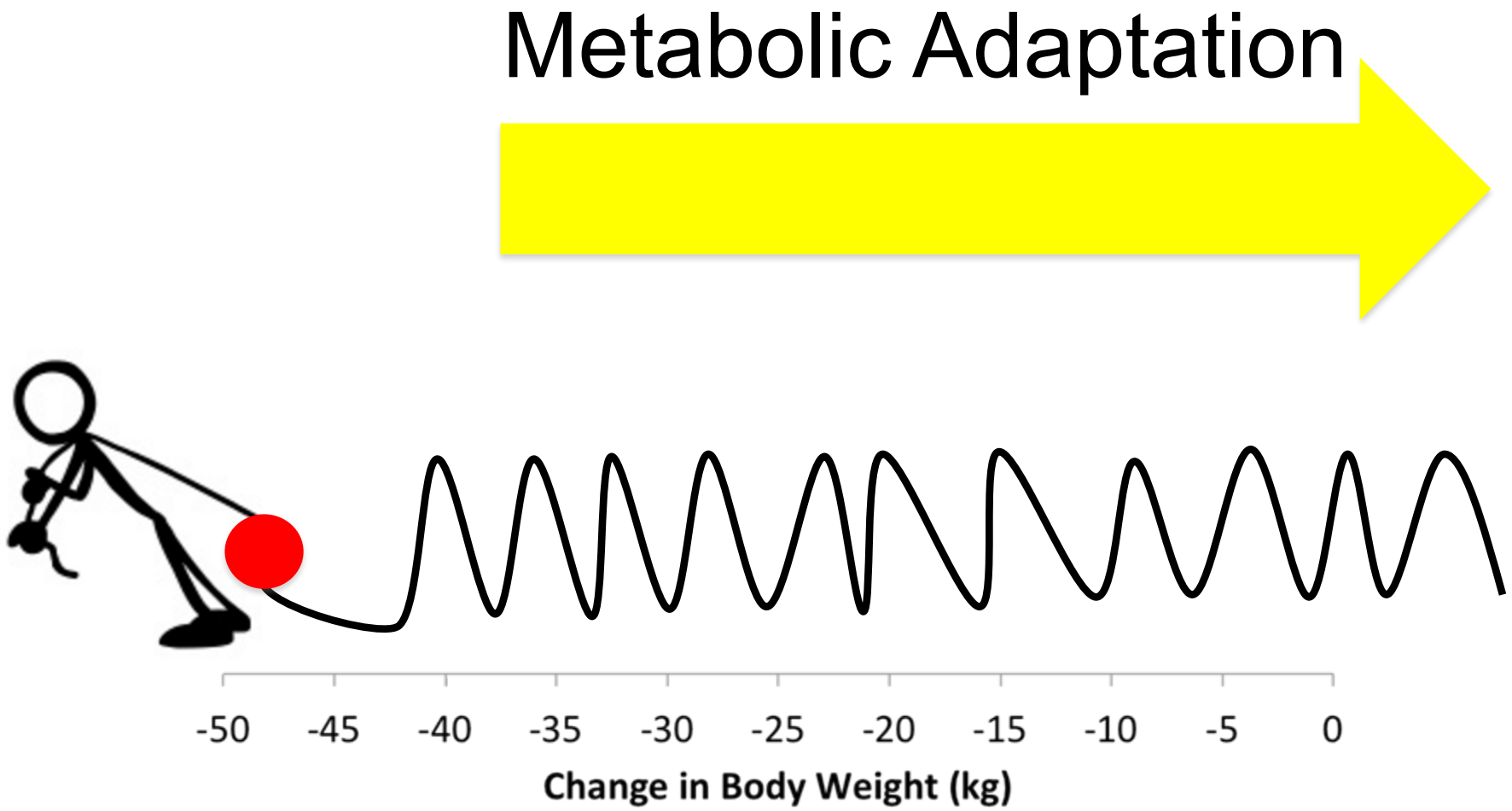
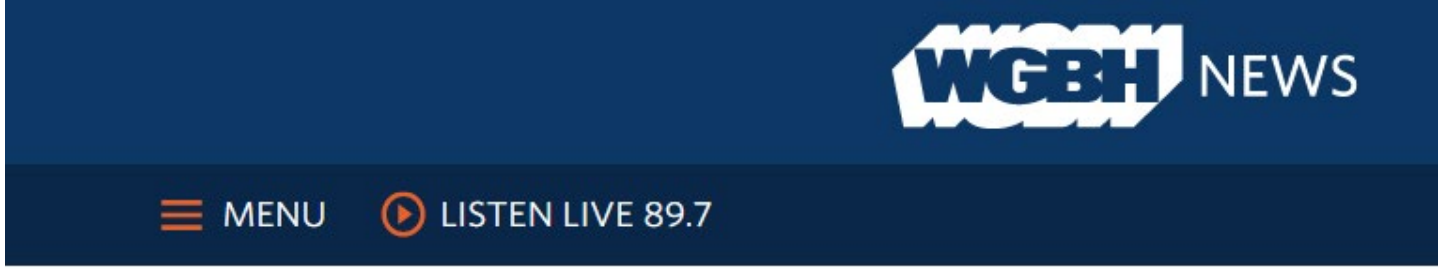


Spring Model of Metabolic Adaptation





“With calorie restriction, sure you lose weight, but then the body fights back with rising hunger and slowing metabolism...

This biological push-back isn’t set in stone…

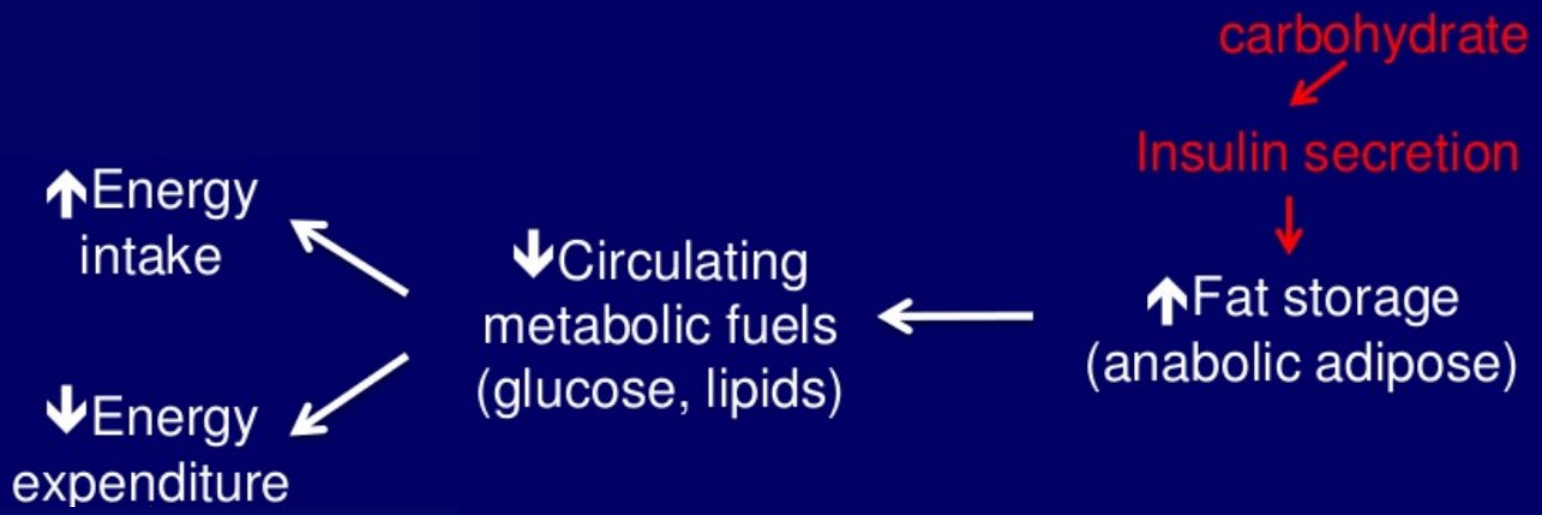
These biological responses that fight against weight loss can be reversed, in potentially as little as one meal in one day.”

Dr. David Ludwig Explains the "Biggest Loser Syndrome"

May 12, 2016

Carbohydrate-Insulin Model of Obesity

Excessive anabolic drive in adipose tissue



"a high-carbohydrate diet … produces postprandial hyperinsulinemia, promotes deposition of calories in fat cells instead of oxidation in lean tissues, and thereby predisposes to weight gain through increased hunger, slowing metabolic rate, or both."

DS Ludwig & CB Ebbeling *JAMA Intern Med* 178:1098-1103 (2018).

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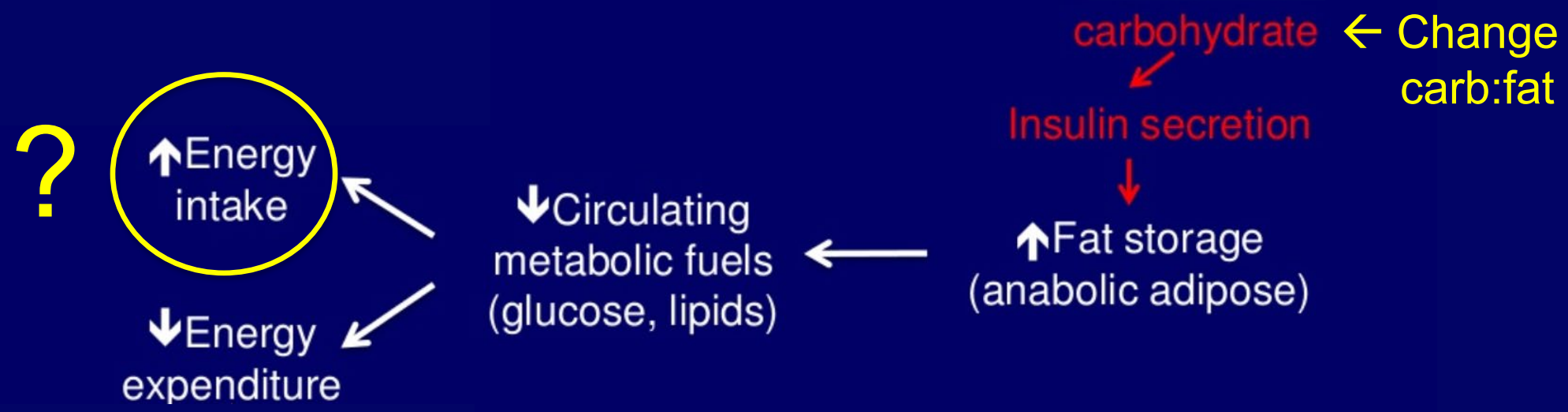

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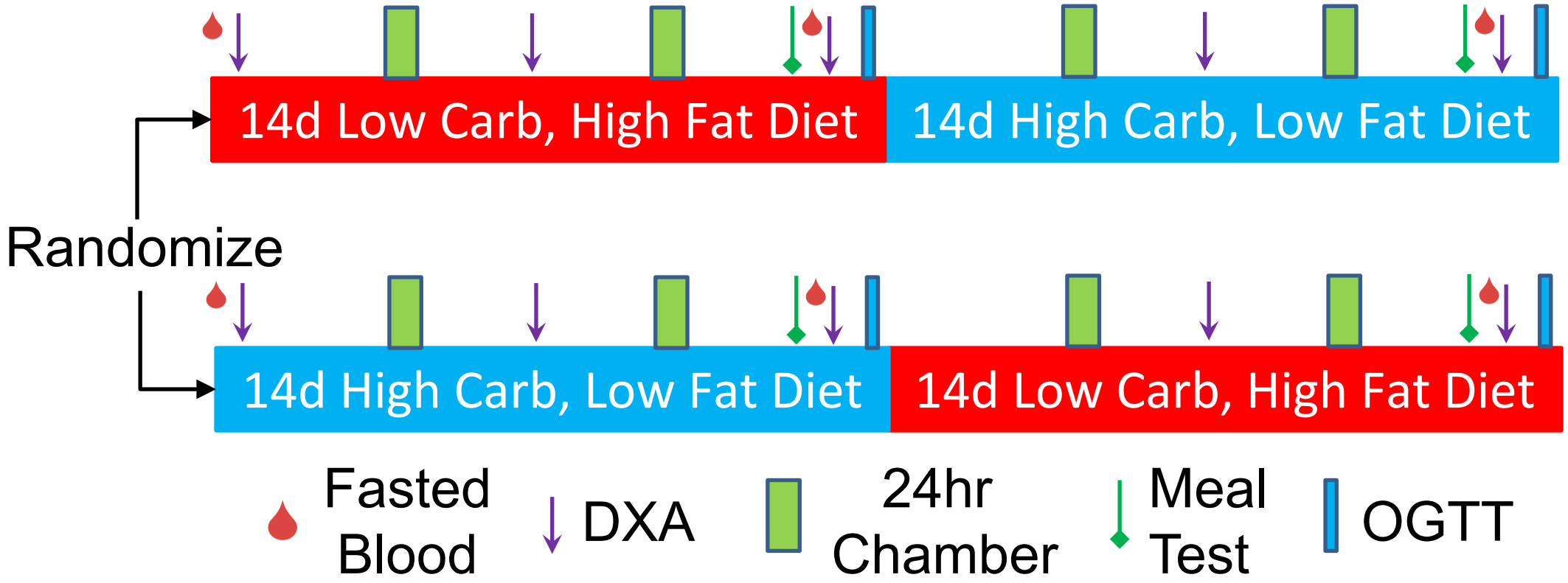
Does Diet Composition Affect Ad Libitum Energy Intake?

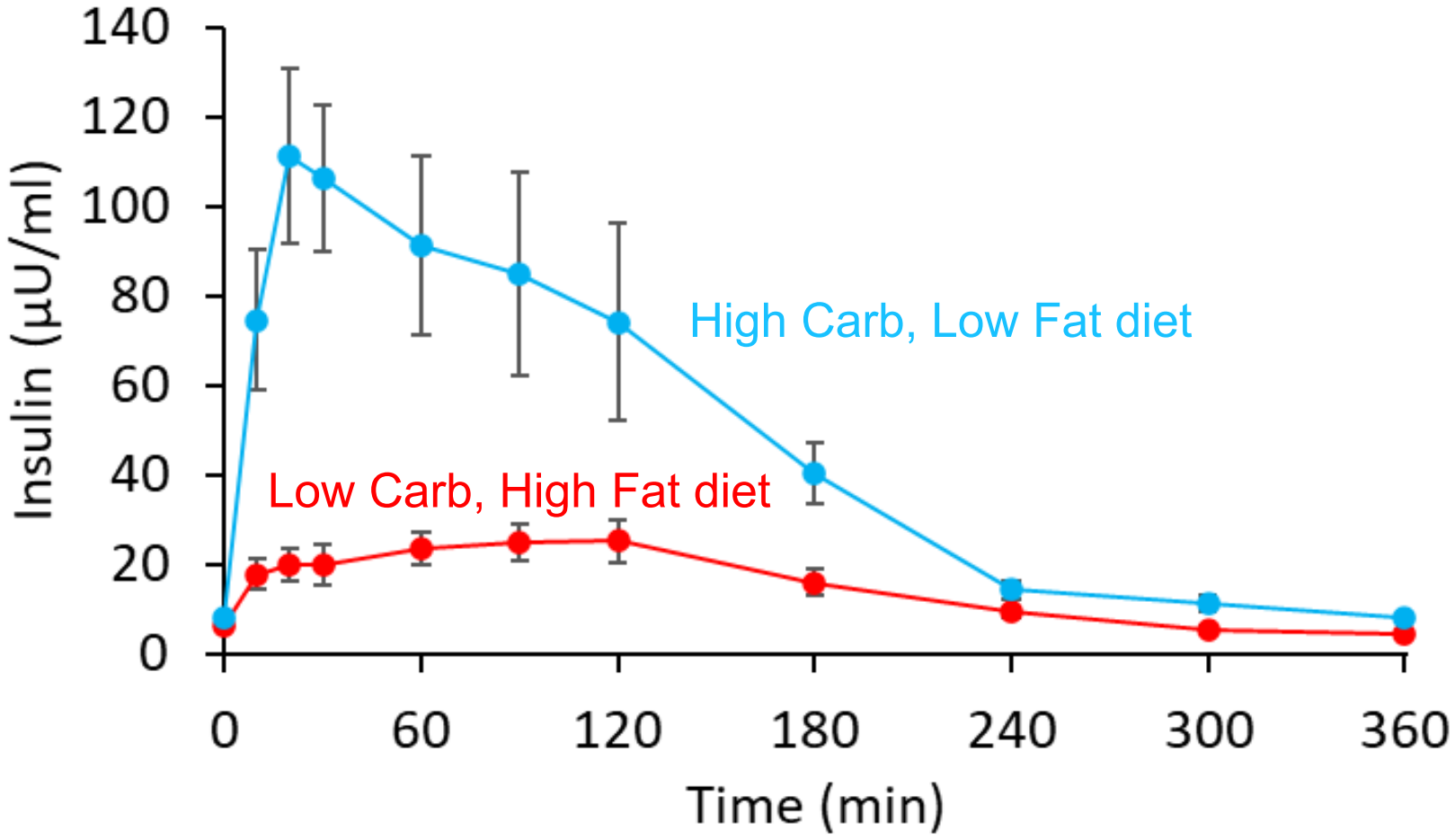


KD Hall et al. *Nature Medicine* 2021 https://doi.org/10.1038/s41591-020-01209-1

High Carb, Low Fat Meals
(75% Carb, 10% Fat, 15% Protein)

Low Carb, High Fat Meals
(10% Carb, 75% Fat, 15% Protein)

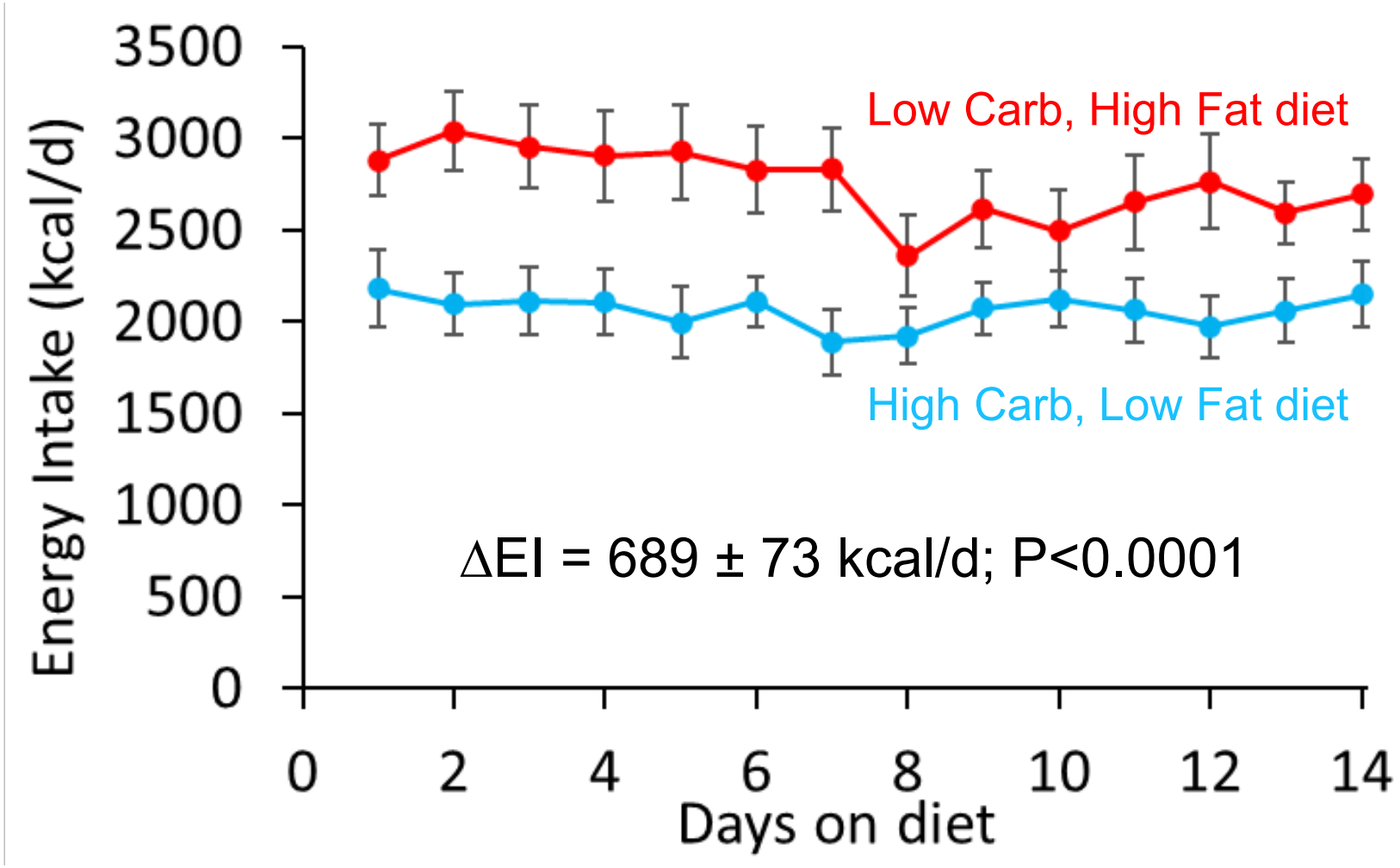
Large Diet Differences in Postprandial Insulin



Mean ± SE

KD Hall et al. *Nature Medicine* 2021 https://doi.org/10.1038/s41591-020-01209-1

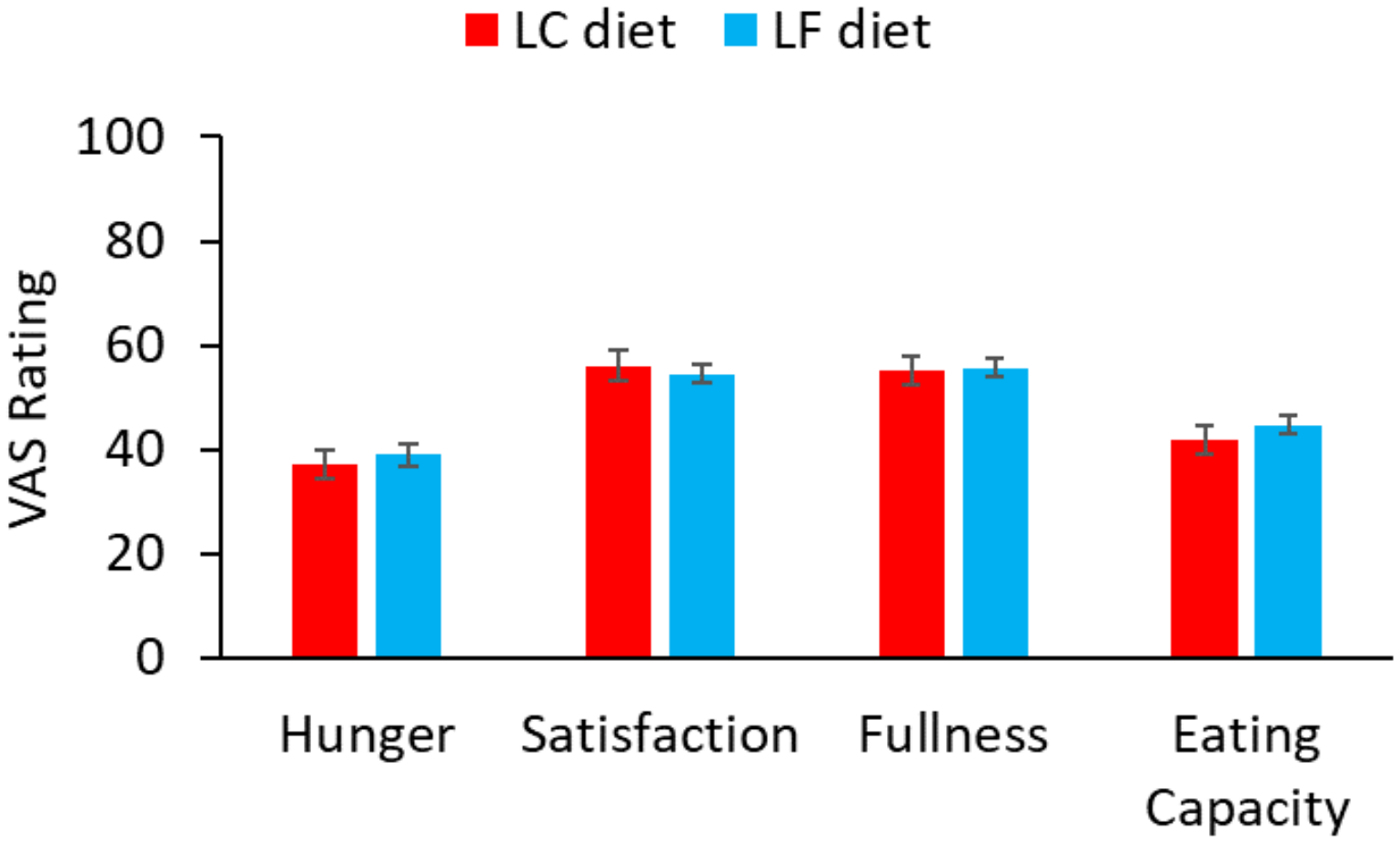
Less Energy Intake on the High Carb, Low Fat Diet



Mean ± SE

KD Hall et al. *Nature Medicine* 2021 https://doi.org/10.1038/s41591-020-01209-1

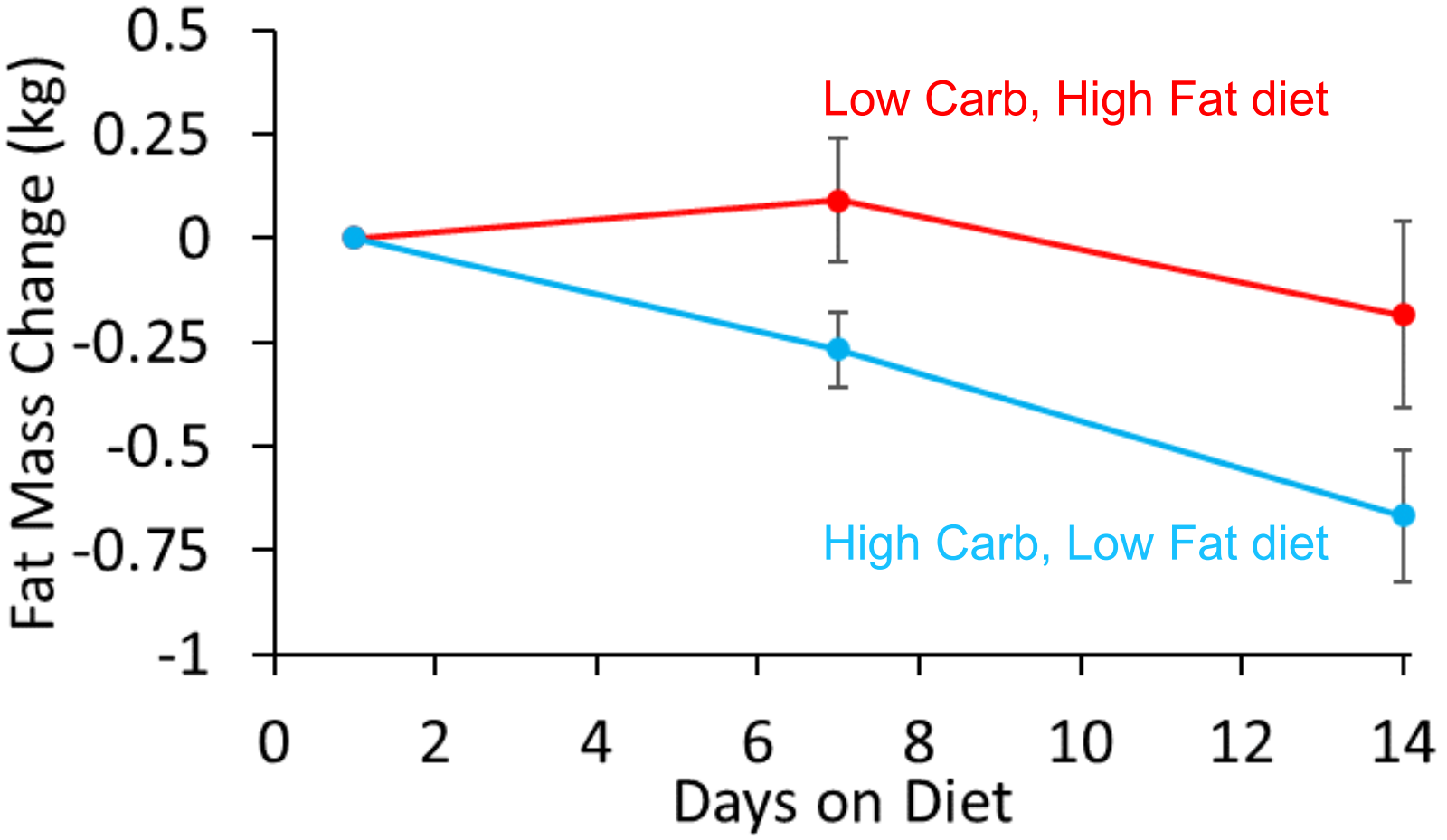
No Differences in Self-Reported Appetite Measures



Mean ± SE

KD Hall et al. *Nature Medicine* 2021 https://doi.org/10.1038/s41591-020-01209-1

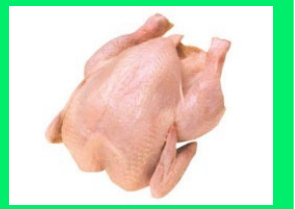
More Body Fat Loss on the High Carb, Low Fat Diet



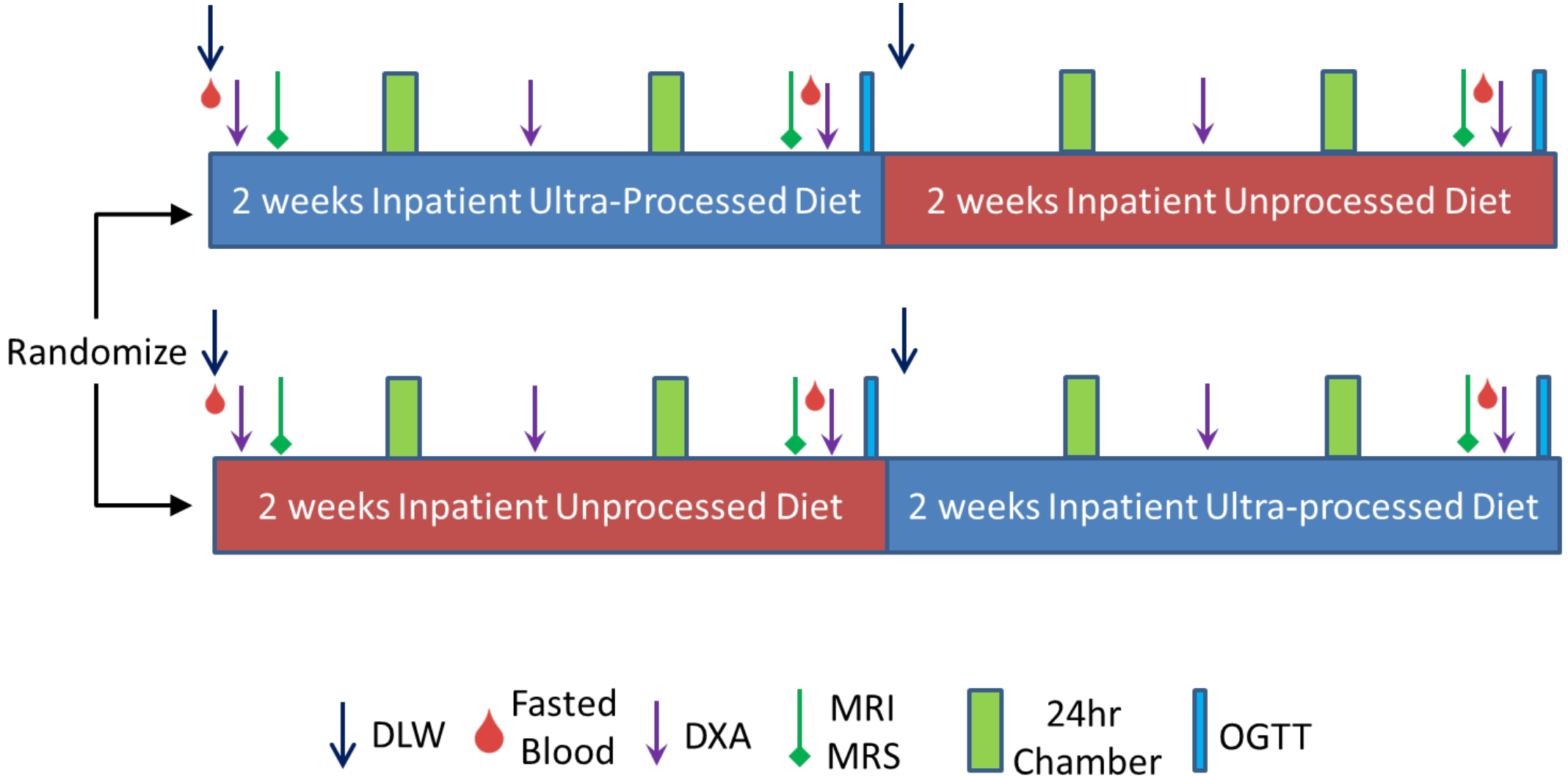
Mean ± SE

KD Hall et al. *Nature Medicine* 2021 https://doi.org/10.1038/s41591-020-01209-1

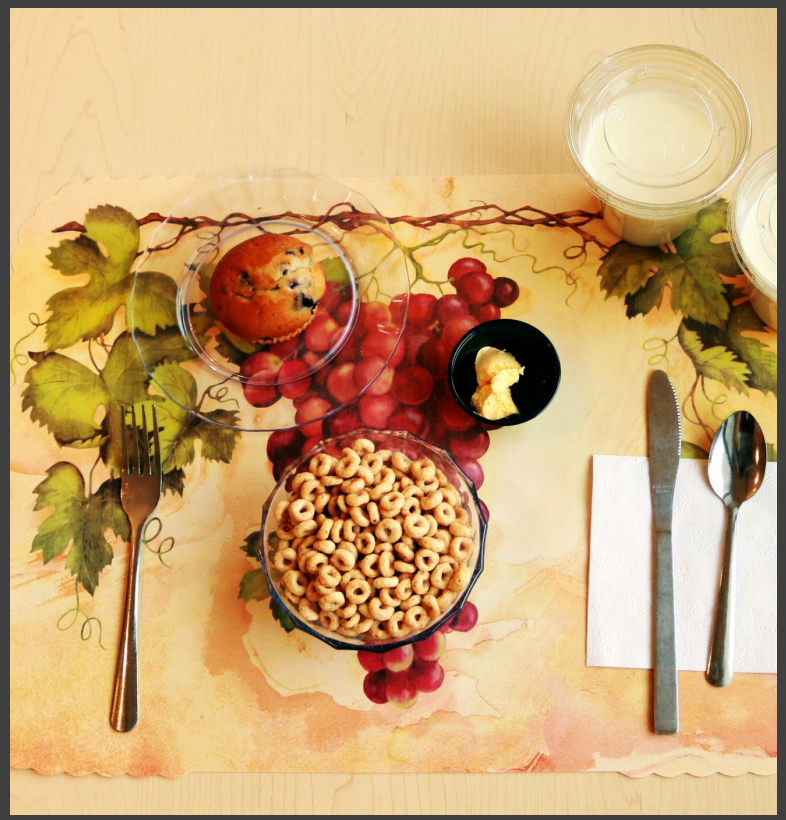

BURRITOS
PIZZA
TABATCHNICK
Vegetable Soup
Split Pea Soup
Potato Soup
Golden
Potato Pancakes
Potato Blintzes
Broccoli Soufflé
Sticks
Eggplant Cutlets
Zucchini Soufflé
ENCHILADA
INDIAN
LEAN POCKETS
HOT POCKETS
PIZZA

NOVA groups	Examples
1) Unprocessed or minimally processed foods Edible parts of plants and animals after separation from nature or preserved by minimal processes (no substances added)	   
2) Processed culinary ingredients Substances extracted from foods or nature and used to prepare, cook and season Group 1 foods	   
3) Processed foods Group 1 foods modified with the addition of Group 2 ingredients aiming food preservation and/or enhancement of its sensory qualities	   
4) Ultra-processed foods Formulations of several ingredients that include original or chemically modified food substances obtained with the fractioning of whole foods and additives used to make the final product palatable or hyper-palatable. The aim is to make convenient, tasteful and low-cost products liable to replace all other NOVA food groups	        

Ultra-processed vs Unprocessed Ad Libitum Diet Study

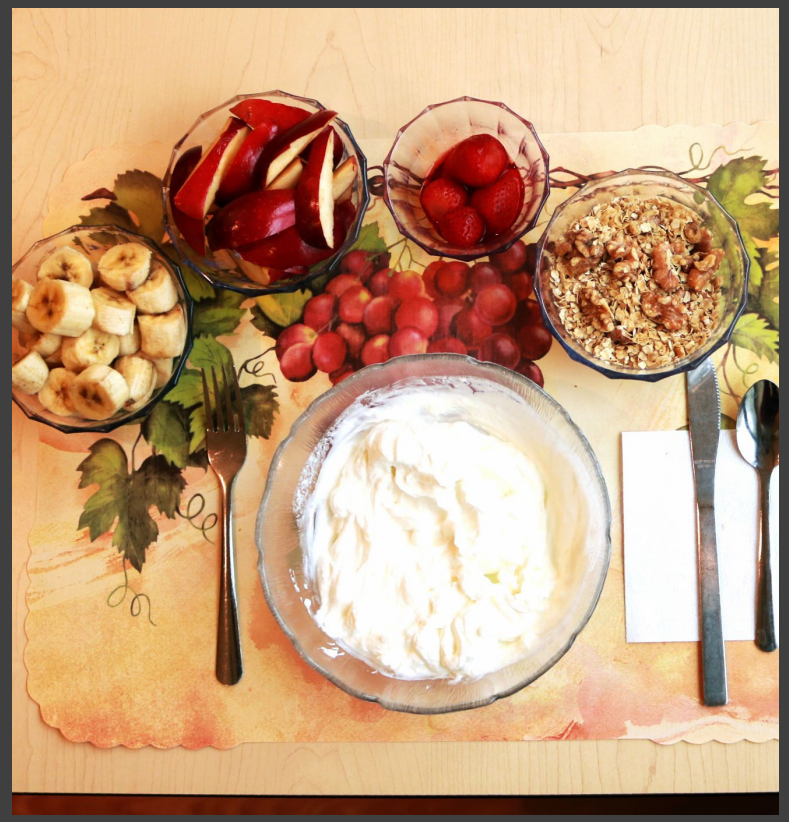


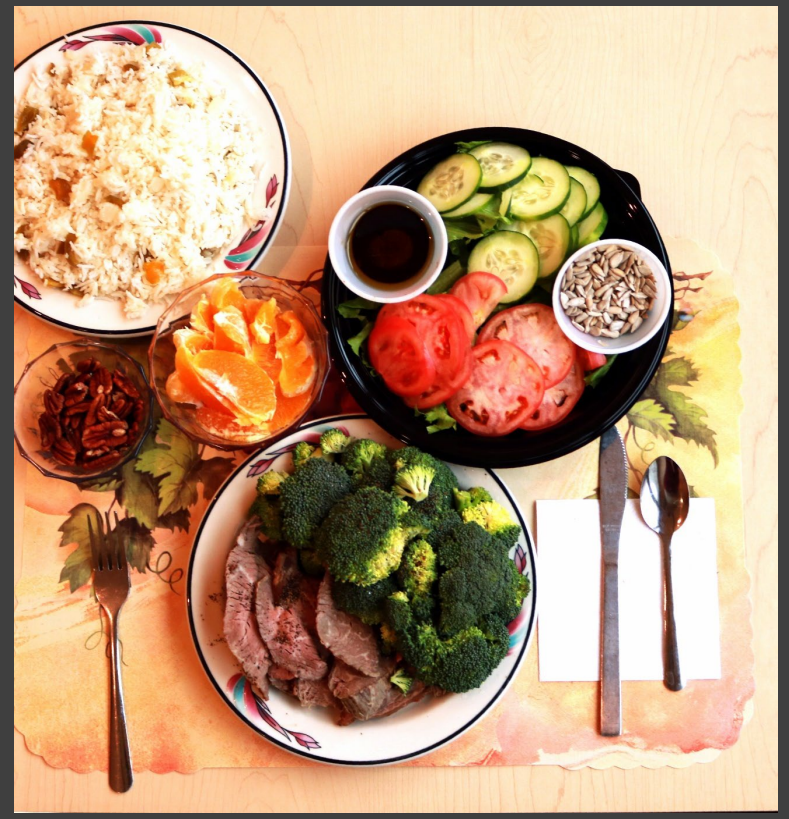
KD Hall et al. *Cell Metabolism* 30:1-11 (2019).



Ultra-processed Meals

Matched for Presented Calories, Fat, Carbs, Sugar, Sodium, Fiber, & Glycemic Load

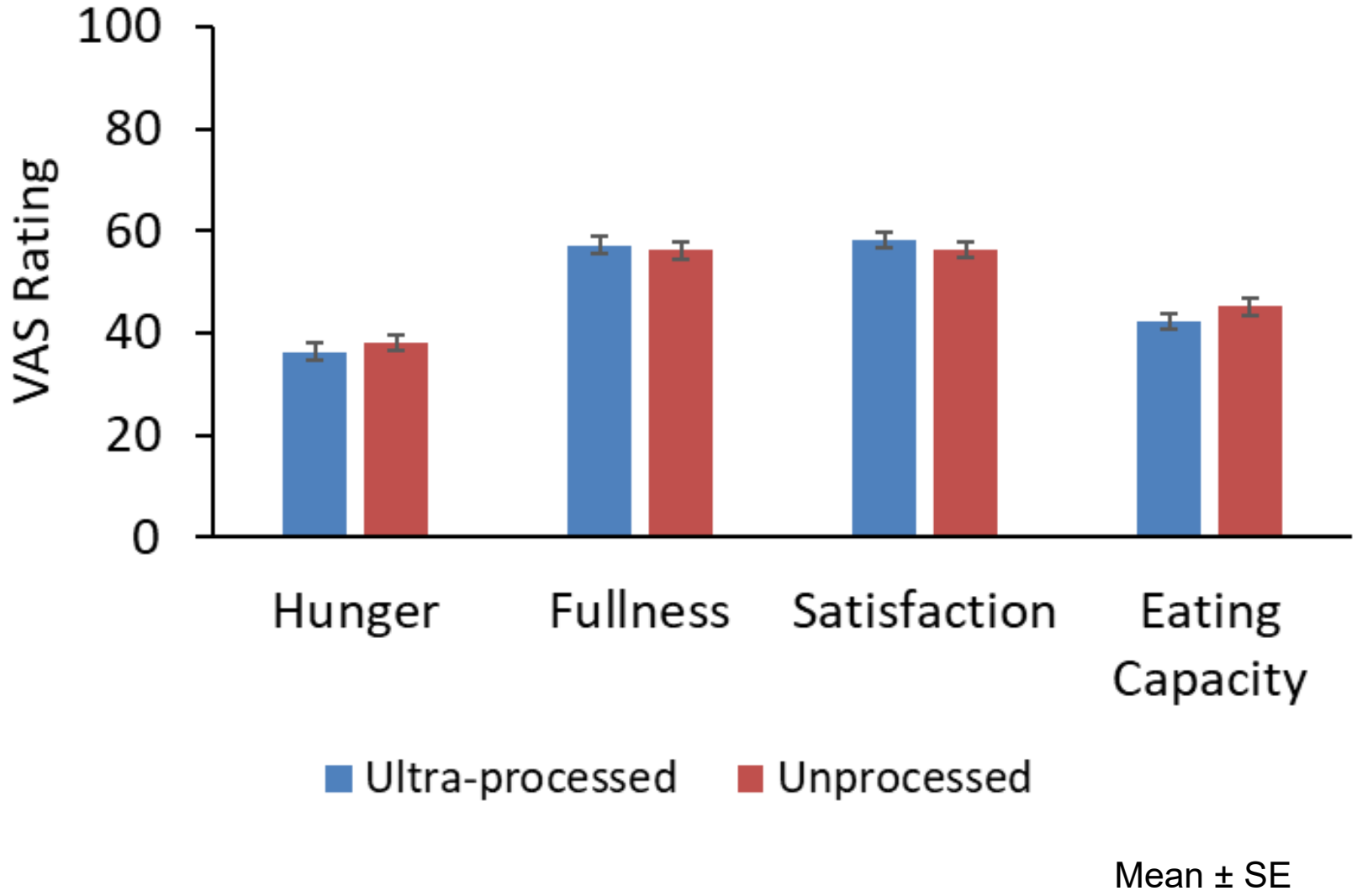




Unprocessed Meals

Matched for Presented Calories, Fat, Carbs, Sugar, Sodium, Fiber, & Glycemic Load

No Differences in Self-Reported Appetite Measures

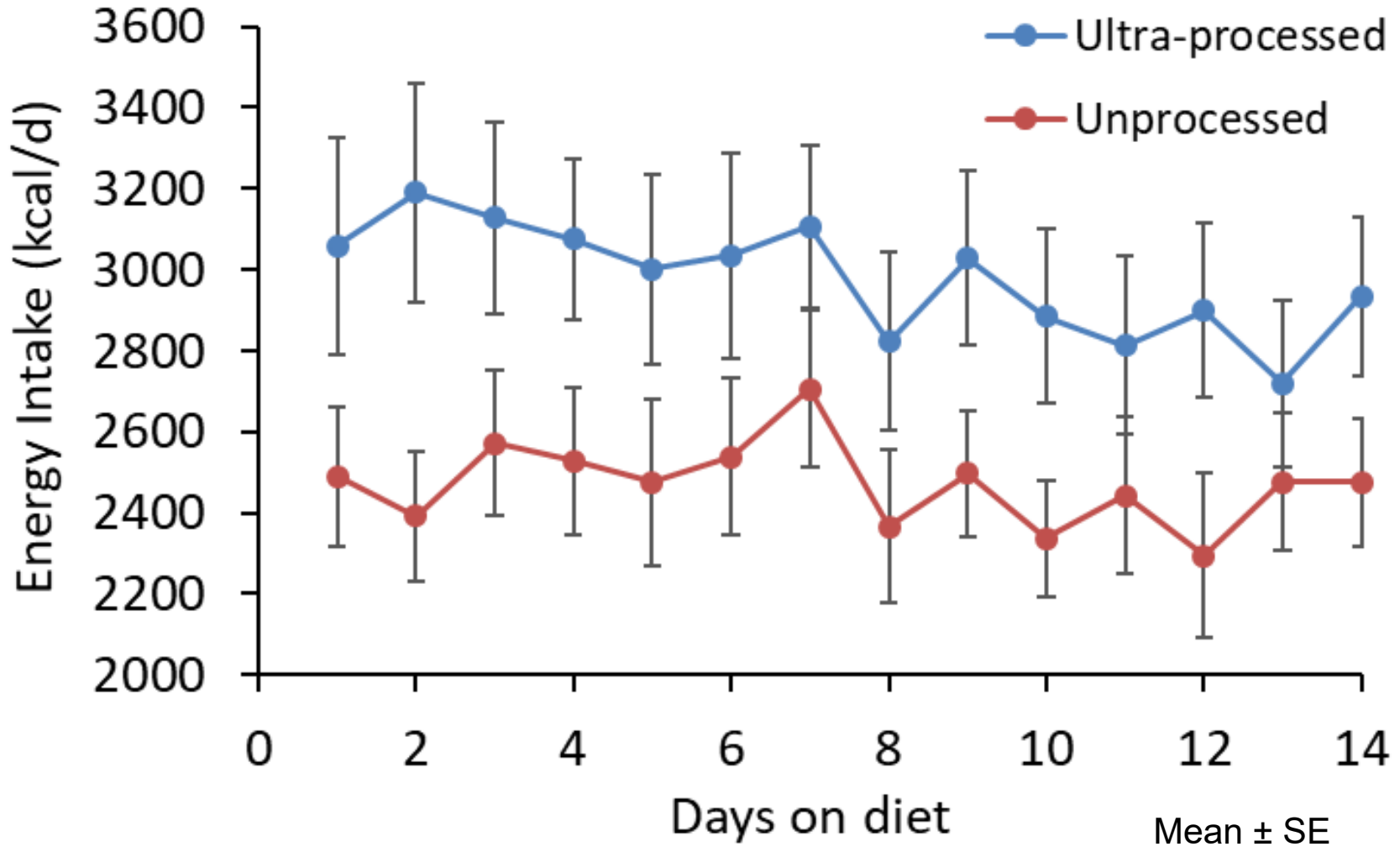


Mean ± SE

KD Hall et al. *Cell Metabolism* 30:1-11 (2019).

Ultra-processed Diets Cause Increased Intake

$\Delta EI = 508 \pm 106$ kcal/d; P=0.0001



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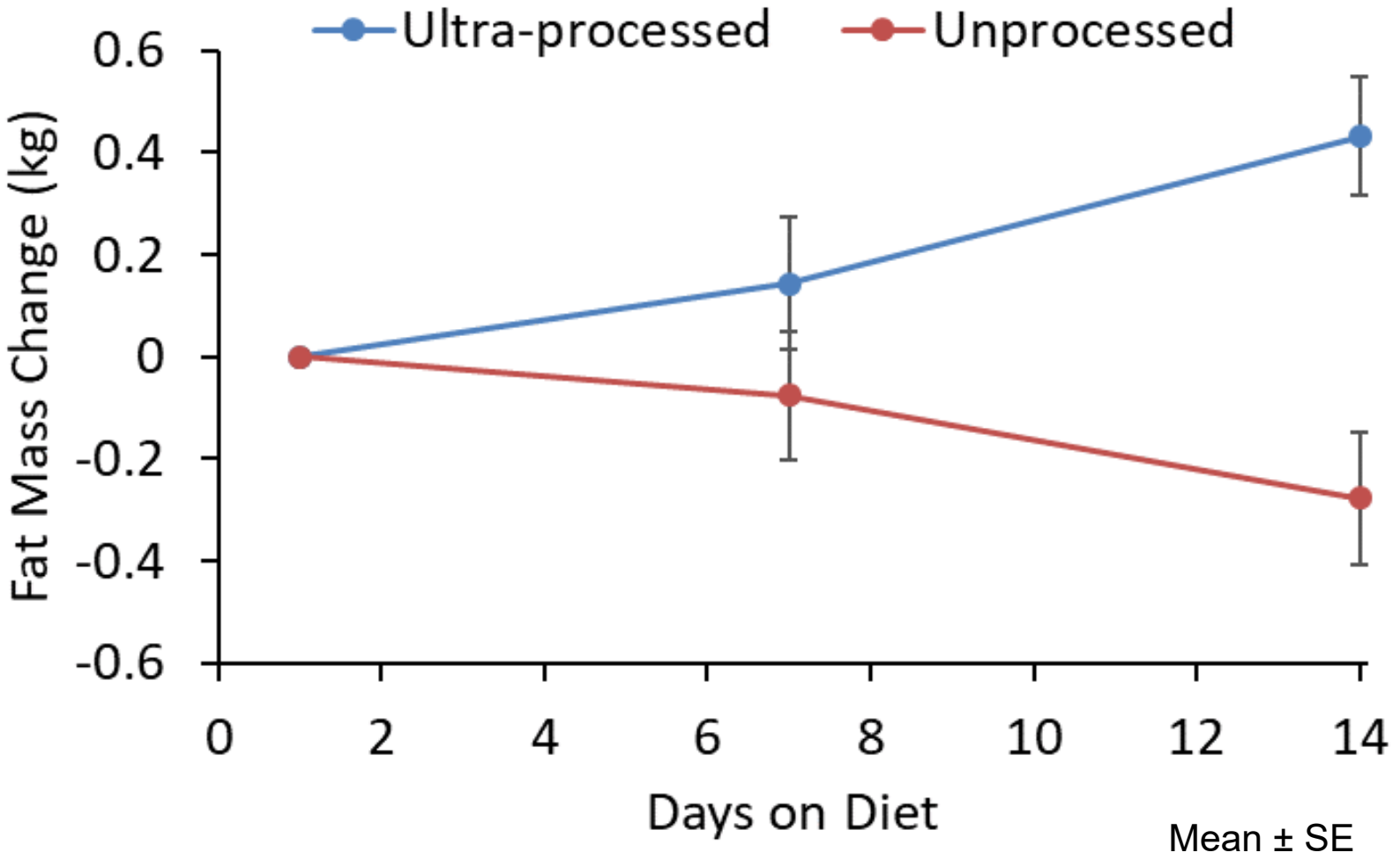
Ultra-processed Diets Cause Body Fat Gain



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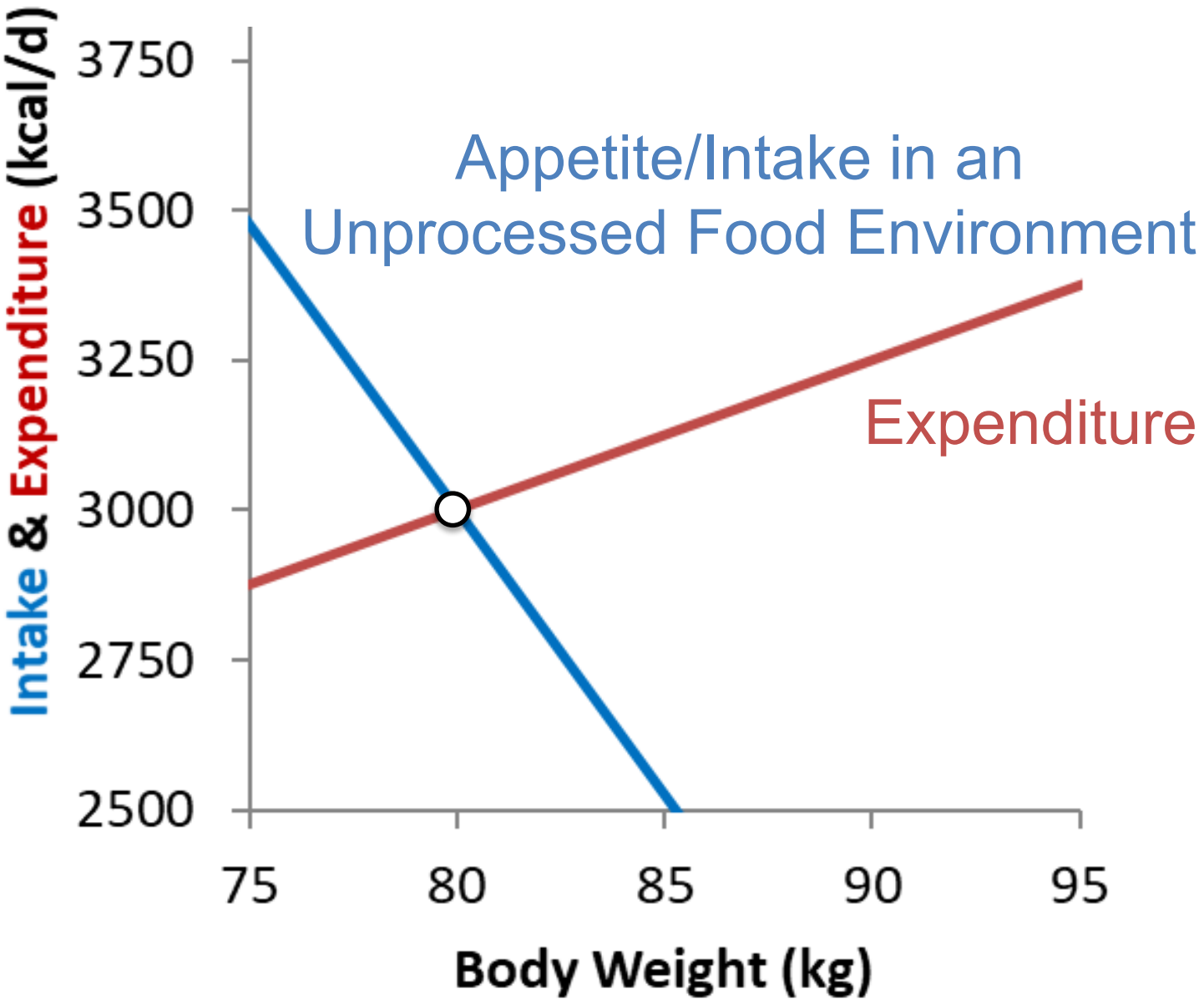
The Food Environment Affects Appetite & Energy Intake



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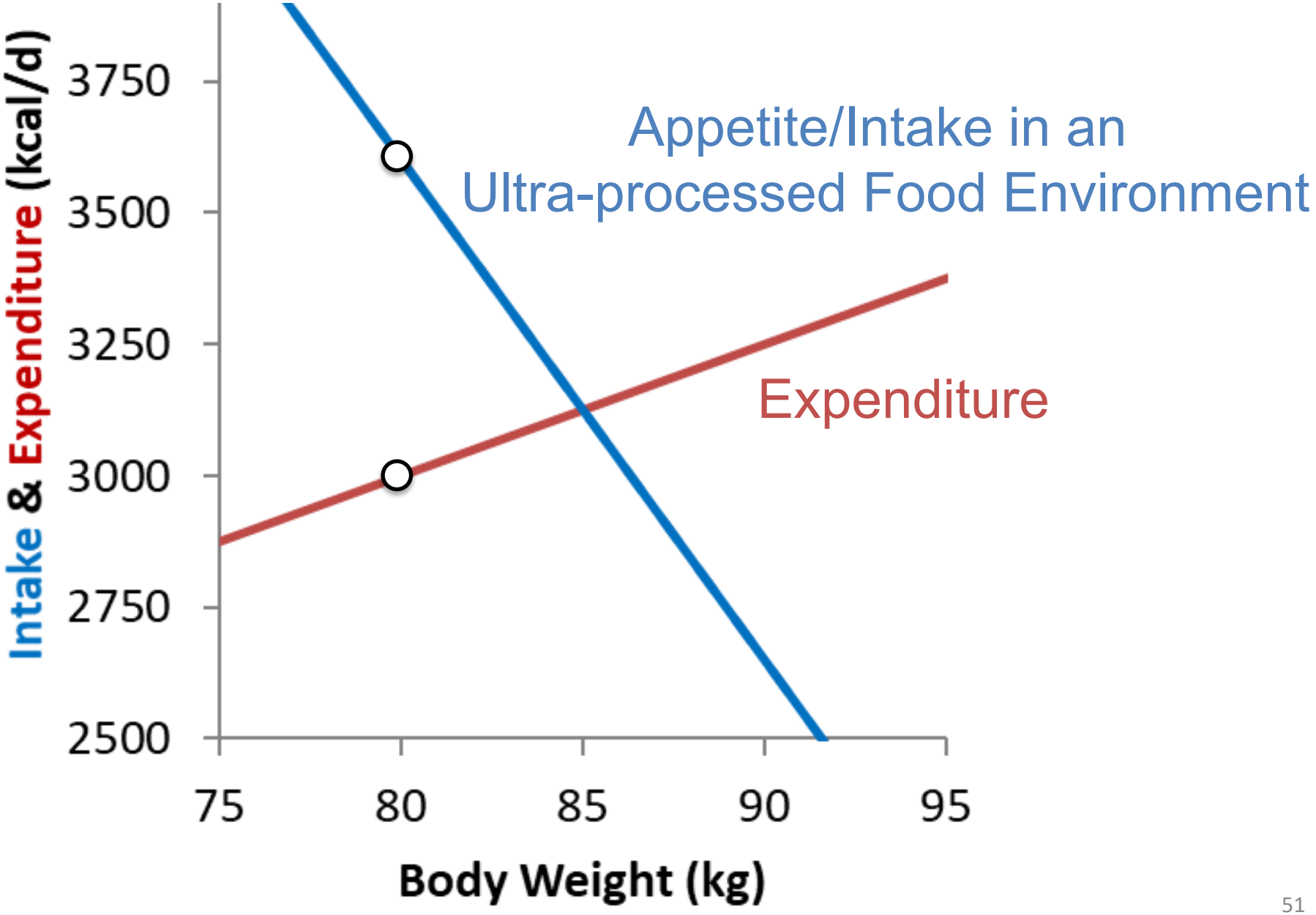
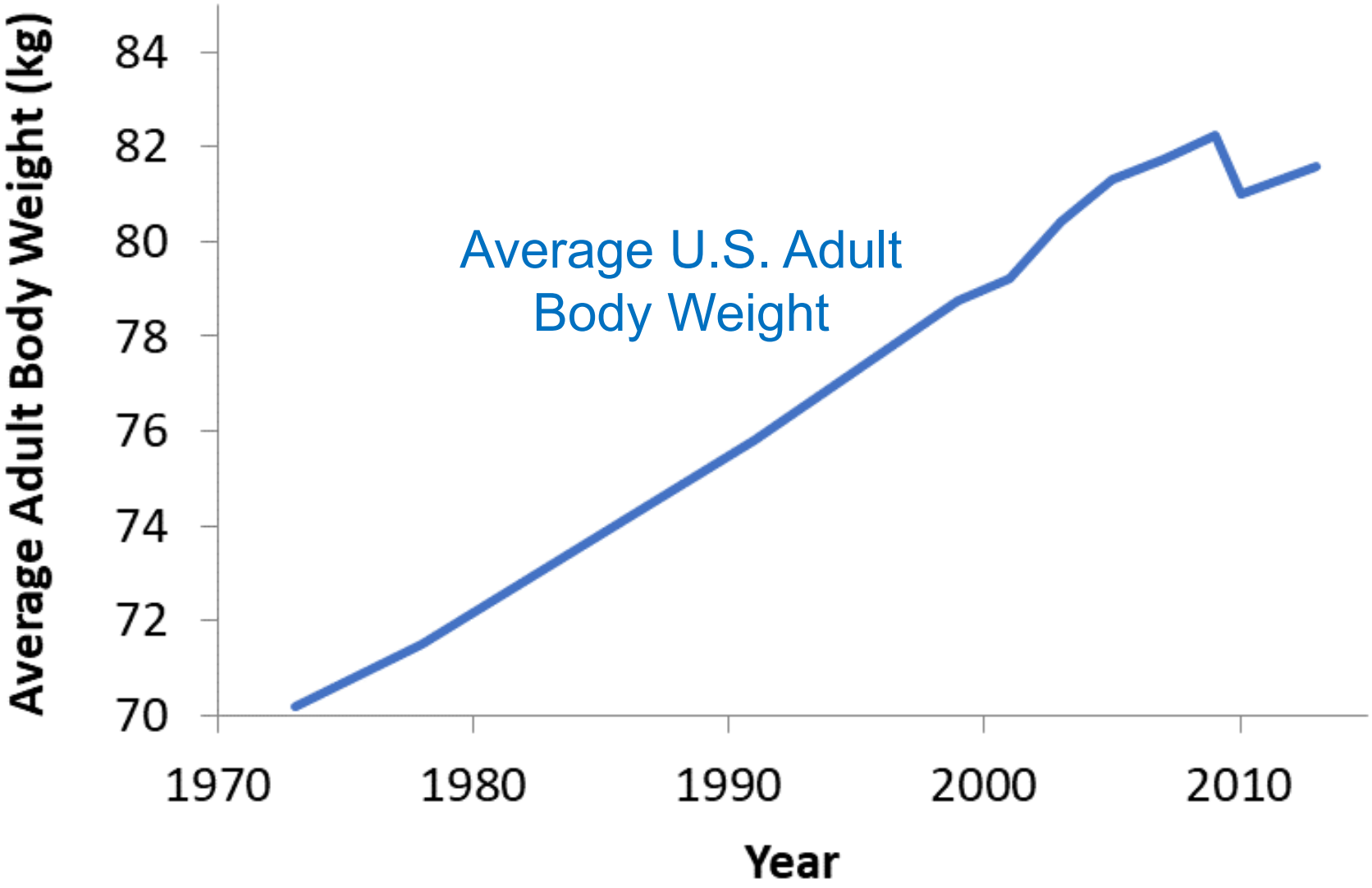
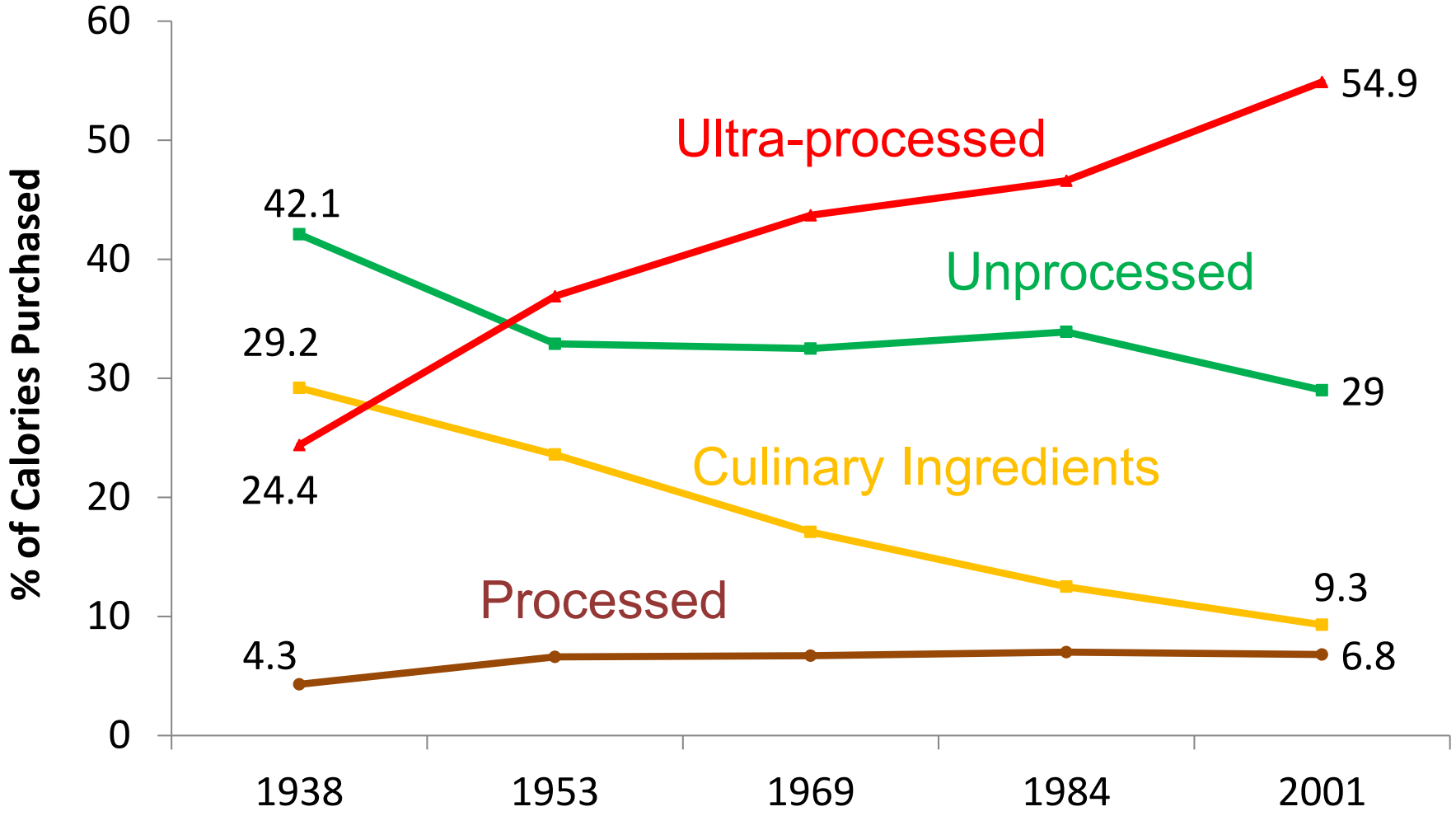


Explaining the Obesity Epidemic in the USA?

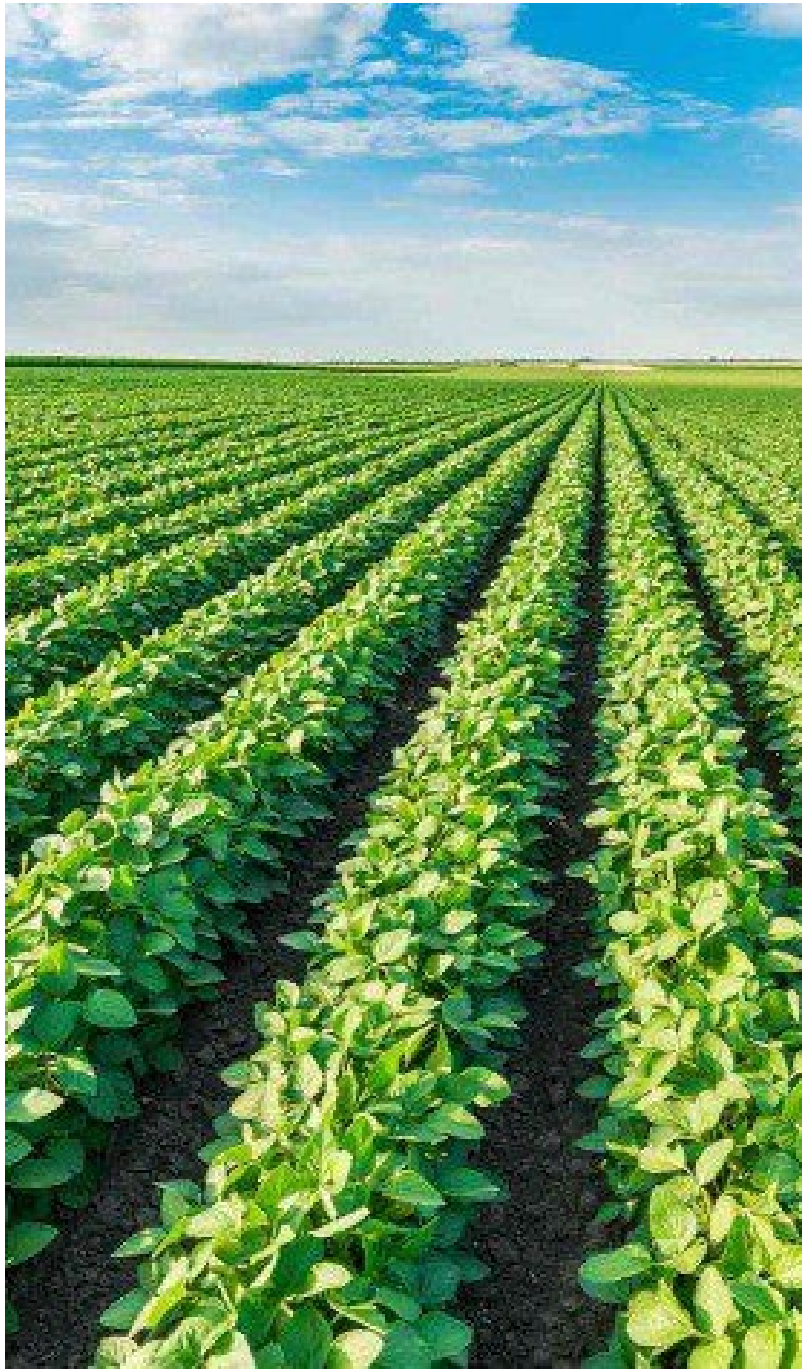
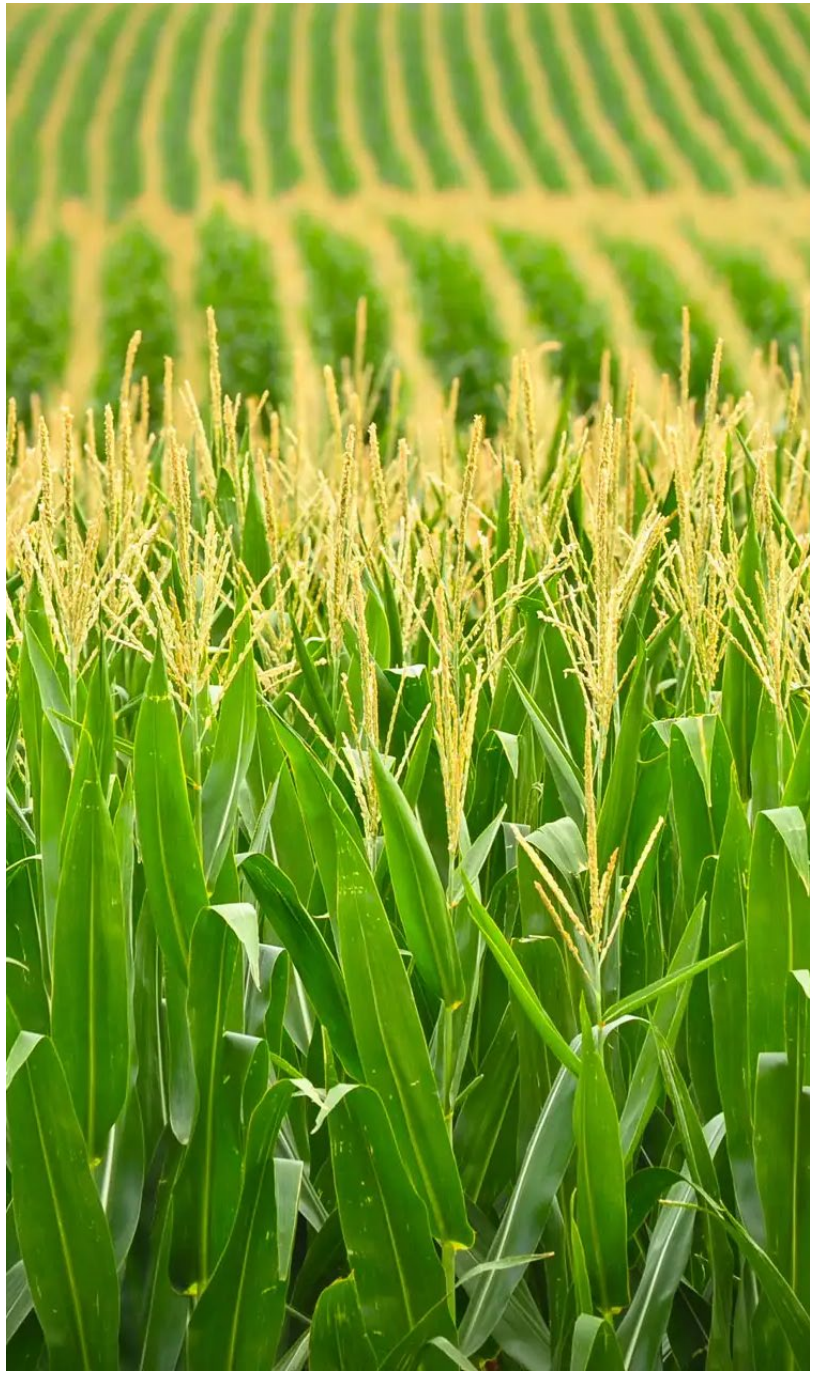


Data from National Health and Nutrition Examination Survey (NHANES)

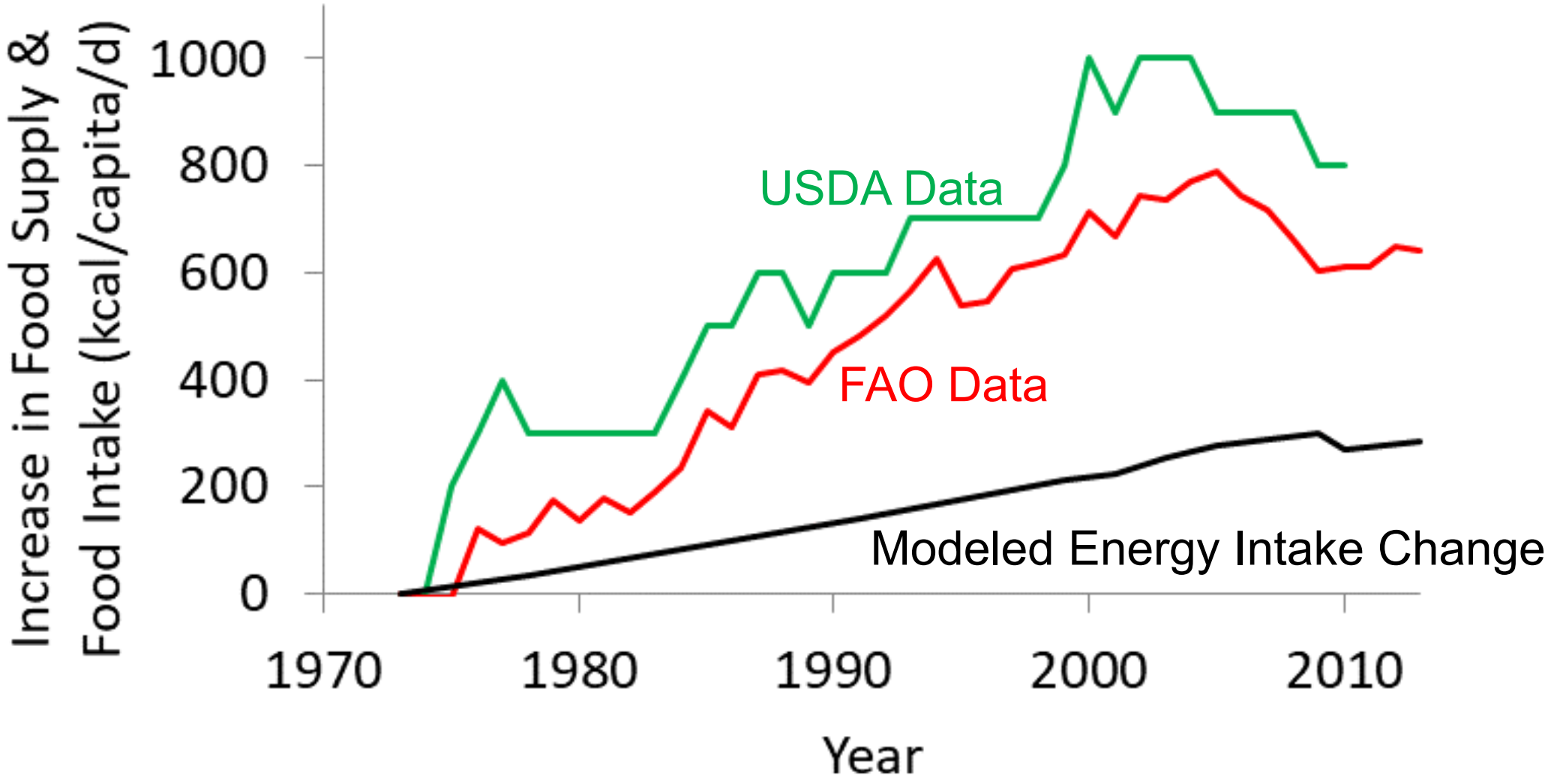
Increasingly Ultra-processed Food Supply



Moubarac et al. *Can J Diet Pract Res*. 75:15-21 (2014)

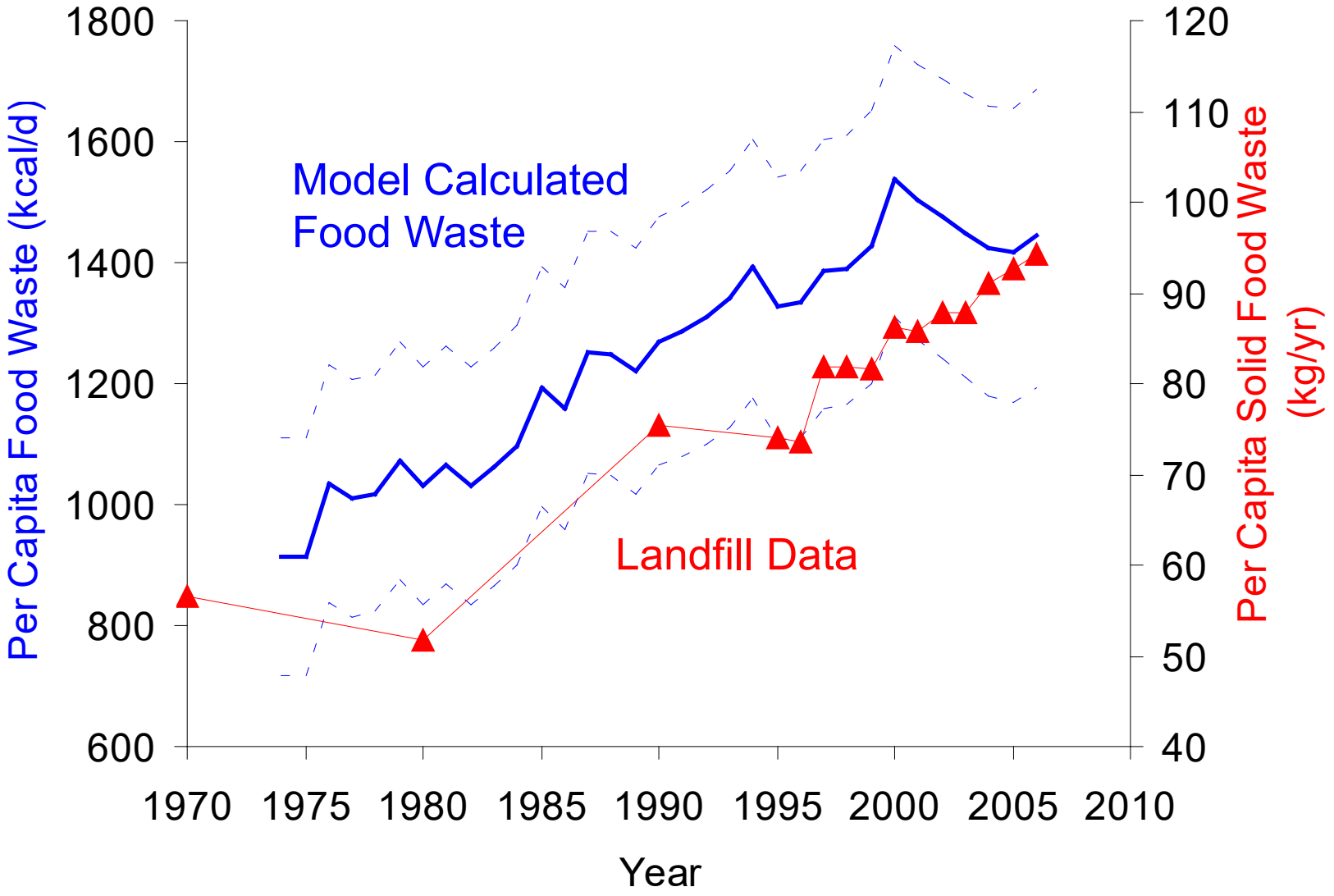




The Increase in US Food Supply Exceeded Energy Intake



KD Hall. *Obesity* 27:1222-1224 (2019)

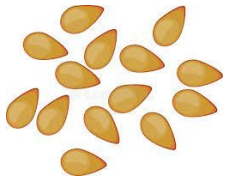
Progressive ~50% Increase in US Food Waste

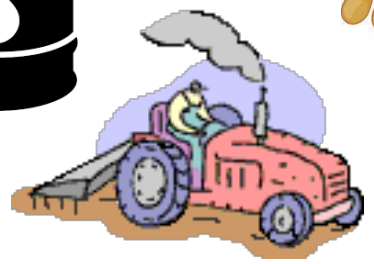


KD Hall, J Guo, M Dore, CC Chow. *PLoS ONE* (2009)

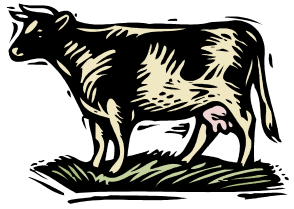
Ultra-processed Food Supply May Have Increased Obesity

Agriculture
Research,
Technology
& Policy

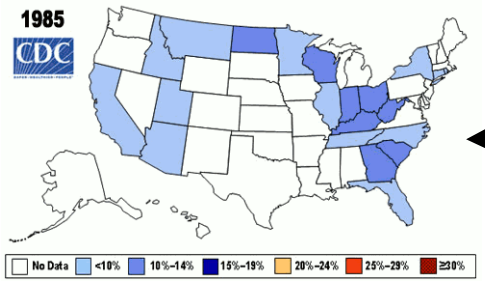




Increased
Production



More,
Convenient,
Inexpensive,
Ultra-processed Food



Increased Obesity

Increased
Food Waste