Calories, Carbs, or Quality?
What Matters Most for Body Weight

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National Institutes of Health

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VIEWPOINT

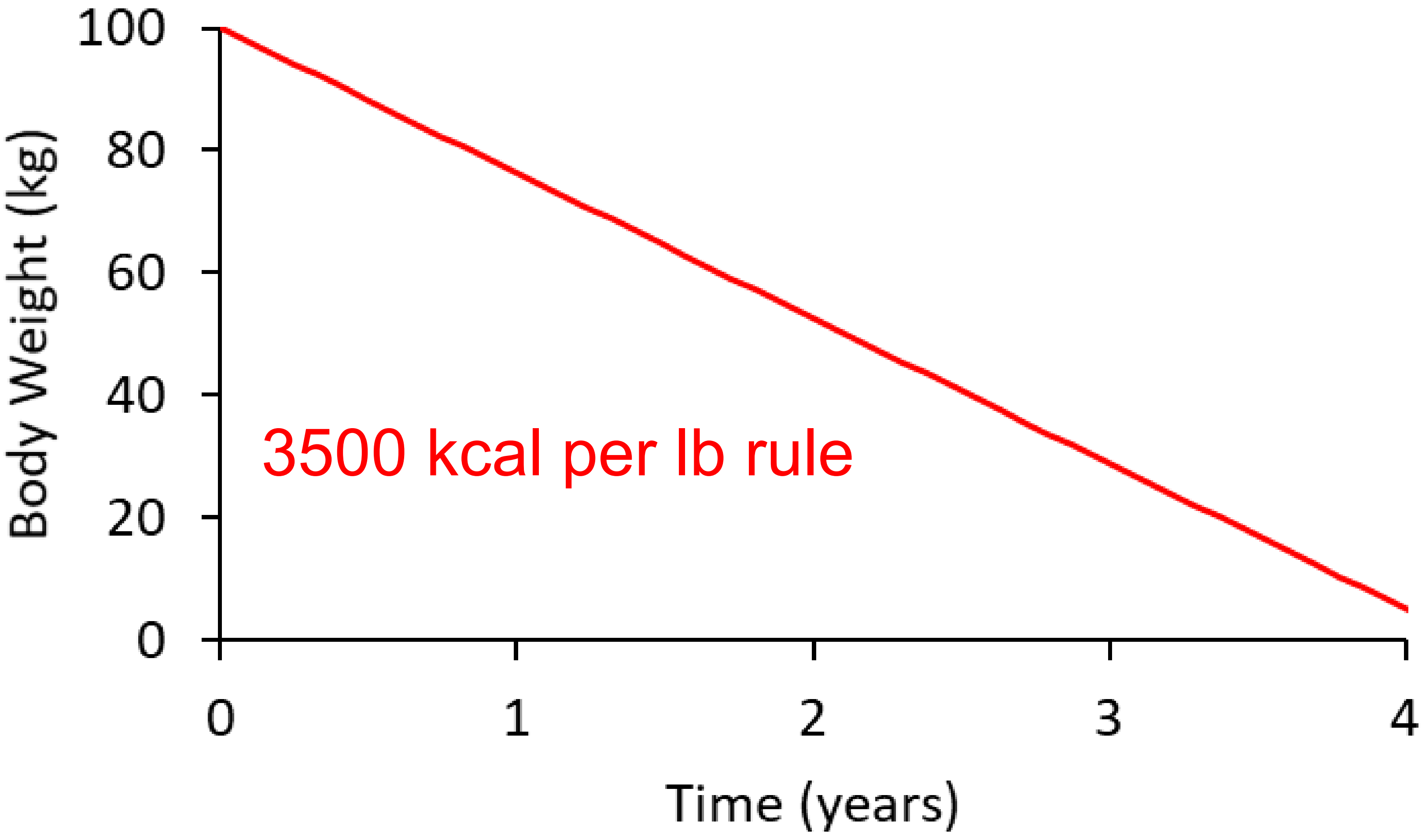
Counting Calo… Approach to Achieve W… Control

JAMA January 16, 2018 Volume 31… 225

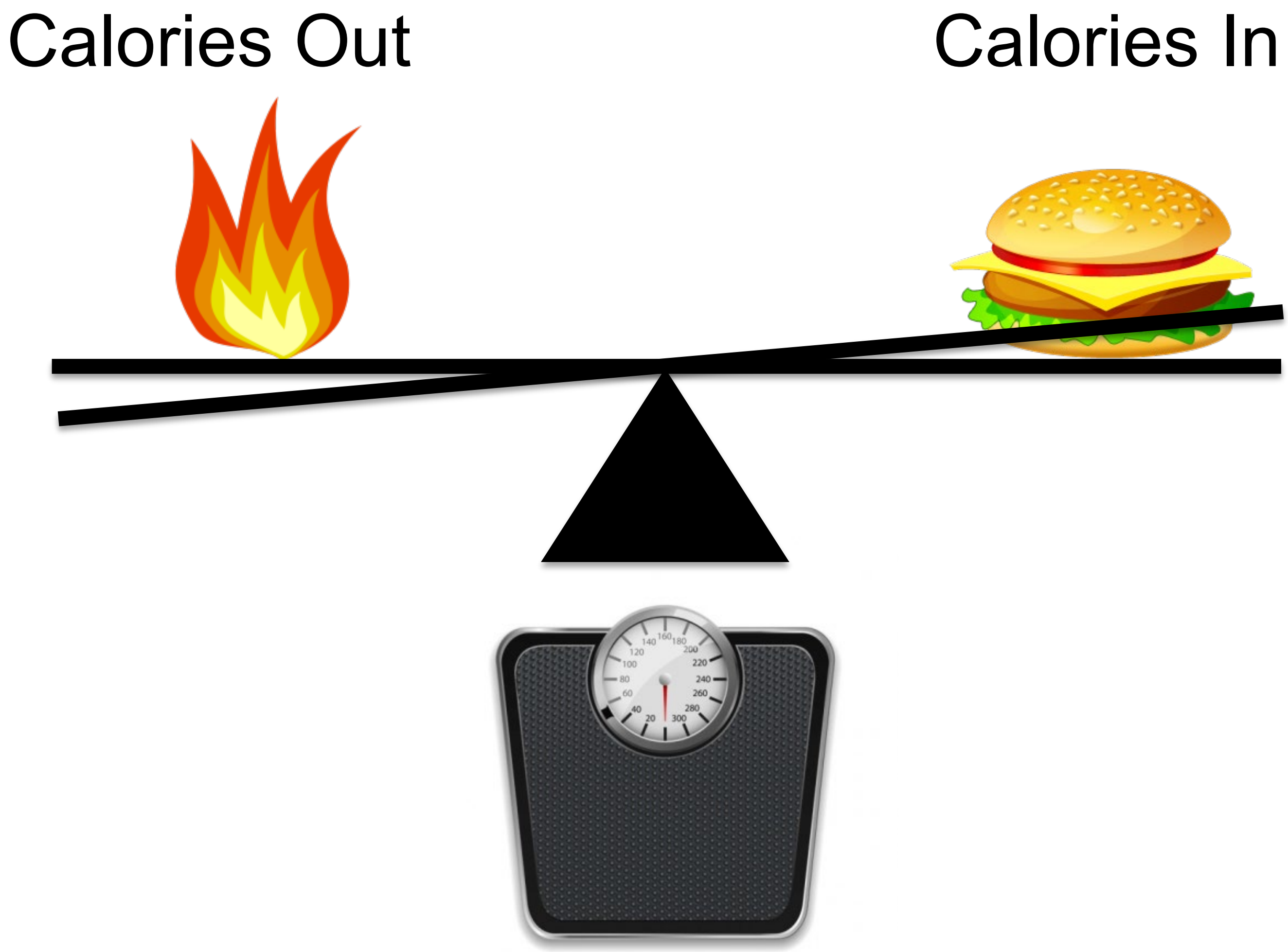
> If a patient reduces … on by 500 calories per day for 7 days … uld lose about 1 lb of body weight per …

Wrong, Wrong, Wrong!

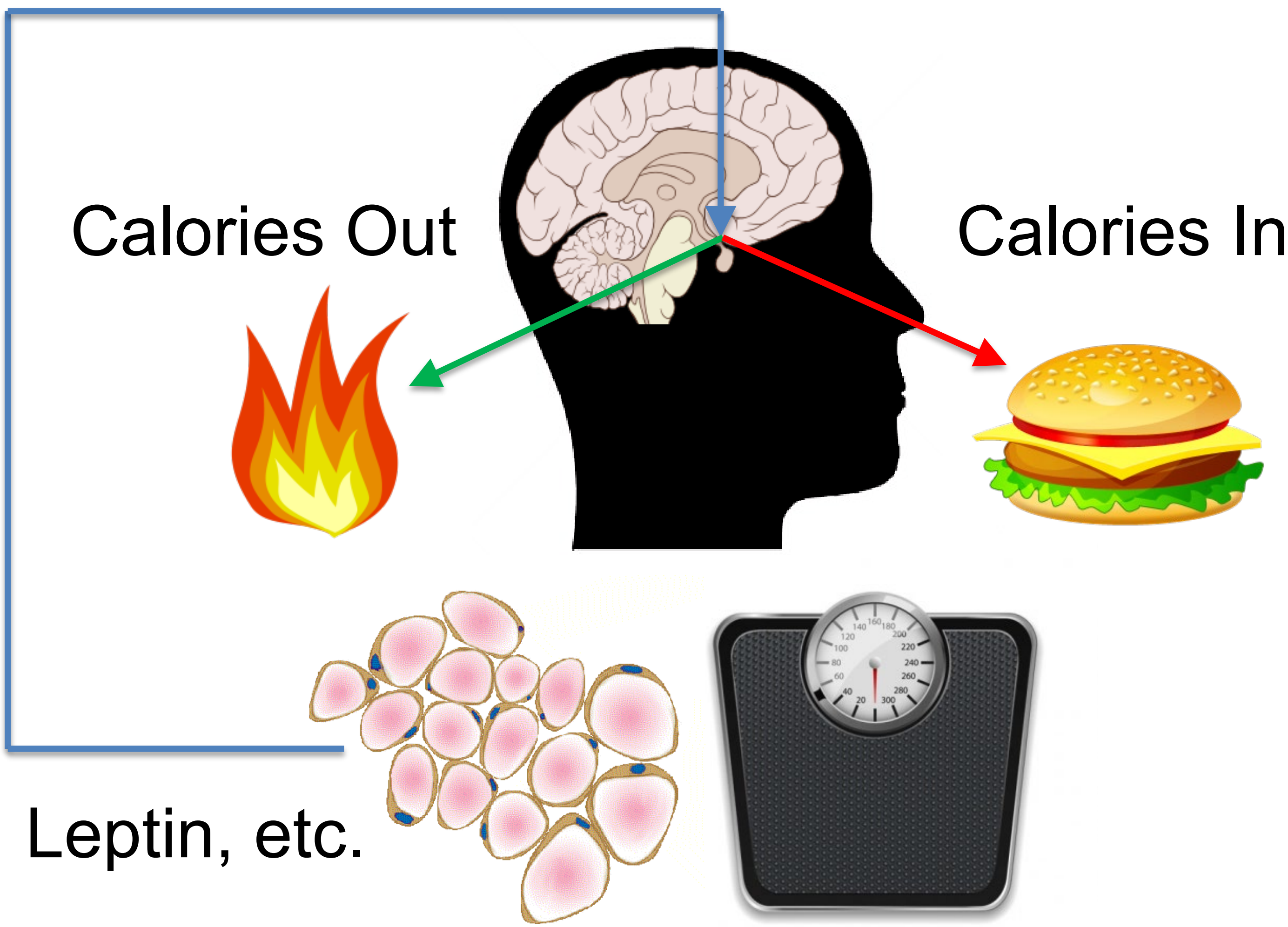
Erroneous Weight Loss Projections



Calories In & Out are NOT Independent



Feedback Regulation of Body Weight



Mathematical Modeling of Metabolism

$$\rho_C \frac{dG}{dt} = CI - DNL + GNG_P + GNG_F - G3P - CarbOx$$

$$\rho_F \frac{dF}{dt} = 3M_{FFA}FI/M_{TG} + \varepsilon_d DNL - KU_{excr} - (1-\varepsilon_k)KTG - FatOx$$

$$\rho_P \frac{dP}{dt} = PI - GNG_P - ProtOx$$

$$FFM = BM + ECF + ECP + LCM$$
$$= BM + ECF + ECP + ICW + P + G + ICS$$
$$= BM + ECF + ECP + I\hat{C}W + P(1+h_P) + G(1+h_G) + ICS$$

$$\frac{dECF}{dt} = \frac{1}{[Na]}\left(\Delta Na_{diet} - \xi_{Na}\left(ECF - ECF_{init}\right) - \xi_{CI}\left(1 - CI/CI_b\right)\right) + \Delta ECF$$

$$\tau_{BW}\frac{d\Delta ECF}{dt} = \xi_{BW}\left(BW - BW_{init}\right) - \Delta ECF$$

$$TEE = TEF + PAE + RMR$$

$$RMR = E_c + \gamma_B M_B + \gamma_{FFM}\left[FFM - M_B - \Delta G\left(1+h_g\right) - \left(ECF - ECF_{init}\right)\right] + \gamma_F F$$
$$+(1-\varepsilon_d)DNL + (1-\varepsilon_g)(GNG_F + GNG_P) + (1-\varepsilon_K)KTG$$
$$+\eta_N N_{excr} + (\eta_P + \varepsilon_P)D_P + \eta_P\frac{dP}{dt} + \eta_F D_F + \eta_F\frac{dF}{dt} + \eta_G D_G + \eta_G\frac{dG}{dt}$$

$$\tau_T \frac{dT}{dt} = \begin{cases} \lambda_1\left(\Delta EI/EI_b\right) - T, & \text{if } EI < EI_b \\ \lambda_2\left(\Delta EI/EI_b\right) - T, & \text{else} \end{cases}$$

$$\hat{\gamma}_{FFM} = \sum_i \gamma_i \frac{dM_i}{dFFM}$$

$$\gamma_{FFM} = \hat{\gamma}_{FFM}\left[1 + (1-\sigma)T\right]$$

$$PAE = \delta\left(1+\sigma T\right)BW + \upsilon BW$$

$$TEF = \alpha_F FI + \alpha_P PI + \alpha_C CI$$

$$CarbOx = GNG_f + GNG_p - G3P + f_C \times T\tilde{E}E$$

$$FatOx = KetOx + f_F \times T\tilde{E}E$$

$$ProtOx = f_P \times T\tilde{E}E$$

$$DNL = \frac{CI \times \left(G/G_{init}\right)^d}{\left(G/G_{init}\right)^d + K_{DNL}^d}$$

$$D_G = \hat{D}_G\left(\frac{G}{G_{init}}\right)$$

$$D_P = \hat{D}_P\left[\left(\frac{P}{P_{Keys}}\right) + \chi\left(\frac{\Delta PI}{PI_b}\right)\right]$$

$$D_F = \hat{D}_F\left(\frac{F}{F_{Keys}}\right)^{\frac{2}{3}}\left[L_{diet} + L_{PA}\right]$$

$$\tau_L \frac{dL_{diet}}{dt} = \frac{K_L^{S_L}\left[1 + \left(A_L - B_L\right)\times\exp\left(-k_L\, CI/CI_b\right) + B_L\right]}{K_L^{S_L} + MAX\left\{0, \left(F/F_{Keys} - 1\right)^{S_L}\right\}} - L_{diet}$$

$$GNG_F = FI\left(\frac{\rho_C M_G}{\rho_F M_{TG}}\right) + D_F \rho_C\left(\frac{M_G}{M_{TG}}\right)$$

$$L_{PA} = \psi\left(\frac{\delta + \upsilon}{\delta_{init} + \upsilon_{init}} - 1\right)$$

$$GNG_P = G\hat{N}G_P\left[\left(\frac{P}{P_{Keys}}\right) - \Gamma_C\left(\frac{\Delta CI}{CI_b}\right) + \left(\Gamma_P + \chi\right)\left(\frac{\Delta PI}{PI_b}\right)\right]$$

$$KTG = \rho_K D_F\left[A_K\left(\frac{D_F/\hat{D}_F}{K_K + D_F/\hat{D}_F}\right)\exp\left(-k_P\frac{PI}{PI_b}\right)\exp\left(-k_G\frac{G}{G_{init}}\right)\right]$$

$$KU_{excr} = \begin{cases} 0, & \text{if } KTG/\rho_K < KTG_{thresh} \\ \dfrac{\rho_K KU_{\max}\left(KTG/\rho_K - KTG_{thresh}\right)}{\left(KTG_{\max} - KTG_{thresh}\right)}, & \text{else} \end{cases}$$

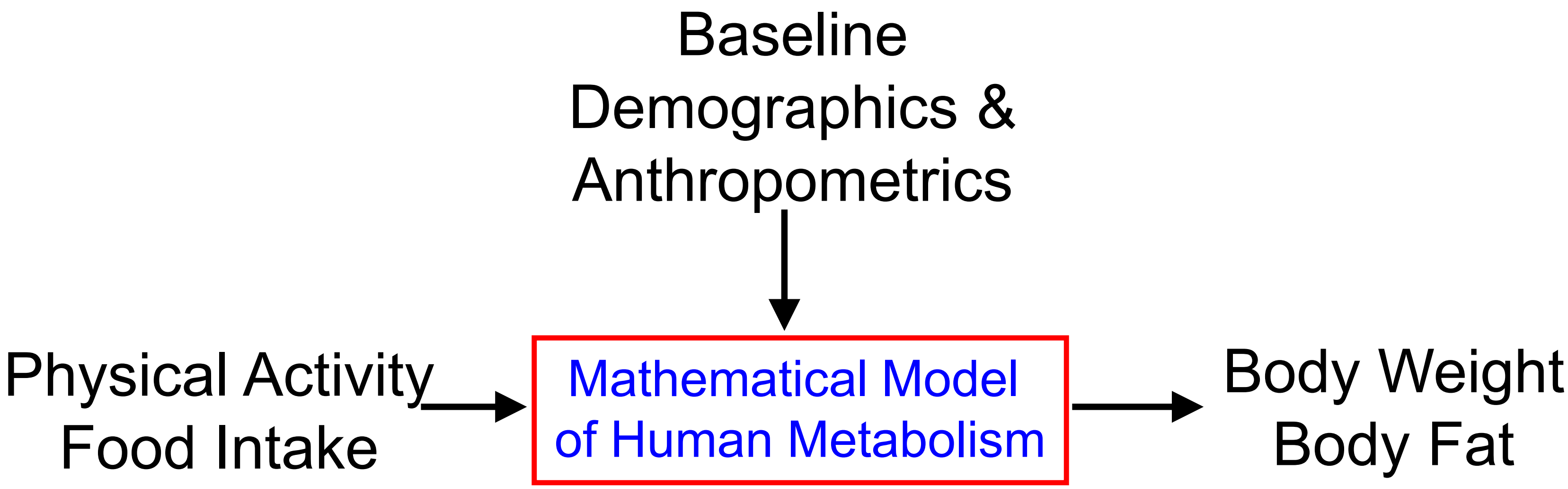
$$f_C = \frac{w_G(D_G/\hat{D}_G) + w_C MAX\left\{0, \left(1 + S_C\,\Delta CI/CI_b\right)\right\} G/\left(G_{\min} + G\right)}{Z}$$

$$f_F = \frac{w_F\left(D_F/\hat{D}_F\right)}{Z}$$

$$f_P = \frac{w_P MAX\left\{0, \left(1 + P_{sig}\right)\right\} + \left(D_P/\hat{D}_P\right)S_A\exp\left(-k_A\left(\delta + \upsilon\right)/\left(\delta_b + \upsilon_b\right)\right)}{Z}$$

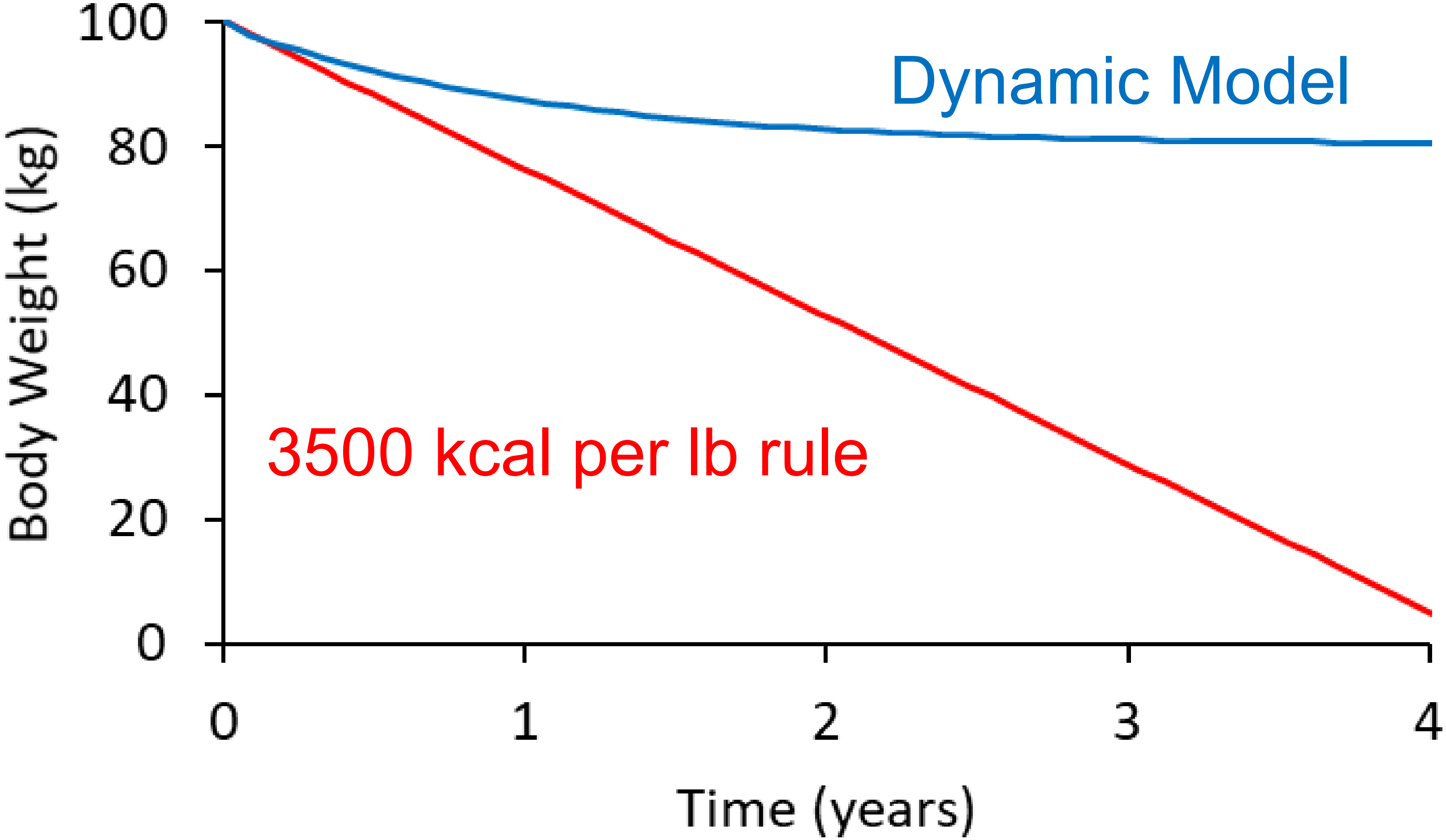
$$\tau_{PI}\frac{dP_{sig}}{dt} = S_P\,\Delta PI/PI_b - P_{sig}$$

Mathematical Modeling of Metabolism



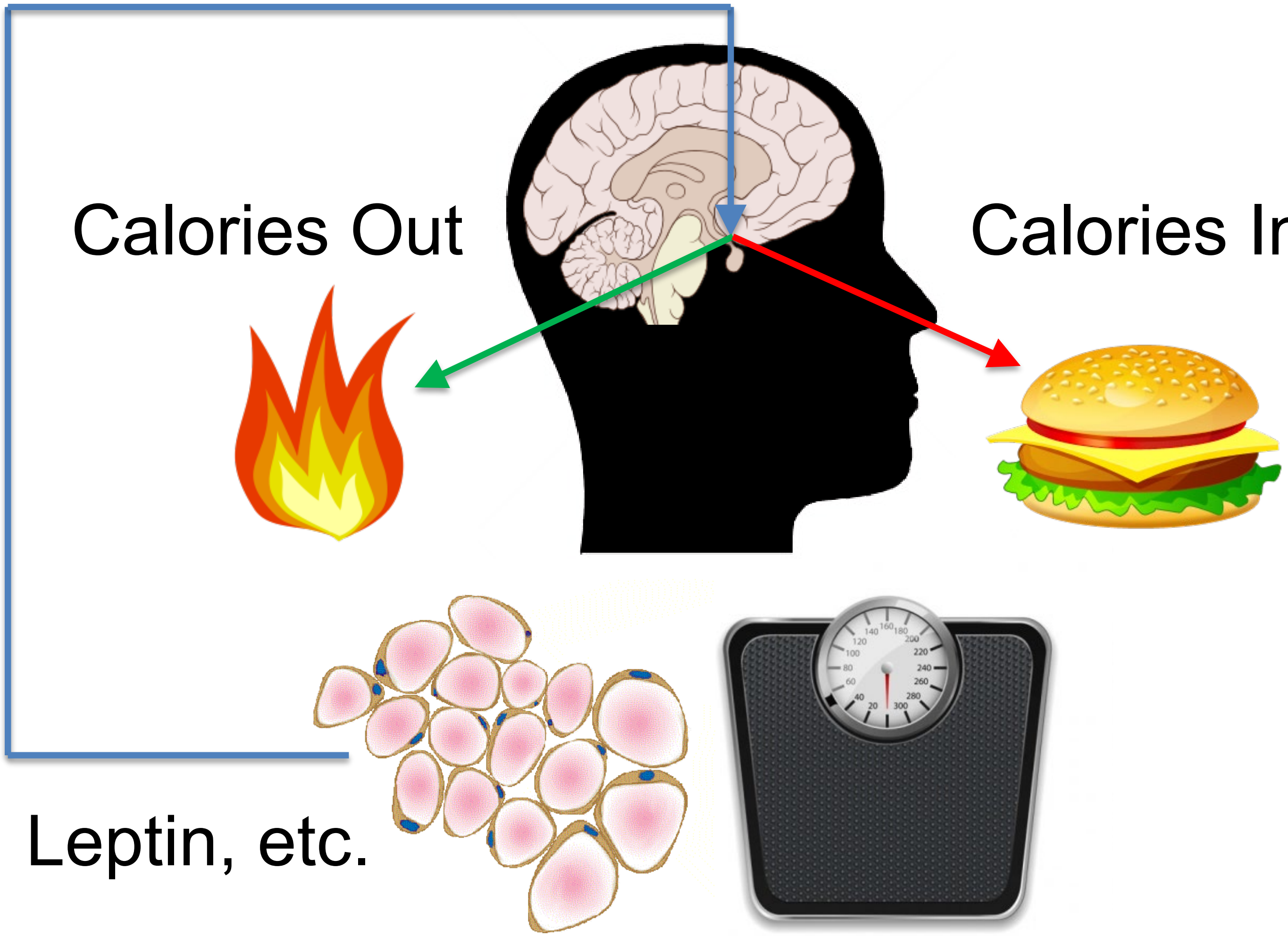
KD Hall et al. *The Lancet* 378:826-37 (2011)

Corrected Weight Loss Projections



KD Hall et al. *The Lancet* 378:826-37 (2011)

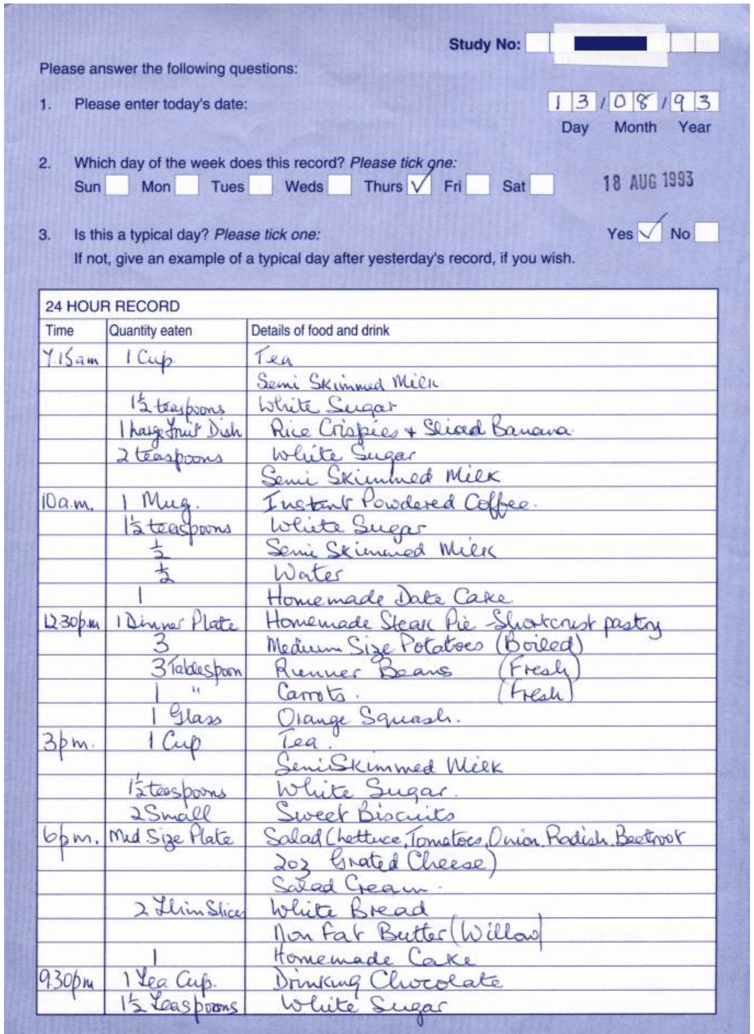
Feedback Control of Appetite?



The fundamental flaw in obesity research

J. T. Winkler

obesity reviews (2005) **6**, 199–202



Study No: [redacted]

Please answer the following questions:

1. Please enter today's date: 13 / 08 / 93 (Day Month Year)

2. Which day of the week does this record? *Please tick one:*
Sun ☐ Mon ☐ Tues ☐ Weds ☐ Thurs ☑ Fri ☐ Sat ☐

18 AUG 1993

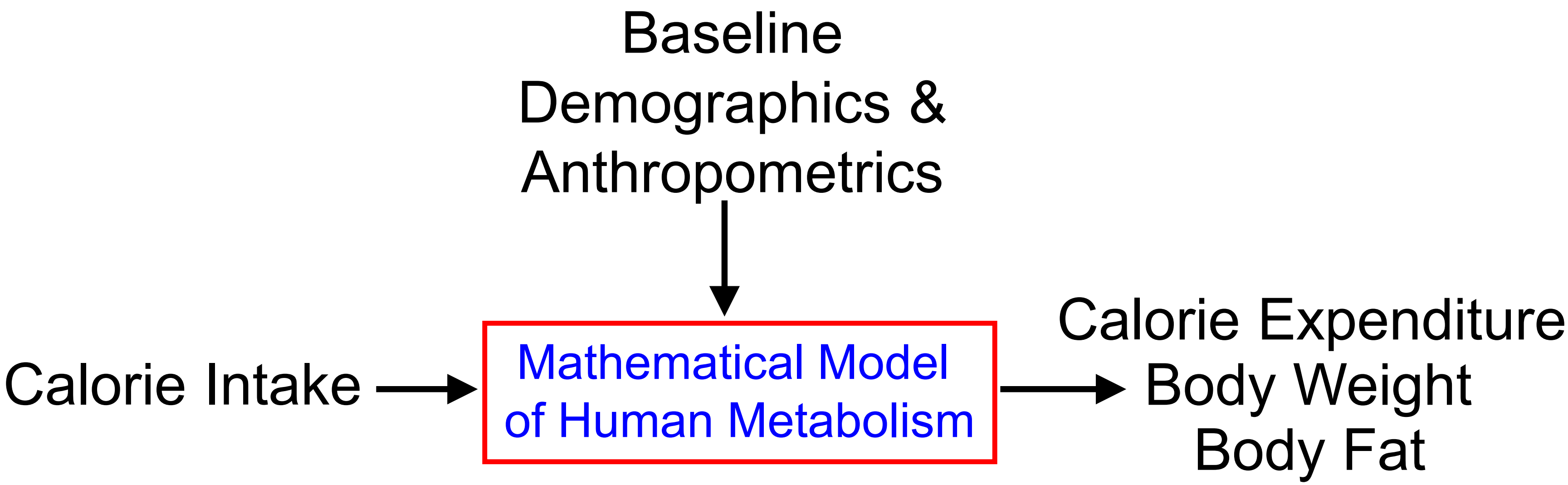
3. Is this a typical day? *Please tick one:* Yes ☑ No ☐
If not, give an example of a typical day after yesterday's record, if you wish.

24 HOUR RECORD

Time	Quantity eaten	Details of food and drink
7.15am	1 Cup	Tea
		Semi Skimmed Milk
	1½ teaspoons	White Sugar
	1 large fruit Dish	Rice Crispies + Sliced Banana
	2 teaspoons	White Sugar
		Semi Skimmed Milk
10a.m.	1 Mug.	Instant Powdered Coffee.
	1½ teaspoons	White Sugar
	½	Semi Skimmed Milk
	½	Water
	1	Homemade Date Cake
12.30pm	1 Dinner Plate	Homemade Steak Pie Shortcrust pastry
	3	Medium Size Potatoes (Boiled)
	3 Tablespoon	Runner Beans (Fresh)
	1 "	Carrots. (Fresh)
	1 Glass	Orange Squash.
3pm.	1 Cup	Tea.
		SemiSkimmed Milk
	1½ teaspoons	White Sugar.
	2 Small	Sweet Biscuits
6pm.	Med Size Plate	Salad (Lettuce, Tomatoes, Onion, Radish, Beetroot
		2oz Grated Cheese)
		Salad Cream.
	2 Thin Slices	White Bread
		Non Fat Butter (Willow)
	1	Homemade Cake
9.30pm	1 Tea Cup.	Drinking Chocolate
	1½ teaspoons	White Sugar

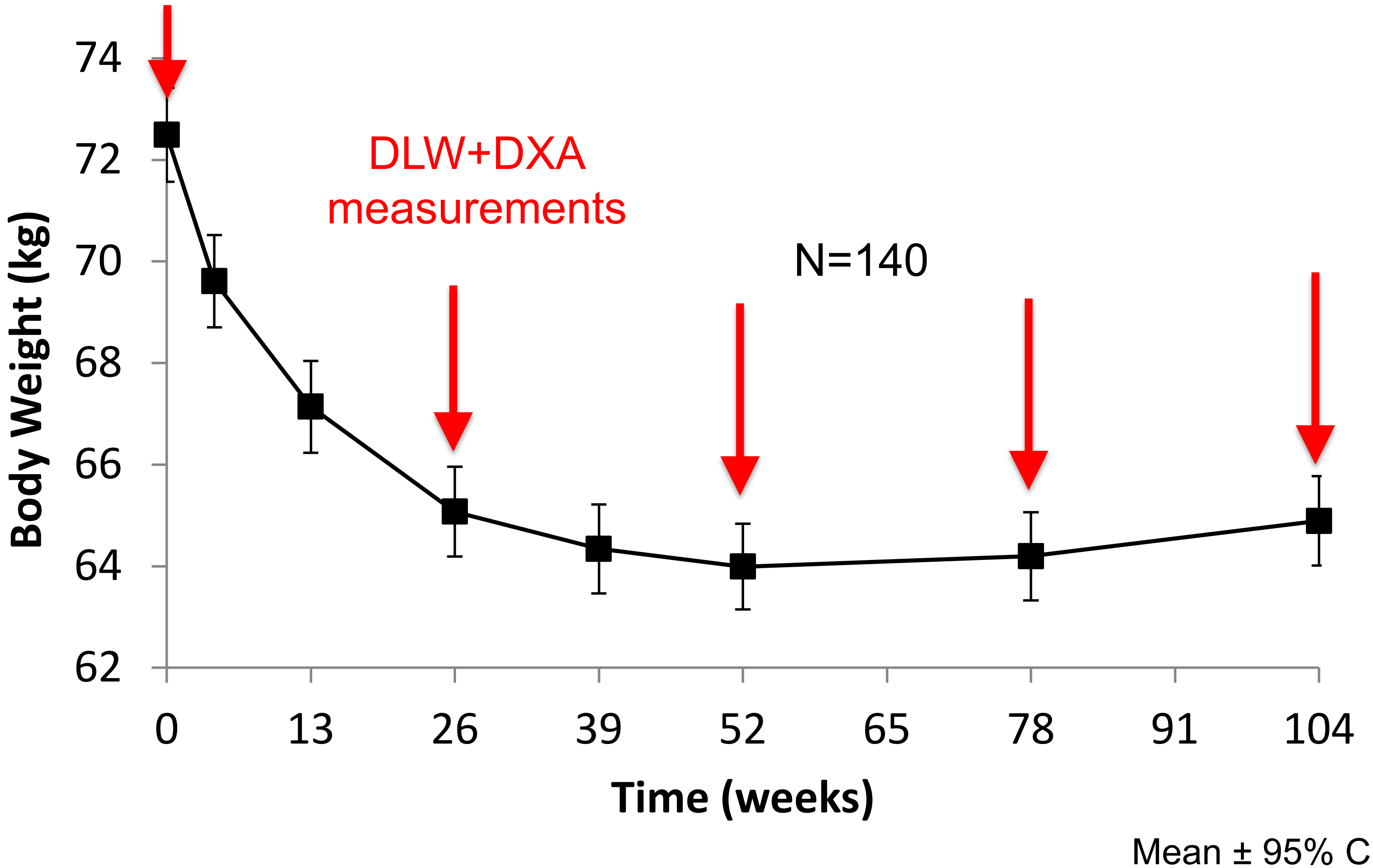
How often, in the past 3 months, did you eat the following?	never	Less than 1 time per week	1-3 times per week	4-6 times per week	1 time per day	2-3 times per day	4 or more times per day	What was your usual serving size, relative to the following?	1	½ or less	1 ½ or more
Fruit (apples, bananas, oranges, etc.)								½ cup raw fruit; ½ medium apple or large orange			
Vegetables (carrots, mushrooms, potatoes, etc.)								½ cup cooked or raw; 1 carrot or stalk celery			
Chicken (fried chicken, in soup, grilled chicken, etc.)								3-4 oz; ½ large or 1 small breast; 2 drumsticks			
Turkey (turkey dinner, turkey sandwich, in soup, etc.)								3-4 oz; 6-8 very thin slices; 1-3 thick slices			
Fish and Seafood (tuna, shrimp, crab, etc.)								3-4 oz; 1 can of tuna; 6 medium shrimp			
Pork (ham, pork chops, ribs, etc.)								3-4 oz; 1 pork chop; 2 ribs; 3-4 slices bacon			
Beef (steak, meatballs, in tacos, etc.)								3-4 oz; ¼ lb burger; 3-6 slices roast beef			
Other Meat (duck, lamb, venison, etc.)								3-4 oz; a piece about the size of your palm			
Nuts (almonds, cashews, walnuts, etc.)								¼ cup or 1 handful; 20 almonds; 2 tbsp nut butter			
Beans (tofu, chickpeas, chili, etc.)								½ cup cooked beans; ¼ cup hummus or tofu			
Dairy (cheese, milk, yogurt, etc.)								3 slices cheese; 1 cup milk; 1 cup yogurt			
Eggs (omelet, in salad, in baked goods, etc.)								1 egg; ¼ cup scrambled eggs or ½ cup egg salad			
Grains (breads, pasta, rice, etc.)								1 slice bread or pizza; ½ cup rice or pasta			
Sweets (candy, cookies, pie, etc.)								2 small cookies; 1 slice cake or pie			
Caffeinated Soft Drinks (cola, diet cola, energy drinks, etc.)								1 can (12 oz) soda; small fountain drink			
Coffee and Tea (hot coffee, iced coffee, black tea, etc.)								6 oz hot coffee or tea; small iced coffee			

Math Models to Calculate Calorie Intake?



A. Sangvhi et al. *Am J Clin Nutr.*102:353-358 (2015)

Validation: Caloric Restriction for 2 Years



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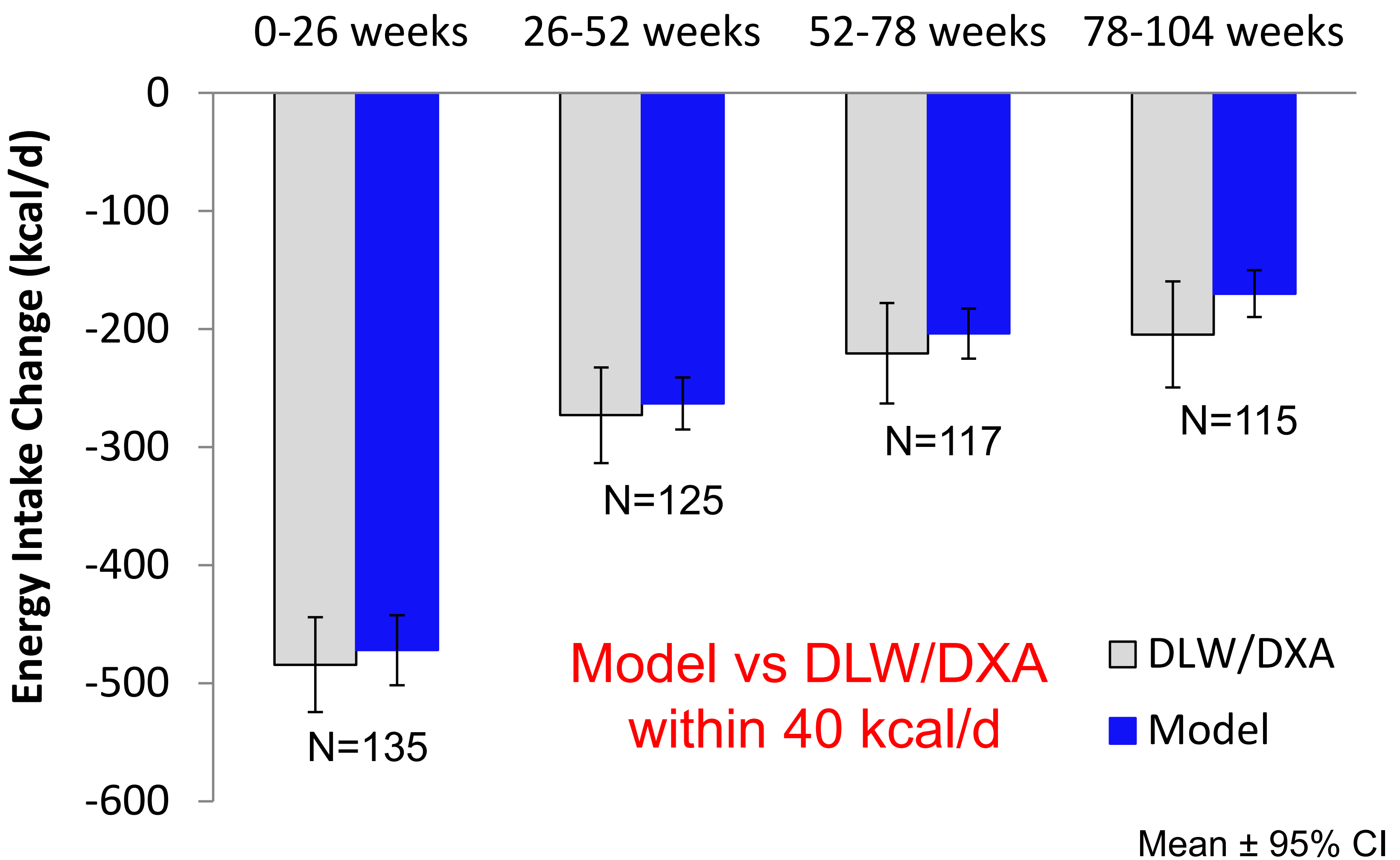
Mean CALERIE 2 Energy Intake Changes



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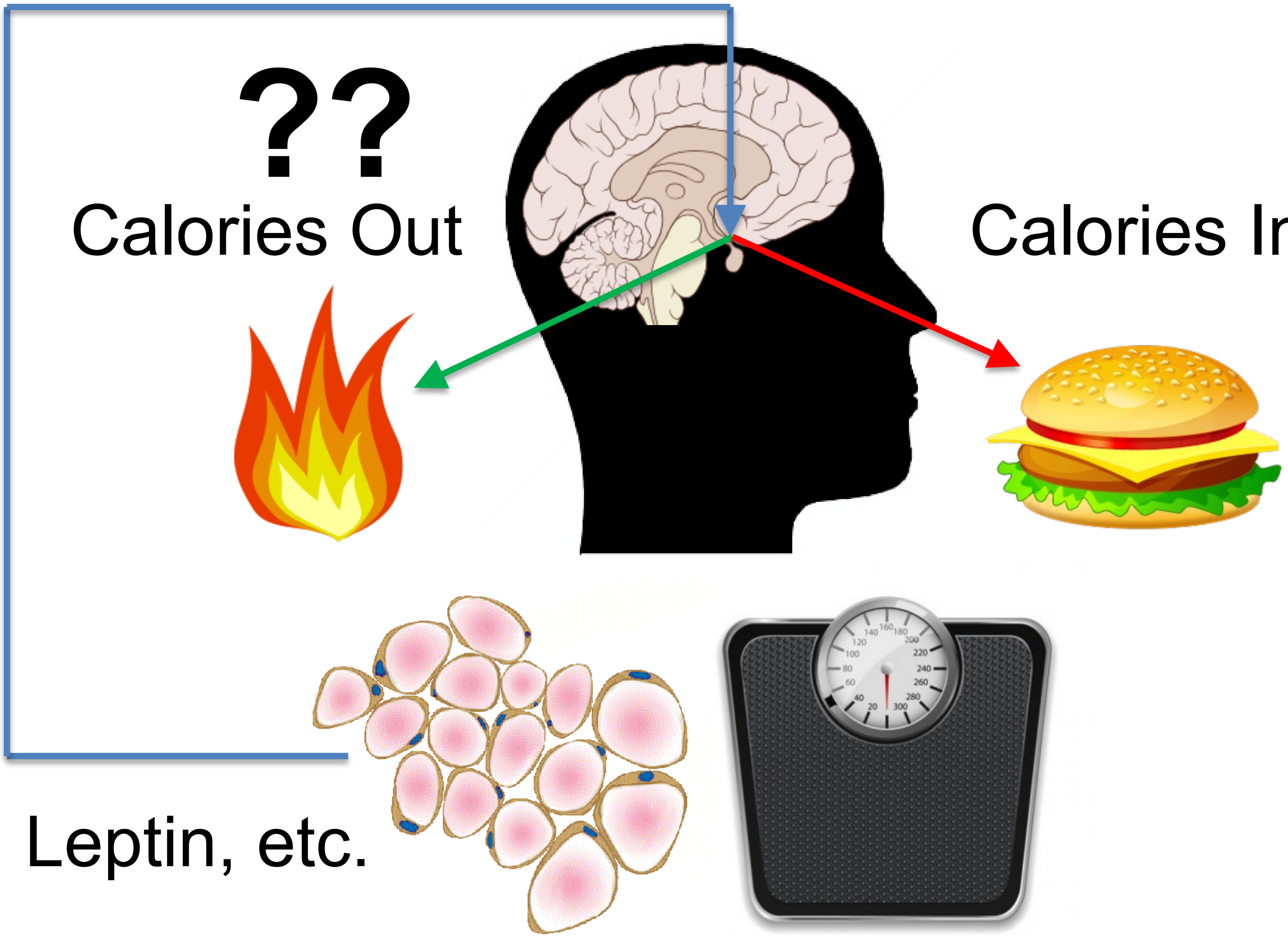
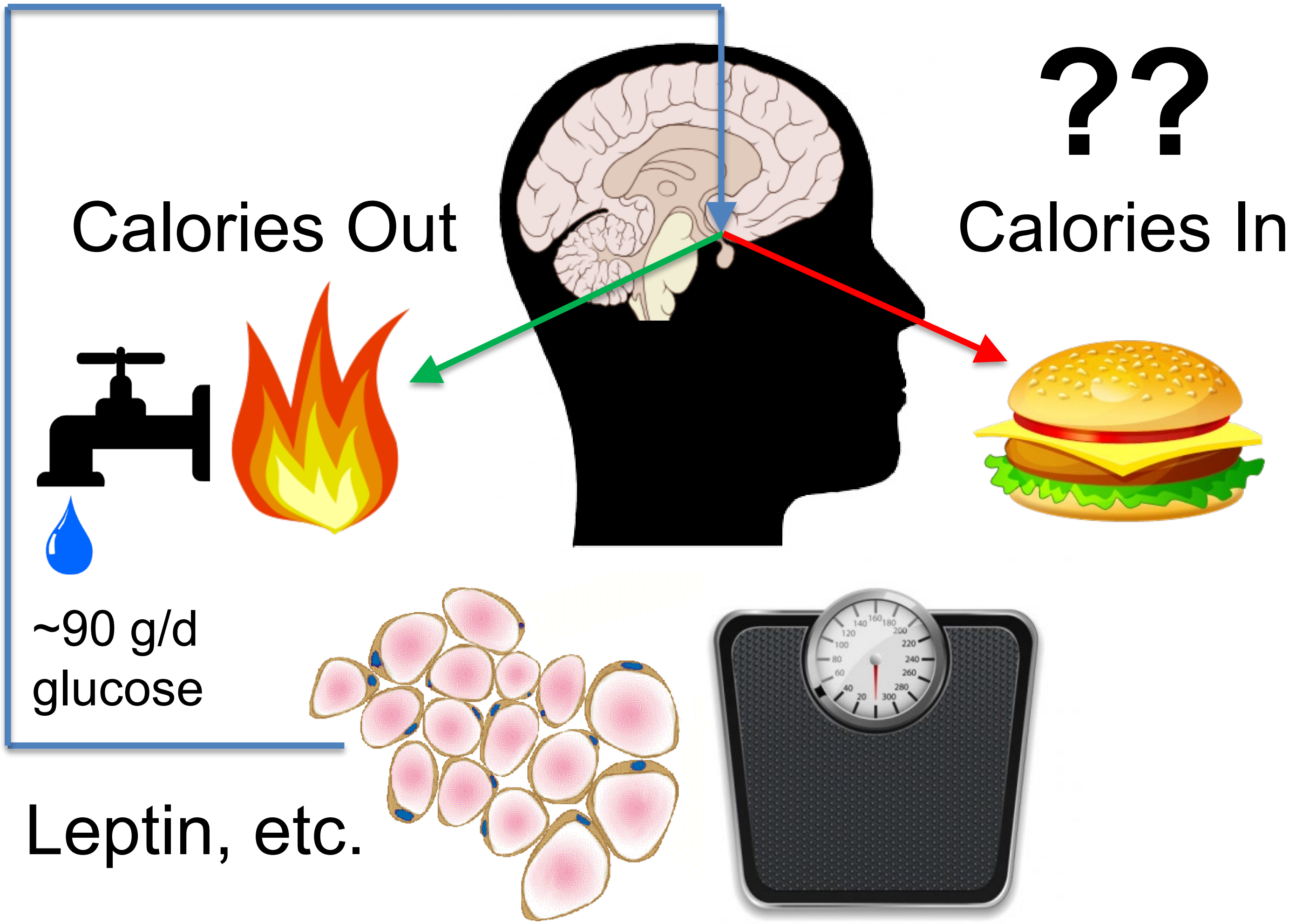
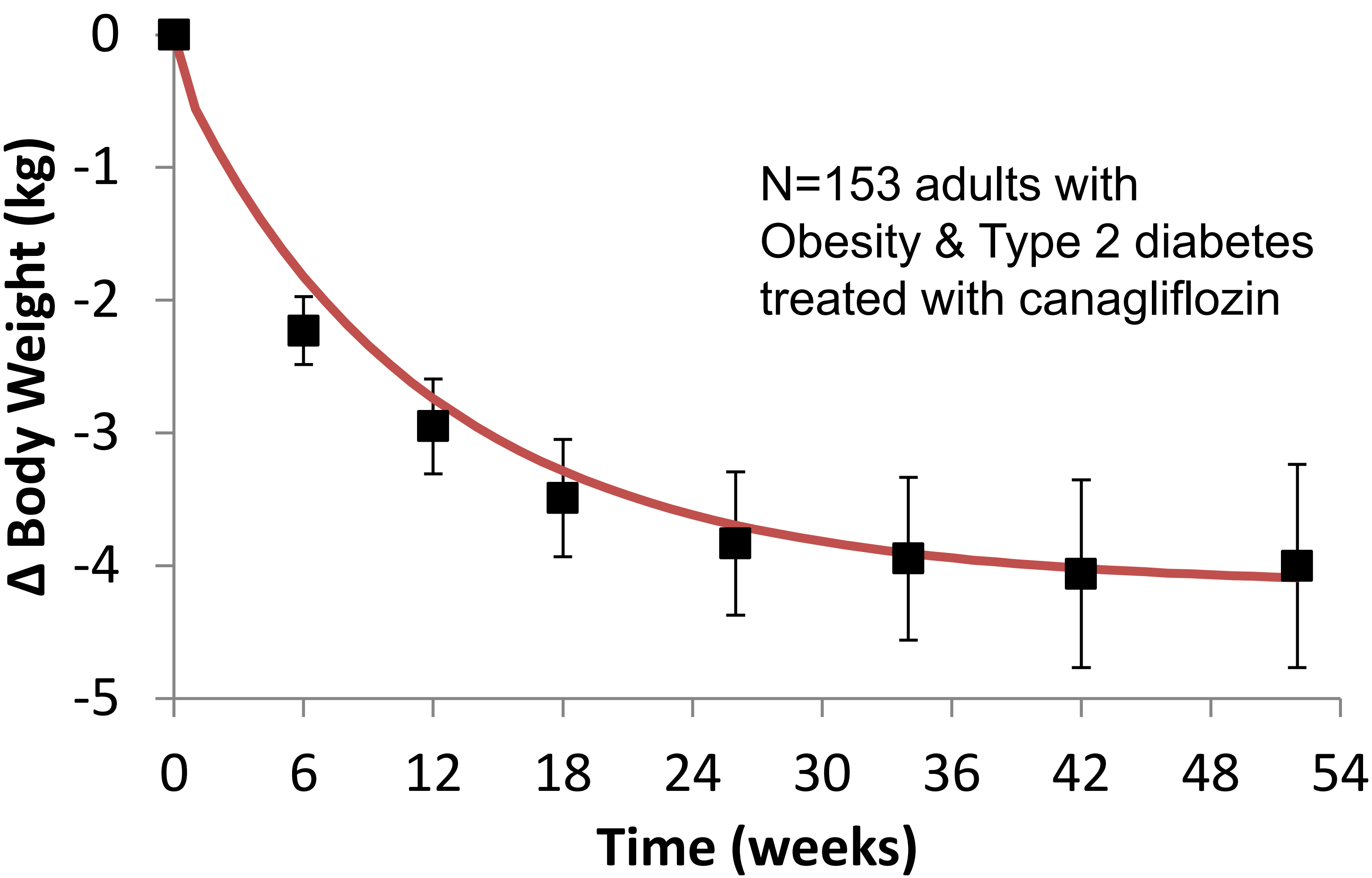
How to Increase Calorie Expenditure?



How to Increase Calorie Expenditure?

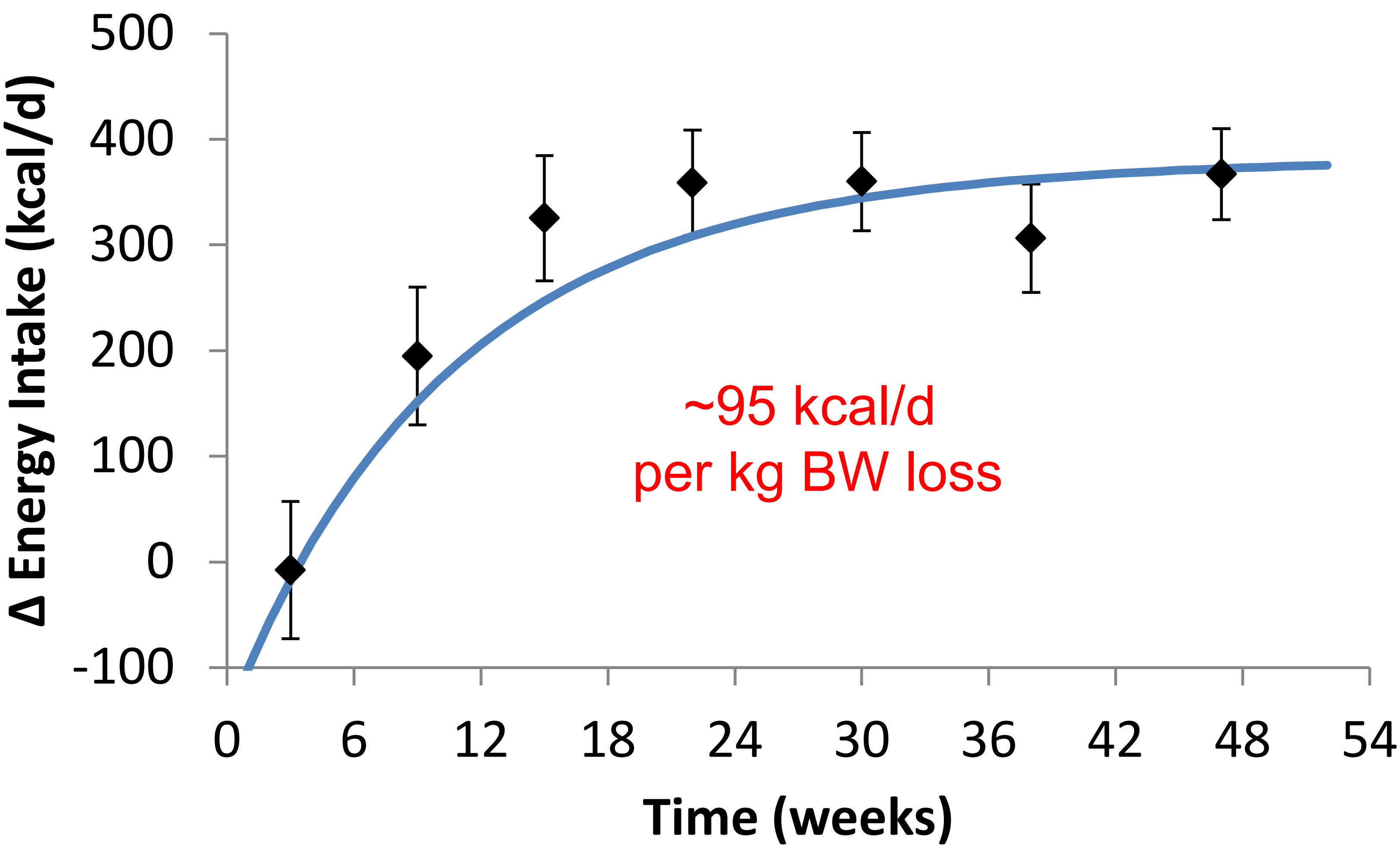


Weight Changes during SGLT2 Inhibition



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

Intake Changes during SGLT2 Inhibition



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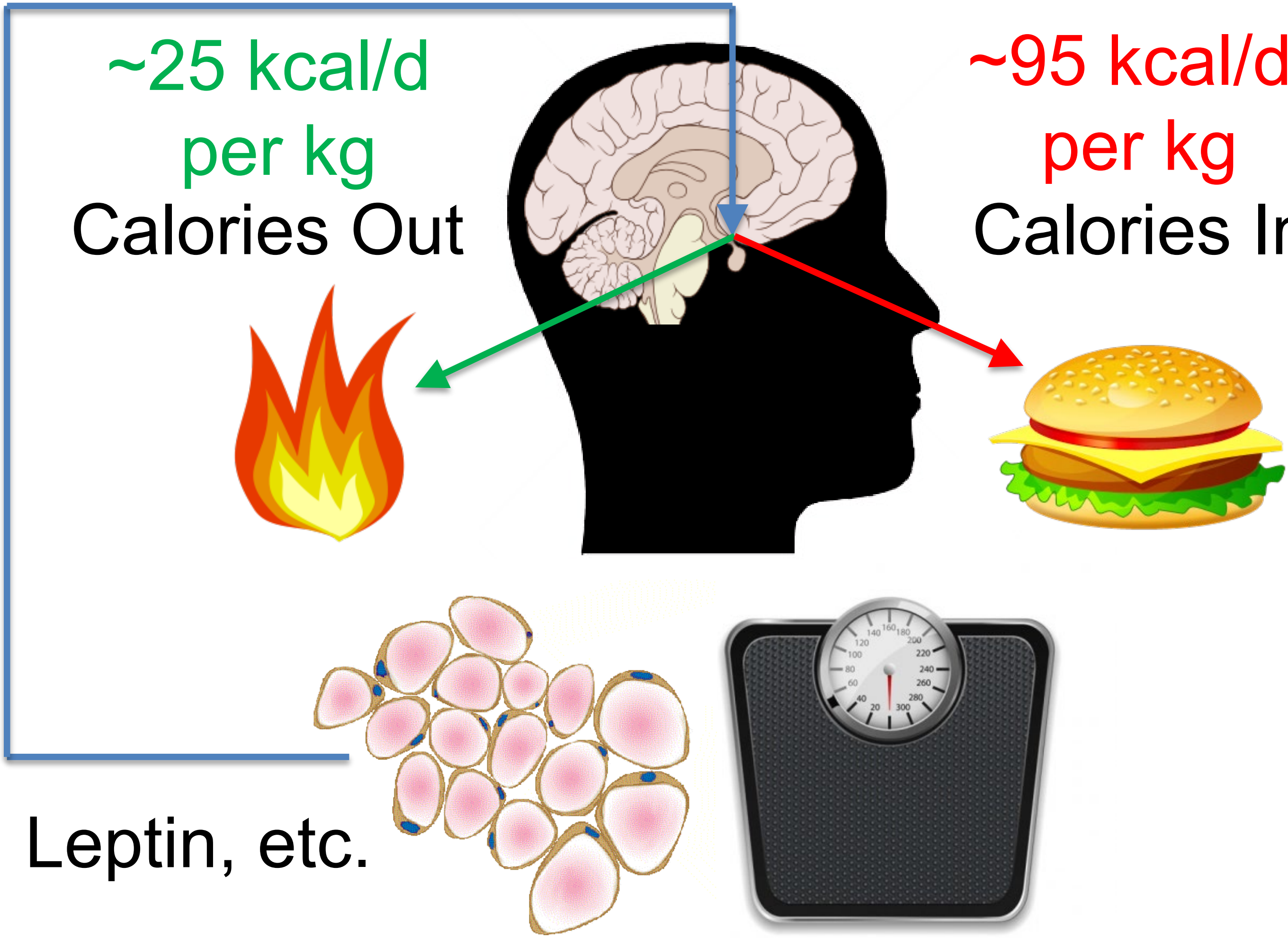
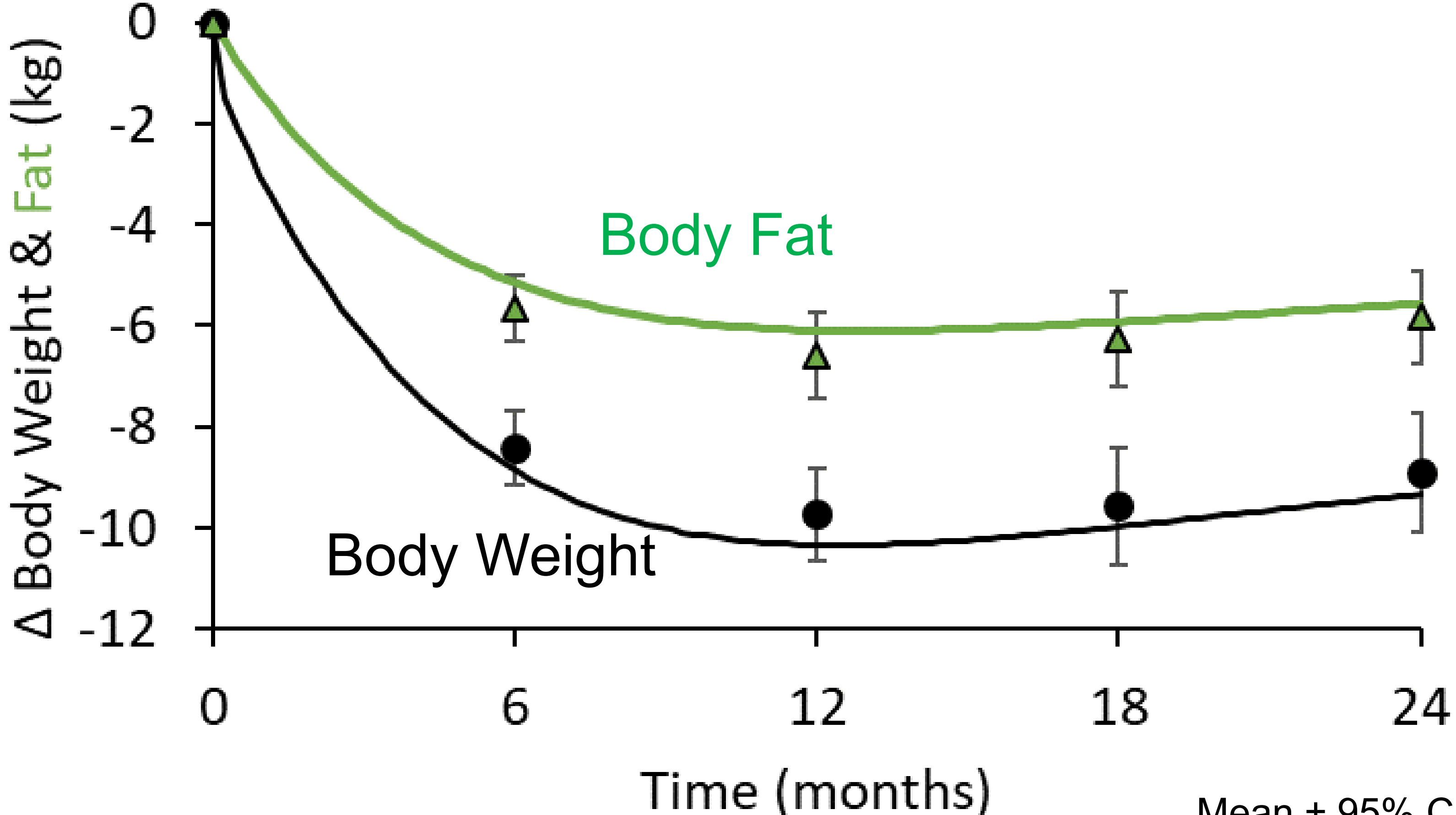
Feedback Regulation of Body Weight



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

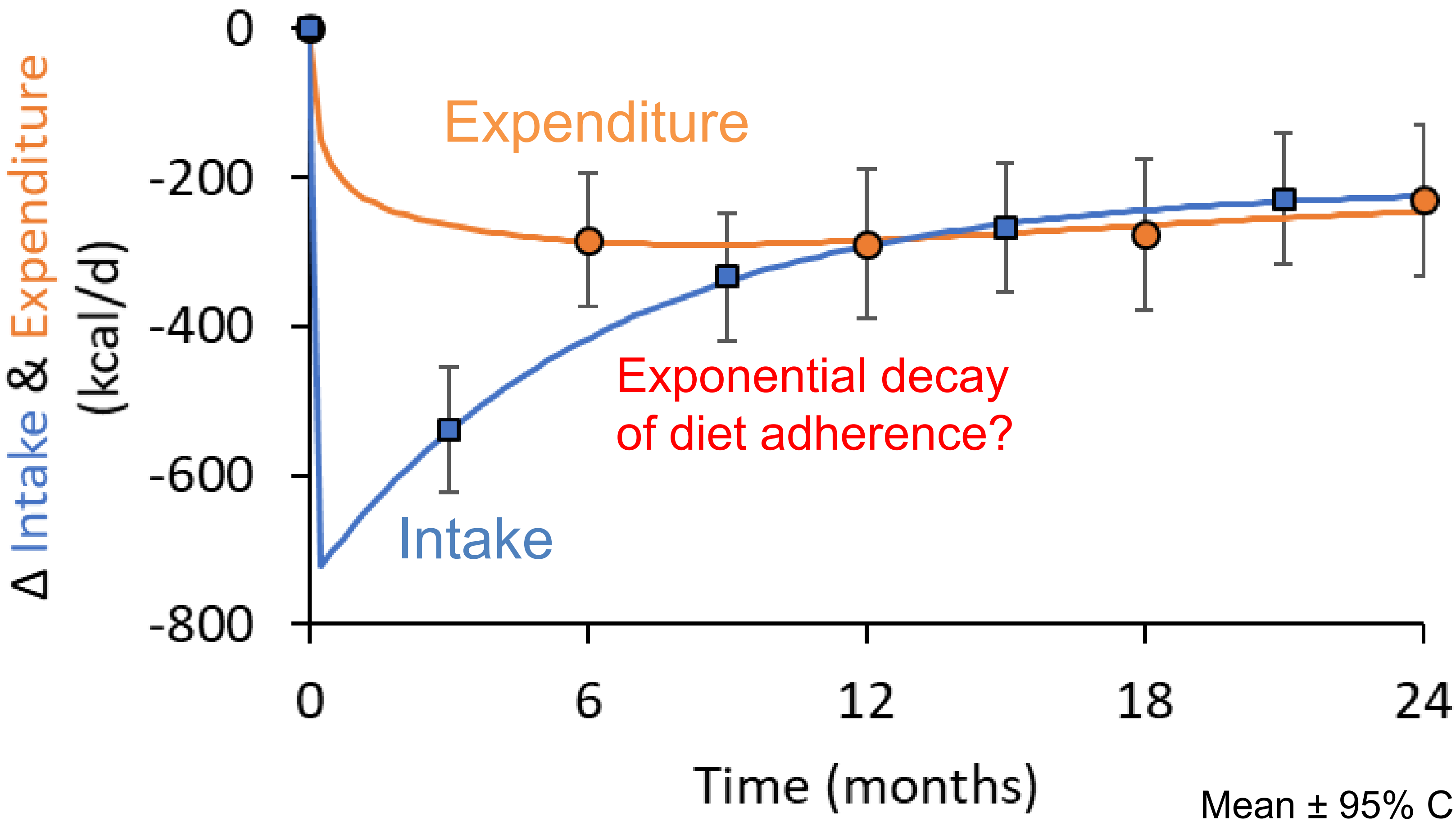
Lifestyle Induced Weight & Fat Loss



Mean ± 95% CI

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

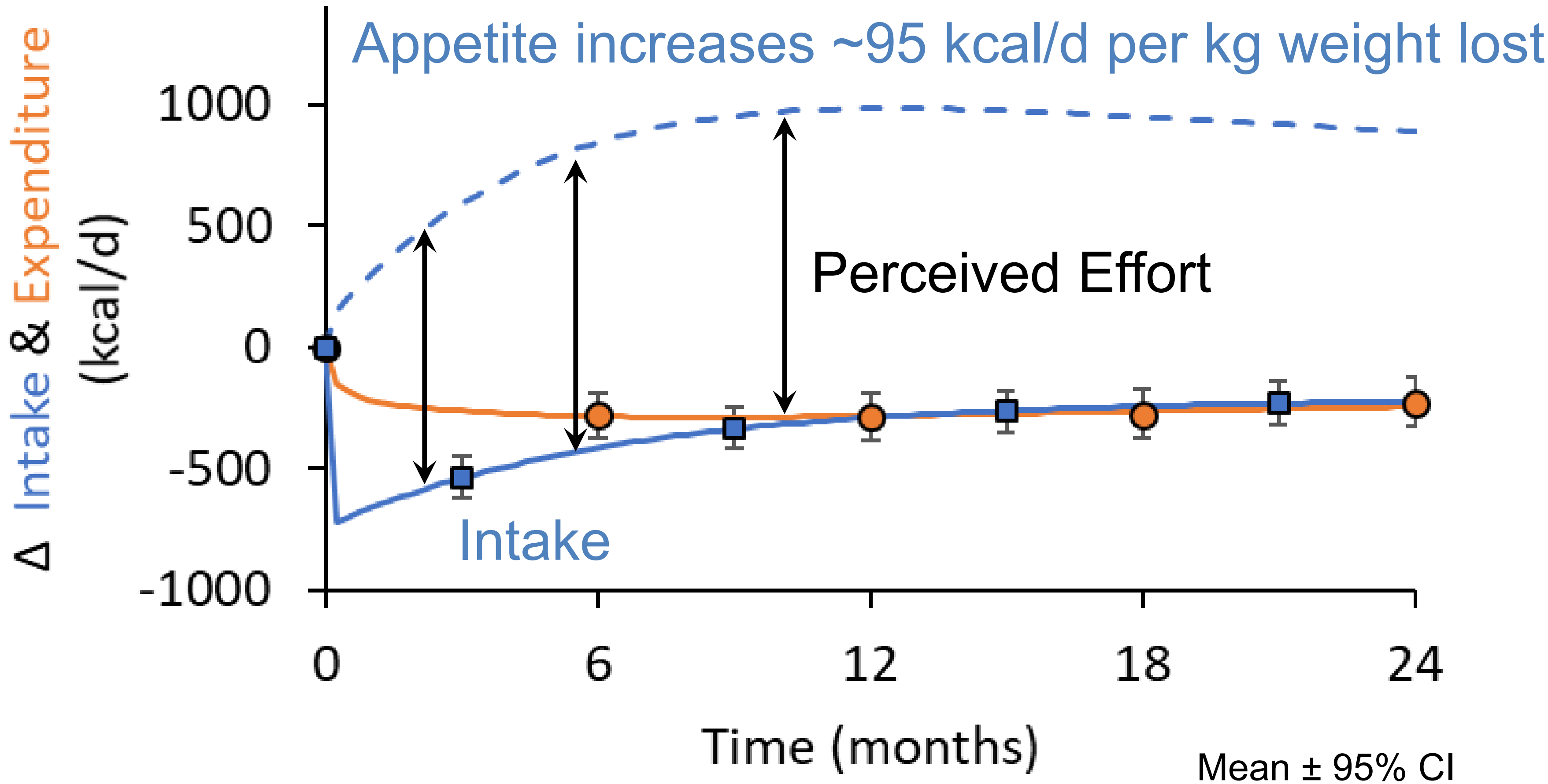
Corresponding Energy Balance Dynamics



Mean ± 95% CI

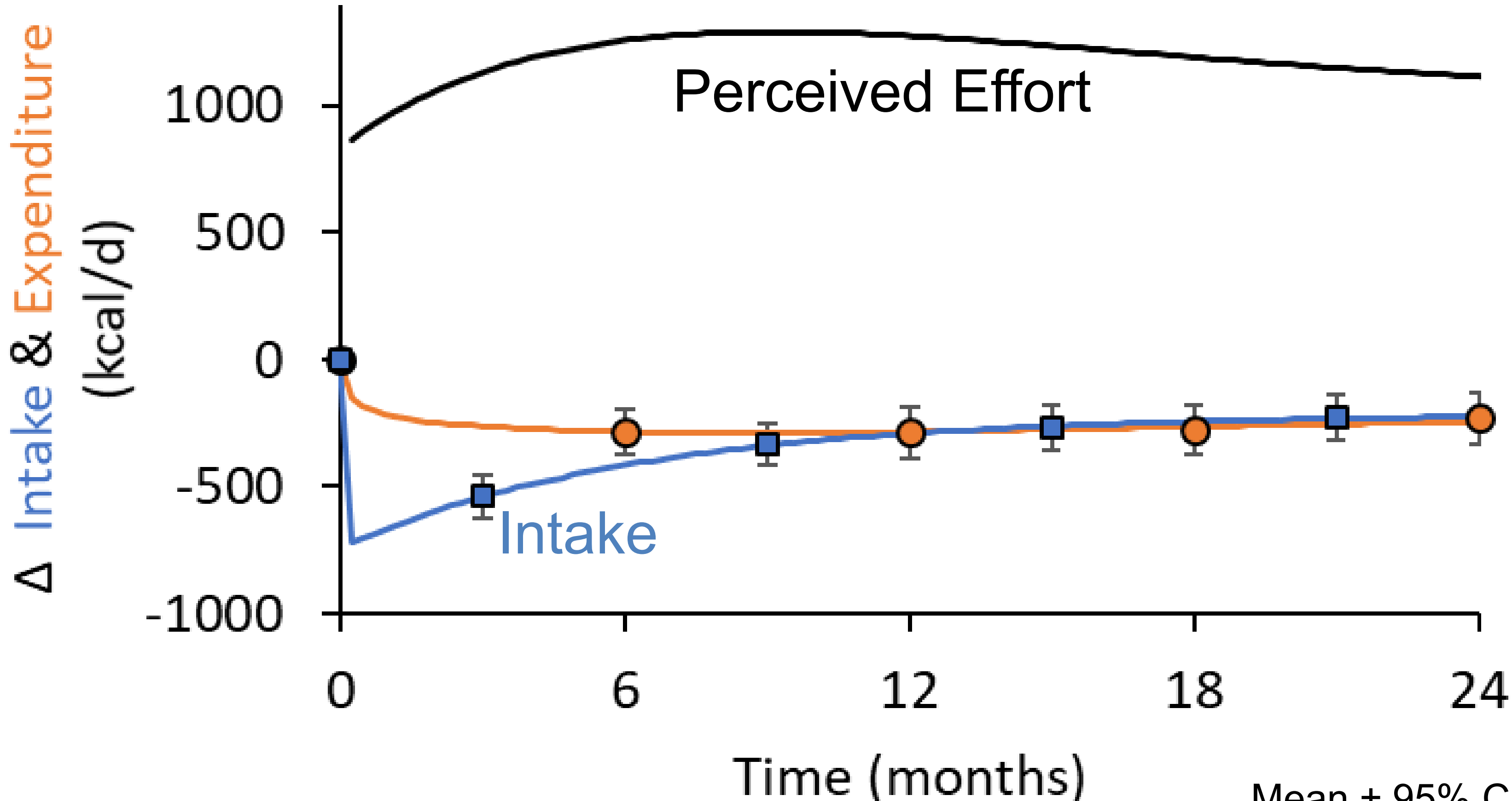
J Guo et al. *Am J Clin Nutr* 107:558–65 (2018).

Interpreting Lifestyle Weight Loss



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

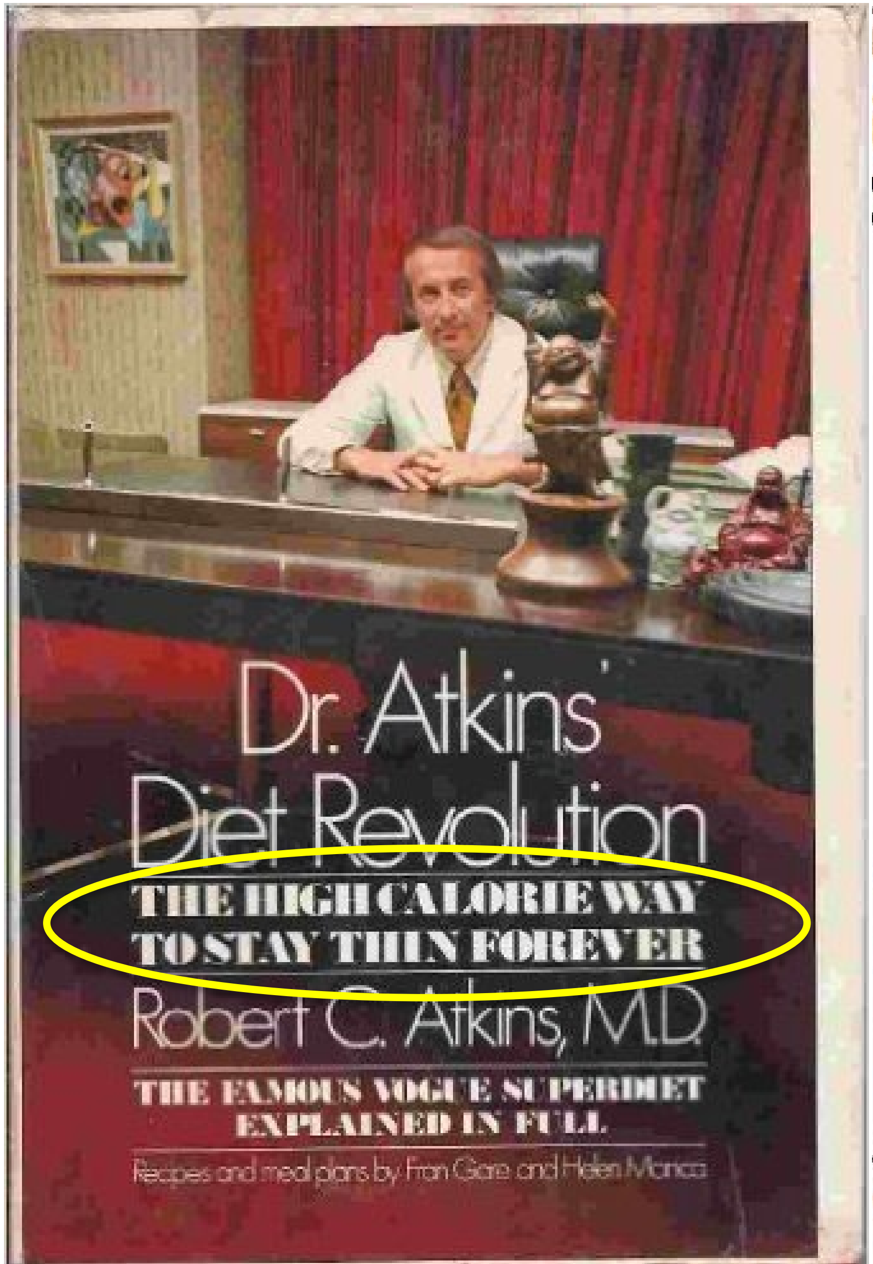
Large & Persistent Perceived Effort

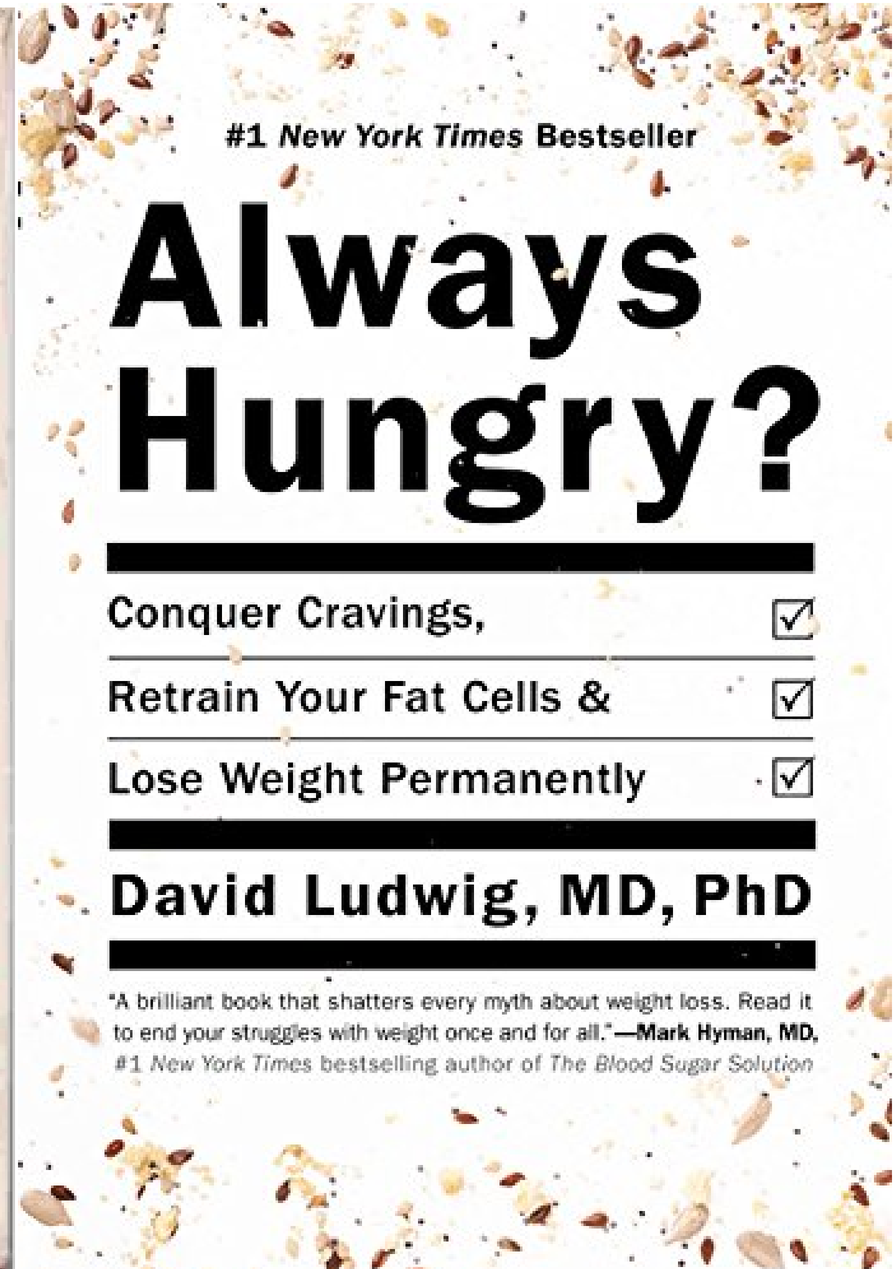


Mean ± 95% CI

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

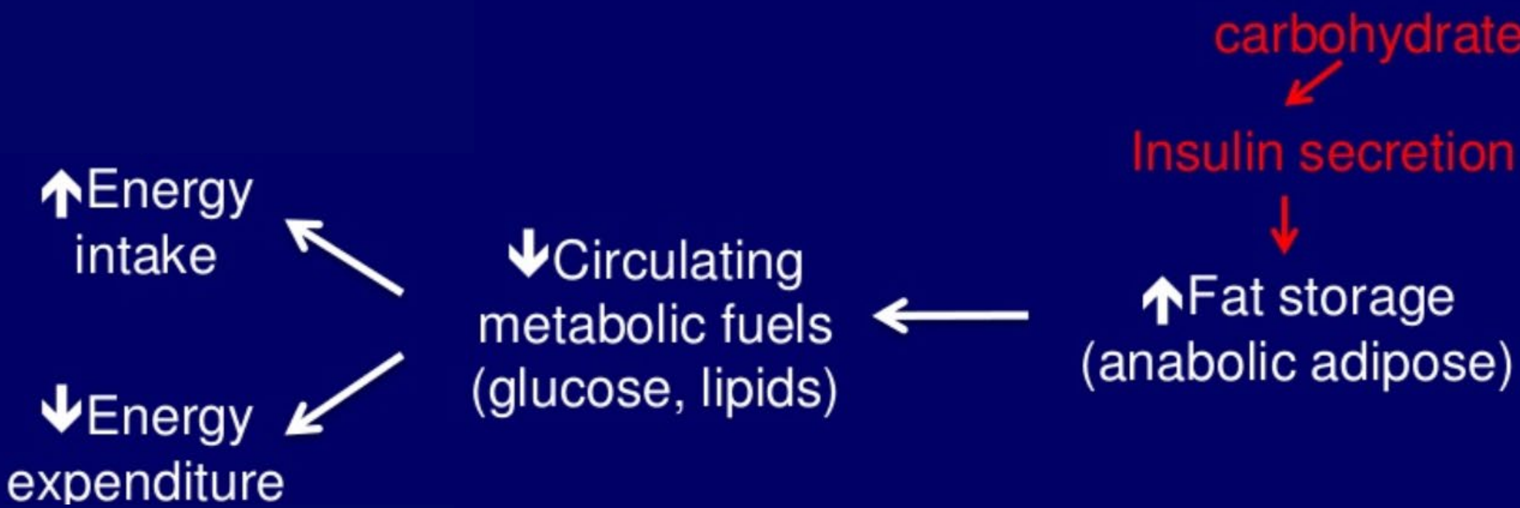
The Promise of Low Carb Diets





Carbohydrate-Insulin Model of Obesity

Excessive anabolic drive in adipose tissue

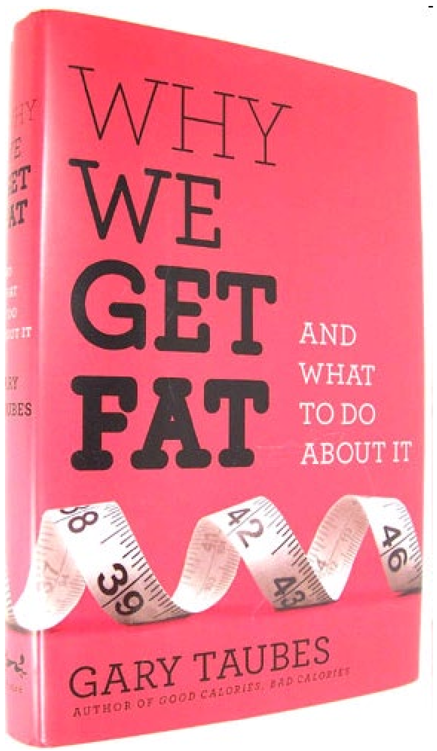


"the metabolic effects of carbohydrate [to increase insulin] cause the adipocyte to take in, store, and trap too many calories. Subsequently, energy expenditure declines and hunger increases"

DS Ludwig & MI Friedman *JAMA* 311:2167-68 (2014).

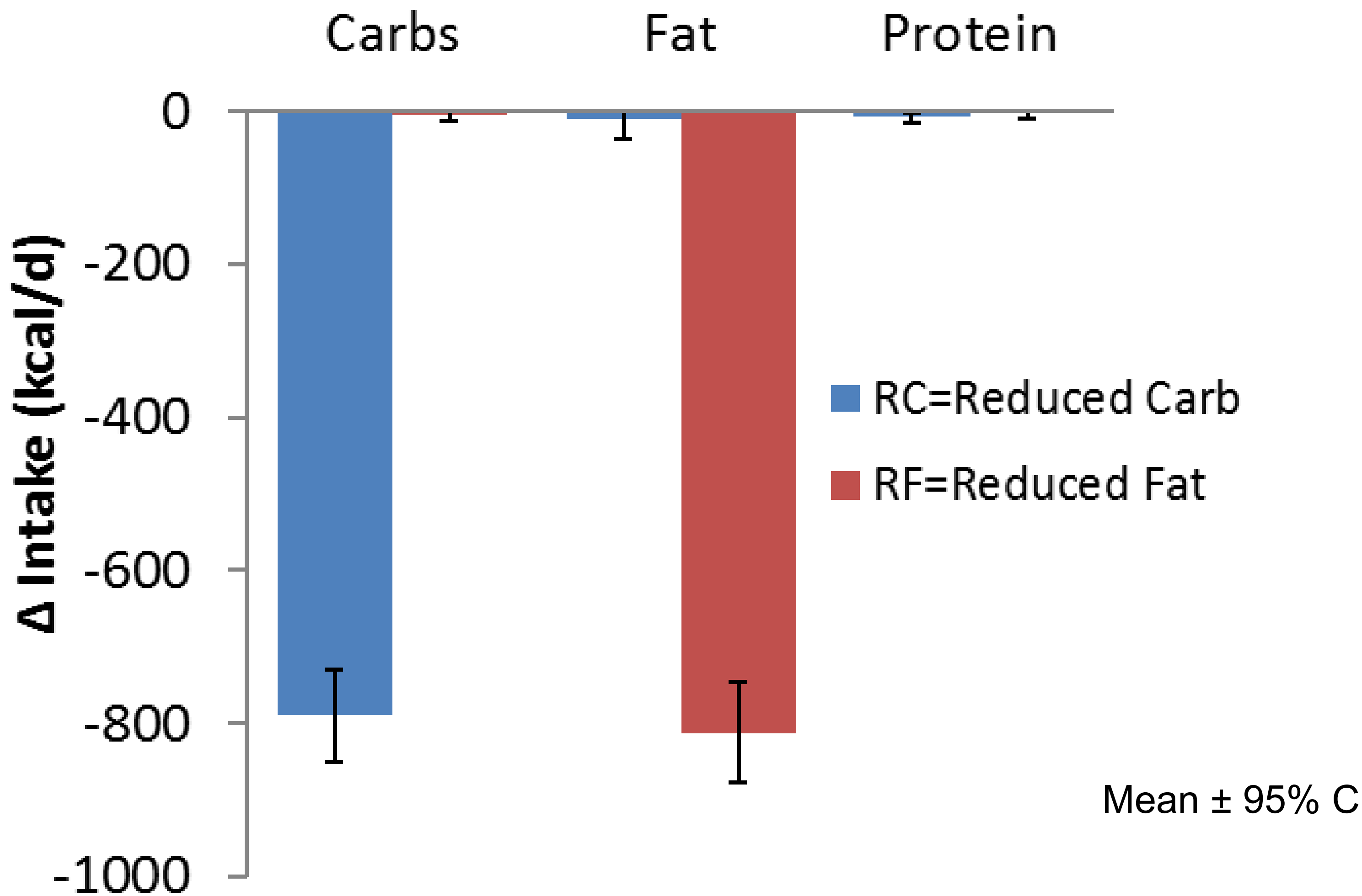
Fat Loss Requires Carbohydrate Reduction?

"Any diet that succeeds does so because the dieter restricts fattening carbohydrates…Those who lose fat on a diet do so because of what they are not eating – the fattening carbohydrates"



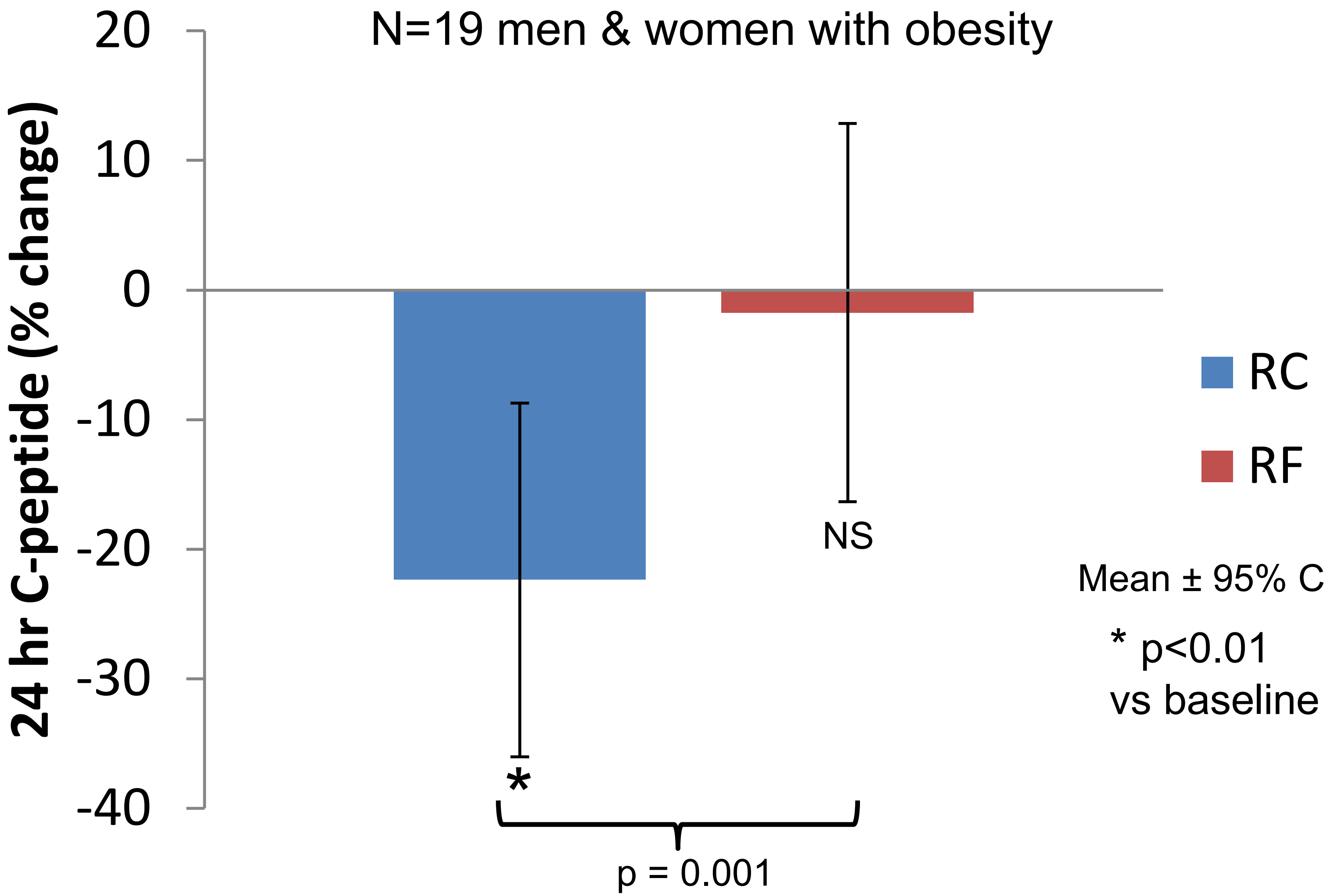
Gary Taubes, W*hy we get fat and what to do about it* (2011).

Isocaloric 30% Calorie Restricted Diets



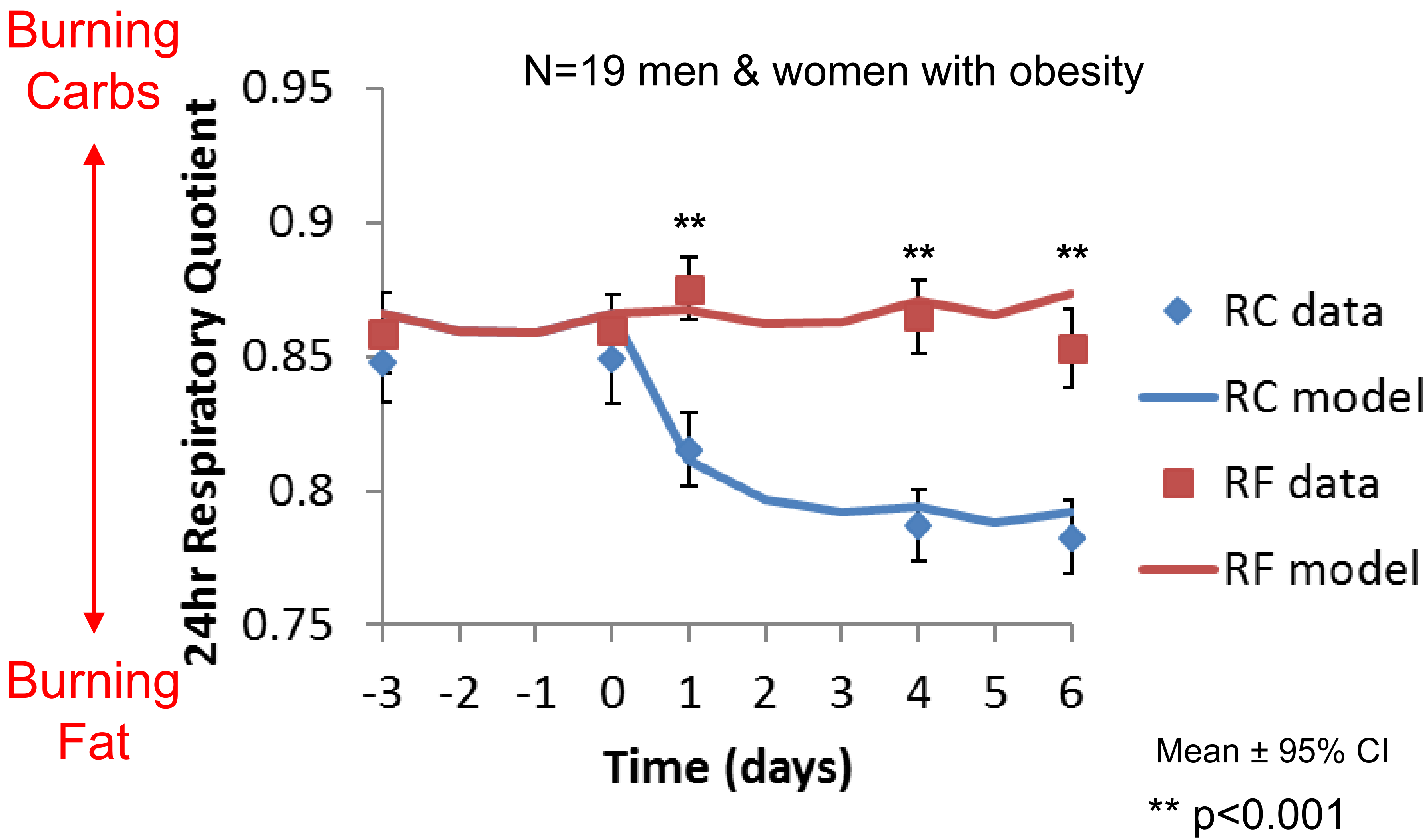
KD Hall et al. *Cell Metabolism* 22:427-436 (2015).

Only RC Diet Decreased Insulin Secretion



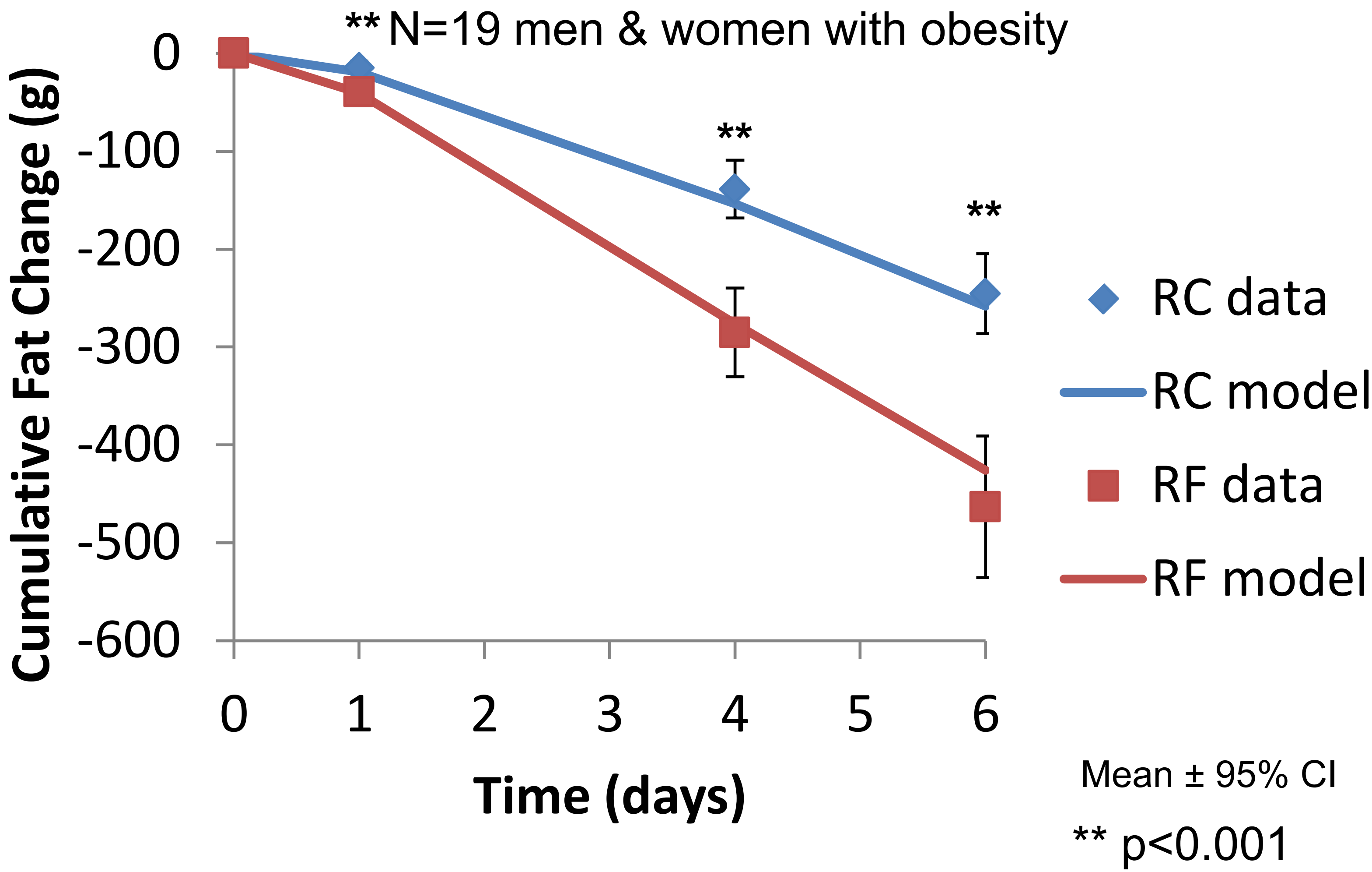
KD Hall et al. *Cell Metabolism* 22:427-436 (2015).

Only RC Diet Increased Fat Oxidation



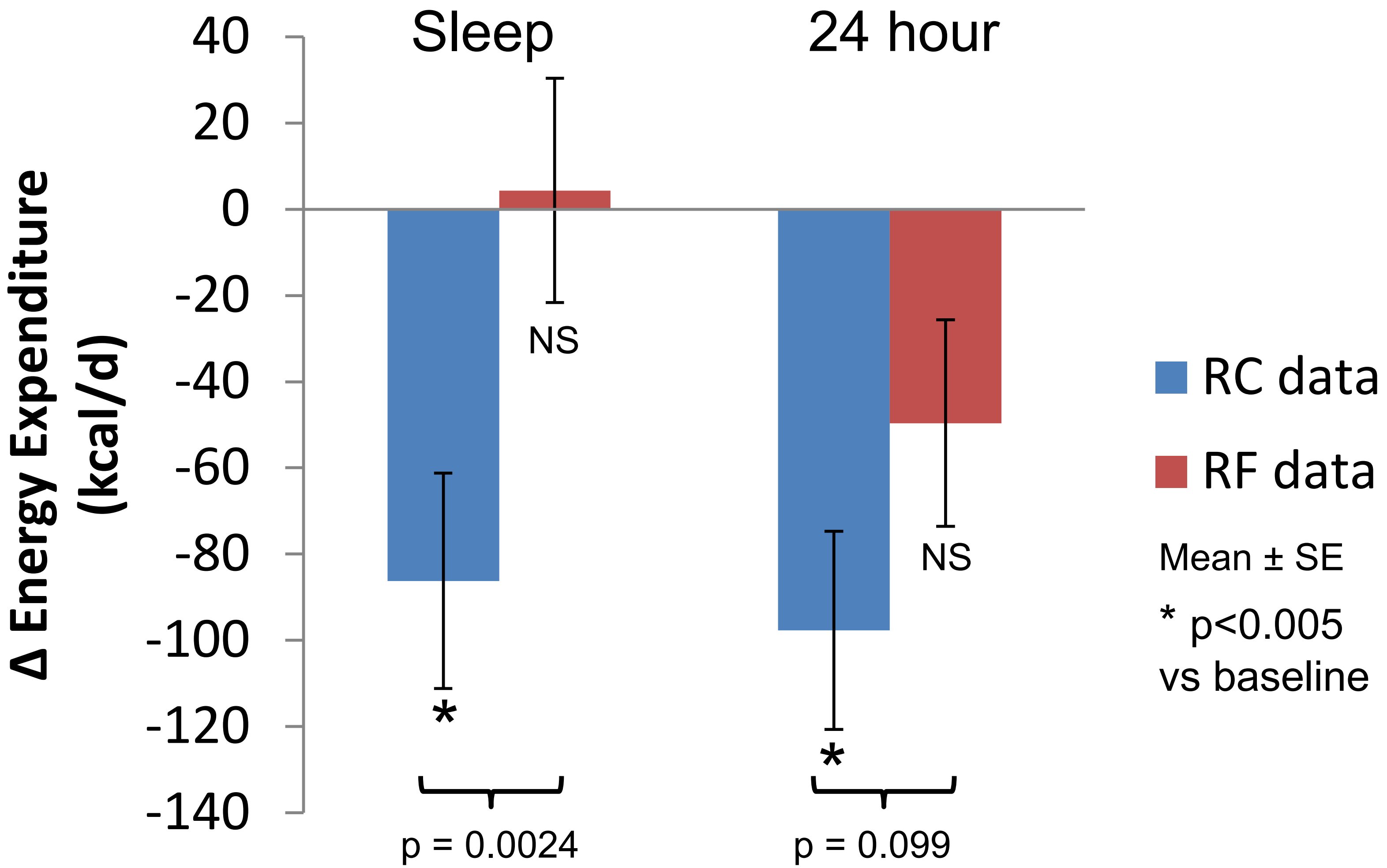
KD Hall et al. *Cell Metabolism* 22:427-436 (2015).

More Cumulative Body Fat Loss with RF



KD Hall et al. *Cell Metabolism* 22:427-436 (2015).

Only RC *Decreases* Energy Expenditure



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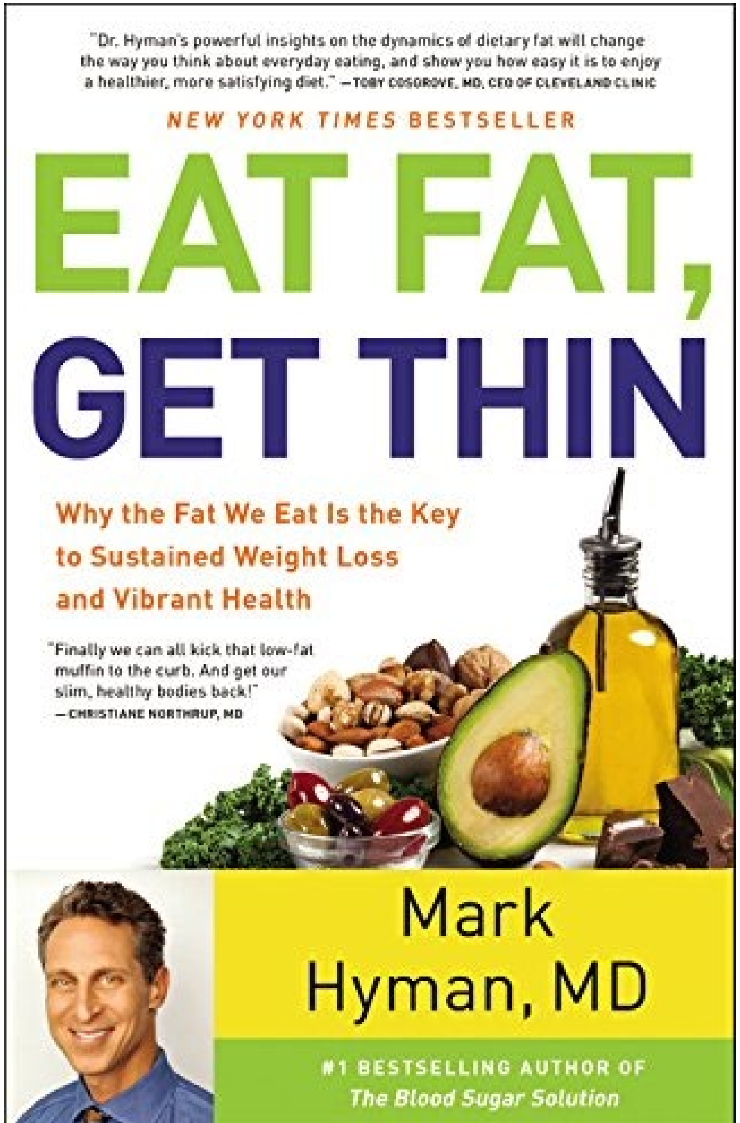
The Low Carb Community Responds

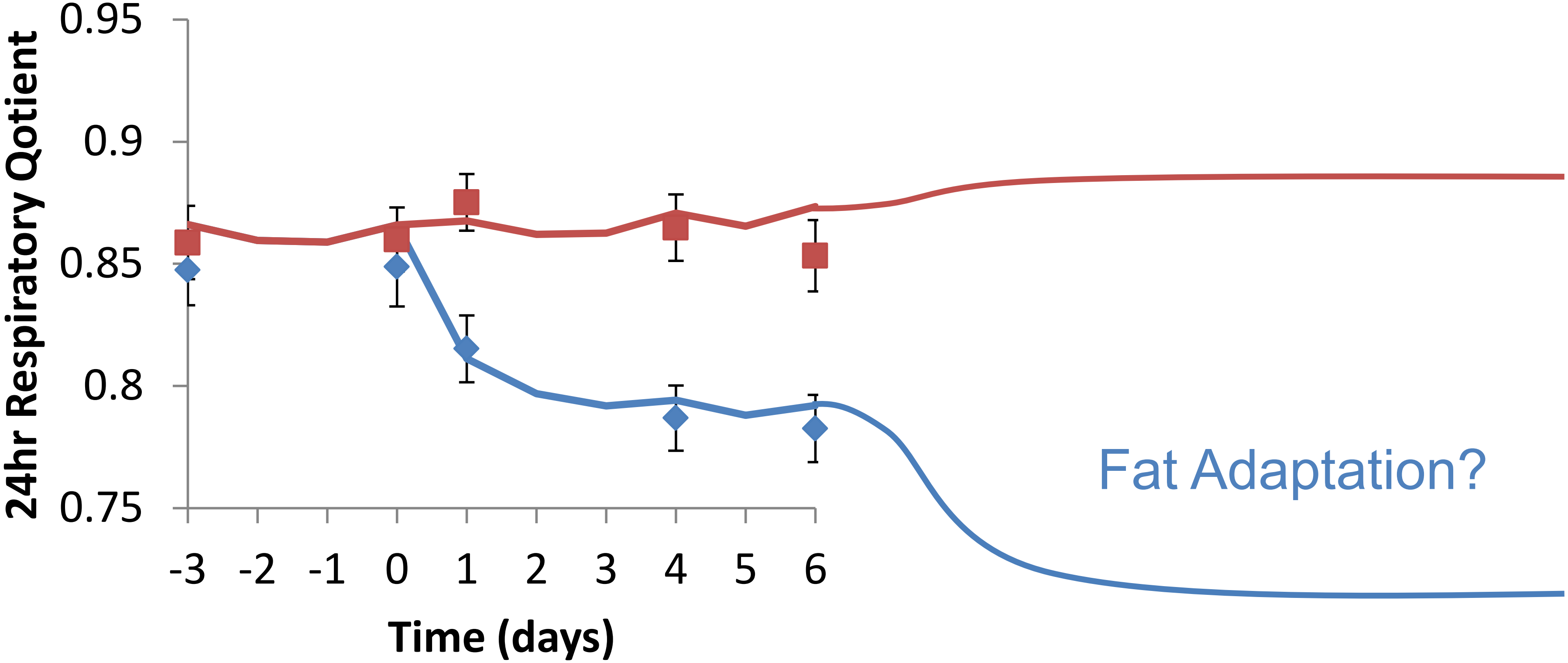


Recently, a study in *Cell Metabolism* by Kevin Hall from the National Institutes of Health attracted a lot of buzz in the news and online…[but] **there were some real problems with the study**

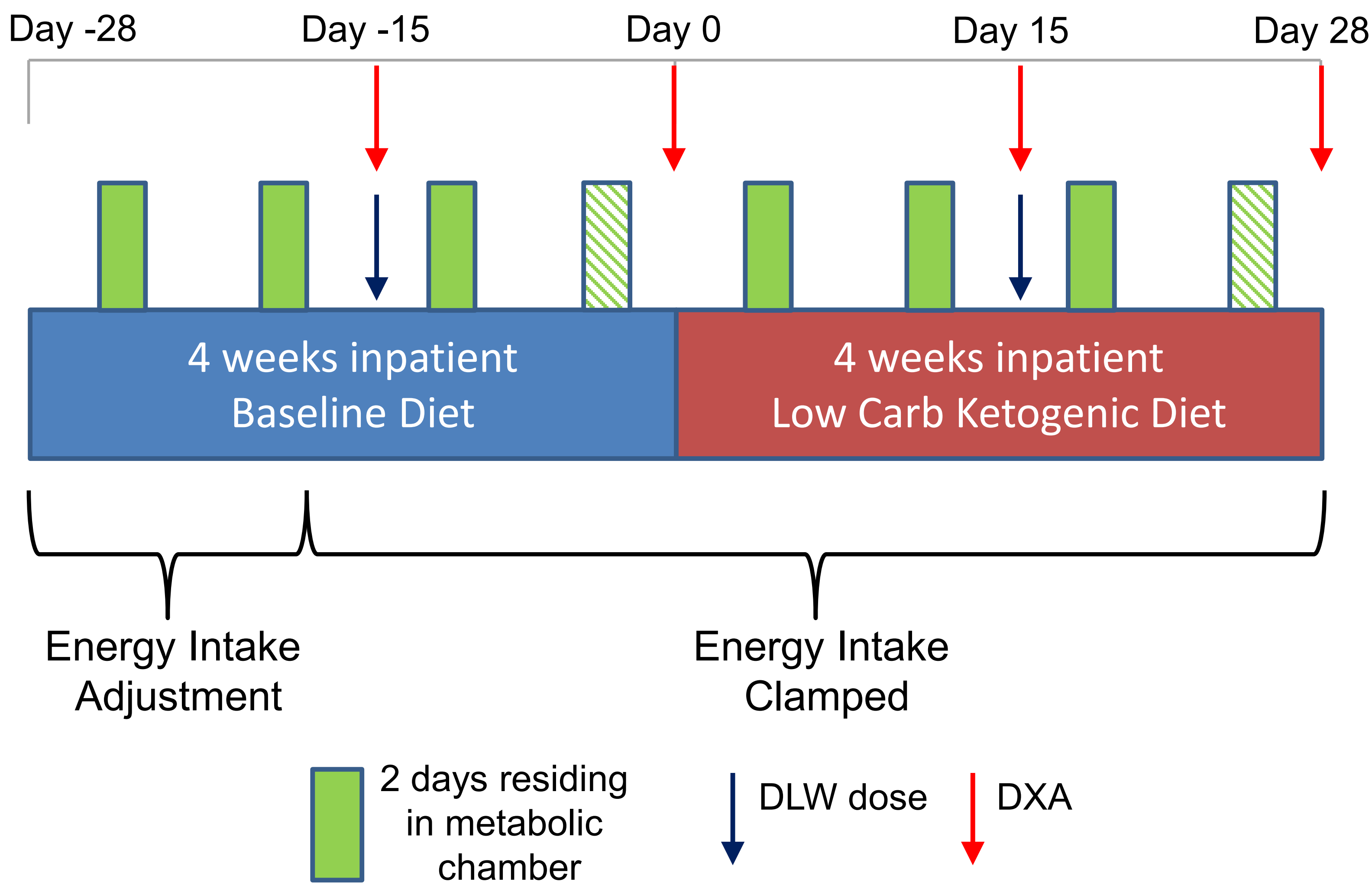
- The **low-carb diet wasn't low at all**, actually, with 29 percent of calories coming from carbs, including refined carbs. A true low-carb diet would have less than 10 percent of calories from carbs.
- It was a **very short-duration study (only six days)** conducted on only nineteen people who were contained in a metabolic ward where all the food was provided…It showed what happened in a vacuum but not in real life.

Mark Hyman, MD
Eat Fat, Get Thin (2016)

Hypothetical Extended Duration Study

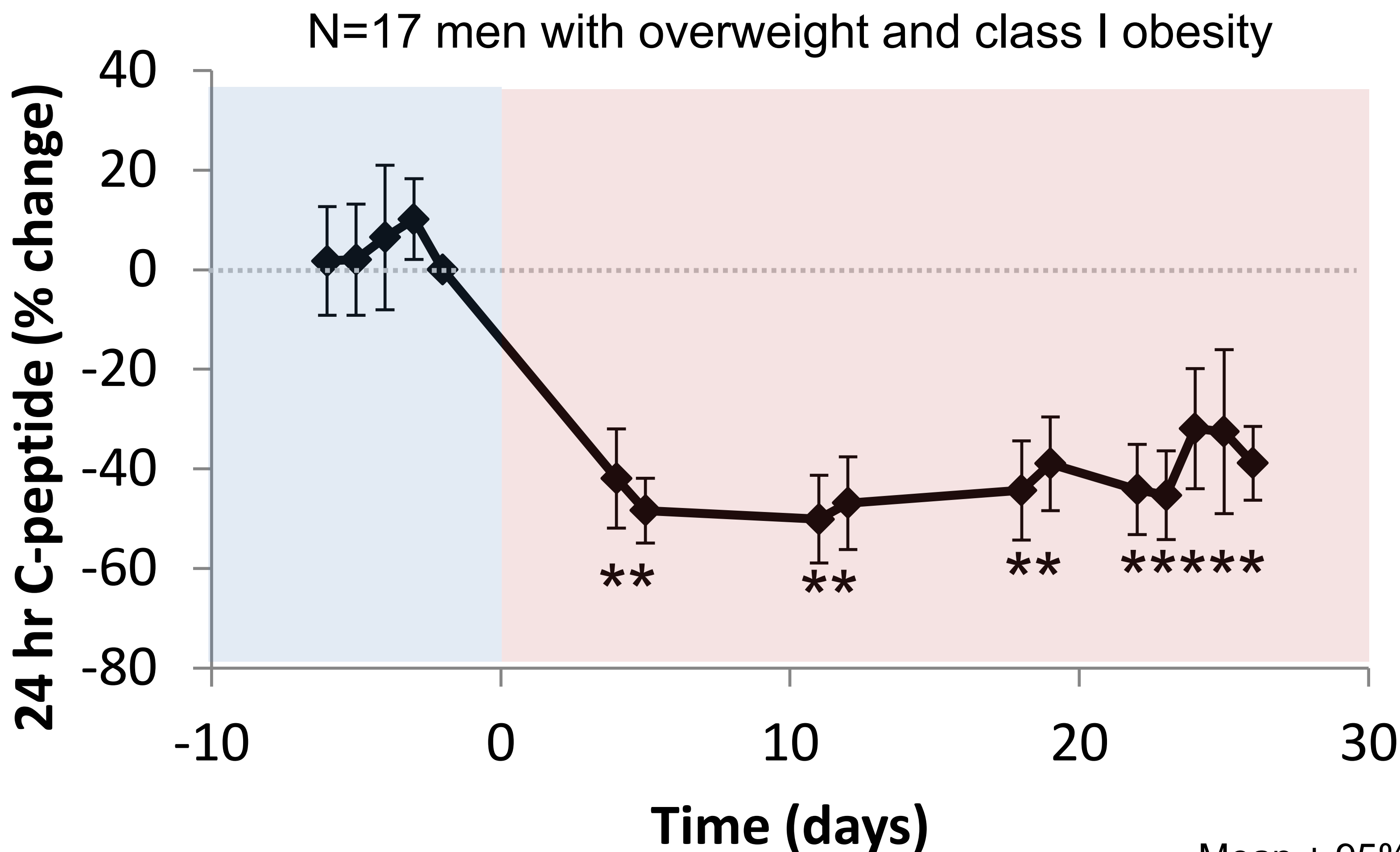


2 Month Isocaloric Ketogenic Diet Study



KD Hall et al. *AJCN 104:324–33* (2016).

Rapid & Persistent Decrease in Insulin Secretion



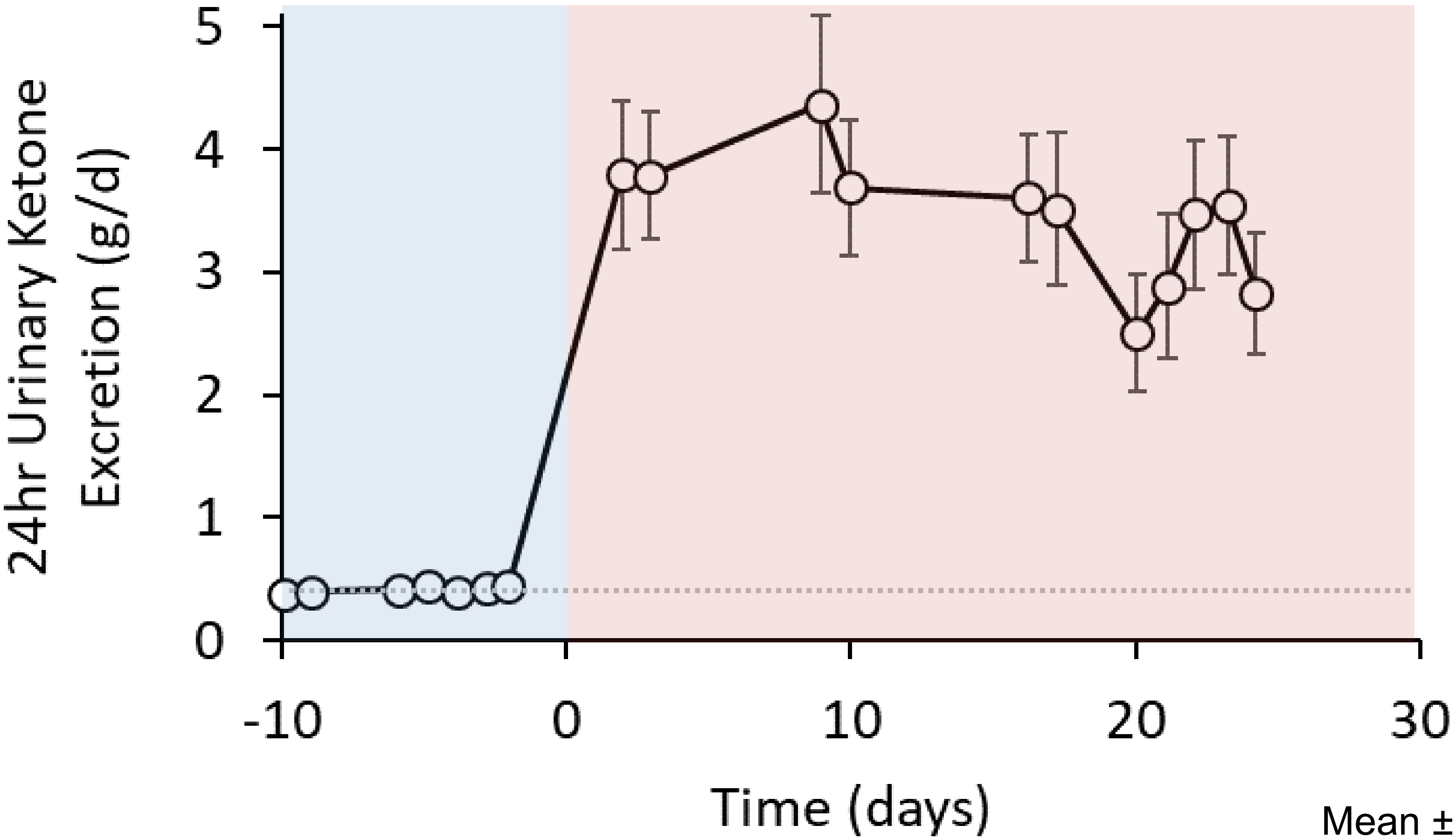
Mean ± 95% CI

* $p<0.0033$

KD Hall et al. *AJCN 104:324–33* (2016).

Rapid & Persistent Increase in Ketosis

N=17 men with overweight and class I obesity

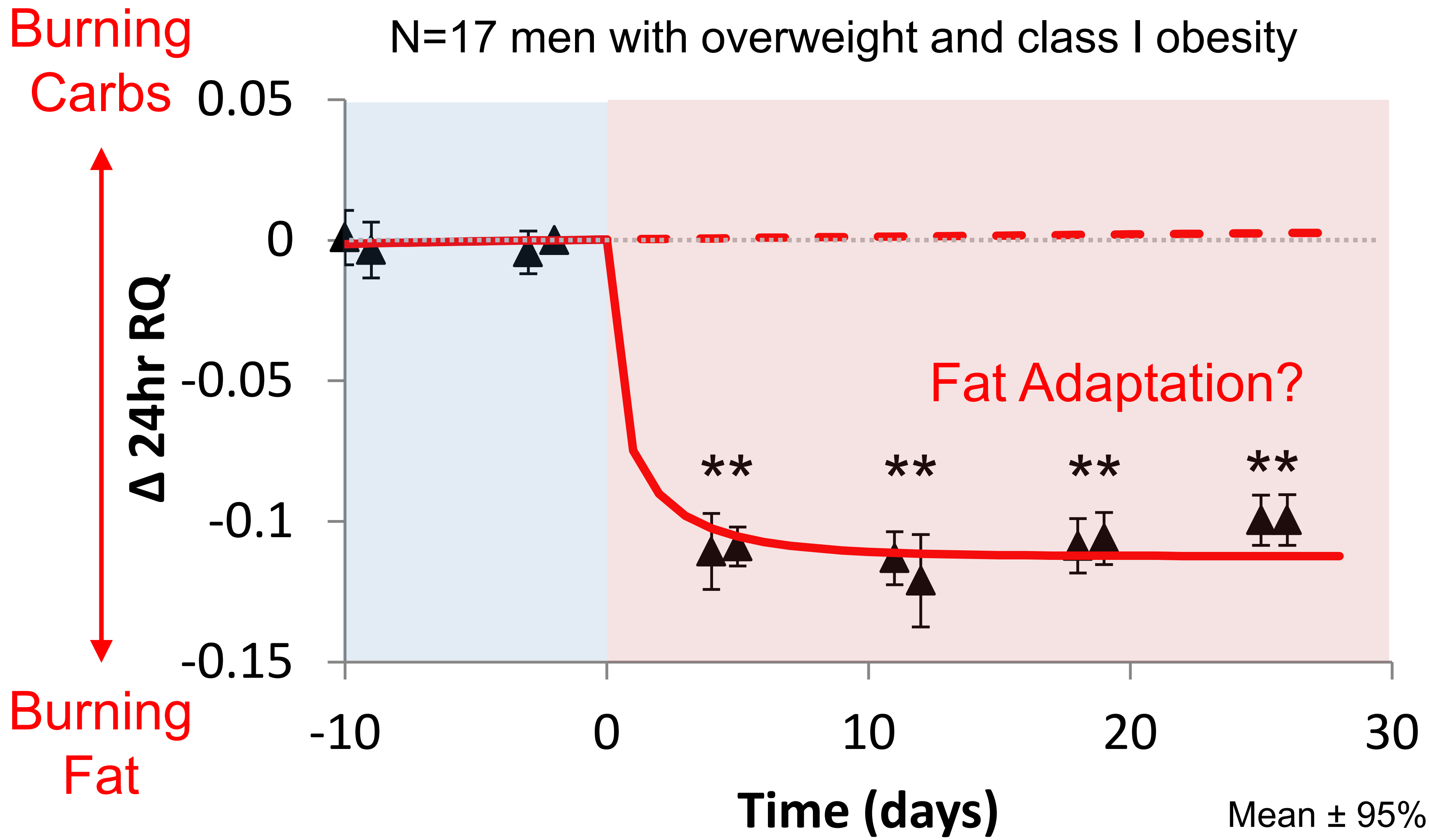


Mean ± SEM

KD Hall et al. *AJCN 104:324–33* (2016).

Rapid & Persistent Shift to Fat Oxidation

N=17 men with overweight and class I obesity

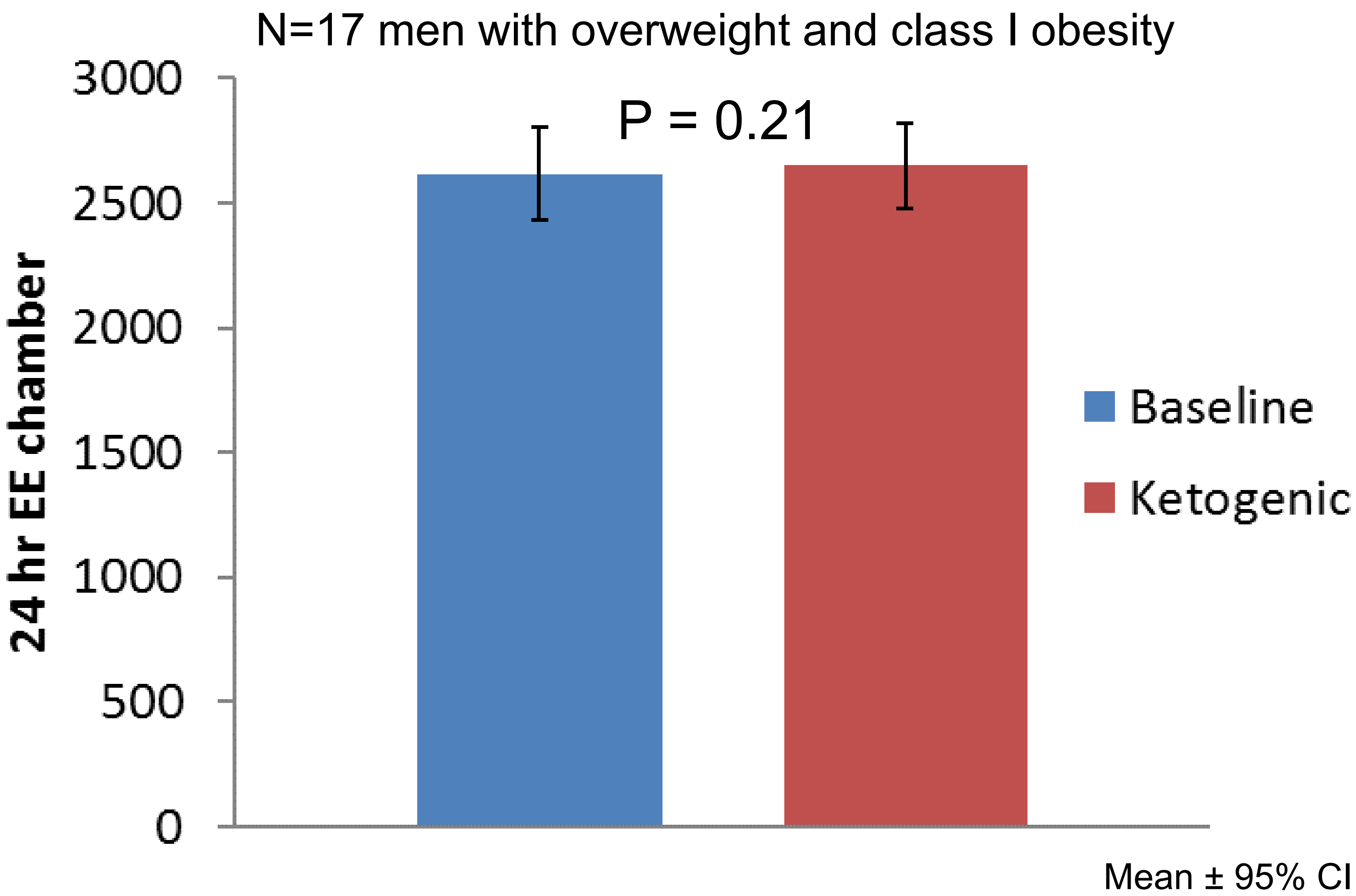


Mean ± 95% CI

*p<0.0045

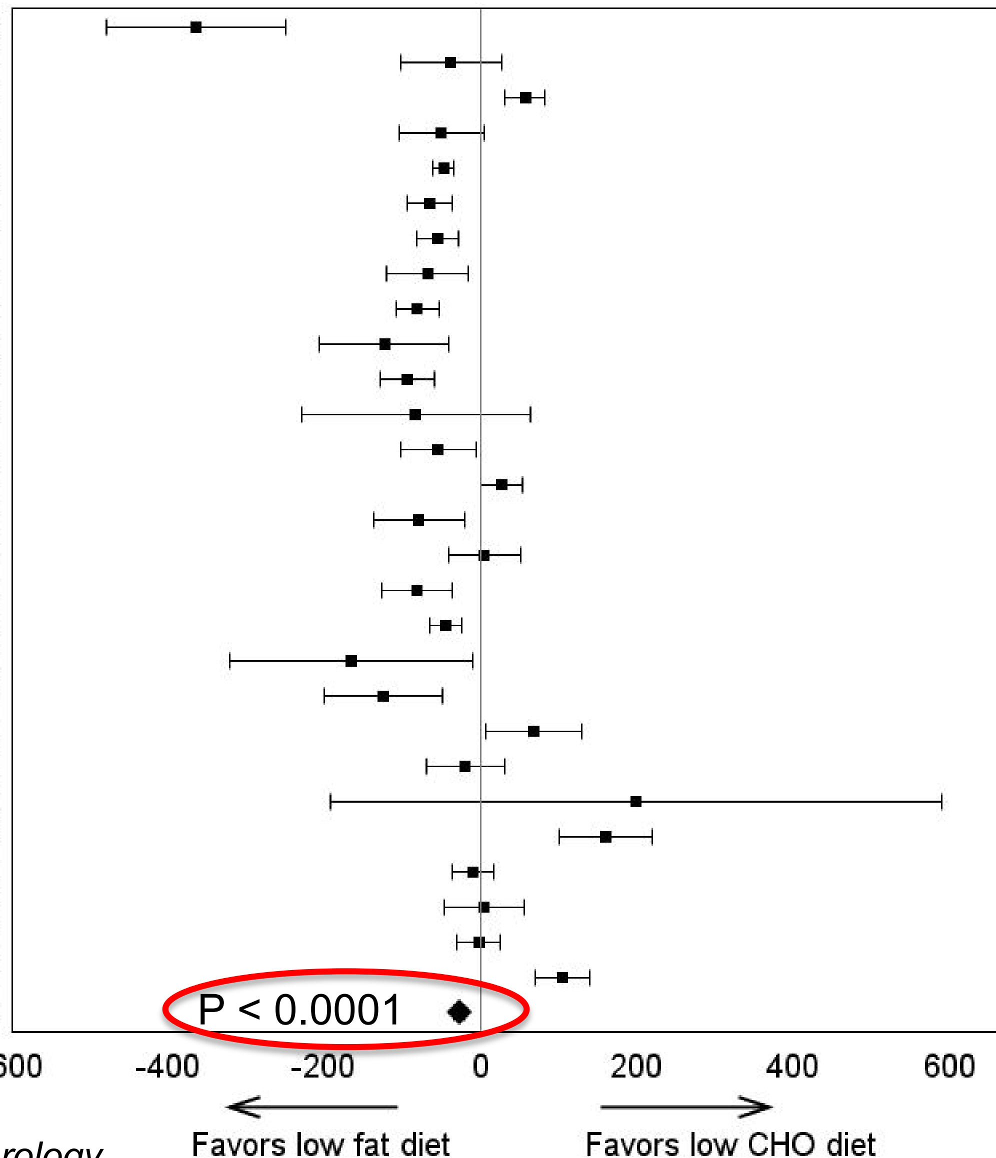
KD Hall et al. *AJCN 104:324–33* (2016).

No Significant Effect on Daily Expenditure



KD Hall et al. *AJCN 104:1488-90* (2016).

Energy Expenditure: Isocaloric Carb vs. Fat

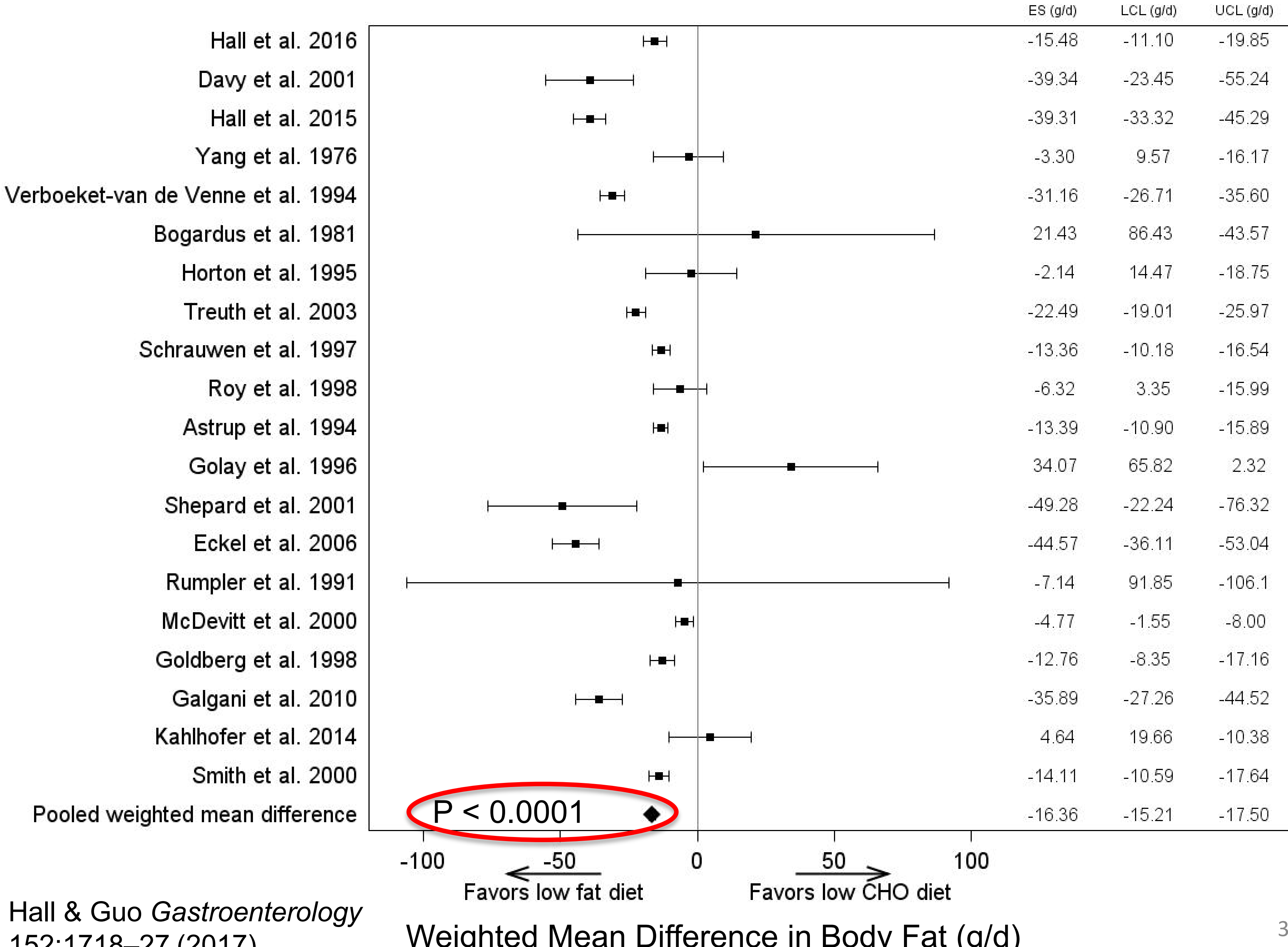


	ES (Kcal/d)	LCL (Kcal/d)	UCL (Kcal/d)
Bandini et al. 1994	-365.0	-479.6	-250.4
Shetty et al. 1994	-38.3	-103.2	26.7
Hall et al. 2016 & 2019	56.6	31.6	81.6
Davy et al. 2001	-50.4	-104.4	3.5
Hall et al. 2015	-48.1	-62.3	-33.9
Verboeket-van de Venne et al. 1994	-65.5	-95.1	-35.9
Verboeket-van de Venne et al. 1996	-55.0	-81.8	-28.2
Hill et al. 1991	-68.6	-121.5	-15.6
Thearle et al. 2013	-80.9	-108.8	-53.0
Hurni et al. 1982	-123.6	-207.2	-40.1
Horton et al. 1995	-94.2	-128.8	-59.5
Schrauwen et al. 2000	-83.7	-230.2	62.8
Bergouignan et al. 2012	-54.3	-102.8	-5.8
Treuth et al. 2003	26.4	-0.0	52.7
Schrauwen et al. 1997	-79.6	-137.8	-21.5
Roy et al. 1998	4.9	-41.0	50.7
Dirlewanger et al. 2000	-81.3	-126.7	-35.9
Astrup et al. 1994	-45.2	-66.3	-24.2
Shepard et al. 2001	-166.3	-321.5	-11.1
Eckel et al. 2006	-125.0	-201.1	-48.9
Abbott et al. 1990	68.0	6.3	129.6
Cooper et al. 2009	-20.4	-70.5	29.7
Rumpler et al. 1991	198.0	-192.5	588.5
Ebbeling et al. 2012	159.0	99.2	218.8
McDevitt et al. 2000	-10.0	-36.9	16.9
Goldberg et al. 1998	4.8	-46.1	55.7
Galgani et al. 2010	-3.0	-29.9	23.9
Smith et al. 2000	105.2	70.5	139.9
Pooled weighted mean difference	-27.5	-34.1	-20.9

Weighted Mean Difference in Energy Expenditure (kcal/d)

Hall & Guo *Gastroenterology* 152:1718–27 (2017)

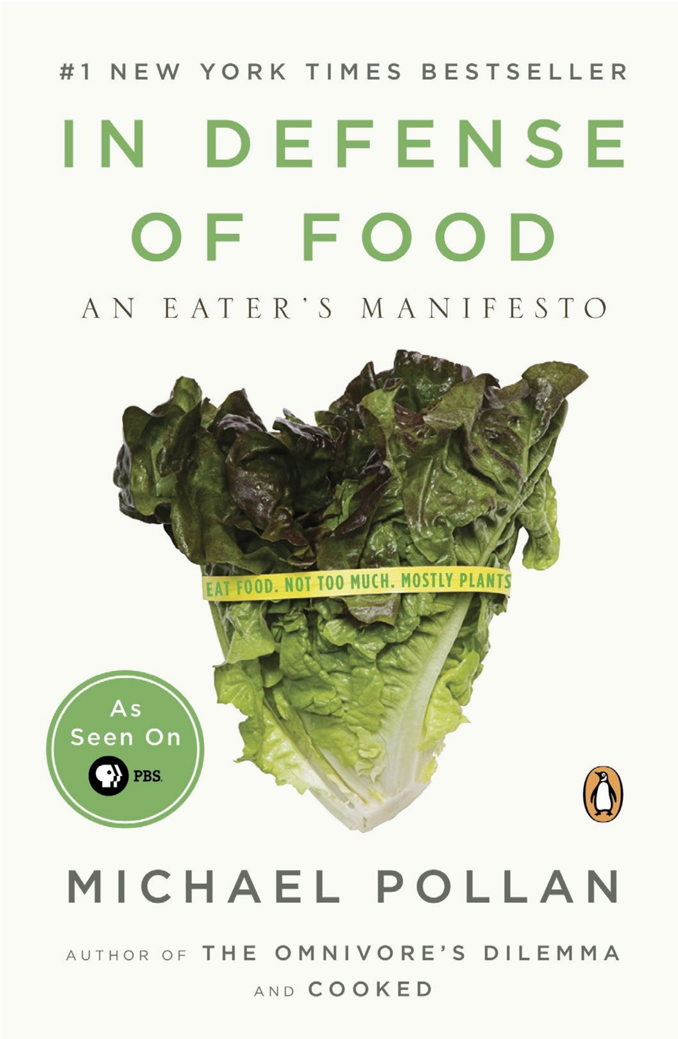
Body Fat: Isocaloric Carb vs. Fat



Hall & Guo *Gastroenterology* 152:1718–27 (2017)

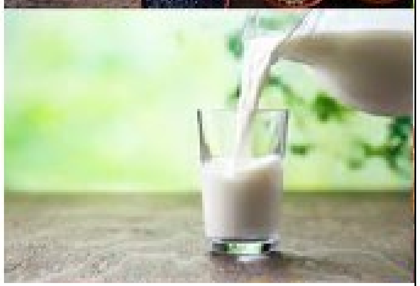
Can We Transcend the Diet Wars?

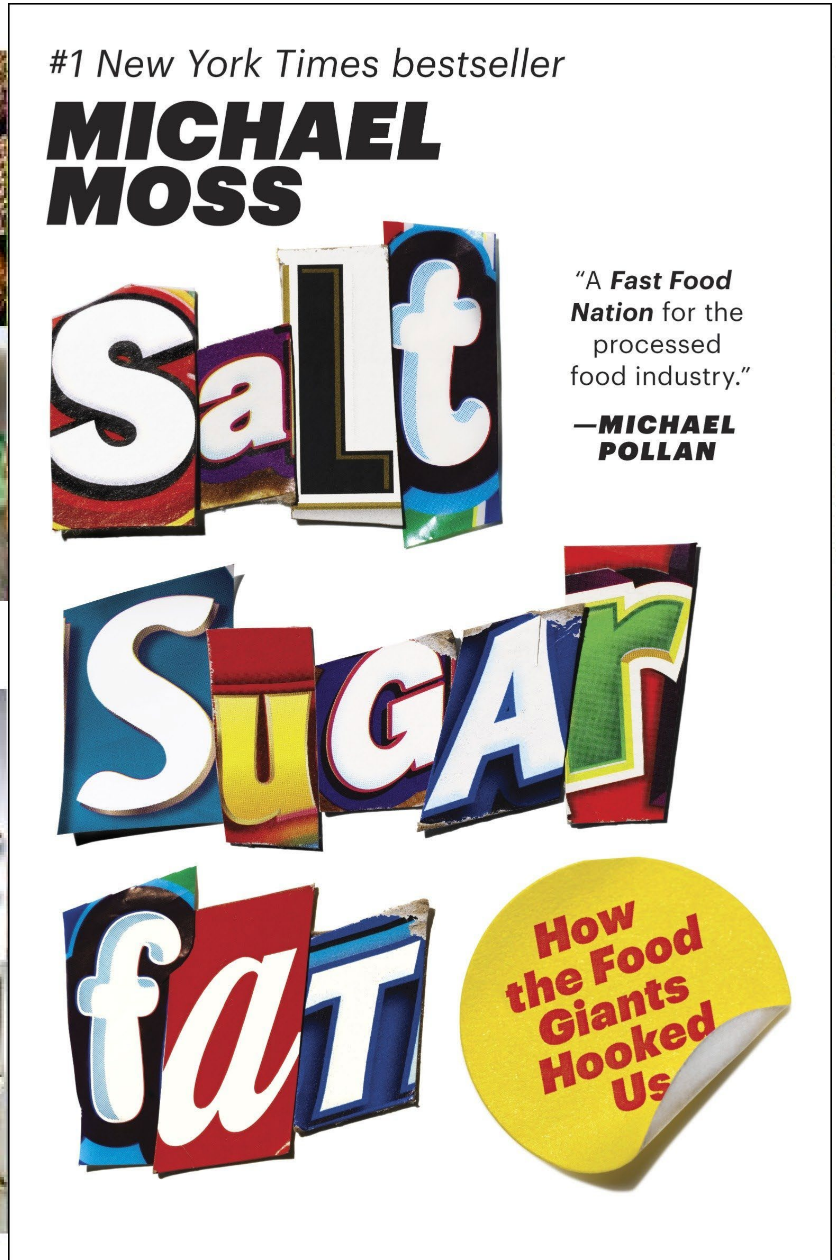
Diet Quality & "Nutritionism"



In the case of nutritionism, the widely shared but unexamined assumption is that the key to understanding food is indeed the nutrient. Put another way: Foods are essentially the sum of their nutrient parts.

Diet Quality & Ultra-processed Food





Unprocessed or minimally processed foods include fresh, dried, or frozen vegetables, grains, legumes, fruits, meats, fish, eggs, and milk. They are the basis of healthy dishes and meals.

Ultra-processed foods include fast food, sugary drinks, snacks, chips, candies, cookies, sweetened milk products, sweetened cereals, and sauce and dressings. They are nutritionally poor.

Ultra-processed vs Unprocessed Diets

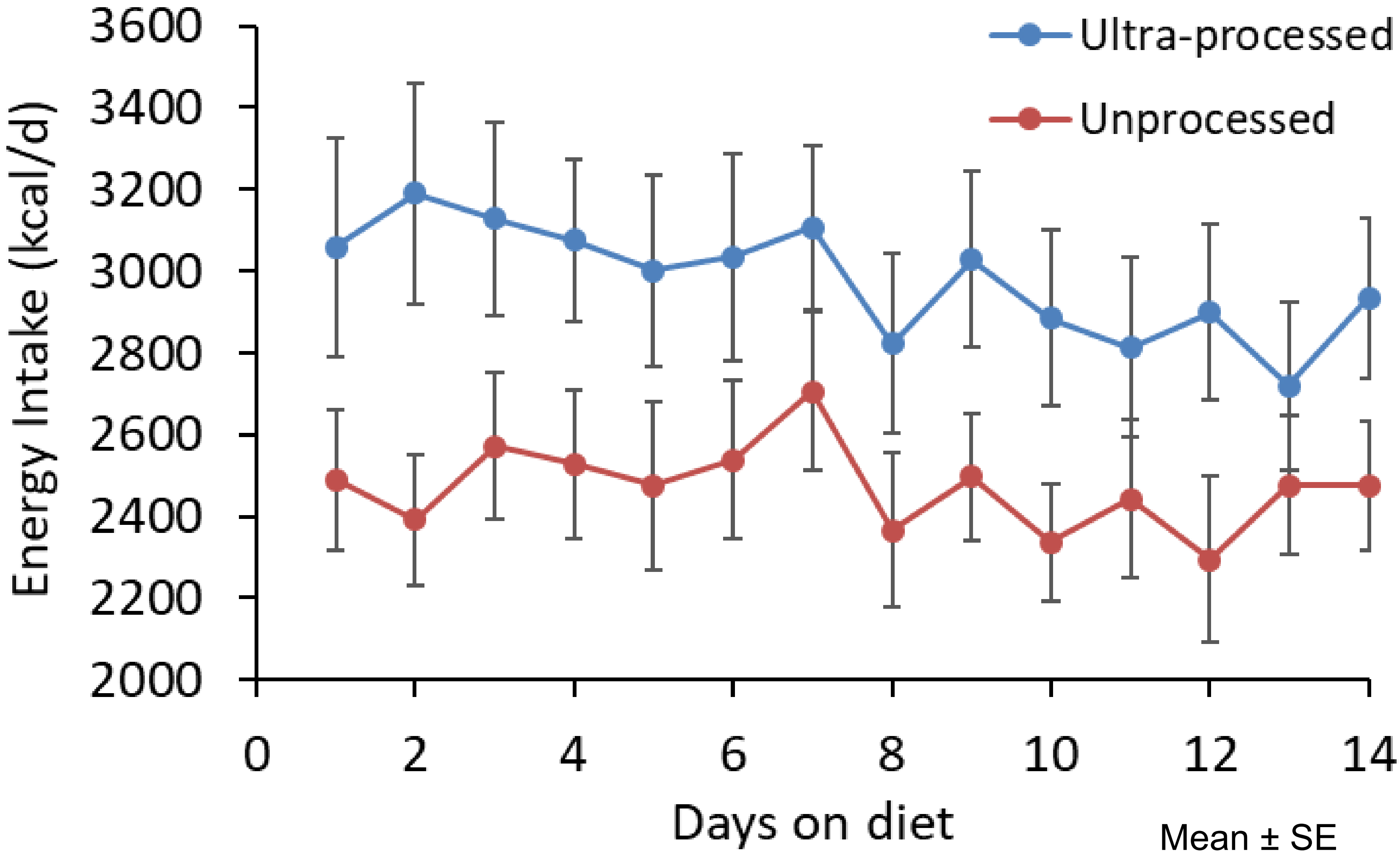
The meals had similar amounts of:
Calories, Carbs, Fat, Protein, Sugar, Sodium, Fiber

20 Adults were instructed to eat as much or as little as desired

Primary Outcome: Energy Intake Differences

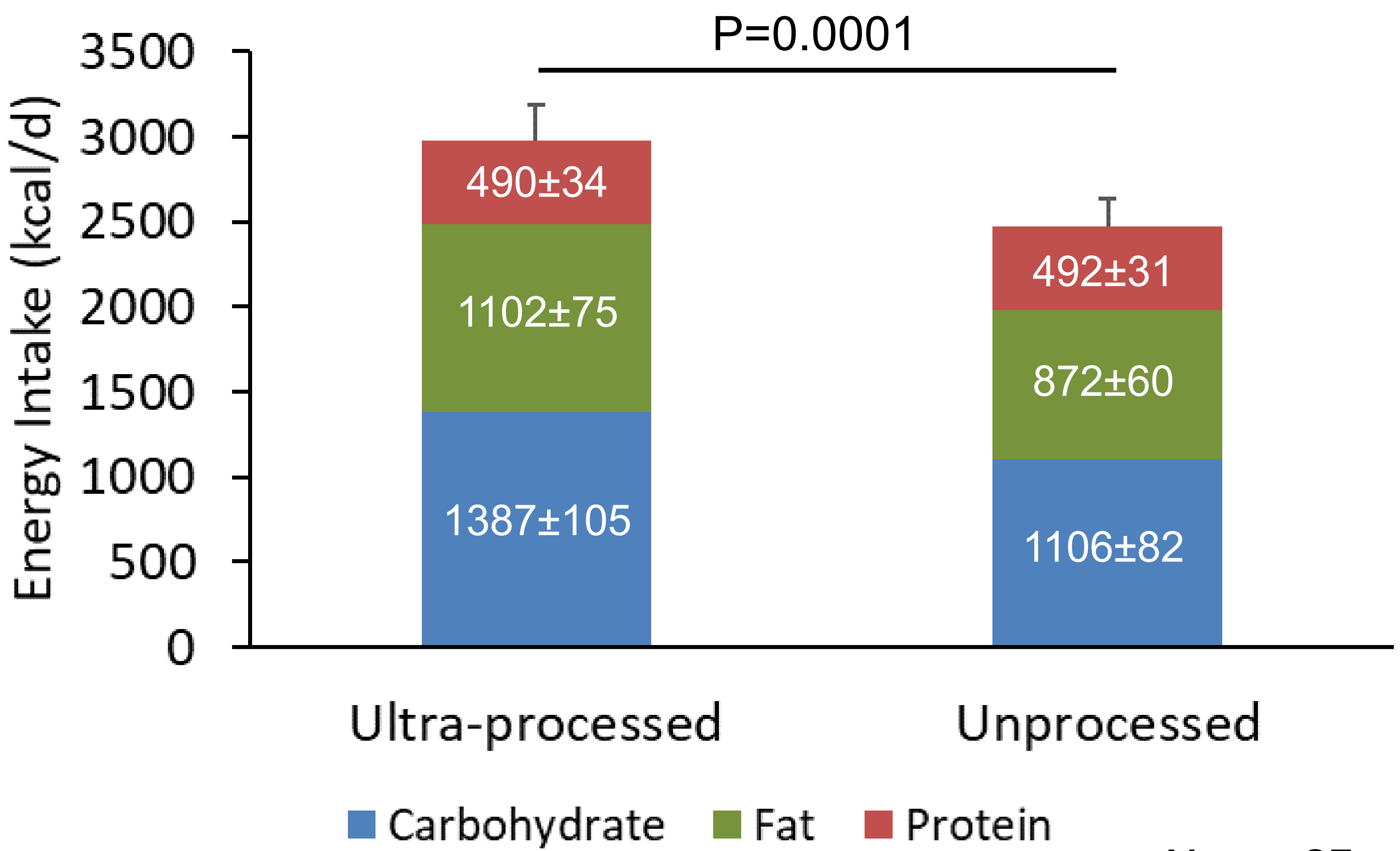
KD Hall et al. *Cell Metabolism* 30:1-11 (2019).

Ultra-processed Diets Cause Increased Intake



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

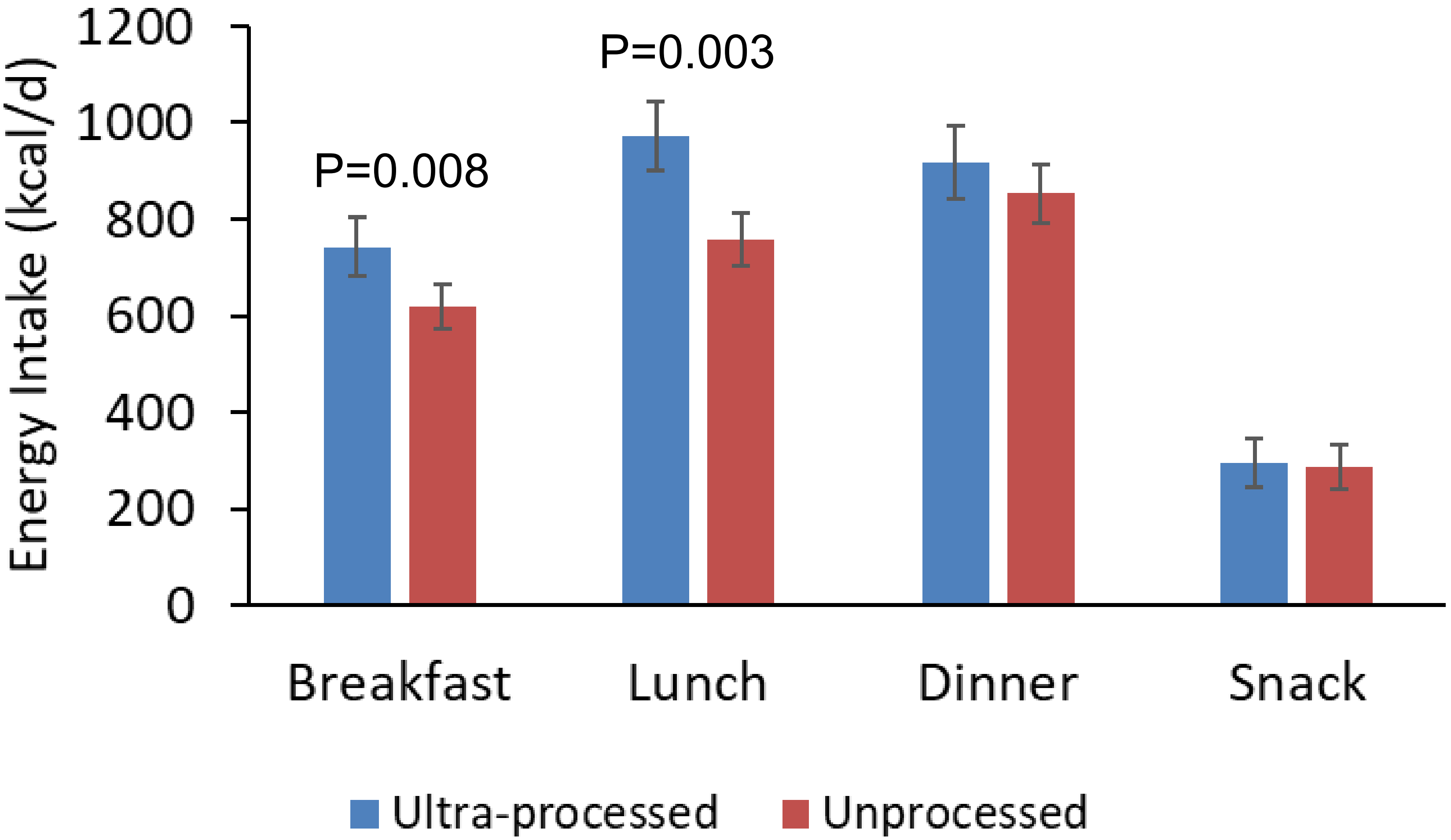
More Carbs & Fat with Ultra-processed Diets



Mean ± SE

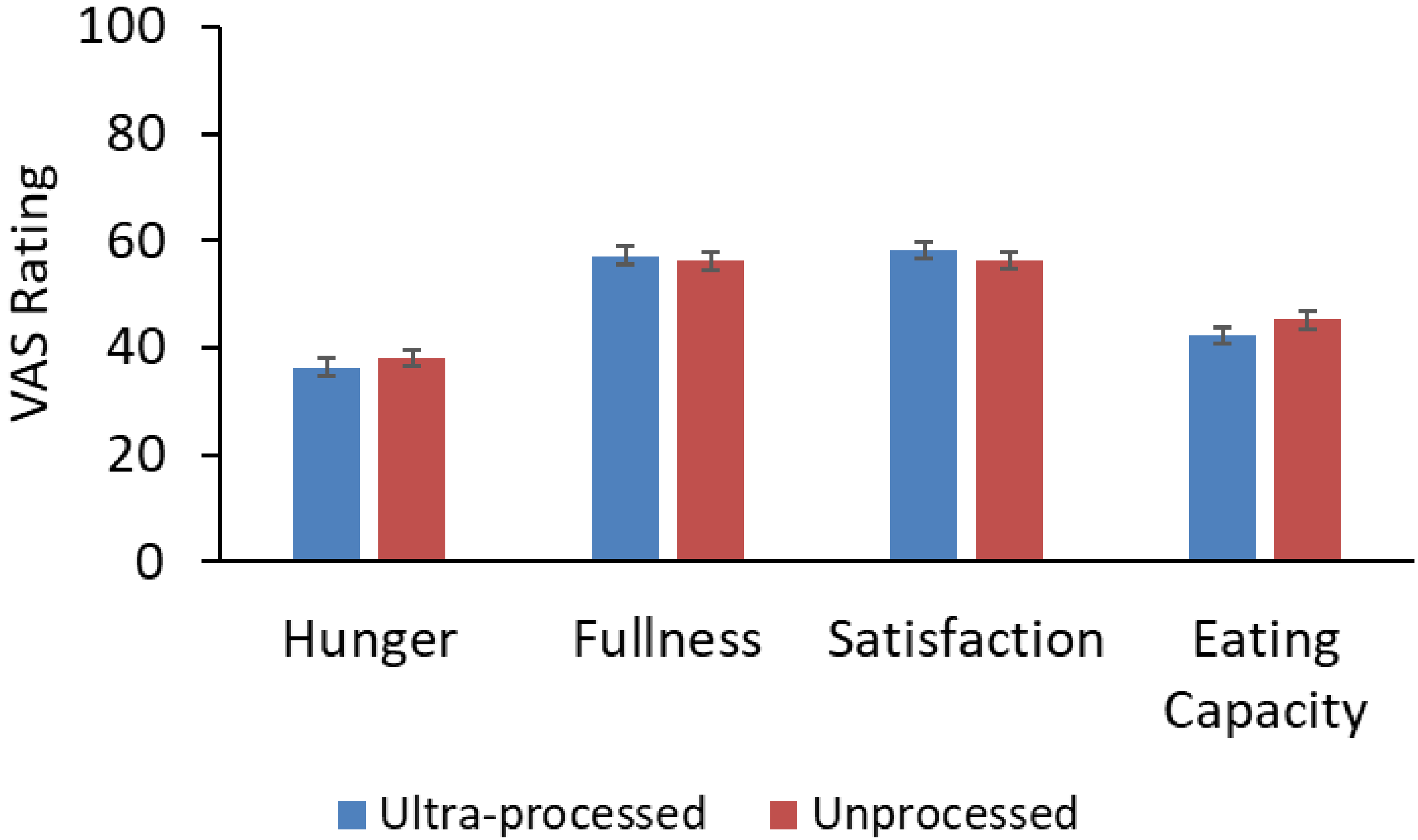
KD Hall et al. *Cell Metabolism* 30:1-11 (2019).

Larger Meals with Ultra-processed Diets



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

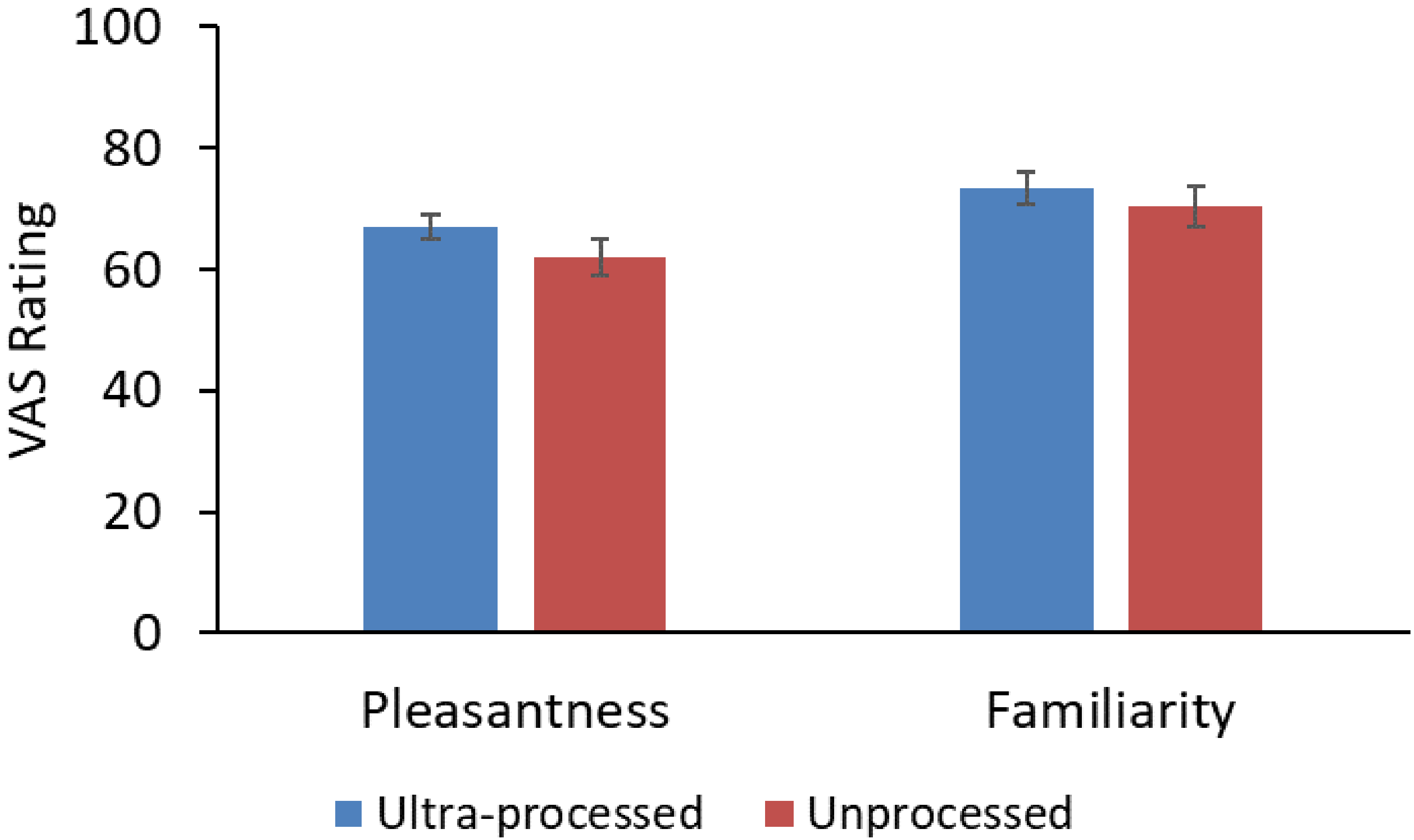
No Differences in Self-Reported Appetite



Mean ± SE

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

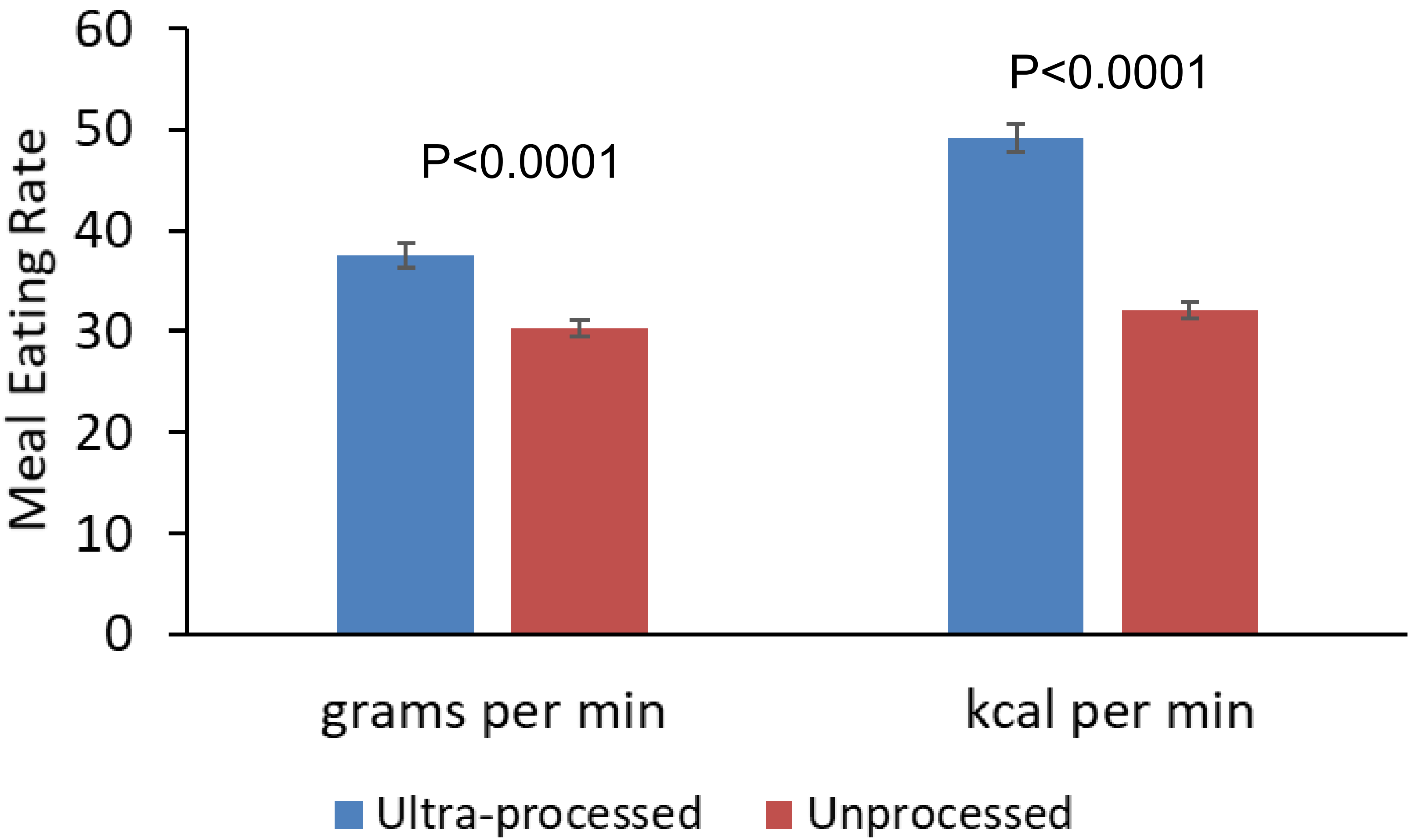
No Differences in Pleasantness or Familiarity



Mean ± SE

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

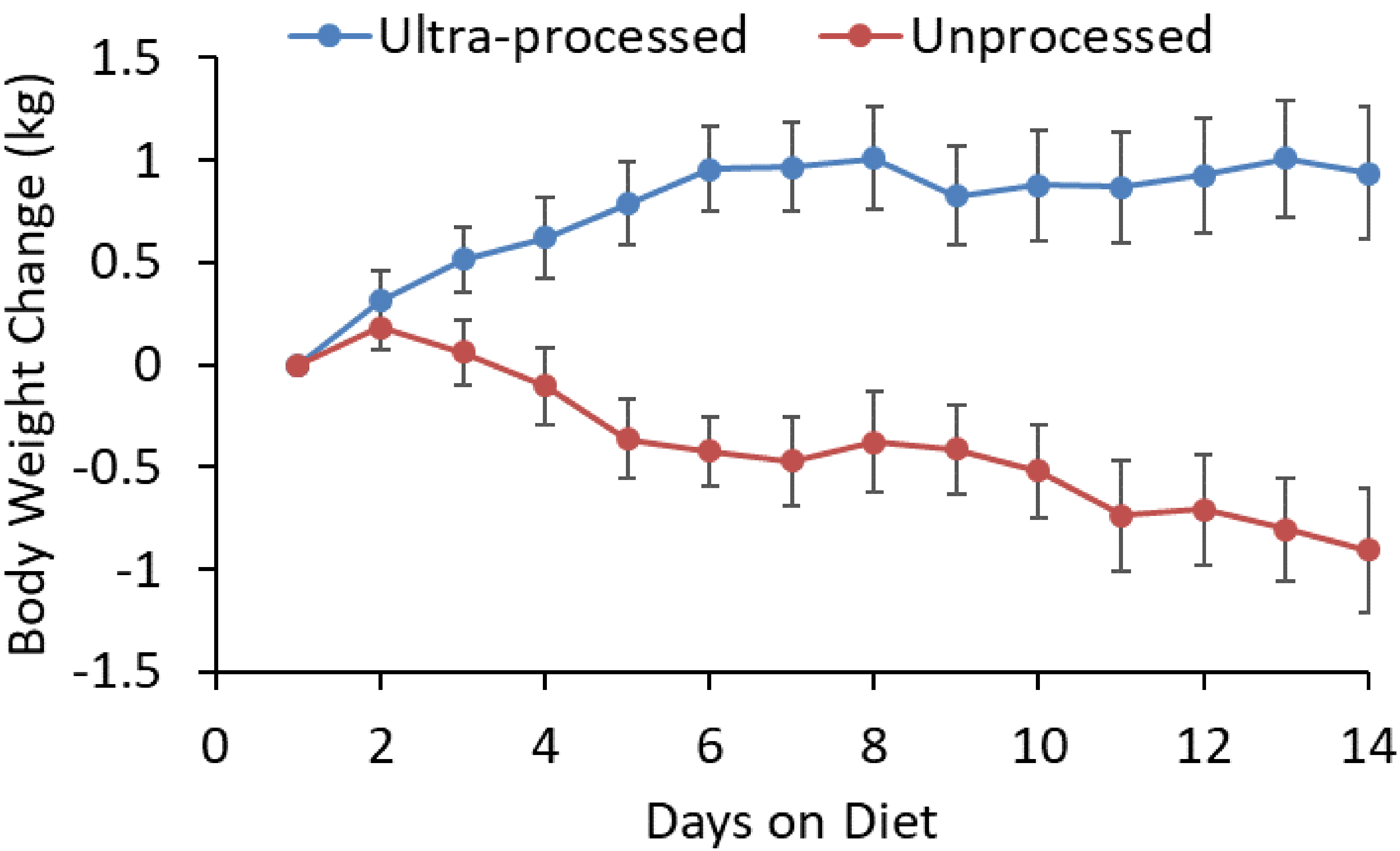
Faster Eating Rate for Ultra-processed Meals



Mean ± SE

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

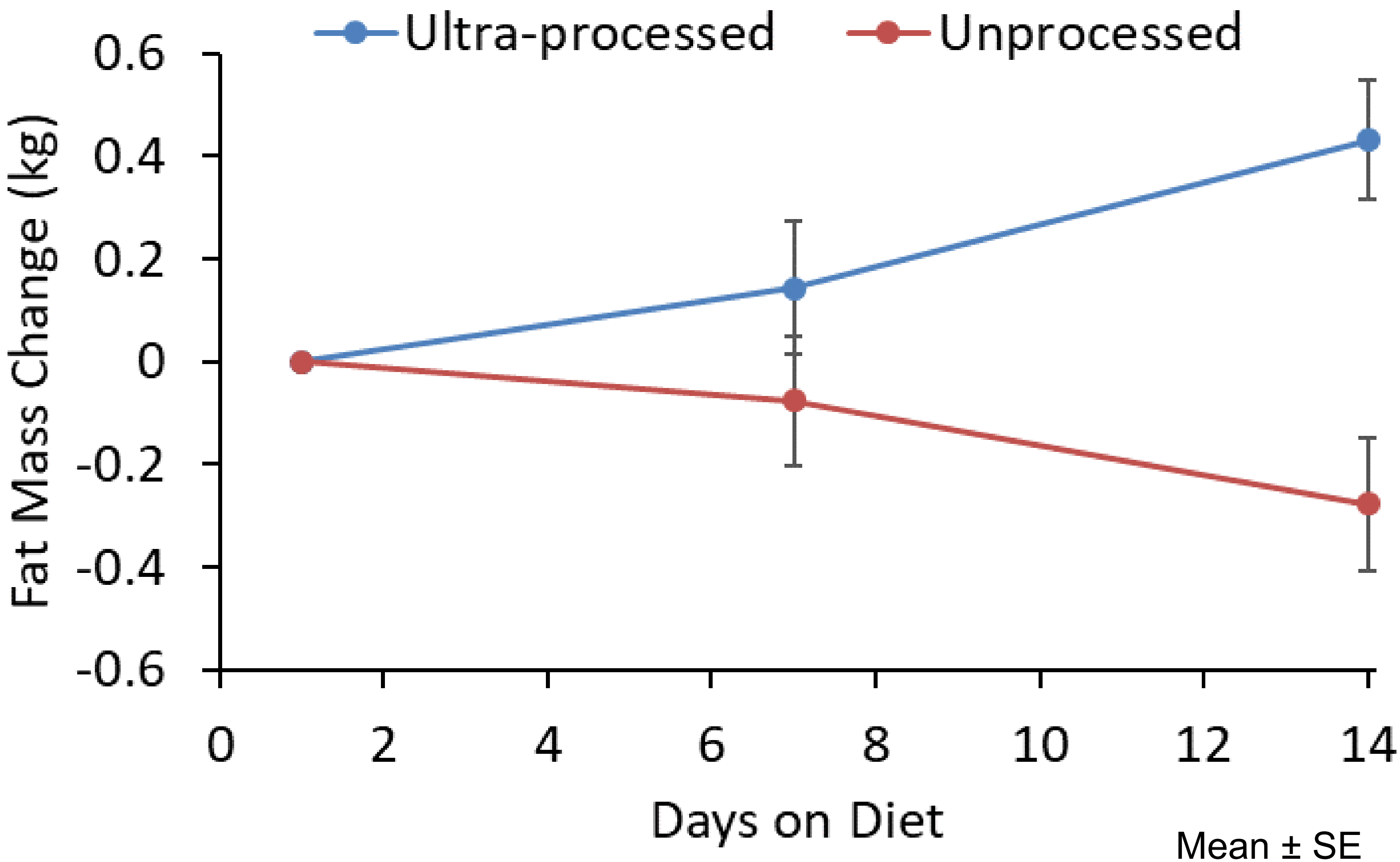
Ultra-processed Diets Cause Weight Gain



Mean ± SE

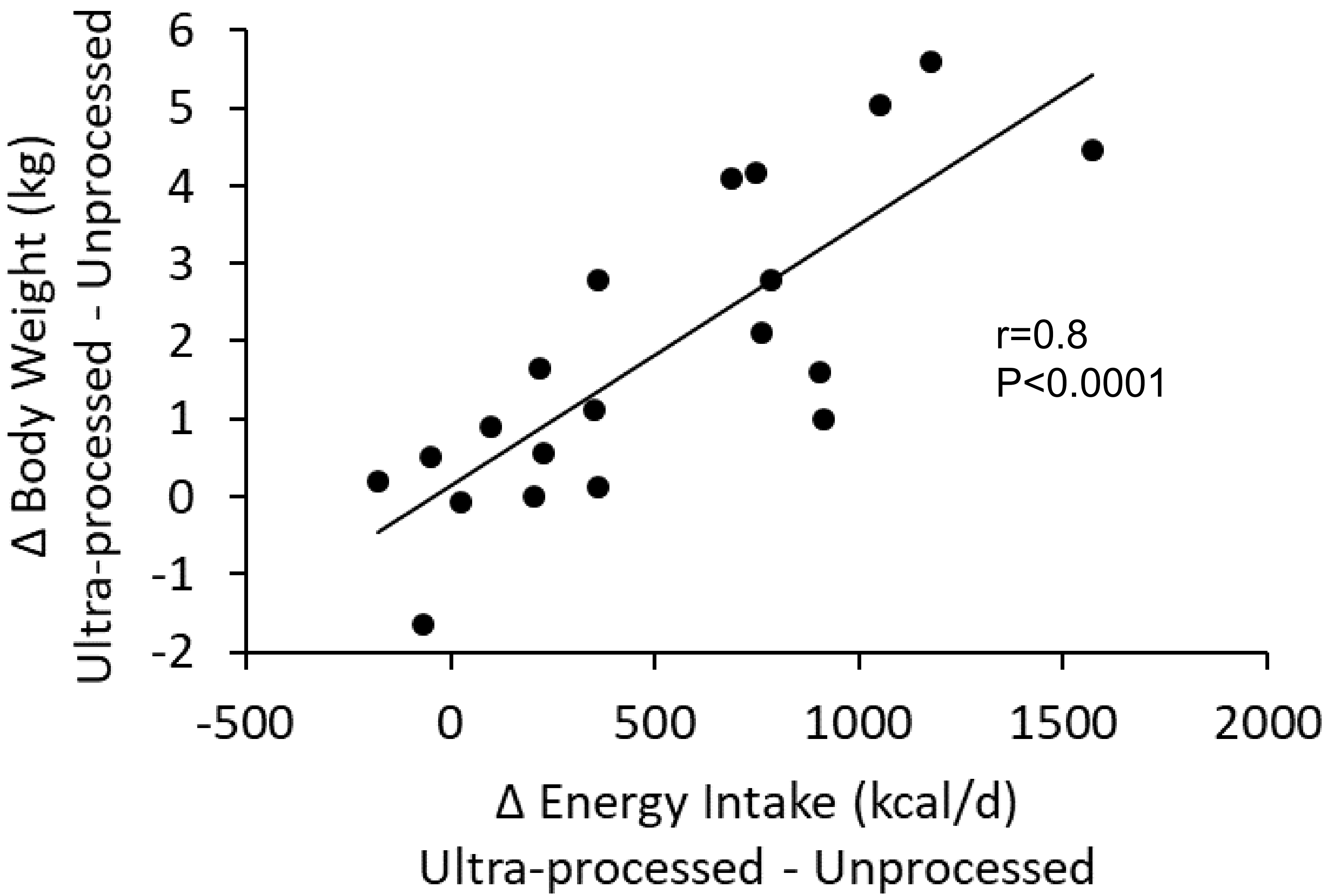
KD Hall et al. *Cell Metabolism* 30:1-11 (2019).

Ultra-processed Diets Cause Fat Gain



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

Substantial Individual Variability



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

Mechanisms?

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one program
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infinite possibilities

irp.nih.gov

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