Obesity Trials

From the Metabolic Ward to the Clinic

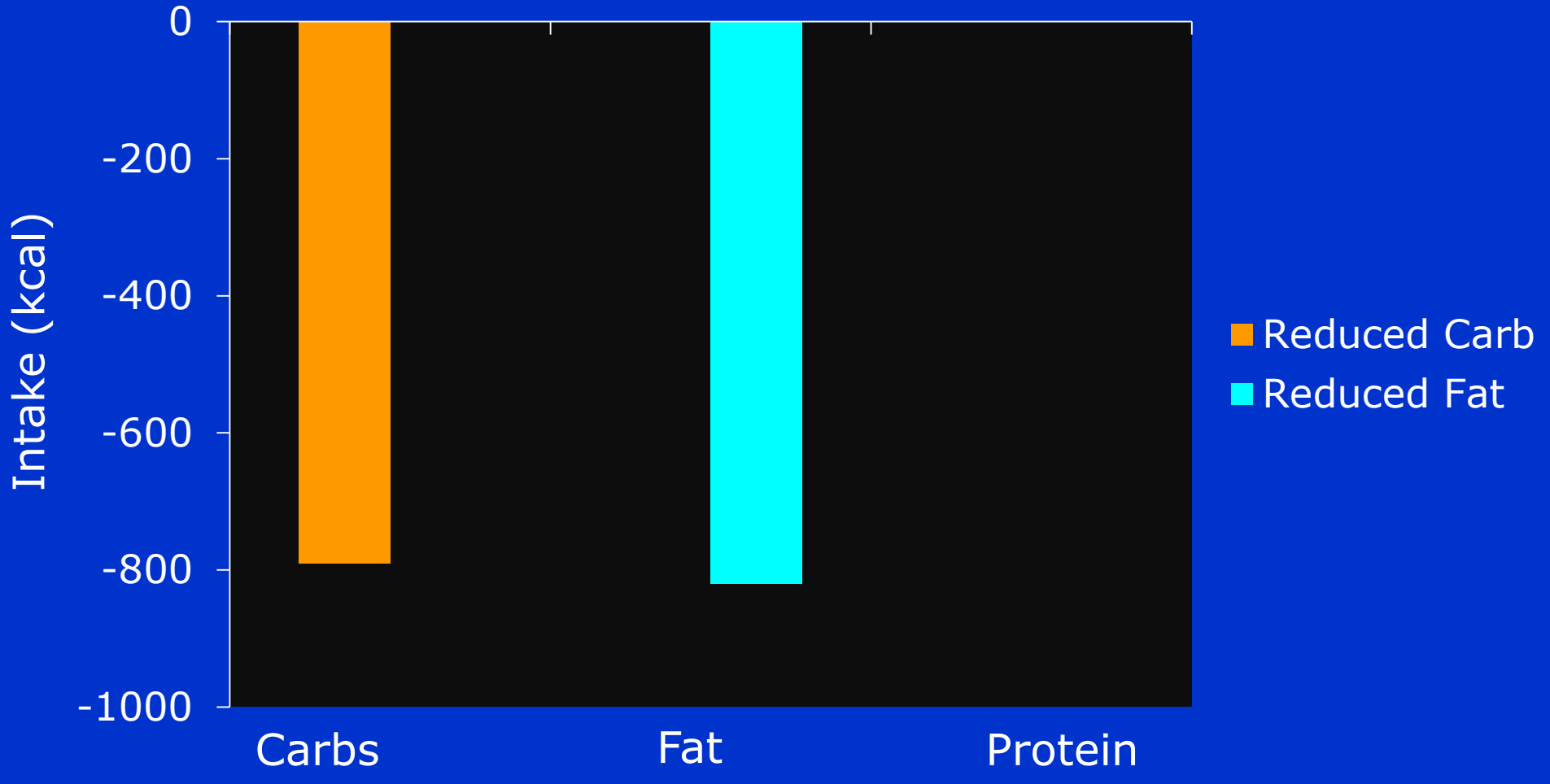
Christopher Case, M.D.

ccase@jcmg.org

Objectives

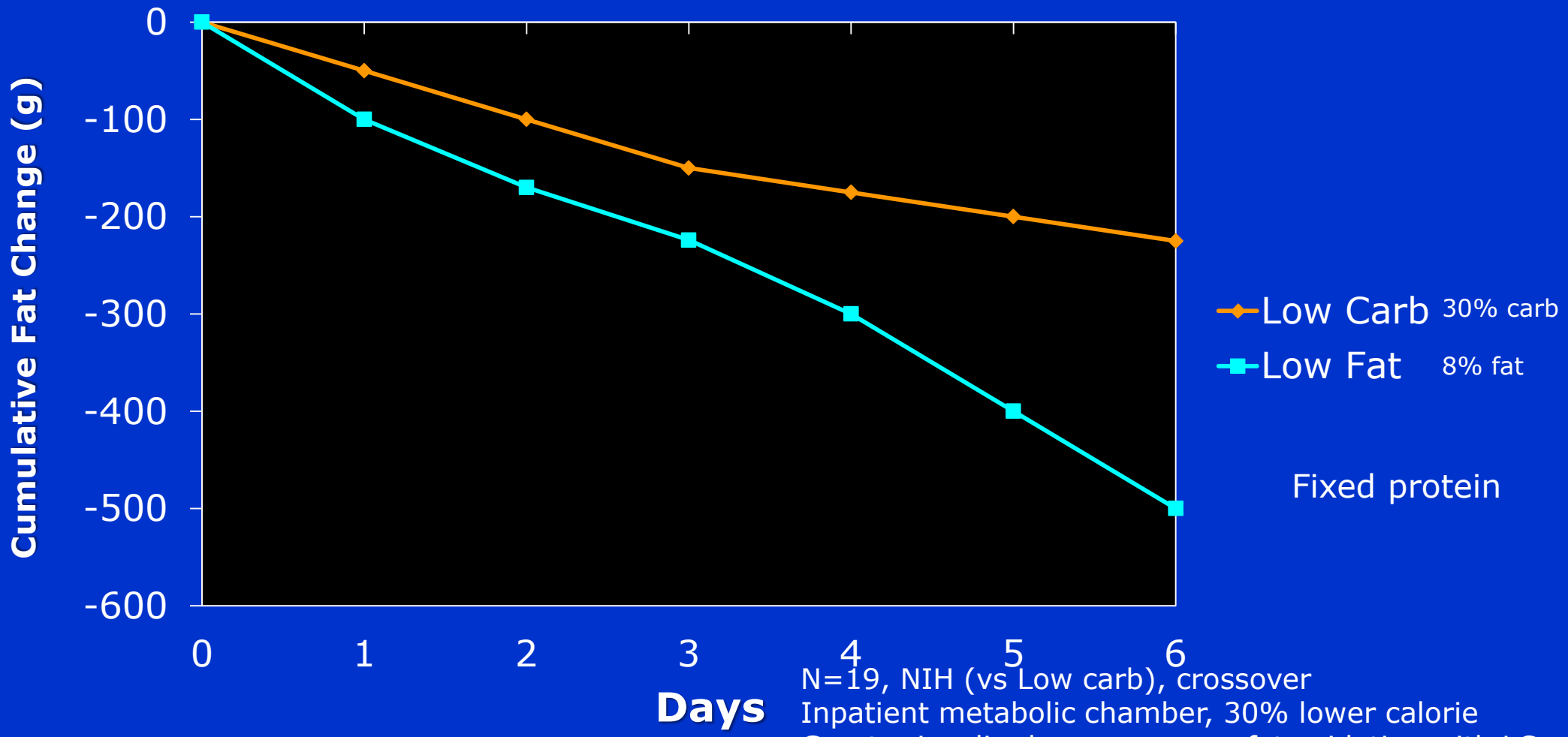
- Review recently published articles conducted in the metabolic wards
- Discuss how to translate and implement these conclusions in the obesity clinic with practical weight maintenance and weight loss techniques

Calorie for Calorie, Dietary Fat Restriction Results in More Body Fat Loss than Carbohydrate Restriction in People with Obesity



Hall et al. 2015, Cell Metabolism 22,1-10. Sept 1.

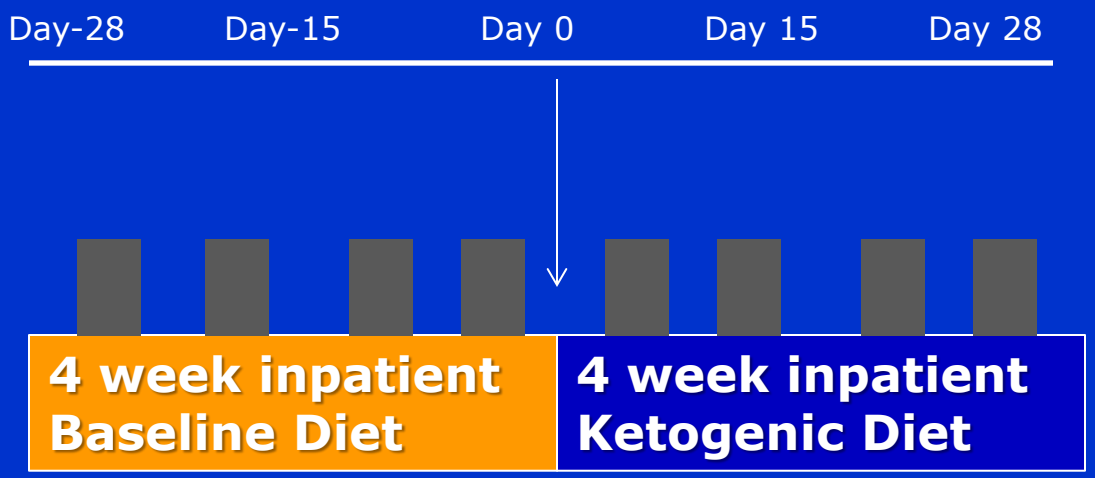
Calorie for Calorie, Dietary Fat Restriction Results in More Body Fat Loss than Carbohydrate Restriction in People with Obesity



N=19, NIH (vs Low carb), crossover
Inpatient metabolic chamber, 30% lower calorie
Greater insulin decrease, more fat oxidation with LC
Reduced carb had lower energy expenditure

Hall et al. 2015, Cell Metabolism 22,1-10. Sept 1.

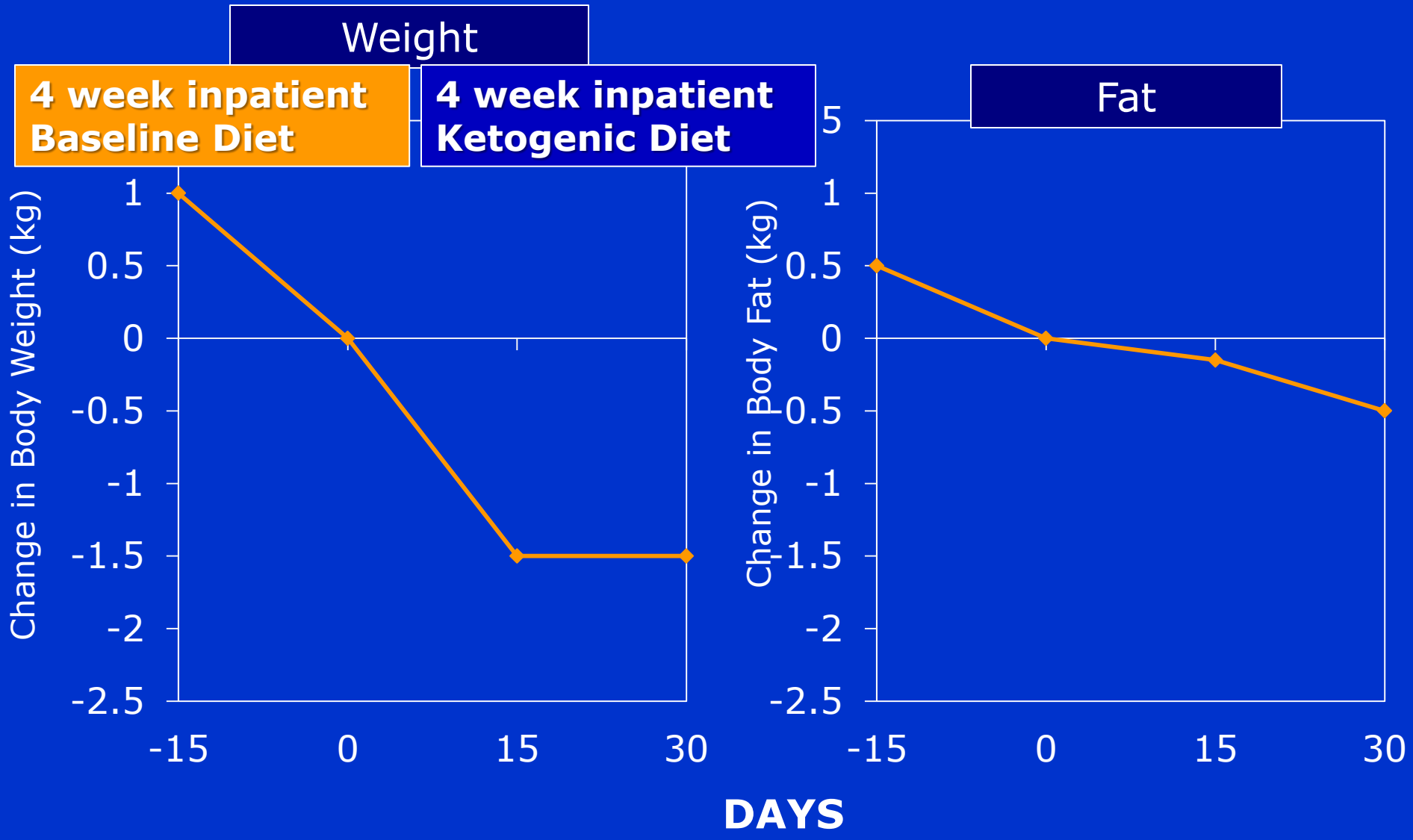
Energy expenditure and body composition changes after an isocaloric ketogenic diet in overweight and obese men



- Carb-insulin model of obesity suggests eating high carb diets sequesters fat in adipocytes and decreases energy expenditure.
- KD increase EE and body fat loss
- N=17
- Baseline high carb for 4 weeks then 4 weeks of isocaloric KD clamped protein (5% carb, fixed protein)
- 2 days in metabolic chamber =
- DXA/ EE - DLW

Hall et al. Am J Clin Nutr doi: 10.3945/acjn.116.133561

Energy expenditure and body composition changes after an isocaloric ketogenic diet in overweight and obese men



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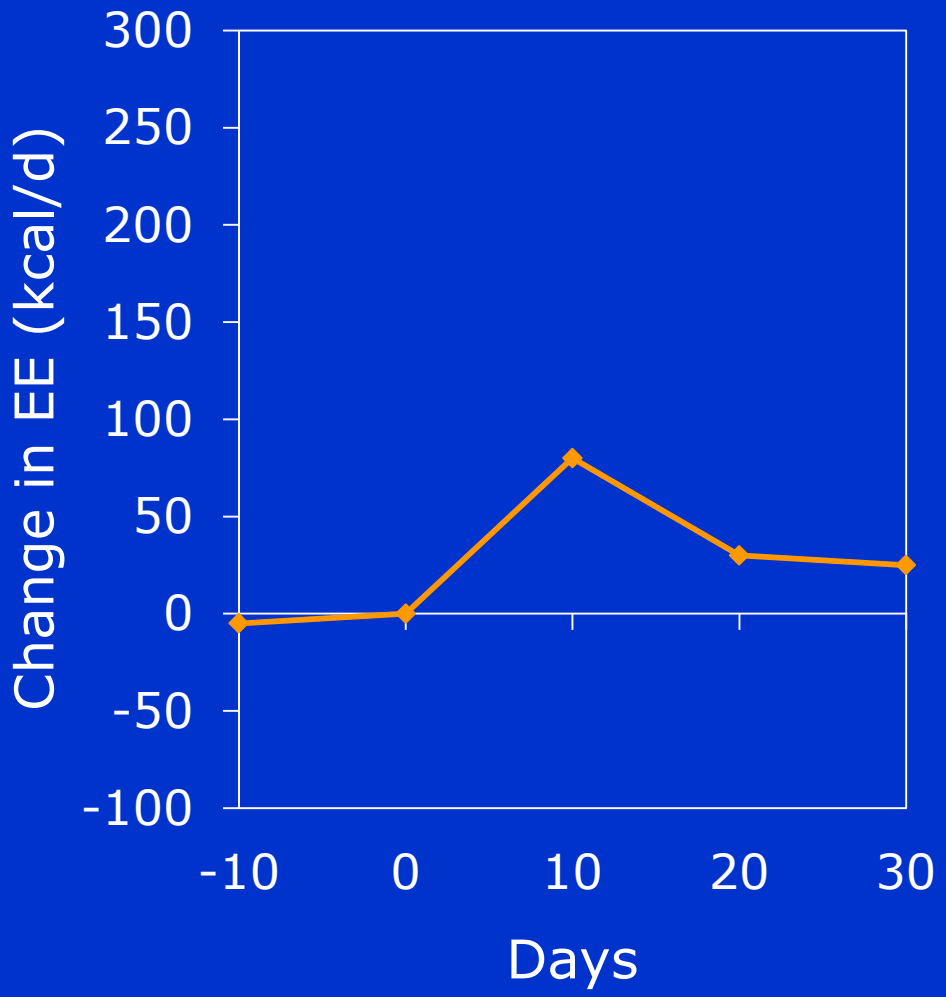
Energy expenditure and body composition changes after an isocaloric ketogenic diet in overweight and obese men



- Subjects lost weight and body fat throughout the study
- RQ decreased within 1 week
- KD increased EE 57 kcal/d
- Body fat loss slowed during KD coinciding with increased protein utilization and loss of fat-free mass

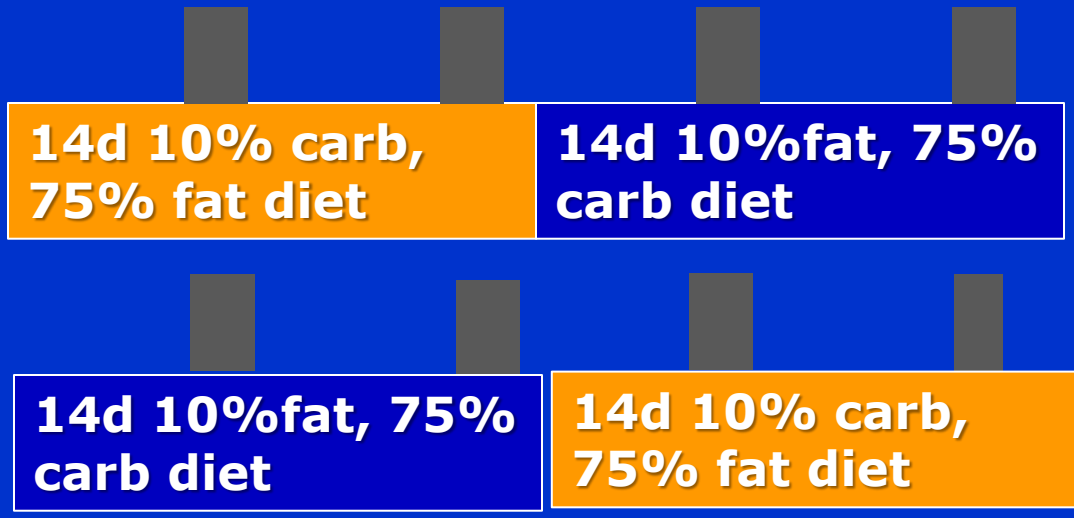
- Authors suggest nullifies insulin/carb theory and confirms "calorie is a calorie" as far as EE/body fat
  - (Inpatient metabolism study, not ad lib diet, not studying effect of changes in insulin, not study of health of calorie)
- Weight loss from water, increase REE was not sustained
- Transient increase EE related to ketogenesis – 1 week reached maximum
- Participants lost fat on low fat diet
- There was increase RMR but authors suggest this is at the limits of detection
- Hall et al. Gastroenterology 152:1718—27 metanalysis – controlled feeding studies increase energy expenditure with low fat -27 kcal/day difference

A plant-based, low-fat diet decreases ad libitum energy intake compared to an animal-based, ketogenic diet: An inpatient randomized controlled trial

- N=20 for 28 days BMI 27.8, age 29
- PBLF (75% carb, 10% fat, ED 1kcal/g) vs ABLC (78% fat, 10% carb, ED 2kcal/g) for 2 weeks then crossover
- 3 meals plus snack at 2 times estimated energy requirement as much or as little as desired

Hall et al. 2020 in press https://osf.io/preprints/nutrixiv/rdjfb/

A plant-based,low fat diet decreases ad libitum energy intake compared to an animal-based, ketogenic diet: An inpatient randomized controlled trial



- Carb-insulin model of obesity suggests eating high carb diets sequesters fat in adipocytes and decreases energy expenditure.
- N=20
- As much as little as they wanted, double energy requirement
- 24 hour in metabolic chamber =
- DXA/meal test/OTT
- Lower insulin and glucose with LC

Hall et al. Am J Clin Nutr doi: 10.3945/acjn.116.133561

ABLC

Veggie Scramble (Egg, shredded cheddar/Monterey jack cheese, heavy cream, butter, onions, broccoli, spinach, salt)

PBLF

Hummus bagel sandwich (plain bagel, hummus, spinach, onions) with soy milk and raisins

ABLC

Beef stir fry (beef roast, broccoli, green pepper, onion, soy sauce, canola oil, salt and peanuts) with cauliflower rice

PBLF

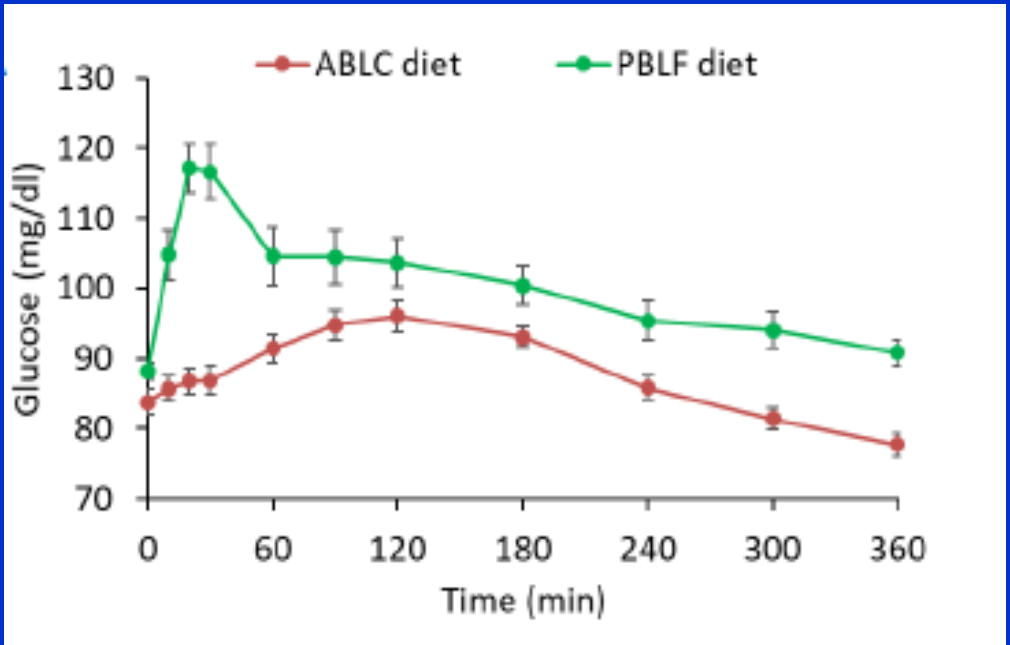
Spaghetti with vegan pasta sauce (marinara sauce, broccoli, green peppers, chickpeas and salt)

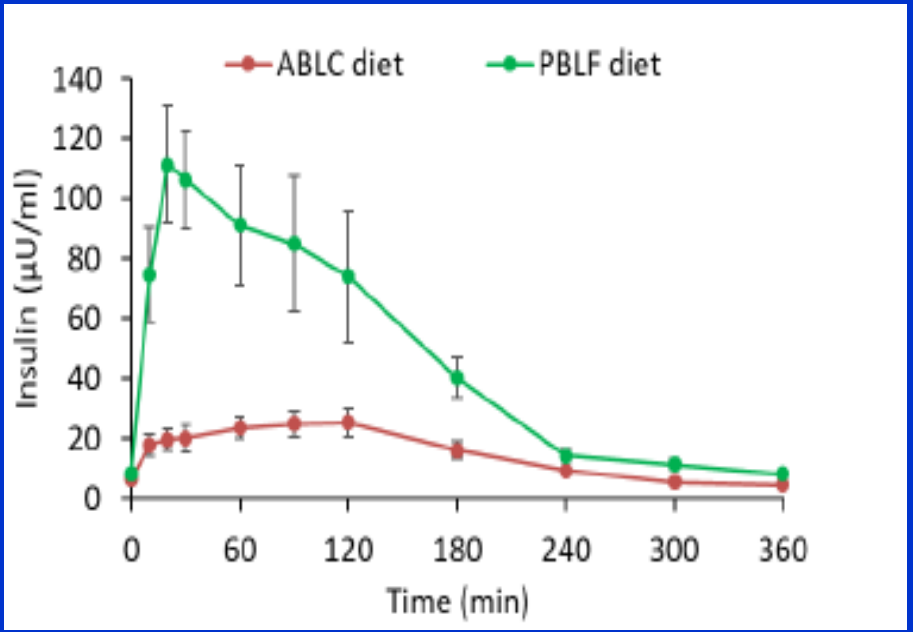
ABLC

Stuffed pepper casserole (ground beef, onion, butter, green pepper, salt, crushed tomatoes and flaxseed) over cauliflower rice and topped with shredded cheddar/Monterey jack cheese

PBLF

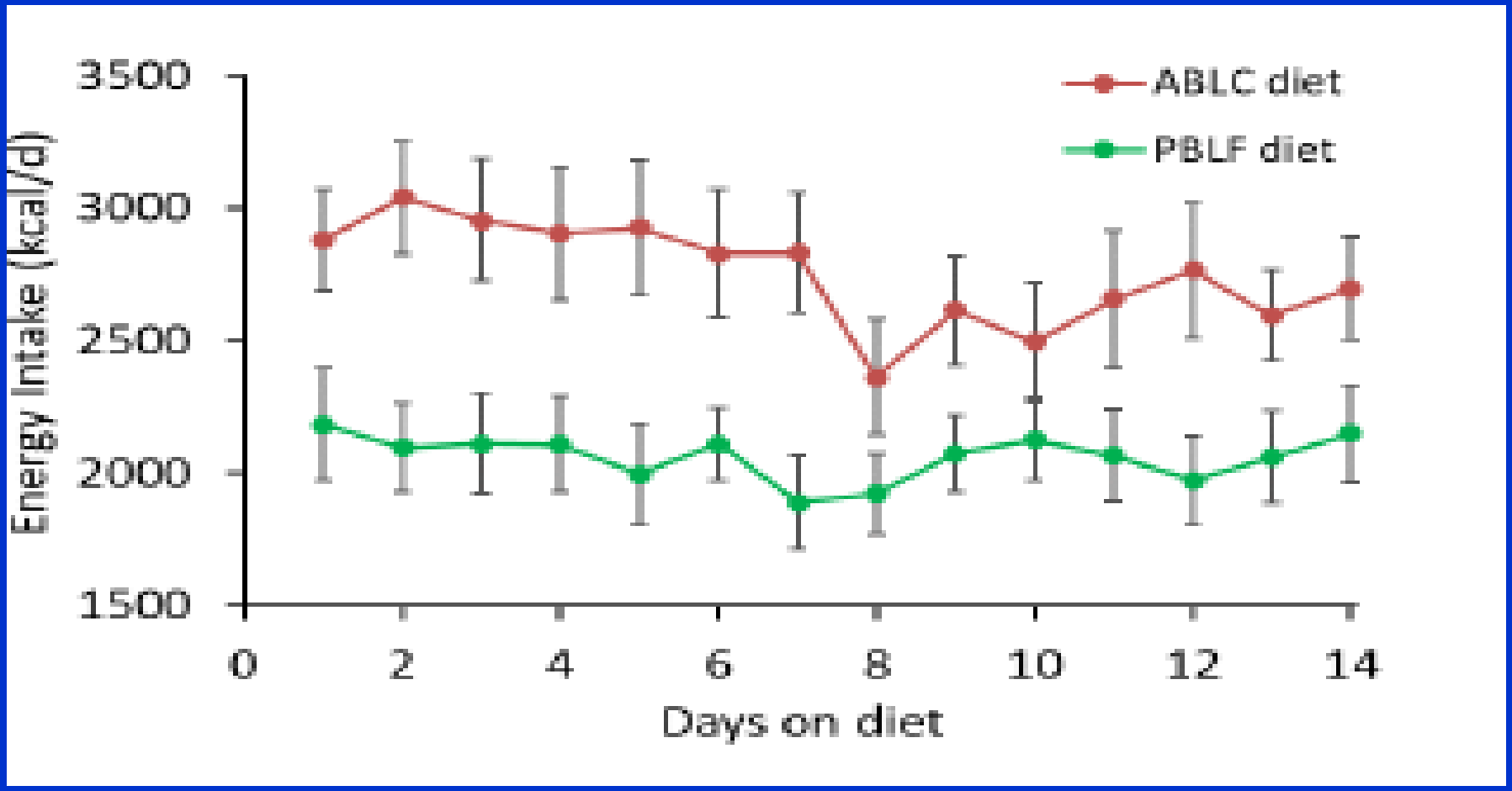
Stuffed baked potatoes (Idaho potatoes, salt, black beans, broccoli and salsa) with a side of grapes

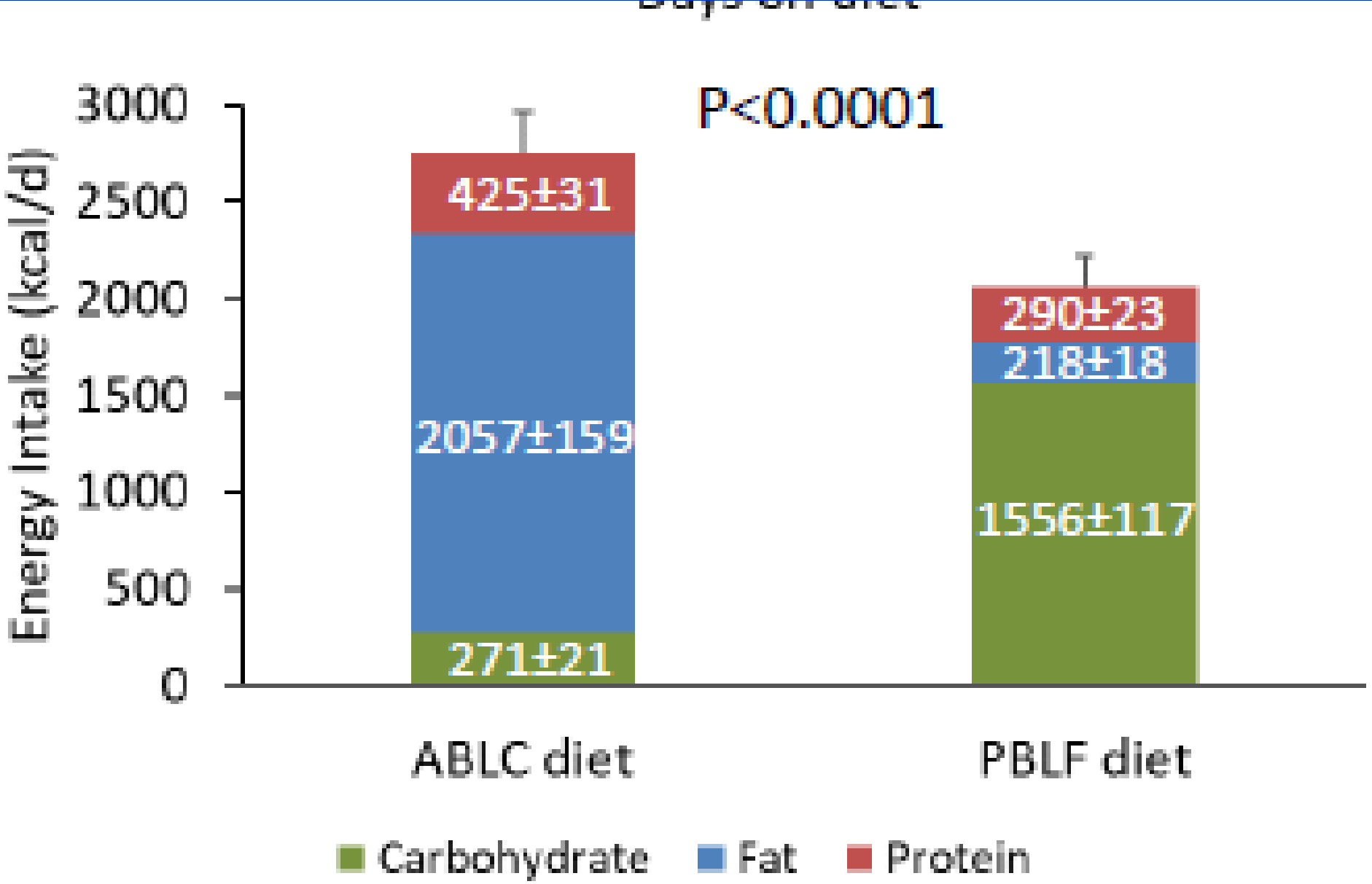

ABLC diet
PBLF diet
Glucose (mg/dl)
130
120
110
100
90
80
70
0
60
120
180
240
300
360
Time (min)


ABLC diet
PBLF diet
Insulin (µU/ml)
140
120
100
80
60
40
20
0
0
60
120
180
240
300
360
Time (min)

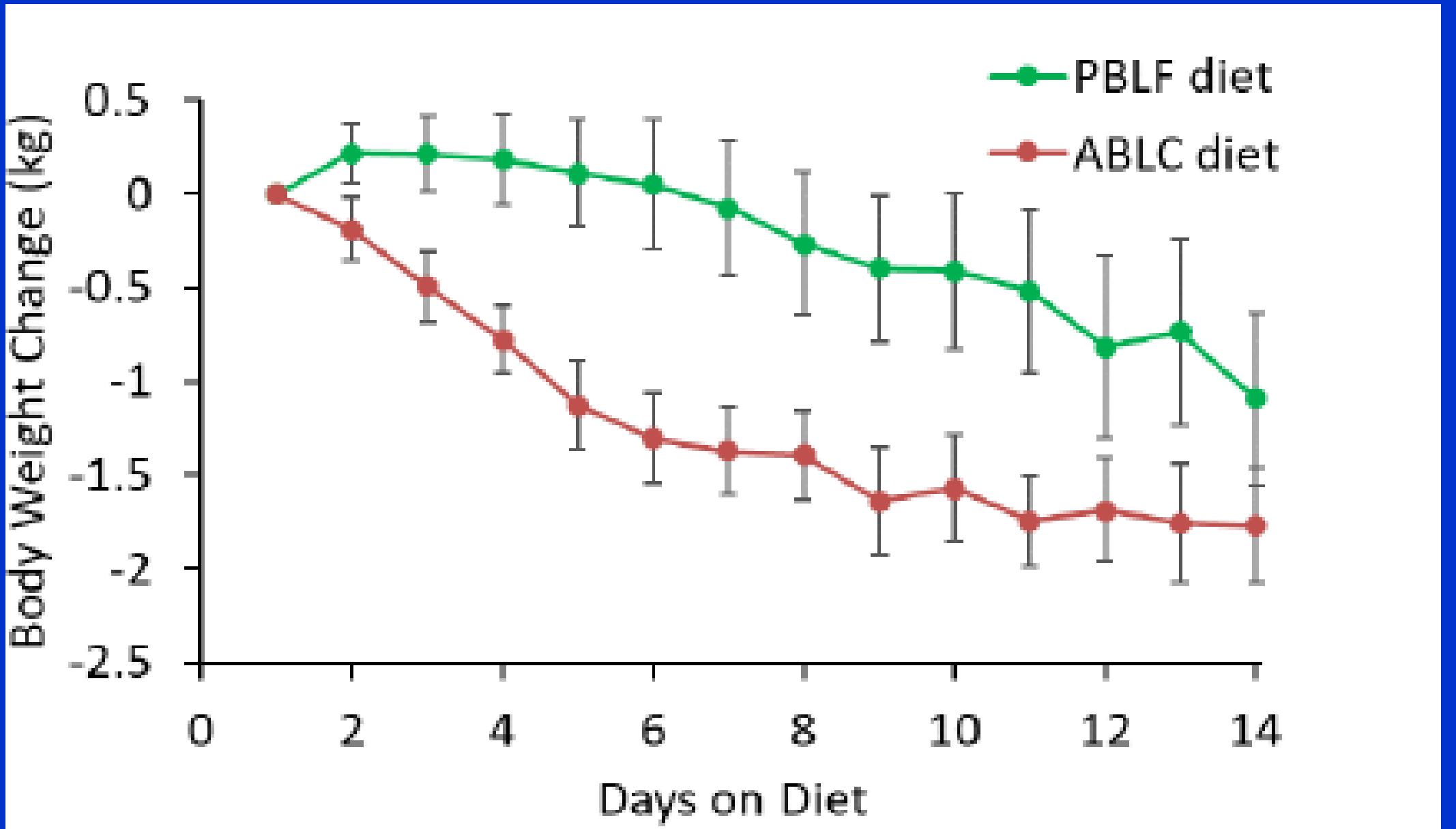
Greater Intake (689 kcal) with ABLC

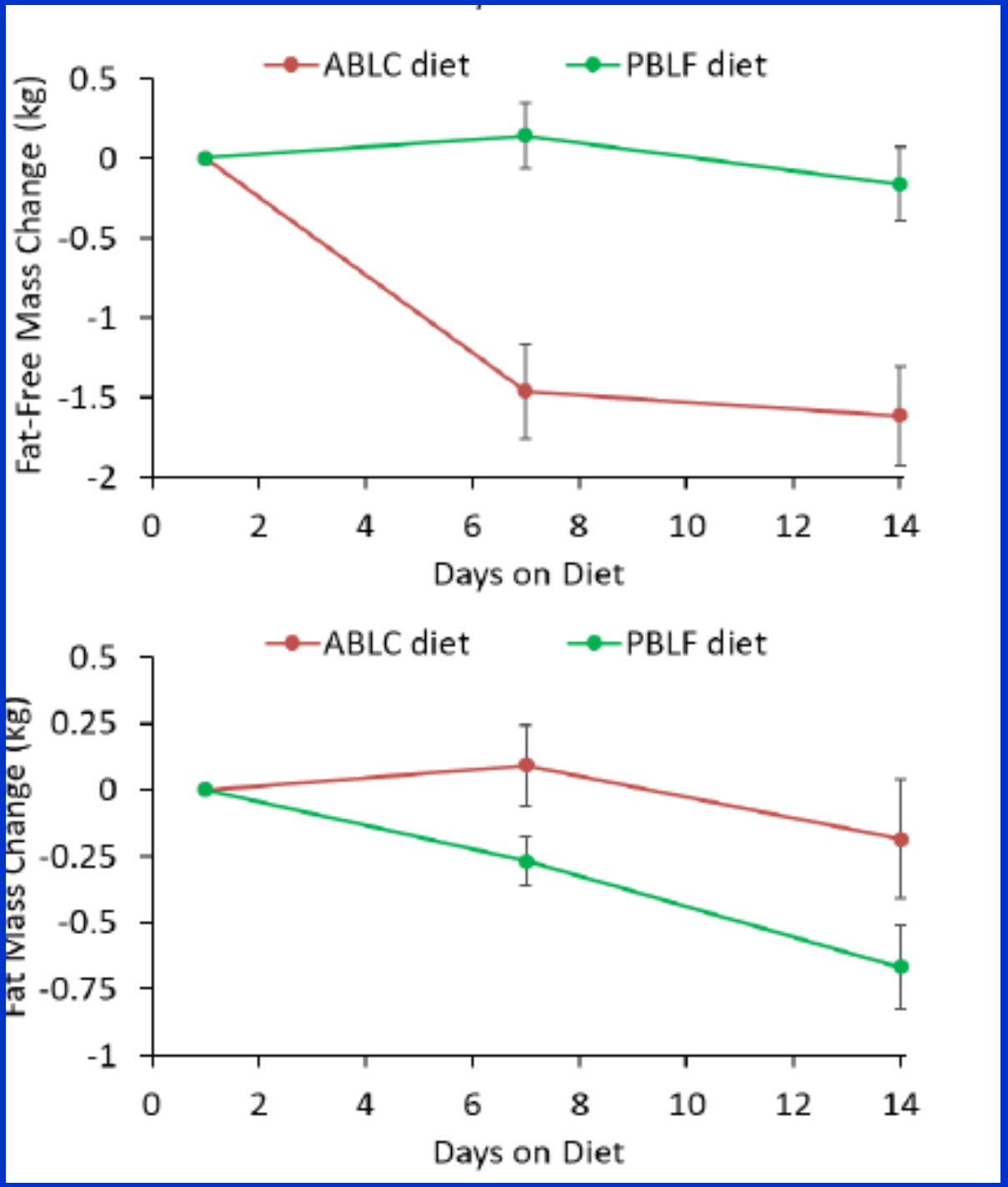
All subjects had lower intake with PBLF

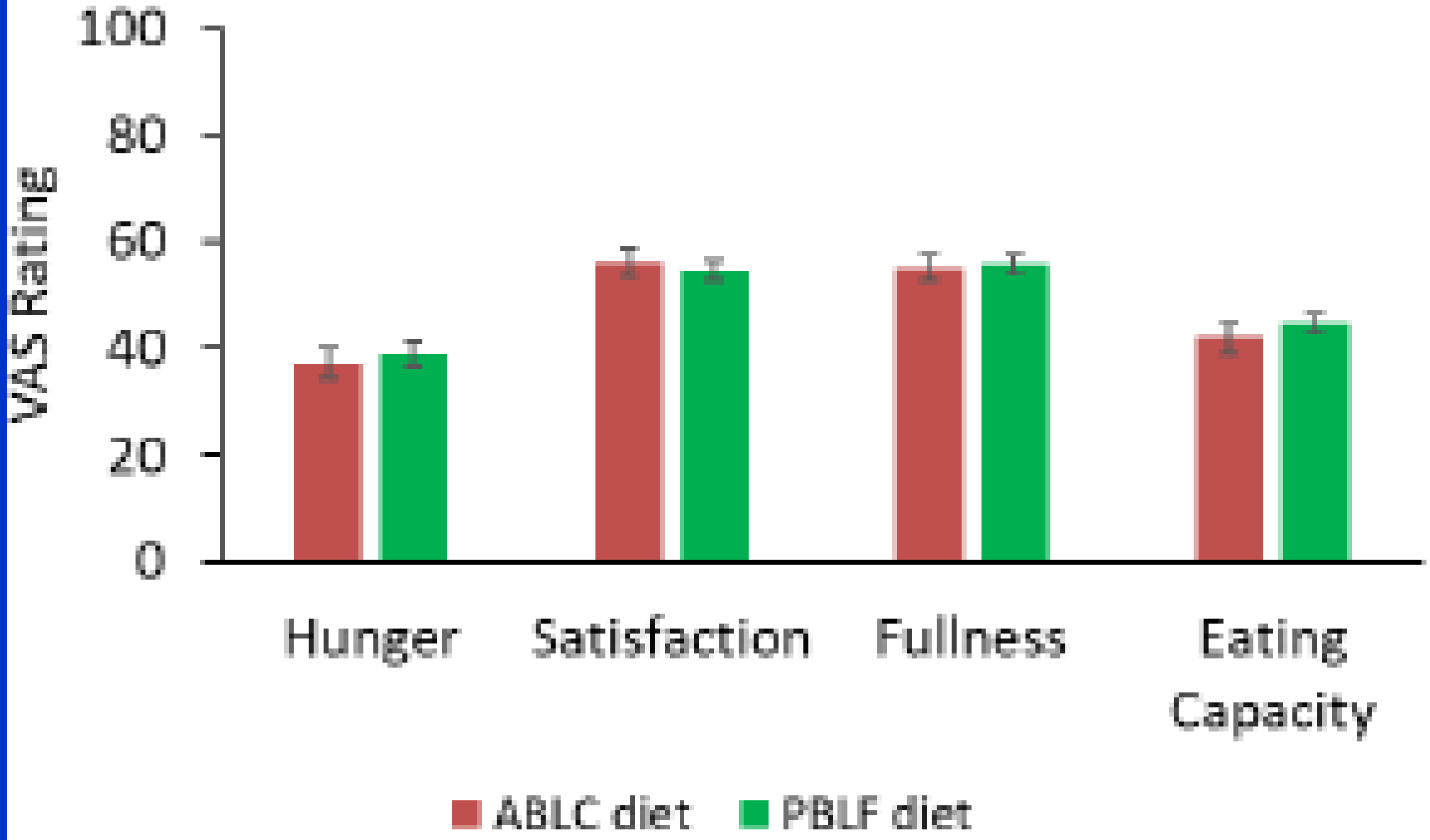


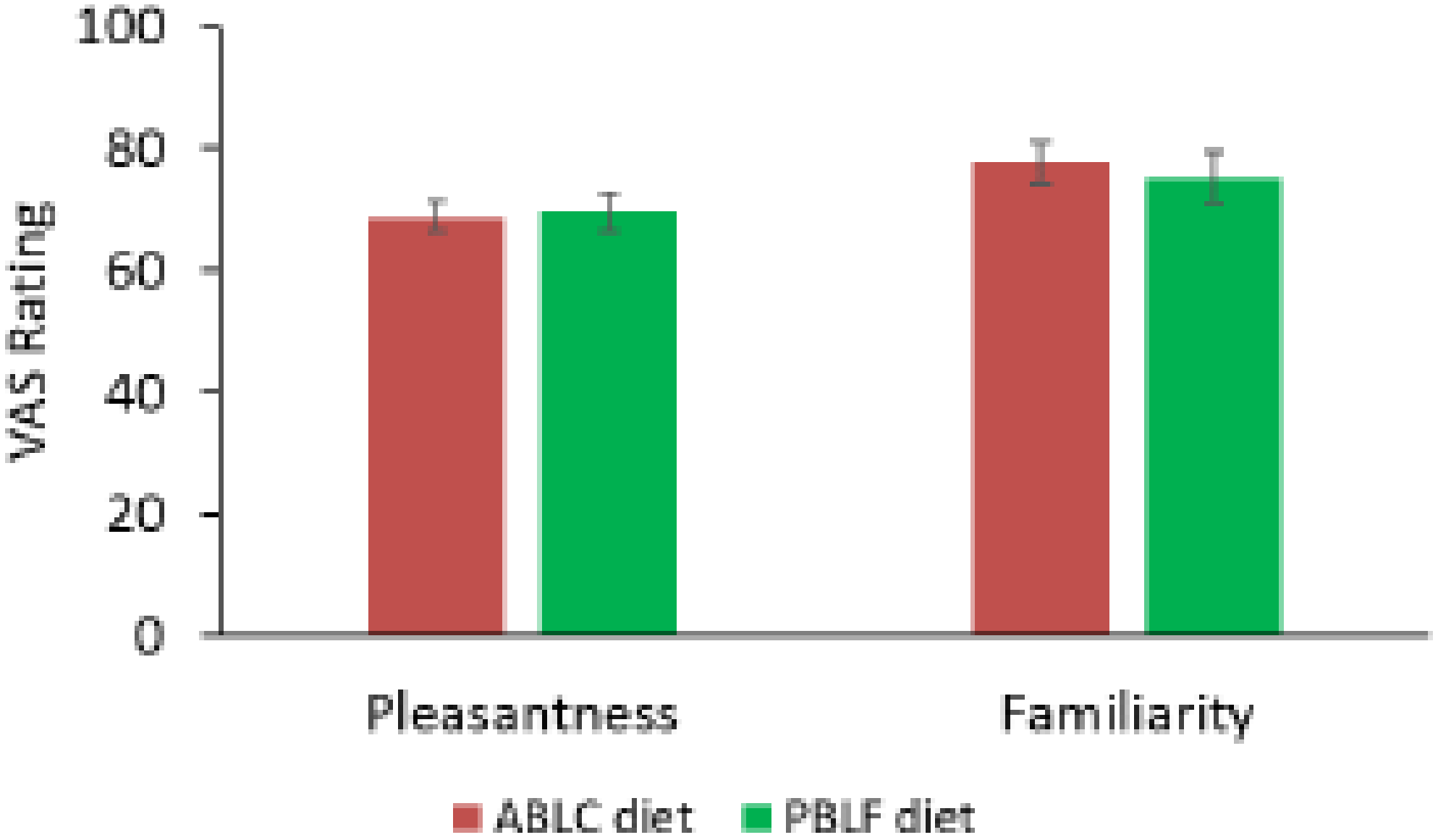


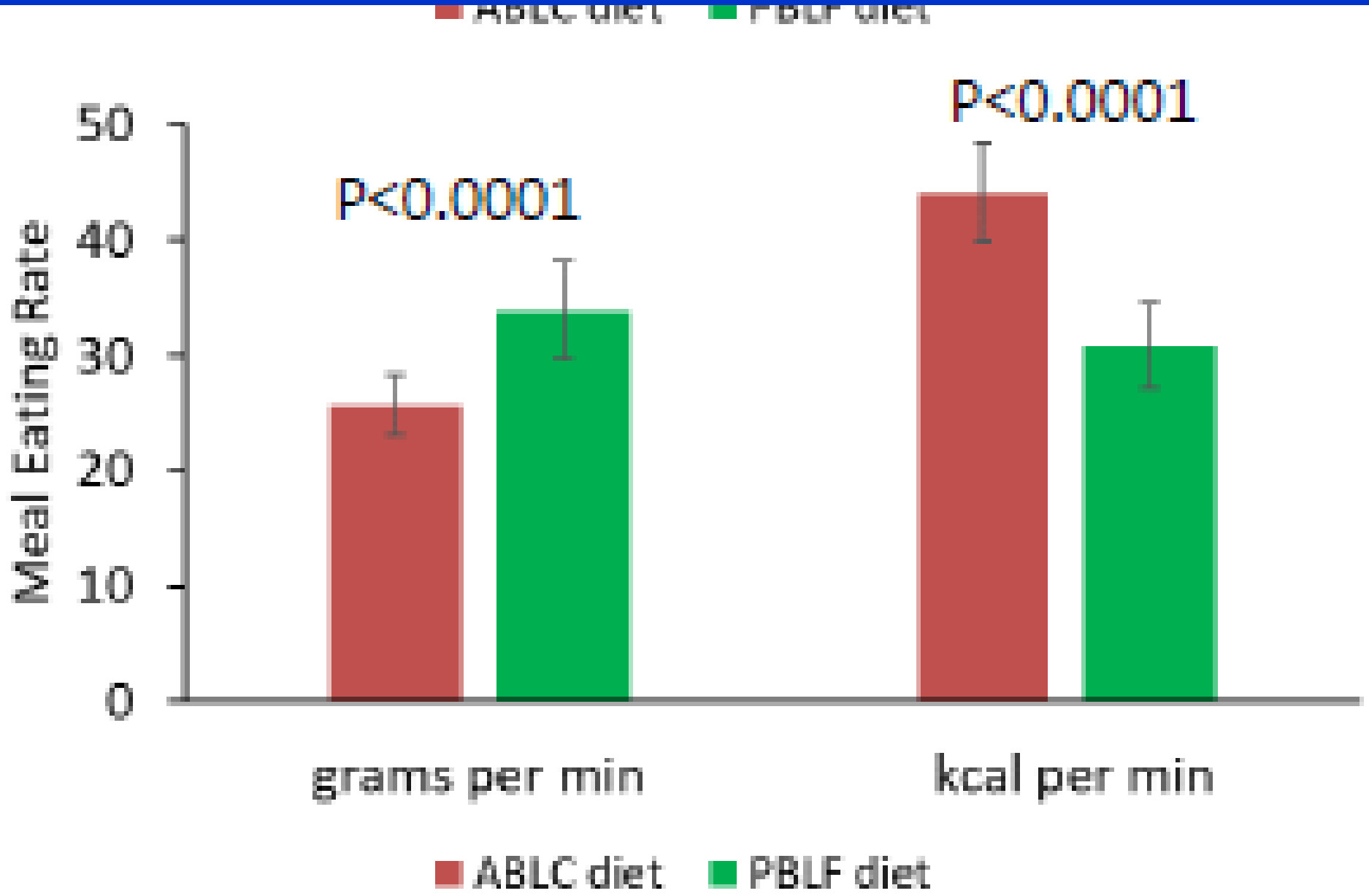
PBLF 60 grams fiber vs 20


PBLF diet
ABLC diet
Body Weight Change (kg)
0.5
0
-0.5
-1
-1.5
-2
-2.5
0
2
4
6
8
10
12
14
Days on Diet


ABLC diet
PBLF diet
Fat-Free Mass Change (kg)
0.5
0
-0.5
-1
-1.5
-2
0
2
4
6
8
10
12
14
Days on Diet
ABLC diet
PBLF diet
Fat Mass Change (kg)
0.5
0.25
0
-0.25
-0.5
-0.75
-1
0
2
4
6
8
10
12
14
Days on Diet


100
80
60
40
20
0
VAS Rating
Hunger
Satisfaction
Fullness
Eating Capacity
ABLC diet
PBLF diet


100
80
60
40
20
0
VAS Rating
Pleasantness
Familiarity
ABLC diet
PBLF diet


ABLC diet
PBLF diet
P<0.0001
P<0.0001
Meal Eating Rate
50
40
30
20
10
0
grams per min
kcal per min
ABLC diet
PBLF diet

Ultra-Processed Diets Cause Excess Calorie Intake and Weight Gain: An Inpatient Randomized Controlled Trial of Ad Libitum Food Intake

- Inpatient
- Ultra-processed – "formulations mostly of cheap

But what makes them altogether different from the other NOVA groups is their use of substances derived from foods seldom if ever used in culinary preparation, such as protein isolates, hydrogenated oils, and modified starches. Or their use of flavors, colors, emulsifiers, and other cosmetic additives designed to mask their basic ingredients and to make the final product attractive to the senses (Monteiro et al., 2019Monteiro C.A. et al. Ultra-processed foods: what they are and how to identify them.*Public Health Nutr.* 2019; 22: 936-941

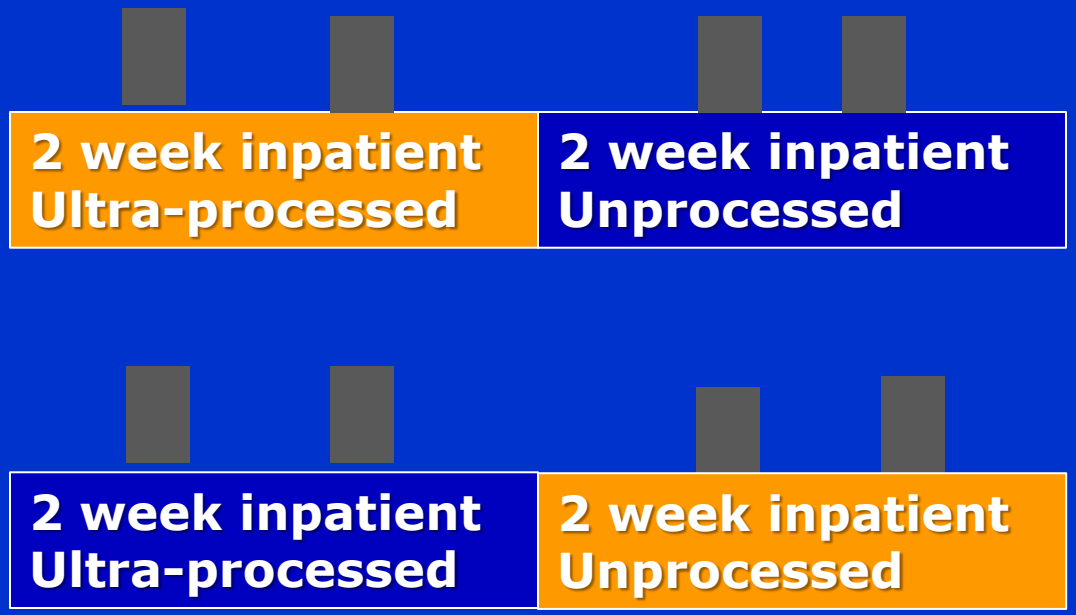
Color ,flavor, texture, taste

kcal/gram)

- McDonalds (+ dextrose, sodium acid pyrophosphage) 230 kcal (3.2 kcal/gram)

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

Ultra-Processed Diets Cause Excess Calorie Intake and Weight Gain: An Inpatient Randomized Controlled Trial of Ad Libitum Food Intake



- N=20 (10M,10F), CROSSOVER
- BMI 27
- 1 days in metabolic chamber =
- DXA/ EE – DLW, MRI
- OGTT

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

Ultra-Processed Diets Cause Excess Calorie Intake and Weight Gain: An Inpatient Randomized Controlled Trial of Ad Libitum Food Intake

- Eat as much of little as desired
- 7 days of menus
- Diets matched for calories, sugar, fat,fiber, macronutrients
- Primary Outcome: Energy Intake

- MATCHED FOR:
  - Salt
  - Sugar
  - Fat

	Ultra-Processed	Unprocessed
Energy (kcal)	3,905	3,871
Carb (%)	49.2	46.3
Fat (%)	34.7	35.0
Protein(%)	16.1	18.7
Fiber (g/1000 kcal)	21.3	20.7
Energy ultra-processed	83.5	0

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

Unprocessed

Greek yogurt (Fage) parfait with strawberries, bananas, with Walnuts (Diamond), Salt and Olive Oil

Apple Slices with Fresh Squeezed Lemon

Ultra-processed

Egg (Papetti's), turkey bacon (Jenni-O) and American cheese (Glenview Farms) on an English muffin (Sara Lee)

Tater tots (Monarch) with ketchup (Heinz)

Orange juice (Sun Cup) with NutriSource Fiber

Unprocessed

Entrée salad with grilled chicken breast, baked sweet potato, corn (Monarch, from frozen), avocado, onions, tomatoes, carrots on green leaf lettuce

Vinaigrette (red wine vinegar (Giant) and olive oil)

Skim milk (Cloverland)

Apple slices with fresh squeezed lemon juice

Ultra-processed

Cheeseburger with American cheese (Glenview Farms) on a Kaiser roll (Anzio & Sons)

French fries (Monarch)

Ketchup (Heinz)

Diet lemonade (Crystal Light) with NutriSource fiber

Unprocessed

Stir fried beef tender roast (Tyson) with broccoli, onions, sweet peppers, ginger, garlic and olive oil

Basmati rice (Roland)

Orange slices

Pecan halves (Monarch)

Salt and Pepper (Monarch)

Ultra-processed

Steak (Tyson) and Cheddar and Monterey Jack Cheese (Glenview Farms) burrito (Pasado Tortilla) with canned black beans (Pasado)

Sour cream (Glenview Farms)

Salsa (del Pasado)

Tortilla chips (Tostitos)

Diet Lemonade (Crystal Light) with NutriSource fiber

Unprocessed

Oatmeal (Quaker) with blueberries and raw almonds

Salt (Monarch)

2% milk (Cloverfield)

Ultra-processed

Honey Nut Cheerios (General Mills)

Whole milk (Cloverland) with NutriSource fiber

Blueberry muffin (Otis Spunkmeyer) Margarine (Glenview Farms)

Unprocessed

Entrée salad with grilled chicken breast, farro (Bob's Red Mill), apples, grapes

Vinaigrette (fresh squeezed lemon juice, apple cider vinegar (Giant), olive oil)

Salt and Pepper (Monarch)

Ultra-processed

Beef ravioli (Chef Boyardee)

Parmesan cheese (Roseli)

White bread (Ottenberg)

Margarine (Glenview Farms)

Diet lemonade (Crystal Light) with NutriSource fiber

Oatmeal raisin cookies (Otis Spunkmeyer)

Unprocessed

Southwest entrée salad with green leaf lettuce, tomatoes, cucumbers, carrots, black beans (cooked from dried), corn (cooked from frozen), and avocado

Vinaigrette (red wine vinegar, fresh squeezed lemon juice and flaxseed oil (International Collection))

Salt and Pepper (Monarch)

Raw almonds (Giant)

Grapes

Ultra-processed

Macaroni and cheese (Stouffer's)

Chicken tenders (Perdue)

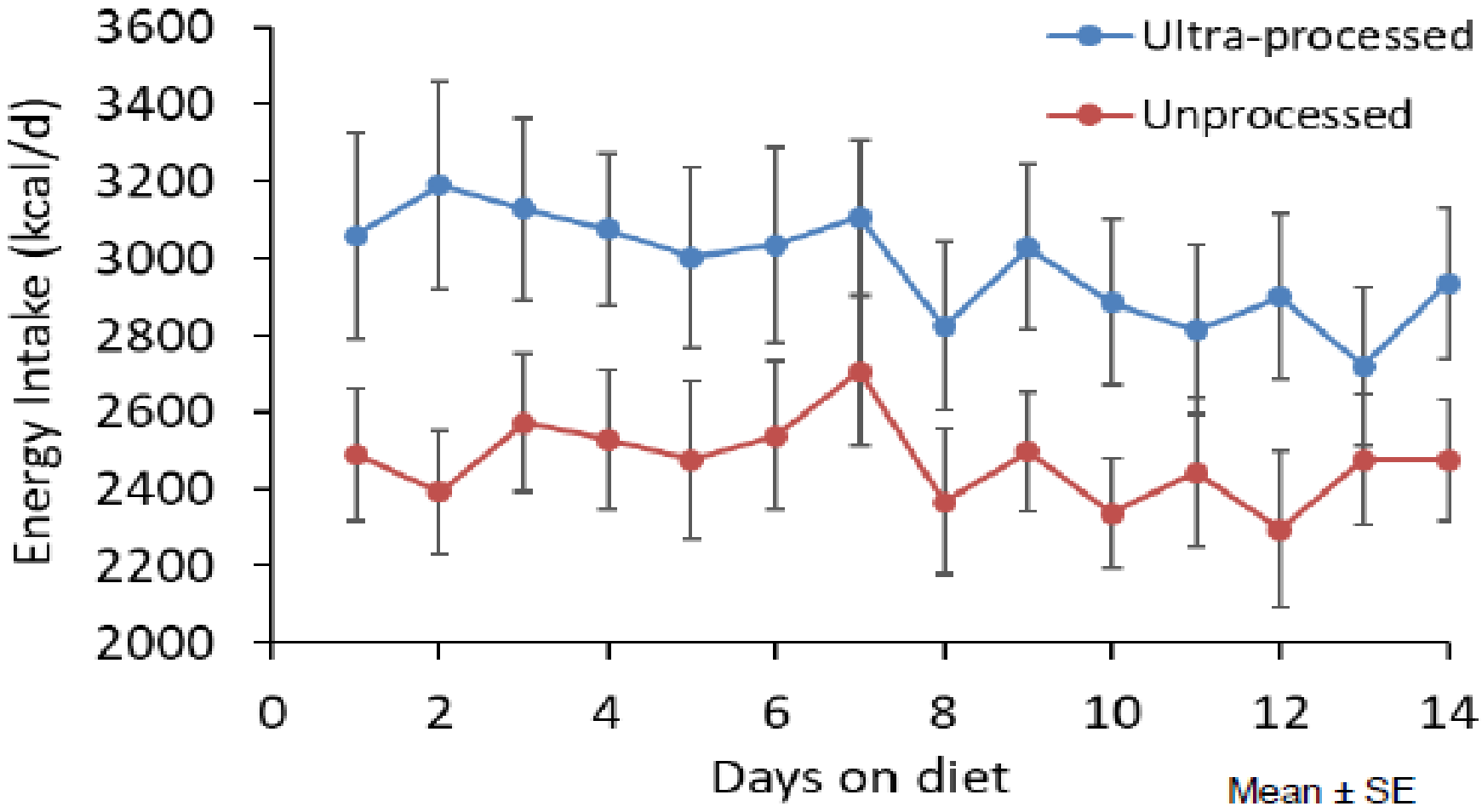
Canned green beans (Giant)

Diet lemonade (Crystal Light) with NutriSource fiber

Unprocessed

Ultra-processed

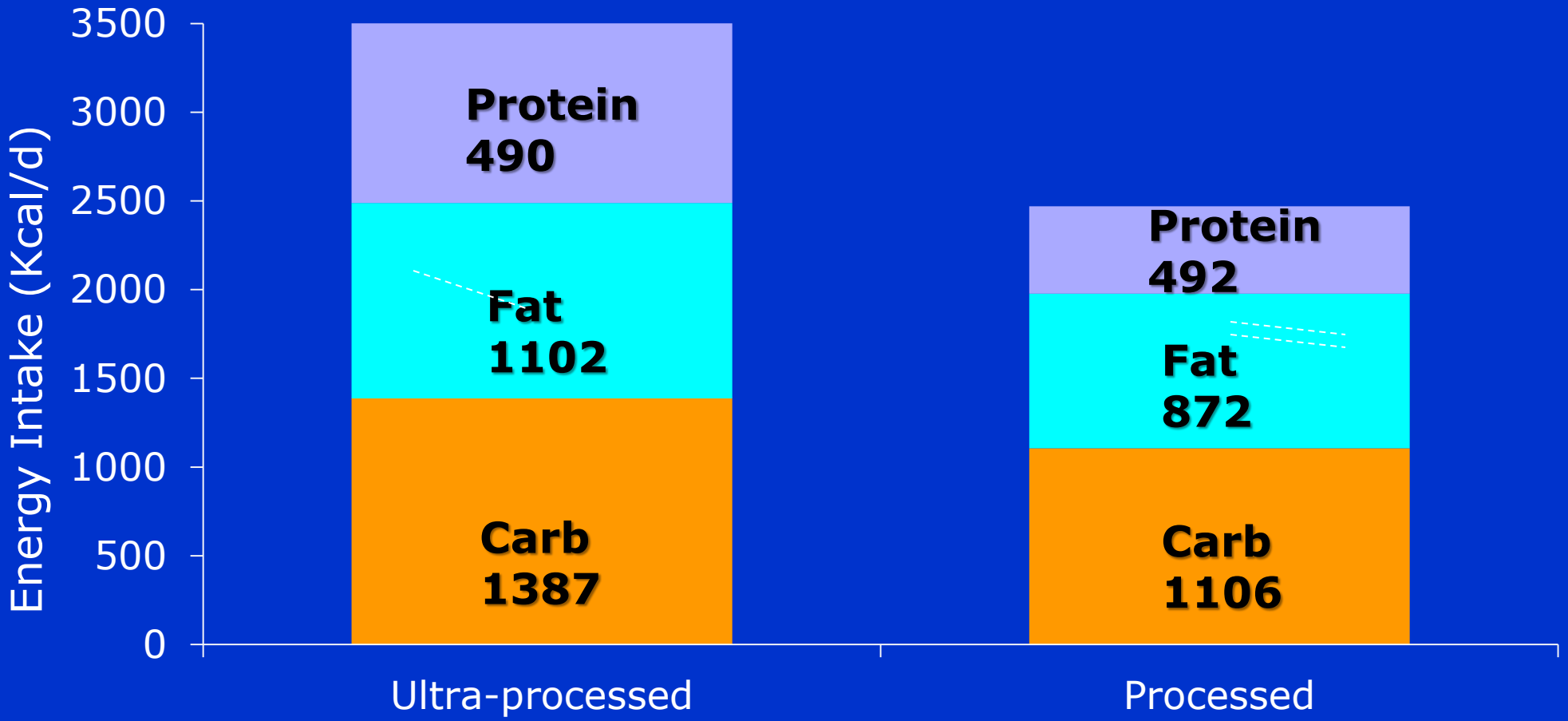
Ultra-processed Diets Cause Increased Intake



+508

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

Ultra-Processed Diets Cause Excess Calorie Intake and Weight Gain: An Inpatient Randomized Controlled Trial of Ad Libitum Food Intake



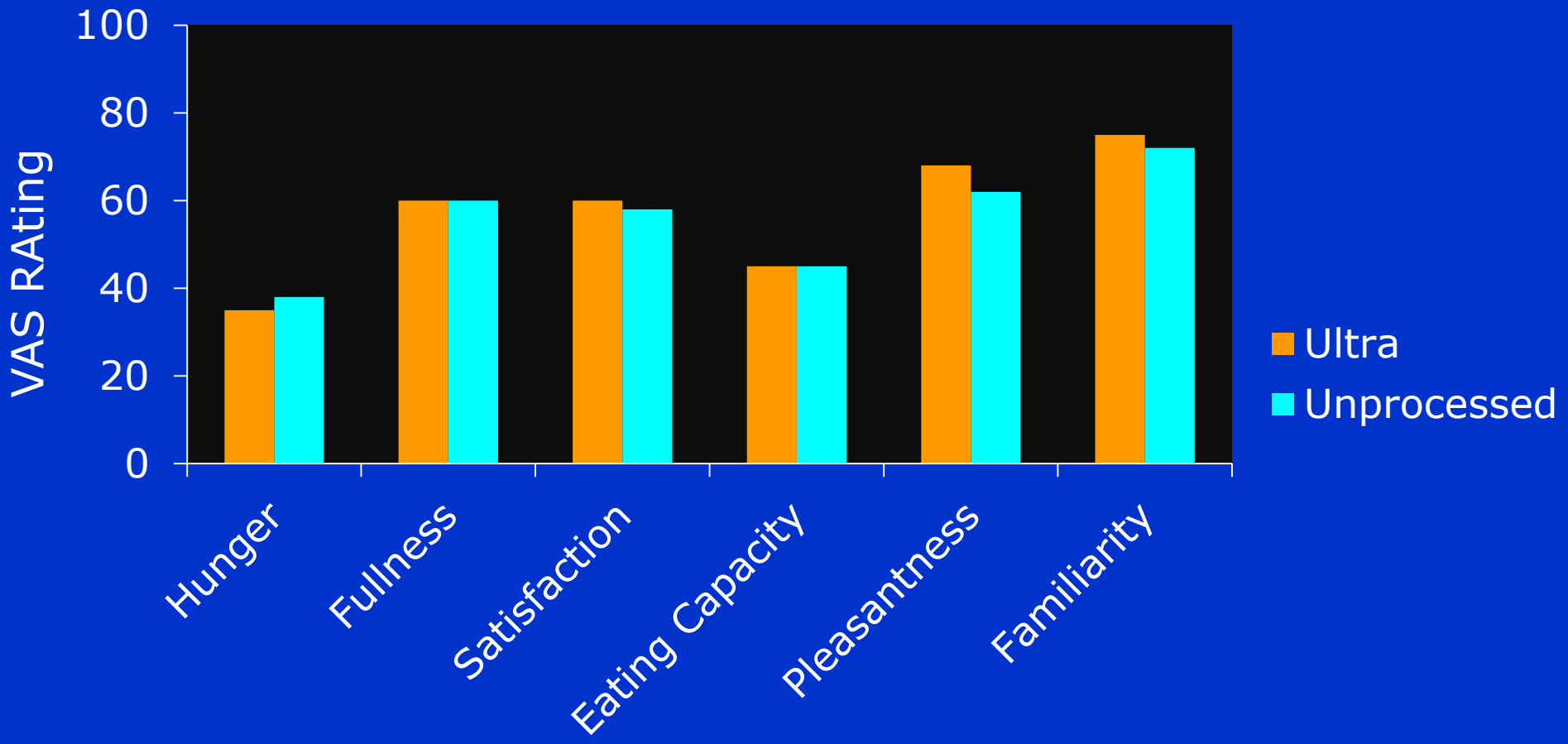
Hall et al. Cell Metabolism 30:1-11 (2019)

Protein is similar

Ultra-Processed Diets Cause Excess Calorie Intake and Weight Gain: An Inpatient Randomized Controlled Trial of Ad Libitum Food Intake

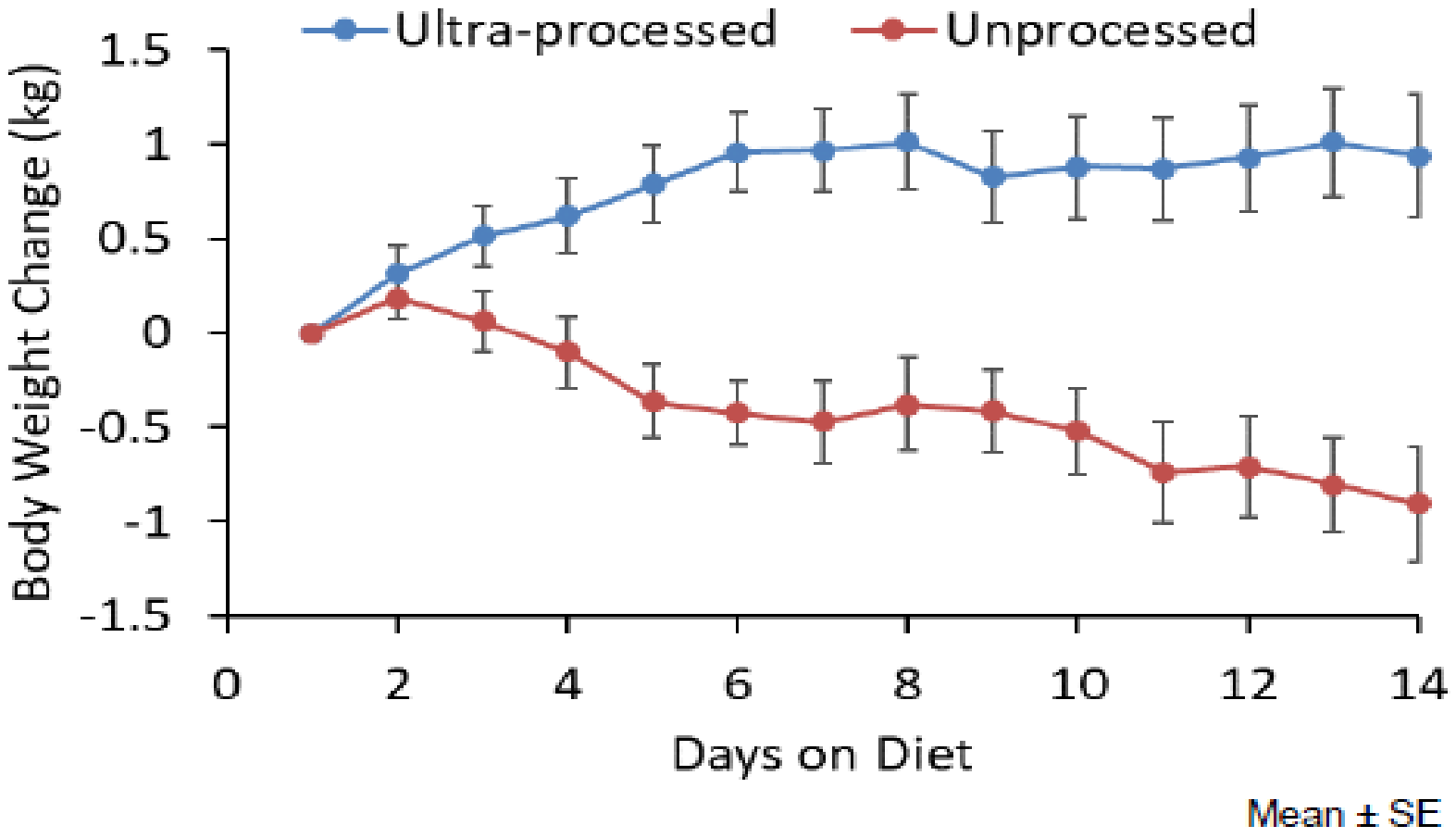
Papkaonstanknou et al. Diabetes and metabolism 44 (2018) 226-234

Self-Reported Appetite/Pleasantness/Familiarity



Veum et al. Am J Clin Nutri. Doi: 10.3945/acjn.115.123463

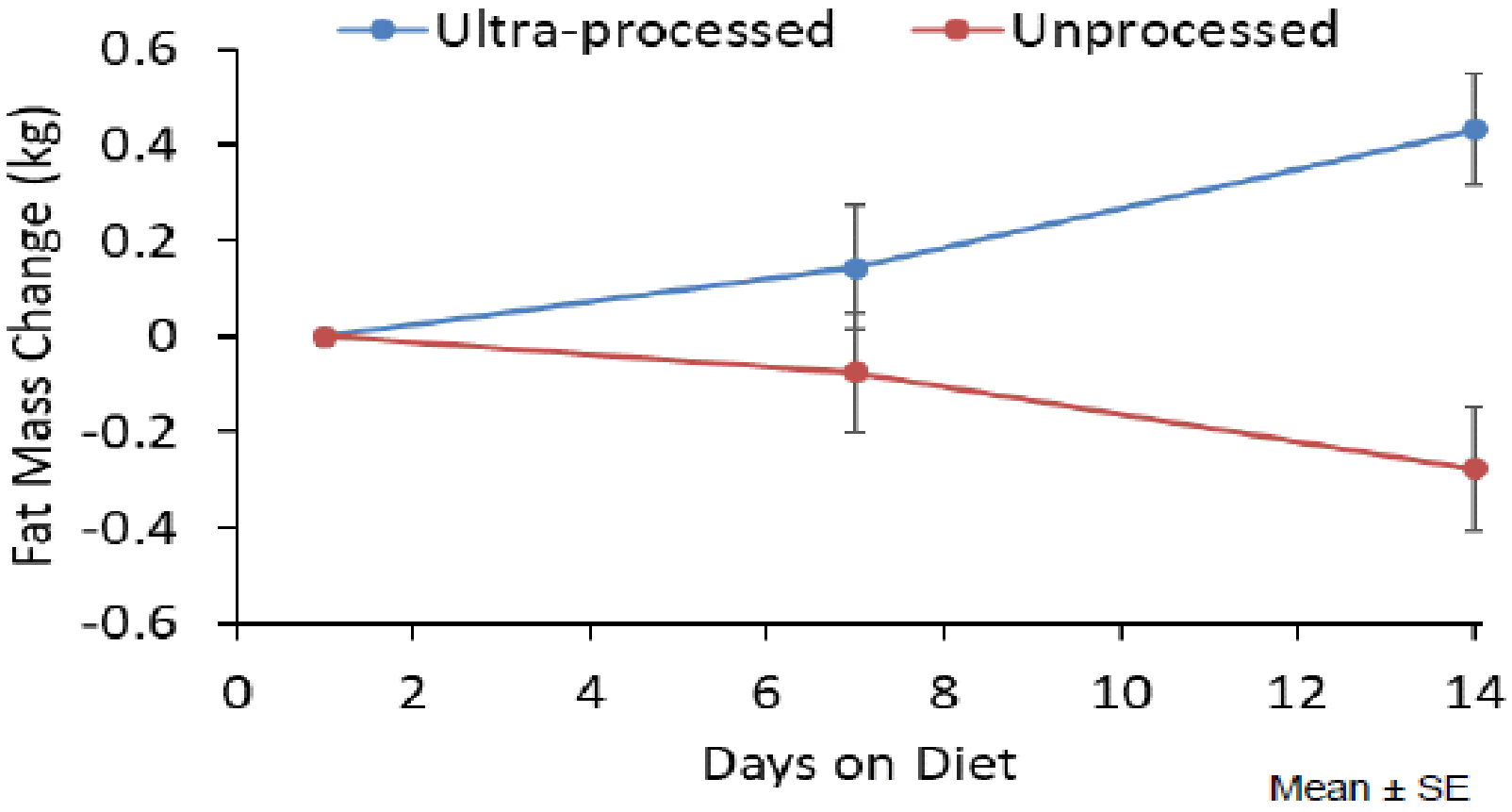
Ultra-processed Diets Cause Weight Gain



Mean ± SE

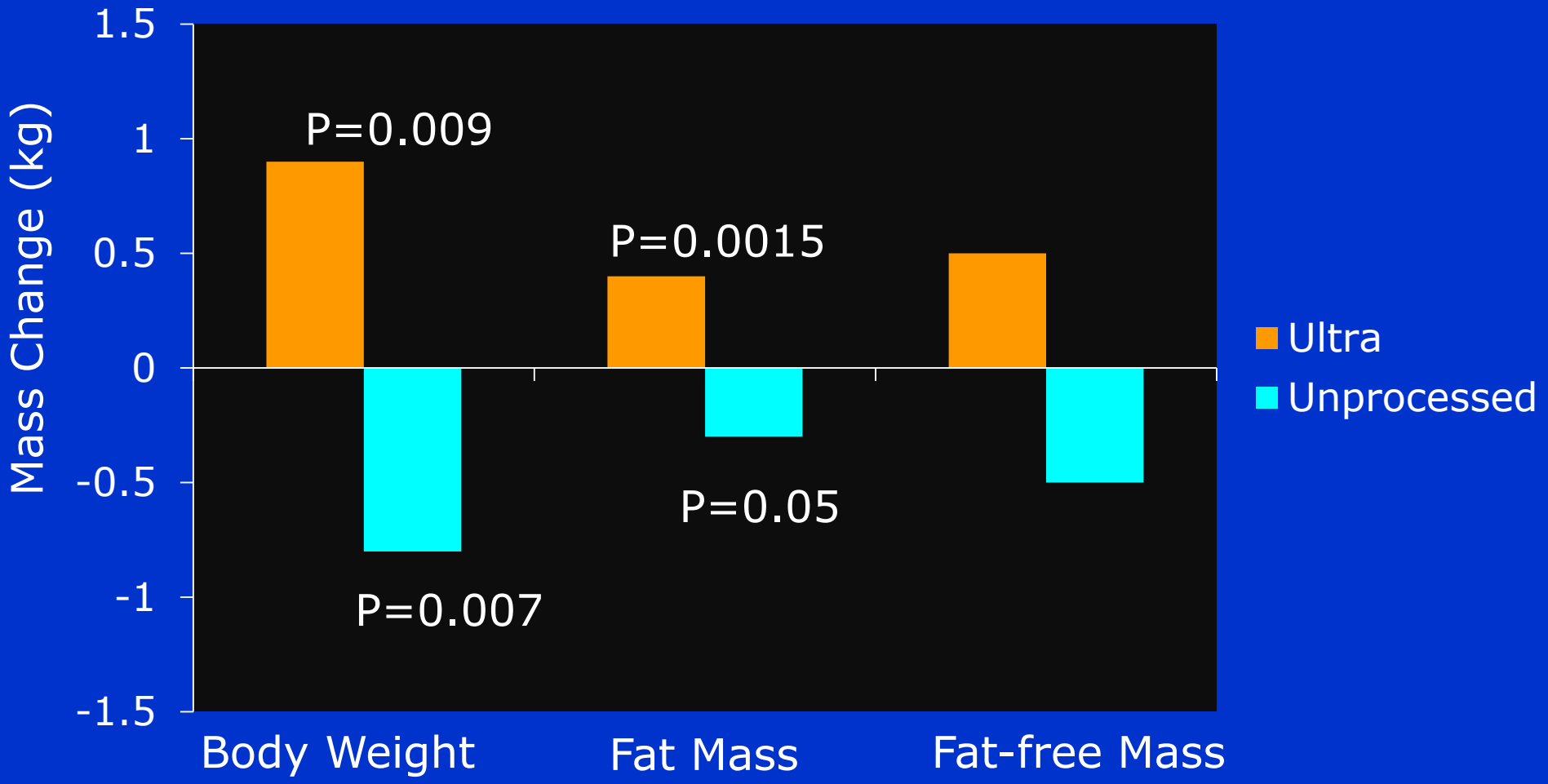
KD Hall et al. *Cell Metabolism* 30:1-11 (2019).

Ultra-processed Diets Cause Fat Gain



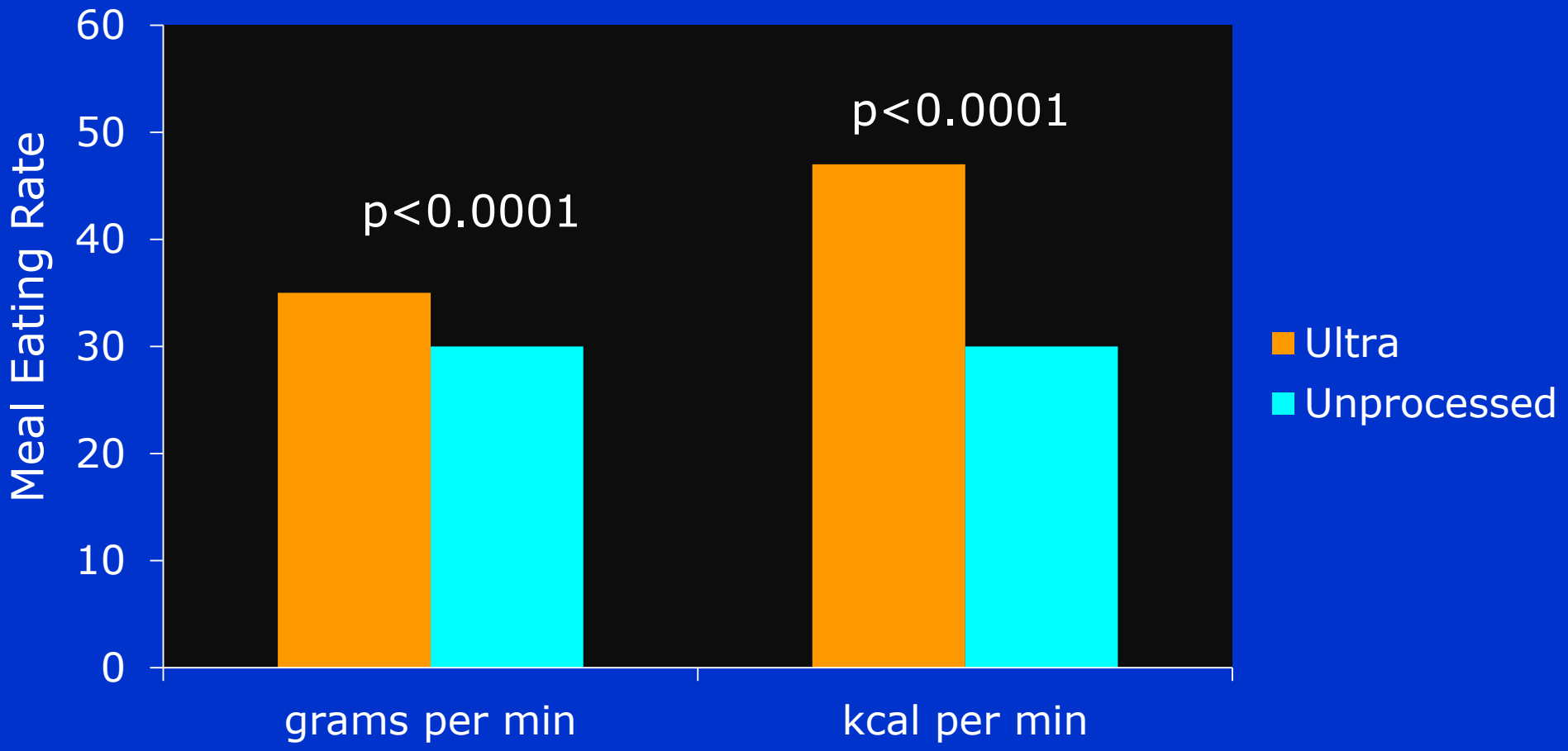
KD Hall et al. *Cell Metabolism* 30:1-11 (2019).

Weight Change



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

Eating Rate



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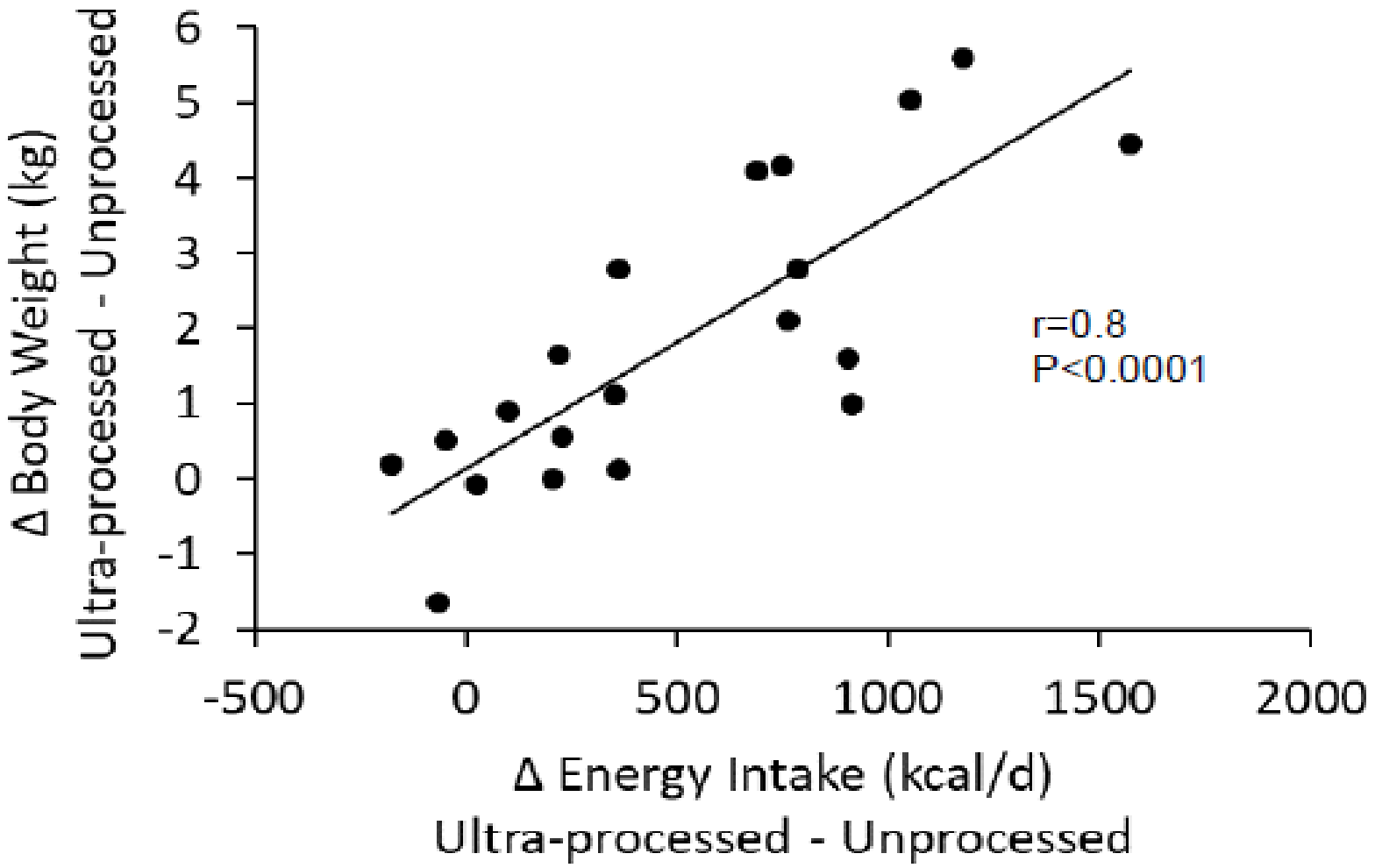
Substantial Individual Variability



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

	Ultra-Processed Diet	Unprocessed Diet
Three Daily Meals		
Energy (kcal/day)	3,905	3,871
Carbohydrate (%)	49.2	46.3
Fat (%)	34.7	35.0
Protein (%)	16.1	18.7
Energy density (kcal/g)	1.024	1.028
Non-beverage energy density (kcal/g)	1.957	1.057
Sodium (mg/1,000 kcal)	1,997	1,981
Fiber (g/1,000 kcal)	21.3	20.7
Sugars (g/1,000 kcal)	34.6	32.7
Saturated fat (g/1,000 kcal)	13.1	7.6
Omega-3 fatty acids (g/1,000 kcal)	0.7	1.4
Omega-6 fatty acids (g/1,000 kcal)	7.6	7.2
Energy from unprocessed (%)[a]	6.4	83.3
Energy from ultra-processed (%)[a]	83.5	0

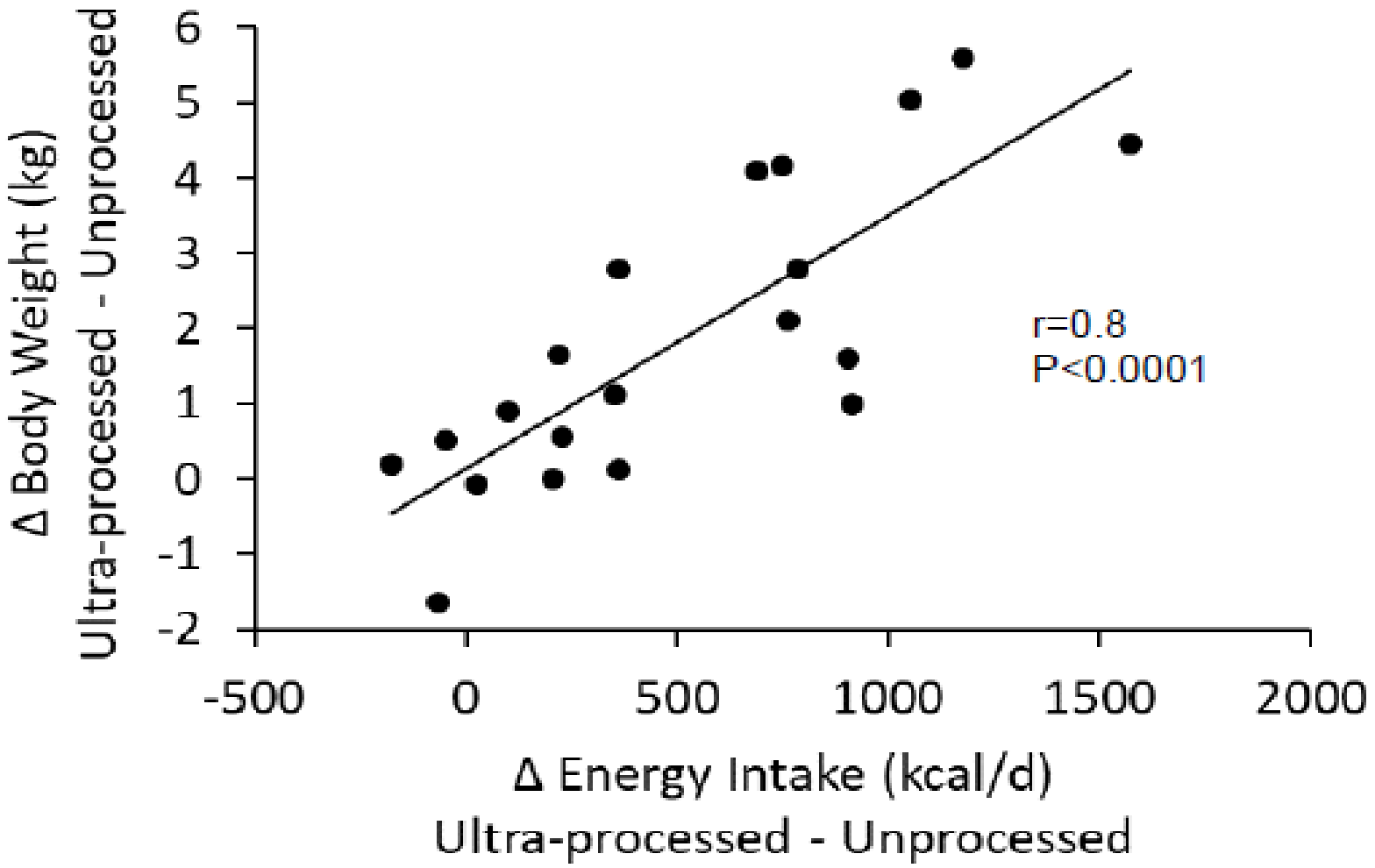
Mechanisms???

- Fat, fiber, sugar?
- Can not rule out palability?
- Hormones? (PYY, Ghrelin) but not variability
- Energy density of non-beverage foods?
- Higher eating rate?
- Ultra-processed?
- Microbiome?
- Eating rate, volume, energy density

Ultra-Processed Diets Cause Excess Calorie Intake and Weight Gain

Some individuals consume more caloric high dense, easy to eat food when presented with unlimited foods in a inpatient setting and thus gain weight

Substantial Individual Variability



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

60% food in US is ultraprocessed

- 570Calories
- 21gTotal Fat
- 470mgSodium
- 87gTotal Carb
- 3gFiber
- 7gProtein

Honey Nut Cheerios (General Mills)

Whole milk (Cloverland) with NutriSource fiber

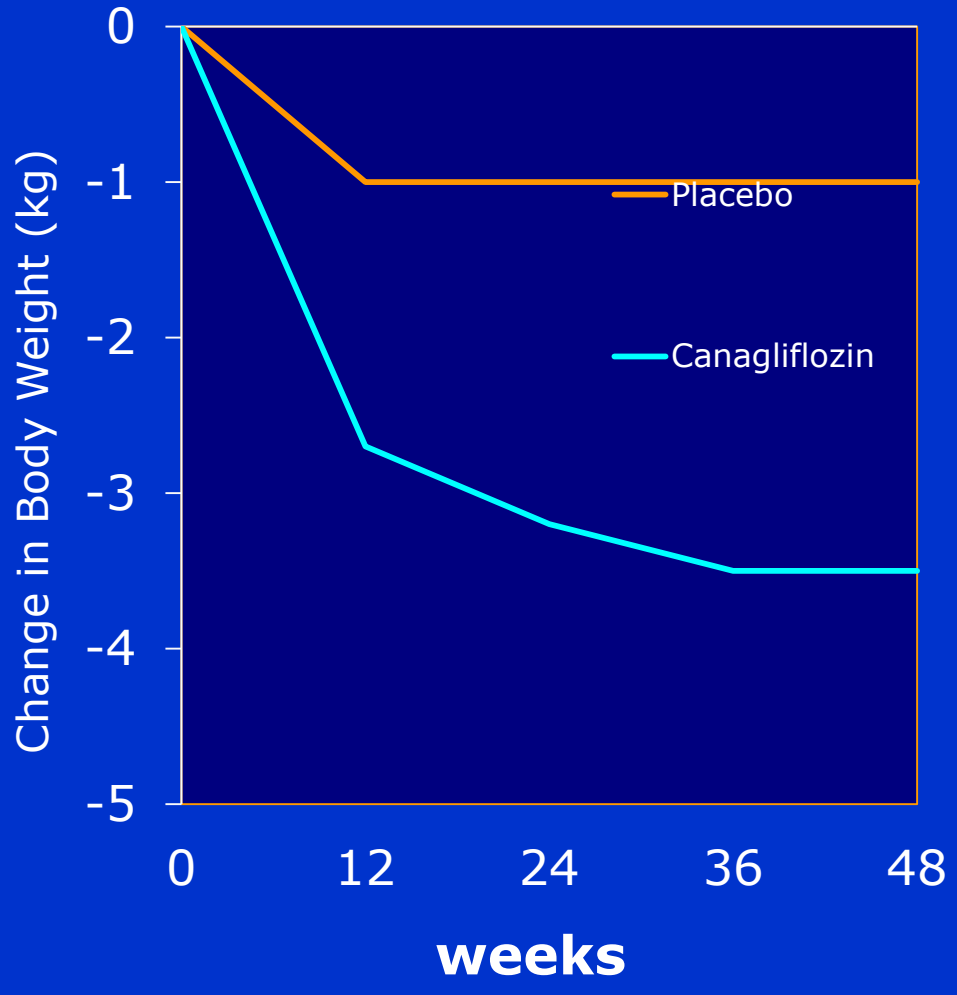
Blueberry muffin (Otis Spunkmeyer) Margarine (Glenview Farms)

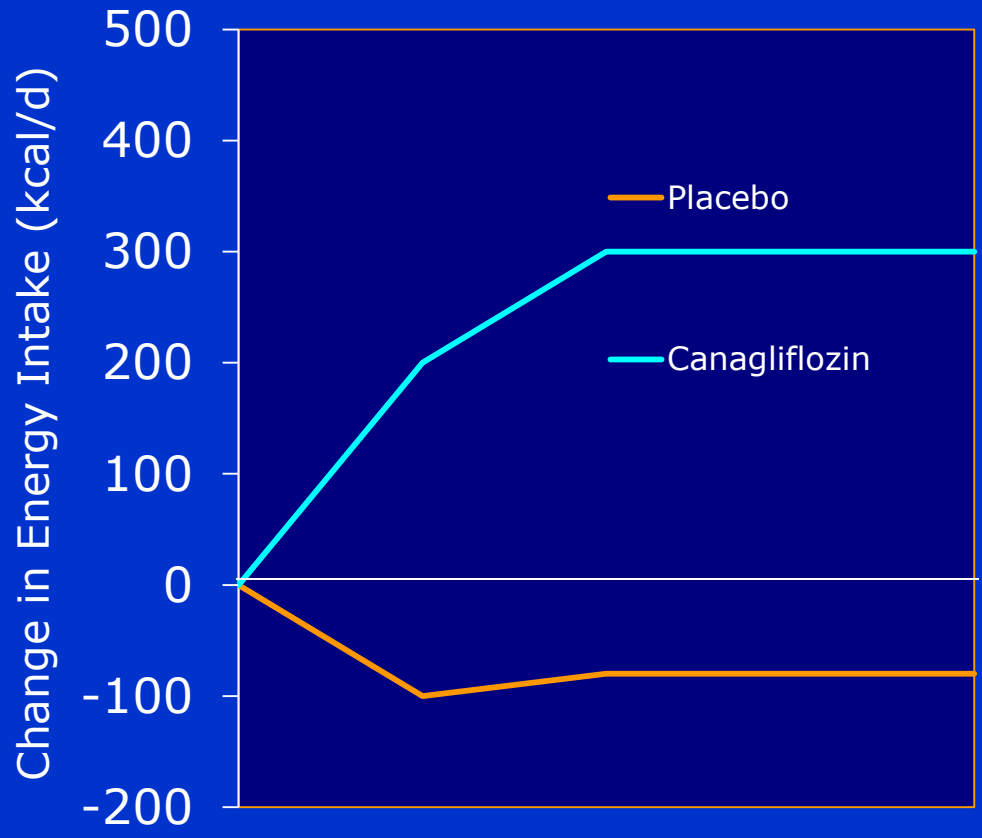
Ultra-Processed Diets Cause Excess Calorie Intake and Weight Gain

Some individuals consume more caloric high dense, easy to eat food when presented with unlimited foods in a inpatient setting and thus gain weight

Many individuals consume more caloric high dense, easy to eat food when presented with semi-unlimited foods at home, at work, at restaurants and thus gain weight

How Strongly Does Appetite Counter Weight Loss? Quantification of the Feedback Control of Human Energy Intake



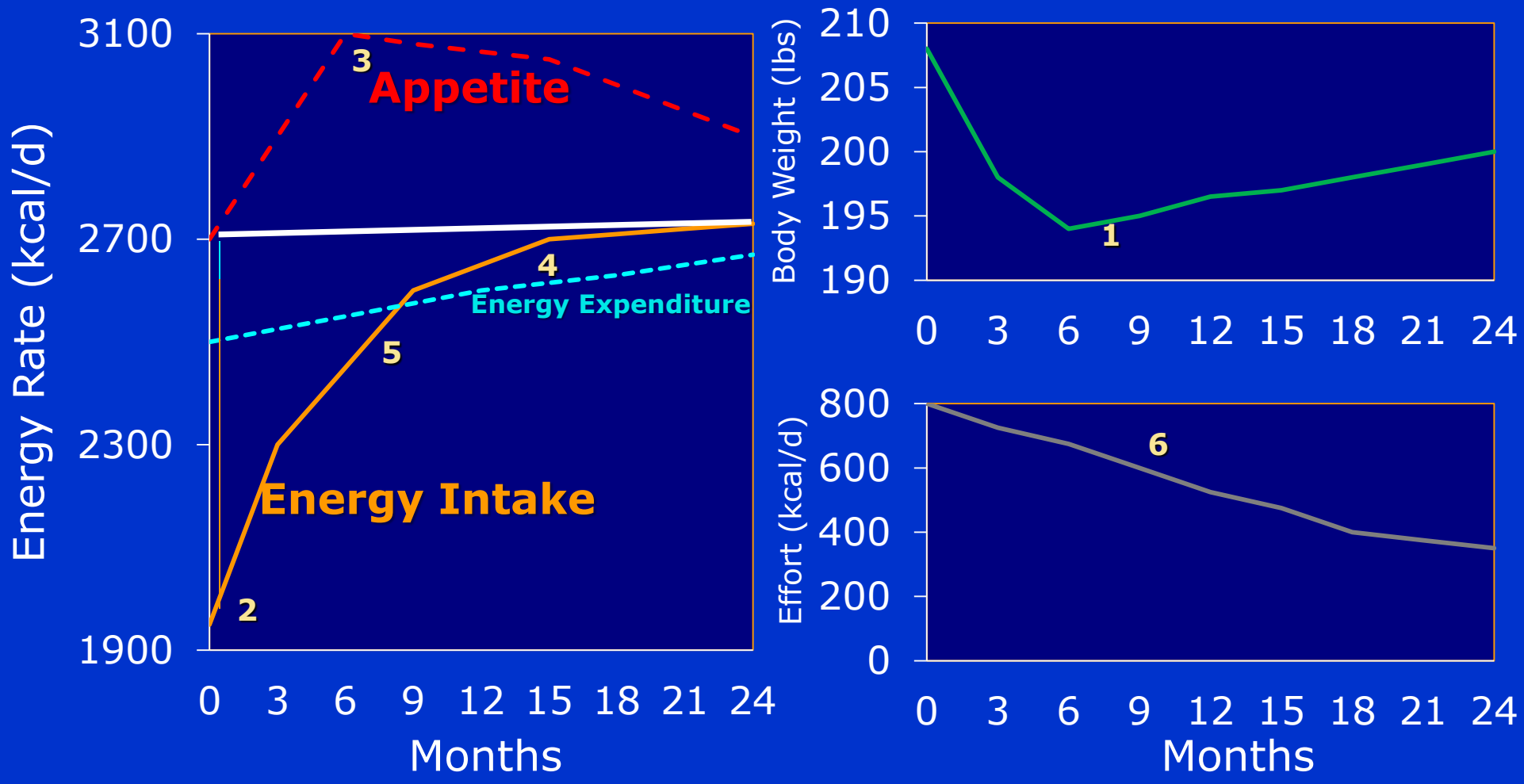


N=153, 90g urinary loss of glucose
Covert manipulation of energy balance
Mathematical model of energy intake
100 kcal increase in intake per kg lost

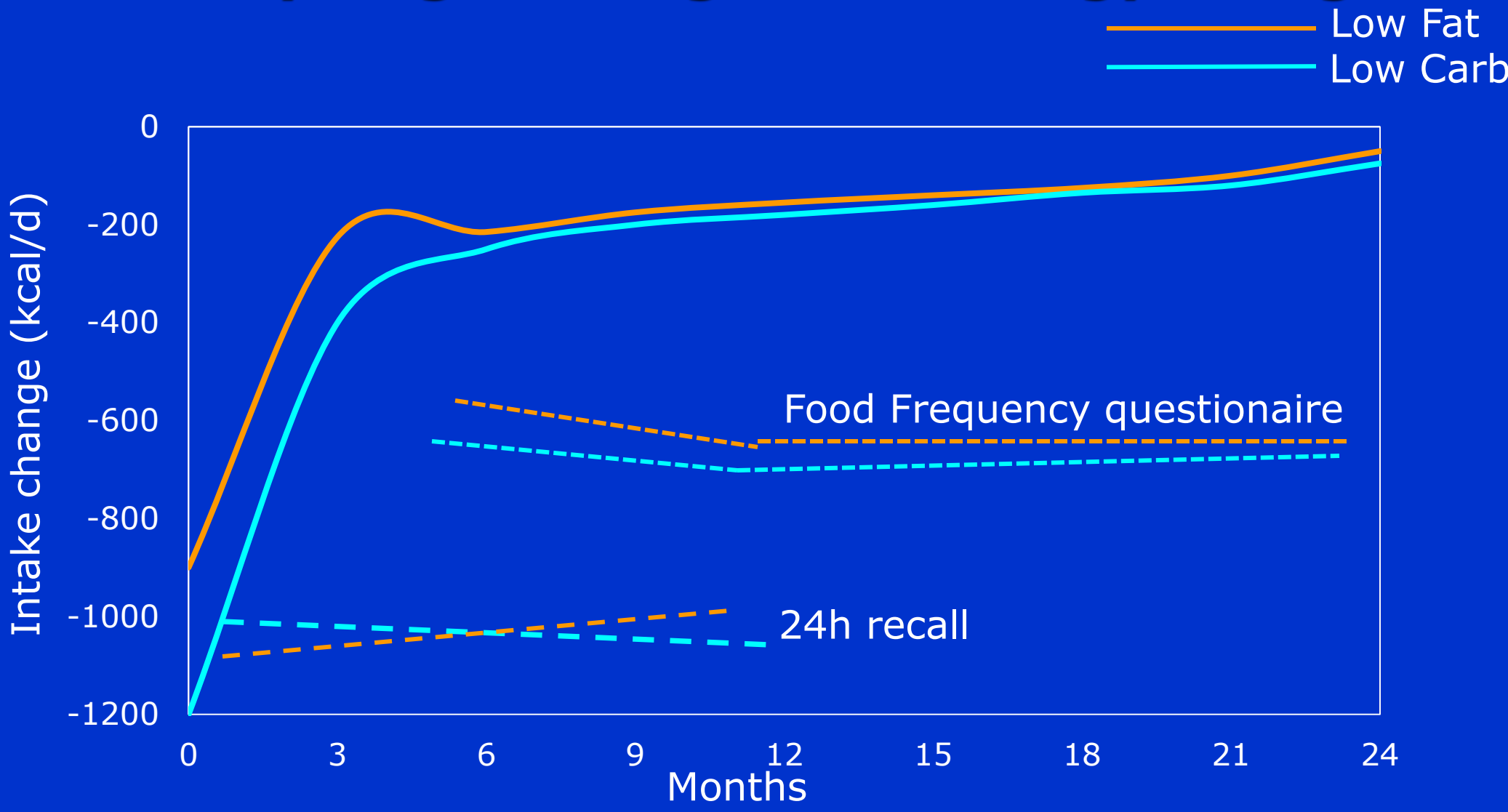
Polidori et al. Obesity (2016) 24, 2289-95

Appetite increased by 100 kcal/day above baseline per kilogram of lost weight – an effort several fold larger than corresponding energy expenditure adaptations. The few individuals who successfully maintain weight loss over time do so by heroic and vigilant efforts to maintain behavior changes in the face of increased appetite along with persistent suppression of energy expenditure in an omnipresent obesogenic environment.

1. Plateau at 6-8 months
2. Initial significant reduction in energy intake
3. Increase in appetite
4. Small decrease in energy expenditure (3>4)
5. Exponential increase in energy intake
6. Effort continues as weight increases



Mean bodyweight changes and energy changes



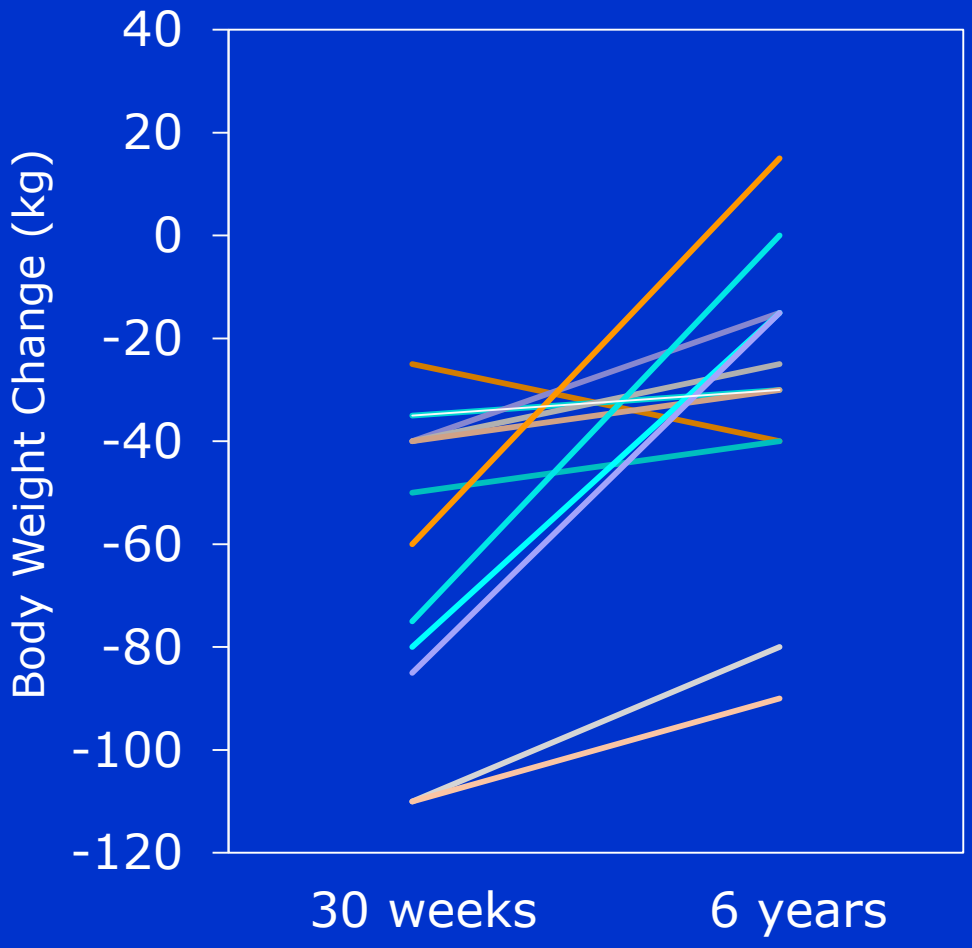
Freedhoff Y. Hall K. *The Lancet* volume 338, 849-51, 2016

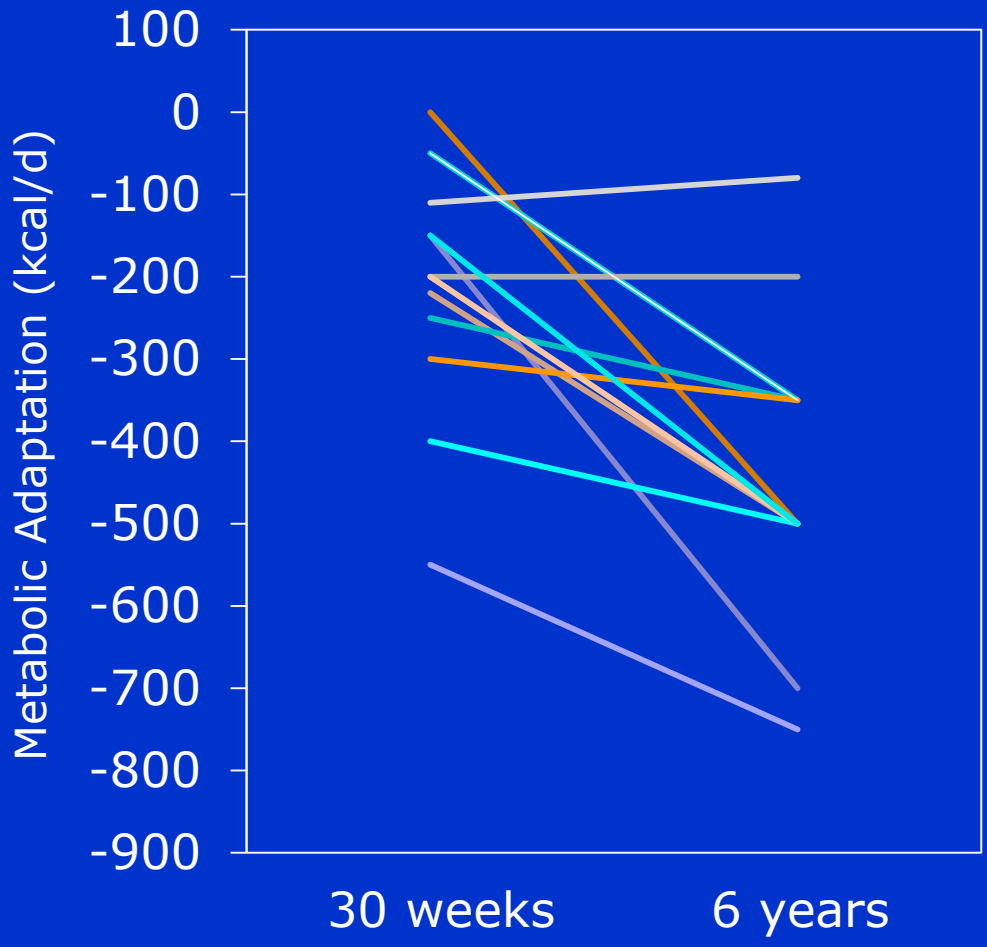
Persistent Metabolic Adaptation 6 Years After "The Biggest Loser" Competition

	Baseline	30 week	6 year	B vs 30	B vs. 6 y	30w vs 6y
Age	34.9	35.4	41.3	<0.0001	<0.0001	<0.0001
Weight (kg)	148.9 (40)	90.6	131.6	<0.0001	0.0294	0.0002
BMI	49.5	30.2	43.8	<0.0001	0.0294	0.0002
%BF	49.3	28.1	44.7	<0.0001	0.0894	0.0003
RMR measured	2,607	1,996	1,903	0.0004	0.0312	0.3481
RMR predicted	2,577	2,272	2,403	<0.0001	0.0058	0.0168
Metabolic adaption	29	-275	-499	0.0061	<0.0001	0.0075
TEE (kcal/d)	3,804	3,002	3,429	0.0014	0.0189	0.0034
Physical activity (kcal/kg/d)	5.6	10.0	10.1	0.0027	0.001	0.8219

Fothergill et al. Obesity 2016. doi:10.1002/oby.21538

Persistent Metabolic Adaptation 6 Years After "The Biggest Loser" Competition





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The Biggest Loser

- Lost 1 lb per day
- 1300 kcal intake/ 5,000 kcal exercise
- Maintained 11.9% +/- 16.8% (57% > 10% weight loss)
- Learned behaviors, no diabetes developed
- Maintained physical activity but intake (appetite) near return to baseline
- Metabolic slowing with massive weight loss despite preservation of fat-free mass
- Metabolic adaptation was not related to weight regain at 6 years
- Greater weight loss (most successful) at 6 years experienced greater metabolic slowing

Inpatient is not Outpatient but…

- Small numbers, healthy, low variables
- Maybe passionately focusing on the macronutrient quantity and not quality, behavior, adherence, portion size lessens success
  - Suggests able lose fat on LF diets
  - KD may not promote satiety (protein) especially with unlimited available food
  - LC decreases insulin, glucose and does not marked increase energy expenditure
- A sustained, increase in physical activity is needed to help sustain weight loss
- Diet recall is not accurate