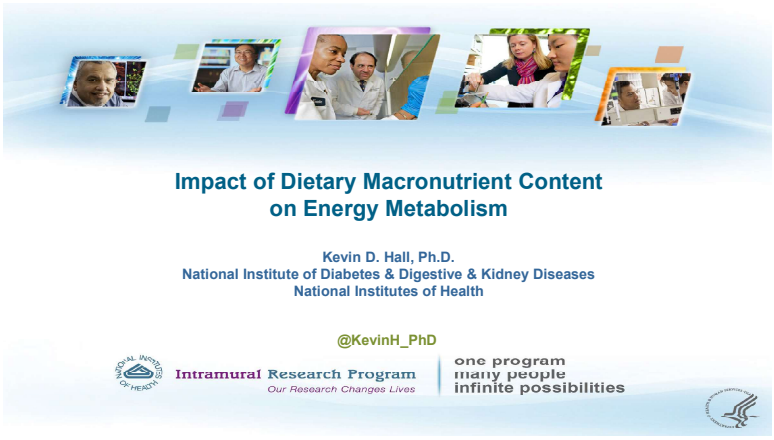

Impact of Dietary Macronutrient Content on Energy Metabolism

Kevin D. Hall, Ph.D.
National Institute of Diabetes & Digestive & Kidney Diseases
National Institutes of Health

@KevinH_PhD

Intramural Research Program
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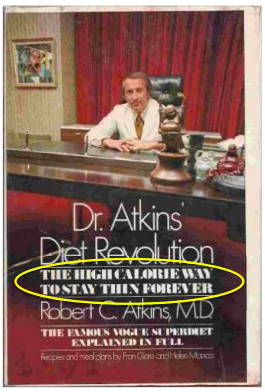
one program
many people
infinite possibilities

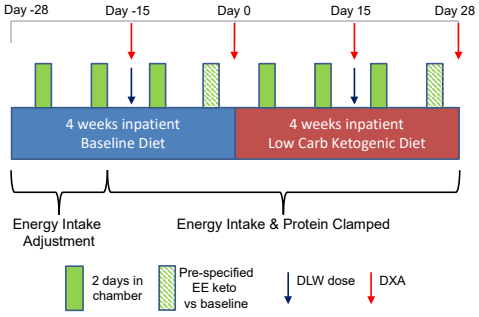
The Promise of Low Carb Diets



"You can eat more calories… as long as no carbohydrates are present [and] still lose weight."

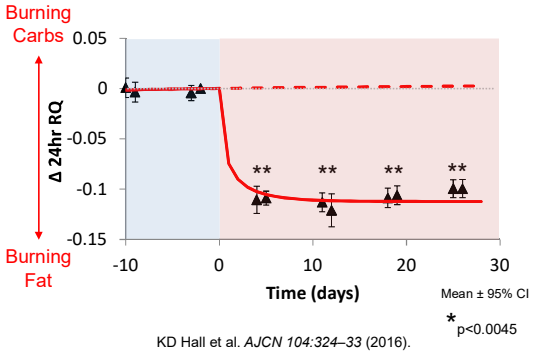
Robert C. Atkins,
Dr. Atkins Diet Revolution:
The High Calorie Way to Stay Thin Forever (1972).

Two Month Inpatient Isocaloric Ketogenic Diet Study



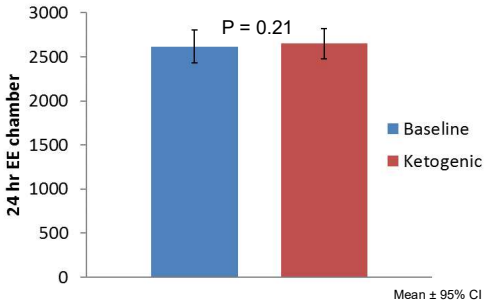
KD Hall et al. *AJCN 104:324–33* (2016).

Rapid & Persistent Shift to Increased Fat Oxidation



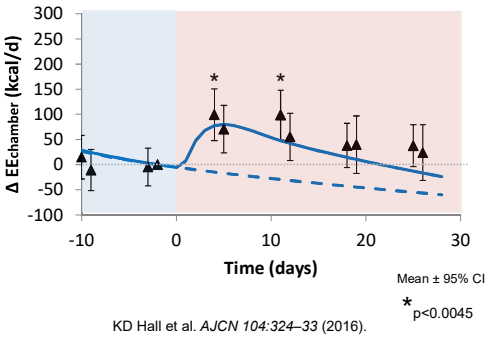
KD Hall et al. *AJCN 104:324–33* (2016).

No Significant Energy Expenditure Difference



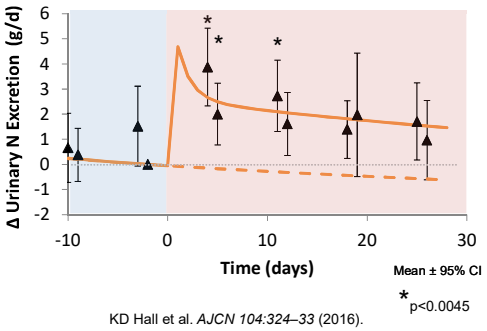
KD Hall et al. *AJCN 104:1488-90* (2016).

Small and Transient Increase in Energy Expenditure



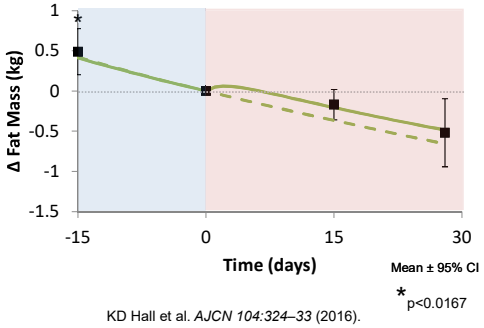
KD Hall et al. *AJCN 104:324–33* (2016).

Increased N Excretion post Ketogenic Diet



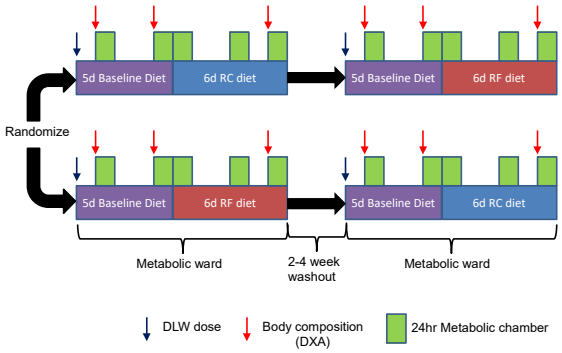
KD Hall et al. *AJCN 104:324–33* (2016).

Loss of Body Fat Slows post Ketogenic Diet



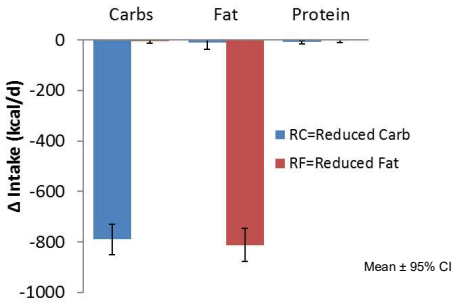
KD Hall et al. *AJCN 104:324–33* (2016).

Isocaloric Selective Reduction of Dietary Carbs vs Fat



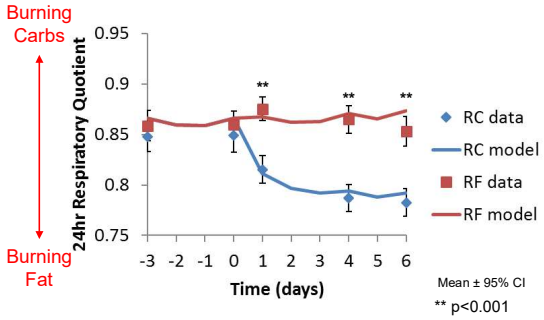
KD Hall et al. *Cell Metabolism* 22:427-436 (2015).

Isocaloric 30% Calorie Restricted Diets



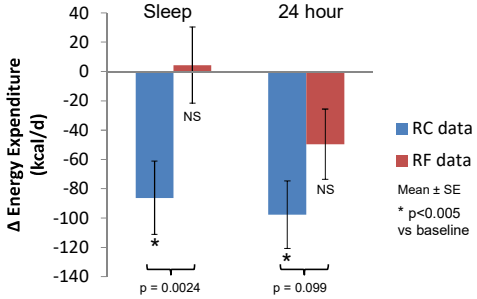
KD Hall et al. *Cell Metabolism* 22:427-436 (2015).

Only the RC Diet Increased Fat Oxidation



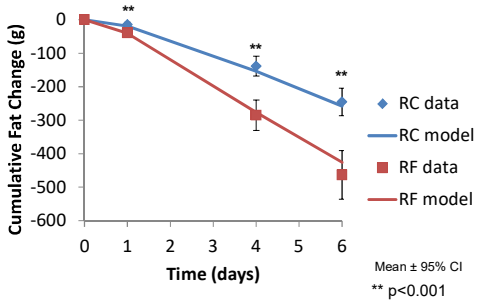
KD Hall et al. *Cell Metabolism* 22:427-436 (2015).

Only the RC Diet Decreased Energy Expenditure



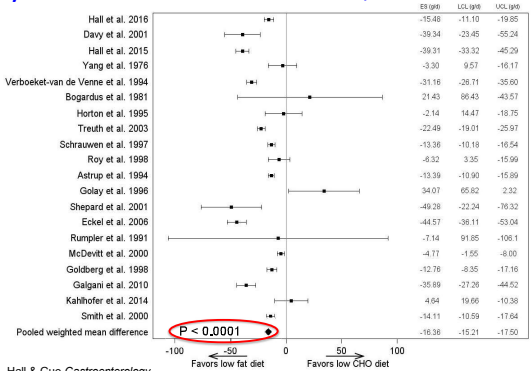
KD Hall et al. *Cell Metabolism* 22:427-436 (2015).

More Cumulative Body Fat Loss with the RF Diet



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

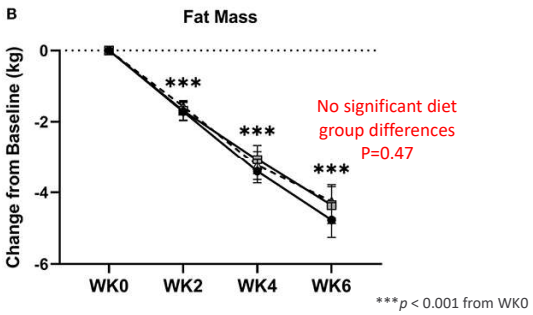
Body Fat: Isocaloric Carb vs. Fat, Matched Protein



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

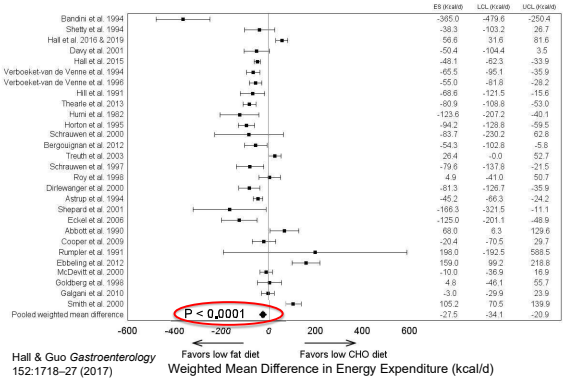
Weighted Mean Difference in Body Fat (g/d)

Since the Meta: Very Low Carb vs. Low Fat Isocaloric Diets



A. Buga et al. *Front. Nutr. March 24,* 2021 https://doi.org/10.3389/fnut.2021.618520

Expenditure: Isocaloric Carb vs. Fat, Matched Protein



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

Weighted Mean Difference in Energy Expenditure (kcal/d)

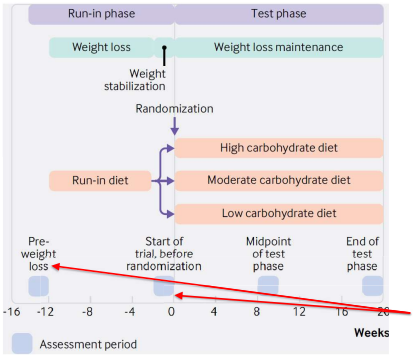
Do Lower-Carbohydrate Diets Increase Total Energy Expenditure? An Updated and Reanalyzed Meta-Analysis of 29 Controlled-Feeding Studies

David S Ludwig,[1] Stephanie L Dickinson,[2] Beate Henschel,[2] Cara B Ebbeling,[1] and David B Allison[2]

[1]New Balance Foundation Obesity Prevention Center, Boston Children's Hospital and Harvard Medical School, Boston, MA, USA; and
[2]Indiana University School of Public Health–Bloomington, Bloomington, IN, USA

Conclusions: Lower-carbohydrate diets transiently reduce TEE, with a larger increase after ~2.5 wk. These findings highlight the importance of longer trials to understand chronic macronutrient effects and suggest a mechanism whereby lower-carbohydrate diets may facilitate weight loss. *J Nutr* 2021;151:482–490.

Ebbeling et al. BMJ 2018 Study Design

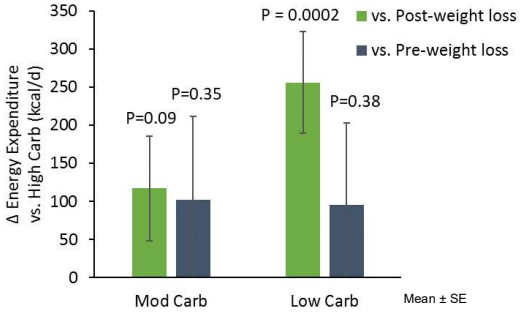


"The pre-weight-loss value…, rather than [post-weight-loss], was ***originally specified in the registry*** as the anchor for calculating change scores, but this error was corrected…"

The pre-specified analysis was not reported in the final paper

Two potential points of comparison:
Pre-Weight Loss vs
Post Weight Loss

Ebbeling et al. BMJ 2018 Reanalysis



Hall, Guo, Speakman. *Int J Obesity* (2019) https://doi.org/10.1038/s41366-019-0456-3

Methodology: Indirect Calorimetry 101

$$EE(\text{kcal}) = 3.85 \times VO_2(\text{L}) + 1.07 \times VCO_2(\text{L})$$

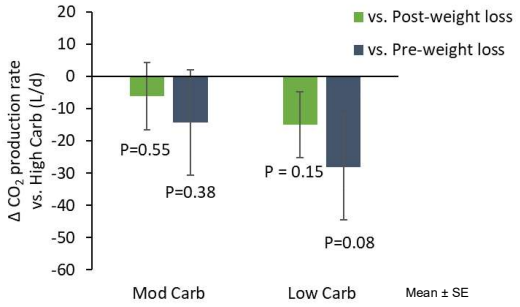
$$EE_{DLW}(\text{kcal}) = \left[\frac{3.85}{RQ} + 1.07\right] \times rCO_2(\text{L})$$

Doubly Labeled Water (DLW) indirectly estimates the daily average CO_2 production rate

DLW also requires estimating the daily average Respiratory Quotient (RQ = VCO_2:VO_2)

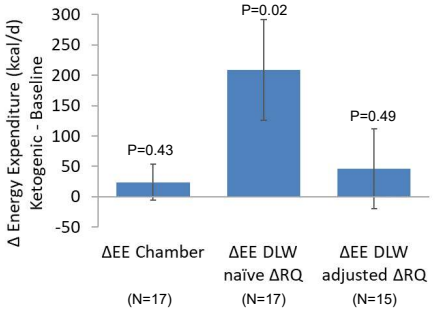
KD Hall et al. *AJCN* 109:1328-1334 (2019)

No Significant Diet Effect on CO_2 Production



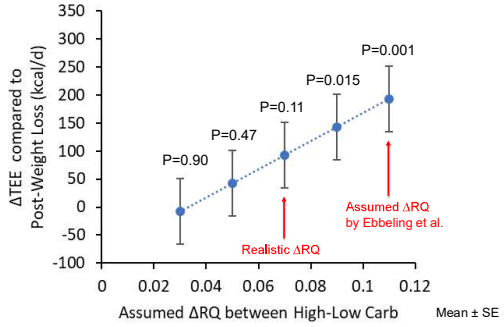
Hall, Guo, Speakman. *Int J Obesity* (2019) https://doi.org/10.1038/s41366-019-0456-3

RQ Sensitivity of ΔExpenditure Keto vs. Baseline Diets



KD Hall et al. *AJCN* 109:1328-1334 (2019)

DLW Expenditure Effect Depends on Assumed ΔRQ



Hall, Guo, Speakman. *Int J Obesity* (2019) https://doi.org/10.1038/s41366-019-0456-3

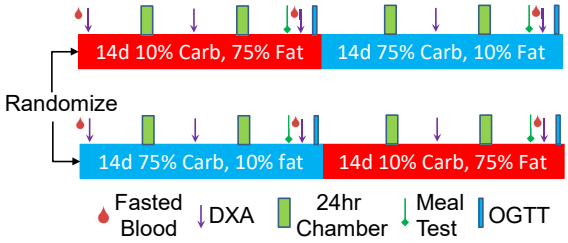
Overestimated Impact of Lower-Carbohydrate Diets on Total Energy Expenditure

Dear Editor:

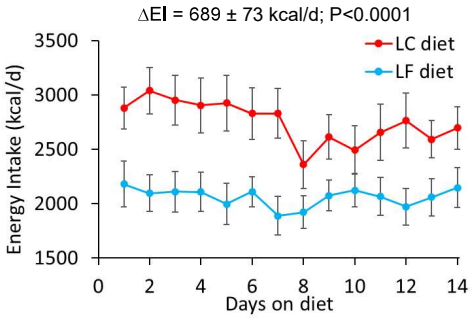
Ludwig et al. (1) report that total energy expenditure (TEE) is greater during isocaloric lower-carbohydrate diets lasting >17 days. However, the reported effect size of 135 kcal/d is likely overestimated, because the TEE differences extracted from several longer-term studies are not the most defensible values. Our reanalysis of the longer-term controlled feeding studies confirms that the TEE effect of lower-carbohydrate diets is statistically significant, but its ~63–74 kcal/d magnitude is smaller than that estimated by Ludwig et al. (1), amounting to an energy equivalent of less than an apple per day.

S Guyenet & KD Hall. *J Nutr* 151:2496-7 (2021).

Does Diet Composition Affect *Ad Libitum* Energy Intake?

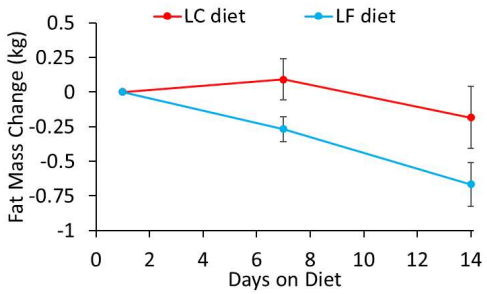


Less Energy Intake on the Low Fat Diet



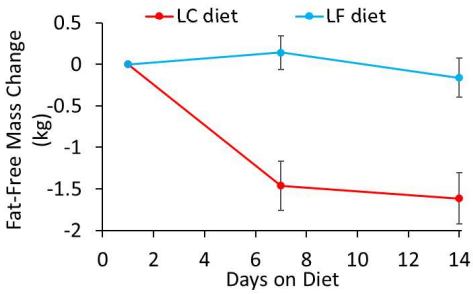
Mean ± SE

More Body Fat Loss on the Low Fat Diet



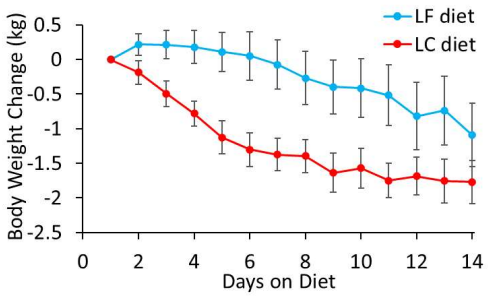
Mean ± SE

Greater Loss of Fat-free Mass on the Low Carb Diet



Mean ± SE

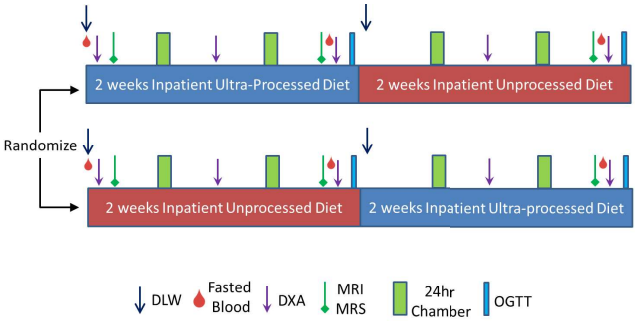
Faster Weight Loss on the Low Carb Diet



Mean ± SE

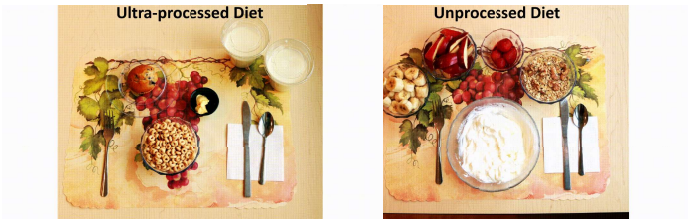
KD Hall et al. *Nature Medicine* 2021 https://doi.org/10.1038/s41591-020-01209-1

Ultra-processed vs Unprocessed Diet Study



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

Ultra-processed vs Unprocessed Diets



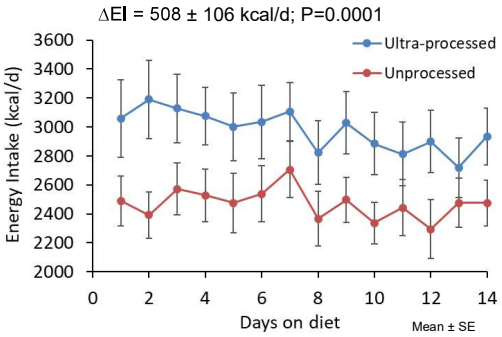
The meals had similar amounts of:
Calories, Carbs, Fat, Sugar, Sodium, Fiber

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

Primary Outcome: Mean Daily Energy Intake Differences

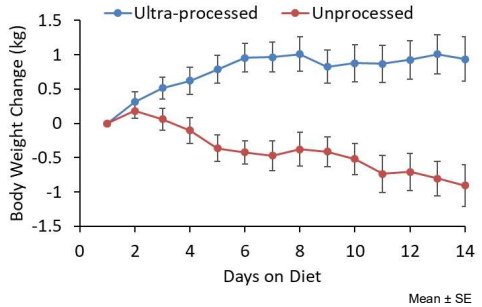
KD Hall et al. *Cell Metabolism* 30:1-11 (2019).

Ultra-processed Diets Cause Increased Intake



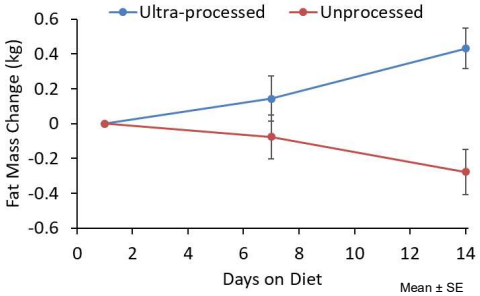
KD Hall et al. *Cell Metabolism* 30:1-11 (2019).

Ultra-processed Diets Cause Weight Gain



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

Ultra-processed Diets Cause Body Fat Gain



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

Summary

- Isocaloric variation in the ratio of dietary carbohydrate:fat
  - has small effects on Energy Expenditure (& methods matter!)
  - has small effects on Body Fat Mass
  - has large effects on metabolic fuel utilization as well as circulating hormones & metabolites (not shown)

- Diet composition has large effects on *ad libitum* Energy Intake
  - Very low carb diets result in greater energy intake than very low fat diets
  - Ultra-processed diets result in greater energy intake than unprocessed diets matched for various nutrients

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B. Tim Walsh (Columbia)

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many people
infinite possibilities

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Special Thanks

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Metabolic Kitchen Staff
Volunteer Study Subjects
Nutrition Science Initiative