

# What's the Best Weight Loss Diet

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19th Annual

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# Disclosures – Donna Ryan

- Advisor or Consultant: Novo Nordisk, Pfizer, Real Appeal, Epitomee, Gila Therapeutics, Xeno Bioscience, Calibrate, Naturally Slim Wondr Health, Lilly Advisory, YSOPIA, Altimmune, IFA Celtic, Ro, Scientific Intake, Amgen, Zealand
- Speakers Bureau: Novo Nordisk
- Ownership Interest: Gila Therapeutics, Xeno Bioscience, Epitomee, Calibrate, Roman and Scientific Intake
- Research: SELECT Steering Committee (Novo Nordisk)



# AHA/ACC/TOS Guidelines Critical Question 3: What is the best diet for weight loss?

- 17 diets reviewed: including AHA step 1, EASD & ADA, low cal, low carb, low fat, low glycemic index/load, vegan, lacto-ovarian vegetarian, Mediterranean, DASH, Zone-like, Atkins-like and others
- For weight loss of at least one year's duration, there was no one clearly superior dietary approach.

# Lacking a superior diet for weight loss, the Obesity Guidelines endorsed behavioral counseling.



- ✓ The diet must be calorie reduced in order to create an energy deficit
  - 1200-1500 kcal/d for women and 1500-1800 kcal/d for men, or
  - 500 kcal/d or 750 kcal/d energy deficit from baseline diet






- ✓ Prescription diets for weight loss should be based on the patient's preferences and health status – there is no 'one diet' for all patients

# Behavioral Strategies for Creating Negative Energy Balance Target Biology

Gastroenterology 2017;152:1728–1738

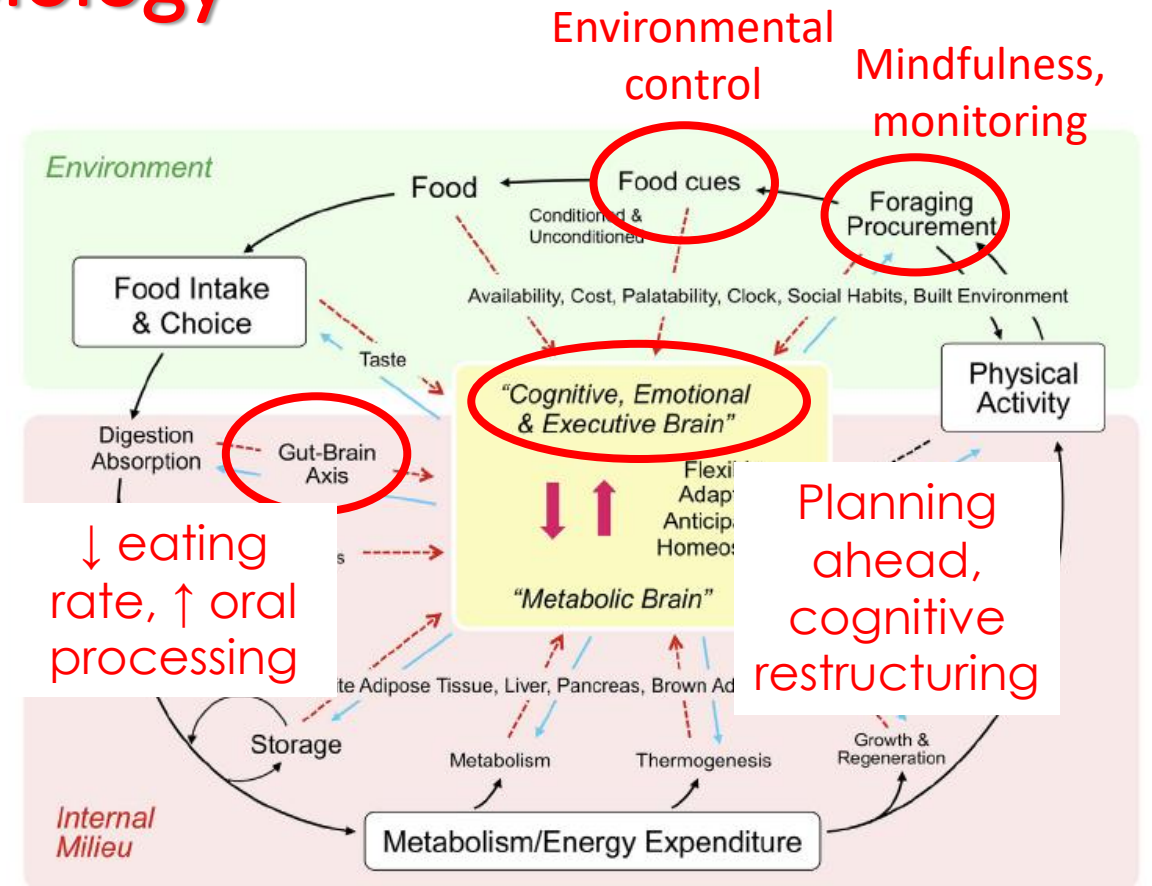
## Blaming the Brain for Obesity: Integration of Hedonic and Homeostatic Mechanisms

Hans-Rudolf Berthoud Heike Münzberg Christopher D. Morrison

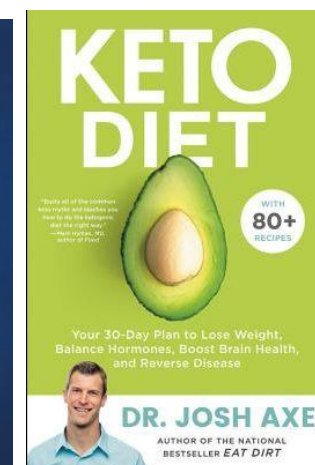
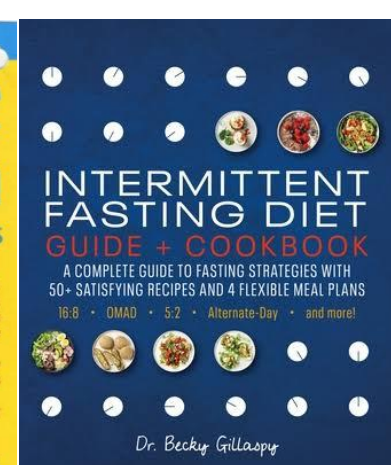
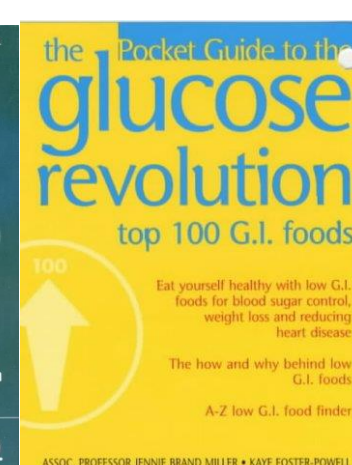
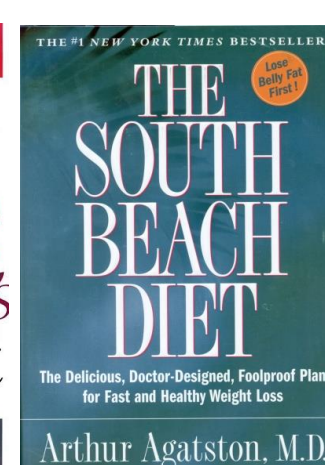
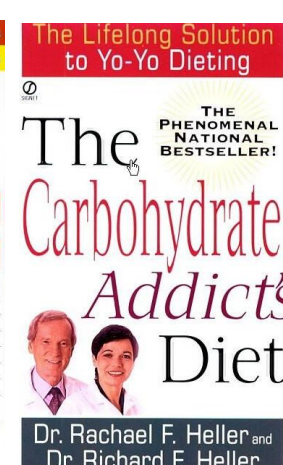
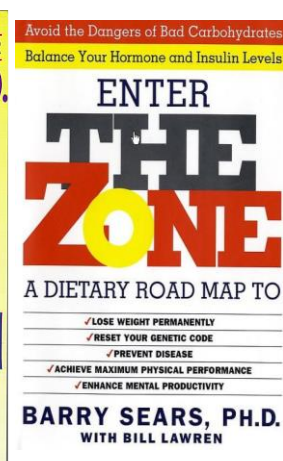
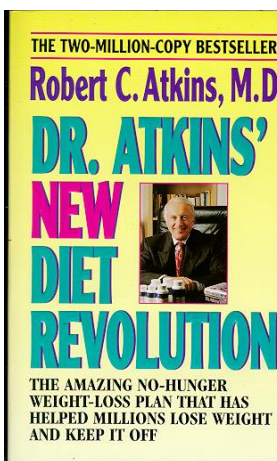
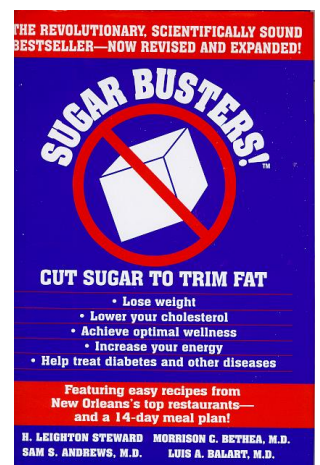
Neurobiology of Nutrition and Metabolism Department, Pennington Biomedical Research Center, Louisiana State University System, Baton Rouge, Louisiana

The brain plays a key role in the controls of energy intake and expenditure, and many genes associated with obesity are expressed in the central nervous system. Technological and conceptual advances in both basic and clinical research have provided enough to compete with other behaviors and had to be learned and passed to future generations. Such a high-energy throughput also requires a large metabolic (M) that capable of efficiently digesting



# The search for a magic diet to promote weight loss

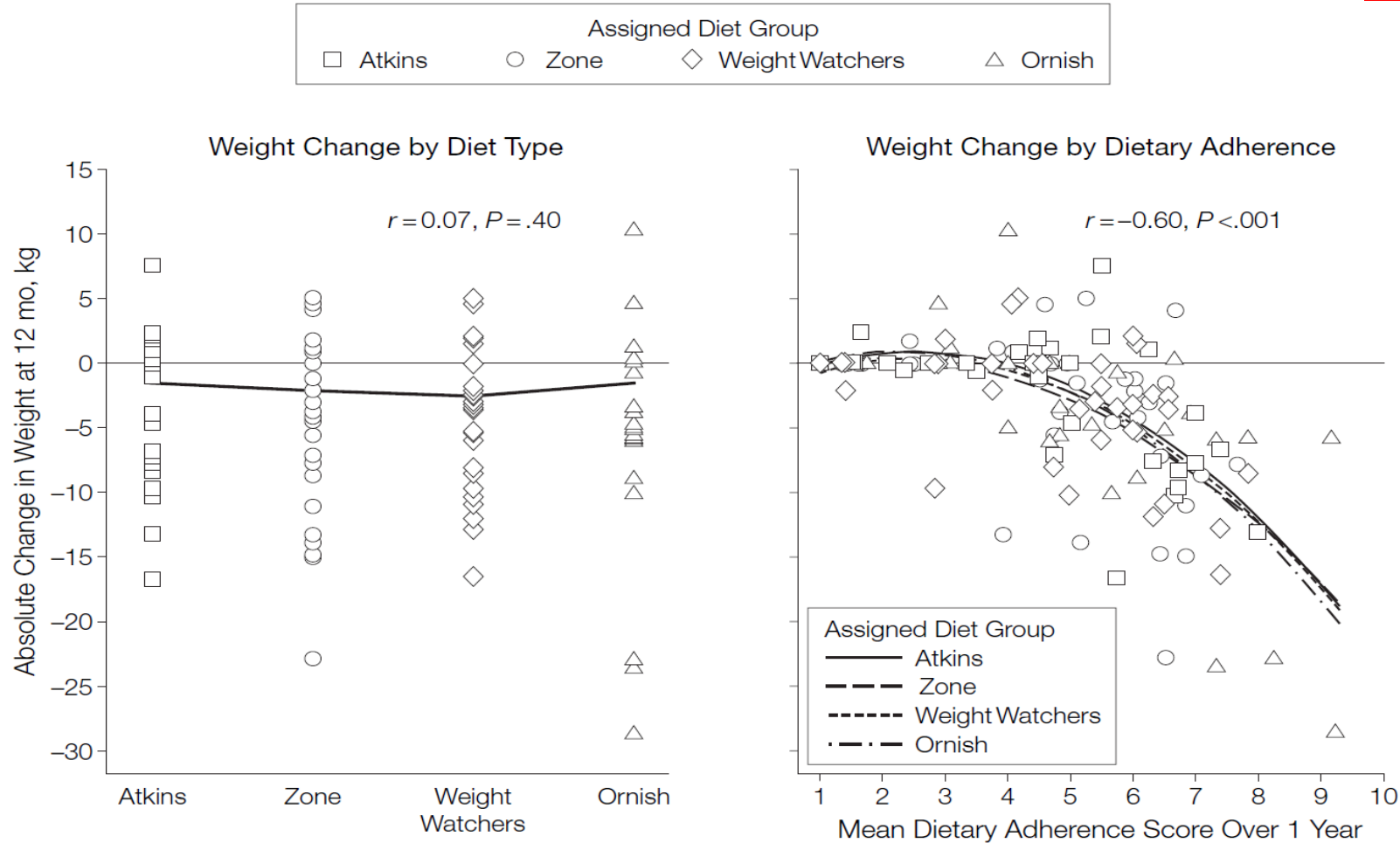
- Simple, easy to follow instructions
  - No weighing, measuring, monitoring and recording
- Lose weight without restricting delicious foods
  - Macronutrient approaches eliminate whole classes of foods, but allow some foods *ad lib*
  - Time restricted eating
- Illustrates how difficult it is for patients to navigate the obesogenic environment
- Distracts from understanding obesity as a disease



1. Heterogeneity of treatment effect

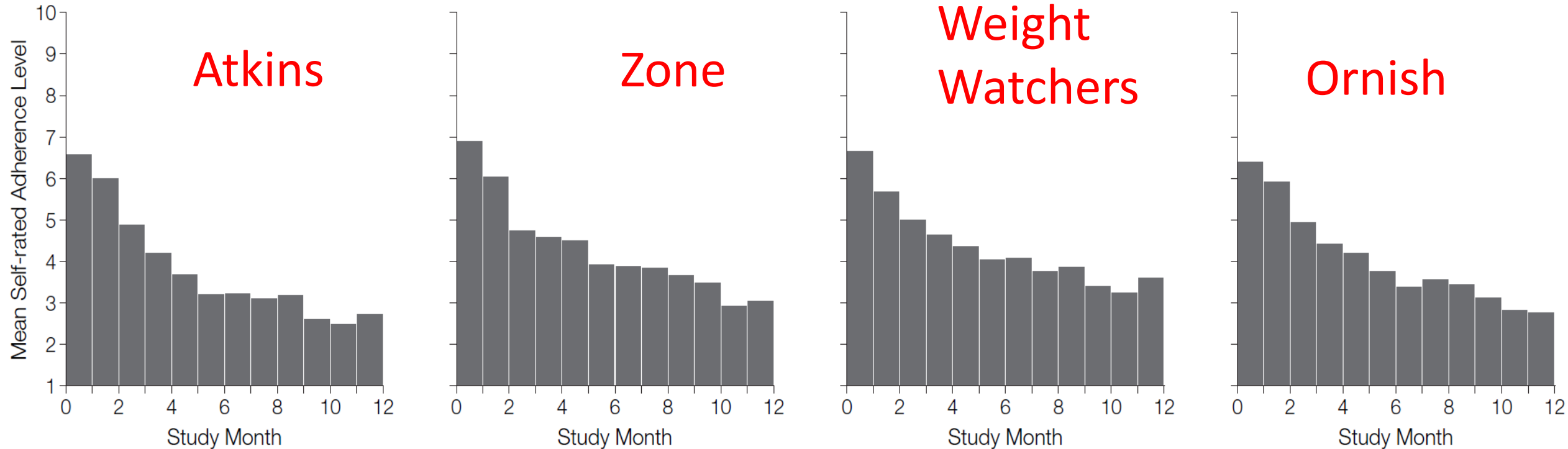
# 4 Popular Diets Atkins, Zone, WW, Ornish

2. Adherence predicts success



# Dietary Adherence Wanes over Time

Mean Self-reported Dietary Adherence by Month for 4 Popular Diets





# Adherence – Not Diet - Predicts Success

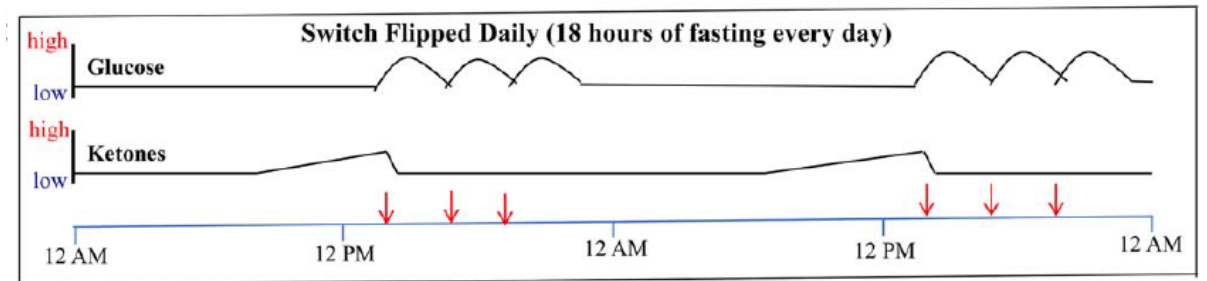
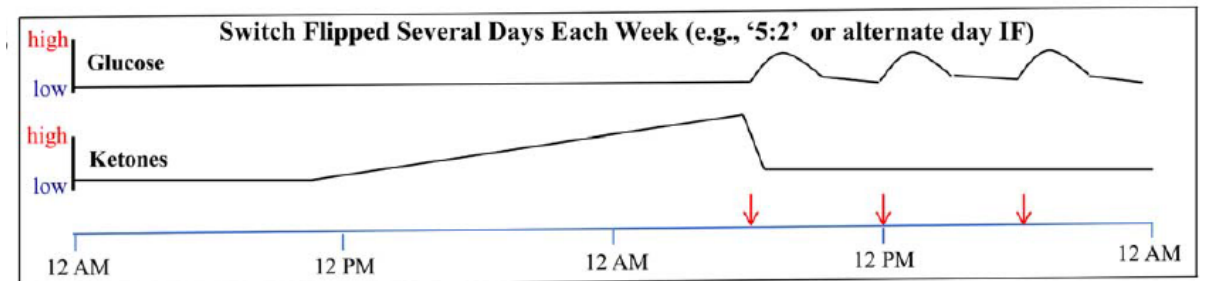
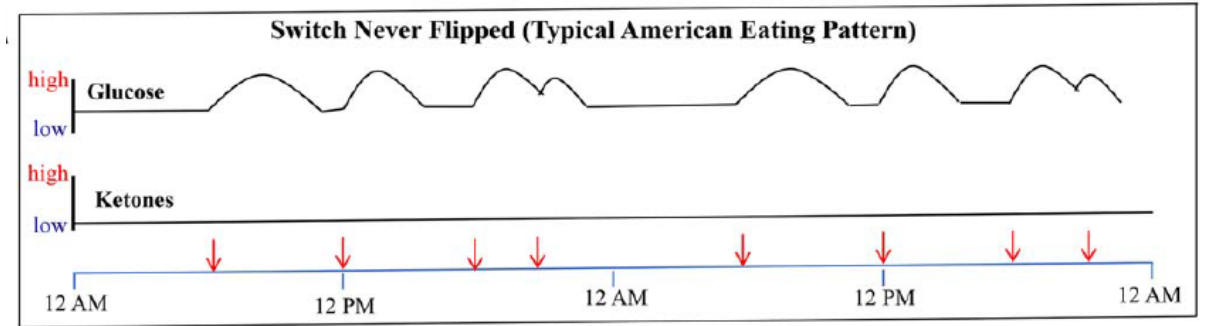
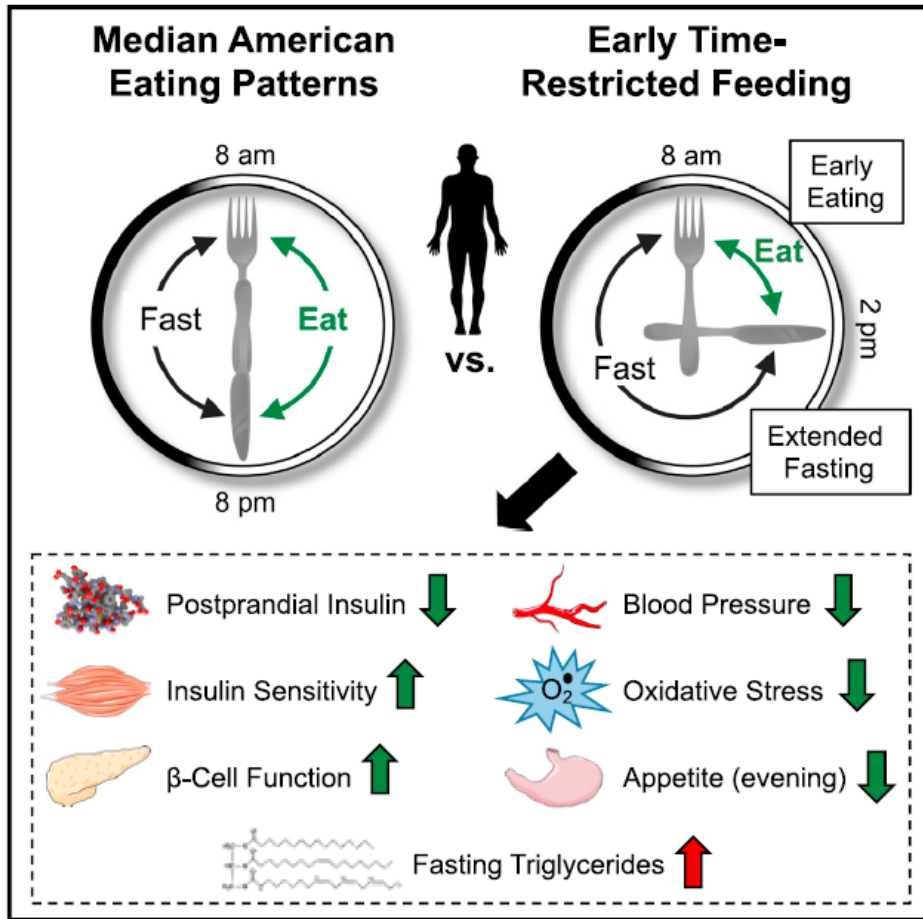
## Choice of Strategy Does Not Improve Weight Loss

- 2012 - Consistent finding in four meta-analyses, each summarizing 13 to 24 trials: adherence was most strongly associated with weight loss<sup>1-4</sup>
  1. Ajala O, et al. *Am J Clin Nutr.* 2013;97(3):505-516.
  2. Wycherley TP, et al. *Am J Clin Nutr.* 2012;96(6):1281-1298.
  3. Hu T, et al. *Am J Epidemiol.* 2012;176 Suppl 7:S44-54.
  4. Bueno NB, et al. *Br J Nutr.* 2013;110(7):1178-1187
- 2014 - Meta-analysis of 48 trials, n = 7,286; conclusion: any diet a patient will adhere to lose weight is best<sup>5</sup>
  5. Johnston BC, et al. *JAMA.* 2014;312(9):923-933.
- 2019 – Systematic Review and Meta-analysis of 12 interventions in 9 studies - Choice vs. No choice did not incur weight loss benefit<sup>6</sup>
  6. Leavy JM, Clifton PM, Keogh JB. The Role of Choice in Weight Loss Strategies: A Systematic Review and Meta-Analysis. *Nutrients.* 2018 Aug 21;10(9):1136.

# Current Diet Trends 2021

- 39% - have followed a specific diet or eating pattern within the past year...Top Diets:
  - Calorie counting (10%)
  - clean eating (9%)
  - Intermittent fasting (8%)
  - ketogenic or high-fat (5%) and low-carb (6%)
- Top motivators for new diets
  - losing weight (39%)
  - protecting long-term health and preventing future health concerns (38%)
  - feeling better and having more energy (38%)
  - improving physical appearance (29%)
  - preventing weight gain (28%)

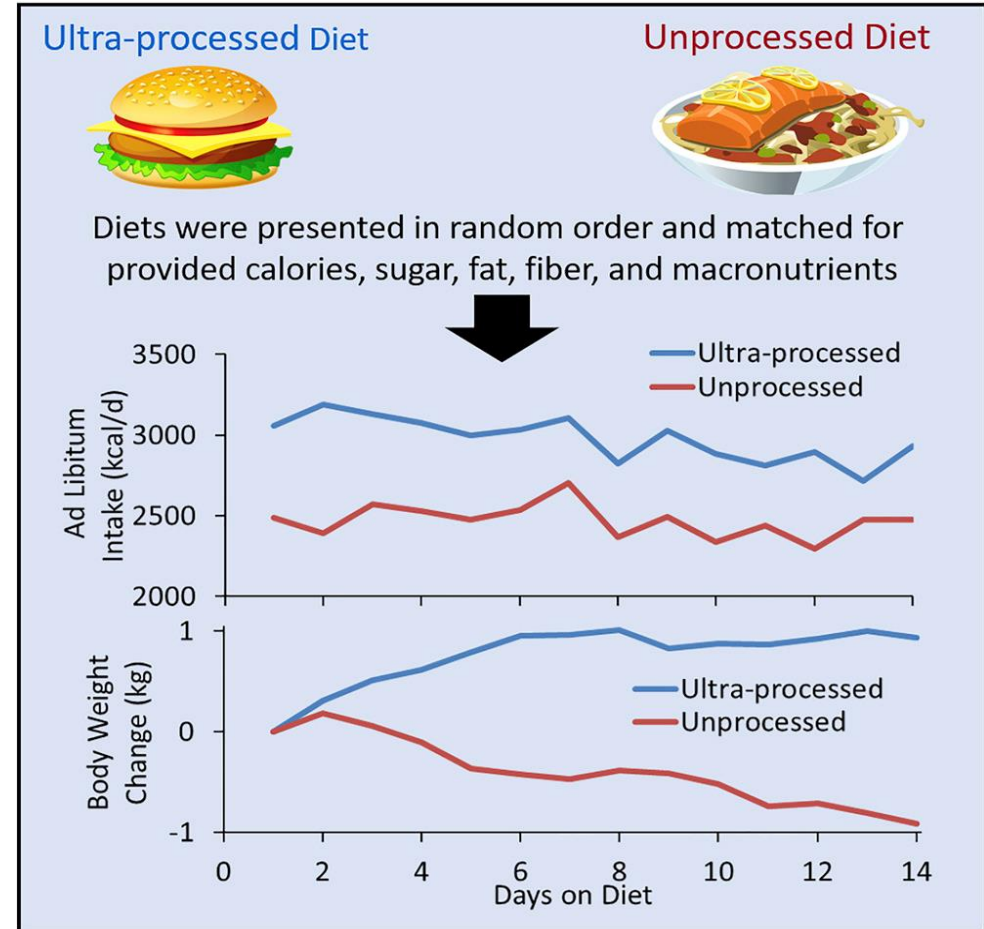
# Trending now... Time Restricted Eating



# Trending now... Clean Eating



Clean eating... avoids processed foods

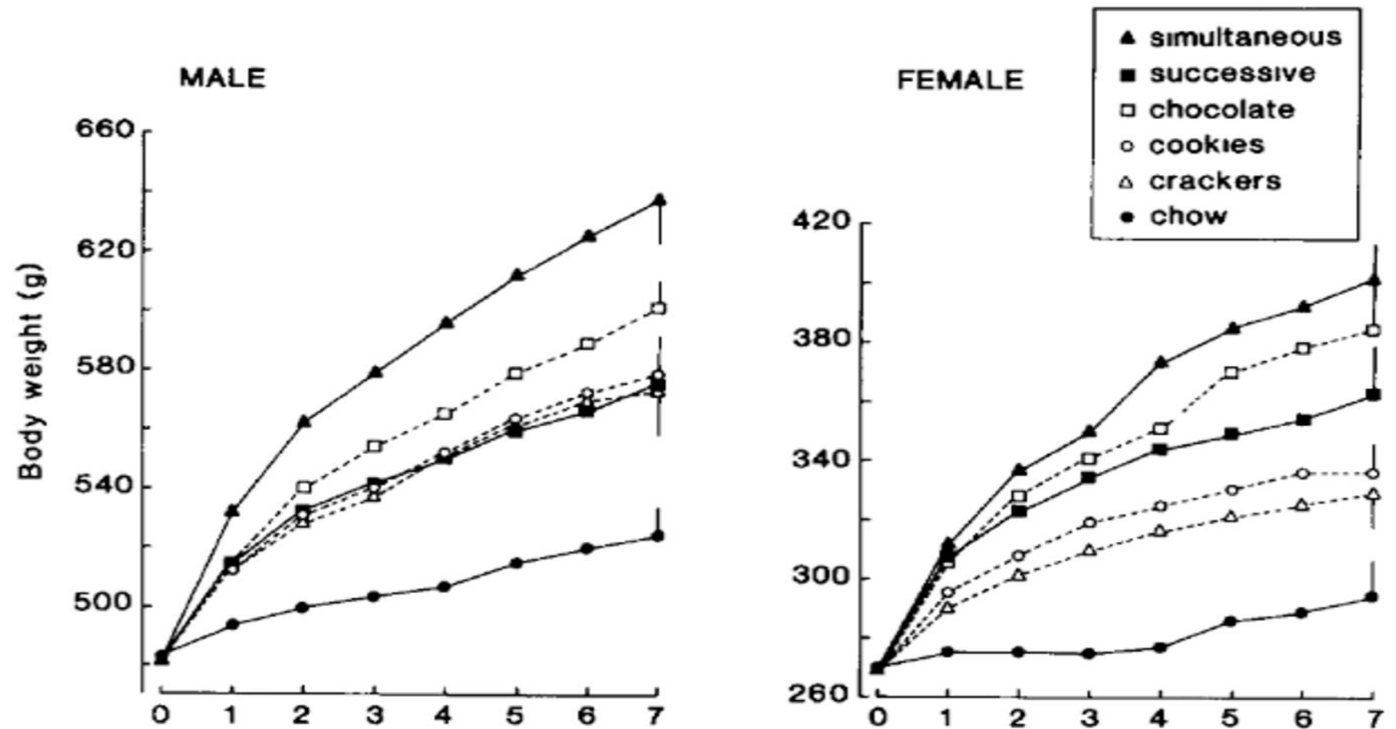


# Trending, but seems to have plateaued – Ketogenic diet

**Ketogenic diet:** very hi fat  
& low carb;  
75% fat, 20% protein, 5% carb

- *excludes* most grains, legumes, fruits, breads, sweets, pastas and starchy vegetables, and sometimes nuts and seeds

If you limit food choices, you will reduce caloric intake.

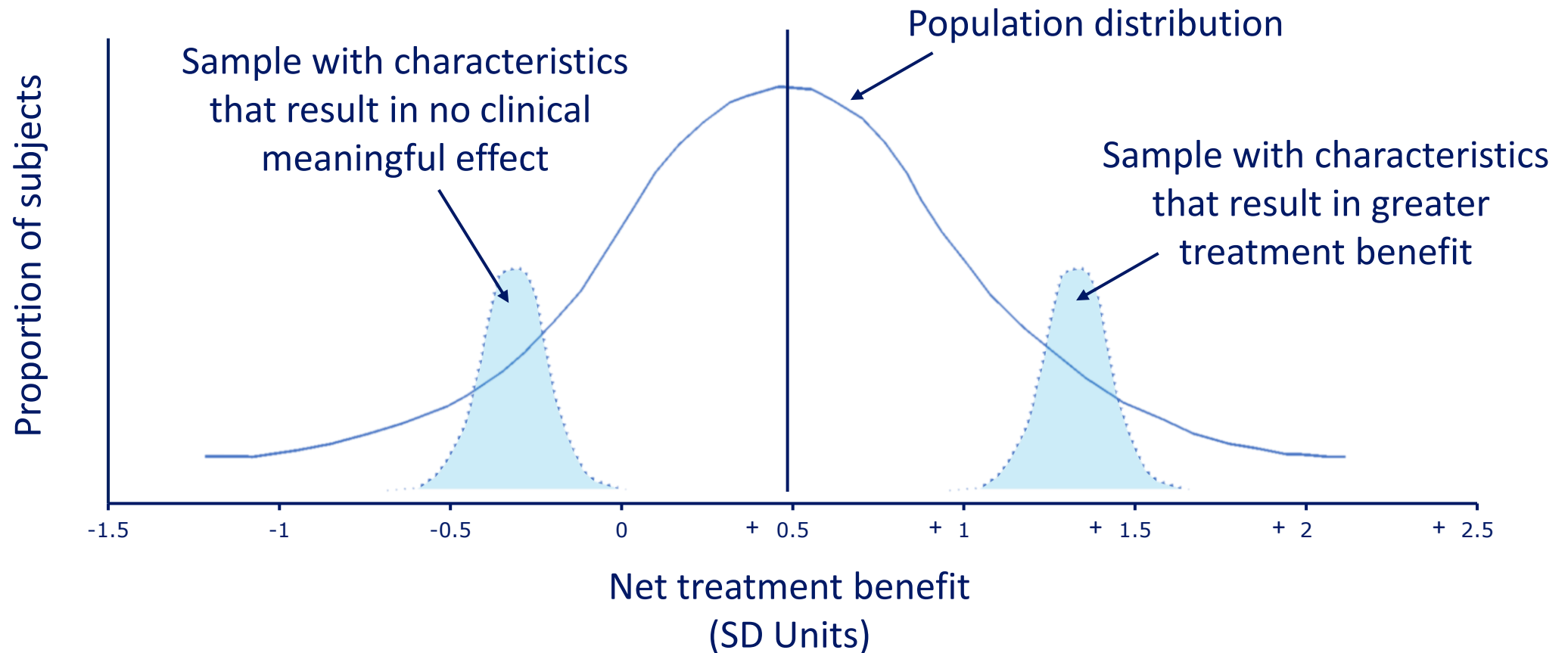


What about a  
personalized  
approach to diet for  
weight loss?

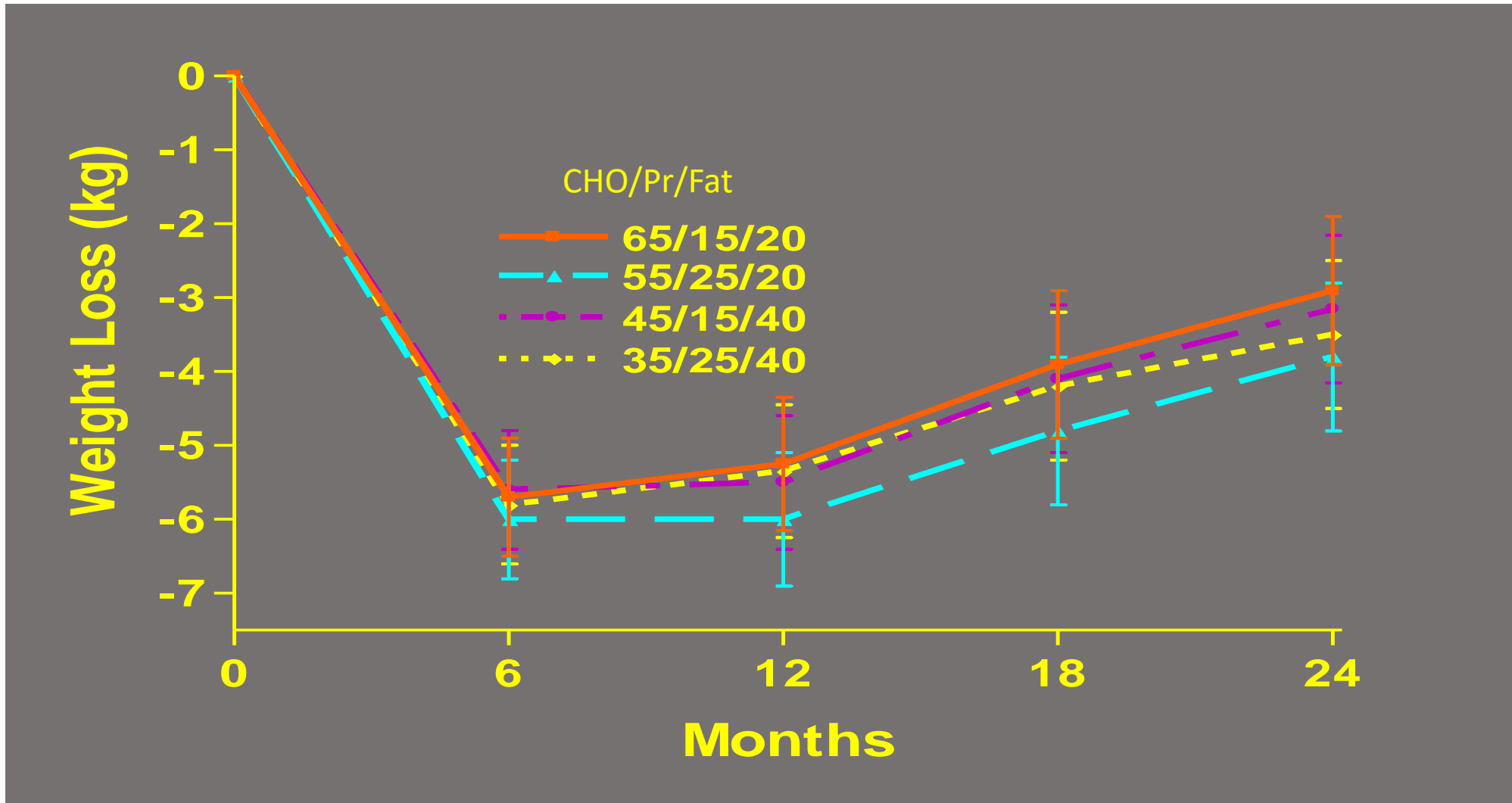


## Heterogeneity of treatment effects occurs when...

there is an interaction between patient characteristics and the treatment delivered

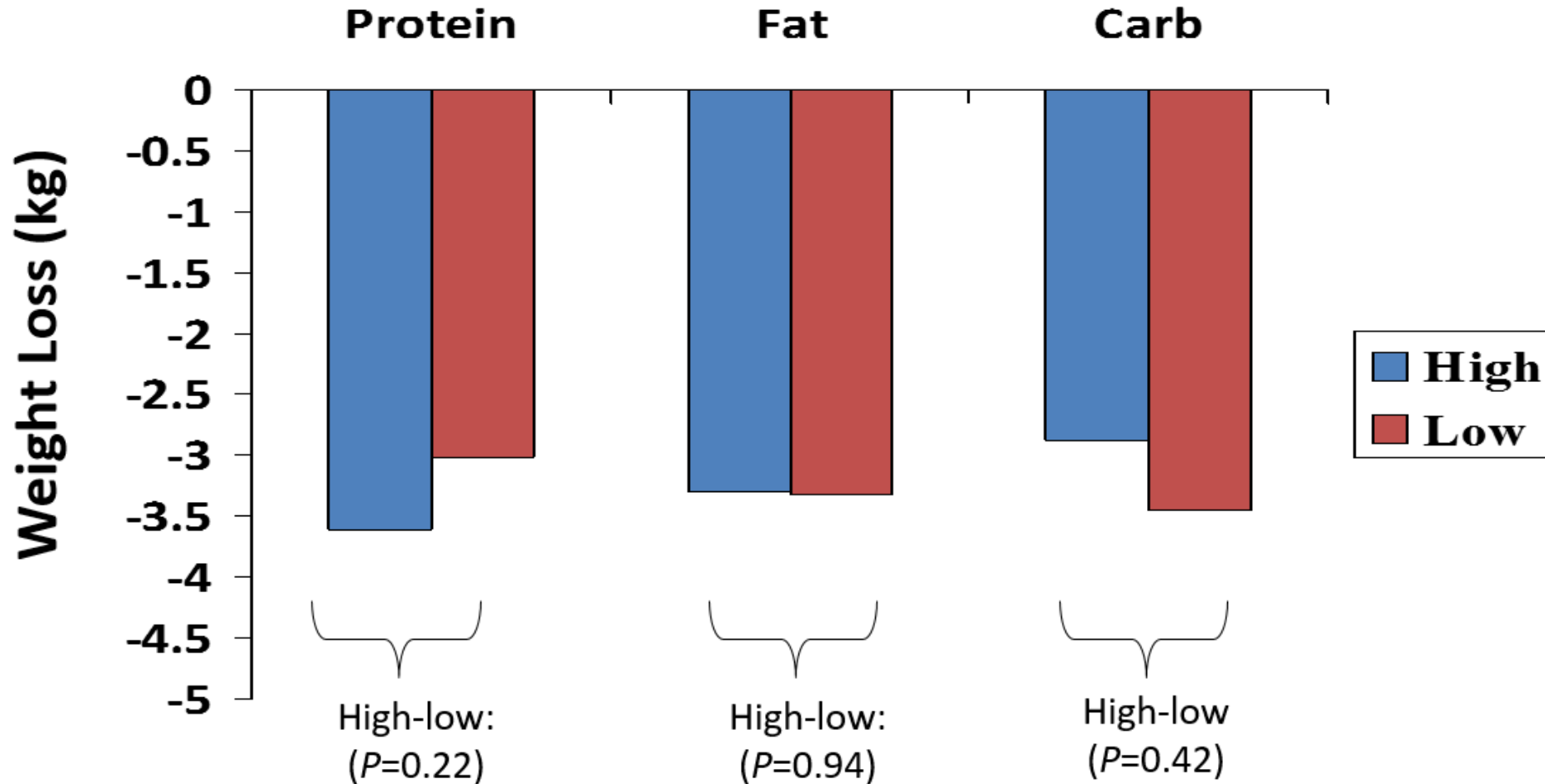


# POUNDS Lost: Weight Change Over 2 years among 4 diets of differing macronutrient composition





# POUNDS LOST: Weight Change from Baseline to 2 years: N=811



# Baseline factors in POUNDS Lost Predicting Weight Loss

<i>Baseline Factor</i>	<i>Outcome</i>
<i>Older age vs younger age</i>	Greater weight loss
<i>Men vs women</i>	Greater weight loss
<i>Married vs unmarried women</i>	Greater weight loss
<i>White participants vs black participants</i>	Greater weight loss
<i>Free triiodothyronine (FT3), Free thyroxine (FT4) higher levels vs low</i>	Greater weight loss,
<i>Lower levels of craving for carbohydrates/starches vs. high</i>	Greater weight loss
<i>Low Restraint on TFEQ vs high levels</i>	Greater weight loss
<i>Perfluoroalkyl compounds (PFAS) low levels vs. high</i>	Greater weight loss

# Post hoc factors in POUNDS Lost Predicting Weight Loss

<i>Post hoc Factor</i>	Outcome
<i>Higher adherence to attendance, monitoring, dietary goals, computer tracking</i>	Greater weight loss
<i>Greater increase in dietary protein intake</i>	Greater weight loss
<i>Greater increase in dietary fiber intake</i>	Greater weight loss

# Genetic predictors of weight loss in POUNDS Lost

<b>Gene</b>	<b>SNP</b>	<b>Weight loss/abdominal fat</b>	<b>Treatment group</b>
<i>AMY1-AMY2</i>	<i>rs11185098</i>	Greater weight loss; -5.1 kg for AA vs GG phenotype	All diets
<i>PPM1K</i>	<i>rs1440581</i>	Greater weight loss -8.2 kg for TT vs -5.1 kg for CC genotype	High fat diet
<i>NPY</i>	<i>rs16147</i>	Greater waist circumference decrease; -8.5cm for CC vs -5 cm reduction for TT genotype	High fat diet
<i>NFATC2IP</i>	<i>rs11150675</i>	Greater weight loss; -6.4 kg for A versus -5.3 for non-A allele	High fat diet
<i>FGF21</i>	<i>rs838147</i>	Decreased total fat; -3.7% for CC vs -15% for TT genotype	High carbohydrate diet
<i>IRS1</i>	<i>rs2943641</i>	Greater weight loss; -6.5kg for CC vs -3.7kg for TT genotype	High carbohydrate diet
<i>MTNR1B</i>	<i>rs7227255</i>	Greater weight loss; -11 kg for GG vs 6.5 kg for CC genotype	Low fat diet
<i>TCFL72</i>	<i>rs122553720</i>	Greater weight loss; -9.5 kg for TT vs 6.4 kg for GG genotype	Low fat diet
<i>HNFA</i>	<i>rs7957197</i>	Greater weight loss-6.1 kg for AA vs -4.5 kg with AT or TT genotype	Low fat diet
<i>LCT</i>	<i>rs4988235</i>	Greater weight loss; -1.3 kg for GG vs -0.4 kg for AA genotype	High protein diet
<i>FTO</i>	<i>rs1558902</i>	Greater weight loss; -8.8 kg for AA vs -4.1 kg for TT genotype	High protein diet

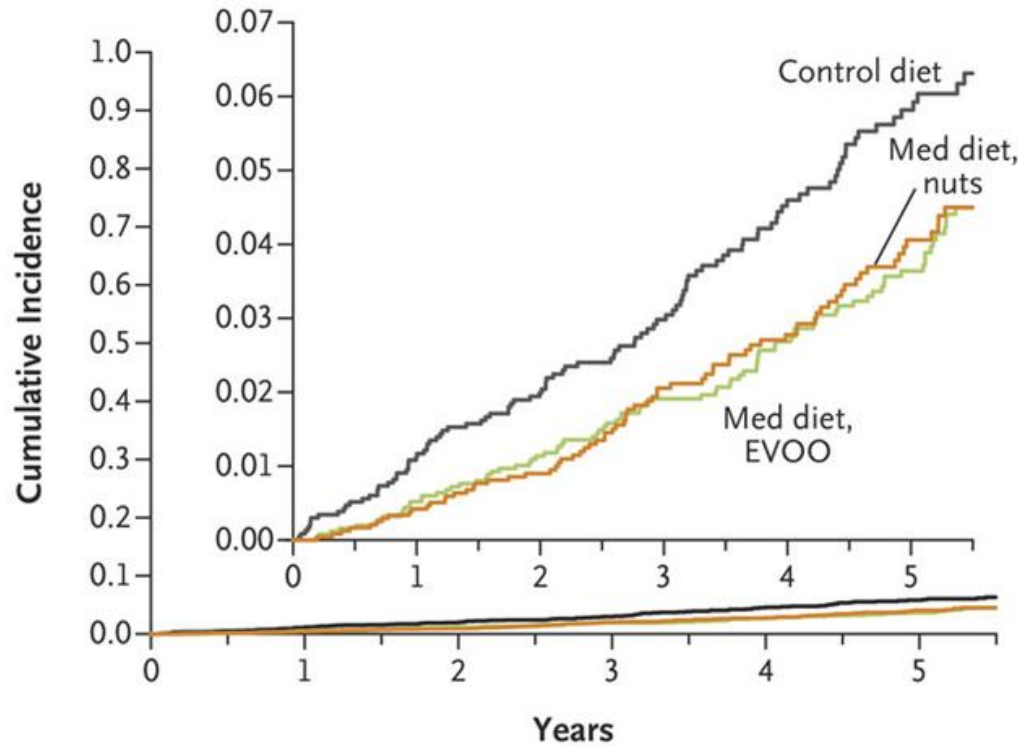
Lacking evidence from  
clinical trials of personalized  
approaches to diet  
prescription for weight loss,  
what are we to do?

# Expert Approaches to Weight Loss Diets

Most experts will

- For diabetes, prediabetes and insulin resistance, advise low carb or low GI approaches.
- Respect patient's choice of diet for weight loss, within bounds of Guidelines.
- Remember, adherence is strongest predictor of weight loss.
- Caloric intake (quantity) is important in weight loss, but dietary quality can have health benefits. The long-term diet should be one that is health-promoting.

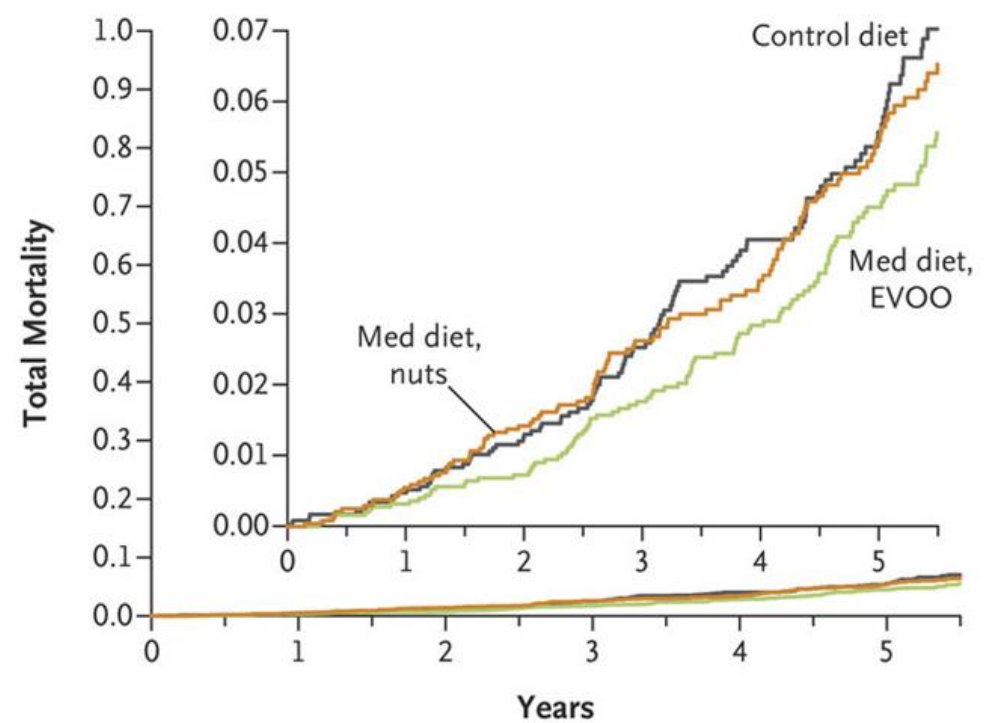
# Mediterranean Diet Reduces CVD Risk and Total Mortality



**Primary Endpoint: Acute MI, Stroke or CVD death**

Med Diet + EVOO HR = 0.69 (CI = 0.53-0.91)

Med Diet + Nuts HR = 0.72 (CI = 0.54-0.95)



**Total Mortality**

Med Diet + EVOO HR = 0.690 (CI = 0.69-1.18)

Med Diet + Nuts HR = 1.12 (CI = 0.86-1.87)

# ARS: Which statement best captures your thoughts about this presentation?

1. The speaker is correct. I agree with her.
2. The speaker is mostly correct, but I disagree with a few things.
3. The speaker is dead wrong. There is a diet that is better than all others to produce weight loss and it is the low carb/low glycemic load diet.
4. The speaker is dead wrong. There is a diet that is better than all others to produce weight loss and it is early time restricted feeding diet.
5. The speaker is dead wrong. There is a diet that is better than all others to produce weight loss and it is the clean food diet.
6. The speaker is dead wrong. There is a diet that is better than all others to produce weight loss and it's not mentioned above.



Thank You!

# Methodology

- What statistical analysis to use?
  - ANCOVA models, Pearson correlations, multiple regression models,  $\chi^2$
- Cluster analysis<sup>1</sup>
  - Identify a set of predictive factors by looking at responders versus non responders
- Signal Detection<sup>2</sup>
  - Hierarchical approach to identifying predictors
- Identification by biological response
  - Drug levels, fMRI, physiological marker