




New Twist on Low Carb vs. Low Fat for Weight Loss

**BOTH appropriate,
but not for everyone**

Christopher Gardner, PhD
Stanford Prevention Research Center
Stanford University, Department of Medicine







**Sponsored by the
University of Arizona
College of Medicine
at the
Arizona Health Sciences Center**



Arizona Health Sciences Center

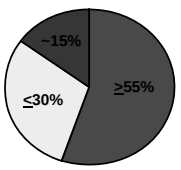
No disclosures

**Clinical Guidelines on the Identification, Evaluation,
and Treatment of Overweight and Obesity in Adults**
The Evidence Report. National Institutes of Health.
Obes Res 1998;6(Suppl)2:51S-209S.

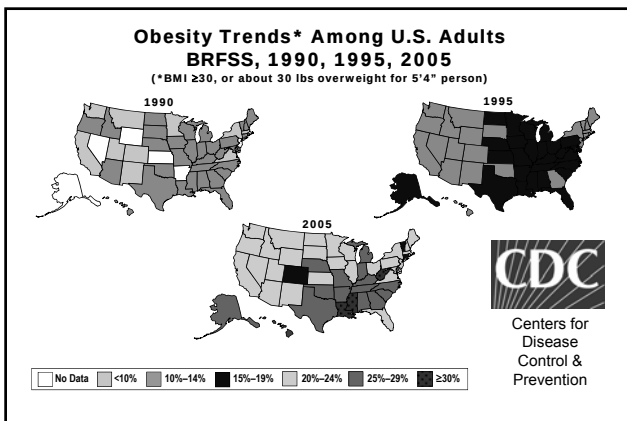
■ Carb

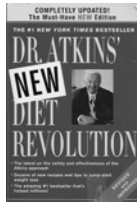
□ Fat

■ Protein



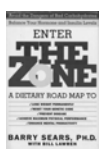
≥55% energy from carbohydrate
 ≤30% energy from fat
 and approximately 15% energy from protein










Low carb ←————→ High carb

Outline

➤ Low-Carb vs. Low Fat: General Conclusions

- *Insulin Resistance: Effect Moderator*
- *Dietary Adherence Differences*
- *Diet X Genotype Interaction*
- *Practical Limitations of the Terms "Low-Carb" and "Low-Fat"*
- *Summary*

Recent Trials 2003-2009

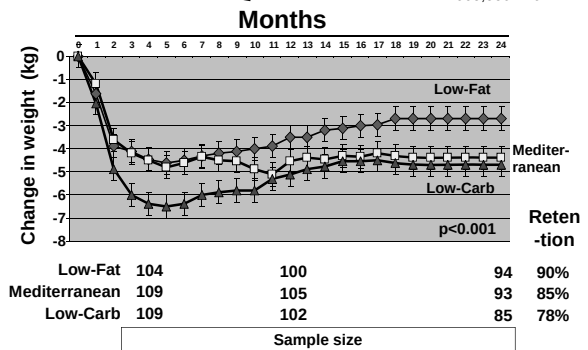
Recent Trials: 2003-2006

Foster GD, N Engl J Med. 2003;348:2082-90.
 Samaha FF, N Engl J Med. 2003;348:2074-81.
 Brehm BJ, J Clin Endocrinol Metab. 2003;88:1617-23.
 Aude Y, Arch Intern Med. 2004;164:2141-6.
 Stern L, Ann Intern Med. 2004;140:778-785.
 Yancy W, Ann Intern Med. 2004;140:769-77.
 Dansinger ML, JAMA. 2005;293:43-53.
 McAuley KA, Diabetologia. 2005;48:8-16.
 McMillan-Price J, Arch Intern Med. 2006;166:1466-75.
 Truby H, BMJ. 2006;332:1309-14.

LIMITATIONS: Small sample sizes, short duration (3-6 months for most), high drop-out rates, inadequate diet assessment

Work-Site Study: Israel

Shai et al, NEJM
 2008;359:229-41



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 February 26, 2009 VOL. 360 NO. 9

Comparison of Weight-Loss Diets with Different Compositions of Fat, Protein and Carbohydrates

Frank M. Sacks, George A. Bray, Vincent J. Carey, Steven R. Smith, Donna H. Ryan, Stephen D. Anton, et al.

DESIGN:

Study Population: n=811 overweight men and women

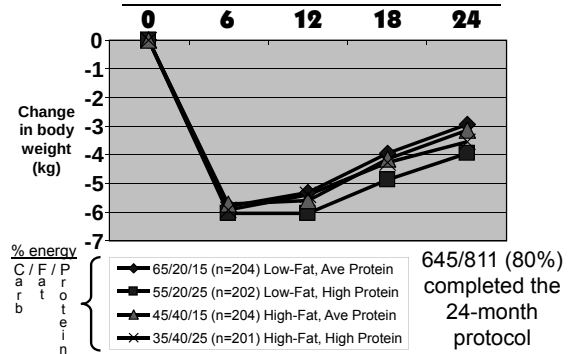
Four Diets: Differing in fat, protein, carbohydrate

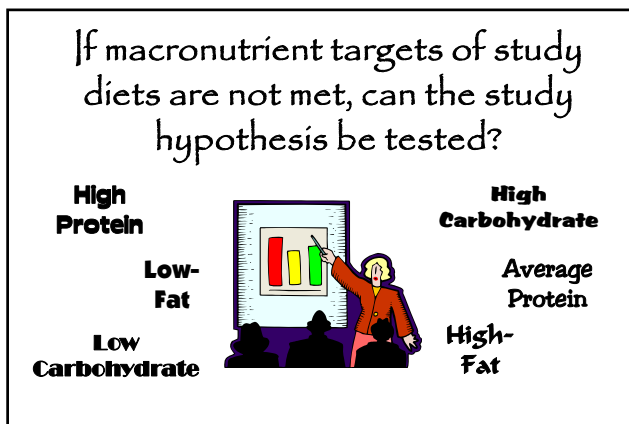
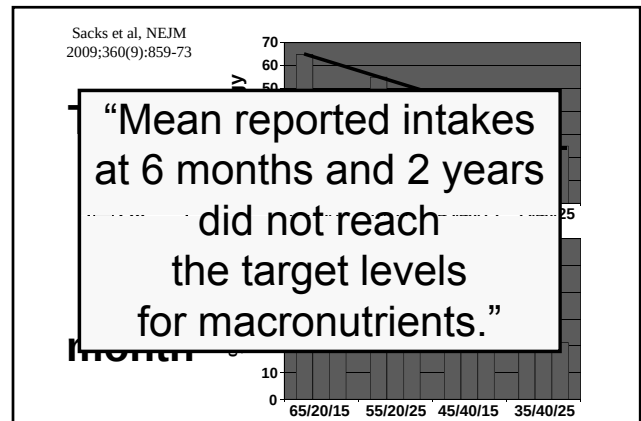
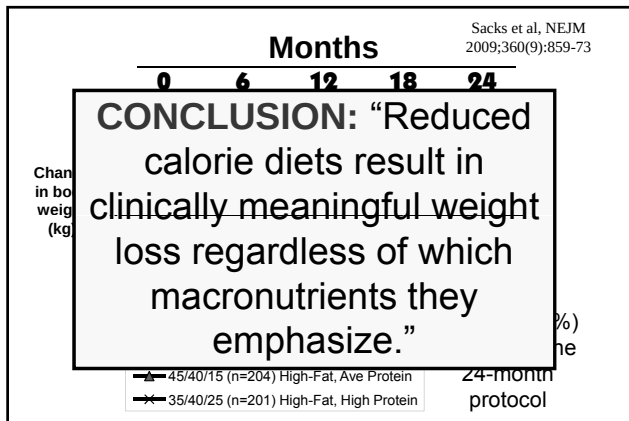
Duration: 2 years

Primary Outcome: 2-year weight change

Months

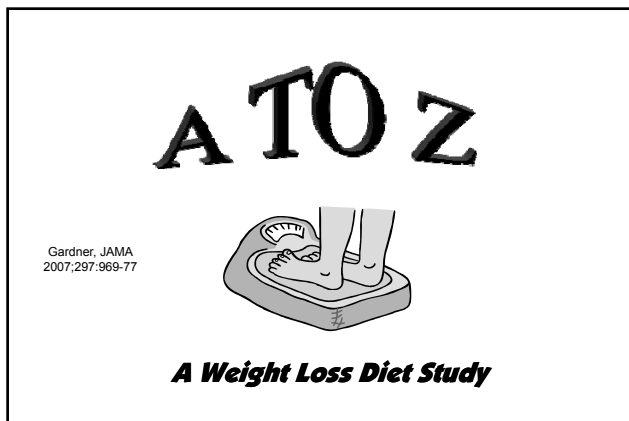
Sacks et al, NEJM
 2009;360(9):859-73





If macronutrient targets of study diets are not met, can the study hypothesis be tested?

If the field's top scientists are unsuccessful in achieving dietary targets among participants..... can it be done?

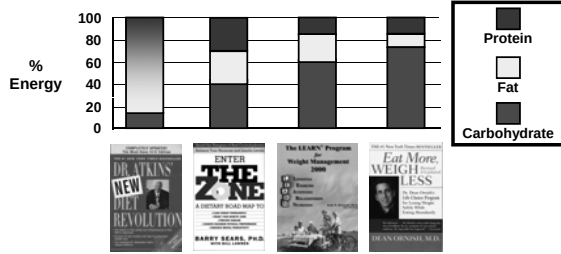


A TO Z

Atkins
Traditional (L.E.A.R.N.)
Ornish
Zone

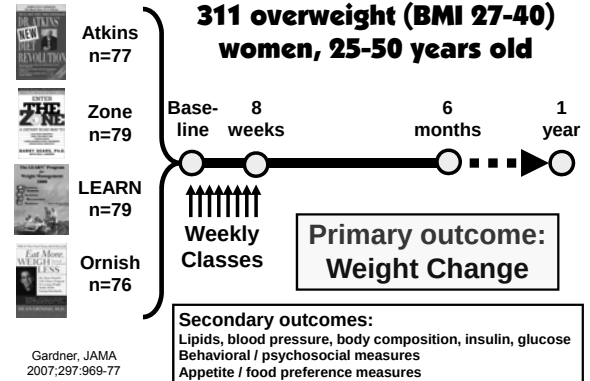
Gardner, JAMA
2007;297:969-77

From Low-Carb to High Carb

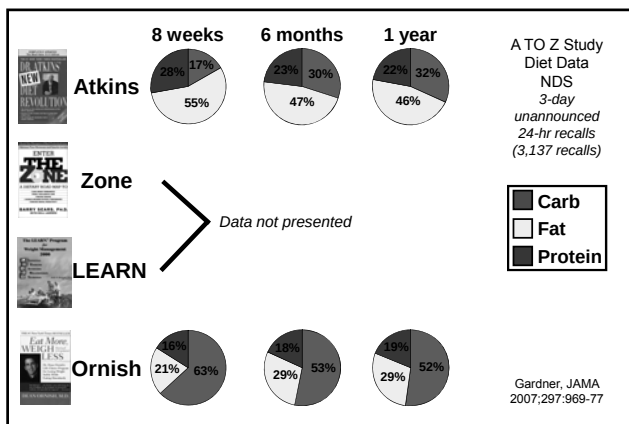


Gardner, JAMA
2007;297:969-77

311 overweight (BMI 27-40) women, 25-50 years old

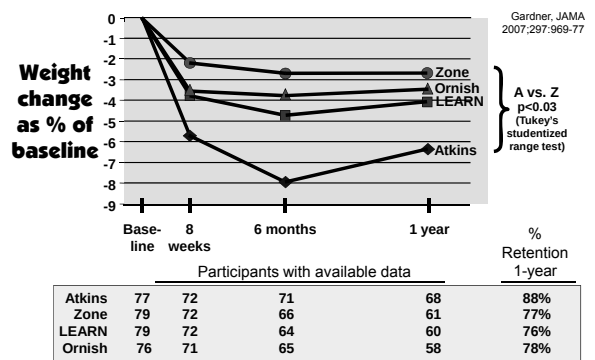


Gardner, JAMA
2007;297:969-77



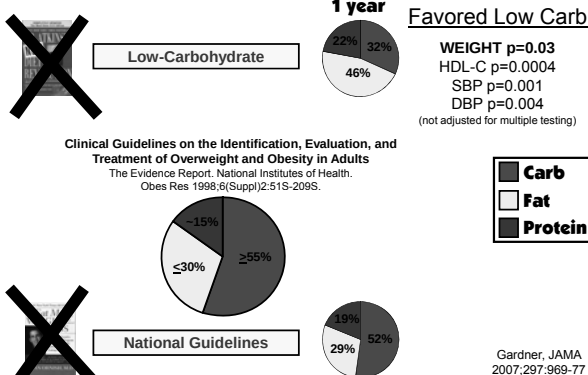
Gardner, JAMA
2007;297:969-77

Percent weight change across time, by group

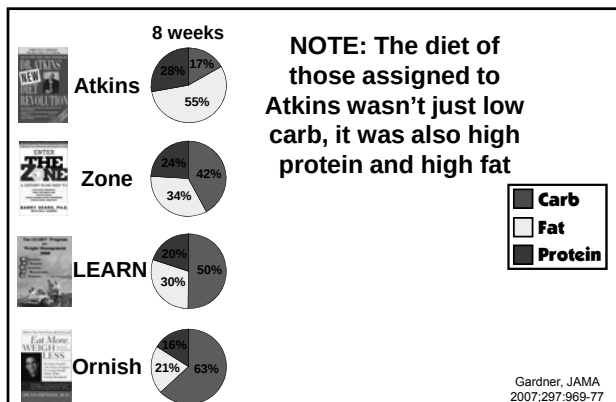


Gardner, JAMA
2007;297:969-77

A vs. Z
p<0.03
(Tukey's studentized range test)



Gardner, JAMA
2007;297:969-77



Gardner, JAMA
2007;297:969-77

Benefits of High PROTEIN?

WEIGHT LOSS, AND RELATED RISK FACTORS

High Protein vs. High Carbohydrate (holding fat constant)

Due, *Int J Obes Relat Metab Disord*. 2004;28:1283-1290.
Farnsworth, *Am J Clin Nutr*. 2003;78:31-39.
Layman, *J Nutr*. 2005;135:1903-1910.
Noakes, *Am J Clin Nutr*. 2005;81:1298-1306.

High Protein vs. High Fat (holding carbohydrate constant)

Luscombe-Marsh, *Am J Clin Nutr*. 2005;81:762-772.
Weigle, *Am J Clin Nutr*. 2005;82:41-48.

BLOOD PRESSURE AND OTHER RISK FACTORS, WEIGHT STABLE

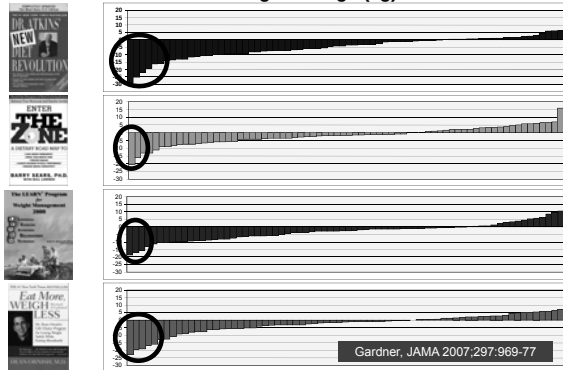
Appel, *OMNI-HEART, JAMA*. 2005;294(19):2455-2464

High PROTEIN – long term risk?

There is no place in your body where extra protein can be “stored”. All protein that is absorbed is either used for functional purposes, or broken down into fat or carbohydrate.

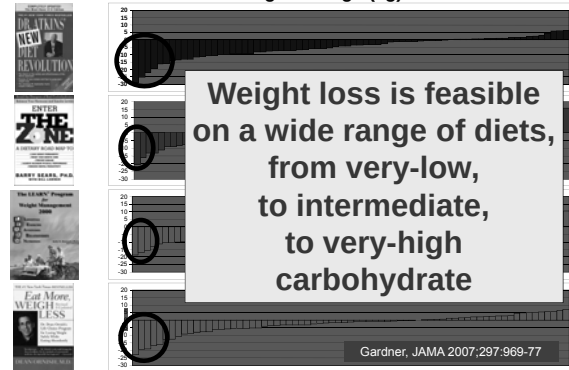
Breaking down and/or eliminating excess protein involves eliminating nitrogen, which will increase demands on the kidney, and may leech calcium from bones.

12-month net weight change (kg): Individual results



Gardner, JAMA 2007;297:969-77

12-month net weight change (kg): Individual results



Weight loss is feasible on a wide range of diets, from very-low, to intermediate, to very-high carbohydrate

Gardner, JAMA 2007;297:969-77

Evidence for role of carbohydrate, fat and protein

Low-Fat **NOT** proven to be superior in recent trials

Low-Carb has been consistently as or more effective for weight loss

Low-Carb is typically also High Protein and High Fat

Average weight loss is modest after 1-2 years (~5 kg)

Long-term adherence to diets is typically poor

Studies are all relatively short, often too short for weight restabilization

Many inherent challenges involved in conducting successful weight loss studies

Outline

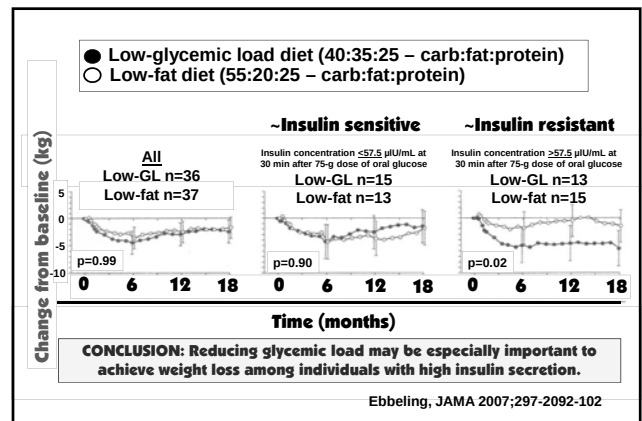
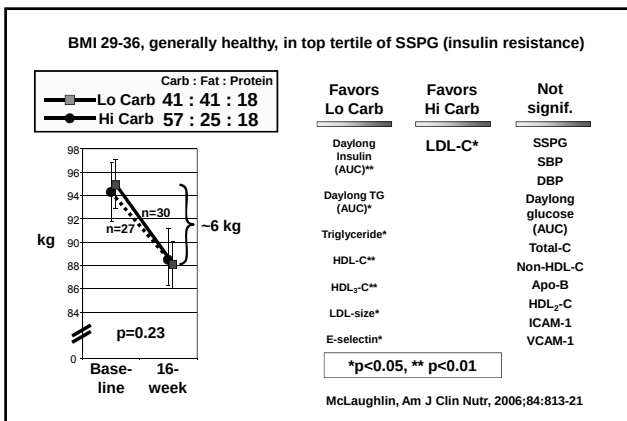
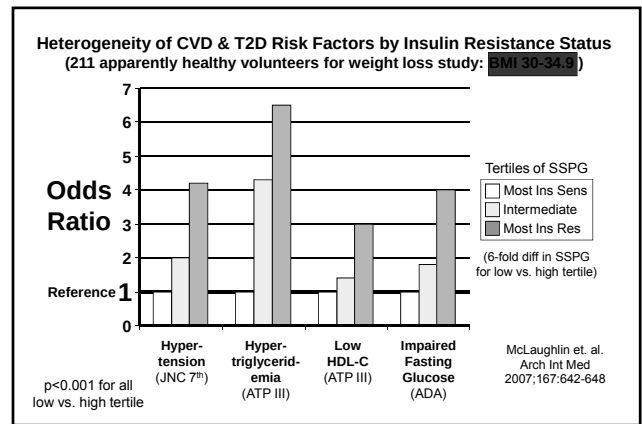
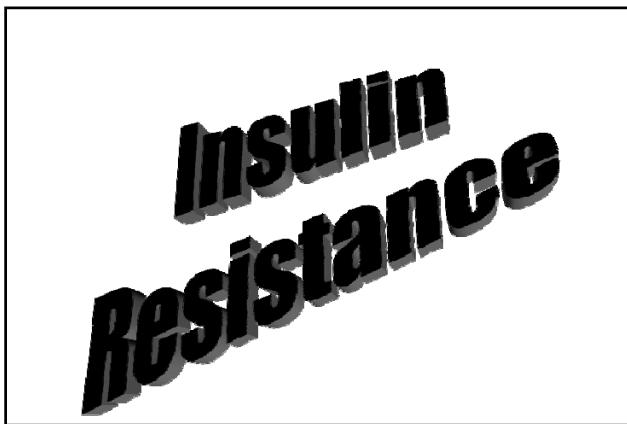
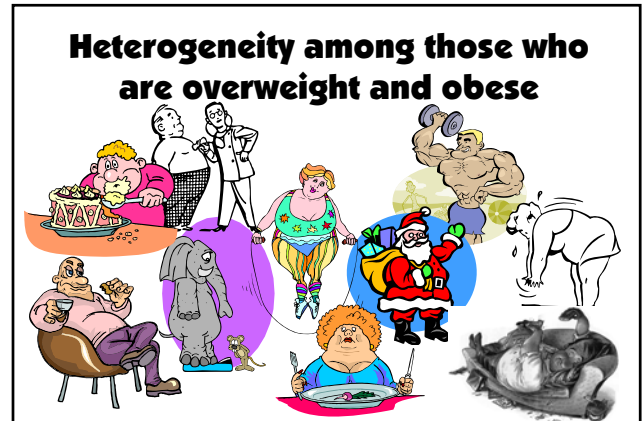
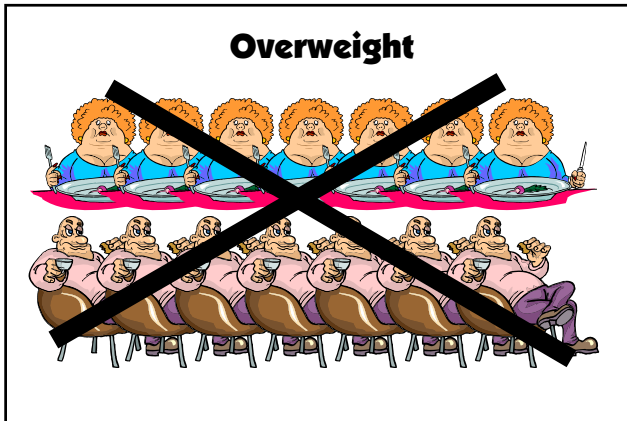
➤ Evidence for Role of Carbohydrate, Fat and Protein

➤ Insulin Resistance: Effect Moderator

➤ Diet X Genotype Interaction

➤ Practical Limitations of the Terms “Low-Carb” and “Low-Fat”

➤ Summary



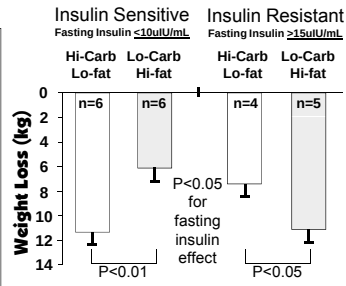
Insulin sensitivity/resistance

Moderator of success with high-carb vs. low-carb weight loss

Obese, non-diabetic women
4-month feeding study
Hypocaloric diet
Hi-Carb/Lo-Fat = 60:20
Lo-Carb/Hi-Fat = 40:40

CONCLUSIONS:

Hi-Carb/Lo-Fat more effective for insulin sensitive women
Lo-Carb/Hi-Fat more effective for insulin resistant women
Differences not explained by changes in intake, activity or resting metabolic rate



Cornier M-A et al. Obesity Research 2005;13(4):703-9

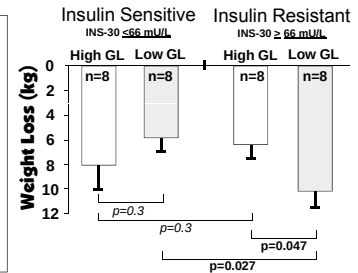
Insulin sensitivity/resistance

Moderator of success with high-carb vs. low-carb weight loss

Overweight (BMI 25-30) w & m
6-month feeding study
Hypocaloric diet (30% restriction)
High GL = 60:20:20 (carb:pro:fat)
Low GL = 40:30:30 (carb:pro:fat)

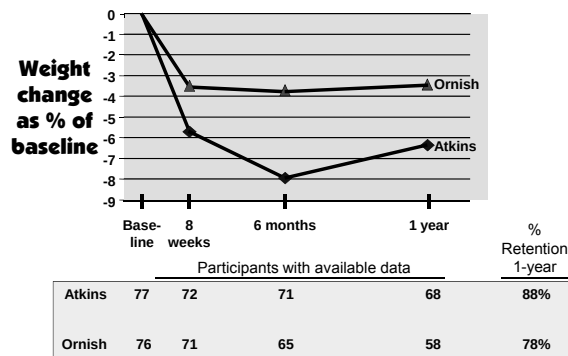
CONCLUSIONS:

Low GL more effective than High GL for insulin resistant adults, but not for insulin sensitive adults.



Pittas al. Diabetes Care 2005;28:2939-2941

Percent weight change across time, by group

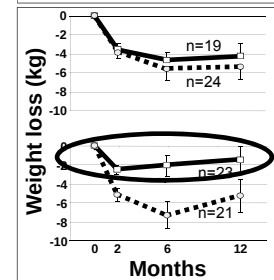


Fasting Insulin Tertiles

A TO Z Study: Exploratory analyses

Ornish Diet (very low fat, high carb)
Atkins (very low carb, unrestricted fat and protein)

Most Insulin Sensitive (<7 μU/mL)
Most Insulin Resistant (>10 μU/mL)
Mean, SEM

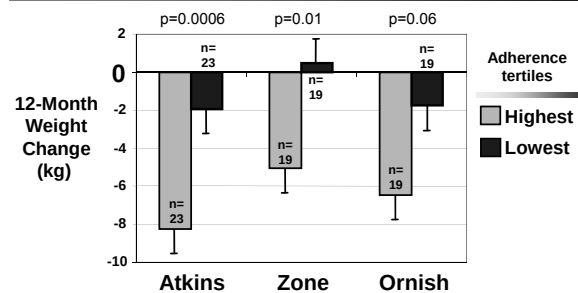


Success with either diet for those who are relatively insulin sensitive

For those who are insulin resistant, traditional low-fat diet ineffective compared to low-carb diet

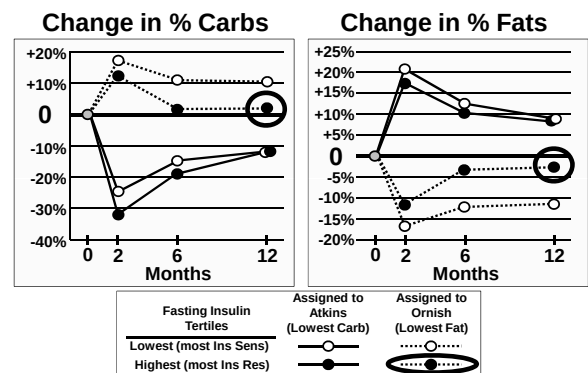
Adherence

Weight Loss by Adherence Tertile (A TO Z Study)



Alhassan, Intl J Obesity, 2008; 57:49-56

Insulin resistance, Low carb vs. Low Fat, & Adherence



Effect Moderator: Insulin Resistance

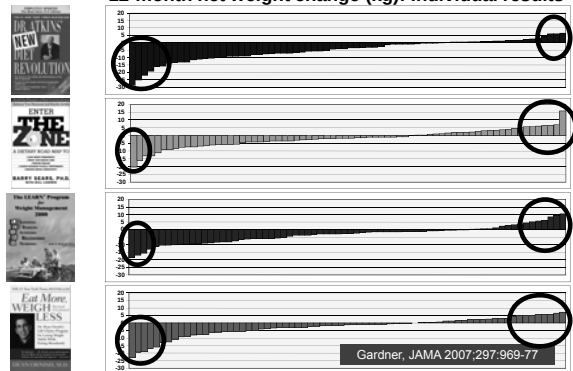
Traditional Low-Fat diet may be particularly ineffective for weight loss for those with insulin resistance

Estimate of metabolic syndrome in US ~23% (Ford, JAMA, 2002)

Insulin resistant individuals may find it inherently more difficult to adhere to a lower-fat/higher-carb diet

Gene-Diet Interaction

12-month net weight change (kg): Individual results



Multi-Locus Genotype Patterns

3 Selection criteria

- Genotype association with obesity/weight management validated in ≥ 3 clinical studies
- Gene variant functional, alters biological mechanisms associated with body weight
- Clinical evidence of gene-diet interaction

200+ genes reviewed, 3 selected

- FABP2 rs 1799883
- PPARG rs 1801282
- ADRB2 rs 1042714

Multi-Locus Genotype Patterns

3 Selection criteria

- Genotype associated with obesity management validated in ≥ 3 clinical trials
- Gene variant functionally biologically plausible
- Causal association with weight loss

2 - gene variants selected

- FABP2 rs1799883
- PPARG rs1801282
- ADRB2 rs1042714

...6 months prior to start of study.

This was a test of PREDEFINED genotype patterns

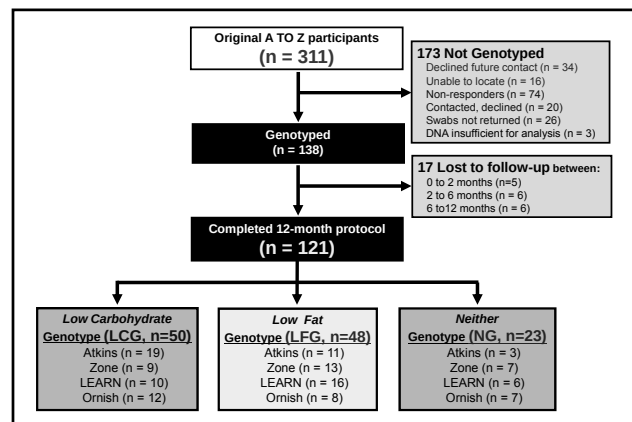
Multi Locus Genotype Patterns

Diet Category	Genotypes			Expected freq of multi-locus pattern†	A to Z Frequency
	FABP2 rs1799883	PPARG rs1801282	ADRB2 rs1042714		
Low-Carb	A/*	G/*	A/*	0.45	0.41
Low-Fat	A/*	C/C	A/*	0.39	0.39
Balanced	G/G	C/C	C/C	0.16	0.20

† Frequencies calculated for Caucasians from Quebec Family Study

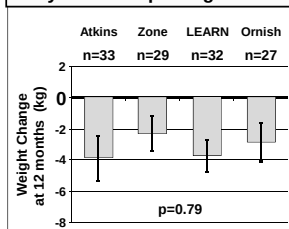
Hypothesis

Overweight/obese women assigned to genotype appropriate diets will lose more weight over 12 months than women assigned to genotype inappropriate diets



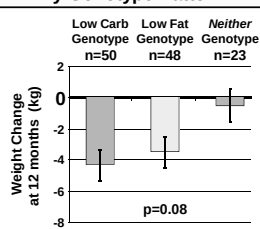
12 Month Weight Loss

By Diet Group Assignment



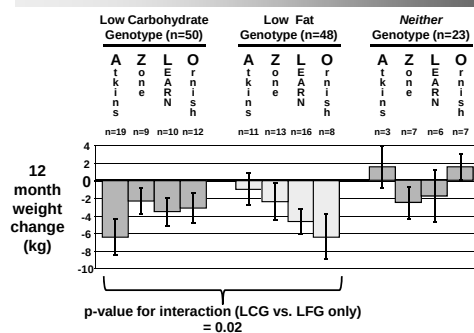
Without taking genotype pattern into consideration

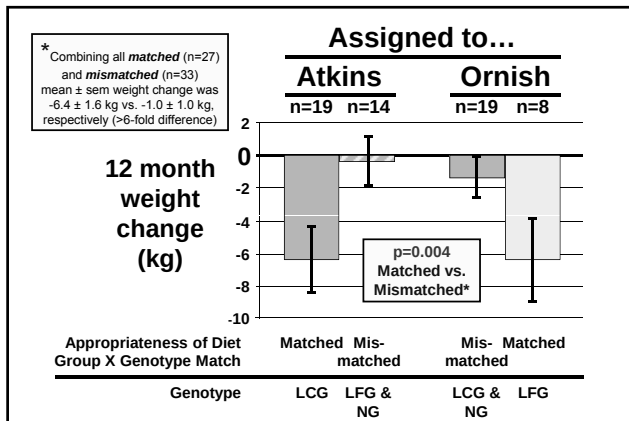
By Genotype Pattern



Without taking diet group assignment into consideration

Diet Group X Genotype





Gene-Diet Interaction

Preliminary evidence suggests simple DNA test could help dieters predict likelihood of greater weight loss success with a low carb vs. low fat diet.

Example may help to explain the substantial variability in weight loss success among different individuals trying to follow the same diet.

Outline

- Evidence for Role of Carbohydrate, Fat and Protein
- Effect Moderators: Insulin Resistance and Genetic Predisposition
- **Practical Limitations of the Terms “Low-Carb” and “Low-Fat”**
- Summary

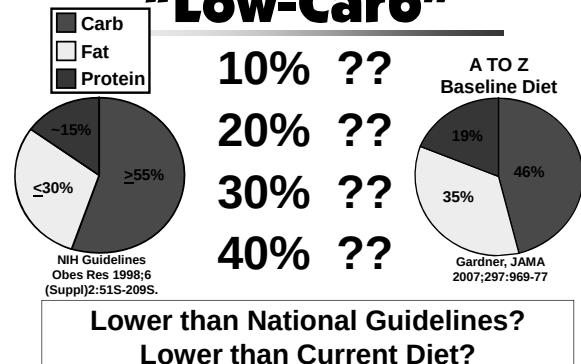
Dietary Macronutrients

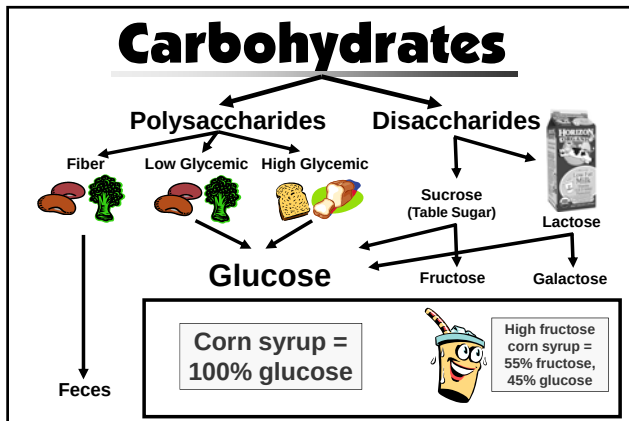
Carb } ~~Low vs. High~~
Fat }
Protein } Overly simplistic

Dietary Macronutrients

Carb	Glycemic Index / Load Complex vs. Refined Fiber-rich
Fat	Monounsaturates/Polyunsaturates /Saturated Omega-3 vs. Omega-6 Marine vs. Plant Omega-3
Protein	Plant, Marine, Animal

“Low-Carb”



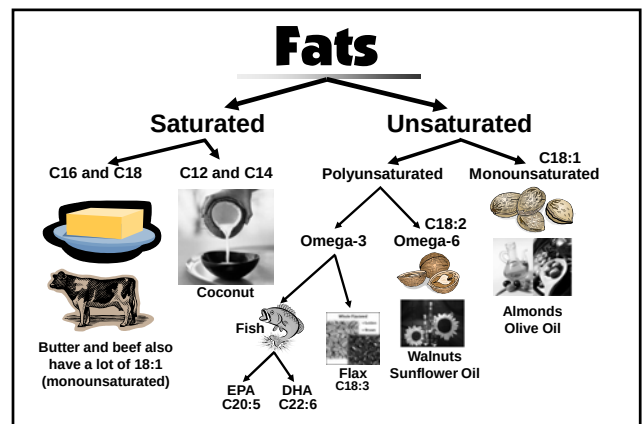
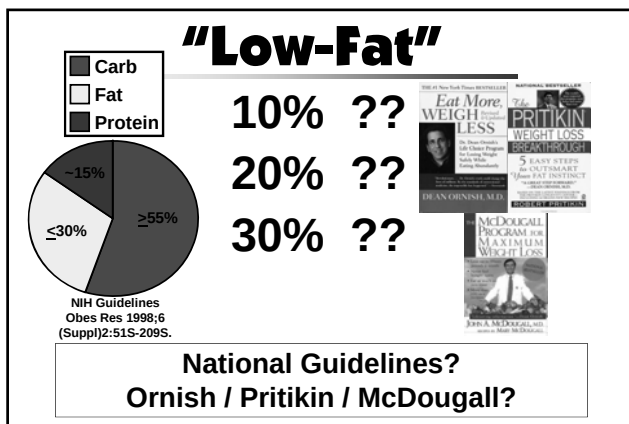


How Low?

How useful is the term "Low-Carb"?

All Carbs?

Or, mainly added sugars?



How Low?

How useful is the term "Low-Fat"?

All Fats?

Mainly saturated?

All saturated?





- Cultured certified organic low fat pasteurized milk
- Pectin
- Cultures



- Cultured certified organic low fat pasteurized milk
- Organic evaporated cane juice
- Organic raspberries
- Pectin
- Natural flavors
- Elderberry juice concentrate (for color)
- Locust bean gum
- Cultures



Calories 90	Fat Cal. 25
% Daily Values	
Total Fat 2.5 g	4%
Sat Fat 1.5 g	8%
Cholest. 10 mg	4%
Sodium 110 mg	4%
Total Carb. 11 g	4%
Dietary Fiber 0 g	0%
Sugars 11 g	
Protein 7 g	15%



Calories 130	Fat Cal. 20
% Daily Values	
Total Fat 2.0 g	3%
Sat Fat 1.5 g	7%
Cholest. 10 mg	3%
Sodium 95 mg	4%
Total Carb. 23 g	8%
Dietary Fiber 0 g	0%
Sugars 22 g	
Protein 6 g	12%



- Cultured certified organic low fat pasteurized milk
- Raspberries (1/2 c)
- Pectin
- Cultures



- Cultured certified organic low fat pasteurized milk
- Organic evaporated cane juice
- Organic raspberries
- Pectin
- Natural flavors
- Elderberry juice concentrate (for color)
- Locust bean gum
- Cultures



Calories 120	Fat Cal. 25
% Daily Values	
Total Fat 3.0 g	4%
Sat Fat 1.5 g	8%
Cholest. 10 mg	4%
Sodium 110 mg	4%
Total Carb. 18 g	4%
Dietary Fiber 4 g	16%
Sugars 14 g	
Protein 8 g	15%



Calories 130	Fat Cal. 20
% Daily Values	
Total Fat 2.0 g	3%
Sat Fat 1.5 g	7%
Cholest. 10 mg	3%
Sodium 95 mg	4%
Total Carb. 23 g	8%
Dietary Fiber 0 g	0%
Sugars 22 g	
Protein 6 g	12%

Practical Limitations of the Terms "Low-Carb" and "Low-Fat"

How "Low" (what percentage)?

Gen'l public – difficulty achieving specific percentages

All types, or specific types?

Packaged food manipulations –
Healthy Junk Food?

LOWER Carb & LOWER fat, choose
low energy density / high nutrient density
FOODS

Overall Summary

For average overweight/obese individual, selected at random:
Low-Fat is not superior to Low-Carb for weight loss
Success with either approach is minimal to negligible

Insulin Resistance:

Lower-Carb more appropriate
Adherence to Lower-Carb better than Lower-Fat

Genetic Predisposition:

May be ~6-fold difference in success when
appropriately matched vs. mismatched

"Low" is relative, and can be deceptive

Thresholds have not been established – try "lower"
Don't oversimplify, "Low" needs to include:
high nutrient density
low energy density