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

BOTH appropriate, but not for everyone

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Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults

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

Obesity Trends* Among U.S. Adults BRFSS, 1990, 1995, 2005 (*BMI ≥30, or about 30 lbs overweight for 5'4" person)

Low carb High carb

Centers for Disease Control & Prevention
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: 2003-2006

- McAuley KA, Diabetologia. 2005;48:8-16.

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

The NEW ENGLAND JOURNAL of MEDICINE

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

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
CONCLUSION: “Reduced calorie diets result in clinically meaningful weight loss regardless of which macronutrients they emphasize.”

Mean reported intakes at 6 months and 2 years did not reach the target levels for macronutrients.

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?
### From Low-Carb to High Carb

#### Energy Distribution

- **Protein**
- **Fat**
- **Carbohydrate**

#### Study Participants
- Atkins: n=77
- Zone: n=79
- LEARN: n=79
- Ornish: n=76

#### Study Design
- **Primary outcome:** Weight Change
- **Secondary outcomes:**
  - Lipids, blood pressure, body composition, insulin, glucose
  - Behavioral / psychosocial measures
  - Appetite / food preference measures

#### Study Outcomes
- **Atkins**
  - 8 weeks: 32%
  - 1 year: 17%
- **Zone**
  - 8 weeks: 46%
  - 1 year: 34%
- **LEARN**
  - 8 weeks: 30%
  - 1 year: 21%
- **Ornish**
  - 8 weeks: 55%
  - 1 year: 28%

#### Weight Change Across Time, by Group

<table>
<thead>
<tr>
<th>Group</th>
<th>8 weeks</th>
<th>6 months</th>
<th>1 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atkins</td>
<td>32%</td>
<td>17%</td>
<td>68%</td>
</tr>
<tr>
<td>Zone</td>
<td>46%</td>
<td>34%</td>
<td>58%</td>
</tr>
<tr>
<td>LEARN</td>
<td>30%</td>
<td>21%</td>
<td>72%</td>
</tr>
<tr>
<td>Ornish</td>
<td>55%</td>
<td>28%</td>
<td>78%</td>
</tr>
</tbody>
</table>

#### Retention
- Atkins: 88%
- Zone: 77%
- LEARN: 72%
- Ornish: 71%

#### Favored Low Carb

- **Low-Carbohydrate**
  - 1 year: 32%
- **National Guidelines**
  - 1 year: 20%

#### Clinical Guidelines

- **Low-Carbohydrate**
  - Weight p<0.03
  - HDL-C p<0.0004
  - SBP p<0.001
  - DBP p<0.004
- **National Guidelines**
  - Not adjusted for multiple testing

#### Note
- The diet of those assigned to Atkins wasn’t just low carb, it was also high protein and high fat.
Benefits of High PROTEIN?

WEIGHT LOSS, AND RELATED RISK FACTORS
High Protein vs. High Carbohydrate (holding fat constant)

High Protein vs. High Fat (holding carbohydrate constant)

BLOOD PRESSURE AND OTHER RISK FACTORS, WEIGHT STABLE

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.

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
Overweight

Heterogeneity among those who are overweight and obese

Insulin Resistance

BMI 29-36, generally healthy, in top tertile of SSPG (insulin resistance)

Heterogeneity of CVD & T2D Risk Factors by Insulin Resistance Status

(211 apparently healthy volunteers for weight loss study: BMI 30-34.9)

- Hyper-tension (JNC 7th)
- Hyper-triglyceridemia (ATP III)
- Low HDL-C (ATP III)
- Impaired Fasting Glucose (ADA)

Odds Ratio

Low vs. high tertile


(6-fold diff in SSPG for low vs. high tertile)
p<0.001 for all low vs. high tertile

Low-glycemic load diet (40:35:25 – carb:fat:protein)

- Insulin sensitive
- Insulin resistant

CONCLUSION: Reducing glycemic load may be especially important to achieve weight loss among individuals with high insulin secretion.

Ebbeling, JAMA 2007;297:2092-102
**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

**Percent weight change across time, by group**

<table>
<thead>
<tr>
<th>Weight change % of baseline</th>
<th>Atkins</th>
<th>Ornish</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>77</td>
<td>76</td>
</tr>
<tr>
<td>8 weeks</td>
<td>72</td>
<td>71</td>
</tr>
<tr>
<td>6 months</td>
<td>71</td>
<td>65</td>
</tr>
<tr>
<td>1 year</td>
<td>68</td>
<td>58</td>
</tr>
</tbody>
</table>

Participants with available data: Atkins 77, Ornish 76
Retention 1-year: Atkins 88%, Ornish 78%

**Fasting Insulin Tertiles**

- Most Insulin Sensitive (<7 µIU/mL)
- Most Insulin Resistant (>10 µIU/mL)

**A TO Z Study: Exploratory analyses**

**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**

**Weight Loss by Adherence Tertile (A TO Z Study)**

Adherence tertiles

- Highest
- Lowest

12-Month Weight Change (kg)

Atkins Zone Ornish
**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**

**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

Selection criteria:
• Genotype associated with obesity/weight management validated in ≥3 clinical studies
• Gene variant functionally altered, mechanisms associated with body weight regulation

2 genes selected
• FABP2 rs1799883
• PPARG rs1801282
• ADRB2 rs1042714

Clinical evidence of gene-diet interaction
…6 months prior to start of study.
This was a test of PREDEFINED genotype patterns

<table>
<thead>
<tr>
<th>Diet Category</th>
<th>Genotypes</th>
<th>Expected freq of multi-locus pattern†</th>
<th>A TO Z Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-Carb</td>
<td>G/G</td>
<td>0.45</td>
<td>0.41</td>
</tr>
<tr>
<td></td>
<td><em>/</em></td>
<td>0.41</td>
<td></td>
</tr>
<tr>
<td>Low-Fat</td>
<td>A/*</td>
<td>0.39</td>
<td>0.39</td>
</tr>
<tr>
<td></td>
<td>G/G</td>
<td>0.39</td>
<td></td>
</tr>
<tr>
<td>Balanced</td>
<td>G/G</td>
<td>0.16</td>
<td>0.20</td>
</tr>
<tr>
<td></td>
<td>C/C</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

† 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

p-value for interaction (LCG vs. LFG only) = 0.79
Combing all matched (n=27) and mismatched (n=33) mean ± sem weight change was -4.4 ± 1.6 kg vs. -1.6 ± 1.0 kg, respectively (6-fold difference).

**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**
  - 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”**

- 10% ??
- 20% ??
- 30% ??
- 40% ??

Lower than National Guidelines?
Lower than Current Diet?
Carbohydrates

Polysaccharides
- Glucose
- Fucrose
- Galactose

Disaccharides
- Sucrose (Table Sugar)
- Lactose
- Fructose

Low Glycemic
High Glycemic

Fiber

Sucrose

Corn syrup = 100% glucose

High fructose corn syrup = 55% fructose, 45% glucose

How Low?

How useful is the term "Low-Carb"?

All Carbs?

Or, mainly added sugars?

"Low-Fat"

10% ??

20% ??

30% ??

National Guidelines?
Ornish / Pritikin / McDougall?

Fats

Saturated
- C16 and C18
- C12 and C14

Unsaturated
- Polyunsaturated
- Omega-3
- Omega-6

C18:1

Butter and beef also have a lot of 18:1 (monounsaturated)

EPA C20:5

DHA C22:6

Low fat yogurt

Plain

Raspberry
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