What’s the Best Diet for the Metabolic Syndrome Patient?

Marc Cornier, M.D.
Associate Professor of Medicine
Division of Endocrinology, Metabolism & Diabetes
Anschutz Health and Wellness Center
University of Colorado School of Medicine
Denver Health Medical Center

The Metabolic Syndrome
What is the Best Diet?

- How do we judge whether one diet is superior to another? Depends on the goals?
  - The diet that leads to the most long-term weight loss?
  - The diet that improves insulin sensitivity?
  - The diet that improves other features of the Metabolic Syndrome such as glycemia, blood pressure, lipids?
  - The diet that helps prevent diabetes?
  - The diet that improves CVD outcomes or survival?
  - The diet that individuals can adhere to?
- Does one size fit all?

Goals for Dietary Interventions in the Metabolic Syndrome

- Weight Loss
  - Need a diet that results in negative energy balance
- Improved Insulin Sensitivity
  - Weight loss is the biggest driver of
- Improved CVD risk – CVD Prevention
  - Weight loss
  - Low sodium for BP control
  - Lower carb for Triglycerides
  - Higher mono/poly unsaturated fats for HDL
- Diabetes Prevention
  - Data supports weight loss, low calorie, low fat diets
The Consequences of the Metabolic Syndrome

- Obesity
- Hyperinsulinemia
- Insulin Resistance
- Diabetes
- Dyslipidemia
- Thrombosis
- Hypertension
- Repro-Endo
- NAFLD
- Macrovascular Disease
- Thrombosis
- Dyslipidemia
- Hypertension
- Repro-Endo
- NAFLD
- Macrovascular Disease

Weight Loss Interventions: Guide to Selecting Treatment

<table>
<thead>
<tr>
<th>BMI</th>
<th>Treatment</th>
<th>25-26.9</th>
<th>27-29.9</th>
<th>30-35</th>
<th>35-40</th>
<th>&gt;40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diet, Exercise</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Pharmacology</td>
<td>w/ co-morbidities</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgery</td>
<td>w/ co-morbidities</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Weigh Loss: “Negative” Energy Balance

<table>
<thead>
<tr>
<th>Kcal/day</th>
<th>Food Intake</th>
<th>Activity</th>
<th>Digestion</th>
<th>Basal Metabolic Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Energy Intake | Energy Expenditure

How do You Reduce the Calories “In”?

- Decrease the portion sizes
- Decrease the energy density
- Decrease snacking
- Watch for calories in beverages
- Change the macronutrient content of the diet
  - Low-Fat Diet?
  - Low-Carb Diet?
  - High Protein Diet?

Low-Fat Diets

- Theory and Positives:
  - High-fat diets are associated with increased food intake, obesity, insulin resistance, diabetes, and CVD
  - Low-fat (esp low-saturated-fat) diets are associated with a reduced LDL-C and lower prevalence of CVD and incidence of diabetes.
  - High-fat foods are energy dense (9 kcal/g), so low-fat diets should result in reduced energy intake and weight loss
  - Adopted by most “guidelines”

- Negatives:
  - High-carb intake may increase TG
  - Low-fat diets may reduce HDL-C
  - High-carb intake may worsen glucose tolerance?
Dietary fat increases energy intake across the range of typical consumption in the United States

Decreasing Dietary Fat is Associated with a Decrease in Body Weight
Analysis of 37 Diet Intervention Studies

Diabetes Prevention Program

- Intensive Lifestyle Intervention
  - Goal 7% wt loss
    - low-calorie, LOW-FAT diet (<30% fat) using the Food Guide Pyramid
    - 150 min/week of moderate-intensity physical activity
    - 16-lesson curriculum

Ornish Diet: The Lifestyle Heart Trial

Very low fat diet (10% fat based on the Pritikin Diet)

Mean Percentage Diameter Stenosis

<table>
<thead>
<tr>
<th>Diameter Stenosis (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
</tr>
<tr>
<td>5</td>
</tr>
<tr>
<td>10</td>
</tr>
<tr>
<td>15</td>
</tr>
<tr>
<td>20</td>
</tr>
<tr>
<td>25</td>
</tr>
<tr>
<td>30</td>
</tr>
<tr>
<td>35</td>
</tr>
</tbody>
</table>

Control
Treatment

*p=0.02
†p=0.001

Are All Carbs Created Equally?

• High-Fiber-Carbohydrate Diets
  – Improved glucose tolerance
  – Improved lipid risk factors
  – Reduced incidence of CHD
  – Reduced incidence of cancer

• Glycemic Index/Load
  – Low GI carbs better than High GI carbs?

Low-Fat Diets: Long-Term Solution or Just Another Diet?

• Pros:
  – They do produce weight loss even in those with insulin resistance
  – Associated with prevention of Type 2 Diabetes and reduced incidence of CHD and cancer
  – May be best diet for maintaining a lower body fat level over time?

• Cons:
  – Paucity of data in the Metabolic Syndrome population
  – Low-fat does not necessarily mean low-calorie
  – May not favorably effect TG, HDL-C, and glucose
What is the Theory Behind Low-Carb Diets?

- Insulin is bad!
- High Glycemic Index Carbs are bad!
- Hyperinsulinemia and “relative” hypoglycemia increase hunger and sugar cravings, leading to excessive food intake and weight gain…

Low-Carb/High-Fat Diets

- Theory and Positives:
  - Despite the “low-fat” craze we’re becoming more obese
  - Low-Carb diets may promote beneficial weight loss
  - Low-Carb intake may improve glucose and insulin metabolism
  - Low-Carb intake may improve fasting triglycerides
  - Higher fat diets that substitute unsaturated fats for saturated fat may reduce LDL-C while maintaining HDL-C

- Negatives:
  - Low-Carb does not necessarily translate to low calorie
  - Higher fat diets may lead to post-prandial hypertriglyceridemia
  - Long-Term effects are unclear
    - Weight loss?
    - Atherosclerosis?
    - Colon cancer?
Recent Trials: 2003-2006

Brehm BJ, J Clin Endocrinol Metab. 2003;88:1617-23.
McAuley KA, Diabetologia. 2005;48:8-16.

LIMITATIONS: Small sample sizes, short duration, high drop-out rates, inadequate diet assessment

---

The Effects of Low-Fat and Low-Carb Diets on Energy Intake

![Bar chart showing energy intake comparison between Low-Fat and Low-Carb diets at baseline and 6 months.](image)

Brehm et al., JCEM. 88:1617; 2003

---

Randomized Controlled Trial of Atkins Diet on Body Weight

![Line graph showing weight change over months.](image)


---
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

CONCLUSIONS:
• Reduced calorie diets result in clinically meaningful weight loss regardless of which macronutrients they emphasize.
• Adherence to the diet was the biggest predictor of weight loss.
Comparison of Weight Loss Diets with Different Compositions of Carbs/Fat/Protein

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Target</th>
<th>Actual</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fat</td>
<td>20 vs 40%</td>
<td>27 vs 35%</td>
</tr>
<tr>
<td>Protein</td>
<td>15 vs 25%</td>
<td>20 vs 21%</td>
</tr>
<tr>
<td>Carbohydrate</td>
<td>35 to 65%</td>
<td>43 to 53%</td>
</tr>
</tbody>
</table>

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

Mean reported intakes 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, then can it be done?

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

**The A to Z Weight Loss Study**

Low carb diet also favored improvements in HDL, BP

Gardner, JAMA 2007;297:969-77
### Low-Carb Diets: Summary

- **Pros:**
  - 6-month data shows more weight loss than on “standard” low fat diets.
  - Improvements in “fasting” lipids at one year
  - Clearly a calorie restricted diet without “limiting” caloric intake

- **Cons:**
  - As in every diet, weight is regained by 1 year
  - Greatest concern is high saturated fat intake and what happens to post-prandial TGs
  - NWCR: <3% are using this diet weight maintenance
  - Few can stay on this long term?

### Low-Carb Diets: Long-Term Solution or Just Another Diet?

- **Pros:**
  - They do produce short-term weight loss
  - Calorie restriction without restricting calories
  - Beneficial effects on fasting lipids
  - Some may be healthier than others

- **Cons:**
  - Paucity of data in this population
  - As in every diet, weight is regained by 1 year; few can maintain these diets long term?
  - Potential for high saturated fat intake, post-prandial hypertriglyceridemia and long-term safety concerns
  - Low Carb does NOT necessarily mean less calories

### Are All Fats Created Equally?

- **Saturated and Trans Fats:**
  - Clearly BAD
  - Associated with CHD and acute events

- **Monounsaturated Fats:**
  - Good
  - Lower cholesterol
  - Associated with improved CVD outcomes

- **Polyunsaturated Fats:**
  - Good
  - Reduce CHD mortality and sudden death
Benefits of High Protein on Weight Loss and Related Risk Factors?

- High Protein vs. High Carbohydrate (holding fat constant)
- High Protein vs. High Fat (holding carbohydrate constant)

Effect of an Ad Libitum High-Protein, Low-Fat* Diet on Body Weight

*30% of total energy from fat.

![Graph showing body weight changes over time for different diets.]

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 leach 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
A to Z: Individual weight change (kg)

~30 kg RANGE of weight change WITHIN each diet group.
From losing 20-25 kg to gaining 5-10 kg

Weight Loss with a Low-Carbohydrate, Mediterranean, or Low-Fat Diet

Mediterranean-Style Diet in Patients with Newly Diagnosed Type 2 Diabetes: A 2-year Randomized Trial
Primary Prevention of CVD with a Mediterranean Diet

- Mediterranean Diets:
  - Recommended: olive oil, tree nuts/peanuts, fresh fruits, vegetables, fish/seafood, legumes, soffrito, white meat, wine with meals
  - Discouraged: soda drinks, commercial bakery goods, sweets and pastries, spread fats, red and processed meats
  - Participants in the two Mediterranean-diet groups received either extra-virgin olive oil (~1 liter/week) or 30g of mixed nuts/d at no cost

- Low-Fat Diet (Control)
  - Recommended: Low-Fat Diary Products, Bread, Potatoes, Pasta, Rice, Fresh Fruits, Vegetables, Lean Fish and Seafood
  - Discouraged: Vegetable Oils, Commercial Bakery Goods, Sweets, Pastries, Nuts and Fried Snacks, Red and Processed Meats, Visible Fat in Meats and Soups, Fatty Fish, Seafood Canned in Oil, Spread Fats, Soffrito

- No calorie restriction or physical activity advised/promoted.
Primary Prevention of CVD with a Mediterranean Diet

Subgroup Analysis

• Mediterranean Diets were Better in Patients with:
  – Diabetes
  – Hypertension
  – Dyslipidemia
  – Elevated Waist Circumference
  – Obesity
  – Better Diet Adherence

“Eat Right for Your Type”

• The Concept:
  – Your blood type tells you what the best diet is for you. This is because your blood type tells you about your genetic background.
  – Different diets are best for people of different phenotypes.
**Change in Body Weight After 16 Weeks of Dietary Intervention in Obese Women**

- Insulin Sensitive: -3.7 kg
- Insulin Resistant: -3.4 kg

**P < 0.05**

21 obese women (fasting insulin ≤ 9 or ≥ 16 μU/mL) randomized to hypocaloric diet:
- HC/LF diet: 60G/20F/20P
- LC/HF diet: 40G/20F/20P

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.

**Insulin sensitivity/resistance**
Moderator of success with high-carb vs. low-carb weight loss

**Conclusions:**
- Low GL more effective than High GL for insulin resistant adults, but not for insulin sensitive adults.

**What is the Best Diet for the Metabolic Syndrome?**

- Paucity of data specifically in this population

**Goals:**
- Weight loss
- Improved insulin sensitivity
- Prevention of diabetes
- Improved lipids
- Improved BP
- Reduced CHD

**Ultimately weight loss occurs with negative energy balance**

Caloric Restriction vs Diet Composition?
Dietary intake clearly has an impact on all of the components of the metabolic syndrome.

- Even though energy deficit is the most important element of weight loss, macronutrient composition of the diet may influence dietary effectiveness and long-term compliance.
- Although individualization is important, it is prudent to recommend a diet low in saturated fat and sodium and higher in unsaturated fats and in complex carbohydrates.

What Should We Recommend to Our Patient?

- An "individualized" diet plan that results in:
  - Negative energy balance
  - Low saturated-fat and cholesterol intake
  - High fiber intake
  - Sustainable weight loss
- In theory, a diet that is high in mono- and poly-unsaturated fats but low in saturated-fats may be ideal...
- If referring for dietary counseling emphasize weight reduction as primary goal?

Conclusions

- Dietary intake clearly has an impact on all of the components of the metabolic syndrome.
- Even though energy deficit is the most important element of weight loss, macronutrient composition of the diet may influence dietary effectiveness and long-term compliance.
- Although individualization is important, it is prudent to recommend a diet low in saturated fat and sodium and higher in unsaturated fats and in complex carbohydrates.

Conclusions

- The treatment goals of the metabolic syndrome should include correcting and/or preventing metabolic and cardiovascular abnormalities.
- Weight reduction is a powerful tool to prevent and treat metabolic syndrome. Because hypocaloric low carbohydrate diets combined with a reduction in saturated fat can improve insulin sensitivity, glucose tolerance, reduce triglycerides, increase HDL, and result in substantial weight loss, it should be recommended as a part of lifestyle modifications in patients with the metabolic syndrome.