SEPARATE EFFECTS OF REDUCED CARBOHYDRATE INTAKE AND WEIGHT LOSS ON ATHEROGENIC DYSLIPIDEMIA.

Kirsten Brown & Juliette Soelberg

Krauss R, Blanche P, Rawlings R, Fernstrom H, Williams P. Separate Effects of Reduce
Carbohydrate Intake and Weight Loss on Atherogenic Dyslipidemia. Am J Clin Nutr.
2006;83:1025-31.

Outline

- Background Information
- Objectives of the Study
- Material and Methods
- Results
  - Table 2: Leah
  - Table 3: Freida
  - Figure 2: Erika
- Conclusions
  - Author's Conclusion
  - Our Conclusion
- Application to the Profession

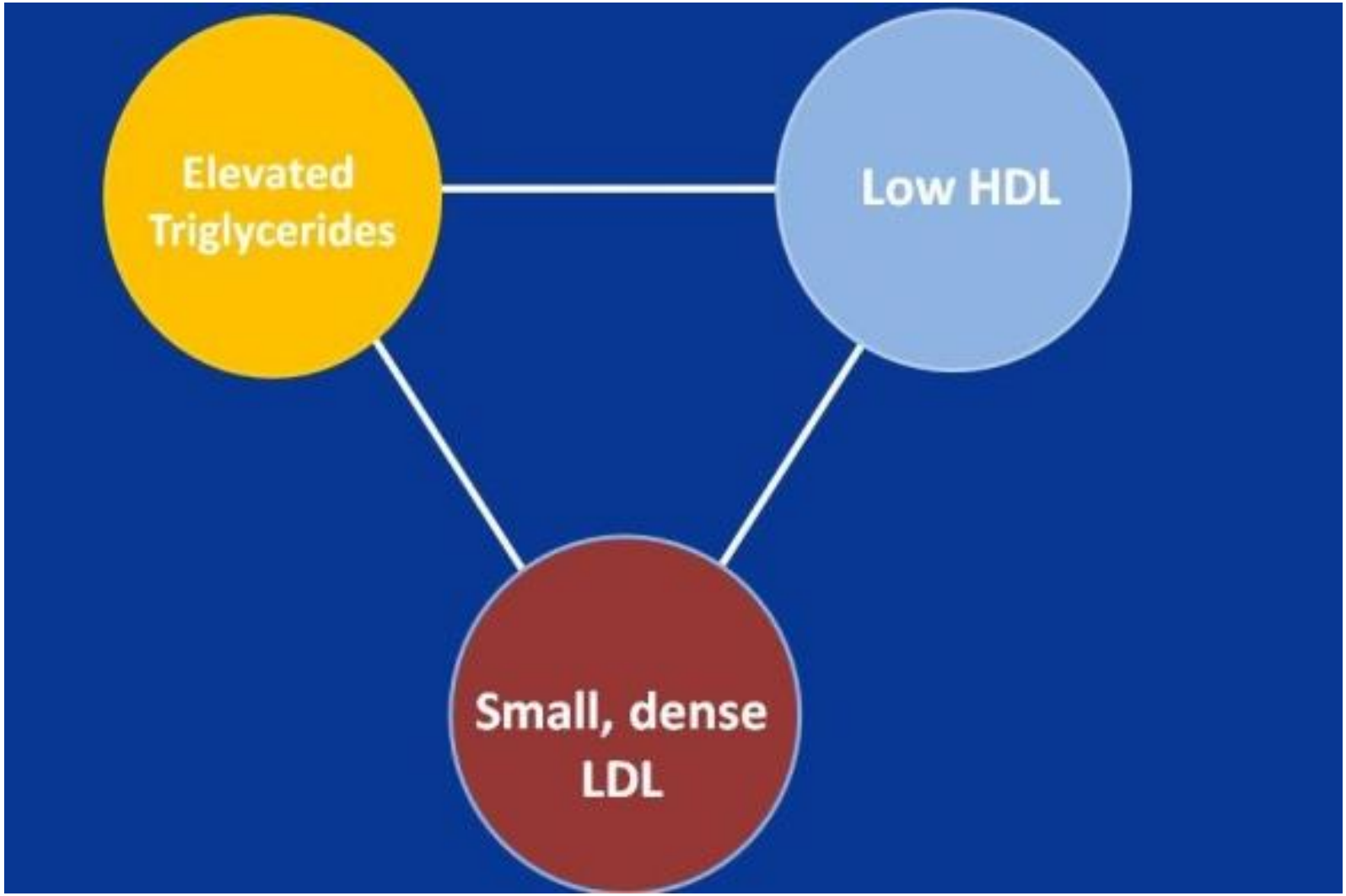
Key Words

- Carbohydrates- Macromolecule consisting of carbon, Hydrogen, and oxygen. Functions primarily to provide the body with **energy**.

- Saturated Fat- Fatty acid with no double bonds between individual carbon atoms of a fatty acid chain. Recommended intake <10% daily intake.

- Lipoproteins- Molecule made of protein and fat. Aids in transportation of lipids in the blood.

What is Atherogenic Dyslipidemia?



Tenenbaum and Fisman *Cardiovascular Diabetology* 2012 **11**:125

Atherogenic Dyslipidemia

- Dietary carbohydrates can promote atherogenic dyslipidemia.
  - Effect the metabolism of plasma triglyceride-rich lipoproteins.

- High-carbohydrate, low-fat diets have been shown to increase concentrations of small, dense LDL and the expression of the small, dense LDL particle phenotype.
  - LDL subclass pattern B phenotype is associated with increased CVD risk.

Krauss et al., 2006

Low Carbohydrate Diets

- Reduce total caloric intake by substitution of protein and/or fat for carbohydrates.
  - Weight loss

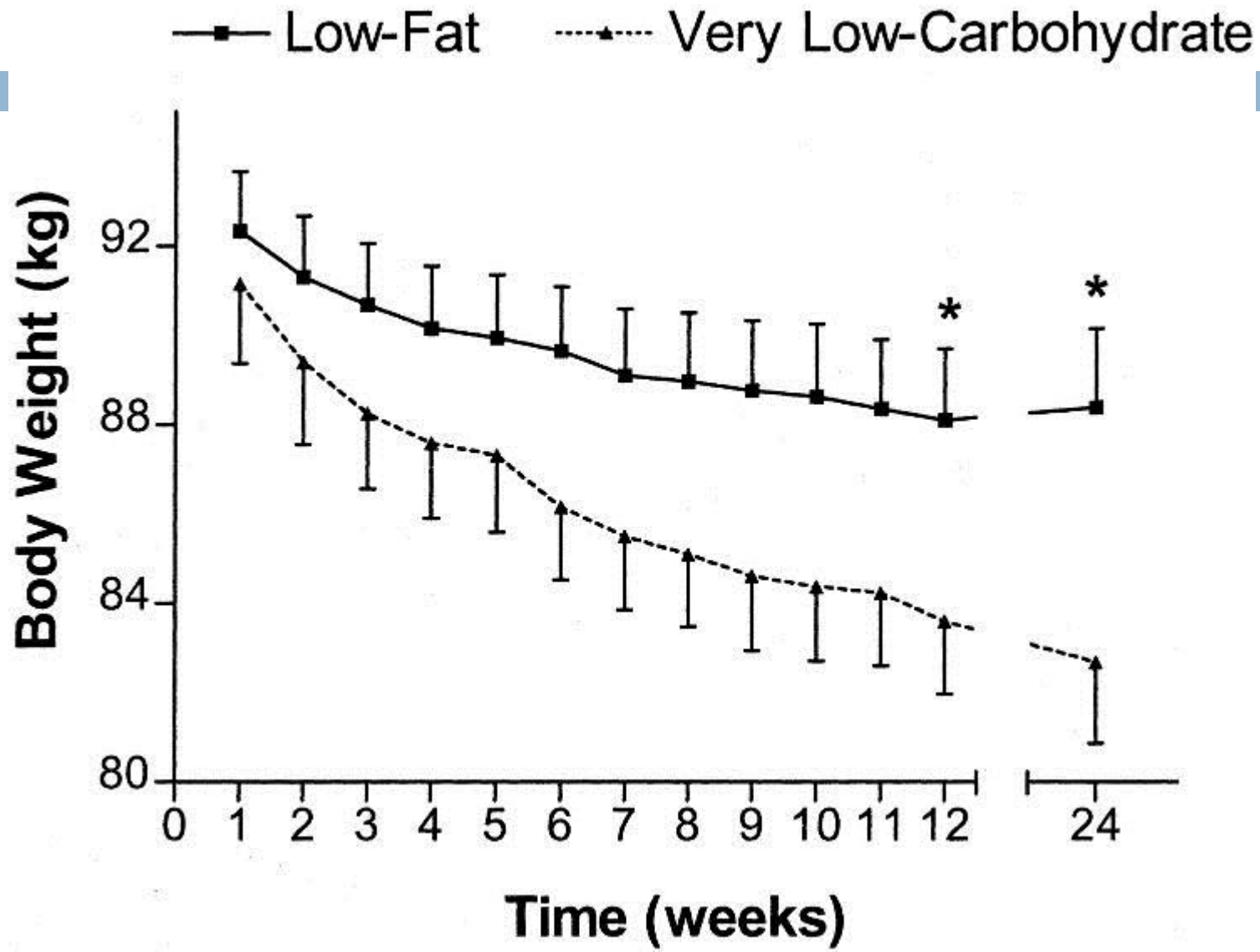
- Manage obesity and subsequent metabolic consequences (reduced plasma triglyceride; Reduction/lack of increased LDL cholesterol).

Krauss et al., 2006

Low-Carbohydrate Diet

Study	Results
Foster et al., 2003	The low-carbohydrate diet produced a greater weight loss and was associated with a greater improvement in risk factors for coronary heart disease than did the conventional diet for the first six months.
Brehm et al., 2003	Very low carbohydrate diet is more effective than a low fat diet for short-term weight loss and is not associated with deleterious effects on important cardiovascular risk factors in healthy women.
Samaha et al., 2003	Greater weight loss during on a carbohydrate-restricted diet than on a calorie- and fat-restricted diet, with a relative improvement in insulin sensitivity and triglyceride levels
Yancy et al., 2004	A low-carbohydrate diet program had greater weight loss, decreased serum triglyceride levels, and increased HDL, then a low-fat diet.

Mean body weight of women randomized to very low carbohydrate and low fat diets over the course of the 6-month trial.



Brehm B J et al. JCEM 2003;88:1617-1623

J.Clin.Endocrinol.Metab., 2003, 88, 4, 1617-1623

Previous Studies:

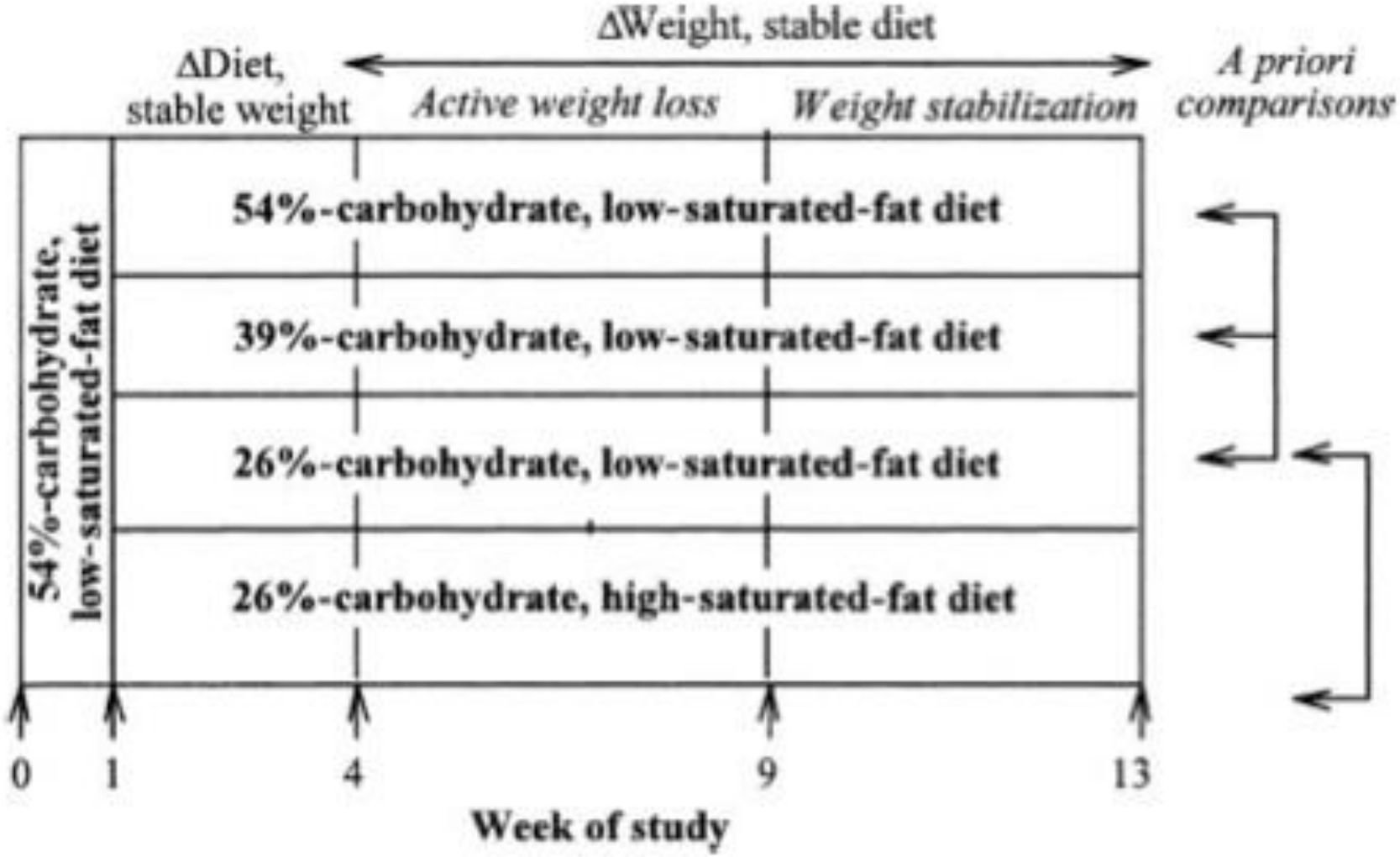
Study	Conclusion
Pelkman et al., 2004	A moderate-fat diet improves the cardiovascular disease risk profile on the basis of favorable changes in lipids and lipoproteins, but not in the low-fat diet.
Archer et al., 2003	The high MUFA diet more favorably affected triglyceride levels, suggesting that it may be preferable to a high CHO diet in cardiovascular disease prevention.
Collette et al., 2003	The MUFA diets showed better effects on serum TG than the CHO rich diet. Results also indicate a protective effect of oleic acid on oxidative stress and SMC proliferation.
Luscombe-Marsh et al., 2005	Weight loss and the improvements in insulin resistance and cardiovascular disease risk factors did not differ significantly between the low-fat, high protein, or high-fat, standard protein diet.

Current Study: Objectives

- To observe the effects of moderate carbohydrate restriction on atherogenic dyslipidemia in overweight and mildly obese men.
- To identify the extent to which changes in lipoprotein with reduction in carbohydrate intake are influenced by dietary saturated fat intake.

Krauss et al., 2006

Study Design



Krauss et al., 2006

Materials and Methods

TABLE 1

Macronutrient composition of the diets[1]

	54% Carbohydrate (basal)	39% Carbohydrate	26% Carbohydrate	26% Carbohydra high saturated f
		% of energy		
Carbohydrate	54	39	26	26
Protein	16	29	29	29
Total fat	30	31	46	45
Saturated	7	8	9	15
Monounsaturated	13	13	27	20
Polyunsaturated	8	8	5	6

[1] Each diet was controlled for other nutrients as follows: cholesterol, 150 mg/1000 kcal; *trans* fatty acids, 2% of energy; fiber, 25 g/2000 kcal plus 2.5 g/5 kcal above 2000; carbohydrate, 50% simple and 50% complex; protein, 50% animal and 50% vegetable; dairy intake, 3 portions of milk, yogurt, or cheese day.

Krauss et al., 2006

Inclusion Criteria:

- Only men (financial and logistical constraints)
  - Higher prevalence of LDL pattern B
- No history of CVD or chronic disease
- BMI ≥26-35
- Total LDL below 95th percentile for age and sex
- Triacylglycerol concentration ≤500 mg/dL
- Fasting Glucose ≤125 mg/dL
- Systolic BP <150 mm Hg, Diastolic BP <90 mm Hg
- No smoking or alcohol consumed during the study

Krauss et al., 2006

Laboratory Measurements

- Express 550 Plus
  - Total cholesterol and triacylglycerol
  - Apo A-I and Apo B
- Dextran sulfate precipitation of plasma
  - HDL
- Friedwald et al formula
  - LDL

Krauss et al., 2006

Laboratory Measurements

- Analytic Ultracentrifugation
  - Measurement of mass concentrations of LDL subfractions.

- LDL subfractions are identified as LDL I-IV, with LDL I being the largest and least dense, to LDL IV being the smallest and most dense.
  - Described by Frieda in Table 2

Krauss et al., 2006

Statistical Procedures

- Comparisons were made by:
  - Analysis of variance
  - Analysis of covariance
  - Post hoc analyses of significance by Scheffe's test

- The study was designed to be able to detect a 50% reduction in the prevalence of LDL-subclass pattern B between groups.

Krauss et al., 2006

RESULTS

Table 2: Leah

Body weight and plasma lipid and lipoprotein measurements at baseline and changes during the low- and high-saturated-fat (SF) diets[1]

	Low-SF diet (7–9%)			High-SF diet (15%)	*P*	
	54% CHO	39% CHO	26% CHO	26% CHO	Low-SF diet (ANOVA)[2]	High- vs low-SF diet (*t* test)[3]
Subjects (*n*)						
Recruited	57	56	59	52	—	—
Dropped out	8	14	12	12	—	—
Final sample size	49	42	47	40	—	—
Weight (kg)						
Baseline	91.6 ± 9.0	92.7 ± 9.1	93.6 ± 9.3	95.6 ± 10.1	NS	NS
ΔDiet, stable weight	−0.0 ± 0.4	−0.2 ± 0.2	−0.9 ± 0.2[4]	−0.5 ± 0.2	0.005	NS
ΔWeight, stable diet	−5.3 ± 0.3	−5.0 ± 0.4	−5.4 ± 0.3	−4.8 ± 0.4	NS	NS
Body fat (%)						
Baseline	27.3 ± 4.0	28.4 ± 4.6	27.5 ± 4.3	28.0 ± 4.2	NS	NS
ΔDiet, stable weight	−0.2 ± 0.1	−0.3 ± 0.1	−0.4 ± 0.1	−0.5 ± 0.2	0.02	NS
ΔWeight, stable diet	−3.5 ± 0.3	−3.5 ± 0.3	−3.6 ± 0.2	−3.3 ± 0.3	NS	NS
Total cholesterol (mg/dL)						
Baseline	203.2 ± 34.6	202.1 ± 23.2	201.1 ± 31.7	203.0 ± 34.8	NS	NS
ΔDiet, stable weight	−7.4 ± 3.0	−9.4 ± 2.8	−21.4 ± 3.2[4,5]	−10.7 ± 3.6	0.002	0.03
ΔWeight, stable diet	−10.6 ± 2.5	−2.1 ± 2.9	7.0 ± 3.1[6]	2.2 ± 3.3	0.0001	NS
LDL cholesterol (mg/dL)						
Baseline	130.1 ± 30.2	125.5 ± 23.1	129.1 ± 25.7	127.8 ± 32.0	NS	NS
ΔDiet, stable weight	−2.6 ± 3.1	−0.6 ± 3.3	−11.2 ± 2.7	−0.7 ± 3.9	0.04	0.03
ΔWeight, stable diet	−8.9 ± 2.5	−1.2 ± 2.5	4.3 ± 2.7[4]	1.1 ± 2.7	0.002	NS
Triacylglycerol (log mg/dL)						
Baseline	2.16 ± 0.20	2.19 ± 0.23	2.10 ± 0.24	2.18 ± 0.25	NS	NS
ΔDiet, stable weight	−0.05 ± 0.02	−0.12 ± 0.03	−0.19 ± 0.03[7]	−0.20 ± 0.03	0.0004	NS
ΔWeight, stable diet	−0.07 ± 0.02	−0.06 ± 0.02	0.01 ± 0.02	−0.03 ± 0.02	0.04	NS
HDL cholesterol (mg/dL)						
Baseline	41.7 ± 8.7	41.6 ± 9.0	43.1 ± 12.4	41.0 ± 11.1	NS	NS
ΔDiet, stable weight	−1.3 ± 0.7	0.6 ± 0.6	0.4 ± 0.9	3.0 ± 1.0	NS	0.06
ΔWeight, stable diet	1.9 ± 0.7	2.0 ± 0.7	2.4 ± 0.8	2.5 ± 0.9	NS	NS
Apolipoprotein B (mg/dL)						
Baseline	102.3 ± 21.7	102.6 ± 18.4	100.0 ± 21.2	104.2 ± 24.7	NS	NS
ΔDiet, stable weight	−4.9 ± 2.0	−9.5 ± 1.8	−15.8 ± 1.9[7]	−12.5 ± 2.1	0.0004	NS
ΔWeight, stable diet	−6.4 ± 1.8	−0.9 ± 2.4	2.3 ± 1.5[4]	−1.4 ± 2.0	0.004	NS
Apolipoprotein A-I (mg/dL)						
Baseline	113.8 ± 15.8	114.0 ± 15.5	111.0 ± 16.4	111.2 ± 14.3	NS	NS
ΔDiet, stable weight	−3.1 ± 1.3	0.8 ± 1.6	0.2 ± 1.7	2.3 ± 1.9	NS	NS
ΔWeight, stable diet	−0.9 ± 1.5	−0.8 ± 1.5	2.9 ± 1.9	0.8 ± 1.7	NS	NS
Total:HDL cholesterol						
Baseline	5.03 ± 1.17	5.09 ± 1.25	4.93 ± 1.30	5.30 ± 1.80	NS	NS
ΔDiet, stable weight	−0.05 ± 0.10	−0.31 ± 0.10	−0.62 ± 0.12[7]	−0.7 ± 0.14	0.001	NS
ΔWeight, stable diet	−0.45 ± 0.08	−0.29 ± 0.11	−0.03 ± 0.09[4]	−0.16 ± 0.08	0.005	NS
LDL peak particle diameter (Å)						
Baseline	258.8 ± 8.7	258.5 ± 8.0	260.3 ± 8.5	258.9 ± 9.2	NS	NS
ΔDiet, stable weight	0.2 ± 0.8	3.5 ± 0.9[8]	3.6 ± 0.9[8]	5.1 ± 1.1	0.007	NS
ΔWeight, stable diet	3.9 ± 1.0	1.3 ± 0.8	0.9 ± 0.7[8]	1.9 ± 0.8	0.02	NS

[1] All baseline values are $\bar{x} \pm$ SD, and all changes (Δ) are $\bar{x} \pm$ SE. To convert cholesterol and triacylglycerol concentrations to SI units (mmol/L), multiply by 0.0259 and 0.0113, respectively. CHO, carbohydrate. There were no significant differences between groups at baseline.

[2] 54%-CHO vs 39%-CHO vs 26%-CHO diet.

[3] 26%-CHO diet only.

[4,6–8] Significantly different from the 54%-CHO control diet (Scheffe test): [4] $P < 0.01$, [6] $P < 0.0001$, [7] $P < 0.001$, [8] $P < 0.05$.

[5] Significantly different from the 39%-CHO diet, $P \leq 0.05$ (Scheffe test).

Krauss et al, 2006

Subjects at Baseline (54% carbohydrate)

- No significant differences between experimental groups
  - Lipids
  - Lipoproteins
  - Apolipoproteins
- No significant differences between ages (P=0.94)

54% Carb, low-saturated fat diet	50.3 ± 9.8 yr
39% Carb, low-saturated fat diet	51.5 ± 11.6 yr
26% Carb, low-saturated fat diet	49.2 ± 9.3 yr
26% Carb, high-saturated fat diet	50.1 ± 11.3 yr

Krauss et al, 2006

Time-by-Diet Interactions

- Significant interactions for all lipoprotein variables *except LDL-III*

Total Cholesterol (P = 0.0008)

LDL Cholesterol (P = 0.005)

Triacylglycerides (P = 0.0006)

HDL Cholesterol (P = 0.005)

Apo B (P = 0.008)

Apo A-I (P = 0.04)

Total:HDL Cholesterol (P = 0.001)

LDL peak particle diameter (P = 0.007)

LDL-I (P = 0.003)

LDL-II (P = 0.004)

LDL-III (P = 0.59)

LDL-IV (P = 0.04)

Krauss et al, 2006

Stage 1: Δ Diet, Stable Weight

- Those on the 26%-carbohydrate, low-saturated fat diet saw more reduction from baseline than those who remained on the 54%-carbohydrate, low-saturated fat diet
  - ↓ Total cholesterol
  - ↓ Triacylglyceride
  - ↓ Apo B
  - ↓ Total:HDL

  } Still significant after unexpected change in weight during stable weight period
- No significant change in HDL for all diets ($p = 0.16$)
- No significant change in Apo A-I

Krauss et al, 2006

TABLE 3

Plasma LDL subfraction total mass concentrations at baseline and changes during the low- and high-saturated-fat (SF) diets[1]

	Low-SF diet (7–9%)			High-SF diet (15%)	*P*	
	54% CHO (n = 49)	39% CHO (n = 42)	26% CHO (n = 47)	26% CHO (n = 40)	Low-SF diet (ANOVA)[2]	High- vs low-SF diet (t test)[3]
LDL-I						
Baseline	90.2 ± 35.1	93.0 ± 32.6	95.4 ± 29.9	94.2 ± 37.1	NS	NS
ΔDiet, stable weight	−3.8 ± 3.6	2.7 ± 3.8	6.3 ± 4.1	16.1 ± 5.4	NS	NS
ΔWeight, stable diet	−0.3 ± 3.9	6.2 ± 3.8	1.1 ± 4.7	−1.6 ± 4.8	NS	NS
LDL-II						
Baseline	100.0 ± 35.1	99.2 ± 30.4	101.5 ± 26.0	98.1 ± 33.0	NS	NS
ΔDiet, stable weight	1.3 ± 3.3	1.8 ± 4.2	−5.5 ± 3.9	3.6 ± 5.5	NS	NS
ΔWeight, stable diet	−7.3 ± 4.1	−0.6 ± 3.6	2.3 ± 4.0	−5.3 ± 4.5	NS	NS
LDL-III						
Baseline	75.3 ± 39.4	71.7 ± 34.9	75.7 ± 38.3	77.9 ± 42.8	NS	NS
ΔDiet, stable weight	−5.3 ± 4.1	−7.3 ± 4.2	−24.5 ± 4.1[4,5]	−24.3 ± 5.1	0.002	NS
ΔWeight, stable diet	−16.1 ± 3.5	−11.6 ± 4.7	−1.2 ± 3.6[6]	−9.6 ± 3.8	0.02	NS
LDL-IV						
Baseline	18.3 ± 15.5	14.1 ± 14.7	16.6 ± 13.5	22.0 ± 21.4	NS	NS
ΔDiet, stable weight	−1.1 ± 1.3	−1.8 ± 2.2	−7.2 ± 1.8[6]	−9.6 ± 2.6	0.03	NS
ΔWeight, stable diet	−6.2 ± 2.0	−2.0 ± 1.8	1.4 ± 1.1[4]	−2.4 ± 1.3	0.007	0.03

[1] All baseline values are $\bar{x} \pm$ SD, and all changes (Δ) are $\bar{x} \pm$ SEM. CHO, carbohydrate. There were no significant differences between groups at baseline.

[2] 54%-CHO vs 39%-CHO vs 26%-CHO diet.

[3] 26%-CHO diet only.

[4,6] Significantly different from the 54%-CHO control diet (Scheffe test): [4]$P < 0.01$, [6]$P < 0.05$.

[5] Significantly different from the 39%-CHO diet, $P \leq 0.05$.

Krauss et al, 2006

Stage 1: Δ Diet, Stable Weight

- LDL peak diameter increased
  - More within 39% and 26 %-carbohydrate, low-saturated fat diets than with 54%-carbohydrate diet
  - Changes were still significant after adjusted for weight change
- LDL-III and LDL-IV decreased greater in 26%-carbohydrate, low-saturated fat diet than in the 54%-carbohydrate diet.
  - After adjusting for weight, significance for LDL-IV reduction was reduced (p=0.07), but significance for LDL-III remained (p=0.01)
- Intermediate changes with 39%-carbohydrate diet compared to 2 other diets
  - LDL-III in 39%-carbohydrate diet significantly different from 26%-carbohydrate, low-saturated fat diet

Krauss et al, 2006

Stage 2: Δ Weight, Diet Stable

- Reductions in variables were significantly greater with 54%-carbohydrate than with 26%-carbohydrate
  - ↓ Total cholesterol
  - ↓ Triacylglyceride
  - ↓ Apo B
  - ↓ Total:HDL
- HDL cholesterol significantly increased after weight loss for all diets combined ($P < 0.0001$)
- No significant changes in apo A-I with either 26%-carb diet
- LDL peak particle diameter did not continue to change with lower-carb diets, but increased with 54%-carb diet

Krauss et al, 2006

Stage 2: Δ Weight, Diet Stable

- Minimal changes with 26%-carb, low-saturated fat
- Significantly greater decrease in LDL-III and LDL-IV with 54%-carb diet
- Changes in LDL peak particle diameter and LDL subfraction concentrations reflected by changes in LDL subclass pattern B expression

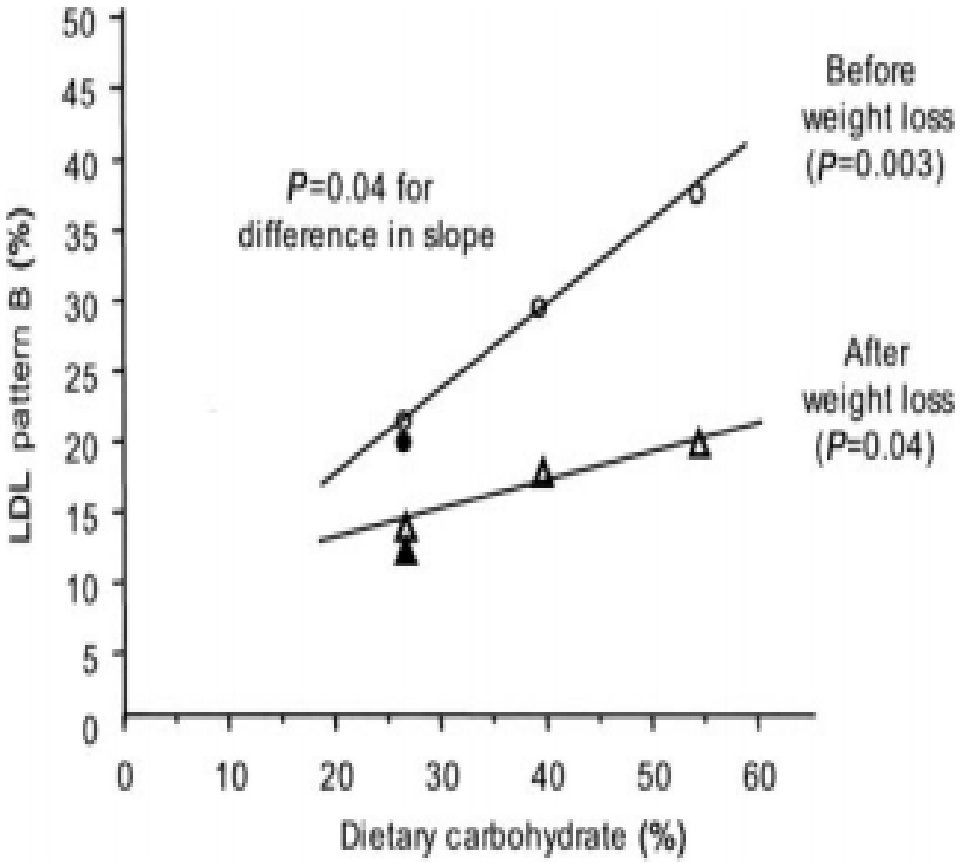


FIGURE 2. Prevalence of LDL subclass pattern B as a function of dietary carbohydrate content for each experimental diet before and after weight loss and stabilization with the diets. Closed symbols represent the low-saturated-fat diet group (n = 49, 42, and 47 for the 54%-, 39%-, and 26%-carbohydrate diets, respectively), and open symbols represent the high-saturated-fat diet group (n = 40).

Krauss et al, 2006

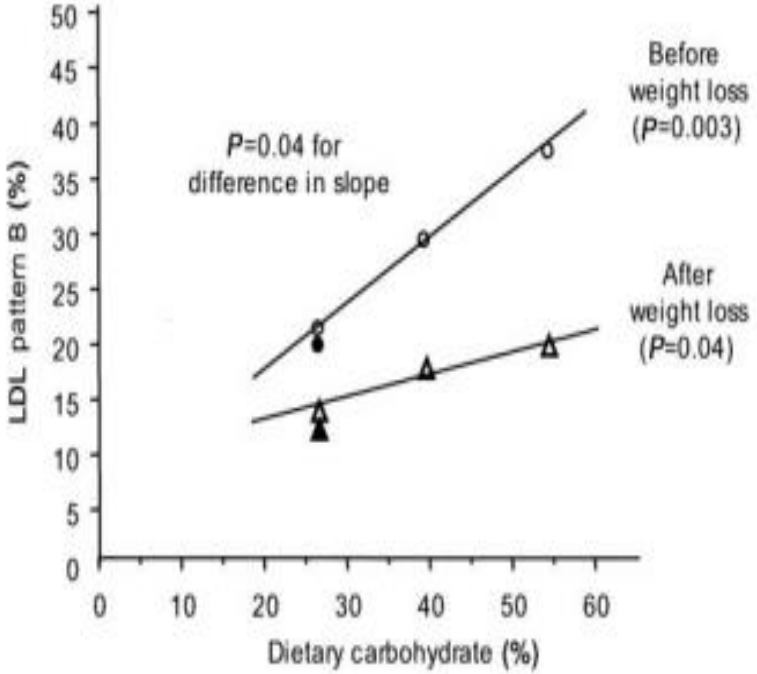
Conclusions

- Comparing 54% and 26%
  - Can't discriminate effects of added protein/monounsaturated fat from effects of reduced carbohydrates
- Changing fat content between 26%-carb diets did not significantly change triacylglycerides, apo B, or total:HDL cholesterol
  - Changes not due primarily to the higher monounsaturated fat content

TABLE 1
Macronutrient composition of the diets[1]

	54% Carbohydrate (basal)	39% Carbohydrate	26% Carbohydrate	26% Carbohydrate, high saturated fat
		% of energy		
Carbohydrate	54	39	26	26
Protein	16	29	29	29
Total fat	30	31	46	45
Saturated	7	8	9	15
Monounsaturated	13	13	27	20
Polyunsaturated	8	8	5	6

Krauss et al, 2006



- Includes 2 diets similar in fat
  - 54%, 39%
- Includes 2 diets similar in protein
  - 39%, 26%
- Can conclude that primary determinant of change in pattern B expression is the reduction in carbohydrates

Krauss et al, 2006

LDL Cholesterol

- Reduction in *total LDL cholesterol* for 26%-carb, low-saturated fat diet was barely significant compared to the other diets
- Must look at subfractions:
  - Significant reduction in small, dense LDL for low-carb diet
  - 26% diet with higher sat-fat produced more large, buoyant LDSL
    - When looked at together, small net change
  - Reductions correlated to reduction in plasma triacylglycerol concent

Krauss et al, 2006

High vs low saturated fat

The two 26%-carb diets did not significantly differ but the higher saturated fat did have more large buoyant LDL

TABLE 3

Plasma LDL subfraction total mass concentrations at baseline and changes during the low- and high-saturated-fat (SF) diets[1]

	Low-SF diet (7–9%)			High-SF diet (15%)	*P*	
	54% CHO (n = 49)	39% CHO (n = 42)	26% CHO (n = 47)	26% CHO (n = 40)	Low-SF diet (ANOVA)[2]	High- vs low-SF diet (t test)[3]
LDL-I						
Baseline	90.2 ± 35.1	93.0 ± 32.6	95.4 ± 29.9	94.2 ± 37.1	NS	NS
ΔDiet, stable weight	−3.8 ± 3.6	2.7 ± 3.8	6.3 ± 4.1	16.1 ± 5.4	NS	NS
ΔWeight, stable diet	−0.3 ± 3.9	6.2 ± 3.8	1.1 ± 4.7	−1.6 ± 4.8	NS	NS

If saturated fat increases large LDL particles, should we eat more saturated fat with a low carb diet?

Weight Loss

- After weight loss, reductions in lipid/lipoprotein indicators of CVS risk was greater with higher (54%) carb diet than with lower (26%)
  - The actual amount of carbs in 54%-carb diet during weight loss stage was less than the actual amount of carbs in the 26%-carb, low-saturated fat diet
- Possible that reduction of either (weight loss or carb %) will have similar results
  - Not as effective together: effect of weight loss is greater with a high carb diet
- Also evidenced by LDL subclass pattern B

Krauss et al, 2006

Dietetics Profession

Weight loss vs. Low-carb diet

What would you recommend??

Questions?