

Citation:

Volek JS, Phinney SD, Forsythe CE, Quann EE, Wood RJ, Puglisi MJ, Kraemer WJ, Bibus DM, Fernandez ML, Feinman RD. Carbohydrate restriction has a more favorable impact on the metabolic syndrome than a low fat diet. *Lipids*. 2009 Apr; 44 (4): 297-309.

PubMed ID: [19082851](#)

Study Design:

Randomized Controlled Trial

Class:

A - [Click here](#) for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To test the effects of consuming diets with differing macronutrient proportions [carbohydrate-restricted diet (CRD) vs. low-fat diet (LFD)] on body weight and metabolic syndrome risk factors in adults.

Inclusion Criteria:

- Men and women aged 18 to 55 years
- Body mass index (BMI) less than 25kg/m²
- Moderately elevated fasting triglycerides (150 to 500mg per dL)
- Low fasting HDL-cholesterol (less than 40mg per dL for males and less than 50mg per dL for females).

Exclusion Criteria:

- Presence of any metabolic or endocrine disorders
- Use of glucose-lowering, lipid-lowering or vasoactive prescriptions or supplements
- Consumption of a CRD at baseline
- Weight loss of more than 5.0kg in the past three months.

Description of Study Protocol:**Design**

A randomized, controlled, dietary intervention trial that compared a CRD to a LFD over a 12-week period in overweight subjects with atherogenic dyslipidemia.

Dietary Intake/Dietary Assessment Methodology

Seven-day weighed food records were kept during weeks one, six and 12 of the intervention and were analyzed for energy and macro- and micronutrient content using Nutritionist PRO software.

Blinding Used

Body mass and composition were measured by a blinded technician.

Intervention

- Subjects received individual and personalized dietary counseling from registered dietitians (RDs) prior to the dietary interventions. Detailed dietary booklets, specific to each dietary treatment, were provided that outlined dietary goals, lists of appropriate foods, recipes, sample meal plans and food record log sheets. All subjects were given a multivitamin/mineral complex that provided micronutrient levels of less than 100% of the RDA and instructed to consume one pill every other day
- No explicit instructions were provided regarding calorie intake for either diet. Subjects received weekly follow-up counseling during which body mass was measured, compliance was assessed and further dietetic education was provided.
 - CRD: The main goal of the carbohydrate-restricted diet was to restrict carbohydrate (CHO) intake to a level that induced a low level of ketosis. Subjects monitored ketosis daily using urine reagent strips that produce a relative color change in the presence of one of the primary ketones, acetoacetic acid. In this diet, there were no restrictions on the type of fat from saturated and unsaturated sources or cholesterol levels. Subjects were instructed to avoid all low-CHO breads and cereal products, and were limited to a maximum of one sugar alcohol-containing, low-CHO snack per day. The final nutrient composition was 1,504kcal per day, with 12% carbohydrate, 59% fat and 28% protein
 - LFD: The low-fat diet was designed to provide less than 10% of total calories from saturated fat and less than 300mg cholesterol. Standard diabetic exchange lists were used to ensure a macronutrient balance of protein (approximately 20%), fat (approximately 25%) and CHO (approximately 55%). The final nutrient composition was 1,478kcal per day, with 56% CHO, 524% fat and 20% protein.

Statistical Analysis

- The mean of two fasting blood draws performed at the same time of day on separate days was used to account for diurnal and day-to-day variation in lipids
- An ANOVA with one between-effect (CRD vs. LFD) and one within effect (week zero vs. week 12) was used to compare responses over time in both groups
- Significant main or interaction effects were further analyzed using a Fishers LSD post-hoc test
- For post-prandial biochemical variables, the area under the curve was calculated using the trapezoidal method
- Relationships among selected variables were examined using Pearson's product-moment correlation coefficient
- The significance level was set at $P < 0.05$.

Data Collection Summary:

Timing of Measurements

- Prior to starting the diet treatment, subjects attended two baseline morning visits after a 12-hour overnight fast and 24-hour abstinence from alcohol and strenuous exercise. The same tests were repeated after the 12-week dietary intervention period
 - On visit one, body mass and body composition were assessed and a blood sample was obtained
 - On visit two, a six-hour oral fat tolerance test was done
 - In females, all blood tests were obtained during the early follicular phase to control for possible effects of menstrual phase on dependent variables
- Seven-day weighed food records were kept during weeks one, six and 12
- Subjects monitored ketosis daily using urine reagent strips.

Dependent Variables

- Body mass was measured in the morning after an overnight fast to the nearest 100g on a calibrated digital scale
- Whole body and regional body composition was assessed by DXA
- Oral fat tolerance test was performed using standard procedures that involved consumption of a high-fat meal, and taking post-prandial blood samples immediately and hourly for hours one through six following the meal
- Whole blood was collected into tubes without preservative or an anticoagulant and centrifuged at 1500 x g for 15 minutes and 4°C, and promptly aliquoted into storage tubes. This blood was used to measure total cholesterol, HDL, triglycerides, LDL, glucose, insulin, LDL and HDL particle size, total ketone bodies, non-esterified fatty acids, Apo A-1, Apo B, leptin, serum RBP4 and fatty acids.

Independent Variables

Macronutrient content of the diet:

- Seven-day weighed food records were kept to assess compliance with the study intervention diets
- Subjects monitored ketosis daily using urine reagent strips.

Control Variables

- Habitual physical activity was maintained throughout the study intervention and was documented daily by all subjects
- Dietary intake was assessed with detailed and weight seven-day food records collected at baseline to assess habitual intake.

Description of Actual Data Sample:

- *Attrition (final N)*: 20 males and 20 females completed the study
 - N=20 for the CRD
 - N=20 for the LFD
- *Age*: CRD, 32.6±11.3 years; LFD, 36.9±12.5 years
- *Anthropometrics*: Between-group comparisons at baseline were not reported
- *Location*: United States.

Summary of Results:

Dietary Intake

- Energy intake did not differ between the two study diets; while macronutrient intake differed according to study design
 - CRD: 1,504kcal per day; 12% CHO, 59% fat and 28% protein
 - LFD: 1,478kcal per day; 56% CHO, 24% fat and 20% protein
- Subjects consuming the LFD reduced saturated fat intake to 7%, compared to 22% for subjects consuming the CRD
- Dietary cholesterol was significantly higher and fiber significantly lower on the CRD compared to the LFD
- During weeks two to 12 of the CRD intervention, subjects reported that presence of urinary ketones above trace on 85% of the days, indicating a high degree of compliance.

Weight Loss and Adiposity

Despite similar reductions in calories, weight loss in the CRD groups was, on average, two-fold greater than in the LFD group. Whole body fat mass and fat mass in the abdominal region also decreased significantly more in CRD subjects than in LFD subjects.

	CRD		LFD		2X2 ANOVA	
	Week 0	Week 12	Week 0	Week 12	Time	TimeXGroup
Body mass (kg)	96.5±13.7	86.4±12.0	94.4±15.2	89.2±13.9	0.000	0.000
BMI (kg/m²)	33.5±5.2	30.0±4.3	32.1±4.1	30.3±3.9	0.000	0.000
Fat mass (kg)	38.7±7.7	33.1±7.9	37.1±10.0	33.4±9.4	0.000	0.009
Lean body mass (kg)	54.4±11.6	51.0±10.9	55.1±10.7	54.1±9.9	0.000	0.009
Percent body fat (%)	40.6±7.3	38.2±8.5	39.0±7.9	36.8±7.9	0.000	NS
Abdominal fat (g)	4,152±1,261	3,325±1,154	4,059±1,165	3,553±1,160	0.000	0.018

Glycemic and Insulin Control

- The CRD resulted in a significant average reduction in 12% in fasting glucose (P<0.0001), while the LFD responses had little average change (NS)
- Fasting insulin response decreased significantly more in subjects following the CRD (-49%) compared to subjects following the LFD (-17%) (P<0.017)
- A significantly greater decrease in leptin was seen with CRD (-42%) compared to LFD (-18%) (P< 0.004).

Changes in Atherogenic Dyslipidemia and Lipoprotein Markers

The CRD improved the features of atherogenic dyslipidemia compared to the LFD.

- CRD showed a more favorable response in fasting TAG (-51 vs. -19%), HDL (+13 vs. -1%),

and TAG/HDL: Ratio (-54 vs. -20%) (P<0.0001)

- Total cholesterol/HDL ratio was reduced more in CRD subjects compared to LFD subjects (-14 vs. -4%; P<0.05), while the Apo B/Apo A-1 ratio improved in CRD subjects and worsened in LFD subjects (-16% vs. +8%; P<0.001)
- LDL particle size shifted from smaller to larger particles in CRD subjects, while there was no change in the size of LDL particles in LFD subjects.

Author Conclusion:

The authors conclude that this study showed that CRDs result in significantly greater weight loss and loss of fat mass, and greater improvement in markers of metabolic syndrome, particularly related to atherogenic dyslipidemia, compared to LFD when followed for 12 weeks.

Reviewer Comments:

- *Relatively short duration limits the understanding of the long-term effects of consuming these types of diets on body weight, adiposity and markers of metabolic syndrome*
- *Small sample size limits the generalizability of these findings*
- *Statistical adjustments were not made for additional factors that may have influence results (e.g., race or ethnicity, age and physical activity).*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

- | | | |
|----|---|-----|
| 1. | Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies) | Yes |
| 2. | Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about? | Yes |
| 3. | Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice? | Yes |
| 4. | Is the intervention or procedure feasible? (NA for some epidemiological studies) | Yes |

Validity Questions

- | | | |
|------|---|-----|
| 1. | Was the research question clearly stated? | Yes |
| 1.1. | Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified? | Yes |
| 1.2. | Was (were) the outcome(s) [dependent variable(s)] clearly indicated? | Yes |

1.3.	Were the target population and setting specified?	Yes
2.	Was the selection of study subjects/patients free from bias?	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	No
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	Were study groups comparable?	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	???
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	Was method of handling withdrawals described?	No
4.1.	Were follow-up methods described and the same for all groups?	No
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	No
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	No
4.4.	Were reasons for withdrawals similar across groups?	???
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A

5.	Was blinding used to prevent introduction of bias?	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	Yes
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were intervening factors described?	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	Were outcomes clearly defined and the measurements valid and reliable?	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	???

7.6.	Were other factors accounted for (measured) that could affect outcomes?	No
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	Was the statistical analysis appropriate for the study design and type of outcome indicators?	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	No
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	No
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	No
9.	Are conclusions supported by results with biases and limitations taken into consideration?	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	Is bias due to study's funding or sponsorship unlikely?	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes