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# Effectiveness of a Carbohydrate Restricted Diet to Treat Non-Alcoholic Fatty Liver Disease in Adolescents with Obesity: Trial Design and Methodology

**Shima Dowla, PhD**[1,2], **May Pendergrass, RD**[3], **Mark Bolding, PhD**[4], **Barbara Gower, PhD**[3], **Kevin Fontaine, PhD**[1], **Ambika Ashraf, MD**[5], **Taraneh Soleymani, MD**[3], **Shannon Morrison, PhD**[6], and **Amy Goss, PhD**[3]

[1]Department of Health Behavior, University of Alabama at Birmingham, Birmingham, Alabama

[2]School of Medicine, University of Alabama at Birmingham, Birmingham, Alabama

[3]Department of Nutrition, University of Alabama at Birmingham, Birmingham, Alabama

[4]Division of Advanced Medical Imaging Research, Department of Radiology, University of Alabama at Birmingham, Birmingham, Alabama

[5]Division of Pediatric Endocrinology, Department of Pediatrics, University of Alabama at Birmingham, Birmingham, Alabama

[6]School of Nursing, University of Alabama at Birmingham, Birmingham, Alabama

## Abstract

**Background—**Non-alcoholic fatty liver disease (NAFLD) is the most common liver disorder among children in the developed world and can progress to cirrhosis, hepatocellular carcinoma, and liver failure. No evidence-based dietary guidelines exist on the most effective diet prescription to treat NAFLD.

**Objective—**To compare the effect of a carbohydrate (CHO)-restricted diet vs fat-restricted diet, the current standard of care, on changes in hepatic fat infiltration, body composition, and metabolic health over an 8-week period among overweight and obese children diagnosed with NAFLD.

**Methods—**In this two-arm, parallel design randomized controlled trial (RCT), 40 participants aged 9 to 18 years were randomized to a CHO restricted diet (<25:>50:25% daily calories from CHO: fat: protein) or control, fat restricted diet (55:20:25% daily calories from CHO: fat: protein). This family-based diet intervention included: (1) a 2-week supply of groceries to feed a four-person household specific to the assigned diet; and (2) extensive education on diet implementation

**Corresponding Author:** Amy M. Goss, PhD, RD, Assistant Professor, Department of Nutrition Sciences, University of Alabama at Birmingham, 1675 University Blvd, Birmingham, AL 35294, amymiski@uab.edu.



**Conflicts of Interest**: None

through biweekly, diet-specific group and individualized counseling sessions with participants and one parent or guardian led by a registered dietitian (RD). The primary outcome measure of this study was hepatic lipid, measured using magnetic resonance spectroscopy (MRS). Secondary outcomes included liver transaminases; markers of inflammation (hsCRP, IL-6, TNF-α); body composition; visceral adipose tissue; and insulin resistance. All testing was conducted at baseline and week 8; hepatic transaminases were also measured at weeks 2 and 4. This RCT is registered with ClinicalTrials.gov (ID: NCT02787668).

**Keywords**

diet intervention; carbohydrate restriction; non-alcoholic fatty liver disease; childhood obesity; adolescent

## 1. Introduction

The prevalence of obesity among children has reached 17% worldwide and affects nearly 13 million children in the United States (1). In parallel with the rate of childhood obesity, the occurrence of non-alcoholic fatty liver disease (NAFLD) is also increasing in this age group. NAFLD is the most common cause of pediatric chronic liver disease, with prevalence estimates reaching 40% in children with obesity (2–4).

NAFLD refers to a spectrum of liver diseases ranging from simple fat infiltration to non-alcoholic steatohepatitis (NASH), a medical condition involving extensive hepatic inflammation, cellular injury, and potentially fibrosis (5). If left untreated, NASH can progress to cirrhosis, hepatocellular carcinoma, and end-stage liver disease (6–7). NAFLD in children, as in adults, is associated with obesity and metabolic syndrome and involves complex interactions between defects in glucose and lipid metabolism and inflammation in multiple organ systems (5, 8 –11). While primary pharmacotherapies target the metabolic disorders associated with fatty liver, no treatment currently exists to directly reverse hepatic fat infiltration.

Observation of NAFLD is becoming a common occurrence among pediatricians; thus, there is urgent need for evidenced-based guidelines on how to treat NAFLD in children and adolescents. Because obesity increases the risk for the progression of fatty liver, weight loss through caloric restriction and exercise is typically the recommended therapy for children (12). However, the dietary recommendation of calorie restriction alone may not be optimal in a pediatric population for multiple reasons including changes in hormonal milieu, growth velocity, lean mass, and bone mineral density that occur with significant weight loss (13–17). Indeed, adults with significant weight loss through caloric restriction have been shown to develop persistent metabolic adaptations over time causing weight regain (13, 18–19). Moreover, RCT's examining the effects of lifestyle interventions have shown limited success potentially due to the difficulty in adhering to long-term physical activity and caloric restrictive regimens (20).

There is evidence that suggests a change in diet composition alone can reduce hepatic fat infiltration. Studies in rodent models and humans have shown that reducing intake of CHO sources such as added sugars, high glycemic grains, and fructose may be an effective

approach to reverse fatty liver by significantly reducing insulin resistance, inflammation, and, primarily, hepatic de novo lipogenesis (DNL) (21–23). Limiting hepatic DNL, a process that converts dietary CHO into triglyceride in the postprandial state, can reduce the accrual of hepatic lipids and simultaneously enhance their disposal via mitochondrial β-oxidation (5, 24–25). A 2-week randomized clinical trial in adults found that a CHO restricted diet (<20 g/day) compared to a reduced calorie, low-fat diet resulted in similar weight loss but greater reduction in hepatic fat (−55% vs. −28%, $p < .001$) (26). This suggests a clear metabolic advantage of CHO-restriction, independent of overall weight loss, in adults with NAFLD. To date, studies have not tested CHO restriction on changes in hepatic fat among children with NAFLD.

The primary purpose of this study is to evaluate the effects of a CHO vs. fat restricted diet on changes in hepatic lipid, aminotransferases, markers of inflammation, insulin resistance, body composition, and visceral adiposity over 8 weeks among overweight/obese children with NAFLD.

## 2. Methods

The Consolidated Standards of Reporting Trials (CONSORT) guidelines were referenced to provide comprehensive and clear information about the methodology of this randomized controlled trial (RCT) (27). Key components of the design and delivery of this diet intervention study are shown in Figure 1.

### 2.1 Study Design

This two-arm, parallel design RCT was designed to compare the effectiveness of a CHO restricted diet (CHO <25%; fat >50%, protein 25%) vs a fat restricted diet (CHO 55%; fat 20%; protein 25%) on improvements in hepatic lipid content among children ages 9 to 18 with NAFLD (n = 40) over an 8-week period. In this family-based diet intervention, each participant and at least one parent or guardian were randomized to one of two diets and received (1) a two week supply of groceries for a four-person household specific to the assigned diet and (2) extensive education on diet implementation through weekly, diet specific group counseling sessions and biweekly individualized dietary counseling sessions led by a registered dietitian (RD). Hepatic lipid content was measured at baseline and week 8 using magnetic resonance imaging (MRI) and MRS. Secondary outcomes include measurement of changes in transaminase levels from a blood draw, body composition via dual-energy x-ray absorptiometry (DXA), visceral adiposity via MRI, insulin resistance (via HOMA-IR), and markers of inflammation (hs-CRP, TNF-a, and IL-6) via fasting blood draw. Average dietary intake and adherence were assessed using 4-day food records at weeks 0, 2, and 4, and analyzed using the Nutrition Data System for Research (NDSR). This RCT is registered with ClinicalTrials.gov (ID: NCT02787668).

### 2.2 Participants and Eligibility Criteria

Recruitment targeted participants who lived within 200 miles of the clinical testing facility in Birmingham, AL. Eligible participants were those between the ages of 9–18 years at the time of initial screening, English speaking, overweight or obese, and diagnosed with

NAFLD through biochemical or radiological testing (Table 1). Exclusion criteria included all other liver diseases, pregnancy, alcohol consumption, history of parenteral nutrition, history of bariatric surgery, and use of medications known to induce steatosis, elevations in liver enzymes, or affect body weight and carbohydrate metabolism. Participants were also excluded if they and their parents/guardians were unwilling or unable to give informed consent, accept random assignment, attend dietary counseling sessions, adhere to treatment prescription, or complete study measures.

### 2.3 Recruitment Strategies

Several strategies were employed to recruit participants, including recruitment letters, flyers, and referrals from clinicians. The study team first identified potential participants by searching the Children's of Alabama electronic medical record (EMR) for patients with ICD-9 billing codes indicating NAFLD (571.8) or elevations in liver transaminases (790.4). Each patient chart with a billing code of interest was then manually reviewed to determine eligibility. All individuals meeting eligibility criteria were mailed a letter with information about the study and how to enroll.

Participants were also recruited from several Children's of Alabama clinics, including the primary care, adolescent, hepatology, endocrinology, and weight management clinics through flyers and clinician referrals. Patients identified by clinicians or study staff as eligible for the study were given the option to contact the study team directly or have a member of the study team contact them at their convenience.

Other recruitment strategies employed included advertisements in the University of Alabama Birmingham (UAB) Reporter, a virtual bulletin board that advertises various clinical trials occurring at UAB, and television. Recruitment flyers were also placed in various locations around the UAB campus and the Jefferson County Department of Public Health.

### 2.4 Screening

All interested individuals were screened via telephone using a telephone interview script. This script provided general information about the study, including purpose, eligibility criteria, the diet intervention, and all tests and procedures.

All eligible individuals were then scheduled for an in-person interview. During this interview, potential participants and their parents/guardians received additional information about the study, provided informed consent and assent, and had the opportunity to view clinic and testing facilities. Unless the interested participant received a recruitment letter or was referred to the study by a clinician, they were required to provide medical documentation confirming NAFLD. Eligible individuals and their parents consenting to all components of the study, including the diet intervention and all testing, were enrolled into the trial and completed baseline testing.

### 2.5 Randomization

Participants were randomly assigned to either the fat restricted diet (control) or CHO restricted diet. A blocked randomization scheme was used to ensure an allocation ratio of

1:1. The random allocation sequence was created using a random number generator by PROC PLAN (SAS Version 9.3). Participants were notified of their diet assignment at their initial diet instruction. Because this was a diet intervention study, it was not possible for participants or study personnel to be blinded to group assignment. However, to minimize potential bias, study personnel involved in data analysis were blinded to randomized assignment.

### 2.6 Diet Intervention

This family-based diet intervention was adapted from the UAB's medically supervised "EatRight" clinic, a lifestyle-oriented weight management program. Although this study focused solely on outcomes of the child and adolescent participants, parents and guardians were strongly encouraged to adopt the prescribed diet for the entire family, as parental and family involvement can predict successful adherence to diet (28–30).

The participant-parent dyad began the 8-week diet intervention after initial diet instruction. This intervention consisted of bi-weekly, diet specific, individual and group counseling sessions led by the study's registered dietitian (RD). Individual meetings with the RD focused on diet instruction, meal planning, goal setting, and a review of nutritional resources. Participants, with the help of their parents, were instructed how to record their dietary intake every two weeks using food journals, and to plan their intake using handouts provided by the study team. These handouts provide lists of common foods broken down by servings per macronutrient.

Dietary adherence was assessed using 4-day food records, which were reviewed with participants and parents at the start of each individual counseling session. To encourage dietary adherence, the RD employed behavioral strategies effective in childhood weight management, such as goal setting, review of food journals, and counseling modification based on the participant's readiness to change (28–30). Diet specific group classes included topics such as label reading, meal planning, healthy substitutions, mindful eating, and other relevant topics important for dietary adherence.

**2.6.1 Initial Diet Instruction—**Following randomization, participants and their parents/guardians attended an initial diet instruction with the RD. During this meeting, the dietitian educated participants on the amount of macronutrients to be consumed each day using food lists. These lists outlined permissible food items organized by food group and macronutrient content, and included information on portion sizes. Participants were also provided with a 14-day sample menu and corresponding recipes.

**2.6.2 Food Provision—**Participants received groceries specific to their 14-day meal plan and recipes at the initial diet instruction meeting. A grocery delivery service was used to minimize the initial burden of shopping on the family and study personnel coordinated with participants to choose a time for grocery pick up or delivery. Each household received sufficient groceries to feed a four-person household for two weeks.

**2.6.5 Diet Prescriptions—**The features of each diet are detailed below with differences highlighted in Table 2.

**Carbohydrate Restricted Diet:** The CHO-restricted diet was designed to minimize intake of refined CHO sources such as added sugars, high glycemic grains, and fructose and provided ≤25% energy from CHO, 25% energy from protein, and ≥50% energy from fat. CHO sources were primarily derived from leafy greens and non-starchy vegetables. Additional CHO sources included in the diet prescription were nuts and nut butters, unsweetened yogurt, and low-glycemic fruits such as apples and berries. Limited amounts of legumes, root vegetables, and "treats" like dark chocolate were permitted. Protein sources included meat, fish, eggs, poultry, and whey protein if appropriate. Saturated fat intake was limited to <10% total energy/day. Other permitted fat sources included olive oil, walnut oil, and other sources of poly- and monounsaturated fatty acids. A multi-vitamin was also encouraged to ensure all micronutrient requirements were met.

**Fat Restricted Diet:** The standard of care in the dietary management of children with NAFLD is a diet low in fat comprised of foods with low energy density, which served as the basis for the control diet group (31–32). The FRD was based on the USDA MyPlate Daily Food Plan for teenagers and consisted of 55:25:20% energy from carbohydrates: protein: fat (33). Participants were discouraged from consuming foods high in fat such as fried foods, butter, cream cheese, and bacon, while foods such as fruits, vegetables (starchy and non-starchy), whole grains, poultry, lean meats, and low-fat dairy products were permitted. Similar to the CHO restricted group, participants were encouraged to supplement meals with a multivitamin.

## 2.7 Outcome Measures

A timetable organizing all outcome measures and time points of data collection is provided in

**2.7.1 Resting Energy Expenditure (REE)—**REE was used to determine participants' caloric requirements, which in turn was used to estimate intake necessary for a weight maintaining diet. After an overnight fast, participants were tested using in an indirect calorimeter (Vmax ENCORE 29N Systems, SensorMedics Corporation, Yorba Linda, CA) at the Nutrition Obesity Research Center (NORC) Metabolism Core Facility for approximately 30 minutes. A clear, plastic, canopy hood was placed over the head and shoulders, and expired air was collected for 20 min after a 10-min equilibration period. Oxygen consumption and carbon dioxide production were measured continuously during this time to estimate 24-hour REE.

**2.7.2 Anthropometric Measurements and Vital Signs—**Height, weight, blood pressure and pulse measurements were taken at baseline, and biweekly at diet counseling sessions using a standardized stadiometer, calibrated electronic scale, and automated blood pressure monitor. Height was measured to the nearest 0.25 inch and weight to the nearest 0.1 pound. Using this information, age, and gender of the participant, BMI percentile and z score were calculated (34).

**2.7.3 Blood Draw and Laboratory Analyses—**Ten milliliters of blood were collected by a phlebotomist at weeks 0, 2, 4, and 8 to measure fasting insulin, glucose, markers of

inflammation (hsCRP, IL-6, TNF-α), lipid profile (total cholesterol (TC), low density lipoprotein (LDL), high density lipoprotein (HDL), and triglyceride), aminotransferases (ALT, AST) and gamma glutamyl transferase (GGT). Blood draws at baseline and week 8 were conducted following a 10-hour fast of all food and beverages except water. Samples were centrifuged, aliquotted, and sera stored at −85°C; concentrations of serum-derived analytes were assayed at the Diabetes Research Center (DRC) Core Laboratory and the UAB Outreach Laboratory. Insulin Resistance (HOMA-IR) was calculated using measurements for fasting glucose and fasting insulin (35–36). Subjects were instructed to avoid strenuous physical activity the day prior to testing, and to avoid all physical activity on the morning of testing.

**2.7.4 Hepatic Lipid (MRI and MRS)—**At baseline and week 8, Magnetic Resonance Spectroscopy (MRS) and 3-point M Dixon MRI were performed to assess liver fat. Both MRS and 3-point M Dixon utilize chemical-shift principles to estimate resonant frequencies of water and methylene groups of triglyceride fatty acid chains. MRS data acquisition involved placement of a single large voxel (≈1–8 cm3) in the liver. Post-processing and quantification involved phase correction signal fitting of the peaks within the acquired spectra, and integration to find the area under each spectral peak of interest. Water – and fat-suppressed images obtained from 3-point M Dixon technique were used to assess hepatic lipid percentage by identifying 3 regions of interest (ROI) free of artifacts and vessels. The signal intesity (SI) of the 3 ROIs, which is based on tissue densities, will be averaged and used to calculate the hepatic fat fraction (fat SI/fat SI+water SI).

**2.7.5 Body Composition—**Body composition was estimated using dual-energy X-ray absorptiometry (DXA) in the NORC/DRC Core Facility. Participants were asked to wear light clothing and lie flat on their backs with arms by their sides during the DXA scan (iDXA; GE Healthcare Lunar, Madison, WI). Total and regional (within the trunk and leg) fat, bone, and lean mass was estimated at baseline and week 8. Girls of childbearing age were required to complete a urine pregnancy test prior to DXA scans. Any female with a positive pregnancy test result were excluded from participating in the study.

**2.7.6 Abdominal Fat Distribution—**Intra-abdominal adipose tissue (IAAT) and subcutaneous abdominal adipose tissue (SAAT) were measured using magnetic resonance imaging (MRI) using Slice-O-Matic software (version 4.3, Tomovision, Montreal, Canada). IAAT and SAAT were computed from segmented regions of interest on non-fat suppressed axial images of the upper abdominal visceral cavity at baseline and 8 weeks.

**2.7.7 Dietary Intake & Adherence—**Dietary intake and adherence were measured and analyzed using 4-day food records and the Nutrition Data System for Research (NDSR) Software Version 2012 (37). Participants were asked to complete 4-day food diaries (three weekdays, one weekend day) at weeks 0, 2, and 4. These records were distributed at baseline testing, collected at initial diet instruction to determine typical dietary intake, and reviewed at every biweekly visit with the RD. Detailed instructions of the food records were provided to participants and their parents/guardians at baseline testing. Food records were inputted into NDSR Software (Version 2012, Nutrition Coordinating Center, University of

Minnesota, Minneapolis, MN) in order to quantify average macronutrient intake. Typical intake on a CHO restricted vs fat restricted diet is shown in Table 4.

### 2.8 Adverse Event Monitoring

Adverse events were routinely queried for at each clinic visit through discussions with both participants and their parents/guardians. The study physician, who provided all medical supervision for the intervention, was on call in the case of an adverse event during testing. The adverse event protocol included immediate reporting of the event to the UAB Institutional Review Board (IRB) and review by the investigative team. If any of these individuals and/or the IRB identified any adverse events related to the study protocol, all study testing would be suspended and the protocol would be amended accordingly.

### 2.9 Sample Size Calculations

The sample size was calculated to detect significant differences in hepatic lipid content. Based on published data by Browning et al, we expected a similar −12.0% absolute reduction in hepatic triglyceride content in the treatment group (low CHO) compared to −5.0% in the control group (low fat) (26). Assuming a standard deviation of 7% and alpha of 0.05, a sample size of 16 in each group will have 80% power to detect a 7% difference in hepatic lipid content between CHO-restricted and fat-restricted diet intervention groups. Allowing for 20% attrition, 20 participants per diet group (total n=40) will be sufficient to detect a statistically significant change in hepatic triglyceride content.

### 2.10 Statistical Analyses

Descriptive statistics such as means, standard deviations, and frequency counts will be used to characterize the study population. To test the hypothesis that CHO compared to fat restriction will induce reductions in hepatic lipid, comparisons between diet groups will be investigated using analysis of covariance (ANCOVA) with follow-up % hepatic lipid content as the dependent variable and diet group as the independent variable adjusted for baseline % hepatic lipid content. Further adjustments will be made for other relevant confounders (e.g., age, gender, ethnicity, change in body weight). Spearman correlation coefficients will be used to determine associations between levels of change in hepatic fat, transaminases, insulin resistance, markers of inflammation, and body composition among all participants combined and by intervention group. All tests will use a .05 alpha level of significance and will be conducted using SAS Version 9.4.

## 3. Discussion

In recent years, NAFLD has become the most common liver disorder in children. Lipid accumulation in the liver may contribute to hepatic insulin resistance and other metabolic abnormalities and, over time, can progress to cirrhosis, cancer, and liver failure if not appropriately managed. Given the increased risk of morbidity and all-cause mortality associated with this condition, therapies are urgently needed to reverse hepatic steatosis.

Dietary CHO restriction holds promise as a treatment for pediatric NAFLD. Diets high in CHO stimulate the post-prandial release of insulin, which increases uptake of glucose into

the liver. In an energy excess state, this glucose is converted into fatty acids via hepatic DNL. A byproduct of fatty acid synthesis, malonyl co-A, further promotes fat accumulation in the liver by inhibiting transport of fatty acid into the mitochondria for ATP production via β-oxidation (5). By restricting sources of glucose in the diet, a CHO restricted diet may effectively reduce hepatic steatosis directly by decreasing the substrate for lipogenesis and indirectly by reducing concentrations of malonyl CoA.

This study will be the first to prospectively test the effects of CHO restriction on changes in hepatic fat infiltration in children with NAFLD using a family-based intervention design. Some epidemiological studies have investigated the link between sugar consumption, glycemic load, and pediatric NAFLD. Similar to glucose, fructose is a simple sugar that serves as the primary sweetener in corn syrup and sugar sweetened beverages. In a cross-sectional study of 592 Australian adolescents, researchers found a strong relationship between fructose consumption and NAFLD in obese children (38). Indeed, in rodent and human studies, fructose has been strongly linked to hepatic steatosis, inflammation and fibrosis through mechanisms involving hepatic DNL (39–41). There is also research investigating low glycemic load diets designed to limit post prandial serum glucose and insulin concentrations. The effects of a low vs high glycemic load diet on change in liver fat was examined in 16 children with MRS-confirmed NAFLD (42). Results of this diet intervention showed no significant differences between diet groups in liver fat, visceral adipose tissue, BMI, ALT, or insulin resistance over 6 months. Children on the low glycemic load diet were provided 40% of daily total calories from CHO, whereas our study limits CHO to < 25% of total calories per day. It may be critical to not only consume low glycemic CHO sources in the diet, but also limit the total amount of energy from CHO below 40% per day to improve hepatic steatosis and other metabolic outcomes in this population. It is also possible that lack of adherence to the low glycemic load diet or a relatively small sample size affected the ability to detect significant between-group differences in change in primary outcomes (43).

This study will be among the first to rigorously test the independent effects of diet composition without caloric restriction on hepatic fat content in children with NAFLD. While inevitable in most diet studies, weight loss can confound the ability to observe differences of macronutrient manipulation on total fat loss and distribution. Moreover, intentional weight loss has been shown to affect growth, puberty, lean mass, bone mineral density in growing children. To address the confounding effects of weight loss, our study utilizes indirect calorimetry to precisely estimate total daily caloric requirements of each participant and tailors each diet to be weight maintaining. This study is also among the first to use MRS imaging to quantify changes in hepatic fat in children on CHO and fat restriction. Although this technology is not currently used in clinical practice, it holds promise as a more accurate and less invasive way of diagnosing and managing NAFLD than standard techniques (e.g. ultrasound and liver biopsy) (44). Additional strengths of this study include attention to a condition with high clinical and public health significance, randomized controlled study design, family-based intervention, and provision of meals to assist with dietary adherence.

To date, there are no evidenced-based dietary guidelines for the standard of care in children and adolescents with NAFLD. The results of this RCT will provide insight into the effects of a reduced CHO dietary pattern on hepatic lipid changes, as well as on insulin resistance and inflammation in adolescents with obesity at high risk of developing type 2 diabetes, metabolic syndrome, and severe liver disease.

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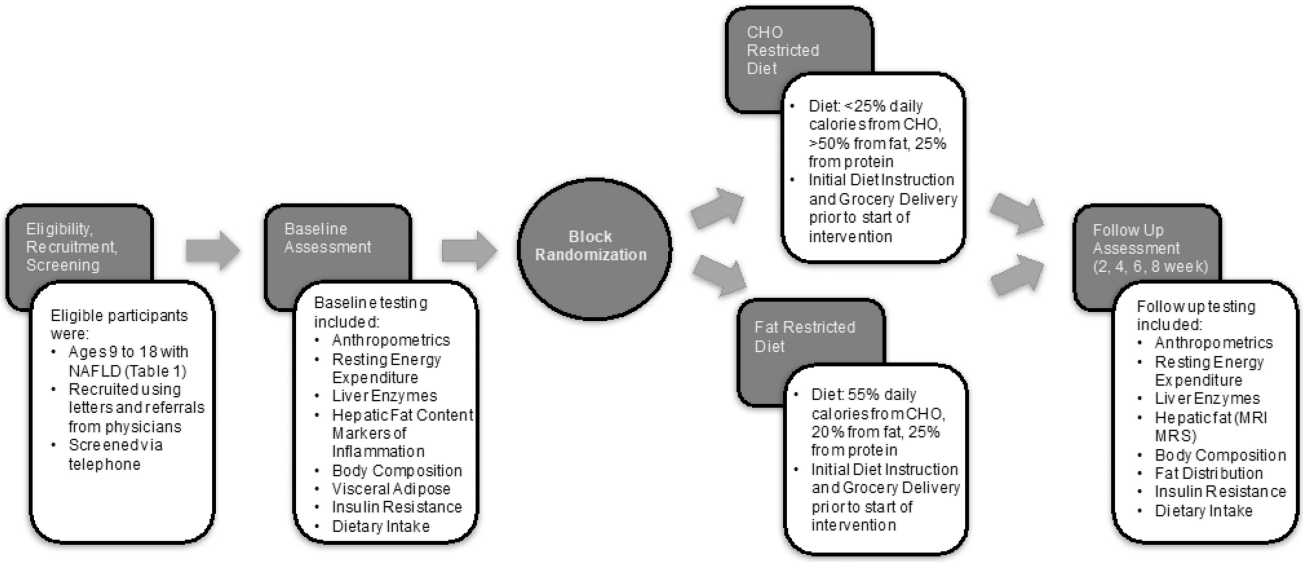


**Figure 1.**
Flow Chart of Diet Intervention Study

**Table 1**

Inclusion and Exclusion Criteria for Participants

| |
|---|
| *Inclusion Criteria* |
| Between the ages of 9–18 years at the time of initial screening |
| Overweight or obese (BMI ≥ 85$^{th}$ percentile) |
| Diagnosis of NAFLD through elevations in serum transaminase (AST or ALT) 1.5 times higher than the reference range or radiological findings (ultrasound, computed tomography, or biopsy) consistent with NAFLD |
| Fluency in English (participants and parents/guardians) |
| *Exclusion Criteria* |
| Pregnant |
| Alcohol consumption |
| History of parenteral nutrition |
| Hepatic virus infections (HCV RNA–polymerase chain reaction negative; hepatitis A, B, C, D, E, and G; cytomegalovirus; and Epstein-Barr virus) |
| Use of medications known to induce steatosis (e.g. valproate, amiodarone, or prednisone), elevation of liver enzymes, or affect body weight and carbohydrate metabolism (within the last 6 months) |
| Autoimmune liver disease, metabolic liver disease, and Wilson's disease |
| Genetic conditions (e.g. glycogen storage disorder) leading to hepatic steatosis |
| History of Bariatric Surgery |
| Participants and parents/guardians unwilling or unable to give informed consent, accept random assignment, attend dietary counseling sessions, adhere to treatment prescription, or complete study measures |
| Inability to speak and comprehend English (participants and parents/guardians) |
| Currently receiving intense lifestyle modification treatment |

Abbreviations: BMI- Body Mass Index; NAFLD- Non-Alcoholic Fatty Liver Disease; AST- Aspartate Aminotransferase; ALT- Alanine Aminotransferase; HCV- Hepatitis C Virus; RNA- ribonucleic acid

**Table 2**

Example Day of CHO- and Fat-Restricted Diet Meal Plan

| | CHO RESTRICTED | FAT RESTRICTED |
|---|---|---|
| **BREAKFAST** | Boiled egg (1 large)<br>Low CHO Pancake (1, 4 in)<br>Cream cheese (2 oz)<br>Eggs (2 large)<br>Almond Flour (2 TB)<br>Splenda (1 Ts)<br>Cinnamon (½ Ts)<br>Serve with sugar-free syrup | Nonfat skim milk (8 fluid oz.)<br>Reduced fat yogurt (6 oz.)<br>Reduced fat granola (1/2 cup)<br>Mixed berries, unsweetened (1 cup) |
| **LUNCH** | Hamburger patty, 93% lean ground beef (4 oz)<br>Lettuce, iceberg (2 large leaves for lettuce wrap)<br>Cream Cheese (2 TB)<br>Celery stalk (5–6 in stick)<br>Low CHO Slaw (1 cup)<br>Broccoli, chopped, frozen, steamed (1 cup) | Hamburger patty, 93% lean ground beef (4 oz)<br>Whole wheat bun (1 large)<br>Reduced fat cheddar cheese (1 slice)<br>Lettuce, iceberg (2 large leaves)<br>Tomato, raw (1 medium slice)<br>Celery stalk (5–6 in stick)<br>Low Fat Cole Slaw (1 cup)<br>Apple (1 medium)<br>Reduced fat dressing (2 TB) |
| **DINNER** | Tilapia, baked, no coating (4 oz)<br>Butter, regular (7 g)<br>Sautéed Spinach (½ cup)<br>Yellow Squash (1 cup)<br>Spinach, frozen, steamed (½ cup)<br>Squash, summer, frozen, steamed (1 cup)<br>Parmesan Cheese, fresh (1 oz)<br>Olive oil (2 TB) | Nonfat skim milk (8 fluid oz.)<br>Tilapia, baked, no coating (4 oz)<br>Spinach, frozen, steamed (1/2 cup)<br>Rice, brown (1 cup)<br>Squash, summer, frozen, steamed (1 cup)<br>Parmesan Cheese, fresh (1 oz)<br>Olive Oil (1 TB)<br>Strawberries (1 cup) |
| **SNACK** | Flax seed muffin (1,42.2 g)<br>Almond Butter (2 TB) | Animal crackers (8 pieces)<br>Raisins (2 TB) |

[1] Composition based on 1800 calorie meal plan

**Table 3**

Outcome Measures

| Measure | Baseline | Week 2 | Week 4 | Week 6 | Week 8 |
|---|---|---|---|---|---|
| Resting Energy Expenditure | X | | | | X |
| Anthropometries | X | X | X | X | X |
| Liver Enzymes | X | X | X | | X |
| Alanine Am inotrasnferase (AST) | | | | | |
| Aspartate Am inotransferase (ALT) | | | | | |
| Gamma Glutamyltransferase(GGT) | | | | | |
| Insulin Resistance | X | | | | X |
| Markers of Inflammation (hsCRP, IL-6, TNF-α) | X | | | | X |
| Lipid Profile (TC, LDL, HDL, Triglyceride) | X | | | | X |
| Hepatic Fat (MRI and MRS) | X | | | | X |
| Body Composition (DXA) | X | | | | X |
| Visceral Fat (MRI) | X | | | | X |
| Dietary Intake and Adherence | X | X | X | | X |

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**Table 4**

Macronutrient Composition (grams) by Diet

| | Total CHO | Added Sugar | Fructose | Total Fat | Total Fiber (g) | SFA | Omega 3 | Protein |
|---|---|---|---|---|---|---|---|---|
| Fat Restriction | 218.9 | 23.2 | 24.2 | 62.7 | 31.5 | 10.1 | 1.9 | 119.9 |
| CHO Restriction | 55.0 | 5.6 | 6.1 | 141.8 | 18.3 | 23.2 | 5.6 | 112.1 |

[1]Composition based on 1800 calorie meal plan