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Long-Term Health Effects of the Three Major Diets Under Self-Management with Advice, Yields High Adherence and Equal Weight Loss, but very different Long-Term Cardiovascular Health Effects as Measured by Myocardial Perfusion Imaging and Specific Markers of Inflammatory Coronary Artery Disease

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Abstract

Background: Obesity is caused by eating behaviours. Adherence to all diets has been extremely poor, thus, comparative data on health effects of different diets over periods of a year or more are limited. This study was designed to treat the root causes of obesity by modifying the eating behaviours and to compare the long-term (one year) cardiovascular health affects using three major diets under isocaloric conditions.

Methods: 120 obese, otherwise healthy, adults were recruited including 63 men and 57 women with a mean age and BMI of 43.7 years and 42.4 respectively. Participants agreed to follow and self-manage diet with follow-up at six-week intervals to achieve 1500-1600 calorie intake of assigned diet type: low-to moderate-fat, lowered-carbohydrate, or vegan. Adherence, weight loss, changes in 14 cardiovascular lipids and coronary blood flow health risk indices were measured.

Results: One-year body mass changes did not differ by diet (P>.999). Effect sizes (R, R2) were statistically significant for all indices. Coronary blood flow, R (CI95%) = .48 to .69, improved with low-to-moderate-fat and declined with lowered carbohydrate diets. Inflammatory factor Interleukin-6 (R = .51 to .71) increased with lowered carbohydrate and decreased with low-to-moderate-fat diets.

Conclusion: One-year lowered-carbohydrate diet significantly increases cardiovascular risks, while a low-to-moderate-fat diet significantly reduces cardiovascular risk factors. Vegan diets were intermediate. Lowered-carbohydrate dieters were least inclined to continue dieting after conclusion of the study. Reductions in coronary blood flow reversed with appropriate dietary intervention. The major dietary effect on atherosclerotic coronary artery disease is inflammation and not weight loss.

Keywords: Heart Disease; Inflammation; FMTVDM; Heart Disease; Weight loss; Diets

Abbreviations: CAD: Coronary Blood Flow; MPI: Myocardial Perfusion Imaging; Veg: Vegan; LMF: Low-To-Moderate-Fat; LoCarb: Lowered-Carbohydrate; TC: Total Cholesterol; LDL: Low-Density Lipoprotein Cholesterol; HDL: High-Density Lipoprotein Cholesterol; VLDL: Very Low-Density Lipoprotein Cholesterol; TG: Triglycerides; CRP: C-Reactive Protein; IL-6: Interleukin-6; Hcy: Homocysteine; Fib: Fibrinogen; Lp (a): Lipoprotein (a); ELISA: Enzyme-Linked Immunosorbent Assay

Introduction

A Centers for Disease Control report showed obesity (Body Mass Index>30) and overweight (25<BMI<30) accounted for 9.1% of all US medical expenditures in 1998 [1]. Lowered carbohydrate diets received general acceptance in 2003 when two widely and popularly publicized studies [2,3] reported low-carbohydrate diets to be effective. By the end of the year, 19% of US adults reported being on "LoCarb" diets [4]. Diet studies attain abysmal participant retention rates, sometimes as low as 50%, while research in non-diet areas can attain rates of 99%. Clearly diets per se have a major impact on participant retention. Despite the magnitude of the censored data problem, no reports of application of statistical methods of survival analysis appear to exist for diet data. Not only is there poor participant survival of diet treatments in general but also there is variation in adherence under different diets [5].

With almost half of the data missing for reasons associated with the treatments, there is little or no basis for generalizing diet studies results to the population. Moreover, given associations of adherence with diet, there is little or no basis in existing research for predicting adherence and consequences when very different (non-directive) treatments are used. The present study examines the effects of non-directive counseling treatment, following well-established behavioural principles to establish self-management, and measures the outcome of subsequent dietary change on weight loss, fourteen (14) cardiovascular disease markers of vascular disease and inflammation and absolute changes in coronary blood flow (CAD) as measured using myocardial perfusion imaging (MPI). A four-month post-intervention analysis was obtained to determine post-intervention treatment, which has not previously been reported in the literature.

Methods

Subject recruitment and monitoring: A total of 673 subjects (Figure 1) were submitted for the study. Final participants included 120 volunteers referred by their primary care physicians as being: obese (Body Mass Index (BMI)>30), age 30-59, nonpregnant, no prior documented heart disease, no medications including over the counter vitamins and supplements, no particular food allergies (e.g., gluten, dairy, peanuts, et cetera), not enrolled in other studies, and free of diabetes, liver, renal, gastrointestinal disease or cancer. Medical history and allergies were confirmed from medical records. Human subject guidelines were followed with informed consent following IRB approval. For a balanced experimental design, participants were randomly assigned by casting a die, to equal diet plan groups: vegan (Veg), low-to-moderate-fat (LMF) and lowered-carbohydrate (LoCarb). The initial design (Figure 1) included subdivision into vitamin supplementation groups but is not further reported here because there was no effect on long-term outcomes resulting from vitamin supplementation. Figure 1 details the study sequence including when each variable was measured.

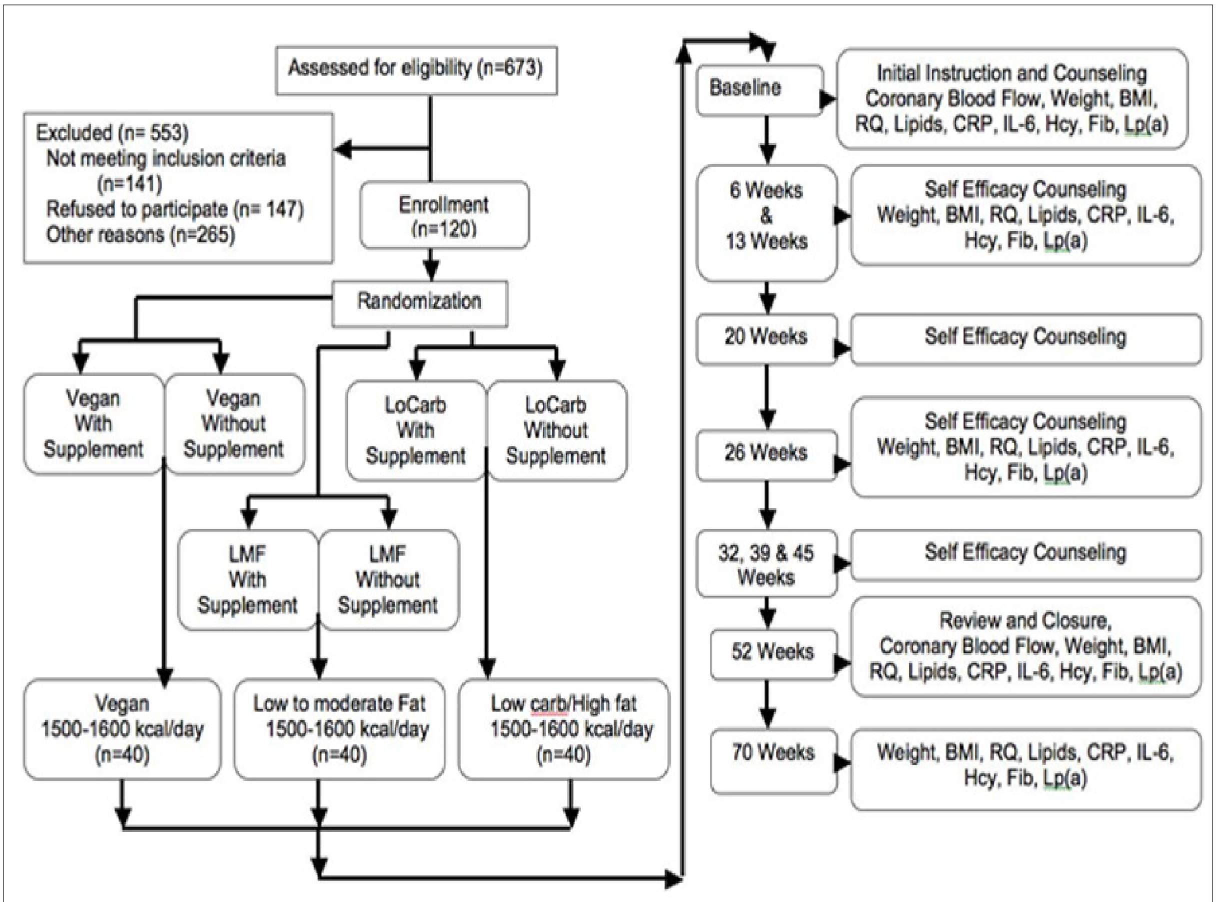

Figure 1: Participant recruitment and study sequence.

Counseling

Participants received supportive nondirective nutritional counseling from the first author/principal investigator for 20 to 30 minutes at 6-week intervals following an initial informational/ instructional entry session of 50 to 60 minutes. Dietary recommendations: As previously reported [6], these dietary-counseling sessions included assessment of total caloric intake with encouragement to maintain an average daily consumption of 1500 to 1600 kcal/day, along with information on sources of protein, carbohydrate and fat [6-9] intake consistent with each of the three regimens [6]. While individual participants determined their own dietary consumption, participants were encouraged to eat more complex carbohydrates and natural foods versus processed or highly refined foods. Vegan dieters were asked to abstain from eating meat, defined as anything moving under its own power while alive (e.g. beef, poultry, pork, fish, et cetera). Dairy products and eggs were also eliminated from the diets of this group. Recommended sources of protein included legumes, beans, nuts and soy products.

Fats were limited to those found in vegetable sources and oils used in the preparation of foods as well as flaxseed. Low-to-moderate fat (LMF) diets included adjustment of fat intake to no more than 15-20% of the total caloric intake. No specific foods were eliminated on this diet if the total fat intake did not exceed this amount with no more than 5 grams of saturated fat consumed per day. During a typical day this would result in 20-25 grams of non-saturated fat and up to 5 grams of saturated fat. Meats (defined as anything which moves under its own power when alive) were incorporated into this regimen with limitations based upon the saturated fat content. Hence, preparation of meat products focused on removing as much saturated fat from the products as possible. Dairy products were limited based on fat content, with emphasis on skim milk and skim or soymilk products. LoCarb diets were higher fat diets with consumption of carbohydrate not exceeding 25% of the recommended daily caloric intake of approximately 100 grams per day. The remainder of the caloric intake was divided between protein (25%) and fat (50%) consumption. There were no restrictions on the amount of saturated fat versus non-saturated fat consumed. Selection depended upon personal preference.

Vitamin Supplement

The study supplement consisted of 2.5mg Folic Acid, 25mg Pyridoxine (B6) and 2mg Cyanocobalamin (B12).

Compliance Biomarkers: Urinalysis for ketones and respiratory quotient to determine dietary intake was measured at each of the follow up evaluations (Figure 1) assuring dietary group adherence.

Exercise Regimen

Participants were asked to follow one of three exercises (walking, bicycling or swimming) three times per week for thirty minutes per session. This could be indoors or outdoors depending upon weather conditions and individual preference. Exercise was for time, not speed or distance. Stationary treadmills or bicycles could be used in the place of non-stationary sources of exercise depending upon personal preference.

Testing Sequence

Anthropometric, exercise, fasting blood work, respiratory quotient, and inflammothrombotic variables were determined for each visit (Figure 1). Assessment of coronary blood flow was conducted at the beginning of the study and at 52 weeks.

Anthropometric Information

Heights were taken upon entry into the study and weights and at each of the follow up evaluations as shown in Figure 1. Calculated BMI's were used as the weight index throughout the study. Fasting venous blood work. At each evaluation, blood samples were obtained and sent to a commercial laboratory service for assay. Fasting blood work [6] was obtained for depository variables (those which are associated with deposition of material within coronary arteries) including total cholesterol (TC), low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), very low-density lipoprotein cholesterol (VLDL), and triglycerides (TG). From this, insulin resistance (TG/HDL) was estimated [10]. The methodology for determination of these variables has been described [11,12] previously in detail. During the evaluations fasting venous blood was also obtained for C-reactive protein (CRP), interleukin-6 (IL-6), homocysteine (Hcy), fibrinogen (Fib), and lipoprotein (a) [Lp (a)]. The methodology for determining these variables has been described [6,8,9] elsewhere except for IL-6. Interleukin-6 was determined from fasting blood samples, which were immediately spun, separated and then frozen for enzyme-linked immunosorbent (ELISA) assay.

Coronary Blood Flow

Myocardial perfusion imaging was completed at entry into the study and one year after following the recommended dietary and supplement protocol. Perfusion imaging was performed [8,9,13] as previously established and described.

Statistical Analysis

The experimental design anticipated use of a general linear model. Venables et al. [14], describe Studentized-residuals, Durbin-Watson, Cook's distance, and other graphic examinations applicable to justifying the selection of a linear model. They also provide a detailed exposition on the software used. Software was R-1.8.0. Coefficients of the linear models lead to confidence intervals for the mean changes for each index on each diet and for the differences between diets. Statistical effect sizes among and between the different diets on cardiovascular disease risk factors were also analyzed using both the coefficient of determination (R2) and the ratio of effect variance to total variance, that is, the multiple correlation (R). Quantile statistics lead to notched box plots showing quartile distributions, outliers, and confidence intervals of medians as alternative statistics not affected by outliers.

Results

The initial characteristics of the 120 men and women enrolled in this study are shown in Table 1 and are representative of the general population who are overweight, which now represents two-thirds of the populations of most affluent societies. Participant retention was 100%, no participants withdrew. With all three diets, participants maintained their weight loss over the four-month period following cessation of the dieting programs and did not show the commonly reported regaining of weight. The Institute of Medicine recommends all health research include an examination of sex effects in all phenomena under study. Using a general linear model to examine all data of this research for sex effects and interactions, no effects or trends were found. The 57 female and 63 male participants were randomly assigned to equal dietary groups by casting a die. There were no statistical demographic differences between group assignments. There were no statistically significant differences, or even trends, between diet groups at the initiation of the study. Since the groups were unequivocally randomized for all fifteen-baseline indices, statistical inference to the initial population, described by Table 1, is appropriate.

Table 1: Initial population characteristics (Mean [SD]).

Variable	All Participants
Females	57
Males	63
Age (years)	43.7[8.40]
Height (inches)	67.9[3.13]
Weight (lbs)	272 [54.7]
Weight (kg)	124 [25.0]
Body Mass Index/BMI (kg/m^2)	42.4[7.55]
Ischemic Index [28]	.082[.054]
Respiratory Quotient (RQ)	.893[.023]
Total Cholesterol/TC (mg/dl)	266 [28.2]
Low Density Lipoprotein/LDL (mg/dl)	185 [27.6]
High Density Lipoprotein/HDL (mg/dl)	42.2[6.01]
TC/HDL	6.43[1.14]
Very Low Density Lipoprotein/VLDL (mg/dl)	39.0[6.99]
Triglycerides/TG (mg/dl)	195 [34.9]
Insulin Resistance (TG/HDL)	4.71[1.11]
C-reactive Protein/CRP (mg/dl)	1.07[1.89]
Interleukin-6/IL (pg/ml)	5.89[3.68]
Homocysteine/Hcy (mmol/L)	15.0[8.31]
Fibrinogen/Fibrin (mg/dl)	327 [64.7]
Lipoprotein(a)/Lp (mg/dl)	23.7[11.6]

The baseline and follow-up results for each measured index for each group are shown in Tables 2-7, including a breakdown by diet and vitamin supplementation. There were no statistical differences for any dietary regimen based upon the inclusion or exclusion of vitamin supplementation. Subsequently the two groups (with and without vitamin supplementation) for each diet regimen (Vegan, LMF and LoCarb) were combined for further analysis. Variances within this study were generally homogeneous except for the Ischemic Index [7,9,15], which is distinctive as shown in Figure 2A with smaller Vegan variance. Robust regression analysis, which minimized the impact of the outliers, yielded much larger coefficients but in the same proportions as did the linear model. Analysis of reduced data sets, with outliers excluded, also yielded larger coefficients and much higher significance levels. Thus the linear fit presented appears to be conservative in its estimates of effects. Using the ANOVA randomization test, the Bonferroni adjusted probability for all fifteen measures and three groups at initiation of the study, $R2 < 0.05$ with P (Bonferroni) = .20. Figure 2A & 2B, for all variates, were constructed with notched box plots. The notches are a form of confidence interval such that non-overlapping notches show a significant ($P<.05$) difference in medians. The boxes encompass the 2nd and 3rd quartiles; the whiskers represent 1.5 times the interquartile range; all outliers beyond that range are shown.

Table 2: 1500-1600 kcal/ day vegetarian diet without vitamin supplement (Mean [SD]).

	Baseline	6 Weeks	3 Months	6 Months	1 Year	4 Months After
II	0.087[0.049]	NA	NA	NA	0.069[0.047]	NA
RQ	0.88[0.02]	0.90[0.02]	0.92[0.02]	0.92[0.03]	0.95[0.02]	0.95[0.03]
Pounds	268.0[63.7]	261.0[62.9]	256.4[62.4]	248.1[61.8]	237.8[60.4]	237.4[59.3]
Kg	121.6[29.1]	118.6[28.5]	116.6[28.4]	112.6[28.1]	108.1[27.5]	107.9[26.9]
BMI	42.0[8.3]	40.9[8.1]	40.3[8.1]	38.9[8.0]	37.2[7.6]	37.2[7.6]
TC	254.8[23.1]	242.0[21.9]	240.0[21.6]	231.9[20.4]	206.2[20.1]	201.2[32.9]
LDL	172.7[24.1]	161.7[20.2]	161.7[20.2]	154.5[19.4]	132.9[16.6]	127.4[31.1]
HDL	43.0[5.9]	44.4[7.6]	44.4[7.6]	46.2[6.6]	48.3[5.4]	49.2[4.9]
TC/HDL	6.0[1.1]	5.6[0.9]	5.5[0.9]	5.1[0.8]	4.3[0.5]	4.1[0.8]
VLDL	39.1[6.1]	35.9[4.6]	33.8[3.9]	31.1[3.7]	25.1[3.0]	24.5[3.6]
TG	195.6[30.7]	179.6[23.1]	169.1[19.3]	155.4[18.3]	125.5[15.2]	122.3[18.0]
TG/HDL	4.6[1.0]	4.1[0.8]	3.9[0.7]	3.4[0.6]	2.6[0.4]	2.5[0.5]
CRP	0.81[1.46]	0.77[1.33]	0.61[1.6]	0.48[0.60]	0.28[0.14]	0.26[0.17]
IL-6	5.28[3.84]	5.11[3.45]	4.22[2.24]	3.51[1.99]	2.63[1.32]	2.11[1.25]
Hcy	15.5[9.4]	16.2[8.3]	15.7[6.9]	14.4[6.9]	11.3[4.1]	15.5[19.9]
Fib	331.5[66.4]	322.9[42.6]	322.3[33.6]	321.9[22.3]	321.4[20.3]	324.1[18.1]
Lp (a)	26.6[13.2]	25.3[11.9]	24.0[11.5]	21.7[10.4]	20.4[9.7]	21.4[9.4]

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Table 3: 1500-1600 kcal/day vegetarian diet with vitamin supplement (Mean [SD]).

s	Baseline	6 Weeks	3 Months	6 Months	1 Year	4 Months After
II	0.080[0.040]	NA	NA	NA	0.071[0.033]	NA
RQ	0.89[0.03]	0.92[0.02]	0.94[0.02]	0.94[0.03]	0.97[0.02]	0.92[0.03]
Pounds	277.2[53.4]	270.4[53.2]	260.3[53.7]	251.1[54.5]	243.5[53.5]	244.9[53.0]
Kg	125.6[24.1]	123.1[24.1]	118.3[24.4]	114.2[24.7]	110.7[24.3]	111.4[24.0]
BMI	42.5[7.7]	41.3[7.6]	39.9[8.2]	38.6[8.2]	37.4[8.0]	37.5[8.2]
TC	264.1[29.0]	249.1[30.5]	228.9[26.3]	224.0[23.9]	192.5[20.7]	189.8[18.0]
LDL	181.7[27.5]	168.6[28.0]	149.9[23.7]	147.4[21.8]	119.0[20.0]	118.6[17.6]
HDL	43.4[4.9]	44.3[4.0]	46.4[4.2]	47.0[4.3]	48.1[4.3]	47.0[4.2]
TC/HDL	6.2[1.0]	5.7[0.8]	5.0[0.6]	4.8[0.6]	4.0[0.6]	4.1[0.5]
VLDL	39.0[6.3]	36.2[5.9]	32.4[5.2]	29.5[5.2]	25.4[5.2]	24.2[4.6]
TG	195.1[31.3]	181.2[29.6]	162.1[25.9]	147.4[26.0]	127.0[26.1]	121.2[23.0]
TG/HDL	4.5[0.8]	4.1[0.7]	3.5[0.6]	3.2[0.6]	2.7[0.6]	2.6[0.5]
CRP	2.34[3.55]	1.49[2.19]	0.76[1.24]	0.45[0.44]	0.28[0.22]	0.40[0.13]
IL-6	5.83[2.98]	5.11[2.91]	4.54[2.28]	4.15[1.76]	3.55[1.69]	3.34[1.31]
Hcy	13.9[6.4]	12.0[5.9]	10.5[5.2]	10.0[4.1]	9.1[3.1]	9.0[3.1]
Fib	327.4[72.1]	327.1[45.4]	327.4[28.3]	325.8[22.1]	329.1[18.2]	329.2[14.9]
Lp (a)	23.4[12.0]	22.7[11.3]	21.4[10.8]	20.2[8.9]	19.0[8.5]	18.1[8.4]

Table 4: 1500-1600 kcal/day low to moderate fat diet without vitamin supplement (Mean [SD]).

	Baseline	6 Weeks	3 Months	6 Months	1 Year	4 Months After
II	0.083[0.055]	NA	NA	NA	0.068[0.041]	NA
RQ	0.90[0.02]	0.93[0.01]	0.93[0.01]	0.92[0.01]	0.92[0.01]	0.92[0.01]
Pounds	276.5[53.2]	268.9[53.2]	263.2[53.2]	254.8[53.0]	246.7[53.3]	243.9[53.3]
Kg	125.7[24.2]	122.4[24.2]	119.6[24.2]	115.8[24.1]	112.2[24.2]	110.9[24.3]
BMI	43.1[7.5]	42.0[7.2]	41.1[7.4]	39.7[7.3]	38.6[7.5]	38.1[7.5]
TC	266.2[23.3]	239.5[22.4]	216.7[20.0]	196.2[21.3]	181.5[16.7]	170.9[28.6]
LDL	183.4[21.3]	158.9[20.5]	136.5[17.4]	120.9[18.9]	108.2[14.1]	98.9[25.0]
HDL	43.4[4.9]	45.4[5.3]	47.3[5.6]	47.0[3.7]	48.3[3.4]	49.0[4.1]
TC/HDL	6.2[0.8]	5.3[0.6]	4.6[0.6]	4.2[0.5]	3.8[0.3]	3.5[0.5]
VLDL	39.5[8.1]	35.3[5.2]	32.8[4.5]	28.2[4.1]	24.9[4.8]	23.0[4.5]
TG	197.4[40.4]	176.3[26.2]	163.8[22.5]	141.0[20.6]	124.6[24.2]	115.1[22.4]
TG/HDL	4.6[1.3]	3.9[0.8]	3.5[0.7]	3.0[0.4]	2.6[0.5]	2.4[0.5]
CRP	0.71[1.02]	0.44[0.49]	0.24[0.14]	0.16[0.11]	0.09[0.09]	0.19[0.09]
IL-6	6.14[4.44]	5.77[3.94]	5.21[3.42]	4.86[3.12]	3.99[2.16]	3.85[2.03]
Hcy	16.0[8.7]	14.0[6.9]	12.9[6.5]	10.9[5.1]	9.2[3.5]	9.2[3.3]
Fib	326.7[61.4]	331.8[51.6]	338.7[42.2]	341.8[22.8]	333.9[20.8]	341.4[16.0]
Lp (a)	22.8[10.1]	21.6[9.6]	19.4[8.7]	17.0[7.1]	15.0[6.6]	13.8[5.8]

Table 5: 1500-1600 kcal/day low to moderate fat diet with vitamin supplement (Mean [SD]).

	Baseline	6 Weeks	3 Months	6 Months	1 Year	4 Months After
II	0.094[0.058]	NA	NA	NA	0.053[0.036]	NA
RQ	0.89[0.02]	0.93[0.02]	0.92[0.01]	0.93[0.02]	0.93[0.01]	0.93[0.01]
Pounds	267.1[55.9]	259.8[54.3]	253.1[54.4]	245.8[54.8]	243.1[53.2]	240.7[53.1]
Kg	121.3[25.3]	118.1[24.6]	115.0[24.8]	111.7[25.0]	110.6[24.2]	109.5[24.0]
BMI	42.1[7.8]	40.9[7.5]	40.0[7.4]	38.8[7.7]	38.5[8.1]	38.0[8.1]
TC	261.9[35.0]	247.9[36.1]	234.3[30.1]	214.4[30.9]	191.9[32.9]	182.8[29.6]
LDL	186.2[37.1]	174.2[36.4]	163.1[31.2]	143.4[30.4]	121.8[33.6]	111.8[31.1]
HDL	39.4[6.3]	40.8[5.6]	41.4[5.2]	44.4[5.8]	46.5[4.8]	47.8[3.9]
TC/HDL	6.9[1.7]	6.2[1.4]	5.8[1.1]	4.9[1.0]	4.2[0.8]	3.9[0.8]
VLDL	36.3[5.2]	32.9[5.4]	29.7[4.7]	26.6[4.1]	23.6[3.3]	23.2[2.9]
TG	181.4[26.1]	164.3[26.8]	148.6[23.7]	133.1[20.3]	118.1[16.5]	116.0[14.3]
TG/HDL	4.7[1.1]	4.1[1.0]	3.7[0.8]	3.1[0.7]	2.6[0.5]	2.4[0.4]
CRP	0.54[0.54]	0.30[0.23]	0.18[0.09]	0.17[0.07]	0.13[0.08]	0.16[0.09]
IL-6	6.02[3.58]	5.33[2.85]	4.40[2.47]	3.78[2.10]	3.33[2.04]	3.54[1.98]
Hcy	13.4[6.5]	12.2[5.4]	9.8[3.1]	8.5[2.6]	7.5[1.7]	7.9[1.9]
Fib	332.6[63.5]	328.8[55.4]	322.9[41.7]	319.8[33.6]	310.4[26.7]	319.8[17.8]
Lp (a)	24.9[11.8]	22.5[10.8]	19.8[9.0]	16.5[7.2]	14.7[6.3]	14.0[6.1]

Table 6: 1500-1600 kcal/day low carbohydrate diet without vitamin supplement (Mean [SD]).

	Baseline	6 Weeks	3 Months	6 Months	1 Year	4 Months After
II	0.081[0.059]	NA	NA	NA	0.119[0.079]	NA
RQ	0.90[0.02]	0.88[0.02]	0.86[0.01]	0.85[0.02]	0.84[0.01]	0.93[0.01]
Pounds	272.1[53.5]	261.4[53.4]	254.5[53.9]	250.0[53.5]	245.7[53.0]	250.0[53.8]
Kg	123.5[24.2]	118.8[24.3]	115.9[24.6]	113.6[24.3]	111.8[24.0]	113.7[24.3]
BMI	42.7[7.0]	41.0[7.0]	40.0[7.0]	39.3[7.0]	38.6[6.9]	39.2[7.1]
TC	287.8[38.7]	274.7[36.9]	259.4[30.9]	269.1[30.6]	280.5[28.3]	280.5[26.4]
LDL	206.5[38.7]	195.1[37.7]	180.9[33.1]	188.1[31.1]	198.3[28.0]	204.4[27.4]
HDL	43.0[6.1]	43.2[5.3]	43.3[4.9]	43.7[5.4]	42.5[3.8]	42.0[3.0]
TC/HDL	6.8[1.1]	6.4[1.1]	6.1[0.9]	6.2[0.9]	6.6[0.8]	6.7[0.7]
VLDL	38.4[6.3]	36.4[5.7]	35.2[5.4]	37.1[5.3]	39.6[5.5]	39.1[9.6]
TG	192.1[31.4]	181.8[28.6]	175.9[26.8]	185.7[26.7]	197.9[27.6]	195.4[48.0]
TG/HDL	4.6[1.1]	4.3[0.9]	4.1[0.7]	4.3[0.7]	4.7[0.7]	4.7[1.1]
CRP	1.07[1.79]	1.00[1.59]	1.34[1.54]	1.19[1.37]	1.26[0.59]	0.80[0.42]
IL-6	6.79[4.34]	8.14[3.76]	10.58[3.72]	10.56[2.50]	10.56[2.49]	9.70[3.10]
Hcy	16.4[10.6]	17.3[9.7]	20.4[12.7]	21.9[11.5]	23.0[10.9]	20.4[10.1]
Fib	311.0[62.7]	317.4[61.8]	330.1[56.8]	337.0[55.1]	340.8[52.2]	339.1[49.9]
Lp (a)	24.3[10.9]	24.9[10.7]	26.3[10.8]	27.6[11.2]	29.9[11.8]	28.7[11.6]

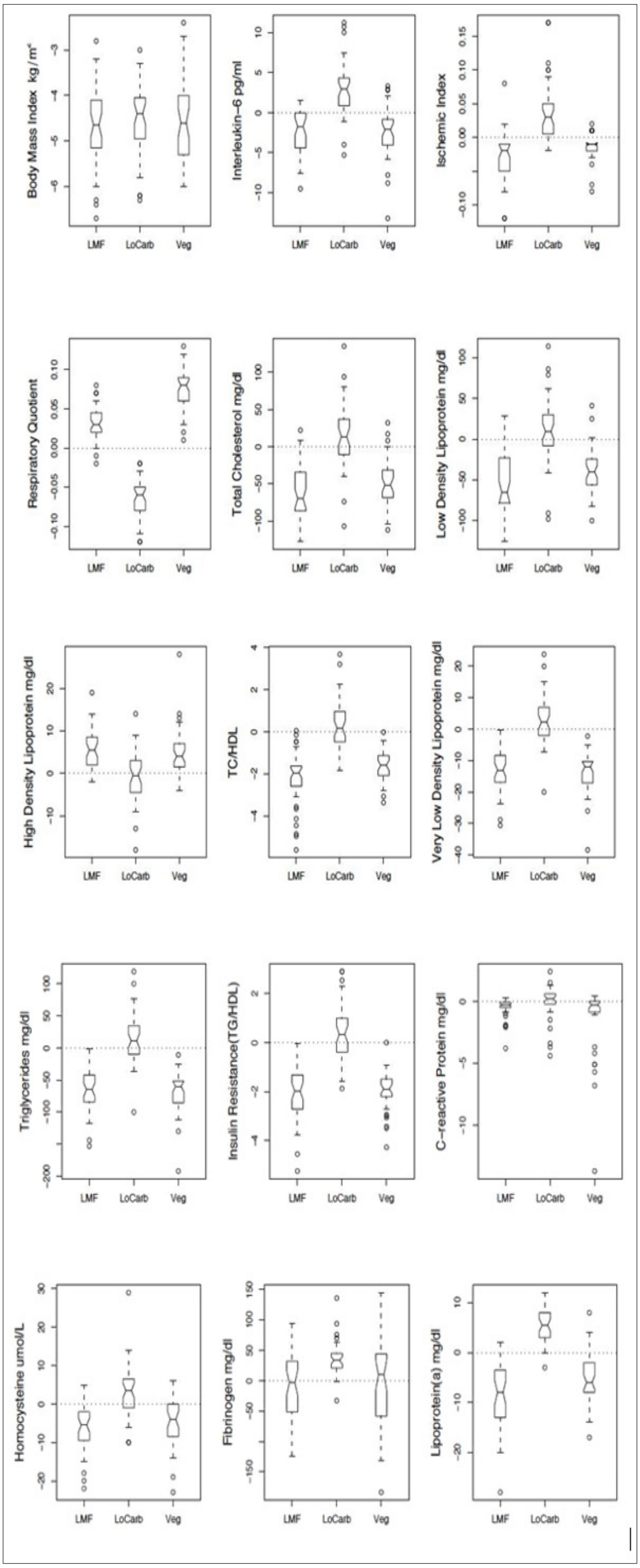

Figure 2A: Outcomes followed twelve (12) months of dietary intervention.

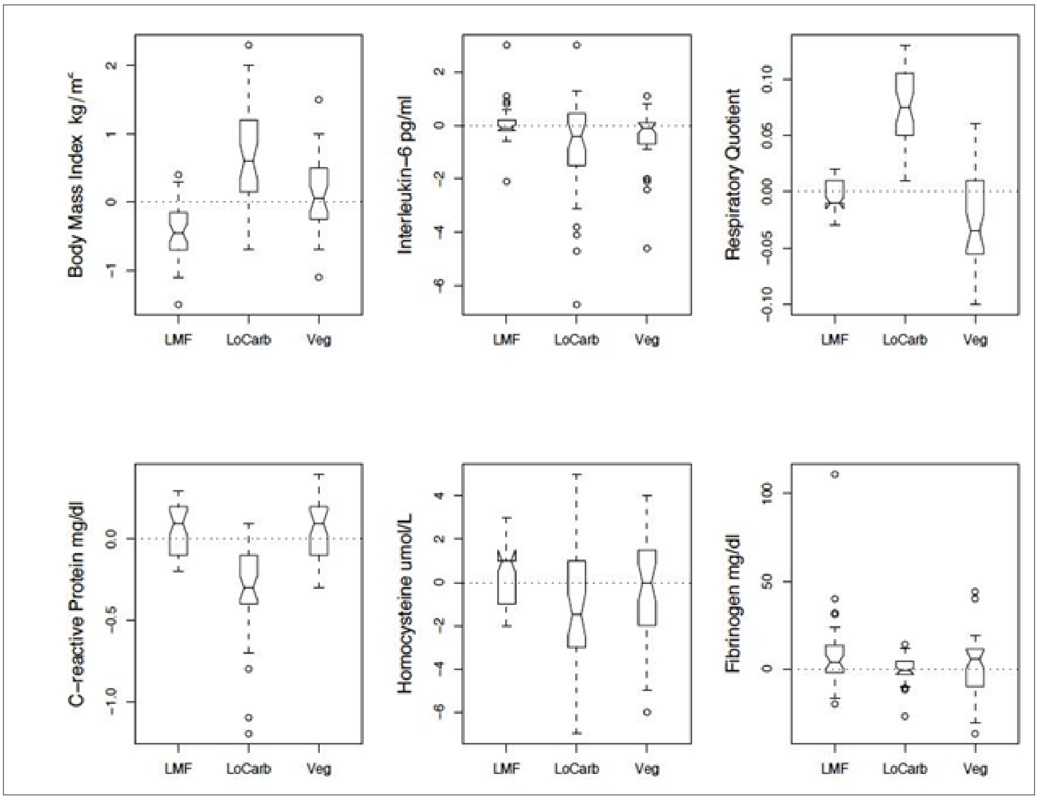

Figure 2B: Outcomes followed four (4) months post intervention.

Table 7: 1500-1600 kcal/day low carbohydrate diet with vitamin supplement (Mean [SD]).

	Baseline	6 Weeks	3 Months	6 Months	1 Year	4 Months After
II	0.066[0.061]	NA	NA	NA	0.116[0.094]	NA
RQ	0.90[0.02]	0.87[0.02]	0.86[0.02]	0.85[0.02]	0.83[0.02]	0.89[0.02]
Pounds	285.8[48.9]	269.0[51.7]	259.1[52.5]	248.3[47.4]	244.3[47.7]	249.0[38.9]
Kg	129.9[22.1]	122.4[23.4]	117.7[23.9]	112.9[21.5]	111.1[21.8]	113.3[17.7]
BMI	43.6[6.7]	42.3[8.2]	39.6[7.4]	38.1[6.8]	37.3[6.8]	38.1[5.4]
TC	286.7[45.3]	277.8[42.1]	276.2[39.3]	288.7[43.6]	315.1[38.1]	315.7[37.5]
LDL	203.8[45.0]	197.5[42.4]	195.8[39.7]	206.1[43.2]	228.3[38.5]	229.1[36.6]
HDL	41.4[7.2]	40.6[5.3]	40.8[4.1]	40.8[3.4]	40.1[3.2]	41.6[2.7]
TC/HDL	7.2[2.2]	7.0[1.9]	6.9[1.6]	7.2[1.5]	7.9[1.4]	7.7[1.3]
VLDL	41.7[9.0]	39.6[8.2]	39.5[7.3]	41.8[6.7]	46.6[8.3]	44.8[7.0]
TG	208.4[45.1]	198.0[40.8]	197.6[36.5]	209.2[33.6]	232.9[41.7]	224.2[35.1]
TG/HDL	5.2[1.3]	5.0[1.3]	4.9[1.1]	5.2[1.1]	5.9[1.2]	5.4[1.1]
CRP	0.96[0.97]	0.79[0.48]	0.68[0.23]	0.74[0.15]	0.62[0.21]	0.42[0.21]
IL-6	5.28[2.86]	5.67[2.67]	6.67[3.40]	7.54[3.20]	7.23[2.62]	6.42[2.45]
Hcy	15.1[8.0]	15.4[6.8]	14.8[6.5]	14.4[5.6]	15.1[4.6]	14.5[4.5]
Fib	332.6[67.3]	340.8[65.0]	351.9[61.5]	360.6[50.2]	372.4[47.5]	373.5[48.1]
Lp (a)	20.2[12.0]	21.9[11.0]	22.9[10.7]	24.0[11.0]	25.5[11.1]	25.8[10.5]

This form of display reveals the data distribution. Though the scale of the display is determined by outliers, the notch intervals retain their relationships and as medians are not influenced by the outliers. Figure 2B displays plots only for those risk factors, which showed significant (F-statistic, P<.05) post-diet changes at the four-month follow-up. Variability increased post-diet and the medians dependent graphic seems a more meaningful representation than the means dependent F-statistic. The cumulative effect of the three diets over the entire 16-month study on the indices is shown in Table 8. The mean weight loss during the 12-month dietary period was 29.25 pounds (13.3 kg) and did not differ by diet. The BMI was similarly reduced without differences between diets (0.75 < P < 1.00). These changes persisted during the 4-month post-diet period. That is, after a year of dieting participants tended to maintain the weight levels achieved. There was significant reduction in homocysteine with the LMF diet and Vegan diet (P<.001) and significant increase with the LoCarb diet (P<.001). Fibrinogen was unaffected by the LMF or Vegan diets but was significantly increased (P<.001) on the LoCarb diet. A significant improvement (reduction) in lipoprotein(a) [Lp(a)], was seen among individuals following the LMF diet (P<.001) and to a lesser extent (p<0.01) the Vegan diet. A significant increase (P<.001) in Lp(a) was seen in the group following the LoCarb regimen. Each of the diets showed an initial improvement in lipids.

Table 8: Analyses of deviance of long-term changes induced by three diets.

Assessment				
Diet Coefficients	Estimate	Std. Error	t value	Pr(>|t|)
Body Mass Index				
(Intercept-LMF)	-5.0675	0.1617	-31.347	< 2e-16*****
LoCarb	1.2525	0.2286	5.479	2.49e-07*****
Vegan	0.5475	0.2286	2.395	0.0182
Respiratory Quotient				
(Intercept-LMF)	0.020000	0.007187	2.783	0.00631
LoCarb	0.011500	0.010164	1.131	0.26024
Vegan	0.050500	0.010164	4.969	2.39e-06 ****
Vitamin	0.021000	0.010164	2.066	0.04108
LoCarb:Vitamin	-0.060500	0.014374	-4.209	5.14e-05 ***
Vegan:Vitamin	-0.059500	0.014374	-4.139	6.70e-05 ***
Total Cholesterol (TC)				
(Intercept-LMF)	-68.075	5.917	-11.506	< 2e-16*****
LoCarb	79.050	8.367	9.447	4.37e-16 *****
Vegan	30.225	8.367	3.612	0.000448 **
Low Density Lipoprotein (LDL)				
(Intercept-LMF)	-60.075	5.624	-10.682	< 2e-16*****
LoCarb	69.425	7.953	8.729	2.10e-14 *****
Vegan	32.000	7.953	4.024	0.000102 ***
High Density Lipoprotein (HDL)				
(Intercept-LMF)	7.0000	0.8762	7.989	1.06e-12 *****
LoCarb	-7.4000	1.2392	-5.972	2.58e-08 *****
Vegan	-2.1000	1.2392	-1.695	0.0928
TC/HDL				
(Intercept-LMF)	-2.4557	0.1805	-13.61	< 2e-16*****
LoCarb	2.6935	0.2552	10.55	< 2e-16****
Vegan	1.0310	0.2552	4.04	9.6e-05***
Very Low Density Lipoprotein (VLDL)				
(Intercept-LMF)	-14.760	1.216	-12.141	< 2e-16 *****
LoCarb	16.665	1.719	9.693	< 2e-16 *****
Vegan	0.040	1.719	0.023	0.981
Triglycerides (TG)				

(Intercept-LMF)	-73.800	6.079	-12.141	<2e-16*****
LoCarb	83.325	8.597	9.693	<2e-16*****
Vegan	0.200	8.597	0.023	0.981
Insulin Resistance (TG/HDL)				
(Intercept-LMF)	-2.2830	0.1713	-13.330	<2e-16*****
LoCarb	2.4635	0.2422	10.171	<2e-16*****
Vegan	0.2513	0.2422	1.037	0.302
C-reactive Protein				
(Intercept-LMF)	-0.5150	0.3983	-1.293	0.1986
LoCarb	0.2450	0.5633	0.435	0.6644
Vegan	-0.0300	0.5633	-0.053	0.9576
Vitamin	0.1300	0.5633	0.231	0.8179
LoCarb: Vitamin	-0.4000	0.7966	-0.502	0.6165
Vegan: Vitamin	-1.5200	0.7966	-1.908	0.0589
Interleukin-6				
(Intercept-LMF)	-2.3875	0.5372	-4.444	2.02e-05 ***
LoCarb	4.4100	0.7598	5.804	5.64e-08 *****
Vegan	-0.4450	0.7598	-0.586	0.559
Homocysteine				
(Intercept-LMF)	-6.100	1.080	-5.648	1.16e-07 *****
LoCarb	7.825	1.527	5.123	1.20e-06 ****
Vegan	1.450	1.527	0.949	0.344
Fibrinogen				
(Intercept-LMF)	0.875	8.938	0.098	0.92218
LoCarb	33.600	12.640	2.658	0.00895
Vegan	-3.650	12.640	-0.289	0.77327
Lipoprotein(a)				
(Intercept)	-10.000	1.006	-9.944	<2e-16*****
LoCarb	15.000	1.422	10.547	<2e-16*****
Vegan	4.775	1.422	3.357	0.00106*

Note: Significance codes: p<: `*****’ 0.000001 `****’ 0.00001 `***’ 0.0001 `**.’ 0.001 `*’ 0.01

However, the results varied after the first few months with those on the Vegan and LMF diets showing improvements (P<.001) in their lipid levels and their insulin resistance (P<.001) as measured by TG/HDL. In contrast, the initial improvements in lipids on the LoCarb diet were short-lived, instead showing significant (P<.001) subsequent gain in risk. By the end of 12 months of dieting TG/HDL had returned to pre-diet levels (P<.001), an effect which persisted 4 months post-diet. CRP changes for each diet were not statistically significant but different trends led to a statistically significant (P < .05) but clinically minimal (R2 = .06) overall CRP effect size. In contrast, interleukin-6 (IL-6), which is a more specific marker of vascular inflammation, was significantly reduced (P<.001) on both the LMF and Vegan diets but increased (P<.001) on the LoCarb diet.

Discussion

“In our experiment, we found that the low carbohydrate, high saturated fat diet worsened all cardiac risk factors and coronary blood flow as determined by myocardial perfusion imaging, despite a mean weight loss of 29 pounds at 1 year. This is in direct contrast to the low/moderate fat and vegan diets which improved all cardiac risk factors and coronary blood flow in association with similar weight loss, demonstrating that not all dietary weight loss strategies improve cardiac risk factors” [16]. That 100% of participants continued their respective diet plans through a full year of dieting contrasts sharply with much of diet research experience with drop outs and with common experience with difficulties of dieting and remaining on diets. This success can be attributed to attention to well-established psychological principles of habit acquisition and extinction and of behavior modification through Bandura [17] counseling. The treatment goal was to change eating habits. Thus the diet must be the diet, or close to the diet, which is to become habitual. If the diet conditioning conditions are not those of the normal life pattern, the original habits are likely to be reinstated when the dieter returns to normal conditions as was seen with the LoCarb and to a lesser extent Vegan group.

Some studies have suggested that LoCarb diets result in greater weight loss than other diets. In both the work of Westman [18] and Samaha [3], the studies showed greater caloric restriction among individuals on the LoCarb diet, than those following other diets. Both studies revealed a greater weight loss with greater caloric restriction, regardless of the diet content. In support of this, Foster [2] and Fleming [6] have both shown similar findings with weight loss contingent upon caloric intake, while Sacks [19] had demonstrated that this weight loss is independent of macronutrients. In this study, compared with other diets, those on the LoCarb diet showed a significantly greater (P<.001) initial reduction in weight and BMI. This difference in initial weight loss and reduction in BMI disappeared throughout the duration of the study, demonstrating no cumulative long-term differences in weight loss among any of the isocaloric diets. The initial reduction follows the expected trend due to the combined effect of fat catabolism and resulting water loss. Alternatively it could represent a steeper response to conditioning due to taste preferences for higher fat foods resulting in reaching asymptotic levels sooner than those following the other diet plans.

A major assumption has been that losing weight automatically lowers ones risk of coronary artery disease. Recent research has suggested that individuals on LoCarb diets may initially lower their cholesterol levels. This is important since cholesterol, particularly LDL cholesterol is considered important in causing many of the initial problems ultimately leading to vascular inflammation, the final common pathway of coronary artery disease. Most of this previous research has shown improvement in lipid levels during the first few months on the diet, with little or no long-term data to substantiate residual effects. These studies have had significant dropout rates and some individuals have been removed from the studies due to increases in cholesterol levels. Given a 40 to 60 percent dropout rates in such studies, it is impossible to determine either a weight or cardiovascular benefit. This effect of subject drop out is problematic because it introduces bias into the results and as such, it is impossible to statistically compare the results of such studies with one in which subject participation is maintained. Long-term effects of a diet cannot be based upon short-term findings, or the removal of individuals who had adverse lipid effects.

Failure to document a significant coronary artery stenosis does not exclude the existence of inflammatory coronary artery disease [15,20-23]. Ischemia can be physiologically determined by reductions in regional [15] coronary blood flow in comparison to regions with normal vasodilatory capacities, which can increase coronary blood flow to meet the physiologic and metabolic demands of the heart. As previously [15,20] described these regions of reduced blood flow can be quantified to determine both the extent and reduction in coronary blood flow throughout the heart, compared to normal blood flow. This cumulative reduction in maximal coronary blood flow is the ischemic index (II) and can be used to detect minor changes in coronary blood flow that can otherwise go clinically undetected unless a "vulnerable inflammatory plaque" ruptures [24,25]. Here, the long-term effect of a LMF diet shows significant improvement in coronary blood flow and in regression of inflammatory coronary artery disease (Figures 2A and 2B). A reduction in coronary blood flow and an increase in inflammatory coronary artery disease indices are evident for a LoCarb diet.

Conclusion

The results support the proposition that public health policies will undoubtedly play a major role in implementing major changes in societal behaviors, which can subsequently reduce atherosclerosis and other inflammatory health problems as they have with smoking cessation and changes in air quality. We now know that these food choices and their impact are at least partially precipitated by the inflammatory effect of our diets given our inability to convert Neu5Ac to Neu5Gc and our bodies immune response to the Neu5Gc present in animal protein [26-34]. This study also emphasizes the importance of answering the question at hand; viz. if we are looking for inflammatory coronary artery disease, we must look for it with a truly quantitative test, which measures [24,25,35] coronary artery disease.

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