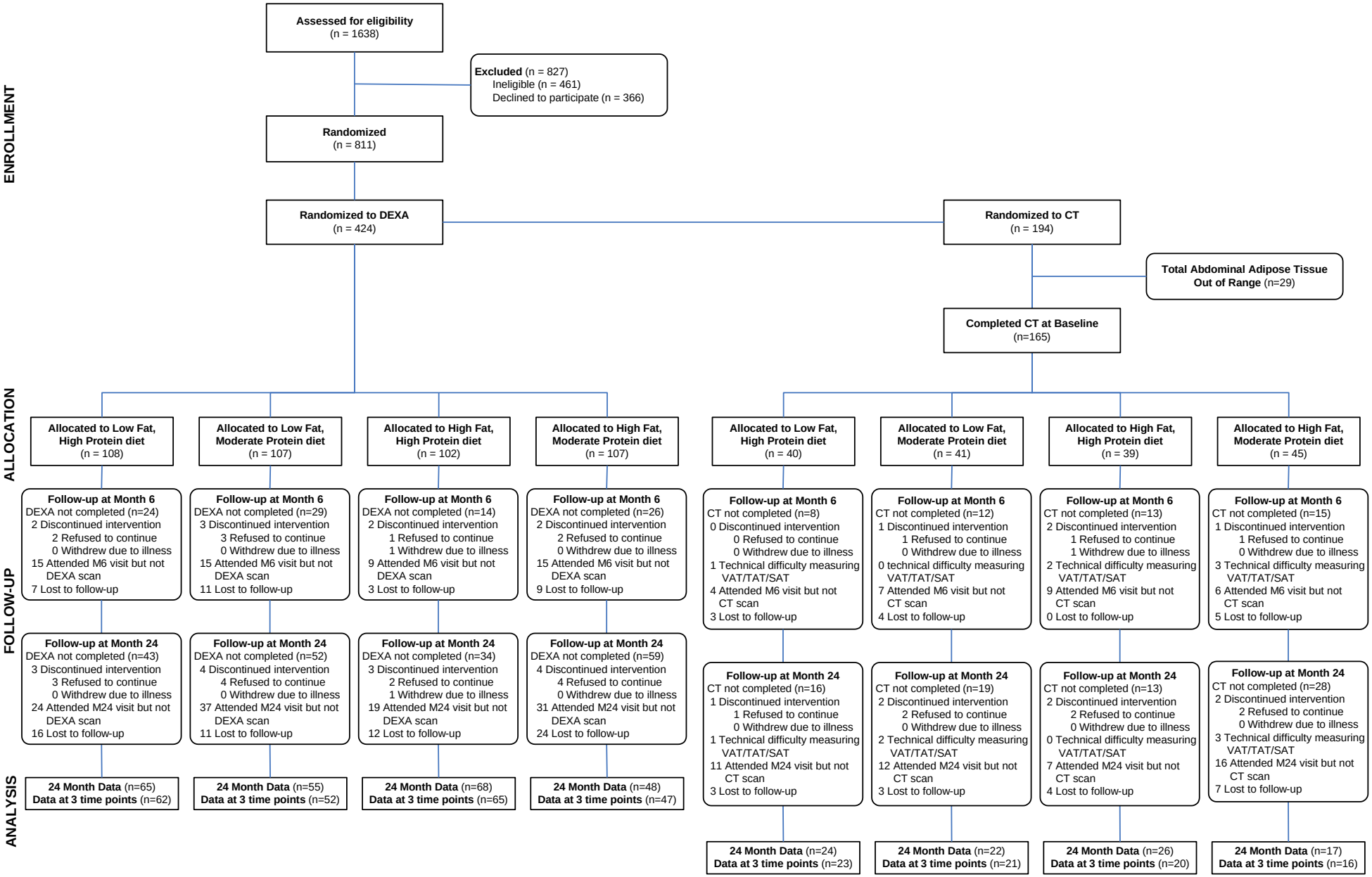
ENROLLMENT
Assessed for eligibility (n = 1638)
Excluded (n = 827)
Ineligible (n = 461)
Declined to participate (n = 366)
Randomized (n = 811)
Randomized to DEXA (n = 424)
Randomized to CT (n = 194)
Total Abdominal Adipose Tissue Out of Range (n=29)
Completed CT at Baseline (n=165)
ALLOCATION
Allocated to Low Fat, High Protein diet (n = 108)
Allocated to Low Fat, Moderate Protein diet (n = 107)
Allocated to High Fat, High Protein diet (n = 102)
Allocated to High Fat, Moderate Protein diet (n = 107)
Allocated to Low Fat, High Protein diet (n = 40)
Allocated to Low Fat, Moderate Protein diet (n = 41)
Allocated to High Fat, High Protein diet (n = 39)
Allocated to High Fat, Moderate Protein diet (n = 45)
FOLLOW-UP
Follow-up at Month 6
DEXA not completed (n=24)
2 Discontinued intervention
2 Refused to continue
0 Withdrew due to illness
15 Attended M6 visit but not DEXA scan
7 Lost to follow-up
Follow-up at Month 6
DEXA not completed (n=29)
3 Discontinued intervention
3 Refused to continue
0 Withdrew due to illness
15 Attended M6 visit but not DEXA scan
11 Lost to follow-up
Follow-up at Month 6
DEXA not completed (n=14)
2 Discontinued intervention
1 Refused to continue
1 Withdrew due to illness
9 Attended M6 visit but not DEXA scan
3 Lost to follow-up
Follow-up at Month 6
DEXA not completed (n=26)
2 Discontinued intervention
2 Refused to continue
0 Withdrew due to illness
15 Attended M6 visit but not DEXA scan
9 Lost to follow-up
Follow-up at Month 6
CT not completed (n=8)
0 Discontinued intervention
0 Refused to continue
0 Withdrew due to illness
1 Technical difficulty measuring VAT/TAT/SAT
4 Attended M6 visit but not CT scan
3 Lost to follow-up
Follow-up at Month 6
CT not completed (n=12)
1 Discontinued intervention
1 Refused to continue
0 Withdrew due to illness
0 technical difficulty measuring VAT/TAT/SAT
7 Attended M6 visit but not CT scan
4 Lost to follow-up
Follow-up at Month 6
CT not completed (n=13)
2 Discontinued intervention
1 Refused to continue
1 Withdrew due to illness
2 Technical difficulty measuring VAT/TAT/SAT
9 Attended M6 visit but not CT scan
0 Lost to follow-up
Follow-up at Month 6
CT not completed (n=15)
1 Discontinued intervention
1 Refused to continue
0 Withdrew due to illness
3 Technical difficulty measuring VAT/TAT/SAT
6 Attended M6 visit but not CT scan
5 Lost to follow-up
Follow-up at Month 24
DEXA not completed (n=43)
3 Discontinued intervention
3 Refused to continue
0 Withdrew due to illness
24 Attended M24 visit but not DEXA scan
16 Lost to follow-up
Follow-up at Month 24
DEXA not completed (n=52)
4 Discontinued intervention
4 Refused to continue
0 Withdrew due to illness
37 Attended M24 visit but not DEXA scan
11 Lost to follow-up
Follow-up at Month 24
DEXA not completed (n=34)
3 Discontinued intervention
2 Refused to continue
1 Withdrew due to illness
19 Attended M24 visit but not DEXA scan
12 Lost to follow-up
Follow-up at Month 24
DEXA not completed (n=59)
4 Discontinued intervention
4 Refused to continue
0 Withdrew due to illness
31 Attended M24 visit but not DEXA scan
24 Lost to follow-up
Follow-up at Month 24
CT not completed (n=16)
1 Discontinued intervention
1 Refused to continue
0 Withdrew due to illness
1 Technical difficulty measuring VAT/TAT/SAT
11 Attended M24 visit but not CT scan
3 Lost to follow-up
Follow-up at Month 24
CT not completed (n=19)
2 Discontinued intervention
2 Refused to continue
0 Withdrew due to illness
2 Technical difficulty measuring VAT/TAT/SAT
12 Attended M24 visit but not CT scan
3 Lost to follow-up
Follow-up at Month 24
CT not completed (n=13)
2 Discontinued intervention
2 Refused to continue
0 Withdrew due to illness
0 Technical difficulty measuring VAT/TAT/SAT
7 Attended M24 visit but not CT scan
4 Lost to follow-up
Follow-up at Month 24
CT not completed (n=28)
2 Discontinued intervention
2 Refused to continue
0 Withdrew due to illness
3 Technical difficulty measuring VAT/TAT/SAT
16 Attended M24 visit but not CT scan
7 Lost to follow-up
ANALYSIS
24 Month Data (n=65)
Data at 3 time points (n=62)
24 Month Data (n=55)
Data at 3 time points (n=52)
24 Month Data (n=68)
Data at 3 time points (n=65)
24 Month Data (n=48)
Data at 3 time points (n=47)
24 Month Data (n=24)
Data at 3 time points (n=23)
24 Month Data (n=22)
Data at 3 time points (n=21)
24 Month Data (n=26)
Data at 3 time points (n=20)
24 Month Data (n=17)
Data at 3 time points (n=16)

Figure S1

Figure S1. ***Participant flow for those randomly selected to receive dual x-ray absorptiometry scans (n=424) and those selected to receive computed tomography scan (n=194) at baseline.***

A total of 331 participants (78%; 153 men and 178 women) provided DXA measurements at both baseline and 6 months, and 236 (58%; 107 men and 129 women) at 2 years. One hundred and seventeen participants (71%; 58 men and 59 women) repeated complete CT measurements at 6 months, and 89 (54%; 39 men and 50 women) at 2 years. A total of 226 participants (53%; 122 women and 104 men) provided DXA and 80 (41%; 43 women and 37 men) provided complete CT on all three measurement occasions.

ON-LINE SUPPLEMENT 1: ALLOMETRIC MODELING

Hallgreen and Hall (1) proposed that changes in visceral fat and fat mass during weight loss were related according to the equation:

$$\Delta\text{VAT}/\Delta\text{FM} = k \ \frac{VAT(kg)}{FM(kg)} \ ,$$

where *k* is a dimensionless constant, when both visceral fat and fat mass change in the same direction. They found that across all interventions, and in both genders, *k*= 1.3±0.1. To test if *k* was a good fit to our data, the primary outcome variable was the coefficient (*k*) of the ratio of change in visceral fat to the change in total fat from baseline to 6 months or 2 years ($\Delta\text{VAT}\ (\text{kg})/\Delta\text{FM}\ (\text{kg})$; dependent variable) regressed on baseline visceral fat to total fat ratio (visceral fat /fat mass; independent variable). We have previously found the standard deviation of repeated VAT measurements to be ≈0.2 kg, and with k=1.3, a 3 kg change in fat mass would be necessary to overcome this imprecision. Given that 60-70% of body weight change is fat mass, this translates to a 5 kg total weight change. For these analyses, we therefore included any participant who provided a measurement of both fat mass and visceral fat at each time point, and lost 5 kg body weight, with losses of both visceral fat and body fat (n=101 at 6 months; n=58 at 2 years). Regression diagnostics indicated the presence of nine influential outliers at 6 months and three at 2 years (Cook's $\text{distance}_{\text{critical}}$>0.0396). The overall r^2 did increase when these outliers were removed, however the estimates of *k* and their standard errors did not change substantially. We therefore included these 12 data points to provide the most robust estimate of *k*. To determine *k*, we fit the regression model:

$$\Delta\text{VAT}\ (\text{kg})/\Delta\text{FM}\ (\text{kg})_{\ 0\text{ to }6\text{ months or }2\text{ years}} = \alpha + k \ \times \ \frac{VAT(kg)}{FM(kg)},$$

using simple linear regression with a no-intercept model (α=0), since a positive intercept would imply visceral fat could decrease even if initial visceral fat were 0. To test the difference in *k* across diets or between genders, we created an indicator variable, *i*, for macronutrient level or gender (where *i*=1 for "high" and *i*=0 for "low/average"; or 1 for "male" and 0 for "female"), and the interaction term, $i \times \frac{VAT(kg)}{FM(kg)}$. We then entered terms for *i*, $\frac{VAT(kg)}{FM(kg)}$, and their interaction into the regression model, and tested the null hypothesis that $k_{\text{high}} = k_{\text{low/average}}$ or $k_{\text{male}} = k_{\text{female}}$ (i.e. the β-coefficient for the interaction term = 0). We present the overall *k* across all diets, and pre-planned contrasts as above to facilitate comparisons with previous literature on this topic.

1. Hallgreen CE, Hall KD. Allometric relationship between changes of visceral fat and total fat mass. Int J Obes (Lond) 2008;32:845-52.

ON-LINE SUPPLEMENT 2: COMPLETERS-ONLY ANALYSES

DXA Measurement	**Completers at 6 months (n=331)**			**Completers at 6 months and 2 years (n=226)**		
	High Protein	**Average Protein**	**P**	**High Protein**	**Average Protein**	**P**
Weight (kg)	-7.4±0.4	-7.5±0.4	0.87	-7.9±0.5	-8.8±0.5	0.22
Fat mass (kg)	-5.3±0.3	-5.0±0.3	0.49	-5.7±0.4	-5.9±0.4	0.70
Lean Mass (kg)	-2.1±0.2	-2.5±0.2	0.06	-2.2±0.2	-2.9±0.2	<0.01
CT Measurement	**Completers at 6 months (n=117)**			**Completers at 6 months and 2 years (n=80)**		
	High Protein	**Average Protein**	**P**	**High Protein**	**Average Protein**	**P**
Total Abdominal Fat (kg)	-3.1±0.3	-3.6±0.19	0.19	-3.4±0.4	-4.0±0.4	0.22
Visceral Abdominal Fat (kg)	-1.2±0.2	-1.3±0.2	0.92	-1.4±0.2	-1.5±0.2	0.83
Subcutaneous Abdominal Fat (kg)	-1.8±0.2	-2.3±0.2	0.04	-2.0±0.3	-2.6±0.3	0.08
	Completers at 6 months (n=147)			**Completers at 6 months and 2 years (n=106)**		
	High Protein	**Average Protein**	**P**	**High Protein**	**Average Protein**	**P**
Hepatic Density (HU)	4.47±0.64	4.23±0.67	0.79	5.58±0.78	5.12±0.83	0.68

Supplemental Table 1. Effect of dietary protein level on changes in body composition at 6 months in those who completed all measurements at 6 months, and in those who would go on to complete all 3 visits for study outcomes. Data expressed as mean ± SEM change using GLM ANOVA models including main effect of diet, with baseline, age, gender and site as covariates. P-values assess the statistical significance of the difference between the change on High (25%) and Average (15%) Protein diet assignment. Increases in hepatic density reflect decreases in hepatic fat content.

DXA Measurement	**Completers at 6 months (n=331)**			**Completers at 6 months and 2 years (n=226)**		
	High Fat	**Low Fat**	**P**	**High Fat**	**Low Fat**	**P**
Weight (kg)	-7.1±0.4	-7.7±0.4	0.35	-8.1±0.5	-8.5±0.5	0.61
Fat mass (kg)	-4.9±0.3	-5.3±0.3	0.32	-5.6±0.4	-5.9±0.4	0.62
Lean Mass (kg)	-2.2±0.2	-2.3±0.2	0.58	-2.5±0.2	-2.6±0.2	0.69
CT Measurement	**Completers at 6 months (n=117)**			**Completers at 6 months and 2 years (n=80)**		
	High Fat	**Low Fat**	**P**	**High Fat**	**Low Fat**	**P**
Total Abdominal Fat (kg)	-3.1±0.3	-3.6±0.3	0.27	-3.6±0.4	-3.8±0.4	0.70
Visceral Abdominal Fat (kg)	-1.1±0.2	-1.4±0.2	0.18	-1.3±0.2	-1.6±0.2	0.29
Subcutaneous Abdominal Fat (kg)	-2.0±0.2	-2.1±0.2	0.59	-2.3±0.3	-2.3±0.3	0.87
	Completers at 6 months (n=147)			**Completers at 6 months and 2 years (n=106)**		
	High Fat	**Low Fat**	**P**	**High Fat**	**Low Fat**	**P**
Hepatic Density (HU)	4.30±0.63	4.60±0.67	0.74	5.56±0.79	5.43±0.79	0.91

Supplemental Table 2. Effect of dietary fat level on weight and body composition change at 6 months in those who completed all measurements at 6 months, and those who would go on to complete all 3 visits for study outcomes. Data expressed as mean ± SEM change using GLM ANOVA models including main effect of diet, with baseline, age, gender and site as covariates. P-values assess the statistical significance of the difference between the change on High (40%) and Low (20%) Fat diet assignment. Increases in hepatic density reflect decreases in hepatic fat content.

DXA Measurement	**Completers at 6 months (n=166)**			**Completers at 6 months and 2 years (n=117)**		
	Highest Carb	**Lowest Carb**	**P**	**Highest Carb**	**Lowest Carb**	**P**
Weight (kg)	-7.6±0.6	-7.0±0.5	0.44	-8.6±0.7	-7.5±0.6	0.25
Fat mass (kg)	-5.1±0.4	-4.9±0.4	0.85	-5.6±0.4	-5.3±0.4	0.63
Lean Mass (kg)	-2.5±0.2	-2.1±0.2	0.09	-2.9±1.9	-2.2±0.3	0.04
CT Measurement	**Completers at 6 months (n=55)**			**Completers at 6 months and 2 years (n=41)**		
	Highest Carb	**Lowest Carb**	**P**	**Highest Carb**	**Lowest Carb**	**P**
Total Abdominal Fat (kg)	-3.5±0.4	-2.6±0.4	0.11	-3.8±0.6	-3.0±0.5	0.29
Visceral Abdominal Fat (kg)	-1.2±0.2	-0.9±0.2	0.23	-1.3±0.2	-1.1±0.2	0.32
Subcutaneous Abdominal Fat (kg)	-2.3±0.3	-1.7±0.3	0.10	-2.4±0.4	-1.9±0.4	0.32
	Completers at 6 months (n=72)			**Completers at 6 months and 2 years (n=54)**		
	Highest Carb	**Lowest Carb**	**P**	**Highest Carb**	**Lowest Carb**	**P**
Hepatic Density (HU)	3.84±0.81	3.46±0.73	0.73	4.37±0.99	4.53±0.90	0.90

Supplemental Table 3. Effect of dietary carbohydrate level on weight and body composition change at 6 months in those who completed all measurements at 6 months, and in those who would go on to complete all 3 visits for study outcomes. Data expressed as mean ± SEM change using GLM ANOVA models including main effect of diet, with baseline, age, gender and site as covariates. P-values assess the statistical significance of the difference between the change on Highest Carbohydrate (65%) and Lowest (35%) Carbohydrate diet assignment. Increases in hepatic density reflect decreases in hepatic fat content.

DXA Measurement	**Completers at 2 years (n=236)**			**Completers at 6 months and 2 years (n=226)**		
	High Protein	**Average Protein**	**P**	**High Protein**	**Average Protein**	**P**
Weight (kg)	-6.1±0.7	-6.3±0.8	0.87	-6.3±0.7	-6.4±0.8	0.91
Fat mass (kg)	-4.1±0.5	-4.0±0.5	0.90	-4.2±0.5	-4.1±0.6	0.87
Lean Mass (kg)	-2.0±0.2	-2.3±0.3	0.48	-2.1±0.2	-2.3±0.3	0.51
CT Measurement	**Completers at 2 years (n=89)**			**Completers at 6 months and 2 years (n=80)**		
	High Protein	**Average Protein**	**P**	**High Protein**	**Average Protein**	**P**
Total Abdominal Fat (kg)	-2.2±0.5	-2.9±0.5	0.33	-2.5±0.5	-3.1±0.6	0.39
Visceral Abdominal Fat (kg)	-1.0±0.2	-1.2±0.2	0.43	-1.1±0.2	-1.3±0.3	0.50
Subcutaneous Abdominal Fat (kg)	-1.3±0.3	-1.7±0.3	0.31	-1.4±0.3	-1.8±0.3	0.36
	Completers at 2 years (n=112)			**Completers at 6 months and 2 years (n=106)**		
	High Protein	**Average Protein**	**P**	**High Protein**	**Average Protein**	**P**
Hepatic Density (HU)	3.56±1.13	4.58±1.22	0.52	4.14±1.20	4.73±1.26	0.72

Supplemental Table 4. Effect of dietary protein level on weight and body composition change at 2 years in those who completed all measurements at 2 years, and in those who completed all 3 visits for study outcomes. Data expressed as mean ± SEM change using GLM ANOVA models including main effect of diet, with baseline, age, gender and site as covariates. P-values assess the statistical significance of the difference between the change on High (25%) and Average (15%) protein diet assignment. Increases in hepatic density reflect decreases in hepatic fat content.

DXA Measurement	**Completers at 2 years (n=236)**			**Completers at 6 months and 2 years (n=226)**		
	High Fat	**Low Fat**	**P**	**High Fat**	**Low Fat**	**P**
Weight (kg)	-5.8±0.7	-6.6±0.7	0.43	-6.0±0.7	-6.6±0.7	0.53
Fat mass (kg)	-3.7±0.5	-4.3±0.5	0.43	-3.9±0.5	-4.4±0.5	0.53
Lean Mass (kg)	-2.0±0.3	-2.3±0.3	0.52	-2.1±0.3	-2.3±0.3	0.61
CT Measurement	**Completers at 2 years (n=89)**			**Completers at 6 months and 2 years (n=80)**		
	High Fat	**Low Fat**	**P**	**High Fat**	**Low Fat**	**P**
Total Abdominal Fat (kg)	-2.4±0.5	-2.7±0.5	0.70	-2.5±0.5	-3.1±0.6	0.39
Visceral Abdominal Fat (kg)	-0.9±0.2	-1.3±0.2	0.24	-1.0±0.2	-1.4±0.2	0.14
Subcutaneous Abdominal Fat (kg)	-1.5±0.3	-1.4±0.3	0.83	-1.5±0.3	-1.6±0.3	0.75
	Completers at 2 years (n=112)			**Completers at 6 months and 2 years (n=106)**		
	High Fat	**Low Fat**	**P**	**High Fat**	**Low Fat**	**P**
Hepatic Density (HU)	3.54±1.15	4.83±1.18	0.43	4.13±1.21	4.95±1.23	0.62

Supplemental Table 5. Effect of dietary fat level on weight and body composition change at 2 years in those who completed all measurements at 2 years, and in those who completed all 3 study visits. Data expressed as mean ± SEM change using GLM ANOVA models including main effect of diet, with baseline, age, gender and site as covariates. P-values assess the statistical significance of the difference between the change on High (40%) and Low (20%) Fat diet assignment. Increases in hepatic density reflect decreases in hepatic fat content.

DXA Measurement	**Completers at 2 years (n=166)**			**Completers at 6 months and 2 years (n=117)**		
	Highest Carb	**Lowest Carb**	**P**	**Highest Carb**	**Lowest Carb**	**P**
Weight (kg)	-5.7±1.0	-5.0±0.9	0.68	-5.5±0.9	-5.2±1.0	0.79
Fat mass (kg)	-3.4±0.6	-3.2±0.7	0.81	-3.4±0.7	-3.3±0.6	0.94
Lean Mass (kg)	-2.1±0.4	-1.8±0.3	0.51	-2.1±0.3	-1.8±0.4	0.58
CT Measurement	**Completers at 2 years (n=48)**			**Completers at 6 months and 2 years (n=41)**		
	Highest Carb	**Lowest Carb**	**P**	**Highest Carb**	**Lowest Carb**	**P**
Total Abdominal Fat (kg)	-2.5±0.6	-1.8±0.7	0.42	-2.8±0.8	-1.7±0.7	0.27
Visceral Abdominal Fat (kg)	-1.1±0.2	-0.6±0.2	0.22	-1.2±0.3	-0.6±0.3	0.13
Subcutaneous Abdominal Fat (kg)	-1.4±0.5	-1.1±0.4	0.62	-1.6±0.5	-1.1±0.5	0.43
	Completers at 2 years (n=61)			**Completers at 6 months and 2 years (n=54)**		
	Highest Carb	**Lowest Carb**	**P**	**Highest Carb**	**Lowest Carb**	**P**
Hepatic Density (HU)	1.69±1.53	0.71±1.36	0.63	1.49±1.65	1.35±1.50	0.95

Supplemental Table 6. Effect of dietary carbohydrate level on weight and body composition change at 2 years in those who completed all measurements at 6 months, and in those who completed all 3 study visits. Data expressed as mean ± SEM change using GLM ANOVA models including main effect of diet, with baseline, age, gender and site as covariates. P-values assess the statistical significance of the difference between the change on Highest Carbohydrate (65%) and Lowest (35%) Carbohydrate diet assignment. Increases in hepatic density reflect decreases in hepatic fat content.