Supplementary table 1a
Percentage weight gain relative to starting weight at week 4 of male C57BL/6NTac mice exposed to HFD for varying lengths of time. n=30 per group

	Units	Control Diet	2 weeks HFD	4 weeks HFD	6 weeks HFD	12 weeks HFD
		Mean ± SEM	Mean ± SEM	Mean ± SEM	Mean ± SEM	Mean ± SEM
Week 5	%	19.9 ± 1.7	23.3 ± 2.2	21.8 ± 2.0	21.1 ± 1.2	28.8 ± 1.7
Week 6	%	29.3 ± 2.0	33.3 ± 2.9	31.1 ± 2.3	29.7 ± 1.3	44.6 ± 2.6
Week 7	%	37.5 ± 1.9	42.9 ± 3.6	40.8 ± 2.6	39.7 ± 1.3	64.3 ± 3.1
Week 8	%	46.0 ± 2.1	51.2 ± 3.8	47.9 ± 2.6	48.1 ± 1.6	81.4 ± 3.5
Week 9	%	54.6 ± 2.2	57.0 ± 3.8	55.4 ± 2.6	56.1 ± 1.9	97.8 ± 3.6
Week 10	%	62.3 ± 2.1	64.1 ± 4.2	62.5 ± 2.7	63.8 ± 2.3	108.7 ± 4.1
Week 11	%	68.6 ± 2.4	69.6 ± 4.4	68.5 ± 2.6	91.7 ± 2.6	121.1 ± 3.5
Week 12	%	74.8 ± 2.7	76.6 ± 4.4	71.6 ± 3.0	106.9 ± 2.7	126.9 ± 4.3
Week 13	%	81.3 ± 2.8	82.0 ± 4.5	100.0 ± 3.0	119.7 ± 3.0	137.1 ± 4.3
Week 14	%	87.8 ± 3.0	86.4 ± 4.6	114.3 ± 3.7	127.5 ± 3.0	141.7 ± 4.6
Week 15	%	93.3 ± 3.0	110.3 ± 5.4	125.5 ± 4.4	133.6 ± 3.2	146.3 ± 4.7
Week 16	%	99.5 ± 3.4	124.2 ± 6.1	135.7 ± 5.2	140.1 ± 3.0	150.1 ± 4.7

Supplementary table 1b
Statistical analysis of percentage weight gain relative to starting weight at week 4 of male C57BL/6NTac mice exposed to HFD for varying lengths of time. n=30 per group. Where p<0.05, an effect size (Cohen's d) has been calculated.

Week 5

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.624		
Control	4 weeks	0.811		
Control	6 weeks	1.000		
Control	12 weeks	0.002	-0.99	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	1.000		
2 weeks	6 weeks	0.509		
2 weeks	12 weeks	0.589		
4 weeks	6 weeks	0.700		
4 weeks	12 weeks	0.205		
6 weeks	12 weeks	0.000	-1.01	

Week 6

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.704		
Control	4 weeks	0.749		
Control	6 weeks	1.000		
Control	12 weeks	0.000	-1.34	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	1.000		
2 weeks	6 weeks	0.507		
2 weeks	12 weeks	0.068		
4 weeks	6 weeks	0.482		
4 weeks	12 weeks	0.009	-1.07	
6 weeks	12 weeks	0.000	-1.45	

Week 7

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.627		
Control	4 weeks	0.416		
Control	6 weeks	1.000		
Control	12 weeks	0.000	-2.03	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	1.000		
2 weeks	6 weeks	0.791		
2 weeks	12 weeks	0.000	-1.23	
4 weeks	6 weeks	0.589		
4 weeks	12 weeks	0.000	-1.59	
6 weeks	12 weeks	0.000	-2.10	

Week 8

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.816		
Control	4 weeks	0.864		
Control	6 weeks	1.000		
Control	12 weeks	0.000	-2.38	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	1.000		
2 weeks	6 weeks	0.893		
2 weeks	12 weeks	0.000	-1.58	
4 weeks	6 weeks	0.936		
4 weeks	12 weeks	0.000	-2.09	
6 weeks	12 weeks	0.000	-2.45	

Week 9

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.993		
Control	4 weeks	0.963		
Control	6 weeks	1.000		
Control	12 weeks	0.000	-2.81	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	1.000		
2 weeks	6 weeks	0.997		
2 weeks	12 weeks	0.000	-2.09	
4 weeks	6 weeks	0.977		
4 weeks	12 weeks	0.000	-2.62	
6 weeks	12 weeks	0.000	-2.86	

Week 10

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.996		
Control	4 weeks	0.951		
Control	6 weeks	1.000		
Control	12 weeks	0.000	-2.82	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	1.000		
2 weeks	6 weeks	1.000		
2 weeks	12 weeks	0.000	-2.07	
4 weeks	6 weeks	0.996		
4 weeks	12 weeks	0.000	-2.61	
6 weeks	12 weeks	0.000	-2.67	

Week 11

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	1.000		
Control	4 weeks	0.959		
Control	6 weeks	0.000	-1.87	
Control	12 weeks	0.000	-3.59	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	1.000		
2 weeks	6 weeks	0.008	-1.27	
2 weeks	12 weeks	0.000	-2.62	
4 weeks	6 weeks	0.000	-1.81	
4 weeks	12 weeks	0.000	-3.48	
6 weeks	12 weeks	0.000	-1.94	

Week 12

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	1.000		
Control	4 weeks	0.847		
Control	6 weeks	0.000	-2.39	
Control	12 weeks	0.000	-2.83	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	1.000		
2 weeks	6 weeks	0.000	-1.71	
2 weeks	12 weeks	0.000	-2.22	
4 weeks	6 weeks	0.000	-2.61	
4 weeks	12 weeks	0.000	-3.00	
6 weeks	12 weeks	0.000	-1.08	

Week 13

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	1.000		
Control	4 weeks	0.000	-1.30	
Control	6 weeks	0.000	-2.66	
Control	12 weeks	0.000	-2.96	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	0.007	-0.96	
2 weeks	6 weeks	0.000	-2.01	
2 weeks	12 weeks	0.000	-2.38	
4 weeks	6 weeks	0.018	-1.32	
4 weeks	12 weeks	0.000	-1.92	
6 weeks	12 weeks	0.001	-0.90	

Week 14

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	1.000		
Control	4 weeks	0.000	-1.62	
Control	6 weeks	0.000	-2.67	
Control	12 weeks	0.000	-2.68	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	0.000	-1.35	
2 weeks	6 weeks	0.000	-2.16	
2 weeks	12 weeks	0.000	-2.27	
4 weeks	6 weeks	0.628		
4 weeks	12 weeks	0.000	-1.26	
6 weeks	12 weeks	0.018	-0.71	

Week 15

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.017	-0.81	
Control	4 weeks	0.000	-1.77	
Control	6 weeks	0.000	-2.63	
Control	12 weeks	0.000	-2.63	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	0.292		
2 weeks	6 weeks	0.086		
2 weeks	12 weeks	0.000	-1.37	
4 weeks	6 weeks	1.000		
4 weeks	12 weeks	0.045	-0.88	
6 weeks	12 weeks	0.052		

Week 16

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.004	-1.04	
Control	4 weeks	0.000	-1.70	
Control	6 weeks	0.000	-2.53	
Control	12 weeks	0.000	-2.36	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	0.747		
2 weeks	6 weeks	0.750		
2 weeks	12 weeks	0.030	-0.91	
4 weeks	6 weeks	1.000		
4 weeks	12 weeks	0.606		
6 weeks	12 weeks	0.182		

Supplementary table 2a
DEXA (dual energy X-ray absorptiometry) results for 16 week old male C57BL/6NTac mice exposed to HFD for varying lengths of time. n=30 per group. Mice were anaesthetised with Ketamine hydrochloride(100mg/kg)/Xylazine hydrochloride (10mg/kg) prior to measurement.

		Control Diet	2 weeks HFD	4 weeks HFD	6 weeks HFD	12 weeks HFD	Trend observed
	Units	Mean ± SEM	Mean ± SEM	Mean ± SEM	Mean ± SEM	Mean ± SEM	
Nose To Tail Base Length	cm	10.3 ± 0.03	10.3 ± 0.04	10.3 ± 0.04	10.3 ± 0.03	10.3 ± 0.04	-
Bone Mineral Density	g/cm²	0.0493 ± 0.0004	0.0512 ± 0.0003	0.0506 ± 0.0003	0.0502 ± 0.0003	0.0497 ± 0.0003	-
Bone Mineral Content	g	0.4616 ± 0.0055	0.4982 ± 0.0063	0.5070 ± 0.0068	0.5130 ± 0.0049	0.5060 ± 0.0054	↑ with HFD
Bone Area	cm²	9.36 ± 0.05	9.73 ± 0.07	10.00 ± 0.08	10.21 ± 0.06	10.17 ± 0.06	↑ with HFD
Lean Mass	g	24.56 ± 0.33	23.52 ± 0.32	24.54 ± 0.36	23.66 ± 0.17	23.77 ± 0.28	-
Fat Mass	g	10.27 ± 0.58	12.91 ± 0.35	15.28 ± 0.37	17.42 ± 0.32	18.14 ± 0.27	↑ with exposure to HFD
Est Total Tissue Mass	g	34.83 ± 0.56	36.43 ± 0.48	39.82 ± 0.57	41.08 ± 0.36	41.91 ± 0.46	↑ with exposure to HFD
Fat Percentage Estimate	%	29.00 ± 1.33	35.34 ± 0.70	38.29 ± 0.62	42.31 ± 0.50	43.26 ± 0.36	↑ with exposure to HFD

Supplementary table 2b
Statistical analysis of DEXA (dual energy X-ray absorptiometry) results for 16 week old male C57BL/6NTac mice exposed to HFD for varying lengths of time. n=30 per group. Where p<0.05, an effect size (Cohen's d) has been calculated.

Fat mass

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.005	-1.01	
Control	4 weeks	0.000	-1.88	
Control	6 weeks	0.000	-2.80	
Control	12 weeks	0.000	-3.29	ANOVA +
2 weeks	4 weeks	0.000	-1.18	Tamhane's
2 weeks	6 weeks	0.000	-2.03	T2 post hoc
2 weeks	12 weeks	0.000	-2.13	testing
4 weeks	6 weeks	0.001	-0.50	
4 weeks	12 weeks	0.000	-0.74	
6 weeks	12 weeks	0.609		

Lean mass

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.228		
Control	4 weeks	1.000		
Control	6 weeks	0.159		
Control	12 weeks	0.512		ANOVA +
2 weeks	4 weeks	0.319		Tamhane's
2 weeks	6 weeks	1.000		T2 post hoc
2 weeks	12 weeks	1.000		testing
4 weeks	6 weeks	0.274		
4 weeks	12 weeks	0.632		
6 weeks	12 weeks	0.329		

Fat percentage estimate

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.001	-1.14	
Control	4 weeks	0.000	-1.74	
Control	6 weeks	0.000	-2.66	
Control	12 weeks	0.000	-3.09	ANOVA +
2 weeks	4 weeks	0.025	-0.82	Tamhane's
2 weeks	6 weeks	0.000	-2.12	T2 post hoc
2 weeks	12 weeks	0.000	-2.73	testing
4 weeks	6 weeks	0.000	-1.31	
4 weeks	12 weeks	0.000	-1.87	
6 weeks	12 weeks	0.744		

Est total tissue mass

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.328		
Control	4 weeks	0.000	-1.57	
Control	6 weeks	0.000	-2.41	
Control	12 weeks	0.000	-2.45	ANOVA +
2 weeks	4 weeks	0.000	-1.18	Tamhane's
2 weeks	6 weeks	0.000	-2.03	T2 post hoc
2 weeks	12 weeks	0.000	-2.13	testing
4 weeks	6 weeks	0.500		
4 weeks	12 weeks	0.060	-0.74	
6 weeks	12 weeks	0.830		

Nose to tail base length

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	1.000		
Control	4 weeks	1.000		
Control	6 weeks	0.991		
Control	12 weeks	0.511		ANOVA +
2 weeks	4 weeks	1.000		Tamhane's
2 weeks	6 weeks	0.993		T2 post hoc
2 weeks	12 weeks	0.548		testing
4 weeks	6 weeks	1.000		
4 weeks	12 weeks	0.769		
6 weeks	12 weeks	0.979		

Bone mineral density

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.004	-0.98	
Control	4 weeks	0.104		
Control	6 weeks	0.455		
Control	12 weeks	0.993		ANOVA +
2 weeks	4 weeks	0.954		Tamhane's
2 weeks	6 weeks	0.260		T2 post hoc
2 weeks	12 weeks	0.017	0.85	testing
4 weeks	6 weeks	0.984		
4 weeks	12 weeks	0.391		
6 weeks	12 weeks	0.936		

Bone mineral content

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.000	-1.15	
Control	4 weeks	0.000	-1.36	
Control	6 weeks	0.000	-1.84	
Control	12 weeks	0.000	-1.51	ANOVA +
2 weeks	4 weeks	0.986		Tamhane's
2 weeks	6 weeks	0.501		T2 post hoc
2 weeks	12 weeks	0.986		testing
4 weeks	6 weeks	0.998		
4 weeks	12 weeks	1.000		
6 weeks	12 weeks	0.984		

Bone area

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.001	-1.07	
Control	4 weeks	0.000	-1.74	
Control	6 weeks	0.000	-2.82	
Control	12 weeks	0.000	-2.57	ANOVA +
2 weeks	4 weeks	0.144		Tamhane's
2 weeks	6 weeks	0.000	-1.35	T2 post hoc
2 weeks	12 weeks	0.000	-1.20	testing
4 weeks	6 weeks	0.356		
4 weeks	12 weeks	0.682		
6 weeks	12 weeks	1.000		

Supplementary table 3a
Clinical chemistry results for 16 week old male C57BL/6NTac mice exposed to HFD for varying lengths of time. n=30 per group. Blood was collected via retro-orbital puncture from mice that were anaesthetised with Ketamine hydrochloride(100mg/kg)/Xylazine hydrochloride (10mg/kg) into lithium heparin coated tubes and plasma analysed on an Olympus AU400 except for tail-tip glucose measured by glucometer and insulin that was meaured by Meso Scale Discovery array technology.

		Units	Control Diet Mean ± SEM	2 weeks HFD Mean ± SEM	4 weeks HFD Mean ± SEM	6 weeks HFD Mean ± SEM	12 weeks HFD Mean ± SEM	Trend observed
Electrolytes								
Sodium	Na+	mmol/L	147.9 ± 0.3	144.9 ± 0.3	144.2 ± 0.3	144.9 ± 0.3	143.0 ± 0.3	↓ with HFD
Potassium	K+	mmol/L	4.0 ± 0.1	3.9 ± 0.1	4.0 ± 0.1	4.1 ± 0.1	4.3 ± 0.1	-
Chloride	Cl-	mmol/L	107.2 ± 0.3	107.5 ± 0.3	107.2 ± 0.3	107.6 ± 0.3	105.8 ± 0.3	-
Metabolic								
Tail tip glucose (pre-anaesthesia)		mmol/L	9.5 ± 0.21	9.4 ± 0.18	9.6 ± 0.16	9.4 ± 0.21	10.3 ± 0.20	-
Glucose (post-anaesthesia)		mmol/L	20.00 ± 0.61	24.99 ± 0.67	25.66 ± 0.83	25.10 ± 0.73	27.86 ± 0.79	↑ with exposure to HFD
Triglycerides	TG	mmol/L	1.49 ± 0.06	0.86 ± 0.03	0.89 ± 0.03	0.82 ± 0.04	0.68 ± 0.02	↓ with HFD
Cholesterol	Chol	mmol/L	2.45 ± 0.08	4.95 ± 0.10	5.18 ± 0.20	6.30 ± 0.21	7.00 ± 0.16	↑ with exposure to HFD
High density Lipoproteins	HDL	mmol/L	1.77 ± 0.06	3.33 ± 0.05	3.39 ± 0.12	3.89 ± 0.12	4.23 ± 0.08	↑ with exposure to HFD
Low density Lipoproteins	LDL	mmol/L	0.38 ± 0.01	1.08 ± 0.03	1.24 ± 0.06	1.68 ± 0.07	2.00 ± 0.07	↑ with exposure to HFD
Non-esterified fatty acids-C	NEFAC	mmol/L	0.380 ± 0.01	0.390 ± 0.01	0.390 ± 0.03	0.485 ± 0.03	0.355 ± 0.02	-
Glycerol		µmol/L	178.7 ± 6.8	218.1 ± 7.9	220.9 ± 6.7	222.3 ± 7.2	174.0 ± 7.8	-
Fructosamine		µmol/L	218.51 ± 1.22	202.66 ± 1.72	203.25 ± 1.70	206.30 ± 1.60	198.52 ± 6.93	↓ with HFD
Insulin		µg/L	0.72 ± 0.10	1.09 ± 0.12	1.02 ± 0.10	1.12 ± 0.11	1.09 ± 0.16	↑ with HFD
Pancreas								
Amylase		U/L	631.9 ± 10.9	741.3 ± 8.0	742.9 ± 9.8	736.2 ± 10.0	736.8 ± 18.1	↑ with HFD
Protein								
Total protein		g/L	45.8 ± 0.3	48.1 ± 0.3	48.6 ± 0.4	50.3 ± 0.5	51.6 ± 0.4	↑ with exposure to HFD
Albumin		g/L	25.07 ± 0.18	25.05 ± 0.19	25.70 ± 0.17	26.42 ± 0.19	26.84 ± 0.16	↑ with exposure to HFD
Liver/Muscle								
Aspartate aminotransferase	AST	U/L	56.2 ± 2.4	81.4 ± 4.1	102.9 ± 10.0	218.7 ± 29.1	270.5 ± 13.4	↑ with exposure to HFD
Alkaline phosphatase	ALP	U/L	67.1 ± 1.5	67.0 ± 1.8	76.6 ± 3.3	102.2 ± 6.6	136.8 ± 4.7	↑ with exposure to HFD
Alanine aminotransferase	ALT	U/L	51.2 ± 3.9	67.5 ± 4.8	108.6 ± 10.1	239.7 ± 27.5	323.9 ± 17.6	↑ with exposure to HFD
Lactate dehydrogenase	LDH	U/L	455.3 ± 21.0	509.5 ± 26.2	896.1 ± 77.3	1145.4 ± 149.9	1702.4 ± 94.5	↑ with exposure to HFD
Total bilirubin		µmol/L	2.0 ± 0.1	1.9 ± 0.1	2.1 ± 0.1	2.4 ± 0.1	2.3 ± 0.0	-
Creatine kinase	CK	U/L	303.6 ± 39.8	312.3 ± 45.5	272.5 ± 44.1	391.5 ± 58.6	387.9 ± 67.0	-
Kidney								
Creatinine		µmol/L	12.2 ± 0.3	9.9 ± 0.2	10.3 ± 0.3	10.4 ± 0.2	10.6 ± 0.3	↓ with HFD
Urea		mmol/L	10.2 ± 0.2	8.6 ± 0.2	7.7 ± 0.2	7.1 ± 0.1	6.5 ± 0.1	↓ with exposure to HFD
Uric acid		µmol/L	28.7 ± 1.2	34.2 ± 2.1	42.3 ± 3.2	35.8 ± 1.7	41.3 ± 2.3	-
Minerals and Iron								
Calcium		mmol/L	2.25 ± 0.01	2.25 ± 0.01	2.26 ± 0.01	2.30 ± 0.01	2.33 ± 0.01	-
Phosphorus		mmol/L	2.2 ± 0.0	2.3 ± 0.1	2.4 ± 0.0	2.4 ± 0.0	2.4 ± 0.0	-
Magnesium		mmol/L	1.05 ± 0.02	0.87 ± 0.01	0.83 ± 0.01	0.87 ± 0.01	0.88 ± 0.01	↓ with HFD
Iron		µmol/L	21.6 ± 0.4	24.1 ± 0.8	28.3 ± 0.7	33.4 ± 0.9	33.5 ± 1.1	↑ with exposure to HFD

Supplementary table 3b
Statistical analysis of clinical chemistry results for 16 week old male C57BL/6NTac mice exposed to HFD for varying lengths of time. n=30 per group. Where p<0.05, an effect size (Cohen's d) has been calculated.

Glucose

Comparison				
Group 1	Group 2	p	Effect size	Test
Control	2 weeks	0.000	-1.43	
Control	4 weeks	0.000	-1.44	
Control	6 weeks	0.000	-1.40	
Control	12 weeks	0.000	-2.06	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	1.000		
2 weeks	6 weeks	1.000		
2 weeks	12 weeks	0.072		
4 weeks	6 weeks	1.000		
4 weeks	12 weeks	0.461		
6 weeks	12 weeks	0.119		

Amylase

Comparison				
Group 1	Group 2	p	Effect size	Test
Control	2 weeks	0.000	-2.11	
Control	4 weeks	0.000	-1.95	
Control	6 weeks	0.000	-1.82	
Control	12 weeks	0.000	-1.32	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	1.000		
2 weeks	6 weeks	1.000		
2 weeks	12 weeks	1.000		
4 weeks	6 weeks	1.000		
4 weeks	12 weeks	1.000		
6 weeks	12 weeks	1.000		

Iron

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.052		
Control	4 weeks	0.000	-2.28	
Control	6 weeks	0.000	-3.48	
Control	12 weeks	0.000	-2.92	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	0.001	-1.06	
2 weeks	6 weeks	0.000	-2.10	
2 weeks	12 weeks	0.000	-1.84	
4 weeks	6 weeks	0.000	-1.18	
4 weeks	12 weeks	0.003	-1.04	
6 weeks	12 weeks	1.000		

Triglycerides

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.000	2.76	
Control	4 weeks	0.000	2.39	
Control	6 weeks	0.000	2.66	
Control	12 weeks	0.000	3.64	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	1.000		
2 weeks	6 weeks	0.977		
2 weeks	12 weeks	0.000	1.33	
4 weeks	6 weeks	0.829		
4 weeks	12 weeks	0.000	1.29	
6 weeks	12 weeks	0.021	0.85	

Aspartate aminotransferase (AST)

Comparison				
Group 1	Group 2	p	Effect size	Test
Control	2 weeks	0.000	-1.41	
Control	4 weeks	0.002	-1.38	
Control	6 weeks	0.000	-1.89	
Control	12 weeks	0.000	-4.95	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	0.520		
2 weeks	6 weeks	0.001	-1.51	
2 weeks	12 weeks	0.000	-3.93	
4 weeks	6 weeks	0.006	-1.08	
4 weeks	12 weeks	0.000	-2.62	
6 weeks	12 weeks	0.699		

Total bilirubin

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.773		
Control	4 weeks	0.996		
Control	6 weeks	0.187		
Control	12 weeks	0.012	-0.94	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	0.155		
2 weeks	6 weeks	0.007	-1.02	
2 weeks	12 weeks	0.000	-1.64	
4 weeks	6 weeks	0.533		
4 weeks	12 weeks	0.115		
6 weeks	12 weeks	1.000		

Cholesterol

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.000	-5.14	
Control	4 weeks	0.000	-3.55	
Control	6 weeks	0.000	-4.86	
Control	12 weeks	0.000	-6.87	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	0.977		
2 weeks	6 weeks	0.000	-1.59	
2 weeks	12 weeks	0.000	-2.86	
4 weeks	6 weeks	0.003	-0.99	
4 weeks	12 weeks	0.000	-1.82	
6 weeks	12 weeks	0.099		

Alkaline phosphatase (ALP)

Comparison				
Group 1	Group 2	p	Effect size	Test
Control	2 weeks	1.000		
Control	4 weeks	0.109		
Control	6 weeks	0.000	-1.59	
Control	12 weeks	0.000	-4.09	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	0.125		
2 weeks	6 weeks	0.000	-1.54	
2 weeks	12 weeks	0.000	-3.90	
4 weeks	6 weeks	0.011	-0.95	
4 weeks	12 weeks	0.000	-2.75	
6 weeks	12 weeks	0.001	-1.12	

Creatinine

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.000	1.59	
Control	4 weeks	0.000	1.22	
Control	6 weeks	0.000	1.41	
Control	12 weeks	0.002	1.02	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	0.968		
2 weeks	6 weeks	0.588		
2 weeks	12 weeks	0.358		
4 weeks	6 weeks	1.000		
4 weeks	12 weeks	0.991		
6 weeks	12 weeks	0.998		

HDL-cholesterol

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.000	-5.21	
Control	4 weeks	0.000	-3.23	
Control	6 weeks	0.000	-4.36	
Control	12 weeks	0.000	-6.45	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	1.000		
2 weeks	6 weeks	0.001	-1.22	
2 weeks	12 weeks	0.000	-2.56	

Alanine Transferase (ALT)

Comparison				
Group 1	Group 2	p	Effect size	Test
Control	2 weeks	0.098		
Control	4 weeks	0.000	-1.49	
Control	6 weeks	0.000	-2.19	
Control	12 weeks	0.000	-4.63	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	0.010	-1.01	
2 weeks	6 weeks	0.000	-1.95	
2 weeks	12 weeks	0.000	-4.18	

Urea

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.000	1.51	
Control	4 weeks	0.000	2.30	
Control	6 weeks	0.000	3.25	
Control	12 weeks	0.000	4.18	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	0.018	0.85	
2 weeks	6 weeks	0.000	1.68	
2 weeks	12 weeks	0.000	2.54	

4 weeks	6 weeks	0.043	-0.77	
4 weeks	12 weeks	0.000	-1.53	
6 weeks	12 weeks	0.175		

LDL-cholesterol

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.000	-5.69	
Control	4 weeks	0.000	-4.42	
Control	6 weeks	0.000	-5.86	
Control	12 weeks	0.000	-6.88	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	0.152		
2 weeks	6 weeks	0.000	-2.23	
2 weeks	12 weeks	0.000	-3.26	
4 weeks	6 weeks	0.000	-1.28	
4 weeks	12 weeks	0.000	-2.14	
6 weeks	12 weeks	0.017	-0.85	

Fructosamine

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.000	1.96	
Control	4 weeks	0.000	1.91	
Control	6 weeks	0.000	1.58	
Control	12 weeks	0.000	0.90	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	1.000		
2 weeks	6 weeks	0.745		
2 weeks	12 weeks	0.886		
4 weeks	6 weeks	0.888		
4 weeks	12 weeks	0.973		
6 weeks	12 weeks	1.000		

Free fatty acids

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	1.000		
Control	4 weeks	1.000		
Control	6 weeks	0.013	-0.93	
Control	12 weeks	0.942		ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	1.000		
2 weeks	6 weeks	0.030	-0.86	
2 weeks	12 weeks	0.683		
4 weeks	6 weeks	0.119		
4 weeks	12 weeks	0.949		
6 weeks	12 weeks	0.002	1.09	

Glycerol

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.004	-0.98	
Control	4 weeks	0.000	-1.14	
Control	6 weeks	0.000	-1.13	
Control	12 weeks	1.000		ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	1.000		
2 weeks	6 weeks	1.000		
2 weeks	12 weeks	0.002	1.02	
4 weeks	6 weeks	1.000		

4 weeks	6 weeks	0.001	-1.27	
4 weeks	12 weeks	0.000	-2.83	
6 weeks	12 weeks	0.123		

Lactate dehydrogenase (LDH)

Comparison				
Group 1	Group 2	p	Effect size	Test
Control	2 weeks	0.709		
Control	4 weeks	0.020	-1.08	
Control	6 weeks	0.001	-1.47	
Control	12 weeks	0.000	-3.94	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	0.100		
2 weeks	6 weeks	0.003	-1.32	
2 weeks	12 weeks	0.000	-3.61	
4 weeks	6 weeks	0.238		
4 weeks	12 weeks	0.000	-2.03	
6 weeks	12 weeks	0.032	-0.83	

Creatine Kinase (CK)

Comparison				
Group 1	Group 2	p	Effect size	Test
Control	2 weeks	1.000		
Control	4 weeks	1.000		
Control	6 weeks	0.995		
Control	12 weeks	1.000		ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	1.000		
2 weeks	6 weeks	1.000		
2 weeks	12 weeks	1.000		
4 weeks	6 weeks	0.994		
4 weeks	12 weeks	0.999		
6 weeks	12 weeks	1.000		

Total Protein

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.000	-1.39	
Control	4 weeks	0.000	-1.57	
Control	6 weeks	0.000	-2.17	
Control	12 weeks	0.000	-3.06	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	0.976		
2 weeks	6 weeks	0.003	-1.04	
2 weeks	12 weeks	0.000	-1.78	
4 weeks	6 weeks	0.044	-0.77	
4 weeks	12 weeks	0.000	-1.44	
6 weeks	12 weeks	0.418		

Albumin

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	1.000		
Control	4 weeks	0.137		
Control	6 weeks	0.000	-1.34	
Control	12 weeks	0.000	-1.93	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	0.130		
2 weeks	6 weeks	0.000	-1.33	
2 weeks	12 weeks	0.000	-1.89	
4 weeks	6 weeks	0.067		

4 weeks	6 weeks	0.075		
4 weeks	12 weeks	0.000	1.48	
6 weeks	12 weeks	0.031	0.81	

Uric Acid

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.237		
Control	4 weeks	0.003	-1.15	
Control	6 weeks	0.013	-0.89	
Control	12 weeks	0.000	-1.32	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	0.311		
2 weeks	6 weeks	1.000		
2 weeks	12 weeks	0.240		
4 weeks	6 weeks	0.549		
4 weeks	12 weeks	1.000		
6 weeks	12 weeks	0.482		

Sodium

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.000	1.76	
Control	4 weeks	0.000	2.34	
Control	6 weeks	0.000	1.78	
Control	12 weeks	0.000	2.84	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	0.816		
2 weeks	6 weeks	1.000		
2 weeks	12 weeks	0.002	1.02	
4 weeks	6 weeks	0.767		
4 weeks	12 weeks	0.051		
6 weeks	12 weeks	0.001	1.05	

Potassium

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.999		
Control	4 weeks	0.995		
Control	6 weeks	0.558		
Control	12 weeks	0.023	-0.83	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	0.551		
2 weeks	6 weeks	0.037	-0.78	
2 weeks	12 weeks	0.000	-1.17	
4 weeks	6 weeks	0.955		
4 weeks	12 weeks	0.073		
6 weeks	12 weeks	0.555		

Chloride

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.998		
Control	4 weeks	1.000		
Control	6 weeks	0.991		
Control	12 weeks	0.003	1.00	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	0.997		
2 weeks	6 weeks	1.000		
2 weeks	12 weeks	0.001	1.08	
4 weeks	6 weeks	0.988		

4 weeks	12 weeks	0.000	1.18	
6 weeks	12 weeks	0.000	1.17	

Tail-tip glucose

Comparison			Effect size (Cohen's	
Group 1	Group 2	p	d)	Test
Control	2 weeks	1.000		
Control	4 weeks	0.983		
Control	6 weeks	1.000		
Control	12 weeks	0.027	-0.73	ANOVA +
2 weeks	4 weeks	0.948		Tukey's
2 weeks	6 weeks	1.000		HSD post
2 weeks	12 weeks	0.015	-0.84	hoc testing
4 weeks	6 weeks	0.959		
4 weeks	12 weeks	0.106		
6 weeks	12 weeks	0.017	-0.77	

Insulin

Comparison			Effect size (Cohen's	
Group 1	Group 2	p	d)	Test
Control	2 weeks	0.026	-0.61	
Control	4 weeks	0.027	-0.55	
Control	6 weeks	0.004	-0.70	
Control	12 weeks	0.035	-0.52	ANOVA +
2 weeks	4 weeks	1.000		Tukey's
2 weeks	6 weeks	0.971		HSD post
2 weeks	12 weeks	1.000		hoc testing
4 weeks	6 weeks	0.967		
4 weeks	12 weeks	1.000		
6 weeks	12 weeks	0.948		

4 weeks	12 weeks	0.000	-1.25	
6 weeks	12 weeks	0.637		

Calcium

Comparison			Effect size (Cohen's	
Group 1	Group 2	p	d)	Test
Control	2 weeks	1.000		
Control	4 weeks	1.000		
Control	6 weeks	0.002	-1.04	
Control	12 weeks	0.000	-1.85	ANOVA +
2 weeks	4 weeks	1.000		Tamhane's
2 weeks	6 weeks	0.002	-1.02	T2 post hoc
2 weeks	12 weeks	0.000	-1.80	testing
4 weeks	6 weeks	0.037	-0.78	
4 weeks	12 weeks	0.000	-1.43	
6 weeks	12 weeks	0.122		

Phosphorus

Comparison			Effect size (Cohen's	
Group 1	Group 2	p	d)	Test
Control	2 weeks	0.867		
Control	4 weeks	0.415		
Control	6 weeks	0.200		
Control	12 weeks	0.034	-0.81	ANOVA +
2 weeks	4 weeks	1.000		Tamhane's
2 weeks	6 weeks	0.999		T2 post hoc
2 weeks	12 weeks	0.929		testing
4 weeks	6 weeks	1.000		
4 weeks	12 weeks	0.987		
6 weeks	12 weeks	0.999		

4 weeks	12 weeks	0.002	1.04	
6 weeks	12 weeks	0.000	1.20	

Magnesium

Comparison			Effect size (Cohen's	
Group 1	Group 2	p	d)	Test
Control	2 weeks	0.000	2.32	
Control	4 weeks	0.000	2.66	
Control	6 weeks	0.000	2.55	
Control	12 weeks	0.000	2.57	ANOVA +
2 weeks	4 weeks	0.536		Tamhane's
2 weeks	6 weeks	1.000		T2 post
2 weeks	12 weeks	1.000		hoc testing
4 weeks	6 weeks	0.198		
4 weeks	12 weeks	0.103		
6 weeks	12 weeks	1.000		

Supplementary table 4a
Wet liver weights of 16 week old male C57BL/6NTac mice exposed to HFD for varying lengths of time. n=30 per group.

		Control Diet	2 weeks HFD	4 weeks HFD	6 weeks HFD	12 weeks HFD	Trend observed
	Units	Mean ± SEM	Mean ± SEM	Mean ± SEM	Mean ± SEM	Mean ± SEM	
Liver weight	g	1.74 ± 0.03	1.94 ± 0.04	2.42 ± 0.12	2.78 ± 0.09	3.43 ± 0.20	↑ with exposure to HFD

Supplementary table 4b
Statistical analysis of wet liver weights of 16 week old C57BL/6NTac male mice exposed to HFD for varying lengths of time. n=30 per group. Where $p<0.05$, an effect size (Cohen's d) has been calculated.

Liver weight

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.012	-1.82	ANOVA + Tukey's HSD post hoc testing
Control	4 weeks	0.003	-2.86	
Control	6 weeks	0.000	-5.80	
Control	12 weeks	0.000	-4.62	
2 weeks	4 weeks	0.037	-1.81	
2 weeks	6 weeks	0.000	-4.08	
2 weeks	12 weeks	0.000	-3.79	
4 weeks	6 weeks	0.262		
4 weeks	12 weeks	0.008	-1.94	
6 weeks	12 weeks	0.121		

Supplementary table 5a

Haematology results for 16 week old male C57BL/6NTac mice exposed to HFD for varying lengths of time. n=30 per group. Blood was collected via retro-orbital puncture from mice that were anaesthetised with Ketamine hydrochloride(100mg/kg)/Xylazine hydrochloride (10mg/kg) into EDTA coated tubes and analysed on a *scil* VetABC analyser.

		Control Diet	2 weeks HFD	4 weeks HFD	6 weeks HFD	12 weeks HFD	Trend observed
	Units	Mean ± SEM	Mean ± SEM	Mean ± SEM	Mean ± SEM	Mean ± SEM	
White blood cells	$x10^3/\mu l$	6.44 ± 0.17	5.88 ± 0.16	6.58 ± 0.20	7.07 ± 0.25	7.49 ± 0.20	-
Red blood cells	$x10^6/\mu l$	10.66 ± 0.07	10.92 ± 0.10	10.82 ± 0.09	11.25 ± 0.05	10.70 ± 0.06	-
Haemoglobin	g/dl	15.53 ± 0.08	15.71 ± 0.16	15.54 ± 0.11	15.97 ± 0.08	15.45 ± 0.08	-
Haematocrit	%	47.52 ± 0.28	48.02 ± 0.42	47.93 ± 0.39	49.49 ± 0.23	47.95 ± 0.25	-
Mean cell volume	fl	45 ± 0.1	44 ± 0.1	44 ± 0.2	44 ± 0.1	45 ± 0.1	-
Mean corpuscular haemaglobin (MCH)	pg	14.58 ± 0.06	14.39 ± 0.05	14.37 ± 0.06	14.20 ± 0.05	14.44 ± 0.07	-
Mean corpuscular haemaglobin concentration (MCHC)	g/dl	32.68 ± 0.12	32.71 ± 0.13	32.44 ± 0.13	32.28 ± 0.10	32.23 ± 0.12	-
Platelets	$x10^3/\mu l$	1461 ± 27	1402 ± 20	1299 ± 29	1250 ± 33	1214 ± 24	↓ with exposure to HFD
Red cell distribution width (RDW)	%	11.49 ± 0.08	11.68 ± 0.07	11.49 ± 0.06	11.45 ± 0.06	11.46 ± 0.07	-
Mean platelet volume (MPV)	fl	5.20 ± 0.02	5.34 ± 0.02	5.32 ± 0.02	5.32 ± 0.02	5.41 ± 0.02	-

Supplementary table 5b
Statistical analysis of haematology results for 16 week old male C57BL/6NTac mice exposed to HFD for varying lengths of time. n=30 per group. Where p<0.05, an effect size (Cohen's d) has been calculated.

White blood cells

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.205		
Control	4 weeks	1.000		
Control	6 weeks	0.359		
Control	12 weeks	0.002	-1.02	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	0.083		
2 weeks	6 weeks	0.002	-1.05	
2 weeks	12 weeks	0.000	-1.61	
4 weeks	6 weeks	0.762		
4 weeks	12 weeks	0.023	-0.82	
6 weeks	12 weeks	0.889		

Red blood cells

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.300		
Control	4 weeks	0.761		
Control	6 weeks	0.000	-1.95	
Control	12 weeks	1.000		ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	0.998		
2 weeks	6 weeks	0.042	-0.83	
2 weeks	12 weeks	0.574		
4 weeks	6 weeks	0.001	-1.19	
4 weeks	12 weeks	0.963		
6 weeks	12 weeks	0.000	1.82	

Haemoglobin

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.977		
Control	4 weeks	1.000		
Control	6 weeks	0.001	-1.05	
Control	12 weeks	0.999		ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	0.994		
2 weeks	6 weeks	0.776		
2 weeks	12 weeks	0.809		
4 weeks	6 weeks	0.024	-0.84	
4 weeks	12 weeks	0.999		
6 weeks	12 weeks	0.000	1.26	

Haematocrit

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.981		
Control	4 weeks	0.993		
Control	6 weeks	0.000	-1.40	
Control	12 weeks	0.950		ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	1.000		
2 weeks	6 weeks	0.039	-0.82	
2 weeks	12 weeks	1.000		
4 weeks	6 weeks	0.012	-0.91	
4 weeks	12 weeks	1.000		
6 weeks	12 weeks	0.000	1.17	

Mean cell volume

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.010	0.95	
Control	4 weeks	0.871		
Control	6 weeks	0.010	0.95	
Control	12 weeks	0.972		ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	0.706		
2 weeks	6 weeks	1.000		
2 weeks	12 weeks	0.000	-1.43	
4 weeks	6 weeks	0.706		
4 weeks	12 weeks	0.174		
6 weeks	12 weeks	0.000	-1.43	

Mean corpuscular haemaglobin (MCH)

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.251		
Control	4 weeks	0.219		
Control	6 weeks	0.000	1.25	
Control	12 weeks	0.800		ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	1.000		
2 weeks	6 weeks	0.097		
2 weeks	12 weeks	1.000		
4 weeks	6 weeks	0.268		
4 weeks	12 weeks	0.998		
6 weeks	12 weeks	0.054	-0.76	

Mean corpuscular haemaglobin concentration (MCHC)

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	1.000		
Control	4 weeks	0.855		
Control	6 weeks	0.109		
Control	12 weeks	0.075		ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	0.823		
2 weeks	6 weeks	0.114		
2 weeks	12 weeks	0.078		
4 weeks	6 weeks	0.981		
4 weeks	12 weeks	0.925		
6 weeks	12 weeks	1.000		

Platelets

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.565		
Control	4 weeks	0.001	1.06	
Control	6 weeks	0.000	1.29	
Control	12 weeks	0.000	1.77	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	0.050	0.77	
2 weeks	6 weeks	0.002	1.06	
2 weeks	12 weeks	0.000	1.56	
4 weeks	6 weeks	0.955		
4 weeks	12 weeks	0.253		
6 weeks	12 weeks	0.993		

Red cell distribution width (RDW)

Comparison				
Group 1	Group 2	p	Effect size (Cohen's d)	Test
Control	2 weeks	0.582		
Control	4 weeks	1.000		
Control	6 weeks	1.000		
Control	12 weeks	1.000		ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	0.361		
2 weeks	6 weeks	0.170		
2 weeks	12 weeks	0.247		
4 weeks	6 weeks	1.000		
4 weeks	12 weeks	1.000		
6 weeks	12 weeks	1.000		

Mean platelet volume (MPV)

Comparison				
Group 1	Group 2	p	Effect size	Test
Control	2 weeks	0.002	-1.05	
Control	4 weeks	0.004	-0.98	
Control	6 weeks	0.001	-1.10	
Control	12 weeks	0.000	-1.82	ANOVA + Tamhane's T2 post hoc testing
2 weeks	4 weeks	1.000		
2 weeks	6 weeks	1.000		
2 weeks	12 weeks	0.246		
4 weeks	6 weeks	1.000		
4 weeks	12 weeks	0.035	-0.79	
6 weeks	12 weeks	0.027	-0.81	

Supplementary table 6
Percentage weight gain relative to starting weight at week 4 of female C57BL/6NTac mice exposed to HFD for varying lengths of time. n=30 per group.

		Control Diet	2 weeks HFD			
	Units	Mean ± SEM	Mean ± SEM	p	Effect size (Cohen's d)	Test
Week 5	%	14.9 ± 0.9	17.2 ± 1.4	0.155		
Week 6	%	26.1 ± 2.2	25.5 ± 1.5	0.721		
Week 7	%	36.0 ± 2.9	33.4 ± 2.1	0.397		
Week 8	%	41.7 ± 2.8	38.2 ± 2.2	0.283		
Week 9	%	48.9 ± 3.4	44.0 ± 2.6	0.222		
Week 10	%	55.0 ± 3.5	48.1 ± 2.2	0.075		Welch's
Week 11	%	61.0 ± 3.6	53.1 ± 2.4	0.056		t-test
Week 12	%	63.9 ± 3.6	55.9 ± 2.6	0.068		
Week 13	%	66.1 ± 3.5	60.8 ± 3.2	0.268		
Week 14	%	71.3 ± 3.9	66.3 ± 3.3	0.337		
Week 15	%	78.9 ± 4.9	92.4 ± 4.8	0.058		
Week 16	%	86.5 ± 5.6	104.7 ± 5.0	0.022	-0.63	

Supplementary table 7
DEXA (dual energy X-ray absorptiometry) results for 16 week old female C57BL/6NTac mice exposed to HFD for varying lengths of time. n=30 per group. Mice were anaesthetised with Ketamine hydrochloride (100mg/kg)/Xylazine hydrochloride (10mg/kg) prior to measurement.

		Control Diet	2 weeks HFD			
	Units	Mean ± SEM	Mean ± SEM	p	Effect size (Cohen's d)	Test
Nose To Tail Base Length	cm	10.1 ± 0.03	10.0 ± 0.03	0.000	-0.45	
Bone Mineral Density	g/cm²	0.0512 ± 0.0002	0.0523 ± 0.0003	0.003	-0.85	
Bone Mineral Content	g	0.4691 ± 0.0041	0.4935 ± 0.0056	0.001	-0.93	
Bone Area	cm²	9.16 ± 0.06	9.42 ± 0.06	0.003	-0.80	Welch's
Lean Mass	g	20.82 ± 0.22	19.84 ± 0.24	0.004	0.78	t-test
Fat Mass	g	6.61 ± 0.53	9.51 ± 0.56	0.000	-0.98	
Est Total Tissue Mass	g	27.43 ± 0.71	29.35 ± 0.77	0.072		
Fat Percentage Estimate	%	23.23 ± 1.28	31.61 ± 1.12	0.000	-1.29	

Supplementary table 8
Clinical chemistry results for 16 week old female C57BL/6NTac mice exposed to HFD for varying lengths of time. n=30 per group. Blood was collected via retro-orbital puncture from mice that were anaesthetised with Ketamine hydrochloride (100mg/kg)/Xylazine hydrochloride (10mg/kg) into lithium heparin coated tubes and plasma analysed on an Olympus AU400.

		Control Diet	2 weeks HFD			
	Units	Mean ± SEM	Mean ± SEM	p	Effect size (Cohen's d)	Test
Electrolytes						
Sodium	mmol/L	145.5 ± 0.2	143.48 ± 0.336	0.000	1.45	
Potassium	mmol/L	3.4 ± 0.0	3.41 ± 0.036	0.839		
Chloride	mmol/L	108.6 ± 0.3	109.27 ± 0.327	0.157		
Metabolic						
Tail tip glucose	mmol/L	7.9 ± 0.1	8.80 ± 0.2	0.000	-1.01	
Glucose	mmol/L	16.45 ± 0.41	20.80 ± 0.444	0.000	-1.88	
Triglycerides	mmol/L	0.84 ± 0.05	0.51 ± 0.016	0.000	1.94	
Cholesterol	mmol/L	2.00 ± 0.05	3.31 ± 0.113	0.000	-2.96	
HDL	mmol/L	1.42 ± 0.03	2.29 ± 0.072	0.000	-3.01	
LDL	mmol/L	0.33 ± 0.01	0.71 ± 0.029	0.000	-3.56	
NEFAC	mmol/L	0.297 ± 0.02	0.34 ± 0.014	0.045	-0.53	
Glycerol	µmol/L	134.9 ± 4.8	179.92 ± 4.559	0.000	-1.77	
Fructosamine	µmol/L	213.32 ± 2.26	194.44 ± 2.204	0.000	1.56	
Insulin	µg/L	0.30 ± 0.03	0.57 ± 0.052	0.000	-1.24	
Pancreas						
Amylase	U/L	543.3 ± 11.8	606.89 ± 10.23	0.000	-1.06	
Protein						
Total protein	g/L	47.2 ± 0.2	48.05 ± 0.31	0.103		Welch's t-test
Albumin	g/L	26.20 ± 0.17	26.36 ± 0.182	0.977		
Liver/Muscle						
AST	U/L	56.9 ± 2.4	78.80 ± 4.88	0.092		
ALP	U/L	104.3 ± 2.3	102.04 ± 2.843	0.116		
ALT	U/L	33.4 ± 1.5	46.87 ± 3.682	0.544		
LDH	U/L	472.8 ± 16.3	442.85 ± 17.54	0.628		
Total bilirubin	µmol/L	1.9 ± 0.1	2.01 ± 0.056	0.452		
CK	U/L	239.2 ± 24.2	165.11 ± 19.82	0.247		
Kidney						
Creatinine	µmol/L	12.6 ± 0.4	8.64 ± 0.183	0.409		
Urea	mmol/L	11.1 ± 0.3	7.77 ± 0.25	0.939		
Uric acid	µmol/L	24.5 ± 1.5	22.01 ± 1.301	0.880		
Minerals and Iron						
Calcium	mmol/L	2.28 ± 0.01	2.26 ± 0.007	0.965		
Phosphorus	mmol/L	2.2 ± 0.0	2.39 ± 0.035	0.005	-1.00	
Magnesium	mmol/L	1.07 ± 0.01	0.83 ± 0.01	0.263		
Iron	µmol/L	26.5 ± 0.7	26.07 ± 0.667	0.956		

Supplementary table 9
Wet liver weights of 16 week old female C57BL/6NTac mice exposed to HFD for varying lengths of time. n=30 per group.

		Control Diet	2 weeks HFD			
	Units	Mean ± SEM	Mean ± SEM	p	Effect size (Cohen's d)	Test
Liver weight	g	1.37 ± 0.03	1.66 ± 0.05	0.000	-1.33	Student's t-test

Supplementary table 10
Haematology results for 16 week old female C57BL/6NTac mice exposed to HFD for varying lengths of time. n=30 per group. Blood was collected via retro-orbital puncture from mice that were anaesthetised with Ketamine hydrochloride (100mg/kg)/Xylazine hydrochloride (10mg/kg) into EDTA coated tubes and analysed on a *scil* VetABC analyser.

		Control Diet	2 weeks HFD			
	Units	Mean ± SEM	Mean ± SEM	p	Effect size (Cohen's d)	Test
White blood cells	$x10^3/\mu l$	5.65 ± 0.20	5.75 ± 0.21	0.731		
Red blood cells	$x10^6/\mu l$	10.76 ± 0.08	10.60 ± 0.08	0.153		
Haemoglobin	g/dl	15.87 ± 0.12	15.44 ± 0.11	0.010	0.70	
Haematocrit	%	47.60 ± 0.35	46.98 ± 0.38	0.241		
Mean cell volume	fl	44.24 ± 0.13	44.33 ± 0.09	0.553		Welch's t-test
MCH	pg	14.75 ± 0.05	14.57 ± 0.05	0.018	0.64	
MCHC	g/dl	33.35 ± 0.13	32.87 ± 0.10	0.005	0.76	
Platelets	$x10^3/\mu l$	1085 ± 19.8	1033.1 ± 15.0	0.040	0.55	
RDW	%	11.69 ± 0.04	11.87 ± 0.04	0.002	-0.84	
MPV	fl	5.31 ± 0.02	5.46 ± 0.02	0.000	-1.42	

Supplementary table 11
Incidence table of microscopic findings for follow-up study for male and female mice given 2 weeks HFD.

Group			C57BL/6NTac Males		C57BL/6NTac Females	
	Finding	Grade	No HFD	HFD	No HFD	HFD
	micro	0	7	0	10	2
		1	0	0	0	1
		2	0	6	0	5
		3	0	1	0	2
	macro	0	7	3	10	2
		1	0	3	0	4
		2	0	1	0	3
		3	0	0	0	1
	Oil Red O	0	7	0	8	0
		1	0	1	2	1
		2	0	3	0	2
		3	0	2	0	5
		4	0	1	0	2

Key
Micro = microvesicular vacuolation predominantly centrilobular
Macro = macrovesicular vacuolation (usually periportal)
ORO grading
1- occasional small lipid droplets
2- mainly small lipid droplets in <50% of cells
3- most cells have small or large lipid droplets
4- virtually all cells have droplets mainly large