

Supplemental Table 1S. Interactions between selected subgroups and adipokine values on the composite endpoint of CV death, non-procedural MI and stroke.

Outcome:	IP Group		IS Group		Inter-action	Below Median		Above Median		Inter-action	
	CV Death/Non-Procedural MI/Stroke					BMI ≤31		BMI >31			
	Events/N in subgroup at baseline	191/1163		173/1167		170/1112		194/1218			
	HR	P	HR	P	P	HR	P	HR	P	P	
	(95% CI)		(95% CI)			(95% CI)		(95% CI)			
Baseline Log leptin	0.8 (0.7, 0.9)	.009	0.9 (0.8, 1.1)	.32	.27	0.7 (0.6, 0.9)	<.001	1.1 (0.9, 1.3)	.62	.01	
Change from Baseline Log leptin	0.8 (0.7, 1.0)	.02	0.8 (0.7, 0.9)	.008	.84	0.8 (0.6, 0.9)	.002	0.9 (0.7, 1.0)	.07	.39	
Baseline Log adiponectin	1.3 (1.1, 1.6)	.002	1.1 (0.9, 1.3)	.34	.12	1.3 (1.1, 1.6)	.01	1.1 (1.0, 1.3)	.13	.84	
Change from Baseline Log adiponectin	1.1 (0.9, 1.4)	.35	1.0 (0.8, 1.2)	.67	.32	1.4 (1.1, 1.7)	.001	0.9 (0.7, 1.0)	.07	.04	
Baseline Log MCP-1	1.0 (0.9, 1.2)	.68	0.8 (0.7, 1.0)	.04	.07	0.8 (0.7, 1.0)	.05	1.0 (0.8, 1.1)	.82	.09	
Change from Baseline Log MCP-1	1.2 (0.9, 1.4)	.15	0.9 (0.7, 1.1)	.33	.09	1.4 (1, 1.8)	.02	0.9 (0.8, 1.1)	.55	.22	
Baseline Log leptin/adiponectin	0.7 (0.6, 0.9)	<.001	0.9 (0.7, 1.1)	.18	.12	0.7 (0.6, 0.8)	<.001	0.9 (0.8, 1.1)	.57	.09	
Change from Baseline Log leptin/adiponectin	0.8 (0.7, 1.0)	.03	0.8 (0.7, 1.0)	.05	.94	0.7 (0.6, 0.8)	<.001	1.0 (0.8, 1.2)	.65	.12	
Baseline Log leptin/BMI	0.8	.009	0.9	.48	.21	0.8	.001	1.0	.79	.03	

Outcome:	IP Group		IS Group		Inter-action	Below Median		Above Median		Inter-action	
						BMI ≤31		BMI >31			
	Events/N in subgroup at baseline	191/1163		173/1167		170/1112		194/1218			
	HR (95% CI)	P	HR (95% CI)	P	P	HR (95% CI)	P	HR (95% CI)	P		
	(0.7, 1.0)		(0.8, 1.1)			(0.7 ,0.9)		(0.9, 1.2)			
Change from Baseline Log leptin/BMI	0.9 (0.7, 1.1)	.16	0.8 (0.6, 0.9)	.01	.46	0.8 (0.7 ,0.9)	.007	0.8 (0.7, 1.0)	.06	.85	
Baseline Log TNF- α	1.3 (1.1, 1.5)	.001	1.2 (1.0, 1.4)	.10	.29	1.4 (1.2 ,1.7)	<.001	1.2 (1.0, 1.3)	.05	.61	
Change from Baseline Log TNF- α	1.2 (1.1, 1.3)	.001	1.1 (1.0, 1.3)	.16	.45	1.1 (0.9 ,1.3)	.23	1.2 (1.1, 1.3)	.001	.02	
Baseline Log CRP	1.6 (1.4, 1.9)	<.001	1.3 (1.1, 1.6)	.002	.12	1.8 (1.5 ,2.2)	<.001	1.3 (1.1, 1.5)	.005	.03	
Change from Baseline Log CRP	1.4 (1.2, 1.7)	<.001	1.2 (1.0, 1.4)	.10	.15	1.1 (0.9 ,1.4)	.20	1.5 (1.2, 1.7)	<.001	.13	
Baseline Log IL-6	1.4 (1.1, 1.7)	.002	1.3 (1.0, 1.5)	.02	.57	1.7 (1.4 ,2.2)	<.001	1.1 (1.0, 1.3)	.14	.03	
Change from Baseline Log IL-6	1.2 (1.0, 1.4)	.04	1.0 (0.9, 1.3)	.66	.27	1.2 (1.0 ,1.6)	.06	1.1 (0.9, 1.2)	.49	.41	
Baseline Log BMI	0.4 (0.2, 0.7)	.004	0.5 (0.2, 0.9)	.02	.28	0.4 (0.2 ,0.8)	.01	1.0 (0.5, 2.2)	.93	<.001	
Change from Baseline Log BMI	0.7 (0.5, 1.0)	.06	0.7 (0.5, 1.0)	.06	.93	0.4 (0.3 ,0.6)	<.001	1.1 (0.8, 1.6)	.52	.001	

Outcome:	IP Group		IS Group		Inter-action	Below Median		Above Median		Inter-action
	Events/N in subgroup at baseline	191/1163	Events/N in subgroup at baseline	173/1167		BMI ≤31	170/1112	194/1218		
	HR (95% CI)	P	HR (95% CI)	P	P	HR (95% CI)	P	HR (95% CI)	P	P
Baseline Log Waist Circumference	1.0 (0.8, 1.4)	.89	1.1 (0.9, 1.5)	.35	.39	0.7 (0.5 ,0.9)	.008	1.5 (1.1, 1.9)	.01	.009
Change from Baseline Log Waist Circumference	1.0 (0.8, 1.4)	.79	0.9 (0.6, 1.2)	.34	.39	0.6 (0.4 ,0.9)	.02	1.2 (0.9, 1.6)	.20	.03

All models fully adjusted.

BMI and waist circumference were measured at the same time as the adipokine values

Supplemental Table 2S. Interactions between sex and adipokine values on the composite endpoint of CV death, non-procedural MI and stroke.

Outcome: CV Death/Non-Procedural MI/Stroke	Females	Males	Interaction
Events/N in subgroup at baseline	127/693	237/1637	
Covariate	HR (95% CI)	HR (95% CI)	P
Baseline Log leptin	0.9 (0.7, 1.2)	0.8 (0.7, 1.0)	.58 .02 .01 .31
Change from Baseline Log leptin	0.8 (0.7, 1.0)	0.8 (0.7, 0.9)	.02 .01 .94
Baseline Log adiponectin	1.3 (1.0, 1.6)	1.2 (1.0, 1.3)	.04 .06 .50
Change from Baseline Log adiponectin	0.9 (0.7, 1.2)	1.1 (0.9, 1.2)	.45 .44 .28
Baseline Log MCP-1	0.9 (0.7, 1.0)	1.0 (0.8, 1.1)	.12 .83 .26
Change from Baseline Log MCP-1	1.1 (0.9, 1.4)	1.0 (0.8, 1.2)	.41 .83 .43
Baseline Log leptin/adiponectin	0.8 (0.7, 1.0)	0.8 (0.7, 0.9)	.05 .004 .85
Change from Baseline Log leptin/adiponectin	0.8 (0.7, 1.0)	0.8 (0.7, 1.0)	.10 .01 .75
Baseline Log leptin/BMI	0.9 (0.8, 1.2)	0.9 (0.7, 1.0)	.51 .03 .49
Change from Baseline Log leptin/BMI	0.8 (0.7, 0.9)	0.8 (0.7, 1.0)	.01 .10 .60

Outcome: CV Death/Non-Procedural MI/Stroke	Females	Males	Interaction		
Events/N in subgroup at baseline	127/693	237/1637			
Covariate	HR	P	HR	P	P
		(95% CI)		(95% CI)	
Baseline Log TNF- α	1.2 (1.0, 1.5)	.05	1.2 (1.1, 1.4)	.003	.99
Change from Baseline Log TNF- α	1.0 (0.9, 1.2)	.74	1.2 (1.1, 1.4)	<.001	.11
Baseline Log CRP	1.1 (0.9, 1.3)	.56	1.0 (0.8, 1.1)	.70	.47
Change from Baseline Log CRP	0.9 (0.8, 1.1)	.50	0.9 (0.8, 1.0)	.15	.82
Baseline Log IL-6	1.2 (1.0, 1.5)	.07	1.6 (1.4, 1.9)	<.001	.03
Change from Baseline Log IL-6	1.1 (0.9, 1.4)	.33	1.4 (1.2, 1.6)	<.001	.14
Baseline Log BMI	0.9 (0.7, 1.1)	.22	1.1 (1.0, 1.3)	.09	.04
Change from Baseline Log BMI	0.8 (0.6, 1.0)	.08	1.3 (1.1, 1.5)	.01	.003
Baseline Log Waist Circumference	0.5 (0.2, 1.1)	.09	0.4 (0.2, 0.9)	.02	.72
Change from Baseline Log Waist Circumference	0.8 (0.6, 1.2)	.28	0.7 (0.5, 0.9)	.01	.44

BMI and waist circumference were measured at the same time as the adipokine values

Table 3S. Effect of adipokines on the composite endpoint of CV death, non-procedural MI and stroke by Baseline BMI quintiles.

Baseline BMI Quintiles	Q1	Q2	Q3	Q4	Q5	Interaction
BMI Range	18<=BMI<27	27<=BMI<30	30<=BMI<32	32<=BMI<36	36<=BMI<66	
Events/N in Quintile at baseline*	71/460	72/462	64/465	75/465	80/458	
	HR (95% CI)	P				
Baseline Log leptin	0.8 (0.6, 1.0)	1.0 (0.8, 1.4)	0.6 (0.4, 0.8)	1.1 (0.7, 1.8)	1.4 (0.9, 2.0)	.03
Change from Baseline Log leptin	0.8 (0.6, 1.0)	1.0 (0.7, 1.3)	0.7 (0.5, 0.9)	0.6 (0.5, 0.9)	1.0 (0.7, 1.3)	.06
Baseline Log adiponectin	1.7 (1.2, 2.2)	1.1 (0.8, 1.6)	1.3 (0.9, 1.7)	0.7 (0.5, 0.9)	1.4 (1.1, 1.9)	.01
Change from Baseline Log adiponectin	0.9 (0.6, 1.3)	0.9 (0.6, 1.2)	1.2 (0.9, 1.7)	1.0 (0.7, 1.4)	1.0 (0.7, 1.4)	.69
Baseline Log MCP-1	1.1 (0.8, 1.4)	1.0 (0.7, 1.3)	0.8 (0.6, 1.0)	1.0 (0.8, 1.3)	0.8 (0.6, 1.1)	.71
Change from Baseline Log MCP-1	1.8 (1.2, 2.7)	1.1 (0.8, 1.6)	0.8 (0.6, 1.1)	0.8 (0.6, 1.1)	1.0 (0.7, 1.4)	.03
Baseline Log leptin/adiponectin	0.7 (0.6, 0.9)	1.0 (0.7, 1.3)	0.6 (0.5, 0.9)	1.5 (1.0, 2.3)	0.9 (0.6, 1.2)	.03
Change from Baseline Log leptin/adiponectin	0.8 (0.6, 1.1)	1.1 (0.7, 1.5)	0.7 (0.5, 0.9)	0.7 (0.5, 0.9)	1.0 (0.7, 1.4)	.06

Baseline Log leptin/BMI	0.8 (0.7, 1.0)	1.0 (0.8, 1.3)	0.7 (0.5, 0.9)	1.2 (0.8, 1.8)	1.3 (0.9, 1.8)	.04
Change from Baseline Log leptin/BMI	0.8 (0.7, 1.1)	1 (0.7, 1.4)	0.8 (0.6, 1.1)	0.6 (0.4, 0.9)	0.9 (0.6, 1.2)	.18
Baseline Log TNF- α	1.6 (1.1, 2.3)	1.5 (1.1, 2.0)	1.1 (0.8, 1.5)	1.0 (0.7, 1.3)	1.2 (0.9, 1.6)	.26
Change from Baseline Log TNF- α	1.2 (1.0, 1.5)	1.4 (1.1, 1.8)	1.0 (0.7, 1.2)	0.9 (0.7, 1.2)	1.3 (1.1, 1.5)	.02
Baseline Log CRP	1.5 (1.1, 2.0)	1.8 (1.3, 2.5)	1.7 (1.3, 2.4)	1.7 (1.2, 2.3)	1.0 (0.7, 1.4)	.06
Change from Baseline Log CRP	1.1 (0.8, 1.5)	1.7 (1.2, 2.2)	1.4 (0.9, 2.0)	1.5 (1.1, 2.0)	1.4 (1.0, 2.0)	.47
Baseline Log IL-6	1.8 (1.3, 2.6)	1.5 (1.1, 2.1)	1.2 (0.9, 1.5)	1.2 (0.9, 1.7)	1.1 (0.8, 1.6)	0.29
Change from Baseline Log IL-6	1.1 (0.8, 1.6)	1.8 (1.3, 2.6)	0.7 (0.5, 0.9)	1.1 (0.8, 1.5)	1.2 (0.9, 1.5)	0.005

All models fully adjusted.

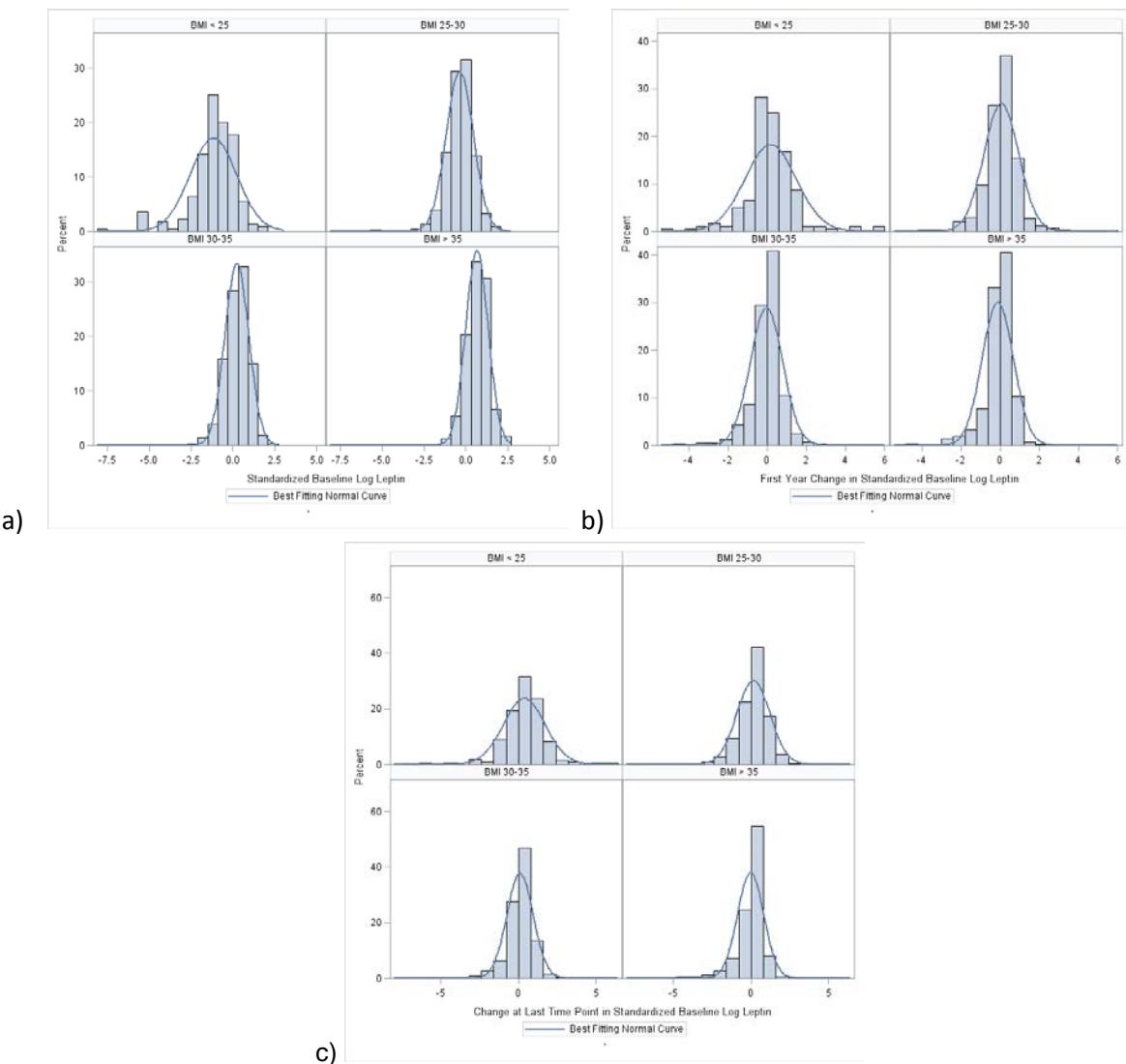
* There were 20 people missing baseline BMI measures, two of which had events. Thus this table represents 2310 participants and 362 events.

Table 4S. Effect of adipokines on the composite endpoint of CV death, non-procedural MI and stroke by leptin/adiponectin quintiles.

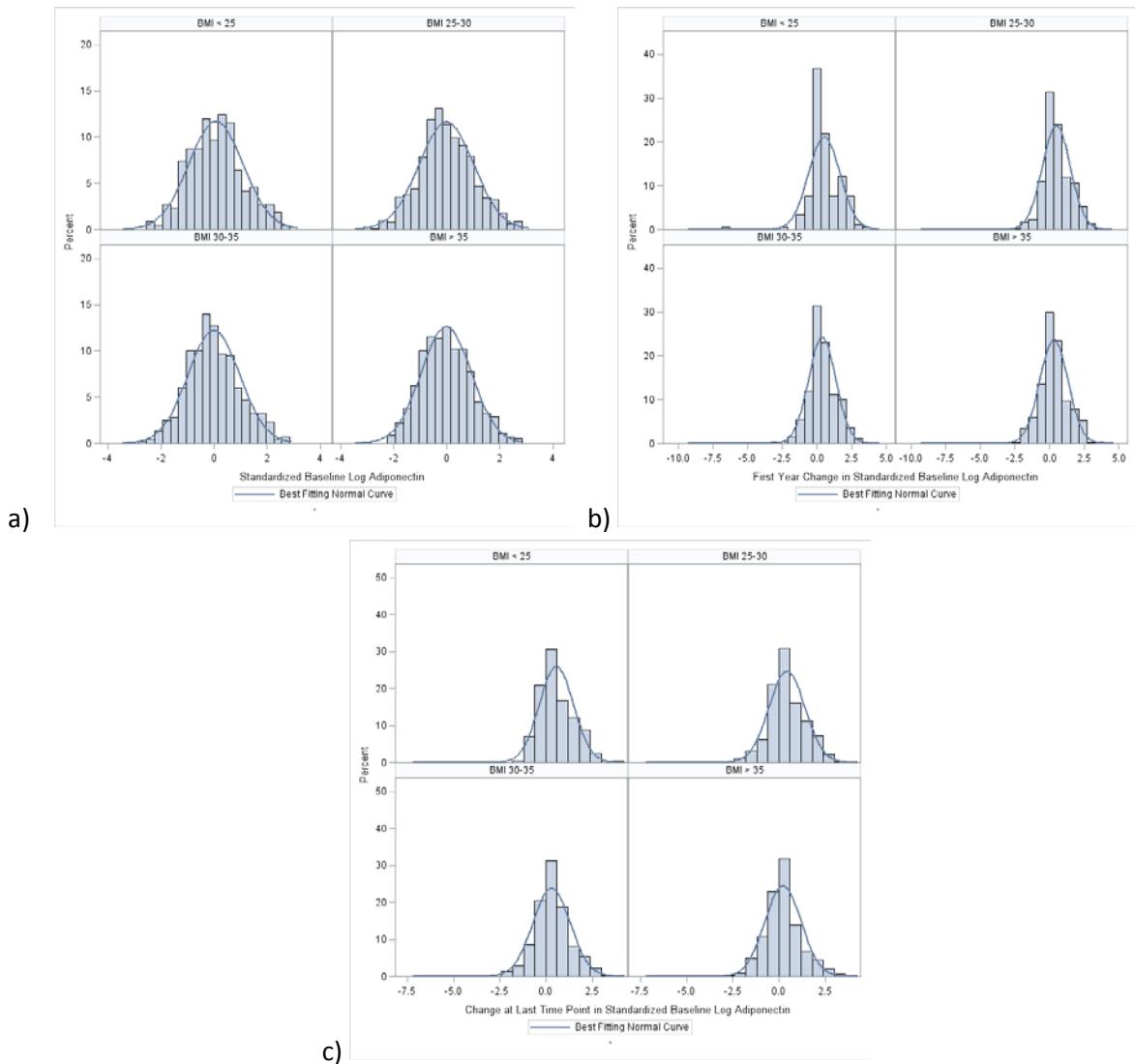
Leptin/Adiponectin Quintiles	Q1	Q2	Q3	Q4	Q5	
	Men: 0.001-1.1	Men: 1.1-2.2	Men: 2.2-4.1	Men: 4.1-7.3	Men: 7.4-116.7	Inter-action
	Women: 0.001-2.2	Women: 2.2-4.3	Women: 4.3-7.5	Women: 7.5-12.5	Women: 12.5-111.2	
Quintile Ranges	0.001-2.2	2.2-4.3	4.3-7.5	7.5-12.5	12.5-111.2	
Events/N in Quintile at baseline	86/476 HR (95% CI)	71/464 HR (95% CI)	56/464 HR (95% CI)	64/462 HR (95% CI)	87/464 HR (95% CI)	P
Baseline Log leptin	0.7 (0.6, 0.9)	1.1 (0.6, 2.0)	1.7 (0.9, 3.1)	1.3 (0.7, 2.3)	1.1 (0.6, 1.8)	.008
Change from Baseline Log leptin	0.8 (0.7, 1.0)	0.8 (0.6, 1.2)	0.7 (0.5, 1.1)	0.9 (0.6, 1.3)	0.9 (0.7, 1.1)	.98
Baseline Log adiponectin	1.2 (0.9, 1.7)	1.1 (0.8, 1.7)	1.8 (1.1, 2.9)	1.2 (0.8, 1.7)	1.0 (0.7, 1.3)	.62
Change from Baseline Log adiponectin	1.1 (0.8, 1.6)	1.0 (0.7, 1.4)	1.2 (0.9, 1.7)	0.9 (0.6, 1.3)	0.9 (0.7, 1.2)	.35
Baseline Log MCP-1	1.2 (0.9, 1.6)	1.0 (0.7, 1.4)	1.1 (0.8, 1.6)	0.9 (0.7, 1.2)	0.7 (0.6, 0.9)	.14
Change from Baseline Log MCP-1	1.6 (1.2, 2.3)	1.0 (0.7, 1.6)	1.1 (0.7, 1.8)	1.1 (0.8, 1.6)	0.8 (0.6, 1.0)	.02
Baseline Log leptin/adiponectin	0.7 (0.5, 0.9)	0.9 (0.2, 4.7)	0.3 (0.0, 2.3)	2.1 (0.2, 18.0)	1.3 (0.7, 2.6)	.95

Change from Baseline Log leptin/adiponectin	0.8 (0.6, 1.0)	0.9 (0.6, 1.3)	0.7 (0.5, 1.1)	1.0 (0.6, 1.5)	0.9 (0.7, 1.1)	.53
Baseline Log leptin/BMI	0.8 (0.6, 0.9)	1.2 (0.7, 2.1)	1.9 (1.1, 3.4)	1.4 (0.8, 2.4)	1.0 (0.7, 1.6)	.01
Change from Baseline Log leptin/BMI	1.0 (0.8, 1.2)	0.8 (0.5, 1.2)	0.6 (0.4, 1.0)	0.9 (0.6, 1.5)	0.8 (0.6, 1.0)	.43
Baseline Log TNF- α	1.3 (1.0, 1.7)	1.5 (1.0, 1.2)	1.2 (0.9, 1.6)	1.0 (0.7, 1.4)	1.3 (1.0, 1.6)	.46
Change from Baseline Log TNF- α	1.3 (1.0, 1.6)	1.2 (1.0, 1.4)	1.1 (0.8, 1.4)	1.3 (0.9, 1.7)	1.2 (1.0, 1.4)	.91
Baseline Log CRP	2.1 (1.6, 2.8)	1.2 (0.9, 1.7)	1.5 (1.0, 2.1)	1.5 (1.1, 2.2)	1.1 (0.8, 1.5)	.007
Change from Baseline Log CRP	1.6 (1.2, 2.1)	1.1 (0.8, 1.6)	1.4 (1.0, 2.0)	1.5 (1.1, 2.2)	1.1 (0.8, 1.4)	.03
Baseline Log IL-6	1.6 (1.2, 2.1)	1.3 (1.0, 1.7)	1.6 (1.1, 2.5)	1.1 (0.7, 1.5)	1.2 (0.9, 1.6)	.51
Change from Baseline Log IL-6	1.2 (0.9, 1.6)	1.1 (0.8, 1.4)	1.3 (0.9, 1.9)	1.2 (0.9, 1.7)	1.1 (0.8, 1.3)	.45

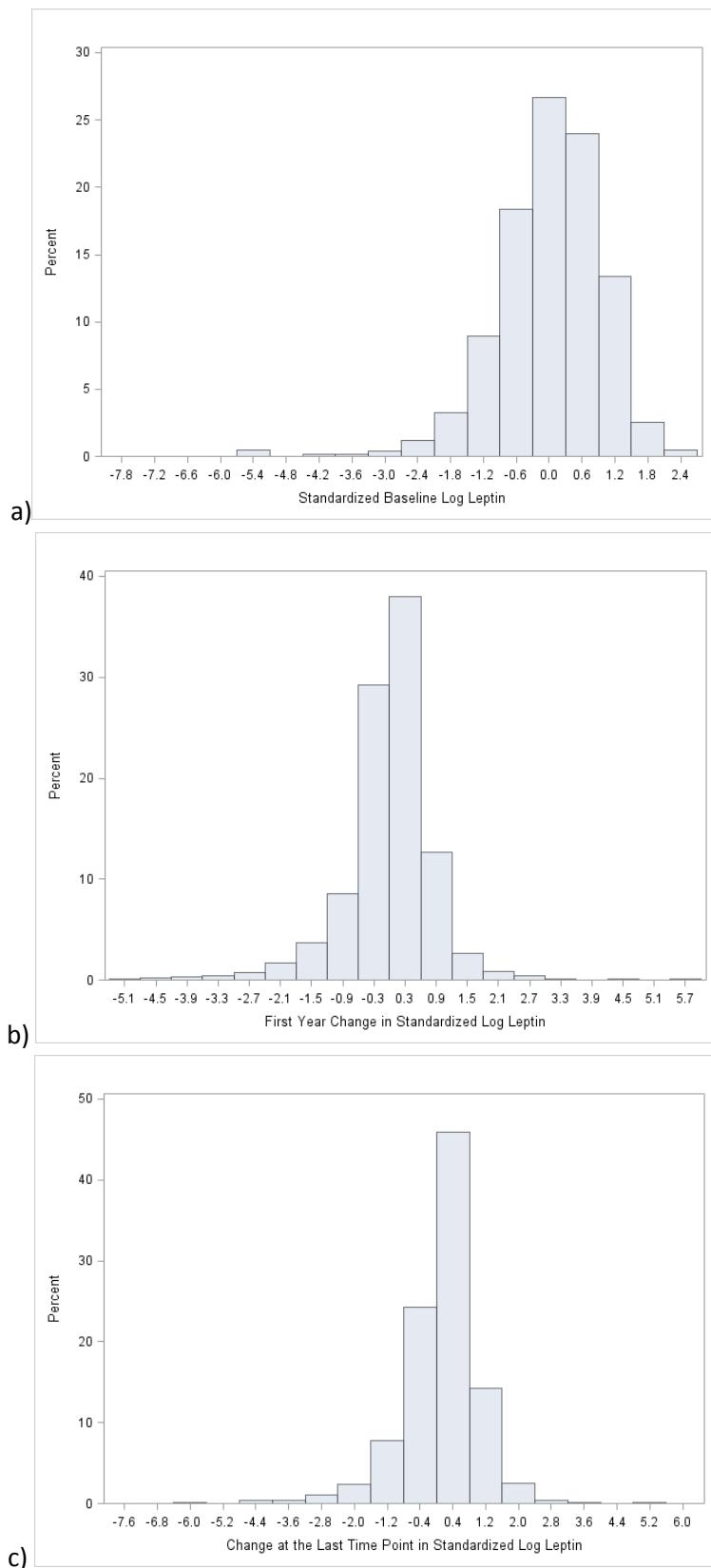
Supplementary Figure 1. Distribution of the Standardized Log Leptin value by BMI quintile at Baseline (a), Year 1 (b), and the Last Time Point (c).



Supplementary Figure 2. Distribution of the Standardized Log Adiponectin value by BMI quintile at Baseline (a), Year 1 (b), and at the Last Time Point (c).



Supplementary Figure 3. Standardized Baseline Log Leptin (a) and Change from Standardized Baseline Log Leptin at Year 1 (b) and at the Last Time Point (c).



Supplementary Figure 4. Standardized Baseline Log Adiponectin (a) and Change from Standardized Baseline Log Adiponectin at Year 1 (b) and at the Last Time Point (c).

