

CONFIDENTIAL

CRCTU Birmingham

A 48-WEEK PHASE II, RANDOMISED, DOUBLE BLINDED
PLACEBO CONTROLLED, PARALLEL-GROUP,
MULTI-CENTRE TRIAL ON LIRAGLUTIDE'S SAFETY,
EFFICACY AND ACTION ON LIVER HISTOLOGY AND
METABOLISM IN OVERWEIGHT PATIENTS WITH
NON-ALCOHOLIC STEATOHEPATITIS, WITH OR WITHOUT
TYPE II DIABETES

Liraglutide Efficacy and Action in Non-alcoholic
steatohepatitis

The word "LEAN" is written in a large, blue, serif font. The letters have a slight 3D effect with a dark blue shadow beneath them.

Prepared by:
Piers Gaunt

Senior Statistician

EudraCT number:
CRCTU reference Number:
ISRCTN number:
Clinicaltrials.gov identifier:

2009-016761-29
HE2013
ISRCTN8577427
NCT01237119

Data For Questionnaires (SF36 and Food/Alcohol)

Contents

1	Questionnaires	1
1.1	The SF36 v2 Health Survey	2
2	Food Questionnaire results	14

1 Questionnaires

At visits 1 (Baseline) 7 (End of Treatment) and 8 (3 month Follow Up) questionnaires were to be completed. A total of 45 patients were in the study at the end of the trial (23 on liraglutide and 22 on placebo). These were the SF36v2 quality of life questionnaire, the Alcohol audit questionnaire and the Food Frequency Questionnaire (FFQ). If a form was not completed then a reason was requested.

The SF36v2 questionnaire was not reported as completed at visit 8 for 3 patients on placebo medication. The reasons were (i) that the patient did not attend (n=2) and (ii) that it was requested from the trial centre but never arrived at site.

The FFQ was reported as not completed at visit 8 for 2 patients on liraglutide. The reasons provided were (i) patient decision and (ii) institutional error. The FFQ was reported as not completed at visit 7 for 2 patients and visit 8 for 4 patients on placebo. The reasons provided for visit 7 were not known (n=2) and for visit 8 were (i) not appropriate (patient was in low mood and unwilling) (ii) that it was requested from the trial centre but never arrived at site and (iii) that the patient did not attend (n=2). The alcohol audit questionnaire was reported as not completed at visit 8 for 2 patients on placebo as they did not attend.

Table 1.1: Questionnaire completion by timepoint

	Baseline (N=52)	End of Treatment (N=45)	3month follow up (N=45)
SF36v2 QoL			
Liraglutide	26	23	23
Placebo	26	22	19
FFQ			
Liraglutide	26	23	21
Placebo	26	20	18
Alcohol Audit			
Liraglutide	26	23	23
Placebo	26	22	20

1.1 The SF36 v2 Health Survey

The N numbers at the top of the tables indicate the number of patients completing all or part of the SF36 v2 Health Survey. The N numbers within the table indicate (for that measure) the number of patients that a score could be determined for. NB: At the follow up visit 8 (3 months post end of treatment) one patient (TNO 28) on Liraglutide did not answer sufficient questions within the Health Survey to enable calculation of some of the individual scales and therefore directly both their overall Physical and Mental Component Summary scores.

The summary data and charts reported here are for the Physical and Mental Component Summary scores.

Table 1.2: SF36 Physical Component Summary by treatment and Visit Number

	Liraglutide			
	1 (N=26)	7 (N=23)	8 (N=22)	Overall (N=71)
PCS				
N	26	23	21	70
Mean (SD)	45 (11)	48 (9)	45 (11)	46 (11)
Median	46	47	45	46
IQR	42, 53	40, 57	39, 54	40, 54
Range	16, 58	30, 61	20, 58	16, 61

	Placebo			
	1 (N=26)	7 (N=22)	8 (N=19)	Overall (N=67)
PCS				
N	26	22	19	67
Mean (SD)	40 (13)	39 (12)	37 (10)	39 (12)
Median	44	39	35	38
IQR	31, 51	31, 48	31, 43	31, 48
Range	15, 63	10, 58	20, 57	10, 63

Figure 1.1: SF36 Physical Component Summary (PCS) Charts

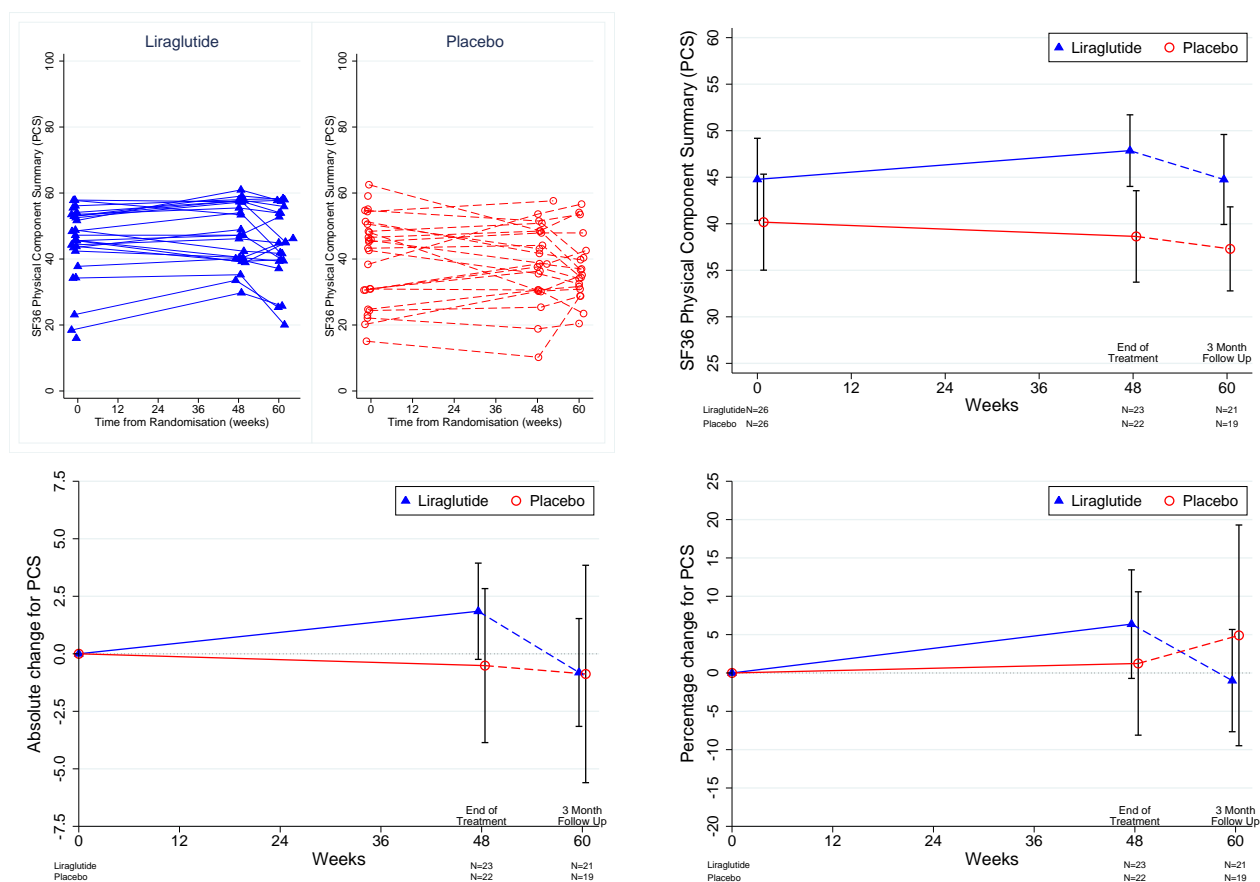


Table 1.3: SF36 Mental Component Summary by treatment and Visit Number

	Liraglutide			
	1 (N=26)	7 (N=23)	8 (N=22)	Overall (N=71)
MCS				
N	26	23	21	70
Mean (SD)	51 (10)	48 (12)	46 (12)	49 (11)
Median	54	53	51	54
IQR	50, 58	34, 57	37, 55	40, 56
Range	27, 61	27, 61	22, 62	22, 62

	Placebo			
	1 (N=26)	7 (N=22)	8 (N=19)	Overall (N=67)
MCS				
N	26	22	19	67
Mean (SD)	45 (14)	41 (16)	40 (16)	42 (15)
Median	47	43	41	44
IQR	33, 56	26, 56	24, 53	29, 55
Range	20, 67	14, 64	11, 63	11, 67

Figure 1.2: SF36 Mental Component Summary (MCS) Charts

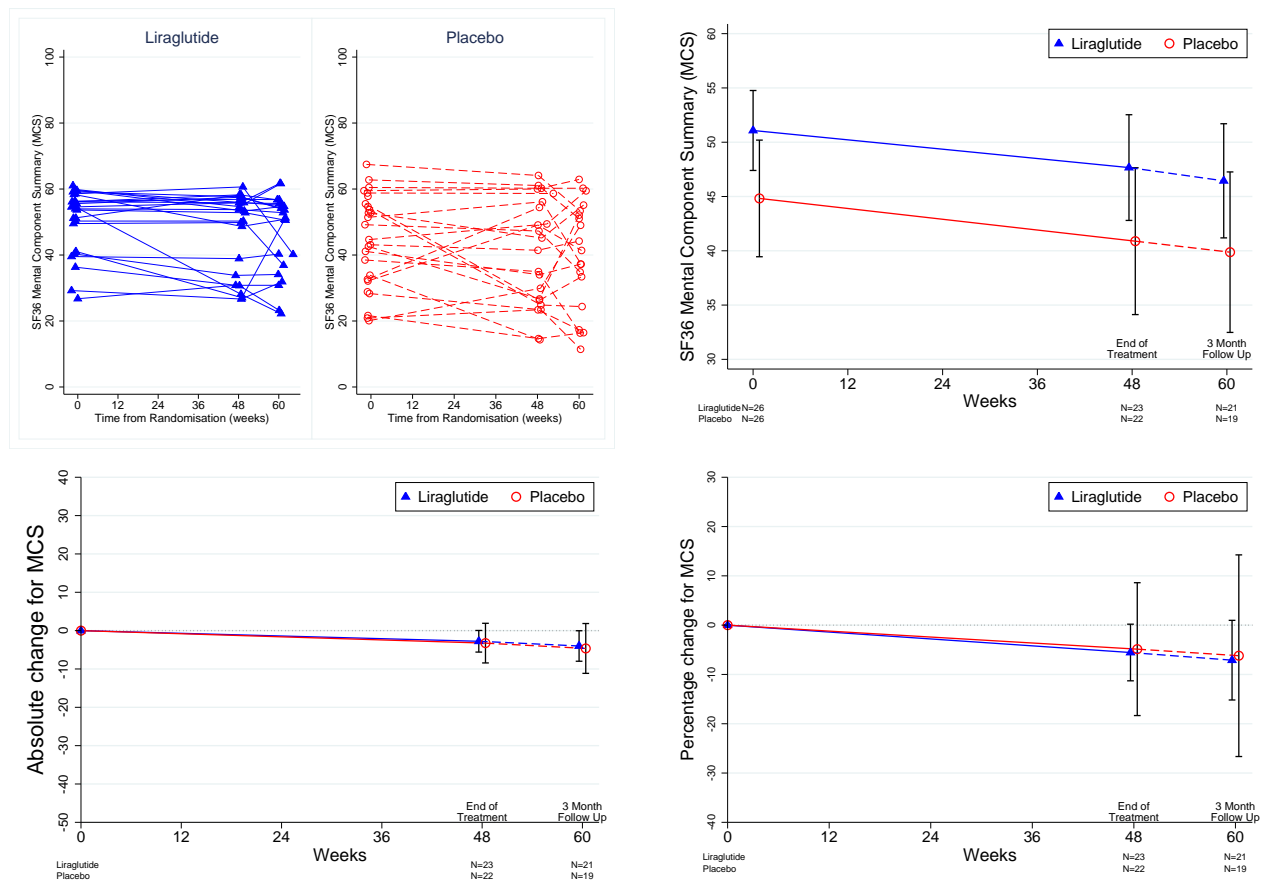


Table 1.4: SF36 Questionnaire changes in scores from baseline to 48 weeks (end of treatment visit)

	Liraglutide (N=26)	Placebo (N=26)	*Adjusted Change from baseline (95%CI)	p-value
Physical Component Summary (PCS)	1.85 (5.12) N=23	-0.51 (8.01) N=22	4.05 (0.20, 7.90)	0.04
Mental Component Summary (MCS)	-2.78 (6.90) N=23	-3.26 (12.37) N=22	1.50 (-4.64, 7.65)	0.62
Physical Functioning (PF)	5.87 (16.28) N=23	-2.15 (17.08) N=22	12.29 (3.19, 21.39)	0.009
Role Physical (RP)	2.17 (19.00) N=23	-1.70 (33.19) N=22	11.55 (-3.71, 26.80)	0.13
Bodily Pain (BP)	1.00 (10.85) N=23	-7.18 (21.10) N=22	12.70 (2.84, 22.56)	0.01
General Health (GH)	-0.26 (14.73) N=23	-1.70 (13.01) N=22	3.57 (-4.28, 11.41)	0.36
Vitality (VT)	-6.79 (12.05) N=23	-3.98 (18.23) N=22	0.19 (-9.38, 9.77)	0.97
Social Functioning (SF)	-1.63 (15.22) N=23	-3.98 (29.22) N=22	7.13 (-6.69, 20.96)	0.30
Role Emotional (RE)	1.45 (15.00) N=23	-4.92 (35.60) N=22	10.54 (-4.71, 25.79)	0.17
Mental Health (MH)	-5.00 (14.77) N=23	-7.05 (18.17) N=22	4.01 (-6.31, 14.34)	0.44

Data are Mean (SD) and N numbers.

*Change from baseline and p-values determined from linear regression analysis using the baseline characteristic score and treatment as covariates

Table 1.5: SF36 Physical Functioning (PF) Summary by treatment and Visit Number

	Liraglutide			
	1 (N=26)	7 (N=23)	8 (N=22)	Overall (N=71)
PF				
N	26	23	22	71
Mean (SD)	73 (28)	81 (19)	74 (26)	76 (25)
Median	82	90	81	85
IQR	70, 95	70, 100	70, 90	70, 95
Range	10, 100	30, 100	15, 100	10, 100

	Placebo			
	1 (N=26)	7 (N=22)	8 (N=19)	Overall (N=67)
PF				
N	26	22	19	67
Mean (SD)	62 (33)	59 (29)	54 (28)	59 (30)
Median	73	65	60	60
IQR	35, 90	35, 85	35, 70	35, 85
Range	0, 100	0, 95	0, 100	0, 100

Figure 1.3: SF36 Physical Functioning (PF) Score Charts

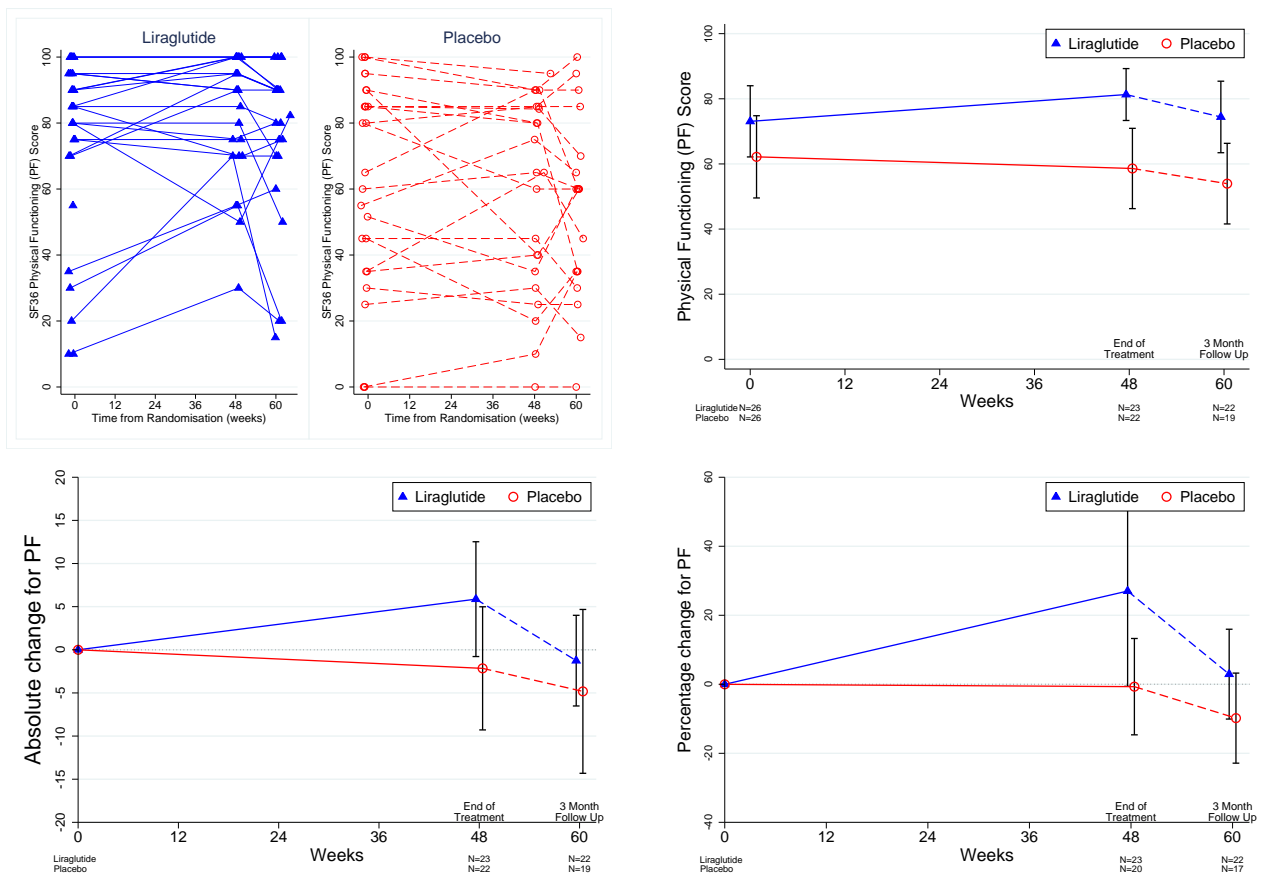


Table 1.6: SF36 Role Physical (RP) Summary by treatment and Visit Number

RP	Liraglutide			
	1 (N=26)	7 (N=23)	8 (N=22)	Overall (N=71)
N	26	23	22	71
Mean (SD)	76 (34)	79 (29)	72 (28)	76 (30)
Median	94	100	75	88
IQR	69, 100	50, 100	50, 100	50, 100
Range	0, 100	19, 100	19, 100	0, 100

RP	Placebo			
	1 (N=26)	7 (N=22)	8 (N=19)	Overall (N=67)
N	26	22	19	67
Mean (SD)	59 (37)	54 (36)	51 (37)	55 (37)
Median	63	63	50	63
IQR	25, 100	13, 81	19, 88	19, 88
Range	0, 100	0, 100	0, 100	0, 100

Figure 1.4: SF36 Role Physical (RP) Score Charts

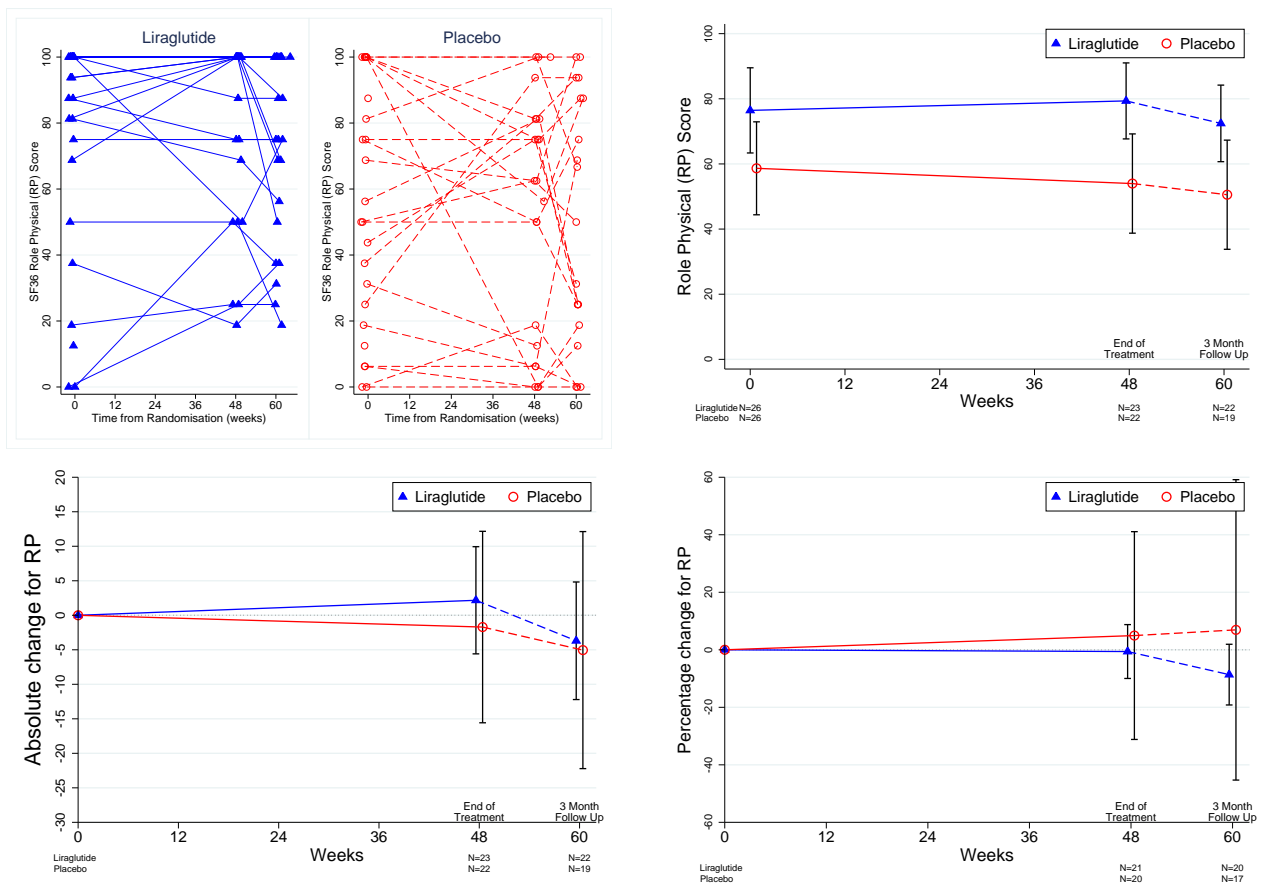


Table 1.7: SF36 Bodily Pain (BP) Summary by treatment and Visit Number

Liraglutide				
	1 (N=26)	7 (N=23)	8 (N=22)	Overall (N=71)
BP				
N	26	23	21	70
Mean (SD)	69 (29)	73 (25)	66 (30)	70 (28)
Median	79	74	74	74
IQR	51, 100	61, 100	41, 100	51, 100
Range	12, 100	22, 100	20, 100	12, 100

Placebo				
	1 (N=26)	7 (N=22)	8 (N=19)	Overall (N=67)
BP				
N	26	22	19	67
Mean (SD)	56 (30)	46 (27)	40 (26)	48 (28)
Median	62	41	41	41
IQR	31, 84	24, 62	21, 52	24, 72
Range	0, 100	0, 100	0, 100	0, 100

Figure 1.5: SF36 Bodily Pain (BP) Score Charts

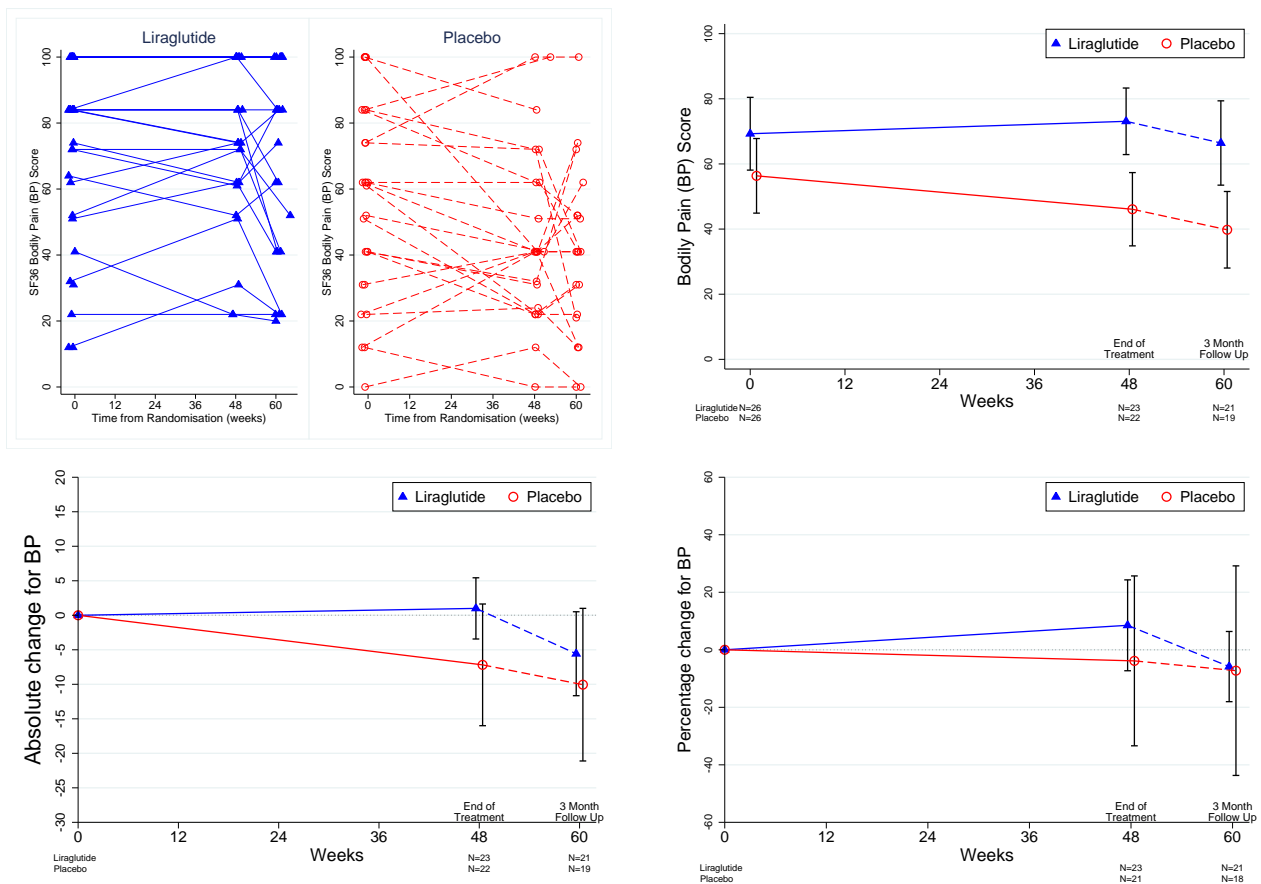


Table 1.8: SF36 General Health (GH) Summary by treatment and Visit Number

Liraglutide				
	1 (N=26)	7 (N=23)	8 (N=22)	Overall (N=71)
GH				
N	26	23	22	71
Mean (SD)	54 (24)	55 (19)	51 (23)	53 (22)
Median	56	52	49	52
IQR	35, 72	42, 72	35, 67	37, 72
Range	10, 92	10, 87	10, 87	10, 92

Placebo				
	1 (N=26)	7 (N=22)	8 (N=19)	Overall (N=67)
GH				
N	26	22	19	67
Mean (SD)	49 (24)	45 (23)	44 (26)	46 (24)
Median	51	49	35	47
IQR	25, 67	25, 62	20, 67	25, 67
Range	10, 100	5, 87	5, 87	5, 100

Figure 1.6: SF36 General Health (GH) Score Charts

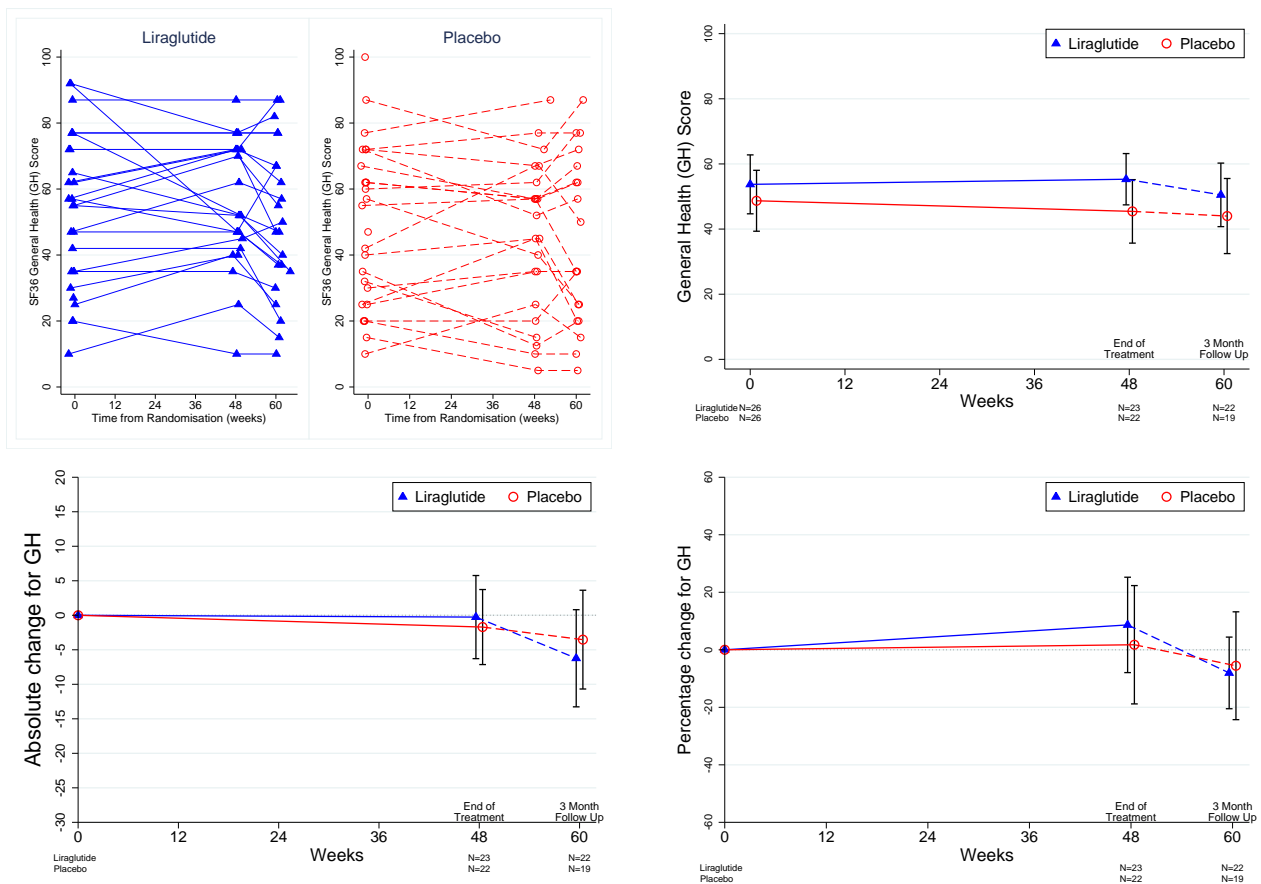


Table 1.9: SF36 Vitality (VT) Summary by treatment and Visit Number

	Liraglutide			
	1 (N=26)	7 (N=23)	8 (N=22)	Overall (N=71)
VT				
N	26	23	21	70
Mean (SD)	54 (23)	47 (25)	47 (26)	50 (25)
Median	56	44	44	50
IQR	38, 69	31, 69	19, 69	31, 69
Range	0, 88	0, 94	6, 88	0, 94

	Placebo			
	1 (N=26)	7 (N=22)	8 (N=19)	Overall (N=67)
VT				
N	26	22	19	67
Mean (SD)	40 (26)	33 (25)	35 (22)	36 (24)
Median	47	31	38	38
IQR	13, 63	13, 56	25, 50	13, 56
Range	0, 81	0, 88	0, 75	0, 88

Figure 1.7: SF36 Vitality (VT) Score Charts

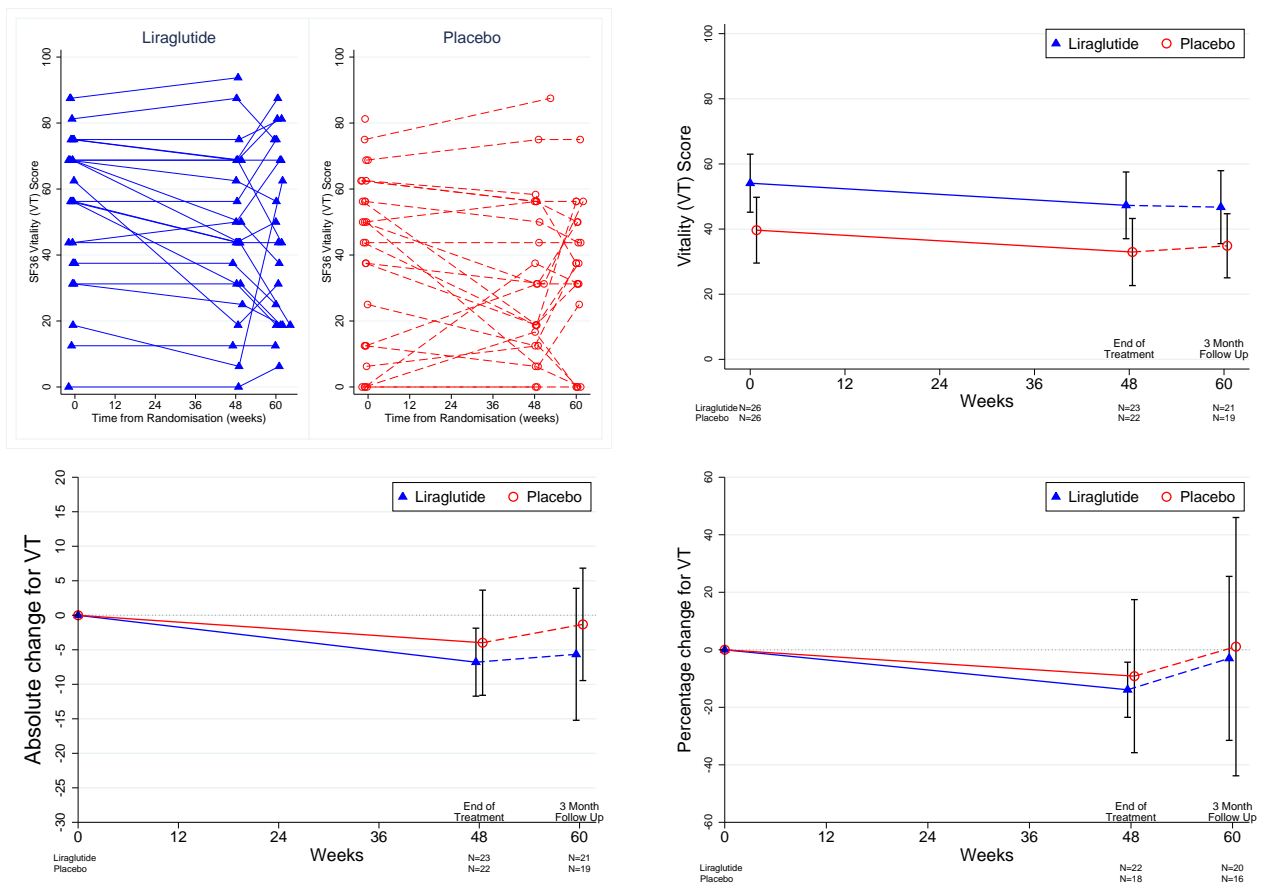


Table 1.10: SF36 Social Functioning (SF) Summary by treatment and Visit Number

Liraglutide				
	1 (N=26)	7 (N=23)	8 (N=22)	Overall (N=71)
SF				
N	26	23	22	71
Mean (SD)	81 (26)	80 (27)	73 (27)	78 (26)
Median	100	88	75	88
IQR	63, 100	63, 100	50, 100	63, 100
Range	13, 100	25, 100	25, 100	13, 100

Placebo				
	1 (N=26)	7 (N=22)	8 (N=19)	Overall (N=67)
SF				
N	26	22	19	67
Mean (SD)	64 (36)	59 (36)	59 (40)	61 (37)
Median	75	63	75	75
IQR	25, 100	25, 100	13, 100	25, 100
Range	0, 100	0, 100	0, 100	0, 100

Figure 1.8: SF36 Social Functioning (SF) Score Charts

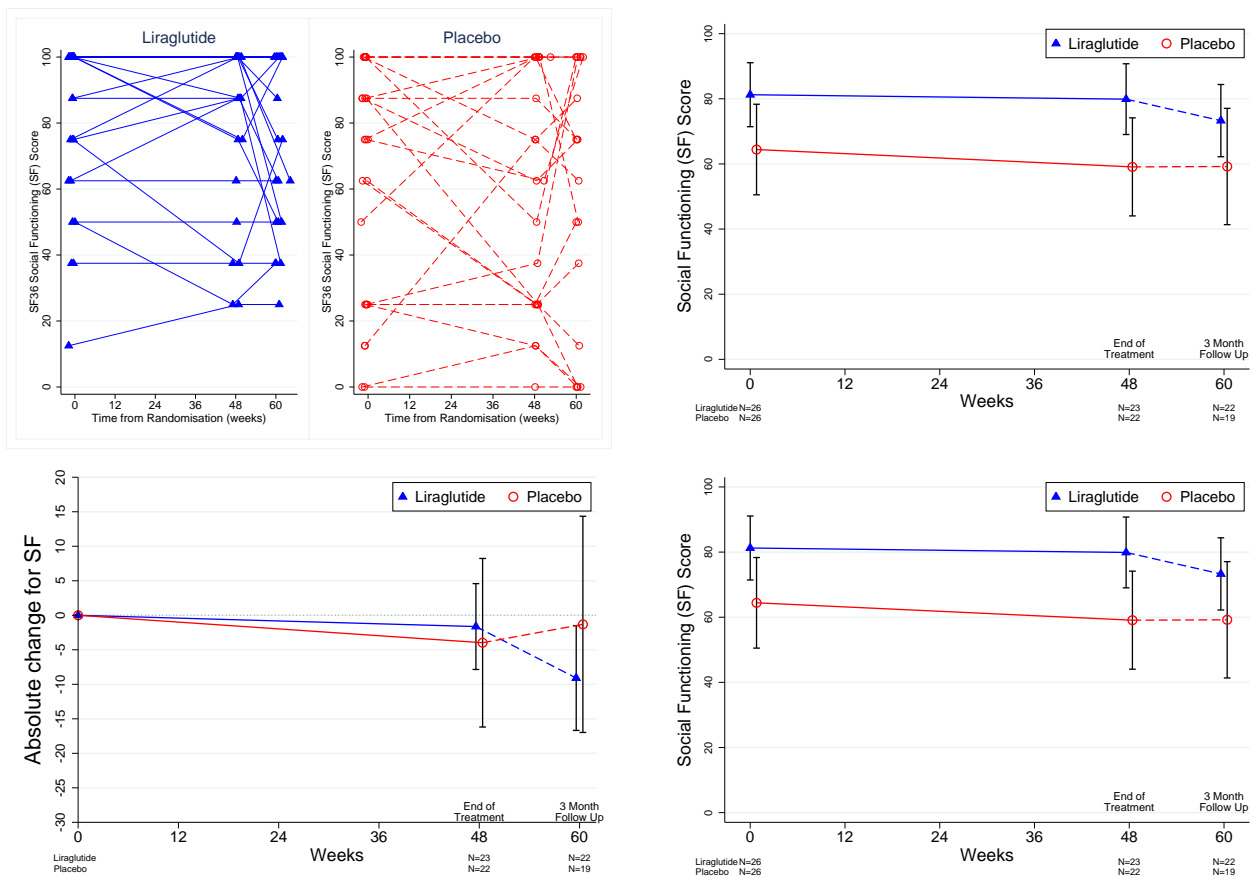


Table 1.11: SF36 Role Emotional (RE) Summary by treatment and Visit Number

RE	Liraglutide			
	1 (N=26)	7 (N=23)	8 (N=22)	Overall (N=71)
N	26	23	21	70
Mean (SD)	85 (27)	84 (26)	79 (28)	83 (27)
Median	100	100	100	100
IQR	83, 100	67, 100	50, 100	67, 100
Range	0, 100	25, 100	25, 100	0, 100

RE	Placebo			
	1 (N=26)	7 (N=22)	8 (N=19)	Overall (N=67)
N	26	22	19	67
Mean (SD)	73 (32)	67 (35)	59 (36)	67 (34)
Median	83	75	58	75
IQR	58, 100	50, 100	25, 92	42, 100
Range	0, 100	0, 100	0, 100	0, 100

Figure 1.9: SF36 Role Emotional (RE) Score Charts

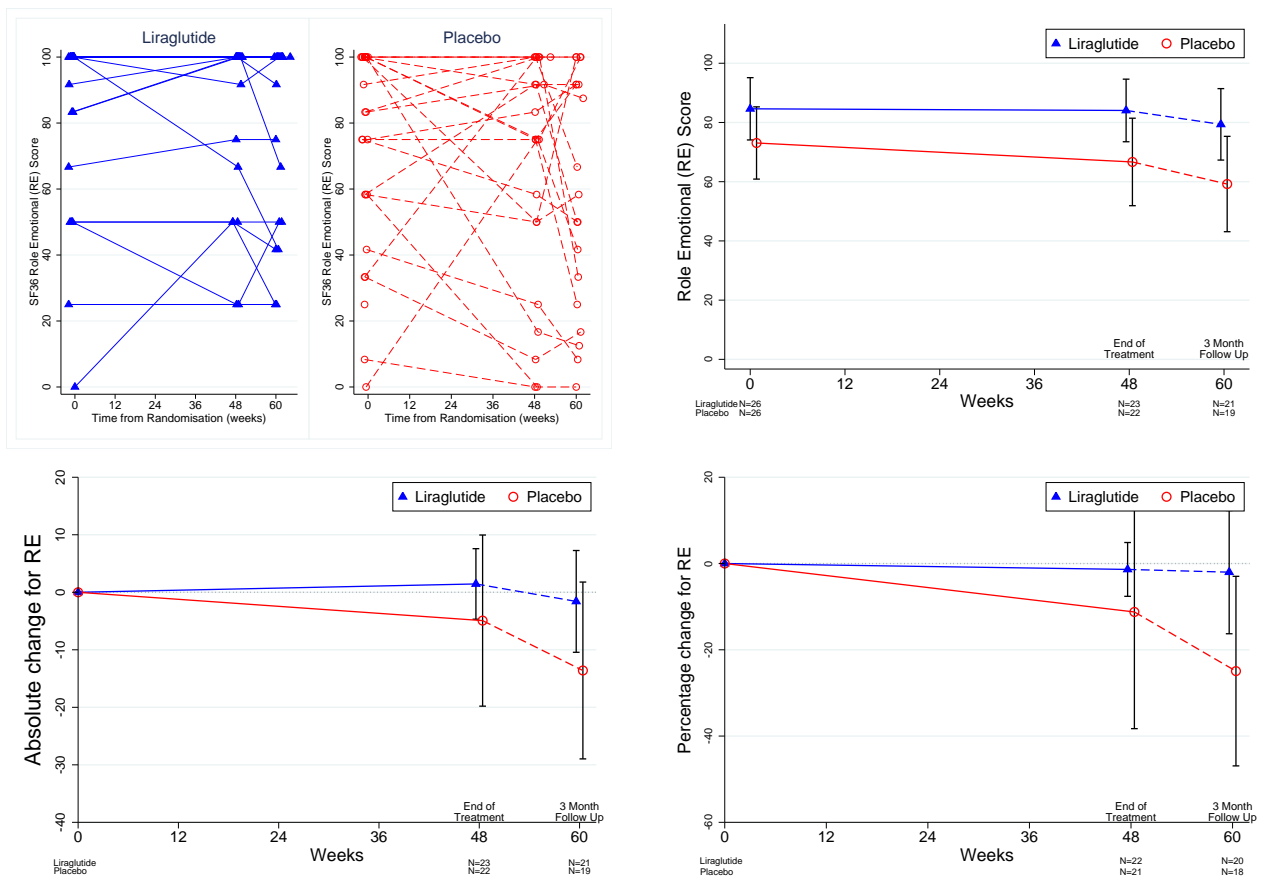
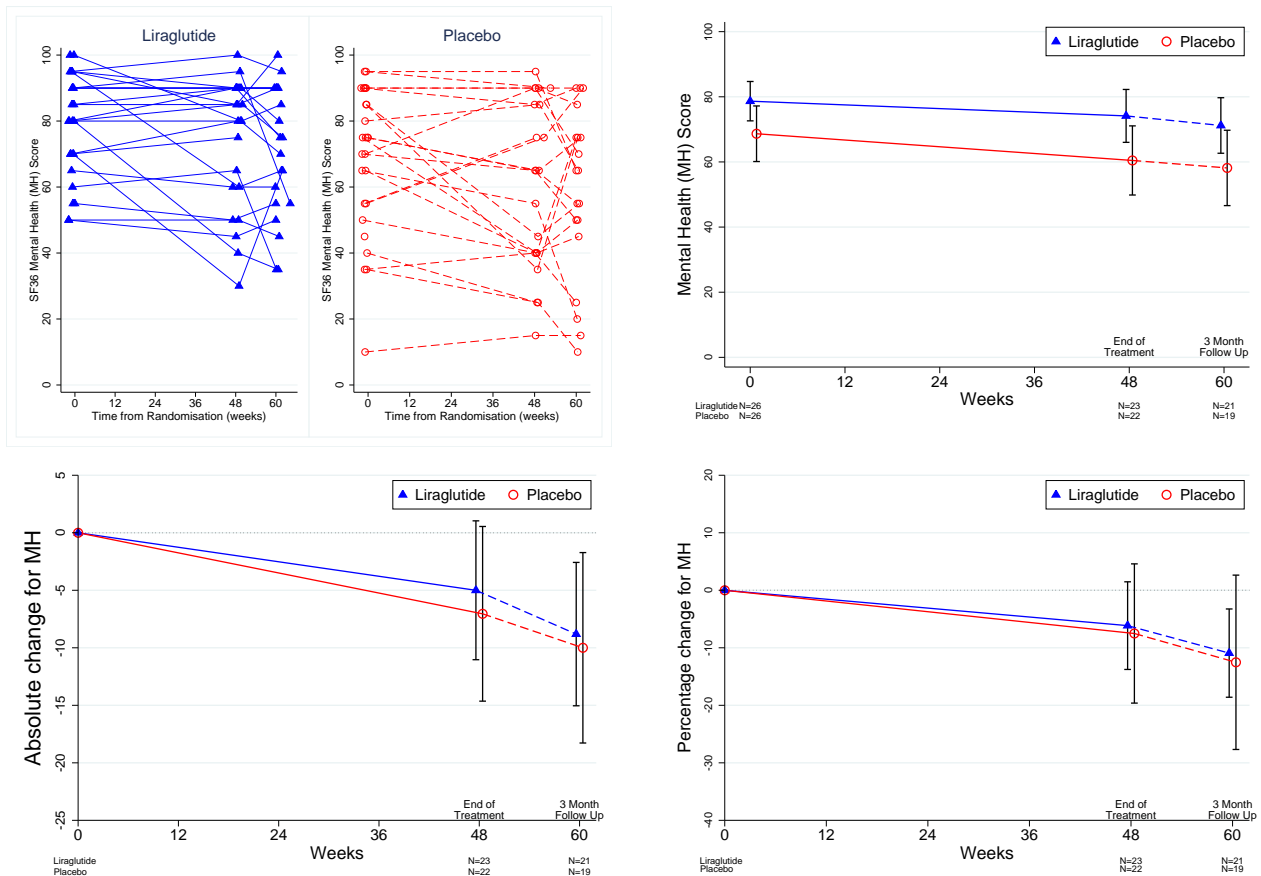


Table 1.12: SF36 Mental Health (MH) Summary by treatment and Visit Number

Liraglutide				
	1 (N=26)	7 (N=23)	8 (N=22)	Overall (N=71)
MH				
N	26	23	21	70
Mean (SD)	79 (16)	74 (20)	71 (20)	75 (18)
Median	80	80	75	80
IQR	70, 90	60, 90	55, 90	60, 90
Range	50, 100	30, 100	35, 100	30, 100

Placebo				
	1 (N=26)	7 (N=22)	8 (N=19)	Overall (N=67)
MH				
N	26	22	19	67
Mean (SD)	69 (22)	60 (25)	58 (26)	63 (24)
Median	75	65	65	65
IQR	55, 90	40, 85	45, 75	45, 85
Range	10, 95	15, 95	10, 90	10, 95

Figure 1.10: SF36 Mental Health (MH) Score Charts



2 Food Questionnaire results

Table 2.1: Calories (KCal) by treatment and Visit Number

	Baseline (N=52)		End of Treatment (N=52)		3 Month Follow Up (N=52)	
	Liraglutide (N=26)	Placebo (N=26)	Liraglutide (N=26)	Placebo (N=26)	Liraglutide (N=26)	Placebo (N=26)
Calories (Kcal)						
N	26	25	23	21	21	18
Mean (SD)	1885 (700)	1926 (677)	1314 (476)	1628 (770)	1306 (494)	1437 (711)
Median	1807	1860	1236	1501	1299	1188
IQR	1379, 2402	1388, 2358	910, 1491	1320, 1935	979, 1614	1041, 1707
Range	456, 3413	829, 3602	714, 2813	469, 3720	278, 2438	601, 3383

Figure 2.1: Calories (Kcal) Charts

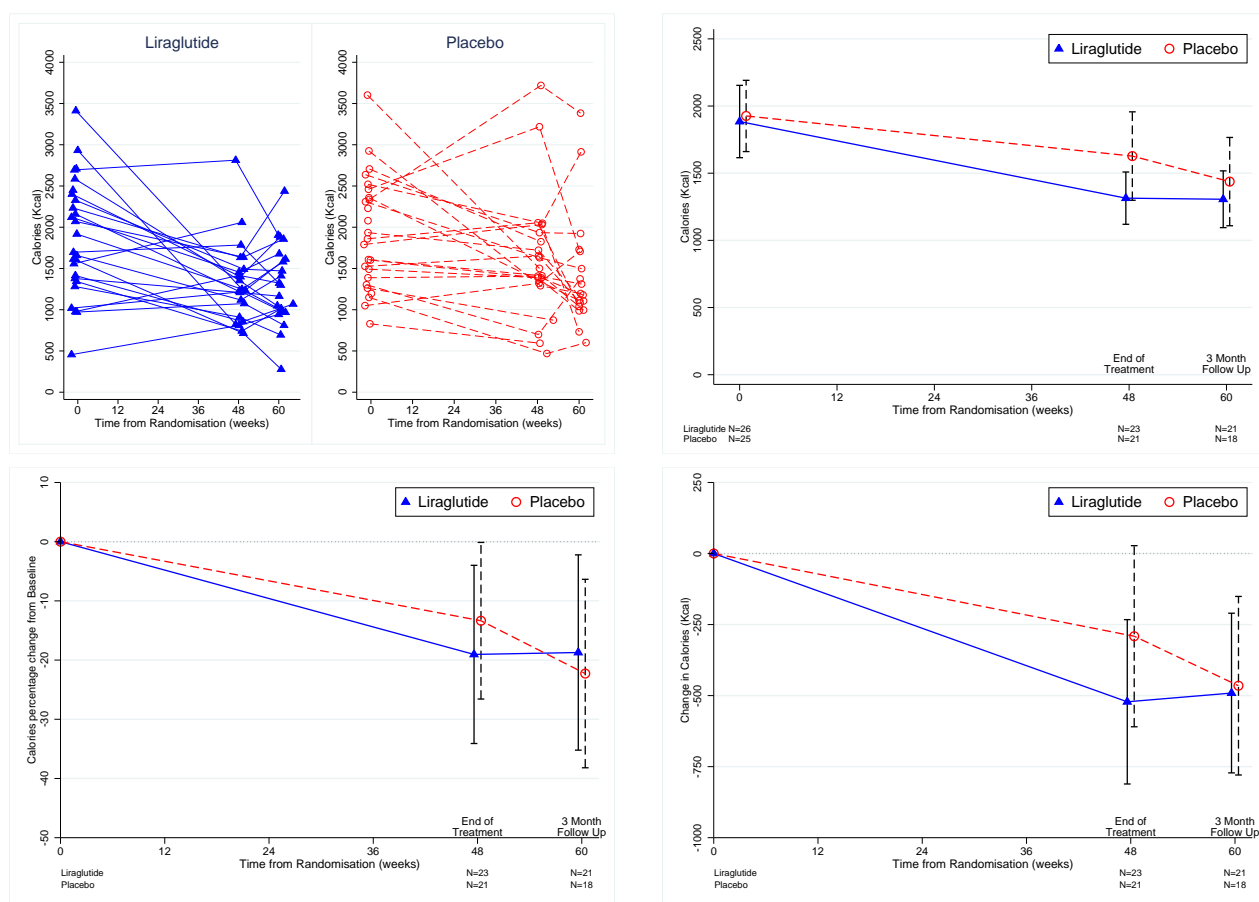


Table 2.2: Protein (g) by treatment and Visit Number

	Baseline (N=52)		End of Treatment (N=52)		3 Month Follow Up (N=52)	
	Liraglutide (N=26)	Placebo (N=26)	Liraglutide (N=26)	Placebo (N=26)	Liraglutide (N=26)	Placebo (N=26)
Protein (g)						
N	26	25	23	21	21	18
Mean (SD)	72 (34)	70 (25)	49 (19)	63 (32)	49 (22)	58 (23)
Median	74	68	50	57	41	53
IQR	44, 91	50, 83	36, 61	41, 80	30, 72	41, 67
Range	14, 163	32, 135	16, 97	19, 142	13, 80	21, 109

Figure 2.2: Protein (g) Charts

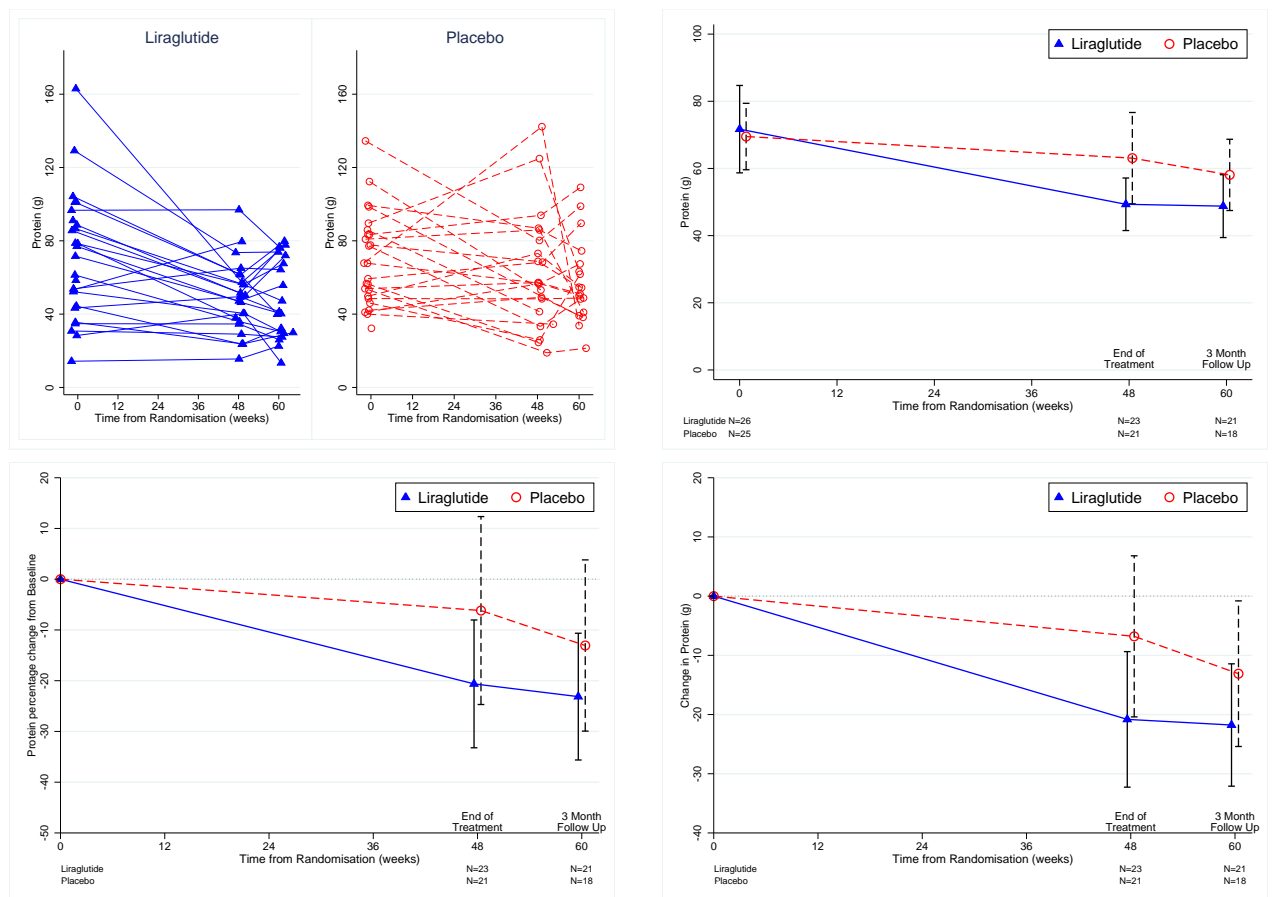


Table 2.3: Total Fat (g) by treatment and Visit Number

	Baseline (N=52)		End of Treatment (N=52)		3 Month Follow Up (N=52)	
	Liraglutide (N=26)	Placebo (N=26)	Liraglutide (N=26)	Placebo (N=26)	Liraglutide (N=26)	Placebo (N=26)
Total Fat (g)						
N	26	25	23	21	21	18
Mean (SD)	71 (30)	74 (35)	46 (15)	56 (33)	47 (18)	52 (25)
Median	69	67	42	47	44	44
IQR	49, 96	52, 87	34, 57	38, 66	37, 56	36, 67
Range	16, 142	27, 167	23, 75	18, 148	14, 81	28, 118

Figure 2.3: Total Fat (g) Charts

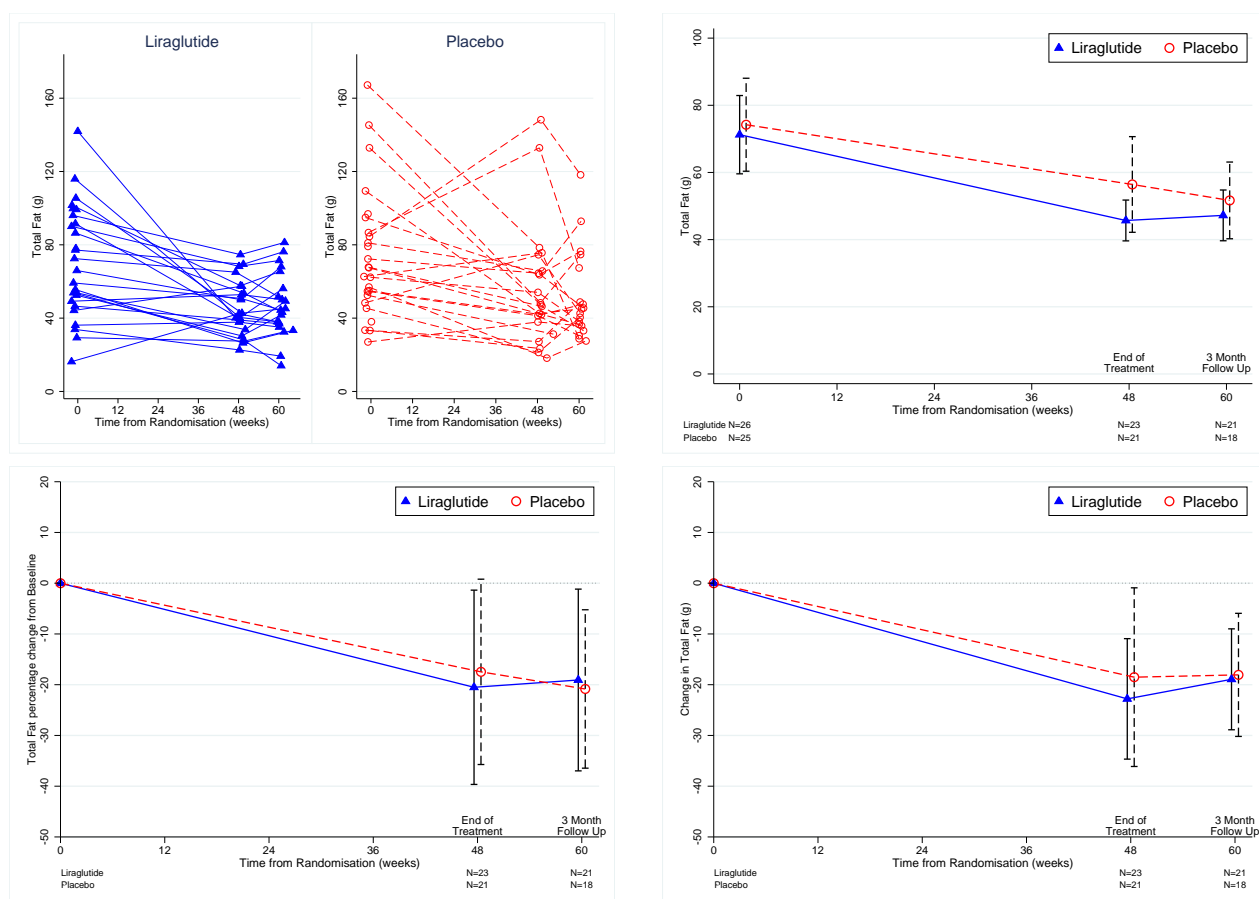


Table 2.4: Carbohydrate (g) by treatment and Visit Number

	Baseline (N=52)		End of Treatment (N=52)		3 Month Follow Up (N=52)	
	Liraglutide (N=26)	Placebo (N=26)	Liraglutide (N=26)	Placebo (N=26)	Liraglutide (N=26)	Placebo (N=26)
Carbohydrate (g)						
N	26	25	23	21	21	18
Mean (SD)	240 (87)	248 (89)	176 (91)	223 (111)	172 (80)	187 (114)
Median	235	256	156	202	163	141
IQR	188, 292	184, 317	119, 197	158, 265	109, 231	119, 209
Range	61, 447	88, 433	72, 496	59, 523	24, 348	70, 482

Figure 2.4: Carbohydrate (g)

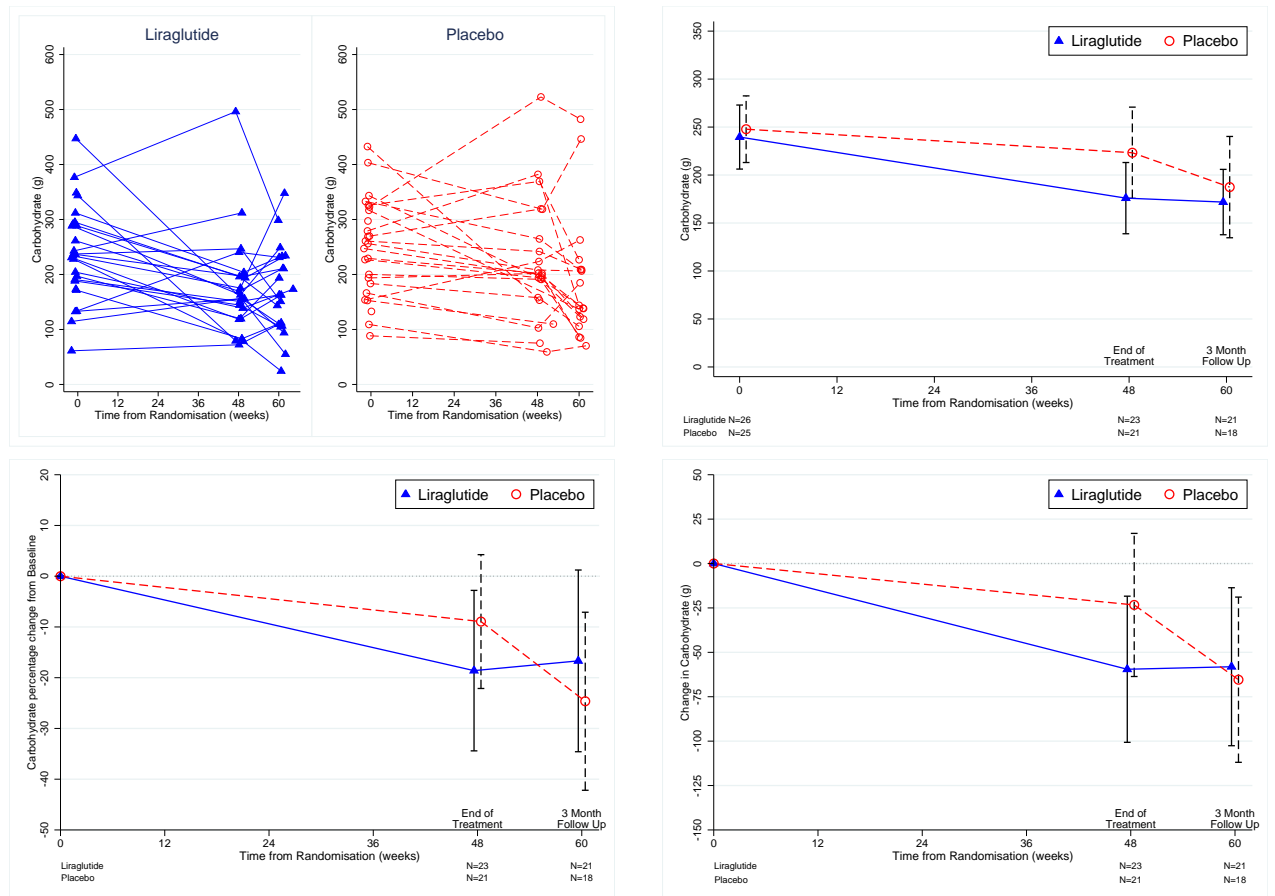


Table 2.5: Vitamin E a-TE by treatment and Visit Number

	Baseline (N=52)		End of Treatment (N=52)		3 Month Follow Up (N=52)	
	Liraglutide (N=26)	Placebo (N=26)	Liraglutide (N=26)	Placebo (N=26)	Liraglutide (N=26)	Placebo (N=26)
Vitamin E (a-TE)						
N	26	25	23	21	21	18
Mean (SD)	8 (3)	9 (4)	5 (2)	7 (5)	6 (2)	6 (3)
Median	8	8	6	6	5	6
IQR	6, 10	6, 11	4, 7	5, 9	4, 6	3, 7
Range	3, 15	4, 17	2, 9	2, 25	2, 10	3, 14

Figure 2.5: Vitamin E (a-TE) Charts

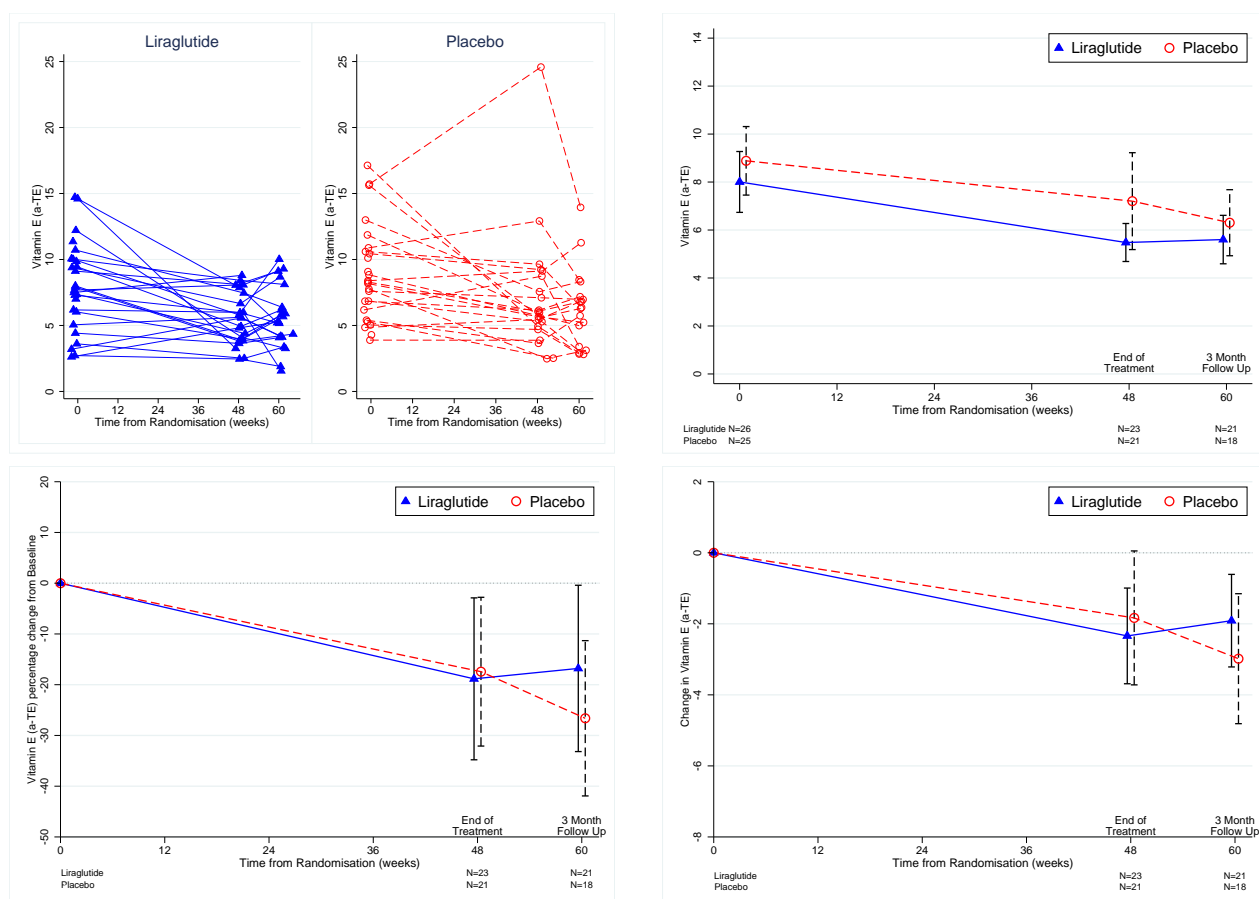


Table 2.6: Caffeine (mg) by treatment and Visit Number

	Baseline (N=52)		End of Treatment (N=52)		3 Month Follow Up (N=52)	
	Liraglutide (N=26)	Placebo (N=26)	Liraglutide (N=26)	Placebo (N=26)	Liraglutide (N=26)	Placebo (N=26)
Caffeine (mg)						
N	26	25	23	21	21	18
Mean (SD)	21.4 (30.1)	26.1 (45.0)	24.1 (56.1)	24.4 (51.9)	21.8 (44.6)	6.6 (14.9)
Median	6.7	3.6	4.3	5.0	2.3	1.2
IQR	0.9, 24.5	1.4, 20.9	1.4, 13.4	0.8, 18.2	1.4, 8.0	0.2, 2.8
Range	0.0, 103.7	0.0, 158.6	0.0, 236.8	0.0, 235.4	0.2, 147.6	0.0, 49.6

Figure 2.6: Caffeine (mg) Charts

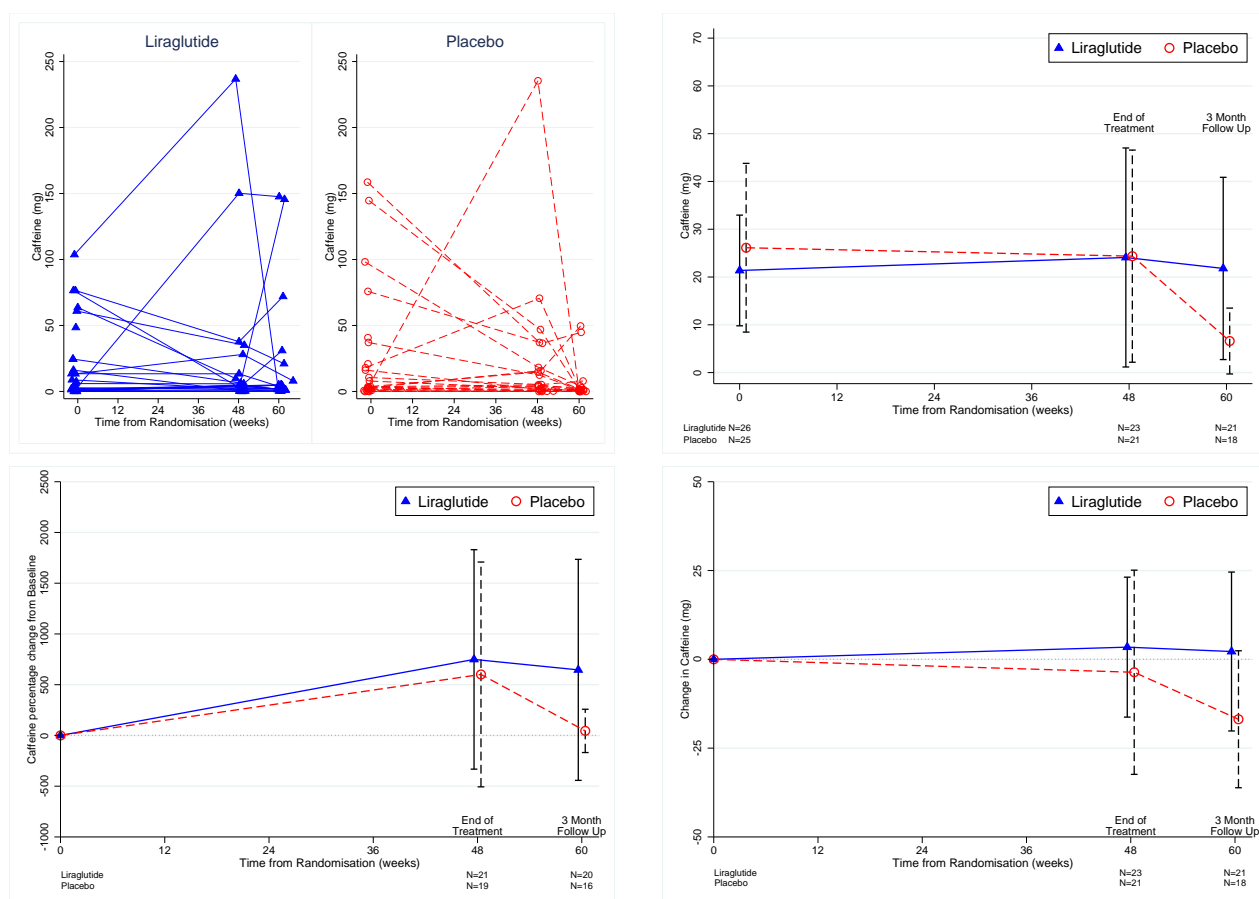


Table 2.7: Alcohol (g) by treatment and Visit Number

	Baseline (N=52)		End of Treatment (N=52)		3 Month Follow Up (N=52)	
	Liraglutide (N=26)	Placebo (N=26)	Liraglutide (N=26)	Placebo (N=26)	Liraglutide (N=26)	Placebo (N=26)
Alcohol (ethanol) (g)						
N	26	25	23	21	21	18
Mean (SD)	6.27 (8.25)	4.77 (8.35)	4.70 (6.37)	2.34 (4.36)	4.15 (4.55)	2.37 (3.53)
Median	4.41	1.47	2.78	0.00	3.20	0.60
IQR	0.23, 8.21	0.00, 4.61	0.00, 7.17	0.00, 2.11	0.00, 7.20	0.00, 3.78
Range	0.00, 36.38	0.00, 30.81	0.00, 26.57	0.00, 13.94	0.00, 15.70	0.00, 10.63

Figure 2.7: Alcohol (Ethanol) Charts

