SUPPLEMENTARY MATERIAL

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Supplementary Table 1. Schedule of procedures

Phase	Baseline metabolic balance study				Treatment period Liraglutide														Treatment metabolic balance study				
Visit day	-3	-2	-1	0	1	11	12	13	14	25	26	27	28	39	40	41	42	50	53	54	55	56	57
Visit type (ward, home, phone)	w	w	w	w	w	p	h	h	p	p	h	h	w	p	h	h	p	p	w	w	w	w	w
Safety assessment																							
Physical examination	x												x						x				
ECG	x												x						x				
Vital signs[1]	x	x	x	x	x								x						x	x	x	x	
Adverse events	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Local tolerability					x								x						x	x	x	x	
Laboratory																							
Standard blood sample		x											x							x			
25-hydroxy-vitamin D (D3+D2)		x																		x			
HbA1c		x											x							x			
Efficacy																							
Metabolic balance study		x	x	x																x	x	x	
Urine collection		x	x	x			x	x		x	x				x	x				x	x	x	
Body composition by DEXA	x																		x				
Body weight	x	x	x	x	x								x						x	x	x	x	
Postprandial hormone profile[2]		x																		x			
Gastric emptying by paracetamol		x																		x			
BMR by indirect calorimetry			x																		x		
Blood flow by ultrasound				x																		x	
Arterial function				x																		x	
Digestive enzymes and bile acid		x																		x			
Stoma nipple size by photography			x																		x		
Completion of QoL questionnaires				x																		x	
Trial material and reminders																							
Completion of diaries (daily)	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	
Injection of liraglutide (daily)					x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	
Remind of urine collection						x				x					x								
Receive urine collection result							x				x					x							
Evaluate for dose up-titration							x				x												
Evaluate for PS volume reduction							x				x												
Return to baseline PS program																	x						
Follow baseline PS program																	x		x	x	x	x	
Return completed diaries																						x	
Oral fasting (22:00 to 8:00)		x	x	x																x	x	x	
Return (partly) used and unused trial product																						x	
Admission to hospital	x																		x				
Hospital discharge					x																		x
Assemble oral fluid program	x																						
Oral fluid fixation		x	x	x			x	x		x	x				x	x			x	x	x	x	

[1] Body weight, height, blood pressure, pulse and temperature. [2] Glucagon-like peptide (GLP)-1, GLP-2, glucose dependent insulinotropic polypeptide, glucagon, gastrin, cholecystokinin.

Abbreviations: ECG – Electrocardiography; DEXA – Dual-energy x-ray absorptiometry; BMR – Basal metabolic rate; QoL – Quality of life; PS – Parenteral support.

Supplementary Table 2. Observed adverse events during eight weeks of liraglutide treatment, with relation and actions.

	Quantity	Related 1: Yes 2: No	Serious Adverse Events (SAE) 0: No 1: Yes	Action 0: None 1: Reduction 2: Paused 3: Terminated
Reduced appetite	6	1	0	0
Nausea	4	1	0	0
Edema of the lower extremity	3	1	0	0
Vomitus	3	1	0	0
Transient stoma nipple growth	3	1	0	0
Weight loss	2	1	0	0
Redness in relation to injection site	2	1	0	0
Asthenia	1	1	0	0
Abdominal pain	1	1	0	0
Increased thirst	1	1	0	0
Laryngitis	1	1	0	0
Low vitamin D levels	1	2	0	0
Receding urine production	1	2	0	0
Abdominal meteorism	1	2	0	0

Supplementary Table 3. Metabolic balance study results

	Baseline			Liraglutide			Effect			*P*
Wet weight										
Diet fluid (g/d)	1801	±	660	1810	±	691	9	±	57	.68
Diet solid (g/d)	941	±	270	922	±	227	-19	±	136	.71
Diet total (g/d)	2743	±	824	2733	±	838	-10	±	128	.83
Ostomy output (g/d)	3249	±	1352	2775	±	1187	-474	±	563	.049
Absolute absorption (g/d)	-506	±	1347	-42	±	1119	464	±	557	.05
Relative absorption (%)	-29.3	±	65.6	-9.3	±	49.6	20.1	±	29.6	.10
Parenteral volume (g/d)	3721	±	2150	3689	±	1907	-32	±	327	.79
Diuresis (g/d)	1543	±	532	2308	±	1138	765	±	759	.02
Energy										
Diet (kJ/d)	10147	±	2584	9875	±	2694	-272	±	1106	.51
Ostomy output (kJ/d)	6904	±	3390	5730	±	3165	-1174	±	877	.01
Absolute absorption (g/d)	3243	±	2357	4146	±	2703	902	±	882	.02
Relative absorption (%)	33.1	±	24.1	41.9	±	24.3	8.8	±	9.2	.03
Carbohydrate										
Diet (g/d)	234	±	66	247	±	63	12	±	23	.17
Ostomy output (g/d)	111	±	68	92	±	60	-19	±	18	.02
Absorption (g/d)	123	±	62	155	±	71	32	±	14	.0003
Relative absorption (%)	53	±	23	62	±	21	9	±	5	.002
Nitrogen										
Diet (g/d)	14	±	5	13	±	4	-0.5	±	2.1	.49
Ostomy output (g/d)	11	±	7	9	±	5	-1.7	±	1.8	.03
Absorption (g/d)	2.9	±	3	4.1	±	3.7	1.2	±	1.9	.12
Relative absorption (%)	24	±	25	31	±	28	7	±	12	.15
Lipids										
Diet (g/d)	100	±	21	94	±	28	-6	±	16	.34
Ostomy output (g/d)	81	±	33	66	±	33	-15	±	11	.01
Absorption (g/d)	19	±	24	28	±	24	9	±	14	.10
Relative absorption (%)	20	±	24	30	±	24	10	±	15	.09
Sodium										
Diet (mmol/d)	131	±	46	115	±	39	-15	±	25	.13
Ostomy output (mmol/d)	309	±	94	272	±	94	-37	±	42	.04
Absolute absorption (mmol/d)	-246	±	118	-157	±	82	22	±	50	.26
Relative absorption (%)	-155	±	109	-147	±	88	7	±	85	.81
Urine (mmol/d)	132	±	115	197	±	178	66	±	68	.03
Potassium										
Diet (mmol/d)	76	±	30	68	±	18	-9	±	19	.25
Ostomy output (mmol/d)	53	±	32	44	±	27	-10	±	12	.04
Absolute absorption (mmol/d)	23	±	19	24	±	27	1	±	15	.85
Relative absorption (%)	32	±	26	35	±	32	3	±	18	.61
Urine (mmol/d)	57	±	16	66	±	18	10	±	15	.12
Calcium										
Diet (mmol/d)	28	±	14	25	±	10	-3	±	6	.19
Ostomy output (mmol/d)	33	±	15	27	±	10	-6	±	7	.05
Absolute absorption (mmol/d)	-4	±	5	-2	±	4	2	±	3	.04
Relative absorption (%)	-20	±	21	-10	±	18	10	±	12	.05
Urine (mmol/d)	4	±	3	5	±	3	1	±	1	.22
Magnesium										
Diet (mmol/d)	11	±	4	10	±	3	-1	±	2	.25
Ostomy output (mmol/d)	16	±	8	14	±	5	-2	±	3	.08
Absolute absorption (mmol/d)	-5	±	9	-3	±	6	1	±	4	.32
Relative absorption (%)	-61	±	124	-42	±	78	20	±	49	.30
Urine (mmol/d)	4	±	3	5	±	3	1	±	1	.01

Data represents means ± standard deviation. *Statistical significance calculated with Student *t* test

Supplementary Table 4. Body composition. Results from the dual energy x-ray absorptiometry (DEXA) scan before and after eight weeks of liraglutide treatment. Data represents means ± standard deviation. Statistical significance calculated with Student t test

	Baseline	Liraglutide	Effect	P
Body weight (kg)	70.6 ± 13.9	70.0 ± 13.7	-0.6 ± 2	.36
Total fat (kg)	21.7 ± 10.6	21.2 ± 10.6	-0.6 ± 45.8	.25
Body fat (%)	29.6 ± 11.2	29.3 ± 11.5	-0.4 ± 19.5	.48
BMC (g/cm^2)	0.926 ± 0.186	0.909 ± 0.165	-0.018 ± 0.033	.18
Total BMC (kg)	2.6 ± 0.7	2.6 ± 0.6	-0.02 ± 0.06	.46
Total lean mass (kg)	46.4 ± 8.0	46.3 ± 8.7	-0.1 ± 1.4	.83

BMC=Bone Mineral Content.

In Supplementary Tables 5–11 we used a One Way Repeated Measures Analysis of Variance with Dunnett's method to isolate the time interval that differ from fasting measurements (-15), where a and b denotes statistical significant differences from fasting measurements. The difference between baseline and liraglutide treatment was tested with a Two Way Repeated Measures Analysis of Variance and the Student-Newman-Keuls Method as post hoc analysis. Data represents before and after eight weeks for liraglutide treatment, and are presented as means ± standard deviation. AUC = Area under the curve.

Supplementary Table 5: Glucagon-Like Peptide-1 profile [pmol/L]

	-15	0	2	5	10	15	20	30	45	60	120	180	P	AUC
Baseline [GLP-1]	9.8±3.1 a	11.6±3.4 a	13.0±4.2 a	13.5±5.4 a	13.8±3.8 b	13.6±4.4 a	14.8±5.1 b	15.0±4.5 b	14.0±4.3 b	13.4±3.8 a	11.9±3.5 a	11.6±2.5 a	.007	2476±627
Liraglutide [GLP-1]	12.0±3.8	13.0±3.1	15.1±3.5	15.1±2.9	15.8±4.4	14.4±4.0	14.6±4.8	15.3±8.1	14.4±3.3	13.5±2.4	13.3±1.0	10.9±1.4	.052	2581±385
p-value	.169	.396	.193	.317	.220	.642	.938	.851	.816	.938	.396	.642		.628

Supplementary Table 6: Glucagon-Like Peptide-2 profile [pmol/L]

	-15	0	2	5	10	15	20	30	45	60	120	180	P	AUC
Baseline GLP-2	8.4±2.4	9.5±4.7	10.8±5.0	12.0±5.0	13.3±9.7	13.9±9.7	17.3±17.1	18.1±17.6 b	16.1±14.3	14.8±12.1	12.3±11.3	10.9±7.1	.110	2575±1986
Liraglutide GLP-2	8.5±3.5	10.1±5.1	12.6±8.2	13.3±5.9	13.1±5.7	12.9±7.1	12.9±7.1	14.1±9.7	12.5±6.5	10.9±3.2	9.9±2.9	9.0±2.6	.082	2082±634
p-value	0.967	.837	.538	.682	.967	.743	.154	.163	.237	.206	.436	.538		.374

Supplementary Table 7: Glucagon profile [pmol/L]

	-15	0	2	5	10	15	20	30	45	60	120	180	P	AUC
Baseline Glucagon	8.1±4.9 a	11.6±5.7 b	11.8±8.3 b	11.9±7.8 b	10.9±6.0 a	9.4±4.3 a	9.5±4.7 a	11.1±4.7 a	9.3±3.8 a	9.6±4.2 a	8.4±3.7 a	8.3±3.1 a	*.008*	1806±737
Liraglutide Glucagon	19.6±27.0	22.1±24.4	19.8±19.4	19.0±19.0	17.1±13.8	14.1±10.5	14.0±9.2	13.1±8.7	10.9±6.0	11.4±7.0	12.8±5.9	10.5±4.3	*.082*	2555±1607
p-value	.041	.059	.140	.185	.242	.369	.394	.740	.755	.737	.407	.667		.217

Supplementary Table 8: Glucose-dependent Insulinotropic Peptide profile [pmol/L]

	-15	0	2	5	10	15	20	30	45	60	120	180	*P*	AUC
Baseline GIP	14±8 a	44±53 a	60±64 a	77±79 b	84±71 b	95±73 b	99±76 b	109±74 b	116±74 b	113±72 b	90±75 b	65±53 a	<.001	17275±12095
Liraglutide GIP	35±44 a	58±50 a	88±67 b	100±71 b	106±80 b	105±78 b	102±87 b	103±80 b	99±60 b	103±62 b	90±59 b	79±60 a	<.001	17459±10868
p-value	.198	.352	.073	.142	.153	.542	.853	.769	.259	.510	.994	.352		.907

Supplementary Table 9: Cholecystokinin profile [pmol/L]

	-15	0	2	5	10	15	20	30	45	60	120	180	*P*	AUC
Baseline CCK	1.1±0.7 a	4.7±5.3 b	5.8±5.1 b	6.4±4.7 b	5.3±3.5 b	4.9±2.7 b	5.1±3.5 b	5.6±3.4 b	5.0±1.7 b	5.7±3.4 b	5.3±6.1 b	3.8±3.1 a	.019	969±707
Liraglutide CCK	2.2±1.4 a	4.3±4.2 a	8.0±4.2 b	9.7±6.3 b	7.6±4.4 b	6.6±3.6 b	6.2±4.4 a	5.5±2.9 a	5.3±2.7 a	6.4±4.1 b	5.0±2.4 a	4.4±2.1 a	<.001	1045±469
p-value	.458	.787	.147	.027	.114	.260	.483	.944	.813	.630	.839	.691		.668

Supplementary Table 10: Gastrin profile [pmol/L]

	-15	0	2	5	10	15	20	30	45	60	120	180	*P*	AUC
Baseline Gastrin	96±91 a	181±87 a	222±111 b	206±108 b	255±205 b	192±105 a	203±148 b	249±216 b	189±119 a	186±124 a	148±108 a	109±94 a	<.001	32554±21041
Liraglutide Gastrin	94±86 a	157±131 b	194±132 b	185±139 b	166±139 b	151±124 a	148±126 a	127±108 a	141±105 a	142±113 a	154±138 b	131±116 a	.002	28003±22791
p-value	.941	.485	.444	.546	.017	.251	.128	.009	.182	.221	.873	.541		.291

Supplementary Table 11: Paracetamol profile [μmol/L]

	-15	0	2	5	10	15	20	30	45	60	120	180	*P*	AUC
Baseline Paracetamol	0.0±0.0 a	0.0±0.0 a	6.9±6.9 a	17.4±17.4 a	37.0±19.1 a	51.5±18.9 b	60.1±16.1 b	80.6±14.0 b	84.4±11.2 b	83.9±11.9 b	80.6±11.8 b	54.4±13.7 b	<.001	12864±5683
Liraglutide Paracetamol	0.0±0.0 a	0.0±0.0 a	17.7±17.7 a	36.2±23.6 a	58.6±22.7 b	68.5±15.7 b	72.8±14.4 b	71.1±9.8 b	85.8±10.5 b	85.9±10.8 b	73.3±13.8 b	62.7±11.2 b	<.001	12938±5256
p-value	1.00	1.00	.097	.059	.006	.108	.146	.838	.832	.758	.538	.430		.937
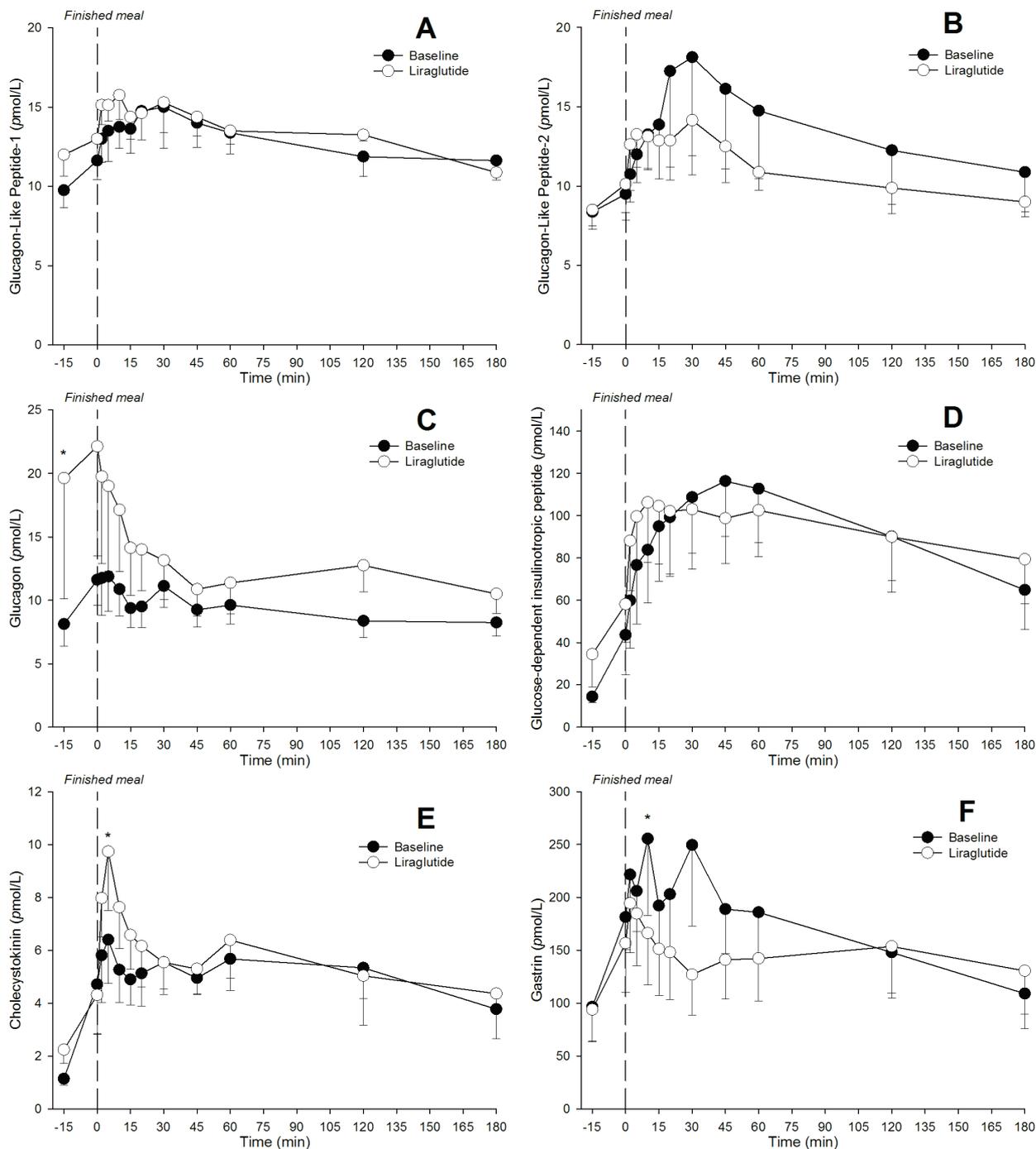
Supplementary Figure 1. Postprandial hormone profiles of glucagon-like peptide (GLP)-1 (A), GLP-2 (B), glucagon (C), glucose-dependent insulinotropic peptide (GIP) (D), cholecystokinin (CCK) (E) and gastrin (F) at fasting (t_{-15}) and for 180 minutes after a mixed meal consisting of 3250 kJ. Black circles = Plasma-levels at baseline. Open circles = Plasma-levels after eight weeks of liraglutide treatment. Mean and Standard error of mean. *denotes $P < .05$ by One Way Repeated Measures Analysis of Variance.
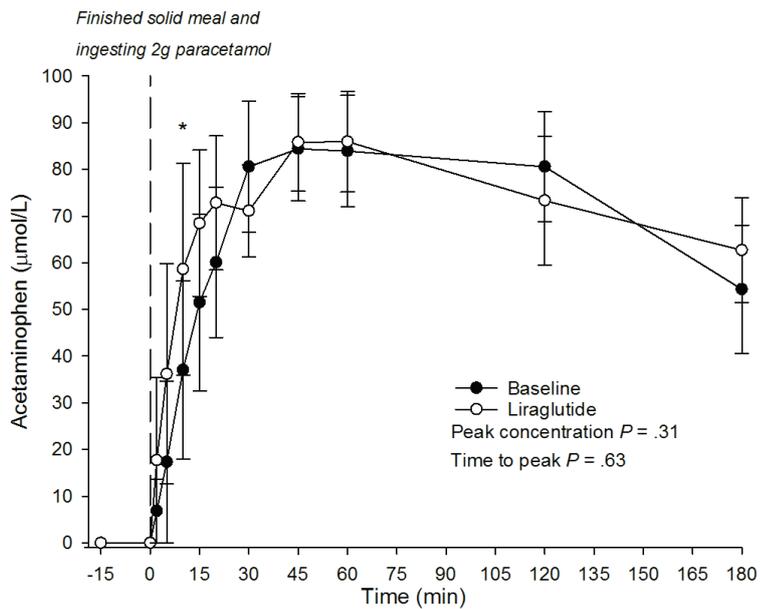
Supplementary Figure 2. Postprandial paracetamol (acetaminophen) profile at fasting (t_{-15}) and for 180 minutes after a mixed meal consisting of 3250 kJ. 2g of soluble paracetamol dissolved in 200g water was ingested between time point t_0 and t_2 minutes. Black circles = Plasma-levels at baseline. Open circles = Plasma-levels after eight weeks of liraglutide treatment. Mean and Standard error of mean. *denotes $P < .05$ by One Way Repeated Measures Analysis of Variance.

Supplementary Table 12. SF-36 questionnaire results before and after eight weeks for liraglutide treatment. The scoring system goes from 0, being the worst, to 100, being the best. Data represents means ± standard deviation. Student *t* test used to determine statistical significance.

SF-36 Domain	Baseline (0-100)	Liraglutide (0-100)	Effect	*P*
Physical functioning	67.5 ± 14.1	73.1 ± 8.8	5.6 ± 10.2	.16
Role-functioning physical	34.4 ± 37.6	53.1 ± 43.2	18.8 ± 45.8	.29
Body pain	71.9 ± 28.9	82.2 ± 27.9	10.3 ± 19.5	.35
General health	52.5 ± 22.5	46.3 ± 19.8	-6.3 ± 22.8	.31
Vitality	49.4 ± 20.3	43.8 ± 26.3	-5.6 ± 14.5	.22
Social functioning	57.8 ± 28.3	51.6 ± 27.1	-6.3 ± 32.7	.61
Role-functioning emotional	50.0 ± 43.6	66.7 ± 35.6	16.7 ± 47.1	.18
Mental health	79.0 ± 16.0	72.0 ± 20.9	-7.0 ± 14.6	.46
Total score	**462 ± 161**	**489 ± 145**	**26 ± 139**	**.61**

Supplementary Table 13. SBS-QoL questionnaire results before and after eight weeks for liraglutide treatment. The scoring system goes from 0, being the best, to 10, being the worst. Data represents means ± standard deviation. Student *t* test used to determine statistical significance.

SBS-QoL Domain	Baseline (0-10)	Liraglutide (0-10)	Effect	*P*
General well-being	4.0 ± 2.0	3.3 ± 1.7	-0.7 ± 2.3	.43
Everyday activities	3.8 ± 3.1	3.2 ± 1.7	-0.6 ± 3.4	.66
Working life/ ability to work	3.2 ± 3.3	4.2 ± 3.3	0.9 ± 1.4	.11
Leisure activities	6.2 ± 3.6	5.0 ± 3.5	-1.2 ± 3.3	.35
Social life	4.0 ± 3.5	5.0 ± 3.2	1.0 ± 2.6	.31
Energy level	4.7 ± 3.0	5.2 ± 3.2	0.5 ± 4.3	.75
Physical health	3.8 ± 3.1	3.9 ± 2.9	0.1 ± 4.3	.94
Mobility and self-care activities	2.3 ± 2.0	1.6 ± 1.6	-0.7 ± 2.5	.44
Pain	2.5 ± 3.2	1.2 ± 1.3	-1.2 ± 2.3	.17
Diet, eating, and drinking habits	4.0 ± 3.6	3.3 ± 2.7	-0.8 ± 2.0	.33
Emotional life	3.9 ± 3.6	4.2 ± 3.4	0.2 ± 1.7	.87
Sleep	2.9 ± 3.8	3.1 ± 3.3	0.2 ± 1.7	.80
Gastrointestinal symptoms	4.1 ± 3.2	2.6 ± 2.1	-1.4 ± 2.8	.20
Fatigue/ weakness	4.1 ± 2.7	5.0 ± 2.9	0.9 ± 2.4	.32
Diarrhoea/stomal output	4.2 ± 3.4	3.2 ± 2.9	-1.0 ± 1.8	.17
Skeleton/muscle symptoms	2.9 ± 3.4	2.1 ± 2.4	-0.8 ± 1.1	.06
Other symptoms/discomfort	3.3 ± 2.8	3.8 ± 3.3	0.6 ± 5.3	.77
Total mean score	**3.7 ± 0.9**	**3.5 ± 1.2**	-0.2 ± 0.8	**.74**