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Supplementary material

Figure S1 – Patients receiving surgery, endocrine therapy, radiotherapy and chemotherapy at each assessment.

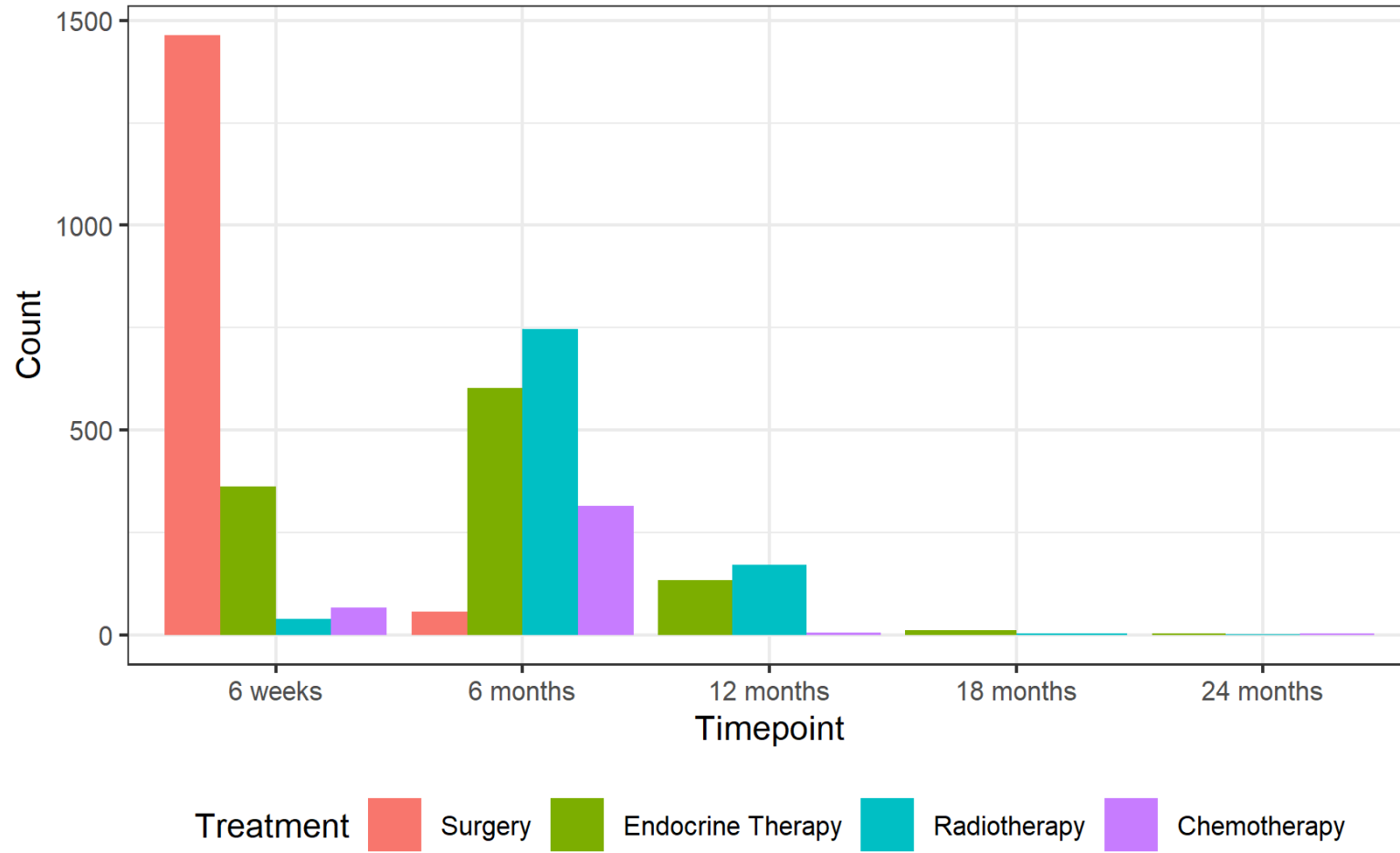


Figure S2 – Completion of the EORTC-QLQ-C30 at each time point.

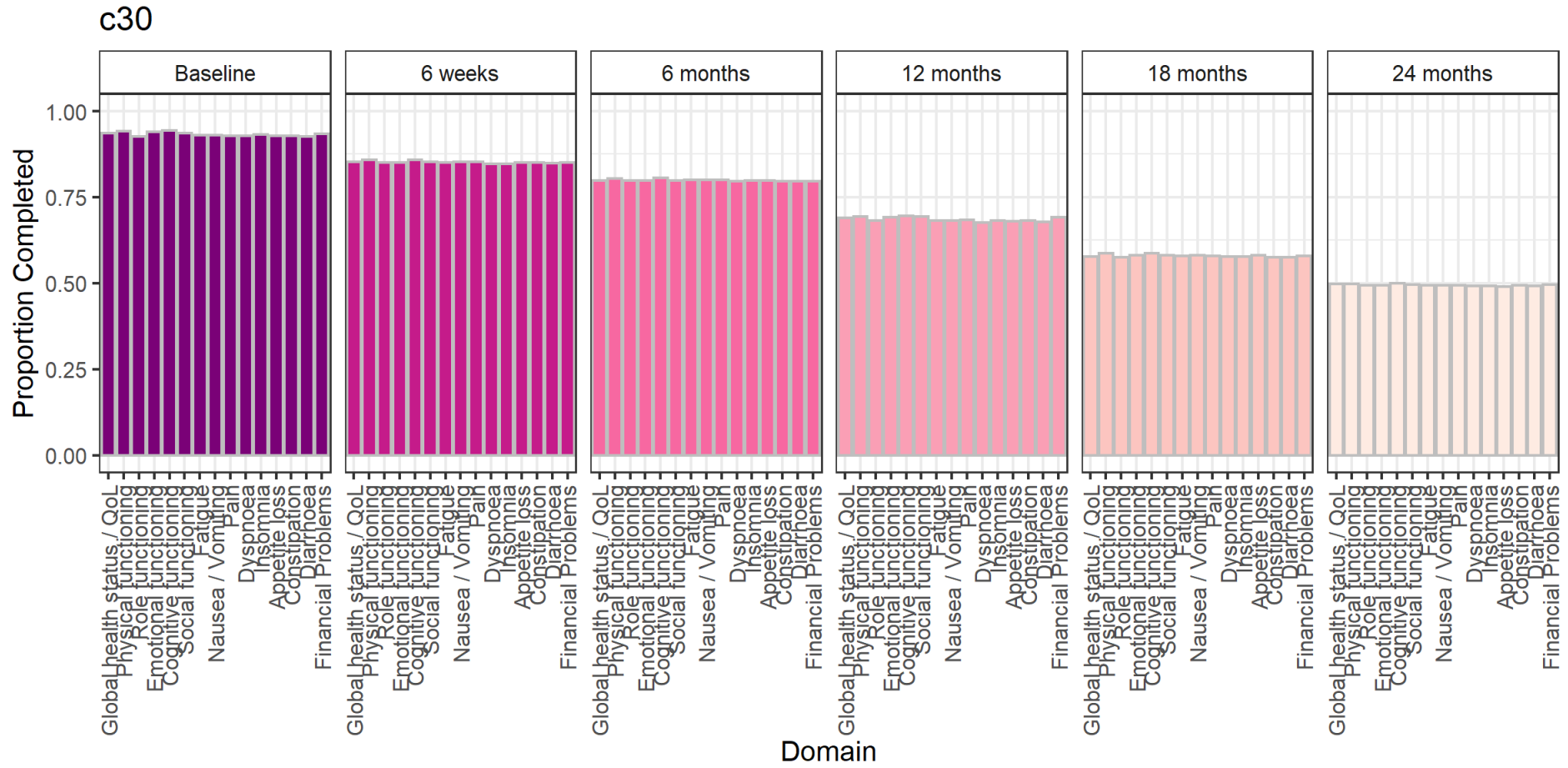


Figure S3 – Completion of the EORTC-QLQ-BR23 at each time point.

br23

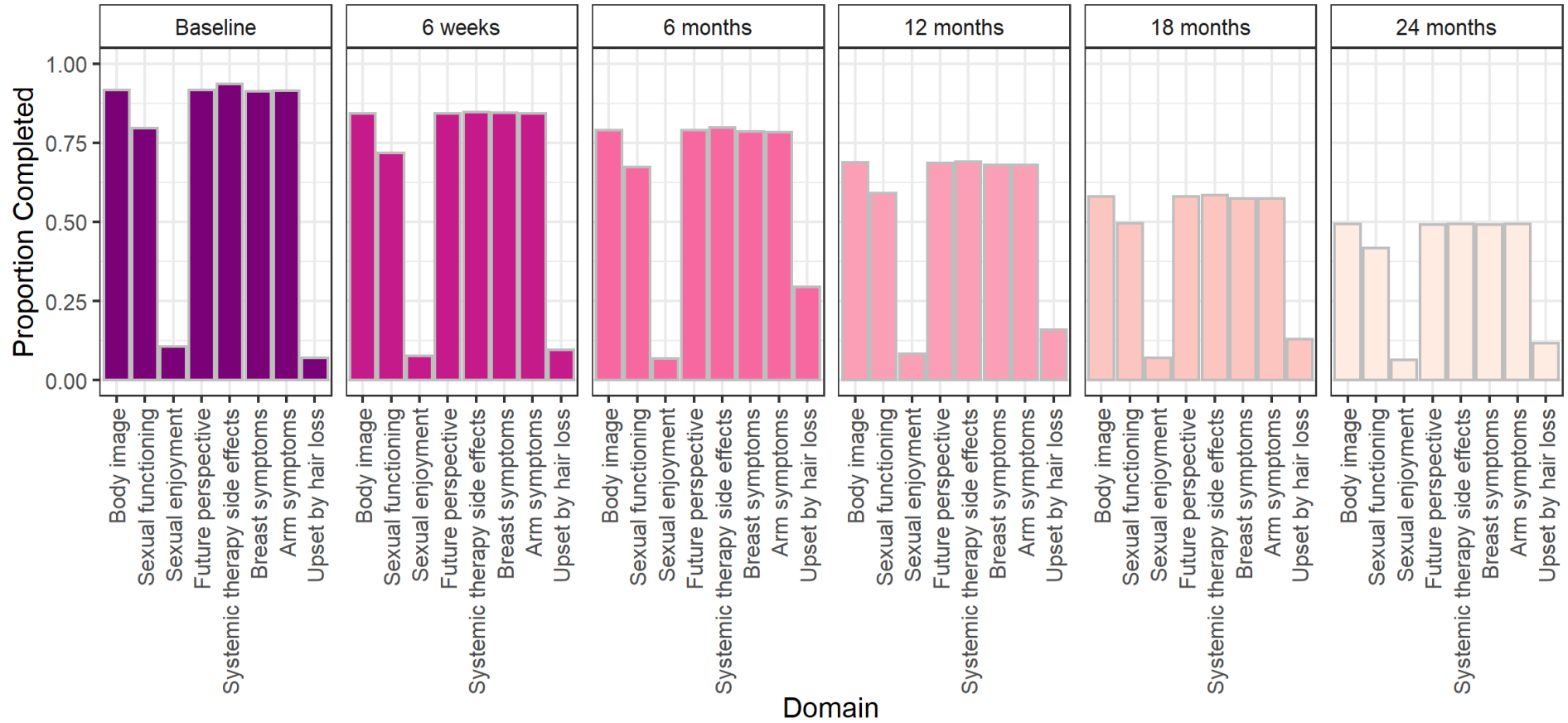


Figure S4 – Completion of the EORTC-QLQ-ELD15 at each time point.

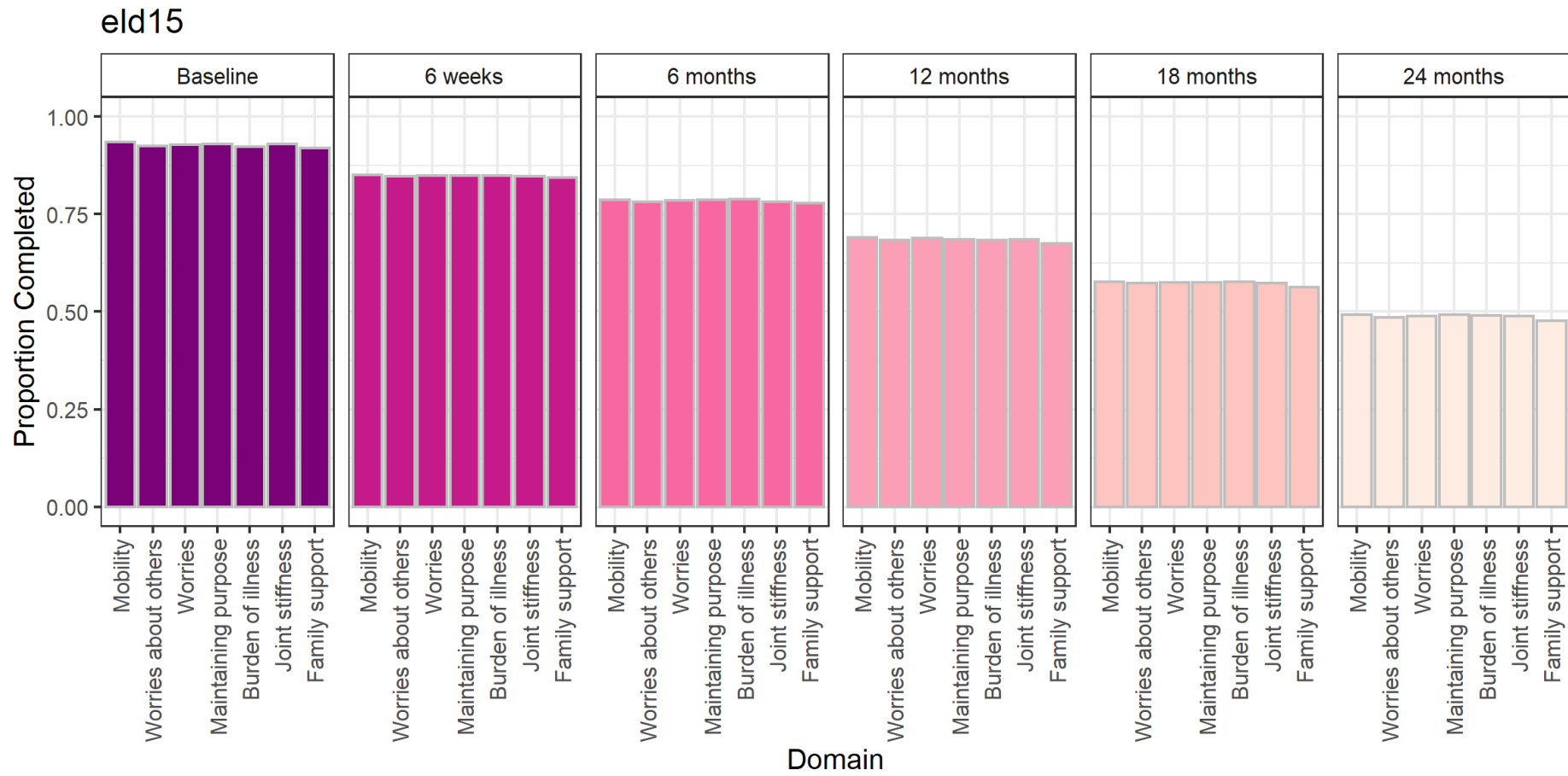


Figure S5 – Mean (95% CI) EORTC-QLQ-C30 global health status/QoL score over timepoints for the matched chemotherapy versus no chemotherapy population.

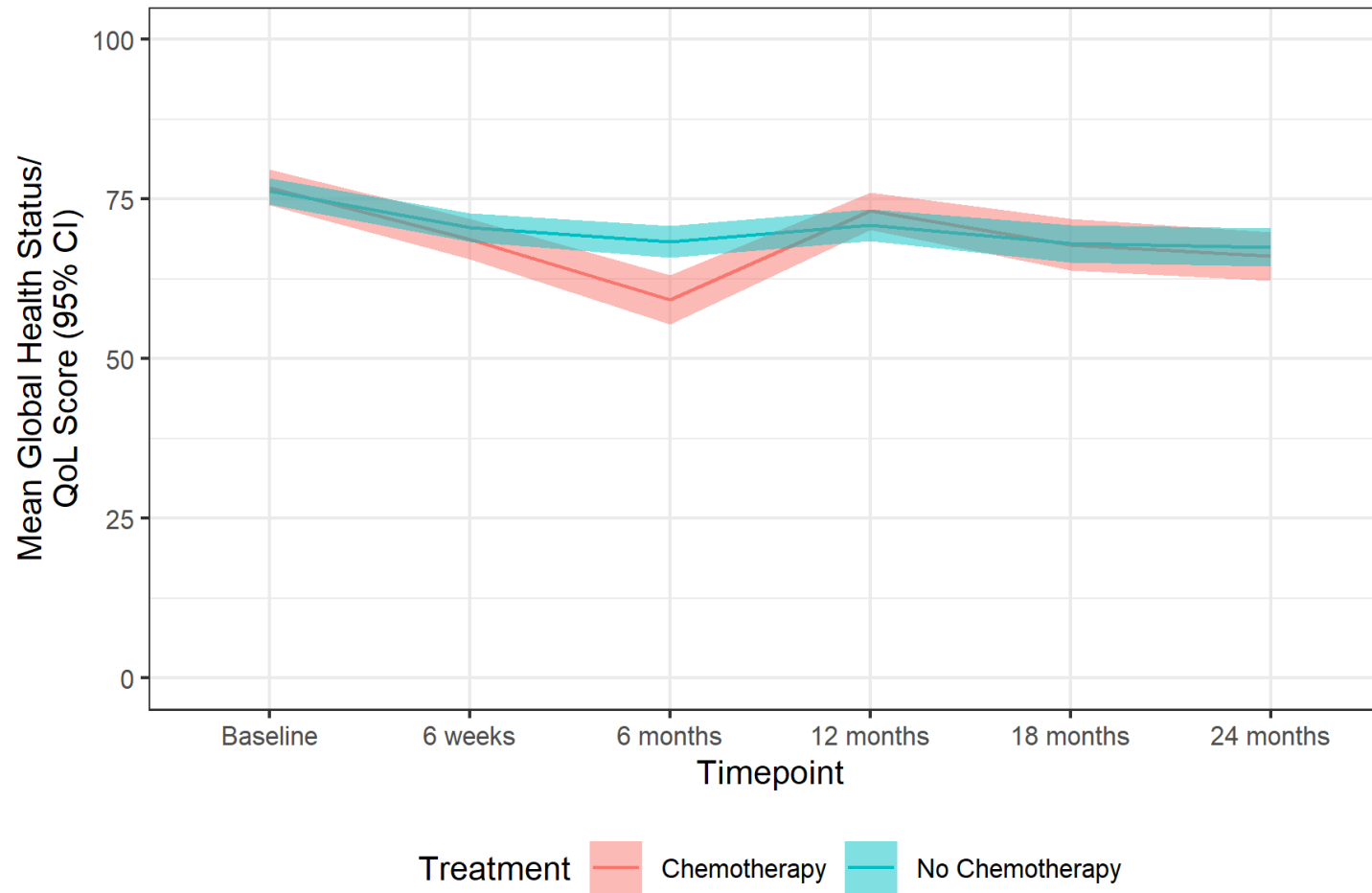


Figure S6 - Estimated marginal mean global health score (95% CI) included in the EORTC-QLQ-C30 score for chemotherapy and no chemotherapy from the matched longitudinal modelling.

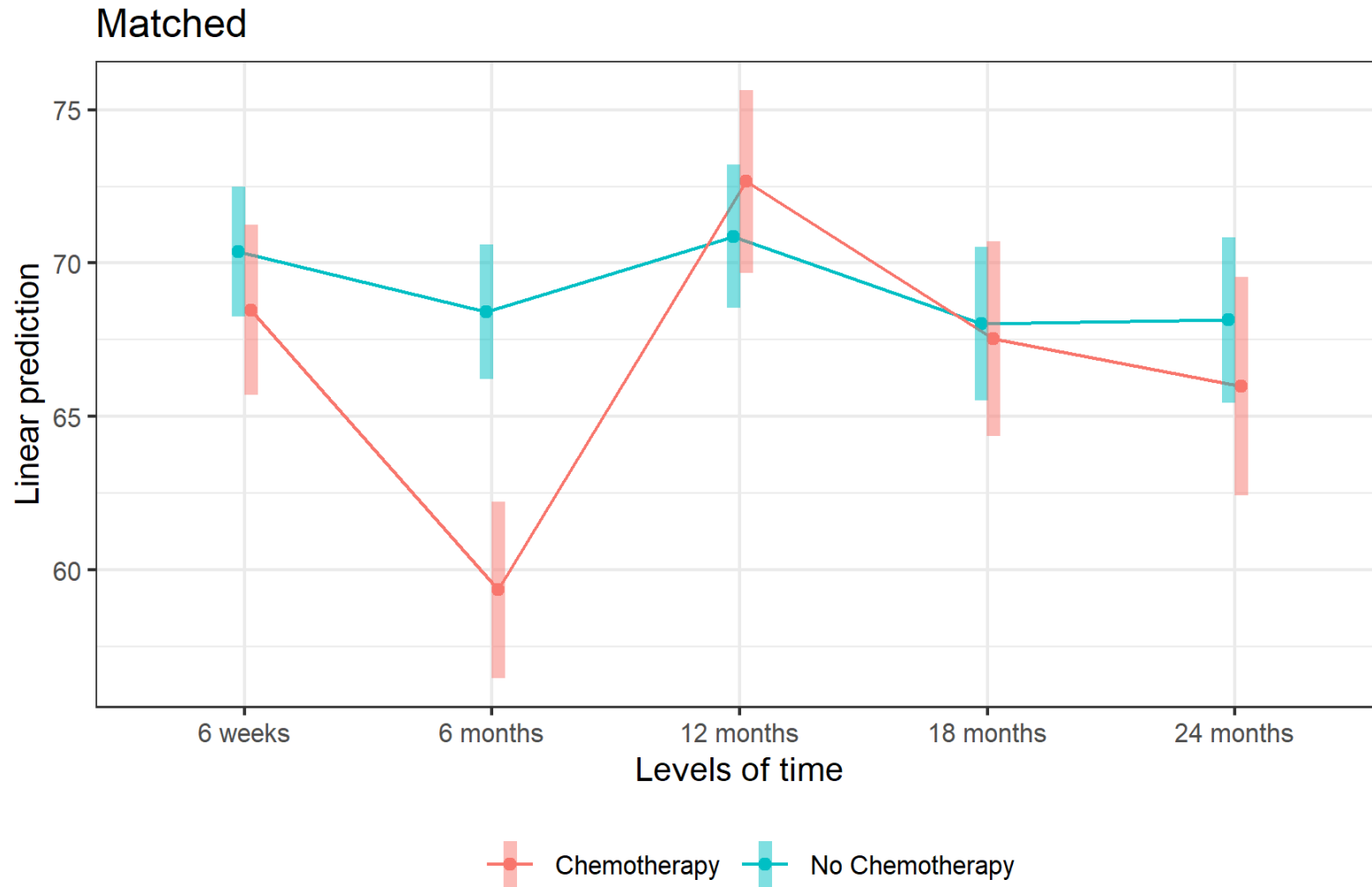


Figure S7 – Mean (95% CI) EORC-QLQ-C30 global health status scores over time points for the chemotherapy versus no chemotherapy population by age group

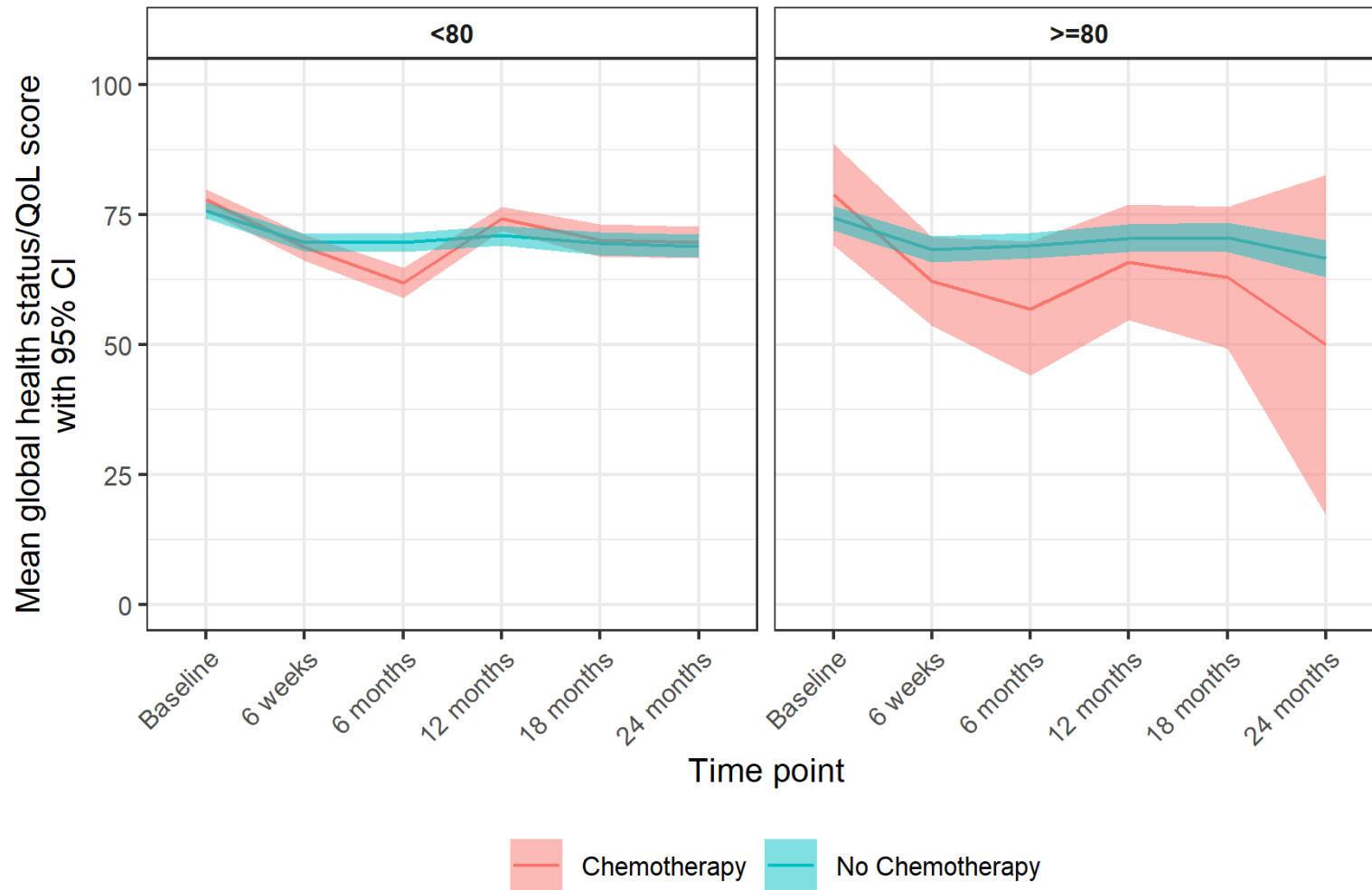


Figure S8 – Mean (95% CI) EQ-5D-5L usual activities score over timepoints for the matched chemotherapy vs no chemotherapy population.

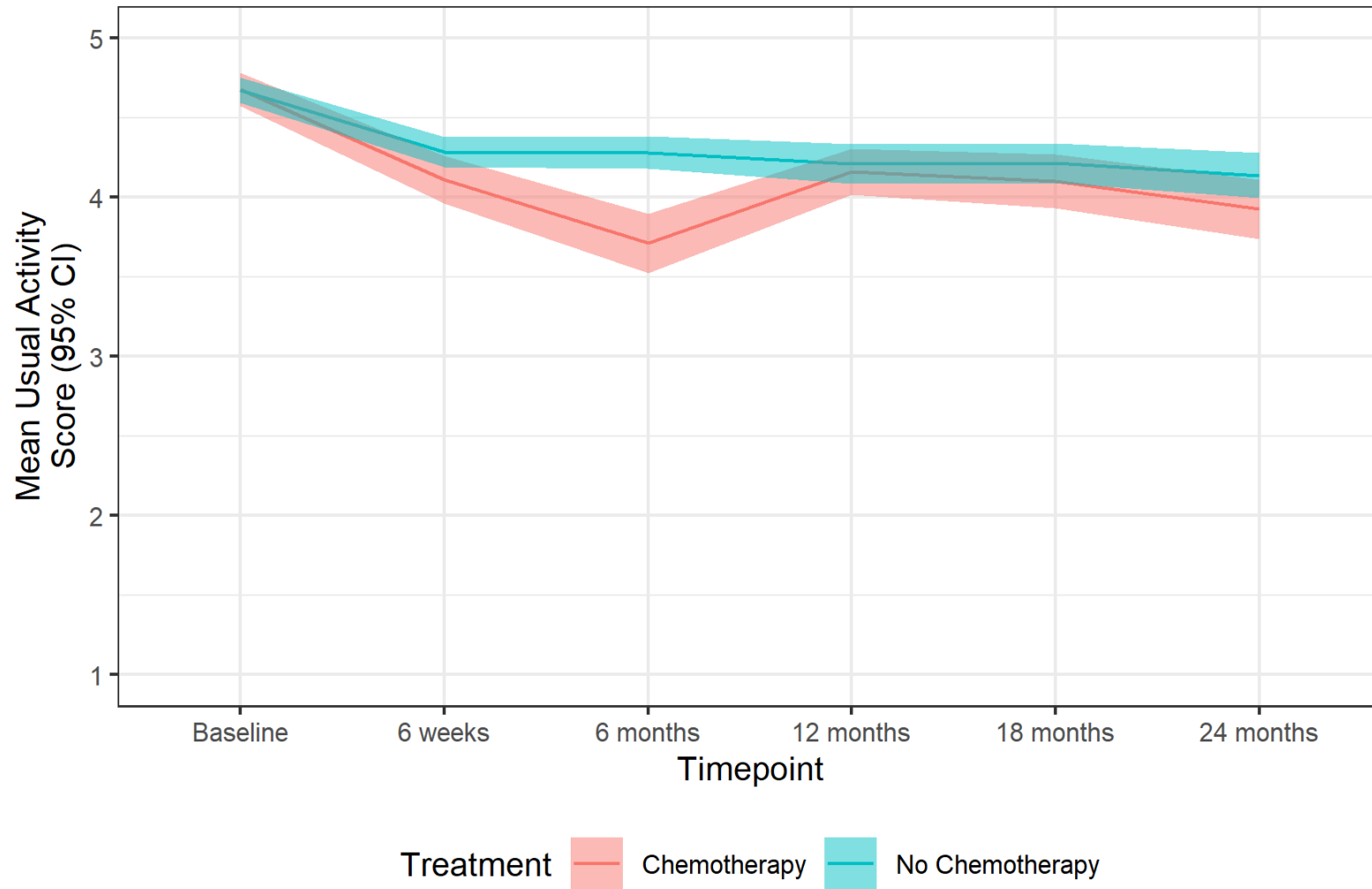


Table S1 - List of participating sites.

	Site Name	Local PI
1	Sheffield	Lynda Wyld and Matt Winter
2	Barnsley	Julia Dicks
3	Doncaster	Clare Rogers
4	Milton Keynes	Amanda Taylor
5	Scunthorpe and Grimsby	Rajesh Vijn (Scunthorpe), Jenny Smith (Grimsby)
6	Leicester	Monika Kaushik
7	Derby	Kwok Leung Cheung
8	East Lancashire	Julie Iddon
9	Harrogate	Matthew Adelekan
10	St Helens and Knowsley	Riccardo Audisio
11	York	Rana Nasr (York and Scarborough)
12	Liverpool	Chris Holcombe
13	Airedale	Claire Murphy
14	Leeds	Kieran Horgan
15	Bradford	Rick Linforth
16	Cardiff	Helen Sweetland
17	Aneurin Bevan Health Board	Simon Waters (Royal Gwent), Theresa Howe (Nevill Hall)
18	Royal Lancaster	Rishi Parmeshwar
19	Coventry	Abigail Tomlins

20	Grantham	Anzors Gvaramadze
21	Lincoln	Anzors Gvaramadze
22	Pilgrim	Anzors Gvaramadze
23	Hull	Peter Kneeshaw
24	Nottingham	Lisa Whisker
25	Southport	Anwar Haq
26	Leighton	Vanessa Pope
27	Royal Marsden	Jenny Rusby
28	Cheltenham General	Sarah Vestey
29	Guys and St Thomas	Michael Douek
30	Dorset County	Caroline Osborne
31	Mid Essex	Sascha Miles-Dua
32	Mid Yorkshire	Jay Naik
33	Bristol	Zoe Winters
34	Chesterfield	Iman Azmy
35	Rotherham	Inder Kumar
36	Darent Valley	Seema Seetharam
37	Kingston	Karyn Shenton
38	Colchester	Mukesh Mukesh
39	Yeovil	Caroline Osborne
40	Croydon	Sanjay Joshi
41	North Tees	Colm Hennessy

42	South Tees	Imtiaz Cheema
43	Luton and Dunstable	Mei-Lin Ah-See
44	Weston General	Rachel Ainsworth
45	Tameside	Stephanie Ridgway
46	Macclesfield	Lisa Barraclough
47	Wrightington, Wigan and Leigh	Angela Power
48	Birmingham	Fiona Hoar
49	Kings Mill	Rebecca Boulton
50	Wythenshawe	Nigel Bundred
51	Aintree	Peter Robson
52	Brighton	Gargi Patel
53	St Margaret's	Ashraf Patel
54	St Marys	Steve Parker
55	Oxford	Asha Adwani
56	Frimley and Wexham	Ruth Davis (Wexham), Raouf Daoud (Frimley)

Table S2 - Definition of risk of breast cancer recurrence based on tumour characteristics on diagnostic biopsy or surgical specimen.

Tumour characteristics	Risk of recurrence	
	High*	Low
ER	Negative	Positive
HER2	Positive	Negative
Grade	3	1-2
Nodal involvement	Yes	No
Oncotype DX Recurrence Score	≥30	<30

**high risk is defined by the presence of ≥1 of the features enlisted.*

Table S3 – Completion of the EORTC-QLQ-C30 at each time point.

		Chemotherapy	No Chemotherapy	Total
		N = 304	N = 816	N = 1120
Baseline	All	276 (90.8%)	736 (90.2%)	1012 (90.4%)
	Some	9 (3.0%)	36 (4.4%)	45 (4.0%)
	None	19 (6.2%)	44 (5.4%)	63 (5.6%)
6 weeks	All	254 (83.6%)	663 (81.2%)	917 (81.9%)
	Some	12 (3.9%)	35 (4.3%)	47 (4.2%)
	None	38 (12.5%)	118 (14.5%)	156 (13.9%)
6 months	All	236 (77.6%)	627 (76.8%)	863 (77.1%)
	Some	12 (3.9%)	29 (3.6%)	41 (3.7%)
	None	56 (18.4%)	160 (19.6%)	216 (19.3%)
12 months	All	217 (71.4%)	511 (62.6%)	728 (65.0%)
	Some	10 (3.3%)	42 (5.1%)	52 (4.6%)
	None	77 (25.3%)	263 (32.2%)	340 (30.4%)
18 months	All	184 (60.5%)	431 (52.8%)	615 (54.9%)
	Some	8 (2.6%)	36 (4.4%)	44 (3.9%)

		Chemotherapy	No Chemotherapy	Total
		N = 304	N = 816	N = 1120
	None	112 (36.8%)	349 (42.8%)	461 (41.2%)
24 months	All	150 (49.3%)	379 (46.4%)	529 (47.2%)
	Some	8 (2.6%)	23 (2.8%)	31 (2.8%)
	None	146 (48.0%)	414 (50.7%)	560 (50.0%)

Table S4 – Completion of the EORTC-QLQ-BR23 at each time point.

		Chemotherapy	No Chemotherapy	Total
		N = 304	N = 816	N = 1120
Baseline	All	2 (0.7%)	4 (0.5%)	6 (0.5%)
	Some	282 (92.8%)	766 (93.9%)	1048 (93.6%)
	None	20 (6.6%)	46 (5.6%)	66 (5.9%)
6 weeks	All	2 (0.7%)	4 (0.5%)	6 (0.5%)
	Some	264 (86.8%)	694 (85.0%)	958 (85.5%)
	None	38 (12.5%)	118 (14.5%)	156 (13.9%)
6 months	All	11 (3.6%)	16 (2.0%)	27 (2.4%)
	Some	236 (77.6%)	633 (77.6%)	869 (77.6%)
	None	57 (18.8%)	167 (20.5%)	224 (20.0%)
12 months	All	2 (0.7%)	15 (1.8%)	17 (1.5%)
	Some	225 (74.0%)	539 (66.1%)	764 (68.2%)
	None	77 (25.3%)	262 (32.1%)	339 (30.3%)
18 months	All	9 (3.0%)	10 (1.2%)	19 (1.7%)
	Some	183 (60.2%)	457 (56.0%)	640 (57.1%)

		Chemotherapy	No Chemotherapy	Total
		N = 304	N = 816	N = 1120
	None	112 (36.8%)	349 (42.8%)	461 (41.2%)
24 months	All	6 (2.0%)	17 (2.1%)	23 (2.1%)
	Some	151 (49.7%)	386 (47.3%)	537 (47.9%)
	None	147 (48.4%)	413 (50.6%)	560 (50.0%)

Table S5 – Completion of the EORTC-QLQ-ELD15 at each time point.

		Chemotherapy	No Chemotherapy	Total
		N = 304	N = 816	N = 1120
Baseline	All	274 (90.1%)	732 (89.7%)	1006 (89.8%)
	Some	9 (3.0%)	33 (4.0%)	42 (3.8%)
	None	21 (6.9%)	51 (6.2%)	72 (6.4%)
6 weeks	All	260 (85.5%)	675 (82.7%)	935 (83.5%)
	Some	4 (1.3%)	14 (1.7%)	18 (1.6%)
	None	40 (13.2%)	127 (15.6%)	167 (14.9%)
6 months	All	232 (76.3%)	625 (76.6%)	857 (76.5%)
	Some	10 (3.3%)	17 (2.1%)	27 (2.4%)
	None	62 (20.4%)	174 (21.3%)	236 (21.1%)
12 months	All	221 (72.7%)	521 (63.8%)	742 (66.2%)
	Some	5 (1.6%)	28 (3.4%)	33 (2.9%)
	None	78 (25.7%)	267 (32.7%)	345 (30.8%)
18 months	All	185 (60.9%)	439 (53.8%)	624 (55.7%)
	Some	5 (1.6%)	18 (2.2%)	23 (2.1%)

		Chemotherapy	No Chemotherapy	Total
		N = 304	N = 816	N = 1120
	None	114 (37.5%)	359 (44.0%)	473 (42.2%)
24 months	All	147 (48.4%)	379 (46.4%)	526 (47.0%)
	Some	6 (2.0%)	20 (2.5%)	26 (2.3%)
	None	151 (49.7%)	417 (51.1%)	568 (50.7%)

Table S6a – Mean (SD) scores for the EORTC QLQ-C30 scale at each time point in the chemotherapy versus no chemotherapy cohorts with adjusted mean difference (95% CI) and p-value.

Domain	Time point		Chemotherapy	No Chemotherapy	Adjusted Mean Difference (95% CI)	P-value	
Global health status / QoL	Baseline	n	282	767			
		Mean (SD)	77.9 (17.7)	75.4 (18.4)	-	-	
	6 weeks	n	263	692			
		Mean (SD)	68.4 (20.1)	69.3 (18.6)	-2.81 (-5.17, -0.44)	0.020	
	6 months	n	243	651			
		Mean (SD)	61.7 (22.3)	69.5 (19.2)	-9.20 (-11.95, -6.44)	<0.001	
	12 months	n	225	548			
		Mean (SD)	73.9 (17.2)	70.9 (18.6)	1.25 (-1.19, 3.69)	0.315	
	18 months	n	190	456			
		Mean (SD)	69.8 (21.2)	69.9 (19.1)	-0.42 (-3.42, 2.59)	0.784	
	24 months	n	157	400			
		Mean (SD)	69.5 (19.2)	68.3 (19.3)	0.53 (-2.70, 3.75)	0.749	
	Physical functioning	Baseline	n	285	769		
			Mean (SD)	87.1 (16.0)	82.1 (19.9)	-	-
6 weeks		n	264	697			
		Mean (SD)	79.3 (18.8)	76.2 (19.9)	-1.25 (-3.08, 0.58)	0.180	
6 months		n	246	655			
		Mean (SD)	71.8 (20.5)	75.7 (20.5)	-8.05 (-10.21, -5.89)	<0.001	
12 months		n	227	551			
		Mean (SD)	76.9 (19.5)	74.9 (21.6)	-2.76 (-4.95, -0.57)	0.014	
18 months		n	191	466			
		Mean (SD)	75.6 (20.9)	74.1 (21.0)	-0.35 (-2.74, 2.04)	0.773	
24 months		n	158	400			
						0.22 (-2.61, 3.06)	0.877

Domain	Time point		Chemotherapy	No Chemotherapy	Adjusted Mean Difference (95% CI)	P-value
Role functioning	Baseline	Mean (SD)	75.8 (19.5)	73.4 (22.0)		
		n	280	757		
	6 weeks	Mean (SD)	89.9 (20.8)	87.1 (23.1)		
		n	263	689	-3.25 (-6.90, 0.40)	0.081
	6 months	Mean (SD)	70.2 (28.5)	71.1 (27.0)		
		n	248	646	-17.59 (-21.24, -13.95)	<0.001
	12 months	Mean (SD)	62.7 (29.3)	77.3 (25.6)		
		n	226	537	-4.41 (-8.17, -0.64)	0.022
	18 months	Mean (SD)	74.7 (26.3)	76.3 (26.1)		
		n	190	455	-3.23 (-7.55, 1.09)	0.143
	24 months	Mean (SD)	74.3 (26.5)	75.6 (27.8)		
		n	156	398	-4.46 (-9.40, 0.48)	0.077
Emotional functioning	Baseline	Mean (SD)	77.0 (19.7)	78.3 (19.2)		
		n	283	769		
6 weeks	Mean (SD)	77.0 (19.7)	78.3 (19.2)			
	n	264	689	0.10 (-2.26, 2.45)	0.936	
6 months	Mean (SD)	78.9 (18.0)	79.5 (19.6)			
	n	244	651	-0.57 (-3.15, 2.00)	0.662	
12 months	Mean (SD)	79.1 (20.0)	80.7 (19.5)			
	n	226	549	0.55 (-2.23, 3.33)	0.699	
18 months	Mean (SD)	80.5 (19.4)	80.0 (20.0)			
	n	191	460	-0.76 (-3.85, 2.33)	0.629	
24 months	Mean (SD)	79.6 (20.8)	80.6 (19.7)			
	n	155	399	-1.90 (-5.08, 1.28)	0.240	
Cognitive functioning	Baseline	Mean (SD)	78.4 (20.3)	80.4 (18.8)		
		n	285	772		
	6 weeks	Mean (SD)	89.6 (15.7)	88.3 (16.0)		
	n	265	697	-1.07 (-3.25, 1.11)	0.335	

Domain	Time point		Chemotherapy	No Chemotherapy	Adjusted Mean Difference (95% CI)	P-value	
	6 months	Mean (SD)	85.8 (16.6)	85.6 (19.0)	-5.55 (-7.97, -3.13)	<0.001	
		n	248	655			
	12 months	Mean (SD)	80.0 (20.8)	84.3 (18.4)	0.49 (-2.02, 2.99)	0.704	
		n	226	553			
	18 months	Mean (SD)	84.0 (16.7)	83.0 (18.8)	-1.66 (-4.37, 1.05)	0.230	
		n	191	466			
	24 months	Mean (SD)	82.7 (19.2)	84.1 (19.8)	-0.90 (-3.70, 1.90)	0.527	
		n	158	401			
	Social functioning	Baseline	Mean (SD)	83.4 (18.1)	83.7 (18.0)	-	-
			n	282	766		
		6 weeks	Mean (SD)	89.4 (19.9)	90.6 (18.6)	-3.57 (-6.71, -0.43)	0.026
			n	263	692		
6 months		Mean (SD)	76.1 (25.3)	79.7 (23.7)	-18.72 (-22.17, -15.27)	<0.001	
		n	244	651			
12 months		Mean (SD)	65.2 (29.1)	84.2 (22.9)	-3.78 (-7.00, -0.56)	0.022	
		n	226	551			
18 months		Mean (SD)	81.4 (22.6)	85.2 (22.2)	-3.21 (-6.87, 0.45)	0.085	
		n	190	460			
24 months		Mean (SD)	82.2 (23.9)	86.0 (23.6)	-2.37 (-6.68, 1.94)	0.280	
		n	156	399			
Fatigue	Baseline	Mean (SD)	80.8 (24.8)	84.4 (24.1)	-	-	
		n	281	761			
	6 weeks	Mean (SD)	18.2 (19.5)	20.2 (20.0)	2.39 (-0.26, 5.04)	0.077	
		n	263	690			
	6 months	Mean (SD)	33.5 (24.1)	32.8 (21.1)	13.09 (9.92, 16.26)	<0.001	
		n	248	648			
	12 months	Mean (SD)	44.3 (26.2)	33.3 (22.7)	3.38 (0.30, 6.46)	0.032	
		n	225	540			

Domain	Time point		Chemotherapy	No Chemotherapy	Adjusted Mean Difference (95% CI)	P-value	
Nausea / Vomiting	18 months	Mean (SD)	33.7 (22.9)	32.2 (21.9)	1.64 (-1.78, 5.05)	0.347	
		n	191	458			
	24 months	Mean (SD)	32.9 (23.1)	31.7 (22.5)	0.86 (-2.62, 4.34)	0.627	
		n	156	397			
	Baseline	Mean (SD)	31.9 (21.4)	32.5 (22.1)	-	-	
		n	281	761			
	6 weeks	Mean (SD)	2.1 (6.5)	2.3 (7.3)	1.27 (-0.33, 2.87)	0.119	
		n	263	691			
	6 months	Mean (SD)	5.4 (13.0)	4.4 (10.6)	5.23 (3.28, 7.17)	<0.001	
		n	247	650			
	12 months	Mean (SD)	9.8 (16.8)	4.6 (11.4)	0.78 (-0.86, 2.42)	0.351	
		n	226	539			
	18 months	Mean (SD)	4.4 (12.2)	4.1 (9.8)	-0.20 (-1.88, 1.48)	0.816	
		n	191	459			
	24 months	Mean (SD)	3.6 (9.1)	4.1 (10.3)	-0.54 (-2.43, 1.35)	0.577	
		n	156	398			
	Pain	Baseline	Mean (SD)	3.7 (10.6)	4.4 (10.4)	-	-
			n	280	759		
6 weeks		Mean (SD)	14.5 (20.2)	15.4 (23.1)	-0.32 (-3.19, 2.55)	0.829	
		n	263	692			
6 months		Mean (SD)	21.1 (21.2)	22.8 (23.6)	1.83 (-1.32, 4.98)	0.255	
		n	247	650			
12 months		Mean (SD)	21.0 (25.5)	20.7 (23.4)	1.92 (-1.64, 5.48)	0.290	
		n	226	540			
18 months		Mean (SD)	23.4 (24.7)	23.6 (25.9)	3.71 (-0.60, 8.03)	0.092	
		n	191	458			
24 months		Mean (SD)	26.7 (29.3)	23.4 (26.4)	0.29 (-4.45, 5.04)	0.903	
		n	155	398			

Domain	Time point		Chemotherapy	No Chemotherapy	Adjusted Mean Difference (95% CI)	P-value
Dyspnoea	Baseline	Mean (SD)	24.3 (28.7)	26.0 (28.1)	-	-
		n	281	758		
	6 weeks	Mean (SD)	9.7 (18.7)	13.7 (22.0)	-2.14 (-4.49, 0.20)	0.073
		n	263	686		
	6 months	Mean (SD)	9.9 (17.8)	15.0 (21.9)	3.86 (0.54, 7.18)	0.023
		n	247	645		
	12 months	Mean (SD)	21.3 (25.6)	21.2 (26.3)	-0.08 (-3.73, 3.58)	0.967
		n	222	536		
	18 months	Mean (SD)	17.6 (24.1)	21.4 (26.9)	0.15 (-3.84, 4.15)	0.941
		n	191	456		
	24 months	Mean (SD)	18.3 (24.6)	20.9 (27.8)	0.94 (-3.36, 5.23)	0.669
		n	155	397		
Insomnia	Baseline	Mean (SD)	20.0 (25.4)	22.1 (26.8)	-	-
		n	281	762		
6 weeks	Mean (SD)	27.9 (29.0)	26.7 (28.6)	3.09 (-0.66, 6.85)	0.106	
	n	261	688			
6 months	Mean (SD)	33.1 (29.8)	29.9 (29.5)	-0.36 (-4.16, 3.45)	0.854	
	n	246	648			
12 months	Mean (SD)	28.9 (29.9)	29.3 (28.9)	-1.87 (-5.88, 2.15)	0.361	
	n	226	537			
18 months	Mean (SD)	29.4 (27.7)	31.7 (29.2)	2.19 (-2.44, 6.81)	0.353	
	n	189	458			
24 months	Mean (SD)	33.3 (30.9)	30.4 (30.2)	0.42 (-4.48, 5.31)	0.868	
	n	153	398			
Appetite loss	Baseline	Mean (SD)	30.7 (28.5)	30.4 (28.9)	-	-
		n	280	759		
	6 weeks	n	262	690	1.29 (-1.70, 4.28)	0.396

Domain	Time point		Chemotherapy	No Chemotherapy	Adjusted Mean Difference (95% CI)	P-value	
	6 months	Mean (SD)	15.9 (23.6)	13.9 (22.2)	13.50 (9.81, 17.19)	<0.001	
		n	247	647			
	12 months	Mean (SD)	26.2 (32.6)	12.7 (22.7)	-0.59 (-4.02, 2.85)	0.738	
		n	225	536			
	18 months	Mean (SD)	12.3 (22.5)	13.4 (22.7)	-1.63 (-5.20, 1.95)	0.372	
		n	191	460			
	24 months	Mean (SD)	10.3 (21.2)	11.7 (22.5)	-1.86 (-5.89, 2.16)	0.363	
		n	156	394			
	Constipation	Baseline	Mean (SD)	11.3 (21.3)	13.1 (22.2)	-	-
			n	281	758		
		6 weeks	Mean (SD)	7.8 (17.0)	9.5 (19.2)	3.43 (0.23, 6.62)	0.035
			n	263	690		
6 months		Mean (SD)	17.0 (26.7)	15.3 (23.7)	3.84 (0.50, 7.18)	0.024	
		n	245	647			
12 months		Mean (SD)	17.1 (26.2)	15.1 (24.1)	-0.33 (-3.76, 3.10)	0.850	
		n	226	538			
18 months		Mean (SD)	12.4 (23.0)	14.8 (23.8)	1.24 (-2.68, 5.16)	0.534	
		n	190	455			
24 months		Mean (SD)	15.3 (25.3)	15.2 (24.3)	-1.67 (-5.75, 2.40)	0.420	
		n	156	398			
Diarrhoea	Baseline	Mean (SD)	12.0 (21.7)	15.1 (24.2)	-	-	
		n	281	757			
	6 weeks	Mean (SD)	3.8 (12.0)	4.4 (13.5)	1.25 (-0.98, 3.48)	0.272	
		n	263	687			
	6 months	Mean (SD)	6.2 (17.5)	5.5 (15.3)	7.68 (5.01, 10.35)	<0.001	
		n	247	644			
	12 months	Mean (SD)	13.0 (24.1)	5.7 (15.2)	4.15 (1.62, 6.68)	0.001	
		n	226	534			

Domain	Time point		Chemotherapy	No Chemotherapy	Adjusted Mean Difference (95% CI)	P-value
Financial Problems	18 months	Mean (SD)	9.0 (19.4)	5.3 (14.5)	1.88 (-0.73, 4.49)	0.159
		n	190	454		
	24 months	Mean (SD)	6.8 (16.3)	5.4 (15.0)	-2.42 (-5.57, 0.74)	0.133
		n	156	395		
	Baseline	Mean (SD)	4.3 (13.5)	6.8 (18.0)	-	-
		n	282	765		
	6 weeks	Mean (SD)	2.5 (9.6)	2.9 (10.7)	1.04 (-0.74, 2.82)	0.253
		n	263	689		
	6 months	Mean (SD)	4.8 (14.3)	4.5 (13.6)	3.28 (1.16, 5.39)	0.002
		n	243	650		
	12 months	Mean (SD)	6.9 (18.1)	4.2 (13.3)	2.50 (0.27, 4.73)	0.028
		n	225	549		
	18 months	Mean (SD)	6.1 (17.5)	4.3 (13.3)	1.36 (-0.72, 3.44)	0.199
		n	190	458		
24 months	Mean (SD)	4.2 (15.1)	2.8 (12.2)	2.60 (-0.09, 5.29)	0.058	
	n	156	400			
		Mean (SD)	5.8 (17.8)	4.0 (14.2)		

Table S6b - Fixed coefficients from the longitudinal model of global health status included in the EORTC QLQ-C30 scale on the matched chemotherapy versus no chemotherapy cohorts.

Term	Level	Effect (95% CI)	P-value
Treatment	Chemotherapy	-1.914 (-5.396, 1.568)	0.282
Time	6 weeks	-	-
	6 months	-1.970 (-4.502, 0.561)	0.127
	12 months	0.492 (-2.171, 3.156)	0.717
	18 months	-2.354 (-5.154, 0.446)	0.100
	24 months	-2.234 (-5.207, 0.738)	0.141
Treatment : Time	Chemotherapy : 6 weeks	-	-
	Chemotherapy : 6 months	-7.153 (-11.317, -2.989)	0.001
	Chemotherapy : 12 months	3.698 (-0.621, 8.017)	0.094
	Chemotherapy : 18 months	1.419 (-3.129, 5.966)	0.541
	Chemotherapy : 24 months	-0.242 (-5.164, 4.681)	0.923
Baseline		0.500 (0.430, 0.569)	<0.001

Table S7 – Mean (SD) scores for the EORTC QLQ-BR23 scale at each time point in chemotherapy versus no chemotherapy cohorts with adjusted mean difference (95% CI) and p-value.

Domain	Time point		Chemotherapy	No Chemotherapy	Adjusted Mean Difference (95% CI)	P-value
Body image	Baseline	n	280	746	-	-
		Mean (SD)	92.7 (13.8)	92.5 (14.8)		
	6 weeks	n	260	685	-0.81 (-3.58, 1.96)	0.565
		Mean (SD)	86.5 (20.8)	86.6 (20.1)		
	6 months	n	244	640	-11.18 (-14.43, -7.94)	<0.001
		Mean (SD)	73.3 (26.0)	84.5 (23.0)		
	12 months	n	224	547	-3.73 (-6.93, -0.52)	0.023
		Mean (SD)	81.8 (22.4)	85.3 (21.3)		
	18 months	n	190	460	-1.59 (-5.19, 2.01)	0.386
		Mean (SD)	84.0 (23.0)	86.1 (21.3)		
	24 months	n	155	397	-1.35 (-5.33, 2.63)	0.506
		Mean (SD)	83.0 (22.7)	84.8 (22.1)		
Sexual functioning	Baseline	n	248	644	-	-
		Mean (SD)	9.2 (18.1)	7.9 (17.6)		
	6 weeks	n	234	569	0.95 (-0.84, 2.74)	0.296
		Mean (SD)	6.1 (13.7)	5.3 (13.3)		
	6 months	n	212	543	-2.57 (-4.60, -0.54)	0.013
		Mean (SD)	4.4 (12.5)	7.2 (16.0)		
	12 months	n	198	465	0.85 (-1.32, 3.03)	0.442
		Mean (SD)	8.0 (16.1)	7.2 (15.8)		
	18 months	n	164	392	2.11 (-0.50, 4.72)	0.113
		Mean (SD)	8.4 (16.4)	7.5 (16.2)		
	24 months	n	129	338	-0.14 (-2.94, 2.67)	0.924
		Mean (SD)	7.4 (15.4)	8.4 (16.8)		
Sexual enjoyment	Baseline	n	42	76	-	-

Domain	Time point		Chemotherapy	No Chemotherapy	Adjusted Mean Difference (95% CI)	P-value	
	6 weeks	Mean (SD)	61.1 (28.4)	61.4 (30.8)	1.41 (-11.23, 14.05)	0.823	
		n	30	55			
	6 months	Mean (SD)	50.0 (30.0)	59.4 (29.9)	-5.19 (-22.01, 11.64)	0.538	
		n	17	59			
	12 months	Mean (SD)	49.0 (31.4)	60.5 (26.6)	-8.82 (-22.57, 4.93)	0.203	
		n	31	61			
	18 months	Mean (SD)	50.5 (27.0)	59.6 (30.5)	-8.67 (-26.09, 8.74)	0.32	
		n	30	48			
	24 months	Mean (SD)	42.2 (26.2)	59.0 (25.9)	1.48 (-14.42, 17.38)	0.852	
		n	17	54			
	Future perspective	Baseline	Mean (SD)	58.8 (32.3)	61.1 (26.5)	-	-
			n	280	747		
		6 weeks	Mean (SD)	66.4 (26.9)	66.0 (27.8)	-7.20 (-10.72, -3.68)	<0.001
			n	260	685		
6 months		Mean (SD)	59.1 (27.6)	66.4 (27.2)	-7.54 (-11.28, -3.80)	<0.001	
		n	243	641			
12 months		Mean (SD)	58.6 (27.5)	66.7 (27.3)	-4.96 (-8.89, -1.03)	0.013	
		n	222	547			
18 months		Mean (SD)	63.1 (28.1)	67.8 (26.6)	-4.97 (-9.37, -0.57)	0.027	
		n	190	459			
24 months		Mean (SD)	63.2 (27.0)	68.4 (27.6)	-3.13 (-7.98, 1.72)	0.205	
		n	154	397			
Systemic therapy side effects		Baseline	Mean (SD)	63.9 (28.3)	66.8 (27.1)	-	-
			n	284	765		
	6 weeks	Mean (SD)	9.1 (10.0)	9.5 (10.6)	3.04 (1.47, 4.61)	<0.001	
		n	260	690			
		Mean (SD)	14.8 (15.0)	12.4 (12.2)			
		n					

Domain	Time point		Chemotherapy	No Chemotherapy	Adjusted Mean Difference (95% CI)	P-value	
	6 months	n	246	648	16.97 (15.00, 18.94)	<0.001	
		Mean (SD)	31.9 (18.5)	15.7 (13.2)			
	12 months	n	225	549	3.32 (1.41, 5.22)	0.001	
		Mean (SD)	18.0 (15.5)	15.7 (13.8)			
	18 months	n	191	463	0.53 (-1.43, 2.49)	0.593	
		Mean (SD)	15.9 (14.6)	15.3 (13.6)			
	24 months	n	155	398	-0.98 (-3.11, 1.15)	0.368	
		Mean (SD)	14.5 (12.9)	16.0 (14.8)			
	Breast symptoms	Baseline	n	276	747	-	-
			Mean (SD)	12.4 (13.9)	11.3 (13.6)		
		6 weeks	n	258	689	-0.80 (-3.46, 1.85)	0.553
			Mean (SD)	22.2 (19.0)	22.7 (18.7)		
6 months		n	241	638	0.07 (-2.23, 2.37)	0.951	
		Mean (SD)	15.5 (16.3)	15.2 (15.2)			
12 months		n	224	537	1.47 (-0.72, 3.66)	0.188	
		Mean (SD)	14.2 (13.8)	13.0 (14.2)			
18 months		n	190	453	1.07 (-1.49, 3.64)	0.412	
		Mean (SD)	13.3 (15.3)	11.8 (14.9)			
24 months		n	154	397	1.03 (-1.51, 3.56)	0.426	
		Mean (SD)	12.4 (14.1)	10.8 (13.4)			
Arm symptoms	Baseline	n	276	748	-	-	
		Mean (SD)	8.3 (14.1)	9.3 (15.1)			
	6 weeks	n	259	685	-0.32 (-3.03, 2.39)	0.819	
		Mean (SD)	17.4 (19.0)	18.8 (19.9)			
	6 months	n	240	638	-1.95 (-4.55, 0.64)	0.14	
		Mean (SD)	12.8 (16.6)	15.7 (18.3)			
	12 months	n	225	537	4.94 (2.18, 7.69)	<0.001	

Domain	Time point		Chemotherapy	No Chemotherapy	Adjusted Mean Difference (95% CI)	P-value	
	18 months	Mean (SD)	18.5 (19.8)	14.6 (17.5)	3.27 (0.01, 6.54)	0.049	
		n	190	453			
	24 months	Mean (SD)	19.5 (23.0)	16.0 (19.1)	4.02 (0.13, 7.90)	0.043	
		n	153	399			
	Upset by hair loss	Baseline	n	19	60	-	-
			Mean (SD)	33.3 (29.4)	31.7 (30.3)		
6 weeks		n	43	64	9.92 (-22.58, 42.42)	0.538	
		Mean (SD)	45.0 (33.2)	29.7 (27.3)			
6 months		n	180	150	-7.58 (-30.35, 15.19)	0.505	
		Mean (SD)	45.9 (35.1)	32.2 (32.4)			
12 months		n	38	141	-10.35 (-55.00, 34.31)	0.639	
		Mean (SD)	50.9 (37.0)	32.4 (31.1)			
18 months		n	36	108	-29.87 (-65.77, 6.03)	0.098	
		Mean (SD)	35.2 (34.7)	35.2 (31.5)			
24 months		n	35	96	-5.05 (-35.78, 25.69)	0.73	
		Mean (SD)	38.1 (36.3)	34.4 (30.8)			

Table S8 – Mean (SD) scores for the EORTC QLQ-ELD15 scale at each timepoint in chemotherapy versus no chemotherapy cohorts with adjusted mean differences and p-values.

Domain	Time point		Chemotherapy	No Chemotherapy	Adjusted Mean Difference (95% CI)	P-value
Mobility	Baseline	n	283	765		
		Mean (SD)	12.0 (19.6)	17.0 (23.1)	-	-
	6 weeks	n	263	689		
		Mean (SD)	19.1 (21.2)	24.6 (24.1)	-0.99 (-3.26, 1.27)	0.389
	6 months	n	241	640		
		Mean (SD)	30.5 (26.5)	25.3 (25.4)	9.82 (6.87, 12.78)	<0.001
	12 months	n	226	547		
		Mean (SD)	25.0 (24.6)	27.6 (27.2)	2.20 (-0.88, 5.27)	0.161
	18 months	n	190	455		
		Mean (SD)	25.6 (25.3)	27.7 (26.8)	-0.21 (-3.62, 3.20)	0.905
	24 months	n	153	399		
		Mean (SD)	27.2 (26.0)	30.2 (28.0)	-0.57 (-4.59, 3.45)	0.782
Worries about others	Baseline	n	280	755		
		Mean (SD)	45.4 (31.0)	41.9 (30.7)	-	-
	6 weeks	n	263	685		
		Mean (SD)	46.8 (29.4)	39.1 (30.7)	5.31 (1.55, 9.07)	0.006
	6 months	n	240	635		
		Mean (SD)	41.1 (29.1)	34.4 (29.3)	6.19 (2.44, 9.95)	0.001
	12 months	n	226	540		
		Mean (SD)	38.1 (28.4)	33.3 (28.8)	4.47 (0.42, 8.52)	0.031
	18 months	n	190	452		
		Mean (SD)	35.2 (29.7)	31.7 (28.6)	3.17 (-1.30, 7.64)	0.164
	24 months	n	152	392		
		Mean (SD)	36.1 (28.3)	31.7 (26.4)	4.41 (-0.24, 9.05)	0.063

Domain	Time point		Chemotherapy	No Chemotherapy	Adjusted Mean Difference (95% CI)	P-value
Worries	Baseline	n	283	757	-	-
		Mean (SD)	37.1 (27.7)	36.5 (26.9)		
	6 weeks	n	264	686	4.09 (0.92, 7.27)	0.011
		Mean (SD)	40.7 (27.4)	35.4 (27.0)		
	6 months	n	241	639	4.18 (0.89, 7.46)	0.013
		Mean (SD)	39.1 (26.6)	34.0 (27.0)		
	12 months	n	226	545	0.01 (-3.57, 3.60)	0.995
		Mean (SD)	34.8 (26.1)	34.6 (26.8)		
	18 months	n	190	454	0.86 (-3.09, 4.80)	0.670
		Mean (SD)	34.5 (24.5)	32.8 (27.2)		
	24 months	n	153	395	0.78 (-3.62, 5.17)	0.729
		Mean (SD)	34.9 (25.5)	34.2 (26.4)		
Maintaining purpose	Baseline	n	283	758	-	-
		Mean (SD)	68.5 (35.0)	64.4 (33.6)		
	6 weeks	n	264	687	0.37 (-4.03, 4.77)	0.870
		Mean (SD)	63.6 (30.2)	62.7 (31.9)		
	6 months	n	241	640	0.71 (-4.09, 5.51)	0.773
		Mean (SD)	64.2 (29.1)	61.8 (33.4)		
	12 months	n	224	544	-0.16 (-5.14, 4.82)	0.950
		Mean (SD)	64.4 (33.4)	63.9 (31.5)		
	18 months	n	190	454	2.90 (-2.66, 8.46)	0.306
		Mean (SD)	65.3 (32.9)	62.0 (32.0)		
	24 months	n	153	398	1.29 (-4.49, 7.08)	0.661
		Mean (SD)	64.6 (29.3)	62.3 (31.8)		
Burden of illness	Baseline	n	281	753	-	-
		Mean (SD)	20.2 (23.1)	20.4 (23.4)		
	6 weeks	n	263	688	4.68 (1.25, 8.11)	0.007
		Mean (SD)	35.8 (26.1)	31.8 (24.9)		

Domain	Time point		Chemotherapy	No Chemotherapy	Adjusted Mean Difference (95% CI)	P-value
Joint stiffness	6 months	n	242	641	21.60 (17.82, 25.39)	<0.001
		Mean (SD)	48.9 (28.5)	28.2 (25.3)		
	12 months	n	225	541	15.21 (11.30, 19.12)	<0.001
		Mean (SD)	38.6 (27.0)	24.5 (24.6)		
	18 months	n	190	455	12.99 (8.81, 17.17)	<0.001
		Mean (SD)	34.3 (26.0)	22.0 (24.5)		
	24 months	n	153	397	8.80 (3.93, 13.66)	<0.001
		Mean (SD)	33.3 (25.6)	24.6 (26.9)		
	Baseline	n	282	759	-	-
		Mean (SD)	25.4 (27.9)	27.1 (28.1)		
	6 weeks	n	262	686	-2.80 (-5.92, 0.33)	0.079
		Mean (SD)	22.4 (26.9)	27.0 (27.7)		
6 months	n	237	639	-0.91 (-4.89, 3.06)	0.652	
	Mean (SD)	36.1 (30.9)	38.6 (29.7)			
12 months	n	225	543	1.46 (-2.57, 5.50)	0.476	
	Mean (SD)	42.2 (29.0)	42.4 (29.4)			
18 months	n	189	453	4.05 (-0.28, 8.38)	0.067	
	Mean (SD)	46.4 (28.0)	41.6 (28.9)			
24 months	n	151	396	0.17 (-4.81, 5.16)	0.946	
	Mean (SD)	43.9 (29.7)	44.0 (30.5)			
Family support	Baseline	n	278	751	-	-
		Mean (SD)	77.9 (31.8)	74.6 (32.0)		
	6 weeks	n	263	681	6.21 (2.26, 10.17)	0.002
		Mean (SD)	81.2 (25.9)	73.2 (30.5)		
	6 months	n	237	634	4.91 (0.26, 9.56)	0.038
		Mean (SD)	76.7 (29.3)	69.6 (32.6)		
	12 months	n	224	531	5.43 (0.39, 10.46)	0.035
		Mean (SD)	71.4 (30.7)	64.3 (34.4)		

Domain	Time point	Chemotherapy	No Chemotherapy	Adjusted Mean Difference (95% CI)	P-value	
	18 months	n	186	444	1.48 (-4.32, 7.29)	0.616
		Mean (SD)	66.0 (34.7)	63.2 (33.6)		
	24 months	n	149	385	-0.73 (-7.13, 5.67)	0.822
		Mean (SD)	62.4 (33.4)	60.5 (34.2)		

Table S9 – Mean scores and 95% confidence intervals (CIs) adjusted for baseline score for the EQ-5D-5L scale at each timepoint in chemotherapy versus no chemotherapy cohorts.

Domain	Time point	Chemotherapy	No Chemotherapy	Adjusted Mean Difference (95% CI)	P-value		
Score	Baseline	n	335	980	-	-	
		Mean (SD)	0.8769 (0.1327)	0.8693 (0.1489)			
	6 weeks	n	299	807	0.0130 (-0.0030, 0.0289)	0.112	
		Mean (SD)	0.8409 (0.1414)	0.8242 (0.1572)	-0.0028 (-0.0231, 0.0175)		
	6 months	n	279	760	-0.0013 (-0.0228, 0.0201)	0.789	
		Mean (SD)	0.8247 (0.1767)	0.8241 (0.1721)	0.0114 (-0.0143, 0.0372)		
	12 months	n	261	659	0.0001 (-0.0286, 0.0288)	0.903	
		Mean (SD)	0.8274 (0.1639)	0.8185 (0.1753)	0.0130 (-0.0030, 0.0289)		
	18 months	n	224	556	-0.0028 (-0.0231, 0.0175)	0.384	
		Mean (SD)	0.8186 (0.1937)	0.8088 (0.1910)	-0.0013 (-0.0228, 0.0201)		
	24 months	n	185	474	0.0114 (-0.0143, 0.0372)	0.994	
		Mean (SD)	0.8013 (0.1787)	0.8020 (0.1968)			
	VAS	Baseline	n	324	951	-	-
			Mean (SD)	78.9 (16.3)	76.9 (16.6)		
6 weeks		n	296	793	-1.44 (-3.52, 0.64)	0.176	
		Mean (SD)	74.5 (17.4)	74.9 (17.0)			
6 months		n	280	757	-6.57 (-8.74, -4.40)	<0.001	
		Mean (SD)	70.1 (18.0)	75.3 (16.7)			
12 months		n	256	656	0.72 (-1.60, 3.05)	0.541	
		Mean (SD)	76.7 (15.8)	74.8 (17.6)			
18 months		n	230	549	0.92 (-1.78, 3.63)	0.503	
		Mean (SD)	74.9 (17.6)	73.6 (18.3)			
24 months		n	185	479	1.48 (-1.41, 4.36)	0.315	
		Mean (SD)	74.7 (16.3)	72.7 (18.2)			