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Supplementary materials

Supplementary Table 1 - 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 Vijh (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)

Supplementary Table 2 – Summary of the Quality-of-Life instruments used in the Age Gap study and their meaning.

Instrument	Question number	Domain number	Domains	No. items	Score positive or negative
Generic cancer EORTC QLQ C30	30	2 visual analogue scales,	Health status	1	High score means higher level of function
			Quality of life	1	
		5 multi-item functional scales	Physical	5	
			Role	2	
			Emotional	4	
			Cognitive	2	
			Social	2	
		9 symptom scales	Fatigue	3	Higher score means higher symptom severity
			Nausea and vomiting	2	
			Pain	2	
			Dyspnoea	1	
			Insomnia	1	
			Appetite loss	1	
			Constipation	1	
			Diarrhoea	1	
			Financial difficulties	1	
Breast cancer specific EORTC QLQ BR23	23	5 multi-item scales	Body image	4	High score means higher level of function
			Sexual function	2	
			Sexual enjoyment	1	
			Future perspectives	1	
		4 single item symptom scales	Systemic therapy side effects	7	Higher score means higher symptom severity
			Breast symptoms	4	
			Arm symptoms	3	
			Upset by hair loss	1	
Older person specific EORTC ELD-14	14	2 functional scales	Family support	2	High score means higher level of function
			Maintaining autonomy and purpose	2	
		3 symptom scales	Mobility	3	Higher score means higher symptom severity
			Future worries	5	
			Burden of illness	2	
Generic EQ5D-5L	5 plus a visual analogue scale	3 functional scales	Mobility	5	All scored from 1-5 with score of 1 being the best outcome, 5 the worst
			Self-care	5	
			Usual activities	5	
		2 symptom scales	Pain/discomfort	5	
			Anxiety/depression	5	
		1 visual analogue scale	How good/bad is health today	1	Scored 1-100 with 100 meaning best health possible

Supplementary Table 3 – Definitions of risk of recurrence and fitness.

Supplementary Table 3a – Definition of risk of recurrence categories.

Tumour characteristics	Risk of recurrence	
	High*	Low
BREAST CONSERVING COHORT		
Tumour size	≥3cm	<3cm
ER	Negative	Positive
HER2	Positive	Negative
Grade	3	1-2
Nodal involvement	Yes	No
MASTECTOMY COHORT		
Tumour size	≥5cm	<5cm
Lymph nodes involved	≥4	<4

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

Supplementary Table 3b – Definition of fitness categories. Overall scores: Fit: 0-2; Vulnerable: 3-8. Frail: ≥9.

Domain	Range	Score		
		0	1	2
ECOG PS	0-4	0-1	2	3-4
ADL	0-10	20	19	≤18
IADL	0-8	8	7	≤6
Charlson comorbidity index	-	0-1	-	≥2
Prescribed medications (excluding vitamins/minerals)	-	≤3	≥4	-
APSGA		0-3	4-8	≥9
MMSE	0-30	≥24	20-24	<20

Supplementary Table 4 - Postoperative tumour, patient and treatment characteristics by receipt of radiotherapy.

		No radiotherapy N = 1058	Radiotherapy N = 1753	Total N = 2811
Age (years)	70-74	374 (35.3%)	799 (45.6%)	1173 (41.7%)
	75-79	318 (30.1%)	581 (33.1%)	899 (32.0%)
	80-84	225 (21.3%)	281 (16.1%)	506 (18.0%)
	≥85	141 (13.3%)	92 (5.2%)	233 (8.3%)
Participation level	Full	784 (74.1%)	1327 (75.7%)	2111 (75.1%)
	Partial	232 (21.9%)	389 (22.2%)	621 (22.1%)
	Consultee	42 (4.0%)	37 (2.1%)	79 (2.8%)
Main side	Right	487 (46.0%)	818 (46.7%)	1305 (46.4%)
	Left	571 (54.0%)	935 (53.3%)	1506 (53.6%)
Tumour size (mm)	≤ 20	432 (40.8%)	847 (48.3%)	1279 (45.5%)
	21-50	530 (50.1%)	755 (43.1%)	1285 (45.7%)
	> 50	66 (6.2%)	122 (7.0%)	188 (6.7%)
	Unknown	30 (2.8%)	29 (1.7%)	59 (2.1%)
Nodal status	pN0	764 (72.2%)	1149 (65.5%)	1913 (68.1%)
	pN1	204 (19.3%)	408 (23.3%)	612 (21.8%)
	pN2	36 (3.4%)	111 (6.3%)	147 (5.2%)
	pN3	21 (2.0%)	56 (3.2%)	77 (2.7%)
	Unknown	33 (3.1%)	29 (1.7%)	62 (2.2%)
Grade	Grade 1	147 (13.9%)	234 (13.3%)	381 (13.6%)
	Grade 2	540 (51.0%)	945 (53.9%)	1485 (52.8%)
	Grade 3	331 (31.3%)	534 (30.5%)	865 (30.8%)
	Unknown	40 (3.8%)	40 (2.3%)	80 (2.8%)
Histology	Ductal carcinoma	685 (64.7%)	1130 (64.5%)	1815 (64.6%)
	Lobular carcinoma	143 (13.5%)	232 (13.2%)	375 (13.3%)
	Tubular carcinoma	5 (0.5%)	24 (1.4%)	29 (1.0%)

		No radiotherapy N = 1058	Radiotherapy N = 1753	Total N = 2811
	Mucinous carcinoma	34 (3.2%)	37 (2.1%)	71 (2.5%)
	Other	107 (10.1%)	159 (9.1%)	266 (9.5%)
	Unknown	84 (7.9%)	171 (9.8%)	255 (9.1%)
ER status	Negative	166 (15.7%)	206 (11.8%)	372 (13.2%)
	Positive	844 (79.8%)	1510 (86.1%)	2354 (83.7%)
	Unknown	48 (4.5%)	37 (2.1%)	85 (3.0%)
HER2 status	Negative	816 (77.1%)	1456 (83.1%)	2272 (80.8%)
	Inconclusive	9 (0.9%)	13 (0.7%)	22 (0.8%)
	Positive	153 (14.5%)	179 (10.2%)	332 (11.8%)
	Unknown	80 (7.6%)	105 (6.0%)	185 (6.6%)
ADL category	No dependency	729 (68.9%)	1275 (72.7%)	2004 (71.3%)
	Mild dependency	125 (11.8%)	183 (10.4%)	308 (11.0%)
	Moderate/severe dependency	120 (11.3%)	158 (9.0%)	278 (9.9%)
	Unknown	84 (7.9%)	137 (7.8%)	221 (7.9%)
IADL category	No dependency	739 (69.8%)	1330 (75.9%)	2069 (73.6%)
	Mild dependency	104 (9.8%)	145 (8.3%)	249 (8.9%)
	Moderate/severe dependency	126 (11.9%)	132 (7.5%)	258 (9.2%)
	Unknown	89 (8.4%)	146 (8.3%)	235 (8.4%)
MMSE category	Normal function	907 (85.7%)	1587 (90.5%)	2494 (88.7%)
	Mild impairment	112 (10.6%)	136 (7.8%)	248 (8.8%)
	Moderate impairment	15 (1.4%)	21 (1.2%)	36 (1.3%)
	Severe impairment	24 (2.3%)	9 (0.5%)	33 (1.2%)
AGP SGA category	Low	805 (76.1%)	1375 (78.4%)	2180 (77.6%)
	Moderate	122 (11.5%)	166 (9.5%)	288 (10.2%)
	High	12 (1.1%)	28 (1.6%)	40 (1.4%)
	Unknown	119 (11.2%)	184 (10.5%)	303 (10.8%)
ECOG performance status	0	675 (63.8%)	1269 (72.4%)	1944 (69.2%)

		No radiotherapy N = 1058	Radiotherapy N = 1753	Total N = 2811
	1	270 (25.5%)	337 (19.2%)	607 (21.6%)
	2	42 (4.0%)	38 (2.2%)	80 (2.8%)
	3	18 (1.7%)	18 (1.0%)	36 (1.3%)
	4	1 (0.1%)	0 (0.0%)	1 (0.0%)
	Unknown	52 (4.9%)	91 (5.2%)	143 (5.1%)
Charlson comorbidity index (no age)	n	1021	1686	2707
	Mean (SD)	1.06 (1.29)	1.02 (1.31)	1.03 (1.30)
	Median (IQR)	1.00 (0.00, 2.00)	0.00 (0.00, 2.00)	1.00 (0.00, 2.00)
	Min, Max	0, 9	0, 9	0, 9
Number of concurrent medications	n	926	1520	2446
	Mean (SD)	4.12 (2.70)	4.03 (2.60)	4.06 (2.64)
	Median (IQR)	4.00 (2.00, 6.00)	4.00 (2.00, 5.00)	4.00 (2.00, 5.75)
	Min, Max	0, 18	0, 15	0, 18
Breast surgery	Breast conserving surgery	284 (26.8%)	1385 (79.1%)	1669 (59.4%)
	Mastectomy	746 (70.5%)	341 (19.4%)	1087 (38.7%)
	Unknown	28 (2.7%)	27 (1.5%)	55 (1.9%)
Axillary surgery	Axillary sample	32 (3.0%)	56 (3.2%)	88 (3.1%)
	Axillary clearance	166 (15.7%)	248 (14.1%)	414 (14.7%)
	Sentinel lymph node biopsy	724 (68.4%)	1256 (71.6%)	1980 (70.4%)
	Internal mammary node biopsy	0 (0.0%)	1 (0.1%)	1 (0.0%)
	No axillary surgery	55 (5.2%)	25 (1.4%)	80 (2.8%)
	Unknown	81 (7.7%)	167 (9.5%)	248 (8.8%)
Chemotherapy	Chemotherapy	146 (13.8%)	251 (14.3%)	397 (14.1%)
	No Chemotherapy	912 (86.2%)	1502 (85.7%)	2414 (85.9%)

Supplementary Table 5 - Postoperative tumour, patient and treatment characteristics by age.

		70-74	75-79	80-84	>=85	Total
		N = 1173	N = 899	N = 506	N = 233	N = 2811
Participation level	Full	926 (78.9%)	674 (75.0%)	368 (72.7%)	143 (61.4%)	2111 (75.1%)
	Partial	225 (19.2%)	209 (23.2%)	123 (24.3%)	64 (27.5%)	621 (22.1%)
	Consultee	22 (1.9%)	16 (1.8%)	15 (3.0%)	26 (11.2%)	79 (2.8%)
Main side	Right	535 (45.6%)	418 (46.5%)	247 (48.8%)	105 (45.1%)	1305 (46.4%)
	Left	638 (54.4%)	481 (53.5%)	259 (51.2%)	128 (54.9%)	1506 (53.6%)
Tumour size (mm)	≤ 20	649 (55.3%)	371 (41.3%)	184 (36.4%)	75 (32.2%)	1279 (45.5%)
	21-50	439 (37.4%)	439 (48.8%)	271 (53.6%)	136 (58.4%)	1285 (45.7%)
	> 50	66 (5.6%)	66 (7.3%)	40 (7.9%)	16 (6.9%)	188 (6.7%)
	Unknown	19 (1.6%)	23 (2.6%)	11 (2.2%)	6 (2.6%)	59 (2.1%)
Tumour size (mm)	N	1154	876	495	227	2752
	Mean (SD)	23.07 (17.68)	26.53 (16.19)	27.55 (15.40)	28.75 (15.74)	25.45 (16.79)
	Median (IQR)	19.00 (12.00, 28.00)	22.00 (16.00, 32.00)	25.00 (17.00, 35.00)	25.00 (19.00, 35.00)	21.00 (15.00, 31.00)
	Min, Max	0, 210	0, 155	0, 120	7, 120	0, 210
Nodal involvement	pN0	867 (73.9%)	573 (63.7%)	326 (64.4%)	147 (63.1%)	1913 (68.1%)
	pN1	212 (18.1%)	223 (24.8%)	117 (23.1%)	60 (25.8%)	612 (21.8%)
	pN2	46 (3.9%)	54 (6.0%)	36 (7.1%)	11 (4.7%)	147 (5.2%)
	pN3	29 (2.5%)	24 (2.7%)	16 (3.2%)	8 (3.4%)	77 (2.7%)
	Unknown	19 (1.6%)	25 (2.8%)	11 (2.2%)	7 (3.0%)	62 (2.2%)
Grade	1	199 (17.0%)	110 (12.2%)	47 (9.3%)	25 (10.7%)	381 (13.6%)
	2	635 (54.1%)	482 (53.6%)	255 (50.4%)	113 (48.5%)	1485 (52.8%)
	3	311 (26.5%)	278 (30.9%)	190 (37.5%)	86 (36.9%)	865 (30.8%)
	Unknown	28 (2.4%)	29 (3.2%)	14 (2.8%)	9 (3.9%)	80 (2.8%)
Histology	Ductal carcinoma	761 (64.9%)	567 (63.1%)	341 (67.4%)	146 (62.7%)	1815 (64.6%)
	Lobular carcinoma	164 (14.0%)	128 (14.2%)	58 (11.5%)	25 (10.7%)	375 (13.3%)
	Tubular carcinoma	21 (1.8%)	5 (0.6%)	3 (0.6%)	0 (0.0%)	29 (1.0%)
	Mucinous carcinoma	18 (1.5%)	28 (3.1%)	12 (2.4%)	13 (5.6%)	71 (2.5%)

		70-74	75-79	80-84	>=85	Total
		N = 1173	N = 899	N = 506	N = 233	N = 2811
ER status	Other	110 (9.4%)	83 (9.2%)	53 (10.5%)	20 (8.6%)	266 (9.5%)
	Unknown	99 (8.4%)	88 (9.8%)	39 (7.7%)	29 (12.4%)	255 (9.1%)
	Negative	141 (12.0%)	117 (13.0%)	74 (14.6%)	40 (17.2%)	372 (13.2%)
	Positive	1002 (85.4%)	753 (83.8%)	414 (81.8%)	185 (79.4%)	2354 (83.7%)
	Unknown	30 (2.6%)	29 (3.2%)	18 (3.6%)	8 (3.4%)	85 (3.0%)
HER2 status	Negative	981 (83.6%)	724 (80.5%)	375 (74.1%)	192 (82.4%)	2272 (80.8%)
	Positive	136 (11.6%)	115 (12.8%)	63 (12.5%)	18 (7.7%)	332 (11.8%)
	Inconclusive	9 (0.8%)	7 (0.8%)	4 (0.8%)	2 (0.9%)	22 (0.8%)
	Unknown	47 (4.0%)	53 (5.9%)	64 (12.6%)	21 (9.0%)	185 (6.6%)
ADL category	No dependency	924 (78.8%)	623 (69.3%)	331 (65.4%)	126 (54.1%)	2004 (71.3%)
	Mild dependency	89 (7.6%)	109 (12.1%)	67 (13.2%)	43 (18.5%)	308 (11.0%)
	Moderate/severe dependency	70 (6.0%)	101 (11.2%)	60 (11.9%)	47 (20.2%)	278 (9.9%)
	Unknown	90 (7.7%)	66 (7.3%)	48 (9.5%)	17 (7.3%)	221 (7.9%)
IADL category	No dependency	955 (81.4%)	679 (75.5%)	332 (65.6%)	103 (44.2%)	2069 (73.6%)
	Mild dependency	54 (4.6%)	78 (8.7%)	70 (13.8%)	47 (20.2%)	249 (8.9%)
	Moderate/severe dependency	67 (5.7%)	70 (7.8%)	55 (10.9%)	66 (28.3%)	258 (9.2%)
	Unknown	97 (8.3%)	72 (8.0%)	49 (9.7%)	17 (7.3%)	235 (8.4%)
MMSE category	Normal function	1059 (90.3%)	805 (89.5%)	444 (87.7%)	186 (79.8%)	2494 (88.7%)
	Mild impairment	91 (7.8%)	74 (8.2%)	50 (9.9%)	33 (14.2%)	248 (8.8%)
	Moderate impairment	11 (0.9%)	12 (1.3%)	5 (1.0%)	8 (3.4%)	36 (1.3%)
	Severe	12 (1.0%)	8 (0.9%)	7 (1.4%)	6 (2.6%)	33 (1.2%)
AGP SGA category	Low	929 (79.2%)	709 (78.9%)	370 (73.1%)	172 (73.8%)	2180 (77.6%)
	Moderate	111 (9.5%)	88 (9.8%)	62 (12.3%)	27 (11.6%)	288 (10.2%)
	High	15 (1.3%)	13 (1.4%)	10 (2.0%)	2 (0.9%)	40 (1.4%)
	Unknown	118 (10.1%)	89 (9.9%)	64 (12.6%)	32 (13.7%)	303 (10.8%)
ECOG performance status	0	930 (79.3%)	619 (68.9%)	305 (60.3%)	90 (38.6%)	1944 (69.2%)
	1	151 (12.9%)	205 (22.8%)	142 (28.1%)	109 (46.8%)	607 (21.6%)

		70-74	75-79	80-84	>=85	Total
		N = 1173	N = 899	N = 506	N = 233	N = 2811
	2	21 (1.8%)	24 (2.7%)	23 (4.5%)	12 (5.2%)	80 (2.8%)
	3	10 (0.9%)	9 (1.0%)	8 (1.6%)	9 (3.9%)	36 (1.3%)
	4	1 (0.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.0%)
	Unknown	60 (5.1%)	42 (4.7%)	28 (5.5%)	13 (5.6%)	143 (5.1%)
Charlson comorbidity index (no age)	N	1133	869	481	224	2707
	Mean (SD)	0.90 (1.21)	1.10 (1.36)	1.19 (1.37)	1.09 (1.30)	1.03 (1.30)
	Median (IQR)	0.00 (0.00, 2.00)	1.00 (0.00, 2.00)	1.00 (0.00, 2.00)	1.00 (0.00, 2.00)	1.00 (0.00, 2.00)
	Min, Max	0, 6	0, 9	0, 9	0, 6	0, 9
Number of concurrent medications	N	973	801	462	210	2446
	Mean (SD)	3.85 (2.66)	4.16 (2.63)	4.26 (2.63)	4.21 (2.53)	4.06 (2.64)
	Median (IQR)	3.00 (2.00, 5.00)	4.00 (2.00, 6.00)	4.00 (2.00, 6.00)	4.00 (2.00, 6.00)	4.00 (2.00, 5.75)
	Min, Max	0, 14	0, 18	0, 14	0, 14	0, 18
Surgery type	Mastectomy	342 (29.2%)	356 (39.6%)	253 (50.0%)	136 (58.4%)	1087 (38.7%)
	Breast conservation	813 (69.3%)	521 (58.0%)	243 (48.0%)	92 (39.5%)	1669 (59.4%)
	Unknown	18 (1.5%)	22 (2.4%)	10 (2.0%)	5 (2.1%)	55 (2.0%)
Axillary surgery	Axillary sampling	38 (3.2%)	30 (3.3%)	11 (2.2%)	9 (3.9%)	88 (3.1%)
	Axillary clearance	134 (11.4%)	134 (14.9%)	99 (19.6%)	47 (20.2%)	414 (14.7%)
	Sentinel lymph node biopsy	881 (75.1%)	633 (70.4%)	336 (66.4%)	130 (55.8%)	1980 (70.4%)
	Internal mammary node biopsy	0 (0.0%)	1 (0.1%)	0 (0.0%)	0 (0.0%)	1 (0.0%)
	No axillary surgery	23 (2.0%)	16 (1.8%)	22 (4.3%)	19 (8.2%)	80 (2.8%)
	Unknown	97 (8.3%)	85 (9.5%)	38 (7.5%)	28 (12.0%)	248 (8.8%)
Chemotherapy use	Yes	256 (21.8%)	120 (13.3%)	20 (4.0%)	1 (0.4%)	397 (14.1%)
	No	917 (78.2%)	779 (86.7%)	486 (96.0%)	232 (99.6%)	2414 (85.9%)
Radiotherapy use	Yes	799 (68.1%)	581 (64.6%)	281 (55.5%)	92 (39.5%)	1753 (62.4%)
	No	374 (31.9%)	318 (35.4%)	225 (44.5%)	141 (60.5%)	1058 (37.6%)

Supplementary Table 6 – Radiotherapy details by treatment side for all women whose primary treatment was breast conserving surgery.

BREAST CONSERVING SURGERY COHORT		
	Left	Right
	N = 741	N = 666
Breast	733 (98.9%)	663 (99.5%)
Breast fractions	n	658
	Mean (SD)	14.99 (2.74)
	Median (IQR)	15.00 (15.00, 15.00)
	Min, Max	1, 40
Axilla	Ticked	24 (3.6%)
Axilla fractions	n	24
	Mean (SD)	14.54 (2.73)
	Median (IQR)	15.00 (15.00, 15.00)
	Min, Max	5, 20
Supraclavicular fossa		38 (5.7%)
Supraclavicular fossa fractions	n	37
	Mean (SD)	14.81 (2.54)
	Median (IQR)	15.00 (15.00, 15.00)
	Min, Max	5, 25
Chest wall		5 (0.8%)
Chest wall fractions	n	5
	Mean (SD)	11.00 (5.48)
	Median (IQR)	15.00 (5.00, 15.00)
	Min, Max	5, 15
Other		15 (2.3%)
Other fractions	n	15
	Mean (SD)	6.78 (3.66)
	Median (IQR)	5.00 (5.00, 7.25)
	Min, Max	3, 16

		MASTECTOMY COHORT	
		Left	Right
		N = 192	N = 148
Breast		48 (25.0%)	43 (29.1%)
Breast fractions*	n	48	43
	Mean (SD)	15.33 (1.23)	15.58 (2.49)
	Median (IQR)	15.00 (15.00, 15.00)	15.00 (15.00, 15.00)
	Min, Max	15, 20	15, 30
Axilla	Ticked	41 (21.4%)	27 (18.2%)
Axilla fractions	n	41	27
	Mean (SD)	15.51 (1.87)	15.52 (2.14)
	Median (IQR)	15.00 (15.00, 15.00)	15.00 (15.00, 15.00)
	Min, Max	15, 25	14, 25
Supraclavicular fossa		83 (43.2%)	70 (47.3%)
Supraclavicular fossa fractions	n	83	67
	Mean (SD)	15.31 (2.57)	15.51 (1.78)
	Median (IQR)	15.00 (15.00, 15.00)	15.00 (15.00, 15.00)
	Min, Max	4, 25	14, 25
Chest wall		145 (75.5%)	102 (68.9%)
Chest wall fractions	n	145	100
	Mean (SD)	15.14 (2.60)	15.35 (2.24)
	Median (IQR)	15.00 (15.00, 15.00)	15.00 (15.00, 15.00)
	Min, Max	2, 30	5, 25
Other		6 (3.1%)	6 (4.1%)
Other fractions	n	6	6
	Mean (SD)	15.67 (6.98)	15.00 (6.32)
	Median (IQR)	15.00 (15.00, 18.75)	15.00 (15.00, 15.00)
	Min, Max	4, 25	5, 25

*This category in the mastectomy cohort includes radiotherapy given to contralateral breast for patients with bilateral breast cancer.

Supplementary Table 7 – Radiotherapy use by site.

Site ID	Availability of radiotherapy on site	n/N (%)
1	No	10/11 (90.9%)
2	Yes	37/41 (90.2%)
3	Yes	66/78 (84.6%)
4	No	21/25 (84.0%)
5	Yes	28/34 (82.4%)
6	No	13/16 (81.2%)
7	Yes	92/117 (78.6%)
8	Yes	29/37 (78.4%)
9	No	42/54 (77.8%)
10	No	37/49 (75.5%)
11	Yes	66/88 (75.0%)
12	No	38/51 (74.5%)
13	Yes	62/85 (72.9%)
14	Yes	72/101 (71.3%)
15	Yes	27/38 (71.1%)
16	No	12/17 (70.6%)
17	No	7/10 (70.0%)
18	No	18/26 (69.2%)
19	No	33/48 (68.8%)
20	No	16/24 (66.7%)
21	No	26/39 (66.7%)
22	No	34/52 (65.4%)
23	No	43/66 (65.2%)
24	No	48/74 (64.9%)
25	No	14/22 (63.6%)
26	No	44/71 (62.0%)
27	Yes	13/21 (61.9%)

Site ID	Availability of radiotherapy on site	n/N (%)
28	No	35/57 (61.4%)
29	Yes	92/153 (60.1%)
30	No	15/25 (60.0%)
31	Yes	3/5 (60.0%)
32	No	77/132 (58.3%)
33	No	90/155 (58.1%)
34	No	8/14 (57.1%)
35	No	25/44 (56.8%)
36	Yes	108/192 (56.2%)
37	Yes	46/82 (56.1%)
38	No	54/98 (55.1%)
39	No	18/33 (54.5%)
40	Yes	6/11 (54.5%)
41	Yes	13/24 (54.2%)
42	Yes	13/24 (54.2%)
43	Yes	23/44 (52.3%)
44	No	29/57 (50.9%)
45	No	3/6 (50.0%)
46	Yes	3/6 (50.0%)
47	No	14/28 (50.0%)
48	No	38/78 (48.7%)
49	No	25/57 (43.9%)
50	No	9/21 (42.9%)
51	No	7/17 (41.2%)
52	No	15/37 (40.5%)
53	No	3/8 (37.5%)
54	No	19/54 (35.2%)
55	Yes	11/37 (29.7%)

Site ID	Availability of radiotherapy on site	n/N (%)
56	No	3/17 (17.6%)

Supplementary Table 8 – Completion of the QoL questionnaires at each time point for patients undergoing BCS or mastectomy.

		BREAST CONSERVING SURGERY COHORT		
		No radiotherapy	Radiotherapy	Total
		N = 210	N = 915	N = 1125
		EORTC-QLQ-C30		
Baseline	All	181 (86.2%)	823 (89.9%)	1004 (89.2%)
	Some	8 (3.8%)	40 (4.4%)	48 (4.3%)
	None	21 (10.0%)	52 (5.7%)	73 (6.5%)
6 weeks	All	157 (74.8%)	758 (82.8%)	915 (81.3%)
	Some	7 (3.3%)	44 (4.8%)	51 (4.5%)
	None	46 (21.9%)	113 (12.3%)	159 (14.1%)
6 months	All	134 (63.8%)	728 (79.6%)	862 (76.6%)
	Some	8 (3.8%)	33 (3.6%)	41 (3.6%)
	None	68 (32.4%)	154 (16.8%)	222 (19.7%)
12 months	All	114 (54.3%)	646 (70.6%)	760 (67.6%)
	Some	11 (5.2%)	33 (3.6%)	44 (3.9%)
	None	85 (40.5%)	236 (25.8%)	321 (28.5%)
18 months	All	101 (48.1%)	531 (58.0%)	632 (56.2%)
	Some	7 (3.3%)	35 (3.8%)	42 (3.7%)
	None	102 (48.6%)	349 (38.1%)	451 (40.1%)
24 months	All	83 (39.5%)	472 (51.6%)	555 (49.3%)
	Some	6 (2.9%)	24 (2.6%)	30 (2.7%)
	None	121 (57.6%)	419 (45.8%)	540 (48.0%)
		EORTC-QLQ-BR23		
Baseline	All	0 (0.0%)	8 (0.9%)	8 (0.7%)
	Some	188 (89.5%)	854 (93.3%)	1042 (92.6%)
	None	22 (10.5%)	53 (5.8%)	75 (6.7%)
6 weeks	All	0 (0.0%)	8 (0.9%)	8 (0.7%)
	Some	164 (78.1%)	789 (86.2%)	953 (84.7%)

	None	46 (21.9%)	118 (12.9%)	164 (14.6%)
6 months	All	7 (3.3%)	22 (2.4%)	29 (2.6%)
	Some	133 (63.3%)	733 (80.1%)	866 (77.0%)
	None	70 (33.3%)	160 (17.5%)	230 (20.4%)
12 months	All	7 (3.3%)	27 (3.0%)	34 (3.0%)
	Some	118 (56.2%)	650 (71.0%)	768 (68.3%)
	None	85 (40.5%)	238 (26.0%)	323 (28.7%)
18 months	All	5 (2.4%)	16 (1.7%)	21 (1.9%)
	Some	102 (48.6%)	548 (59.9%)	650 (57.8%)
	None	103 (49.0%)	351 (38.4%)	454 (40.4%)
24 months	All	2 (1.0%)	26 (2.8%)	28 (2.5%)
	Some	87 (41.4%)	472 (51.6%)	559 (49.7%)
	None	121 (57.6%)	417 (45.6%)	538 (47.8%)
EORTC-QLQ-ELD15				
Baseline	All	182 (86.7%)	820 (89.6%)	1002 (89.1%)
	Some	6 (2.9%)	36 (3.9%)	42 (3.7%)
	None	22 (10.5%)	59 (6.4%)	81 (7.2%)
6 weeks	All	161 (76.7%)	777 (84.9%)	938 (83.4%)
	Some	1 (0.5%)	16 (1.7%)	17 (1.5%)
	None	48 (22.9%)	122 (13.3%)	170 (15.1%)
6 months	All	134 (63.8%)	715 (78.1%)	849 (75.5%)
	Some	7 (3.3%)	29 (3.2%)	36 (3.2%)
	None	69 (32.9%)	171 (18.7%)	240 (21.3%)
12 months	All	119 (56.7%)	646 (70.6%)	765 (68.0%)
	Some	5 (2.4%)	27 (3.0%)	32 (2.8%)
	None	86 (41.0%)	242 (26.4%)	328 (29.2%)
18 months	All	101 (48.1%)	531 (58.0%)	632 (56.2%)
	Some	5 (2.4%)	23 (2.5%)	28 (2.5%)
	None	104 (49.5%)	361 (39.5%)	465 (41.3%)

24 months	All	88 (41.9%)	473 (51.7%)	561 (49.9%)
	Some	0 (0.0%)	18 (2.0%)	18 (1.6%)
	None	122 (58.1%)	424 (46.3%)	546 (48.5%)
MASTECTOMY COHORT				
		No radiotherapy	Radiotherapy	Total
		N = 459	N = 169	N = 628
EORTC-QLQ-C30				
Baseline	All	416 (90.6%)	151 (89.3%)	567 (90.3%)
	Some	19 (4.1%)	7 (4.1%)	26 (4.1%)
	None	24 (5.2%)	11 (6.5%)	35 (5.6%)
6 weeks	All	384 (83.7%)	130 (76.9%)	514 (81.8%)
	Some	18 (3.9%)	5 (3.0%)	23 (3.7%)
	None	57 (12.4%)	34 (20.1%)	91 (14.5%)
6 months	All	354 (77.1%)	129 (76.3%)	483 (76.9%)
	Some	19 (4.1%)	7 (4.1%)	26 (4.1%)
	None	86 (18.7%)	33 (19.5%)	119 (18.9%)
12 months	All	285 (62.1%)	98 (58.0%)	383 (61.0%)
	Some	22 (4.8%)	9 (5.3%)	31 (4.9%)
	None	152 (33.1%)	62 (36.7%)	214 (34.1%)
18 months	All	237 (51.6%)	78 (46.2%)	315 (50.2%)
	Some	13 (2.8%)	11 (6.5%)	24 (3.8%)
	None	209 (45.5%)	80 (47.3%)	289 (46.0%)
24 months	All	204 (44.4%)	80 (47.3%)	284 (45.2%)
	Some	10 (2.2%)	6 (3.6%)	16 (2.5%)
	None	245 (53.4%)	83 (49.1%)	328 (52.2%)
EORTC-QLQ-BR23				
Baseline	All	2 (0.4%)	1 (0.6%)	3 (0.5%)
	Some	430 (93.7%)	158 (93.5%)	588 (93.6%)
	None	27 (5.9%)	10 (5.9%)	37 (5.9%)

6 weeks	All	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Some	403 (87.8%)	134 (79.3%)	537 (85.5%)
	None	56 (12.2%)	35 (20.7%)	91 (14.5%)
6 months	All	3 (0.7%)	3 (1.8%)	6 (1.0%)
	Some	368 (80.2%)	132 (78.1%)	500 (79.6%)
	None	88 (19.2%)	34 (20.1%)	122 (19.4%)
12 months	All	10 (2.2%)	1 (0.6%)	11 (1.8%)
	Some	296 (64.5%)	106 (62.7%)	402 (64.0%)
	None	153 (33.3%)	62 (36.7%)	215 (34.2%)
18 months	All	6 (1.3%)	1 (0.6%)	7 (1.1%)
	Some	245 (53.4%)	88 (52.1%)	333 (53.0%)
	None	208 (45.3%)	80 (47.3%)	288 (45.9%)
24 months	All	7 (1.5%)	2 (1.2%)	9 (1.4%)
	Some	207 (45.1%)	84 (49.7%)	291 (46.3%)
	None	245 (53.4%)	83 (49.1%)	328 (52.2%)
EORTC-QLQ-ELD15				
Baseline	All	408 (88.9%)	151 (89.3%)	559 (89.0%)
	Some	16 (3.5%)	7 (4.1%)	23 (3.7%)
	None	35 (7.6%)	11 (6.5%)	46 (7.3%)
6 weeks	All	391 (85.2%)	130 (76.9%)	521 (83.0%)
	Some	11 (2.4%)	3 (1.8%)	14 (2.2%)
	None	57 (12.4%)	36 (21.3%)	93 (14.8%)
6 months	All	356 (77.6%)	131 (77.5%)	487 (77.5%)
	Some	14 (3.1%)	3 (1.8%)	17 (2.7%)
	None	89 (19.4%)	35 (20.7%)	124 (19.7%)
12 months	All	291 (63.4%)	99 (58.6%)	390 (62.1%)
	Some	12 (2.6%)	8 (4.7%)	20 (3.2%)
	None	156 (34.0%)	62 (36.7%)	218 (34.7%)
18 months	All	234 (51.0%)	84 (49.7%)	318 (50.6%)

24 months	Some	12 (2.6%)	4 (2.4%)	16 (2.5%)
	None	213 (46.4%)	81 (47.9%)	294 (46.8%)
	All	200 (43.6%)	80 (47.3%)	280 (44.6%)
	Some	13 (2.8%)	6 (3.6%)	19 (3.0%)
	None	246 (53.6%)	83 (49.1%)	329 (52.4%)

Supplementary Table 9 - Mean (SD) scores for the EORTC QLQ-BR23 scale at each time point in the radiotherapy versus no radiotherapy cohorts with adjusted mean difference (95% CI) and p-value.

BREAST-CONSERVING SURGERY COHORT (N=1042)*					
Time point	Domain	No radiotherapy	Radiotherapy	Treatment Effect	P value
6 weeks	Body image	92.81 (90.84, 94.78)	92.08 (91.24, 92.92)	-0.73 (-2.88, 1.41)	0.502
	Sexual functioning	7.79 (5.22, 10.35)	8.08 (7.01, 9.14)	0.29 (-2.49, 3.07)	0.837
	Sexual enjoyment	60.30 (46.13, 74.46)	60.35 (54.38, 66.32)	0.06 (-15.33, 15.44)	0.994
	Future perspective	70.17 (66.42, 73.92)	67.01 (65.42, 68.61)	-3.16 (-7.24, 0.92)	0.128
	Systemic therapy side effects	11.14 (9.54, 12.73)	12.61 (11.93, 13.28)	1.47 (-0.26, 3.20)	0.095
	Breast symptoms	21.12 (18.15, 24.10)	22.26 (20.97, 23.54)	1.13 (-2.11, 4.38)	0.493
	Arm symptoms	13.03 (10.47, 15.60)	14.75 (13.64, 15.85)	1.71 (-1.08, 4.51)	0.229
	Upset by hair loss	49.27 (28.22, 70.32)	29.56 (20.71, 38.40)	-19.71 (-42.52, 3.10)	0.088
6 months	Body image	90.93 (88.36, 93.50)	91.29 (90.25, 92.32)	0.36 (-2.41, 3.14)	0.798
	Sexual functioning	11.30 (8.40, 14.20)	9.09 (7.95, 10.23)	-2.21 (-5.33, 0.90)	0.163
	Sexual enjoyment	59.01 (46.32, 71.71)	53.04 (47.74, 58.34)	-5.97 (-19.68, 7.74)	0.389
	Future perspective	69.73 (65.45, 74.01)	69.77 (68.05, 71.50)	0.04 (-4.57, 4.66)	0.985
	Systemic therapy side effects	16.88 (14.82, 18.95)	15.87 (15.03, 16.71)	-1.01 (-3.24, 1.21)	0.373
	Breast symptoms	11.00 (8.30, 13.71)	17.27 (16.16, 18.38)	6.27 (3.34, 9.19)	<0.001
	Arm symptoms	11.73 (8.83, 14.62)	13.71 (12.53, 14.89)	1.98 (-1.14, 5.11)	0.213
	Upset by hair loss	43.90 (16.78, 71.03)	36.32 (26.65, 45.99)	-7.58 (-36.43, 21.26)	0.598
12 months	Body image	90.06 (87.31, 92.80)	91.38 (90.27, 92.48)	1.32 (-1.64, 4.28)	0.382
	Sexual functioning	9.54 (6.60, 12.49)	9.53 (8.35, 10.71)	-0.02 (-3.20, 3.16)	0.992
	Sexual enjoyment	53.44 (35.79, 71.10)	59.54 (53.53, 65.56)	6.10 (-12.30, 24.49)	0.510
	Future perspective	66.61 (62.18, 71.04)	69.27 (67.48, 71.05)	2.65 (-2.12, 7.43)	0.276
	Systemic therapy side effects	16.06 (13.94, 18.18)	15.75 (14.90, 16.61)	-0.31 (-2.60, 1.98)	0.793
	Breast symptoms	9.90 (7.35, 12.45)	13.79 (12.74, 14.83)	3.89 (1.13, 6.64)	0.006
	Arm symptoms	14.05 (10.92, 17.19)	13.29 (12.00, 14.57)	-0.77 (-4.16, 2.62)	0.657
	Upset by hair loss	54.96 (32.04, 77.87)	41.52 (31.63, 51.41)	-13.44 (-38.42, 11.55)	0.283
18 months	Body image	89.80 (86.73, 92.88)	90.84 (89.55, 92.13)	1.04 (-2.30, 4.37)	0.542

24 months	Sexual functioning	9.85 (6.36, 13.34)	8.81 (7.39, 10.24)	-1.03 (-4.81, 2.74)	0.591
	Sexual enjoyment	52.47 (31.38, 73.55)	56.69 (49.52, 63.86)	4.22 (-17.76, 26.21)	0.701
	Future perspective	72.24 (67.25, 77.23)	69.73 (67.63, 71.83)	-2.51 (-7.92, 2.90)	0.363
	Systemic therapy side effects	16.28 (13.94, 18.61)	15.89 (14.91, 16.87)	-0.39 (-2.92, 2.14)	0.764
	Breast symptoms	9.96 (7.24, 12.67)	12.18 (11.02, 13.34)	2.22 (-0.73, 5.18)	0.140
	Arm symptoms	13.92 (10.67, 17.18)	13.08 (11.69, 14.46)	-0.85 (-4.38, 2.69)	0.638
	Upset by hair loss	43.14 (14.33, 71.96)	40.63 (27.30, 53.96)	-2.52 (-34.27, 29.24)	0.872
	Body image	88.24 (84.98, 91.51)	91.15 (89.83, 92.47)	2.91 (-0.61, 6.43)	0.105
	Sexual functioning	9.43 (5.78, 13.07)	9.48 (8.00, 10.96)	0.05 (-3.88, 3.99)	0.979
	Sexual enjoyment	60.67 (41.22, 80.11)	52.27 (45.36, 59.18)	-8.40 (-28.85, 12.05)	0.414
	Future perspective	69.22 (63.96, 74.49)	70.25 (68.10, 72.40)	1.02 (-4.66, 6.71)	0.724
	Systemic therapy side effects	17.06 (14.59, 19.52)	15.80 (14.80, 16.79)	-1.26 (-3.92, 1.39)	0.351
	Breast symptoms	8.63 (6.08, 11.17)	10.01 (8.95, 11.06)	1.38 (-1.38, 4.14)	0.325
	Arm symptoms	15.01 (11.18, 18.84)	12.84 (11.25, 14.43)	-2.17 (-6.32, 1.97)	0.304
	Upset by hair loss	73.42 (40.92, 105.93)	38.16 (26.93, 49.38)	-35.27 (-69.79, -0.75)	0.046
MASTECTOMY COHORT (N=588)*					
Time point	Domain	No radiotherapy	Radiotherapy	Treatment Effect	P value
6 weeks	Body image	81.92 (79.78, 84.05)	81.76 (78.19, 85.32)	-0.16 (-4.31, 4.00)	0.940
	Sexual functioning	4.04 (2.96, 5.11)	4.39 (2.53, 6.26)	0.36 (-1.79, 2.51)	0.745
	Sexual enjoyment	46.17 (31.77, 60.57)	61.86 (35.67, 88.05)	15.69 (-13.94, 45.31)	0.282
	Future perspective	69.71 (67.19, 72.23)	67.91 (63.70, 72.12)	-1.81 (-6.72, 3.10)	0.470
	Systemic therapy side effects	12.45 (11.44, 13.45)	12.05 (10.35, 13.74)	-0.40 (-2.37, 1.57)	0.689
	Breast symptoms	23.49 (21.65, 25.32)	23.84 (20.75, 26.94)	0.36 (-3.24, 3.96)	0.845
	Arm symptoms	19.46 (17.57, 21.36)	20.15 (16.95, 23.34)	0.68 (-3.03, 4.39)	0.718
	Upset by hair loss	37.37 (22.14, 52.61)	64.87 (36.01, 93.73)	27.50 (-4.90, 59.90)	0.091
6 months	Body image	80.37 (78.01, 82.74)	79.99 (76.21, 83.77)	-0.38 (-4.84, 4.08)	0.866
	Sexual functioning	5.38 (4.06, 6.70)	6.01 (3.96, 8.06)	0.63 (-1.81, 3.07)	0.611
	Sexual enjoyment	67.61 (57.31, 77.90)	55.31 (39.45, 71.17)	-12.30 (-30.57, 5.98)	0.176
	Future perspective	70.59 (68.04, 73.13)	67.71 (63.62, 71.80)	-2.87 (-7.70, 1.95)	0.242

12 months	Systemic therapy side effects	15.51 (14.43, 16.60)	14.46 (12.72, 16.21)	-1.05 (-3.10, 1.00)	0.316
	Breast symptoms	12.19 (10.66, 13.71)	17.71 (15.30, 20.12)	5.52 (2.67, 8.37)	<0.001
	Arm symptoms	14.80 (13.05, 16.56)	16.87 (14.10, 19.64)	2.07 (-1.21, 5.35)	0.215
	Upset by hair loss	37.36 (22.01, 52.71)	51.20 (28.92, 73.48)	13.84 (-13.42, 41.10)	0.300
	Body image	81.27 (78.79, 83.75)	81.28 (77.24, 85.32)	0.01 (-4.73, 4.75)	0.997
	Sexual functioning	5.85 (4.37, 7.33)	5.27 (2.86, 7.69)	-0.57 (-3.41, 2.26)	0.690
	Sexual enjoyment	53.70 (41.21, 66.19)	45.79 (24.53, 67.05)	-7.91 (-33.12, 17.30)	0.521
	Future perspective	69.82 (66.89, 72.75)	67.04 (62.23, 71.86)	-2.78 (-8.42, 2.86)	0.333
	Systemic therapy side effects	15.94 (14.61, 17.27)	17.05 (14.84, 19.25)	1.11 (-1.46, 3.69)	0.396
	Breast symptoms	10.04 (8.43, 11.65)	17.16 (14.57, 19.75)	7.12 (4.07, 10.17)	<0.001
	Arm symptoms	12.00 (10.24, 13.77)	18.35 (15.49, 21.20)	6.34 (2.99, 9.70)	<0.001
	Upset by hair loss	40.20 (23.58, 56.83)	51.73 (28.06, 75.40)	11.53 (-17.27, 40.33)	0.415
18 months	Body image	82.33 (79.68, 84.97)	81.68 (77.43, 85.93)	-0.65 (-5.65, 4.36)	0.800
	Sexual functioning	6.07 (4.28, 7.86)	5.74 (2.82, 8.65)	-0.33 (-3.75, 3.08)	0.848
	Sexual enjoyment	54.24 (37.66, 70.81)	41.98 (19.11, 64.86)	-12.26 (-40.34, 15.83)	0.372
	Future perspective	71.04 (67.85, 74.23)	65.22 (60.07, 70.38)	-5.82 (-11.88, 0.25)	0.060
	Systemic therapy side effects	15.69 (14.19, 17.18)	17.85 (15.43, 20.28)	2.16 (-0.68, 5.01)	0.135
	Breast symptoms	9.81 (8.08, 11.55)	11.29 (8.45, 14.13)	1.48 (-1.85, 4.80)	0.383
	Arm symptoms	13.98 (11.84, 16.13)	17.02 (13.47, 20.58)	3.04 (-1.11, 7.18)	0.150
	Upset by hair loss	48.18 (29.58, 66.77)	72.33 (49.30, 95.35)	24.15 (-5.31, 53.61)	0.099
24 months	Body image	81.84 (78.85, 84.83)	78.66 (74.08, 83.23)	-3.19 (-8.66, 2.28)	0.253
	Sexual functioning	6.15 (4.14, 8.16)	5.40 (2.51, 8.29)	-0.75 (-4.27, 2.77)	0.674
	Sexual enjoyment	59.71 (46.62, 72.80)	46.58 (28.38, 64.78)	-13.13 (-36.10, 9.83)	0.245
	Future perspective	69.58 (66.03, 73.13)	64.91 (59.49, 70.34)	-4.66 (-11.15, 1.82)	0.158
	Systemic therapy side effects	16.40 (14.78, 18.02)	17.67 (15.18, 20.16)	1.27 (-1.71, 4.24)	0.402
	Breast symptoms	10.17 (8.24, 12.10)	12.87 (9.95, 15.79)	2.70 (-0.79, 6.20)	0.129
	Arm symptoms	15.31 (12.58, 18.05)	21.50 (17.35, 25.66)	6.19 (1.21, 11.17)	0.015
	Upset by hair loss	33.81 (11.03, 56.59)	88.36 (56.49, 120.22)	54.55 (14.54, 94.55)	0.016

*patients with questionnaires available at baseline.

Supplementary Table 10 - Mean (SD) scores for the EORTC QLQ-C30 scale at each time point in the radiotherapy versus no radiotherapy cohorts with adjusted mean difference (95% CI) and p-value.

BREAST-CONSERVING SURGERY COHORT					
Time point	Domain	No radiotherapy	Radiotherapy	Treatment Effect	P value
6 weeks	Global health status / QoL	71.50 (68.98, 74.01)	71.58 (70.49, 72.67)	0.09 (-2.66, 2.83)	0.951
	Physical functioning	79.75 (78.01, 81.49)	79.01 (78.26, 79.76)	-0.74 (-2.64, 1.16)	0.445
	Role functioning	76.53 (72.79, 80.27)	74.47 (72.85, 76.09)	-2.06 (-6.14, 2.02)	0.322
	Emotional functioning	79.89 (77.28, 82.51)	79.39 (78.24, 80.54)	-0.50 (-3.36, 2.35)	0.729
	Cognitive functioning	86.97 (84.58, 89.36)	87.35 (86.31, 88.38)	0.38 (-2.22, 2.98)	0.775
	Social functioning	85.98 (82.79, 89.17)	82.46 (81.08, 83.85)	-3.51 (-7.00, -0.03)	0.048
	Fatigue	28.84 (26.02, 31.66)	30.85 (29.63, 32.07)	2.01 (-1.06, 5.08)	0.199
	Nausea / Vomiting	4.51 (2.90, 6.11)	4.27 (3.58, 4.96)	-0.24 (-1.98, 1.51)	0.791
	Pain	20.14 (16.98, 23.30)	21.99 (20.62, 23.37)	1.85 (-1.60, 5.29)	0.293
	Dyspnoea	14.09 (11.13, 17.04)	14.66 (13.38, 15.95)	0.58 (-2.64, 3.80)	0.725
	Insomnia	29.22 (25.21, 33.23)	30.26 (28.53, 31.99)	1.04 (-3.33, 5.40)	0.641
	Appetite loss	11.76 (8.84, 14.68)	11.29 (10.03, 12.56)	-0.47 (-3.65, 2.72)	0.773
	Constipation	14.11 (10.99, 17.23)	13.53 (12.18, 14.89)	-0.58 (-3.97, 2.82)	0.739
	Diarrhoea	3.34 (1.16, 5.52)	5.14 (4.20, 6.08)	1.80 (-0.58, 4.18)	0.138
	Financial Problems	4.49 (2.68, 6.31)	4.06 (3.26, 4.85)	-0.44 (-2.42, 1.55)	0.665
6 months	Global health status / QoL	71.64 (68.92, 74.36)	72.06 (70.93, 73.18)	0.41 (-2.53, 3.36)	0.783
	Physical functioning	78.52 (76.39, 80.65)	78.55 (77.67, 79.43)	0.03 (-2.28, 2.34)	0.978
	Role functioning	77.19 (73.38, 80.99)	79.46 (77.90, 81.01)	2.27 (-1.84, 6.38)	0.279
	Emotional functioning	79.80 (76.82, 82.77)	79.99 (78.75, 81.23)	0.19 (-3.03, 3.42)	0.906
	Cognitive functioning	83.92 (81.23, 86.62)	85.25 (84.14, 86.36)	1.33 (-1.59, 4.25)	0.373
	Social functioning	86.43 (83.07, 89.79)	86.23 (84.86, 87.60)	-0.20 (-3.83, 3.43)	0.913
	Fatigue	30.43 (27.02, 33.84)	31.28 (29.88, 32.67)	0.85 (-2.84, 4.54)	0.652
	Nausea / Vomiting	5.79 (3.91, 7.67)	3.76 (3.00, 4.53)	-2.03 (-4.06, 0.00)	0.050
	Pain	22.20 (18.57, 25.84)	22.73 (21.24, 24.22)	0.52 (-3.40, 4.45)	0.794

	Dyspnoea	22.60 (18.89, 26.31)	18.98 (17.47, 20.50)	-3.62 (-7.63, 0.39)	0.077
	Insomnia	28.06 (23.47, 32.64)	30.24 (28.36, 32.12)	2.18 (-2.77, 7.14)	0.388
	Appetite loss	14.63 (11.19, 18.07)	10.28 (8.87, 11.69)	-4.35 (-8.06, -0.63)	0.022
	Constipation	14.33 (10.41, 18.25)	14.76 (13.16, 16.36)	0.43 (-3.80, 4.66)	0.842
	Diarrhoea	6.80 (4.16, 9.43)	5.05 (3.98, 6.12)	-1.75 (-4.59, 1.10)	0.229
	Financial Problems	4.12 (2.20, 6.05)	3.52 (2.72, 4.31)	-0.61 (-2.69, 1.47)	0.567
12 months	Global health status / QoL	68.21 (65.33, 71.09)	71.40 (70.24, 72.55)	3.19 (0.08, 6.29)	0.044
	Physical functioning	77.82 (75.45, 80.19)	77.85 (76.89, 78.82)	0.03 (-2.53, 2.60)	0.980
	Role functioning	75.44 (71.10, 79.78)	78.62 (76.86, 80.38)	3.18 (-1.51, 7.87)	0.183
	Emotional functioning	76.91 (73.60, 80.23)	80.00 (78.65, 81.36)	3.09 (-0.49, 6.67)	0.090
	Cognitive functioning	83.85 (80.93, 86.77)	84.45 (83.26, 85.64)	0.60 (-2.55, 3.76)	0.707
	Social functioning	84.54 (80.87, 88.21)	86.95 (85.46, 88.43)	2.41 (-1.56, 6.37)	0.233
	Fatigue	32.29 (28.83, 35.74)	29.33 (27.93, 30.73)	-2.96 (-6.69, 0.77)	0.120
	Nausea / Vomiting	2.70 (1.11, 4.28)	3.60 (2.96, 4.24)	0.91 (-0.80, 2.61)	0.298
	Pain	24.68 (20.35, 29.01)	23.85 (22.10, 25.61)	-0.83 (-5.50, 3.84)	0.728
	Dyspnoea	22.28 (18.09, 26.46)	19.86 (18.16, 21.56)	-2.42 (-6.94, 2.11)	0.295
	Insomnia	29.58 (24.72, 34.45)	32.52 (30.55, 34.49)	2.94 (-2.31, 8.19)	0.272
	Appetite loss	11.71 (7.81, 15.61)	11.05 (9.47, 12.64)	-0.66 (-4.88, 3.56)	0.759
	Constipation	15.12 (10.99, 19.25)	14.52 (12.84, 16.19)	-0.61 (-5.07, 3.85)	0.789
	Diarrhoea	5.52 (2.81, 8.23)	4.98 (3.89, 6.06)	-0.55 (-3.47, 2.37)	0.713
	Financial Problems	5.43 (3.31, 7.55)	3.05 (2.19, 3.91)	-2.38 (-4.67, -0.09)	0.041
18 months	Global health status / QoL	69.00 (65.77, 72.24)	71.01 (69.63, 72.40)	2.01 (-1.52, 5.54)	0.264
	Physical functioning	76.87 (74.28, 79.45)	76.20 (75.09, 77.30)	-0.67 (-3.50, 2.16)	0.642
	Role functioning	72.91 (68.03, 77.80)	78.22 (76.14, 80.29)	5.30 (-0.02, 10.63)	0.051
	Emotional functioning	79.09 (75.71, 82.47)	80.81 (79.36, 82.27)	1.73 (-1.96, 5.41)	0.358
	Cognitive functioning	82.36 (79.08, 85.63)	84.68 (83.29, 86.07)	2.33 (-1.23, 5.89)	0.199
	Social functioning	84.40 (80.39, 88.41)	88.01 (86.30, 89.72)	3.61 (-0.75, 7.98)	0.105
	Fatigue	31.27 (27.45, 35.09)	29.70 (28.07, 31.33)	-1.57 (-5.73, 2.60)	0.460
	Nausea / Vomiting	6.86 (4.66, 9.07)	3.33 (2.40, 4.27)	-3.53 (-5.93, -1.14)	0.004

	Pain	28.18 (23.55, 32.80)	24.06 (22.09, 26.03)	-4.11 (-9.14, 0.91)	0.109
	Dyspnoea	21.09 (16.65, 25.54)	19.36 (17.47, 21.24)	-1.74 (-6.57, 3.10)	0.481
	Insomnia	31.91 (26.63, 37.20)	30.65 (28.43, 32.87)	-1.26 (-6.99, 4.47)	0.666
	Appetite loss	13.60 (9.70, 17.49)	9.86 (8.22, 11.51)	-3.73 (-7.97, 0.50)	0.084
	Constipation	16.70 (12.11, 21.28)	14.18 (12.26, 16.11)	-2.51 (-7.49, 2.46)	0.322
	Diarrhoea	4.69 (1.69, 7.69)	5.94 (4.69, 7.19)	1.25 (-2.00, 4.49)	0.451
	Financial Problems	5.43 (3.24, 7.62)	2.41 (1.48, 3.35)	-3.02 (-5.40, -0.63)	0.013
24 months	Global health status / QoL	69.80 (66.08, 73.52)	69.76 (68.24, 71.28)	-0.04 (-4.07, 3.98)	0.983
	Physical functioning	74.42 (71.33, 77.51)	75.69 (74.42, 76.97)	1.27 (-2.08, 4.63)	0.456
	Role functioning	72.87 (67.68, 78.07)	77.88 (75.74, 80.03)	5.01 (-0.62, 10.64)	0.081
	Emotional functioning	80.77 (77.20, 84.34)	79.95 (78.49, 81.41)	-0.82 (-4.68, 3.04)	0.676
	Cognitive functioning	80.64 (77.18, 84.10)	85.15 (83.74, 86.56)	4.51 (0.78, 8.25)	0.018
	Social functioning	84.45 (79.68, 89.23)	86.73 (84.81, 88.65)	2.28 (-2.87, 7.42)	0.385
	Fatigue	32.48 (28.40, 36.56)	29.32 (27.65, 30.99)	-3.16 (-7.58, 1.25)	0.160
	Nausea / Vomiting	5.84 (3.69, 7.99)	3.41 (2.52, 4.30)	-2.43 (-4.76, -0.10)	0.041
	Pain	25.25 (20.20, 30.30)	23.88 (21.79, 25.96)	-1.37 (-6.84, 4.09)	0.622
	Dyspnoea	24.79 (19.88, 29.70)	20.17 (18.16, 22.19)	-4.62 (-9.93, 0.69)	0.088
	Insomnia	33.09 (27.39, 38.79)	30.48 (28.14, 32.83)	-2.61 (-8.77, 3.55)	0.406
	Appetite loss	13.70 (9.44, 17.96)	10.27 (8.50, 12.04)	-3.43 (-8.05, 1.18)	0.145
	Constipation	17.54 (12.65, 22.43)	13.67 (11.64, 15.70)	-3.87 (-9.16, 1.42)	0.152
	Diarrhoea	7.27 (3.62, 10.92)	6.08 (4.58, 7.58)	-1.19 (-5.13, 2.75)	0.554
	Financial Problems	4.31 (1.95, 6.67)	3.18 (2.23, 4.14)	-1.13 (-3.67, 1.42)	0.386
MASTECTOMY COHORT					
Time point	Domain	No radiotherapy	Radiotherapy	Treatment Effect	P value
6 weeks	Global health status / QoL	69.78 (68.19, 71.37)	66.60 (63.90, 69.31)	-3.18 (-6.32, -0.04)	0.047
	Physical functioning	75.75 (74.47, 77.02)	71.82 (69.67, 73.98)	-3.93 (-6.43, -1.42)	0.002
	Role functioning	68.38 (65.80, 70.96)	67.58 (63.25, 71.91)	-0.80 (-5.84, 4.24)	0.756
	Emotional functioning	80.93 (79.28, 82.59)	79.85 (77.03, 82.66)	-1.09 (-4.35, 2.18)	0.514
	Cognitive functioning	85.98 (84.47, 87.48)	84.79 (82.23, 87.34)	-1.19 (-4.16, 1.77)	0.429

	Social functioning	80.38 (78.17, 82.59)	77.11 (73.35, 80.87)	-3.27 (-7.63, 1.09)	0.141
	Fatigue	33.22 (31.44, 34.99)	34.78 (31.78, 37.78)	1.56 (-1.92, 5.05)	0.379
	Nausea / Vomiting	3.80 (2.85, 4.76)	4.25 (2.64, 5.86)	0.45 (-1.42, 2.32)	0.637
	Pain	23.53 (21.40, 25.66)	22.13 (18.54, 25.71)	-1.40 (-5.57, 2.77)	0.510
	Dyspnoea	14.74 (13.15, 16.33)	14.14 (11.47, 16.81)	-0.59 (-3.70, 2.52)	0.709
	Insomnia	27.54 (24.95, 30.12)	27.45 (23.09, 31.82)	-0.08 (-5.16, 4.99)	0.974
	Appetite loss	13.99 (11.88, 16.11)	14.98 (11.42, 18.55)	0.99 (-3.15, 5.14)	0.638
	Constipation	14.05 (11.87, 16.24)	15.66 (12.00, 19.33)	1.61 (-2.66, 5.88)	0.459
	Diarrhoea	4.60 (3.22, 5.99)	4.39 (2.03, 6.74)	-0.21 (-2.94, 2.52)	0.878
	Financial Problems	3.60 (2.44, 4.75)	4.54 (2.57, 6.51)	0.94 (-1.34, 3.22)	0.416
	Global health status / QoL	69.95 (68.14, 71.76)	69.31 (66.40, 72.21)	-0.64 (-4.06, 2.78)	0.714
6 months	Physical functioning	75.42 (74.05, 76.78)	73.82 (71.60, 76.03)	-1.60 (-4.20, 1.00)	0.227
	Role functioning	77.98 (75.59, 80.37)	77.33 (73.45, 81.20)	-0.65 (-5.20, 3.90)	0.779
	Emotional functioning	82.45 (80.71, 84.20)	81.47 (78.65, 84.28)	-0.99 (-4.30, 2.33)	0.558
	Cognitive functioning	83.72 (82.09, 85.34)	84.23 (81.60, 86.87)	0.52 (-2.58, 3.61)	0.743
	Social functioning	86.23 (84.04, 88.42)	83.77 (80.23, 87.30)	-2.46 (-6.62, 1.70)	0.245
	Fatigue	30.40 (28.45, 32.35)	34.85 (31.72, 37.98)	4.45 (0.77, 8.14)	0.018
	Nausea / Vomiting	3.91 (2.91, 4.91)	4.36 (2.76, 5.97)	0.45 (-1.44, 2.34)	0.639
	Pain	20.22 (18.17, 22.27)	18.51 (15.22, 21.80)	-1.71 (-5.58, 2.16)	0.386
	Dyspnoea	19.57 (17.39, 21.76)	20.81 (17.28, 24.34)	1.23 (-2.92, 5.39)	0.559
	Insomnia	26.85 (24.28, 29.42)	26.74 (22.59, 30.88)	-0.12 (-5.00, 4.77)	0.963
	Appetite loss	10.56 (8.41, 12.71)	13.00 (9.56, 16.45)	2.44 (-1.62, 6.50)	0.238
	Constipation	12.12 (10.06, 14.18)	15.81 (12.51, 19.11)	3.69 (-0.20, 7.58)	0.063
	Diarrhoea	5.88 (4.50, 7.27)	2.88 (0.65, 5.12)	-3.00 (-5.63, -0.37)	0.026
	Financial Problems	4.64 (3.27, 6.00)	2.99 (0.78, 5.20)	-1.65 (-4.24, 0.95)	0.213
	Global health status / QoL	71.13 (69.26, 73.00)	71.04 (67.92, 74.15)	-0.09 (-3.72, 3.53)	0.960
	Physical functioning	73.50 (71.97, 75.02)	71.89 (69.39, 74.40)	-1.60 (-4.54, 1.33)	0.284
	Role functioning	76.24 (73.50, 78.97)	74.72 (70.29, 79.16)	-1.52 (-6.73, 3.69)	0.567
	Emotional functioning	82.44 (80.40, 84.49)	76.75 (73.34, 80.15)	-5.70 (-9.67, -1.73)	0.005
12 months	Global health status / QoL	71.13 (69.26, 73.00)	71.04 (67.92, 74.15)	-0.09 (-3.72, 3.53)	0.960
	Physical functioning	73.50 (71.97, 75.02)	71.89 (69.39, 74.40)	-1.60 (-4.54, 1.33)	0.284
	Role functioning	76.24 (73.50, 78.97)	74.72 (70.29, 79.16)	-1.52 (-6.73, 3.69)	0.567
	Emotional functioning	82.44 (80.40, 84.49)	76.75 (73.34, 80.15)	-5.70 (-9.67, -1.73)	0.005

	Cognitive functioning	82.50 (80.64, 84.35)	82.44 (79.36, 85.52)	-0.06 (-3.65, 3.54)	0.975
	Social functioning	86.22 (84.00, 88.43)	83.55 (79.89, 87.21)	-2.67 (-6.94, 1.60)	0.220
	Fatigue	29.95 (27.76, 32.15)	37.22 (33.63, 40.80)	7.26 (3.07, 11.46)	0.001
	Nausea / Vomiting	2.87 (1.80, 3.94)	4.57 (2.81, 6.33)	1.70 (-0.36, 3.76)	0.105
	Pain	21.42 (18.92, 23.93)	24.90 (20.80, 29.01)	3.48 (-1.32, 8.28)	0.154
	Dyspnoea	19.22 (16.60, 21.84)	27.35 (23.07, 31.63)	8.13 (3.11, 13.14)	0.002
	Insomnia	27.21 (24.40, 30.02)	29.26 (24.61, 33.90)	2.04 (-3.38, 7.47)	0.459
	Appetite loss	11.99 (9.54, 14.44)	17.00 (12.98, 21.03)	5.01 (0.31, 9.72)	0.037
	Constipation	12.18 (9.87, 14.49)	14.65 (10.87, 18.42)	2.47 (-1.96, 6.89)	0.273
	Diarrhoea	6.06 (4.22, 7.90)	5.56 (2.51, 8.62)	-0.49 (-4.06, 3.08)	0.786
	Financial Problems	3.63 (2.16, 5.10)	6.72 (4.29, 9.15)	3.09 (0.26, 5.93)	0.033
18 months	Global health status / QoL	70.24 (67.95, 72.54)	66.05 (62.23, 69.86)	-4.20 (-8.63, 0.24)	0.064
	Physical functioning	72.15 (70.44, 73.87)	69.62 (66.85, 72.39)	-2.54 (-5.80, 0.72)	0.127
	Role functioning	75.63 (72.48, 78.79)	70.46 (65.30, 75.62)	-5.17 (-11.23, 0.89)	0.094
	Emotional functioning	82.82 (80.73, 84.91)	78.79 (75.36, 82.22)	-4.03 (-8.04, -0.02)	0.049
	Cognitive functioning	84.09 (82.01, 86.16)	79.87 (76.48, 83.25)	-4.22 (-8.19, -0.26)	0.037
	Social functioning	86.97 (84.40, 89.54)	83.50 (79.31, 87.69)	-3.47 (-8.38, 1.44)	0.165
	Fatigue	31.71 (29.22, 34.21)	37.15 (33.05, 41.24)	5.44 (0.64, 10.23)	0.026
	Nausea / Vomiting	3.51 (2.20, 4.81)	5.25 (3.11, 7.38)	1.74 (-0.76, 4.24)	0.173
	Pain	21.95 (18.93, 24.98)	26.00 (21.08, 30.92)	4.05 (-1.72, 9.81)	0.168
	Dyspnoea	21.96 (19.26, 24.67)	22.45 (18.04, 26.85)	0.48 (-4.67, 5.64)	0.853
	Insomnia	27.20 (24.30, 30.10)	30.54 (25.78, 35.30)	3.35 (-2.20, 8.89)	0.236
	Appetite loss	10.86 (8.17, 13.55)	17.05 (12.65, 21.45)	6.19 (1.04, 11.34)	0.019
	Constipation	14.65 (11.93, 17.38)	14.99 (10.52, 19.45)	0.33 (-4.90, 5.56)	0.900
	Diarrhoea	4.71 (2.94, 6.48)	5.91 (3.03, 8.78)	1.19 (-2.18, 4.57)	0.487
	Financial Problems	3.35 (1.97, 4.72)	3.81 (1.52, 6.10)	0.46 (-2.20, 3.13)	0.734
24 months	Global health status / QoL	69.61 (67.13, 72.09)	65.45 (61.58, 69.31)	-4.17 (-8.75, 0.42)	0.075
	Physical functioning	70.82 (68.63, 73.02)	69.03 (65.67, 72.39)	-1.79 (-5.80, 2.22)	0.380
	Role functioning	71.81 (68.11, 75.51)	70.44 (64.73, 76.16)	-1.37 (-8.17, 5.44)	0.693

Emotional functioning	82.60 (80.38, 84.81)	78.03 (74.59, 81.47)	-4.57 (-8.66, -0.47)	0.029
Cognitive functioning	83.03 (80.90, 85.17)	80.46 (77.14, 83.79)	-2.57 (-6.52, 1.38)	0.201
Social functioning	82.67 (79.60, 85.74)	82.35 (77.56, 87.14)	-0.32 (-6.00, 5.36)	0.912
Fatigue	32.31 (29.71, 34.92)	38.88 (34.85, 42.91)	6.56 (1.76, 11.37)	0.008
Nausea / Vomiting	4.11 (2.74, 5.48)	4.44 (2.31, 6.57)	0.33 (-2.20, 2.87)	0.796
Pain	25.39 (22.14, 28.64)	28.59 (23.54, 33.64)	3.20 (-2.80, 9.20)	0.295
Dyspnoea	21.52 (18.41, 24.63)	22.84 (17.99, 27.68)	1.31 (-4.45, 7.08)	0.654
Insomnia	27.25 (23.82, 30.69)	32.29 (26.95, 37.63)	5.04 (-1.30, 11.37)	0.119
Appetite loss	13.49 (10.54, 16.44)	13.78 (9.13, 18.43)	0.29 (-5.22, 5.80)	0.917
Constipation	12.85 (10.00, 15.70)	17.33 (12.92, 21.75)	4.48 (-0.77, 9.73)	0.094
Diarrhoea	5.52 (3.26, 7.78)	8.92 (5.45, 12.40)	3.40 (-0.73, 7.53)	0.106
Financial Problems	3.40 (1.72, 5.08)	4.86 (2.23, 7.49)	1.47 (-1.65, 4.59)	0.356

Supplementary table 11 - Fixed coefficients from the longitudinal model of global health status included in the EORTC QLQ-C30 scale.

BREAST-CONSERVING SURGERY COHORT			
Term	Level	Effect (95% CI)	P-value
Treatment	Radiotherapy	-0.819 (-3.856, 2.219)	0.597
Time	6 weeks	-	-
	6 months	-0.153 (-3.446, 3.141)	0.928
	12 months	-3.142 (-6.595, 0.311)	0.075
	18 months	-4.525 (-8.096, -0.954)	0.013
	24 months	-2.378 (-6.288, 1.531)	0.233
Treatment : Time	Radiotherapy:6 weeks	-	-
	Radiotherapy:6 months	0.720 (-2.851, 4.291)	0.693
	Radiotherapy:12 months	2.729 (-1.006, 6.464)	0.152
	Radiotherapy:18 months	3.816 (-0.066, 7.698)	0.054
	Radiotherapy:24 months	0.021 (-4.198, 4.241)	0.992
Baseline		0.504 (0.456, 0.551)	<0.001
Age		-0.196 (-0.363, -0.030)	0.021
CCI	1	-	-
	2	-0.876 (-3.531, 1.780)	0.518
MMSE	Normal Function	-	-
	Mild impairment	-0.119 (-2.924, 2.687)	0.934
	Moderate impairment	-9.399 (-17.491, -1.307)	0.023
	Severe	3.895 (-17.826, 25.617)	0.725
ECOG	Mild	-	-
	Moderate	-8.512 (-14.434, -2.590)	0.005
	High	-7.824 (-15.243, -0.405)	0.039
Medications		-0.446 (-0.789, -0.104)	0.011
MASTECTOMY COHORT			
Term	Level	Effect (95% CI)	P-value

Treatment	Radiotherapy	-3.129 (-6.587, 0.329)	0.076
Time	6 weeks	-	-
	6 months	-0.164 (-2.172, 1.843)	0.872
	12 months	1.180 (-0.963, 3.324)	0.281
	18 months	-0.359 (-2.649, 1.931)	0.759
	24 months	-1.785 (-4.239, 0.669)	0.154
Treatment : Time	Radiotherapy:6 weeks	-	-
	Radiotherapy:6 months	2.581 (-1.301, 6.462)	0.193
	Radiotherapy:12 months	3.340 (-0.869, 7.549)	0.120
	Radiotherapy:18 months	-0.129 (-4.649, 4.390)	0.955
	Radiotherapy:24 months	4.214 (-0.427, 8.856)	0.075
Baseline		0.489 (0.420, 0.557)	<0.001
Age		-0.154 (-0.382, 0.075)	0.188
CCI	1	-	-
	2	-1.161 (-4.327, 2.005)	0.473
MMSE	Normal function	-	-
	Mild impairment	1.068 (-2.456, 4.591)	0.553
	Moderate impairment	-6.152 (-17.462, 5.159)	0.287
ECOG	Mild	-	-
	Moderate	-7.067 (-13.113, -1.020)	0.022
	High	1.900 (-10.931, 14.731)	0.772
Medications		-0.844 (-1.296, -0.391)	<0.001

Supplementary Table 12 - Mean (SD) scores for the EORTC QLQ-ELD15 scale at each time point in the radiotherapy versus no radiotherapy cohorts with adjusted mean difference (95% CI) and p-value.

BREAST-CONSERVING SURGERY COHORT					
Time point	Domain	No radiotherapy	Radiotherapy	Treatment Effect	P value
6 weeks	Mobility	21.41 (18.86, 23.97)	20.76 (19.66, 21.86)	-0.65 (-3.44, 2.14)	0.648
	Worries about others	39.10 (35.12, 43.07)	38.14 (36.43, 39.86)	-0.96 (-5.29, 3.37)	0.664
	Worries	32.56 (29.10, 36.02)	34.17 (32.67, 35.67)	1.61 (-2.15, 5.38)	0.401
	Maintaining purpose	67.52 (62.58, 72.47)	64.70 (62.55, 66.85)	-2.82 (-8.21, 2.57)	0.305
	Burden of illness	29.48 (25.92, 33.04)	28.93 (27.39, 30.47)	-0.56 (-4.43, 3.32)	0.779
	Joint stiffness	29.29 (25.74, 32.83)	26.08 (24.53, 27.62)	-3.21 (-7.08, 0.66)	0.104
	Family support	74.72 (70.13, 79.30)	74.38 (72.39, 76.36)	-0.34 (-5.34, 4.66)	0.893
6 months	Mobility	23.97 (20.99, 26.94)	22.23 (21.00, 23.46)	-1.74 (-4.97, 1.49)	0.291
	Worries about others	33.97 (29.53, 38.41)	33.58 (31.75, 35.41)	-0.39 (-5.19, 4.41)	0.874
	Worries	32.53 (28.57, 36.48)	32.25 (30.63, 33.87)	-0.28 (-4.55, 4.00)	0.899
	Maintaining purpose	59.97 (54.26, 65.67)	63.22 (60.85, 65.59)	3.26 (-2.92, 9.43)	0.301
	Burden of illness	20.06 (16.22, 23.90)	25.55 (23.96, 27.13)	5.49 (1.33, 9.64)	0.010
	Joint stiffness	39.78 (35.29, 44.26)	38.71 (36.85, 40.57)	-1.06 (-5.92, 3.79)	0.667
	Family support	67.10 (61.91, 72.29)	69.99 (67.83, 72.14)	2.89 (-2.73, 8.51)	0.313
12 months	Mobility	25.13 (21.78, 28.47)	23.75 (22.39, 25.11)	-1.38 (-4.99, 2.24)	0.455
	Worries about others	33.51 (28.81, 38.22)	31.48 (29.58, 33.39)	-2.03 (-7.11, 3.05)	0.433
	Worries	34.62 (30.39, 38.85)	32.00 (30.27, 33.72)	-2.62 (-7.19, 1.95)	0.261
	Maintaining purpose	59.69 (53.74, 65.65)	63.28 (60.85, 65.71)	3.58 (-2.85, 10.02)	0.275
	Burden of illness	18.80 (14.73, 22.87)	21.67 (20.02, 23.32)	2.87 (-1.52, 7.26)	0.200
	Joint stiffness	42.31 (37.71, 46.92)	41.70 (39.81, 43.59)	-0.61 (-5.58, 4.37)	0.810
	Family support	61.37 (55.43, 67.31)	65.58 (63.17, 67.98)	4.20 (-2.21, 10.62)	0.199
18 months	Mobility	26.75 (23.06, 30.44)	25.38 (23.80, 26.96)	-1.37 (-5.41, 2.67)	0.506
	Worries about others	32.56 (27.73, 37.40)	29.94 (27.90, 31.99)	-2.62 (-7.87, 2.63)	0.327
	Worries	30.90 (26.19, 35.62)	31.68 (29.69, 33.68)	0.78 (-4.34, 5.91)	0.764

24 months	Maintaining purpose	57.80 (51.56, 64.05)	63.81 (61.14, 66.48)	6.01 (-0.78, 12.80)	0.083
	Burden of illness	16.45 (12.23, 20.67)	18.20 (16.42, 19.97)	1.74 (-2.83, 6.32)	0.454
	Joint stiffness	44.80 (39.96, 49.63)	42.11 (40.05, 44.17)	-2.69 (-7.94, 2.57)	0.316
	Family support	58.77 (52.09, 65.44)	62.21 (59.39, 65.04)	3.45 (-3.80, 10.70)	0.351
	Mobility	28.77 (24.55, 32.99)	26.50 (24.75, 28.25)	-2.27 (-6.85, 2.31)	0.331
	Worries about others	34.92 (29.84, 40.01)	28.72 (26.64, 30.79)	-6.21 (-11.70, -0.71)	0.027
	Worries	32.74 (27.70, 37.79)	32.66 (30.59, 34.73)	-0.09 (-5.54, 5.37)	0.975
	Maintaining purpose	62.09 (55.44, 68.75)	65.55 (62.80, 68.29)	3.45 (-3.75, 10.65)	0.347
	Burden of illness	20.73 (16.04, 25.41)	18.44 (16.51, 20.36)	-2.29 (-7.35, 2.77)	0.374
	Joint stiffness	45.46 (39.86, 51.05)	41.44 (39.11, 43.76)	-4.02 (-10.08, 2.03)	0.193
	Family support	65.26 (58.06, 72.46)	59.91 (56.92, 62.91)	-5.35 (-13.14, 2.45)	0.179
	MASTECTOMY COHORT				
Time point	Domain	No radiotherapy	Radiotherapy	Treatment Effect	P value
6 weeks	Mobility	26.86 (25.25, 28.47)	27.80 (25.07, 30.53)	0.94 (-2.23, 4.11)	0.561
	Worries about others	36.60 (33.96, 39.24)	39.96 (35.46, 44.46)	3.36 (-1.86, 8.59)	0.207
	Worries	33.35 (31.04, 35.65)	36.38 (32.44, 40.31)	3.03 (-1.53, 7.59)	0.193
	Maintaining purpose	65.34 (62.28, 68.41)	62.62 (57.45, 67.80)	-2.72 (-8.74, 3.30)	0.375
	Burden of illness	30.00 (27.61, 32.40)	35.54 (31.50, 39.59)	5.54 (0.84, 10.24)	0.021
	Joint stiffness	28.45 (26.18, 30.72)	26.54 (22.73, 30.36)	-1.90 (-6.35, 2.54)	0.400
	Family support	76.33 (73.60, 79.05)	75.36 (70.72, 80.00)	-0.97 (-6.36, 4.42)	0.724
6 months	Mobility	27.43 (25.38, 29.48)	26.41 (23.14, 29.69)	-1.02 (-4.89, 2.85)	0.605
	Worries about others	31.96 (29.52, 34.40)	32.47 (28.54, 36.40)	0.51 (-4.13, 5.15)	0.829
	Worries	30.46 (28.26, 32.66)	33.31 (29.77, 36.86)	2.86 (-1.32, 7.03)	0.180
	Maintaining purpose	62.74 (59.11, 66.37)	65.91 (60.13, 71.68)	3.17 (-3.65, 9.99)	0.362
	Burden of illness	23.64 (21.00, 26.29)	33.31 (29.08, 37.54)	9.66 (4.67, 14.66)	<0.001
	Joint stiffness	38.93 (36.27, 41.60)	34.23 (29.96, 38.50)	-4.70 (-9.73, 0.33)	0.067
	Family support	67.57 (64.18, 70.96)	73.73 (68.29, 79.18)	6.16 (-0.26, 12.59)	0.060
12 months	Mobility	30.35 (28.10, 32.60)	31.69 (28.06, 35.31)	1.34 (-2.94, 5.62)	0.539
	Worries about others	33.71 (30.72, 36.69)	35.25 (30.32, 40.19)	1.55 (-4.23, 7.32)	0.599

	Worries	34.25 (31.62, 36.88)	35.01 (30.68, 39.34)	0.76 (-4.31, 5.83)	0.769
	Maintaining purpose	62.74 (59.07, 66.42)	66.24 (60.23, 72.24)	3.50 (-3.54, 10.53)	0.329
	Burden of illness	20.69 (17.89, 23.49)	26.39 (21.82, 30.96)	5.70 (0.34, 11.06)	0.037
	Joint stiffness	43.05 (40.13, 45.96)	43.49 (38.79, 48.19)	0.44 (-5.09, 5.97)	0.875
	Family support	62.88 (59.13, 66.64)	64.35 (58.07, 70.63)	1.47 (-5.86, 8.81)	0.693
18 months	Mobility	31.35 (28.89, 33.80)	33.12 (29.27, 36.98)	1.78 (-2.81, 6.36)	0.446
	Worries about others	30.12 (26.97, 33.27)	32.71 (27.61, 37.81)	2.59 (-3.42, 8.59)	0.397
	Worries	30.62 (27.70, 33.54)	34.66 (29.97, 39.35)	4.04 (-1.49, 9.56)	0.152
	Maintaining purpose	62.34 (58.06, 66.61)	63.63 (56.83, 70.43)	1.29 (-6.73, 9.31)	0.752
	Burden of illness	18.49 (15.53, 21.44)	26.68 (21.98, 31.37)	8.19 (2.64, 13.74)	0.004
	Joint stiffness	41.22 (37.83, 44.61)	43.32 (37.98, 48.66)	2.10 (-4.22, 8.42)	0.514
	Family support	64.45 (60.06, 68.84)	63.54 (56.47, 70.60)	-0.92 (-9.24, 7.41)	0.829
24 months	Mobility	33.91 (30.96, 36.86)	37.10 (32.70, 41.51)	3.19 (-2.11, 8.49)	0.237
	Worries about others	30.91 (27.45, 34.37)	32.49 (27.21, 37.77)	1.58 (-4.73, 7.89)	0.622
	Worries	33.03 (29.73, 36.33)	34.19 (29.14, 39.25)	1.16 (-4.87, 7.20)	0.704
	Maintaining purpose	61.34 (56.85, 65.82)	56.54 (49.78, 63.30)	-4.80 (-12.90, 3.30)	0.245
	Burden of illness	23.35 (19.43, 27.26)	31.68 (25.77, 37.59)	8.34 (1.25, 15.43)	0.021
	Joint stiffness	41.93 (38.22, 45.65)	47.60 (42.05, 53.16)	5.67 (-1.02, 12.35)	0.096
	Family support	61.53 (56.76, 66.30)	59.73 (52.47, 66.99)	-1.81 (-10.49, 6.88)	0.682

Supplementary Table 13 - Mean scores and 95% confidence intervals (CIs) adjusted for baseline score for the EQ-5D-5L scale at each timepoint in radiotherapy versus no radiotherapy cohorts.

BREAST-CONSERVING SURGERY COHORT					
Time point	Score	No radiotherapy	Radiotherapy	Treatment Effect	P value
6 weeks	Score	0.85 (0.83, 0.86)	0.84 (0.83, 0.85)	-0.0081 (-0.0264, 0.0102)	0.385
	VAS	76.22 (74.22, 78.23)	76.46 (75.59, 77.33)	0.23 (-1.96, 2.42)	0.835
6 months	Score	0.84 (0.81, 0.86)	0.83 (0.82, 0.84)	-0.0021 (-0.0271, 0.0229)	0.871
	VAS	76.64 (74.28, 79.00)	76.24 (75.27, 77.20)	-0.40 (-2.96, 2.15)	0.757
12 months	Score	0.81 (0.79, 0.84)	0.83 (0.82, 0.84)	0.0145 (-0.0130, 0.0420)	0.300
	VAS	73.62 (71.01, 76.23)	76.03 (75.00, 77.07)	2.41 (-0.40, 5.22)	0.093
18 months	Score	0.81 (0.78, 0.84)	0.82 (0.81, 0.83)	0.0107 (-0.0204, 0.0418)	0.501
	VAS	73.02 (69.87, 76.16)	75.01 (73.72, 76.30)	1.99 (-1.41, 5.40)	0.251
24 months	Score	0.83 (0.80, 0.86)	0.82 (0.80, 0.83)	-0.0148 (-0.0493, 0.0197)	0.399
	VAS	73.53 (70.21, 76.85)	74.56 (73.21, 75.90)	1.03 (-2.56, 4.61)	0.574
MASTECTOMY COHORT					
Time point	Score	No radiotherapy	Radiotherapy	Treatment Effect	P value
6 weeks	Score	0.83 (0.81, 0.84)	0.80 (0.79, 0.82)	-0.0202 (-0.0431, 0.0028)	0.085
	VAS	74.76 (73.30, 76.22)	74.03 (71.57, 76.49)	-0.73 (-3.59, 2.13)	0.615
6 months	Score	0.83 (0.82, 0.84)	0.82 (0.80, 0.84)	-0.0095 (-0.0329, 0.0140)	0.429
	VAS	75.77 (74.33, 77.20)	75.45 (73.14, 77.76)	-0.31 (-3.03, 2.40)	0.820
12 months	Score	0.82 (0.81, 0.84)	0.80 (0.78, 0.82)	-0.0254 (-0.0537, 0.0029)	0.079
	VAS	74.98 (73.31, 76.66)	74.70 (71.99, 77.40)	-0.29 (-3.47, 2.89)	0.859
18 months	Score	0.81 (0.79, 0.83)	0.77 (0.74, 0.80)	-0.0387 (-0.0735, -0.0040)	0.029
	VAS	74.29 (72.44, 76.15)	71.83 (68.89, 74.77)	-2.46 (-5.94, 1.01)	0.164
24 months	Score	0.81 (0.80, 0.83)	0.76 (0.73, 0.79)	-0.0511 (-0.0858, -0.0165)	0.004
	VAS	73.77 (71.70, 75.85)	72.29 (69.12, 75.45)	-1.49 (-5.27, 2.29)	0.439

Supplementary Table 14 - Radiotherapy adverse events for patients receiving radiotherapy after breast-conserving surgery.

	Events N = 1385	Individuals N = 1385
Any adverse event	629	620 (44.8%)
Skin erythema	532	526 (38.0%)
Pain	218	216 (15.6%)
Breast oedema	77	76 (5.5%)
Breast shrinkage	13	13 (0.9%)

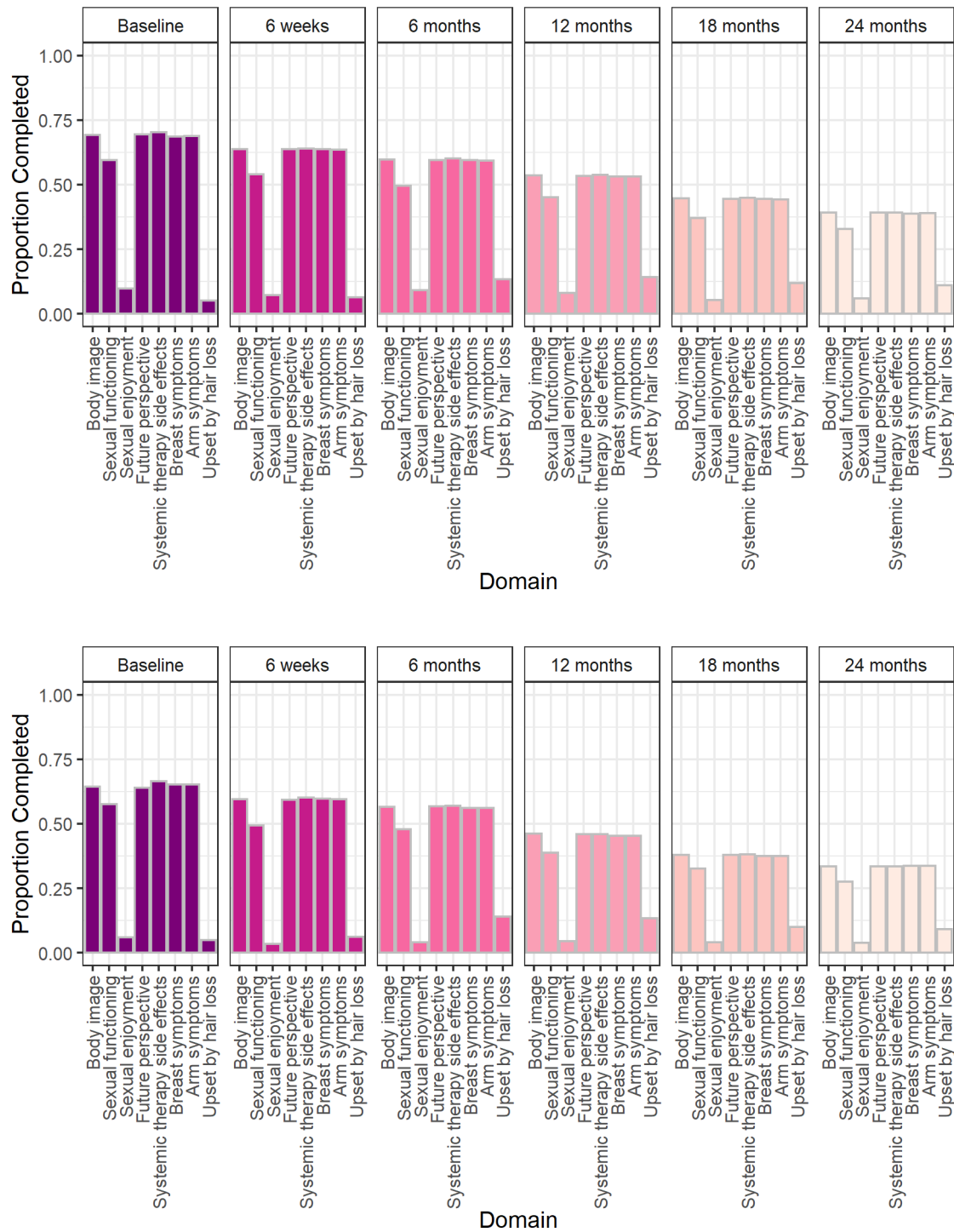
Supplementary Table 15 - Radiotherapy adverse events for patients receiving radiotherapy after a mastectomy.

	Events N = 341	Individuals N = 341
Any adverse event	158	157 (46.0%)
Skin erythema	136	135 (39.6%)
Pain	50	50 (14.7%)
Chest wall oedema	12	12 (3.5%)

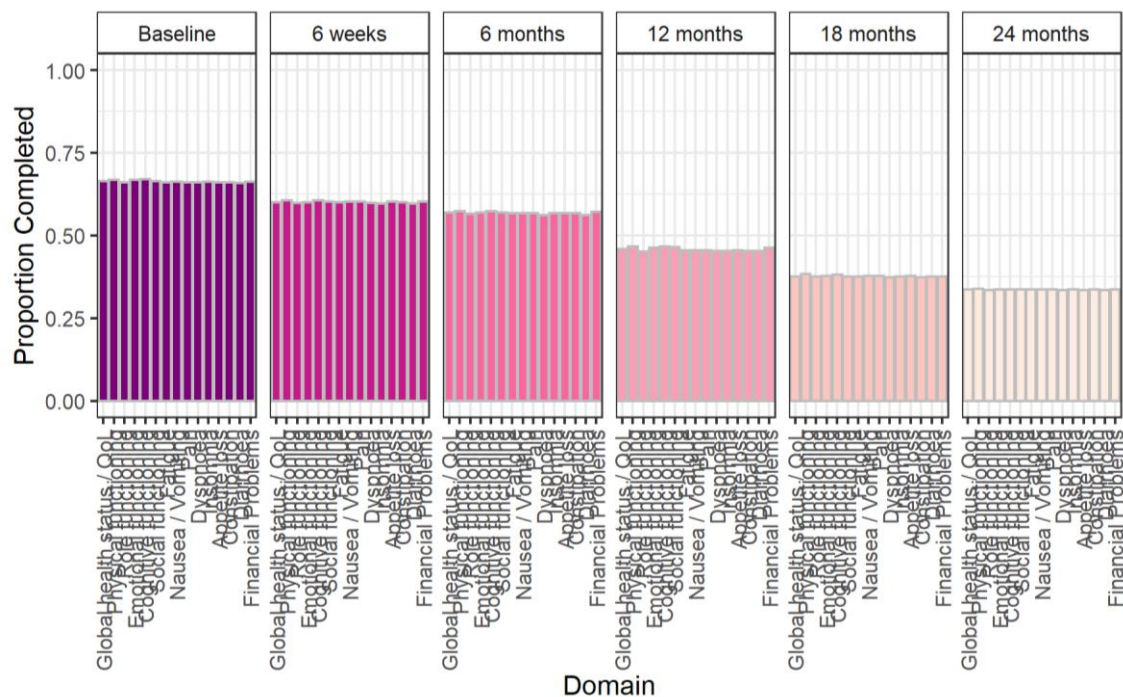
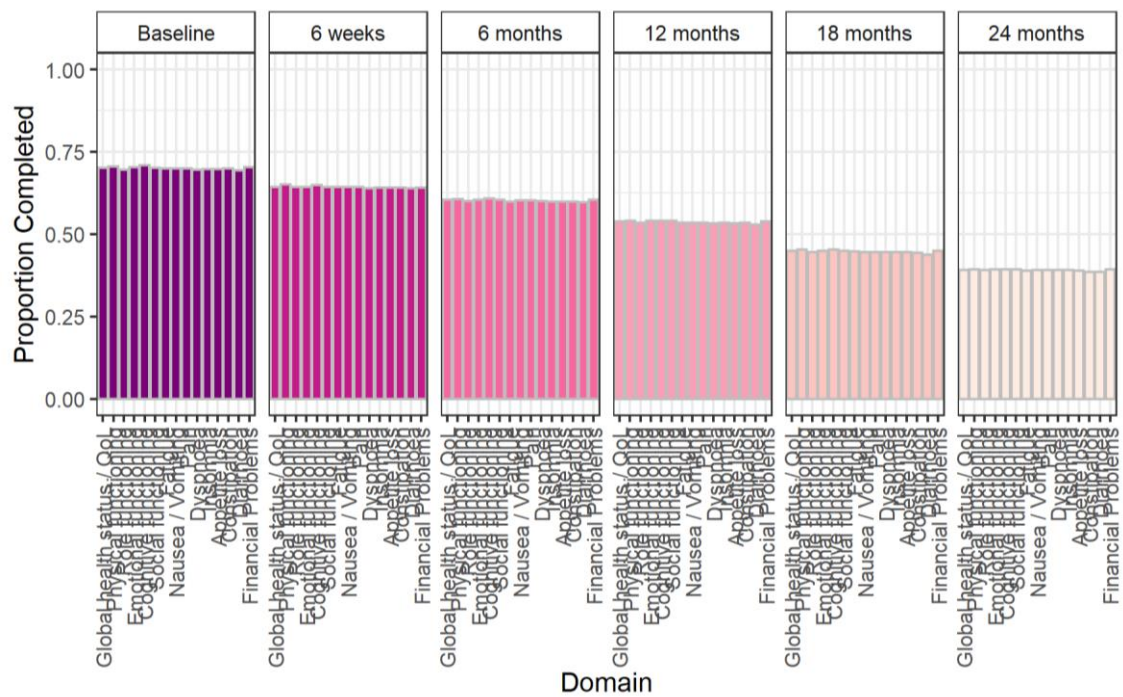
Supplementary Table 16 – Mortality rates in the overall cohort, in the breast-conserving surgery cohort and in the mastectomy cohort.

		OVERALL COHORT		
		No radiotherapy	Radiotherapy	Total
		N = 1058	N = 1753	N = 2811
Overall death (any cause)	n	1041	1716	2757
	No	824 (79.2%)	1469 (85.6%)	2293 (83.2%)
	Yes	217 (20.8%)	247 (14.4%)	464 (16.8%)
Death due to breast cancer-related cause	n	1032	1706	2738
	No	955 (92.5%)	1590 (93.2%)	2545 (93.0%)
	Yes	77 (7.5%)	116 (6.8%)	193 (7.0%)
BREAST-CONSERVING SURGERY COHORT				
		No radiotherapy	Radiotherapy	Total
		N = 284	N = 1385	N = 1669
Overall death (any cause)	n	277	1354	1631
	No	229 (82.7%)	1205 (89.0%)	1434 (87.9%)
	Yes	48 (17.3%)	149 (11.0%)	197 (12.1%)
Death due to breast cancer-related cause	n	276	1348	1624
	No	267 (96.7%)	1297 (96.2%)	1564 (96.3%)
	Yes	9 (3.3%)	51 (3.8%)	60 (3.7%)
MASTECTOMY COHORT				
		No radiotherapy	Radiotherapy	Total
		N = 746	N = 341	N = 1087
Overall death (any cause)	n	737	336	1073
	No	574 (77.9%)	243 (72.3%)	817 (76.1%)
	Yes	163 (22.1%)	93 (27.7%)	256 (23.9%)
Death due to breast cancer-related cause	n	730	332	1062
	No	665 (91.1%)	269 (81.0%)	934 (87.9%)
	Yes	65 (8.9%)	63 (19.0%)	128 (12.1%)

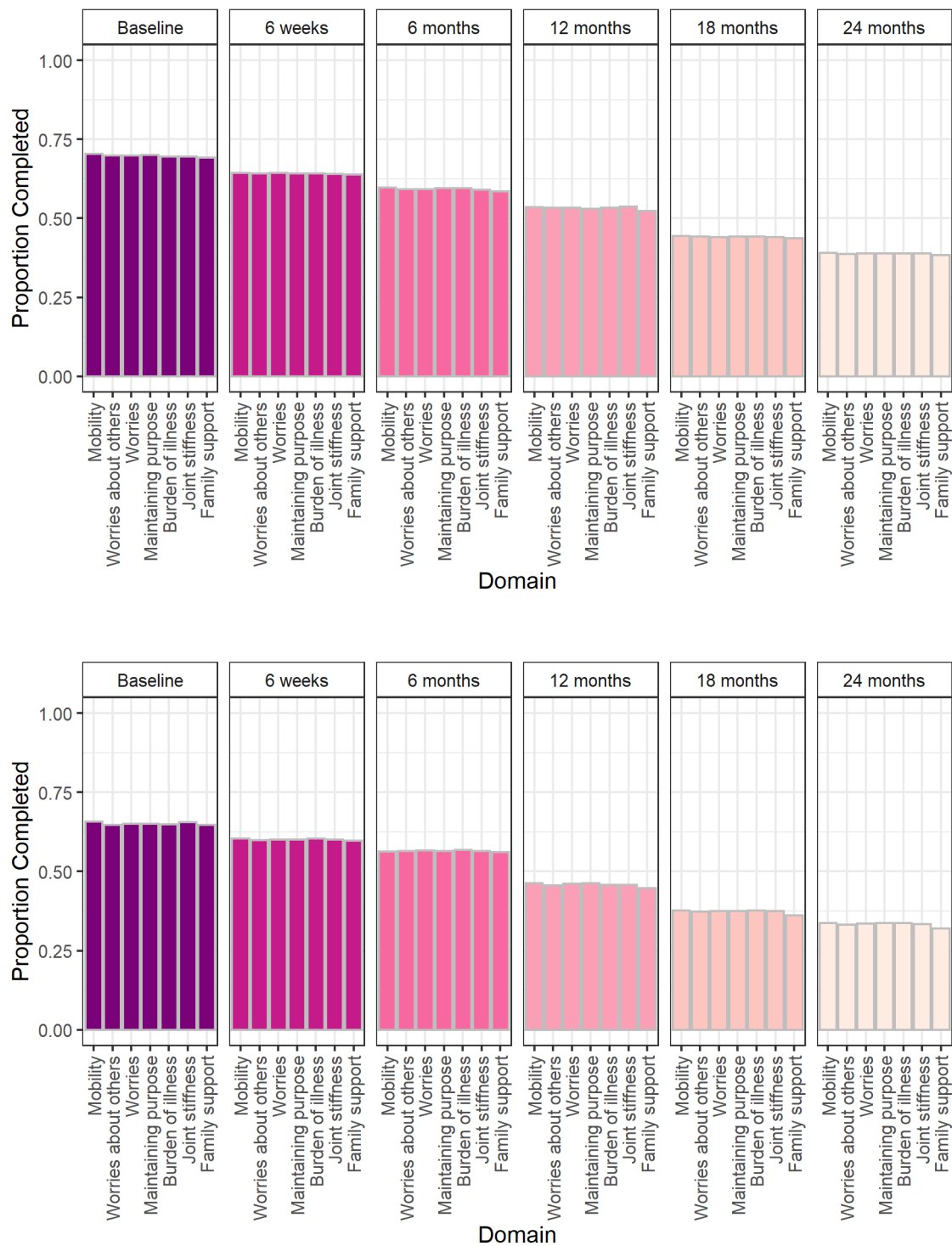
Supplementary Figure 1 – Completion of the EORTC-QLQ-BR23 at each time point in patient undergoing breast-conserving surgery (top) and in those undergoing a mastectomy (bottom).



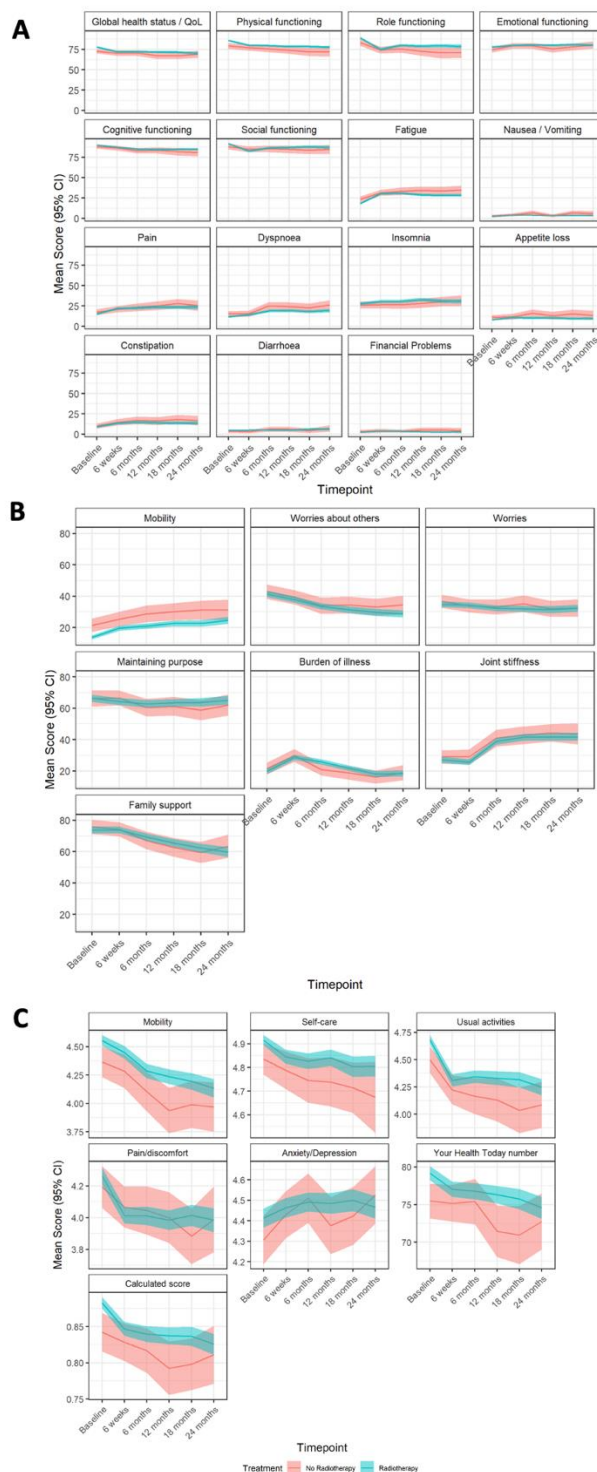
Supplementary Figure 2 – Completion of the EORTC-QLQ-C30 at each time point in patient undergoing breast-conserving surgery (top) and in those undergoing a mastectomy (bottom).



Supplementary Figure 3 – Completion of the EORTC-QLQ-ELD15 at each time point in patient undergoing breast-conserving surgery (top) and in those undergoing a mastectomy (bottom).



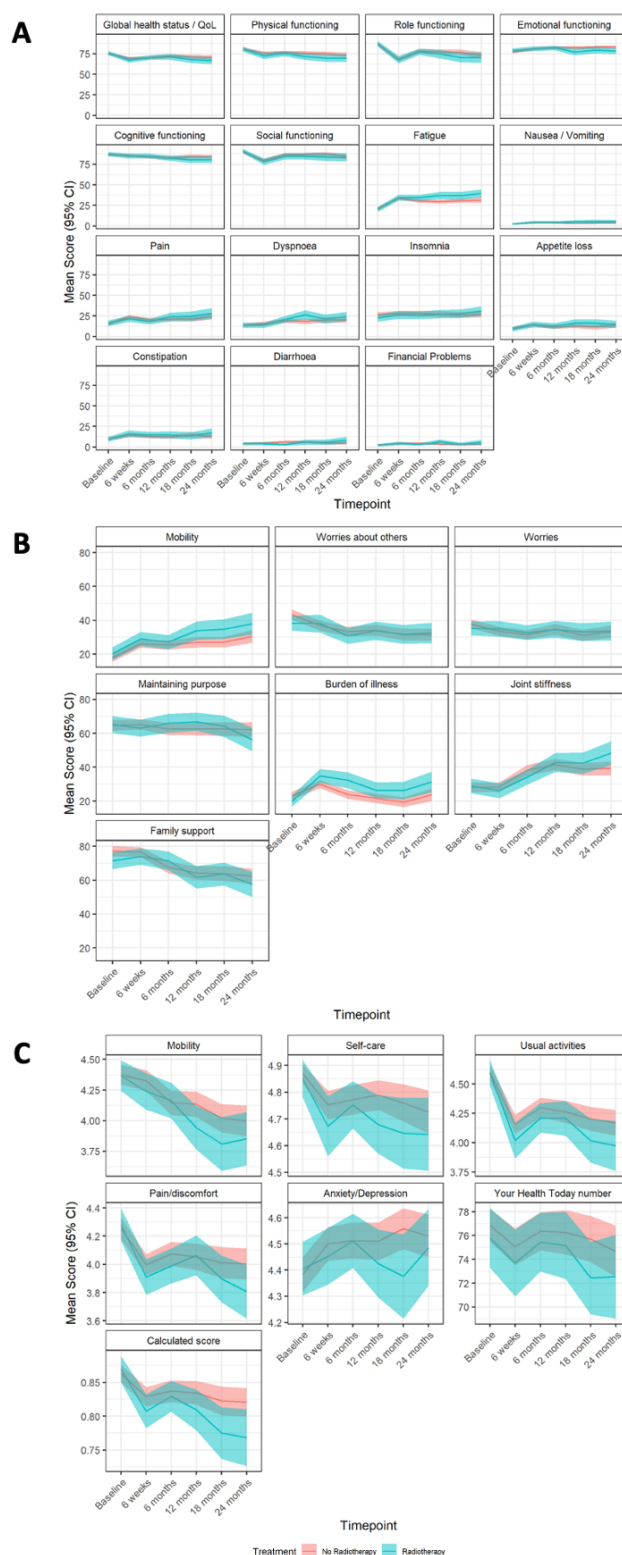
Supplementary Figure 4 – Mean (95% CI) scores over time points for the radiotherapy versus no radiotherapy population measured on the EORTC-QLQ-C30 (A), ELD15 (B) and EQ-5D-5L* scale (C) in patients undergoing breast-conserving surgery.[^]



**the calculated score is a single summary number (index value) which reflects the health state in the context of the preferences of the general population of a country/region and is derived by applying a formula attaching weights to each of the levels in each dimension as per the EQ-5D-5L User Guide.*

[^]A high score for a functional scale represents a high/healthy level of functioning; a high score for the global health status/QoL represents a high QoL, whilst a high score for a symptom scale represents a high level of symptomology/problems.

Supplementary Figure 5 – Mean (95% CI) scores over time points for the radiotherapy versus no radiotherapy population measured on the EORTC-QLQ-C30 (A), ELD15 (B) and EQ-5D-5L* scale (C) in patients undergoing a mastectomy.^



**the calculated score is a single summary number (index value) which reflects the health state in the context of the preferences of the general population of a country/region and is derived by applying a formula attaching weights to each of the levels in each dimension as per the EQ-5D-5L User Guide.*

^A high score for a functional scale represents a high/healthy level of functioning; a high score for the global health status/QoL represents a high QoL, whilst a high score for a symptom scale represents a high level of symptomology/problems.