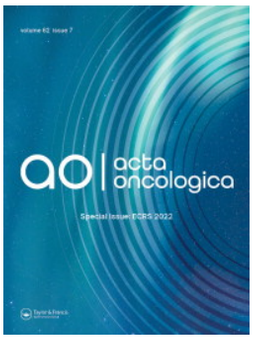

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ORIGINAL ARTICLE

Sexual functioning, sexual enjoyment, and body image in Norwegian breast cancer survivors: a 12-year longitudinal follow-up study and comparison with the general female population

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ABSTRACT

Background: Given the scarcity of evidence concerning the long-term sexual health of breast cancer (BC) survivors (BC-Pop), we aimed to assess how BC treatments affect short- and long-term sexual functioning, sexual enjoyment, and body image, and compare with aged-matched women in the Norwegian general population (F-GenPop).

Material and Methods: The 349 patients in BC-Pop treated at Trondheim University Hospital in 2007–2014, were assessed in clinical controls at the hospital; before starting radiotherapy (T1, baseline), immediately after ending radiotherapy (T2), and after 3, 6, and 12 months (T3–T5), and at a long-term follow-up 7–12 years after baseline (T6). Meanwhile, F-GenPop included 2254 age-matched women in the Norwegian general population. The impact of BC treatment on sexual functioning was examined using a Linear Mixed Model. Sexual functioning, sexual enjoyment, and body image were assessed with the EORTC's QLQ-BR23 scales and compared between the populations in the four age groups (30–49, 50–59, 60–69, and 70+ years) using means with 95% confidence intervals and Student *t*-test. Linear regression, adjusted for age and comorbidity was applied to estimate individual scores.

Result: BC survivors treated with mastectomy had overall lower sexual functioning than patients who had received breast-conserving surgery ($p = 0.017$). Although BC survivors treated with chemotherapy had lower sexual functioning than those treated without chemotherapy at T1–T5 ($p = 0.044$), both groups showed the same level of functioning at T6. BC-Pop exhibited significantly poorer sexual functioning ($p < 0.001$), lower sexual enjoyment ($p < 0.05$), and better body image ($p < 0.001$) than F-GenPop in all age groups.

Conclusion: The impact of specific BC treatments on sexual functioning was modest; only mastectomy had a persistent negative influence. Nevertheless, all age groups in BC-Pop displayed significantly poorer sexual functioning than F-GenPop at both 12 months and up to 12 years after treatment.

Abbreviations: BC-Pop: Breast cancer populations; EORTC: European organization for research and treatment of cancer; RT: Radiotherapy; BC: Breast cancer; LMM: Linear mixed models; BCS: Breast conserving surgery; F-GenPop: General female population; DAG: Directed acyclic graph

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KEYWORDS
Sexual functioning; breast cancer; survivorship; EORTC QLQ-BR23; Norwegian general population

Background

Improvements in breast cancer (BC) treatment in recent decades [1,2] have increased the population of BC survivors [3], all of whom may suffer from late effects capable of diminishing health-related quality of life (HRQOL) [4]. Of all the late effects, fatigue [5], pain [6,7], and psychological problems [8,9] have received most attention in research and clinical practice, whereas sexual problems have been handled more discreetly among both clinicians and patients [10]. Female sexual dysfunction, which includes persistent and recurrent difficulties in sexual desire, arousal, lubrication, orgasm, and dyspareunia [9,11], ranks among the most common late effects in BC survivors. Because female sexual dysfunction may be affected by biological-, psychological-, interpersonal-, and sociocultural factors [9,11–13], sexual functioning can be directly or indirectly affected by distress, mood disorders,

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body image, relationship with partner, comorbidities, and side effects of cancer treatment [9].

Treatment for BC is multimodal and may include surgery, chemotherapy, radiotherapy (RT), endocrine therapy, immune therapy and various targeted systemic therapies [14]. A meta-analysis of 16 studies revealed that patients treated with breast-conserving surgery (BCS) and breast reconstruction, had better physical health and body image than patients treated with mastectomy, although evidence regarding sexual functioning was inconclusive [15]. Even so, a short-term study with assessments conducted before, during and after RT showed no differences in sexual function, enjoyment, or body image between patients treated with BCS versus mastectomy [16]. In other studies, chemotherapy has been shown to negatively influence sexual health, particularly among younger BC patients [17–19]. Even so, more recent longitudinal studies have shown that chemotherapy-effects on health-related quality of life (HRQoL) are usually resolved within 18 months after treatment [19,20]. Meanwhile, endocrine therapy, particularly using aromatase inhibitors [21–23], but also tamoxifen [24], has been found to influence sexual function, most frequently in postmenopausal women [19]. Despite all of the above, evidence of BC treatments' long-term impact on sexual function remains limited, because most studies have small sample sizes [13], cross-sectional study designs [21–23,25], and, if longitudinal, then follow-up time has been limited to maximum 5 years [9,16,26].

The risk of developing sexual dysfunction is found to be 3.5-fold greater in women with BC than women without cancer [9]. A recent review of longitudinal studies with follow-up times from 6 months to 5 years, examining sexual dysfunction in female patients with cancer, revealed that sexual dysfunction was present in 30–80% of cases [9]. Moreover, as the review and other studies have shown, BC and gynecological cancer are the female cancers most associated with sexual dysfunction [9,13]. A meta-analysis of 19 studies addressing sexual dysfunction among European, U.S., and Asian BC survivors revealed an overall high prevalence of sexual dysfunction (73%) and significant geographic heterogeneity, with less prevalence in Europe than in Asia and the United States [12].

Distinguishing sexual problems following BC disease and treatment versus changes related to normal aging processes is challenging. Although comparisons of sexual health problems in BC populations with various control populations have attempted to overcome that challenge, the results have been conflicting [27,28], probably due to the heterogeneity of both the controls and the assessment tools. By contrast, comparing sexual health in the BC population with the general female population may be a superior strategy.

Against that backdrop, the aim of our study was to assess the impact of BC treatments on long-term sexual functioning and compare short- and long-term sexual functioning, sexual enjoyment, and body image among BC survivors with age-matched women in the general population of Norway. We hypothesized that BC treatment modalities have different impacts on sexual functioning, sexual enjoyment, and body image, and that BC survivors have lower sexual functioning, sexual enjoyment, and body image than the female general population.

Material and methods

The paper presents data from a longitudinal 12-year follow-up study of two BC cohorts (BC-Pop) and a large nation-wide electronic and postal cross-sectional survey in the Norwegian female general population (F-GenPop).

The breast cancer population (BC-Pop)

Figure 1 displays the flowchart for the longitudinal BC-Pop cohorts. Cohort I consisted of 250 patients referred to post-operative conventional RT at Trondheim University Hospital in 2007–2008. The inclusion flowchart and the characteristics of patients and treatment have previously been published [29]. Chemotherapy was administered as six anthracycline-based courses, or four anthracycline-based courses, followed by 12 weeks of taxanes. The RT was given in 2 Gy fractions, to 50 Gy 5 days a week to the breast or chest wall. Endocrine therapy was administered as tamoxifen or aromatase inhibitors according to menopausal status, TNM stage, and molecular classification. Cohort II consisted of 99 BC patients from the TARGIT study (ClinicalTrials.gov: NCT00983684) who were referred to BCS at Trondheim University Hospital in the period from 2008 to 2012. Patients at least 45 years old with early-stage BC were randomized before surgery to single dose (i.e., 20 Gy) intra-operative irradiation (IORT) or standard external whole-breast RT. The chemotherapy and endocrine treatments were administered similarly to Cohort I. After the final histopathology report, supplementary external RT was given to 13% of patients in the IORT-arm.

BC-Pop: procedures and measures

All assessments in the BC cohort were performed during clinical visits as part of extended outpatient follow-up at the hospital. The baseline assessment (T1) was performed before RT in Cohort I and before surgery and IORT in Cohort II. Follow-up assessments were completed immediately after external RT (T2), and at 3 months (T3), 6 months (T4) and 12 months (T5) after baseline, whereas the long-term follow-up was between 7 and 12 years after baseline (T6). T5 was defined as *short-term follow-up*, because the acute effects of treatments are expected to have decreased at that time.

Comorbidity was registered at clinical controls by the oncologists. At each visit, patients completed the European Organization for Research and Treatment of Cancer's (EORTC) questionnaires QLQ-C30 and the breast module QLQ-BR23. Treatment modalities were dichotomized into type of surgery (*BCS vs mastectomy*), chemotherapy (*yes vs no*), extent of RT (*local vs locoregional*) and endocrine therapy (*yes vs no*). Patients treated with IORT only ($n = 42$) were categorized in the local RT group, whereas patients who had received additional external radiation after IORT ($n = 13$) were categorized according to their external RT (*local vs locoregional*).

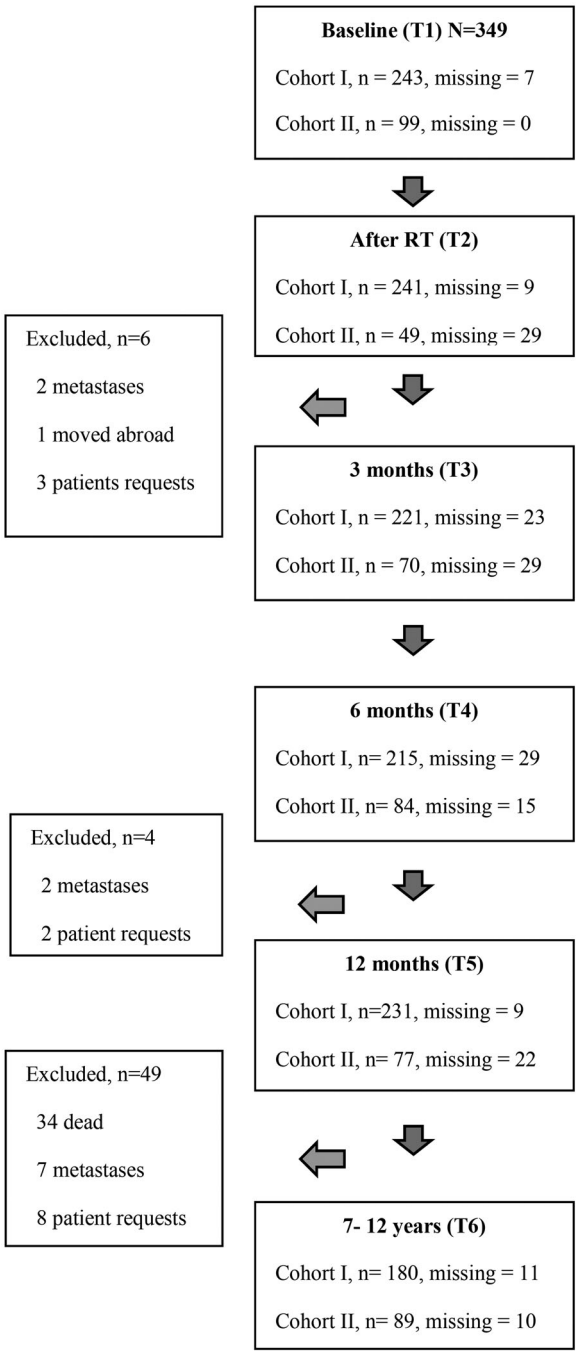


Figure 1. Flowchart for Cohort I and Cohort II in the BC-Pop and responses on the EORTC's QLQ-BR23 at baseline, 3, 6, and 12 months, and after 7–12 years. Patients in Cohort II had no scheduled assessment at T2 and only some patients with external RT filled out the questionnaire. Excluded patients at left panel. "Missing" are patients who did not meet at clinical visits, did not deliver the EORTC questionnaire or did not answer the EORTC sexual items. All excluded patients participated in Cohort I.

The general female population (F-GenPop)

Data from the general female population were obtained from a survey conducted in 2021 [30]. From the total sample ($n = 5135$), the female participants were selected ($n = 2735$), and respondents less than 30 years old were excluded to achieve an age distribution similar to that in BC-Pop ($n = 2254$) (Table 1). Individuals in F-GenPop with previous cancer diagnoses were not excluded, because they are considered to be part of a general population. Morbidity was self-reported using the Self-Administered Comorbidity Questionnaire (SCQ) [31]. Total morbidity was defined as having or have had one or more of the selected health conditions that limited their daily activities/overall functioning.

Table 1. Characteristics for the breast cancer cohort (BC-Pop) and the female general population (F-GenPop).

	BC-Pop $N = 349$ (%)	F-GenPop $N = 2254$ (%)
Age (Mean ± St. Dev.)	59 (9.2)	52 (13.2)
30–49 years	48 (13.7)	989 (39.8)
50–59 years	119 (34.0)	540 (23.9)
60–69 years	133 (38.1)	454 (20.1)
70–79 years	27 (7.7)	271 (12.0)
Marital status		
Living alone	79 (22.6)	577 (25.7)
Married/ cohabitant	256 (73.4)	1666 (74)
Missing	14 (4)	11 (0.5)
Comorbidity	103 (30.7)	653 (29.0)*
Anxiety and/or depression	12 (3.4)	241 (10.7)*
Diabetes mellitus	9 (2.6)	134 (5.9)
Stroke	3 (0.9)	42 (1.8)
Cardiovascular disease	39 (11.2)	86 (3.8)
Respiratory disease	17 (4.9)	94 (4.2)*
Musculoskeletal	23 (6.6)	375 (16.6)*
Cancer (F-GenPop)		221 (9.8)
Medical characteristics		
AJCC (stage)		
0	20 (5.7)	
I	208 (59.6)	
II	93 (26.7)	
III	15 (4.3)	
Grade		
I	81 (23.2)	
II	152 (43.6)	
III	106 (30.4)	
To little tissue	9 (2.4)	
Surgery		
Conservative	276 (79.1)	
Mastectomy	73 (20.9)	
Radiotherapy (RT)		
Local	210 (60.2)	
Locoregional	96 (27.5	
IORT	43 (12.3)	
Chemotherapy	135 (39.2)	
FEC 60	68 (19.9)	
FEC 100	29 (8.5)	
FEC/ taxemes/others	38 (10.8)	
Endocrine therapy	181 (53.0)	
Tamoxifen	125 (36.4)	
Aromatase inhibitors	56 (16.4)	

AJCC, American Joint Committee on Cancer, a classification system for describing the extent of disease in cancer patients. In BC-Pop comorbidity was registered by clinicians at the clinical controls and from medical records. In F-GenPop morbidity is self-reported and based on the criteria of having one or more of the given conditions. Morbidities with * in F-GenPop means having one or more morbidity that limits activities.

Assessment of sexual functioning in BC-Pop and F-GenPop

Sexual functioning, *sexual enjoyment* and *body image* were measured with the sexual domains in the EORTC's QLQ-BR23. *Sexual functioning* contains two items regarding sexual interest and activity, with or without intercourse. *Sexual enjoyment* contains one item addressing sexual enjoyment, which was questioned only to sexually active individuals. *Body image* contains four items whereof two items concern dissatisfaction with one's body and the last two items ask whether disease

and treatment has interfered their femininity or attractiveness. Response options were 1(*not at all*), 2(*a little*), 3(*quite a bit*) and 4(*very much*), and for the F-GenPop, we listed 'not relevant' as an additional response option on the two treatment-related items on the *body image* scale. Scale scores were calculated according to the EORTC scoring manual and transformed to a scale ranging from 0 to 100, with higher scores indicating better functioning. As in past studies, a functional score of 33 or lower was regarded as problematically low and thus of high clinical significance [32,33].

Statistical analyses

The longitudinal impact of treatment modalities on *sexual functioning* was analyzed in a linear mixed model (LMM), which is highly suitable for analyzing data with repeated measures due to including a random effect to account for within-patient correlations. Because LMMs also allow missing values at single time points, all data from each assessment was utilized. The *sexual functioning* scale was the dependent variable in the model, while the patients ID (study number) was included as a random effect. To make clinically relevant adjustments, we used a directed cyclic graph as a working tool (Supplementary Figure I). Age and comorbidities were treated as confounders and adjusted for in the model. Comorbidity was defined as 'have or have had one or more conditions that limit current activities/functioning'. The independent variables were time of measurement (i.e., T1–T6, reference coded to T1), age, comorbidity, treatment modality, and the interaction between time and treatment. The treatment variable represented the difference in sexual functioning between the groups at T1, and the time-treatment interaction tested whether the groups developed differently over time.

Sexual functioning, *sexual enjoyment*, and *body image* scores in the BC-Pop (i.e., overall mean) and F-GenPop groups were described as mean values with 95% confidence intervals (CI) in the four age-groups (Figure 3), and differences were tested with Student *t*-test (Table 2).

To enable a more precise estimation of scale values in BC individuals or groups, adjusted for age and comorbidity, and related to normative population values, we performed multivariable regression (Table 2). The analyses were performed in SPSS, Stata, and MatLab.

Table 2. Mean EORTC scores on sexual functioning, sexual enjoyment, and body image in the breast cancer cohort (BC-Pop) and the female general population (F-GenPop).

	BC-Pop						BC-Pop*	F-Gen Pop	Mean diff.	*p*-values
	T1	T2	T3	T4	T5	T6				
Sexual functioning	26.1	23.8	28.7	30.2	31.0	23.2	27.3	55.7	−19.5	<0.001
St. Dev.	24.0	23.4	24.1	24.8	24.0	24.0	24.2	20.3		
Sexual enjoyment	64.5	65.6	63.7	64.5	65.2	65.0	64.7	70.7	−6.3	<0.001
Std. Dev.	26.8	26.2	27.1	27.6	25.2	29.3	26.9	26.9		
Body image	86.9	84.1	87.1	87.1	88.0	88.4	87.0	70.8	13.3	<0.001
St. Dev.	20.4	21.3	19.3	20.3	19.1	19.5	20.0	26.8		

T1–T6 are mean values at given time-points in BC-Pop. The overall mean scores in BC-Pop* (average sample mean score from T1 to T6) were compared with mean scores in F-GenPop and differences were tested with Student *t*-tests.

Ethics

The study was approved by the Regional Committee for Medical and Health Research Ethics in central Norway (REK 2020/58888).

Results

The response rates in the BC-Pop were 98% at T1, 87% at T2, 85% at T3, 87% at T4, 91% at T5, and 93% at T6 (Figure 1). In the F-GenPop, the response rate was 35%. The mean age in BC-pop was 59 years at inclusion, compared with 52 years in F-GenPop. Most women were married or cohabitating (Table 1).

The impact of BC treatment modalities on long-term sexual functioning, sexual enjoyment, and body image

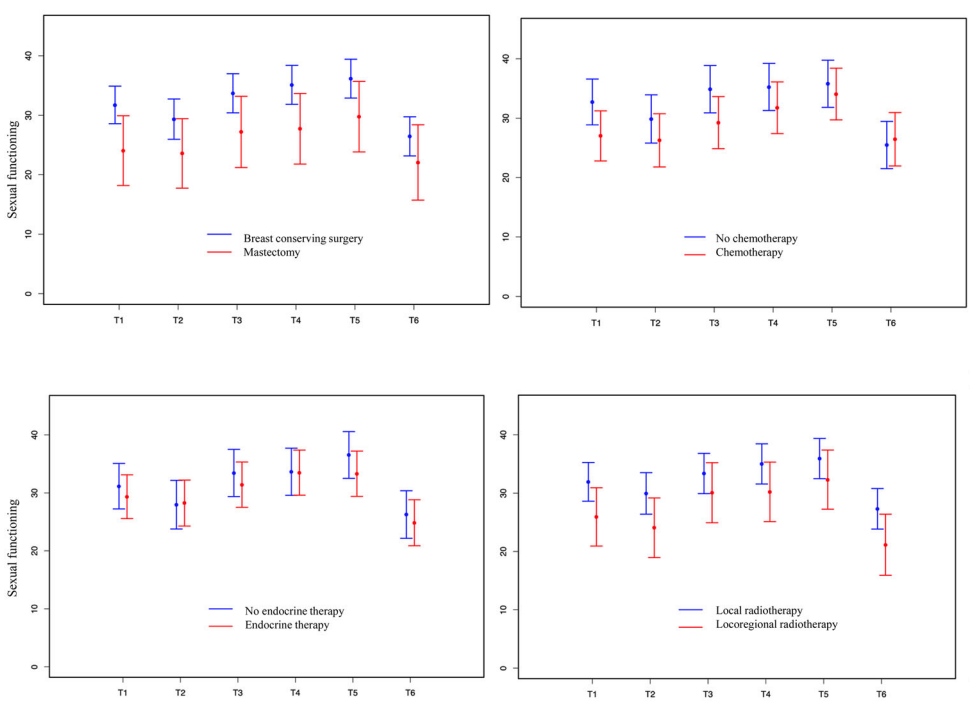
The four treatment groups showed the same pattern in sexual functioning, measured as activity and interest, with a slightly deterioration from baseline to T2, but an improvement from baseline to T3–T5. At T6, all four treatment groups showed significant reduction from baseline.

Patients treated with mastectomy had significantly lower sexual functioning at baseline than patients treated with BCS (mean difference = 7.6, $p = 0.017$) (Figure 2). Over time, both groups showed the same significant improvement in sexual functioning from baseline to T4 and T5, and thereafter a significant decrease to T6 (estimate = −5.3, $p < 0.001$). There was a significant age difference between patients with mastectomy versus BCS, mean age 56 versus 59 years ($p = 0.016$).

Patients treated with chemotherapy showed significantly lower sexual functioning at baseline than patients treated without chemotherapy (mean difference = −5.7, $p < 0.044$, Figure 2). Both groups followed the same pattern in the first year after baseline. At T6, both groups showed significant decreases in sexual functioning scores compared with baseline, but with smaller decrease in the patients treated with chemotherapy, resulting in almost equal mean values in patients treated with and without chemotherapy at T6.

Patients receiving endocrine treatment showed the same pattern as patients not receiving endocrine treatment, and similarly there was no additional effect from extent of RT (Figure 2, Supplementary Table I). Furthermore, overall mean values of sexual functioning did not significantly differ between the tamoxifen and aromatase inhibitor groups (mean values 25 vs 27, $p > 0.05$).

Body image and *sexual enjoyment* were not significantly impacted by any BC treatment.



A) Sexual functioning	Coef.	95 % CI	P
Surgery			
mastectomy	7.6	(-14.0, -1.4)	0.017
Age	-0.4	(-0.7, -0.2)	<0.001
(Co)morbidity	-7.7	(-12.3, -3.1)	0.001
Time			
1 (T2)	-2.4	(-5.1, 0.3)	0.083
2 (T3)	2.0	(-0.6, 4.5)	0.130
3 (T4)	3.4	(0.8, 5.9)	0.009
4 (T5)	4.4	(1.9, 7.0)	0.001
5 (T6)	-5.3	(0.0, -14.0)	<0.001
Interaction			
Time * Type of surgery			
1 (T2)	1.9	(-3.7, 7.5)	0.500
2 (T3)	1.1	(-4.5, 6.9)	0.685
3 (T4)	0.3	(-5.3, 5.9)	0.919
4 (T5)	1.3	(-4.3, 6.9)	0.657
5 (T6)	3.3	(-2.8, 9.3)	0.286
cons	57.7	(43.7, 71.7)	<0.001

B) Sexual functioning	Coef.	95 % CI	P
Chemotherapy			
yes	-5.7	(-11.3, -0.2)	0.044
Age	-0.5	(-0.8, -0.2)	<0.001
(Co)morbidity	-8.0	(-12.7, -3.9)	0.001
Time			
1 (T2)	-2.9	(-5.9, 0.2)	0.065
2 (T3)	2.2	(-0.8, 5.0)	0.151
3 (T4)	2.5	(-0.4, 5.5)	0.090
4 (T5)	3.0	(0.2, 6.0)	0.039
5 (T6)	-7.3	(-10.2, -4.3)	<0.001
Interaction			
Time * Chemotherapy			
1 (T2)	2.1	(-2.7, 6.9)	0.387
2 (T3)	0.9	(-4.6, 4.7)	0.971
3 (T4)	2.2	(-2.4, 6.8)	0.349
4 (T5)	4.0	(-0.6, 8.6)	0.087
5 (T6)	6.7	(1.9, 11.5)	0.006
cons	60.6	(44.2, 77.0)	<0.001

Figure 2. Sexual functioning scores after different BC treatment modalities for 12 years follow-up. T1= before radiotherapy (RT, $n = 333$), baseline, T2 = immediately after RT ($n = 251$), T3 = 3 months after RT ($n = 279$), T4 = 6 months after RT ($n = 285$), T5 = 12 months after RT ($n = 290$), T6 = 7–12 years after RT ($n = 262$). The four figure panels represent longitudinal estimated sexual functioning scores (mean and 95% confidence intervals) based on type of surgery, use of chemotherapy, use of endocrine treatment and the extent of RT. The panels to the right show the LMM with estimates for the significant impact of surgery and chemotherapy on sexual functioning. The LMM for RT and endocrine treatment is displayed in Supplementary Table 1. To calculate more precise estimates of scale values in BC individuals or groups, adjusted for age and comorbidity, the numbers in the LMM model can be used as follows: for a 55-year-old woman without comorbidities who has undergone BCS, estimated sexual functioning score is 57.7 (cons) – 0.4*55 (age) = 35.7 at baseline. A woman of same age and comorbidity-status who underwent mastectomy, will have an estimated sexual functioning score of 57.7 (cons) – 0.4*55 (age) – 7.6 (mastectomy) = 28.1 at baseline.

Table 3. Sexual functioning, body image, and sexual enjoyment in breast cancer patients (BC-Pop) and female general population (F-GenPop) by age and comorbidity.

Intercept (GenPop-reference)		BC-Pop		Age		Comorbidity	
		Coeff.	*p*-value	Coeff.	*p*-value	Coeff	*p*-value
Sexual functioning at T5	57.4	−12.2	<0.001	−0.3	<0.001	−4.3	<0.001
Sexual functioning at T6	57.1	−14.0	<0.001	−5.7	<0.001	−3.6	<0.001
Sexual enjoyment at T5	75.6	−3.6	0.019	−0.15	0.002	−2.5	0.053
Sexual enjoyment at T6	75.1	−3.7	0.040	−0.1	0.008	−2.2	0.094
Body image at T5	67.0	6.4	<0.001	0.5	<0.001	−9.9	<0.001
Body image at T6	68.5	5.8	<0.001	−5.7	<0.001	−10.7	<0.001

T5 = 1 year after radiotherapy, T6 = 7–12 years after treatment. F-GenPop is compared to the BC-Pop on Sexual Functioning, Body Image and Sexual Enjoyment (among sexually active women) at short-term (T5) and long-term (T6) follow up. The regression analyses are adjusted for age and comorbidity.

Short- and long-term sexual functioning, sexual enjoyment, and body image among BC survivors compared with age-matched women in the general population

Table 2 presents the observed mean values at each time point and the overall mean score (average T1–T6)) for BC-Pop, along with mean values for F-GenPop. Overall mean scores on sexual functioning and sexual enjoyment were significantly lower in BC-Pop than in F-GenPop, with respective mean differences 19.5 and 6.3 (both $p < 0.001$). Overall mean score on body image was significantly higher in BC-Pop than in F-GenPop (mean difference = 13.3, $p < 0.001$). Table 3 shows the regression models for *sexual functioning*, *sexual enjoyment*, and *body image* in BC-Pop versus F-GenPop. Sexual functioning in BC-Pop at short-term (T5) and long-term (T6) was significantly lower than in F-GenPop (mean differences = −12.2, $p < 0.001$ and −14.0, $p < 0.001$, respectively). Slightly, but significantly lower sexual enjoyment, was found in BC-Pop at T5 and T6 compared with F-GenPop (mean difference = −3.6, $p < 0.05$ and −3.7, $p < 0.05$). BC-Pop had better body image at T5 and T6 than F-GenPop (mean difference = 5.8, $p < 0.01$ and 6.4, $p < 0.001$). Age and morbidity had a significant negative impact on short- and long-term sexual functioning ($p < 0.001$).

Figure 3 illustrates *sexual functioning* by age groups in BC-Pop at 12 months (T5) and 7–12 years (T6) after treatment compared with normative F-GenPop values. Sexual functioning in BC-Pop at both T5 and T6 was significantly lower than in F-GenPop in all age groups, and largest differences between the populations were observed in the youngest and oldest groups. Sexual enjoyment was relatively stable across age-groups for both BC-Pop and F-GenPop and lowest among the oldest in BC-Pop. Body image was better in BC-Pop than in F-GenPop and improved with advanced age in both populations.

Discussion

In our long-term follow-up study reviled that BC survivors had significantly lower sexual functioning and sexual enjoyment, but better body image than the general female population, both in the short and long term after cancer

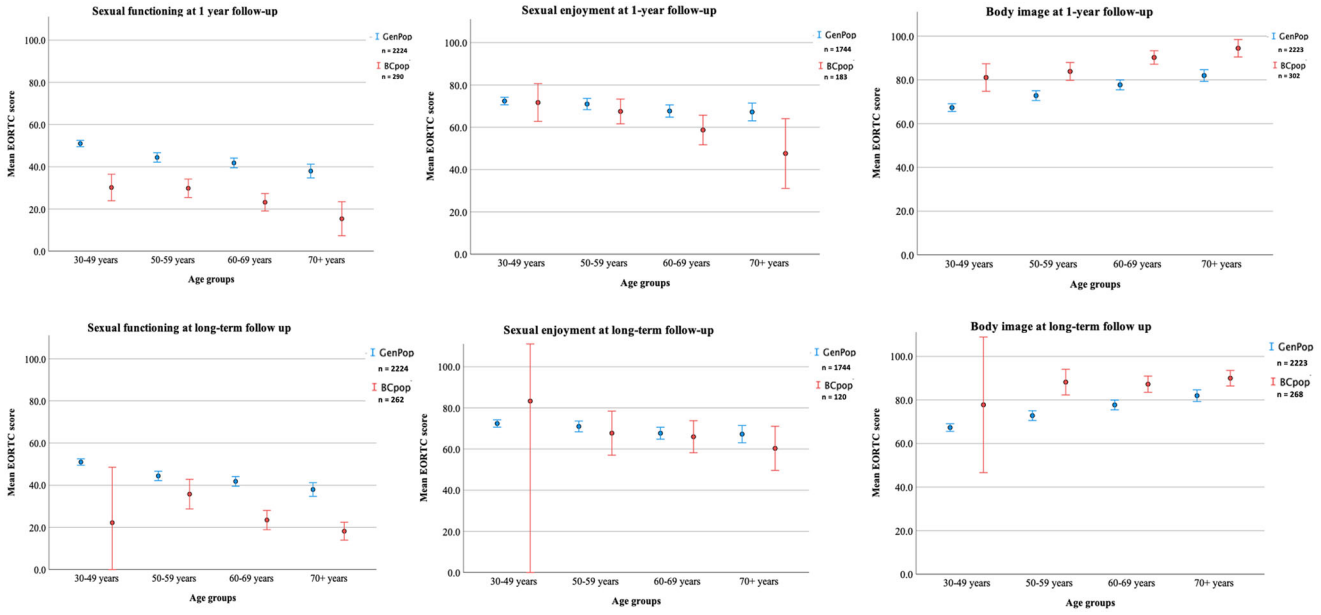


Figure 3. Sexual functioning, sexual enjoyment, and body image by age among BC survivors (BC-Pop) compared with the general female population (F-GenPop) at short-term (T5) and long-term (T6) follow-up after BC treatment. Mean EORTC scores and 95% confidence intervals are displayed on *Y*-axis, and age groups displayed on the *X*-axis.

treatment. Surgery was the only treatment with a significant persistent impact on sexual functioning. Women who had undergone mastectomy displayed modest, but significantly lower sexual functioning than those with BCS up to 12 years after treatment. BC survivors treated with chemotherapy had lower sexual functioning during the first year after treatment than those who did not receive this treatment, but at the long-term follow-up the groups had equal level of sexual functioning.

We found a small, but significant impact of mastectomy on long-term sexual functioning. In agreement with our results, a cross-sectional study using the same EORTC QLQBR23, revealed that sexual functioning was diminished 12 months after mastectomy [34], and a short-term follow-up study after RT found lower sexual enjoyment among patients treated with mastectomy than among patients treated with BCS [16]. Further, a recent study using the sexual health questionnaire EORTC QLQ-SHQ22, showed a lower feeling of security with onés partner and less femininity among patients treated with mastectomy than among those treated with BCS [35]. The negative impact of mastectomy on sexual functioning may be related to complications with scaring, pain, loss of sensation, or even phantom sensations in the removed breast [36,37]. The female breast is often associated with sexuality and could be a source of erotic pleasure. Its loss could therefore influence body image and loss of sexuality [38]. Today, surgical procedures have changed, and most patients are offered breast reconstruction, which probably has contributed to improved sexual health in BC survivors [38].

The small short-term and lack of long-term impact of chemotherapy on sexual functioning corroborates past results on chemotherapýs temporary influence on sexual functioning in the first 12–18 months after treatment [18–20]. By contrast, a small 12-month follow-up study of sexual health in BC patients receiving endocrine treatment, revealed no short-term association between chemotherapy and sexual satisfaction [35]. Indeed, some cross-sectional studies have shown associations between chemotherapy and long-term sexual activity [21], but to document the real impact of chemotherapy we need longitudinal studies with baseline assessment before chemotherapy using sensitive sexual health outcome measures.

No significant difference in sexual functioning was apparent between patients who had received local versus locoregional RT, which agrees with previous evidence [35]. In our study, sexual functioning was not influenced by endocrine therapy, which is in line with a large French study evaluating two-year trajectories of multiple EORTC outcomes in BC survivors [19]. However, cross-sectional studies have shown associations between endocrine treatment, particularly aromatase inhibitors, and sexual dysfunction, in both the short term [23,39] and in long term [21]. In our BC sample, most endocrine positive patients received Tamoxifen, which may explain the non-significant difference between the groups.

Most importantly, and despite minor treatment impacts, in our 12-year longitudinal study, BC patients reported poor sexual functioning from baseline and throughout follow-up, in line with a comparable study [40] As baseline assessments in most prospective studies are never collected before diagnosis and rarely before all kinds of treatments, baseline scores are most likely influenced by emotional- or physical conditions related to the disease. Therefore, normative general population values are useful as a substitute for real baseline assessments, but are also valuable in the long-term follow-up when disease- and treatment-related HRQoL deteriorations are assumed to be resolved.

Sexual functioning and sexual enjoyment decreased with age among the Norwegian BC survivors as well as the general female population. BC survivors reported significantly poorer sexual functioning than the general female population, and differences ranging from 15 to 32 EORTC points are

definitively of high clinical significance [41]. Because normative general population data for EORTC's measures of sexual health exist only for the Norwegian population, comparison with similar studies is impossible. Nevertheless, poorer sexual functioning and sexual enjoyment were also found in German BS survivors compared to other nonmalignant breast-disease patient groups [28].

Interestingly, BC survivors reported significantly better body image at both the short- and long-term follow up than the general female population, which aligns with results in European, Asian, and Arabic populations [28,42,43]. Even so, poorer body image has been reported in some subgroup of BC patients, that is, patients with mastectomy [38], and in patients with lymphedema [44]. Despite bodily changes, good body image may be due to a shift in perspectives following diagnosis and treatment, with a greater appreciation of the body and widened limits of normality [45].

Among the limitations in our study, the relative narrow measure of sexual functioning in the EORTC QLQ-BR23 is regarded as most crucial as it probably miss important elements of sexual concerns in these patients. However, the study was designed many years ago aiming to register different late effects after RT, among which sexual functioning was not the primary focus. Of the same reason, our baseline measure before RT was not optimal to capture the impact of chemotherapy. We recommend future follow-up studies of cancer patients with high likelihood of sexual health deterioration to apply a more sensitive measure such as the recently validated EORTC QLQ-SHQ22 [46]. Lastly, when comparing data from a long-lasting follow-up study with recently developed normative data, the assessment times were naturally different in the two populations. Based on the same reason, comorbidity was assessed differently in the two populations: by clinicians in BC-Pop and self-reported in F-GenPop. However, to hinder overreporting of morbidity in F-GenPop, only conditions limiting daily functioning were considered.

Our study is the first to provide long-term longitudinal data on sexual functioning in a BC population with comparison to a country specific general female population. The BC-Pop was well defined with excellent compliance over a 12-year period, based on closely monitored assessments at clinical visits. Lastly, our study is the first to compare the EORTC sexual dimensions with normative data [30] accounted for age and comorbidity, as recommended in a recent EORTC publication [47].

Conclusion

Twelve-year longitudinal data on BC survivors' sexual functioning compared with age-matched women in the general population contributes bridging a knowledge gap on sexual challenges after BC treatment. The treatments' impact on sexual functioning were modest; mastectomy was associated with a small long-term deterioration, chemotherapy had a small impact the first year after treatment, which thereafter attenuated, while the extent of RT and endocrine treatment had no impact in our BC population. Most importantly, the level of sexual functioning in Norwegian BC survivors is considered as problematic low, and significantly lower than levels in the general female population. The poor sexual functioning in long-term BC survivors is of highly clinical relevance and actions should therefore be taken to accommodate this partly under-communicated health issue in the follow-up of BC patients.

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Data availability statement

The data are available on request to the corresponding author, randi.j.reidunsdatter@ntnu.no.

References

[1] Early Breast Cancer Trialists' Collaborative Group. Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. The Lancet. 2005;365(9472):1687–1717.
[2] Cancer registry of Norway. Cancer in Norway 2021.
[3] Early Breast Cancer Trialists' Collaborative Group. Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10 801 women in 17 randomised trials. The Lancet. 2011;378(9804):1707–1716.
[4] Ewertz M, Jensen AB. Late effects of breast cancer treatment and potentials for rehabilitation. Acta Oncol. 2011;50(2):187–193. doi: 10.3109/0284186X.2010.533190.
[5] Abrahams H, Gielissen M, Schmits I, et al. Risk factors, prevalence, and course of severe fatigue after breast cancer treatment: a meta-analysis involving 12 327 breast cancer survivors. Ann Oncol. 2016;27(6):965–974. doi: 10.1093/annonc/mdw099.
[6] Andersen KG, Kehlet H. Persistent pain after breast cancer treatment: a critical review of risk factors and strategies for prevention. J Pain. 2011;12(7):725–746. doi: 10.1016/j.jpain.2010.12.005.
[7] Mejdahl MK, Andersen KG, Gärtner R, et al. Persistent pain and sensory disturbances after treatment for breast cancer: six year nationwide follow-up study. BMJ. 2013;346:f1865. doi: 10.1136/bmj.f1865.
[8] Wang X, Wang N, Zhong L, et al. Prognostic value of depression and anxiety on breast cancer recurrence and mortality: a systematic review and meta-analysis of 282,203 patients. Mol Psychiatry. 2020;25(12):3186–3197. doi: 10.1038/s41380-020-00865-6.
[9] Sousa Rodrigues Guedes T, Barbosa Otoni Gonçalves Guedes M, de Castro Santana R, et al. Sexual dysfunction in women with cancer: a systematic review of longitudinal studies. Int J Environ Res Public Health. 2022;19(19):11921. doi: 10.3390/ijerph191911921.

[10] Reese JB, Sorice K, Beach MC, et al. Patient-provider communication about sexual concerns in cancer: a systematic review. J Cancer Surviv. 2017;11(2):175–188. doi: 10.1007/s11764-016-0577-9.
[11] Parish SJ, Cottler-Casanova S, Clayton AH, et al. The evolution of the female sexual disorder/dysfunction definitions, nomenclature, and classifications: a review of DSM, ICSM, ISSWSH, and ICD. Sex Med Rev. 2021;9(1):36–56. doi: 10.1016/j.sxmr.2020.05.001.
[12] Jing L, Zhang C, Li W, et al. Incidence and severity of sexual dysfunction among women with breast cancer: a meta-analysis based on female sexual function index. Support Care Cancer. 2019;27(4):1171–1180. doi: 10.1007/s00520-019-04667-7.
[13] Maiorino MI, Chiodini P, Bellastella G, et al. Sexual dysfunction in women with cancer: a systematic review with meta-analysis of studies using the female sexual function index. Endocrine. 2016; 54(2):329–341. doi: 10.1007/s12020-015-0812-6.
[14] NBCG. Behandlingsskjemaer 2020
[15] Zehra S, Doyle F, Barry M, et al. Health-related quality of life following breast reconstruction compared to total mastectomy and breast-conserving surgery among breast cancer survivors: a systematic review and meta-analysis. Breast Cancer. 2020;27(4):534–566. doi: 10.1007/s12282-020-01076-1.
[16] Munshi A, Dutta D, Kakkar S, et al. Comparison of early quality of life in patients treated with radiotherapy following mastectomy or breast conservation therapy: a prospective study. Radiother Oncol. 2010;97(2):288–293. doi: 10.1016/j.radonc.2010.04.008.
[17] Azim H, Jr De Azambuja E, Colozza M, et al. Long-term toxic effects of adjuvant chemotherapy in breast cancer. Ann Oncol. 2011;22(9):1939–1947. doi: 10.1093/annonc/mdq683.
[18] Malinovszky K, Gould A, Foster E, et al. Quality of life and sexual function after high-dose or conventional chemotherapy for high-risk breast cancer. Br J Cancer. 2006;95(12):1626–1631. doi: 10.1038/sj.bjc.6603454.
[19] Ferreira A, Di Meglio A, Pistilli B, et al. Differential impact of endocrine therapy and chemotherapy on quality of life of breast cancer survivors: a prospective patient-reported outcomes analysis. Ann Oncol. 2019;30(11):1784–1795. doi: 10.1093/annonc/mdz298.
[20] Battisti NML, Reed MW, Herbert E, et al. Bridging the age gap in breast cancer: impact of chemotherapy on quality of life in older women with early breast cancer. Eur J Cancer. 2021;144:269–280. doi: 10.1016/j.ejca.2020.11.022.
[21] Smedsland SK, Vandraas KF, Bøhn SK, et al. Sexual activity and functioning in long-term breast cancer survivors; exploring associated factors in a nationwide survey. Breast Cancer Res Treat. 2022;193:139–149. doi: 10.1007/s10549-022-06544-0.
[22] Schover LR, Baum GP, Fuson LA, et al. Sexual problems during the first 2 years of adjuvant treatment with aromatase inhibitors. J Sex Med. 2014;11(12):3102–3111. doi: 10.1111/jsm.12684.
[23] Gandhi C, Butler E, Pesek S, et al. Sexual dysfunction in breast cancer survivors. Am J Clin Oncol. 2019;42(6):500–506. doi: 10.1097/COC.0000000000000552.
[24] Juliato P, Rodrigues A, Stahlschmidt R, et al. Can polyacrylic acid treat sexual dysfunction in women with breast cancer receiving tamoxifen? Climacteric. 2017;20(1):62–66. doi: 10.1080/13697137.2016.1258396.
[25] Howes BH, Watson DI, Xu C, et al. Quality of life following total mastectomy with and without reconstruction versus breast-conserving surgery for breast cancer: a case-controlled cohort study. J Plast Reconstr Aesthet Surg. 2016;69(9):1184–1191. doi: 10.1016/j.bjps.2016.06.004.
[26] Lee C, Sunu C, Pignone M. Patient-reported outcomes of breast reconstruction after mastectomy: a systematic review. J Am Coll Surg. 2009;209(1):123–133. doi: 10.1016/j.jamcollsurg.2009.02.061.
[27] Oberguggenberger A, Martini C, Huber N, et al. Self-reported sexual health: breast cancer survivors compared to women from the general population–an observational study. BMC Cancer. 2017; 17(1):599. doi: 10.1186/s12885-017-3580-2.
[28] Karsten MM, Roehle R, Albers S, et al. Real-world reference scores for EORTC QLQ-C30 and EORTC QLQ-BR23 in early breast cancer patients. Eur J Cancer. 2022;163:128–139. doi: 10.1016/j.ejca.2021.12.020.
[29] Reidunsdatter RJ, Albrektsen G, Hjermstad MJ, et al. One-year course of fatigue after post-operative radiotherapy in Norwegian breast cancer patients–comparison to general population. Acta Oncol. 2013;52(2):239–248. doi: 10.3109/0284186X.2012.742563.
[30] Åsberg RE, Nilsen M, Hjermstad MJ, et al. Norwegian general population normative data for the EORTC questionnaires; the core QLQ-C30, the sexual health questionnaire QLQ-SHQ22, and the sexual domains of the QLQ-BR23/BR45. Eur J Cancer. 2023; 190:112943. doi: 10.1016/j.ejca.2023.112943.
[31] Sangha O, Stucki G, Liang MH, et al. The self-administered comorbidity questionnaire: a new method to assess comorbidity for clinical and health services research. Arthritis Rheum. 2003;49(2): 156–163. doi: 10.1002/art.10993.
[32] Alawadi SA, Ohaeri JU. Health - related quality of life of kuwaiti women with breast cancer: a comparative study using the EORTC quality of life questionnaire. BMC Cancer. 2009;9(1):222. doi: 10.1186/1471-2407-9-222.
[33] Ahn S, Park B, Noh D, et al. Health-related quality of life in disease-free survivors of breast cancer with the general population. Ann Oncol. 2007;18(1):173–182. doi: 10.1093/annonc/mdl333.
[34] Pačarić S, Kristek J, Mirat J, et al. The quality of life of croatian women after mastectomy: a cross-sectional single-center study. BMC Public Health. 2018;18(1):999. doi: 10.1186/s12889-018-5929-0.
[35] Aptecar L, Fiteni F, Jarlier M, et al. Prospective evaluation of sexual health in breast cancer women during the first year of adjuvant hormonal treatment using a cancer patient's dedicated questionnaire: a glaring gap of communication between health professionals and patients. Breast Cancer Res Treat. 2021;186(3): 705–713. doi: 10.1007/s10549-020-06062-x.
[36] Fakhari S, Pourfathi H, Farzin H, et al. Post-mastectomy phantom breast syndrome. JOGCR. 2018;3(4):1–6. doi: 10.30699/jogcr.3.4.1.
[37] Farthmann J, Hanjalic-Beck A, Veit J, et al. The impact of chemotherapy for breast cancer on sexual function and health-related quality of life. Support Care Cancer. 2016;24(6):2603–2609. doi: 10.1007/s00520-015-3073-2.
[38] Martins Faria B, Martins Rodrigues I, Verri Marquez L, et al. The impact of mastectomy on body image and sexuality in women with breast cancer: a systematic review. PSIC. 2021;18(1):91–115. doi: 10.5209/psic.74534.
[39] Baumgart J, Nilsson K, Evers AS, et al. Sexual dysfunction in women on adjuvant endocrine therapy after breast cancer. Menopause. 2013;20(2):162–168. doi: 10.1097/gme.0b013e31826560da.
[40] Koch L, Jansen L, Herrmann A, et al. Quality of life in long-term breast cancer survivors–a 10-year longitudinal population-based study. Acta Oncol. 2013;52(6):1119–1128. doi: 10.3109/0284186X.2013.774461.
[41] Osoba D, Rodrigues G, Myles J, et al. Interpreting the significance of changes in health-related quality-of-life scores. J Clin Oncol. 1998;16(1):139–144. doi: 10.1200/JCO.1998.16.1.139.
[42] Imran M, Al-Wassia R, Alkhayyat SS, et al. Assessment of quality of life (QoL) in breast cancer patients by using EORTC QLQ-C30 and BR-23 questionnaires: a tertiary care center survey in the Western region of Saudi Arabia. PLoS One. 2019;14(7):e0219093. doi: 10.1371/journal.pone.0219093.
[43] Tan ML, Idris DB, Teo LW, et al. Validation of EORTC QLQ-C30 and QLQ-BR23 questionnaires in the measurement of quality of life of breast cancer patients in Singapore. Asia Pac J Oncol Nurs. 2014;1(1):22–32. doi: 10.4103/2347-5625.135817.
[44] Teo I, Novy DM, Chang DW, et al. Examining pain, body image, and depressive symptoms in patients with lymphedema secondary to breast cancer. Psychooncology. 2015;24(11):1377–1383. doi: 10.1002/pon.3745.
[45] Nilsen M, Stalsberg R, Sand K, et al. Meaning making for psychological adjustment and quality of life in older long-term breast cancer survivors. Front Psychol. 2021;12:734198. doi: 10.3389/fpsyg.2021.734198.

[46] Oberguggenberger AS, Nagele E, Inwald EC, et al. Phase 1–3 of the cross-cultural development of an EORTC questionnaire for the assessment of sexual health in cancer patients: the EORTC SHQ-22. Cancer Med. 2018;7(3):635–645. doi: 10.1002/cam4.1338.

[47] Pilz MJ, Gamper EM, Efficace F, et al. EORTC QLQ-C30 general population normative data for Italy by sex, age and health condition: an analysis of 1,036 individuals. BMC Public Health. 2022; 22(1):1040. doi: 10.1186/s12889-022-13211-y.