



## Original article

# Body image problems in women with and without breast cancer 6–20 years after bilateral risk-reducing surgery – A prospective follow-up study



Lucy Bai <sup>a,\*</sup>, Brita Arver <sup>a</sup>, Hemming Johansson <sup>a</sup>, Kerstin Sandelin <sup>b</sup>, Marie Wickman <sup>b,c</sup>, Yvonne Brandberg <sup>a</sup>

<sup>a</sup> Department of Oncology-Pathology, Karolinska Institutet, Stockholm, Bioclinicum J5:17, SE-171 64, Solna, Sweden

<sup>b</sup> Department of Molecular Medicine and Surgery, Karolinska Institutet, Karolinska University Hospital, Solna (L1:00), SE-171 76, Stockholm, Sweden

<sup>c</sup> Sophiahemmet University, Stockholm, Sweden

## ARTICLE INFO

## Article history:

Received 14 August 2018

Received in revised form

25 January 2019

Accepted 31 January 2019

Available online 1 February 2019

## Keywords:

Breast cancer

Risk

Prophylactic mastectomy

Breast reconstruction

Quality of life

Body image

Sexuality

Anxiety

Depressive symptoms

## ABSTRACT

**Purpose:** To prospectively follow-up and investigate women's perceptions of the cosmetic outcome of their implant-based breast reconstruction, body image, sexuality, anxiety/depressive symptoms, and health-related quality of life (HRQoL) 6–20 years after bilateral risk-reducing mastectomy (RRM), or complementary RRM after breast cancer diagnosis, due to increased risk of hereditary breast cancer.

**Patients and methods:** Women with and without previous breast cancer diagnosis that underwent RRM between March 1997 and September 2010 were invited ( $n = 200$ ). We compared 146 (73%) sets of long-term questionnaire responses (e.g., EORTC QLQ-BRR26, Body Image Scale, Sexuality Activity Questionnaire, Hospital Anxiety and Depression Scale, and SF-36) with responses one year after surgery. Women with and without previous breast cancer were compared at the long-term assessment point.

**Results:** The HRQoL and anxiety/depressive symptoms remained unchanged compared with one year after surgery, and there were no between-group differences. The negative impact on body image persisted in both groups for most of the items. 'Sexual discomfort' increased significantly for women with previous breast cancer ( $p = 0.016$ ). Women with previous breast cancer also reported more problems with 'Disease treatment/surgery related symptoms' ( $p = 0.006$ ) and 'Sexuality' ( $p = 0.031$ ) in the EORTC QLQ-BRR26 questionnaire.

**Conclusion:** Problems with body image appeared to persist long time post-RRM. No differences in HRQoL were found at the long-term follow-up between women with and without previous breast cancer. The results of this investigation might be of use in improving future counselling before risk-reducing surgery for women in the decision-making process.

© 2019 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## 1. Introduction

Risk-reducing breast/ovarian surgery is offered to women with increased hereditary risk of breast/ovarian cancer or confirmed *BRCA1/BRCA2* mutation. The demands on outcome after risk-reducing mastectomy (RRM) with immediate breast reconstruction (IBR) are equally high for asymptomatic individuals as for

those with previous breast cancer diagnosis. RRM should fulfil the goals of safety, retained body image, and health-related quality of life (HRQoL). Though bilateral RRM shows a risk-reduction of approximately 90% for developing breast cancer in asymptomatic individuals [1–4], the need for reoperations, due to postoperative complications and/or revisions to achieve satisfying cosmetic results after implant-based reconstruction, still exists [5,6].

Previous prospective short-term follow-up studies have shown high overall cosmetic satisfaction six months and one year post-RRM, corresponding to the women's expectations, and no negative impact on anxiety/depressive symptoms, or HRQoL [7,8]. Body image and sexuality were negatively affected the first years after surgery [9–12]. Long-term effects of risk-reducing surgery have

\* Corresponding author.

E-mail addresses: [lucy.bai@ki.se](mailto:lucy.bai@ki.se) (L. Bai), [brita.arver@gmail.com](mailto:brita.arver@gmail.com) (B. Arver), [hemming.johansson@sl.se](mailto:hemming.johansson@sl.se) (H. Johansson), [kerstin.sandelin@ki.se](mailto:kerstin.sandelin@ki.se) (K. Sandelin), [marie.wickman@ki.se](mailto:marie.wickman@ki.se), [marie.wickman.chantereau@sophiahemmet.se](mailto:marie.wickman.chantereau@sophiahemmet.se) (M. Wickman), [yvonne.brandberg@ki.se](mailto:yvonne.brandberg@ki.se) (Y. Brandberg).

been studied retrospectively, indicating high procedure satisfaction, but decreased levels of satisfaction with the physical appearance [13–17]. There is, however, a lack of long-term prospective psychosocial follow-up studies [17].

This prospective follow-up study aimed to investigate women's perceptions of the cosmetic outcome of their breast reconstruction, body image, sexuality, anxiety/depressive symptoms, and HRQoL, 6–20 years post-RRM. Differences between women with or without previous breast cancer at follow-up, as well as changes over time from the one-year assessment to follow-up, were evaluated.

## 2. Material and methods

### 2.1. Patients and procedure

Between March 1997 and September 2010, 298 women underwent RRM at Karolinska University Hospital in Stockholm, Sweden due to increased hereditary risk for breast cancer. Individual risk for breast cancer was based on *BRCA* tests/family history of breast cancer. A total of 188 (63%) 'women without cancer' underwent bilateral RRM, while 110 (37%) 'women with (previous breast) cancer' underwent complementary/contralateral RRM (depending on if they previously had breast conservation or mastectomy). No women underwent risk-reducing surgery concomitantly with their cancer surgery. The RRM was performed at a mean time of 56 (range 16–254) months after breast cancer surgery. Ninety-five percent had IBR with expandable or permanent implants, placed under total muscular cover. At the time of surgery, the most common procedure was removal of the nipples and subsequent regrafting or with other techniques. Surgical details have been described in our previous studies [10,11,18].

We started a prospective psychosocial follow-up study in connection to RRM in 1997, and short-term results have been published [8–10]. No power calculations were made since it was not planned in the initial study design in 1997. The previously collected psychosocial questionnaire data from the same instruments used in the current study were available in a database, including the responses of the eligible 200 women. Women declining future participation in data collection, and those diagnosed with breast/other cancer(s) after RRM were excluded from the present study.

An information letter regarding the current follow-up study was sent to the women's home addresses during November–December 2016. An informed consent form asking for permission to review medical records in order to investigate clinical aspects post-RRM, the questionnaires, and a prepaid return envelope were also attached. One reminder was sent if no answer was obtained after one month, the last were sent January 2017. Questionnaire-data collection proceeded until May 31, 2017. After completion, the participants sent questionnaires and consent forms via the prepaid envelope to the study coordinator (LB) at the Department of Oncology-Pathology, Karolinska Institutet.

### 2.2. Instruments

The European Organisation for Research and Treatment of Cancer Breast Reconstruction Questionnaire (EORTC QLQ-BRR26) assesses satisfaction with the results after breast reconstruction. The questionnaire was validated/tested for reliability in a set of breast cancer patients after breast reconstruction [19,20]. It consists of 26 items constituting three scales with scores ranging from 1 ('Not at all') to 4 ('A lot'). The Swedish version has been formally translated, and was a part of the development of this questionnaire [19,20].

*The Body Image Scale (BIS)* is a 10-item scale measuring the impact of surgery on self-consciousness, physical/sexual attractiveness, femininity, satisfaction with body/scars, body integrity, and avoidance behaviour after surgery for cancer patients [21]. The development of the scale did not rely on a particular theoretical model, as there was no consensus on the definition of body image disturbance in 1997, when the first study was carried out. Scores per item ranges from 0 ('Not at all') to 3 ('Very much'), creating a total score of 0–30/patient. A higher total score translates to more problems. The Swedish version was translated at Karolinska University Hospital in 1997. It has not been formally validated/reliability-tested, but the Cronbach  $\alpha$  coefficient for the study sample at the six-month assessment was 0.85 [9].

*The Sexuality Activity Questionnaire (SAQ)* consists of a 10-item scale assessing sexual activity: 'Pleasure' (desire, enjoyment, and satisfaction; higher scores indicate more pleasure (range 0–18)), 'Discomfort' (dryness and pain; higher scores indicate more discomfort (range 0–6)), and 'Sexual habit' (<0.33 indicate less frequent than usual (range 0–3)) [22]. The Swedish translation has not been formally validated, but the English version was shown to be valid/reliable as a measure of women's sexual functioning [22].

*The Hospital Anxiety and Depression (HAD)* scale assesses anxiety/depressive symptoms [23]. It consists of 14 items (seven items assessing 'Anxiety' and 'Depressive symptoms' each), scored 0 to 3, yielding a summated score per scale between 0 and 21. Cut-offs for clinically relevant anxiety/depressive symptoms have been established [23]. Less than 8 points indicate normal levels of problems, 8–10 points indicate possible clinical cases, and  $\geq 11$  points indicate clinical cases. The Swedish version has been validated against diaries in a sample of breast cancer patients [24].

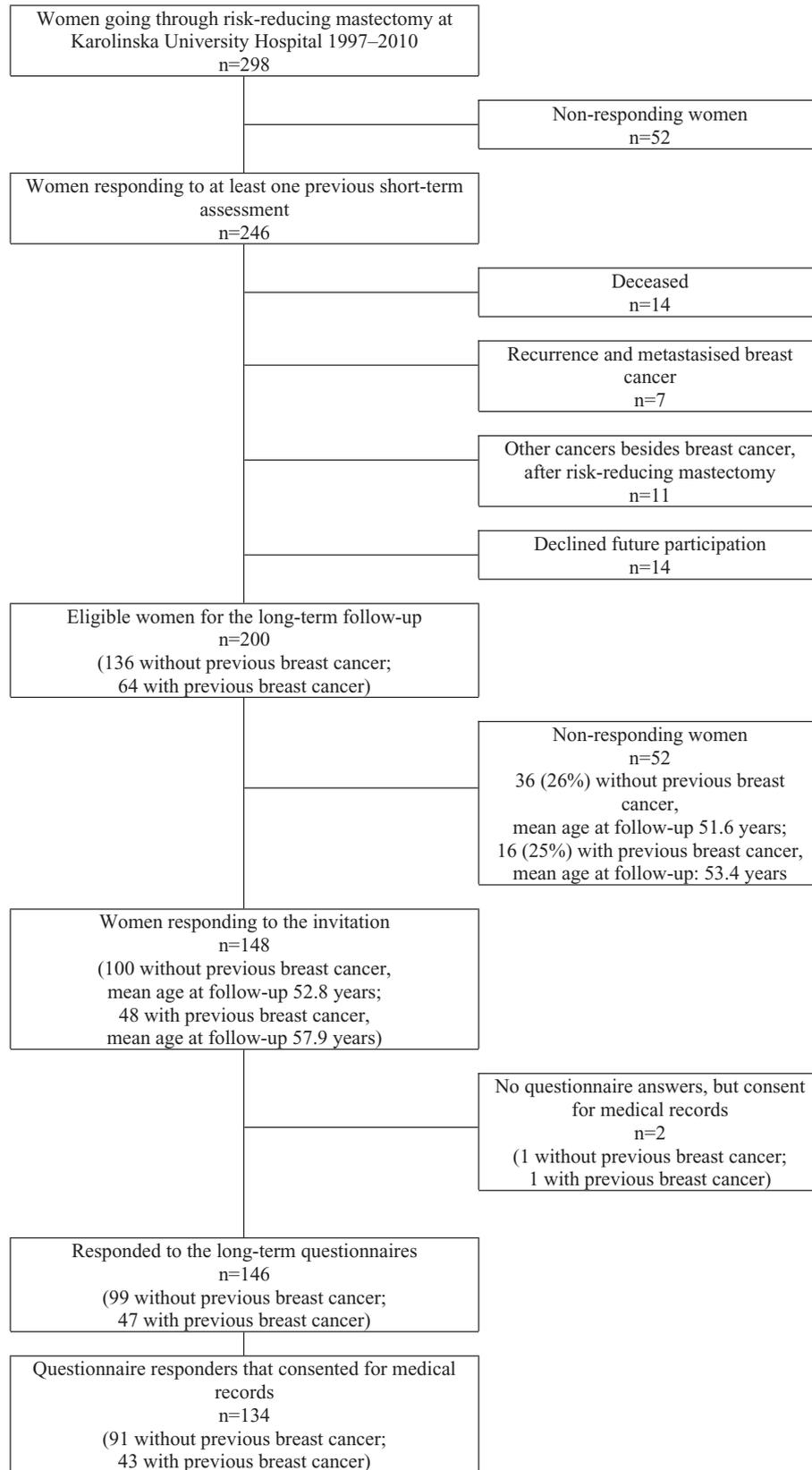
*The Swedish Short Term-36 Health Survey (SF-36)* measures HRQoL [25]. It covers eight-domains by 36 items. For each domain, mean scores were transformed to a 0 to 100 scale, where a higher number represents higher functioning.

### 2.3. Statistical analysis

Differences in scores between the one-year and long-term assessments were investigated using paired *t*-tests. Mean paired differences are presented together with 95% confidence intervals. Unpaired comparisons between women with or without previous breast cancer were performed by linear regression models. Factors included in the adjusted models were: scores one year post-RRM, time since RRM, age at long-term follow-up, mutation-status, bilateral prophylactic salpingo-oophorectomy, and body mass index (BMI; kg/m<sup>2</sup>). Results from these models are presented as mean differences with 95% confidence intervals. For SF-36, clinically meaningful differences were determined according to Osoba [26]. A difference of 5–9 points was considered as 'small' (S), 10–19 as 'moderate' (M), and  $\geq 20$  as 'large' (L). Reported *p*-values are two-sided and refer to Wald tests. The statistical significance level was set to 0.05. All analyses were performed using STATA/IC 14.2 for Mac, StataCorp, TX, USA.

## 3. Results

The Consort diagram (Fig. 1) presents the 148 (74%) women who returned the envelopes, of whom 146 (73%) (99 without previous breast cancer; 47 with previous breast cancer) completed the questionnaires. Demographic/clinical data for 136 (68%) women who consented to data collection from medical records are presented in Table 1. For the women who completed the questionnaires without giving permission to extract data from their medical records, some missing data were replaced using the research



**Fig. 1.** Consort diagram, including details about written consent for clinical data collection from medical records.

**Table 1**

Demographic and clinical data of women that have undergone bilateral or contralateral risk-reducing surgery that have consented to extraction of clinical data from medical journals for the long-term follow-up study.

Variable	Cancer <sup>a</sup>	No cancer
	n (%)	n (%)
Number of women	44	92
Age at risk-reducing surgery (year)		
Range	30–69	26–68
Mean	46.5	41.2
Median	45	39
Age at return of questionnaires (year)		
35–44	1 (2)	16 (17)
45–54	20 (46)	42 (46)
55–64	12 (27)	19 (21)
≥65	11 (25)	15 (16)
BRCA mutation status		
BRCA1/BRCA2/BRCA <sup>b</sup>	33 (75)	50 (54)
No mutation or unknown	11 (25)	42 (46)
BMI		
<18.5	2 (5)	4 (4)
18.5–24.9	31 (70)	62 (67)
25–29.9	7 (15)	10 (11)
≥30	2 (5)	6 (7)
Missing	2 (5)	10 (11)
Bilateral prophylactic salpingo-oophorectomy		
Yes	28 (64)	52 (57)
No	15 (34)	39 (42)
Missing	1 (2)	1 (1)
Type of breast cancer		92 (100)
None		
In situ	6 (14)	
Invasive	35 (84)	
Missing	1 (2)	
Type of breast cancer surgery prior risk-reducing surgery		
Breast conserving cancer surgery	20 (48)	
Mastectomy (cancer surgery)	22 (52)	
Type of risk-reducing surgery		
Mastectomy with immediate breast reconstruction	42 (95)	87 (95)
Mastectomy without immediate breast reconstruction		2 (2)
Reduction/mastopexy	1 (2)	3 (3)
Radiotherapy		
Yes	28 (64)	
No	13 (29)	
Missing	3 (7)	
Chemotherapy		
Yes	28 (64)	
No	13 (29)	
Missing	3 (7)	
Endocrine therapy		
Yes	22 (50)	
No	18 (41)	
Missing	4 (9)	
Reoperations (unforeseen) after risk-reducing breast surgery <sup>c</sup>		
Yes	29 (66)	48 (52)
No	15 (34)	40 (44)
Missing		4 (4)

<sup>a</sup> Women with previous breast cancer  $n = 42$ , and gynaecological cancer  $n = 2$ .

<sup>b</sup> BRCA<sup>b</sup> = women with breast cancer and/or ovarian cancer, screened negative for BRCA1 and BRCA2, and with family history of breast cancer.

<sup>c</sup> Nipple reconstructions were not included.

group's established database. The mean follow-up time from date of risk-reducing surgery was 11.5 (range 6.0–19.7) years. Limited information about the non-responders was available as we never obtained consent to extract data from their medical charts.

### 3.1. Satisfaction with breast reconstruction (EORTC QLQ-BRR26)

This questionnaire was used only at follow-up, thus not allowing for analysis over time. Women with previous breast cancer were generally more dissatisfied with the results of the surgery versus women without cancer, Table 2. Statistically significant group

differences were found in the adjusted analyses for the subscales 'Disease treatment/surgery related symptoms' ( $p = 0.006$ ), and 'Sexuality' ( $p = 0.031$ ), with lower levels of problems and higher satisfaction in the group without cancer. Concerning 'Satisfaction with reconstructed nipple', a between-group difference was found in the unadjusted analyses ( $p = 0.020$ ) in the same direction. Clinical significant differences were noted for 'Disease treatment/surgery related symptoms' (S), 'Sexuality' (M), and 'Satisfaction with reconstructed nipple' (M). No other between-group differences were found.

### 3.2. Body image (BIS)

The long-term mean BIS summated scores (range 0–30) reported by women with and without previous breast cancer were 7.7 (SD 5.8) and 4.9 (SD 5.2), respectively. An unadjusted mean difference was 2.8 (95% CI, 0.9 to 4.7). When adjusting for confounding factors, no statistical significant difference was found. Fig. 2 shows the proportions of women reporting any level of problem (1–3) for each item at the one-year and the follow-up assessments for both groups. There was a statistical significant improvement in self-consciousness at long-term versus the one-year assessment for women without cancer ( $p = 0.026$ ). No other statistically significant group differences, or differences at the long-term follow-up were observed for the body image items.

### 3.3. Sexuality (SAQ)

At the long-term assessment, 20 (43%) women with and 57 (61%) without previous breast cancer reported a 'current active sex-life', versus 22 (63%) and 52 (76%) at the one-year assessment, respectively. A statistical significant increase in 'Discomfort' was found at the long-term assessment, versus one year post-RRM for women with previous breast cancer ( $p = 0.016$ ), see Table 3. Women without breast cancer showed a statistical significant increase in 'Sexual habit' over time ( $p = 0.031$ ). No statistical significant differences between the groups were observed at the long-term follow-up for 'Pleasure', 'Discomfort', or 'Sexual habit' after adjusting for confounding factors.

### 3.4. Anxiety and depression (HAD)

The mean anxiety scores reported by women with cancer at the one-year and long-term assessment were 5.0 (SD 4.1) and 6.2 (SD 4.3), respectively. Corresponding figures for women without cancer at one-year and long-term were 4.2 (SD 3.7) and 4.5 (SD 4.3). The mean depression scores reported by women with cancer at one-year and long-term were 2.1 (SD 2.3) and 3.1 (SD 3.2), respectively, while it was 1.9 (SD 2.5) and 2.6 (SD 3.0) for women without cancer at one-year and long-term, respectively. There was a statistical significant increase in depression score when comparing long-term- with one-year-scores for women without cancer ( $p = 0.042$ ). No significant between-group difference was observed at the long-term assessment.

### 3.5. Health-related quality of life (SF-36)

There was a statistical significant decrease in 'General health' at the long-term assessment versus one year post-RRM for both groups ( $p \leq 0.05$ ), Table 3. There were no between-group differences in HRQoL at the long-term assessment.

## 4. Discussion

This is, to our knowledge, the furthestmost prospective long-

**Table 2**  
Satisfaction of results after breast reconstruction (EORTC QLQ-BRR26): mean and standard deviation (SD) for all women responding at the long-term assessment; unadjusted and adjusted mean differences (MD) between women with and without previous breast cancer.

Parameter	Long-term assessment		Unadjusted mean difference		Adjusted <sup>a</sup> mean difference	
	Cancer (n = 34–47)	No cancer (n = 84–99)	MD (95% CI) (n = 141–146)	p	MD (95% CI) (n = 99–120)	p
	Mean (SD)	Mean (SD)				
Disease treatment/surgery related symptoms	13.1 (2.8)	4.5 (1.1)	8.6 <sup>S</sup> (3.6–13.5)	0.001	8.7 <sup>S</sup> (2.6–14.8)	0.006
Problems finding a well-fitting bra	31.9 (5.7)	31.3 (3.6)	0.6 (–12.1 to 13.4)	0.922	–3.3 (–18.3 to 11.8)	0.666
Sexuality	45.3 (4.6)	28.8 (2.5)	16.6 <sup>M</sup> (6.9–26.2)	0.001	12.8 <sup>M</sup> (1.2–24.5)	0.031
Cosmetic outcome breast	59.0 (3.6)	64.3 (2.5)	–5.3 (–14.1 to 3.4)	0.228	–3.4 (–13.2 to 6.4)	0.491
Cosmetic outcome donor site <sup>b</sup>	15.0 (4.9)	11.9 (4.4)	3.1 (–11.7 to 17.9)	0.651	15.5 <sup>M</sup> (–115.2 to 146.2)	0.373
Satisfaction with reconstructed nipple	31.9 (4.1)	45.0 (3.1)	–13.2 <sup>M</sup> (–24.2 to –2.1)	0.020	–19.1 <sup>M</sup> (–21.6 to 1.4)	0.086
Problems with losing the nipple <sup>c</sup>	29.6 (6.7)	30.6 (8.7)	–0.9 (–25.2 to 23.3)	0.937	8.7 <sup>S</sup> (–28.7 to 46)	0.600

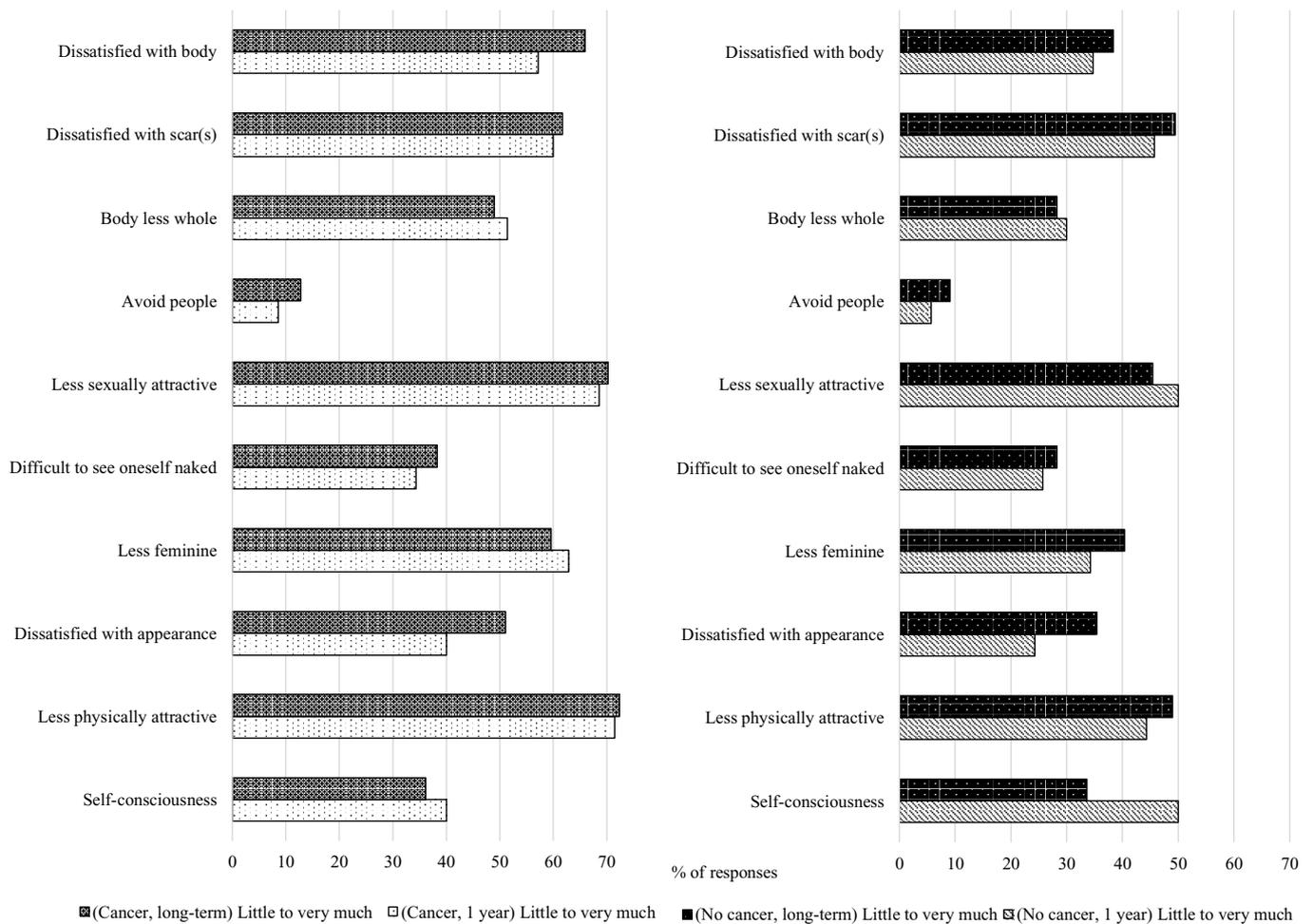
Range 0–100, where higher scores indicate higher satisfaction for ‘Satisfaction with reconstructed nipple’ and ‘Cosmetic outcome of breast’, and vice versa for the rest of the measures.

<sup>S</sup> Small and <sup>M</sup> moderate clinical significant differences [26].

<sup>a</sup> Adjusted for age at long-term follow-up, time since risk-reducing surgery, mutation, bilateral prophylactic salpingo-oophorectomy, and body mass index (BMI; kg/m<sup>2</sup>).

<sup>b</sup> Too few observations: n = 9–12.

<sup>c</sup> Too few observations: n = 16–21.



**Fig. 2.** Body Scale Image (BIS): percentage of women with and without previous breast cancer reporting ‘little’ to ‘very much’-body image problems at the one year and long-term assessment after the risk-reducing breast surgery with immediate breast reconstruction. The y-axis illustrates the ten items included in the BIS. The data is presented in terms of proportions (%) of women responding at each time of assessment, where  $n(\text{cancer, 1 year}) = 35$ ,  $n(\text{cancer, long-term}) = 46–47$ ,  $n(\text{no cancer, 1 year}) = 69–70$ , and  $n(\text{no cancer, long-term}) = 98–99$ .

term follow-up study about psychosocial outcomes for women with increased hereditary risk for breast cancer post-RRM and IBR. HRQoL, anxiety/depressive symptoms appeared to remain rather unchanged in the long-term, with one exception. ‘General health’ decreased over time in both groups. Body image problems noted at

the one-year assessment did not change at the long-term assessment, and there were no differences between the groups, except from improved self-consciousness over time for women without breast cancer, and significantly increased ‘Sexual discomfort’ over time for women with breast cancer.

**Table 3**

Sexual activity – pleasure and discomfort subscales, and habit item (SAQ), and Health-related quality of life (SF-36): mean and standard deviation (SD) at one year and long-term for all respondents at each assessment point, and for women responding at both occasions; long-term changes in sexual activity and health-related quality of life compared with one year after risk-reducing surgery for women with and without previous breast cancer.

Variable	Women responding at each assessment				Difference over time Women responding at both assessments							
	Cancer		No cancer		Cancer				No cancer			
	One year Mean (SD)	Long-term Mean (SD)	One year Mean (SD)	Long-term Mean (SD)	One year Mean (SD)	Long-term Mean (SD)	Difference (95% CI)	p	One year Mean (SD)	Long-term Mean (SD)	Difference (95% CI)	p
Number of women	28	25–28	58–59	71–74	21–22				44–46			
Sexual activity												
Pleasure	9.4 (3.1)	8.2 (4.6)	11.3 (3.9)	10.2 (4.4)	9.8 (3.0)	8.6 (3.9)	-1.2 (-2.9 to 0.4)	0.138	11.5 (3.7)	10.8 (4.4)	-0.7 (-1.9 to 0.5)	0.265
Discomfort	2.1 (2.1)	2.8 (2.3)	1.0 (1.4)	1.5 (1.8)	1.2 (2.0)	3.0 (2.2)	1.2 (0.3–2.1)	0.016	0.9 (1.2)	1.5 (1.8)	0.6 (-0.02 to 1.2)	0.058
Habit	0.6 (0.6)	0.8 (0.5)	0.7 (0.5)	0.9 (0.5)	0.7 (0.6)	0.8 (0.5)	0.1 (-0.2 to 0.4)	0.540	0.8 (0.5)	1.0 (0.5)	0.2 (0.02–0.4)	0.031
Number of women	31–35	46–47	66–70	95–99	31–35				65–70			
Health-related quality of life												
Physical Functioning <sup>a</sup>	87 (20)	85 (21)	92 (13)	89 (19)	87 (20)	85 (21)	-3 (-10 to 5)	0.510	92 (13)	92 (16)	-1 (-5 to 3)	0.726
General health <sup>b</sup>	82 (20)	71 (24)	84 (20)	77 (24)	82 (19)	74 (24)	-9 (-16 to -2)	0.018	84 (19)	79 (23)	-5 (-11 to -0)	0.042
Vitality <sup>b</sup>	66 (25)	62 (24)	68 (22)	63 (25)	66 (25)	63 (24)	-3 (-12 to 6)	0.531	68 (22)	65 (23)	-2 (-8 to 3)	0.320
Mental health <sup>c</sup>	79 (18)	74 (19)	82 (18)	77 (19)	79 (18)	77 (17)	-2 (-8 to 5)	0.645	83 (18)	79 (18)	-4 (-8 to 1)	0.094
Role-Physical <sup>a</sup>	79 (38)	84 (34)	87 (31)	83 (34)	79 (38)	85 (34)	5 (-3 to 14)	0.223	87 (30)	85 (32)	-2 (-11 to 7)	0.691
Role-Emotional <sup>a</sup>	85 (27)	83 (33)	86 (30)	85 (32)	85 (27)	82 (34)	-3 (-16 to 10)	0.620	86 (30)	85 (30)	-1 (-9 to 7)	0.851
Social functioning <sup>c</sup>	91 (18)	88 (22)	92 (20)	86 (23)	91 (18)	87 (22)	-4 (-12 to 4)	0.344	93 (19)	88 (22)	-5 (10–1)	0.091
Bodily pain <sup>a</sup>	76 (24)	77 (25)	82 (24)	82 (26)	76 (24)	76 (25)	0 (-9 to 9)	0.978	83 (23)	83 (24)	1 (-7 to 8)	0.882

SAQ:  
 Pleasure: higher scores indicate more pleasure [range 0–18].  
 Discomfort: higher scores indicate more discomfort [range 0–6].  
 Habit: < 0.33 = less frequent than usual [range 0–3].  
 SF-36 [range 0–100, higher scores indicate better well-being]:  
<sup>a</sup> Physical health.  
<sup>b</sup> Overall representation of both physical and psychic/mental health. Both scales are bipolar. A median of Vitality and General Health implies absence of fatigue and no negative values of health in general, respectively.  
<sup>c</sup> Psychic/mental health, where Mental Health is a bipolar scale, mid-value implies absence of anxious/depressive symptoms or psychosocial impairment, 100 indicates best possible well-being.

The EORTC QLQ-BRR26 has no published comparable data yet. The long-term results showed an expected group difference in 'Disease treatment/surgery related symptoms', as the primary cancer surgery often involves axillary dissection of different degrees [27]. This subscale involves questions about numbness/tingling in the arm/shoulder and fullness under the arm. Implant rupture/symptomatic leakage and radiation induced fibrosis (causing capsular contracture/deformity/pain) can occur long time after radiation [28]. Satisfaction with the reconstructed nipple was rated moderately clinically higher by women without cancer, possible also due to side-effects from radiotherapy in the other group [28,29].

The sexuality-subscale in EORTC-BRR26 involves questions about body feeling less whole, loss of sexual attractiveness, at ease in intimate situations, role of breast as part of sexuality, and loss of pleasurable sensations to the breast. Women without cancer reported lower levels of problems on the sexuality-subscale than women with cancer. This result was mirrored in the SAQ-assessment, where women 'with cancer reported a higher level of 'Discomfort' than the other group. As women in both groups have gone through bilateral surgery, the surgical impact on sensation ought to cancel out each other in the comparison, and might not explain the significant difference between the groups. In addition, radiotherapy has not been shown to affect the recovery of sensation postmastectomy [30,31]. The higher level of sexual problems in the breast cancer group could be due to late effects of anti-cancer treatment and recommendations of avoiding hormone replacement therapy after bilateral prophylactic salpingo-oophorectomy,

which affects the vaginal mucosa and causes vaginal dryness [32–34]. More than 50% in both groups had undergone prophylactic salpingo-oophorectomy, where women without breast cancer could use hormonal replacement therapy. This could explain the higher levels of sexual discomfort associated with intercourse among the cancer patients.

The BIS results showed several problems appearing to persist many years post-RRM. A number of reconstructed women underwent several revision surgeries including replacement of implants. Some women also received autologous reconstruction after implant failure during the follow-up time. Approximately 70% of the women with cancer and 45–50% of the women without cancer reported sexual/physical attractiveness problems at the long-term follow-up. In addition, large proportions of women in both groups were dissatisfied with their scars at the long-term assessment, 62% of the women with cancer and 49% of the women without cancer. Other body image problems, such as feeling less feminine after the surgery, difficulties with seeing oneself naked, or body feeling less whole, were also relatively persistent. Problems with body image post-RRM have previously been reported [10–12,35,36]. However, this is the first study contributing with long-term prospective results, clinically significant for preoperative consultations. The items in the BIS questionnaire refer to 'after the surgery', thus it is likely that the women attribute these perceptions to RRM.

The levels of HRQoL persisted from the one-year assessment to the long-term follow-up. HRQoL has been previously reported to not change from pre-RRM to one year post-RRM for women

without previous breast cancer [9]. Similar results were obtained in our prospective two-year follow-up study of women with cancer who had complementary/contralateral RRM [8]. Thus, going through RRM does not seem to affect HRQoL. The decrease in 'General health' over time might be explained by aging.

The strengths of this study includes the prospective design with baseline data previously collected one year after surgery, the robust response rates long time post-RRM, and the use of several validated questionnaires [37]. A limitation is the lack of clinical/demographic information about the non-responders. In addition, the number of responders at the one-year assessment was 164 women. Thus, only 107 women responded at both assessments. In order to make it possible for the reader to evaluate the correspondence between data from those who have responded only at *one* time point and from those who responded at *both* assessments, we have added data in the tables and figures for the questionnaires from all women responding at *each* time of assessment. The results should be interpreted with caution due to the small sample size, which is mirrored in the size of the confidence intervals.

In summary, problems with body image seemed to persist long time post-RRM, regardless of previous breast cancer or not. A decline in 'General health' appeared over time, but no HRQoL differences were found at the long-term follow-up between women with and without cancer. The long-term results of this study might be of clinical importance for women considering RRM in order for them to make an informed decision.

## Appendix

### Funding sources

This study received financial support from the Swedish Cancer Society, Swedish Research Council, Radiumhemmets forskningsfonder, and Breast cancer patient organisation fund (Bröstcancerfonden). It has been used for administrative costs for data collection, analysis, interpretation of the data, in the writing of the report, and in the decision to submit the article for publication.

### Conflict of interest statement

None to declare.

### Ethical approval

The study was approved by the Regional Ethics Committee in Stockholm (dnr 2015/735-31/4).

## References

- Hartmann LC, Schaid DJ, Woods JE, Crotty TP, Myers JL, Arnold PG, et al. Efficacy of bilateral prophylactic mastectomy in women with a family history of breast cancer. *N Engl J Med* 1999;340:77–84. <https://doi.org/10.1056/NEJM199901143400201>.
- Hartmann LC, Thomas A, Schaid DJ, Thomas S, Soderberg CL, Sitta L, et al. Efficacy of bilateral prophylactic mastectomy in BRCA1 and BRCA2 gene mutation carriers. *Cancer* 2001;93:1633–7.
- Meijers-Heijboer H, van Geel B, van Putten WL, Henzen-Logmans SC, Seynaeve C, Menke-Pluymers MB, et al. Breast cancer after prophylactic mastectomy in women with a BRCA1 or BRCA2 mutation. *N Engl J Med* 2001;345:159–64. <https://doi.org/10.1056/NEJM200107193450301>.
- Rebbeck TR, Friebel T, Lynch HT, Neuhausen SL, Van't Veer L, Garber JE, et al. Bilateral prophylactic mastectomy reduces breast cancer risk in BRCA1 and BRCA2 mutation carriers: the PROSE study group. *J Clin Oncol* 2004;22:1055–62. <https://doi.org/10.1200/JCO.2004.04.188>.
- Koskenvuo L, Svarvar C, Suominen S, Aittomäki K, Jähkola T. The frequency and outcome of breast cancer risk-reducing surgery in Finnish BRCA1 and BRCA2 mutation carriers. *Scand J Surg* 2014;103:34–40. <https://doi.org/10.1177/1457496913490460>.
- Arver B, Isaksson K, Atterhem H, Baan A, Bergkvist L, Brandberg Y, et al. Bilateral prophylactic mastectomy in Swedish women at high risk of breast cancer: a national survey. *Ann Surg* 2011;253:1147–54. <https://doi.org/10.1097/SLA.0b013e318214b55a>.
- Brandberg Y, Arver B, Johansson H, Wickman M, Sandelin K, Liljegren A. Less correspondence between expectations before and cosmetic results after risk-reducing mastectomy in women who are mutation carriers: a prospective study. *Eur J Surg Oncol* 2012;38:38–43. <https://doi.org/10.1016/j.ejso.2011.10.010>.
- Unukovych D, Sandelin K, Liljegren A, Arver B, Wickman M, Johansson H, et al. Contralateral prophylactic mastectomy in breast cancer patients with a family history: a prospective 2-years follow-up study of health related quality of life, sexuality and body image. *Eur J Cancer* 2012;48:3150–6. <https://doi.org/10.1016/j.ejca.2012.04.023>.
- Brandberg Y, Sandelin K, Erikson S, Jurell G, Liljegren A, Lindblom A, et al. Psychological reactions, quality of life, and body image after bilateral prophylactic mastectomy in women at high risk for breast cancer: a prospective 1-year follow-up study. *J Clin Oncol* 2008;26:3943–9. <https://doi.org/10.1200/JCO.2007.13.9568>.
- Gahm J, Wickman M, Brandberg Y. Bilateral prophylactic mastectomy in women with inherited risk of breast cancer – prevalence of pain and discomfort, impact on sexuality, quality of life and feelings of regret two years after surgery. *Breast* 2010;19:462–9. <https://doi.org/10.1016/j.breast.2010.05.003>.
- Gahm J, Hansson P, Brandberg Y, Wickman M. Breast sensibility after bilateral risk-reducing mastectomy and immediate breast reconstruction: a prospective study. *J Plast Reconstr Aesthetic Surg* 2013;66:1521–7. <https://doi.org/10.1016/j.bjps.2013.06.054>.
- Gopie JP, Mureau MAM, Seynaeve C, Ter Kuile MM, Menke-Pluymers MBE, Timman R, et al. Body image issues after bilateral prophylactic mastectomy with breast reconstruction in healthy women at risk for hereditary breast cancer. *Fam Cancer* 2013;12:479–87. <https://doi.org/10.1007/s10689-012-9588-5>.
- Frost MH, Schaid DJ, Sellers TA, Slezak JM, Arnold PG, Woods JE, et al. Long-term satisfaction and psychological and social function following bilateral prophylactic mastectomy. *Jama* 2000;284:319–24.
- Frost MH, Slezak JM, Tran NV, Williams CI, Johnson JL, Woods JE, et al. Satisfaction after contralateral prophylactic mastectomy: the significance of mastectomy type, reconstructive complications, and body appearance. *J Clin Oncol* 2005;23:7849–56. <https://doi.org/10.1200/JCO.2005.09.233>.
- Borgen PI, Hill ADK, Tran KN, Van Zee KJ, Massie MJ, Payne D, et al. Patient regrets after bilateral prophylactic mastectomy. *Ann Surg Oncol* 1998;5:603–6. <https://doi.org/10.1007/BF02303829>.
- Montgomery LL, Tran KN, Heelan MC, Van Zee KJ, Massie MJ, Payne DK, et al. Issues of regret in women with contralateral prophylactic mastectomies. *Ann Surg Oncol* 1999;6:546–52. <https://doi.org/10.1007/s10434-999-0542-1>.
- Hartmann LC, Lindor NM. The role of risk-reducing surgery in hereditary breast and ovarian cancer. *Obstet Gynecol Surv* 2016;71:598–9. <https://doi.org/10.1097/01.ogx.0000499510.12280.54>.
- Wickman M, Sandelin K, Arver B. Technical aspects and outcome after prophylactic mastectomy and immediate breast reconstruction in thirty consecutive high-risk patients. *Plast Reconstr Surg* 2003;111:1069–77.
- Thomson HJ, Winters ZE, Brandberg Y, Didier F, Blazebly JM, Mills J. The early development phases of a European Organisation for Research and Treatment of Cancer (EORTC) module to assess patient reported outcomes (PROs) in women undergoing breast reconstruction. *Eur J Cancer* 2013;49:1018–26. <https://doi.org/10.1016/j.ejca.2012.09.021>.
- Winters ZE, Balta V, Thomson HJ, Brandberg Y, Oberguggenberger A, Sinove Y, et al. Phase III development of the European organization for research and treatment of cancer quality of life questionnaire module for women undergoing breast reconstruction. *Br J Surg* 2014;101:371–82. <https://doi.org/10.1002/bjs.9397>.
- Hopwood P, Fletcher I, Lee A, Al Ghazal S. A body image scale for use with cancer patients. *Eur J Cancer* 2001;37:189–97.
- Thirlaway K, Fallowfield L, Cuzick J. The Sexual Activity Questionnaire: a measure of women's sexual functioning. *Qual Life Res* 1996;5:81–90.
- Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;67:361–70.
- Arving C, Glimelius B, Brandberg Y. Four weeks of daily assessments of anxiety, depression and activity compared to a point assessment with the Hospital Anxiety and Depression Scale. *Qual Life Res* 2008;17:95–104. <https://doi.org/10.1007/s11136-007-9275-4>.
- Sullivan M, Karlsson J, Ware JEJ. The Swedish SF-36 Health Survey-I. Evaluation of data quality, scaling assumptions, reliability and construct validity across general populations in Sweden. *Soc Sci Med* 1995;41:1349–58.
- Osoba D, Rodrigues G, Myles J, Zee B, Pater J. Interpreting the significance of changes in Health-Related Quality-of-Life scores. *J Clin Oncol* 1998;16:139–44. <https://doi.org/10.1200/jco.1998.16.1.139>.
- Krag D, Weaver D, Ashikaga T, Moffat F, Klimberg VS, Shriver C, et al. The sentinel node in breast cancer — a multicenter validation study. *N Engl J Med* 1998;339:941–6. <https://doi.org/10.1056/NEJM199810013391401>.
- Quinn TT, Miller GS, Rostek M, Cabalag MS, Rozen WM, Hunter-Smith DJ. Prosthetic breast reconstruction: indications and update. *Gland Surg* 2016;5:174–86. <https://doi.org/10.3978/j.issn.2227-684X.2015.07.01>.
- Berbers J, Van Baardwijk A, Houben R, Heuts E, Smidt M, Keymeulen K, et al. "Reconstruction: before or after postmastectomy radiotherapy?" A systematic review of the literature. *Eur J Cancer* 2014;50:2752–62. <https://doi.org/>

- 10.1016/j.ejca.2014.07.023.
- [30] Tomita K, Yano K, Hosokawa K. Recovery of sensation in immediate breast reconstruction with latissimus dorsi myocutaneous flaps after breast-conservative surgery and skin-sparing mastectomy. *Ann Plast Surg* 2011;66:334–8. <https://doi.org/10.1097/SAP.0b013e3181ee73cf>.
- [31] Khan A, Zhang J, Sollazzo V, Mohammed K, Gui G. Sensory change of the reconstructed breast envelope after skin-sparing mastectomy. *Eur J Surg Oncol* 2016;42:973–9. <https://doi.org/10.1016/j.ejso.2016.03.018>.
- [32] Couzi RJ, Helzlsouer KJ, Fetting JH. Prevalence of menopausal symptoms among women with a history of breast cancer and attitudes toward estrogen replacement therapy. *J Clin Oncol* 1995;13:2737–44. <https://doi.org/10.1200/JCO.1995.13.11.2737>.
- [33] Panjari M, Bell RJ, Davis SR. Sexual function after breast cancer. *J Sex Med* 2011;8:294–302. <https://doi.org/10.1111/j.1743-6109.2010.02034.x>.
- [34] Johansen N, Liavaag AH, Tanbo TG, Dahl AA, Pripp AH, Michelsen TM. Sexual activity and functioning after risk-reducing salpingo-oophorectomy: impact of hormone replacement therapy. *Gynecol Oncol* 2016;140:101–6. <https://doi.org/10.1016/j.ygyno.2015.11.016>.
- [35] Hopwood P, Lee A, Shenton A, Baidam A, Brain A, Lalloo F, et al. Clinical follow-up after bilateral risk reducing ('prophylactic') mastectomy: mental health and body image outcomes. *Psycho Oncol* 2000;9:462–72. [https://doi.org/10.1002/1099-1611\(200011/12\)9:6<462::AID-PON485>3.0.CO;2-J](https://doi.org/10.1002/1099-1611(200011/12)9:6<462::AID-PON485>3.0.CO;2-J).
- [36] Lostumbo L, N. E. Carbine, Wallace J, Ezzo J, Dickersin K. Prophylactic mastectomy for the prevention of breast cancer. *Cochrane Database Syst Rev* 2004;(4), CD002748. <https://doi.org/10.1002/14651858.CD002748.pub2>.
- [37] Winters ZE, Benson JR, Pusic AL. A systematic review of the clinical evidence to guide treatment recommendations in breast reconstruction based on patient-reported outcome measures and health-related quality of life. *Ann Surg* 2010;252:929–42. <https://doi.org/10.1097/SLA.0b013e3181e623db>.