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Patient Factors Associated with Increased Cancer Worry, Fatigue, and Impact on Work Following a Breast Cancer Diagnosis: A Cross-Sectional Analysis

Analyse transversale des facteurs liés au patient associés à une plus grande inquiétude face au cancer et à de la fatigue, et répercussions professionnelles après un diagnostic de cancer du sein

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Abstract

Introduction: A breast cancer diagnosis may result in disabling effects which may persist after treatment. The aim of this study was to identify patient factors that are associated with increased cancer worry, fatigue, and impact on work. **Methods:** Women with a history of breast cancer, aged ≥18 years, and English-speaking were recruited through the Love Research Army between October and November 2019. Participants completed demographic and clinical questions alongside the BREAST-Q Cancer Worry, Fatigue, and Impact on Work scales. Univariable and multivariable regression analyses were used to identify participant characteristics associated with each scale. **Results:** Cancer Worry, Fatigue, and Impact on Work scales were completed by $n = 1680$, $n = 1037$, and $n = 873$ participants, respectively. Most participants were older than 50 ($n = 1,470$, 87.5%), married ($n = 1229$, 73.2%), white ($n = 1557$, 92.7%), and had undergone surgery for cancer treatment ($n = 1,472$, 87.6%). Increased Cancer Worry was significantly associated ($P < .04$) with younger age, less time since diagnosis, pain related to cancer/treatment, recurrence, prior chemotherapy, and ongoing breast edema. Increased Fatigue was significantly associated ($P < .01$) with elevated BMI, less time since diagnosis, ethnicity, employment status, recurrence, prior chemotherapy, ongoing pain, and difficulty sleeping secondary to treatment. Decreased Impact on Work scores was significantly associated ($P < .04$) with chemotherapy administration, shorter time since diagnosis, employment, fatigue related to treatment, breast edema, and ongoing pain. **Conclusion:** This study reveals patient characteristics associated with increased cancer worry, fatigue, and a negative impact on work following a breast cancer diagnosis. These findings can inform clinical and research initiatives to better support patients through treatment and survivorship.

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Résumé

Introduction: Un diagnostic de cancer du sein peut avoir des effets dévastateurs qui persistent après le traitement. Le but de cette étude était d'identifier les facteurs liés au patient qui sont associés à une augmentation de l'inquiétude face au cancer, à la fatigue et aux répercussions sur l'activité professionnelle. **Méthodes:** Des femmes ayant eu un cancer du sein, âgées ≥ 18 ans, anglophones, ont été recrutées par le biais du programme Love Research Army entre octobre et novembre 2019. Les participantes ont rempli des questionnaires démographiques et cliniques, ainsi que les échelles BREAST-Q Cancer Worry (inquiétude), Fatigue et impact sur le travail. Des analyses en régression uni- et multifactorielles ont été utilisées pour identifier les caractéristiques des participantes associées à chaque échelle. **Résultats:** Les échelles Cancer Worry, Fatigue and Impact on Work ont été remplies par, respectivement, $n = 1680$, $n = 1037$ et $n = 873$ participantes. La plupart des participantes étaient âgées de plus de 50 ans ($n = 1470$, 87,5%), mariées ($n = 1229$, 73,2%), blanches ($n = 1557$, 92,7%) et avaient subi une chirurgie à visée thérapeutique du cancer ($n = 1472$, 87,6%). L'inquiétude face au cancer était significativement ($P < 0,04$) augmentée parmi les plus jeunes patientes, avec un délai plus court depuis le diagnostic, une douleur liée au cancer/son traitement, une récidive, une chimiothérapie antérieure et un œdème mammaire persistant. L'augmentation de la fatigue était significativement associée ($P < 0,01$) avec un IMC élevé, un délai plus court depuis le diagnostic, l'ethnicité, le statut face à l'emploi, la récidive, une chimiothérapie antérieure, une douleur persistante et des troubles du sommeil secondaires au traitement. La baisse des scores de répercussion sur le travail était significativement associée ($P < 0,04$) avec l'administration d'une chimiothérapie, un délai plus court depuis le diagnostic, l'emploi, la fatigue liée au traitement, un œdème du sein et une douleur persistante. **Conclusion:** Cette étude révèle les caractéristiques des patients associées à une augmentation de l'inquiétude face au cancer, à la fatigue, et aux répercussions négatives sur le travail après un diagnostic de cancer du sein. Ces constatations peuvent informer les initiatives dans le domaine clinique et celui de la recherche pour mieux soutenir les patientes pendant leur traitement et leur survie.

Keywords

breast cancer, BREAST-Q, cancer worry, fatigue, patient-reported outcome measure

Mots-clés

Cancer du sein, BREAST-Q, inquiétude du cancer, fatigue, résultats rapportés par les patients

Introduction

Breast cancer is the most common malignancy in women, with treatment typically requiring surgical resection with or without systemic or focused neoadjuvant or adjuvant therapies.[1] While women who undergo breast cancer surgery generally demonstrate favorable outcomes with respect to health-related quality of life (HRQL), disabling symptoms associated with surgery and concomitant treatment may persist after the treatment period.[2] Specifically, patient HRQL concerns pertaining to fear of cancer progression/recurrence,[2,3] chronic fatigue[4] as well as impaired return to work or pretreatment activities are commonly reported in the literature.[5]

Despite known sequelae of breast cancer and its treatment, there exists a paucity of evidence which seeks to prognosticate which patients are likely to struggle following a breast cancer diagnosis. As such, efforts by clinicians and researchers to identify patients at high-risk of poor HRQL outcomes following a breast cancer diagnosis can aid resource allocation to ensure these individuals are adequately supported. Specifically, Park et al[6] advocate for targeted survivorship care in breast cancer survivors to improve HRQL outcomes.

To understand the impact of breast cancer and its treatment on patient HRQL, condition-specific patient-reported outcome measures (PROMs) are required.[7,8] To date, the BREAST-Q is the most frequently used PROM to measure HRQL outcomes in this patient population.[8] Specifically, the BREAST-Q Breast Cancer module utilizes independently functioning scales to measure the outcomes that matter to patients with a breast cancer diagnosis. Specifically, our research team developed and validated three novel BREAST-Q Breast Cancer module scales that measure HRQL outcomes specific to cancer worry, fatigue, and impact on work.[9,10] These scales are designed for patients who have undergone either breast reconstruction, mastectomy without reconstruction, or breast-conserving therapy.

In this study, the authors sought to perform an exploratory analysis using patient data collected from the PROM field-test validation study of the BREAST-Q Cancer Worry, Fatigue, and Impact on Work scales. The primary aim was to identify which patient clinical and demographic characteristics are associated with poor HRQL outcomes following a breast cancer diagnosis.

Methods

This cross-sectional study was approved by two respective research ethics boards sites and the Love Research Army (LRA; formerly known as the Army of Women) Scientific Advisory Committee.

Sample and Recruitment

A convenience sample of participants were recruited through the LRA as part of a larger field-test study to validate the

novel BREAST-Q Breast Cancer Worry, Fatigue and Impact on Work scales. LRA members in the United States were sent an electronic recruitment email (ie, e-blast) describing the study and given access to a REDCap survey link (hosted at participating hospital). Data collection took place between October and November 2019. Participants were included if: (1) they were 18 years or older; (2) English-speaking; and (3) had a prior breast cancer diagnosis. Women who self-selected to meet the inclusion criteria completed demographic and breast cancer-specific questions alongside the Cancer Worry, Fatigue, and Impact on Work scales. All participants completed the Cancer Worry scale. The Fatigue scale was only administered to participants who endorsed fatigue related to breast cancer and/or its treatment, and the Impact on Work scale was only completed by participants who indicated they worked in a job (for pay) in the past six months.

Scoring of BREAST-Q Scales

All three BREAST-Q scales are continuous outcomes, scored from 0 to 100. For the Cancer Worry scale (ie, 10 items), *higher* scores reflect *more* cancer worry, whereas for the Fatigue (ie, 10 items) and Impact on Work (ie, 8 items) scales, *higher* scores correspond to *better* HRQL outcomes. Each scale takes approximately 1-4 min to complete.

Data Analysis

Descriptive statistics were used to evaluate participant demographic and clinical characteristics. Predictor variables hypothesized to be clinically relevant to the Breast Cancer Worry, Fatigue, and Impact on Work scales were selected *a priori* by the study authors. A univariable regression analysis was used to evaluate the existence of a linear relationship between each predictor variable and the BREAST-Q scales. Statistical significance was determined using a Wald test (ie, continuous variables) or Partial F-Test (ie, categorical variables). Predictors demonstrating a statistically significant linear relationship from this univariable analysis were included in a multivariable linear regression model for each scale. Standardized coefficients (β*) were used to compare the relative importance of predictor variables. The total variability explained through this model was summarized using the coefficient of determination (R^2). An a priori Variance Inflation Factor (VIF) > 5 was used to denote definite multicollinearity. Given a sample size rule of thumb of 10-20 participants per predictor established by Harrell,[11,12] the sample size for each scale was considered sufficient. Pairwise deletion (ie, available case analysis) was performed to address missing data within regression analyses. Statistical significance was considered at $P \leq .05$. All analyses were performed using SPSS ® version 26.0 (IBM Corporation, Armonk NY, USA for Windows®).

Results

Of the 1717 participants who opened the REDCap link, $n = 1680$ (97.8%) completed at least one scale. The Cancer Worry, Fatigue, and Impact on Work scales were completed by $n = 1680$, $n = 1037$, and $n = 873$ participants, respectively. Participants had a mean (± standard deviation, SD) age of 61.9 (±10.1) years and body mass index (BMI) of 26.9 kg/m^2 (±5.8). Common characteristics of the cohort included respondents being married/common law (73.2%), Caucasian (92.7%), had started or obtained a College/University diploma (48.2%) or Master's/Doctoral degree (48.4%), and were working full time (33.5%) or retired (43.5%). With respect to their oncologic status, most participants had surgery (89.2%) and/or radiation (71.7%) for treatment of their breast cancer and had not experienced a cancer recurrence (87.4%). Participant demographic characteristics are reported in Table 1.

Cancer Worry Scale

The participant sample ($n = 1680$) demonstrated a normal distribution of BREAST-Q Cancer Worry scores with a mean of 45.4 (±17.7) (Figure S1 and Table 2).

Following a univariable linear regression analysis (Table 3), more Cancer Worry (ie, higher scores) was significantly associated with younger participant age [β −0.55, 95% CI −0.64 to −0.48, $P < .01$], increasing BMI [β 0.20, 95% CI 0.05 to 0.35, $P < .01$], shorter duration since breast cancer diagnosis ($P < .01$) and working full- or part-time relative to being retired ($P < .01$). Additionally, participants who reported ongoing pain secondary to breast cancer [β 9.44, 95% CI 7.80 to 11.08, $P < .01$], a higher breast cancer stage at diagnosis ($P < .01$), triple positive disease ($P < .01$), breast cancer recurrence [β 4.01, 95% CI 1.45 to 6.58, $P < .01$], treatment with chemotherapy [β 4.61, 95% CI 2.88 to 6.34, $P < .01$], radiation [β 3.62, 95% CI 1.74 to 5.50, $P < .01$], or anti-estrogen therapy [β 3.80, 95% CI 1.98 to 5.61, $P < .01$], ongoing breast lymphedema [β 10.46, 95% CI 8.18 to 6.65, $P < .01$], positive lymph nodes [β 4.21, 95% CI 2.32 to 6.10, $P < .01$], and those who underwent a lumpectomy relative a unilateral or bilateral mastectomy ($P < .01$) reported more cancer worry.

When statistically significant variables were included in a multivariable linear regression model, only younger participant age [β −0.33, 95% CI −0.46 to −0.20, $P < .01$], shorter duration of time since initial breast cancer diagnosis ($P < .01$), ongoing pain related to breast cancer or treatment [β 4.97, 95% CI 3.15 to 6.79, $P < .01$], history of breast cancer recurrence [β 4.82, 95% CI 1.93 to 7.70, $P < .01$], ongoing breast edema/lymphedema [β 5.70, 95% CI 3.25 to 8.16, $P < .01$], and treatment with chemotherapy [β 2.53, 95% CI 0.16 to 4.89, $P = .04$] remained statistically significant after adjusting for all other variables in the model (Table 3). Using standardized coefficients (β*), participant age was determined to be the most important predictor variable for the BREAST-Q Cancer Worry score [$\beta^* = -0.19$] (Figure 1). Overall, the multivariable model explained 22.4% of the variance in Cancer Worry Scores [$R^2 = 0.22$, $F(27,1290) = 13.79$, $P < .01$].

Table 1. Demographic Characteristics

Participant characteristics	*N* = 1680	*N*%
Age		
≤49	210	12.5
50-59	431	25.7
60-69	637	37.9
≥70	402	23.9
BMI (kg/m^2)		
Underweight (≤18.5)	31	1.8
Normal (18.5-24.9)	698	41.5
Overweight (25-29.9)	534	31.8
Obese (≥30)	412	24.5
Missing	5	0.3
Relationship status		
Single, never married	178	10.6
Married/common law	1229	73.2
Separated/divorced	170	10.1
Widowed	84	5.0
Other	19	1.1
Ethnicity		
Caucasian	1557	92.7
African American	38	2.3
Hispanic/Latino	35	2.1
Asian	22	1.3
Other	21	1.2
Missing	7	0.4
Education level		
High school equivalent or less	53	3.2
College/Trade/University diploma	809	48.2
Master's/Doctoral degree	813	48.4
Missing	5	0.3
Employment status		
Retired	728	43.3
Working full time	562	33.5
Working part time	217	12.9
Other	168	10.0
Missing	5	0.3
Breast cancer stage at diagnosis		
Stage 0 (DCIS/LCIS)	296	17.6
Stage 1	591	35.2
Stage 2	510	30.4
Stage 3 or 4	251	14.9
Missing	35	1.9
Bra cup size		
A cup	134	8.0
B cup	399	23.8
C cup	540	32.1
D cup	293	17.4
DD cup and larger	196	11.7
Missing	118	7.0
Time since initial breast cancer diagnosis, years		
≤5	474	28.2
6-10	398	23.7
11-15	395	23.5
≥16	413	24.6
Presence of cancer recurrence		
Yes	208	12.4
No	1469	87.4
Missing	3	0.2
Pain from breast cancer treatment		
No	792	47.1
Yes	888	52.9
Working for pay in the last 6 months?		
No	793	47.2
Yes	887	52.8
HR and HER2 associated with Breast cancer at diagnosis		
HR−/HER2−	113	6.7
HR−/HER2+	108	6.4
HR+/HER2−	658	39.2
HR+/HER+	218	13.0
Triple negative	163	9.7
Triple positive	67	4.0
Not tested	28	1.7
Do not know	325	19.3
Diagnosed with breast cancer in one or both of your breasts?		
Unilateral	1498	89.2
Bilateral	182	10.8
History of surgery for treatment of breast cancer		
No	208	12.4
Yes	1472	87.6
History of chemotherapy for treatment of breast cancer		
No	644	38.3
Yes	1036	61.7
History of radiation for treatment of breast cancer		
No	475	28.3
Yes	1205	71.7
History of anti-estrogen therapy for treatment of breast cancer	534	31.8
No	1146	
Yes		68.2
Presence of breast lymphedema		
No swelling	1365	81.3
Swelling	265	15.8
Missing	50	3.0
Presence of arm lymphedema secondary to cancer treatment		
No	1295	77.1
Yes	359	21.4
Missing	26	1.5
Problems with arms secondary to cancer treatment (ie, pain, swelling, difficulty moving arms)	938	55.8
No	742	44.2

(continued)

Table 1. (continued)

Participant characteristics	N = 1680	N%
Yes		
Difficulty sleeping from breast cancer treatment		
Never	714	42.5
Sometimes (1-2 nights/week)	495	29.5
Often (3-4 nights/week)	254	15.1
Very often (5-7 nights/week)	217	12.9
Fatigue from breast cancer treatment		
None of the time	630	37.5
A little of the time	359	21.4
Some of the time	441	26.3
Most of the time	192	11.4
All of the time	58	3.5
Type of breast surgery performed (n = 1472)		
Lumpectomy one or both breast	670	45.4
Mastectomy one breast	338	23.0
Mastectomy both breasts	463	31.5
Missing	1	0.1
Nipple areolar complex removed at time of surgery (n = 801)		
NAC not removed	86	5.1
NAC removed	715	42.6
Lymph node status (n = 1359)		
No—lymph nodes cancer-free	842	62.0
Yes—lymph nodes had breast cancer	517	38.0
Breast reconstruction surgery (n = 801)		
No	263	32.8
Yes	538	67.2

Table 2. BREAST-Q Cancer Worry, Fatigue and Work-Life Scale Scores

BREAST-Q Scale	Mean (SD)	Minimum	Maximum	N Participants reporting maximum scale score (%)
Cancer Worry N = 1680	45.4 (17.7)	0	100	8 (0.5)
Fatigue N = 1037	69.4 (20.0)	0	100	138 (13.3)
Work-life N = 873	73.0 (28.1)	0	100	318 (36.4)

N, frequency; SD, standard deviation.

Fatigue Scale

A sample of $n = 1037$ participants completed the BREAST-Q Fatigue scale and demonstrated a mean scale score of 69.4 (±20.0). Scale distributions were skewed (Figure S1).

Following a univariable analysis (Table 4), worse participant Fatigue (ie, lower scores) was associated with younger age [β 0.26, 95% CI 0.14 to 0.38, $P < .01$], increasing BMI [β −0.43, 95% CI −0.64 to −0.22 $P < .01$], shorter time since diagnosis ($P < .01$), participant ethnicity ($P < .01$), employment status ($P < .01$), self-reported pain related to breast cancer or cancer treatment [β −10.68, 95% CI −13.03 to−8.32, $P < .01$], higher breast cancer stage at diagnosis relative to stage 0 disease ($P < .01$), increased difficulty sleeping relative to no difficulty sleeping ($P < .01$), cancer recurrence [β −4.48, 95% CI −8.17 to −0.79, $P = .02$], history of surgical treatment for breast cancer [β −3.76, 95% CI −7.45 to −0.06, $P = .04$] or chemotherapy [β −4.31, 95% CI −6.80 to −1.81, $P < .01$], ongoing breast edema/lymphedema [β −8.33, 95% CI −11.66 to −5.00, $P < .01$], and self-reported problems with arms secondary to cancer treatment (eg, pain, swelling, difficulty moving arms) [β −7.36, 95% CI −9.78 to −4.95, $P < .01$].

Again, when statistically significant variables were included in a multivariable linear regression model only increasing BMI [β −0.30, 95% CI −0.49 to −0.10, $P < .01$], participant ethnicity ($P < .01$), employment status ($P < .01$), ongoing pain [β −6.61, 95% CI −9.07 to −4.14, $P < .01$], history of cancer recurrence [β −4.60, 95% CI −8.15to −1.05, $P < .01$], treatment with chemotherapy [β −3.67, 95% CI −6.56 to −0.78, $P = .01$], and increased frequency of difficulty sleeping ($P < .01$) were significantly associated with BREAST-Q Fatigue scores after adjusting for other variables in the model. Using standardized coefficients (β*), difficulty sleeping "very often (5 to 7 nights/week)" and "pain related to cancer or related treatments" were determined to be the most important predictors for the BREAST-Q fatigue score [$\beta^* = -0.17$] (Figure 2). Overall, the multivariable model explained 22.3% of the variance in Fatigue Scores [$R^2 = 0.22$, $F(24,973) = 11.64$, $P < .01$].

Impact on Work Scale

A sample of $n = 873$ participants completed the BREAST-Q Impact on Work scale and demonstrated a mean scale score of 73.0 (±28.1). Scale distributions were skewed (Figure S1).

Following univariable regression (Table 5), worse participant Impact on Work (ie, lower scale scores) was associated with younger participant age [β 0.33, 95% CI 0.15 to 0.52, $P < .01$], shorter time since initial breast cancer diagnosis ($P < .01$, part-time employment status relative to retirement ($P < .01$), ongoing pain related to breast cancer or associated treatments [β −13.82, 95% CI −17.44 to −10.19, $P < .01$], higher cancer stage at diagnosis ($P < .01$), increased difficulty sleeping secondary to breast cancer/treatment ($P < .01$), worse self-reported fatigue frequency ($P < .01$), history of chemotherapy [β −8.09, 95% CI −11.89 to −4.29, $P < .01$], ongoing breast edema/lymphedema [β −14.09, 95% CI −11.89 to −4.29, $P < .01$], problems with arms secondary to cancer treatment [β −12.46, 95% CI −16.12 to −8.79, $P < .01$], and separated/divorced relationship status relative to married participants ($P = .03$).

When these statistically significant variables were included in a multivariable linear regression model (Table 5), only

Table 3. Univariable and Multivariable Linear Regression of BREAST-Q Cancer Worry Scale on Participant Variables

	Univariable regression			Multivariable regression				
Variable	β	*P*-value	95% CI	B	β*	*P*-value	95% CI	VIF
Age, years	−0.55	**<.01****	−0.64 to −0.48	−0.33	−0.19	**<.01****	−0.46 to −0.20	2.26
BMI (kg/m^2)	0.20	**<.01****	0.05 to 0.35	0.09	0.03	.22	−0.06 to −0.25	1.04
Time since initial breast cancer diagnosis, years (ref = ≤5)		**<.01****				**<0.01****		
6-10	−2.88		−5.17 to −0.59	−2.55	−0.06		−4.99 to −0.11	1.48
11-15	−6.10		−8.40 to −3.81	−4.89	−0.12		−7.43 to −2.34	1.60
≥16	−11.79		−14.06 to −9.53	−6.70	−0.16		−9.53 to −3.87	2.04
Employment status (ref = Retired)		**<.01****				.07		
Working full time	7.28		5.38 to 9.18	−1.18	−0.03		−3.81 to 1.45	2.12
Working part time	7.55		4.93 to 10.17	1.67	0.03		−1.30 to 4.65	1.37
Other	11.27		8.37 to 14.17	2.38	0.04		−1.05 to 5.81	1.46
Pain related to breast cancer or cancer-related treatment (ref = no)	9.44	**<.01****	7.80 to 11.08	4.97	0.14	**<.01****	3.15 to 6.79	1.14
Breast cancer stage at diagnosis (ref = stage 0)		**<.01****				.60		
Stage 1	4.55		2.11 to 7.00	1.90	0.05		−0.87 to 4.67	2.42
Stage 2	6.72		4.21 to 9.22	1.74	0.05		−1.36 to 4.85	2.83
Stage 3 or 4	9.31		6.34 to 12.25	1.69	0.03		−2.05 to 5.43	2.48
Hormone receptor associated with Breast cancer (ref = Do not know)		**<.01****				.17		
HR−/HER2−	0.21		−3.49 to 3.91	−1.15	−0.02		−5.03 to 2.74	1.30
HR−/HER2+	7.18		3.41 to 10.94	1.63	0.02		−2.54 to 5.79	1.43
HR+/HER2−	8.66		6.37 to 10.96	2.30	0.06		0.32 to 4.93	2.26
HR+/HER+	8.89		5.93 to 11.86	4.09	0.08		0.86 to 7.31	1.61
Triple negative	6.85		3.60 to 10.11	0.91	0.02		−3.02 to 4.84	1.86
Triple positive	14.00		9.46 to 18.55	4.44	0.05		0.54 to 9.42	1.31
Not tested	−3.42		−10.10 to 3.25	−0.98	−0.01		−7.99 to 6.03	1.11
History of breast cancer recurrence (ref = No)	4.01	**<.01****	1.45 to 6.58	4.82	0.09	**<.01****	1.93 to 7.70	1.24
History of chemotherapy for treatment of breast cancer (ref = No)	4.61	**<.01****	2.88 to 6.34	2.53	0.07	**.04****	0.16 to 4.89	1.81
History of radiation for treatment of breast cancer (ref = No)	3.62	**<.01****	1.74 to 5.50	2.43	0.06	.06	−0.14 to 5.00	1.84
History of anti-estrogen therapy for treatment of breast cancer (ref = No)	3.80	**<.01****	1.98 to 5.61	1.31	0.03	.27	−1.03 to 3.64	1.63
Presence of breast lymphedema (ref = No)	10.46	**<.01****	8.18 to 12.75	5.70	0.12	**<.01****	3.25 to 8.16	1.13
Positive lymph nodes (ref = negative nodes)	4.21	**<.01****	2.32 to 6.10	0.81	0.02	.49	−1.48 to 3.11	1.71
Type of breast surgery performed (ref = Lumpectomy one or both breast)		**<.01****				.12		
Mastectomy one breast	−3.13		−5.43 to −0.83	−1.25	−0.03		−4.01 to 1.52	1.85
Mastectomy both breasts	3.69		1.61 to 5.77	2.24	0.06		−0.32 to 4.80	1.94

(continued)

Table 3. (continued)

	Univariable regression			Multivariable regression				
Variable	β	*P*-value	95% CI	B	β*	*P*-value	95% CI	VIF
Bra cup size (ref = A cup)		.32						
B cup	0.38		−3.07 to 3.84					
C cup	1.21		−2.14 to 4.55					
D cup	1.78		−1.83 to 5.39					
DD cup and larger	3.35		−0.54 to 7.23					
Relationship status (ref = Married/common law)		.09						
Single, never married	−0.70		−3.48 to 2.09					
Separated/divorced	0.93		−1.91 to 3.78					
Widowed	−5.17		−9.08 to −1.25					
Other	2.24		−5.79 to 10.27					
Ethnicity (ref = Caucasian)		.42						
African American	−1.62		−7.34 to 4.10					
Hispanic/Latino	1.91		−4.05 to 7.86					
Asian	2.06		−5.41 to 9.54					
Other	6.68		−0.97 to 14.33					
Education level (ref = High school/equivalent)		.42						
College/Trade/University	1.12		−3.82 to 6.05					
Master's/Doctoral	−0.03		−4.96 to 4.90					
Unilateral versus bilateral breast cancer (ref = Unilateral)	0.84	.55	−1.89 to 3.57					
History of surgery for treatment of breast cancer (ref = No)	1.84	.16	−0.74 to 4.42					
Nipple areolar complex removed at time of surgery (ref = No)	−1.63	.42	−5.56 to 2.30					
Breast reconstruction (ref = no)	1.30	.33	−1.29 to 3.89					

Not applicable

**, denotes statistical significance; ref, denotes reference value; β, represents the average change in scale score for every one-unit change in covariate (continuous variables) or the average difference in scores compared to the reference value (categorical variables); *P*-value, corresponds to Wald test (*t* distribution) for each β coefficient; β*, denotes standardized coefficient; VIF, refers to the variance inflation factor (ie, > 5 was used to denote definite multicollinearity). Level of statistical significance is $P \leq 0.05$.

time since initial breast cancer diagnosis ($P < .01$), employment status ($P < .01$), presence of pain related to breast cancer [β −5.20, 95% CI −8.85 to −1.55, $P < .01$], increased self-reported fatigue frequency ($P < .01$), treatment with chemotherapy ($P = .01$), and presence of breast lymphedema [β −5.17, 95% CI −9.99 to −0.34, $P = .04$] remained statistically significant after adjusting for all other variables in the model. Using the standardized coefficients (β*), participant self-reported fatigue described as "Most of the time" [$\beta^* = -0.25$] and "All of the time" [$\beta^* = -0.23$] was determined to be the most important predictor variable for the BREAST-Q Impact on Work score. Overall, this multivariable model explained 28.2% of the variance in scores [$R^2 = 0.28$, $F(25,823) = 12.04$, $P < .01$].

Discussion

This analysis provides evidence of patient characteristics that may be associated with increased breast cancer worry, fatigue and impact on work following a breast cancer diagnosis in a well-educated and predominantly white cohort of women. For clinicians and researchers, this analysis is hypothesis generating and identifies patient characteristics that may influence HRQL outcomes in this patient population. The results of this study can be used to identify patients at high-risk of poor HRQL outcomes following a breast cancer diagnosis and can aid resource allocation to ensure these individuals are adequately supported in survivorship.

In-keeping with the findings of Lebel et al,[13] who concluded that younger patient age was associated with more fear of cancer recurrence among breast cancer patients, we identified a statistically significant association between younger participant age and breast cancer worry such that each additional 1-year increase in age was associated with a 0.55 reduction in Cancer Worry score (Table 3). This result corresponds to an average reduction of −5.55 points for a 10-year increase in participant age. When standardized coefficients are compared in this multivariable model, age has the largest absolute value ($\beta^*_{Age} = -0.19$) and suggests that a change of 1 standard

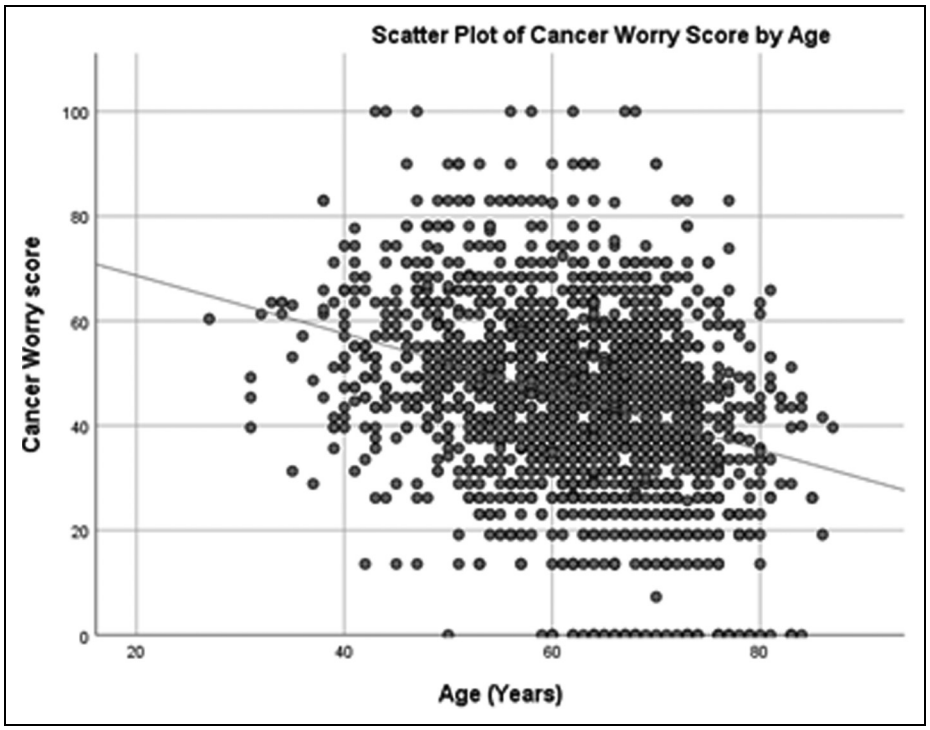

Figure 1. Scatter plot of cancer worry score by age (years).

deviation in participant age will result in an average change of 0.19 standard deviation units in Cancer Worry score, given all other variables are included. As such, participant age appears to have the greatest impact on Cancer Worry score after adjusting for other clinically relevant variables in our multivariable regression model. To address fear of cancer recurrence, Lebel et al[13] advocates for the implementation of clinical interventions which focus on anxiety management. Specifically, a randomized control trial comparing cognitive-behavioral group therapy (CBT) or supportive therapy versus standard treatment in reducing fear of disease progression in cancer patients by Herschbach et al[14] demonstrated a moderate reduction in fear of disease progression after four sessions over a 12-month period.

Moreover, this analysis identified increasing difficulty sleeping and pain related to breast cancer or related treatments to be the most important predictors for the BREAST-Q Fatigue scale. Specifically, relative to those participants who reported "never" for difficulty sleeping, those who selected "very often (5 to 7 nights/week)" demonstrated a 16.5-point reduction in Fatigue scale scores. Additionally, those participants who reported ongoing pain related to breast cancer or cancer-related treatment demonstrated, on average, a 10.7-point reduction in Fatigue scores. These participant variables remained statistically significant following inclusion in a multivariable linear regression model and were determined to be the most important variables following a comparison of standardized coefficients. This finding is consistent with Okuyama et al[15] who reported that fatigue in breast cancer survivors was significantly correlated with insufficient sleep, and this association was independent of other psychological factors such as depression. Furthermore, the association between pain and fatigue is supported by Schreier et al[16] who concluded that pain intensity was positively correlated with fatigue and described correlations between pain interference, sleep disturbance, and anxiety. To address fatigue in breast cancer patients, Okuyama et al[15] advocate for the treatment of concurrent symptoms (eg, dyspnea and insomnia) as well as the implementation of psychosocial interventions which have demonstrated some effectiveness—although additional research is required.[15]

Finally, the authors identified participant self-reported fatigue to be the most important predictor of negative work-life HRQL such that, relative to those who reported no fatigue, those who endorsed fatigue "Most of the time" and "All of the time" scored, on average, 30.1 and 44.5 points lower on the BREAST-Q Impact on Work scale, respectively. This finding is in keeping with Schmidt et al[5] who identified an association between impaired return to work and increased fatigue at 1.5 years after surgery in a breast cancer sample. In this study, fatigue was the most frequently cited reason for impaired return to work and persistent fatigue at 1.5 years following treatment remained a significant long-term determinant for work-life impairment. These results are further supported by several studies which corroborate an association between fatigue and impaired return to work in cancer patients.[17–20] Again, the implementation of psychosocial interventions may

Table 4. Univariable and Multivariable Linear Regression of BREAST-Q Fatigue Scale on Participant Variables

	Univariable regression			Multivariable regression				
Variable	β	*P*-value	95% CI	β	β*	*P*-value	95% CI	VIF
Age, years	0.26	**<.01****	0.14 to 0.38	0.08	0.04	.33	−0.08 to 0.24	2.17
BMI (kg/m^2)	−0.43	**<.01****	−0.64 to −0.22	−0.30	−0.09	**<.01****	−0.49 to −0.10	1.04
Time since initial breast cancer diagnosis, years (ref = ≤ 5)		**<.01****				**<.01****		
6-10	2.64		−0.71 to 6.00	3.37	0.07		0.21 to 6.53	1.47
11-15	6.91		3.55 to 10.27	6.97	0.15		3.67 to 10.26	1.59
≥16	8.00		4.68 to 11.32	6.78	0.15		3.16 to 10.41	1.98
Ethnicity (ref = Caucasian)			−19.35 to −3.07			**<.01****		
African American	−11.21	**<.01****		−9.57	0.07		−17.09 to −2.04	1.02
Hispanic/Latino	−1.16		−9.63 to 7.32	4.61	0.03		−3.25 to 12.48	1.03
Asian	11.71		1.07 to 22.35	9.13	0.05		−0.66 to 18.92	1.01
Other	−15.17		−26.06 to −4.28	−11.93	−0.07		−22.00 to −1.85	1.03
Employment status (ref = Retired)		**<.01****				**<.01****		
Working full time	−0.52		−3.27 to 2.23	4.69	0.11		1.26 to 8.12	2.13
Working part time	−1.04		−4.82 to 2.75	2.63	0.04		−1.22 to 6.48	1.36
Other	−13.84		−18.03 to −9.65	−7.10	−0.11		−11.58 to −2.62	1.47
Pain related to breast cancer or cancer-related treatment (ref = no)	−10.68	**<.01****	−13.03 to −8.32	−6.61	−0.17	**<.01****	−9.07 to −4.14	1.23
Breast cancer stage at diagnosis (ref = stage 0)		**<.01****				.11		
Stage 1	−2.61		−6.13 to 0.92	0.09	0.02		−3.29 to 3.47	2.14
Stage 2	−3.23		−6.84 to 0.39	1.69	0.04		−2.16 to 5.54	2.58
Stage 3 or 4	−9.69		−13.93 to −5.44	−2.74	−0.05		−7.30 to 1.81	2.18
Difficulty Sleeping from breast cancer treatment (ref = Never)		**<.01****				**<.01****		
Sometimes (1-2 nights/week)	−0.70		−3.50 to 2.10	3.90	0.09		1.08 to 6.72	1.35
Often (3-4 nights/week)	−9.55		−13.04 to −6.06	−3.57	−0.06		−7.08 to −0.05	1.29
Very often (5-7 nights/week)	−16.46		−20.16 to −12.75	−10.38	−0.17		−14.11 to −6.64	1.27
History of breast cancer recurrence (ref = No)	−4.48	**.02****	−8.17 to −0.79	−4.60	−0.08	**.01****	−8.15 to −1.05	1.12
History of surgery for treatment of breast cancer (ref = No)	−3.76	**.04****	−7.45 to −0.06	−1.97	−0.03	.26	−5.40 to 1.46	1.04
History of chemotherapy for treatment of breast cancer (ref = No)	−4.31	**<.01****	−6.80 to −1.81	−3.67	−0.09	**.01****	−6.56 to −0.78	1.60
Presence of breast lymphedema (ref = No)	−8.33	**<.01****	−11.66 to −5.00	−1.92	−0.04	.25	−5.21 to 1.37	1.20
Problems with arms secondary to cancer treatment (ie, pain, swelling, difficulty moving arms) (ref = No)	−7.36	**<.01****	−9.78 to −4.95	−2.03	−0.05	0.12	−4.57 to 0.51	1.29
Working for pay in the last 6 months? (ref = No)	1.88	.13	−0.56 to 4.32	***Not applicable***				
Breast reconstruction surgery (ref = no)	−0.13	.94	−3.83 to 3.56					
Type of breast surgery performed (ref = Lumpectomy one or both breast)		.41						

(continued)

Table 4. (continued)

	Univariable regression			Multivariable regression				
Variable	β	*P*-value	95% CI	β	β*	*P*-value	95% CI	VIF
Mastectomy one breast	−1.18		−5.08 to 1.53					
Mastectomy both breasts	−1.77		−4.77 to 1.22					
Relationship status (ref = Married/common law)		.23						
Single, never married	−2.90		−6.90 to 1.11					
Separated/divorced	−4.02		−8.11 to 0.06					
Widowed	−2.49		−8.12 to 3.14					
Other	−2.54		−14.08 to 9.00					
Education level (ref = High school/equivalent)		.43						
College/Trade/University	2.39		−4.69 to 9.48					
Master's/Doctoral	3.63		−3.45 to 10.71					
Unilateral versus bilateral breast cancer (ref = Unilateral)	3.08	.12	−0.84 to 7.00					
History of radiation for treatment of breast cancer (ref = No)	0.67	.63	−2.04 to 3.37					
History of anti-estrogen therapy for treatment of breast cancer (ref = No)	−0.29	.83	−2.91 to 2.33					

**, denotes statistical significance; ref, denotes reference value; β, represents the average change in scale score for every one-unit change in covariate (continuous variables) or the average difference in scores compared to the reference value (categorical variables); P-value, corresponds to Wald test (t distribution) for each β coefficient; β*, denotes standardized coefficient; VIF, refers to the variance inflation factor (ie, > 5 was used to denote definite multicollinearity). Level of statistical significance is $P \leq 0.05$.

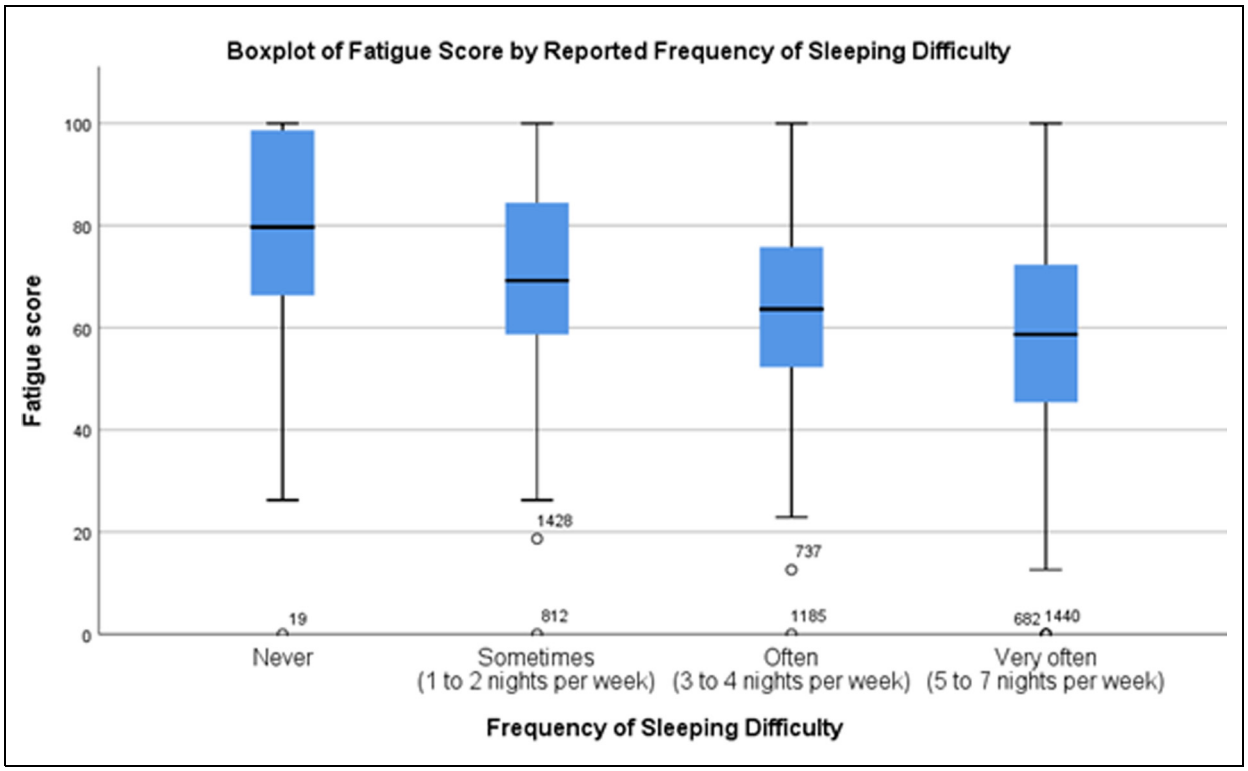

Figure 2. Box plot demonstrating relationship between self-reported frequency of sleeping difficulty and BREAST-Q fatigue scores.

Table 5. Univariable and Multivariable Linear Regression of BREAST-Q Impact on Work Scale on Participant Variables

	Univariable regression			Multivariable regression				
Variable	β	*P*-value	95% CI	β	β*	*P*-value	95% CI	VIF
Age, years	0.33	**<.01****	0.15 to 0.52	0.23	0.08	.06	−0.01 to 0.48	2.22
Time since initial breast cancer diagnosis, years (ref = ≤ 5)		**<.01****				**<.01****		
6-10	10.85		5.76 to 15.94	9.68	0.15		5.046 to 14.31	1.47
11-15	11.41		6.31 to 16.51	8.39	0.13		3.56 to 13.22	1.58
≥ 16	15.44		10.40 to 20.48	10.82	0.17		5.58 to 16.07	1.92
Employment status (ref = Retired)		**<.01****				**<.01****		
Working full time	3.16		−1.09 to 7.40	13.24	0.22		8.18 to 18.29	2.15
Working part time	−9.83		−15.68 to −3.99	−3.16	−0.04		−8.81 to 2.48	1.36
Other	−7.85		−14.32 to −1.38	6.52	0.07		−0.08 to 13.12	1.49
Pain related to breast cancer or cancer-related treatment (ref = no)	−13.82	**<.01****	−17.44 to −10.19	−5.20	−0.09	**<.01****	−8.85 to −1.55	1.25
Breast cancer stage at diagnosis (ref = stage 0)		**<.01****				.29		
Stage 1	−8.09		−13.41 to −2.76	−3.00	−0.05		−7.91 to 1.91	2.09
Stage 2	−11.91		−17.37 to −6.44	−4.16	−0.07		−9.75 to 1.44	2.53
Stage 3 or 4	−18.66		−25.07 to −12.24	−6.63	−0.09		−13.30 to 0.04	2.17
Difficulty Sleeping from breast cancer treatment (ref = Never)		**<.01****				.33		
Sometimes (1-2 nights/week)	−7.67		−12.01 to −3.33	1.71	0.03		−2.78 to 6.20	1.58
Often (3-4 nights/week)	−17.67		−23.09 to −12.25	−3.16	−0.04		−8.72 to 2.40	1.50
Very often (5-7 nights/week)	−16.40		−22.14 to −10.65	1.22	0.02		−4.72 to 7.16	1.50
Fatigue from breast cancer treatment (ref = None of the time)		**<.01****				**<.01****		
A little of the time	−5.72		−10.32 to −1.11	−1.44	−0.02		−6.38 to 3.49	1.54
Some of the time	−14.90		−19.22 to −10.58	−9.51	−0.15		−14.47 to −4.54	1.80
Most of the time	−30.81		−36.54 to −25.07	−21.63	−0.25		−28.09 to −15.17	1.60
All of the time	−44.50		−54.05 to −34.95	−35.86	−0.23		−45.93 to −27.79	1.28
History of chemotherapy for treatment of breast cancer (ref = No)	−8.09	**<.01****	−11.89 to −4.29	−5.33	−0.09	**.01****	−9.56 to −1.09	1.60
Presence of breast lymphedema (ref = No)	−14.09	**<.01****	−19.13 to −9.05	−5.17	−0.07	**.04****	−9.99 to −0.34	1.20
Problems with arms secondary to cancer treatment (ie, pain, swelling, difficulty moving arms) (ref = No)	−12.46	**<.01****	−16.12 to −8.79	−2.75	−0.05	.15	−6.50 to 1.00	1.31
Relationship status (ref = Married/common law)		**.03****				.23		
Single, never married	−0.12		−6.23 to 5.99	−0.99	−0.01		−6.40 to 4.42	1.05
Separated/divorced	−9.06		−15.29 to −2.83	−5.97	−0.06		−11.53 to −0.41	1.06
Widowed	6.47		−2.12 to 15.06	3.73	0.03		−4.06 to 11.53	1.09
Other	−0.70		−18.31 to 16.90	1.38	0.01		−14.14 to 16.90	1.02
Education level (ref = High school/equivalent)	−5.36	.48	−16.21 to 5.49					
College/Trade/University	−6.41		−17.25 to 4.44					
Master's/Doctoral								
Unilateral versus bilateral breast cancer (ref = Unilateral)	2.72	.37	−3.28 to 8.73					

Not applicable

(continued)

Table 5. (continued)

	Univariable regression			Multivariable regression				
Variable	β	*P*-value	95% CI	β	β*	*P*-value	95% CI	VIF
History of radiation for treatment of breast cancer (ref = No)	−2.44	.25	−6.58 to 1.70					
History of anti-estrogen therapy for treatment of breast cancer (ref = No)	2.65	.19	−1.35 to 6.66					
BMI (kg/m^2)	−0.32	.05	−0.64 to 0.01					
Ethnicity (ref = Caucasian)		.21						
African American	−4.90		−17.42 to 7.62					
Hispanic/Latino	5.89		−7.14 to 18.93					
Asian	−4.92		−21.29 to 11.45					
Other	−17.24		−34.00 to −0.49					
History of breast cancer recurrence (ref = No)	−1.99	.49	−7.65 to 3.67					
History of surgery for treatment of breast cancer (ref = No)	−2.16	.46	−7.82 to 3.51					
Breast reconstruction surgery (ref = no)	5.35	.06	−0.13 to 10.83					
Type of breast surgery performed (ref = Lumpectomy one or both breast)		.52						
Mastectomy one breast	1.11		−3.93 to 6.15					
Mastectomy both breasts	−1.90		−6.47 to 2.66					

**, statistical significance; ref, reference value; β, the average change in scale score for every one-unit change in covariate (continuous variables) or the average difference in scores compared to the reference value (categorical variables); *P*-value corresponds to Wald test (*t* distribution) for each β coefficient; β*, standardized coefficient; VIF, the variance inflation factor (ie, >5 was used to denote definite multicollinearity). Level of statistical significance is $P \leq 0.05$.

be effective at reducing fatigue strategy in breast cancer patients.[15]

There are several limitations to this analysis. Firstly, there is no minimal clinical important difference established for the BREAST-Q Cancer Worry, Fatigue, and Impact on Work scales yet. As such, we are unable to precisely interpret the independent effect of predictor variables that results in a clinically meaningful difference in HRQL outcomes. Secondly, the BREAST-Q Fatigue and Impact on Work scales demonstrate a highly skewed distribution with 13.3% and 36.4% of participants scoring 100 (ie, best HRQL), respectively. To ensure the normality and homoscedasticity assumptions for linear regression were met, the authors examined residuals using visual inspection and p-p plots. Moreover, regression remains robust to violations of the normality assumption and does not noticeably impact results in large sample sizes (eg, where the number of observations per variable is >10).[21] The skewed distribution of the data is therefore unlikely to impact our results. Thirdly, as the demographic and clinical data provided by the sample are self-reported, the accuracy of the data cannot be verified. Lastly, given that our cross-sectional sample was largely Caucasian, educated, non-working, and resided in the United States, further research is needed to ensure these associations remain applicable to other ethnic and socioeconomic groups in other settings and countries. The results of this analysis should be viewed with these limitations in mind.

Conclusions

The BREAST-Q Cancer Worry, Fatigue, and Impact on Work HRQL scales are rigorously developed, and validated PROMs designed for use in patients with a breast cancer diagnosis. For outcomes researchers, this analysis is hypothesis generating and identifies patient variables that may influence scale scores in this population. Clinicians and study investigators should follow-up with patients who endorse predictors significantly associated with reduced HRQL outcomes, address areas of concern in participant scale scores, and ensure patients are offered further supports, if necessary. The results of this study can be used to identify patients at high-risk of poor HRQL outcomes following a breast cancer diagnosis and can aid resource allocation to ensure these individuals are adequately supported. Future research is necessary to confirm these associations in a diverse, prospective patient sample and establish minimal clinical important differences for these scale scores.

Author Contributions

All authors contributed to the study design, analysis, and manuscript preparation.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: The BREAST-Q is owned by Memorial Sloan Kettering Cancer Center, Mass General Brigham, and McMaster University. Drs Pusic and Klassen are co-developers and receive royalty for use in for-profit studies.

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Research Ethics and Patient Consent

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. This study was approved by the research ethics boards at Brigham and Women's Hospital (BWH, Boston, MA, USA), McMaster University (Hamilton, ON, Canada), and the Love Research Army (LRA; formerly known as the Army of Women) Scientific Advisory Committee.

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Supplemental Material

Supplemental material for this article is available online.

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