Support Care Cancer (2016) 24:4017–4023
DOI 10.1007/s00520-016-3242-y

ORIGINAL ARTICLE

Socio-demographic and clinical variables associated with psychological distress 1 and 3 years after breast cancer diagnosis

Sven Alfonsson[1] · Erik Olsson[1] · Timo Hursti[2] · Marie Høyer Lundh[1,3] · Birgitta Johansson[4]

Received: 22 December 2015 / Accepted: 24 April 2016 / Published online: 29 April 2016

Abstract
Purpose A large group of women (20–30 %) report psychological distress shortly after breast cancer diagnosis, and some experience continued or increased symptoms over time. The aim of this study was to investigate socio-demographic and clinical variables associated with sustained psychological distress in this patient group.
Methods Women with breast cancer ($n = 833$) completed self-report questionnaires regarding socio-demographic and clinical variables shortly after (T1) and 3 years after diagnosis (T2) while data on illness severity were collected from a quality register. The Hospital Anxiety and Depression Scale was used as a measure of psychological distress at both time points.
Results The number of participants who reported elevated levels of anxiety was 231 (28 %) at T1 and 231 (28 %) at T2 while elevated depressive symptoms was reported by 119 (14 %) women at T1 and 92 (11 %) at T2. Despite non-significant differences in mean scores over time, 91 (15 %) participants reported increased anxiety symptoms and 47 (7 %) reported increased depressive symptoms. Poor financial situation, lack of social support, previous psychiatric treatment, and high levels of fatigue were associated with both anxiety and depressive symptoms. Reporting high levels of fatigue was the variable most strongly associated with increased psychological distress over time.
Conclusion Most participants reported decreased psychological distress over time, but there were subgroups of women who experienced sustained or increased symptoms of anxiety or depression. Participants with poor financial status, previous psychological problems, or high levels of fatigue may be at increased risk of psychological distress. Such individuals may benefit most from psychosocial interventions.

Keywords Breast cancer · Distress · Anxiety · Depression · Longitudinal

✉ Sven Alfonsson
sven.alfonsson@pubcare.uu.se

[1] Department of Public Health and Caring Sciences, Uppsala University, Box 564, 751 22 Uppsala, Sweden

[2] Department of Psychology, Uppsala University, Box 1225, 751 42 Uppsala, Sweden

[3] Department of Nursing, Metropolitan University College, 2200 Copenhagen N, Denmark

[4] Department of Immunology, Genetics and Pathology, Uppsala University Hospital, 751 85 Uppsala, Sweden

Introduction

Though treatment advances have improved the prognosis for patients with breast cancer, many women (20–30 %) report elevated levels of anxiety and depressive symptoms shortly after diagnosis [1]. This is probably due both to the psychological shock of having a potentially life threatening disease and to the negative physiological effects of the disease and its treatment. While anxiety and depressive symptoms are sometimes grouped together as psychological distress (e.g., [2]), anxiety and depressive symptoms have overlapping but different neurological and etiological characteristics [3, 4]. The socio-demographic and clinical variables associated with sustained anxiety and depressive symptoms over time are relatively understudied [5].

Anxiety is an evolutionary developed response to environmental threats and uncertain dangers [6]. Breast cancer can be a serious danger to a person's health depending on the disease stage, treatment intensity and possible cancer recurrence and consequently, patients with more severe forms of the illness

often report higher levels of anxiety symptoms [7]. While anxiety is characterized by a stress reaction and activation of the sympathetic nervous system, depressive symptoms are better characterized by reduced activity and a loss of motivation. The typical environmental trigger for depressive symptoms is a major routine disruption such as a decrease in behaviors that have been positively reinforced. One of the most common symptoms among patients during cancer treatment is severe fatigue, a loss of both physical and mental energy [8]. High levels of fatigue may lead to decreased activity levels and social withdrawal which may in turn increase the risk of developing depressive symptoms [9]. While previous studies have shown that breast cancer is associated with increased levels of anxiety and depressive symptoms, at least in the short term, we know less about the underlying mechanisms [10].

In breast cancer, psychological symptoms often decrease over time and 2 years after diagnosis, mean levels are only marginally higher compared with the general population [11]. However, for some women, the distress prevails [12]. Previous studies have shown that after breast cancer, several psychosocial factors such as younger age, comorbidities, low socio-economic status, and lack of social support are associated with psychological distress but this association seems to be independent of the illness [13]. Psychological symptoms are often assessed at specific time points, but there could be groups of patients who experience different development of psychological symptoms over time. To find such subgroups, one must use methods that focus on individual development rather than changes in the mean values of groups [14].

In general, psychological distress seems to decrease over time after breast cancer diagnosis but some women may report increased psychological symptoms for reasons that are largely unknown. The aim of this study was to investigate demographic, psychosocial, and clinical variables associated with symptoms of anxiety and depression at 1 and 3 years after diagnosis. A further aim was to study subgroups of patients who report changes in psychological symptoms over time and to assess predictor variables for such change.

Methods

Participants and data collection

A total of 1573 patients with breast cancer were approached, and of these, 1086 patients (69 %) chose to participate and 833 (53 %) had complete clinical and self-report data for the planned analyses [11]. Data from two time points were used: T1 at 1–9 months (MD = 4) after diagnosis and T2 at 35–42 months (MD = 38) after diagnosis. The data collection procedure and sample characteristics have previously been reported [13]. The study was approved by the Regional Ethics Review Board in Uppsala, Sweden.

Measurements

Psychological symptoms were measured with the Hospital Anxiety and Depression Scale (HADS; [15]). The HADS has two subscales, Anxiety and Depression, and a score above 7 is often used as a cutoff for a possible risk of psychological distress in the respective domain.

Based on previous findings [1, 8, 11–13], five socio-demographic variables were extracted at both T1 and T2: the quartile with lowest age (<51 years), marital status (single or married/cohabitant), lack of social support within the family ("Do you have someone in the family that you can confide in and get support from?," yes or no), previous treatment for anxiety or depression during the last year (yes or no) and self-assessed/perceived financial situation, scored from 0 = "worst possible situation" to 10 = "best possible situation." Self-assessed/perceived financial situation was dichotomized into poor financial situation (yes or no) using the lowest 10th percentile (a score <4), to allow comparison with other variables. Each variable was collected through a project specific self-report questionnaire [16].

There are few established risk factors for illness severity in the literature [17], but four clinical variables were identified and extracted from the Breast Cancer Quality Register in the Uppsala-Örebro health care region in Sweden: distant metastases at diagnosis, use of preoperative chemotherapy and postoperative chemotherapy, and/or Trastuzumab treatment. These variables were coded into dichotomous variables (yes or no).

Fatigue was measured with the Fatigue scale of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30; [18]). The index was transformed into a dichotomous variable by recoding participants in the highest quartile as having high levels of fatigue and the rest as having low levels of fatigue. The other scales of the EORTC QLQ-C30 were only used to compare participants with incomplete data to those included in the analyses.

Statistical analyses

Prior to further analyses, participants with complete data were compared with participants with incomplete data, all variables were scrutinized for outliers and all variable distributions were investigated. Differences between groups of participants were investigated with Analysis of Variance and χ^2 depending on variable type. HADS change scores were calculated by subtracting the score at T1 from the score at T2 for each participant. The score on the HADS was used to classify participants into two groups for each subscale at the two time points. Participants with a score of 0 to 7 were classified as *non-cases* (N) and a score of 8 or more as *possible cases* (P). The classifications at the two time points were coded for each

participant representing development over time. Participants who were classified as no cases at both T1 and at T2 were coded as NN, participants who were classified as no cases at T1 and possible cases at T2 were coded as NP, participants who were classified as possible cases at T1 and no cases at T2 were coded as PN, and participants who were classified as possible cases at both T1 and T2 were coded as PP.

The HADS classifications were used as outcome variables in multivariate logistic regression analyses using maximum-likelihood estimation. Only independent variables that showed to be significantly associated with the outcome variables in bivariate regression analyses were entered into the multiple logistic regression analyses. All variables were entered simultaneously using first one-step regression analyses for T1 only and then two-step analyses for T1 and T2. For variables that were measured both at T1 and T2, data from the time point that contributed the least to the model, as measured by the change in R^2 or were insignificant, was removed. Before regression analyses, independence of errors, homoscedasticity, distribution of errors, and multicollinearity were assessed and found to be satisfactory in this dataset. Cox and Snell R^2 (R^2_{CS}) and Nagelkerke R^2 (R^2_N) were used as measures of model fit. The number of participants was deemed large enough to allow for at least ten independent variables in the regression analyses. A p value of 0.05 was used as the cutoff for statistical significance. SPSS 20.0 was used for all statistical analyses.

Results

In the sample of 833 women, the mean age at diagnosis was 60.6 years (SD = 11.6, range = 25–94) and 264 (32 %) had attended university. About one third was working (n = 265, 32 %), 268 (21 %) were on sick leave or on disability pension, and 309 (37 %) had retired. The proportion of participants with distant metastases (n = 7, 1 %) and/or preoperative chemotherapy (n = 11, 1.3 %) were too small to allow for statistical analyses, and these variables were thus removed in the subsequent analyses (Table 1). Participants with incomplete data were significantly older (mean difference = 6.2 years, F = 13.10, p < 0.001), more often single rather than married/cohabitant (χ^2 = 4.55, p = 0.03) and reported worse Physical functioning on the EORTC QLQ-C30 (mean difference = 9.5, F = 13.62, p < 0.001) than participants with complete data in the original dataset.

The mean scores on the HADS anxiety were slightly below the clinical cutoff at both T1 and T2 (Table 2). In contrast, the mean scores on the HADS depression were well below the clinical cutoff at both T1 and T2. There was no significant change in reported mean scores or number of possible case classification for either anxiety or depression between T1 and T2.

Table 1 Distribution of predictor variables at T1 (1–9 months after diagnosis) and T2 (35–42 months after diagnosis) (n = 833)

Predictor variable	T1 (n (%))	T2 (n (%))
Low age (<51 years at diagnosis)	176 (23 %)	–[a]
Marital status: single	204 (24 %)	241 (29 %)
Lack of social support	70 (8 %)	86 (10 %)
Poor financial situation	97 (13 %)	97 (13 %)
Previous treatment for anxiety	43 (5 %)	–[a]
Previous treatment for depression	61 (7 %)	–[a]
Distant metastases at diagnosis	7 (1 %)	–[a]
Preoperative chemotherapy	11 (1 %)	–[a]
Postoperative chemotherapy	308 (37 %)	–[a]
Postoperative Trastuzumab treatment	67 (8 %)	–[a]
High levels of fatigue	210 (25 %)	223 (27 %)

[a] Data from T1 was used in all analyses of these variables

Anxiety symptoms classification and development

Despite the non-significant changes in mean scores in the whole sample, 91 of 617 participants (15 %) classified as non-cases at T1 reported increased levels of anxiety and were classified as possible cases at T2 while 105 (45 %) participants who were classified as possible cases at T1 improved and were classified as non-cases at T2 (Table 3).

There were no bivariate associations between marital status and postoperative chemotherapy on the one hand and HADS anxiety classification at T1 on the other hand so these variables were removed from the multivariate analysis. Of the remaining variables, all were significantly and independently associated with HADS anxiety classification at T1 (Table 4). For the whole model, $\chi^2(7) = 119.266$, $p < 0.001$, $R^2_{CS} = 0.14$, $R^2_N = 0.21$.

In the two-step logistic regression analysis, T1 measurements of lack of social support, poor financial situation, previous anxiety treatment and high levels of fatigue could significantly predict HADS anxiety classification at T2 (Table 4). However, when adding the variables measured at T2, lack of social support and high levels of fatigue measured at T1 were no longer significant and were removed from the model. For the whole model, $\chi^2(7) = 91.619$, $p < 0.001$, $R^2_{CS} = 0.11$, $R^2_N = 0.16$.

Most participants (n = 511, 61 %) were non-cases at both T1 and T2. A small group of 91 (15 %) participants changed from non-cases at T1 to possible cases at T2 and were thus classified as NP. In bivariate regression analyses, none of the variables measured at T1 could significantly predict NP using NN as a reference group. Only high levels of fatigue measured at T2 (B = 1.29 (0.27), χ^2 = 22.57, p < 0.001, OR = 3.65 (2.14–6.22)) was significantly associated with being classified as type NP. Also, high levels of fatigue measured at T2

Table 2 HADS mean values and categorizations at variables at T1 (1–9 months after diagnosis) and T2 (35–42 months after diagnosis) ($n = 833$)

Scale	T1			T2		
	m (SD)	Non-case (*n*)	Possible case (*n*)	m (SD)	Non-case (*n*)	Possible case (*n*)
HADS anxiety	5.18 (4.25)	602 (72 %)	231 (28 %)	5.30 (3.56)	616 (74 %)	217 (26 %)
HADS depression	3.69 (3.47)	714 (86 %)	119 (14 %)	3.64 (2.93)	741 (89 %)	92 (11 %)

($B = 0.77$ (0.33), $\chi^2 = 5.57$, $p = 0.018$, OR = 2.16 (1.14–4.09)) was the only variable significantly associated with PP (being classified as Possible case at both T1 and T2) using PN (being classified as possible case at T1 and as no case at T2) as a reference group, indicating that symptoms of fatigue were associated with both developing and having sustained anxiety.

Depressive symptoms classification and development

While the mean score of the HADS depression subscale remained unchanged in the whole sample, 47 (7 %) changed classification from non-case at T1 to possible case at T2 while 74 (62 %) went from possible case at T1 to non-case at T2 (Table 5).

Low age was not associated with HADS depression classification at T1 and was therefore not included in the multivariate regression analysis while marital status, postoperative chemotherapy, and Trastuzumab treatment were significantly associated with depression classification in the bivariate analysis but not in the multivariate analysis (Table 6). For the whole model, $\chi^2(9) = 136.338$, $p < 0.001$, $R^2_{CS} = 0.16$, $R^2_N = 0.29$.

Low age, marital status, postoperative chemotherapy, and Trastuzumab treatment were not significantly associated with depression classification at T2 in the initial bivariate analyses and were thus removed from the multivariate analysis. However, all the remaining variables at T1 could significantly predict depression classification at T2 (Table 6). When adding the variables measured at T2, lack of social support and high levels of fatigue measured at T1 were no longer significant and were removed from the model. For the whole model, $\chi^2(5) = 85.592$, $p < 0.001$, $R^2_{CS} = 0.10$, $R^2_N = 0.21$.

To investigate the predictors for developing depressive symptoms after an initial low level, type NP was compared with type NN in multiple logistic regression analyses. Previous treatment for depression ($B = 1.12$ (0.49), $\chi^2 = 5.23$, $p = 0.022$, OR = 3.08 (1.17–8.05) and high levels of fatigue ($B = 1.05$ (0.35), $\chi^2 = 9.15$, $p = 0.002$, OR = 2.85 (1.45–5.60) at T1 significantly predicted being classified as type NP while low age ($B = -0.87$ (0.34), $\chi^2 = 6.35$, $p = 0.012$, OR = 0.42 (0.22–0.83) significantly predicted being classified as type NN. At T2, only lack of social support (B = 1.37 (0.54), $\chi^2 = 6.59$, $p = 0.010$, OR = 3.94 (1.38–11.23) and high levels of fatigue ($B = 1.79$ (0.36), $\chi^2 = 25.32$, $p < 0.001$, OR = 5.99 (2.98–12.04)), were significantly associated with being classified as Type NP. Developing depressive symptoms was thus associated with previous treatment for depression, high levels of fatigue and lack of social support at T2. All variables were further investigated in both bivariate and multiple logistic regression analyses in order to assess whether variables could predict whether a participant would have sustained as compared with improved depressive symptoms (i.e., comparing predictors for type PP and type PN), but no variable in the analyses reached statistical significance.

Discussion

The socio-demographic variables associated with elevated levels of anxiety shortly following breast cancer in this study were low age, lack of social support, poor financial situation,

Table 3 HADS anxiety mean values and change scores for each HADS anxiety development category variables at T1 (1–9 months after diagnosis) and T2 (35–42 months after diagnosis) ($n = 833$)

Classification at T1	Classification at T2	Type	Number (%)	M (SD) T1	M (SD) T2	Anxiety change score (M (SD))
No case ($n = 602$)	Non-case	NN	511 (85 %)	2.79 (2.32)	3.34 (2.12)	0.55 (2.48)
	Possible case	NP	91 (15 %)	4.48 (2.18)	9.33 (1.33)	4.85 (2.44)
Possible case ($n = 231$)	Non-case	PN	105 (45 %)	9.87 (2.01)	4.87 (1.77)	−4.99 (2.64)
	Possible case	PP	126 (55 %)	11.46 (3.05)	10.67 (2.27)	0.80 (3.17)

NN non-case (T1) and non-case (T2), *NP* non-case (T1) and possible case (T2), *PN* possible case (T1) and non-case (T2), *PP* possible case (T1) and possible case (T2)

Table 4 Independent variables for HADS anxiety "possible case" classification at T1 ($n = 833$, non-cases = 602, possible cases = 231) and T2 ($n = 833$, non-cases = 616, possible cases = 217)

	B (SE)	χ^2	*P* value	OR	95 % CI
Possible case T1					
Low age (<51)	0.60 (0.18)	11.23	0.001	1.82	1.28–2.59
Lack of social support	1.13 (0.29)	15.76	<0.001	3.10	1.72–5.41
Poor financial situation	0.92 (0.25)	13.75	<0.001	2.51	1.54–4.08
Previous treatment for anxiety	1.37 (0.37)	13.54	<0.001	3.94	1.90–8.19
Postoperative Trastuzumab treatment	0.66 (0.29)	5.08	0.024	1.93	1.09–3.42
High levels of fatigue	1.01 (0.19)	28.60	<0.001	2.74	1.90–3.97
Possible case T2					
Step 1 ($R^2_{CS} = 0.08$, $R^2_N = 0.11$)					
Low age (T1)	0.18 (0.18)	1.04	0.31	1.20	0.85–1.70
Lack of social support (T1)	0.63 (0.29)	4.89	0.027	1.88	1.07–3.29
Poor financial situation (T1)	0.91 (0.24)	13.86	<0.001	2.47	1.54–3.98
Previous anxiety treatment (T1)	0.89 (0.35)	6.34	0.012	2.43	1.22–4.86
Postoperative Trastuzumab treatment (T1)	−0.02 (0.31)	0.01	0.95	0.98	0.53–1.82
High levels of fatigue (T1)	0.77 (0.19)	16.10	<0.001	2.15	1.48–3.13
Step 2 ($R^2_{CS} = 0.11$, $R^2_N = 0.16$)					
Low age (T1)	0.27 (0.18)	2.28	0.13	1.30	0.92–1.83
Poor financial situation (T1)	0.73 (0.24)	9.17	0.002	2.08	1.30–3.34
Previous anxiety treatment (T1)	0.92 (0.36)	6.71	0.010	2.51	1.25–5.03
Postoperative Trastuzumab treatment (T1)	0.30 (0.31)	0.95	0.33	1.35	0.74–2.45
Lack of social support (T2)	0.61 (0.26)	5.39	0.020	1.84	1.10–3.08
High levels of fatigue (T2)	1.23 (0.18)	45.99	<0.001	3.43	2.40–4.90

and previous treatment for anxiety while clinical variables included postoperative Trastuzumab treatment and high levels of fatigue. Similarly for depressive symptoms, lack of social support, poor financial situation, previous treatment for depression, and high levels of fatigue were significantly associated with high symptom levels. Treatment with Trastuzumab, indicating a more intensive treatment regime for HER2+ breast cancer, thus seems to be associated with anxiety rather than depressive symptoms in the year after diagnosis. Even after taking the level of fatigue into account, poor financial situation and previous psychiatric treatment could predict elevated levels of anxiety and depressive symptoms 3 years after diagnosis. Somewhat unexpectedly, indicators of intensive treatment regimes, postoperative chemotherapy, and treatment with Trastuzumab, were not strongly associated with psychological distress over time.

While the largest group of participants showed a pattern of low and stable symptoms of anxiety and depression over 3 years following breast cancer, a subgroup reported high or rising levels of symptoms of anxiety ($n = 91$, 15 %) and depression ($n = 47$, 7 %) over time. No psychosocial or clinical variables except fatigue could predict either increased or sustained levels of anxiety 3 years after cancer diagnosis. Developing depressive symptoms was associated with high levels of fatigue but also with previous treatment for depression and lack of social support. Similarly to previous studies, symptoms of fatigue were thus strongly associated with an increase in anxiety and depressive symptoms over time [19]. Fatigue is a common problem in most cancer treatments, but the symptoms also overlap to some extent with symptoms of anxiety and to a large extent with depression [20]. Consequently, it is difficult to assess whether experienced

Table 5 HADS depression mean values and change scores for each HADS depression development category variables at T1 (1–9 months after diagnosis) and T2 (35–42 months after diagnosis) ($n = 833$)

Classification at T1	Classification at T2	Type	Number (%)	M (SD) T1	M (SD) T2	Depression change score (M (SD))
No case ($n = 714$)	No case	NN	667 (93 %)	2.47 (2.14)	2.73 (1.99)	0.25 (2.39)
	Possible case	NP	47 (7 %)	4.45 (1.90)	9.11 (1.38)	4.66 (2.32)
Possible case ($n = 119$)	No case	PN	74 (62 %)	9.63 (2.27)	4.27 (1.92)	−5.20 (2.84)
	Possible case	PP	45 (38 %)	11.11 (2.28)	10.24 (1.94)	0.87 (2.88)

NN non-case (T1) and non-case (T2), *NP* non-case (T1) and possible case (T2), *PN* possible case (T1) and non-case (T2), *PP* possible case (T1) and possible case (T2)

Table 6 Predictor variables for HADS depression "possible case" classification at T1 ($n = 833$, non-cases = 714, possible cases = 119) and T2 ($n = 833$, non-cases = 741, possible cases = 92)

	B (SE)	χ^2	*P* value	OR	95 % CI
Possible case T1					
Marital status: single	0.38 (0.25)	2.19	0.14	1.46	0.89–2.40
Lack of social support	0.96 (0.33)	8.30	0.004	2.62	1.36–5.03
Poor financial situation	1.05 (0.28)	13.76	<0.001	2.86	1.64–4.99
Previous treatment for depression	0.78 (0.36)	4.84	0.028	2.19	1.09–4.39
Postoperative chemotherapy	0.28 (0.26)	1.23	0.27	1.33	0.81–2.19
Postoperative Trastuzumab treatment	0.65 (0.36)	3.31	0.07	1.92	0.95–3.88
High levels of fatigue	1.85 (0.24)	58.54	<0.001	6.35	3.96–10.20
Possible case T2					
Step 1 ($r^2_{CS} = 0.07$, $R^2_N = 0.14$)					
Lack of social support (T1)	0.87 (0.34)	6.59	0.010	2.38	1.23–4.63
Poor financial situation (T1)	0.97 (0.30)	10.69	0.001	2.63	1.47–4.68
Previous treatment for depression (T1)	0.80 (0.36)	5.00	0.025	2.22	1.10–4.50
High levels of fatigue (T1)	0.95 (0.25)	14.18	<0.001	2.60	1.58–4.27
Step 2 ($R^2_{CS} = 0.10$, $R^2_N = 0.21$)					
Poor financial situation (T1)	0.90 (0.29)	9.61	0.002	2.45	1.39–4.32
Previous treatment for depression (T1)	0.69 (0.35)	3.80	0.050	1.99	1.00–3.96
Lack of social support (T2)	0.95 (0.31)	9.68	0.002	2.59	1.42–4.73
High levels of fatigue (T2)	1.58 (0.25)	40.25	<0.001	4.84	2.97–7.88

fatigue measured in this study was truly independent of the psychological distress after breast cancer [21]. Furthermore, the possible causal mechanisms between fatigue on the one hand and anxiety and depressive symptoms on the other is still unclear [19, 22].

The change score for participants who went from no cases to possible cases were substantial for both HADS anxiety (M = 4.85, SD = 2.44) and HADS depression (M = 4.66, SD = 2.32) corresponding to clinically relevant aggravations in symptoms over time. While identifying possible risk factors, the analyses in this study could not explain by what mechanisms these changes in distress occur. This highlights the need for more thorough investigation of these processes at a more detailed level guided by well-founded psychological models. Whether specific interventions for patients at risk of developing psychological distress may be effective in the long term is still uncertain [23].

Problems of anxiety and depression typically overlap and in this study the risk factors for anxiety and depressive symptoms were identical with a few exceptions. Low age and treatment with Trastuzumab were risk factors for anxiety but not for depressive symptoms in the short term (T1) while low age was a specific risk factor for anxiety but not for depressive symptoms in the long term (T2). That low age is specifically associated with anxiety has been seen in other studies as well and may be a sign of more severe cancer types in younger patients. Lack of social support and poor financial situation were general risk factors for both anxiety and depressive symptoms which support the notion that people who are socially bereaved may be more vulnerable to different kinds of psychological problems.

A limitation of the current study was the narrow scope of the instruments used for measuring psychological distress (the HADS) and fatigue (the EORTC fatigue subscale). The study was designed to investigate quality of life in cancer patients in a broad sense and the number and extent of instruments was constrained for practical reasons. More specific and valid instruments may have provided data of higher quality and in subsequent studies, instruments such as the State Trait Anxiety Inventory and FACIT Fatigue Scale have been included to further assess the variables that were found to be important [24]. A further limitation was the lack of good proxy variables of illness severity in this patient group. While the chosen clinical variables in this study are often indicators of cancer aggressiveness and prognosis, they may not capture the full range of important prognostic variables in cancer treatment. Strengths of the current study include the rather large sample size, the population-based recruitment and the high level of participant retention. The follow-up time of 35–42 months (MD = 38) after diagnosis is arguably sufficient since many patients have by then completed active treatments and started to go back to their everyday lives [16].

Clinically, there seems to be reasons to focus the efforts on the subgroup of patients with prolonged and elevated distress after breast cancer [14]. The behavioral and psychological mechanisms for sustained or increased psychological distress

are unclear and effective interventions have to be evaluated for these patients [25]. The results of the current study confirm that socio-demographic variables and fatigue are important factors in predicting psychological distress [26]. While the causal associations are unknown, specific interventions to ameliorate fatigue are warranted and have shown some promise [27, 28]. Most participants reported decreased psychological distress over time, but there were subgroups of women who experienced sustained or increased symptoms of anxiety or depression. Participants with low socio-economic status, previous psychological problems or high levels of fatigue may be at increased risk of psychological distress. Such individuals may benefit most from psychosocial interventions.

Acknowledgments This study was partly funded by the Swedish government strategic grant U-CARE to Uppsala University.

Compliance with ethical standards

Conflicts of interest The author declares that they have no conflict of interest.

References

1. Knobf MT (2011) Clinical update: psychosocial responses in breast cancer survivors. Semin Oncol Nurs 27:e1–e14. doi:10.1016/j.soncn.2011.05.001
2. Iwatani T et al (2013) Predictive factors for psychological distress related to diagnosis of breast cancer. Psycho-Oncology 22.3:523–529. doi:10.1002/pon.3023
3. Antony MM, Stein MB (2009) Oxford handbook of anxiety and related disorders. Oxford University Press, New York
4. Richards CS, O'Hara MW (2014) The Oxford handbook of depression and comorbidity. Oxford University Press, New York
5. Stafford L et al (2015) Anxiety and depression symptoms in the 2 years following diagnosis of breast or gynaecologic cancer: prevalence, course and determinants of outcome. Support Care Cancer 23(8):2215–2224. doi:10.1007/s00520-014-2571-y
6. Grupe DW, Nitschke JB (2013) Uncertainty and anticipation in anxiety: an integrated neurobiological and psychological perspective. Nat Rev Neurosci 14:488–501. doi:10.1038/nrn3524
7. Stark DPH, House A (2000) Anxiety in cancer patients. Br J Cancer 83:1261. doi:10.1054/bjoc.2000.1405
8. Bower JE, Ganz PA, Desmond KA, Rowland JH, Meyerowitz BE, Belin TR (2000) Fatigue in breast cancer survivors: occurrence, correlates, and impact on quality of life. J Clin Oncol 18:743
9. Servaes P, Verhagen C, Gijs B (2002) Fatigue in cancer patients during and after treatment: prevalence, correlates and interventions. Eur J Cancer 38.1:27–43. doi:10.1016/S0959-8049(01)00332-X
10. Raison CL, Miller AH (2003) Depression in cancer: new developments regarding diagnosis and treatment. Biol Psychiatry 54:283–94. doi:10.1016/S0006-3223(03)00413-X
11. Burgess C, Cornelius V, Love S, Graham J, Richards M, Ramirez A (2005) Depression and anxiety in women with early breast cancer: five year observational cohort study. BMJ 330:702. doi:10.1136/bmj.38343.670868.D3
12. Mitchell AJ, Ferguson DW, Gill J, Paul J, Symonds P (2013) Depression and anxiety in long-term cancer survivors compared with spouses and healthy controls: a systematic review and meta-analysis. Lancet Oncol 14:721–32. doi:10.1016/S1470-2045(13)70244-4
13. Høyer M, Johansson B, Nordin K, Bergkvist L, Ahlgren J, Lidin-Lindqvist A et al (2011) Health-related quality of life among women with breast cancer—a population-based study. Acta Oncol 50:1015–26. doi:10.3109/0284186X.2011.577446
14. Bidstrup PE, Christensen J, Mertz BG, Rottmann N, Dalton SO, Johansen C (2015) Trajectories of distress, anxiety, and depression among women with breast cancer: looking beyond the mean. Acta Oncol 54:789–96. doi:10.3109/0284186X.2014.1002571
15. Zigmond AS, Snaith RP (1983) The Hospital Anxiety and Depression Scale. Acta Psychiatr Scand 67:361–70. doi:10.1111/j.1600-0447.1983.tb09716.x
16. Lundh MH, Lampic C, Nordin K, Ahlgren J, Bergkvist L, Lambe M et al (2013) Changes in health-related quality of life by occupational status among women diagnosed with breast cancer—a population-based cohort study. Psychooncology 22:2321–31. doi:10.1002/pon.3285
17. Bardwell WA, Natarajan L, Dimsdale JE, Rock CL, Mortimer JE, Hollenbach K et al (2006) Objective cancer-related variables are not associated with depressive symptoms in women treated for early-stage breast cancer. J Clin Oncol 24:2420–7. doi:10.1200/JCO.2005.02.0081
18. Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ et al (1993) The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst 85:365–76. doi:10.1093/jnci/85.5.365
19. Brown LF, Kroenke K (2009) Cancer-related fatigue and its associations with depression and anxiety: a systematic review. Psychosomatics 50:440–7. doi:10.1016/S0033-3182(09)70835-7
20. Jacobsen PB, Weitzner MA (2003) Evaluating the relationship of fatigue to depression and anxiety in cancer patients. In: Bruera E, Portenoy RK (eds) Issues in palliative care research. Oxford University Press, New York, pp 127–50
21. Okuyama T, Akechi T, Kugaya A, Okamura H, Imoto S, Nakano T et al (2000) Factors correlated with fatigue in disease-free breast cancer patients: application of the cancer fatigue scale. Support Care Cancer 8:215–22. doi:10.1007/s005200050288
22. Levy MR (2008) Cancer fatigue: a neurobiological review for psychiatrists. Psychosomatics 49:283–91. doi:10.1176/appi.psy.49.4.283
23. Fors EA, Bertheussen GF, Thune I, Juvet LK, Elvsaas IKØ, Oldervoll L et al (2011) Psychosocial interventions as part of breast cancer rehabilitation programs? Results from a systematic review. Psychooncology 20:909–18. doi:10.1002/pon.1844
24. Mattsson S, Alfonsson S, Carlsson M, Nygren P, Olsson E, Johansson B (2013) Internet-based stepped care with interactive support and cognitive behavioral therapy for reduction of anxiety and depressive symptoms in cancer—a clinical trial protocol. BMC Cancer 13(1):1
25. Berger AM, Gerber LH, Mayer DK (2012) Cancer-related fatigue. Cancer 118:2261–9. doi:10.1002/cncr.27475
26. Servaes P, Verhagen S, Bleijenberg G (2002) Determinants of chronic fatigue in disease-free breast cancer patients: a cross-sectional study. Ann Oncol 13:589–98. doi:10.1093/annonc/mdf082
27. Kangas M, Bovbjerg DH, Montgomery GH (2008) Cancer-related fatigue: a systematic and meta-analytic review of non-pharmacological therapies for cancer patients. Psychol Bull 134:700. doi:10.1037/a0012825
28. Benjamin HJ, Campos MPO (2014) Cancer-related fatigue. In: Mostofsky DI (ed) The handbook of behavioral medicine. Wiley & Sons Ltd, Oxford, pp 105–124. doi:10.1002/9781118453940.ch6