ann. behav. med. (2008) 36:141–148
DOI 10.1007/s12160-008-9061-8

ORIGINAL ARTICLE

Course of Distress in Breast Cancer Patients, Their Partners, and Matched Control Couples

Chris Hinnen, Ph.D. · Adelita V. Ranchor, Ph.D. · Robbert Sanderman, Ph.D. · Tom A. B. Snijders, Ph.D. · Mariët Hagedoorn, Ph.D. · James C. Coyne, Ph.D.

Published online: 17 September 2008

Abstract
Background Previous studies offer a limited perspective on the dynamic course of distress in cancer patients and their partners, owing to a restricted number of assessment points and the absence of comparison controls drawn from the general population.
Purpose This study investigated the course of distress among breast cancer patients and their partners (N=92 couples) in comparison to matched control couples (N=64). Furthermore, the influence of neuroticism on distress was investigated.
Method The Hospital Anxiety and Depression Scale was administered nine times over a 12-month period, and neuroticism was assessed at the beginning of the study using the Eysenck Personality Questionnaire.
Results Multilevel analyses revealed that patients were more distressed during the first 15 months after diagnosis than nonpatients. A significant portion of the distress that could not be explained by the cancer experience was explained by neuroticism.
Conclusion Differences in distress between patients and comparison-control women are relatively small and decreased over time, while distress in male partners was not elevated in comparison to their controls.

Keywords Anxiety · Depression · Neuroticism · Multi-level analysis · Intervention

C. Hinnen · A. V. Ranchor · R. Sanderman · M. Hagedoorn · J. C. Coyne
Department of Health Sciences,
Graduate School for Health Research,
University Medical Center Groningen, University of Groningen,
Groningen, The Netherlands

T. A. B. Snijders
Department of Sociology, University of Groningen,
Groningen, The Netherlands

T. A. B. Snijders
Department of Statistics, University of Oxford,
Oxford, UK

J. C. Coyne
School of Medicine, University of Pennsylvania,
Philadelphia, PA, USA

A. V. Ranchor (✉)
Department of Health Sciences,
University Medical Center Groningen, University of Groningen,
P.O. Box 196, 9700 AD Groningen, The Netherlands
e-mail: a.v.ranchor@med.umcg.nl

Introduction

Diagnosis and treatment of breast cancer are life-altering experiences that may evoke considerable emotional distress in patients and their intimates [1, 2]. Feelings of anxiety and depression may be understandable reactions to the changes imposed by the illness and its treatment—threat of death, loss of mobility, tiredness, or changes in social and leisure activities. However, when high levels of distress persist over time, they may become the focus of clinical concern. Claims are widespread that cancer may induce enduring high levels of distress in patients and partners [3]. In accordance, the design of clinical trials testing interventions for the reduction of psychological distress in couples facing cancer—in either patients or their partners—has typically been guided by the implicit assumption that, as a population, unselected couples or individuals facing cancer are sufficiently distressed to register a benefit for intervention [4]. However, recruitment of patient samples lacking in sufficient distress to respond positively has been offered as a post hoc explanation of null findings in

intervention trials [5, 6]. The risk is that psychosocial interventions will be labeled as inefficacious when they would have been shown to be efficacious when administered to a sample with greater distress [4]. Thus, statements that a substantial portion of the cancer patients suffer from enduring distress *in response to* diagnosis and treatment of breast cancer may be premature or at least in need of greater precision, particularly given the cross-sectional design and lack of a control-comparison group [7, 8] in most descriptive studies. Indeed some studies have even found that the distress levels in women with breast cancer are comparable to the levels of distress found in primary-care samples or individuals of the general population [2, 8–11]. In general, based on such comparisons, sustained elevations in distress in couples facing cancer appear to be moderate, at best [12].

Studies that do follow breast cancer patients over time [13–15] show a decrease in distress within the first months after the diagnosis (see, for an exception, [2]). Although these studies offer valuable insights into levels of distress over time, they typically make use of a restricted number of assessment points, limiting the understanding that they provide of the dynamic course of distress. Moreover, there is a lack of agreement concerning when to expect declines or increases in distress. For example, some claim an initial increase following diagnosis that persists during treatment [16], whereas others indicate that the major threat of distress lies at the end of treatment [17]. Furthermore, in the absence of matched comparison controls, it is not clear whether and when distress levels decrease to the levels found in the general population. The few longitudinal studies that include comparison controls offer inconsistent results [2, 7]. Analyses of the only longitudinal study investigating distress in couples facing breast cancer and comparison controls did not take into account the correlated, nonindependent nature of distress scores within individuals over time and between individuals within couples [2]. Ignoring that nonindependence of distress scores—i.e., accepting each observation of a distress score as independent—may bias standard errors of statistical tests, increasing type-I error rates and inflating the statistical significance of the results.

Distress levels found in cancer patients and their partners may not only simply be the result of illness-related factors [18, 19], but may also be explained by personality or background factors [20]. If a substantial portion of distress is not explained by cancer experiences but by enduring personality characteristics, this may have implications for interventions, as there would be a lower expectation for alleviating this distress with formal cancer-specific interventions [21, 22]. A candidate personality trait is the concept of neuroticism, one of the basic dimensions in the Big Five model of personality. Neuroticism is indicative of emotional instability, increasing people's proneness to distress in general and in situations of stress specifically [23]. Its stability has been established across the life span, indicating that neuroticism is a relatively stable trait that shows only minor gradual changes over time [24, 25]. Moderate to strong correlations have been found between neuroticism and distress, raising discussion about possible contamination. Several studies [25, 26] have shown that, while distress was susceptible to change as a result of life events, neuroticism remained stable, favoring its position as a trait. In addition, it was found that neuroticism is a predictor of the distress induced by life events, supporting its importance when examining distress (e.g., [21, 27–29]). There are some indications that it is also predictive of distress in persons with cancer [30–31]. Taken together, these results point at the importance of taking neuroticism into account when examining the course of distress in cancer patients.

The aim of the present study is to extend previous research by investigating the level and course of distress in women with breast cancer and their partners in comparison to matched controls from the general population, making use of nine assessment points between 3 and 15 months after diagnosis. This number of assessments will provide more detailed insight into fluctuations in distress over time, allowing for fewer assessment points in future observational trials and also providing a guide for the choice of appropriate times for psychosocial interventions. A recent meta analysis suggests that we should aim for addressing the short-term burden of distress for some cancer patients, rather than expecting long-term effects [32]. We seek to give more precision to this suggestion. Patients and partners were investigated both as individuals and as part of a couple, and the nonindependence of scores over time within individuals and between individuals within couples was handled appropriately by means of multilevel analysis. Moreover, distress not explained by cancer was expected to be partly explained by neuroticism.

Method

Study Design and Participants

Participants were recruited from five hospitals in the Netherlands. Inclusion criteria were: living with a partner, willingness by both female patients and male partners to participate in the study, woman's age between 30 and 75 years, prognosis of at least 15 months survival, no previous cancer history for either the women or partner, and both being fluent in Dutch. In a procedure required by the hospital Institutional Review Board, women received a letter from their physician inviting the couple to participate

in the study. Women interested were encouraged to enlist their partners and to mail back consent forms. After approximately 4 weeks, couples who did not return the consent form were contacted by the study team with a letter reminding them about the study. In addition, comparison-control couples were selected from a community sample, matched on age and geographical region. An exclusion criterion for both female and male controls was a history of cancer. Control couples enrolled in the study only if both partners were willing to participate.

Data Collection

After recruitment, participants were assessed nine times. The first assessment took place 3 months after diagnosis, followed by questionnaires every 6 weeks. A total of 284 patient couples were asked to consider participation. In the end, 92 couples (a response rate of 32%) participated in the study of which almost all (94%) remained in the study. This response rate reflects (a) the burden of the intensive design of the study as patients were asked to complete a broad range of questionnaires, and (b) perhaps more importantly, the consent procedure required by the Institutional Review Board and the initiative it required from the patients to enroll in the study. Nonetheless, this percentage is comparable to what has been found in some well-resourced studies investigating couples [33, 34]. The main reason (31%) for not participating was that couples indicated that participating was too great a burden. In addition, 28% of the couples were simply not interested; in 15% of the cases, a partner was not willing to participate; 10% indicated that they wanted to close the cancer history; and another 16% of the couples gave other reasons for not participating in the study.

Control couples were selected from a large community sample (N=2500) of women aged between 30 and 75 years living with a partner, taken from the registries of the municipalities in areas covered by the participating hospitals. After inclusion of a new patient couple, a matching control female of this sample along with her male partner were approached by a mailed letter containing information about the study for participation. Control couples had to respond by mail when they wanted to participate. When a control couple refused, a similar procedure was applied until a matching control couple was found. When a sufficiently large sample of control couples was derived, the matching procedure was stopped, while the patient inclusion continued. The matching was continuously checked at group level to ascertain that the two groups were adequately matched. In total, N=347 control females were approached for participation, of whom N=66 were enrolled along with their partners, indicating a participation rate of 19%.

Measures

Distress

Participants completed the Hospital Anxiety and Depression Scale (HADS) [35, 36], a 14-item self-report scale assessing feelings of anxiety and depressive symptoms over the last week on a four-point scale (0 to 3). In the present study, the total score was calculated with a higher score representing more distress. Cronbach's alpha for the total score, averaged over nine assessments, was high, 0.91 for patients, 0.90 for partners, 0.89 for comparison-control women, and 0.85 for comparison-control men, supporting the use of the total scale in this study.

Neuroticism

A short, 12-item version of the widely used Eysenck Personality Questionnaire [37] was used to assess neuroticism at T1 (e.g., "Does your mood often go up and down?" or "Are your feelings easily hurt?"). Response alternatives were "yes" or "no," and scores ranged from 0 to 12. Cronbach's alpha was 0.83 for patients, 0.84 for partners, 0.84 for comparison-control women, and 0.83 for comparison-control men.

Analysis

Patient characteristics and the association between self-reported treatment characteristics (i.e., being in treatment and type of treatment: chemo-, radio-, hormonal-, or alternative therapy), cancer stage, and distress were explored. Furthermore, multilevel analysis [38], also called hierarchical linear modeling, was used to investigate the differences in level and course of distress between patients, partners, and comparison controls. This is a generalization of regression analysis designed for nested data sets. In our data set, repeated measurements were nested in individuals, and individuals were nested in couples. The correlation patterns followed from this nesting structure. Thus, the multilevel analysis accounted simultaneously for the inter-correlation of distress scores between partners of a dyad and for the longitudinal character of the data [39]. Analyses were carried out using MLwiN [40]. Since MLwiN allows the number of observations per assessment to differ, missing data were not imputed. A sequence of models was fitted, and the random effects of these models were tested using deviance statistics.

First, we investigated the distribution of the variance in distress across the different levels on the basis of the interclass correlation coefficient of the unconditional model (model 1). Next, we tested whether differences in distress could be explained by being male versus female, by being

part of a patient couple versus a comparison-control couple, and by being a patient versus a nonpatient (model 2). Furthermore, time since diagnosis was entered as a potential source of variation (model 3). Graphical analysis of the mean distress scores of all participants at the different moments in time showed that the distress trajectory was best represented by a linear equation (i.e., a steady decrease in distress over time), with a discrepancy from this linear effect at T1. To test this discrepancy, T1 distress was included in the model as a dummy variable, representing distress at 3 months after diagnosis versus later assessments. Differences between individuals and between couples in the course of distress were represented by random coefficients for time and the dummy variable for T1. To achieve a good model fit, we tested whether the effects of these random effects varied between individuals and whether they differed between couples, and the significant random effects were retained. Next, interactions between groups and the two time variables were tested (model 4). We also investigated the effect of neuroticism on distress and whether entering neuroticism into the model changed earlier results (model 5). Finally, we investigated the level and rate of distress in the different groups at the end of the study (T9). In this analysis, distress at T9 is the dependent variable.

Results

Descriptive Statistics

Participants' characteristics are presented in Table 1. Patients and partners were properly matched with comparison controls on age, employment status, and education level. All women with breast cancer received surgery, and 90% (N=83) received additional treatment (i.e., radiotherapy and/or chemotherapy and/or hormonal therapy). Sixteen patients (17%) were diagnosed with stage 1, 69 (75%) with stage 2, and seven (8%) with stage 3 breast cancer. Among patients, there was no association of stage, active treatment status, and type of treatment at the first and last assessment with level of distress, and so these variables were excluded from further analysis. In Fig. 1, distress trajectories of patients, partners, and comparison controls are shown. The distress trajectory of patient and comparison-control couples in Fig. 1 is the mean distress score at the couple level.

Level and Course of Distress

The total variance in distress was partitioned over the three levels; couples, individuals, and time. The amount of variance was assessed using interclass correlation coefficient of the unconditional model (i.e., a model without explanatory variables). The unconditional model (model 1) showed that a total of 26% of the variance in distress was at the couple level (10.96/10.96+15.66+15.46), 37% at the individual level, and 37% at the time level, which indicates that distress varies between couples, between individuals, and over time.

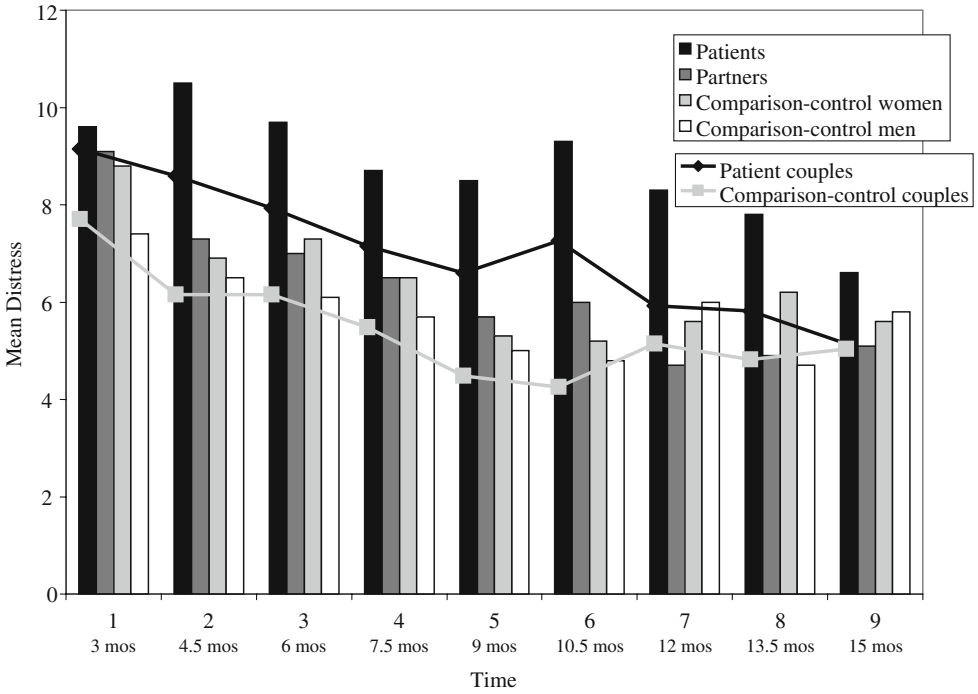
Next, we entered explanatory variables in four sequential steps. First, we entered group into the equation (i.e., male, patient-couple, patient). This model (model 2) fitted the data better than the model without explanatory variables (χ^2=23, df=4, p<0.001) and showed that the average distress score of comparison-control women was 6.62 (SE= 0.65) and that patients were more distressed than comparison-control women, β=1.78 (SE=0.91), p<0.05. Men were not significantly less distressed than women, β= −0.71 (SE=0.70), p>0.05, and patient couples (aggregated scores for patients and partners) were not significantly more distressed than comparison-control couples, β=0.64 (SE= 0.85), p>0.05.

Table 1 Descriptive characteristics

	Patients	Comparison-control women	Partners	Comparison-control men
Mean age (SD)	53 (9.3)	53 (10.0)	54 (9.4)	56 (9.9)
Employment (yes)	44 (49%)	32 (50%)	62 (67%)	43 (67%)
Education level				
Lower level	28 (30%)	18 (28%)	28 (30%)	10 (16%)
Secondary level	40 (44%)	24 (38%)	33 (36%)	22 (34%)
Higher level	24 (26%)	22 (34%)	31 (34%)	32 (50%)
Patients		at T1	at T9	
In treatment (yes)		59 (64%)[a]	28 (33%)[a]	
Chemotherapy		27 (46%)[b]	0	
Radiotherapy		22 (37%)[b]	0	
Hormonal therapy		13 (22%)[b]	24 (86%)[b]	
Alternative therapy		4 (7%)[b]	7 (25%)[b]	

[a] Percentage of the total number of patients included in the study at T1 (N=92) and T2 (N=84)
[b] Percentage of the number of people in treatment

Fig. 1 Course of distress



Second, we entered time, both as a linear equation coefficient and as a dummy variable for T1 (model 3). Since the effect of time on distress may differ between individuals and couples, we allowed the time variables to vary randomly at both the couple and individual level. Deviance tests revealed that time as a linear equation had a random effect at the couple level (χ^2=13, *df*=1, p<0.001) but not at the individual level (χ^2=3, *df*=1, p>0.05), indicating that individuals within couples showed rather similar distress trajectories, while couples were more distinct. Time at T1 had a random effect at both the individual (χ^2=25, *df*=1, p<0.001) and the couple level (χ^2=30, *df*=1, p<0.001), indicating that large differences in initial distress scores existed between couples and between individuals. This model fitted the data significantly better than the model without explanatory time variables (χ^2=255, *df*=5, p<0.001). The fixed part of the model showed that participants reported significantly more distress at T1, β=0.72 (SE=0.35), p<0.05, and that distress decreased over time, β=−0.29 (SE=0.05), p<0.001.

Third, interactions between group and the two time variables were entered into the equation and the significant fixed effects were retained (model 4). Patient couples showed a stronger decrease in distress over time, β=−0.23 (SE=0.09), p<0.05, than comparison-control couples. Patients scored relatively low on distress at T1, β=−2.33 (SE=0.62), p<0.001, in comparison to their subsequent scores. This finding shows that the discrepancy in the steady decrease in distress over time observed at T1, as shown in the preliminary graphical analyses, was due to the fact that patients reported greater distress at several points other than T1. The model with the two significant interaction effects fitted the data better than the previous model (χ^2=16, *df*=2, p<0.001).

Fourth, we entered neuroticism into the equation at the individual level (model 5). Results showed that a large part of the variation in distress between individuals, which was not explained by group and time, was explained by neuroticism (χ^2=301, *df*=2, p<0.001). Individuals who scored higher on neuroticism were more distressed, β=0.90 (SE=0.08), p<0.01. This association was not qualified by group but was qualified by time. That is, the association between neuroticism and distress decreased over time, β=−0.03 (SE=0.01), p<0.001. See Table 2.[1]

Finally, we investigated the results at the end of the study (i.e., T9). Results showed that, 15 months after the diagnosis, patients were more distressed than comparison-control women, β=1.94 (SE=0.75), p<0.01.[2]

[1] To test whether the skewness of the continuous distress measure impacted the results, the residual variance was allowed to differ between patients and nonpatients. These additional analyses showed no differences in the effects tested.

[2] A separate investigation of the anxiety and depression subscales of the HADS produced a similar pattern of the results as the full scale with only two exceptions. That is, males scored significantly lower on anxiety than women β=−0.98 (SE=0.42), p<0.05, but no differences between men and women were found in depressive symptoms, β=0.26 (SE=0.35), p>0.05. Moreover, overall, patients were not found to report more anxiety, β=0.72 (SE=0.55), p>0.05, but they were found to report more depressive symptoms than control women β=1.06 (SE=0.45), p<0.05.

Table 2 Predictors of distress

	Distress as Continuous variable									
	Model 1		Model 2		Model 3		Model 4		Model 5	
	β	SE	β	SE	β	SE	β	SE	β	SE
Fixed effect										
Intercept	7.17***	0.36	6.62***	0.65	7.91***	0.70	7.08***	0.74	6.71***	0.65
Male			−0.71	0.70	−0.79	0.69	−0.80	0.69	0.16	0.56
Patient couple			0.64	0.85	0.38	0.80	1.53	0.89	1.35	0.76
Patient			1.78*	0.91	1.45	0.90	2.02*	0.92	1.94**	0.75
Time					−0.29***	0.05	−0.15*	0.07	−0.16*	0.07
Time_1[a]					0.72*	0.35	1.40***	0.39	1.40***	0.40
Patient × Time_1							−2.33***	0.62	−2.36***	0.63
Patient couple × Time							−0.23*	0.09	−0.22*	0.09
Neuroticism									0.90***	0.08
Neuroticism × Time									−0.03**	0.01
Random effect										
Couple level										
Intercept[b]	10.96***	2.45	11.34***	2.35	21.45***	3.86	20.97***	3.81	18.82***	3.21
Time					0.25***	0.05	0.24***	0.05	0.24***	0.05
Time_1					3.40	2.49	3.88	2.41	4.68	2.49
Individual level										
Intercept[b]	15.66***	2.00	13.75***	1.78	14.91***	1.90	14.84***	1.89	9.33***	1.27
Time_1					9.54**	2.7	7.87**	2.56	7.60**	2.54
Time level										
Intercept[b]	15.46***	0.45	15.46***	0.45	12.37***	0.40	12.37***	0.40	12.36***	0.41

Significance was tested two-tailed
*$p<0.05$; **$p<0.01$; ***$p<0.001$
[a] Time_1=dummy variable of distress at T1
[b] The variance in distress at the Couple, Individual and Time levels

Discussion

Results showed that women with breast cancer had enduring but only modestly higher levels of distress than comparison-control women. Although the level of distress decreased over time, 15 months after diagnosis, patients were still more distressed than comparison-controls and also more than their partners. Peak levels of distress followed by a decline thereafter were observed at T2 (during adjuvant treatment) and T6 (after end of treatment). While some researchers claim an initial increase in distress after diagnosis that persists during treatment [16], our findings indicate a decline after treatment. It also corroborates the claim of an increase after end of treatment [17], although this change seems to be only transient.

A possible explanation for the relatively high levels of distress at T2 and T6 might be found in treatment characteristics. In the Netherlands, across hospitals, the same standardized treatment protocol for breast cancer patients is applied [41]. Almost all women undergo surgery within 2–4 weeks after diagnosis followed by adjuvant treatment in more than 80% of the cases. Adjuvant therapy includes radiation therapy and/or chemotherapy. Radiation therapy will take approximately 7 weeks while chemotherapy may take more than 12 weeks. Taking into account an average 4-week waiting period after the procedure, treatment intensity will be at its peak around T2 (approximately 18 weeks after diagnosis). This may explain the relatively high distress in patients at this assessment point. Six months later, patients will have ended treatment which may explain the relatively high levels of distress in patients at T6. Ending treatment might be associated with an increase in distress as people may lose the security associated with being in treatment and in regular contact with healthcare professionals it provides [42]. Future studies may investigate this possibility further by paying more attention to the emotional impact of specific illness events (see for an example, [14]).

The findings in the present study may have implications for intervention studies. First, it could be concluded that, although women with breast cancer reported more distress than comparison controls, over time, women with breast cancer and comparison controls become more similar. Consequently, trials should be implemented relatively soon after diagnosis (e.g., within the first 6 months after diagnosis) with a limited time to follow-up, as otherwise

effects of the intervention will dissipate with time and would require patients to become less distressed than members of the general community in order for an effect to be registered. This finding is in accordance with a recent meta-analysis suggesting that we should aim for addressing the short-term burden of distress for some cancer patients rather than expecting long-term effects [32].

The finding that differences in distress between patients and comparison-control women are small and decrease over time also indicates that interventions aimed at alleviating distress would require a very large number of unselected patients to detect a treatment effect relative to the decrease in distress that is likely to occur without a formal intervention. Therefore, instead of treating all patients, it may be much more effective to pre-select patients with elevated distress scores, consistent with recent recommendations [43, 44]. The few studies to date that do find a treatment by group effect [45, 46] tended to pre-select patients with elevated distress scores. In both of these studies, patients were selected for heightened distress, and both the treatment and control condition had at least 50 patients each. However, the bulk of the psychological interventions for cancer patients do not pre-select clinically distressed patients and have fewer than 50 patients in the small condition [47]. Therefore, most psychological interventions studied in oncology may be underpowered and otherwise target an unselected sample of patients unlikely to register an effect. A consequence may be that many interventions are dismissed as lacking in efficacy that might have proven efficacious in a sufficiently powered trial with patients pre-selected for distress [48].

Furthermore, the present results suggest that partners of women with breast cancer are not a suitable target for intervention studies directed at alleviating their distress, as they were not found to be more distressed than male comparison controls. It might be more useful to engage partners in efforts to address relationship issues or as collaborators in efforts to reduce the distress in women with breast cancer [29]. Finally, the finding that neuroticism was a strong predictor of psychological distress may have implications for interventions, since distress experienced by individuals scoring high on neuroticism may be less responsive to interventions [26, 27].

Our study has some distinct strengths, such as a longitudinal design with multiple assessments, the inclusion of patients and partners as well as comparison controls, and the use of a more sophisticated method of analysis, but it also has some notable limitations. The response rate in the patient group was relatively low. This may have affected the findings, in particular, the level of distress among patient couples. The more distressed couples may have been more likely to refuse participation, causing an underestimation of the actual level of distress in the larger pool of patient couples. We strongly suspect that the response rate was affected by the conditions of recruitment imposed by the Institutional Review Board (e.g., not being allowed to offer an even minimal financial incentive to patients or to approach patients directly, thus leaving the initiative to them). Given that other studies might increasingly face similar constraints, it is important to investigate whether such recruitment strategies actually yield different levels in observed distress than what might be found in a population that investigators were able to access directly. Nonetheless, it should be noted though that the level and course of distress found in the present study of partnered patients are in line with other studies using the HADS in women with breast cancer [9, 10, 49, 50].

Different mechanisms likely underlie the recruitment rate in the control group. They might have lacked the motivation that their participation would contribute to an understanding of how the predicament of women suffering from breast cancer and their partners adjust to the disease. This was underscored by a more impersonal recruitment strategy, unconnected with a setting in which they were receiving any treatment. In general, characteristics of comparison control patients leading to their recruitment and retention in studies may differ from those of medically ill patients, a reasonable assumption that deserves further investigation.

Acknowledgment This research was funded by a grant from the Dutch Cancer Society (NKB RUG 99–2002).
The authors would like to thank the following hospitals for their collaboration in the data collection: Martini Ziekenhuis Groningen, Nij Smellinghe Drachten, Wilhelmina Ziekenhuis Assen, Universitair Medisch Centrum Groningen, and Medisch Centrum Leeuwarden.

References

1. Hagedoorn M, Buunk BP, Kuijer RG, Wobbes T, Sanderman R. Couples dealing with cancer: role and gender differences regarding psychological distress and quality of life. *Psychooncology.* 2000; 9: 232–242.
2. Northouse LL, Templin T, Mood D, Oberst M. Couples' adjustment to breast cancer and benign breast disease: A longitudinal analysis. *Psychooncology.* 1998; 7: 37–48.
3. Bultz BD, Carlson LE. Emotional distress: The sixth vital sign in cancer care. *J Clin Oncol*. 2005; 23: 6440–6441.
4. Coyne JC, Lepore SJ, Palmer SC. Efficacy of psychosocial interventions in cancer care: Evidence is weaker than it first looks. *Ann Behav Med*. 2006; 32: 104–110.
5. Sandgren AK, McCaul KD. Long-term telephone therapy outcomes for breast cancer patients. *Psychooncology.* 2007; 16: 38–47.
6. Classen C, Kraemer H, Blasey C, et al. Supportive-expressive group therapy for primary breast cancer patients: a randomized prospective multicenter trial. *Psychooncology.* 2008; 17: 438–447.

7. Andersen BL, Anderson B, deProsse C. Controlled prospective longitudinal study of women with cancer: II. Psychological outcomes. *J Consult Clin Psychol*. 1989; 57: 692–697.
8. Fechner-Bates S, Coyne JC, Schwenk TL. The relationship of self-reported distress to depressive disorders and other psychopathology. *J Consult Clin Psychol*. 1994; 62: 550–559.
9. Groenvold M, Fayers PM, Sprangers MAG, et al. Anxiety and depression in breast cancer patients at low risk of recurrence compared with the general population: A valid comparison? *J Clin Epidemiol*. 1999; 52: 523–530.
10. Osborne RH, Elsworth GR, Sprangers MAG, Oort FJ, Hopper JL. The value of the Hospital Anxiety and Depression Scale (HADS) for comparing women with early onset breast cancer with population-based reference women. *Qual Life Res*. 2004; 13: 191–206.
11. Coyne JC, Palmer SC, Shapiro PJ, Thompson R, DeMichele A. Distress, psychiatric morbidity, and prescriptions for psychotropic medication in a breast cancer waiting room sample. *Gen Hosp Psych*. 2004; 26: 121–128.
12. Hagedoorn M, Sanderman R, Bolks N, Tuinstra J, Coyne JC. Distress in couples coping with cancer: A meta-analysis and critical review of role and gender effects. *Psychol Bull*. 2008; 134: 1–30.
13. Koopman C, Butler LD, Classen C, et al. Traumatic stress symptoms among women with recently diagnosed primary breast cancer. *J Trauma Stress*. 2002; 15: 277–287.
14. Heim E, Valach L, Schaffner L. Coping and psychosocial adaptation: Longitudinal effects over time and stages in breast cancer. *Psychosom Med*. 1997; 59: 408–418.
15. Greimel E, Thiel I, Peintinger F, Cegnar I, Pongratz E. Prospective assessment of Quality of Life of female cancer patients. *Gynecol Oncol*. 2002; 85: 140–147.
16. Epping-Jordan JE, Compas BE, Osowiecki DM, et al. Psychological adjustment to breast cancer: Processes of emotional distress. *Health Psychol*. 1999; 18: 315–326.
17. Stanton AL, Ganz PA, Rowland JH, et al. Promoting adjustment after treatment for cancer. *Cancer*. 2005; 104: 2608–2613.
18. Burgess C, Cornelius V, Love S, et al. Depression and anxiety in women with early breast cancer: Five year observational cohort study. *BMJ*. 2005; 330: 702–705.
19. Wong-Kim EC, Bloom JR. Depression experienced by young women newly diagnosed with breast cancer. *Psychooncology*. 2005; 14: 564–573.
20. Bardwell WA, Natarajan L, Dimsdale JE, et al. Objective cancer-related variables are not associated with depressive symptoms in women treated for early-stage breast cancer. *J Clin Oncol*. 2006; 24: 2420–2427.
21. Cameron LD, Petrie KJ, Ellis CJ, Buick D, Weinman JA. Trait negative affectivity and responses to a health education intervention for myocardial infarction patients. *Psychol Health*. 2005; 20: 1–18.
22. Jang Y, Clay OJ, Roth DL, Haley WE, Mittelman MS. Neuroticism and longitudinal change in caregiver depression: impact of a spouse-caregiver intervention program. *Gerontologist*. 2004; 44: 311–317.
23. Ormel J, Wohlfarth T. How neuroticism, long-term difficulties and life situation change influence psychological distress—a longitudinal model. *J Pers Soc Psychol*. 1991; 60: 744–755.
24. Terracciano A, McCrae RR, Brant LJ, Costa PT. Hierarchical linear modeling analyses of the NEO-PI-R scales in the Baltimore longitudinal study of aging. *Psychol Aging*. 2005; 20: 493–506.
25. Ormel J. Neuroticism and well-being inventories—measuring traits or states. *Psychol Med*. 1983; 13: 165–176.
26. Costa PT, Herbst JH, McCrae RR, Siegler IC. Personality at midlife: stability, intrinsic maturation, and response to life events. *Assessment*. 2000; 7: 365–378.
27. Boland A, Cappeliez P. Optimism and neuroticism as predictors of coping and adaptation in older women. *Pers Individ Differ*. 1997; 22: 909–919.
28. Gunthert KC, Cohen LH, Armeli S. The role of neuroticism in daily stress and coping. *J Pers Soc Psychol*. 1999; 77: 1087–1100.
29. Kokkonen M, Pulkkinen L. Extraversion and neuroticism as antecedents of emotion regulation and dysregulation in adulthood. *Eur J Pers*. 2001; 15: 407–424.
30. Ranchor AV, Sanderman R, Steptoe A, et al. Pre-morbid predictors of psychological adjustment to cancer. *Qual Life Res*. 2002; 11: 101–113.
31. Millar K, Purushotham AD, McLatchie E, George WD, Murray GD. A 1-year prospective study of individual variation in distress, and illness perceptions, after treatment for breast cancer. *J Psychosom Res*. 2005; 58: 335–342.
32. Osborn RL, Demoncada AC, Feuerstein M. Psychosocial interventions for depression, anxiety, and quality of life in cancer survivors: Meta-analyses. *Int J Psychiatry Med*. 2006; 36: 13–34.
33. Manne SL, Ostroff JS, Winkel G, et al. Couple-focused group intervention for women with early stage breast cancer. *J Consult Clin Psychol*. 2005; 73: 634–646.
34. Manne SL, Ostroff J, Norton TR, et al. Cancer-related relationship communication in couples coping with early stage breast cancer. *Psychooncology*. 2006; 15: 234–247.
35. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scan*. 1983; 67: 361–370.
36. Spinhoven Ph, Ormel J, Sloekers PPA, et al. A validation study of the Hospital Anxiety and Depression Scale (HADS) in different groups of Dutch subjects. *Psychol Med*. 1997; 27: 363–370.
37. Eysenck SBG, Eysenck HJ, Barrett P. A revised version of the Psychoticism scale. *Pers Indiv Differ*. 1985; 6: 21–29.
38. Snijders TAB, Bosker RJ. *Multilevel analysis: An introduction to basic and advanced multilevel analysis*. London: Sage; 1999.
39. Gibbons RD, Hedeker D, Elkin I, et al. Some conceptual and statistical issues in analysis of longitudinal psychiatric data: Application to the NIMH treatment of depression collaborative research-program dataset. *Arch Gen Psychiatry*. 1993; 50: 739–750.
40. Rasbash J, Steele F, Browne W, Prosser B. A user's guide to MLwiN version 2.0. University of Bristol; 2005.
41. Nationaal Borstkanker Overleg Nederland. Richtlijn behandeling van het mammacarcinoom [Treatment protocol mamma carcinoma]. Alphen aan den Rijn: Van Zuiden Communications BV; 2002.
42. Cohen L, De Moor C, Amato RJ. The association between treatment-specific optimism and depressive symptomathology in patients enrolled in a phase I cancer clinical trial. *Cancer*. 2001; 91: 1949–1955.
43. Coyne JC, Lepore SJ. Rebuttal. The black swan fallacy in evaluating psychological interventions for distress in cancer patients. *Ann Behav Med*. 2006; 32: 115–118.
44. Linden W, Satin JR. Avoidable pitfalls in behavioral medicine outcome research. *Ann Behav Med*. 2007; 33: 143–147.
45. Greer S, Moorey S, Baruch JDR, et al. Adjuvant psychological therapy for patients with cancer: a prospective randomized trial. *BMJ*. 1992; 304: 675–680.
46. Nezu AM, Nezu CM, Felgoise SH, McClure KS, Houts PS. Project Genesis: Assessing the efficacy of problem-solving therapy for distressed adult cancer patients. *J Consul Clin Psychol*. 2003; 71: 1036–1048.
47. Newell SA, Sanson-Fisher RW, Savolainen NJ. Systematic review of psychological therapies for cancer patients: overview and recommendations for future research. *J Natl Cancer Inst*. 2002; 94: 558–584.
48. Lepore SJ, Coyne JC. Psychological interventions for distress in cancer patients: A review of reviews. *Ann Behav Med*. 2006; 32: 85–92.
49. McArdle JMC, George WD, McArdle CS, et al. Psychological support for patients undergoing breast cancer surgery: A randomised study. *BMJ*. 1996; 312: 813–816.
50. Sellick SM, Edwardson AD. Screening new cancer patients for psychological distress using the Hospital anxiety and depression scale. *Psychooncology*. 2007; 16: 534–542.