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ONSET AND RELAPSE OF PSYCHIATRIC DISORDERS FOLLOWING EARLY
BREAST CANCER. A CASE-CONTROL STUDY.

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ABSTRACT

Objective: Our objective is to evaluate the mental status of primary early breast cancer survivors according to DSM-IV criteria, distinguishing new psychiatric diagnosis which started after the cancer diagnosis from relapse. **Methods:** A comparative study of 144 breast cancer survivors and 125 women without previous history of cancer was carried out. Neuropsychiatric symptomatology was assessed retrospectively using standardized psychiatric examinations (MINI, Watson's PTSD Inventory) over three successive periods, "before cancer" (from childhood to three years before the interview), "around cancer event" (the three last years including the time of diagnosis and treatment), and "currently" (the last two weeks). **Results:** Increased rates of anxiety and mood disorders were observed following a diagnosis of breast cancer compared to controls (generalized anxiety disorder (GAD) and major depressive disorder (MDD); 10.4 vs. 1.6% and 19.4 vs. 8.8%, respectively). The cancer disease promoted the development of dysthymia (n=4 new cases/6 two-year prevalent cases) and post-traumatic stress disorder (7/7) and the re-emergence of MDD (n=21 relapses/28 three-year prevalent cases) and GAD (10/15). No improvement in serious mood disorders such as MDD (16.0 vs. 7.2%) and dysthymia (4.2 vs. 0%) was reported at the time of interview, more than 1.75 years (median time) after the cancer surgery, the prevalence being 2-4 times greater in breast cancer survivors than in controls. **Conclusion:** Despite significant advances in treatment, a diagnosis of breast cancer is highly associated with various forms of psychopathology, regardless of the psychiatric history, some of which persist after treatment. These results may assist clinicians in planning mental health care for women with breast cancer.

Key words: breast cancer; **oncology**; **psychiatric disorders**, PTSD, relapse.

PTSD = post-traumatic stress disorder; **MDD** = major depressive disorder; **MDE** = Major depressive episode; **GAD** = generalized anxiety disorder; **MINI** = Mini International Neuropsychiatric Interview

INTRODUCTION

While cancer patients are known to have high rates of psychological morbidity, they are low consumers of psychiatric care, especially for clinically severe disorders [1]. Moreover, patient requests for psychosocial support is not correlated with severity of psychological distress [2]. The failure to detect patients with psychological distress has principally been attributed to lack of communication between health care professionals and patients [3, 4]. This is probably largely based on the shared feeling that anxiety and depression are normal reactions to both, the diagnosis and treatment of cancer, as well as the clinical assumption that such suffering will diminish with time. Although adaptive responses are commonly observed in cancer patients, nonetheless severe disorders such as major depression disorder (MDD), phobia and post-traumatic stress disorder (PTSD) have been observed to occur [5, 6].

To improve the response of health care professionals to psychological suffering in breast cancer, more accurate clinical information is thus required relating to the frequency, type of pathologies occurring at the time of diagnosis and during the treatment and recovery periods, as well as the life-time psychiatric vulnerability of the patients. The adverse long-term effects on mental health of cancer diagnosis and treatment in early stages of cancer are well documented [7, 8], however little is known about the long-term prevalence and risk factors for clinically severe disorders such as MDD, generalised anxiety (GAD), and phobia which are rarely explored. In addition although history of psychiatric disorders is a risk factor for relapses, the life-time prevalence has however not been considered and many studies have been limited by their failure to differentiate incident and chronic cases. Although cancer has been recognized as a traumatic event able to cause PTSD in the DSM-IV [9] and PTSD has been diagnosed in cancer survivors [10-12], the validity of current PTSD criteria in relation to cancer is currently questioned. In particular the question is raised as to whether traumatic reactions observed in relation to cancer are symptomatically the same as those observed in PTSD due to other causes [13-16].

The main objective of this retrospective study was to evaluate the life-time prevalence of a wide range of psychiatric disorders including PTSD, in primary early breast cancer survivors distinguishing onset after the cancer diagnosis from relapses, in comparison with women without a previous history of cancer. We hypothesized that "breast cancer event" would be associated with psychiatric disorders, both during the treatment and beyond the recovery period and could be considered as a traumatic event susceptible of promoting PTSD symptoms, comparable in severity to other traumatic events of the civilian life.

METHODS

Participants

Subjects in the breast cancer group were consecutive referrals to the Regional Cancer Hospital Val d'Aurelle-Paul Lamarque in Montpellier, France, between November 2002 and April 2004. They were aged from 18 to 75 years, subject to clinical follow-up examinations but with no active treatment (except for hormonal treatment). All subjects had received a diagnosis of primary breast cancer (stage I-III, American Joint Committee on Cancer, 1989[17]) one to three years earlier and were in remission. Among the 169 women contacted, 159 accepted to participate (94.1%). Reasons for refusal were, "lack of interest in participating" (n=6), "not having time" (n=1), "being too tired" (n=1) and "not wishing to speak about illness" (n=2).

Women of the "comparison group" were recruited in waiting rooms of specialist breast radiologists between November 2002 and April 2004 in the context of a routine screening program of breast cancer, proposed to French women. The inclusion conditions were being aged from 18 to 75 years, not having experienced any serious life-threatening disease and having a mammography. To recruit women which are socio-demographically comparable to women of the "cancer group", we chose radiologists in the city centre (a University Hospital Lapeyronie and a private specialist breast Radiologist, Center Victor Hugo), and radiologists moving with an equipped truck in rural areas ("Mammobile34"). The women were interviewed after their mammogram was taken. Among the 256 women contacted, 192 accepted to participate (75%). Reasons for refusal were principally "not having time" (n=37). Only 165 women were eligible for the study. Among the 27 non-eligible women, 22 (81.5%) have had a cancer history or received, the day of the examination, information about the possibility to have a breast cancer, 2 (7.4%) were not able to understand the sense of the questions and 3 (11.1%) did not complete the interview.

Of the 324 participant recruited in the study, only women with complete psychiatric evaluation and no missing data for the variables considered in the analysis were included. The present analysis was thus conducted on 269 subjects (144 exposed to breast cancer and 125 non-exposed). At time of interview these women did not differ from those excluded from the analysis in age ($p=0.56$), marital status ($p=0.36$), education ($p=0.83$) or place of residence ($p=0.28$).

Ethics approval for the study was given by the national ethics committee of the National Institute of Health and Medical research (Inserm, France). All participants gave their signed consent for participation of the study.

Diagnosis measures

A standardized psychiatric interview, the Mini International Neuropsychiatric Interview (MINI; DSM-IV criteria; French version 5.00), which has been validated by Lecrubier (1997), was used to investigate both lifetime and current MDD, mania, phobia, GAD, obsessive-

compulsive disorder (OCD), panic disorder with and without agoraphobia, substance abuse-related disorders and current dysthymic disorder [18]. The MINI does not use a hierarchical approach and comorbidity was recorded under each disorder. Psychiatric disorders were retrospectively evaluated on three successive periods, the first period being from childhood to three years before the interview, the second covered the three last years including the time of diagnosis, and the third period corresponded to the present (the last two weeks). These periods thus correspond to a pre-cancer period, the period around diagnosis and treatment, and the current post-treatment period. This interview was administered by only one experienced research nurse who has been initially formed and trained by a psychiatrist.

The Watson's PTSD Inventory (PTSD-I, DSM-III-R; internal consistency, $\alpha=0.92$ and test-retest reliability total score= 0.95) [19] was used to obtain both lifetime and current diagnoses of Post-Traumatic Stress Disorder (PTSD), using the validated French hetero-questionnaire version [20, 21]. The first question identifies past traumatic events spontaneously evoked by the participants. The second question, concerning the most frightening personal experience in the past, was only asked if there was no response to the first question. If this experience is a traumatic event as defined in DSM-IV, the questionnaire is continued focusing on the most traumatic event. This questionnaire thus lists all past traumatic events experienced by the subjects, including cancer when reported as such. The next 17 items correspond to specific DSM-III-R symptoms. Subjects answer each question using a 7-point Likert scale ranging from "1-(never)" to "7-(extremely)". A "4-(commonly)" is considered to be sufficient to meet the relevant DSM symptom criterion. A severity score which is the sum of the symptom rating was also calculated. The main advantage of PTSD-I compared to the PTSD diagnosis of the MINI is its capacity to provide continuous measures of the severity of the disorder for every symptom. In addition, this assessment tool allows measuring partial PTSD. Partial PTSD subjects in this study were defined as endorsing symptoms sufficient to meet criteria for two of three PTSD symptom clusters [22].

Statistical analysis

Comparisons between the two groups were carried out using the Chi-square test or the Fisher's exact test for categorical variables, and Wilcoxon's test for quantitative variables. The associations of breast cancer with mental disorders and MDD, for the 3 years following the cancer diagnosis were adjusted on age, education, marital status, using logistic regression. The results from two-sided tests are reported. Significant level was set to $p \leq 0.05$. Test p values < 0.10 are reported as trends. Data analysis was performed using the v9.1 SAS software.

RESULTS

Subject characteristics

The cancer and comparison groups were found to differ with regard to place of residence ($p=0.02$) but not age at time of interview ($p=0.82$), occupational activities ($p=0.26$), education level ($p=0.08$) or marital status ($p=0.43$) (Table 1). With regard to breast cancer treatment, 30.6% of the women in the cancer group had undergone mastectomy and 69.4% had a tumorectomy with breast conservation (Table 2). Most of these women (94.4%) received post-surgical treatment and were taking hormone chemotherapy at the time of the interview (68.8%; Table 2). Interviews with the women in the cancer group took place after a median period of 1.75 years (range=0.67-3.0) after surgery.

Lifetime and current psychiatric status

Table 3 shows rates of lifetime and current psychiatric disorder (except for PTSD which will be considered separately), during three successive periods, namely pre-cancer period, the period around diagnosis and treatment, and the current post-treatment period. None of the subjects in either of the two groups have a history of substance abuse (data not shown).

The frequency of past psychiatric disorders during the first period did not differ significantly between the two groups, irrespective of the disorder. More than 30% of subjects reported past MDD and 13-23% experienced past GAD or phobia. Regarding lifetime MDD ($n=95$) there was no significant difference between the two groups regarding the number of major depressive episodes (MDE) (median value (Q25-Q75)=2 (1-3) for the two groups; $p=0.68$). This suggests that the two groups are comparable in terms of mental health during the first period before diagnosis.

In contrast during the second period of observation there was a significantly higher rate of MDD (19.4% compared to 8.8%), GAD (10.4% vs. 1.6%) or panic disorder (4.2% vs. 0%) in the cancer group compared to the controls (Table 3). When the first psychiatric diagnoses occurring during the last three years were considered separately (Table 3), no significant difference was found between both groups with regard to MDD, GAD or panic disorder, but there was a trend for an increase in incident cases of phobia ($p=0.06$). This suggests that a cancer diagnosis and/or related treatments can induce both a reactivation of a previous history of MDD or GAD and the development of a first episode of phobia.

At the time of interview, although active treatment had been terminated for several months in the cancer group, current rates of MDD and dysthymic disorder remained significantly increased, whereas rates of current anxiety disorders and particularly GAD were comparable to the comparison group (Table 3).

Higher rates of current anxiety (PTSD, Panic disorder, phobia, OCD and GAD) and current mood disorders (MDD, dysthymic and manic disorders) co-morbidity were observed in the cancer group compared to controls (14.6% vs. 6.4%, $p=0.03$), consistent with the

increase in psychiatric disorders in this group. Considering only women with psychiatric disorders (n=51 in the cancer group and n=38 in the comparison group) the cancer group was observed to be more severely affected (41.2% vs. 21.1% p=0.045; data not shown).

In order to evaluate the effect of cancer on diagnosis of mental disorders we conducted a logistic regression analysis, controlling for age, education and marital status. This multivariate model confirmed that cancer disease is a strong predictor of psychiatric disorders (odds ratio=4.10; 95% confidence interval=2.11-7.92) and MDD (odds ratio=3.27; 95% confidence interval =1.48-7.22) during the three last years period as well as a strong predictor of MDD (odds ratio=2.51; p=0.03, 95% confidence interval, 1.09-5.79) at the time of interview (current period).

PTSD prevalence and severity in breast cancer survivors and controls

Among women who have had cancer, 8.3% (n=12) spontaneously declared this as a traumatic event and 14.8% (n=21) as the most frightening experience of their life. The other most often declared traumatic events both in the comparison and cancer groups were "the sudden, unexpected death of a parent or a loved one" (26.4% and 22.2%, respectively), "a serious accident" (4.8% and 3.5%, respectively), and "violent physical aggression" (1.6% and 3.5%, respectively). Similar patterns were also observed for the most often reported frightening experience in the two groups. "The sudden, unexpected death of a parent or a loved one" was the most commonly reported event (20.8% and 17.4% for the comparison and the cancer groups, respectively) and "a serious accident" (2.4% and 0.7%, respectively) was the second. No significant difference regarding declarations of traumatic events or frightening experiences was observed between the two groups.

During the first period of observation before the cancer diagnosis (from childhood until three years before the interview), the two groups were not found to significantly differ regarding the rate of traumatic events, the prevalence of life-time PTSD and life-time partial PTSD (Table 4). Similarly, the age of life-time PTSD development (median value (Q25-Q75)=40 years (20-50) and 22 years (13-43), for the comparison group and the cancer group, respectively; p= 0.32), or the severity score of the life-time PTSD (median value (Q25-Q75)=64 (56-76) and =60 (55-66), respectively; p=0.68; data not shown) were not significantly different between the two groups. On the other hand, during the second period (last three years), the number of traumatic events reported was significantly higher in the cancer group compared to controls (22.2 vs. 1.6%) as well as past partial PTSD prevalence (5.6 vs. 0.8%). The difference in life-time PTSD prevalence was also nearly significant (p=0.07).

At the time of interview, rates of current PTSD in the cancer group were comparable to that of the comparison group. This absence of difference could not be attributable to an improvement in the PTSD cancer group (six on seven cases of PTSD induced by "cancer event" and diagnosed during the second period are currently persistent) but rather to the

distinct evolution of life-time PTSD between the two groups. Indeed, five on eight cases of PTSD diagnosed in the comparison group during the first period (childhood to 3 years before interview) were persistent at the time of interview but only one on six cases in the cancer group.

Finally to compare the prevalence and severity of PTSD specifically related to cancer as opposed to other traumatic events, we compared women who declared the cancer as a unique traumatic event (n=22) with controls declaring only one traumatic event (n=23); the most frequent traumatic event in the latter group being "the sudden, unexpected death of a parent or a close one" (69.6%). No significant differences in the expression of the three clusters of symptoms (re-experiencing the event, avoidance and numbing or increased arousal) or in the median symptom severity scores were observed between these two subgroups (Table 5). A comparison of symptom expression profiles between these two subgroups did not show any significant qualitative difference (data not shown). There was no significant difference between the two subgroups either for the full PTSD syndrome or for the partial syndrome (Table 5).

DISCUSSION

The present study examined life-time psychiatric diagnoses in breast cancer survivors. At the time of interview, adjuvant chemotherapy or radiation treatment had been completed seven to thirty-one months before. These women no longer felt the acute physical effects of treatments, but were close enough in time to the diagnosis to remember their symptom at this time. Women who had experienced breast cancer reported significantly more psychiatric episodes over the past three years than controls, comparable with regard to age, marital status and past psychiatric history. The most common psychiatric disorders in the cancer group compared to controls were MDD (19.4% vs. 8.8%), GAD (10.4% vs. 1.6%), PTSD (4.9% vs. 0.8%) and panic disorder (4.2% vs. 0%). A nearly significant increase in incident cases of phobia was noticed (3.5% vs. 0%). At the time of interview, 1 to 3 years after diagnosis, current prevalence of mood disorders, MDD (16.0% vs. 7.2%) and dysthymic disorder (4.2% vs. 0%), remained significantly higher in the breast cancer group. The analysis adjusted on potential risk factors (age, education, marital status) confirmed a higher prevalence of total psychiatric diagnosis and MDD during the last three years in cancer group as well as a higher prevalence of MDD at the time of interview.

Over the past decade, several studies have investigated the psychological and psychiatric consequences of diagnosis or treatments of cancers, mainly focusing on the first months of the disease. These studies have reported an MDD prevalence between 8% and 25% [5, 12, 23-29] and a prevalence of anxious disorders between 6% and 50% [12, 27, 28, 30, 31]. The large differences in observed rates are probably related to different methodologies and case identification procedures [8].

There have been very few studies comparing psychiatric prevalence rates in cancer patients with subjects never experiencing a life-threatening illness; most studies referring to psychiatric prevalence rates from the general population. Globally these comparisons suggested higher psychiatric morbidity in cancer patients [7, 27, 32, 33], notably for mood disorders [8], but not systematically [1]. The present study has three original aspects: we have examined prevalence rates of most DSM-IV axis I disorders in women with breast cancer, we have compared cancer subjects with controls who have also undergone the stress of cancer screening, and we have also differentiated three different periods of time for the onset of psychopathology (before diagnosis, the diagnosis and treatment period, at the end of treatment). We have thus shown that the psychiatric disorders occurring in response to a diagnosis of breast cancer can persist for a long time after the period of life-threatening illness and curative cancer treatments, in particular severe mood disorders such as MDD and dysthymic disorder. Our results are in partial disagreement with that of Burgess et al. who did not observe modifications in the prevalence of depressive and/or anxious disorders beyond the first year after diagnosis in a cohort of 222 early breast cancer patients compared to the general population [5]. Our results are, however, compatible with the meta-analysis of Van't Spijker et al. which suggests persistence of depressive disorders and a decrease of anxious disorders in cancer survival patients after 1 year [8].

A further original aspect of our study is the distinction between subjects experiencing a relapse of previous episodes of psychiatric disorder from first episodes. We observed that the diagnosis of cancer promoted not only the re-emergence of MDD (75% of the cases, n=21) and GAD (67% of cases, n=10), but also the development of other psychiatric disorders not previously diagnosed, notably phobia (50% of cases, n=5) and dysthymia (67% of current cases, n=4) and probably panic disorder (50% of cases, n=3), although in this latter case the small numbers does not allow us to demonstrate significance. Past psychiatric morbidity is generally recognized as a risk factor for psychiatric disorder following cancer [1, 5], however only four studies, to our knowledge, have evaluated psychiatric relapse focusing on depressive disorder in cancer patients with relapse rates of 54%, 62.5%, 33.5% and 29% respectively [12, 27, 33, 34].

Very few data were available on the possible association between cancer disease and dysthymic disorder [35] or phobia [32, 33], and none of these studies could establish that this occurs after diagnosis or treatment. The study of Aragona et al. suggested that dysthymic disorder could be present before diagnosis and contribute to the onset of breast cancer [35, 36]. In our study 2.8% of the women with breast cancer reported symptoms of dysthymic disorder for the first time after diagnosis. However we cannot exclude the possibility that these women were suffering from a sub-syndromic dysthymic disorder before disease onset or that the dysthymic disorder was the consequence of inadequately-treated MDD.

The prevalence of current PTSD in our study (4.9%) is comparable to rates previously reported, 2.4% to 6% [10-12, 28, 37, 38], although some authors have reported higher rates, 12 to 18% [39, 40]. The prevalence of PTSD observed during the last three years tended to be higher in the cancer group than in controls (4.9 vs. 0.8%, $p=0.07$) but not at the time of interview (i.e. 1 to 3 years after the breast cancer diagnosis). This lack of difference in current PTSD diagnosis between groups is not explained by the improvement of post-traumatic symptoms in the cancer group but rather by the high long-term persistence of life-time PTSD in the comparison group. These results are in agreement with observations which showed relatively low rates of full-PTSD induced by breast cancer but significant persistent clinical distress evidenced by symptoms of re-experiencing and arousal associated or not with depression symptoms [10-12, 37-39].

Our results did not show quantitative (regarding life-time prevalence of full- or partial-PTSD) or qualitative differences (expression and severity of post-traumatic symptoms) between the women who declared the breast cancer as a unique life traumatic event in the cancer group and those who declared any other unique traumatic event in the comparison group. These data suggest that the diagnosis and treatment of cancer is an event comparable in gravity to other severe traumatic events and should be considered as such in DSM-IV. A limitation of this last comparison is its retrospective nature. The cancer event occurred on a median period of 1.87 years (range=1-3) before the interview whereas the traumatic event in the comparison sub-group occurred on a median period of 15.87 years (range=0.34-57.42) before. This could influence the recall and the declaration of some symptoms in the

comparison sub-group and artificially decrease the difference in symptomatic expression between the two sub-groups.

Concerning the severity of post-traumatic symptoms in the cancer sub-group, the rates of patients who fulfilled diagnostic criteria for symptom clusters such as avoidance or increased arousal were higher than those previously described by some authors [11, 12] but comparable to those observed by Palmer et al. [38]. This could be explained by sample differences. In our study the diagnosis of PTSD was completed only in women who spontaneously cited cancer as traumatic event or as the most frightening event in their life. Thus our patient sample is qualitatively closer to that of Palmer et al. which corresponds to a sub-group of selected patients fulfilling A1 and A2 criteria of the PTSD diagnosis (DSM-IV) than that of Alter et al. or of Green et al. which included all women affected by breast cancer (A1 criteria of the PTSD diagnosis) [11, 12, 38]. In the latter case an undetermined proportion of patients may not have experienced breast cancer as a traumatic event and consequently would not express post-traumatic symptoms.

This study has several limitations. At the beginning of our study PTSD-I, based on DSM-III-R, was the only validated instrument translated in French language, available for both a PTSD diagnosis and an evaluation of post-traumatic symptoms severity. We considered, however, this was only a minor drawback compared to the extensive information this questionnaire has provided. Besides, as in retrospective studies, there is a bias of memory related to lifetime recollection of symptoms which is probably not different between both groups. We have however, observed a higher decrease of life-time PTSD diagnoses of the first period (childhood to three years before the interview) not related to the cancer event, in the cancer group compared to the comparison group. One explanation could be that the "cancer event" may have obscured the recall of previous PTSD symptoms and then artificially decreased the measure of current PTSD symptoms for the women of the cancer group who have declared a traumatic event prior to the cancer disease.

In conclusion, this large study of psychiatric disorder in breast cancer survivors underlines the fact that in spite of important treatment advances and increases in survival time, the diagnosis and treatment of breast cancer event continues to have an important psychological effect on women, regardless of their psychiatric history. Our results underline the importance of detecting mood and anxiety disorders in breast cancer patients during therapeutic follow-up.

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Conflict of interest

All the authors declare that they have no conflicts of interest.

REFERENCES

1. Kadan-Lottick NS, Vanderwerker LC, Block SD, Zhang B and Prigerson HG. Psychiatric disorders and mental health service use in patients with advanced cancer: a report from the coping with cancer study. *Cancer* 2005; **104**:2872-81.
2. Sollner W, Maislinger S, Konig A, Devries A and Lukas P. Providing psychosocial support for breast cancer patients based on screening for distress within a consultation-liaison service. *Psychooncology* 2004; **13**:893-7.
3. Maguire P. Improving the recognition of concerns and affective disorders in cancer patients. *Ann Oncol* 2002; **13 Suppl 4**:177-81.
4. Maguire P and Pitceathly C. Improving the psychological care of cancer patients and their relatives. The role of specialist nurses. *J Psychosom Res* 2003; **55**:469-74.
5. Burgess C, Cornelius V, Love S, Graham J, Richards M and Ramirez A. Depression and anxiety in women with early breast cancer: five year observational cohort study. *Bmj* 2005; **330**:702.
6. Helgeson VS, Snyder P and Seltman H. Psychological and physical adjustment to breast cancer over 4 years: identifying distinct trajectories of change. *Health Psychol* 2004; **23**:3-15.
7. Derogatis LR, Morrow GR, Fetting J, Penman D, Piasetsky S, Schmale AM, Henrichs M and Carnicke CL, Jr. The prevalence of psychiatric disorders among cancer patients. *Jama* 1983; **249**:751-7.
8. van't Spijker A, Trijsburg RW and Duivendoorn HJ. Psychological sequelae of cancer diagnosis: a meta-analytical review of 58 studies after 1980. *Psychosom Med* 1997; **59**:280-93.
9. American Psychiatric Association. 4th ed. Diagnostic and Statistical Manual Of Mental Disorders. Washington, DC. 1994
10. Cordova MJ, Andrykowski MA, Kenady DE, McGrath PC, Sloan DA and Redd WH. Frequency and correlates of posttraumatic-stress-disorder-like symptoms after treatment for breast cancer. *J Consult Clin Psychol* 1995; **63**:981-6.
11. Alter CL, Pelcovitz D, Axelrod A, Goldenberg B, Harris H, Meyers B, Grobois B, Mandel F, Septimus A and Kaplan S. Identification of PTSD in cancer survivors. *Psychosomatics* 1996; **37**:137-43.
12. Green BL, Rowland JH, Krupnick JL, Epstein SA, Stockton P, Stern NM, Spertus IL and Steakley C. Prevalence of posttraumatic stress disorder in women with breast cancer. *Psychosomatics* 1998; **39**:102-11.
13. Andrykowski MA and Cordova MJ. Factors associated with PTSD symptoms following treatment for breast cancer: test of the Andersen model. *J Trauma Stress* 1998; **11**:189-203.
14. Cordova MJ, Studts JL, Hann DM, Jacobsen PB and Andrykowski MA. Symptom structure of PTSD following breast cancer. *J Trauma Stress* 2000; **13**:301-19.
15. DuHamel KN, Ostrof J, Ashman T, Winkel G, Mundy EA, Keane TM, Morasco BJ, Vickberg SM, Hurley K, Burkhalter J, Chhabra R, Scigliano E, Papadopoulos E, Moskowitz C and Redd W. Construct validity of the posttraumatic stress disorder checklist in cancer survivors: analyses based on two samples. *Psychol Assess* 2004; **16**:255-66.
16. Shelby RA, Golden-Kreutz DM and Andersen BL. Mismatch of posttraumatic stress disorder (PTSD) symptoms and DSM-IV symptom clusters in a cancer sample: Exploratory factor analysis of the PTSD Checklist-Civilian Version. *J Trauma Stress* 2005; **18**:347-57.
17. American Joint Committee on Cancer. Manual for staging for breast carcinoma. 3th rev. 1989

18. Lecrubier Y, Sheehan DV, Weiller E, Amorim P, Bonora I, Harnett Sheehan K, Janavs J and Dunbar GC. The MINI International Neuropsychiatric Interview (MINI). A short diagnostic structured interview: reliability and validity according to the CIDI. *Eur Psychiatry* 1997; **12**:224-231.
19. Watson CG, Juba MP, Manifold V, Kucala T and Anderson PE. The PTSD interview: rationale, description, reliability, and concurrent validity of a DSM-III-based technique. *J Clin Psychol* 1991; **47**:179-88.
20. Brunet A (1995): Evaluation de la version française auto-administrée du PTSD-I. In (ed)^(eds), *IV Conférence Européenne sur le Stress Traumatique*, ed, Vol. Paris, pp.
21. Jehel L, Duchet C, Paterniti S and Louville P. Construction et étude de validité d'un autoquestionnaire de l'état de stress post-traumatique issu du PTSD-Interview: leQSPT. *Revue Française de Psychiatrie et de Psychologie Médicale* 1999; **24**:203-5.
22. Carlier IV and Gersons BP. Partial posttraumatic stress disorder (PTSD): the issue of psychological scars and the occurrence of PTSD symptoms. *J Nerv Ment Dis* 1995; **183**:107-9.
23. Fallowfield LJ, Hall A, Maguire GP and Baum M. Psychological outcomes of different treatment policies in women with early breast cancer outside a clinical trial. *Bmj* 1990; **301**:575-80.
24. Maguire GP, Lee EG, Bevington DJ, Kuchemann CS, Crabtree RJ and Cornell CE. Psychiatric problems in the first year after mastectomy. *Br Med J* 1978; **1**:963-5.
25. Coyne JC, Palmer SC, Shapiro PJ, Thompson R and DeMichele A. Distress, psychiatric morbidity, and prescriptions for psychotropic medication in a breast cancer waiting room sample. *Gen Hosp Psychiatry* 2004; **26**:121-8.
26. Kissane DW, Clarke DM, Ikin J, Bloch S, Smith GC, Vitetta L and McKenzie DP. Psychological morbidity and quality of life in Australian women with early-stage breast cancer: a cross-sectional survey. *Med J Aust* 1998; **169**:192-6.
27. Kissane DW, Grabsch B, Love A, Clarke DM, Bloch S and Smith GC. Psychiatric disorder in women with early stage and advanced breast cancer: a comparative analysis. *Aust N Z J Psychiatry* 2004; **38**:320-6.
28. Mehnert A and Koch U. Prevalence of acute and post-traumatic stress disorder and comorbid mental disorders in breast cancer patients during primary cancer care: a prospective study. *Psychooncology* 2007; **16**:181-8.
29. Mundy EA, Blanchard EB, Cirenza E, Gargiulo J, Maloy B and Blanchard CG. Posttraumatic stress disorder in breast cancer patients following autologous bone marrow transplantation or conventional cancer treatments. *Behav Res Ther* 2000; **38**:1015-27.
30. Hall A, A'Hern R and Fallowfield L. Are we using appropriate self-report questionnaires for detecting anxiety and depression in women with early breast cancer? *Eur J Cancer* 1999; **35**:79-85.
31. Fallowfield LJ, Hall A, Maguire P, Baum M and A'Hern RP. Psychological effects of being offered choice of surgery for breast cancer. *Bmj* 1994; **309**:448.
32. Honda K and Goodwin RD. Cancer and mental disorders in a national community sample: findings from the national comorbidity survey. *Psychother Psychosom* 2004; **73**:235-42.
33. Harter M, Reuter K, Aschenbrenner A, Schretzmann B, Marschner N, Hasenburger A and Weis J. Psychiatric disorders and associated factors in cancer: results of an interview study with patients in inpatient, rehabilitation and outpatient treatment. *Eur J Cancer* 2001; **37**:1385-93.
34. Kangas M, Henry JL and Bryant RA. The course of psychological disorders in the 1st year after cancer diagnosis. *J Consult Clin Psychol* 2005; **73**:763-8.

35. Aragona M, Muscatello MR and Mesiti M. Prevalence of depressive mood disorders in breast cancer patients of southern Italy. *Ann N Y Acad Sci* 1996; **784**:482-5.
36. Aragona M, Muscatello MR and Mesiti M. Depressive mood disorders in patients with operable breast cancer. *J Exp Clin Cancer Res* 1997; **16**:111-8.
37. Andrykowski MA, Cordova MJ, Studts JL and Miller TW. Posttraumatic stress disorder after treatment for breast cancer: prevalence of diagnosis and use of the PTSD Checklist-Civilian Version (PCL-C) as a screening instrument. *J Consult Clin Psychol* 1998; **66**:586-90.
38. Palmer SC, Kagee A, Coyne JC and DeMichele A. Experience of trauma, distress, and posttraumatic stress disorder among breast cancer patients. *Psychosom Med* 2004; **66**:258-64.
39. Tjemslund L, Soreide JA and Malt UF. Posttraumatic distress symptoms in operable breast cancer III: status one year after surgery. *Breast Cancer Res Treat* 1998; **47**:141-51.
40. Amir M and Ramati A. Post-traumatic symptoms, emotional distress and quality of life in long-term survivors of breast cancer: a preliminary research. *J Anxiety Disord* 2002; **16**:195-206.

Table 1: Baseline personal characteristics of women recently recovered from breast cancer.

		At time of interview			
		Comparison group n=125	Cancer group n=144	p-value	
Median age (Q25-Q75)	54 (47-60)	53 (48-61)		0.82	
	n	%	n	%	
Marital status					0.43
Single	7	5.60	11	7.64	
Married/cohabiting	97	77.60	104	72.22	
Widowed	7	5.60	5	3.47	
Divorced/separated	14	11.20	24	16.67	
Education (years)					0.08
≤ 5	18	14.40	33	22.92	
6-9	43	34.40	55	38.19	
10-12	19	15.20	23	15.97	
> 12	45	36.00	33	22.92	
Place of residence					0.02
Country-side	21	16.80	42	29.17	
City-side	104	83.20	102	70.83	

Table 2: Baseline clinical characteristics of women with first diagnosis of breast cancer (n=144)

	n	%
Localisation		
Unifocal	119	82.64
Multifocal	25	17.36
Stage		
0	8	5.56
1	57	39.58
2	58	40.28
3	5	3.47
Unknown	16	11.11
Type of operation		
Mastectomy	44	30.56
Tumorectomy	100	69.44
Post-operative Treatment		
None	8	5.56
Chemotherapy	1	0.69
Radiotherapy	60	41.67
Chemother. + radiother.	75	52.08
Hormonotherapy		
None	44	30.56
Yes	99	68.75
Not known	1	0.69

Table 3: Retrospective determination of life time mental health diagnoses of women recently recovered from breast cancer.

Variable	Childhood to 3 years before the interview			3 last years before the interview			Current prevalence							
	Diagnosed episodes			Diagnosed episodes			Diagnosed episodes							
	Comparison group	Cancer group	p-value	Comparison group	Cancer group	p-value	Comparison group	Cancer group	p-value					
MDD	40	32.0	0.29	11	8.8	0.01	4	3.2	0.49	9	7.2	23	16.0	0.03
Dysthymia [†]							0		0.13	0	0	6	4.2	0.04
Manic Episode	4	3.2	0.76	2	1.6	0.99	0	0		7	5.6	5	3.5	0.40
Panic disorder	6	4.8	0.80	0	6	0.03	0	3	0.25	4	3.2	4	2.8	0.99
Phobia	25	20.0	0.13	4	3.2	0.17	0	5	0.06	11	8.8	9	6.3	0.43
OCD	1	0.8	0.99	0	1	0.99	0	1	0.99	1	0.8	3	2.1	0.63
GAD	29	23.2	0.30	2	1.6	0.003	1	0.8	0.22	15	12.0	22	15.3	0.44

[†]: Determinations of the life-time dysthymic disorder diagnosis and dysthymic disorder relapses were not feasible with the MINI. The "first diagnosis prevalence" of this psychiatric disorder was established for the 2 last years before the interview instead of the 3 last years used for the other disorders.

Table 4: Traumatic story of breast cancer survivors.

Variable	Childhood to 3 years before interview			3 last years before the interview			Current prevalence			
	Comparison group n=125	Cancer group n=144	p-value	Comparison group n=125	Cancer group n=144	p-value	Comparison group n=125	Cancer group n=144	p-value	
Experience of traumatic event	24	19.2	30	20.8	0.74	2	1.6	32	22.2	<0.0001
PTSD	8	6.4	6	4.2	0.41	1	0.8	7	4.9	0.07
Partial PTSD	2	1.6	5	3.5	0.46	1	0.8	8	5.6	0.04
								6	4.8	0.98
								2	1.6	0.45
								5	3.5	

Table 5: Lifetime prevalence and severity of PTSD induced by breast cancer. Comparison with other traumatic events of the civilian life.

Variable	Any traumatic event n=23		Cancer event n=22		p-value
	n	%	n	%	
Re-experiencing symptoms cluster	16	69.6	12	54.6	0.30
Avoidance symptoms cluster	9	39.1	7	31.8	0.61
Increased arousal symptoms cluster	10	43.5	8	36.4	0.72
Life time PTSD	8	34.8	4	18.2	0.21
Life time Partial PTSD	2	8.7	5	22.7	0.24
	Median	Median	Median	Median	
	(Q25-Q75)	(Q25-Q75)	(Q25-Q75)	(Q25-Q75)	
Severity score	38 (25-56)	41 (30-50)			0.70