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## Original article

# The course of anxiety and depression over 5 years of follow-up and risk factors in women with early breast cancer: Results from the UK Standardisation of Radiotherapy Trials (START)

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## ABSTRACT

Prospective data are limited on the course of anxiety and depression and their determinants in women with early breast cancer. These parameters were assessed before adjuvant radiotherapy (RT) and over 5 years follow-up.

Of 2208 women recruited to the START QOL study, 35% reported clinically relevant levels of anxiety and/or depression pre-RT; there was no significant change in these proportions over time. However, 75% women with high baseline anxiety recorded further high scores over time whilst one in six had high scores at every follow-up point. Depression showed a similar pattern with lower frequencies at all time points; very few with initial normal scores developed clinically relevant anxiety or depression over time. Lower educational level predicted worse anxiety and depression over time; younger age predicted worse anxiety and chemotherapy predicted worse depression. Scores in the borderline or case range for anxiety or depression at baseline were both significantly associated with worse mood states over 5 years.

These findings indicate the course of anxiety and depression in women with specific risk factors. This subgroup of patients requires greater clinical attention.

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## Introduction

Depression in early breast cancer has been widely reported, but prevalence rates vary considerably,<sup>1</sup> reflecting different patient cohorts and methodological approaches, whilst anxiety disorders have received less attention. Studies conducted in the context of modern multimodal treatment have suggested good psychological health on completion of treatment<sup>2</sup> and in the longer term,<sup>3-8</sup> which compare favourably with population samples, despite adverse effects of treatment on other aspects of quality of life. These outcomes suggest a level of psychological resilience, although increased emotional distress has been observed in younger breast cancer patients<sup>9–11</sup> relative to older breast cancer populations.<sup>11–13</sup> However, long-term *prospective* data in large samples of breast cancer patients across the age range are limited<sup>14</sup> and general measures of distress sometimes lack clinical interpretation. Therefore, we lack an understanding of how anxiety and depression change over the longer term and need to determine associated predictors.<sup>15</sup> This would indicate which

patients retain vulnerability over time and develop repeated or chronic episodes of anxiety and/or depression. This large national clinical trial provides an opportunity to clarify these issues.

The START trials<sup>16,17</sup> comprised two parallel multicentre randomised clinical trials to determine the effects of hypofractionated radiotherapy regimens against an international standard in women with early breast cancer. In trial A, experimental doses of 41.6 Gy and 39Gy, each delivered in 13 fractions over 5 weeks were compared to the global standard of 50 Gy delivered in 25 fractions over 5 weeks.<sup>16</sup> In trial B, a commonly used regimen in the UK of 40 Gy delivered in 15 fractions over 3 weeks was compared with the same standard regimen.<sup>17</sup> Quality of life endpoints were integral to the trials<sup>18</sup> and included assessments from 2208 participants with a wide range of patient age and a geographic distribution. Results of the randomised comparisons in Trials A and B have now been published<sup>16,17</sup> and showed no significant differences in local tumour control compared with the global standard but a tendency for reduced levels of adverse effects on normal tissues was observed for the 39 Gy and 40 Gy regimens respectively; in Trial A results for the 41.6 Gy regimen were similar to the 50 Gy regimen.

In our analysis of the quality of life study at baseline (after surgery, and chemotherapy where appropriate but pre-

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radiotherapy) we found higher levels of anxiety (32.4% borderline and/or case) compared with depression (12.0% borderline and/or case), using the Hospital Anxiety and Depression Scale (HADS)).<sup>18</sup> There was a higher proportion of 'cases' of anxiety and depression in 735 (33.3%) patients who had received chemotherapy (p < 0.001). In multivariate analysis, which included age and key clinical factors (type of breast surgery, use of chemotherapy and endocrine therapy) there was a significant decrease in the proportion of anxiety cases with increasing age (p < 0.001 for trend) whilst this was not found for depression; clinical factors were not significantly associated. Data for the 5-year follow-up period are now available and this report aims to add knowledge on the course of anxiety and depression for this cohort and to assess the stability of age and other key demographic and treatment variables as predictors in the longer term.

#### Objectives

The main aim of this paper is to examine the course of anxiety and depression over the longer term (5 years) to determine individual patient outcomes over time.

Second, factors examined at baseline that may continue to contribute to adjustment over time were tested to predict anxiety and depression over a 5-year period following treatment. These are age, education, and key treatment factors (type of surgery, receiving adjuvant chemotherapy and endocrine therapy). Baseline anxiety and depression categories were included in the model to account for the effect of these co-morbidities.

We hypothesised that age and education would be predictive of anxiety and depression over time but that clinical factors would not.

## Materials and methods

#### Study participants

Women aged over 18 years with early breast cancer who had completed breast surgery (breast-conserving surgery (BCS) or mastectomy (Mx), without reconstruction, undergone adjuvant chemotherapy (CT), where appropriate, had commenced endocrine therapy and had been prescribed radiotherapy, were eligible for entry into the START trials.<sup>16,17</sup> Participation in the trials was open to all UK centres providing radiotherapy treatment for patients with early breast cancer between February 1999 and October 2002. The trials were run in parallel with centres choosing whether to participate in Trial A or B. Centres could also choose whether or not to participate in the QOL study and all patients in participant centres were potentially eligible to take part; they were invited to participate by the clinical team. The START trials were approved by the relevant local ethics committees of all participating centres.

Data from the trials A and B have been combined, as a comparison of the randomised radiotherapy schedules was not the purpose of this paper. This provides a unique cohort of UK women receiving treatment for early breast cancer.

#### Procedures

Written informed consent for the QOL study was obtained at the patient's planned visit by staff in the participating centres prior to randomisation. Patients also completed a baseline QOL questionnaire booklet in the clinic before randomisation. Follow-up questionnaires were mailed from the Trials Office at The Institute of Cancer Research for completion at home at 6,12 24 and 60 months after randomisation, having first checked the patient's current health status with their clinical team. Telephone or mailed prompts were sent within 3 weeks if questionnaires were not returned. Patients who relapsed were approached according to advice from the responsible clinical team.

#### Measures

#### Demographic information

Age at randomisation was recorded for all patients and educational level was collected at 1 year (as part of a health economics (HE) assessment). The HE assessments were mailed to patients' homes with the QOL booklets and returned in a prepaid envelope to the Trials Centre. Ethnicity and civil status were not routinely collected in the trial.

*Clinical characteristics* used in the analysis, available from the clinical database included type of surgery (Mx or BCS), use of adjuvant chemotherapy and endocrine therapy.<sup>18</sup>

Quality of Life booklets comprised the following:

Anxiety and Depression were measured using the Hospital Anxiety and Depression Scale.<sup>19</sup> This comprised two 7-item subscales for symptoms of anxiety and depression respectively; each item was rated on a 4-point scale (scored 0–3). This measure has shown stable dimensional structure and reliability across settings and age groups with modest effects of demographics on scores<sup>20–22</sup> in population samples. An advantage is the use of threshold scores for possible (borderline) or probable clinical (case) levels of anxiety and depression.

*Body image* was evaluated using the 10-item Body Image Scale (BIS) designed for use with cancer patients<sup>23</sup> and *Quality of Life* was evaluated using the EORTC QOLQ-C30 general cancer quality of life scale<sup>24</sup> and the 23 item breast cancer module (BR23).<sup>25</sup> The BIS and QOL measures were not included in this analysis.

#### Scoring and statistical analysis

Recommended threshold scores were used to estimate levels of anxiety and depression, scores $\geq 11$  on either the anxiety or depression subscales indicated probable case disorder; those between 8 and 10 indicated borderline disorder and those between 0 and 7 were considered normal, according to recommended thresholds.<sup>19</sup>

Patterns of change in the course of Anxiety and Depression were examined by plotting the frequencies of case, borderline and normal subscale categories of anxiety and depression respectively over time for subgroups of women who scored in each of these categories at baseline. Women with baseline scores and at least one additional HADS assessment were included. Frequencies were calculated separately for women who completed all assessments.

The repeated measurements of anxiety (normal, borderline, case) from baseline to 5 years follow-up were analysed using the proportional odds logistic model with random intercepts. This model analyses the cumulative probabilities of borderline and case anxiety, appropriately taking account of the within-patient correlation induced by repeated measurements. The gllamm command<sup>26</sup> implemented in the STATA software (STATA 9.2) was used to fit this model. An identical modelling strategy was used for depression.

Predictors included in these models were years from randomisation to questionnaire completion, patients' demographic and clinical characteristics. Baseline levels of depression were included in the prediction model for anxiety and vice versa. As the regression modelled all anxiety (or depression) data from baseline to 5 years, it was unnecessary to include baseline anxiety (or depression) as a predictor in the corresponding model. Results are presented as odds ratios (OR) with 95% confidence intervals (CI) and p-values. The interpretation of the OR for anxiety is that for a one-unit

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increase in an adverse predictor variable, the odds of borderline and case combined versus normal are OR-fold larger, and the odds of case versus borderline and normal combined are OR-fold larger. In other words, for a one-unit increase in the risk predictor, we would expect an OR-fold deterioration of the anxiety status. The same interpretation applies to the depression model.

No formal account for missing data was carried out as rates of incomplete assessments (not due to death) were very low. The regression models were performed on patients with available data for all of the predictors and at least one repeated measurement for the outcome variable in question.

## Results

#### Participant characteristics

A total of 2208 patients were recruited to the QOL study (1129 from 13 UK centres in START Trial A and 1079 from 21 UK centres in START Trial B); this represented 49% of the overall trial cohorts. The median proportion per centre of trial patients entered into the QOL study out of those eligible for QOL was 91.3% (IQR 75.0–96.9%). Uptake rates varied between centres; reasons for non-accrual were not routinely collected but anecdotally were found largely due to resource limitations involved in approaching patients; the number of patients declining was not recorded.

The cohort had a median age of 56.5 years (range 26–86 years): 518 (23.5%) were aged under 50 years at baseline assessment (considered pre-menopausal). Most women (82.9%) underwent breast-conserving surgery (BCS) and 94.2% received adjuvant systemic therapy; of these 34.6 had received chemotherapy (24.4% with and 10.2% without tamoxifen). Similar proportions of younger and older women had BCS but a greater proportion of younger women (66.2%) than older women (25.0%) received chemotherapy. Educational level and clinical characteristics are shown in Table 1.

#### Compliance and missing data

A total of 281 (10%) patients died or withdrew during the quality of life study period; the numbers of patients who withdrew or died at 6 months, 1, 2 and 5 years were 21, 31, 61 and 168, respectively. Reasons for withdrawal or refusal were not requested. Allowing for deaths and withdrawals, completion rates for the self-report measures were high: 2181 patients (98.8%) at baseline and 94.7%, 93.3%, 91.3% and 91.2% at 6 months, 1, 2 and 5 years, respectively.

Educational status was available for 1807 women (82%) at year 1 when this information was first collected; 27 patients had withdrawn, 28 had died, 126 did not return forms, 118 did not supply their educational status and 102 received an earlier version of the questionnaire which did not ask for this information.

#### Point prevalence of anxiety and depression over time

The prevalence of borderline or case anxiety, depression or both was 34.9% at baseline. Only 9.4% patients had co-existing anxiety and depression at the borderline or case level at this time point. Results for the separate anxiety and depression subscales are shown in Fig. 1; these show that rates for anxiety were three times higher than those for depression. There was no clinically significant change in the absolute proportions of patients exhibiting anxiety and depression over time or in the relative increase of anxiety over depression.

Women aged under 50 at baseline (proxy pre-menopausal) had higher rates of borderline and case levels of anxiety compared with women aged 50 and over (41.5% vs. 29.6) whilst depression rates were similar between the age groups (14.9% vs. 11.0%, respectively).

| Table |  |
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Demographic and clinical characteristics of 2208 patients in the START QOL study.

| Patient characteristic   | Number of patients (%)  |
|--|---|
| Age<br>20–29<br>30–39<br>40–49<br>50–59<br>60–69<br>70–79<br>80–89   | 11 (0.5)<br>116 (5.3)<br>391 (17.7)<br>858 (38.9)<br>573 (26.0)<br>241 (10.9)<br>18 (0.8) |
| Mean (SD)<br>Median (IQR)[ range]  | 56.9 (10.4)<br>56.5 (50.5–63.9)   |
| Education (at 1 year)<br>School certificate or equivalent<br>'A' level or equivalent<br>Professional qualification, degree level or above<br>None of the above | 528 (29.2%)<br>115 (6.4%)<br>439 (24.3%)<br>725 (40.1%)                                   |
| Surgery<br>Breast conserving surgery <sup>a</sup><br>Mastectomy  | 1831 (82.9)<br>377 (17.1))  |
| Pathological tumour size (cm)<br>0-0.9<br>1.0-1.9<br>2.0-2.9<br>≥3.0<br>Unknown  | 182 (8.2)<br>1007 (45.6)<br>618 (28.0)<br>390 (17.7)<br>11 (0.5)                          |
| Tumour grade<br>1<br>2<br>3<br>Unknown   | 516 (23.4)<br>1030 (46.6)<br>612 (27.7)<br>50 (2.3)                                       |
| Histological type<br>Ductal<br>Lobular<br>Mixed ductal and lobular<br>Special types <sup>b</sup><br>Not reported   | 1722 (78.0)<br>282 (12.8)<br>47 (2.1)<br>113 (5.1)<br>44 (1.9)                            |
| Node status<br>Positive<br>Negative<br>Unknown   | 692 (31.3)<br>1451 (65.7)<br>65 ( 2.9)  |
| Axillary surgery<br>Yes<br>No  | 2144 (97.1)<br>64 (2.9)   |
| Adjuvant treatment<br>None<br>Tamoxifen only<br>Chemotherapy only<br>Chemotherapy + tamoxifen<br>Other <sup>c</sup><br>Unknown                                 | 128 ( 5.8)<br>1266 (57.3)<br>224 (10.1)<br>537 (24.3)<br>42 (1.9)<br>11 (0.5)             |

<sup>a</sup> BCS includes patients who had undergone quadrantectomy,<sup>1</sup> partial mastectomy,<sup>4</sup> lumpectomy<sup>1</sup> and radiologically guided excision biopsy.<sup>8</sup>

<sup>b</sup> Special types include tubular and medullary tumours.

<sup>c</sup> Forty two received endocrine therapy with drugs other than tamoxifen.

When 10-year age groups were considered, a gradient of decreasing levels of anxiety with increasing age was observed but there was little variation in the frequency of depression by age (Fig. 2a and b); the age effect was consistent over time and is shown at 5 years (Fig. 2c and d).

The proportion of women with case anxiety varied little over time (from 14.4% to 12.6% at 60 months) whilst the pattern for women with case depression was similar, although numbers were very small (3.1% at baseline and 3.3% at 60 months, respectively) as shown in Fig. 1. A limitation of these subscale prevalence rates over time is the lack of detail as to which women have repeated high scores and how many improve or worsen at different time

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| Anxiety    | Baseline     | Month 6      | Month 12     | Month 24     | Month 60     |
|------------|--------------|--------------|--------------|--------------|--------------|
| Normal     | 1472 (67.6%) | 1416 (69.3%) | 1402 (70.8%) | 1326 (70.4%) | 1231 (71.5%) |
| Borderline | 392 (18.0%)  | 316 (15.5%)  | 317 (16.0%)  | 333 (17.7%)  | 274 (15.9%)  |
| Case       | 313 (14.4%)  | 312 (15.3%)  | 260 (13.1%)  | 225 (11.9%)  | 216 (12.6%)  |
| Missing    | 4            | 137          | 202          | 297          | 460          |
| Total      | 2181         | 2181         | 2181         | 2181         | 2181         |
|            |              |              |              |              |              |
| Depression | Baseline     | Month 6      | Month 12     | Month 24     | Month 60     |
| Normal     | 1914 (87.9%) | 1800 (88.1%) | 1765 (89.2%) | 1689 (89.6%) | 1529 (88.8%) |
| Borderline | 193 (8.9%)   | 163 (8.0%)   | 151 (7.6%)   | 135 (7.2%)   | 134 (7.8%)   |
| Case       | 67 (3.1%)    | 81 (4.0%)    | 63 (3.2%)    | 58 (3.1%)    | 57 (3.3%)    |
| Missing    | 4            | 137          | 202          | 297          | 460          |
| Total      | 2181         | 2181         | 2181         | 2181         | 2181         |

*Missing* includes forms not returned or HADS section of QOL-questionnaire not completed for reason not due to death or withdrawal. Reasons for non compliance were not routinely recorded.

Fig. 1. Observed distributions of anxiety and depression over time.

points. We therefore examined these changes over all 4 follow-up points.

The course of anxiety and depression over time: analysis of individual patient scores

We observed different patterns of continuation, improvement, or resolution of anxiety and depression over time when frequencies were examined for those women who were categorised at baseline as having case, borderline or normal levels of anxiety or depression on the respective subscales (Fig. 3). Considering the course of anxiety, 313 women reported case anxiety at baseline and 306 (97.8%) had at least one follow-up assessment (range 1–4). Of these, three quarters (228 women) rated as cases on at least one further occasion and hence only a quarter did not have a further episode over time. A total of 193 (61.7%) of the 313 women had all follow-up assessments and of these one in six (18.8%) rated as cases at all four follow-ups over 5 years whilst 74.6% rated as cases on at least one subsequent assessment.

With respect to depression, 67 women reported case levels of depression at baseline and nearly two-thirds (42/66) with at least one follow-up (range 1–4) reported case depression on a further occasion over 5 years. A total of 38 (57%) women completed all four follow-ups and of these only 5 (13.2%) rated as cases on all occasions whilst over two-thirds (68.4%) rated as cases on at least one occasion. As shown in Fig. 3, there was a gradual decrease in the proportion of women who reported a further case level of anxiety or depression at successive time points.

In contrast, very few women with normal scores at baseline reported an increase in anxiety or depression to borderline or case level over time as shown in Fig. 3. Allowing for missing data, only 4.1–5.2% became anxiety cases at any successive follow-up point and so there was a high likelihood of remaining in the normal range for anxiety over time given a normal score at baseline. As shown in Fig. 3, an even lower rate was observed for depression.

Fig. 3 also shows that women with initial borderline anxiety or depression showed a pattern of greater recovery (the proportion of

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Fig. 2. Distribution of anxiety and depression levels by age groups at baseline and 5 years.

normal scores over time) than deterioration (the proportion of case level scores) over successive time points. This was examined further by quantifying the changes over time for these borderline groups in more detail. With respect to anxiety, 38.7% (146/377) of women with at least one follow-up showed a deterioration of mood on at least one follow-up occasion. Of 262 (67.1%) with all four follow-ups, only 10 scored in the case range on all occasions and just over a third (38.4%) rated at this level on at least one occasion. Considering those with borderline depression at baseline, 27.9% with at least one follow-up showed a deterioration to case level of depression whilst for those with all follow-up data (112, 58%) only one rating of case depression at every assessment was observed and just over a quarter (26.8%) recorded a deterioration of mood on at least one occasion. Therefore, considering reciprocal changes, a higher proportion of women with borderline anxiety or depression at baseline showed no deterioration or an improvement in mood over time than a worsening and this course was more frequent for those with initial borderline depression than borderline anxiety.

### Predictors of anxiety and depression

The multivariate regression analyses for anxiety and depression respectively from baseline to 60 months were each performed on 1801 patients with data available for all the candidate predictors, including the baseline depression category (in the anxiety model) and baseline anxiety category (in the depression model). Educational level was the only common predictor for both anxiety and depression (p < 0.01;test for trend) in each model (Tables 2a and 2b).

Anxiety status improved with follow-up time (p = 0.041) whilst younger age (p < 0.001) and worse baseline depression (borderline or case versus normal category; p < 0.001 for each) were significant in predicting worse anxiety over time (Table 2a). Clinical factors had no significant effect on the risk of anxiety over time (Table 2a).

The severity of depression (normal, borderline or case) was not affected by follow-up time or age (Table 2b) but increased in women who had received adjuvant chemotherapy (p = 0.011); other clinical factors had no effect. Case or borderline anxiety scores

at baseline also significantly increased the risk of worse depression compared to those with anxiety scores in the normal range (p < 0.001 for each) (Table 2b).

### Discussion

An important and novel finding of this study is that different frequencies and patterns of change over time can be distinguished for different levels of severity of anxiety and depression at the time of presentation for radiotherapy treatment. Most women who presented with a probable case level of anxiety before starting radiotherapy treatment reported repeated high anxiety over time. A similar course was observed for depression, albeit with many fewer women with clinically relevant depression scores at baseline. This finding was observed for women with all follow-up assessments as well as those with one or more missing evaluations so that the rate of repeat episodes did not appear to be related to the number of ratings completed. In marked contrast, far fewer women with a normal level of anxiety or depression at baseline experienced increases in these mood states over time, reflecting a stable level of well-being for these women. The course of both borderline anxiety and borderline depression was intermediate between these two very different patterns and generally showed more improvement in their mood state over time than deterioration. These findings from the analysis of individual patient scores need to be considered in the context of the results of the change in group proportions of anxiety and depression over time (Fig 1), in which no significant change in the rates of borderline or case anxiety and depression were observed over 5 years of follow-up. This is an important outcome in itself but we have shown that a different approach is warranted to examine individual variation and identify women at risk of increased psychological morbidity.

We cannot comment on the duration of episodes of anxiety and depression and this is an area that warrants more research to inform intervention studies. Burgess et al., <sup>6</sup> conducted a detailed study of psychological morbidity over 5 years and reported that 40% of women aged 60 or less had episodes lasting 90 days or more but the authors did not discriminate between anxiety and depression

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Fig. 3. Patterns of change over time for baseline frequencies of case, borderline and normal categories of anxiety and depression.

or severity of distress. The detriment in well-being due to anxiety may not be apparent in studies that have focussed on depression: overall, 90% of anxious women in the START trial reported no concurrent depressive symptoms, so ignoring this morbidity will lead to underreported distress.

Our findings are comparable with other studies with other studies using the HADS with respect to prevalence rates of anxiety and depression,<sup>27</sup> risk factors <sup>27–29</sup> and increased anxiety over population rates.<sup>28</sup> The vulnerability of younger women to psychological distress was consistent with other research <sup>4,9–11,30</sup> but in our cohort there was a clear linear increase in rates of anxiety with decreasing age but no age effect on rates of depression. Research has been less consistent in the association of mood disorder and older women, where both good mental health <sup>2,5</sup> and deterioration over time were observed <sup>12,13</sup> and methodological factors may account for these differences.

Education was a predictor of both anxiety and depression in this study which also confirms other reports. However, achieving an 'A' level of attainment was not significantly different from education below the minimum school certificate level in the START trial and this is likely to be due to relatively smaller numbers in this subgroup; the largest subgroup (40%) was for women not achieving the lowest level of attainment. Several studies have found no effect for type of surgery, as in our study, and have also failed to observe a significant predictive effect for systemic therapy,<sup>2,3,5,6,28–31</sup> whilst receiving adjuvant chemotherapy increased the risk of depression in the START cohort, in contrast to our finding at baseline. This is unexplained but the onset of the menopause and oestrogen decline, which result from chemotherapy, have been associated with depression in some reports.

Patients' initial ratings of anxiety and depression were a clinically relevant risk factor for further episodes of mood disorder and

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#### Table 2a

Results of prediction model for anxiety (normal, borderline, case).

| Predictor                                    | Odds ratio (95% CI)  | p-value |
|--|----------------------|---------|
| Follow-up time (per year increase)           | 0.96 (0.93-0.998)    | 0.041   |
| Age (per year increase)                      | 0.94 (0.92-0.96)     | < 0.001 |
| Type of surgery (mastectomy vs.              | 0.79 (0.53-1.19)     | 0.265   |
| conservative surgery)                        |                      |         |
| Chemotherapy (yes vs. no)                    | 1.24 (0.78-1.99)     | 0.366   |
| Endocrine therapy (yes vs. no)               | 0.89 (0.61-1.30)     | 0.547   |
| Time since surgery (per 10% increase)        | 0.98 (0.95-1.00)     | 0.051   |
| Education (school certificate or             | 0.57 (0.40-0.81)     | 0.002   |
| equivalent vs. no qualification)             |                      |         |
| Education (A-level or equivalent vs.         | 0.81 (0.45-1.47)     | 0.485   |
| no qualification)                            |                      |         |
| Education (professional qualification/degree | 0.39 (0.27-0.57)     | < 0.001 |
| or above vs. no qualification)               |                      |         |
| Depression month 0 (borderline vs. normal)   | 17.72 (10.86-28.90)  | < 0.001 |
| Depression month 0 (case vs. normal)         | 81.17 (37.11-177.55) | < 0.001 |

\*The trend effect was significant (p < 0.01).

may be the most pragmatic indicator of risk for clinical teams. Since the HADS is very well accepted by patients, it could form a role as a screening tool in clinical practice.<sup>32–34</sup>

Our findings highlight the value of QOL sub-studies in cancer therapy trials, in generating well-defined patient samples across a wide age and geographic range with long-term follow-up, which are strengths of our study. A further strength was the high level of compliance with guestionnaire completion over 5 years and low level of missing data, in comparison with many psychosocial studies. However, a limitation of the trial setting is the lack of an assessment prior to all cancer treatment and lack of coverage of some demographic and psychosocial factors of relevance, such as social support and past psychiatric history. Moreover, trial cohorts even with guite broad entry criteria do not represent all patients in clinical care. The sample was drawn from all parts of the UK but the proportions from London and the South of England were overrepresented in comparison with the annual distribution of new breast cancer cases for these areas<sup>35</sup> (46.3% vs. 35%, respectively) and any effect of this bias is unknown.

All self-report measures have limitations in their accuracy of measuring psychological morbidity and although the HADS is very widely used in research it could underestimate depression in cancer patients<sup>36</sup> and so true diagnostic rates should not be directly extrapolated from these data. Clinical psychological assessments can take account of individual risk and resilience and monitor the process of adjustment and coping, which is often necessary before providing further intervention. The assessment of psychological

#### Table 2b

Results of prediction model for depression (normal, borderline, case).

| Predictor                                    | Odds ratio (95% CI) | p-value |
|--|---------------------|---------|
| Follow-up time (per year increase)           | 1.02 (0.97-1.07)    | 0.436   |
| Age (per year increase)                      | 1.00 (0.98-1.02)    | 0.874   |
| Type of surgery (mastectomy vs.              | 0.94 (0.60-1.49)    | 0.799   |
| conservative surgery)                        |                     |         |
| Chemotherapy (yes vs. no)                    | 2.07 (1.18-3.62)    | 0.011   |
| Endocrine therapy (yes vs. no)               | 1.23 (0.79-1.92)    | 0.359   |
| Time since surgery (per 10% increase)        | 0.99 (0.97-1.02)    | 0.737   |
| Education (school certificate or             | 0.64 (0.43-0.96)    | 0.032   |
| equivalent vs. no qualification)             |                     |         |
| Education (A-level or equivalent vs.         | 0.85 (0.44-1.67)    | 0.641   |
| no qualification)                            |                     |         |
| Education (professional qualification/degree | 0.42 (0.26-0.65)    | < 0.001 |
| or above vs. no qualification)               |                     |         |
| Anxiety month 0 (borderline vs. normal)      | 7.82 (5.11-11.98)   | < 0.001 |
| Anxiety month 0 (case vs. normal)            | 57.27 (36.04-91.00) | < 0.001 |

\*The trend effect was significant (p < 0.01).

morbidity is a priority, however, as its associations with other detriments in quality of life are often reported.

#### Conclusion

Women presenting with probable case anxiety and/or depression before their radiotherapy treatment are at high risk for further episodes whilst those with normal mood are likely to remain psychologically well over time. Demographic rather than clinical factors affected risk profiles; these findings are useful indicators of risk and resilience for clinical teams managing women with early breast cancer.

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#### **Conflict of interest statement**

None declared.

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