Can a brief psychological intervention prevent anxiety or depressive disorders in cancer patients? A randomised controlled trial

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Received 7 March 2008; revised 17 October 2008; accepted 21 October 2008

Background: We tested whether a brief psychological intervention could prevent anxiety or depressive disorders among newly diagnosed cancer patients.

Patients and methods: Patients free of anxiety or depressive disorder were randomised to receive immediate intervention (start of cancer treatment), delayed intervention (8 weeks after starting treatment) or usual care. They were stratified according to risk of developing anxiety or depressive disorders. Primary outcome was measured using a standardised psychiatric interview to detect any anxiety or depressive disorder at 6 and 12 months following the cancer diagnosis. Analyses used conditional odds logistic regression models adjusting for age, gender, concerns and past history to compare outcome of all intervention patients with usual care.

Results: A total of 465 patients were recruited. In all, 313 (79%) of the 397 well enough to be interviewed completed the study. At 12 months, there was no difference between the groups receiving the intervention and usual care [odds ratio (OR) = 0.69, 95% confidence interval (CI) 0.41–1.17, P = 0.17]. In high-risk patients, those who received the intervention were less likely to develop an anxiety or depressive disorder compared with those who received usual care (OR = 0.54, 95% CI 0.29–1.00, P = 0.050). In low-risk patients, there was no difference (OR = 1.50, 95% CI 0.51–4.43, P = 0.47).

Conclusion: A brief intervention, delivered by nonspecialists, promoted adjustment among newly diagnosed cancer patients at high risk of developing anxiety or depressive disorders.

Key words: anxiety or depressive disorder, cancer patients, psychological intervention, randomised controlled trial

introduction

While most cancer patients report distress within the first year of diagnosis, 25%–40% develop anxiety or depressive disorders which impair quality of life for patients and their families [1–5]. These anxiety or depressive disorders are predicted by previous history of disorder and by difficulty coping with cancer-related concerns [6, 7]. Psychological interventions have been developed to reduce symptoms of anxiety and depression by improving coping [8, 9], although the evidence for their efficacy is still not scientifically robust [10–12]. No previous study has attempted to prevent, rather than treat, anxiety or depressive disorders in a broad range of newly diagnosed cancer patients, though such preventive intervention has been recommended [13]. Evidence from the noncancer field suggests that prevention is most likely to be successful if a ‘high-risk’ group is targeted for treatment; the strongest evidence relates to cognitive behavioural interventions used to prevent anxiety or depressive disorders [14]. There is some evidence that such treatment might carry a slight risk of worsening depression in some patients [15, 16].

The design of our trial was influenced by the fact that relatively few psychiatrists and psychologists work in the cancer field, so a successful intervention carried out by such specialists would stand little chance of becoming part of routine care [17, 18]. Our therapists were drawn from nursing and social work backgrounds. In addition, it is not known whether a psychological intervention could benefit, or even hinder adjustment, in cancer patients considered to be at low risk of developing anxiety or depressive disorders [10]. We included both high- and low-risk patients.

The optimal timing for a preventive intervention is uncertain: delay may allow spontaneous adjustment [8], but anxiety or depressive disorders can develop within weeks of a cancer diagnosis [6]. In view of this uncertainty, our trial design included both immediate and delayed interventions.

We tested the hypothesis that a brief intervention, delivered by nonspecialists, would be superior to usual care in preventing the development of new anxiety or depressive disorders.
during the year after starting treatment for cancer. We compared the effectiveness of the intervention (i) in patients at high and low risk of developing anxiety or depressive disorders and (ii) when given immediately or 8 weeks after the start of cancer treatments.

**patients and methods**

**sample**

Participants were patients recruited consecutively from clinics at a regional centre for the treatment of cancer in Manchester. Patients were included if they were between 18 and 70 years of age, newly diagnosed with a first episode of cancer, judged to have a life expectancy of at least 2 years (as identified by their clinicians) and consented to the trial. All were beginning chemotherapy or radiotherapy as part of the planned treatment either soon after diagnosis or after an initial surgical intervention.

Patients were excluded if they had current generalised anxiety, major depressive or panic disorder or if they were currently receiving psychological treatment or psychotropic medication.

Patients were invited to join the trial by their physician at an outpatient appointment before their chemotherapy or radiotherapy commenced. Their suitability for inclusion was assessed by one of the research staff, who ascertained whether the patient met inclusion or exclusion criteria.

This trial received ethical approval from South Manchester MREC (ERP/05/035) and all participants signed informed consent forms before commencing the study.

**measures to determine risk of developing anxiety or depressive disorders**

Patients were included in the trial only if they did not have an anxiety or depressive disorder at baseline but they were categorised as high or low risk of developing ‘subsequent’ anxiety or depressive disorder.

Patients were asked whether they had previously experienced any episodes of anxiety or depression, before the cancer diagnosis, for which they had consulted a general practitioner or mental health specialist. Such a past history is a risk factor for subsequent anxiety or depressive disorder after a cancer diagnosis [6].

Patients completed the ‘concerns checklist’, a 14-item checklist of physical, practical, relationship and existential concerns related to the cancer and its treatments [19]. Each concern is rated on a five-point scale of worry, summed to achieve an overall concerns score (range 0–56). A score of 8 or more is a risk factor for subsequent development of depressive disorder in cancer patients [6].

**definition of high risk**

Patients were regarded as high risk if, at recruitment, they reported a score of 8 or more on the concerns checklist and/or they reported a history of prior episodes of anxiety or depression for which treatment had been sought.

Patients were recruited in the proportion of 3 : 2 high to low risk to ensure that the majority of patients in the sample were at high risk of developing anxiety or depressive disorder. Initially patients were recruited consecutively regardless of risk. Once adequate low-risk patients had been recruited, only high-risk patients were recruited until the desired sample size was achieved.

**outcome measures**

The Structured Clinical Interview for DSM IIIR (SCID) [20] was the primary outcome measure. It was administered by trained interviewers at 6 and 12 months to identify any episodes of anxiety or depressive disorder (i.e., major depressive disorder, generalised anxiety disorder or panic disorder) that had developed at any time during the trial, even if the episode had resolved by the time of the interview. Patients were asked whether they had experienced symptoms listed in the SCID (i) during the past month and (ii) at any time over the previous 6 months.

An interrater reliability study was conducted with the three independent researchers who administered the SCID and 9.5% of the 666 SCID interviews were independently rated. All the intraclass correlation coefficients fell within the ‘almost perfect’ range of benchmark values (0.81–1.00) of Landis and Koch [21].

The Hospital Anxiety and Depression Scale (HADS) [22] is a standardised measure of psychological distress frequently used in cancer research [23]. It was used in this trial as a secondary outcome measure. We used it also at recruitment to screen out potential participants if they had an anxiety or depressive disorder. Any potential participants who scored a total of 16 or over on the HADS [22, 24] were assessed by the study psychiatrist, who used the SCID to ensure that we only included in the trial patients who did not fulfil criteria for an anxiety or depressive disorder at baseline [20].

Assessment of the main outcome, development of anxiety or depressive disorder, was made at 6 and 12 months after baseline. Assessments were conducted by researchers who were blind to treatment group.

**randomisation and assessment**

After baseline, assessments were completed and consent signed participants were randomly allocated to one of three study arms: immediate intervention (within a week of starting treatment), delayed intervention (~8 weeks after starting treatment) or usual care. The nature and duration of the intervention were identical in the immediate and delayed groups. There was no attempt to standardise usual care.

Allocation to intervention group was conducted by an independent statistician using a computer-generated minimisation programme. The study arms were stratified for gender, disease site and risk of developing anxiety or depressive disorder (high or low).

**the intervention**

The intervention followed the principles and processes of cognitive behavioural therapy [25]. Three structured intervention sessions took place over a 6-week period. The first 90-min session was conducted face-to-face with the therapist; the subsequent sessions, 2 and 6 weeks later, lasted 45 min and were conducted by telephone.

**intervention process**

At the first session, therapists invited patients to retell their experience of the detection, diagnosis and initial experience of cancer. Using a collaborative style, therapists helped patients explore their thoughts and beliefs about the illness and illness-related events, the effectiveness of their coping strategies in managing cancer-related concerns and the helpfulness of support from health professionals, family and friends. Patients were offered a booklet, designed for the study, as a psychoeducational resource to support and reinforce learning. The booklet provided examples of maladaptive coping, e.g., setting unrealistic goals (like ‘I must not get upset’ or ‘I should be coping better than I am’) which are bound to lead to disappointment. The therapists helped patients identify strategies to manage current concerns that could be tried between sessions. The main purpose of the two telephone sessions was to review and reinforce those efforts. The key points of the intervention are summarised in Table 1.

**therapist training**

The two therapists (a nurse and a social worker) were given 20 h training by the clinical psychologist (MP). This involved an introduction to theories of coping, the use of cognitive behavioural methods and observation of the psychologist conducting the intervention with patients not included in the study. The therapists received supervision for 1.5 h, every 2 weeks throughout the study, using tape recordings of their sessions. A manual...
The data were analysed on an intention-to-treat basis using the statistical software Stata version 9.1 and SPSS version 13.0.1 [26, 27]. Separate analyses were conducted to investigate whether the outcome (i) differed between immediate and delayed intervention groups and (ii) differed between the high- and low-risk patients and (c) was associated with age, gender, previous psychiatric history, concerns score or disease site. The overall effect of the intervention was determined with a conditional odds logistic regression that estimated the odds of a patient developing an anxiety or depressive disorder across the 12-month time period of the investigation [28]. This model simultaneously looked at the effect of the intervention on the probability of developing a depressive or anxiety disorder in the first 6 months and the probability of developing such a disorder in the second 6 months, conditional on staying well in the first 6 months.

Dropouts were adjusted for by calculating the probability of staying in the trial, during each of the two time periods separately, using logistic regression, with baseline variables as potential predictors. The baseline variables found to predict dropout were age, gender, previous psychiatric history and concern’s score. The product of the reciprocals of the probabilities obtained for the two periods were then used to create inverse probability weights for the subsequent conditional odds logistic regression analysis of the main outcome variable.

The logic behind the weighting procedure is described in detail by Everitt and Pickles [29].

The mean HADS total scores between intervention and usual care groups were compared using analysis of covariance to adjust for age, sex, past history, baseline concerns and baseline total HADS scores. This was repeated for high- and low-risk groups separately. The number of participants who had a HADS total score of 17 or more at any follow-up assessment was also calculated.

### sample size
To reduce the rate of new anxiety or depressive disorders from 21% to 10.5% with a ratio of 2 : 1 in the treated and usual care groups, it was calculated that 300 patients in the treatment group and a 150 in the treatment as usual group would be needed to have 80% power.

### role of the funding source
Cancer Research UK (the funding source) had no involvement in the study design, collection, analysis or interpretation of data, writing the report or submitting it for publication.

### results
#### patients
From 1995 to 2000, 613 patients commencing chemotherapy or radiotherapy were approached for the study; 41 (6.7%) patients refused immediately and 107 (17.5%) patients were excluded: 55 patients were taking antidepressant or anxiolytic medication, 40 patients had an anxiety or depressive disorder, 22 of 311 (10.3%) of those offered the intervention refused it and a further six were too ill or had died before the intervention commenced.

The mean age of the sample was 51.4 years (SD 13.04); 321 (69%) of 465 patients were female and 343 (74%) patients were married or cohabiting. The most common diagnoses were breast cancer, lymphoma and gynaecological cancer. There...
were no differences in age, gender, marital status, disease site or risk of anxiety or depressive disorder across the study arms (Table 2). At baseline, 277 (59.6%) patients were judged to be at high risk of developing anxiety or depressive disorders according to study criteria.

**follow-up assessments**

At 6 months, we assessed outcome in 355 patients (Figure 1); we were unable to assess 85 of 311 patients (27.3%) in the intervention arms and 25 of 154 patients (16.2%) in the usual care group (Fisher’s exact test, \( P = 0.008 \)). At 12 months, we assessed outcome in 355 patients (6.7%) could not be contacted and 53 (11.4%) chose to withdraw during the study (Figure 1). All those followed up at 12 months had participated also in the 6-month interview. The baseline variables found to predict dropout were age, gender, previous psychiatric history and concerns score.

At the 6-month assessment, 16 (14.3%) of 112 immediate intervention patients had developed anxiety or depressive disorders compared with 14 (12.3%) of 114 patients in the delayed intervention group (Fisher’s exact test, \( P = 0.70 \)). The two intervention groups were therefore considered together for the main analyses. Neither gender nor disease site was associated with outcome. Younger age was a significant predictor of developing an anxiety or depressive disorder [odds ratio (OR) = 0.97, 95% confidence interval (CI) 0.96–0.99, \( P = 0.005 \), as was concerns score (OR = 1.07, 95% CI 1.03–1.10, \( P < 0.001 \)).

A total of 71 patients were diagnosed with an anxiety or depressive disorder during the study (Table 3). Thirteen patients were diagnosed with anxiety or depressive disorders at both the 6- and 12-month assessment interviews so are included only once in the main analysis.

**outcome: odds of developing anxiety or depressive disorder**

There was no difference between the groups receiving the intervention and usual care (OR = 0.69, 95% CI 0.41–1.17, \( P = 0.17 \)), adjusting for age, gender, concerns and past history. Subsequent analysis showed a trend toward a significant risk \( \times \) group interaction (\( P = 0.098 \)) and we present below the results separately for high- and low-risk patients.

For patients in the high-risk group, the odds of developing an anxiety or depressive disorder were lower for the patients who had received the intervention compared with patients who had received usual care, OR = 0.54, 95% CI 0.29–1.00, \( P = 0.050 \), adjusting for age, gender, concerns and past history.

For patients in the low-risk group, the odds of developing an anxiety or depressive disorder were slightly higher, but not significantly so, in the intervention arm compared with patients in the usual care group (OR = 1.50, 95% CI 0.51–4.43, \( p = 0.47 \)), adjusting for age, gender, concerns and past history.

**outcome scores for anxiety and depression**

These are shown in Table 4. The scores, adjusted for age, sex, past history, baseline concerns and HADS scores, were significantly lower at 2 and 4 months for the intervention group compared with usual care. For the high-risk group only, the differences were significant at 4 and 6 months. Figure 2 shows the data for the high-risk group only; the reduction of total HADS score is greatest between baseline and 2 months for the immediate (early) intervention group and between 2 and 4 months for the delayed intervention group. Of the high-risk group, the number of participants who scored a HADS total of 17 or more at any follow-up assessment was 28 of 160 (17.5%) for the intervention group and 26 of 89 (29.2%) for usual care (\( P = 0.032 \)).
During the study, 14 patients accepted referral to the psychologist or psychiatrist: seven (3.1%) in the intervention group and seven (5.4%) in the usual care group. Others who had a depressive or anxiety disorder at SCID interview were recommended to seek help from their general practitioner but we do not know whether they did so.

**Discussion**

Our three-session psychological intervention was shown to be a promising intervention in preventing the development of anxiety or depressive disorders only in those newly diagnosed cancer patients at high risk of developing such disorders. Cognitive behavioural interventions prevent 12%–19% of new cases of anxiety and depressive disorders in noncancer high-risk groups [15]; our result (13%) is within this range. To our knowledge, this is the first randomised controlled trial to confirm the potential of a psychological intervention to prevent rather than treat depressive and anxiety disorders in a cancer setting. In patients with a low risk of developing anxiety or depressive disorders, there was no effect. This must be regarded as a preliminary result, which requires replication. Our trial was powered on the basis that all participants would be analysed together in the main analysis with delayed and intervention groups combined and both high- and low-risk groups included. This analysis showed no benefit from the intervention. We could not predict whether there would be sufficient statistical power to examine the high-risk group independently through lack of previous data. This was, however, a preplanned analysis and our sample size did prove adequate to show benefit, at the conventional level of statistical significance, for patients in the high-risk group who received the intervention. We found also that there was no difference between early and delayed intervention, which allowed us to combine these two intervention groups for analysis. We found no evidence that the intervention provoked depression or anxiety disorders in the low-risk group, a potential hazard of early psychological intervention [16].

Our brief intervention with two telephone sessions proved highly acceptable (90% take-up). A longer intervention might have conferred greater benefits [30], but would have excluded more patients involved in demanding chemotherapy and radiotherapy treatment regimes [31]. The dropout...
rate from the intervention groups in the first 6 months suggests that a minority of patients (~10%) do not wish to discuss their concerns and worries during the early stages of their treatment.

Table 4. Total HADS scores by intervention and usual treatment groups

<table>
<thead>
<tr>
<th></th>
<th>Intervention Mean</th>
<th>Usual care Mean</th>
<th>Comparison P</th>
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<tbody>
<tr>
<td></td>
<td>SEM n</td>
<td>SEM n</td>
<td></td>
</tr>
<tr>
<td>Whole sample</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>8.1 0.22 311 8.4</td>
<td>0.31 154 0.41</td>
<td></td>
</tr>
<tr>
<td>2 months</td>
<td>7.1 0.30 272 8.1</td>
<td>0.41 146 0.045*</td>
<td></td>
</tr>
<tr>
<td>4 months</td>
<td>5.8 0.32 238 7.2</td>
<td>0.42 135 0.007**</td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>6.0 0.33 226 7.0</td>
<td>0.44 129 0.072</td>
<td></td>
</tr>
<tr>
<td>12 months</td>
<td>5.4 0.37 200 6.8</td>
<td>0.50 113 0.37</td>
<td></td>
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<tr>
<td>High-risk patients</td>
<td></td>
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<tr>
<td>Baseline</td>
<td>10.4 0.32 185 10.8</td>
<td>0.45 92 0.45</td>
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<tr>
<td>2 months</td>
<td>8.8 0.44 160 10.3</td>
<td>0.60 89 0.051</td>
<td></td>
</tr>
<tr>
<td>4 months</td>
<td>7.1 0.47 136 9.0</td>
<td>0.60 82 0.012*</td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>6.9 0.48 128 8.5</td>
<td>0.62 76 0.045*</td>
<td></td>
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<tr>
<td>12 months</td>
<td>6.1 0.52 113 7.2</td>
<td>0.70 63 0.20</td>
<td></td>
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<tr>
<td>Low-risk patients</td>
<td></td>
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</tr>
<tr>
<td>Baseline</td>
<td>4.8 0.26 126 4.8</td>
<td>0.37 62 0.87</td>
<td></td>
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<tr>
<td>2 months</td>
<td>4.4 0.34 112 4.9</td>
<td>0.48 57 0.38</td>
<td></td>
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<tr>
<td>4 months</td>
<td>4.0 0.38 102 4.7</td>
<td>0.53 53 0.24</td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>4.7 0.41 98 5.0</td>
<td>0.55 53 0.66</td>
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<tr>
<td>12 months</td>
<td>4.5 0.51 87 4.5</td>
<td>0.68 50 0.97</td>
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</tr>
</tbody>
</table>

*aComparison of intervention and usual care groups was by analysis of covariance, adjusting for age, sex past history and concerns and HADS total baseline scores.

*bP < 0.05; **P < 0.01.

HADS, Hospital Anxiety and Depression Scale; SEM, standard error of the mean.

**strengths and limitations**

Strengths of our study include standardised measures, made by blind assessors, assignment through randomisation, an intention-to-treat analysis and a good response rate [17, 18]. The intervention followed an explicit structure and is now manualised. Conditions for a high-quality trial [12] were met except that it was impossible for participants to be blind to treatment group. Our therapists were trained and regularly supervised, but it is a limitation of the trial that no independent assessment of their fidelity to the model or competence in delivering the intervention was made. Another limitation was our screening of potential participants with the HADS instead a full SCID interview at baseline to avoid undue burdening of patients beginning cancer treatments. We lost quite a large number of patients during the trial through serious illness or death in spite of including only patients predicted to survive for 2 years. Our analysis did allow for the variables associated with dropout.

The design of our trial was pragmatic, i.e. we used a ‘treatment as usual’ comparison group rather than an attention-placebo control. In theory, the improvement in the intervention group might have resulted from the additional time with the therapist rather than the specific intervention. Since this was an effectiveness rather than an efficacy trial, however, the clinical benefits are important whatever the mechanism.

We conclude that a brief, structured intervention delivered by nonspecialists shows promise as an effective intervention in those at high risk of developing anxiety or depressive disorder, when such patients were identified by the criteria of past psychiatric history and a raised concerns score. Such patients can be identified readily, so this intervention could be transferred to clinical practice in many cancer treatment settings. As the timing of the intervention conferred no differential benefits, this may be determined by patients’ needs and wishes.

Our design is congruent with a model of service provision that delivers a brief psychological intervention to all high-risk patients.
patients with specialist referral only when necessary, i.e. patients who are experiencing great difficulty coping with their cancer-related concerns and/or who develop an anxiety or depressive disorder. The intervention, when delivered by healthcare providers without a professional counselling or psychotherapeutic training, is consistent with UK NICE Guidance recommendations for a level 2 psychological intervention [32]. In the light of current knowledge, it does not seem to be appropriate to recommend our intervention for low-risk patients.

**funding**

Cancer Research UK (C322/A5888).

**acknowledgements**

We acknowledge advice in the development phase of the study from Prof. Nicholas Tarrier and the contributions of Cathy Heaven, nurse therapist on the study, Laurence Yusupoff and Adriana Summers who supervised the therapists, Alison Mather and Emma Winter who coordinated the project in its latter stages. We are grateful for statistical advice received from Graham Dunn. Contributors: CP provided treatment, MP contributed to the design, analysis, interpretation and writing the manuscript. All authors obtained funding, coordinated the running of the study and coordinated data analysis and led on writing the paper. PM contributed to the design of the study, trained the therapists and supervised the raters. FC contributed to the development and implementation of the intervention [32]. In the light of current knowledge, it does not seem to be appropriate to recommend our intervention for low-risk patients.

**references**