The effectiveness of treatment for depression/depressive symptoms in adults with cancer: a systematic review

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CRD summary
This review concluded there was some evidence of effectiveness of pharmacological interventions for cancer patients with depression but there was a paucity of data on tolerability. Data was limited on the efficacy of psychotherapeutic interventions. The authors' cautious conclusions appropriately reflect the variable quality of the included trials.

Authors' objectives
To evaluate the efficacy and safety of psychotherapeutic and antidepressant treatment for cancer patients with depression or depressive symptoms.

Searching
PubMed, CINAHL, Cochrane Library databases, DARE and PsycARTICLES were searched up to 2005. Search terms were reported. Manual searches were also conducted and relevant articles were retrieved from key papers, reports, theses and dissertations. Only English language studies were eligible.

Study selection
Randomised controlled trials (RCTs) evaluating the efficacy and safety of pharmacological and psychotherapeutic interventions for the treatment of depression or depressive symptoms in adult cancer patients were eligible for inclusion. Trials evaluating psychotherapeutic interventions and pharmacological therapy together were excluded. Trials evaluating complementary and alternative medicines, including meditation, education or information interventions, were also excluded. Depressive symptoms or diagnosed clinical depression were outcomes measured by a wide variety of published rating scales.

Pharmacological interventions in the included RCTs were: selective serotonin reuptake inhibitors including fluoxetine (20 mg per day) and paroxetine (ranging from 10 mg to 40 mg per day); and a tricyclic antidepressant, mianserin (30 mg increasing to 60 mg per day). Duration of pharmacological therapy varied.

Psychotherapeutic therapies in the included RCTs were: cognitive behavioural therapy (CBT); computer based assessment and individually tailored care plans; and singly or in combination, education, counselling, relaxation, psychotherapy, information, social support or specialist support. Most RCTs also had co-interventions.

Half the pharmacological RCTs and a large proportion of the psychotherapeutic RCTs were single centre design only. The average age of the included participants ranged from 49 to 64 years and the proportion of women ranged from 41 to 100%. Included participants were being treated for cancer at various sites including skin, breast, colon, lung, gynaecological, testicular and prostate.

The authors did not state how papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
Validity was assessed using published criteria. Studies were assessed on the following criteria: adequacy of sample size; randomisation, blinding, method of allocation concealment; clear description of treatment; representative source of subjects; use of diagnostic criteria; number and reasons for withdrawal; methods of analysis; clear description of outcomes; use of validated instruments; and measures to control for potential confounding factors.

The authors did not state how many reviewers performed the validity assessment.

Data extraction
Data were extracted independently onto a standard form by two reviewers and checked for accuracy.
Methods of synthesis
The studies were grouped by intervention category and combined in a narrative synthesis with additional information presented in tables. Effect sizes and p-values were reported in text and tables.

Results of the review
Twenty four randomised controlled trials (RCTs) were included in the review (n=3,348 participants).

Methodological quality:
In six pharmacological RCTs, sample size was reported as adequate in two trials, method of randomisation was adequately described in all trials, method of allocation concealment was adequately described in three trials, blinding was reported in all trials. In addition, all RCTs clearly reported interventions, had a representative group of participants, and provided the number and reasons for withdrawals.

In all 18 psychotherapeutic RCTs, subjects were randomly allocated to treatment groups, and method of randomisation was adequately described in all trials, method of allocation concealment was adequately reported in six trials, blinding of investigators was only reported in two trials. All RCTs provided a clear description of intervention and had a representative source of subjects. Sixteen RCTs reported attrition rates, with reasons for withdrawal being reported in 13 trials. All RCTs clearly described and used reliable outcome measures.

Pharmacological studies:
Paroxetine: Three RCTs (n=683 participants) reported that paroxetine was significantly more effective than placebo in reducing depression and depressive symptoms. Only one trial reported on tolerability; three of 20 participants in the paroxetine group experienced retinal haemorrhage.

Fluoxetine: Two RCTs (n=254 participants) compared fluoxetine with placebo; one trial reported a significant improvement in depression, and the other did not. In one of the RCTs there was a significantly higher frequency of vomiting in the treatment group compared to the placebo group. The other study did not observe any differences in side effects between the groups.

Mianserin: One RCT (n=55 participants) found a reduction in depressive symptoms in breast cancer patients receiving mianserin compared with placebo (p=0.004). No significant differences between groups were reported for tolerability.

Psychotherapeutic studies:
Depression: One RCT (n=200 participants) reported significant improvements in depression for counseling/psychotherapy compared to control group. One RCT (n=53) reported that counselling and relaxation therapy significantly improved depression compared to control group. One RCT (n=450) reported that computer based assessments and individually tailored care plans were associated with a reduction in the proportion of moderately or severely depressed cancer patients compared to control. However, one RCT (n=53) found no significant effects of cognitive behavioural therapy together with problem solving therapy.

Cognitive behavioural therapy: Seven RCTs (n=959 participants) reported a significant reduction in depressive symptoms for cognitive behavioural therapy compared to placebo. However, two RCTs (n=103) found no significant differences on depressive symptoms. One RCT (n=36) reported a significant reduction in depressive symptoms undergoing counselling and psychotherapy.

Counselling/psychotherapy: One RCT (n=53 participants) reported counselling and relaxation to be effective in reducing mild to moderate depressive symptoms but not for severe depressive symptoms 6 weeks after therapy.

Supportive: One RCT (n=79 participants) reported that the provision of group social support was found to be as effective as cognitive behavioural therapy in reducing depressive symptoms. Significant reductions in depressive symptoms were reported for other supportive interventions compared to control including: peer support (one RCT, n=46 participants); web based social support group (one RCT, n=72 participants); computer-based assessments and individually tailored care plans together with emotional support and counselling by nurses (one RCT, n=109 participants); computer-based assessments and individually tailored care plans (one RCT, n=450 participants). One
RCT (n=11 participants) reported reductions in depressive symptoms after support from a breast care nurse alone, but not for other combined interventions.

**Authors' conclusions**
There was some evidence that pharmacological interventions were effective for cancer patients with depression but there was a paucity of data on tolerability. However, data was limited on the efficacy of psychotherapeutic interventions in treating depression or depressive symptoms in cancer patients. The majority of the included trials were of small sample size and lacked control of potential confounding factors.

**CRD commentary**
The review addressed a broad research question, encompassing a wide range of interventions. Several relevant sources were searched and attempts were made to locate unpublished studies, thus limiting the possibility of publication bias. However, restriction to English language studies may have resulted in the loss of some relevant data. Methods were used to minimise reviewer errors and bias in the extraction of data, but it was not clear whether similar steps were taken in study selection or validity assessment. A narrative synthesis was appropriate given the differences between trials. The authors highlighted several limitations with the evidence including a lack of consistent avoidance or monitoring of use of co-interventions, small sample sizes, and no attempt to control for confounding factors. The authors also noted that tolerability data were not always reported in the pharmacological studies. Consequently, the authors' cautious conclusions appropriately reflect the variable quality of the included trials.

**Implications of the review for practice and research**

**Practice:** The authors stated that the lack of clinical trial data should not equate to evidence of ineffectiveness, and that cancer patients should not be denied access to treatment for depression or depressive symptoms because of a lack of data on effectiveness.

**Research:** The authors stated there is a need for rigorous clinical trials to investigate the efficacy of pharmacological and psychotherapeutic interventions, including avoidance and monitoring of other co-interventions. Further trials are also required comparing the efficacy of psychotherapeutic versus pharmacological interventions. In addition, trials should investigate the known side effects and possible stimulation of malignant growth by pharmacological therapy.

**Funding**
Not stated.

**Bibliographic details**

**PubMedID**
16465173

**DOI**
10.1038/sj.bjc.6602949

**Original Paper URL**
http://www.nature.com/bjc/journal/v94/n3/pdf/6602949a.pdf

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Antidepressive Agents /therapeutic use; Depression /drug therapy /etiologic; Depressive Disorder /drug therapy /etiologic; Humans; Neoplasms /complications; Randomized Controlled Trials as Topic; Treatment Outcome
AccessionNumber
12006001011

Date bibliographic record published
04/07/2007

Date abstract record published
02/09/2009

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.