Meta-analysis of efficacy of interventions for elevated depressive symptoms in adults
diagnosed with cancer

Hart SL, Hoyt MA, Diefenbach M, Anderson DR, Kilbourn KM, Craft LL, Steel JL, Cuipers P, Mohr DC, Berendsen M, Spring B,
Stanton AL

CRD summary
The authors' conclusion that psychotherapeutic or pharmacologic treatments for depression are more effective than control for depressed patients is unlikely to be erroneous, however it is difficult to be clear about the magnitude of these effects or the differences between treatment options due to analytical choices, differences between trials and potential for missed studies.

Authors' objectives
To evaluate the efficacy of psychotherapeutic and pharmacologic interventions for depression in cancer patients.

Searching
Five databases were searched (MEDLINE and EMBASE included) from inception to October 2011. Search terms were reported and references were checked. The searches were limited to publications in English.

Study selection
Randomised controlled trials with participants over the age of 18 years who had a diagnosis of any cancer and elevated depressive symptoms on entry to the trial were eligible for inclusion. Relevant interventions included cognitive-behaviour therapy, physical activity, collaborative care, mind-body approaches or pharmacological components. Trials were required to include a control arm of usual care, placebo, attention control or a waiting list control condition.

Most of the included trials enrolled participants with mixed cancer types and stages, mean time of cancer diagnosis ranged from six or fewer weeks to seven years. Studies either compared psychotherapeutic interventions (problem-solving therapy or cognitive-behaviour therapy) with a control condition or pharmacological treatment (mianserin, fluoxetine, desipramine, paroxetine) with a placebo. Three of the problem-solving therapy trials also included antidepressant medication as treatment option. Most participants were women and the mean age was between 47 and 60 years. Baseline depressive symptoms levels ranged from mild to moderate. Most studies systematically screened participants for entry and assessed depressive symptoms using validated scales or interviews.

Studies were selected by pairs of independent raters. Any discrepancy was resolved by discussion with a third rater.

Assessment of study quality
The PEDro quality assessment tool (11 criteria including randomisation procedures, blinding and analysis) was used to assess study quality. Three items that covered treatment fidelity and provision of loss to follow-up information were added to the tool.

Studies were assessed by pairs of independent raters. Any discrepancy was resolved by discussion.

Data extraction
Continuous data from assessments of depressive symptoms were extracted to calculate effect sizes. Author definitions of responder/remitter and associated rates were not used. Hedge's g was calculated for each trial. The mean of effect sizes was used where outcome data for more than one measure of depressive symptoms was reported for a single study. Where trials contained two separate intervention arms, effect sizes were calculated for each arm. The assessment closest in time to completion of the intervention was used to calculate the post-treatment effect size.

Data were extracted by pairs of independent reviewers. Any discrepancy was resolved by discussion. Authors were contacted for additional information where necessary.

Methods of synthesis
A random-effects model was used throughout the analyses to pool effect sizes across trials. Distribution of effect sizes
was examined to identify any extreme values for exclusion. Subgroup analyses used mixed effects models and Bonferroni correction to explore moderators (specific treatment approaches, trial quality criteria, participant characteristics and intervention characteristics). Heterogeneity was considered using the Q-test and $I^2$ statistic. Continuous moderators were explored using meta-regression and the method of moments estimator. Publication bias was assessed using funnel plots, trim and fill and Egger's test. Fail safe N was calculated.

**Results of the review**
Ten trials (1,362 participants) were included in this review. At least three trials were excluded due to authors being unable to provide essential data. Post intervention assessments ranged from eight weeks to 12 months in the psychotherapy trials and 28 days to 12 weeks in pharmacologic trials. Only four psychotherapy trials reported follow-up assessments (six to 24 months). Trial quality varied (trials met between nine and 12 out of 14 criteria).

The main analysis compared any intervention with control conditions and found a significant effect in favour of treatment (Hedge's $g$ 1.01, 95% CI 0.48 to 1.54) with high heterogeneity ($I^2=93\%$). Removal of one trial with two intervention arms (150 participants) as an outlier found a smaller effect with no heterogeneity (hedge's $g$ 0.43, 95% CI 0.30 to 0.56). Using the lowest reported effect size where multiple outcomes had been reported did not substantially alter this result.

Analyses based on follow-up data from four psychotherapy trials reported significant benefits remaining at six to eight months (three trials) and 12 to 18 months (two trials) but not at 24 months (one trial).

Subgroup analyses that compared cognitive-behaviour therapy versus problem solving therapy versus pharmacologic interventions reported statistically significant benefits over control conditions in all cases. Pair-wise comparisons found a significant difference between the two kinds of psychotherapy but not between either kind of psychotherapy compared to medication.

None of the continuous variables examined through meta-regression were associated with overall effect size. There was no indication of significant publication bias and the fail-safe N was 106.

See the full paper for further details of the analyses.

**Authors' conclusions**
Psychological and pharmacological approaches can be targeted productively toward cancer patients with elevated depressive symptoms.

**CRD commentary**
The review addressed a clear clinical question with appropriate inclusion criteria and a reasonable search of the literature. The restriction to papers in English, lack of clarity around the eligibility of unpublished studies and necessary omission of three trials due to lack of available data suggested that the review may not have included all of the eligible and relevant trials. Review processes were generally well reported and likely to minimise error/bias. The studies were assessed for quality and the results were reported clearly.

The synthesis used various techniques although the degree to which these were appropriate was unclear. Removal of a large important trial because it was an outlier without further exploration was difficult to justify and may have influenced the results. The subgroupings were not clearly explained. Meta-regression was unlikely to be informative when so few studies were included.

The conclusion that psychotherapeutic or pharmacologic treatments for depression were more effective than control for depressed patients was unlikely to be erroneous. However it was difficult to be clear about the magnitude of these effects, differences between treatment options due to analytical choices, differences between trials and potential for missed studies.

**Implications of the review for practice and research**
**Practice**: Patients who display elevated symptoms of depression should be referred for treatment.

**Research**: The authors recommend that further research was needed to maximise effectiveness, accessibility and
integration into clinical care of interventions for depressed cancer patients.

**Funding**
Supported in part by grants from National Cancer Institute of the National Institutes of Health.

**Bibliographic details**

**PubMedID**
22767203

**DOI**
10.1093/jnci/djs256

**Original Paper URL**
http://jnci.oxfordjournals.org/content/104/13/990.abstract

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Adaptation, Psychological; Adult; Antidepressive Agents /therapeutic use; Cognitive Therapy; Confounding Factors (Epidemiology); Databases, Factual; Depression /diagnosis /drug therapy /epidemiology /etiology /therapy; Depressive Disorder, Major /etiology /therapy; Humans; Neoplasms /psychology; Problem Solving; Publication Bias; Randomized Controlled Trials as Topic; Risk Factors; Severity of Illness Index; Stress, Psychological /complications; Treatment Outcome

**AccessionNumber**
12012036734

**Date bibliographic record published**
22/10/2012

**Date abstract record published**
22/02/2013

**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.