Reducing relapse and recurrence in unipolar depression: a comparative meta-analysis of cognitive-behavioral therapy's effects

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CRD summary
This review found that for adults with major depression who respond to acute-phase treatment, relapse and recurrence are significantly lower among those treated acutely with cognitive-behavioural therapy (CBT) than among those treated with pharmacotherapy. Continuation-phase CBT appears to reduce subsequent relapse and recurrence rates in this group significantly more than other treatments. Methodological limitations mean that these conclusions should be treated with caution.

Authors' objectives
To evaluate the role of cognitive-behavioural therapies (CBT) in preventing relapse and/or recurrence in major depressive disorder.

Searching
MEDLINE and PsycINFO were searched from inception to July 2006; the search terms were reported. The reference lists of published studies and reviews were checked and experts in the field were consulted. There were no language restrictions. Preliminary findings were presented at a conference and the audience was asked to suggest additional studies.

Study selection
Study designs of evaluations included in the review
There were no explicit inclusion criteria relating to the types of studies eligible for inclusion. Randomised controlled trials (RCTs) and uncontrolled studies were included.

Specific interventions included in the review
Studies of CBT were eligible. The interventions in the included studies were described as cognitive or behavioural therapy, or addressed cognition as a primary therapeutic technique. A formal restrictive definition of CBT was not used. The included studies assessed group and individual CBT. CBT was given either at the acute phase or as continuation treatment, or both. The comparison interventions in studies that included a control group were acute phase or continuation treatment with pharmacotherapy (followed in one study by pill placebo and combined with clinical management in another), behavioural couples therapy, treatment as usual, interpersonal psychotherapy, psychodynamic interpersonal therapy and reduced acute-phase CBT.

Participants included in the review
Studies of adults (older than 18 years) with a primary diagnosis of major (unipolar) depression were eligible for inclusion. The participants in the review were in- or out-patients with above-threshold scores for depression symptoms on the Beck Depression Inventory (BDI), Hamilton Rating Scale for Depression (HRSD), Inventory for Depressive Symptomatology-Clinician Version (IDSC) or Geriatric Depression Scale (GDS). One study was restricted to patients with nonmelancholic depressive diagnoses (major depression, dysthymia or neurotic depression). The majority of patients were middle aged (mean or median age 42 years), female (67%) and (where stated) white (94%).

Outcomes assessed in the review
Studies that reported the number of patients responding to acute-phase treatment, that conducted follow-up assessment after the acute-phase treatment and reported the number or proportion of relapse-recurrences among responders to acute-phase CBT or the recurrence of depression during follow-up, were eligible. Acute phase was defined as occurring during the depressive episode. Studies that did not define acute-phase treatment responders and relapse or recurrence in categorical terms (i.e. rather than using quantitative symptom scores) were excluded. Relapse-recurrence was defined in the review as increased depressive symptoms among patients who first experience remission-recovery in acute-phase treatment.

In the included studies, acute-phase treatment response was defined as an absence of depression or major depressive
episodes using diagnostic criteria, and/or as scores below predetermined thresholds on the HRSD, BDI, GDS, IDSC and/or Scale for Suicidal Ideation. Relapse-recurrence was defined as a diagnosis of depression, and/or symptom scores on the above tools above predetermined thresholds (for periods ranging from 2 weeks to 2 months, where stated), and/or re-treatment or hospitalisation for depression. The timing of the outcome measures varied in the included studies: outcomes were reported at the end of treatment and/or at the longest follow-up time after treatment (these ranged from 1 to 2 years post-intervention for acute-phase treatment and from 10 to 255 weeks post-intervention for continuation-phase treatment).

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
The authors did not state how many reviewers performed the data extraction. Effect sizes were calculated from the proportion of patients experiencing relapse or recurrence at the longest available follow-up time. Estimates of relapse-recurrence within a treatment modality were calculated as raw proportions, which were transformed to logits prior to analysis. Differences between treatments were expressed as areas under the curve (AUC), calculated as 0.5 (proportion relapsing in comparison group minus the proportion relapsing in CBT group, plus 1).

Methods of synthesis
How were the studies combined?
A random-effects model was used to pool relapse proportions and the AUCs, weighted by their inverse variance. Summary AUCs were used to estimate the pooled risk differences (RDs) and the numbers-needed-to-treat (NNT) (formulae given).

How were differences between studies investigated?
Heterogeneity was evaluated using the Q statistic (p<0.10 was considered to provide evidence of heterogeneity). Statistically significant heterogeneity was investigated using random-effects, weighted analysis of variance and regression models with maximum likelihood evaluation.

Results of the review
The review included 28 studies (n=1,880): 24 RCTs, 2 non-randomised controlled studies and 2 uncontrolled studies.

Prevalence of post-therapy relapse-recurrence among responders to acute phase CBT (13 studies, n=364).
Thirty-nine per cent (95% confidence interval, CI: 29, 50) of patients relapsed over a mean of 74 weeks (range: 1 to 2 years). There was statistically significant evidence of heterogeneity (p<0.05). Higher rates of relapse were associated with longer follow-up (p<0.01), use of survival analysis rather than simple proportions (p=0.09), reporting of assessment of CBT therapists’ competence (p=0.02), and use of major depressive episode diagnostic criteria in relapse-recurrence definitions (p=0.04). Lower rates of relapse-recurrence were associated with assessment of CBT therapist adherence (p=0.02), gaps in time in the follow-up assessment (p<0.01), and use of a tool-based threshold in the definition of relapse-recurrence (p<0.01).

Acute-stage CBT compared with active controls.
Acute-stage CBT reduced post-therapy relapse-recurrence more than acute pharmacotherapy (7 RCTs, n=335; AUC 0.61, 95% CI: 0.54, 0.67, p<0.05; RD 22%; NNT 5). Acute-stage CBT plus pharmacotherapy reduced post-therapy relapse-recurrence rates more than pharmacotherapy alone (6 RCTs, n=285; AUC 0.61, 95% CI: 0.54, 0.68, p<0.05; RD 23%; NNT 4). There was no difference in post-therapy relapse-recurrence rates between acute-stage CBT plus pharmacotherapy when compared with acute-stage CBT alone (3 RCTs, n=136; AUC 0.51, 95% CI: 0.42, 0.61) or between acute-stage CBT and other depression-specific psychotherapies (4 studies, n=194; AUC 0.50, 95% CI: 0.42, 0.58). There was no evidence of statistically significant heterogeneity for any of these comparisons (p>0.10).
Continuation-phase CBT compared with non-active controls.

Continuation-phase CBT reduced rates of relapse-recurrence at the end of 35 to 53 weeks' continuation treatment more than non-active controls (assessment only) (4 studies, n=234; AUC 0.61, 95% CI: 0.53, 0.68, p<0.05; RD 21%; NNT 5). It also reduced relapse-recurrence rates 69 to 312 weeks after the end of continuation treatment significantly more than non-active controls (assessment only or clinical management) (5 studies, n=232; AUC 0.64, 95% CI: 0.57, 0.72, p<0.05; RD 29%; NNT 4). There was no evidence of statistically significant heterogeneity for either of these comparisons (p>0.10).

Continuation-phase CBT compared with active controls.

There was a non significant trend towards a greater reduction in relapse-recurrence rates with continuation-phase CBT compared with active controls at the end of 20 to 52 weeks' continuation treatment (5 studies, n=359; AUC 0.56, 95% CI: 0.50, 0.62, p<0.10). Continuation-phase CBT also reduced relapse-recurrence rates 10 to 255 weeks after the end of continuation treatment significantly more than active controls (8 studies, n=626; AUC 0.57, 95% CI: 0.52, 0.61, p<0.05; RD 14%; NNT 8). There was no evidence of statistically significant heterogeneity for either of these comparisons (p>0.10).

Authors' conclusions

Among adults with major depression who respond to acute-phase treatment, relapse and recurrence are significantly lower among those treated acutely with CBT than those treated with pharmacotherapy. Continuation-phase CBT appears to reduce subsequent relapse-recurrence rates in this group significantly more than other treatments. Methodological limitations mean that these conclusions should be treated cautiously.

CRD commentary

The authors' objective was clear and inclusion criteria were defined in terms of the intervention, participants and outcomes. Some relevant sources were searched but the review was limited to published studies, so the review may be subject to publication bias. It is not clear whether appropriate procedures were undertaken when selecting studies for inclusion or extracting the data, thus the potential for reviewer bias and error cannot be determined. Study quality was not formally assessed and the exact design of the non-RCTs included in the review was unclear; the reliability of the review findings is therefore uncertain. There was little information about compliance rates with treatment or the intensity and duration of the interventions, which makes it difficult to assess the generalisability of the findings. Statistical heterogeneity was assessed and, where present, was appropriately investigated. In view of possible publication bias and the failure to assess study quality, the authors’ conclusions should be treated with caution.

Implications of the review for practice and research

Practice: The authors stated that the preventive effect of CBT should be considered when selecting acute-phase treatment and that continuation CBT should be considered after remission to reduce the risk of relapse and (possibly) recurrence.

Research: The authors stated that more research is needed on the role of CBT in delaying or preventing the recurrence of major depression, in particular comparisons of CBT with other depression-specific psychotherapies and the inclusion of ethnically diverse samples. They recommended longitudinal follow up, time-to-event analysis, standard definition of terms, and the testing and reporting of variables that may moderate treatment effects.

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