

**Hackett ML, Anderson CS, House A, Halteh C. Interventions for preventing depression after stroke. Cochrane Database of Systematic Reviews 2008; Issue 3, Art. # CD003689.**

Design: Meta-analysis of randomized clinical trials

PICOS:

- **Patient population:** Patients with a confirmed history of stroke where there was an explicit intention to provide an intervention to prevent depression associated with stroke
  - o Subarachnoid hemorrhage was excluded because of its different natural history and management strategy
  - o Similarly, trials that included mixed populations of patients with stroke and with head injury were excluded from the analysis unless results for stroke patients were reported separately
  - o Patients with cognitive and communication difficulties, as well as those with diagnoses of depression at baseline, were also excluded
- **Interventions:** Two kinds of intervention were considered and analyzed separately; pharmacological treatments and psychological therapy
  - o Psychological therapy required direct patient-provider interaction
  - o Interventions where the sole content was educational or occupational, or which involved visits from stroke support workers, were excluded
- **Comparison/control interventions:**
  - o For pharmacological treatments: placebo
  - o For psychological treatments: standard care
- **Outcomes:** Primary analysis was the proportion of patients meeting diagnostic criteria for depression at the end of follow up:
  - o DSM-III-R or DSM IV criteria for depression, dysthymia, or minor depression
  - o Scoring above cut points for depressive disorder, as defined by symptom scores on standard rating scales
- **Study types:** randomized trials which compared interventions with placebo
  - o Crossover trials were excluded
  - o RCT which compared two active interventions were excluded from analysis

Study selection:

- Databases included the trials registers of the Cochrane Stroke Group, MEDLINE, and other electronic databases through May 2006, as well as contacting researchers and pharmaceutical firms for information about unpublished trials
- Two authors reviewed all citations for inclusion in the review, and estimated the risk of bias by documenting method of randomization, allocation concealment, blinding and the success of blinding, intention to treat analysis, and accounting for withdrawals and dropouts

- Disagreements between article raters were resolved through discussion or through consultation with a third author

Pertinent results:

- Two basic types of intervention were studied: pharmacotherapy and psychological therapy
- For pharmacotherapy, data were available for 11 placebo-controlled trials with 591 patients
  - o 3 compared an SSRI, 2 compared trazodone, 2 compared a tetracyclic drug, 1 compared a tricyclic drug, and 3 compared other drugs (piracetam, indeloxazine, and methylphenidate)
  - o Antidepressants and other drugs (psychostimulants) were analyzed separately
  - o Neither antidepressants nor psychostimulants were shown to produce benefit on depression scales, cognition, disability, or activities of daily living
  - o The effect of antidepressants on the proportion of patients meeting criteria for depression, although lower for antidepressant-treated patients, was not consistent, and meta-analysis was not done
- For psychological therapy, data was available from 4 trials with 902 patients
  - o There was a small significant benefit of psychotherapy in decreasing the proportion of patients diagnosed as depressed at the end of treatment; the pooled odds ratio was 0.64 (95% confidence interval was 0.42 to 0.98)

Authors' conclusions:

- There is inadequate evidence to support the routine use of antidepressants or psychostimulants for prevention of depression in stroke patients
- There is a small benefit of psychological therapy to support the use of more structured approaches to the delivery of education and advice, but evidence to support routine use of psychological approaches in stroke rehabilitation is limited
- Significant difficulties attend the interpretation of clinical trials in this area of stroke medicine
  - o There is considerable heterogeneity in design and analysis of studies; for example, the time from the onset of stroke in various studies varies from a few days to several months
  - o Many studies do not specify clearly the methods used to diagnose stroke
  - o Inadequate concealment of randomization and high attrition rates also create difficulties in interpreting outcomes
- The lack of evidence of an effect of treatment can be attributed to the limited number of studies and weaknesses in study design; it is not necessarily due to the lack of efficacy of the interventions

Comments:

- The extent of the search for relevant studies is more wide-reaching than many other Cochrane reviews are able to report; the search for studies not published in electronic databases should be expected to find most studies which are germane to the topic of the review
- Thus, even though the review is high-quality, the evidence in support of drug and psychological interventions is limited, due to the limitations in the literature identified by the authors
- The authors' conclusion about the effect of psychological therapy is not clear as stated, but appears to have been influenced by a recent study (Watkins 2007) which examined the effect of "motivational interviewing" after stroke
  - o This consisted of 4 weekly sessions of 30 to 60 minutes, in which the therapist elicited the patient's personal goals for recovery and the perceived blocks to recovery
- The psychotherapy paragraph of the review states that outcomes data were available for 4 studies involving 902 participants, but the summary odds ratio of 0.64 is based on only two studies with 520 participants (Analyses 3.1 and 3.2)
- The odds ratio of 0.64, implying a treatment effect of a 36% risk reduction, slightly inflates the effect size based on an actual risk ratio which is closer to 0.72 (a 28% risk reduction)



Assessment: High quality review which supports "some evidence" that structured psychotherapy may be effective in preventing the development of clinical depression following a cerebrovascular stroke

Reference: Watkins CL, Auton MF, et al. Motivational Interviewing Early After Acute Stroke. Stroke 2007;38:1004-1009.