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| Title    | Pharmacological, Psychological, and Noninvasive Brain Stimulation Interventions for Treating Depression After Strokes.   |
| Type     | Article  |
| URL      | <a href="https://clock.uclan.ac.uk/34198/">https://clock.uclan.ac.uk/34198/</a>  |
| DOI      | <a href="https://doi.org/10.1161/STROKEAHA.120.029239">https://doi.org/10.1161/STROKEAHA.120.029239</a>  |
| Date     | 2020   |
| Citation | Allida, Sabine, Cox, Katherine L, Hsieh, Cheng-Fang, Lang, Helen, House, Allan and Hackett, Maree (2020) Pharmacological, Psychological, and Noninvasive Brain Stimulation Interventions for Treating Depression After Strokes. <i>Stroke</i> , 51 (9). ISSN 0039-2499 |
| Creators | Allida, Sabine, Cox, Katherine L, Hsieh, Cheng-Fang, Lang, Helen, House, Allan and Hackett, Maree  |

It is advisable to refer to the publisher's version if you intend to cite from the work.  
<https://doi.org/10.1161/STROKEAHA.120.029239>

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## **Pharmacological, psychological, and non-invasive brain stimulation interventions for treating depression after stroke**

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*Keywords:* Stroke; Depression; Antidepressants; Psychological therapy; Brain stimulation; Randomised controlled trial; Review

Depression is common after stroke. This substantive update including new and combination interventions expands on our previous Cochrane Reviews published in 2004 and updated in 2008.

### **Search methods**

We searched electronic databases from inception to August 2018, clinical trial registers, conference proceedings, and contacted study authors.

### **Selection criteria**

Randomised controlled trials comparing (1) pharmacological interventions with placebo; (2) non-invasive brain stimulation with sham stimulation/usual care; (3) psychological therapy with usual care/attention control; (4) pharmacological and psychological therapy with pharmacological intervention and usual care/attention control; (5) non-invasive brain stimulation and pharmacological intervention with pharmacological intervention and sham stimulation/usual care; to treat depression. Four comparisons are not reported because we found no trials.

### **Results**

49 trials (56 comparisons) with 3342 participants. Data were available for intervention (1) with 20 comparisons; (2) with 8; (3) with 16; (4) with 2; and (5) with 10 comparisons.

We have very little confidence in the following results due to the methodological limitations of many of the included trials.

Pharmacological interventions may decrease the number of people with diagnosable depression (RR 0.70, 95% CI 0.55-0.88; 8 trials, 1025 participants, see Figure), and with <50% reduction in depression scale scores at end of treatment (RR 0.47, 95% CI 0.32-0.69; 6 trials, 511 participants) compared to placebo. There was an increase in adverse events related to the central nervous system (CNS) (RR 1.55, 95% CI 1.12-2.15; 5 trials, 488 participants) and gastrointestinal adverse events (RR 1.62, 95% CI 1.19-2.19; 4 trials, 473 participant) compared to placebo.

Psychological therapy may decrease the number of people with diagnosable depression at end of treatment (RR 0.77, 95% CI 0.62-0.95; 6 trials, 521 participants) with no evidence of death or adverse events compared to usual care/attention control.

There were no trials of non-invasive brain stimulation or combination therapies that reported the prevalence of diagnosable depression at end of treatment. Non-invasive brain stimulation interventions and combination therapies resulted in no deaths.

**Figure.** Effect of pharmacotherapy versus placebo on depression at the end of treatment, grouped by method used to determine depression

## **Discussion**

We lack confidence in the results for pharmacological and psychological interventions showing evidence of benefit and harm. The harm (in pharmacological trials) is concerning given the small number of trials in which harm was recorded and reported.

Large, well-designed trials, with proper collection of adverse events, for moderate/severe depression identified by standardised case-finding in the first six months after stroke are needed. In the absence of such trials, the best clinical advice is: restrict antidepressant prescription to people with persistent depression of moderate-severe intensity, and exercise caution in people with a history of falls, fracture or gastrointestinal bleeding.

## **Disclosures**

The original review was supported by a travel grant from the Stroke Society of Australasia and non-financial support from the Academic Unit of Psychiatry, The University of Leeds and the Department of Clinical Neurosciences, University of Edinburgh. M Hackett receives salary funding from an Australian National Health and Medical Research Council Fellowship.

This paper is based on a Cochrane Review published in The Cochrane Library 2020 (see [www.thecochranelibrary.com](http://www.thecochranelibrary.com) for information). Cochrane Reviews are regularly updated as new evidence emerges and in response to feedback, and The Cochrane Library should be consulted for the most recent version of the review.

## **References**

Allida S, Cox KL, Hsieh CF, Lang H, House A, Hackett ML (2020). Pharmacological, psychological, and non-invasive brain stimulation interventions for treating depression after stroke. *Cochrane Database of Systematic Reviews*, Issue 1. Art. No.: CD003437.

<http://dx.doi: 10.1002/14651858.CD003437.pub4>.