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Pharmacological, non-invasive brain stimulation and psychological interventions, and their combination, for treating depression after stroke (Review)

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TABLE OF CONTENTS

[Intervention Review]

Pharmacological, non-invasive brain stimulation and psychological interventions, and their combination, for treating depression after stroke

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ABSTRACT

Background

Depression is an important morbidity associated with stroke that impacts on recovery, yet is often undetected or inadequately treated.

Objectives

To evaluate the benefits and harms of pharmacological intervention, non-invasive brain stimulation, psychological therapy, or combinations of these to treat depression after stroke.

Search methods

This is a living systematic review. We search for new evidence every two months and update the review when we identify relevant new evidence. Please refer to the Cochrane Database of Systematic Reviews for the current status of this review.

We searched the Specialised Registers of Cochrane Stroke, and Cochrane Depression Anxiety and Neurosis, CENTRAL, MEDLINE, Embase, five other databases, two clinical trials registers, reference lists and conference proceedings (February 2022). We contacted study authors.

Selection criteria

Randomised controlled trials (RCTs) comparing: 1) pharmacological interventions with placebo; 2) non-invasive brain stimulation with sham stimulation or usual care; 3) psychological therapy with usual care or attention control; 4) pharmacological intervention and psychological therapy with pharmacological intervention and usual care or attention control; 5) pharmacological intervention and non-invasive brain stimulation with pharmacological intervention and sham stimulation or usual care; 6) non-invasive brain stimulation and psychological therapy versus sham brain stimulation or usual care and psychological therapy; 7) pharmacological intervention and psychological therapy with placebo and psychological therapy; 8) pharmacological intervention and non-invasive brain stimulation with placebo and non-invasive brain stimulation; and 9) non-invasive brain stimulation and psychological therapy versus non-invasive brain stimulation and usual care or attention control, with the intention of treating depression after stroke.

Data collection and analysis

Two review authors independently selected studies, assessed risk of bias, and extracted data from included studies. We calculated mean difference (MD) or standardised mean difference (SMD) for continuous data, and risk ratio (RR) for dichotomous data, with 95% confidence intervals (CIs). We assessed heterogeneity using the I^2 statistic and certainty of the evidence according to GRADE.

Main results

We included 65 trials (72 comparisons) with 5831 participants. Data were available for: 1) 20 comparisons; 2) nine comparisons; 3) 25 comparisons; 4) three comparisons; 5) 14 comparisons; and 6) one comparison. We found no trials for comparisons 7 to 9.

Comparison 1: Pharmacological interventions
Very low-certainty evidence from eight trials suggests pharmacological interventions decreased the number of people meeting the study criteria for depression (RR 0.70, 95% CI 0.55 to 0.88; P = 0.002; 8 RCTs; 1025 participants) at end of treatment and very low-certainty evidence from six trials suggests that pharmacological interventions decreased the number of people with inadequate response to treatment (RR 0.47, 95% CI 0.32 to 0.70; P = 0.0002; 6 RCTs; 511 participants) compared to placebo. More adverse events related to the central nervous system (CNS) (RR 1.55, 95% CI 1.12 to 2.15; P = 0.008; 5 RCTs; 488 participants; very low-certainty evidence) and gastrointestinal system (RR 1.62, 95% CI 1.19 to 2.19; P = 0.002; 4 RCTs; 473 participants; very low-certainty evidence) were noted in the pharmacological intervention than in the placebo group.

Comparison 2: Non-invasive brain stimulation
Very low-certainty evidence from two trials show that non-invasive brain stimulation had little to no effect on the number of people meeting the study criteria for depression (RR 0.67, 95% CI 0.39 to 1.14; P = 0.14; 2 RCTs; 130 participants) and the number of people with inadequate response to treatment (RR 0.84, 95% CI 0.52, 1.37; P = 0.49; 2 RCTs; 130 participants) compared to sham stimulation. Non-invasive brain stimulation resulted in no deaths.

Comparison 3: Psychological therapy
Very low-certainty evidence from six trials suggests that psychological therapy decreased the number of people meeting the study criteria for depression at end of treatment (RR 0.77, 95% CI 0.62 to 0.95; P = 0.01; 521 participants) compared to usual care/attention control. No trials of psychological therapy reported on the outcome inadequate response to treatment. No differences in the number of deaths or adverse events were found in the psychological therapy group compared to the usual care/attention control group.

Comparison 4: Pharmacological interventions with psychological therapy
No trials of this combination reported on the primary outcomes. Combination therapy resulted in no deaths.

Comparison 5: Pharmacological interventions with non-invasive brain stimulation
Non-invasive brain stimulation with pharmacological intervention reduced the number of people meeting study criteria for depression at end of treatment (RR 0.77, 95% CI 0.64 to 0.91; P = 0.002; 3 RCTs; 392 participants; low-certainty evidence) but not the number of people with inadequate response to treatment (RR 0.95, 95% CI 0.69 to 1.30; P = 0.75; 3 RCTs; 392 participants; very low-certainty evidence) compared to pharmacological therapy alone. Very low-certainty evidence from five trials suggest no difference in deaths between this combination therapy (RR 1.06, 95% CI 0.27 to 4.16; P = 0.93; 487 participants) compared to pharmacological therapy intervention and sham stimulation or usual care.

Comparison 6: Non-invasive brain stimulation with psychological therapy
No trials of this combination reported on the primary outcomes.

Authors' conclusions

Very low-certainty evidence suggests that pharmacological, psychological and combination therapies can reduce the prevalence of depression while non-invasive brain stimulation had little to no effect on the prevalence of depression. Pharmacological intervention was associated with adverse events related to the CNS and the gastrointestinal tract. More research is required before recommendations can be made about the routine use of such treatments.

PLAIN LANGUAGE SUMMARY

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

Review question
Do pharmacological treatments, non-invasive brain stimulation (electrodes are placed on the scalp and a finely controlled electric current is applied to change brain activity), psychological treatments, or combination treatments reduce the proportion of people with depression or the extent of depressive symptoms after stroke?

Background
Depression is common after stroke yet often is not detected or is inadequately treated.

Search date

We identified studies by searches conducted on 8 February 2022. This is a living systematic review. We search for new evidence every two months and update the review when we identify relevant new evidence. Please refer to the Cochrane Database of Systematic Reviews for the current status of this review.

Study characteristics

We included trials that reported on the use of pharmacological, non-invasive brain stimulation, psychological, and combined interventions to treat depression after stroke. We described the main outcomes as the number of people meeting the criteria for depression (scoring above a predefined scoring threshold) and inadequate response (scoring below 50% of the predefined scoring threshold). Average age of participants ranged from 54 to 78 years. Studies were from Asia (39), Europe (12), America (6), South America (1) and Australia (3).

Key results

We included 65 trials (72 comparisons) involving 5831 participants. Pharmacological treatments resulted in fewer people meeting the study criteria for depression at end of treatment and with inadequate response to treatment. Non-invasive brain stimulation did not reduce the number of people meeting the study criteria for depression at end of treatment and with inadequate response to treatment. Psychological therapy reduced the number of people meeting the study criteria for depression at end of treatment. The combination of pharmacological treatment and non-invasive brain stimulation resulted in fewer people meeting the study criteria for depression but did not affect those with inadequate response to treatment. More people in the pharmacological treatment group reported central nervous system (e.g. confusion, sedation, tremor; in five trials) and gastrointestinal side effects (e.g. constipation, diarrhoea; in four trials) than in the placebo groups. Information on side effects of other treatments was not provided.

Certainty of the evidence

Estimates of treatment effects were imprecise due to small numbers in most studies and recruitment of people with very different baseline characteristics. We rated the certainty of evidence as low to very low due to these and other limitations in study design.

Conclusion

Antidepressant drugs may benefit people with persistent depressive symptoms after stroke, but care is required in their use, as little is known about their effects on overall stroke recovery. Non-invasive brain stimulation may not be of benefit while psychological and combination therapies may offer a treatment option. Future research should include a broader group of people with stroke.

SUMMARY OF FINDINGS

Summary of findings 1. Pharmacological interventions compared to placebo for treating depression after stroke

Pharmacological interventions compared to placebo for treating depression after stroke

Patient or population: people with depression after stroke
Setting: hospital, community or mixed
Intervention: pharmacological intervention
Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with pharmacological interventions				
Depression: meeting study criteria for depression at end of treatment (primary outcome)	596 per 1000	417 per 1000 (328 to 525)	RR 0.70 (0.55 to 0.88)	1025 (8 RCTs)	⊕⊖⊖⊖ Very low[a,b,c]	
Depression: < 50% reduction in scale scores at end of treatment (primary outcome)	725 per 1000	348 per 1000 (232 to 507)	RR 0.48 (0.32 to 0.70)	511 (6 RCTs)	⊕⊖⊖⊖ Very low[a,c,d]	
Depression: mean scores at end of treatment (secondary outcome)	See comment	See comment	-	1535 (15 RCTs)	-	No totals
Depression: meeting study criteria for depression at end of follow-up (secondary outcome)	See comment	See comment	-	(0 RCTs)	-	No data available
Adverse events: death (secondary outcome)	18 per 1000	12 per 1000 (4 to 37)	RR 0.64 (0.20 to 2.07)	848 (9 RCTs)	⊕⊖⊖⊖ Very low[a,e]	
Adverse events: all - central nervous system events (e.g. confusion, sedation, tremor) (secondary outcome)	153 per 1000	238 per 1000 (172 to 329)	RR 1.55 (1.12 to 2.15)	488 (5 RCTs)	⊕⊖⊖⊖ Very low[a,e]	
Adverse events: all - gastrointestinal effects (e.g. constipation, diarrhoea) (secondary outcome)	179 per 1000	291 per 1000 (213 to 393)	RR 1.62 (1.19 to 2.19)	473 (4 RCTs)	⊕⊖⊖⊖ Very low[a,d]	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: confidence interval; **OR:** odds ratio; **RCTs:** randomised controlled trials; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]We downgraded the certainty of evidence by two points as several studies were rated as having high or unclear risk for multiple risk of bias domains.
[b]We downgraded the certainty of evidence by two points due to substantial heterogeneity (50% to 89%) observed.
[c]We downgraded the certainty of evidence by one point as the confidence intervals were wide.
[d]We downgraded the certainty of evidence by one point due to moderate heterogeneity (30% to 49%) observed.
[e]We downgraded the certainty of evidence by two points as the confidence intervals were very wide.

Summary of findings 2. Non-invasive brain stimulation compared to sham non-invasive brain stimulation and/or usual care for treating depression after stroke

Non-invasive brain stimulation compared to sham non-invasive brain stimulation and/or usual care for treating depression after stroke

Patient or population: people with depression after stroke
Setting: hospital, community or mixed
Intervention: non-invasive brain stimulation
Comparison: sham non-invasive brain stimulation and/or usual care

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with sham non-invasive brain stimulation and/or usual care	Risk with non-invasive brain stimulation				
Depression: meeting study criteria for depression at end of treatment (primary outcome)	754 per 1000	505 per 1000 (294 to 859)	RR 0.67 (0.39 to 1.14)	130 (2 RCTs)	⊕⊖⊖⊖ Very low[a,b,c]	
Depression: < 50% reduction in scale scores at end of treatment (primary outcome)	785 per 1000	659 per 1000 (408 to 1000)	RR 0.84 (0.52 to 1.37)	130 (2 RCTs)	⊕⊖⊖⊖ Very low[a,b,c]	
Depression: mean scores at end of treatment (secondary outcome)	Ranges from a mean of 10.3 to 19.2	MD 6.51 lower (-9.64 to -3.38)	-	505 (8 RCTs)	⊕⊖⊖⊖ Very low[a,c,d]	

Depression: meeting study criteria for depression at end of follow-up (secondary outcome)	See comment	See comment	-	(0 RCTs)	-	No data available
Adverse events: death - at end of treatment (secondary outcome)	See comment	See comment	-	393 (4 RCTs)	-	No deaths reported across the 4 studies
Adverse events: all - central nervous system events (e.g. confusion, headache, tremor) (secondary outcome)	88 per 1000	54 per 1000 (20 to 144)	RR 0.61 (0.23 to 1.64)	183 (4 RCTs)	⊕⊕⊖⊖ Low[e,f]	
Adverse events: all - other events - not listed above (e.g. dysuria, neck pain, eye discomfort) (secondary outcome)	99 per 1000	46 per 1000 (16 to 137)	RR 0.47 (0.16 to 1.39)	183 (4 RCTs)	⊕⊕⊖⊖ Low[e,f]	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: confidence interval; **MD:** mean difference; **OR:** odds ratio; **RCTs:** randomised controlled trials; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]We downgraded the certainty of evidence by two points as the studies were rated as having unclear risk in multiple risk of bias domains.
[b]We downgraded the certainty of evidence by two points due to substantial heterogeneity (50% to 89%) observed.
[c]We downgraded the certainty of evidence by two points as the confidence intervals were very wide.
[d]We downgraded the certainty of evidence by two points due to considerable heterogeneity (90% to 100%) observed.
[e]We downgraded the certainty of evidence by one point as the confidence intervals were wide.
[f]We downgraded the certainty of evidence by two points as several studies were rated as having high or unclear risk in multiple risk of bias domains.

Summary of findings 3. Psychological therapy compared to usual care and/or attention control for treating depression after stroke

Psychological therapy compared to usual care and/or attention control for treating depression after stroke
Patient or population: people with depression after stroke **Setting:** hospital, community or mixed **Intervention:** psychological therapy **Comparison:** usual care and/or attention control

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with usual care and/or attention control	Risk with psychological therapy				
Depression: meeting study criteria for depression at end of treatment (primary outcome)	703 per 1000	541 per 1000 (436 to 668)	RR 0.77 (0.62 to 0.95)	521 (6 RCTs)	⊕⊖⊖⊖ Very low[a,b]	
Depression: < 50% reduction in scale scores at end of treatment (primary outcome)	See comment	See comment	-	(0 RCTs)	-	No data available
Depression: mean scores at end of treatment (other outcome)	See comment	See comment	-	1568 (17 RCTs)	-	No totals
Depression: meeting study criteria for depression at end of follow-up (secondary outcome)	543 per 1000	462 per 1000 (320 to 657)	RR 0.85 (0.59 to 1.21)	201 (3 RCTs)	⊕⊖⊖⊖ Very low[a,b]	
Adverse events: death - at end of treatment (secondary outcome)	27 per 1000	17 per 1000 (7 to 44)	RR 0.65 (0.26 to 1.66)	889 (9 RCTs)	⊕⊖⊖⊖ Very low[a,b]	
Adverse events: all - central nervous system events (e.g. suicidal intentions) (secondary outcome)	48 per 1000	42 per 1000 (10 to 189)	RR 0.87 (0.20 to 3.90)	126 (2 RCTs)	⊕⊖⊖⊖ Very low[a,b]	
Adverse events: all - other events - not listed above (e.g. fall, too ill) (secondary outcome)	31 per 1000	19 per 1000 (4 to 95)	RR 0.62 (0.13 to 3.09)	254 (3 RCTs)	⊕⊖⊖⊖ Very low[a,b]	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: confidence interval; **OR:** odds ratio; **RCTs:** randomised controlled trials; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]We downgraded the certainty of evidence by two points as several studies were rated as having unclear or high risk in multiple risk of bias domains.
[b]We downgraded the certainty of evidence by one point as confidence intervals were wide.

Summary of findings 4. Pharmacological intervention and psychological therapy (combination) compared to a pharmacological intervention and usual care or attention control (single) for treating depression after stroke

Pharmacological intervention and psychotherapy (combination) compared to a pharmacological intervention and usual care or attention control (single) for treating depression after stroke

Patient or population: people with depression after stroke
Setting: hospital, community or mixed
Intervention: pharmacological intervention and psychotherapy (combination)
Comparison: a pharmacological intervention and usual care or attention control (single)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with a pharmacological intervention and usual care or attention control (single)	Risk with pharmacological intervention and psychotherapy (combination)				
Depression: meeting study criteria for depression at end of treatment (primary outcome)	See comment	See comment	-	(0 RCTs)	-	No data available
Depression: < 50% reduction in scale scores at end of treatment (primary outcome)	See comment	See comment	-	(0 RCTs)	-	No data available
Depression: mean scores at end of treatment (secondary outcome)	Ranges from a mean of 10.1 to 30.2	MD 1.60 lower (-2.13 -to -1.08 lower)	-	278 (3 RCTs)	⊕⊖⊖⊖ Very low[a,b,c]	
Depression: meeting study criteria for depression at end of follow-up (secondary outcome)	See comment	See comment	-	(0 RCTs)	-	No data available
Adverse events: death - at end of treatment (secondary outcome)	See comment	See comment	-	54 (1 RCT)	-	Unable to perform a meta-analysis as there was only 1 study
Adverse events: all - gastrointestinal effects (e.g. constipation, diarrhoea) (secondary outcome)	See comment	See comment	-	54 (1 RCT)	-	Unable to perform a meta-analysis as there was only 1 study

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **MD:** mean difference **OR:** odds ratio; **RCTs:** randomised controlled trials; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]We downgraded the certainty of evidence by one point as both studies were rated as having unclear risk in multiple risk of bias domains.
[b]We downgraded the certainty of evidence by two points as substantial heterogeneity (50% to 89%) was observed.
[c]We downgraded the certainty of evidence by two points as the confidence intervals were very wide.
[d]We downgraded the certainty of evidence by two points as considerable heterogeneity (90% to 100%) was observed.

Summary of findings 5. Pharmacological intervention and non-invasive brain stimulation (combination) compared to a pharmacological intervention and sham stimulation or usual care (single) for treating depression after stroke

Pharmacological intervention and non-invasive brain stimulation (combination) compared to a pharmacological intervention and sham stimulation or usual care (single) for treating depression after stroke

Patient or population: people with depression after stroke
Setting: hospital, community or mixed
Intervention: non-invasive brain stimulation and a pharmacological intervention (combination)
Comparison: a pharmacological intervention and sham stimulation or usual care (single)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with a pharmacological intervention and sham stimulation or usual care (single)	Risk with non-invasive brain stimulation and a pharmacological intervention (combination)				
Depression: meeting the criteria for depression at end of treatment (primary outcome)	640 per 1000	493 per 1000 (410 to 582)	RR 0.77 (0.64 to 0.91)	392 (3 RCTs)	⊕⊖⊖⊖ Low[a,d]	

Depression: < 50% reduction in scale scores at end of treatment (primary outcome)	645 per 1000	613 per 1000 (445 to 839)	RR 0.95 (0.69 to 1.30)	392 (3 RCTs)	⊕⊕⊖⊖ Very low[a,b,d]	
Depression: mean scores at end of treatment (secondary outcome)	Hamilton Depression Rating scale mean scores range from 12.8 to 27.26. The trial using the Stroke Depression scale had a mean score of 23.16.	SMD 1.06 lower (-1.60 to -0.52)	-	1055 (12 RCTs)	⊕⊖⊖⊖ Very low[a,b,c]	
Depression: meeting study criteria for depression at end of follow-up (secondary outcome)	See comment	See comment	-	(0 RCTs)	-	No data available
Adverse events: death (secondary outcome)	16 per 1000	17 per 1000 (4 to 67)	RR 1.06 (0.27 to 4.16)	487 (5 RCTs)	⊕⊖⊖⊖ Very low[a,c]	
Adverse events: all - central nervous system events (e.g. headache, seizures) (secondary outcome)	11 per 1000	6 per 1000 (1 to 61)	RR 0.50 (0.05 to 5.28)	342 (3 studies)	⊕⊖⊖⊖ Very low[a,c]	
Adverse events: all - other events - not listed above (e.g. insomnia, discomfort, headaches) (secondary outcome)	0 per 1000	0 per 1000 (0 to 0)	RR 7.00 (0.38 to 129.93)	120 (2 RCTs)	⊕⊖⊖⊖ Very low[a,c]	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: confidence interval; **MD:** mean difference; **OR:** odds ratio; **RCTs:** randomised controlled trials; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]We downgraded the certainty of evidence by two points as several studies were rated as having unclear or high risk in multiple risk of bias domains.
[b]We downgraded the certainty of evidence by two points as substantial heterogeneity (50% to 89%) was observed.
[c]We downgraded the certainty of evidence by two points as the confidence intervals were very wide.
[d]We downgraded the certainty of evidence by one point as the confidence intervals were wide.

BACKGROUND

Description of the condition

Depression and anxiety disorders are important sequelae of stroke. These mood disorders occur in up to half of people during the first year after onset of stroke, although estimates differ between studies due to varying definitions, populations, exclusion criteria, and timing of assessments (Ayerbe 2013; Hackett 2014). Inconsistent research findings are also due to the complexity of recognition, assessment, and diagnosis of an underlying mood disorder associated with acute stroke and cognitive, language, and other impairments. In addition, people with stroke may experience a variety of behavioural syndromes that are more specific to brain injury, including indifference, emotional lability, disinhibition, unawareness of illness (anosognosia), and difficulties with verbal emotional expression (aprosody). In particular, much of the controversy surrounding 'stroke-associated depression' as a specific type of depressive syndrome hinges on concern about whether the tools normally used for diagnosis of major depression and other depressive illnesses may mis-attribute features of ischaemic brain injury to depression (House 1987; Johnson 1991). Although several depression screening tools have been validated (against a structured clinical interview) for use in people with stroke (Burton 2015; Turner 2012), in practice, researchers use a range of methods to diagnose depression - a psychiatric interview to apply standard diagnostic criteria such as those provided in the *Diagnostic and Statistical Manual of Mental Disorders* (e.g. DSM-IIIR, DSM-IV, DSM 5) (APA 1987; APA 1994; APA 2013), or psychiatric rating scales such as the Montgomery Åsberg Depression Rating Scale (MADRS) (Montgomery 1979), or a rating scale of mood based on self-assessment.

Although controversy continues about whether depression after stroke is predominantly caused by physical factors (such as stroke lesion location) (Carson 2000; Towfighi 2017), or by a person's psychological response to stroke, evidence suggests that clinically diagnosed stroke-associated depression is similar in frequency and nature to depression amongst older people with other chronic illnesses (Burvill 1996; Burvill 1997; Ladwig 2018; Sharpe 1990). Although it was previously thought that the period of greatest risk appeared to be within the first few months of stroke onset (Burvill 1995a; Herrmann 1998; House 1991), this was not apparent in systematic reviews of high-quality observational studies (Hackett 2014). Although some people recover spontaneously, apparently undergoing a grief-like depressive adjustment reaction, up to one-third of people have depression that persists during the first year or longer after stroke onset (Astrom 1996; Herrmann 1998). Those with 'anxious depression' and those with more severe symptoms at presentation appear less responsive to treatment and have a worse long-term prognosis (Astrom 1996).

Evidence of a causal relationship between stroke-associated depression and adverse outcomes is complicated by potential confounding factors such as age, gender, social class, physical disability, and comorbid conditions. However, abnormal mood may impair physical function (Ayerbe 2013; Blöchl 2019), cognitive function (Robinson 1986), and contribute to stress on carers (Anderson 1995a; Roth 2020). Furthermore, stroke-associated depression may be associated with increased risk of death (House 2001; Morris 1993b), including death by suicide (Stenager 1998). Depressive illness amongst older people, in general, is associated with greater morbidity and dependency, higher use of drugs and alcohol, increased use of healthcare resources, and poor compliance with treatment of comorbid conditions (Katona 1995). Aside from exploration of biomarkers to inform prognosis and treatment outcomes, it has been decades since we have seen any major therapeutic advances for people with depression (Herrman 2022).

Description of the intervention

We considered three broad interventions.

- Pharmacological interventions designed to treat depression: several classes of relevant pharmacological agents include selective serotonin reuptake inhibitors (SSRIs) (e.g. fluvoxamine, fluoxetine, sertraline, citalopram, paroxetine), serotonin-norepinephrine reuptake inhibitors (SNRIs) (e.g. venlafaxine, milnacipran, sibutramine), monoamine oxidase inhibitors (MAOIs) (e.g. moclobemide), tricyclic antidepressants (TCAs) (e.g. nortriptyline, imipramine, clomipramine), and other antidepressant medications including psychostimulants (e.g. methylphenidate), mood stabilisers (e.g. lithium), or benzodiazepines.
- Non-invasive brain stimulation: electroconvulsive therapy (ECT) involves the brief passage of an electrical current through the brain via electrodes applied to the scalp to induce a generalised seizure (i.e. a fit or convulsion). The seizure comprises two components: a central element - the ictus involving depolarisation (i.e. discharge of neurotransmitter chemicals) of brain cells - and a peripheral element consisting of convulsive, jerking movements of the body, although this is now modified due to use of a short-acting anaesthetic and muscle relaxant, as part of what is called modified ECT. Modified ECT replaced the crude equipment and techniques of unmodified ECT used in the mid-1950s. The seizure is detected by electrodes placed on the scalp to monitor brain electrical activity (i.e. EEG). The ECT electrodes can be placed on both sides of the head (bilateral placement), or on one side - usually the right side of the head (unilateral placement). Passage of an electrical current through the skull to the brain is necessary to trigger a seizure. In this update, we broadened the review to include other non-invasive brain stimulation techniques such as 1) transcranial magnetic stimulation or repetitive transcranial magnetic stimulation (TMS or rTMS, where a magnetic 'coil' is placed near the head of the person receiving the treatment without making physical contact); 2) transcranial direct current stimulation (tDCS, where a constant, low current is delivered directly to the brain area of interest via small electrodes); 3) cerebrovascular function therapy (CVFT, where a non-invasive percutaneous mastoid electrical stimulator (PMES) device and stimulation electrode are placed on the mastoid area behind the ear to deliver low-voltage electrical current to the fatty tissue below the skin, near the area of a specific nerve, or to the nerve endings situated in the local area; 4) cranial electrotherapy stimulation (CES, where a small, pulsed electrical current is applied across a patient's head); and 5) magnetic seizure therapy (MST), a type of convulsive therapy that involves replacing the electrical stimulation used in ECT with a rapidly alternating strong magnetic stimulation.
- Psychological therapy (talking therapy) designed to treat depression: as many therapies are available, we included any psychological therapy that involved direct patient-professional interaction. The content of the interaction could vary from

counselling to specific psychotherapy, provided it was directed at helping people develop their social problem-solving skills and adjust to the emotional impact of stroke. All interventions had to have a psychological component - talking, listening, support, advice; they had to be based on a theory of talking therapy; had to be structured and timetabled as a talking therapy; and had to be delivered by somebody with some explicitly stated training in and supervision of therapies. The person-professional interaction could take place in person, via telephone, or through other media. We did not include web-based interventions even if mediated by a healthcare professional. We did not include interventions based upon self-management or supported self-management.

We further considered these combinations of three broad interventions.

- Pharmacological intervention and one of various forms of psychological therapy versus pharmacological intervention and usual care and/or attention control.
- Pharmacological intervention and non-invasive brain stimulation versus pharmacological intervention and sham stimulation or usual care.
- Non-invasive brain stimulation and one of various forms of psychological therapy versus sham brain stimulation or usual care and psychological therapy.
- Pharmacological intervention and one of various forms of psychological therapy versus placebo and psychological therapy.
- Pharmacological intervention and non-invasive brain stimulation versus placebo and non-invasive brain stimulation.
- Non-invasive brain stimulation and one of various forms of psychological therapy versus non-invasive brain stimulation and usual care and/or attention control.

Earlier versions of this review had the title 'Pharmacological, psychological, and non-invasive brain stimulation interventions for treating depression after stroke'. The new title better reflects all the interventions considered for inclusion in the living review and presents the interventions in the same order they are covered in the review.

How the intervention might work

Pharmacological interventions are thought to alter the synaptic transmission process within the brain to increase neurotransmission, for example, SSRIs are intended to block the resorption of serotonin, SNRIs are designed to increase the levels of serotonin and norepinephrine, and TCAs are designed to block the reuptake of norepinephrine.

During modified ECT, a small amount of electrical current is passed briefly across the brain to cause an artificial epileptic fit that affects the entire brain. Repeated ECT is believed to alter chemical pathways in the brain that are responsible for depression. The exact mechanism of action of rTMS, tDCS, PMES and CES remains unclear. They are thought to induce intracerebral current flow and increase or decrease neuronal excitability and/or activate nerve cells in the specific area being stimulated. rTMS involves replacing the electrical stimulation used in ECT with a magnetic stimulus, which is purported to produce similar clinical effects but without the cognitive side effects.

Psychological therapy focuses on changing thinking, emotional, behavioural, and relationship patterns. During psychological therapies, trained therapists work with individuals to help them see patterns in their thoughts, emotions, behaviours, or relationships that may be problematic. The therapist's role is to help a person understand these patterns while assist that person in developing ways to overcome them.

Why it is important to do this review

This topic lends itself to a living systematic review approach for several reasons.

Although depression may influence recovery and outcomes following stroke, many (perhaps most) people with stroke do not receive effective treatment because their mood disorder is undiagnosed or is inadequately treated. The UK National Sentinel Audit found that 25% of patients were not screened for depression, and only 60% of those identified as needing support received it. Ebrahim 1987a found that few people with stroke-associated depression had been given antidepressants following discharge from hospital, and House 1989 reported that general practitioners and hospital doctors had a passive attitude towards therapy. On the other hand, some studies have found antidepressant prescribing persisting long term but with little attempt to match prescribing to need (Paul 2006). Although this variability may reflect problems with the diagnosis of a 'significant' mood state amongst older people with disability, it still also reflects uncertainty amongst clinicians as to the balance of benefits and risks (including side effects) of therapies in this setting. For example, it is not clear that in other settings, antidepressants are of benefit for mild or moderate depression of the sort that is common after stroke (Fournier 2010). Recent evidence from trials of the SSRI fluoxetine to improve function after stroke has shown an increased risk of fractures (AFFINITY Trial Collaboration 2020; EFFECTS Trial Collaboration 2020; FOCUS Trial Collaboration 2019). This has increased the level of clinical uncertainty about the balance of benefit and risk when using fluoxetine and other SSRIs to treat depression. We believe it is important to incorporate new evidence relating to SSRIs for treating depression in a timely manner.

Indirect evidence of the effectiveness of pharmacological and psychological treatments for depression (and anxiety) for older people in general, and for those with associated physical illness, is available in several published reviews (Gill 2000; Kirsch 2008; Lima 2001; McCusker 1998; Mittmann 1997; Wilkinson 1997). However, because of the possibility that depression after stroke may differ in important ways, it may be inappropriate to extrapolate these data to people with stroke. Use of rTMS, tDCS, PMES and CES in people with stroke is relatively new, and few data have been available to guide clinical decision-making. We are aware of an increasing number of completed and ongoing trials of non-invasive brain stimulation to treat depression after stroke. As such, this systematic review has been transformed into a Living Systematic Review where new evidence from all randomised controlled trials (published and unpublished) of pharmacological agents, non-invasive brain stimulation, psychological therapies, or their combination for treatment of depression after stroke are incorporated rapidly after it is identified.

This Cochrane Review was first published in 2004, and updated in 2008 and 2020.

OBJECTIVES

To evaluate the benefits and harms of pharmacological therapy, non-invasive brain stimulation, psychological therapy, or combinations of these interventions to treat depression after stroke.

METHODS

Criteria for considering studies for this review

Types of studies

We restricted the review to all relevant randomised controlled trials (RCTs) only. There was no restriction on eligibility of RCTs on the basis of language, sample size, duration of follow-up, or publication status. Trials that met all inclusion criteria, but from which no outcome data were available (neither from the report of the trial nor from the study authors), could not contribute meaningfully to a pooled estimate of effect. These trials were regarded as 'dropouts' rather than as ineligible.

Types of participants

We defined stroke according to clinical criteria, including cerebral infarction, intracerebral haemorrhage, and 'uncertain' pathological subtypes. We excluded trials of people with subarachnoid haemorrhage (SAH) only, as this entity has a different natural history and management strategy from other stroke subtypes. However, we did include trials with mixed stroke subtypes, including small numbers of people with SAH. There were no restrictions on the basis of age, sex, or other characteristics. Participants were required to have depression (diagnosed by psychiatric interview, mood scale, or treating clinician) on recruitment. We excluded trials with participants who were not depressed at recruitment, but that measured depression as the primary outcome at follow-up. These trials were included in a review of interventions for preventing depression after stroke (Allida 2020a).

The diagnostic categories of depression considered were:

- depressive disorder, as defined by symptom scores on a standard screening instrument - scoring above a predefined scoring threshold;
- major depression, as defined by the American Psychiatric Association *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IIIR APA 1987, DSM-IV APA 1994, DSM-V APA 2013), or similar diagnostic criteria; and
- dysthymia or minor depression, as defined by DSM or other standard diagnostic criteria.

Trials that included mixed populations (such as those with stroke and head injury or other central nervous system (CNS) disorders) were excluded unless separate results for people with stroke could be identified. Trials were excluded if participants were being treated primarily for a stroke-associated pain syndrome, even if depression was measured as a secondary outcome.

Types of interventions

We included the following interventions.

- Comparison between a pharmacological intervention and placebo for treatment of depression after stroke. Specific pharmacological agents included tricyclic antidepressants (e.g. nortriptyline, imipramine, clomipramine), selective serotonin reuptake inhibitors (SSRIs) (e.g. fluvoxamine, fluoxetine, sertraline, citalopram, paroxetine), monoamine oxidase inhibitors (MAOIs) (e.g. moclobemide), and other antidepressant medications. Trials of mood stabilisers (e.g. lithium) or of benzodiazepines and psychostimulants (e.g. methylphenidate) were analysed separately.
- Comparison between non-invasive brain stimulation and sham stimulation or usual care for treatment of depression associated with stroke.
- Comparison between psychological therapy and usual care and/or attention control for treatment of depression after stroke. We included any psychological therapy that involved direct person-professional interaction. The content of the interaction could vary from counselling to specific psychological therapy, provided it was directed at helping people adjust to the emotional, social or physical impact of stroke in ways that were likely to improve mood. All interventions had to have a psychological component - talking, listening, support, advice - and had to be based on a theory of talking therapy; had to be structured and time-tabled as a talking therapy; and had to be delivered by somebody with some explicitly stated training in and supervision of therapies.

Alternatively, we included their combinations.

- Pharmacological intervention and one of various forms of psychological therapy versus pharmacological intervention and usual care and/or attention control.
- Pharmacological intervention and non-invasive brain stimulation versus pharmacological intervention and sham stimulation or usual care.
- Non-invasive brain stimulation and one of various forms of psychological therapy versus sham brain stimulation or usual care and psychological therapy.
- Pharmacological intervention and one of various forms of psychological therapy versus placebo and psychological therapy.
- Pharmacological intervention and non-invasive brain stimulation versus placebo and non-invasive brain stimulation.
- Non-invasive brain stimulation and one of various forms of psychological therapy versus non-invasive brain stimulation and usual care and/or attention control.

Exclusions included the following.

- Interventions with an agent or therapy that was being evaluated primarily for other reasons (e.g. to improve physical function, to provide neuroprotection, to facilitate neuroregeneration), even if the intervention was a recognised treatment for depression, and even if a standardised depression scale was administered at baseline and at outcome assessment (these trials are included in a separate systematic review, with depression as a secondary endpoint (Mead 2012)). Where the intervention and the trial are designed to treat depression, but the primary endpoint is safety or feasibility e.g. a pilot or feasibility trial, the trial will be included if the intervention is clearly described as targeting depression and depression is measured as the main secondary endpoint.

- Interventions provided with the sole purpose of educating or providing information.
- Occupational therapy (including leisure therapy and other rehabilitation services).
- Acupuncture or electro-acupuncture.
- Herbal medicines.
- Interventions that involved visits from stroke support workers, unless there was a clearly defined psychological component. Attention control in psychological therapy trials can include nonspecific interventions such as relaxation classes or follow-up with a clinician who has no psychological training.

Types of outcome measures

Primary outcomes

Primary analyses focused on the prevalence of diagnosable depression and included the following.

- Meeting the criteria for depression at end of treatment, as defined by DSM or similar standard diagnostic criteria.
- Inadequate response to treatment defined as less than 50% reduction in depression scale scores at end of treatment.

Secondary outcomes

- Depression scores as measured on scales such as the Hamilton Depression Rating Scale (HDRS; Hamilton 1960), the Montgomery Åsberg Depression Rating Scale (MADRS; Montgomery 1979), the Geriatric Depression Scale (GDS; Gompertz 1993), the Beck Depression Inventory (BDI; Beck 1961), and the Hospital Anxiety and Depression Scale (HADS Depression subscale; Zigmond 1983) at end of treatment and at follow-up.
- Meeting the criteria for depression at end of follow-up, as defined by DSM or similar standard diagnostic criteria.
- Less than 50% reduction in depression scale scores at end of follow-up.
- Psychological distress scores, as measured on composite scales such as the General Health Questionnaire (GHQ; Goldberg 1972) at end of treatment.
- Anxiety scores, as measured on scales such as the Hamilton Anxiety Scale, the Beck Anxiety Inventory, and the Hospital Anxiety and Depression Scale (HADS Anxiety subscale; Zigmond 1983) at end of treatment.
- Cognitive function scores, as measured on scales such as the Mini-Mental State Examination (MMSE; Folstein 1975) at end of treatment.
- Activities of daily living scores, as measured on scales such as the Barthel Index (BI; Mahoney 1965) at end of treatment.
- Disability scores, as measured on scales such as the Functional Independence Measure (FIM; Deutsch 1997).
- Neurological function scores, as measured on scales such as the National Institutes of Health Stroke Scale (NIHSS; Lyden 2001).
- Disadvantages of treatment recorded as adverse events, grouped by death, all events, and leaving the study early (including death).

Participants' reasons for withdrawal from trials were examined as a marker of acceptance.

Search methods for identification of studies

This is a Living Systematic Review updating a previously published Cochrane Review update (Allida 2020). The first review was published in 2004 (Hackett 2004), and subsequently updated in 2008 (Hackett 2008). For this update, we searched all databases from inception until February 2022. We searched for relevant trials in all languages and arranged for translation of trial reports when necessary.

Cochrane Stroke Specialised Register

The Cochrane Stroke Group Information Specialist searched the Specialised Register of Cochrane Stroke on 8 February 2022.

Electronic searches

We searched the following bibliographic databases.

- Cochrane Stroke Group Specialised Register of Trials (last searched February 2022).
- Cochrane Central Register of Controlled Trials (CENTRAL; Issue 5 of 12, February 2022) in the Cochrane Library (last searched February 2022).
- MEDLINE (OVID): 1946 to February 2022.
- Embase (OVID): 1980 to February 2022.
- APA PsycINFO (OVID): 1967 to February 2022.
- Cumulative Index to Nursing and Allied Health Literature (CINAHL) (EBSCO): 1982 to February 2022.
- Science Citation Index - Expanded (SCI-EXPANDED) - 1900 to present, Social Sciences Citation Index (SSCI) - 1900 to present, and Arts & Humanities Citation Index (A&HCI) - 1975 to present within Web of Science (last searched February 2022).

We developed the MEDLINE search strategy (Appendix 1) with the help of the Cochrane Stroke Group Information Specialist and adapted it for the other databases. The stroke and depression search terms have been linked to the Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE: sensitivity- and precision-maximising version (2008 revision); Ovid format, as referenced in the Box 3.d in the Technical Supplement to Chapter 4: Searching for and selecting studies in the *Cochrane Handbook for Systematic Reviews of Interventions* Version 6.1.0 (updated February 2022) (Lefebvre 2021).

The updated search strategies used for this update are presented in Appendix 2.

The search strategies used for the 2018 update are presented in Appendix 3. Biological Abstracts has now been superseded by ISI Web of Science, which includes the Arts and Humanities Index. Several databases/citation indexes (Applied Science and Technology Plus; Biological Abstracts; BIOSIS Previews; General Science Plus; Dissertations and Theses) listed in Appendix 4 were not used in the 2018 update.

Living systematic review considerations

The last search was 8 February 2022. We will re-run bi-monthly searches after this. We are incorporating new evidence rapidly after it is identified. We will reconsider search methods and strategies once a year to ensure they reflect any terminology changes in the topic area or in the databases.

Searching other resources

We searched the following resources using "stroke" or "brain infarction" and "depression" or "low mood" and "interventional" from inception to 8 February 2022.

- US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (www.clinicaltrials.gov).
- World Health Organization International Clinical Trials Registry Platform (WHO ICTRP) (www.who.int/ictrp/en/).

Data collection and analysis

Selection of studies

Five review authors (ARS, KC, KP, SA and MH) reviewed all new citations and discarded those that were irrelevant based on the title of the publication and its abstract. When any suggestion was made that an article was possibly relevant, we retrieved the full-length article for further assessment. Three review authors (KC, MH and SA) independently selected the new trials for inclusion in the review from the culled citation list. Potentially relevant Chinese articles were translated by another study author (C-FH). We resolved disagreements by discussion, and AH and MH confirmed the final list and adjudicated any persisting differences of opinion. The selection for the most recent search process is presented in a PRISMA flow diagram (Figure 1). We listed the included studies under Characteristics of included studies and studies that we ultimately excluded under Characteristics of excluded studies, and we provided the primary reasons for exclusion. A PRISMA flow diagram of the preceding search is also available (Appendix 5).

Figure 1. Study flow diagram for living review update (to February 2022). Details of searches for previous versions of this review are available in those reviews

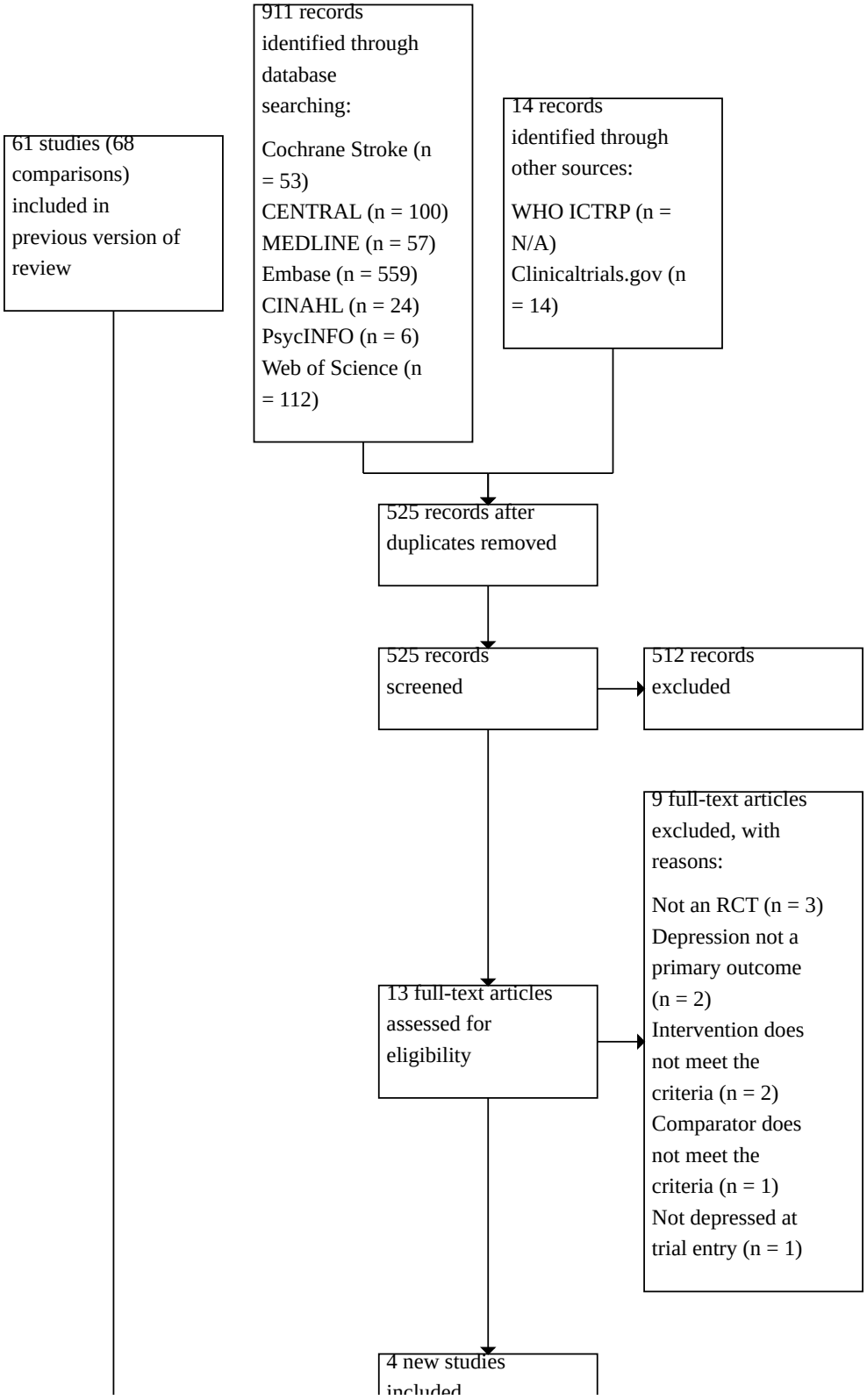
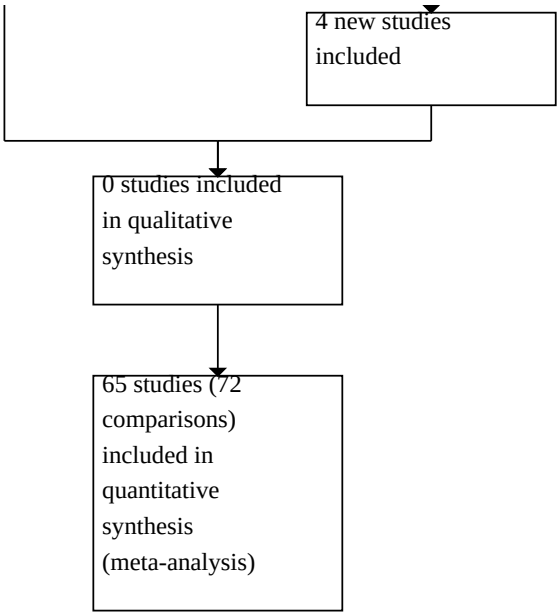


Figure 1. (Continued)



Living systematic review considerations

We will immediately screen any new citations retrieved during the bi-monthly searches.

Data extraction and management

Four review authors (C-FH, KC, MH and SA) independently extracted study characteristics and outcome data from included studies and entered them on specially designed forms. We cross-checked and entered the data into Review Manager 5 (Review Manager 2020), and Review Manager Web (RevMan Web 2020). We resolved disagreements by discussion or through consultation with two other review authors (AH or MH). We obtained missing information from the study authors when possible. Information on funding sources is mentioned in the notes sections of the Characteristics of included studies table.

We collected data on:

- the report: author, year, and source of publication;
- the study: sample characteristics, social demography, and definition and criteria used for depression;
- the participants: stroke sequence (first ever vs recurrent), social situation, time elapsed since stroke onset, history of psychiatric illness, current neurological status, current treatment for depression, and history of coronary artery disease;
- the research design and features: sampling mechanism, treatment assignment mechanism, adherence, non-response, and length of follow up;
- the intervention: type, duration, dose, timing, and mode of delivery; and
- the effect size: sample size, nature of outcome, estimate, and standard error.

To allow for intention-to-treat (ITT) analysis, we sought the data irrespective of adherence and fidelity of the intervention, and regardless of whether participants were subsequently deemed ineligible or were otherwise excluded from treatment or follow-up. When study authors used multiple measures to assess depression, we extracted data from the measure the study authors stated was used to assess the primary outcome. For measures assessing secondary outcomes, we extracted data from the most commonly used measure. When data for the same trial endpoint were conflicting across multiple publications, we extracted data from the first publication reporting data for that outcome.

We checked all extracted data for agreement between review authors. We obtained missing information from the primary investigators whenever possible. To avoid introducing bias, we obtained this unpublished information in writing, on forms designed for the purpose, and entered it into RevMan.

Assessment of risk of bias in included studies

Four review authors (SA, KC, C-FH, MH) independently assessed risk of bias for each study using the criteria outlined in Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We resolved any disagreements by discussion or by consultation with another review author (MH). Although a number of scales have been devised to assess the quality of RCTs, no convincing evidence shows that complex and time-consuming scales are more effective than simple scales (Verhagen 2001). We assessed risk of bias according to the following domains.

- Random sequence generation.
- Allocation concealment: if allocation was performed using opaque envelopes, we also categorised this as 'high risk' as it is not tamper-proof.

- Blinding of participants and personnel: for psychological interventions, we recognise that participants are unlikely to remain blinded; however we also categorised this as 'high risk'.
- Blinding of outcome assessment.
- Incomplete outcome data.
- Selective outcome reporting: if a published trial had no corresponding published or registered protocol, this was assessed as unclear risk.
- Other bias.

We also provided a quote from the study to justify our judgement in the Risk of bias in included studies table. When considering treatment effects, we have taken into account the risk of bias for studies that contributed to that outcome.

Measures of treatment effect

Dichotomous data

For all dichotomous outcomes, we calculated risk ratios (RRs) with 95% confidence intervals (CIs) when appropriate, using random-effects analyses.

Continuous data

For continuous data, if ordinal scale data appeared to be normally distributed, or if the analysis suggested that parametric tests were appropriate, we treated outcome measures as continuous. If at least two studies reported the same outcomes, then we calculated a mean difference (MD) with 95% CI across trials. When different outcome measures were used, we calculated a standardised mean difference (SMD) with 95% CI.

Unit of analysis issues

We predicted that randomisation would occur at the level of the individual participant in most, if not all, trials. Outcomes are reported at end of treatment and at end of follow-up when data are available. When trials included two or more active intervention arms and only one control arm (placebo, attention control, or usual care), we compared data from each treatment arm with data from the total number of participants in the control arm divided by the number of active intervention arms. Comparisons are presented as separate trials.

Dealing with missing data

We wrote to the authors of all included, ongoing, and dropout trials to request data that were unavailable or ambiguous in published articles.

Assessment of heterogeneity

Clinical and methodological heterogeneity were assessed by examining the study characteristics. We used the I^2 statistic to measure heterogeneity amongst the trials in each analysis (Deeks 2021). If at least two trials reported the same outcomes, we reviewed the data for appropriateness of pooling. We interpreted the amount of heterogeneity as low (0% to 29%), moderate (30% to 49%), substantial (50% to 89%), and considerable (90% to 100%) using I^2 values. We reported similarities between interventions, participants, design, and outcomes in the Description of studies subsection.

Assessment of reporting biases

We assessed publication bias by using a funnel plot only if 10 or more trials were included (Higgins 2011). We attempted to avoid language bias by including trials irrespective of language of publication, and we provided translation when needed by native speakers of that language.

In some cases, similarities between trial reports indicated the possibility of multiple publications from the same trial. We contacted study authors to check whether these publications were duplicates. In the absence of a response and explicit cross-referencing, we judged articles to be from the same trial if they met the following criteria: 1) evidence suggested overlapping recruitment sites, trial dates, and grant funding numbers, and 2) similar or identical patient characteristics were reported by trial authors.

Data synthesis

We analysed data using Review Manager software (Review Manager 2020), and pooled data for meta-analysis when studies assessed similar treatments and had similar outcomes. We conducted a meta-analysis using available or calculated MD or SMD for continuous outcomes, and RR for dichotomous outcomes. We included measures of uncertainty in the results, such as 95% CIs and estimates of I^2.

Subgroup analysis and investigation of heterogeneity

If at least two trials reported the same outcomes, we reviewed the data for appropriateness of pooling. If we found definitive evidence of heterogeneity (I^2 > 50%), we explored potential reasons for differences by performing subgroup analyses and meta-regression (Normand 1999). If heterogeneity could not be explained, we combined trials using random-effects analyses with cautious interpretation, or we did not combine them at all. When possible, we performed subgroup analyses to examine the impact of treatment type and duration, and of stroke severity. We reported two subgroup analyses. Further subgroup analyses were not performed due to the small number of trials in a subgroup, limited data available about the intervention to determine appropriate subgroups, unavailability of risk of bias data, or we were unable to determine which trials to exclude for sensitivity analyses.

Sensitivity analysis

We explored the sensitivity of the combined estimate of individual trials for all outcomes, when feasible, by leaving one study out if we noted high risk of bias and methodological differences. We then calculated the combined effect of the remaining trials and compared these results with the combined effect based on all trials.

Methods for future updates

We will review scope and methods approximately yearly, or more frequently if appropriate, in light of potential changes in the topic area or the evidence being included in the review (e.g. additional comparisons, interventions, subgroups or outcomes, or new methods becoming available).

We will make decisions about whether to stop updating when appropriate (e.g. if conclusions are unlikely to change with future updates; no meaningful effect is likely to be found; the review question is no longer a priority for decision-making; or no new

evidence is likely), and will be guided by ongoing research in this area.

Summary of findings and assessment of the certainty of the evidence

We assessed the certainty of evidence according to GRADE by constructing Summary of findings tables for the outcomes below, per comparison, using the GRADEPro tool (GRADEproGDT 2020; Schünemann 2021).

These data were available for: 1) pharmacological interventions versus placebo (with 20 comparisons); 2) one of various forms of non-invasive brain stimulation versus sham stimulation or usual care (with 10 comparisons); 3) one of various forms of psychological therapy versus usual care and/or attention control (with 23 comparisons); 4) pharmacological intervention and various forms of psychological therapy versus pharmacological intervention and usual care and/or attention control (with two comparisons); and 5) non-invasive brain stimulation and pharmacological intervention versus pharmacological intervention and sham stimulation or usual care (with 12 comparisons).

For comparison 1, 'pharmacological intervention versus placebo', we reported certainty of evidence for the following outcomes: meeting study criteria for depression at end of treatment, < 50% reduction in depression scale scores at end of treatment, mean neurological function scores at end of treatment, adverse events related to CNS and gastrointestinal tract and death at end of treatment.

For comparison 2, 'non-invasive brain stimulation versus sham or usual care', we reported certainty of evidence for the following outcomes: meeting study criteria for depression at end of treatment, < 50% reduction in depression scale scores at end of treatment; mean depression scores at end of treatment, mean neurological function scores at end of treatment, death at end of treatment and adverse events related to CNS and other events.

For comparison 3, 'psychological intervention versus usual care or attention control', we reported certainty of evidence for the following outcomes: meeting the study criteria for depression at end of treatment, < 50% reduction in depression scale scores at end of treatment, mean depression scores at end of treatment, meeting the study criteria for depression at end of follow-up and death at end of treatment.

For comparison 4, 'pharmacological intervention and a form of psychological therapy (combination) versus pharmacological intervention and usual care or attention control (single)', we reported certainty of evidence for meeting the study criteria for depression at end of treatment, < 50% reduction in depression scale scores at end of treatment, mean depression scores at end of treatment, mean activities of daily living at end of treatment, and death at end of treatment.

For comparison 5, 'pharmacological intervention and non-invasive brain stimulation (combination) versus pharmacological intervention and sham stimulation or usual care (single)', we reported certainty of evidence for the following outcomes: meeting the study criteria for depression at end of treatment, < 50% reduction in depression scale scores at end of treatment, mean depression scores at end of treatment, mean depression scores at end of follow-up, death at end of treatment, and adverse events related to CNS and other events.

For comparison 6, 'non-invasive brain stimulation and one of various forms of psychological therapy versus sham brain stimulation or usual care plus psychological therapy' we found only one comparison. This result was not summarised using the GRADEPro tool (GRADEproGDT 2020; Schünemann 2021).

We found no trials for the following comparisons: 7) pharmacological intervention and various forms of psychological therapy interventions versus placebo and psychological therapy; 8) pharmacological intervention and non-invasive brain stimulation versus placebo plus non-invasive brain stimulation; and 9) non-invasive brain stimulation and one of various forms of psychological therapy versus non-invasive brain stimulation plus usual care and/or attention control.

Living systematic review considerations

Whenever we find new evidence (i.e. trials, data or information) meeting the review inclusion criteria, we will extract the data, assess risk of bias, and incorporate it in the synthesis every four months, as appropriate. We will incorporate any new trial data into existing meta-analyses using the standard approaches outlined in the Data synthesis section. Formal sequential meta-analysis approaches will not be used for updated meta-analyses.

RESULTS

Description of studies

Results of the search

We identified 925 records; of these, we retrieved 911 through database searching. We found 14 additional references by searching other resources. After 400 duplicates were removed, we screened 525 titles and abstracts and excluded 512 irrelevant records. We retrieved full-text reports for the remaining 13 studies. After reading the full texts, we excluded nine trials as they did not meet the review eligibility criteria. We have provided the primary reasons for exclusions in the Characteristics of excluded studies table and in Figure 1. We identified four trials that met the inclusion criteria (Hjelle 2019; Kim 2019; Li 2016; Yu 2021). However, data were not available for depressed participants only (Hjelle 2019), and were not in a format suitable for meta-analysis (Kim 2019; Li 2016; Yu 2021). These trials are considered 'dropouts' (Table 1). In the previously published version of this review, 17 trials met the inclusion criteria but were considered 'dropouts' (Bramanti 1989; Chang 2011; Choi-Kwon 2006; Delbari 2011; Downes 1995; Hadidi 2014; Jorge 2004; Jorge 2008; Kim 2017; Kim 2017a; Kootker 2012; Mauri 1988; Meara 1998; Ohtomo 1985; Raffaele 1996; Robinson 2000; Sun 2000): outcome data were not available for depressed participants only (Chang 2011; Choi-Kwon 2006; Delbari 2011; Hadidi 2014; Jorge 2004; Jorge 2008; Kim 2017; Kim 2017a; Ohtomo 1985; Raffaele 1996; Robinson 2000; Sun 2000), outcome data were not available at all (Downes 1995), or outcome data were not presented in a format suitable for meta-analysis (Bramanti 1989; Kootker 2012; Meara 1998; Mauri 1988). See Table 1 for more detailed information on these studies.

We contacted the study authors to ask for information on ongoing studies or to request additional study data and, in some instances, additional analyses. For this update, we received responses

with additional data regarding two new trials (Hordacre 2021; Valiengo 2017). We have received responses with additional data or information from the authors of 16 studies across the previous updates (Andersen 1994; Cullen 2018; Downes 1995; Fang 2017; Fruehwald 2003; Hoffmann 2015; Kerr 2018; Kirkness 2017a; Lai 2006a; Lincoln 2003; Murray 2002; Mitchell 2002; Reding 1986, Robinson 2008a; Towle 1989; Watkins 2007).

Included studies

This present review includes 65 trials (72 comparisons) with 5831 participants (Alexopoulos 2012; Andersen 1994; Cao 2009a; Cao 2009b; Chen 2005a; Cullen 2018; Du 2005; Fan 2010; Fan 2014; Fang 2017; Fruehwald 2003; Gao 2017a; Gao 2017b; Gu 2016; Hoffmann 2015; Hordacre 2021; Huang 2002; Jiang 2001a; Jiang 2001b; Jiang 2014a; Jiang 2014b; Jin 2013; Kerr 2018; Kirkness 2017a; Kirkness 2017b; Kong 2007; Lai 2006a; Li 2008; Li 2009; Li 2013; Li 2014; Li 2019a; Liang 2015; Lincoln 2003; Lipsey 1984; Liu 2015; Liu 2020; Lu 2016; Lu 2018; Lu 2020; Meng 2015; Mitchell 2002; Murray 2002; Ohtomo 1991; Ponzio 2001; Rampello 2005; Reding 1986; Robinson 2008a; Robinson 2008b; Sun 2013; Tao 2008; Terachinda 2021; Thomas 2007; Thomas 2016; Tian 2010; Towle 1989; Valiengo 2017; Wang 2004a; Wang 2005; Wang 2005a; Wang 2019; Watkins 2007; Wei 2021; Wiart 2000; Wu 2019; Yang 2002; Yang 2013; Yang 2014a; Yang 2014b; Zhang 2013; Zhao 2004; Zheng 2016).

Lincoln 2003 compared an active treatment with an attention control (time spent by participants in the treatment group with a trained therapist was controlled in the attention control group by participants spending an equal amount of time in focused conversation), as well as another control (standard care). We combined data from the attention control and control groups, and we compared these with data from the treatment group.

Jiang 2001a and Robinson 2008a compared two active treatment arms versus a placebo arm. We compared data from both treatment arms against data from half the number of participants in the placebo arm and presented the results as two separate comparisons (Jiang 2001a; Jiang 2001b; Robinson 2008a; Robinson 2008b).

Cao 2009a and Jiang 2014a were parallel RCTs with four arms. We compared data from both treatment arms with their respective control arms and presented the results as separate comparisons (Cao 2009a; Cao 2009b; Jiang 2014a; Jiang 2014b).

Gao 2017a and Kirkness 2017a compared two active treatment arms versus a usual care or attention control arm. We compared data from both treatment arms with data from half the number of participants in the usual care or attention control arm and presented the results as separate comparisons (Gao 2017a; Gao 2017b; Kirkness 2017a; Kirkness 2017b).

Yang 2014a compared two active treatment arms versus a sham non-invasive brain stimulation arm. We compared data from both treatment arms with data from half the number of participants in the sham non-invasive brain stimulation arm (Yang 2014a; Yang 2014b).

More detailed information is provided in Characteristics of included studies table.

Participants

All trials in this review included men and women. The mean age of participants ranged from 52 to 78 years. Most trial authors reported the time since stroke and randomisation into the trial. The time since stroke for trials of pharmacological intervention ranged from five days to 437 days, non-invasive brain stimulation from three days to 426 days, psychological therapy from 0 days to 1734 days and combination therapy from 0 days to 460 days. Most trials included participants with ischaemic stroke, diagnosed via a combination of standard clinical and computed tomography (CT) or magnetic resonance imaging (MRI) criteria. For more detailed information on each included trial, please refer to the Characteristics of included studies table.

Interventions and comparators

We reported results from the following comparisons: 1) pharmacological intervention versus placebo; 2) non-invasive brain stimulation versus sham non-invasive brain stimulation; 3) one of various forms of psychological therapy versus usual care and/or attention control; 4) pharmacological intervention and one of various forms of psychological therapy versus pharmacological intervention and usual care and/or attention control; 5) pharmacological intervention and non-invasive brain stimulation versus pharmacological intervention and sham stimulation or usual care; and 6) non-invasive brain stimulation and one of various forms of psychological therapy versus sham brain stimulation or usual care and psychological therapy. In 18 trials, 20 pharmacological comparisons were assessed against placebo (Andersen 1994; Fruehwald 2003; Gao 2017a; Huang 2002; Jiang 2001a/Jiang 2001b; Kong 2007; Lai 2006a; Li 2008; Lipsey 1984; Murray 2002; Ohtomo 1991; Ponzio 2001; Rampello 2005; Reding 1986; Robinson 2008a/Robinson 2008b; Wang 2005; Wiart 2000; Yang 2002). Eight trials (nine comparisons) reported on non-invasive brain stimulation comparisons versus sham or usual care (Chen 2005a; Gu 2016; Hordacre 2021; Jiang 2014a; Meng 2015; Valiengo 2017; Yang 2014a; Yang 2014b; Zheng 2016), and the authors of 22 trials (23 comparisons) assessed various forms of psychological therapy compared to usual care or attention control (Alexopoulos 2012; Cao 2009b; Cullen 2018; Fang 2017; Gao 2017b; Hoffmann 2015; Kerr 2018; Kirkness 2017a/Kirkness 2017b; Li 2009; Li 2019a; Liang 2015; Lincoln 2003; Lu 2018; Mitchell 2002; Tao 2008; Thomas 2007; Thomas 2016; Tian 2010; Towle 1989; Wang 2004a; Wang 2019; Watkins 2007; Wei 2021; Zhao 2004). In three trials (three comparisons), a combination of pharmacological interventions and psychological therapy was assessed against pharmacological intervention and usual care and/or attention control (Cao 2009a; Fan 2010; Wang 2005a). In 14 trials, a combination of non-invasive brain stimulation and pharmacological intervention was compared to pharmacological intervention and sham stimulation or usual care (Du 2005; Fan 2014; Jiang 2014b; Jin 2013; Li 2013; Li 2014; Liu 2015; Liu 2020; Lu 2016; Lu 2020; Sun 2013; Terachinda 2021; Yang 2013; Zhang 2013). One trial reported on non-invasive brain stimulation with psychological therapy versus psychological therapy plus usual care (Wu 2019).

We found no trials for the following comparisons: 7) pharmacological intervention and one of various forms of psychological therapy compared to placebo and psychological therapy; 8) pharmacological intervention and non-invasive brain stimulation versus placebo and non-invasive brain stimulation;

and 9) non-invasive brain stimulation and one of various forms of psychological therapy versus non-invasive brain stimulation and usual care and/or attention control.

Pharmacological interventions

There were 18 trials, 20 comparisons (1829 participants) of pharmacological interventions assessed against placebo. Amongst these trials, 12 compared an SSRI against placebo (citalopram: Andersen 1994; Gao 2017a; fluoxetine: Fruehwald 2003; Huang 2002; Kong 2007; Li 2008; Wang 2005; Wiart 2000; paroxetine: Lai 2006a; Ponzio 2001; Yang 2002; sertraline: Murray 2002); two trials compared a tricyclic antidepressant against placebo (amitriptyline: Jiang 2001a; nortriptyline: Lipsey 1984); and six trials compared other treatments with antidepressant effects (Deanxit: Jiang 2001b; Aniracetam: Ohtomo 1991; reboxetine: Rampello 2005; trazodone: Reding 1986; nefiracetam: Robinson 2008a; Robinson 2008b). We found no trials of mood stabilisers (e.g. lithium) or benzodiazepines. We found one trial of psychostimulants (e.g. methylphenidate), which was considered a 'dropout' as outcome data for those with depression at entry could not be separated from data for those without (Delbari 2011). Duration of treatment ranged from one to six months and only five trials treated participants for at least four months.

Non-invasive brain stimulation

There were eight trials, nine comparisons (516 participants) of non-invasive brain stimulation compared to sham or usual care.

Amongst trials reporting on non-invasive brain stimulation interventions, seven compared rTMS versus sham rTMS or usual care (no changes to antidepressant dosage and medication) (Chen 2005a; Gu 2016; Meng 2015; Yang 2014a; Yang 2014b; Zheng 2016). In only one trial, TMS was compared with usual care (Jiang 2014a). Three trials compared high-frequency rTMS versus sham or usual care (Hordacre 2021; Yang 2013; Yang 2014a), one trial compared low-frequency rTMS versus sham stimulation or usual care (Yang 2014b), and another trial compared tdCS versus sham stimulation (Valiengo 2017). We found no trials of ECT. Any future trials will be included but analysed separately.

Psychological therapy

There were 22 trials, 23 comparisons (1764 participants) of psychological therapy compared to usual care or attention control. Forms of psychological therapy included structured cognitive-behavioural therapy delivered by trained psychologists or nurses (Gao 2017b; Hoffmann 2015; Lincoln 2003; Mitchell 2002; Thomas 2007; Thomas 2016); motivational interviewing (MI) delivered by nurses or non-clinical psychologists (Kerr 2018; Watkins 2007); psychosocial therapy delivered by psychosocial nurse practitioner therapists in person or via telephone (Fang 2017; Kirkness 2017a; Kirkness 2017b); group psychotherapy (Cao 2009b); and psychotherapy with an ecosystem aspect (Alexopoulos 2012); treatments focused on psychological support (Li 2009; Li 2019a; Liang 2015; Lu 2018; Tao 2008; Tian 2010; Wang 2004a; Wang 2019; Wei 2021), problem-solving therapy with counselling delivered by social workers (Towle 1989), and a supportive psychological intervention including education delivered by special personnel (Cullen 2018; Zhao 2004).

Combination therapy

There were three trials, three comparisons (278 participants) of pharmacological interventions and psychological therapy compared to pharmacological intervention and usual care and/or attention control. In two trials, a combination of psychotherapy and an SSRI was compared with an SSRI alone (fluoxetine: Cao 2009a; paroxetine: Wang 2005a). One trial did not specify the name and class of antidepressants used with the psychotherapy (Fan 2010).

There were 14 trials (1194 participants) of pharmacological intervention and non-invasive brain stimulation compared to pharmacological intervention and sham stimulation or usual care. In eight trials, rTMS and an SSRI were compared with an SSRI (fluoxetine: Du 2005; Li 2014; Zhang 2013; citalopram: Liu 2015; sertraline: Jiang 2014b; Jin 2013; Terachinda 2021; paroxetine: Liu 2020). In two trials, rTMS and an SNRI were compared with an SNRI alone (duloxetine: Fan 2014; Lu 2016). In one trial, rTMS and another antidepressant medication were compared with an antidepressant alone (mirtazapine: Li 2013), while another trial did not specify the name and class of antidepressant used in combination with rTMS (Yang 2013). One trial compared PMES and an SSRI (sertraline: Lu 2020). Only one trial compared rTMS and a combination of antipsychoactive agents and tricyclic antidepressants (flupenthixol and melitracen: named Deanxit) versus Deanxit alone (Sun 2013).

One trial (82 participants) compared non-invasive brain stimulation (rTMS) and one of various forms of psychological therapy with sham brain stimulation or usual care and psychological therapy (Wu 2019).

Outcomes

Primary outcome: depression

In 17 trials (18 comparisons), outcome data for meeting the study criteria for depression at end of treatment were assessed and reported (Alexopoulos 2012; Andersen 1994; Fang 2017; Fruehwald 2003; Kirkness 2017a/Kirkness 2017b; Lincoln 2003; Lipsey 1984; Liu 2020; Lu 2020; Mitchell 2002; Murray 2002; Ohtomo 1991; Ponzio 2001; Valiengo 2017; Watkins 2007; Yang 2002; Zhao 2004). For the outcome less than 50% reduction in depression scale scores at end of treatment, nine trials contributed data (Andersen 1994; Lai 2006a; Li 2008; Liu 2020; Lu 2020; Murray 2002; Valiengo 2017; Wiart 2000; Yang 2002).

Secondary outcomes

A variety of additional outcomes were assessed in each trial as shown in the table.

Study and year	Depression	Psychological distress	Anxiety	Cognitive function	Activities of daily living	Disability	Neurological function	Adverse events
Alexopoulos 2012	x					x		x
Andersen 1994	x							x
Cao 2009a	x				x			
Cao 2009b	x				x			
Chen 2005a	x					x		
Cullen 2018	x		x					
Du 2005	x			x	x			x
Fan 2010	x							
Fan 2014	x				x			
Fang 2017	x		x					x
Fruehwald 2003	x					x		x
Gao 2017a	x			x	x			x
Gao 2017b	x			x	x			x
Gu 2016	x							x
Hoffmann 2015	x		x		x			
Hordacre 2021;	x							x
Huang 2002	x						x	x
Jiang 2001a	x						x	x
Jiang 2001b	x						x	x
Jiang 2014a	x						x	x

Jiang 2014b	x							x	x
Jin 2013	x							x	
Kerr 2018	x		x		x				
Kirkness 2017a	x				x				
Kirkness 2017b	x				x				
Kong 2007	x				x			x	
Lai 2006a	x								
Li 2008	x				x				x
Li 2009	x								
Li 2013	x								
Li 2014	x				x				
Li 2019a	x								
Liang 2015	x		x					x	
Lincoln 2003	x	x			x				x
Lipsey 1984	x								x
Liu 2015	x							x	x
Liu 2020	x								x
Lu 2016	x					x			
Lu 2018	x								
Lu 2020	x			x					x
Meng 2015	x				x			x	x
Mitchell 2002	x				x				x

Murray 2002	x											x
Ohtomo 1991	x											
Ponzio 2001	x											x
Rampello 2005	x											
Reding 1986	x											
Robinson 2008a	x											x
Robinson 2008b	x											x
Sun 2013	x								x			
Tao 2008	x											
Terachinda 2021	x						x					x
Thomas 2007	x											x
Thomas 2016	x											x
Tian 2010	x											
Towle 1989	x											x
Valiengo 2017	x				x		x					x
Wang 2004a	x								x			
Wang 2005	x				x							
Wang 2005a	x			x								x
Wang 2019	x											
Watkins 2007	x	x							x			x
Wei 2021	x			x	x		x			x		x
Wiart 2000	x				x				x			

Wu 2019	x			
Yang 2002	x			
Yang 2013	x		x	
Yang 2014a	x			
Yang 2014b	x			
Zhang 2013	x			
Zhao 2004	x			
Zheng 2016	x			x

Excluded studies

We excluded a total of nine trials at the full-text review stage for a variety of reasons, including 1) not an RCT (n = 3); 2) depression not the primary outcome of the study (n = 2); 3) intervention does not meet the criteria (n = 2); 4) comparator does not meet the criteria (n = 1); 5) not depressed at trial entry (n = 1). See Characteristics of excluded studies.

Ongoing studies

Nineteen trials are ongoing: pharmacological intervention: Ding 2021; Xu 2016, non-invasive brain stimulation: ChiCTR1800020468; ChiCTR1900024245; ChiCTR1900025440; ChiCTR1900027686; ChiCTR2000029809; ChiCTR2000035582; ChiCTR2100041707; IRCT2017030921965N4; NCT03056287; Tang 2017, psychological therapy: ACTRN12620000165987; Kirkevold 2018; NCT03645759; NCT04941482; NCT04985838NCT05097040, and combination therapy (non-invasive brain stimulation with psychological therapy): IRCT20090716002195N3.

Studies awaiting classification

There are 22 trials (26 comparisons) listed as awaiting classification (Chen 2002a/Chen 2002b; Ding 2005; Evans 1985; Finkenzeller 2009; Hanspal 2007; He 2003; He 2005; Huang 2005; IRCT201008214607N1; Katz 1998; Kuriakose 2020; Latow 1983; Lee 2005; Li 2019; Liu 2010; Pearson 2005; Razazian 2016; Tang 2002; Wang 2015; Yan 2010a/Yan 2010b/Yan 2010c/Yan 2010d; Yu 2019; Zhang 2021). We were unable to obtain more information or outcome data from these trials despite multiple attempts to contact the study authors (Evans 1985; Hanspal 2007; He 2003; Katz 1998; Latow 1983; Lee 2005; Pearson 2005). For four trials (5 comparisons), we were unsure if depression was the primary outcome (Chen 2002a/Chen 2002b; IRCT201008214607N1; Kuriakose 2020; Razazian 2016). In 11 trials (14 comparisons), no information was provided for the psychotherapy component of the intervention to help us determine if it met our review criteria (Ding 2005; Finkenzeller 2009; He 2005; Huang 2005; Li 2019; Liu 2010; Tang 2002; Wang 2015; Yan 2010a/Yan 2010b/Yan 2010c/Yan 2010d; Yu 2019; Zhang 2021).

Dropout studies

In this review, 21 trials met the inclusion criteria (Bramanti 1989; Chang 2011; Choi-Kwon 2006; Delbari 2011; Downes 1995; Hadidi 2014; Hjelle 2019; Jorge 2004; Jorge 2008; Kim 2017; Kim 2017a; Kim 2019; Kootker 2012; Li 2016; Mauri 1988; Meara 1998; Ohtomo 1985; Raffaele 1996; Robinson 2000; Sun 2000; Yu 2021). However, outcome data were not available for depressed participants only (Chang 2011; Choi-Kwon 2006; Delbari 2011; Hadidi 2014; Hjelle 2019; Jorge 2004; Jorge 2008; Kim 2017; Kim 2017a; Ohtomo 1985; Raffaele 1996; Robinson 2000; Sun 2000), or outcome data were not available at all (Downes 1995), or outcome data were not presented in a format suitable for meta-analysis (Bramanti 1989; Kim 2019; Kootker 2012; Li 2016; Meara 1998; Mauri 1988; Yu 2021). We considered these trials as 'dropouts' and have provided more detailed information in Table 1.

Risk of bias in included studies

We present a graphical summary of risk of bias assessments performed by review authors for the included trials in Figure 2, based on the seven risk of bias domains. Figure 3 provides a summary of risk of bias for each included trial. We have provided the reasons for judgements in the Risk of bias in included studies tables.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies

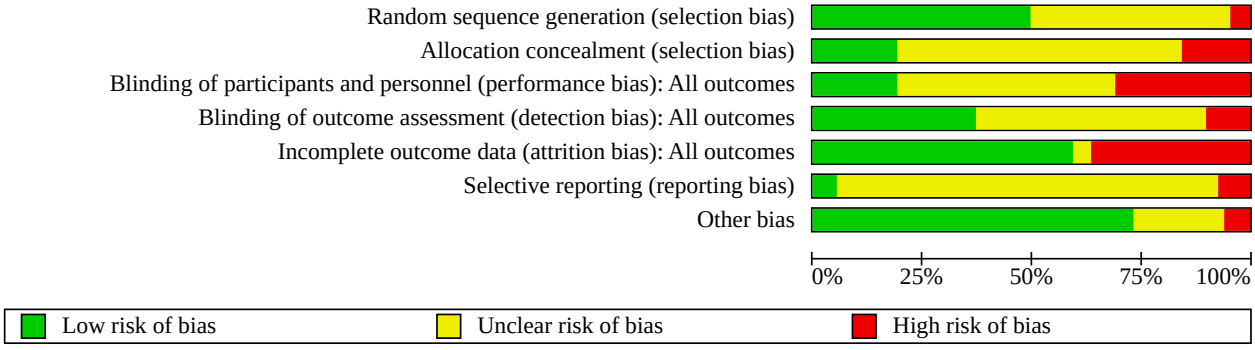


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study

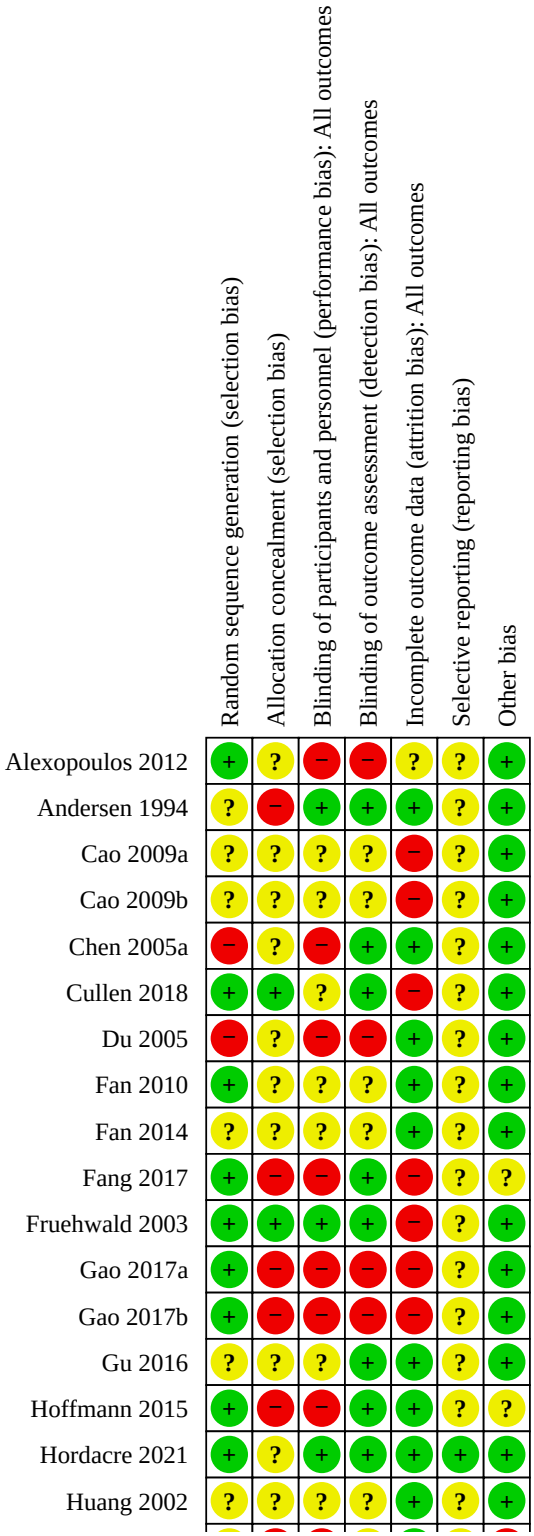


Figure 3. (Continued)

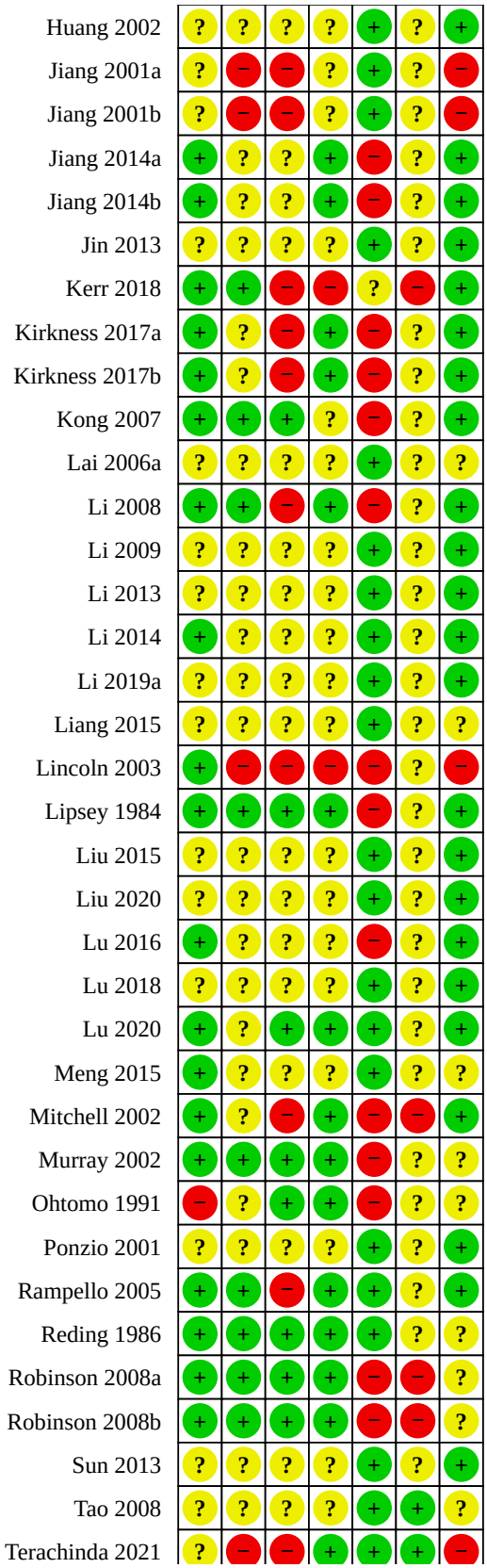
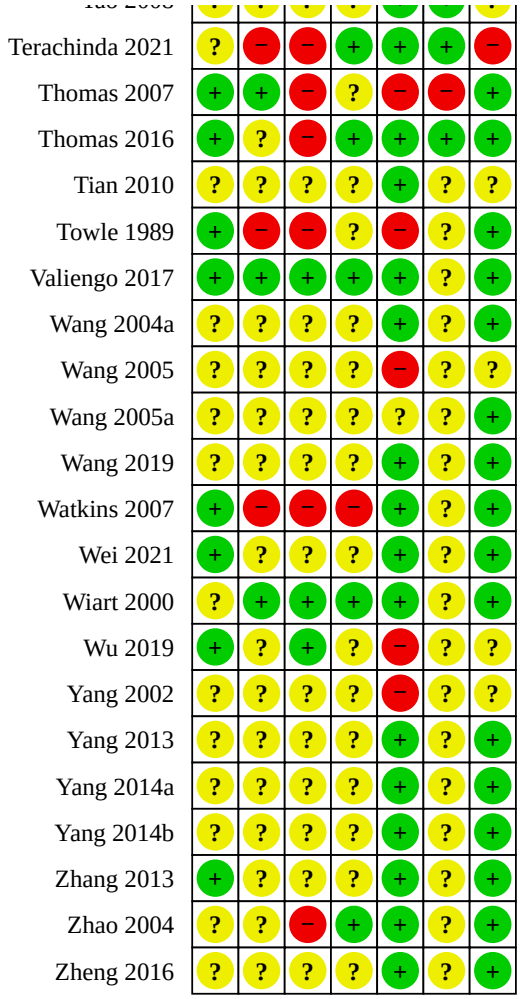


Figure 3. (Continued)



Allocation

Sequence generation

The randomisation sequence was appropriately generated in 50% of the trials; thus we rated them as low risk (Alexopoulos 2012; Cullen 2018; Fang 2017; Fruehwald 2003; Gao 2017a/Gao 2017b; Hoffmann 2015; Hordacre 2021; Jiang 2014a/Jiang 2014b; Kerr 2018; Kirkness 2017a/Kirkness 2017b; Kong 2007; Li 2008; Li 2014; Lincoln 2003; Lipsey 1984; Lu 2016; Lu 2020; Meng 2015; Mitchell 2002; Murray 2002; Rampello 2005; Reding 1986; Robinson 2008a/Robinson 2008b; Thomas 2007; Thomas 2016; Towle 1989; Valiengo 2017; Watkins 2007; Wei 2021; Wu 2019; Zhang 2013). However, 45% of the trials did not describe their method of sequence generation, and were rated as having unclear risk (Andersen 1994; Cao 2009a/Cao 2009b; Fan 2010; Fan 2014; Gu 2016; Huang 2002; Jiang 2001a/Jiang 2001b; Jin 2013; Lai 2006a; Li 2009; Li 2013; Liang 2015; Liu 2015; Liu 2020; Lu 2018; Ponzio 2001; Sun 2013; Tao 2008; Tian 2010; Wang 2004a; Wang 2005; Wang 2005a; Wang 2019; Wiart 2000; Yang 2002; Yang 2013; Yang 2014a/Yang 2014b; Zhao 2004; Zheng 2016). Five per cent of the trials were rated as having high risk, as generation of sequence was controlled by the investigators (Ohtomo 1991), or the method was drawing lots which could be manipulated (Chen 2005a; Du 2005).

Allocation concealment

We rated 23% of the trials as having low risk, as an appropriately generated and clearly concealed allocation procedure was used in the study (Cullen 2018; Fan 2010; Fruehwald 2003; Kerr 2018; Kong 2007; Li 2008; Li 2009; Lipsey 1984; Lu 2018; Murray 2002; Rampello 2005; Reding 1986; Robinson 2008a/Robinson 2008b; Tao 2008; Thomas 2007; Tian 2010; Valiengo 2017; Wang 2019; Wiart 2000). Thirty-eight per cent of the trials did not describe adequate concealment allocation, and we rated them as having unclear risk (Alexopoulos 2012; Cao 2009a/Cao 2009b; Chen 2005a; Du 2005; Fan 2014; Gu 2016; Hordacre 2021; Huang 2002; Jiang 2014a/Jiang 2014b; Jin 2013; Kirkness 2017a/Kirkness 2017b; Lai 2006a; Li 2013; Li 2014; Liang 2015; Liu 2015; Liu 2020; Lu 2016; Lu 2020; Meng 2015; Mitchell 2002; Ohtomo 1991; Ponzio 2001; Sun 2013; Thomas 2016; Wang 2004a; Wang 2005; Wang 2005a; Wei 2021; Wu 2019; Yang 2002; Yang 2013; Yang 2014a/Yang 2014b; Zhang 2013; Zhao 2004; Zheng 2016). We rated 15% of the trials as having high risk for allocation concealment, as they used sealed opaque envelopes, which could be tampered with (Andersen 1994; Fang 2017; Gao 2017a/Gao 2017b; Hoffmann 2015; Jiang 2001a/Jiang 2001b; Lincoln 2003; Terachinda 2021; Towle 1989; Watkins 2007).

Blinding

Blinding of participants and personnel

Twenty-three per cent of the trials reported that participants and personnel were blinded to the treatment allocation, and so we rated these trials as having low risk for performance bias (Andersen 1994; Fruehwald 2003; Hordacre 2021; Kong 2007; Lipsey 1984; Lu 2020Murray 2002; Ohtomo 1991; Reding 1986; Robinson 2008a/Robinson 2008b; Valiengo 2017; Wiart 2000; Wu 2019). We rated 50% of the trials as having unclear risk, as they did not provide information about blinding of participants and personnel (Cao 2009a/Cao 2009b; Cullen 2018; Fan 2010; Fan 2014; Gu 2016; Huang 2002; Jiang 2014a/Jiang 2014b; Jin 2013; Lai 2006a; Li 2009; Li 2013; Li 2014; Liang 2015; Liu 2015; Liu 2020; Lu 2016; Lu 2018; Ponzio 2001; Sun 2013; Tao 2008; Tian 2010; Wang 2004a; Wang 2005; Wang 2005a; Wang 2019; Wei 2021; Yang 2002; Yang 2013; Yang 2014a/Yang 2014b; Zhang 2013; Zheng 2016). Twenty-seven per cent of the trials were rated as having high risk for performance bias, as participants or personnel were not blinded to treatment allocation (Alexopoulos 2012; Chen 2005a; Du 2005; Fang 2017; Gao 2017a/Gao 2017b; Hoffmann 2015; Jiang 2001a/Jiang 2001b; Kerr 2018; Kirkness 2017a/Kirkness 2017b; Li 2008; Lincoln 2003; Rampello 2005; Terachinda 2021; Thomas 2016; Towle 1989; Watkins 2007; Zhao 2004).

Blinding of assessors

We rated 40% of the trials as having low risk for detection bias, as outcome assessors were blinded to treatment allocation (Andersen 1994; Chen 2005a; Cullen 2018; Fang 2017; Fruehwald 2003; Gu 2016; Hoffmann 2015; Hordacre 2021; Jiang 2014a/Jiang 2014b; Kirkness 2017a/Kirkness 2017b; Li 2008; Lipsey 1984; Lu 2020; Mitchell 2002; Murray 2002; Ohtomo 1991; Rampello 2005; Reding 1986; Robinson 2008a/Robinson 2008b; Terachinda 2021; Thomas 2016; Valiengo 2017; Wiart 2000; Zhao 2004). Forty-five per cent of the trials did not provide information about blinding of outcome assessors, and we rated them as having unclear risk of detection bias (Cao 2009a/Cao 2009b; Fan 2010; Fan 2014; Huang 2002; Jin 2013; Kong 2007; Jiang 2001a/Jiang 2001b; Lai 2006a; Li 2009; Li 2013; Li 2014; Liang 2015; Liu 2015; Liu 2020; Lu 2016; Lu 2018; Meng 2015; Ponzio 2001; Sun 2013; Tao 2008; Thomas 2007; Tian 2010; Towle 1989; Wang 2004a; Wang 2005; Wang 2005a; Wang 2019; Wei 2021; Wu 2019; Yang 2002; Yang 2013; Yang 2014a/Yang 2014b; Zhang 2013; Zheng 2016). We rated 15% of the trials as having high risk because they did not use blinded outcome assessment (Alexopoulos 2012; Du 2005; Gao 2017a/Gao 2017b; Kerr 2018; Lincoln 2003; Watkins 2007).

Incomplete outcome data

We rated 60% of the trials as having low risk, as they provided ITT analyses (Andersen 1994; Chen 2005a; Du 2005; Fan 2010; Fan 2014; Hoffmann 2015; Hordacre 2021; Huang 2002; Jiang 2001a/Jiang 2001b; Jin 2013; Lai 2006a; Li 2009; Li 2013; Li 2014; Liang 2015; Liu 2015; Liu 2020; Lu 2018; Lu 2020; Meng 2015; Ponzio 2001; Rampello 2005; Reding 1986; Sun 2013; Tao 2008; Terachinda 2021; Thomas 2016; Tian 2010; Valiengo 2017; Wang 2004a; Wang 2005; Wang 2019; Watkins 2007; Wei 2021; Wiart 2000; Yang 2013; Yang 2014a/Yang 2014b; Zhang 2013; Zhao 2004; Zheng 2016). We rated 35% of the trials as having high risk for attrition bias, as they reported per-protocol analyses only (Cullen 2018; Fang 2017; Fruehwald 2003; Gao 2017a/Gao 2017b; Jiang 2014a/Jiang 2014b; Kirkness 2017a/Kirkness 2017b; Kong 2007; Li 2008; Lincoln 2003; Lipsey 1984; Lu 2016; Mitchell 2002; Murray 2002; Ohtomo 1991; Robinson 2008a/Robinson 2008b; Thomas 2007; Towle 1989; Wu 2019; Yang 2002). The method of analysis was unclear in 5% of the trials (Alexopoulos 2012; Cao 2009a/Cao 2009b; Kerr 2018; Wang 2005a).

Selective reporting

We rated 85% of the trials as having unclear risk for reporting bias, as no trial protocol was available to compare a priori outcomes versus those reported in publications (Alexopoulos 2012; Andersen 1994; Cao 2009a/Cao 2009b; Chen 2005a; Cullen 2018; Du 2005; Fan 2010; Fan 2014; Fang 2017; Fruehwald 2003; Gao 2017a/Gao 2017b; Gu 2016; Hoffmann 2015; Huang 2002; Jiang 2001a/Jiang 2001b; Jiang 2014a/Jiang 2014b; Jin 2013; Kirkness 2017a/Kirkness 2017b; Kong 2007; Lai 2006a; Li 2008; Li 2009; Li 2013; Li 2014; Liang 2015; Lincoln 2003; Lipsey 1984; Liu 2015; Liu 2020; Lu 2016; Lu 2018; Lu 2020; Meng 2015; Murray 2002; Ohtomo 1991; Ponzio 2001; Rampello 2005; Reding 1986; Sun 2013; Tao 2008; Tian 2010; Towle 1989; Valiengo 2017; Wang 2004a; Wang 2005; Wang 2005a; Wang 2019; Watkins 2007; Wei 2021; Wiart 2000; Wu 2019; Yang 2002; Yang 2013; Yang 2014a/Yang 2014b; Zhang 2013; Zhao 2004; Zheng 2016). We rated 10% of the trials as having high risk, as one or two outcomes mentioned in the study protocol or trial registry information page were not reported in the primary results' publication (Kerr 2018; Mitchell 2002; Robinson 2008a/Robinson 2008b; Thomas 2007).

Other potential sources of bias

We rated 75% of the trials as having low risk for other bias, as baseline demographics and depression scores were balanced between groups (Alexopoulos 2012; Andersen 1994; Cao 2009a/Cao 2009b; Chen 2005a; Cullen 2018; Du 2005; Fan 2010; Fan 2014; Fruehwald 2003; Gao 2017a/Gao 2017b; Gu 2016; Hordacre 2021; Huang 2002; Jiang 2001a/Jiang 2001b; Jiang 2014a/Jiang 2014b; Jin 2013; Kerr 2018; Kirkness 2017a/Kirkness 2017b; Kong 2007; Li 2008; Li 2009; Li 2013; Li 2014; Lipsey 1984; Liu 2015; Lu 2016; Lu 2018; Mitchell 2002; Ponzio 2001; Rampello 2005; Sun 2013; Terachinda 2021; Thomas 2007; Thomas 2016; Towle 1989; Valiengo 2017; Wang 2004a; Wang 2005a; Wang 2019; Watkins 2007; Wei 2021; Wiart 2000; Yang 2013; Yang 2014a/Yang 2014b; Zhang 2013; Zhao 2004; Zheng 2016). We rated 20% of the trials as unclear, as no information about baseline demographics and depression scores between groups was provided (Fang 2017; Hoffmann 2015; Lai 2006a; Liang 2015; Liu 2020; Lu 2020; Meng 2015; Murray 2002; Ohtomo 1991; Reding 1986; Robinson 2008a/Robinson 2008b; Tao 2008; Tian 2010; Wang 2005; Wu 2019; Yang 2002). We rated 5% of the trials as high risk, as baseline demographic or depression scores were uneven between groups (Jiang 2001a/Jiang 2001b; Lincoln 2003; Lu 2020).

Effects of interventions

See: **Summary of findings 1** Pharmacological interventions compared to placebo for treating depression after stroke; **Summary of findings 2** Non-invasive brain stimulation compared to sham non-invasive brain stimulation and/or usual care for treating depression after stroke; **Summary of findings 3** Psychological therapy compared to usual care and/or attention control for treating depression after stroke; **Summary of findings 4** Pharmacological intervention and psychological therapy (combination) compared to a pharmacological intervention and usual care or attention control (single) for treating depression

after stroke; **Summary of findings 5** Pharmacological intervention and non-invasive brain stimulation (combination) compared to a pharmacological intervention and sham stimulation or usual care (single) for treating depression after stroke

Overall, we included 5831 participants in this review. In view of the large number and heterogeneous nature of the outcome measures (multiple measures often used for the same endpoint with no primary measure stated) and the reporting of results, we considered it inappropriate to pool outcome data for many endpoints. For details of all comparisons made for the trials with outcome data, refer to the Data and analyses section.

See Summary of findings 1; Summary of findings 2; Summary of findings 3; Summary of findings 4; and Summary of findings 5 for comparisons.

Primary outcomes

Prevalence of diagnosable depression

Meeting study criteria for depression at end of treatment

Comparison 1: eight trials (eight comparisons) on pharmacological interventions reported on the outcome meeting study criteria for depression at end of treatment (Andersen 1994; Fruehwald 2003; Lipsey 1984; Murray 2002; Ohtomo 1991; Ponzio 2001; Wang 2005; Yang 2002). We observed treatment effects favouring pharmacological interventions compared to placebo (risk ratio (RR) 0.70, 95% confidence interval (CI) 0.55 to 0.88, P = 0.002; 1025 participants, very low-certainty evidence; Analysis 1.1). However, substantial heterogeneity (I^2 = 68%) and wide confidence intervals were evident across individual trials. We performed subgroup analysis to explore whether treatment type would make any difference to this outcome and observed a treatment effect favouring SSRIs compared to placebo (RR 0.69, 95% CI 0.50 to 0.95, P = 0.0006; 6 RCTs; 701 participants with substantial heterogeneity I^2 = 77%).

Comparison 2: two trials of non-invasive brain stimulation reported on this outcome (Valiengo 2017; Zheng 2016). There was no difference in the treatment effect between non-invasive brain stimulation and sham stimulation or usual care (RR 0.67, 95% CI 0.39 to 1.14; P = 0.14; 2 RCTs; 130 participants; very low-certainty of evidence) (Valiengo 2017; Zheng 2016). We observed substantial heterogeneity (I^2 = 74%) and wide confidence intervals (Analysis 2.1).

Comparison 3: five trials (six comparisons) of psychological therapy reported on the outcome meeting study criteria for depression at end of treatment and demonstrated an effect favouring psychological therapy over usual care and/or attention control (RR 0.77, 95% CI 0.62 to 0.95; P = 0.01; 6 RCTs; 521 participants; very low-certainty evidence) (Alexopoulos 2012; Fang 2017; Kirkness 2017a/Kirkness 2017b; Mitchell 2002; Watkins 2007). We observed minimal heterogeneity (I^2 = 36%) and wide confidence intervals (Analysis 3.1).

Comparison 4: no trials of pharmacological interventions combined with psychological therapy versus pharmacological intervention with usual care or attention control assessed this outcome (Analysis 4.1).

Comparison 5: two trials of non-invasive brain stimulation with pharmacological intervention (combination) versus pharmacological intervention and sham stimulation or usual care (single) reported on this outcome (Du 2005; Lu 2020). We observed a treatment effect between favouring combination therapy over single therapy (RR 0.77, 95% CI 0.64 to 0.91; P = 0.002; 3 RCTs; 392 participants; low-certainty evidence). There was no heterogeneity observed (Analysis 5.1).

Comparison 6: no trials of non-invasive brain stimulation and one of various forms of psychological therapy versus sham brain stimulation or usual care and psychological therapy assessed this outcome (Analysis 6.1).

Inadequate response to treatment

Comparison 1: six trials (six comparisons) of pharmacological interventions reported on this outcome (Andersen 1994; Lai 2006a; Li 2008; Murray 2002; Wiart 2000; Yang 2002). We observed treatment effects favouring pharmacological therapy amongst those who received a pharmacological intervention compared with placebo (RR 0.48, 95% CI 0.32 to 0.70; P = 0.002; 6 RCTs; 511 participants; very low-certainty evidence). We observed substantial heterogeneity (I^2 = 66%) and wide confidence intervals (Analysis 1.2).

Comparison 2: two trials of non-invasive brain stimulation assessed this outcome (Valiengo 2017; Zheng 2016). We did not observe treatment effects amongst those who received non-invasive brain stimulation compared with sham stimulation (RR 0.84, 95% CI 0.52 to 1.37; P = 0.49; 2 RCTs; 130 participants; very low-certainty of evidence). We observed considerable heterogeneity (I^2 = 81%) and wide confidence intervals (Analysis 2.2).

Comparisons 3, 4 and 6: no trials of psychological interventions versus usual care and/or attention control; pharmacological intervention and psychological therapy (combination) versus pharmacological intervention and usual care or attention control (single); non-invasive brain stimulation and one of various forms of psychological therapy (combination) versus sham brain stimulation or usual care and psychological therapy (single) assessed this outcome (Analysis 3.2; Analysis 4.2; Analysis 6.2).

Comparison 5: two trials (Li 2013; Lu 2020) reported data on this outcome and demonstrated no difference in treatment effect between non-invasive brain stimulation and pharmacological intervention (combination) compared to pharmacological therapy alone (RR 0.95, 95% CI 0.69 to 1.30; P = 0.75; 3 RCTs; 392 participants; very low-certainty evidence). We observed considerable heterogeneity (I^2 = 79%) (Analysis 5.2).

Secondary outcomes

Depression scores

Average change in scores between baseline and end of treatment

Comparison 1: we did not perform a meta-analysis on this outcome for the comparison pharmacological interventions versus placebo (Analysis 1.3) due to the heterogenous nature of the outcome measures and single trials using multiple measures for this outcome without specifying a primary outcome measure.

Comparison 3: two trials (3 comparisons) found an effect favouring psychological therapy over usual care and/or attention control (mean difference (MD) -6.20, 95% CI -8.24 to -4.16; P < 0.00001; 3

RCTs; 189 participants; very low-certainty evidence; Analysis 3.3) (Kirkness 2017a/Kirkness 2017b; Mitchell 2002).

Mean scores at end of treatment

Comparison 1: we did not perform a meta-analysis on this outcome for the comparisons: pharmacological interventions versus placebo due to single trials using multiple measures for this outcome without specifying a primary outcome measure (Analysis 1.4).

Comparison 2: we observed a treatment effect for non-invasive brain stimulation compared to sham or usual care at end of treatment in trials measuring depression using the HDRS tool (MD -6.51, 95% CI -9.64 to -3.38; I^2 = 98%; P = 0.13; 8 RCTs; 505 participants; very low-certainty evidence; Analysis 2.3). The data from the other outcome measures did not demonstrate a treatment effect. Heterogeneity was considerable (I^2 = 98%) and confidence intervals were very wide.

Comparison 3: we did not perform a meta-analysis on this outcome for the comparison: psychological therapy versus usual care and/or attention control due to the heterogenous nature of the psychological therapies and outcome measures and single trials using multiple measures for this outcome without specifying a primary outcome measure (Analysis 3.4).

Comparison 4: we also observed a beneficial effect for combination therapy (pharmaceutical intervention and psychological therapy) compared to pharmaceutical intervention alone at end of treatment (MD -1.60, 95% CI -2.13 to -1.08; P < 0.00001; 3 RCTs; 278 participants; very low-certainty evidence; Analysis 4.3 subgroup 4.3.1). Heterogeneity was substantial (I^2 = 75%) and confidence intervals were very wide.

Comparison 5: we also observed this effect amongst those who received a combination of non-invasive brain stimulation and pharmacological intervention in comparison to those who received pharmacological intervention alone at end of treatment (SMD -1.06, 95% CI -1.06 to -0.02; P = 0.00001; 12 RCTs; 1055 participants; very low-certainty evidence; Analysis 5.3 subgroup 5.3.1). Heterogeneity was considerable (I^2 = 97%). We performed subgroup analysis to explore whether treatment duration would make any difference to this outcome and observed a treatment effect favouring combination treatments of four weeks duration (MD -4.66, 95% CI -6.60 to -2.73, P = 0.00001; 7 RCTs; 503 participants with substantial heterogeneity I^2 = 89%).

Comparison 6: we did not perform a meta-analysis, as only one trial reported data for this outcome (Analysis 6.3).

Mean scores at end of follow-up

Comparisons 2 and 3: due to the heterogenous nature of the outcome measures, we did not perform a meta-analysis on this outcome for the comparisons: non-invasive brain stimulation versus sham stimulation or usual care and psychological therapy versus usual care and/or attention control (Analysis 2.4; Analysis 3.7).

Comparison 5: two trials of combination treatment (non-invasive brain stimulation and pharmacological interventions) compared with single treatment (pharmacological intervention alone) reported data on this outcome (Jiang 2014b; Terachinda 2021). We observed treatment effects favouring combination treatment over single treatment (MD -3.00, 95% CI -3.39, -2.60; P < 0.00001; 3 RCTs; 147 participants; very low-certainty evidence; Analysis 5.4). We did not observe heterogeneity in this analysis.

Meeting study criteria for depression at end of follow-up

Comparison 3: two trials (3 comparisons) of psychological therapy assessed this outcome and showed no treatment effect for those who received psychological therapy compared to usual care and/or attention control (RR 0.85, 95% CI 0.59 to 1.21; P = 0.36; 3 RCTs; 201 participants; very low-certainty evidence; I^2 = 11%; Analysis 3.5) (Kirkness 2017a/Kirkness 2017b; Mitchell 2002).

Psychological distress scores

Comparison 3: no significant effect was observed in those who received psychological therapy compared to usual care and/or attention control on the outcome average change in scores between baseline and end of treatment (MD -0.21, 95% CI -1.89 to 1.48; P = 0.81; 2 RCTs; 377 participants; very low-certainty evidence) (Lincoln 2003; Watkins 2007). Nor did we observe a significant effect on mean psychological distress scores at end of treatment (MD -0.43, 95% CI -2.17 to 1.31; P = 0.63; 2 RCTs; 377 participants; very low-certainty evidence). See Analysis 3.8 subgroup 3.8.1 and Analysis 3.9 subgroup 3.9.1.

Anxiety scores

Mean scores at end of treatment

Comparison 3: we did not perform a meta-analysis on this outcome for comparison of psychological therapy versus usual care and/or attention control due to the heterogenous nature of the outcome measures and single trials using multiple measures for this outcome without specifying a primary outcome measure (Analysis 3.11).

Mean scores at end of follow-up

Comparison 3: we did not perform a meta-analysis on this outcome for comparison: psychological therapy versus usual care and/or attention control due to the heterogenous nature of the outcome measures and single trials using multiple measures for this outcome without specifying a primary outcome measure (Analysis 3.12).

Cognitive function scores

Comparisons 1 and 2: we did not perform a meta-analysis, as only one trial reported data for this outcome (Analysis 1.6; Analysis 2.5)

Comparisons 3 and 4: no trials of psychological interventions versus usual care and/or attention and pharmacological intervention and psychological therapy (combination) versus pharmacological intervention and usual care or attention control (single) control assessed this outcome.

Comparison 5: two trials assessed this outcome (Du 2005; Lu 2020). We observed treatment effects favouring combination of non-invasive brain stimulation and pharmacological interventions over pharmacological interventions alone (SMD -0.25, 95% CI -0.48, -0.03; P = 0.03; 2 RCTs; 318 participants; Analysis 5.5). We observed considerable heterogeneity (I^2 = 96%) and very wide confidence intervals.

Activities of daily living (ADL) scores

Average change in scores between baseline and end of treatment

Comparison 1: two trials (2 comparisons) revealed that pharmacological intervention compared to placebo had no significant effect on the average change in scores between baseline and end of treatment (MD -8.00, 95% CI -24.18 to 8.18; P = 0.33; 2 RCTs; 256 participants; very low-certainty evidence) (Ponzio 2001; Reding 1986) (Analysis 1.8, subgroup 1.8.1).

Comparison 3: similarly, two trials (2 comparisons) also showed that psychological therapy compared to usual care and/or attention control had no significant effect on the average change in scores between baseline and end of treatment (SMD -0.03, 95% CI -0.24 to 0.18; P = 0.78; 2 RCTs; 377 participants; very low-certainty evidence; Analysis 3.13) (Lincoln 2003; Watkins 2007).

Mean scores at end of treatment

Comparison 1: three trials of pharmacological interventions (3 comparisons) found no significant effect on mean ADL scores at end of treatment compared with placebo (MD 3.14, 95% CI -0.97 to 7.26; P = 0.13; 3 RCTs; 316 participants; very low-certainty evidence; Analysis 1.9 subgroup 1.9.1) (Gao 2017a; Kong 2007; Li 2008).

Comparison 2: three trials (3 comparisons) demonstrated no effect amongst those who received non-invasive brain stimulation compared to sham or usual care (SMD 1.31, 95% CI -0.62 to 3.24; P = 0.18; 3 RCTs; 256 participants; very low-certainty evidence; Analysis 2.6) (Jiang 2014a; Meng 2015; Valiengo 2017). However, we observed considerable heterogeneity (I^2 = 98%) and very wide confidence intervals.

Comparison 3: we did not perform a meta-analysis on this outcome for comparison: psychological therapy versus usual care and/or attention control (Analysis 3.14), due to the heterogenous nature of the outcome measures and single trials using multiple measures for this outcome without specifying a primary outcome measure.

Comparison 4: two trials (2 comparisons) found that a combination of pharmacological intervention and psychological therapy had minimal beneficial effect on mean ADL scores compared to a single pharmacological intervention at end of treatment (MD 11.83, 95% CI 0.27 to 23.40; P = 0.04; 2 RCTs; 198 participants; very low-certainty evidence; Analysis 4.5 subgroup 4.5.1) (Cao 2009a; Wang 2005a).

Comparison 5: similarly, five trials (5 comparisons) showed that combination therapy (non-invasive brain stimulation and pharmacological intervention) had a beneficial effect on mean ADL scores compared to pharmacological intervention alone (single) (SMD 2.03, 95% CI 1.21 to 2.85; P < 0.00001; 5 RCTs; 403 participants; very low-certainty evidence; Analysis 5.6) (Du 2005; Fan 2014; Jiang 2014b; Li 2013; Li 2014). However, the two comparisons showed considerable heterogeneity (I^2 = 94% and I^2 = 91%) and very wide confidence intervals.

Mean scores at end of follow-up

Comparisons 3 and 5: we did not perform a meta-analysis, as only one trial reported data on this outcome (Analysis 3.15; Analysis 5.7).

Disability scores

Comparison 3: two trials (2 comparisons) found that psychological therapy had no effect on mean disability scores at end of treatment compared to usual care and/or attention control (SMD -0.16, 95% CI -0.48 to 0.17; P = 0.35; 2 RCTs; 162 participants; very low-certainty evidence; Analysis 3.16) (Alexopoulos 2012; Gao 2017b).

Comparison 5: two trials (2 comparisons) reported that non-invasive brain stimulation and pharmacological intervention (combination) had an effect on mean disability scores at end of treatment compared to pharmacological intervention alone (MD -10.02, 95% CI -20.14 to 0.11; P = 0.05; 2 RCTs; 180 participants; very low-certainty evidence; Analysis 5.8 subgroup 5.7.1) (Lu 2016; Sun 2013).

Neurological function scores

Mean scores at end of treatment

Comparison 1: four trials (4 comparisons) showed that pharmacological interventions had an effect on mean scores at end of treatment compared to placebo (SMD -0.95, 95% CI -1.44 to -0.45; P = 0.0002; 4 RCTs; 304 participants; very low-certainty evidence; Analysis 1.13) (Huang 2002; Jiang 2001a; Kong 2007; Wang 2005). Heterogeneity was substantial (I^2 = 75%) and confidence intervals were very wide.

Comparison 2: similarly, we observed an effect amongst those who received non-invasive brain stimulation compared to sham or usual care (SMD -2.21, 95% CI -3.32 to -1.09; P = 0.0001; 3 RCTs; 290 participants; very low-certainty evidence; Analysis 2.9) (Meng 2015; Jiang 2014a; Zheng 2016). However, we noted considerable heterogeneity (I^2 = 93%) and wide confidence intervals.

Comparison 3: two trials (2 comparisons) also showed that psychological therapy had an effect on the mean neurological function scores compared to usual care/attention control at end of treatment (MD -1.19, 95% CI -1.56 to -0.83; P < 0.00001; 2 RCTs; 158 participants; Analysis 3.17) (Liang 2015; Wei 2021). However, we also noted considerable heterogeneity (I^2 = 84%) and wide confidence intervals.

Comparison 4: we did not perform a meta-analysis for this comparison: pharmacological intervention and psychological therapy versus pharmacological intervention alone (Analysis 4.6 subgroup 4.6.1), as only one trial reported data on this outcome.

Comparison 5: in contrast, four trials (4 comparisons) found that a combination of non-invasive brain stimulation and pharmacological intervention had an effect on mean scores at end of treatment compared to pharmacological intervention alone (MD -2.78, 95% CI -4.13 to -1.44; P < 0.0001; 4 RCTs; 280 participants; very low-certainty evidence; Analysis 5.9 subgroup 5.8.1) (Jiang 2014b; Jin 2013; Li 2013; Liu 2015). Heterogeneity was substantial (I^2 = 82%) and confidence intervals were very wide.

Adverse events: death

Comparison 1: nine trials (9 comparisons) found that pharmacological intervention had no effect on adverse events compared to placebo: death (RR 0.64, 95% CI 0.20 to 2.07; P = 0.46; 9 RCTs; 848 participants; very low-certainty evidence; Analysis 1.14 subgroup 1.14.1) (Andersen 1994; Fruehwald 2003; Gao 2017a; Huang 2002; Li 2008; Lipsey 1984; Murray 2002; Ponzio 2001; Wiart 2000). Although no heterogeneity was observed (I^2 = 0%), confidence intervals were very wide.

Comparison 2: four trials (4 comparisons) reported that non-invasive brain stimulation resulted in no deaths (Gu 2016; Hordacre 2021; Jiang 2001a; Valiengo 2017) (Analysis 2.10).

Comparison 3: eight trials (8 comparisons) found that psychological therapy had no effect on adverse events compared to usual care or attention control: death (RR 0.65, 95% CI 0.26 to 1.66; P = 0.37; 8 RCTs; 831 participants; very low-certainty evidence; Analysis 3.18 subgroup 3.17.1) (Alexopoulos 2012; Fang 2017; Gao 2017b; Lincoln 2003; Mitchell 2002; Thomas 2007; Towle 1989; Watkins 2007). We observed no heterogeneity (I^2 = 0%) but confidence intervals were very wide.

Comparison 5: five trials reported no difference in deaths between combination therapy (non-invasive brain stimulation and pharmacological intervention) compared to single therapy (pharmacological intervention and sham stimulation or usual care) (RR 1.06, 95% CI 0.27 to 4.16; P = 0.93; 5 RCTs; 487 participants; very low-certainty evidence; Analysis 5.10 subgroup 5.9.1) (Du 2005; Jiang 2014b; Liu 2015; Lu 2020; Terachinda 2021).

Adverse events: all

Comparison 1: significant evidence of harm was demonstrated amongst adverse events, in particular, CNS effects (RR 1.55, 95% CI 1.12 to 2.15; P = 0.008; 5 RCTs; 488 participants; very low-certainty evidence; I^2 = 31%) (Andersen 1994; Lipsey 1984; Murray 2002; Ponzio 2001; Wiart 2000), along with gastrointestinal effects (RR 1.62, 95% CI 1.19 to 2.19; P = 0.002; 4 RCTs; 473 participants; very low-certainty evidence) (Li 2008; Murray 2002; Ponzio 2001; Wiart 2000), amongst those who received pharmacological interventions compared with placebo (see Analysis 1.15 subgroup 1.15.1 and 1.15.5). We observed no heterogeneity (I^2 = 0%), but the confidence intervals were very wide.

Comparison 2: four trials reported that non-invasive brain stimulation resulted in no significant adverse events related to CNS (RR 0.61, 95% CI 023 to 1.64; P = 0.33; 4 RCTs; 183 participants; low-certainty evidence) or other adverse events - not listed above (e.g. dysuria, neck pain, eye discomfort) (RR 0.47, 95% CI 0.16 to 1.39; P = 0.17; 4 RCTs; 183 participants; low-certainty evidence; Analysis 2.11) (Gu 2016; Hordacre 2021; Jiang 2014a; Valiengo 2017).

Comparison 3: four trials (4 comparisons) found that psychological therapy resulted in no significant adverse events (recurrent stroke - RR 5.0, 95% CI 0.24 to 103.12; P = 0.30; 1 RCT; 254 participants; vascular events - RR 0.71, 95% CI 0.23 to 2.19; P = 0.56; 1 RCT; 254 participants; very low-certainty evidence), nor other events - not listed above (e.g. too ill) (RR 1.02, 95% CI 0.15 to 6.81; P = 0.56; 2 RCTs; 206 participants; very low-certainty evidence). See Analysis 3.19 (Mitchell 2002; Thomas 2007; Towle 1989; Watkins 2007).

Comparison 5: two trials (2 comparisons) found that a combination of non-invasive brain stimulation and pharmacological intervention resulted in no significant adverse events (other events - not listed above, e.g. insomnia, discomfort, headache) (RR 7.0, 95% CI 0.38 to 129.93; P = 0.19; 2 RCTs; 120 participants; very low-certainty evidence). See Analysis 5.11 (Du 2005; Jiang 2014b).

Adverse events: leaving the study early (including death)

Comparison 1: 12 trials (13 pharmacological comparisons) reported on this outcome (Andersen 1994; Fruehwald 2003; Gao 2017a; Huang 2002; Kong 2007; Li 2008; Lipsey 1984; Murray 2002; Ponzio 2001; Robinson 2008a/Robinson 2008b; Wang 2005; Wiart 2000). Pharmacological interventions had no effect on the proportion of participants leaving the study early (including death) compared to placebo (RR 1.07, 95% CI 0.82 to 1.39; P = 0.62; 13 RCTs; 1165 participants; Analysis 1.16 subgroup 1.16.1). Although we observed no heterogeneity (I^2 = 0%), confidence intervals were very wide.

Comparison 3: seven trials (8 comparisons) revealed that psychological therapy had no effect on the proportion of participants leaving the study early (including death) compared to usual care and/or attention control (RR 0.83, 95% CI 0.42 to 1.63; P = 0.59; 8 RCTs; 784 participants; Analysis 3.20 subgroup 3.19.1) (Alexopoulos 2012; Gao 2017b; Kirkness 2017a/Kirkness 2017b; Lincoln 2003; Mitchell 2002; Towle 1989; Watkins 2007). Although we observed no heterogeneity (I^2 = 0%), confidence intervals were very wide.

Comparison 5: four combination therapy trials (rTMS and pharmacological interventions) (4 comparisons) reported on this outcome. A combination of rTMS and pharmacological interventions had no effect on the proportion of people leaving the study early (including death) compared to pharmacological intervention alone (RR 1.33, 95% CI 0.32 to 5.58; P = 0.11; 4 RCTs; 300 participants) (Du 2005; Jiang 2014b; Liu 2015; Lu 2016). See Analysis 5.12 subgroup 5.11.1. We observed no heterogeneity (I^2 = 0%), but confidence intervals were very wide.

DISCUSSION

Summary of main results

In this review update, we included 65 trials (72 comparisons) involving 5831 participants that met our criteria.

Data were available for these comparisons: 1) pharmacological interventions versus placebo (with 20 comparisons); 2) one of various forms of non-invasive brain stimulation versus sham stimulation or usual care (with 9 comparisons); 3) one of various forms of psychological therapy versus usual care and/or attention control (with 25 comparisons); 4) pharmacological intervention and various forms of psychological therapy versus pharmacological intervention and usual care and/or attention control (with three comparisons); 5) non-invasive brain stimulation and pharmacological intervention versus pharmacological intervention and sham stimulation or usual care (with 14 comparisons); and 6) non-invasive brain stimulation and psychological therapy with psychological therapy plus usual care (with 1 comparison).

Pharmacological intervention vs placebo

Comparing pharmacological intervention to placebo, we found very low-certainty pooled evidence suggesting benefit in treating depression to remission and reducing depressive symptom scores on mood rating scales, along with evidence of harm (more central nervous system and gastrointestinal adverse events). These results are largely unchanged from previous versions of this review. For pharmacological trials, a key requirement is that a therapeutic dose of the medication must be achieved for an adequate period of time. Guidelines from the American College of Physicians suggest that antidepressants should be continued for at least four months beyond initial recovery, and that treatment should be changed if no response has been shown by six weeks (Snow 2000). In this review, the interventions in most pharmacological trials probably were not

given for an adequate length of time to show maximal or sustained response. Therefore, we are unable to comment on the long-term effects of antidepressant therapy, or to provide information on the most appropriate duration or dose of treatment; nor can we say if one group of antidepressants is more efficacious or provide stopping rules for antidepressant therapy in this group.

Non-invasive brain stimulation vs sham stimulation or usual care

Comparing non-invasive brain stimulation to usual care or sham stimulation, we found very low-certainty pooled evidence suggesting that repetitive transcranial magnetic stimulation (rTMS) has little to no effect in treating depression to remission but reduces depressive symptom scores at end of treatment and after follow-up, from treatment in trials measuring depression using the HDRS tool. No adverse events were reported. The duration of treatment in these trials was short, ranging from one to four weeks. The impact of many different facets of interventions such as rTMS (including electrode placement, number of sessions, or particular frequencies on outcomes) is not within the scope of this review.

Psychological therapy vs usual care and/or attention control

Comparing psychological therapy to usual care and/or attention control, we found very low-certainty pooled evidence of benefit in treating depression to remission at end of treatment, but this benefit was not sustained to the end of follow-up from treatment. We did not pool data related to changes in depression symptom scores due to use of multiple measures across and within studies with no a priori primary outcome measure identified. Pooled evidence for adverse events included benefit and harm. These results are different from findings of previous versions of this review, which demonstrated no treatment effects. For psychological therapy trials, good evidence shows that efficacy is linked to delivery of adequate exposure to the intervention. This means that therapists should be trained and supervised in the therapy they are delivering, and should use a standardised, prespecified framework for therapy. To achieve this in psychological therapy trials, therapy is determined with use of a manual, and research therapists are trained and supervised in use of the manual. Success in brief therapy is linked to adherence to the therapeutic model, as well as to the therapists' characteristics. Future stroke psychological therapy trials should adhere to these standard psychological therapy research guidelines if there is to be any probability of demonstrating consistency and response.

Pharmacological intervention and psychological therapy vs pharmacological intervention and usual care and/or attention control

Comparing combined pharmacological intervention and psychological therapy to pharmacological intervention plus usual care or attention control, we found very low-certainty pooled evidence of benefit in reducing depressive symptom scores on mood rating scales. No reported data were related to remission.

Pharmacological intervention and non-invasive brain stimulation vs pharmacological intervention and sham stimulation or usual care

Comparing pharmacological intervention and non-invasive brain stimulation to pharmacological intervention and sham stimulation or usual care, we found very low-certainty pooled evidence of benefit in treating depression to remission and reducing depressive symptom scores on mood rating scales. No reported data were related to remission. Pooled evidence for adverse events included benefit and harm.

We found only one trial of non-invasive brain stimulation and one of various forms of psychological therapy versus sham brain stimulation or usual care plus psychological therapy. We found no trials for these comparisons: 7) pharmacological intervention and one of various forms of psychological therapy versus placebo and psychological therapy; 8) pharmacological intervention and non-invasive brain stimulation versus placebo and non-invasive brain stimulation; and 9) non-invasive brain stimulation and one of various forms of psychological therapy versus non-invasive brain stimulation and usual care and/or attention control.

Evidence demonstrating benefit must continue to be considered alongside several basic methodological limitations of many of these trials, including the short duration of many interventions, variation in the types of trial participants recruited and in the methods used to diagnose depression, lack of an a priori measurable endpoint, and high risk of bias in many trials. Of particular concern is the evidence of harm (more adverse events) given the small number of trials in which adverse events were systematically recorded and reported, making reliable assessment of the benefits and risks of treatments impossible.

The trials in this review included participants with depression occurring several days to more than two years following stroke. However, depression occurring in the early phase of stroke is likely to be different from that occurring several months or years after the event. Survivors in the first weeks following stroke are coping with the consequences of experiencing a potentially life-threatening event, as well as recovering from the disabling effects of the stroke itself. In the medium to long term, survivors of stroke are more likely to be adjusting to the prospects of permanent disability and changes in social and financial circumstances. It is difficult to summarise the evidence from such mixed populations, and even in doing so, whether it could be considered meaningful, especially given the high risk of relapse of depression in the first few months of recovery, which declines over time (Snow 2000).

In contrast to the wide range in the length of time between stroke onset and entry into the trial, many trials included participants with narrow demographic and clinical characteristics, in particular, they excluded people with communication problems, cognitive loss, or previous psychiatric illness. This reinforces a common criticism of depression research - that trial participants are not representative of those requiring treatment in the 'real world' (Zimmerman 2002). It would appear that this criticism is also applicable to trials of depression following stroke, where up to half of survivors may be excluded on the basis of such criteria (Turner-Stokes 2003). Given the older age of most people with stroke and the frequent presence of neurological impairments, aphasia, and comorbid medical conditions, the fact that up to half of all survivors of stroke are excluded limits the external validity (generalisability) of the results. Use of a large list of exclusions means that the results are applicable to only a small proportion of stroke survivors who have a narrow range of comorbidities and other characteristics. Such exclusions may be justifiable for trials of psychological therapy, in which participants are required to actively participate in therapy by talking, but the exclusions seem inappropriate for pharmacotherapy trials. Ideally, participants

should be heterogeneous with regard to stroke diagnosis, which requires the use of standard diagnostic criteria and neuroimaging in a high proportion of cases. Given differences in the natural history and management of subarachnoid haemorrhage, it could be argued that this form of stroke should be examined separately.

Lack of a consistent method to diagnose depression at trial entry and outcomes in the included trials is a concern and a reflection of the general lack of a standard definition for a 'healthy state' amongst people with mood disorders (Keller 2003). Few trials have stated whether the primary goal of therapy was remission (no longer meeting the baseline criteria for depression), response (> 50% reduction in mood scores from baseline), or simply a greater reduction in mood scores (or difference in scores) in one of the randomised groups. Complete remission of symptoms is arguably the most meaningful endpoint for the patient, whereas the significance of a small reduction in mood scores on a continuous scale is generally difficult to interpret for the patient and for the treating physician. These problems with outcome assessment were further confounded by frequent use of multiple scales and selective reporting of findings between and within trials. Any one scale was used across only eight trials at most, and significantly different cut-points were used to determine depression at entry and at trial end. Given the practical difficulties and high costs of conducting psychiatric interviews in clinical trials, it seems appropriate to adopt a pragmatic approach to assess depression on the basis of a validated mood questionnaire or structured interview. It is hoped that the compulsory registration of trial protocols on publicly available databases will reduce, if not eliminate, the opportunity for selective reporting of results. It has been suggested that more than one-third of efficacy outcomes and half of harm outcomes are inadequately reported (Chan 2004). Several other methodological deficiencies in trials further limit the conclusions that can be drawn from this review. Many trials were small; less than half reported adequate concealment of the randomisation sequence, and dropout rates were high in several trials. Additionally, blinding of investigators and outcome assessors was seldom stated.

Overall completeness and applicability of evidence

The present review included 65 trials (72 comparisons) with 5831 participants. Data were available for 20 pharmacological comparisons, nine non-invasive brain stimulation comparisons, 25 psychological therapy comparisons, and 20 combination therapy trials. Overall, consistent methods used to diagnose depression were lacking, and we considered it inappropriate to pool outcome data for many endpoints. The accuracy of the findings of this systematic review and meta-analysis must be considered in light of the basic methodological limitations described in the Risk of bias in included studies table. Eighteen trials are considered dropouts, 21 trials are awaiting classification, and at least five ongoing trials may contribute further evidence to future updates of this review.

Quality of the evidence

We rated the certainty of evidence for all comparisons by using the five GRADE considerations (study limitations, consistency of effect, indirectness, imprecision, and publication bias; Schünemann 2021). We created a summary of findings table for each comparison. Certainty assessment was low to very low.

Limitations in study design or execution

For the comparison of pharmacological interventions versus placebo, we downgraded the certainty of evidence by two points for the following outcomes: meeting the criteria for depression at end of treatment, less than 50% reduction in depression scale scores, mean neurological function scores at end of treatment, and adverse events - death at end of treatment, all CNS events, and gastrointestinal events - as we rated several studies as having high or unclear risk for multiple risk of bias domains (Summary of findings 1).

For the comparison of non-invasive brain stimulation versus sham, we downgraded the certainty of evidence by two points for the following outcomes: meeting the criteria for depression at end of treatment, less than 50% reduction in depression scale scores, mean depression scores at end of treatment, mean neurological function scores at end of treatment, adverse events - death at end of treatment and adverse events - other, as we rated several studies as having high or unclear risk for multiple risk of bias domains (Summary of findings 2).

For the comparison of psychological therapy versus usual care and/or attention control, we downgraded the certainty of evidence by two points for the following outcomes: meeting the criteria for depression at end of treatment, meeting study criteria for depression at end of follow-up, and adverse events - death at end of treatment as we rated several studies, as having high or unclear risk for multiple risk of bias domains (Summary of findings 3).

For the comparison of pharmacological interventions and psychological therapy (combination) versus pharmacological intervention and usual care and/or attention control (single), we downgraded the certainty of evidence by two points for the following outcomes: mean depression scores at end of treatment and mean activities of daily living scores at end of treatment, as we rated two studies as having unclear risk for multiple risk of bias domains, related to allocation concealment and blinding of participants, personnel, and outcome assessors (Summary of findings 4).

For the comparison of non-invasive brain stimulation and pharmacological intervention (combination) versus pharmacological intervention with sham or usual care (single), we downgraded by two points the certainty of evidence for meeting the criteria for depression at end of treatment, less than 50% reduction in depression scale scores, mean depression scores at end of treatment, mean depression scores at end of follow-up, adverse events - death at end of treatment and adverse events - other, as we rated the study as having high risk for multiple risk of bias domains, related to blinding of participants, personnel, and outcome assessors (Summary of findings 5).

Inconsistency of results

For the comparison of pharmacological interventions versus placebo, we downgraded by two points the certainty of evidence for the following outcomes: meeting the criteria for depression, less than 50% reduction in depression scale scores, and mean neurological function scores at end of treatment, as we observed substantial heterogeneity (50% to 89%). We also downgraded the certainty of evidence by one point for gastrointestinal events, as we observed moderate heterogeneity (30% to 49%) (Summary of findings 1).

For the comparison of non-invasive brain stimulation versus sham, we downgraded the certainty of evidence by two points for meeting the criteria for depression at end of treatment and less than 50% reduction in depression scale scores due to substantial heterogeneity (50% to 89%) and mean depression scores and mean neurological function scores at end of treatment due to considerable heterogeneity (90% to 100%) (Summary of findings 3).

For the comparison of pharmacological interventions and psychological therapy (combination) versus pharmacological intervention and usual care and/or attention control (single), we downgraded by two points the certainty of evidence for mean depression scores at end of treatment due to substantial heterogeneity (50% to 89%), and by two points for mean activities of daily living scores at end of treatment for considerable heterogeneity (90% to 100%) observed (Summary of findings 4).

For the comparison of non-invasive brain stimulation and pharmacological intervention (combination) versus pharmacological intervention with sham or usual care (single), we downgraded by one point the certainty of evidence for less than 50% reduction in depression scale scores due to substantial heterogeneity (50% to 89%). We also downgraded by two points the certainty of evidence for mean depression scores at end of treatment due to considerable heterogeneity (90% to 100%) (Summary of findings 5).

Indirectness of evidence

All included trials addressed the main review questions (PICO). Thus, we did not downgrade any outcomes for indirectness of evidence (Summary of findings 1; Summary of findings 2; Summary of findings 3; Summary of findings 4; Summary of findings 5).

Imprecision

For the comparison of pharmacological interventions versus placebo, we downgraded the certainty of evidence by one point for the following outcomes: meeting the criteria for depression and less than 50% reduction in depression scale scores at end of treatment, as the confidence intervals were wide. We also downgraded by two points the certainty of evidence for mean neurological scores and adverse events - death, CNS events, and gastrointestinal events at end of treatment, as the confidence intervals were very wide (Summary of findings 1).

For the comparison of non-invasive brain stimulation versus sham, we downgraded the certainty of evidence by two points for the following outcomes: mean depression scores at end of treatment, as the confidence intervals were very wide. We also downgraded by one point the certainty of evidence for meeting the criteria for depression at end of treatment, less than 50% reduction in depression scale scores, mean neurological function scores at end of treatment, adverse events - CNS and other, as the confidence intervals were wide (Summary of findings 2).

For the comparison of psychological therapy versus usual care and/or attention control, we downgraded the certainty of evidence by one point for meeting the criteria for depression at end of treatment, meeting criteria for depression at end of follow-up and adverse events - death at end of treatment, as the confidence intervals were wide. (Summary of findings 3).

For the comparison of pharmacological interventions and psychological therapy (combination) versus pharmacological intervention and usual care and/or attention control (single), we downgraded the certainty of evidence by two points for mean depression scores and activities of daily living scores at end of treatment, as the confidence intervals were very wide (Summary of findings 4).

For the comparison of non-invasive brain stimulation and pharmacological intervention (combination) versus pharmacological intervention with sham or usual care (single), we downgraded the certainty of evidence by two points for the following outcomes: mean depression scores at end of treatment, mean depression scores at end of follow-up, adverse events - death at end of treatment and adverse events - other, as the confidence intervals were very wide. We also downgraded the certainty of evidence by one point for meeting the criteria for depression at end of treatment and less than 50% reduction in depression scale scores, as the confidence intervals were wide (Summary of findings 5).

Publication bias

We assessed publication bias using funnel plots for the outcome meeting study criteria for depression at end of treatment for pharmaceutical interventions versus placebo; Figure 4; Figure 5 and Figure 6 shows no evidence of publication bias for this outcome. We did not assess publication bias using funnel plots for the other outcomes in each comparison due to the small number of studies (< 10 studies) contributing to the analysis. Therefore, we did not downgrade the certainty of evidence for publication bias for any outcomes per comparison (Summary of findings 1; Summary of findings 2; Summary of findings 3; Summary of findings 4; Summary of findings 5).

Figure 4. Funnel plot of comparison: 1 Pharmacological interventions versus placebo, outcome: 1.1 Depression: meeting study criteria for depression at end of treatment

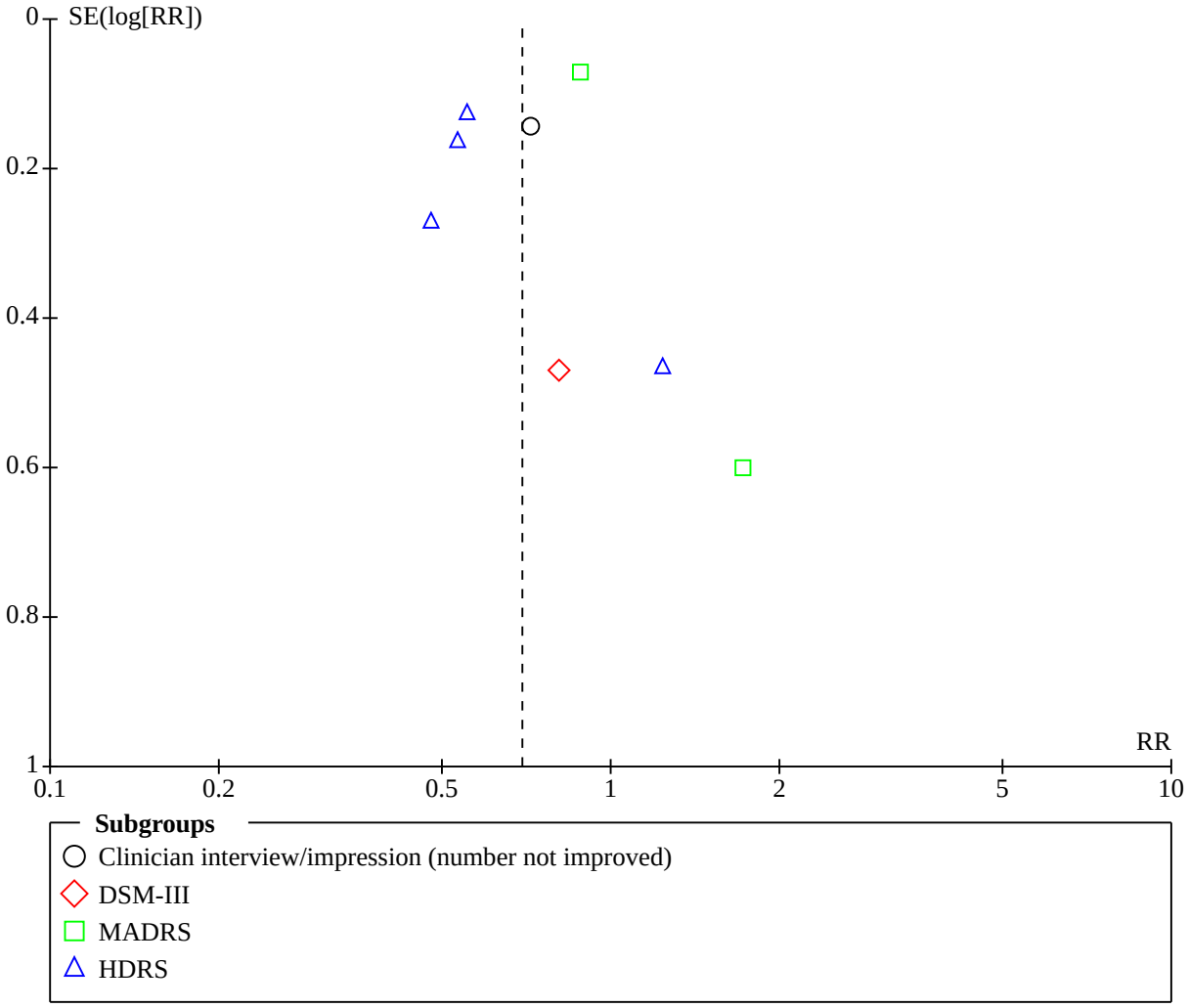


Figure 5. Funnel plot of comparison: 2 Non-invasive brain stimulation versus sham non-invasive brain stimulation or usual care, outcome: 2.1 Depression: mean scores at end of treatment

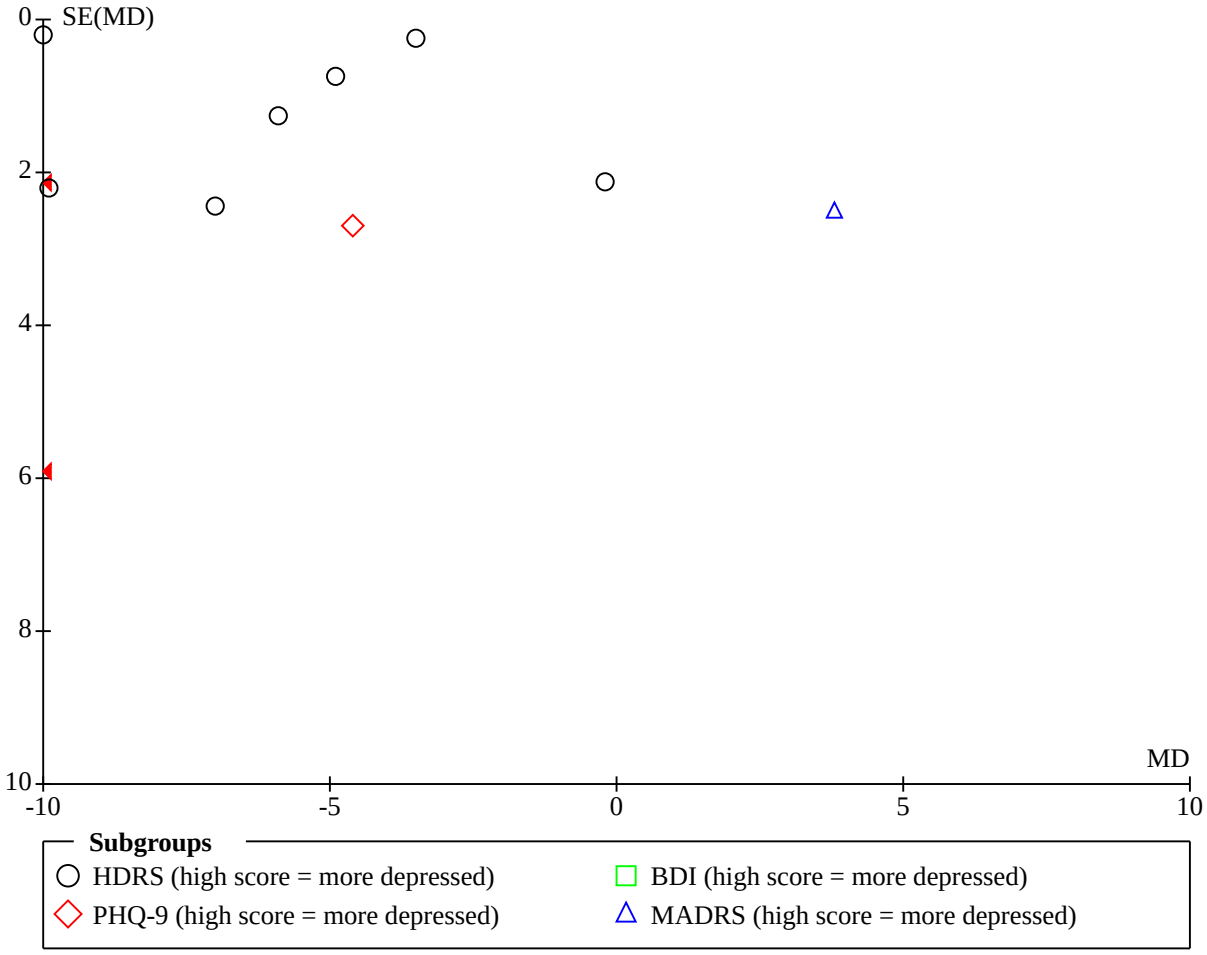
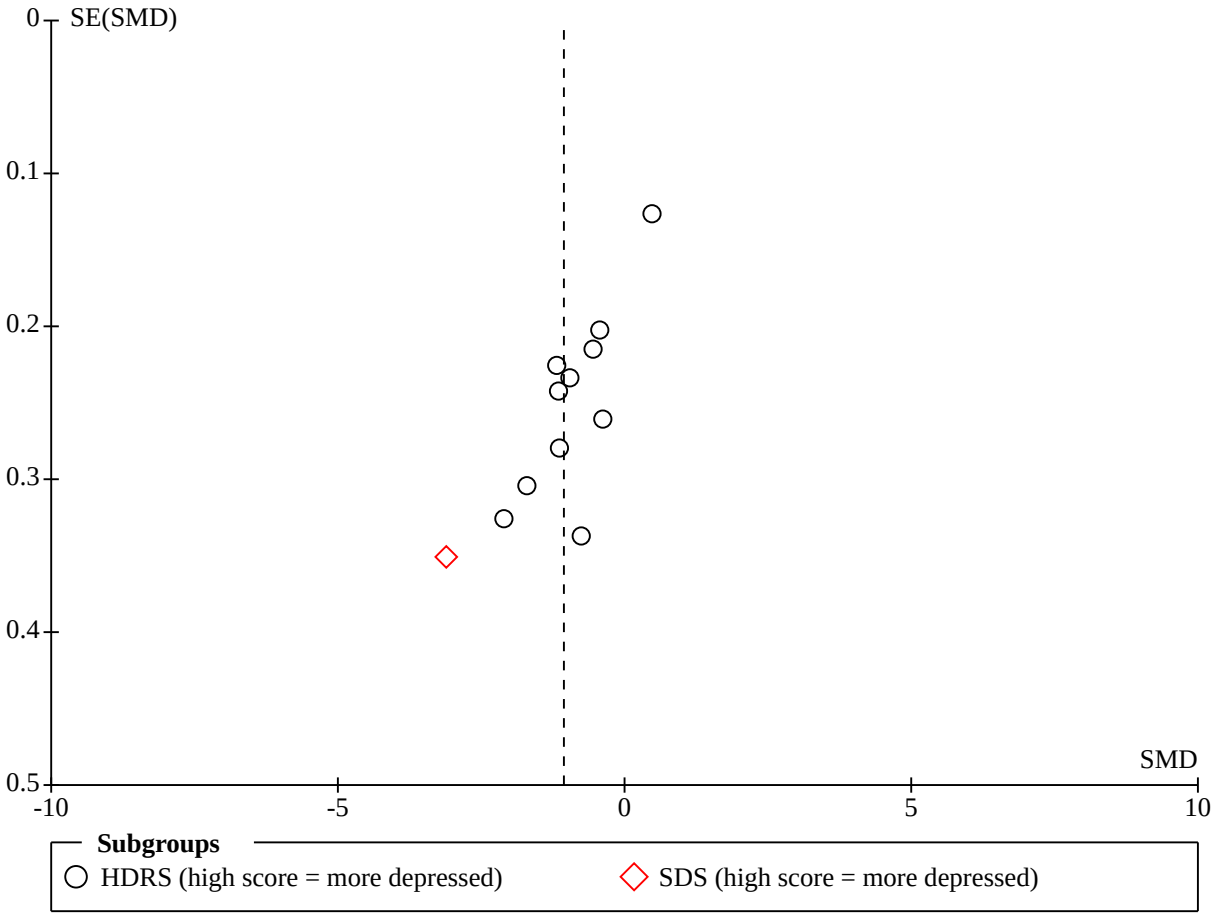


Figure 6. Funnel plot of comparison: 2 Non-invasive brain stimulation and a pharmacological intervention versus pharmacological intervention and sham stimulation or usual care, outcome: 2.1 Depression: mean scores at end of treatment



Potential biases in the review process

Strengths and weaknesses of this review

This review has rigorously adhered to Cochrane methods for performing systematic reviews. During the review process, we tried to avoid and minimise any biases. We undertook extensive searches of databases and additional resources. We did not apply any language restrictions during the search process. Thus, we believe that we have identified and included in this review all potentially relevant trials. We arranged for any relevant and non-relevant non-English full-text trials to be translated into English, to finalise the eligibility process. Furthermore, at least two review authors independently extracted and managed the data.

The main weaknesses of this review are the heterogeneous nature of the outcome measures and the frequent use of multiple scales between and within trials. Inadequate reporting of some trials has led us to rate some of these trials across categories as having unclear risk of bias, with an overall rating of 'very low' certainty of evidence.

Agreements and disagreements with other studies or reviews

To date, no other systematic reviews have been as comprehensive as this current review.

We found one other systematic review comparing effects of pharmacotherapy versus placebo in the stroke population (Chen 2006). Although this review appears similar, there were important differences in the inclusion criteria. We included trials of people with depression on recruitment and excluded trials with participants who were not depressed at recruitment (included in Hackett 2008a). Other reviews included trials of people with and without diagnosed depression at recruitment. This limits our ability to directly compare results. One network meta-analysis comparing pharmacotherapy to placebo in people with a diagnosis of major depressive disorder (but not stroke) also found low-quality pooled evidence of benefit of pharmacotherapy in treating depression to remission (Cipriani 2018). Many trials in that review also provided inadequate information about randomisation and allocation concealment, which restricts interpretation of their results. This indicates that limitations in study design in pharmacotherapy trials are not limited to stroke. A Cochrane

systematic review of SSRIs for stroke recovery included 76 trials (Legg 2021), 38 requiring participants to have depression to be included. In six included trials with a low risk of bias (none required depression at trial entry), SSRIs were found to increase seizures (RR 1.40, 95% CI 1.00 to 1.98; 6080 participants, moderate-quality evidence) and bone fractures (RR 2.35, 95% CI 1.62 to 3.41; 6080 participants, high-quality evidence). This evidence suggests that investigators should explicitly assess these adverse effects in future trials of SSRIs to treat depression after stroke.

One systematic review compared effects of rTMS with sham rTMS and a combination of rTMS and pharmacotherapy versus usual care or sham rTMS and pharmacotherapy in treating depression after stroke (Shen 2017). Those review authors included 22 trials (24 comparisons), of which 13 trials (15 comparisons) were also included in our review (Chen 2005a; Fan 2014; Jiang 2014a; Jiang 2014b; Jin 2013; Li 2013; Li 2014; Liu 2015; Lu 2016; Meng 2015; Yang 2013; Yang 2014a; Yang 2014b; Zhang 2013; Zheng 2016), and two trials (three comparisons) are awaiting classification (Liu 2010; Yan 2010a; Yan 2010b). Seven of the trials included in Shen 2017 did not meet our review criteria for the type of intervention. These trials compared rTMS and pharmacotherapy versus pharmacotherapy alone (with no sham rTMS or usual care). This review also found low-quality pooled evidence that rTMS and a combination of rTMS and pharmacotherapy reduced depressive symptom scores at end of treatment and after follow-up. However, these findings must also be considered in light of the same limitations in study design and heterogeneity.

Another systematic review also evaluated the effects of rTMS with sham rTMS and a combination of rTMS and pharmacotherapy versus usual care or sham rTMS and pharmacotherapy in treating depression after stroke (Liu 2019). Seventeen trials were included in the meta-analysis, of which seven were also included in our review (Gu 2016; Jin 2013; Li 2014; Liu 2015; Yang 2013; Yang 2014a/Yang 2014b; Zhang 2013), and two are awaiting classification (Wang 2015; Yan 2010a/Yan 2010b/Yan 2010c/Yan 2010d). Three of the trials (Jorge 2004; Jorge 2008; Li 2016) included in Liu 2019 were classified as dropouts in our review as data were not available for depressed and not depressed individuals separately. Five trials that were not included in our review were conducted and published in China, and none were identified by our search strategy, nor were they accessible during this update. We will endeavour to locate, translate, and assess these five trials in time for the next update of this review. Their analysis demonstrated that high-frequency rTMS reduced depressive symptoms at end of treatment. Nonetheless, we cannot compare their results to ours as they pooled the trials of rTMS vs sham rTMS with combination therapy (rTMS + pharmacotherapy) vs single therapy. Another systematic review compared effects of non-invasive brain stimulation (which includes rTMS and transcranial direct current stimulation (tDCS)) versus sham stimulation or usual care (Bucur 2018). Review authors included seven studies (case studies and randomised controlled trials (RCTs)), of which one trial was also included in our review (Gu 2016), and two trials were considered 'dropouts', as outcome data were not reported grouped by depressed/non-depressed participants at baseline (Jorge 2004; Valiengo 2017). Review authors did not perform a meta-analysis and only narratively described the included studies.

One systematic review reported on effects of cognitive-behavioural therapy (CBT) in treating depression after stroke (Wang 2018). The review authors included 23 trials, two of which were included in our review (Gao 2017b; Lincoln 2003), and one was considered a 'dropout' as the outcome data (reported median and interquartile ratio (IQR)) were not suitable for pooling (Kootker 2012). The 20 trials that were not included in our review were conducted and published in China, and none were identified by our search strategy, nor were they accessible during this update. We will endeavour to locate, translate, and assess these 20 trials in time for the next update of this review. Another systematic review evaluated the efficacy of psychological nursing in treating depression after stroke (Liao 2020). None of their 12 included trials with 1013 participants were included in our review. We located and translated these trials, of which nine were subsequently included in this update (Fan 2010; Li 2009; Li 2019a; Liang 2015; Lu 2018; Tao 2008; Tian 2010; Wang 2019; Zhang 2013). Three of the trials did not meet the intervention criteria for our review. Their review found a significant difference in the HDRS score between the psychological nursing and usual care groups, which is similar to our results if we had pooled the trials for this outcome. However, this was not possible due to the heterogenous nature of the outcome measures and the frequent use of multiple scales between and within trials.

Identification of ongoing studies and those awaiting classification indicates that this is an area of stroke research for which further evidence will evolve over the short and longer term.

AUTHORS' CONCLUSIONS

Implications for practice

Evidence from trials in people with stroke tentatively supports the use of prescription antidepressants or psychological therapy to treat depression, but this must be considered in light of evidence of an associated increase in harm. Antidepressants may produce a remission or a response in terms of lower scores on mood rating scales but may also increase adverse events. Psychological therapy does not appear to have the same associated risks. Any use of pharmacological agents in people with persistent depressive disorder after stroke would require caution, as little is known about the risks, especially of seizures, falls, delirium, and interaction with other medications.

Implications for research

We recommend that further research is needed in this area. Future trials investigating effects of pharmacological, psychological, and non-invasive brain stimulation interventions, alone and in combination, for treatment of depression in people after stroke should:

- review and refine the methods for trials of psychological endpoints in people with physical illness;
- recruit an adequate number of participants, so that variables such as time passed between stroke and recruitment, inclusion of participants with dysphasia, and subarachnoid haemorrhage (SAH) can be controlled, and modest but clinically important effects can be detected;
- recruit a representative 'real-world' sample of participants to enable results to be generalised to most stroke survivors;
- provide treatment for sufficient duration and follow-up, so that rates of relapse or maintenance of remission can be assessed;
- carefully specify and monitor psychological interventions;

- describe interventions in sufficient detail to allow their replication;
- include careful, prospective assessment and complete reporting of adverse events;
- define a priori and unambiguous, measurable primary endpoint; and
- limit the number of secondary outcomes to three or four and report results for all outcomes.

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The following people conducted the editorial process for this review update

Sign-off Editor (final editorial decision): Dr Alex Todhunter-Brown, Glasgow Caledonian University

Managing Editor (provided editorial guidance to authors, edited the review, selected peer reviewers, and collated peer-reviewer comments): Hazel Fraser, Cochrane Stroke

Statistical Editor (provided comments): Aryelly Rodriguez, Edinburgh Clinical Trials Unit (ECTU) at the University of Edinburgh

Copy Editor (copy-editing and production): Anne Lethaby, Cochrane Copy Edit Support.

Peer reviewers (provided comments and recommended an editorial decision):

- Dr Amanda Barugh, Associate Editor, Cochrane Stroke Group
- Dr Alex Todhunter-Brown, Glasgow Caledonian University
- Linda S Williams, MD VA HSR&D Center for Health Information and Communication Professor of Neurology, Indiana University School of Medicine Research Scientist, Regenstrief Institute, Inc.

One reviewer provided comments but requested not to be acknowledged.

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CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Alexopoulos 2012

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2

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Allida S, Cox KL, Hsieh CF, Lang H, House A, Hackett ML. Pharmacological, psychological, and non-invasive brain stimulation interventions for treating depression after stroke. *Stroke* 2020;**51**:e259-e260. [DOI: 10.1161/STROKEAHA.120.029239]

* Indicates the major publication for the study

Alexopoulos 2012 *(Continued)*

	Treatment arm: ecosystem focused therapy (EFT) **Control arm:** attention control
Participants	**Geographical location:** USA **Setting:** inpatient **Stroke criteria:** ischaemic and haemorrhagic stroke **Method of stroke diagnosis:** not reported **Time since stroke:** not reported **Inclusion criteria:** (1) aged 60 years or older; (2) had an ischaemic, embolic, or haemorrhagic stroke; (3) diagnosis of unipolar major depression by DSM-IV **Exclusion criteria:** (1) moderately severe dementia (MMSE score < 20); (2) greater than moderate aphasia (NIHSS best language > 1); (3) expectation to be discharged to a nursing home; (4) psychotic depression (by DSM-IV); (5) suicidal intent or plan; (6) inability to speak English **Depression criteria:** structured clinical interview for DSM-IV-TR and PHQ-9 cut-off score ≥ 10 **Total number randomised in this trial:** 24 **Number randomised to treatment group:** 12 (50% men, mean age 72 years, SD 7) **Number randomised to control group:** 12 (58% men, mean age 69 years, SD 10) **Total number included in the final analysis:** 24 **Number included in treatment group for final analysis:** 12 (50% men, mean age 72 years, SD 7) **Number included in control group for final analysis:** 12 (58% men, mean age 69 years, SD 10)
Interventions	**Treatment:** 12 weekly 45-minute personalised sessions of EFT were offered. Treatment was designed to increase patient participation in rehabilitation and social activities, focusing on adherence, problem-solving, goal-setting, and co-ordination of care **Administered by:** therapist trained in EFT using manuals; qualification of therapist not stated **Attention control:** 12 weekly 45-minute sessions of Education on Stroke and Depression (ESD) **Administered by:** therapist trained in ESD using manuals; qualification of therapist not stated **Supervision:** 3 practice cases of EFT and ESD were supervised; qualifications of the supervisor not stated **Intervention fidelity:** all EFT and ESD sessions were audio-taped and rated by reviewers who were not members of the research team, using specially devised EFT and ESD fidelity scales (5 grades: 1 = poor, 5 = excellent). Mean EFT scores ranged from 4.0 to 4.4; mean ESD scores ranged from 4.6 to 4.9, indicating good intervention fidelity for both arms **Duration:** 12 weeks **Follow-up:** none
Outcomes	**Primary outcomes** • Depressive symptoms measured using the HDRS **Secondary outcomes** • Remission of depression (HDRS < 10) • Disability measured using the WHODAS-II

Alexopoulos 2012 *(Continued)*

Notes	**Author contact:** emailed study authors to ask how missing data were handled and to ask for information on sample size calculation 19 November 2018

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Quote:** "the subjects were randomly assigned to EFT or ESD using random numbers". (p. 1055)
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	**Quote:** "four therapists were trained and offered both EFT and ESD…" (p. 1056) **Comment:** due to the nature of the trial, it was not possible to mask participants, therapists, or researchers to the treatment allocation.
Blinding of outcome assessment (detection bias) All outcomes	High risk	**Quote:** "… the raters could not be blinded to the treatment condition, although they were unaware of the study hypotheses". (p. 1058)
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	**Comment:** in the intervention arm, 2 died, 1 LTF was reported; in the control arm, 1 discontinued treatment. Analysis includes all patients (ITT), but how missing data were handled was not reported.
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes were reported. No trial protocol or registry record available to compare with the publication
Other bias	Low risk	**Comment:** no statistically significant differences in demographic characteristics, age of depression between EFT- and ESD-treated participants

Andersen 1994

Study characteristics

Methods	**Study design:** parallel design **Number of arms:** 2 **Treatment arm:** citalopram (SSRI) **Control arm:** matched placebo
Participants	**Geographical location:** Denmark **Setting:** mixed outpatient and inpatient **Stroke criteria:** ischaemic stroke and primary intracerebral haemorrhage **Method of stroke diagnosis:** diagnosis via clinical signs and CT (100%) **Time since stroke:** 2 to 52 weeks (average time 12 weeks) **Inclusion criteria:** (1) had stroke 2 to 52 weeks before randomisation

Andersen 1994 *(Continued)*

	Exclusion criteria: (1) patients with subarachnoid haemorrhage or Binswanger's disease; (2) with previous degenerative or expansive neurological disease (such as multiple sclerosis, amyotrophic lateral sclerosis, tumour, and hydrocephalus); (3) with history of psychiatric illness (except depression more than 1 year earlier); (4) decreased consciousness; (5) dementia; (6) aphasia to such a degree that they could not explain themselves or gave conflicting verbal and non-verbal signals **Depression criteria:** HDRS score > 12 (score transformed to appropriate DSM-III-R criteria) **Total number randomised in this trial:** 66 **Number randomised to treatment group:** 33 (36% men, mean age 68 years, SD 4) **Number randomised to control group:** 33 (66% men, mean age 66 years, SD 9) **Total number included in the final analysis:** 66 **Number included in treatment group for final analysis:** 33 (36% men, mean age 68 years, SD 4) **Number included in control group for final analysis:** 33 (66% men, mean age 66 years, SD 9)
Interventions	**Treatment:** citalopram (SSRI), 10 mg in participants > 66 years, 20 mg in participants < 67 years, daily; dose doubled if no response to treatment within 3 weeks **Control:** matched placebo **Duration:** 6 weeks; treatment continued only for responders at 6 weeks (these data not included in review) **Follow-up:** none
Outcomes	**Primary outcomes** • Depression measured using the HDRS • Proportion no longer meeting entry criteria (HDRS score < 13) • Depression measured using the Melancholia Scale **Secondary outcomes** • Disability measured using the BI • Social functioning measured using the Social Activities Index • Cognitive functioning measured using the MMSE
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Quote:** "to ensure approximately equal numbers of patients in the treatment groups, randomization was carried out in groups of 4, with 2 assigned to citalopram". **Comment:** method of sequence generation not reported
Allocation concealment (selection bias)	High risk	**Comment:** opaque envelopes with codes concealed until end of the study were used. After study authors were contacted for more information, this detail was provided.
Blinding of participants and personnel (performance bias)	Low risk	**Quote:** "the trial was designed as a randomized, double-blind, placebo-controlled study". (p. 1100) **Comment:** who was blinded was not reported.

Andersen 1994 *(Continued)*
All outcomes

Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Quote:** "the trial was designed as a randomized, double-blind, placebo-controlled study". (p. 1100) **Comment:** who was blinded was not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** ITT analysis (all participants including dropout were included). See Table 2 (p. 1101) for last observation for dropout carried forward.
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol or registry record available to compare with the publication.
Other bias	Low risk	**Comment:** there were no differences in baseline demographic characteristics between groups.

Cao 2009a

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Treatment arm:** fluoxetine (SSRI) + psychotherapy + usual care **Control arm:** fluoxetine (SSRI) + usual care
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** cerebral haemorrhage and infarct **Method of stroke diagnosis:** not reported **Time since stroke:** not reported **Inclusion criteria:** (1) 24-item HDRS score > 20; (2) can sign informed consent; (3) voluntary participation; (4) strong desire to change themselves; (5) willingness to communicate with others; (6) completion of 12 therapy sessions (treatment arm only) **Exclusion criteria:** (1) history of psychiatric illness; (2) severe cognitive impairment; (3) verbal communication barrier; (4) severe illness (e.g. myocardial infarction) **Depression criteria:** Chinese version of 24-item HDRS score > 20 **Total number randomised in this trial:** 144 (48% of total group men; mean age of total group 60 years, SD 9) **Number randomised to treatment group:** 72 (as above) **Number randomised to control group:** 72 **Total number included in the final analysis:** 144 (48% of total group men; mean age of total group 60 years, SD 9) **Number included in treatment group for final analysis:** 72 (as above) **Number included in control group for final analysis:** 72 (as above)

Cao 2009a *(Continued)*

Interventions	**Treatment:** fluoxetine (SSRI) 20 mg/d + group psychotherapy with 4 phases: an introductory session to build group security and trust **Administered by:** each group has 1 leader and 1 assistant. 2 neurologists qualified with group psychotherapy (national counsellors, grade 2) serve as leaders, and 3 nurses with professional training serve as assistants. **Supervision:** not reported **Intervention fidelity:** not reported **Control:** fluoxetine (SSRI) 20 mg/d **Duration of psychotherapy:** 30 to 40 minutes, once/week for 12 weeks **Duration of fluoxetine:** first depression 4 to 6 months, then taper and discontinue; recurrent depression: extended additional 3 to 6 months; depression episodes ≥ 3 times: more prolonged period **Follow-up:** none
Outcomes	**Primary outcomes** • Depression measured using 24-item HDRS **Secondary outcomes** • Disability measured using BI
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Comment:** method of sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** blinding of participants and personnel not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** blinding of outcome assessment not reported
Incomplete outcome data (attrition bias) All outcomes	High risk	**Comment:** ITT; no missing data reported, but randomised participants who did not complete the 12 sessions appear to have been excluded; dropouts/cross-overs not reported
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol or registry record to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline 24-item HDRS and BI. Baseline demographic information not reported

Cao 2009b

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Treatment arm:** psychotherapy + usual care **Control arm:** usual care
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** cerebral haemorrhage and infarct **Method of stroke diagnosis:** not reported **Time since stroke:** not reported **Inclusion criteria:** (1) 24-item HDRS score > 20; (2) can sign informed consent; (3) voluntary participation; (4) strong desire to change themselves; (5) willingness to communicate with others; (6) completion of 12 therapy sessions (treatment arm only) **Exclusion criteria:** (1) history of psychiatric illness; (2) severe cognitive impairment; (3) verbal communication barrier; (4) severe illness (e.g. myocardial infarction) **Depression criteria:** Chinese version of 24-item HDRS > 20 **Total number randomised in this trial:** 144 (48% of total group men; mean age of total group 60 years, SD 9) **Number randomised to treatment group:** 72 (as above) **Number randomised to control group:** 72 (as above) **Total number included in the final analysis:** 144 (48% of total group men; mean age of total group 60 years, SD 9) **Number included in treatment group for final analysis:** 72 (as above) **Number included in control group for final analysis:** 72 (as above)
Interventions	**Treatment:** group psychotherapy with 4 phases: an introductory session to build group security and trust **Administered by:** each group has 1 leader and 1 assistant. 2 neurologists qualified with group psychotherapy (national counsellors, grade 2) serve as leaders, and 3 nurses with professional training serve as assistants. **Supervision:** not reported **Intervention fidelity:** not reported **Control:** usual care **Duration of psychotherapy:** 30 to 40 minutes, once/week for 12 weeks **Follow-up:** none
Outcomes	**Primary outcomes** • Depression measured using 24-item HDRS

Cao 2009b *(Continued)*

	Secondary outcomes • Disability measured using BI
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Comment:** method of sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** blinding of participants and personnel not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** blinding of outcome assessment not reported
Incomplete outcome data (attrition bias) All outcomes	High risk	**Comment:** ITT; no missing data reported but randomised participants who did not complete the 12 sessions appear to have been excluded; dropouts/cross-overs not reported
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol or registry record to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline 24-item HDRS and BI; baseline demographic information not reported

Chen 2005a

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Treatment arm:** rTMS + cerebrovascular disease routine care **Control arm:** cerebrovascular disease routine care
Participants	**Geographical location:** China **Setting:** mixed outpatient and inpatient **Stroke criteria:** ischaemic stroke **Method of stroke diagnosis:** diagnosis consistent with diagnostic criteria for stroke formulated by the Fourth National Symposium on Cerebrovascular Disease in 1995; confirmation by brain CT or MRI **Time since stroke:** 2 months

Chen 2005a *(Continued)*

	Inclusion criteria: (1) disease course of stroke on average > 2 months; (2) patients and family gave informed consent **Exclusion criteria:** (1) history of psychiatric illness; (2) obvious comprehension impairment; (3) obvious aphasia; (4) severe physical illness; (5) epilepsy **Depression criteria:** depression was diagnosed by clinical interview according to the CCMD-2-R; 17-item HDRS score > 17 **Total number randomised in this trial:** 32 **Number randomised to treatment group:** 16 (62% men, mean age 61 years, SD 4.9; modified SSS 18.3, SD 4.8) **Number randomised to control group:** 16 (56% men, mean age 61.2 years, SD 4.7; modified SSS 17.5, SD 4.4) **Total number included in final analysis:** 32 **Number included in treatment group for final analysis:** 16 (62% men, mean age 61 years, SD 4.9; modified SSS 18.3, SD 4.8) **Number included in control group for final analysis:** 16 (56% men, mean age 61.2 years, SD 4.7; modified SSS 17.5 SD, 4.4)
Interventions	**Treatment:** low-frequency rTMS, fixed-dose 0.72 Tesla (60% of maximal stimulation intensity), frequency 0.5 Hz, 1 sequence included 30 stimulations in each side of the pre-frontal lobe; plus cerebrovascular disease routine care **Control:** cerebrovascular disease routine care **Treatment duration:** 1 sequence a day for 7 successive days **Administration:** unclear **Follow-up:** none
Outcomes	**Primary outcomes** • Depression measured using 17-item HDRS • Impairments measured using modified SSS **Secondary outcomes** • Adverse events
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	**Comment:** randomisation performed by drawing lots, which is prone to bias
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	**Comment:** participants and personnel not blinded to group allocation. Study used a prospective, randomised open-blinded endpoint (PROBE) design.

Chen 2005a *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Comment:** outcome assessors blinded to group allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** ITT analysis reported; no missing data
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol or registry record to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline demographic characteristics between groups

Cullen 2018

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Treatment arm:** brief positive psychotherapy + usual care **Control arm:** usual care
Participants	**Geographical location:** Scotland **Setting:** outpatient **Stroke criteria:** cerebrovascular infarct and haemorrhagic stroke **Method of stroke diagnosis:** confirmed by local clinician based on clinical and/or radiological evidence **Time since stroke:** 3 to 36 months **Inclusion criteria:** (1) adults aged 18 or over; (2) diagnosis of acquired, non-progressive brain injury; (3) between 3 and 12 months post-injury at time of recruitment; (4) presence of emotional distress (score in moderate or above range on at least 1 subscale of the DASS-21; (5) medically stable; (6) able to consent **Exclusion criteria:** (1) significant communication impairment; (2) diagnosis of mild traumatic brain injury; (3) comorbid developmental learning disability or degenerative neurological condition **Depression criteria:** presence of emotional distress (score in moderate or above range on at least 1 subscale of the DASS-21) **Total number randomised in this trial (stroke participants only):** 24 **Number included in treatment group:** 12 (67% men; mean age 55 years, SD 10) **Number included in control group:** 12 (67% men; mean age 60 years, SD 9) **Total number included in final analysis** (stroke participants only)*:* 24 **Number included in treatment group for final analysis:** 12 (67% men; mean age 55 years, SD 10) **Number included in control group for final analysis:** 12 (67% men; mean age 60 years, SD 9)

Cullen 2018 *(Continued)*

Interventions	**Treatment:** participants in intervention arm received a brief positive psychotherapy intervention delivered over 8 weeks, in addition to accessing usual care within the clinical service. Study intervention followed a manualised programme designed by the research team and based on aspects of a programme, incorporating psychoeducation about ABI and positive psychology (week 1), a range of therapeutic exercises, and homework focused on using signature character strengths and reflecting on positive events (weeks 2 to 7 inclusive, with mid-point review at week 4), and final review and plan for maintenance (week 8) (Rashid 2013) **Administered by:** not reported **Supervision:** not reported **Intervention fidelity:** not reported **Control:** participants in control arm received usual care within the clinical service; the content of usual care was not standardised: input varied between services and participants, but all participants could access clinical psychology input if required. **Duration:** 8 weeks **Follow-up:** 20 weeks
Outcomes	**Primary outcomes** • Depression measured using DASS-21 Depression • Anxiety measured using DASS-21 Anxiety • Stress measured using DASS-21 Stress • Depression measured using AHI **Secondary outcomes** • Overall function measured using Mayo-Portland Adaptability Inventory-4 (MPAI-4) total (participant) • Overall function measured using MPAI-4 total (informant) • Caregiver strain measured using Modified-Caregiver Strain Index
Notes	**Author contact:** emailed study authors to request mean, SD for DASS-21 Depression and AHI post-treatment/end of follow-up (received reply from study author with mean SD for DASS-21 Depression, AHI, and DASS-21 Anxiety for stroke patients only 09/11/2018).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Quote:** "stratified randomisation with blocking was used to allocate participants to two groups of equal size, stratified by service setting (stroke versus CTCBI). Because service setting was a proxy for injury type (stroke versus non-stroke) and for the nature of usual care that would be available to participants, either of which could have influenced outcomes, including this as a stratification factor ensured these aspects would be balanced across the intervention and control groups" (p. 24). **Comment:** computer-generated numbers were used based on correspondence with author.
Allocation concealment (selection bias)	Low risk	**Quote:** "the allocation system was managed by the Robertson Centre for Biostatistics and was accessed via an automated telephone service after the baseline assessment had been completed" (p. 24).

Cullen 2018 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Quote:** "screening, baseline assessments, allocation and interventions were carried out by one RA (who was blinded to randomisation block length), and the interim and follow-up measures were administered by a second RA, each of whom was blind to the other's findings. The second RA was blind to participant allocation; a standard script was used to prevent unblinding during follow-up telephone calls, and postal materials included clear instructions to participants not to reveal treatment allocation information" (p. 24). **Comment:** due to the nature of the intervention, it is unlikely that participants were blinded to the group allocation.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Quote:** "a blinded assessor administered the DASS-21 and the AHI at 5, 9 and 20 weeks post-baseline. Of 27 participants randomised (median age 57; 63% men; 82% ischaemic stroke survivors; median 5.7 months post-injury), 14 were assigned to positive psychotherapy, of whom 8 completed treatment" (p. 31).
Incomplete outcome data (attrition bias) All outcomes	High risk	**Comment:** per-protocol analysis reported only; 11/27 participants not included in the analysis
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol or registry record available to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline demographic characteristics between groups

Du 2005

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Treatment arm:** rTMS + fluoxetine (SSRI) **Control arm:** fluoxetine (SSRI)
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** stroke, types not stated **Method of stroke diagnosis:** diagnosis consistent with diagnostic criteria for stroke formulated by the Fourth National Symposium on Cerebrovascular Disease in 1995; confirmation by brain CT or MRI **Time since stroke:** not reported **Inclusion criteria:** (1) 17-item HDRS score ≥ 8 points; (2) can sign informed consent **Exclusion criteria:** (1) previous depression or psychiatric illness history; (2) aphasia; (3) severe cardiac, pulmonary, hepatic, and renal impairment **Total number randomised in this trial:** 60 **Number randomised to treatment group:** 30 (53% men; age range 59 to 82 years) **Number randomised to control group:** 30 (53% men; age range 56 to 83 years) **Total number included in final analysis:** 60

Du 2005 *(Continued)*

	Number included in treatment group for final analysis: 30 **Number included in control group for final analysis:** 30
Interventions	**Treatment:** low-frequency rTMS + 20 mg fluoxetine (SSRI) daily. Patients' bilateral frontal lobes were stimulated with 60% of maximal stimulus intensity, 30 times for each side. Frequency was 0.5 Hz, 1 sequence every day continuous for 5 days as a course, with an interval of 2 days between courses. **Control:** 20 mg fluoxetine (SSRI) daily **Treatment duration:** 4 weeks **Follow-up:** none
Outcomes	**Primary outcomes** • Depression measured using 17-item HDRS • Cognitive functioning measured using MMSE • Disability measured using BI
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	**Comment:** drawing lots used to generate randomisation sequence; this method of sequence generation is prone to bias.
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	**Comment:** participants and personnel not blinded to group allocation
Blinding of outcome assessment (detection bias) All outcomes	High risk	**Comment:** outcome assessors not blinded to group allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** ITT; no missing data reported
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol or registry record available to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline demographic characteristics between groups

Fan 2010

Study characteristics

Methods	**Study design:** parallel design

Fan 2010 *(Continued)*

	Number of arms: 2
	Treatment arm: psychological nursing + antidepressant (name and class not reported)
	Control arm: antidepressant (name and class not reported) + usual care
Participants	**Geographical location:** China
	Setting: inpatient
	Stroke criteria: stroke, types not stated
	Method of stroke diagnosis: confirmed cerebral infarction, cerebral haemorrhage or subarachnoid haemorrhage by transcranial CT or MRI
	Time since stroke: not reported
	Depression criteria: meets the CCMD-II diagnostic criteria for post-stroke depression and a HAMD > 17 score
	Inclusion criteria: (1) confirmed cerebral infarction, cerebral haemorrhage or subarachnoid haemorrhage by transcranial CT or MRI; (2) no prior history of organic diseases and neuropsychiatric diseases; (3) clear consciousness, survival time 30 days; (4) diagnosed by two psychiatrists as meeting the CCMD-II diagnostic criteria for post-stroke depression; (5) meets HAMD > 17 score
	Exclusion criteria: not reported
	Total number randomised in this trial: 80
	Number randomised to treatment group: 40 (55% men and mean age 58.2 SD 5.6 years)
	Number randomised to control group: 40 (52.5% men and mean age 61.6 SD 4.8 years)
	Total number included in final analysis: 80
	Number included in treatment group for final analysis: 40
	Number included in control group for final analysis: 40
Interventions	**Treatment:** psychological nursing, twice a day, 30 minutes each time, for 6 weeks + antidepressant (name and class not reported)
	Administered by: not reported
	Supervision: not reported
	Intervention fidelity: not reported
	Control: antidepressant (name and class not reported) + usual care
	Treatment duration: 6 weeks
	Follow-up: none
Outcomes	**Primary outcomes:** • Depression measured using HDRS-17 • Motor function measured using Scandinavian Stroke Scale
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Fan 2010 *(Continued)*

Random sequence generation (selection bias)	Low risk	**Quote:** "The grouping method uses a random number table..." p. 1335
Allocation concealment (selection bias)	Unclear risk	**Comment:** Method of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** Information on blinding of participants and personnel was not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** Information on blinding of outcome assessment was not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** All 80 patients were included in the final analysis.
Selective reporting (reporting bias)	Unclear risk	**Comment:** All outcomes reported; no trial protocol or registry record available to compare with the publication
Other bias	Low risk	**Quote:** "It can be seen from Table 1 that there was no difference in the total scores of the two groups of HAMD at the time of entry." p. 1336

Fan 2014

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** rTMS + duloxetine (SNRI) + stroke usual care **Control arm:** duloxetine (SNRI) + stroke usual care
Participants	**Geographical location:** China **Setting:** unclear **Stroke criteria:** not reported **Method of stroke diagnosis:** not reported **Time since stroke:** not reported **Inclusion criteria:** (1) meeting diagnostic criteria of the CCMD-2-R for depression; (2) 17-item HDRS score ≥ 8; (3) stable condition; (4) could tolerate rTMS; (5) patient or family member can sign informed consent; (6) age 18 to 80 years **Exclusion criteria:** (1) with previous depression, psychiatric illness history; (2) without 1-week washout period of previous antidepressants; (3) consciousness disturbance or severe cognitive impairment; (4) with epilepsy or severe cardiac, pulmonary, hepatic, or renal disease; (5) critical conditions or unstable acute stage of stroke **Depression criteria:** must meet diagnostic criteria of the CCMD-2-R for depression and the 17-item HDRS score ≥ 8

Fan 2014 *(Continued)*

	Total number randomised in this trial: 90 **Number randomised to treatment group:** 45 (42% men, mean age 61.43, SD 8.74) **Number randomised to control group:** 45 (51% men, mean age 64.78, SD 7.23) **Total number included in final analysis:** 90 **Number included in treatment group for final analysis:** 45 (42% men, mean age 61.43, SD 8.74) **Number included in treatment group for final analysis:** 45 (51% men, mean age 64.78, SD 7.23)
Interventions	**Treatment:** rTMS (frequency: 1 Hz, intensity: 100% motor threshold, 30 times for a series, 10 series for each treatment; location: bilateral dorsolateral pre-frontal) + duloxetine (SNRI) 60 mg/d + stroke usual care (routine medication and rehabilitation) **Control:** duloxetine (SNRI) + stroke usual care **Duration:** 4 weeks **Follow-up:** none
Outcomes	**Primary outcomes** • Depression measured using 17-item HDRS • Disability measured using MBI
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Comment:** method of sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** double-blind stated but who was blinded not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** double-blind stated but who was blinded not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** ITT analysis; no missing data reported
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline demographics between groups

Fang 2017

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** constructive integrative psychosocial intervention (CIPI) **Control arm:** standard care
Participants	**Geographical location:** Singapore **Setting:** inpatient **Stroke criteria:** ischaemic and haemorrhagic stroke **Method of stroke diagnosis:** clinically diagnosed new stroke **Time since stroke:** 1 week **Inclusion criteria:** (1) had satisfactory mental status MMSE > 23; (2) had clinically diagnosed new stroke within a week; (3) only patients who spoke English or Mandarin **Exclusion criteria:** (1) other non-stroke-related neurological conditions such as brain tumour or traumatic brain injury; (2) patients discharged to a nursing home **Depression criteria:** HADS score ≥ 8 **Total number randomised in this trial:** 42 **Number randomised to treatment group:** 23 (% men, age not recorded in the study) **Number randomised to control group:** 19 (% men, age not recorded in the study) **Total number included in final analysis:** 19 **Number included in treatment group for final analysis:** 13 (% men, age not recorded in the study) **Number included in control group for final analysis:** 6 (% men, age not recorded in the study)
Interventions	**Treatment:** CIPI results in a positive construction of experience of illness by patients and significant others. This addresses their cognitions related to living with stroke and related behavioural response to the stroke experience. Key qualities include evidence-supported components of psychosocial-behavioural intervention life review and education. **Administered by:** not reported **Supervision:** not reported **Intervention fidelity:** not reported **Control:** standard care **Duration:** 6 months **Follow-up:** none
Outcomes	**Primary outcome** • Depression measured using HADS at 1, 3, and 6 months **Secondary outcome** • Cognitive functioning measured using MMSE at 1, 3, and 6 months

Fang 2017 *(Continued)*

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Quote:** "it used a randomized control group in an acute stroke unit with pretest–posttest…." **Comment:** based on study authors' responses; random number tables used
Allocation concealment (selection bias)	High risk	**Comment:** based on study authors' responses; sealed envelopes used to conceal allocation. This method of allocation concealment can be tampered with.
Blinding of participants and personnel (performance bias) All outcomes	High risk	**Comment:** due to the nature of the trial, it was not possible to mask participants, clinicians, and researchers to treatment allocation.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Comment:** based on study authors' responses: outcome assessors blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	**Comment:** per-protocol analysis reported; 3/23 in treatment group not included in the analysis
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Unclear risk	**Comment:** baseline demographic information not reported

Fruehwald 2003

Study characteristics

Methods	**Study design:** parallel design **Number of arms:** 2 **Treatment arm:** fluoxetine (SSRI) **Control arm:** matched placebo
Participants	**Geographical location:** Austria **Setting:** inpatients **Stroke criteria:** ischaemic stroke and primary intracerebral haemorrhage **Method of stroke diagnosis:** diagnosis via clinical signs and CT (100%) **Time since stroke:** 11 days **Inclusion criteria:** (1) stroke on average 11 days before randomisation **Exclusion criteria:** (1) MMSE < 20, more than mild communication deficit; (2) disease of the CNS and previous degenerative or expansive neurological disorder

Fruehwald 2003 *(Continued)*

	Depression criteria: psychiatric interview and HDRS score > 15 **Total number randomised in this trial:** 54 **Number randomised to treatment group:** 28 (46% men, mean age 65 years, SD 14) **Number randomised to control group:** 26 (71% men, mean age 64 years, SD 14) **Total number included in final analysis:** 40 **Number included in treatment group for final analysis:** 22 (% men and mean age not reported) **Number included in control group for final analysis:** 18 (% men and mean age not reported)
Interventions	**Treatment:** fluoxetine (SSRI) 20 mg daily; dose escalation at 4 weeks if HDRS score > 13 **Control:** matched placebo **Duration:** 12 weeks. Open-label treatment was continued for a further 15 months for all (these data not included in the review) **Follow-up:** 18 months
Outcomes	**Primary outcomes** • Depression measured using HDRS, BDI, and CGI Scale-1 • Proportion of responders (HDRS < 13) **Secondary outcomes** • Stroke impairment measured using SSS • Adverse events
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Quote:** "the randomization code list was generated by a computer program in a random permuted block design for each centre" (p. 348).
Allocation concealment (selection bias)	Low risk	**Quote:** "all patients were randomly assigned to either fluoxetine or placebo treatment by the drug company independently of the research teams and the study centres" (p. 348).
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Quote:** "… neither patients nor relatives, clinical examiners nor nursing staff were aware of the drug treatment being given" (p. 348).
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Quote:** "… neither patients nor relatives, clinical examiners nor nursing staff were aware of the drug treatment being given" (p. 348).
Incomplete outcome data (attrition bias) All outcomes	High risk	**Comment:** per-protocol analysis reported only; 4/54 (7.4%) not included in analyses
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported. No trial protocol or registry record available to compare with the publication
Other bias	Low risk	**Comment:** non-significant trends towards more women and right-sided lesion strokes in treatment group

Gao 2017a

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Treatment arm:** citalopram (SSRI) + 'attention control' psychological intervention (group B) **Control arm:** placebo + 'attention control' psychological intervention (group A)
Participants	**Geographical location:** China **Setting:** outpatient **Stroke criteria:** ischaemic stroke **Method of stroke diagnosis:** occurrence of an ischaemic stroke that met the standards of WHO diagnostic criteria. Radiological MRI confirmation of an anatomical infarct observed on diffusion-weighted acute MRI **Time since stroke:** not reported **Inclusion criteria:** (1) first-ever acute ischaemic stroke; (2) no history of depression; (3) no antidepressant treatments received before our interventions; (4) over 18 years of age **Exclusion criteria:** (1) presence of pre-stroke disease leading to pre-stroke disability; Barthel Index < 10 **Depression criteria:** 20-item BDI scores > 10 **Total number randomised in this trial:** 136 **Number randomised to treatment group:** 91 (50% men, mean age 66 years, SD 7) **Number randomised to control group:** 45** (53% men, mean age 67 years, SD 10) **Total number included in final analysis:** 128 **Number included in treatment group for final analysis:** 85 (% men and mean age were not reported) **Number included in control group for final analysis:** 43** (% men and mean age were not reported)
Interventions	**Treatment:** patients received active citalopram tablets (SSRI) and participated in similar placebo psychological discussions as group A **Control:** patients received placebo tablets and participated in a placebo psychological intervention, 1-hour discussions with non-psychological clinical doctors twice a week for 3 months; discussions focused on inquiries about stroke recovery and changes in daily life **Administered by:** non-psychological clinical doctors **Supervision:** not reported **Duration:** 3 months **Follow-up:** none
Outcomes	**Primary outcomes** • Depression measured using HDRS • Depression measured using Melancholia Scale

Gao 2017a *(Continued)*

	Secondary outcomes • Disability measured using BI
Notes	**Author contact:** emailed study authors to request AE tables with numbers for all groups 23 October 2018

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Quote:** "randomization into one of three intervention groups was undertaken by an independent researcher using computer-generated random number sequences" (p. 73).
Allocation concealment (selection bias)	High risk	**Quote:** "... were prepared in advance and placed in consecutively numbered, sealed, opaque envelopes" (p. 73). **Comment:** sealed, opaque envelopes can be tampered with.
Blinding of participants and personnel (performance bias) All outcomes	High risk	**Quote:** "when patients were enrolled, they were told to participate in drug therapy, talk with doctors, and engage in rehabilitation at the same time. No breaches in blinding were detected during the trial" (p. 74). "the study therapists were asked not to divulge any treatment information to their patients" (p. 75). **Comment:** therapists delivering the intervention were not blinded to group allocation.
Blinding of outcome assessment (detection bias) All outcomes	High risk	**Quote:** "the study therapists acted as clinical evaluators…" (p. 74)
Incomplete outcome data (attrition bias) All outcomes	High risk	**Comment:** per-protocol analysis reported only; 5/91 in control, 6/91 in treatment not included in the analysis
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol or registry record available to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline demographic characteristics between groups

Gao 2017b

Study characteristics

Methods	**Study design:** parallel design **Number of arms:** 2 **Treatment arm:** 'active' psychological intervention + placebo (group C) **Control arm:** 'attention control' psychological intervention + placebo (group A)
Participants	**Geographical location:** China

Gao 2017b *(Continued)*

	Setting: outpatient **Stroke criteria:** ischaemic stroke **Method of stroke diagnosis:** occurrence of an ischaemic stroke that met the standards of WHO diagnostic criteria. Radiological MRI confirmation of an anatomical infarct observed on diffusion-weighted acute MRI **Time since stroke:** not reported **Inclusion criteria:** (1) first-ever acute ischaemic stroke; (2) no history of depression; (3) no antidepressant treatments received before our interventions; (4) over 18 years of age **Exclusion criteria:** (1) presence of pre-stroke disease leading to pre-stroke disability; Barthel Index < 10 **Depression criteria:** 20-item BDI scores > 10 **Total number randomised in this trial:** 138 **Number randomised to treatment group:** 92 (52% men, mean age 65 years, SD 8) **Number randomised to control group:** 46** (53% men, mean age years 67, SD 10) **Total number included in final analysis:** 130 **Number included in treatment group for final analysis:** 87 (% men and mean age not reported) **Number included in control group for final analysis:** 43** (% men and mean age not reported)
Interventions	**Treatment:** patients received placebo tablets and had an 'active' psychological intervention: professional cognitive-behavioural therapy with psychologists who were trained by a professional cognitive therapist for 1 week. The manual-based treatment included cognitive and behavioural courses that consisted of education, activities, graded task assignments, and identifying and modifying useless beliefs and thoughts. Interventional measures were altered to meet individual demands. **Administered by:** psychologist trained in professional cognitive therapy **Supervision:** not reported **Control:** patients received placebo tablets and participated in a placebo psychological intervention; 1-hour discussions with non-psychological clinical doctors twice a week for 3 months; discussions focused on inquiries about stroke recovery; and changes in daily life. **Administered by:** non-psychological clinical doctors **Supervision:** not reported **Intervention fidelity:** not reported **Duration:** 3 months **Follow-up:** none
Outcomes	**Primary outcomes** • Depression measured using HDRS • Depression measured using Melancholia Scale **Secondary outcomes** • Disability measured using BI

Gao 2017b *(Continued)*

Notes	**Author contact:** emailed study authors to request AE tables with numbers for all groups 23 October 2018

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Quote:** "randomization into one of three intervention groups was undertaken by an independent researcher using computer-generated random number sequences" (p. 73).
Allocation concealment (selection bias)	High risk	**Quote:** "….were prepared in advance and placed in consecutively numbered, sealed, opaque envelopes" (p. 73). **Comment:** sealed, opaque envelopes can be tampered with.
Blinding of participants and personnel (performance bias) All outcomes	High risk	**Quote:** "when patients were enrolled, they were told to participate in drug therapy, talk with doctors, and engage in rehabilitation at the same time. No breaches in blinding were detected during the trial" (p. 74). "the study therapists were asked not to divulge any treatment information to their patients" (p. 75). **Comment:** therapists delivering the intervention not blinded to group allocation
Blinding of outcome assessment (detection bias) All outcomes	High risk	**Quote:** "the study therapists acted as clinical evaluators …" (p. 74).
Incomplete outcome data (attrition bias) All outcomes	High risk	**Comment:** per-protocol analysis reported only; 5/91 in control, 6/91 in treatment not included in the analysis
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol or registry record available to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline demographic characteristics between groups

Gu 2016

Study characteristics

Methods	**Study design:** parallel design **Number of arms:** 2 **Treatment arm:** rTMS **Control arm:** sham rTMS
Participants	**Geographical location:** South Korea **Setting:** unclear **Number of participants:** 24

Gu 2016 *(Continued)*

	Stroke criteria: infarct and haemorrhage **Method of stroke diagnosis:** not reported **Time since stroke:** > 6 months **Inclusion criteria:** (1) absence of depression or medication history of antidepressants before stroke onset; (2) absence of severe cognitive dysfunction or aphasia; (3) absence of serious medical complications such as pneumonia or cardiac problems; (4) admitted > 6 months after stroke onset; (5) aged between 21 and 80 years only **Exclusion criteria:** (1) history of depression before stroke onset; (2) medication history of antidepressants before stroke onset; (3) serious medical complications such as pneumonia or cardiac problems **Depression criteria:** BDI scores > 12 and 17-item HDRS scores > 6 **Total number randomised in this trial:** 24 **Number randomised to treatment group:** 12 (50% men, mean age 58 years, SD 9) **Number randomised to control group:** 12 (42% men, mean age 58 years, SD 8) **Total number included in final analysis:** 24 **Number included in treatment group for final analysis:** 12 (50% men, mean age 58 years, SD 9) **Number included in control group for final analysis:** 12 (42% men, mean age 58 years, SD 8)
Interventions	**Treatment:** Magstim Super Rapid Magnetic Stimulator (The Magstim Company, Wales, UK) with 70-mm, air-cooled coil in the shape of a figure of 8. The coil was held with the handle posterior and oriented sagittally. rTMS was performed over the left F3 on the scalp according to the 10/20 electroencephalography system (i.e. the DLPFC). For patients in the rTMS group, rTMS was delivered over the DLPFC at 10 Hz, at an intensity of 110% of the motor threshold, duration of 5 seconds, and total of 20 trains separated by 1-minute pauses (total of 1000 pulses). Each patient underwent 10 consecutive sessions (Monday to Friday, 5 times per week for 2 weeks) **Control:** sham stimulation was delivered using the same protocol, except that the angle of the coil was at 90 perpendicular to the skull rather than tangential to it. Thus, the magnetic field could not penetrate the brain, although patients could hear the sound that was produced. **Administered by:** psychiatrist **Duration:** 2 weeks **Follow-up:** 4 weeks
Outcomes	**Primary outcomes** • Depression measured using BDI and 17-item HDRS **Secondary outcomes** • Motor function measured using Upper limb Motoricity Index (MI-UE), lower limb MI-LE, Modified Brunnstrom Classification (MBC), and Functional Ambulatory Category (FAC)
Notes	**Author contact:** emailed study authors for method of randomisation, details of blinding of patients, method of stroke diagnosis, number of patients screened/eligible, and sample size calculations 24 October 2018

Risk of bias

Bias	Authors' judgement	Support for judgement

Gu 2016 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	**Quote:** "all patients were randomly assigned to two groups, the rTMS and sham groups**…**"**(**p. 271) **Comment:** method of sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Quote:** "a psychiatrist who was blinded to the study protocol performed rTMS using a Magstim Super Rapid Magnetic Stimulator" (p. 271). **Comment:** double-blind stated but not reported whether participants were blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Quote:** "the experimenters who applied the rTMS or sham stimulations were different from the experimenters who assessed the degree of depression and motor function. The experimenters who assessed depression and motor function were blinded to the group assignment" (p. 271).
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** ITT analysis reported; all participants included in the analysis
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol or registry record available to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline BDI scores and demographic characteristics between groups

Hoffmann 2015

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** cognitive-behavioural therapy **Control arm:** usual care
Participants	**Geographical location:** Australia **Setting:** inpatient **Stroke criteria:** unclear **Method of stroke diagnosis:** diagnosis of stroke confirmed by chart review **Time since stroke:** not reported **Inclusion criteria:** (1) > 18 years old; (2) adequate cognitive capacity to provide informed consent; (3) adequate English and expressive and receptive communication skills **Exclusion criteria:** (1) neurodegenerative disorder (e.g. dementia); (2) living > 50 km away from hospital **Depression criteria:** depression score not an entry criteria. For unpublished analysis, HADS ≥ 8 used for depression criteria

Hoffmann 2015 *(Continued)*

	Total number randomised in this trial: 22 **Number randomised to treatment group:** 12 (75% men; mean age 60.8, SD 11.7) **Number randomised to control group:** 10 (60% men; mean age 57.0, SD 14.2) **Total number included in final analysis:** 17 **Number included in treatment group for final analysis:** 12 (75% men; mean age 60.8, SD 11.7) **Number included in control group for final analysis:** 5 (60% men; mean age 57.0, SD 14.2)
Interventions	**Treatment:** 8 × 1-hour cognitive-behavioural coping skills sessions delivered by clinical psychologist with first 2 sessions in hospital, then 6 delivered at home **Administered by:** clinical psychologist **Supervision:** psychologist **Intervention fidelity:** 9/11 patients received 8 sessions; 7/11 received sessions in the intended location **Control:** usual care **Duration:** 8 weeks **Follow-up:** 3 months
Outcomes	**Primary outcomes** • Depression measured using HADS and MADRS • Anxiety measured using HADS **Secondary outcomes** • Disability measured using MBI • Self-efficacy measured using Stroke Self Efficacy Questionnaire • Functional capacity measured using Nottingham EADL • Knowledge of stroke measured using Stroke Knowledge Questionnaire • Quality of life measured using SAQoL
Notes	This trial had 3 arms (self-management therapy, cognitive-behavioural therapy, and usual care), but only data from cognitive-behavioural therapy compared with usual care (n = 17 participants) are presented here.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Quote:** "... randomly allocated using a predetermined computer generated randomisation sequence ..." (p. 118)
Allocation concealment (selection bias)	High risk	**Comment:** sealed opaque envelopes reported; this method of allocation concealment can be tampered with.
Blinding of participants and personnel (performance bias) All outcomes	High risk	**Comment:** due to the nature of the trial, it was not possible to mask participants, personnel delivering the intervention, and researchers to treatment allocation.

Hoffmann 2015 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Quote:** "outcomes were assessed in a face-to-face interview conducted by a research assistant (a registered psychologist) who was blind to group allocation" (p. 118).
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Quote:** "analysis was completed using ... and on an intention to treat basis and missing data were addressed using the last observation carried forward procedure" (p. 120). **Comment:** ITT analysis reported. From whole data set, including depressed and non-depressed; 1 intervention and 1 control withdrew post randomisation
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Unclear risk	**Comment:** baseline demographic information not reported

Hordacre 2021

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Treatment arm:** rTMS **Control arm:** sham rTMS
Participants	**Geographical location:** Australia **Setting:** unclear **Stroke criteria:** unclear **Method of stroke diagnosis:** unclear **Time since stroke:** overall not reported. rTMS group (mean 5.5, SD 3.3 years) and sham group (mean 3.9, SD 3.0 years) **Inclusion criteria:** (1) aged > 18 years; (2) had depression (PHQ-9 > 5) with onset of symptoms occurring after stroke; (3) no change in antidepressant medication for 6 months prior to participation or during the trial; (4) no contraindications to TMS such as metallic implants, pregnancy or a history of seizures; and (5) no history of craniotomy or craniectomy as skull defects are known to affect electroencephalography (EEG) signal **Exclusion criteria:** (1) unable to communicate; and (2) provide informed consent **Depression criteria:** PHQ-9 > 5 with onset of symptoms occurring after stroke **Total number randomised in this trial:** 11 **Number randomised to treatment group:** 6 (83% men; mean age 63.3, SD 11) **Number randomised to control group:** 5 (80% men; mean age 61.6, SD 12.4) **Total number included in final analysis:** 11 **Number included in treatment group for final analysis:** 6 (83% men; mean age 63.3, SD 11) **Number included in control group for final analysis:** 5 (80% men; mean age 61.6, SD 12.4)

Hordacre 2021 *(Continued)*

Interventions	**Treatment:** focal rTMS was administered using a Magstim Super Rapid (Magstim, UK) connected to an active 70 mm figure-8 air-cooled coil (part number 3910-23-00). For all participants, rTMS was applied at 110% RMT to the left DLPFC (F3 from the 10–20 EEG system). At each treatment session, 3000 pulses were applied at 10 Hz (4 s on and 26 s off; total duration 37.5 min) with a total of 10 rTMS sessions completed at a similar time of day over a 2-week period **Administered by:** not reported **Supervision:** n/a **Intervention fidelity:** all participants completed all 10 rTMS sessions **Control:** sham rTMS was administered using a Magstim Super Rapid (Magstim, UK) connected to a placebo coil that was identical, but did not produced an electromagnetic field (part number 3950–23-00). **Duration:** 2 weeks **Follow-up:** 1 month
Outcomes	**Primary outcome** • Depression measured using BDI **Secondary outcomes** • Depression measured using PHQ-9 • Self-efficacy measured using Stroke Self Efficacy Questionnaire • EEG readings • MRI images • Adverse events
Notes	The study was funded by a Research Themes Investment Scheme — University of South Australia grant.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Quote:** "sequence generation was from a random number generator" p. 1475.
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Quote:** "both participants and outcome assessors were blind to allocation. Participants were informed that there was an Active and Sham group and they would be unable to determine the difference between conditions" p. 1475.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Quote:** "both participants and outcome assessors were blind to allocation. Participants were informed that there was an Active and Sham group and they would be unable to determine the difference between conditions" p. 1475.
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** all 11 participants completed all 10 rTMS sessions and all clinical and neurophysiological assessments.
Selective reporting (reporting bias)	Low risk	**Comment:** all prespecified outcomes reported but no trial protocol available to compare the publication

Hordacre 2021 *(Continued)*

Other bias	Low risk	**Quote:** "There were no group differences in age, sex, time since stroke, lesion characteristics, RMT or baseline BDI, PHQ-9 and SSEQ (all P ≥ 0.42)" p. 1475.

Huang 2002

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** fluoxetine (SSRI) **Control arm:** matched placebo
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** first-ever ischaemic or haemorrhagic stroke **Method of stroke diagnosis:** diagnosis is consistent with the diagnostic criteria for acute stroke formulated by the Chinese Medical Association with 1 single and unilateral lesion confirmed by brain CT or MRI. **Time since stroke:** unclear **Inclusion criteria:** none reported **Exclusion criteria:** (1) history of psychiatric illness; (2) severe heart disease; (3) previous organic brain disease; (4) severe liver or kidney disease; (5) history of drug allergy **Depression criteria:** psychiatric interview to confirm diagnosis meets depression diagnostic criteria of the CCMD-2-R **Total number randomised in this trial:** 80 (overall percentage of men 45%; 80 patients were a depressive subgroup of 168 patients whose mean age was 62.2 years, SD 8.1) **Number randomised to treatment group:** 40 (% men and mean age in treatment group not reported) **Number randomised to control group:** 40 (% men and mean age in control group not reported; total group as above) **Total number included in final analysis:** 80 (overall percentage of men 45%; 80 patients were a depressive subgroup of 168 patients whose mean age was 62.2 years, SD 8.1) **Number included in treatment group for final analysis:** 40 (% men and mean age in treatment group not reported) **Number included in control group for final analysis:** 40 (% men and mean age in control group not reported; total group as above)
Interventions	**Treatment:** fluoxetine (SSRI) 20 mg/d in the morning **Control:** matched placebo **Duration:** 4 weeks **Follow-up:** none
Outcomes	**Primary outcomes**

Huang 2002 *(Continued)*

- Depression measured using CCMD-2-R and 17-item HDRS

Secondary outcomes

- Neurological impairment measured using CSS
- Adverse events

Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Comment:** method of sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** blinding of participants and personnel not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** blinding of outcome assessors not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** ITT analysis reported; no missing data reported
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline HAMD and CSS scores between groups

Jiang 2001a

Study characteristics

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** amitriptyline (TCA) **Control arm:** placebo (not matched)
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** unclear **Method of stroke diagnosis:** diagnosis via CT or MRI (100%) **Time since stroke:** 0 to 7 days

Jiang 2001a *(Continued)*

	Inclusion criteria: (1) Chinese Stroke Scale score > 8; (2) can independently complete HDRS, aged < 80 years; (3) no severe negative life events in past year; (4) first stroke; (5) no previous psychosis; (6) no antidepressant medication **Exclusion criteria:** (1) with history of psychosis; (2) on antidepressant medication **Depression criteria:** HDRS > 8 **Total number randomised in this trial:** 45 **Number randomised to treatment group:** 30 (57% men, mean age 62 years, SD 14) **Number randomised to control group:** 15** (60% men, mean age 63 years, SD 15) **Total number included in final analysis:** 45 **Number included in treatment group for final analysis:** 30 (57% men, mean age 62 years, SD 14) **Number included in control group for final analysis:** 15** (60% men, mean age 63 years, SD 15)
Interventions	**Treatment:** amitriptyline (TCA) 50 mg increasing by 25 mg per day to 200 mg daily **Control:** placebo (not matched) 2 tablets per day **Duration:** 6 months **Follow-up:** none
Outcomes	**Primary outcomes** • Depression measured using HDRS **Secondary outcomes** • Impairment measured using CSS • Adverse events
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Comment:** method of sequence generation not reported
Allocation concealment (selection bias)	High risk	**Comment:** 3-armed trial. Placebo frequency matched to Deanxit (intervention in third arm) - not to amitriptyline
Blinding of participants and personnel (performance bias) All outcomes	High risk	**Comment:** participants blinded but personnel not blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** blinding of outcome assessment not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** ITT analysis reported (complete follow-up of all randomised participants)
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication

Jiang 2001a *(Continued)*

Other bias	High risk	**Comment:** intervention group was younger and had higher HDRS score and lower CSS score.

Jiang 2001b

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** Deanxit **Control arm:** placebo (not matched)
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** unclear **Method of stroke diagnosis:** diagnosis via CT or MRI (100%) **Time since stroke:** 0 to 7 days **Inclusion criteria:** (1) CSS score > 8; (2) can independently complete HDRS, aged < 80 years; (3) no severe negative life events in past year; (4) first stroke; (5) no previous psychosis; (6) no antidepressant medication **Exclusion criteria:** (1) with history of psychosis; (2) on antidepressant medication **Depression criteria:** HDRS > 8 **Total number randomised in this trial:** 45 **Number randomised to treatment group:** 30 (58% men, mean age 62 years, SD 14) **Number randomised to control group:** 15** (60% men, mean age 63 years, SD 15) **Total number included in final analysis:** 45 **Number included in treatment group for final analysis:** 30 (58% men, mean age 62 years, SD 14) **Number included in control group for final analysis:** 15** (60% men, mean age 63 years, SD 15)
Interventions	**Treatment:** Deanxit 2 tablets daily **Control:** placebo (not matched but frequency matched) **Duration:** 6 months **Follow-up:** none
Outcomes	**Primary outcomes** • Depression measured using HDRS **Secondary outcomes** • Impairment measured using CSS • Adverse events
Notes	
Risk of bias	

Jiang 2001b *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Comment:** method of sequence generation not reported
Allocation concealment (selection bias)	High risk	**Comment:** 3-armed trial. Placebo frequency matched to Deanxit (intervention in third arm) - not to amitriptyline
Blinding of participants and personnel (performance bias) All outcomes	High risk	**Comment:** participants blinded but personnel not blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** blinding of outcome assessment not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** ITT analysis reported (complete follow-up of all randomised participants)
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	High risk	**Comment:** intervention group was younger and had higher HDRS score and lower CSS score

Jiang 2014a

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** TMS + acute stroke usual care **Control arm:** acute stroke usual care
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** Internal carotid artery territory infarct **Method of stroke diagnosis:** clinical diagnosis plus confirmation by imaging that a relevant lesion needed to be visible **Time since stroke:** 3 to 10 days **Inclusion criteria:** (1) first-ever stroke; (2) age 30 to 70 years; (3) NIHSS at admission 8 to 20 points; (4) GCS scale score > 8; (5) education level: at least high school, able to complete questionnaires; (6) no communication barriers, able to communicate with medical staff; (7) can sign informed consent **Exclusion criteria:** (1) comorbid severe organ failure; (2) history of epilepsy or consciousness disturbance; (3) contraindication for transcranial magnetic stimulation such as pacemaker implanted, severe cardiac dysrhythmia; (4) worsened clinical condition, new infarct, or haemorrhagic transformation **Depression criteria:** not reported

Jiang 2014a *(Continued)*

	Total number randomised in this trial: 100 **Number randomised to treatment group:** 50 (% men and mean age not reported) **Number randomised to control group:** 50 (% men and mean age not reported) **Total number included in final analysis:** 100 **Number included in treatment group for final analysis:** 50 (% men and mean age not reported) **Number included in control group for final analysis:** 50 (% men and mean age not reported)
Interventions	**Treatment:** TMS + acute stroke usual care; frequency: start 3 to 10 days after stroke onset, 2 times a day, 20 minutes each time, for successive 14 days; location: motor cortex on the healthy side **Control:** acute stroke usual care **Duration:** 12 weeks **Follow-up:** 3 months
Outcomes	**Primary outcomes** • Depression measured using HDRS • Impairment measured using NIHSS • Activities of daily living measured using ADL
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Comment:** random numbers table used for sequence generation
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** information about blinding of participants and personnel not reported
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Comment:** outcome assessors blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	**Comment:** per-protocol analysis reported only; 1 participant dropped out and was not included in the analysis
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline demographics between groups

Jiang 2014b

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** TMS + sertraline (SSRI) + acute stroke usual care **Control arm:** sertraline (SSRI) + acute stroke usual care
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** internal carotid artery territory infarct **Method of stroke diagnosis:** clinical diagnosis plus confirmation by imaging that a relevant lesion needed to be visible **Time since stroke:** 3 to 10 days **Inclusion criteria:** (1) first-ever stroke; (2) age 30 to 70 years; (3) NIHSS at admission 8 to 20 points; (4) GCS scale score > 8; (5) education level: at least high school, able to complete questionnaires; (6) no communication barriers, able to communicate with medical staff; (7) can sign informed consent **Exclusion criteria:** (1) comorbid severe organ failure; (2) history of epilepsy or consciousness disturbance; (3) contraindication for transcranial magnetic stimulation such as pacemaker implanted, severe cardiac dysrhythmia; (4) worsening clinical condition, new infarct, or haemorrhagic transformation **Depression criteria:** not reported **Total number randomised in this trial:** 100 **Number randomised to treatment group:** 50 (% men and mean age not reported) **Number randomised to control group:** 50 (% men and mean age not reported) **Total number included in final analysis:** 99 **Number included in treatment group for final analysis:** 50 **Number included in control group for final analysis:** 49
Interventions	**Treatment:** TMS + sertraline (SSRI) 50 mg/d + acute stroke usual care; frequency: start 3 to 10 days after stroke onset, 2 times a day, 20 minutes each time, for successive 14 days, location: motor cortex on the healthy side **Control:** sertraline (SSRI) 50 mg/d + acute stroke usual care **Duration:** 12 weeks **Follow-up:** 3 months
Outcomes	**Primary outcomes** • Depression measured using HDRS • Impairment measured using NIHSS • Activities of daily living measured using ADL
Notes	
Risk of bias	

Jiang 2014b *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Comment:** random numbers table used for sequence generation
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** information about blinding of participants and personnel not reported
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Comment:** outcome assessors blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	**Comment:** per protocol analysis reported only; 1 participant dropped out and was not included in the analysis
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline demographics between groups

Jin 2013

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** rTMS + sertraline (SSRI) + usual care **Control arm:** sertraline (SSRI) + usual care
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** ischaemic stroke **Method of stroke diagnosis:** clinical diagnosis plus confirmation by imaging that a relevant lesion needed to be visible **Time since stroke:** not reported **Inclusion criteria:** (1) without cerebral haemorrhage; (2) cerebral infarct history; (3) without epilepsy history; (4) EEG showing no epileptiform discharge; (5) without head injury or intracranial infection history; (6) without intracranial metal or other foreign body **Exclusion criteria:** not reported **Depression criteria:** 17-item HDRS score ≥ 17 **Total number randomised in this trial:** 60

Jin 2013 *(Continued)*

	Number randomised to treatment group: 30 (63% men; mean age 56.0, SD 9.8) **Number randomised to control group:** 30 (51% men; mean age 54.0, SD 10.2) **Total number included in final analysis:** 60 **Number included in treatment group for final analysis:** 30 **Number included in control group for final analysis:** 30
Interventions	**Treatment:** rTMS + sertraline (SSRI) 100 mg/d + usual care; frequency: 10 Hz, intensity: 80% resting motor threshold, with each stimulation lasting 4 seconds with an interval of 56 seconds, total 20 minutes each treatment, 1 treatment per day, 5 treatments per week, location: left DLPFC **Control:** sertraline (SSRI) 100 mg/d + usual care **Duration:** 4 weeks **Follow-up:** none
Outcomes	**Primary outcomes** • Depression measured using 17-item HDRS • Impairment measured using NIHSS
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Comment:** method of sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** information about blinding of participants and personnel not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** information about blinding of outcome assessors not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** ITT analysis reported; no missing data
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline demographics between groups

Kerr 2018

Study characteristics

Kerr 2018 *(Continued)*

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** individual motivational interviewing **Control arm:** usual care
Participants	**Geographical location:** Australia **Setting:** inpatient **Stroke criteria:** cerebral infarction/intracerebral haemorrhage **Method of stroke diagnosis:** medical diagnosis confirmed by neurologist in the medical notes **Time since stroke:** not reported **Inclusion criteria:** (1) acute presentation after acute stroke (cerebral infarction/intracerebral haemorrhage; (2) cognitively alert **Exclusion criteria:** (1) subarachnoid haemorrhage; (2) mental health conditions, including depressive symptoms requiring professional support within 1 month; (3) severe communication problems (e.g. significant dysphasia or aphasia); (4) myocardial infarction; (5) concurrent neurological disease/trauma **Depression criteria:** none **Total number randomised in this trial (stroke participants only):** 10 **Number randomised to treatment group:** 4 (25% men, mean age 57 years, SD 20.8) **Number randomised to control group:** 6 (50% men, mean age 65.8 years, SD 12.9) **Total number included in final analysis (stroke participants only):** 9 **Number randomised to treatment group:** 4 **Number included in control group:** 5
Interventions	**Treatment:** the over-arching principle of the intervention was to support the stroke survivor in adjusting to life after stroke. The purpose of Session 1 was to set the agenda and encourage the patient to talk about adjustment to stroke. In Session 2, the patient was encouraged to identify realistic goals for recovery and barriers to achieving goals. In Session 3, the goals were to identify any ambivalence that the patient had about achieving goals; to support the patient's optimism and self-efficacy, and to assist in identification of solutions to problems. Participants were encouraged to summarise their goals and commitment and to clarify any information from the first 2 sessions. Sessions were scheduled for 30 minutes. **Administered by:** trained facilitators **Supervision:** not stated **Intervention fidelity:** not reported **Control:** usual care **Duration:** not reported **Follow-up:** 1 month and 3 months
Outcomes	**Primary outcomes** • Feasibility (application, recruitment, and retention) **Primary clinical outcomes**

Kerr 2018 *(Continued)*

- Depression measured using HADS and PHQ-9
- Anxiety measured using HADS
- Quality of life measured using quality of life Index

Secondary outcomes

- Disability measured using MBI

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Quote:** "a computer-generated block randomisation list equally divided all numbers between 1 and 60 into either treatment or control groups" (p. 3).
Allocation concealment (selection bias)	Low risk	**Quote:** "allocation to the intervention or control arms was concealed from participants until after recruitment and baseline data collection. Envelopes were prepared by the Principal Investigator and stored in a locked cupboard in the ward. The envelopes were numbered sequentially, indicating the order in which participants were enrolled into the study (e.g. the first participant received the envelope labelled "Number 1", the second participant received the envelope "Number 2", etc.). A note in the envelope indicated the allocation (to intervention or control group), concealed by coloured paper to protect the identity of the allocation group. The project manager opened the randomisation envelopes after baseline data collection" (p. 3).
Blinding of participants and personnel (performance bias) All outcomes	High risk	**Quote:** "allocation to the intervention or control arms was concealed from participants until after recruitment and baseline data collection" (p. 3). "Although intentionally blinded, the research assistant may have become aware of the allocation in conversation with the participant" (p. 5).
Blinding of outcome assessment (detection bias) All outcomes	High risk	**Quote:** "the research assistant, a nurse with significant research experience, was employed to collect data at the 2 follow-up time points. Although intentionally blinded, the research assistant may have become aware of the allocation in conversation with the participant" (p. 5).
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	**Comment:** per-protocol analysis reported only; 10/48 participants not included in the analysis
Selective reporting (reporting bias)	High risk	**Comment:** Barthel Index not reported in the publication
Other bias	Low risk	**Comment:** no differences in baseline demographic characteristics between groups

Kirkness 2017a

Study characteristics

Methods

Study design: parallel design

Number of arms: 2

Experimental arm: brief psychosocial-behavioural intervention (in-person)

Kirkness 2017a *(Continued)*

	Control arm: usual care
Participants	**Geographical location:** USA **Setting:** outpatient **Stroke criteria:** ischaemic or haemorrhagic stroke **Method of stroke diagnosis:** ischaemic or haemorrhagic stroke (verified by CT or MRI) **Time since stroke:** 4 months **Inclusion criteria:** (1) those with ischaemic or haemorrhagic stroke; (2) GDS score > 11; (3) within 4 months of stroke onset **Exclusion criteria:** (1) GDS score < 11; (2) not within 4 months of stroke onset **Depression criteria:** GDS score < 11 **Total number randomised in this trial:** 49 **Number randomised to treatment group:** 35 (48.6% men, mean age 58.5 years, SD not reported) **Number randomised to control group:** 14** (50% men, mean age 60.7 years, SD not reported) **Total number included in final analysis:** 44 **Number included in treatment group for final analysis:** 31 **Number included in control group for final analysis:** 13**
Interventions	**Treatment:** brief in-person psychosocial-behavioural intervention (had 1 in-person orientation session with the psychosocial nurse practitioner therapist, either at home or at our study offices. Participant received participant manuals, discussed goals and expectations of each session, and learned how to fill out homework sections. **Administered by:** psychosocial nurse practitioner therapist **Supervised by:** not reported **Treatment fidelity:** not reported **Control:** usual care (participants reported on their progress at follow-up visits in their homes from research nurses at 8 weeks, 21 weeks, and 12 months following entry to the study). **Duration:** 8 weeks **Follow-up:** 10 months
Outcomes	**Primary outcomes** • Response (per cent reduction in HDRS) • Remission (HDRS score < 10) at 8 weeks and 12 months post-treatment
Notes	Emailed study authors to request mean and SD for HDRS, BI, and NIHSS score at 8 weeks and 12 months post-treatment for all 3 groups 23 October 2018 (reply received - mean SD and remission for HDRS and BI for all treatment groups sent by study author 06/11/2018)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Quote:** "the algorithm was based on an imbalance score which measured, for a given set of random assignments, how far out of balance the study would be

Kirkness 2017a *(Continued)*

		within strata for each factor and then summed over factors. When a new subject was available for randomization, we computed what the imbalance score would be if this subject were assigned to usual care, or to telephone intervention, or to in-person intervention. Then randomization was done to allocate two intervention participants to each control with each new assignment having a higher probability of less imbalance. The schema did not require equal numbers in each arm" (p. 4).
Allocation concealment (selection bias)	Unclear risk	**Quote:** "the study statistician generated the algorithm, which was securely stored and accessible only by the statistician and research nurse supervisor" (p. 5). **Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	**Quote:** "participants were asked not to reveal their study arm to the outcome assessors" (p. 5). **Comment:** blinding of personnel not reported
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Quote:** "... masking outcome assessors to the participant's randomization status. Participants were asked not to reveal their study arm to the outcome assessors. We did not detect any breaches in masking" (p. 5).
Incomplete outcome data (attrition bias) All outcomes	High risk	**Comment:** per-protocol analysis reported only. 9 participants not included in the analysis
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline demographic characteristics between groups

Kirkness 2017b

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** brief psychosocial-behavioural intervention (telephone) **Control arm:** usual care
Participants	**Geographical location:** USA **Setting:** outpatient **Stroke criteria:** ischaemic or haemorrhagic stroke **Method of stroke diagnosis:** ischaemic or haemorrhagic stroke (verified by CT or MRI) **Time since stroke:** 4 months **Inclusion criteria:** (1) ischaemic or haemorrhagic stroke; (2) GDS score > 11; (3) within 4 months of stroke onset **Exclusion criteria:** (1) GDS score < 11; (2) not within 4 months of stroke onset

Kirkness 2017b *(Continued)*

	Depression criteria: GDS score < 11 **Total number randomised in this trial:** 51 **Number randomised to treatment group:** 37 (51.4% men, mean age 61.7 years, SD not reported) **Number randomised to control group:** 14** (50% men, mean age 60.7 years, SD not reported) **Total number included in final analysis:** 47 **Number included in treatment group for final analysis:** 34 **Number included in control group for final analysis:** 13**
Interventions	**Treatment:** brief telephone psychosocial-behavioural intervention (had 1 in-person orientation session with psychosocial nurse practitioner therapist, either at home or at our study offices). Participants received participant manuals, discussed goals and expectations of each session, and learned how to fill out homework sections **Administered by:** psychosocial nurse practitioner therapist **Supervised by:** not reported **Treatment fidelity:** not reported **Control:** usual care (participants reported on their progress at follow-up visits in their homes from research nurses at 8 weeks, 21 weeks, and 12 months following entry to the study) **Duration:** 8 weeks **Follow-up:** 10 months
Outcomes	**Primary outcomes** • Response (per cent reduction in HDRS) • Remission (HDRS score < 10) at 8 weeks and 12 months post-treatment
Notes	Emailed study authors to request mean and SD for HDRS, BI, and NIHSS score at 8 weeks and 12 months post-treatment for all 3 groups 23/10/2018 (reply received - mean SD and remission for HDRS and BI for all treatment groups sent by trial author 06/11/2018)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Quote:** "the algorithm was based on an imbalance score which measured, for a given set of random assignments, how far out of balance the study would be within strata for each factor and then summed over factors. When a new subject was available for randomization, we computed what the imbalance score would be if this subject were assigned to usual care, or to telephone intervention, or to in-person intervention. Then randomization was done to allocate two intervention participants to each control with each new assignment having a higher probability of less imbalance. The schema did not require equal numbers in each arm" (p. 4).
Allocation concealment (selection bias)	Unclear risk	**Quote:** "the study statistician generated the algorithm, which was securely stored and accessible only by the statistician and research nurse supervisor" (p. 5). **Comment:** method of allocation concealment not reported

Kirkness 2017b *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	**Quote:** "participants were asked not to reveal their study arm to the outcome assessors" (p. 5). **Comment:** blinding of personnel not reported
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Quote:** "….masking outcome assessors to the participant's randomization status. Participants were asked not to reveal their study arm to the outcome assessors. We did not detect any breaches in masking" (p. 5).
Incomplete outcome data (attrition bias) All outcomes	High risk	**Comment:** per-protocol analysis reported only; 9 participants not included in the analysis
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline demographic characteristics between groups

Kong 2007

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** fluoxetine (SSRI) 20 mg/d **Control arm:** placebo
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** ischaemic stroke **Method of stroke diagnosis:** diagnosis met the diagnostic criteria of various cerebrovascular diseases formulated at the 4th National Cerebrovascular Disease Conference and confirmed as stroke by skull CT or MRI. **Time since stroke:** < 7 days **Inclusion criteria:** (1) all patients were < 7 days from their first-ever stroke; (2) able to understand and carry out verbal instructions **Exclusion criteria:** (1) diagnosis of major depression at evaluation or at any earlier period during the index episode; (2) active suicidal ideation; (3) bipolar disorder, schizophrenia, or other psychotic disorder; (4) currently taking antidepressants; (5) MMSE score ≤ 23; (6) medical contraindication to fluoxetine; (7) history of allergy to fluoxetine; (8) history of substance abuse; (9) obvious liver and renal function deficit **Depression criteria:** 24-item HDRS score ≥ 8 and ≤ 20 **Total number randomised in this trial:** 90 **Number randomised to treatment group:** 48 (60% men; mean age 64 years, SD 7; 62% ischaemic; NIHSS 14.6, SD 5.8) **Number randomised to control group:** 42 (58% men; mean age 62 years, SD 7; 58% ischaemic; NIHSS 14.3, SD 6.1)

Kong 2007 *(Continued)*

	Total number included in final analysis: 73 **Number included in treatment group for final analysis:** 37 **Number included in control group for final analysis:** 36
Interventions	**Treatment:** fluoxetine (SSRI) 20 mg/d; no further details given **Control:** placebo (vitamin C). Dose not specified but capsules described as identical to treatment capsules **Duration:** 8 weeks **Follow-up:** none
Outcomes	**Primary outcomes** • Depression measured using 24-item HDRS **Secondary outcomes** • Functional capacity measured using BI • Impairment measured using NIHSS
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Quote:** "treatment allocation was based on a computer-generated list of treatment numbers" (p. 163).
Allocation concealment (selection bias)	Low risk	**Quote:** "….were given as a single morning dose in identical capsules in coded boxes" (p. 163)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Quote:** "the patient, relatives and the researchers were not aware of the drug being given" (p. 163). **Comment:** blinding of those who delivered the intervention not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** blinding of outcome assessors not reported
Incomplete outcome data (attrition bias) All outcomes	High risk	**Quote:** "seventy-three of the 90 randomized patients accomplished the trial. In the treatment group, 11 patients dropped out, including insufficient clinical response (n = 4), somatic side effects (n = 2), intervening medical illness (n = 1), hypomania (n = 3), and other reasons (n = 2). In the placebo group, 6 patients exited, including insufficient clinical response (n = 2), somatic side effects (n = 1) and other reasons (n = 3)". **Comment:** per-protocol analysis reported only
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline demographic characteristics between groups

Lai 2006a

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** paroxetine (SSRI) **Control arm:** placebo
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** acute stroke **Method of stroke diagnosis:** diagnosis via CT **Time since stroke:** unclear **Inclusion criteria:** not reported **Exclusion criteria:** not reported **Depression criteria:** HDRS score > 6 **Total number randomised in this trial:** 80 **Number included in treatment group:** 40 (54% men in total, mean age 60 years, SD 14) **Number included in control group:** 40 (54% men in total, mean age 60 years, SD 14) **Total number included in final analysis:** 80 **Number included in treatment group for final analysis:** 40 **Number included in control group for final analysis:** 40
Interventions	**Treatment:** paroxetine (SSRI) 20 mg/d **Control:** placebo **Duration:** 2 months **Follow-up:** not reported
Outcomes	**Primary outcomes** • Depression measured using HDRS and ZDS • Impairment measured using SSS **Secondary outcomes** • Death • Adverse events
Notes	

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	**Comment:** method of sequence generation not reported

Lai 2006a *(Continued)*

Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** blinding of participants and personnel not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** blinding of outcome assessment not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** ITT analysis reported (complete follow-up of all randomised participants)
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Unclear risk	**Comment:** baseline demographic information not reported

Li 2008

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** fluoxetine (SSRI) **Control arm:** matched placebo
Participants	**Geographical location:** China. **Setting**: unclear **Stroke criteria:** ischaemic or haemorrhagic stroke **Method of stroke diagnosis:** each patient evaluated for inclusion by a neuro-psychiatrist. Presence of recent < 6 weeks ischaemic or haemorrhagic stroke documented by CT or MRI before the study **Time since stroke:** 4.78 days **Inclusion criteria:** (1) lack of treatment with antidepressants during the 2 weeks before this study; (2) only single ischaemic and haemorrhagic stroke **Exclusion criteria:** (1) cognitive impairment (MMSE < 23); (2) severe aphasia; (3) history of alcoholism, abnormal thyroid, or epilepsy **Depression criteria:** HDRS score > 20 **Total number randomised in this trial:** 90 **Number randomised to treatment group:** 60 (47% men; mean age 68.5 years, SD 4.1; mean time since stroke 4.83 weeks, SD 0.57) **Number randomised to control group:** 30 (57% men; mean age 67.8 years, SD 3.9; mean time since stroke 4.82, SD 0.67) **Total number included in final analysis:** 86

Li 2008 *(Continued)*

	Number included in treatment group for final analysis: 58 **Number included in control group for final analysis:** 28
Interventions	**Treatment:** fluoxetine (SSRI) 20 to 40 mg depending on tolerability together with placebo to make up 6 tablets **Control:** matched placebo (composition not specified) 18 grams in 6 tablets twice daily **Duration:** 8 weeks **Follow-up:** none
Outcomes	**Primary outcomes** • Depression measured using HDRS (mean HDRS score at end of trial) • Percentage of responders (measure of clinical response defined as > 50% reduction in HDRS score compared with baseline score) **Secondary outcomes** • Depression measured using HDRS (at 4 weeks)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Quote:** "a computer-generated randomisation was carried out…" (p. 843).
Allocation concealment (selection bias)	Low risk	**Quote:** "both placebo and herbal tablets were prepared to be identical to the fluoxetine…" (p. 842).
Blinding of participants and personnel (performance bias) All outcomes	High risk	**Quote:** "neither the examiners involved nor the patients were aware of the type of the administered medications" (p. 842). **Comment:** physician initiated and moderated treatment dose based on patient's tolerability and response. It is likely that the physician was not blinded.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Quote:** "neither the examiners involved nor the patients were aware of the type of the administered medications" (p. 842).
Incomplete outcome data (attrition bias) All outcomes	High risk	**Comment:** 2/60 patients in the fluoxetine group withdrew from the study due to recurrent stroke; 2/30 withdrew due to increased depressive symptoms within 4 weeks of the start of the trial. Per-protocol analysis reported only
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline demographic characteristics between groups

Li 2009

Study characteristics

Li 2009 *(Continued)*

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** psychological nursing + usual care **Control arm:** usual care
Participants	**Geographical location:** China **Setting**: inpatient **Stroke criteria:** ischaemic or haemorrhagic stroke **Method of stroke diagnosis:** the diagnostic criteria for stroke developed by the Fourth National Cerebrovascular Disease Academic Conference Standard and cerebral CT or MRI shows evidence of cerebral haemorrhage or cerebral ischaemia. **Time since stroke:** not reported **Inclusion criteria:** (1) first-ever stroke; (2) only single ischaemic and haemorrhagic stroke; (3) no aphasia **Exclusion criteria:** (1) previous history or family history of mental illness; (2) mental retardation, epilepsy and a history of brain trauma or other encephalopathy and other serious physical diseases **Depression criteria:** self-evaluation on admission Scale (SDS) rating ≥ 30 points; HDRS rating score ≥ 8 points; in line with the CCMD-II **Total number randomised in this trial:** 114 **Number randomised to treatment group:** 58 (75.8% men and mean age 58 SD 9.3 years) **Number randomised to control group:** 56 (67.8% men and mean age 59.3 SD 8.5 years) **Total number included in final analysis:** 114 **Number included in treatment group for final analysis:** 58 **Number included in control group for final analysis:** 56
Interventions	**Treatment:** psychological intervention, 3 times a week, 30 minutes each time, for 6 weeks + usual care **Administered by:** not reported **Supervision:** not reported **Intervention fidelity:** not reported **Control:** usual care **Duration:** 6 weeks **Follow-up:** none
Outcomes	**Primary outcomes** • Depression measured using HDRS-17 • Neurological function measured using Chinese Stroke Scale (CNS)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Li 2009 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	**Comment:** Method of sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	**Comment:** Method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** Information on blinding of participants and personnel was not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** Information on blinding of outcome assessment not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** All 80 patients were included in the final analysis.
Selective reporting (reporting bias)	Unclear risk	**Comment:** All prespecified outcomes reported; no trial protocol or registry record available to compare with the publication
Other bias	Low risk	**Comment:** There was no statistically significant difference between the groups in baseline characteristics.

Li 2013

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** rTMS + mirtazapine (atypical tetracyclic) + stroke usual care **Control arm:** mirtazapine + stroke usual care
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria**: not reported **Method of stroke diagnosis:** clinical diagnosis plus confirmation by imaging that a relevant lesion needed to be visible **Time since stroke:** not reported **Inclusion criteria:** (1) aged over 65 years; (2) patient or guardian can sign informed consent; (3) meeting diagnostic criteria of the CCMD-3 for depression **Exclusion criteria:** (1) comorbid with aphasia, comprehension, or expression impairment, or severe mental retardation; (2) with severe cardiac, hepatic, or renal disease, or with epilepsy; (3) intracranial metal implant, possible history of allergy to mirtazapine **Depression criteria:** meeting diagnostic criteria of the CCMD-3 for depression and 17-item HDRS score ≥ 17 **Total number randomised in this trial:** 60

Li 2013 *(Continued)*

	Number included in treatment group: 30 (56% men; mean age 64.8, SD 5.4) **Number included in control group:** 30 (53% men; mean age 65.2, SD 4.8) **Total number included in final analysis:** 60 **Number included in treatment group for final analysis:** 30 **Number included in control group for final analysis:** 30
Interventions	**Treatment:** rTMS + mirtazapine (starting from 15 mg/d at night, if tolerable, increase to 30 mg/d in 2 to 3 days) + stroke usual care (medications + rehabilitation). Frequency: 1 Hz, intensity: 90% motor threshold, each treatment lasting for 20 minutes, 5 treatments a week, location: right DLPFC **Control:** mirtazapine + stroke usual care **Duration:** 4 weeks **Follow-up:** none
Outcomes	**Primary outcomes** • Depression measured using HDRS **Secondary outcomes** • Impairment measured using NIHSS
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Comment:** method of sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** information about blinding of participants and personnel not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** information about blinding of outcome assessors not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** ITT analysis reported; no missing data
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Low risk	**Comment:** no significant differences in baseline demographics between groups

Li 2014

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** rTMS + fluoxetine (SSRI) + stroke usual care **Control arm:** fluoxetine (SSRI) + stroke usual care
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** ischaemic and haemorrhagic stroke **Method of stroke diagnosis:** clinical diagnosis plus confirmation by imaging that a relevant lesion needed to be visible **Time since stroke:** not reported **Inclusion criteria:** (1) meeting diagnostic criteria of the CCMD-3 for depression; (2) 17-item HDRS score ≥ 18 **Exclusion criteria:** not reported **Depression criteria:** meeting diagnostic criteria of the CCMD-3 for depression and for 17-item HDRS score ≥ 18 **Total number randomised in this trial:** 93 **Number randomised to treatment group:** 47 (49% men; mean age 57.6, SD 6.8) **Number randomised to control group:** 46 (52% men; mean age 56.5, SD 6.7) **Total number included in final analysis:** 93 **Number included in treatment group for final analysis:** 47 **Number included in control group for final analysis:** 46
Interventions	**Treatment:** rTMS + fluoxetine (SSRI) 20 mg/d + stroke usual care (medications + rehabilitation) Frequency: 10 Hz, intensity: 80% motor threshold, with each series lasting 4 seconds with an interval of 56 seconds, successive 20 series per day, 5 treatments a week, location: left DLPFC **Control:** fluoxetine (SSRI) + stroke usual care **Duration:** 4 weeks **Follow-up:** none
Outcomes	**Primary outcomes** • Depression measured using HDRS • Disability measured using MBI
Notes	

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

Li 2014 *(Continued)*

Random sequence generation (selection bias)	Low risk	**Comment:** random number table used for sequence generation
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** information about blinding of participants and personnel not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** information about blinding of outcome assessors not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** ITT analysis reported; no missing data
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline demographics between groups

Li 2019a

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Treatment arm:** routine nursing intervention + early psychological nursing intervention **Control arm:** routine nursing intervention
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** ischaemic and haemorrhagic stroke **Method of stroke diagnosis:** confirmed by both brain CT and MRI and in line with stroke diagnostic criteria **Time since stroke:** 1-5 months **Depression criteria:** none **Inclusion criteria:** (1) stroke diagnosed by both brain CT and MRI; (2) stroke in line with the diagnostic criteria for stroke and (3) informed consent **Exclusion criteria:** (1) severe primary disease; (2) previous history of mental illness and; (3) unconsciousness **Total number randomised in this trial:** 60 **Number randomised to treatment group:** 30 (46% men and mean age 63 SD 10 years)

Li 2019a *(Continued)*

	Number randomised to control group: 30 (50% men and 64 SD 10 years) **Total number included in final analysis:** 60 **Number included in treatment group for final analysis:** 30 **Number included in control group for final analysis:** 30
Interventions	**Treatment:** routine nursing intervention + early psychological nursing intervention **Administered by:** not reported **Supervision:** not reported **Intervention fidelity:** not reported **Control:** routine nursing intervention **Treatment duration:** unclear **Follow-up:** unclear
Outcomes	**Primary outcomes:** • Depression measured using HDRS-17 • Neurological function measured using NIHSS • Activites of daily living measured using Barthel Index • Quality of life measured using WHOQoL-BREF
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Comment:** Method of sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	**Comment:** Method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** Information on blinding of participants and personnel was not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** Information on blinding of outcome assessment not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** All 60 patients were included in the final analysis.
Selective reporting (reporting bias)	Unclear risk	**Comment:** All prespecified outcomes reported; no trial protocol or registry record available to compare with the publication
Other bias	Low risk	**Quote:** "In general data comparison, the differences were not statistically significant (P > 0.05)." p. 2102

Liang 2015

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** psychological nursing care + usual care **Control arm:** usual care
Participants	**Geographical location:** China **Setting:** unclear **Stroke criteria:** not reported **Method of stroke diagnosis:** not reported **Time since stroke:** unclear **Depression criteria:** unclear **Inclusion criteria:** unclear **Exclusion criteria:** unclear **Total number randomised in this trial:** 89 **Number randomised to treatment group:** 45 **Number randomised to control group:** 44 **Total number included in final analysis:** 89 **Number included in treatment group for final analysis:** 45 **Number included in control group for final analysis:** 44
Interventions	**Treatment:** psychological nursing care + usual care **Control:** usual care **Duration:** unclear **Follow-up:** unclear
Outcomes	**Primary outcomes** • Depression measured using 24-item HDRS • Quality of life measured using WHOQoL-BREF
Notes	

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	**Comment:** method of sequence generation not reported

Liang 2015 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** all participants were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes were reported; no trial protocol available to compare with the publication
Other bias	Unclear risk	**Comment:** not reported

Lincoln 2003

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 3 **Experimental arm:** cognitive-behavioural therapy **Control arm 1:** attention control **Control arm 2:** usual care
Participants	**Geographical location:** UK **Setting:** outpatient **Stroke criteria:** all subtypes **Method of stroke diagnosis:** diagnosis via clinical signs and symptoms and CT **Time since stroke:** 1 to 6 months **Inclusion criteria:** not reported **Exclusion criteria:** (1) blindness; (2) deafness; (3) participant did not speak English; (4) dementia documented in medical records; (5) treated for depression in previous 5 years; (6) lived outside specified locality; (7) participant could not complete questionnaire unaided **Depression criteria:** psychiatric interview (SCAN), BDI score > 10, WDI score > 18 **Total number randomised in this trial:** 123 **Number randomised to treatment group:** 39 (51% men, mean age 67 years, SD 13) **Number randomised to attention control and usual care group^:** 84 (51% men, mean age 66 years, SD 14) **Total number included in final analysis:** 111

Lincoln 2003 *(Continued)*

	Number included in treatment group for final analysis: 34 **Number included in control group for final analysis:** 77
Interventions	**Treatment:** cognitive-behavioural therapy (techniques included education, graded task assignment, activity scheduling, and identification and modification of unhelpful thoughts and beliefs. Interventions were tailored to meet the individual's needs. Frequency and duration of sessions were 10 × 1 hour sessions over 13 weeks. **Administered by:** trained therapist **Supervision:** therapist received training and clinical supervision by experienced cognitive therapist **Intervention fidelity:** not reported **Attention control:** no formal therapeutic intervention; conversation focused on day-to-day occurrences and discussion regarding physical effects of stroke and life changes (10 × 1-hour visits over 13 weeks) **Control:** usual care (no contact) **Duration:** 13 weeks **Follow-up:** 3 months
Outcomes	**Primary outcomes** • Depression measured using BDI, WDI, GHQ 28 • Activities of daily living measured using EADL scale • Leaving the study early • Death
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Quote:** "a computer generated random number sequence was prepared in advance and sealed in opaque, consecutively numbered envelopes by an independent researcher" (p. 112).
Allocation concealment (selection bias)	High risk	**Quote:** "….prepared in advance and sealed in opaque, consecutively numbered envelopes by an independent researcher" (p. 112). **Comment:** this method of allocation concealment can be tampered with.
Blinding of participants and personnel (performance bias) All outcomes	High risk	**Comment:** due to the nature of the intervention, it was not possible to mask participants, CBT therapists, or researchers to treatment allocation.
Blinding of outcome assessment (detection bias) All outcomes	High risk	**Quote:** "outcome assessments were administered by an assistant psychologist, who was blind to the group allocation, 3 and 6 months after randomization. The primary outcome measures were the BDI and WDI, which were sent for patients to complete prior to a visit" (p. 112).
Incomplete outcome data (attrition bias) All outcomes	High risk	**Comment:** per-protocol analysis reported only; 5/121 (4.1%) not included in analyses

Lincoln 2003 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes were reported; no trial protocol available to compare with the publication
Other bias	High risk	**Comment:** significantly more participants in the treatment group with an ICD-10 diagnosis of depression

Lipsey 1984

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** nortriptyline (TCA) **Control arm:** matched placebo
Participants	**Geographical location:** USA **Setting:** mixed **Stroke criteria:** ischaemic stroke and primary intracerebral haemorrhage **Method of stroke diagnosis:** diagnosis via clinical signs and CT (100%) **Time since stroke:** 262 ± 437 days **Inclusion criteria:** (1) included outpatients who requested treatment for post-stroke depressive disorder **Exclusion criteria:** (1) current treatment for depression; (2) severe comprehension deficit; (3) medical contraindication to nortriptyline **Depression criteria:** psychiatric interview (PSE, DSM-III) **Total number randomised in this trial:** 39 **Number randomised to treatment group:** 17 **Number randomised to control group:** 22 **Total number included in final analysis:** 34 **Number included in treatment group for final analysis:** 14 (64% men, mean age 62 years, SD 9) **Number included in control group for final analysis:** 20 (65% men, mean age 60 years, SD 12)
Interventions	**Treatment:** nortriptyline (TCA) 20 to 100 mg daily; 2 treatment regimens combined; dose escalation over treatment period to 100 mg **Control:** matched placebo **Duration:** 4 to 6 weeks **Follow-up:** not reported
Outcomes	**Primary outcomes** • Depression (proportion no longer meeting entry criteria (DSM-III), measured using HDRS and ZDS)^† **Secondary outcomes** • Death

Lipsey 1984 *(Continued)*

- Adverse events

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Quote:** "all patients were randomly assigned to nortriptyline or placebo treatment by means of a random number table" (p. 297).
Allocation concealment (selection bias)	Low risk	**Quote:** "nortriptyline and placebo were supplied in identical capsules" (p. 297).
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Quote:** "patients and their families, clinical examiners and nursing staff were unaware of the drug treatment being given" (p. 297).
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Quote:** "patients and their families, clinical examiners and nursing staff were unaware of the drug treatment being given" (p. 297).
Incomplete outcome data (attrition bias) All outcomes	High risk	**Comment:** per-protocol analysis reported; 5/39 (13%) not included in analyses
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline demographic characteristics between groups

Liu 2015

Study characteristics

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** rTMS + citalopram (SSRI) + short-term benzodiazepines (BZDs) if needed for insomnia **Control arm:** citalopram (SSRI) + short-term BZDs if needed for insomnia
Participants	**Geographical location:** China **Setting:** mixed **Stroke criteria:** ischaemic stroke **Method of stroke diagnosis:** clinical diagnosis plus confirmation by imaging that a relevant lesion needed to be visible **Time since stroke:** not reported **Inclusion criteria:** (1) can sign informed consent; (2) 17-item HDRS score ≥ 17

Liu 2015 *(Continued)*

	Exclusion criteria: (1) drug dependence history in recent 6 months; (2) bleeding tendency, severe hepatic or renal impairment, or other physical illness; (3) epilepsy history, head injury with consciousness loss history, history of cranial operation, metal implant or electronic devices in the body **Depression criteria:** 17-item HDRS score ≥ 17 **Total number randomised in this trial:** 60 **Number included in treatment group:** 30 (56% men; mean age 64.2, SD 3.1) **Number included in control group:** 30 (53% men; mean age 65.1, SD 3.5) **Total number included in final analysis:** 60 **Number included in treatment group for final analysis:** 30 **Number included in control group for final analysis:** 30
Interventions	**Treatment:** rTMS + citalopram (SSRI), starting from 10 mg/d in the morning, may titrate up to 20 mg/d according to the patient's condition + short-term BZDs (only for difficulty in falling asleep; combined duration: less than 1 week) Frequency: 10 Hz, intensity: 80% resting motor threshold, 1 stimulation lasts 5 seconds and stops for 20 seconds, total treatment time: 20 minutes, 1 treatment per day, 5 treatments a week, total 4 weeks, location: left DLPFC **Control:** citalopram (SSRI) + short-term BZDs **Duration:** 4 weeks **Follow-up:** none
Outcomes	**Primary outcome** • Depression measured using 17-item HDRS **Secondary outcome** • Impairment measured using NIHSS
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Comment:** method of sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** information about blinding of participants and personnel not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** information about blinding of outcome assessors not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** ITT analysis reported; no missing data

Liu 2015 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline demographics between groups

Liu 2020

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** rTMS + paroxetine (SSRI) **Control arm:** paroxetine (SSRI)
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** unclear **Method of stroke diagnosis:** unclear **Time since stroke:** not reported **Inclusion criteria:** (1) diagnosed with PSD according to the third edition of the Chinese Diagnostic Criteria for Mental Disorders (CCMD-3); (2) with complete information and able to cooperate with treatment; (3) not received treatment in the past month; (4) < 80 years old **Exclusion criteria:** (1) with contraindications to experimental drugs; (2) incomplete information; (3) family history and medical history of mental disorders; (3) with major depression, severe movement disorder and confusion **Depression criteria:** meeting diagnostic criteria of ICD-10 for depression and 24-item HDRS score ≥ 20 **Total number randomised in this trial:** 74 **Number randomised to treatment group:** 37 (62% men; mean age 56, SD 5.3) **Number randomised to control group:** 37 (43% men; mean age 55.2, SD 6.2) **Total number included in final analysis:** 74 **Number included in treatment group for final analysis:** 37 **Number included in control group for final analysis:** 37
Interventions	**Treatment:** rTMS (delivered 20 minutes each time, 5 times each week for 2 months + paroxetine (20 mg once daily) **Control:** paroxetine (20 mg once daily) **Duration:** 2 months **Follow-up:** none
Outcomes	**Primary outcomes** • Depression measured using Self-rating Depression Scale

Liu 2020 *(Continued)*

- Serum-related indicators

Secondary outcomes

- Quality of life measured using SF-36
- Adverse events

Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Comment:** method of sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** information about blinding of participants and personnel not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** information about blinding of outcome assessors not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** all participants were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Low risk	**Quote:** "There was no significant difference in general information between the two groups (P > 0.05)." p. 7882

Lu 2016

Study characteristics

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** rTMS + duloxetine (SNRI) + ischaemic stroke routine care **Control arm:** duloxetine (SNRI) + ischaemic stroke routine care
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** ischaemic stroke **Method of stroke diagnosis:** clinical diagnosis plus confirmation by imaging that a relevant lesion needed to be visible

Lu 2016 *(Continued)*

	Time since stroke: not reported **Inclusion criteria:** (1) clear consciousness; (2) 24-item HDRS score ≥ 20; (3) meeting diagnostic criteria of ICD-10 for depression **Exclusion criteria:** (1) cognitive impairment; (2) no language impairment; (3) severe cardiac or pulmonary disease, hepatic or renal impairment; (4) bleeding tendency **Depression criteria:** meeting diagnostic criteria of ICD-10 for depression and 24-item HDRS score ≥ 20 **Total number randomised in this trial:** 80 **Number randomised to treatment group:** 40 (57.5% men; mean age 65.3, SD 8.8) **Number randomised to control group:** 40 (52.5% men; mean age 63.8, SD 8.4) **Total number included in final analysis:** 73 **Number included in treatment group for final analysis:** 36 **Number included in control group for final analysis:** 37
Interventions	**Treatment:** rTMS + duloxetine (SNRI) 60 mg/d + ischaemic stroke routine care. Frequency: 3.0 Hz, intensity: 110% resting motor threshold, 1 treatment lasts 5 minutes, 5 treatments a week, location: left temporoparietal area **Control:** duloxetine (SNRI) + ischaemic stroke routine care **Duration:** 4 weeks **Follow-up:** none
Outcomes	**Primary outcomes** • Depression measured using MADRS • Depression measured using 24-item HDRS • Dependence measured using SDS
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Comment:** random numbers table used for sequence generation
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** information about blinding of participants and personnel not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** information about blinding of outcome assessors not reported
Incomplete outcome data (attrition bias)	High risk	**Comment:** per-protocol analysis reported only; 7/80 not included in the analysis

Lu 2016 *(Continued)*
All outcomes

Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline demographics between groups

Lu 2018

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Treatment arm:** routine nursing intervention + psychological intervention **Control arm:** routine nursing intervention
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** ischaemic and haemorrhagic stroke **Method of stroke diagnosis:** meet the diagnostic criteria of the Fourth National Cerebrovascular Academic Conference Criteria **Time since stroke:** not reported **Depression criteria:** meet the CCMD-III on the diagnostic criteria of mental disorders caused by cerebrovascular diseases and HDRS-17 score ≥ 7 points **Inclusion criteria:** (1) meet the diagnostic criteria of the Fourth National Cerebrovascular Academic Conference Criteria; (2) meet the CCMD-III on the diagnostic criteria of mental disorders caused by cerebrovascular diseases; (3) HDRS-17 score ≥ 7 points; (4) patients and their families were informed of this study and sign the consent form **Exclusion criteria:** (1) those with aphasia, under a coma or have cognitive impairment; (2) those who have a history of depression; (3) serious diseases such as heart, liver and kidney disease **Total number randomised in this trial:** 60 **Number randomised to treatment group:** 30 (60% men and mean age 60.4 SD 2.52 years) **Number randomised to control group:** 30 (63% men and mean age 60.27 SD 2.43 years) **Total number included in final analysis:** 60 **Number included in treatment group for final analysis:** 30 **Number included in control group for final analysis:** 30
Interventions	**Treatment:** routine nursing intervention + early psychological nursing intervention **Administered by:** not reported **Supervision:** not reported **Intervention fidelity:** not reported **Control:** routine nursing intervention

Lu 2018 *(Continued)*

	Treatment duration: unclear **Follow-up:** unclear
Outcomes	**Primary outcomes:** • Depression measured using HDRS-17 • Motor function measured using Fugl-Meyer Assessment • Activities of daily living measured using Barthel Index
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Comment:** Method of sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	**Comment:** Method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** Information on blinding of participants and personnel was not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** Information on blinding of outcome assessment not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** All 60 patients were included in the final analysis.
Selective reporting (reporting bias)	Unclear risk	**Comment:** All prespecified outcomes reported; no trial protocol or registry record available to compare with the publication
Other bias	Low risk	**Quote:** "There is no statistically significant difference in the above-mentioned data such as age and gender between the two groups (P > 0.05)." p. 2066

Lu 2020

Study characteristics

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** percutaneous mastoid electrical stimulation (PMES) + sertraline (SSRI) **Control arm:** sham PMES + sertraline (SSRI)
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** first-ever ischaemic stroke within 14 days

Lu 2020 *(Continued)*

Method of stroke diagnosis: ischaemic stroke was confirmed by brain CT or MRI

Time since stroke: not reported

Inclusion criteria: (1) admission for first-ever ischaemic stroke within 14 days; (2) no neurological or psychiatric disease before stroke; (3) no aphasia; (4) no drug abuse; (5) no severe hearing deficit; (6) right-handed; (7) no serious dysarthria; (8) able to cooperate; (9) no active malignancies and; (10) capable of appropriate communication

Exclusion criteria: not reported

Depression criteria: diagnosis of clinical depression that was verified by a diagnostic interview using DSM-V criteria and 30-item GDS ≥ 11

Total number randomised in this trial: 288

Number randomised to treatment group: 144

Number randomised to control group: 144

Total number included in final analysis: 258

Number included in treatment group for final analysis: 125 (56% men; mean age 65.0, SD 8.82)

Number included in control group for final analysis: 133 (48.7% men; mean age 66.1, SD 8.37)

Interventions	**Treatment:** PMES + sertraline (SSRI) 50 mg/d. The dose of sertraline was adjusted starting from day 7 to 100 mg/day (maximum dose: 400 mg/day). Frequency: 1.8 kHz, current: 10 mA, 1 treatment lasts 45 minutes daily for 6 months, location: mastoid area behind the ear **Control:** sham PMES + sertraline (SSRI) **Duration:** 6 months **Follow-up:** none
Outcomes	**Primary outcomes** • Treatment response (≥ 50% reduction in 24-item HDRS score) • Depression remission (24-item HDRS score ≤ 9) **Secondary outcomes** • Cognitive function measured using Montreal Cognitive Assessment Scale (MoCA < 26)
Notes	The study was funded by the Health and Family Planning Commission of Chengdu (2015009).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Quote:** "a computer-generated block randomization list was prepared by the Clinical Research Unit of The Second People's Hospital of Chengdu" p. 3.
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Quote:** "the patients, investigators and all study personnel were blinded to the treatment allocation. The PMES and sham stimulators had the same external appearances, user manuals and electrodes. They could not be distinguished by their external appearance. We took the following measures to guarantee double-blinding: enrolled patients were not acquainted with each other, there was no physical contact or communication (such as sensory perception)

Lu 2020 *(Continued)*

		between patients during visits, and all of the patients would be told when enrolled that it was not possible to accurately judge whether they were receiving true or sham stimulation based only on the surface sensations" p. 4.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Quote:** "the patients, investigators and all study personnel were blinded to the treatment allocation" p. 4.
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** a total of 288 patients were enrolled in this study (sham group, N = 144; PMES group, N = 144). 12 were lost to follow-up, 10 had a recurrent stroke and 8 died. A total of 258 patients were finally analysed (sham group, N = 133; PMES group, N = 125).
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol or registry record available to compare the publication
Other bias	Low risk	Quote: "there were also no significant group differences in the baseline HDRS and MoCA scores (P > 0.05)" p. 4.

Meng 2015

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** rTMS **Control arm:** sham rTMS
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** ischaemic stroke **Method of stroke diagnosis:** brain CT or MRI confirmed cerebral infarct **Time since stroke:** not reported **Inclusion criteria:** (1) normal expression ability; (2) first stroke; (3) clear consciousness, can sign informed consent, right-handedness; (4) HDRS score ≥ 8 **Exclusion criteria:** (1) history of psychiatric illness; (2) cerebral haemorrhage, history of epilepsy, contraindication for TMS, not finishing treatment course **Depression criteria:** HDRS score ≥ 8 **Total number randomised in this trial:** 108 **Number randomised to treatment group:** 54 (62.9% men; mean age 64.2, SD 4.2) **Number randomised to control group:** 54 (64.8% men; mean age 65.8, SD 4.0) **Total number included in final analysis:** 108 **Number included in treatment group for final analysis:** 54 **Number included in control group for final analysis:** 54

Meng 2015 *(Continued)*

Interventions	**Treatment:** rTMS + usual care (which includes antidepressants if already on them, no change of antidepressant dosage or medication during treatment). Frequency: 10 Hz, intensity: 80% motor threshold, 1 stimulation lasts 4.9 seconds and stops for 20 seconds, 86 cycles a day, total 1960 impulses a day, location: left DLPFC **Control:** sham rTMS, keeping coils at 90-degree angles with the scalp + usual care (which includes antidepressants if already on them, no change in antidepressant dosage or medication during treatment) **Duration:** 2 weeks **Follow-up:** 4 weeks
Outcomes	**Primary outcomes** • Depression measured using HDRS • Disability measured using BI • Impairment measured using CSS
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Comment:** random numbers table used for sequence generation
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** information about blinding of participants and personnel not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** information about blinding of outcome assessors not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** ITT analysis reported; no missing data
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Unclear risk	**Comment:** significant differences in age between groups

Mitchell 2002

Study characteristics

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** cognitive-behavioural therapy plus problem-solving

Mitchell 2002 *(Continued)*

	Control arm: written information from the Stroke Association including information about depression
Participants	**Geographical location:** USA **Setting:** outpatient **Stroke criteria:** ischaemic stroke **Method of stroke diagnosis:** verified by CT or MRI **Time since stroke:** within 4 months **Inclusion criteria:** (1) stroke within 4 months; (2) 21 years of age and older **Exclusion criteria:** (1) subarachnoid or intracranial haemorrhagic stroke; (2) global aphasia; (3) reduced level of consciousness (GCS < 15) **Depression criteria:** diagnosis of depression validated by the Diagnostic Interview and Structured Hamilton among those who scored > 10 on the GDS **Total number randomised in this trial:** 101 **Number randomised to treatment group:** 48 (60% men, mean age 57 years, age range 25 to 88 years) **Number randomised to control group:** 53 (60% men, mean age 57 years, age range 29 to 88 years) **Total number included in final analysis:** 92 **Number included in treatment group for final analysis:** 44 **Number included in control group for final analysis:** 48
Interventions	**Treatment:** cognitive-behavioural therapy plus problem-solving. Sessions were focused on the individual; however, a participant could opt to have a family member or an informal caregiver join these sessions. The brief psychosocial–behavioural intervention was adapted from the "Seattle Protocols" shown to reduce disability associated with depression in Alzheimer disease. All participants received written information from the Stroke Association including information about depression. Participants could receive antidepressant medication at the discretion of their usual care provider. Frequency and duration: 9 sessions over 8 weeks **Administered by:** therapists **Supervision:** all therapists met monthly with the clinical psychologist who developed the intervention **Intervention fidelity:** sessions were audio-taped, and session content was compared to the content specified for each visit **Control:** all participants received written information from the Stroke Association including information about depression. Participants could receive antidepressant medication at the discretion of their usual care provider. **Duration:** 8 weeks **Follow-up:** 12 months
Outcomes	**Primary outcomes** • Depression measured using HDRS • Adverse event data systematically collected included worsening of depression, suicidal ideation, and suicide attempts.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Mitchell 2002 *(Continued)*

Random sequence generation (selection bias)	Low risk	**Quote:** "randomization status was generated by a computerized adaptive randomisation procedure…" (p. 3075).
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	**Comment:** due to the nature of the trial, it was not possible to mask participants, clinicians, and researchers to treatment allocation.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Quote:** "all outcome assessors were masked to the participant's randomization status at each data collection point. We did not detect any breaches in masking" (p. 3075).
Incomplete outcome data (attrition bias) All outcomes	High risk	**Comment:** 9/101 participants were not included in the analysis (per-protocol analysis reported only).
Selective reporting (reporting bias)	High risk	**Comment:** caregiving burden and benefit (Sense of Competence Scale) outcome in the protocol not reported in the publication
Other bias	Low risk	**Comment:** no differences in baseline demographic characteristics between groups

Murray 2002

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** sertraline (SSRI) **Control arm:** matched placebo
Participants	**Geographical location:** Sweden **Setting:** mixed **Stroke criteria:** all subtypes **Method of stroke diagnosis:** diagnosis via clinical signs and CT (100%) **Time since stroke:** 12 months **Inclusion criteria:** (1) > 17 years of age; (2) stroke within previous 12 months **Exclusion criteria:** (1) under 18 years of age; (2) severely impaired communication; (3) apparent difficulties in adhering to study protocol; (4) acute myocardial infarction; (5) psychiatric illness other than depression; (6) significant risk of suicide; (7) antidepressants during the month before randomisation; (8) current use of psychotropic medication or opiate analgesic drugs; (9) < 20% reduction in MADRS score at 6 weeks **Depression criteria:** psychiatric interview (DSM-IV, major and minor) and MADRS > 9 **Total number randomised in this trial:** 123 **Number randomised to treatment group:** 62 (52% men, mean age 71 years, SD 10)

Murray 2002 *(Continued)*

	Number randomised to control group: 61 (44% men, mean age 71 years, SD 10) **Total number included in final analysis:** 123 **Number included in treatment group for final analysis:** 62 **Number included in control group for final analysis:** 61
Interventions	**Treatment:** sertraline (SSRI) 50 mg daily; possible dose escalation to 100 mg after 4 weeks **Control:** matched placebo **Duration:** 26 weeks **Follow-up:** not reported
Outcomes	**Primary outcomes** • Depression measured using MADRS (change in scores from baseline to end of treatment on MADRS) **Secondary outcomes** • Death • Adverse events
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Quote:** "a centralised randomization procedure was applied. The Central Pharmacy in Stockholm kept the randomization list" (p. 709).
Allocation concealment (selection bias)	Low risk	**Quote:** "each centre pharmacy received a consecutive series of presealed treatment packages" (p. 709).
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Quote:** "patients received double-blind identical capsules of either sertraline 50 mg or placebo, once a day as a starting dose" (p. 709).
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Comment:** double-blind placebo-controlled trial, which suggests that outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	**Quote:** "efficacy analyses were based on the intention to treat (ITT), last observation carried forward population…" (p. 710). "… response and remission rates were calculated for those patients who completed the study" (p. 710). **Comment:** continuous outcomes analysed by ITT; dichotomous outcomes analysed per-protocol (data reported for 38/62, 61% intervention participants; 31/61, 51% control participants)
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Unclear risk	**Comment:** significant trend towards more left hemisphere lesion strokes in treatment group

Ohtomo 1991

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** Aniracetam (nootropic agent) **Control arm:** matched placebo
Participants	**Geographical location:** Japan **Setting:** unclear **Stroke criteria:** ischaemic stroke **Method of stroke diagnosis:** not reported **Time since stroke:** not reported **Inclusion criteria:** not reported **Exclusion criteria:** not reported **Depression criteria:** based on physician's impression, no scale used for evaluation **Total number randomised in this trial:** 285 **Number randomised to treatment group:** 150 (details unclear) **Number randomised to control group:** 135 (details unclear) **Total number included in final analysis:** 206 **Number included in treatment group for final analysis:** unclear **Number included in control group for final analysis:** unclear
Interventions	**Treatment:** Aniracetam (nootropic agent) 600 mg twice daily **Control:** matched placebo **Duration:** 12 weeks **Follow-up:** not reported
Outcomes	**Primary outcomes** • Depression measured by physician assessment of change in depression from baseline to end of treatment • Anxiety measured by physician assessment of change
Notes	

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	**Comment:** generation sequence controlled by Professor Furukawa
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported

Ohtomo 1991 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Comment:** double-blind reported and matched placebo used
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Comment:** double-blind reported, so likely that outcome assessment was blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	**Comment:** per-protocol analyses reported only; 79/285 (27.3%) missing from depression analyses
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported. No trial protocol available to compare with the publication
Other bias	Unclear risk	**Comment:** differences in baseline demographics between groups not reported

Ponzio 2001

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** paroxetine (SSRI) **Control arm:** matched placebo
Participants	**Geographical location:** Italy **Setting:** outpatient **Stroke criteria:** unclear **Method of stroke diagnosis:** not reported **Time since stroke:** not reported **Inclusion criteria:** (1) 18 to 85 years of age; (2) MMSE score > 23 **Exclusion criteria:** (1) concurrent predominant psychiatric disorders; (2) receiving psychotropic pharmacotherapy; (3) with substance abuse/dependence; (4) participation in other clinical trials; (5) suicide risk; (6) concomitant medication intolerance to paroxetine **Depression criteria:** MADRS > 18 **Total number randomised in this trial:** 229 **Number randomised to treatment group:** 112 (54% men, mean age 64 years, SD 11) **Number randomised to control group:** 117 (55% men, mean age 66 years, SD 11) **Total number included in final analysis:** 229 **Number included in treatment group for final analysis:** 112 **Number included in control group for final analysis:** 117
Interventions	**Treatment:** paroxetine (SSRI) 20 to 40 mg daily **Control:** matched placebo

Ponzio 2001 *(Continued)*

	Duration: 8 weeks **Follow-up:** not reported
Outcomes	**Primary outcomes** • Depression (change in scores from baseline to end of treatment) measured using MADRS and CGI **Secondary outcomes** • Proportion scoring < 7 on MADRS and responders on CGI • Disability (change in scores from baseline to end of treatment) measured using BI • Functional capacity (change in scores from baseline to end of treatment) measured using Rankin scale • Adverse events
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Quote:** "subjects randomised to paroxetine…" (p. 1) **Comment:** method of sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Quote:** "blinding of study medication was maintained by referring to dosage…" (p. 1). **Comment:** in study design, it stated that this study was a 'double-blind, placebo-controlled' trial, but in treatment, this was a 'single-blind placebo' trial.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** in study design, it stated that this was a 'double-blind, placebo controlled' trial, but in treatment, this was a 'single-blind placebo' trial.
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Quote:** "the primary analysis (post-stroke depression) population was the intention-to-treat (ITT) population…." (p. 1).
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline demographic characteristics between groups

Rampello 2005

Study characteristics

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** reboxetine (NRI)

Rampello 2005 *(Continued)*

	Control arm: matched placebo
Participants	**Geographical location:** Italy **Setting:** outpatient **Stroke criteria:** single ischaemic or haemorrhagic stroke **Method of stroke diagnosis:** diagnosis via CT and MRI **Time since stroke:** 2 weeks **Inclusion criteria:** (1) presence of major or minor depression; (2) presence of retarded depression; (3) lack of treatment with antidepressants 2 weeks before randomisation; (4) absence of treatment with neuroleptic drugs during 3 months before enrolment; (5) can sign informed consent **Exclusion criteria:** (1) previous degenerative or expansive neurological disease; (2) tumour, multiple sclerosis, amyotrophic sclerosis, hydrocephalus, SAH, Binswanger's disease; (3) history of psychiatric illness (other than depression); (4) severe aphasia; (5) severe cognitive deficit; (6) chronic alcoholism **Depression criteria:** psychiatric interview, HDRS > 20, BDI > 15 **Total number randomised in this trial:** 31 **Number randomised to treatment group:** 16 (44% men, mean age 78 years, SD 4) **Number randomised to control group:** 15 (46% men, mean age 77 years, SD 4) **Total number included in final analysis:** 31 **Number included in treatment group for final analysis:** 16 **Number included in control group for final analysis:** 15
Interventions	**Treatment:** reboxetine (NRI) 4 mg twice daily **Control:** matched placebo **Duration:** 16 weeks **Follow-up:** not reported
Outcomes	**Primary outcomes** • Depression measured using HDRS and BDI **Secondary outcomes** • Adverse events
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Quote:** "a computer-generated randomization was carried out by a physician who was not involved in the evaluation of patients…" (p. 277).
Allocation concealment (selection bias)	Low risk	**Quote:** "the generator of randomization assigned a code number (0) to patients who were treated with reboxetine, and a different code (1) was given to patients treated with placebo. Code 0 was stuck on totally white boxes, without any marks, sealed, containing the tablets of..." (p. 278).
Blinding of participants and personnel (performance bias) All outcomes	High risk	**Quote:** "the generator of randomization handed over, for each patient, the box marked with the code and containing the tablets that should be taken" (p. 279).

Rampello 2005 *(Continued)*

		Comment: participants were blinded but the personnel who delivered the intervention knew the treatment allocation.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Quote:** "the other physician was in charge of the follow-up visits and of the evaluation of the outcome measures" (p. 279).
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** follow-up of all participants was complete; ITT analysis reported
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol to compare with the publication
Other bias	Low risk	Quote: "the sample represented in each of the two subgroups was homogeneous for age, sex, side of lesions, and depression stage at baseline" (p. 279).

Reding 1986

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** trazodone-HCl (TCA) **Control arm:** matched placebo
Participants	**Geographical location:** USA **Setting:** inpatients **Stroke criteria:** all subtypes **Method of stroke diagnosis:** diagnosis via clinical signs and CT (% not reported) **Time since stroke:** 45 to 48 days **Inclusion criteria:** not reported **Exclusion criteria:** (1) myocardial infarction within previous month; (2) on anti-arrhythmic medication **Depression criteria:** psychiatric interview (DSM-III, major and minor) **Total number randomised in this trial:** 17 **Number randomised to treatment group:** 11 (66% men, mean age 68 years, SE 2) **Number randomised to control group:** 6 (73% men, mean age 68 years, SE 3) **Total number included in final analysis:** 17 **Number included in treatment group for final analysis:** 11 **Number included in control group for final analysis:** 6
Interventions	**Treatment:** trazodone-HCl (TCA) 50 mg daily; dose escalation every 3 days to target dose of 200 mg **Control:** matched placebo **Duration:** 32 ± 6 days (treatment group) and 24 ± 4 days (control group) **Follow-up:** not reported

Reding 1986 *(Continued)*

Outcomes	**Primary outcomes** • Depression measured using clinical diagnosis of depression and ZDS **Secondary outcomes** • Disability measured using BI
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Quote:** "patients were assigned to either treatment or placebo groups according to a table of random numbers" (p. 763).
Allocation concealment (selection bias)	Low risk	**Quote:** "…or placebo in an identical capsule was administered orally…" (p. 763).
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Quote:** "…or placebo in an identical capsule was administered orally…" (p. 763).
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Quote:** "if the attending physician, unaware of treatment group assignment…." (p. 764)
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** follow-up of all participants was complete; ITT analysis reported in table
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol to compare with the publication
Other bias	Unclear risk	**Comment:** baseline demographic information not reported

Robinson 2008a

Study characteristics

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** nefiracetam (nootropic agent) **Control arm:** matched placebo
Participants	**Geographical location:** USA **Setting**: unclear **Stroke criteria:** ischaemic and primary intracerebral haemorrhage **Method of stroke diagnosis:** unclear **Time since stroke:** 10 days to 3 months

Robinson 2008a *(Continued)*

	Inclusion criteria: not reported **Exclusion criteria:** (1) other psychiatric or neurological disease (e.g. Alzheimer's disease, Parkinson's disease); (2) depression or suicidal plans requiring psychiatric hospitalisation; (3) on psychotropic medication (excluding benzodiazepines or insomnia medication); (4) comprehension deficit precluding verbal interview; (5) life-threatening illness; (6) previous subarachnoid haemorrhage **Depression criteria:** psychiatric interview to confirm DSM-IV diagnosis of "depression due to stroke with major depressive-like episode" plus HDRS score ≥ 18 **Total number randomised in this trial:** 76 **Number randomised to treatment group:** 48 (40% men; mean age 68.1, SD 11.9) **Number randomised to control group:** 28** (54% men; mean age 66.8, SD 13.0) **Total number included in final analysis:** 66 **Number included in treatment group for final analysis:** 41 **Number included in control group for final analysis:** 25**
Interventions	**Treatment:** nefiracetam (nootropic agent) 900 mg, 3 × 150 mg capsule twice/d **Control:** matching placebo 3 × 150 mg capsule twice/d **Duration:** 12 weeks **Follow-up:** not reported
Outcomes	**Primary outcomes** • Depression measured using HDRS • Depression measured using BDI **Secondary outcomes** • Apathy measured using Apathy Scale • Leaving the trial early • Adverse events
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Comment:** based on the study author's responses, sequence generation was attained with computer-generated numbers.
Allocation concealment (selection bias)	Low risk	**Quote:** "nefiracetam or placebo was administered double-blind in three identical 150 mg capsules…" (p. 179).
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Comment:** study author stated that this study was double-blinded but did not state who was blinded.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Comment:** study author stated that this study was double-blinded but did not state who was blinded.

Robinson 2008a *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	High risk	**Quote:** "...missing data points were estimated using LOCF..." (p. 146). "attrition related bias cannot be ruled out" (p. 149). **Comment:** the number of dropouts reported and the number analysed are inconsistent within and between publications.
Selective reporting (reporting bias)	High risk	**Comment:** study author reported that a number of measures were assessed but did not provide details of these measures in the publication.
Other bias	Unclear risk	**Comment:** baseline demographic information was not reported.

Robinson 2008b

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** nefiracetam (nootropic agent) **Control arm:** matched placebo
Participants	**Geographical location:** USA **Setting**: unclear **Stroke criteria:** ischaemic and primary intracerebral haemorrhage **Method of stroke diagnosis:** unclear **Time since stroke:** 10 days to 3 months **Inclusion criteria:** not reported **Exclusion criteria:** (1) other psychiatric or neurological disease (e.g. Alzheimer's disease, Parkinson's disease); (2) depression or suicidal plans requiring psychiatric hospitalisation; (3) on psychotropic medication (excluding benzodiazepines or insomnia medication); (4) comprehension deficit precluding verbal interview; (5) life-threatening illness; (6) previous subarachnoid haemorrhage **Depression criteria:** psychiatric interview to confirm DSM-IV diagnosis of "depression due to stroke with major depressive-like episode" plus HDRS score ≥ 18 **Total number randomised in this trial:** 83 **Number included in treatment group:** 55 (40% men; mean age 64.7, SD 11.9) **Number included in control group:** 28** (54% men; mean age 66.8, SD 13.0) **Total number included in final analysis:** 72 **Number included in treatment group for final analysis:** 47 **Number included in control group for final analysis:** 25**
Interventions	**Treatment:** nefiracetam 600 mg, 3 × 150 mg capsule twice/d **Control:** matching placebo 3 × 150 mg capsule twice/d **Duration:** 12 weeks **Follow-up:** not reported

Robinson 2008b *(Continued)*

Outcomes	**Primary outcomes** • Depression measured using HDRS • Depression measured using BDI **Secondary outcomes** • Apathy measured using Apathy Scale • Leaving the trial early • Adverse events
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Comment:** based on the study author's responses, sequence generation was attained with computer-generated numbers.
Allocation concealment (selection bias)	Low risk	**Quote:** "nefiracetam or placebo was administered double-blind in three identical 150 mg capsules…" (p. 179).
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Comment:** study author stated that this study was double-blinded but did not state who was blinded.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Comment:** study author stated that this study was double-blinded but did not state who was blinded.
Incomplete outcome data (attrition bias) All outcomes	High risk	**Quote:** "...missing data points were estimated using LOCF..." (p. 146). "attrition related bias cannot be ruled out" (p. 149). **Comment:** the number of dropouts reported and the number analysed were inconsistent within and between publications.
Selective reporting (reporting bias)	High risk	**Comment:** study author reported that a number of measures were assessed but did not provide details of these measures in the publication.
Other bias	Unclear risk	**Comment:** baseline demographic information was not reported.

Sun 2013

Study characteristics

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** rTMS + Deanxit (flupentixol and melitracen) **Control arm:** Deanxit (flupentixol and melitracen)
Participants	**Geographical location:** China

Sun 2013 *(Continued)*

	Setting: inpatient **Stroke criteria:** ischaemic stroke **Method of stroke diagnosis:** clinical diagnosis plus confirmation by imaging that a relevant lesion needed to be visible **Time since stroke:** 8 days **Inclusion criteria:** (1) meeting diagnostic criteria of the CCMD-3 for depression; (2) clear consciousness, no obvious aphasia or comprehension impairment; (3) no severe cardiac disease history; (4) first stroke or previous stroke without sequelae; (5) internal carotid system cerebral infarct, no epilepsy or head injury history, can sign informed consent **Exclusion criteria:** (1) cerebral haemorrhage, progressive stroke, intracranial infection, intracranial tumour, seizure attack or consciousness disturbance, severe cardiac event (heart function class ≥ 3), pulmonary (respiratory failure) and renal (uremia) impairment, mental implant in the body (e.g. pacemaker, metal stent), pregnancy or children **Depression criteria:** meeting diagnostic criteria of the CCMD-3 for depression **Total number randomised in this trial:** 100 **Number randomised to treatment group:** 50 (78% men, mean age 64.6, SD 11.4) **Number randomised to control group:** 50 (68% men, mean age 66.5, SD 11.1) **Total number included in final analysis:** 100 **Number included in treatment group for final analysis:** 50 **Number included in control group for final analysis:** 50
Interventions	**Treatment:** rTMS + Deanxit (flupentixol and melitracen), 10.5 mg/d in the morning, starting on day 8 after stroke onset. Frequency: 1 Hz, intensity: 90% motor threshold, 30 stimulations for 1 series, 1 series a day, location: bilateral pre-frontal area, starting on day 8 after stroke onset **Control:** Deanxit (flupentixol and melitracen) **Duration:** 2 weeks **Follow-up:** none
Outcomes	**Primary outcomes** • Depression measured using HDRS • Depression measured using SDS
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Comment:** method of sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias)	Unclear risk	**Comment:** information about blinding of participants and personnel not reported

Sun 2013 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** information about blinding of outcome assessors not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** ITT analysis reported; no missing data
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline demographics between groups

Tao 2008

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Treatment arm:** routine nursing intervention + systematic psychological nursing **Control arm:** routine nursing intervention
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** ischaemic stroke **Method of stroke diagnosis:** ischaemic stroke as diagnosed according to the 2nd National Cerebrovascular Disease Conference Diagnosis criteria and CT or MRI examination **Time since stroke:** not reported **Depression criteria:** Symptom diagnostic criteria of organic depression syndrome, HDRS ≥ 7 points **Inclusion criteria:** (1) those diagnosed according to the symptom diagnostic criteria of organic depression syndrome; (2) met HDRS ≥ 7 points; (3) no complicated heart failure and respiratory failure or acute phase of other diseases; (4) with language comprehension and expression skills **Exclusion criteria:** not reported **Total number randomised in this trial:** 62 **Number randomised to treatment group:** 32 (percentage of men and mean age not reported) **Number randomised to control group:** 30 (percentage of men and mean age not reported) **Total number included in final analysis:** 62 **Number included in treatment group for final analysis:** 32 **Number included in control group for final analysis:** 30
Interventions	**Treatment:** routine nursing intervention + systematic psychological nursing **Administered by:** not reported

Tao 2008 *(Continued)*

	Supervision: not reported **Intervention fidelity:** not reported **Control:** routine nursing intervention **Treatment duration:** 4 weeks **Follow-up:** 8 weeks
Outcomes	**Primary outcomes:** • Depression measured using HDRS-17 • Activities of daily living measured using modified Barthel Index
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Comment:** Method of sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	**Comment:** Method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** Information on blinding of participants and personnel was not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** Information on blinding of outcome assessment not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** All 62 patients were included in the final analysis.
Selective reporting (reporting bias)	Low risk	**Comment:** All prespecified outcomes reported; no trial protocol or registry record available to compare with the publication
Other bias	Unclear risk	**Comment:** The difference in baseline characteristics between groups was not reported.

Terachinda 2021

Study characteristics

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** rTMS + sertraline (SSRI) **Control arm:** sham rTMS + sertraline (SSRI)
Participants	**Geographical location:** Thailand

Terachinda 2021 *(Continued)*

	Setting: inpatient **Stroke criteria**: ischaemic stroke **Method of stroke diagnosis:** evidence of ischaemic stroke obtained from neuroimaging **Time since stroke:** overall not reported. Treatment group (mean 34.0, SD 11.3 days) and control group (mean 59.8, SD 45.5 days) **Inclusion criteria:** (1) aged 18 years and over; (2) within 6 months after stroke onset; (3) had evidence of ischaemic stroke obtained from neuroimaging; (4) had depressive episode after the stroke onset according to the DSM-IV criteria - mood disorder due to medical condition (stroke); (5) antidepressive agent had not been given or had been withdrawn longer than 5 times of its half-life before study enrolment **Exclusion criteria:** (1) had other neurological disorders, i.e. Parkinson's disease, dementia (2) had depressive symptoms before the onset of stroke or had other psychiatric disorders; (3) were contraindicated to rTMS and/or sertraline; (4) were unable to communicate or; (5) had cognitive impairment, scored < 23 on the Thai Mental State Examination (TMSE) **Depression criteria:** depressive episode after the stroke onset according to the DSM-IV criteria - mood disorder due to medical condition (stroke) **Total number randomised in this trial:** 9 **Number randomised to treatment group:** 5 (60% men, mean age 60.6 years, SD 11.1) **Number randomised to control group:** 4 (50% men, mean age 62.3 years, SD 8.5) **Total number included in final analysis:** 8 **Number included in treatment group for final analysis:** 4 **Number included in control group for final analysis:** 4
Interventions	**Treatment:** rTMS + sertraline (SSRI) 50 mg/d. Frequency: 10 Hz, intensity: 110% resting motor threshold for 5 seconds for each train with 60 second-intertrain interval were given, totally 1000 pulses/session. 5 sessions a week, for a total of 10 sessions over 2 weeks, location: left dorsolateral pre-frontal cortex (DLPFC) **Administered by:** study investigators **Intervention fidelity:** not reported **Control:** sham rTMS + sertraline (SSRI) 50 mg/d **Duration:** rTMS was delivered for 2 weeks, sertraline was administered for 14 weeks **Follow-up:** 14 weeks
Outcomes	**Primary outcomes** • Treatment response (≥ 50.0% reduction in baseline symptom severity sustained for 3 consecutive weeks) • Remission (17-item HAMD-Thai version score of ≤ 7 for 3 consecutive weeks) **Secondary outcomes** • Independence in ADL measured using MBI-Thai version • Motor recovery measured by Brunnstrom stages of motor recovery • Adverse events (through subject interviews and medical records)
Notes	This study was funded by Ratchadapiseksompotch Fund, Faculty of Medicine, Chulalongkorn University, grant number RA57/019.

Risk of bias

Terachinda 2021 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Comment:** not detailed
Allocation concealment (selection bias)	High risk	**Quote:** “allocation sequence was sealed in envelopes” p. 72.
Blinding of participants and personnel (performance bias) All outcomes	High risk	**Quote:** “in the sertraline group, sham rTMS was given. Same stimulus parameters were used but the coil was laid perpendicular to the scalp. Other two investigators opened the envelopes and performed rTMS" p. 72.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Quote:** “in current study, a psychologist, who was blinded to the allocation, was trained in using HAM-D by a psychiatrist and performed the evaluation of depression severity at baseline and each time point.” page 72 **Quote:** “All secondary outcomes were assessed by a blinded assessor.” page 73
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Quote**: "missing data were imputed using last observation carried forward method” p. 73. **Comment:** outcome data reported for all participants
Selective reporting (reporting bias)	Low risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare the publication
Other bias	High risk	**Quote:** “… unequal baseline HAM-D score among groups although no statistically significant difference in baseline score was found. Subjects in the combined group had milder symptoms whereas those in the rTMS group had more severe symptoms at baseline” p. 77.

Thomas 2007

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** behavioural psychotherapy **Control arm:** usual care
Participants	**Geographical location:** UK **Setting:** mixed **Stroke criteria**: unclear **Method of stroke diagnosis:** not reported **Time since stroke:** 8.85 days **Inclusion criteria:** (1) presence of aphasia confirmed by a speech and language therapist (hospital or community participants) or using the Sheffield Screening Test for Acquired Language Disorders (voluntary sector participants) **Exclusion criteria:** (1) receiving treatment for depression pre-stroke (at the time of stroke), (2) with dementia, (3) blind or deaf; (4) unable to speak English before stroke

Thomas 2007 *(Continued)*

	Depression criteria: using the 'sad' item of the VAMS and the 10-item hospital version of the SAD-Q, completed by a nurse, relative, or carer. Those identified as having low mood on the 'sad' item of the VAMS (cut-off > 50) or the SAD-Q (cut-off > 6) **Total number randomised in this trial:** 105 **Number randomised to treatment group:** 51 (57% men, mean age 68.5 years, SD 13.1) **Number randomised to control group:** 54 (69% men, mean age 65.5 years, SD 13.9) **Total number included in final analysis:** 89 **Number included in treatment group for final analysis:** 43 **Number included in control group for final analysis:** 46
Interventions	**Treatment 1:** behavioural psychotherapy up to 20 sessions of treatment over 3 months, with each session lasting approximately 1 hour. The manual had been developed from studies of cognitive-behavioural therapy for depression after stroke and with older adults, and from guidelines on conducting cognitive-behavioural therapy with people with aphasia. The intensity of therapy was left to the discretion of the assistant psychologist. The intervention was tailored to the individual's needs, and communication resources such as pictures, photographs, and letter charts were used. **Administered by:** assistant psychologist **Supervision:** therapy was delivered by an assistant psychologist supervised weekly by a clinical psychologist. All assistant psychologists attended a joint monthly supervision meeting with a consultant clinical neuropsychologist. Assistant psychologists received training in supported communication from speech and language therapists and were provided with a therapy manual. **Intervention fidelity:** delivery of therapy was monitored by observation of therapy sessions by the chief investigator. The content of therapy was documented using record forms completed by the assistant psychologist after each session. **Control:** usual care **Duration:** 3 months **Follow-up:** 3 months
Outcomes	**Primary outcomes** • Depression measured using the 21-item hospital version of the SAD-Q – an observational measure of mood completed by a relative or primary carer • Depression measured using the 'sad' item of VAMS **Secondary outcomes** • Self-esteem measured using Visual Analogue Self-Esteem Scale • Activities of daily measured using Nottingham Leisure Questionnaire • Caregiver strain measured using CSI • Patient and carer satisfaction with care measured using 100-mm VAS
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Quote:** "participants were randomly allocated to one of two groups…..using a computer generated pseudo-random list…" (p. 400).

Thomas 2007 *(Continued)*

Allocation concealment (selection bias)	Low risk	**Quote:** "the assistant psychologist providing treatment accessed the allocation by logging into a secure computer server, thus ensuring concealment of allocation" (p. 400).
Blinding of participants and personnel (performance bias) All outcomes	High risk	**Comment:** due to the nature of the trial, not possible to mask participants, personnel, and researchers to treatment allocation
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** primary endpoint self-assessed by relative or carer who was aware of treatment allocation. Secondary endpoints assessed using a blinded assessor
Incomplete outcome data (attrition bias) All outcomes	High risk	**Quote:** "outcomes were analysed by intention to treat" (p. 401). "...missing data using the last observation carried forward on the assumption of no change…" (p. 402) **Comment:** only per-protocol analysis reported
Selective reporting (reporting bias)	High risk	**Comment:** one secondary outcome measure (Extended Activities of Daily Living Scale) not reported in the publication
Other bias	Low risk	**Comment:** no differences in baseline demographic characteristics between groups

Thomas 2016

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** behavioural activation therapy **Control arm:** usual care
Participants	**Geographical location:** UK **Setting:** mixed **Stroke criteria:** ischaemic or haemorrhagic stroke **Method of stroke diagnosis:** not reported **Time since stroke:** 3 months to 5 years **Inclusion criteria:** (1) had a diagnosis of stroke; (2) were aged ≥ 18 years; (3) were living in community settings, including home or nursing home; (4) were a minimum of 3 months and a maximum of 5 years post-stroke; (5) were identified as depressed, defined as a score of ≥ 10 points on the PHQ-9 (two or fewer missing items within the questionnaire may be imputed); (6) a score of at least 50 out of 100 points on the VAMS 'Sad' item **Exclusion criteria:** (1) had a diagnosis of dementia, based on self-report or carer report, prior to their stroke; (2) reported receiving medical or psychological treatment for depression at the time at which they had their stroke; (3) were currently receiving a psychological intervention; (4) had communication difficulties that would have an impact on their capacity to take part in the intervention, based on assessment with the Consent Support Tool 60 (CST) for people with aphasia; (5) had visual or hearing im-

Thomas 2016 *(Continued)*

	pairments that would have an impact on their capacity to take part in the intervention based on their therapist's opinion at baseline assessment; (6) were unable to communicate in English prior to the stroke; (7) did not have mental capacity to consent to take part in the trial **Depression criteria:** score of ≥ 10 points on the PHQ-9 (two or fewer missing items within the questionnaire may be imputed) and a score of at least 50 out of 100 points on the VAMS 'Sad' item **Total number randomised in this trial:** 48 **Number randomised to treatment group:** 25 (68% men and mean age 62.6 SD 14.5 years) **Number randomised to control group:** 23 (52.2% men and mean age 68.8 SD 12.1 years) **Total number included in final analysis:** 48 **Number included in treatment group for final analysis:** 25 **Number included in control group for final analysis:** 23
Interventions	**Treatment:** behavioural activation (BA) therapy is a structured and individualised treatment that aims to increase people's level of activity, particularly the frequency of pleasant or enjoyable events, to improve mood. Maximum of 15 sessions of BA over 4 months, with an expected average of 10 sessions. Therapy sessions were face-to-face on an individual basis, at participants' residences, and lasted about 1 hour. A BA treatment manual was developed. **Administered by:** assistant psychologist **Supervision:** not reported **Intervention fidelity:** not reported **Control:** usual care **Duration:** 4 months **Follow-up:** 6 months
Outcomes	**Primary outcome** • Depression measured using PHQ-9, SAD-Q Hospital version (observer-rated depression) **Secondary outcomes** • Activities of daily living measured using Nottingham Leisure Questionnaire • Functional outcome measured using Nottingham EADL • Health-related quality of life measured using EQ5D-5L
Notes	The study was funded by the National Institute for Health Research.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Quote:** "Randomisation was conducted using a computer-generated list with random permuted blocks of varying sizes, created and hosted by the Sheffield CTRU in accordance with their standard operating procedures and was held on a secure server. Once a participant had consented to the study, the therapist logged into the remote, secure, internet-based randomisation system and entered basic demographic information. The allocation for that participant was then revealed to the researcher." p. 42
Allocation concealment (selection bias)	Unclear risk	**Quote:** "Access to the allocation sequence was restricted to those with authorisation. The sequence of treatment allocations was concealed until interven-

Thomas 2016 *(Continued)*

		tions had been assigned and recruitment, data collection and analyses were complete." p.42 **Comment:** The method of allocation concealment not detailed
Blinding of participants and personnel (performance bias) All outcomes	High risk	**Quote:** "Neither the participants nor the therapists were blind to which treatment the participants were receiving." p. 42
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Quote:** "The outcome assessors were blind to the treatment received and there was no requirement for them to know the treatment allocation at any stage. As a result, a procedure for breaking the code was not necessary." p. 42
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Quote:** "The intention-to-treat (ITT) population includes all participants for whom consent was obtained and who were randomised to treatment, regardless of whether they received the intervention. This is the primary analysis set and end points were summarised for the ITT population unless otherwise stated." p. 43
Selective reporting (reporting bias)	Low risk	**Comment:** All prespecified outcomes in the protocol were reported.
Other bias	Low risk	**Comment:** Baseline demographic characteristics were balanced across the groups.

Tian 2010

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Treatment arm:** conventional nursing care and health education + comprehensive psychological intervention **Control arm:** conventional nursing care and health education
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** haemorrhagic and ischaemic stroke **Method of stroke diagnosis:** meets the diagnostic criteria of the Chinese Academy of Sciences and the Chinese Society of Neurosurgery and through head CT **Time since stroke:** not reported **Depression criteria:** HDRS score ≥ 17 points **Inclusion criteria:** (1) stroke according to the relevant diagnostic criteria of the Chinese Academy of Sciences and the Chinese Society of Neurosurgery and confirmed through head CT; (2) have no history of consciousness disorder, aphasia and mental illness; (3) depression and anxiety (HARS score ≥ 14 points and HDRS score ≥ 17 points). **Exclusion criteria:** not reported **Total number randomised in this trial:** 100

Tian 2010 *(Continued)*

	Number randomised to treatment group: 50 (69% men overall and age range 39-84 years) **Number randomised to control group:** 50 (69% men overall and age range 39-84 years) **Total number included in final analysis:** 100 **Number included in treatment group for final analysis:** 50 **Number included in control group for final analysis:** 50
Interventions	**Treatment:** conventional nursing care and health education + comprehensive psychological intervention **Administered by:** not reported **Supervision:** not reported **Intervention fidelity:** not reported **Control:** conventional nursing care and health education **Treatment duration:** 3 weeks **Follow-up:** none
Outcomes	**Primary outcomes:** • Depression measured using HDRS-17 • Anxiety measured using HARS
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Comment:** Method of sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	**Comment:** Method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** Information on blinding of participants and personnel was not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** Information on blinding of outcome assessment not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** All 100 patients were included in the final analysis.
Selective reporting (reporting bias)	Unclear risk	**Comment:** All prespecified outcomes reported; no trial protocol or registry record available to compare with the publication
Other bias	Unclear risk	**Comment:** The difference in baseline characteristics between groups was not reported.

Towle 1989

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** pragmatic approach (counselling) **Control arm:** custom-designed information booklet
Participants	**Geographical location:** UK **Setting:** outpatients **Stroke criteria:** all subtypes **Method of stroke diagnosis:** diagnosis via clinical signs **Time since stroke:** 6 to 7 months **Inclusion criteria:** (1) able to complete questionnaires unaided **Exclusion criteria:** (1) stroke < 1 year before randomisation; (2) residence in hospital or residential care **Depression criteria:** WDI score > 17 or GHQ-28 score > 9 **Total number randomised in this trial:** 44 **Number randomised to treatment group:** 21 (43% men, mean age 70 years, SD 9) **Number randomised to control group:** 23 (30% men, mean age 69 years, SD 7) **Total number included in final analysis:** 43 **Number included in treatment group for final analysis:** 21 **Number included in control group for final analysis:** 22
Interventions	**Treatment:** pragmatic approach dealing with problems identified by social worker and patients; included counselling the patient and caregiver, giving opportunity to reflect upon their situation and express their feelings (duration: 2 to 11 visits over 16 weeks, mean visits 6.8 ± 2.8; however, length and content of visits varied) **Administered by:** not reported **Supervision:** not reported **Intervention fidelity:** unclear; no report of formal evaluation of the quality or content of therapy provided **Control:** custom-designed information booklet (covered areas believed to be of use and interest to stroke survivors and their families, such as details on housing and financial benefits; aids to daily living; addresses of stroke clubs and self-help groups; telephone number of local social services department), 1 visit, no ongoing visits **Administered by:** social worker **Duration:** 16 weeks **Follow-up:** not reported
Outcomes	**Primary outcomes** • Depression (change in scores from baseline to end of treatment) measured using WDI and GHQ-28
Notes	

Towle 1989 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Quote:** "the order of the envelopes had been decided before the study using random number tables" (p. 520).
Allocation concealment (selection bias)	High risk	**Quote:** "the patients were then allocated randomly to one of two groups using sealed envelopes each containing a slip of paper stating either "treatment" or "no treatment" " (p. 520).
Blinding of participants and personnel (performance bias) All outcomes	High risk	**Quote:** "the patients were then allocated randomly to one of two groups using sealed envelopes each containing a slip of paper stating either "treatment" or "no treatment" " (p. 520). **Comment:** due to the nature of the trial, it was not possible to mask participants or social worker to treatment allocation.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Quote:** "each patient was visited 8 weeks and 16 weeks later by the independent assessor who repeated the pre-intervention questionnaires". **Comment:** it is unclear whether the independent assessor was blinded to treatment allocation.
Incomplete outcome data (attrition bias) All outcomes	High risk	**Comment:** 1/44 participants were excluded from the analysis; only per-protocol analysis reported
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline demographic characteristics between groups

Valiengo 2017

Study characteristics

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** active transcranial direct current stimulation (tDCS) **Control arm:** sham tDCS
Participants	**Geographical location:** Brazil **Setting:** outpatient **Stroke criteria:** ischaemic stroke **Method of stroke diagnosis:** diagnosed by a trained physician and confirmed by both an anamnesis of a neurological condition (stroke) and a physical examination **Time since stroke:** not reported **Inclusion criteria:** (1) aged 30-90 years; (2) HDRS-17 score ≥ 17; (3) only a first stroke episode or it had to occur ≤ 5 years prior to the interview; (4) low suicide risk according to the clinical interview and the

Valiengo 2017 *(Continued)*

	suicide item in the HDRS-17 (3rd item) had to be scored ≤ 2; (5) DSM-IV diagnosis of "mood disorder due to a general medical condition (stroke) with a major depressive-like episode" **Exclusion criteria:** (1) other current Axis I disorders (except for anxiety disorders); (2) specific contraindications for tDCS, such as metallic plates in the head; (3) other neurological disorders, including dementia and epilepsy; (4) life-threatening clinical conditions; (5) use of any antidepressants, antipsychotic, sedative or hypnotic drug **Depression criteria:** HDRS-17 score ≥ 17 and DSM-IV diagnosis of mood disorder **Total number randomised in this trial:** 48 **Number randomised to treatment group:** 24 (50% men; mean age 62.2, SD 12.3) **Number randomised to control group:** 24 (50% men; mean age 61.3, SD 10.6) **Total number included in final analysis:** 48 **Number included in treatment group for final analysis:** 24 **Number included in control group for final analysis:** 24
Interventions	**Treatment:** active tDCS; intensity: 2 mA, 12 30 min sessions, administered over 6 weeks (once daily on weekdays for 2 weeks, then 1 session every other week) location: right DLPFC **Control:** sham tDCS, brief stimulation period (60 s), to mimic common skin effects experienced just after stimulation, followed by no stimulation during the remaining period **Duration:** 6 weeks **Follow-up:** none
Outcomes	**Primary outcomes** • Depression measured using 17-item HDRS **Secondary outcomes** • Clinical response (defined as ≥ 50% reduction from the baseline HDRS score) • Remission (categorical, defined as an endpoint HDRS score < 8) • Depression measured using MADRS • Functional recovery measured using Rankin scale • Disability measured using Barthel Index
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Quote:** "Randomisation was conducted with an automated device that produced sham or active stimulation, according to a number code. Number codes were randomised by a research assistant not involved in any other aspect of the trial, and typed out by the study nurse, who was blinded to the group condition" p. 170-171.
Allocation concealment (selection bias)	Low risk	**Quote:** "Allocations were concealed with a central randomisation method" p. 170-171.
Blinding of participants and personnel (performance bias)	Low risk	**Quote:** "Raters, operators and patients were blinded to treatment allocations. Contact between participants was avoided to enhance study blinding" p. 171.

Valiengo 2017 *(Continued)*
All outcomes

Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Quote:** "Raters, operators and patients were blinded to treatment allocations. Contact between participants was avoided to enhance study blinding" p. 171.
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Quote:** "…48 patients were included and 43 completed the study" p. 172. **Comment:** 5 dropped out (2/24 in the intervention and 3/24 in the control groups).
Selective reporting (reporting bias)	Unclear risk	Comment: All prespecified outcomes reported; no trial protocol available to compare the publication
Other bias	Low risk	**Quote:** "The groups had similar baseline clinical and demographic characteristics. Only 16.6% of patients were previously using antidepressants and required a drug washout" p. 172.

Wang 2004a

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** psychological therapy **Control arm:** usual care
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria**: not reported **Method of stroke diagnosis:** diagnosis consistent with diagnostic criteria for stroke formulated by the Fourth National Symposium on Cerebrovascular Disease in 1995 and confirmation by brain CT **Time since stroke:** not reported **Inclusion criteria:** (1) first-ever stroke **Exclusion criteria:** (1) history of psychiatric illness; (2) previous neurological disease or uncooperative with examination **Depression criteria:** psychiatric interview to confirm diagnosis meets depression diagnostic criteria of the CCMD-2-R **Total number randomised in this trial:** 70 **Number randomised to treatment group:** 35 (57% men; mean age 56, SD 8) **Number randomised to control group:** 35 (54% men; mean age 56, SD 7) **Total number included in final analysis:** 70 **Number included in treatment group for final analysis:** 35 **Number included in control group for final analysis:** 35
Interventions	**Treatment:** psychological therapy 1 hour twice/week administered by a psychiatrist. Psychological therapy entailed psychological support and explanation, relaxing training, and music therapy.

Wang 2004a *(Continued)*

	Administered by: not reported **Supervision:** not reported **Intervention fidelity:** not reported **Control:** usual care **Duration:** 5 weeks **Follow-up:** none
Outcomes	**Primary outcomes** • Depression measured using ZDS • Cognition measured by P300
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Comment:** method of sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** blinding of participants and personnel not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** blinding of outcome assessment not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** ITT analysis reported; no missing data
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline demographic characteristics between groups

Wang 2005

Study characteristics

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** fluoxetine (SSRI)

Wang 2005 *(Continued)*

	Control arm: matched placebo
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** all stroke **Method of stroke diagnosis:** diagnosis consistent with Diagnostic Criteria for Cerebrovascular Disease formulated by the Fourth National Conference of Chinese Medical Association in 1995 **Time since stroke:** not reported **Inclusion criteria:** not reported **Exclusion criteria:** (1) history of psychiatric illness; (2) dementia; (3) aphasia; (4) disturbance of consciousness **Depression criteria:** HDRS scores > 17 **Total number randomised in this trial:** 108 **Number randomised to treatment group:** 54 (57% men, mean age 58.9 years for total sample) **Number randomised to control group:** 54 (57% men, mean age 58.9 years for total sample) **Total number included in final analysis:** 108 **Number included in treatment group for final analysis:** 54 **Number included in control group for final analysis:** 54
Interventions	**Treatment:** fluoxetine (SSRI) 20 to 40 mg/d. If reduction in HDRS scores ≤ 5 points after 2 weeks of treatment, increase dosage to 40 mg/d **Control:** matched placebo **Duration:** 4 weeks **Follow-up:** none
Outcomes	**Primary outcomes** • Depression measured using HDRS (remission: no depression symptoms and HDRS < 7; improved depression symptoms: reduction of HDRS scores by ≥ 5; ineffective: severely depressed mood and reduction in HDRS scores < 4) **Secondry outcomes** • Neurological Impairment measured using CSS • Leaving the trial early
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Comment**: method of sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	**Comment**: method of allocation concealment not reported

Wang 2005 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment**: single-blind reported but who was blinded not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** blinding of outcome assessment not reported
Incomplete outcome data (attrition bias) All outcomes	High risk	**Comment:** ITT (last-observation-carried-forward) for dichotomous endpoints; unclear for continuous endpoints
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Unclear risk	**Comment:** difference in baseline demographic characteristics not reported

Wang 2005a

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** combined psychotherapy + paroxetine (SSRI) **Control arm:** paroxetine (SSRI)
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** ischaemic and haemorrhagic stroke; haemorrhagic subtypes not specified **Method of stroke diagnosis:** diagnosis consistent with diagnostic criteria for cerebrovascular disease formulated by the National Symposium on Cerebrovascular Disease of Chinese Medical Association in 1995 and confirmation by brain CT or MRI **Time since stroke:** 21.85 days **Inclusion criteria:** (1) first-ever stroke **Exclusion criteria:** (1) history of psychiatric illness, depressive phase of bipolar disorders; (2) antidepressants and antipsychotics in the previous 3 months; (3) severe cognitive impairment, aphasia; (4) severe cardiac impairment, hepatic or renal impairment; (5) coma; (6) too severe clinical condition to receive interview; (7) allergy to paroxetine **Depression criteria:** meeting both organic depression and organic anxiety diagnostic criteria of the CCMD-3 **Total number randomised in this trial:** 54 **Number included in treatment group:** 27 (52% men; mean age 64.0, SD 5.3) **Number included in control group:** 27 (52% men; mean age 62.4, SD 6.1) **Total number included in final analysis:** 54 **Number included in treatment group for final analysis:** 27

Wang 2005a *(Continued)*

	Number included in control group for final analysis: 27
Interventions	**Treatment:** combined psychotherapy, 1 session/week variable length 30 to 60 minutes administered by a psychotherapist + SSRI (paroxetine) 20 mg/d in the morning. Psychotherapy was described as having a supportive focus **Administered by:** not reported **Supervision:** not reported **Intervention fidelity:** not reported **Control:** paroxetine (SSRI) 20 mg/d in the morning **Duration:** 6 weeks **Follow-up:** none
Outcomes	**Primary outcomes** • Depression measured using HDRS **Secondary outcomes** • Anxiety measured using HARS • Disability measured using BI • Impairment measure using SSS
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Comment**: method of sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	**Comment**: method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment**: blinding of participants and personnel not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** blinding of outcome assessment not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	**Comment:** 2/54 treatment and 0/54 control dropped out. ITT for categorical outcome variable: clinical efficacy of participants with missing data regarded as ineffective; analysis by allocation for continuous outcomes analysis not reported
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline demographic characteristics between groups

Wang 2019

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Treatment arm:** routine nursing care + psychological counselling nursing **Control arm:** routine nursing care
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** stroke **Method of stroke diagnosis:** meets the diagnostic criteria of the Chinese Academy of Sciences and the Chinese Society of Neurosurgery and through head CT **Time since stroke:** not reported **Depression criteria:** HDRS score ≥ 17 points **Inclusion criteria:** (1) clinical symptoms meet the diagnostic criteria for stroke; (2) the diagnosis of depression conforms with the Chinese Mental Disease Classification Scheme and Diagnostic criteria; (3) with major diseases such as heart, liver, kidney and metabolic diseases **Exclusion criteria:** (1) patients with cognitive impairment and congenital malformations; (2) all non-cooperators **Total number randomised in this trial:** 50 **Number randomised to treatment group:** 25 (68% men and mean age 61.7 SD 3.7 years) **Number randomised to control group:** 25 (56% men overall and mean age 64.5 SD 7.6 years) **Total number included in final analysis:** 50 **Number included in treatment group for final analysis:** 25 **Number included in control group for final analysis:** 25
Interventions	**Treatment:** routine nursing care + psychological counselling nursing **Administered by:** not reported **Supervision:** not reported **Intervention fidelity:** not reported **Control:** routine nursing care **Treatment duration:** 4 weeks **Follow-up:** none
Outcomes	**Primary outcomes:** • Depression measured using HDRS-17 • Activities of daily living measured using Activities of Daily Living Scale
Notes	

Wang 2019 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Comment:** method of sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** information on blinding of participants and personnel was not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** information on blinding of outcome assessment not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** all 50 patients were included in the final analysis.
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol or registry record available to compare with the publication
Other bias	Low risk	**Quote:** "Comparison of general clinical data such as time, the difference is not significant (P > 0.05)" p. 2528.

Watkins 2007

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** motivational interviewing **Control arm:** usual care
Participants	**Geographical location:** UK **Setting:** inpatient **Stroke criteria:** all subtypes **Method of stroke diagnosis:** diagnosis via clinical signs and CT (100%) **Time since stroke:** 5 to 28 days **Inclusion criteria:** (1) over 18 years of age **Exclusion criteria:** (1) severe cognitive and communication problems; (2) moving out of the area after discharge; (3) already receiving psychiatric or clinical psychology intervention **Depression criteria:** GHQ score > 4 **Total number randomised in this trial:** 254 **Number randomised to treatment group:** 127 (52% men, mean age 68 years, SD 12)

Watkins 2007 *(Continued)*

	Number randomised to control group: 127 (53% men, mean age 68 years, SD 12) **Total number included in final analysis:** 254 **Number included in treatment group for final analysis:** 127 **Number included in control group for final analysis:** 127
Interventions	**Treatment:** motivational interviewing, up to 4 sessions, 1 per week, with same therapist **Administered by:** therapists **Supervision:** therapists received 4 days of training in motivational interviewing by a specialist followed by up to 10 practice sessions until competent and confident of the technique. Therapists were supervised by a clinical psychologist through team meetings and 1-to-1 clinical supervision sessions on a monthly basis with additional informal support throughout the study. **Intervention fidelity:** therapy sessions were audio recorded. The quality of the application of motivational interviewing was assessed by analysing a purposive sample of 60 sessions from different patients. A clinical psychologist reviewed the content of 20 therapist utterances around the midpoint of each session using a structured evaluation tool, "Motivational Interviewing Skill Code (version 2)". Utterances that were rated motivational interviewing-consistent included open questions, reflections, advise with permission, affirm, emphasise control, reflect, re-frame, and support. Utterances that were rated motivational interviewing-inconsistent included advise without permission, confront, direct, raise concern without permission, and warn. The percentage of motivational interviewing-consistent utterances was determined (total MI-consistent/(total MI-consistent plus MI-inconsistent)). Unclear if or how this information was fed back to therapists **Control:** usual care **Delivered by:** nurses and non-clinical psychologists **Duration:** 4 weeks **Follow-up:** none
Outcomes	**Primary outcomes** • Depression (proportion no longer meeting study criteria for depression, change in scores from baseline to end of treatment) measured using GHQ-28 • Disability measured using BI • Stroke Impairment measured using Stroke Expectations Questionnaire
Notes	Additional unpublished data provided by study authors

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Quote:** "a research nurse randomized patients (1:1 ratio) to either usual care (control) or MI (intervention) using minimization over sex, age (65 and 65 years), baseline function in activities of daily living (ADL; Barthel: 18 to 20; 11 to 17; 0 to 10), and location (acute stroke unit)".
Allocation concealment (selection bias)	High risk	**Quote:** "the same nurse then assigned intervention group patients to 1 of 4 therapists using an opaque sealed envelope in a pseudorandomized blocked design" (p. 1957).
Blinding of participants and personnel (performance bias) All outcomes	High risk	**Quote:** "the same nurse then assigned intervention group patients to 1 of 4 therapists using an opaque sealed envelope in a pseudorandomized blocked design" (p. 1957).

Watkins 2007 *(Continued)*

		Comment: due to the nature of the intervention, it was not possible to mask participants, nurses, and researchers to treatment allocation.
Blinding of outcome assessment (detection bias) All outcomes	High risk	**Quote:** "surviving patients were sent a questionnaire. Patients not returning questionnaires within 2 weeks were telephoned by a second research nurse, blind to group allocation, and given the option of declining, having a further questionnaire posted, completing the questionnaire over the telephone, or receiving a home visit to assist" (p. 1957).
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Quote:** "where data were missing, imputations were performed as described previously" (p. 1958). **Comment:** ITT analysis reported
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported. No trial protocol available to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline demographic characteristics between groups

Wei 2021

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** psycho-cardiology + usual care **Control arm:** usual care
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** ischaemic and haemorrhagic stroke **Method of stroke diagnosis:** meets the diagnostic criteria of stroke in Guidelines for Diagnosis and Treatment of Acute Ischaemic Stroke in China 2018 confirmed by MRI and CT **Time since stroke:** 57 months **Depression criteria:** meets diagnostic criteria of depression in ICD-10 Classification of Mental and Behavioral Disorders and HDRS score ≥ 8 **Inclusion criteria:** (1) meets the diagnostic criteria of stroke in Guidelines for Diagnosis and Treatment of Acute Ischaemic Stroke in China 2018, and they were diagnosed by MRI and CT; (2) meets the diagnostic criteria of depression in ICD-10 Classification of Mental and Behavioral Disorders; (3) patients with elementary education level or above, can communicate and complete the in-study scale evaluation on their own or with the help of professionals); (4) HDRS score ≥ 8, and HARS score ≥ 7 and; (5) have signed the informed consent form for the study **Exclusion criteria:** (1) deaf-mute patients with severe arrhythmia, myocardial infarction, heart failure and coronary heart disease; (2) with severe hepatic and renal inadequacy; (3) with brain tumour; (4) who died during the study; (5) with suicidal tendencies; (6) with drug or alcohol dependence and psychoactive substance abuse and; (7) with comorbidities such as schizophrenia, bipolar disorder, and other severe mental disorders **Total number randomised in this trial:** 78

Wei 2021 *(Continued)*

	Number randomised to treatment group: 39 (41% men, mean age 68, SD 6.2) **Number randomised to control group:** 39 (46% men, mean age 68, SD 6.7) **Total number included in final analysis:** 78 **Number included in treatment group for final analysis:** 39 **Number included in control group for final analysis:** 39
Interventions	**Treatment:** psycho-cardiology (which included psychotherapy, behavioural therapy, exercise and relaxation) + usual care. **Administered by:** study nurse **Supervision:** not reported **Intervention fidelity:** not reported **Control:** usual care **Duration:** unclear **Follow-up:** unclear
Outcomes	**Primary outcomes** • Mental state measured using HDRS • Anxiety measured using HARS • Neurological function measured using NIHSS • Cognitive function measured using MMSE • Prognostic indicators measured using the Fugl-Meyer Assessment (FMA) and BI **Secondary outcomes** • Adverse events • Nursing satisfaction
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Quote:** "They were randomly divided into two groups according to the random number table method…" p. 8022.
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** blinding of participants and personnel not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** blinding of outcome assessors not reported
Incomplete outcome data (attrition bias)	Low risk	**Comment:** all participants were included in the analysis.

Wei 2021 *(Continued)*
All outcomes

Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Low risk	**Quote:** "There was no significant difference in the baseline data such as gender, age, course of stroke, type of stroke and underlying diseases between the two groups (P > 0.05)." p. 8024

Wiart 2000

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** fluoxetine (SSRI) **Control arm:** matched placebo
Participants	**Geographical location:** France **Setting:** not reported **Stroke criteria:** ischaemic stroke and primary intracerebral haemorrhage **Method of stroke diagnosis:** diagnosis via clinical signs and CT (100%) **Time since stroke:** 48 days **Inclusion criteria:** (1) all antidepressant or neuroleptic drugs stopped 10 days before enrolment **Exclusion criteria:** (1) severe psychiatric problems that required hospitalisation; (2) severe cognitive impairment; (3) chronic alcoholism; (4) chronic associated handicapping pathology; (5) contraindication to fluoxetine **Depression criteria:** psychiatric interview (ICD-10 criteria) and MADRS score > 19 **Total number randomised in this trial:** 31 **Number randomised to treatment group:** 16 (56% men, mean age 66 years, SD 7) **Number randomised to control group:** 15 (40% men, mean age 69 years, SD 12) **Total number included in final analysis:** 31 **Number included in treatment group for final analysis:** 16 **Number included in control group for final analysis:** 15
Interventions	**Treatment:** fluoxetine (SSRI) 20 mg daily **Control:** matched placebo **Duration:** 45 days **Follow-up:** none
Outcomes	**Primary outcomes** • Depression (change in scores from baseline to end of treatment, 50% reduction in score) measured using MADRS **Secondary outcomes**

Wiart 2000 *(Continued)*

- Functional capacity measured using FIM
- Cognitive function measured using MMSE
- Motor function measured using Motoricity Index
- Leaving the study early
- Adverse events
- Death

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Comment:** method of sequence generation not reported
Allocation concealment (selection bias)	Low risk	**Quote:** "treatment lasted up to 45 days (endpoint) and was given in the form of identical white capsules containing 20 mg of either fluoxetine or placebo, delivered in boxes coded by the central pharmacy of the University Hospital complex of Bordeaux" (p. 1829).
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Quote:** "treatment lasted up to 45 days (endpoint) and was given in the form of identical white capsules containing 20 mg of either fluoxetine or placebo, delivered in boxes coded by the central pharmacy of the University Hospital complex of Bordeaux" (p. 1829).
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Comment:** double-blind reported but who was blinded not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Quote:** "an intent-to-treat statistical analysis was conducted in which the last visit recorded was used as an endpoint" (p. 1830). **Comment:** missing data were handled using last-observation-carried-forward method.
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline demographic characteristics between groups

Wu 2019

Study characteristics

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** rTMS + cognitive therapy + routine stroke treatment **Control arm:** cognitive therapy + routine stroke treatment
Participants	**Geographical location:** China **Setting:** outpatient

Wu 2019 *(Continued)*

	Stroke criteria: ischaemic and haemorrhagic stroke **Method of stroke diagnosis:** meets stroke diagnostic criteria and confirmed by brain CT and MRI **Time since stroke:** 13 months **Depression criteria:** meets HDRS cut-off scores: < 7, no depression, > 17 mild or moderate depression, > 24 severe depression) and MADRS cut-off scores not described **Inclusion criteria:** (1) meets stroke diagnostic criteria and confirmed by brain CT and MRI; (2) stable condition; (3) age 40-85; (4) first stroke; (5) stable condition **Exclusion criteria:** (1) depression before stroke, organic brain disease such as brain tumour and previous psychiatric abnormalities; (2) severe cognitive and communication impairment, unable to cooperate; (3) recurrent stroke; (4) heart, lung, liver, kidney insufficiency and malignant hypertension and other complications that restrict activities **Total number randomised in this trial:** 82 **Number randomised to treatment group:** unclear (17.5% men, mean age 58, SD 12) **Number randomised to control group:** unclear (27.5% men, mean age 66, SD 9) **Total number included in final analysis:** 80 **Number included in treatment group for final analysis:** 40 **Number included in control group for final analysis:** 40
Interventions	**Treatment:***rTMS* (1200 pulses each time, 20 sequences, continuous stimulation 15 minutes each time, every day, location: right dorsolateral pre-frontal, for 4 weeks); + *cognitive therapy* (once a week, lasting for one hour, total 4 weeks): 1) understand depression severity, mood and emotional expression; 2) advise on unfavourable emotional expression, its negative effects, possible causes and corrective methods, and promote realistic behavior and understanding; 3) help to overcome negative emotions, change defensive behaviours, and facilitate to correct thinking patterns, reshape personality and beliefs; 4) encourage participation in entertainment activities, establish interests and hobbies, encourage family members to participate, form a joint participation model, and encourage them to build beliefs; + *routine stroke treatment*: anti-platelet aggregation, blood pressure control, blood sugar control and other treatments for ischemic stroke, dehydration to lower intracranial pressure, blood pressure adjustment, and prevention of continued bleeding for haemorrhagic stroke **Control:***cognitive therapy* (once a week, lasting for one hour, total 4 weeks): 1) Understand depression severity, mood and emotional expression; 2) Advise on unfavourable emotional expression, its negative effects, possible causes and corrective methods, and promote realistic behavior and understanding; 3) help to overcome negative emotions, change defensive behaviours, and facilitate to correct thinking patterns, reshape personality and beliefs; 4) encourage participation in entertainment activities, establish interests and hobbies, encourage family members to participate, form a joint participation model, and encourage them to build beliefs; + *routine stroke treatment*: anti-platelet aggregation, blood pressure control, blood sugar control and other treatments for ischemic stroke, dehydration to lower intracranial pressure, blood pressure adjustment, and prevention of continued bleeding for haemorrhagic stroke **Duration:** 4 weeks **Follow-up:** None
Outcomes	**Primary outcome** • Depression measured using 24-item HDRS and Montgomery Asberg Depression Rating Scale (MADRS) • Neurological function measured using NIHSS

Wu 2019 *(Continued)*

- Functional capacity measured using modified Rankin Scale

Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Comment:** using Excel random function to allocate experiment or control group according to visit sequences
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Comment:** double-blind method was used; scales were assessed by one single person who did not participate in allocation, treatment or analysis.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** blinding of outcome assessors not reported
Incomplete outcome data (attrition bias) All outcomes	High risk	**Comment:** 2/82 participants withdrew from the study due to poor compliance, but it was unclear what their group allocation was.
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Unclear risk	**Comment:** participants in the treatment group were younger than those in the control group (58.30 ± 11.90 vs. 66.10 ± 8.74, P = 0.0013), but had no significant differences in sex, time from stroke and stroke type.

Yang 2002

Study characteristics

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** paroxetine (SSRI) **Control arm:** matched placebo
Participants	**Geographical location:** China **Setting:** outpatient **Stroke criteria:** ischaemic and haemorrhagic stroke **Method of stroke diagnosis:** not reported **Time since stroke:** not reported **Inclusion criteria:** not reported **Exclusion criteria:** not reported **Depression criteria:** HDRS score > 7

Yang 2002 *(Continued)*

	Total number randomised in this trial: 121 **Number included in treatment group:** 64 (63% men, mean age 64 years, SD 3) **Number included in control group:** 57 (56% men, mean age 63 years, SD 5) **Total number included in final analysis:** 110 **Number included in treatment group for final analysis:** unclear **Number included in control group for final analysis:** unclear
Interventions	**Treatment:** paroxetine (SSRI) 20 mg daily **Control:** matched placebo **Duration:** 4 months **Follow-up:** none
Outcomes	**Primary outcomes** • Depression (50% reduction in scores from baseline to end of treatment) measured using HDRS
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Comment:** method of sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** blinding of participants and personnel not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** blinding of outcome assessment not reported
Incomplete outcome data (attrition bias) All outcomes	High risk	**Comment:** per-protocol analysis reported only; 11/121 (9%) excluded from analysis
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Unclear risk	**Comment:** no other bias detected

Yang 2013

Study characteristics

Methods	**Study design:** parallel design **Number of arms:** 2

Yang 2013 *(Continued)*

	Experimental arm: high-frequency rTMS + antidepressants **Control arm:** sham rTMS + antidepressants
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** ischaemic stroke **Method of stroke diagnosis:** confirmed brain CT or MRI **Time since stroke:** not reported **Inclusion criteria:** (1) 24-item HDRS score ≥ 8; (2) first stroke; (3) right-handedness; (4) clear consciousness; (5) able to express personal will **Exclusion criteria:** (1) history of epilepsy, metal implant in the body; (2) history or family history of psychiatric illness **Depression criteria:** 24-item HDRS score ≥ 8 **Total number randomised in this trial:** 38 **Number randomised to treatment group:** 19 (63% men; mean age 61, SD 8) **Number randomised to control group:** 19 (52.6% men; mean age 60, SD 9) **Total number included in final analysis:** 38 **Number included in treatment group for final analysis:** 19 **Number included in control group for final analysis:** 19
Interventions	**Treatment:** high-frequency rTMS + antidepressants. Frequency: 10 Hz, intensity: 80% motor threshold, 1 stimulation lasts 4.9 seconds and stops for 20 seconds, total impulse number: 1960/d, 16 minutes per day, for 10 working days, location: left DLPFC **Control:** sham rTMS + antidepressants. Keeping the coils at 90-degree angles with the scalp **Duration:** 2 weeks **Follow-up:** 4 weeks
Outcomes	**Primary outcomes** • Depression measured using HDRS
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Comment:** method of sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias)	Unclear risk	**Comment:** information about blinding of participants and personnel not reported

Yang 2013 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** information about blinding of outcome assessors not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** ITT analysis reported; no missing data
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline demographics between groups

Yang 2014a

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** high-frequency rTMS **Control arm:** sham rTMS
Participants	**Geographical location:** China **Setting:** mixed **Stroke criteria:** not reported **Method of stroke diagnosis:** clinical diagnosis plus confirmation by imaging that a relevant lesion needed to be visible **Time since stroke:** not reported **Inclusion criteria:** (1) meeting diagnostic criteria of the CCMD-3 for depression; (2) 24-item HDRS score ≥ 8; (3) first stroke; (4) clear consciousness; (5) able to express personal will and to sign informed consent **Exclusion criteria:** (1) history or family history of psychiatric illness; (2) unable to co-operate with the examination due to obvious aphasia or severe cognitive dysfunction; (3) history of epilepsy, metal implant in the body **Depression criteria:** meeting diagnostic criteria of the CCMD-3 for depression and 24-item HDRS score ≥ 8 **Total number randomised in this trial:** 56 **Number randomised to treatment group:** 37 (75.6% men; mean age 56.6, SD 13.6) **Number randomised to control group:** 19** (73% men; mean age 53.3, SD 14.6) **Total number included in final analysis:** 55 **Number included in treatment group for final analysis:** 37 **Number included in control group for final analysis:** 19**

Yang 2014a *(Continued)*

Interventions	**Treatment:** high-frequency rTMS. Frequency: 10 Hz, intensity: 90% motor threshold, 1 stimulation lasts 5 seconds and stops for 35 seconds, total impulse number: 1500, location: left DLPFC **Control:** sham rTMS. With coils kept at 90-degree angles with the scalp and with coils contacting the scalp, participants could hear the click sounds. **Duration:** 2 weeks **Follow-up:** 4 weeks
Outcomes	**Primary outcomes** • Depression measured using HDRS
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Comment:** method of sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** information about blinding of participants and personnel not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** information about blinding of outcome assessors not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** ITT analysis reported; no missing data
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline demographics between groups

Yang 2014b

Study characteristics

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** low-frequency rTMS **Control arm:** sham rTMS
Participants	**Geographical location:** China

Yang 2014b *(Continued)*

	Setting: mixed **Stroke criteria**: not reported **Method of stroke diagnosis:** clinical diagnosis plus confirmation by imaging that a relevant lesion needed to be visible **Time since stroke:** not reported **Inclusion criteria:** (1) meeting diagnostic criteria of the CCMD-3 for depression; (2) 24-item HDRS score ≥ 8; (3) first stroke; (4) clear consciousness; (5) able to express personal will and to sign informed consent **Exclusion criteria:** (1) history or family history of psychiatric illness; (2) unable to co-operate with the examination due to obvious aphasia or severe cognitive dysfunction; (3) history of epilepsy, metal implant in the body **Depression criteria:** meeting diagnostic criteria of the CCMD-3 for depression and 24-item HDRS score ≥ 8 **Total number randomised in this trial:** 55 **Number randomised to treatment group:** 37 (81% men; mean age 52.3, SD 11) **Number randomised to control group:** 18** (73% men; mean age 53.3, SD 14.6) **Total number included in final analysis:** 55 **Number included in treatment group for final analysis:** 37 **Number included in control group for final analysis:** 18**
Interventions	**Treatment:** low-frequency rTMS. Frequency: 1 Hz, intensity: 90% motor threshold, 1 stimulation lasts 10 seconds and stops for 2 seconds, total impulse number: 1000, location: left DLPFC **Control:** sham rTMS. With coils kept at 90-degree angles with the scalp and with coils contacting the scalp, participants could hear the click sounds. **Duration:** 2 weeks **Follow-up:** 4 weeks
Outcomes	**Primary outcomes** • Depression measured using HDRS
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Comment:** method of sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** information about blinding of participants and personnel not reported

Yang 2014b *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** information about blinding of outcome assessors not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** ITT analysis reported; no missing data
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline demographics between groups

Zhang 2013

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** rTMS + fluoxetine + stroke medications **Control arm:** fluoxetine + stroke medications
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** ischaemic and haemorrhagic stroke **Method of stroke diagnosis:** complying with diagnostic criteria for cerebral infarction and cerebral haemorrhage formulated by the Fourth National Conference on Cerebrovascular Diseases **Time since stroke:** not reported **Inclusion criteria:** (1) meeting diagnostic criteria of the CCMD-3 for depression; (2) 17-item HDRS score ≥ 17; (3) no history of psychiatric illness and history of drug abuse or alcohol; (4) not taking any antipsychotic drugs 2 weeks before enrolment; (5) relatively stable clinical condition, able to clearly express feelings, no communication obstacle; (6) age 40 to 70 years, Han ethnic group, co-operative during treatment, able to complete all exams and to sign informed consent, educational level: junior high school or above **Exclusion criteria:** not reported **Depression criteria:** meeting diagnostic criteria of the CCMD-3 for depression and 17-item HDRS score ≥ 17 **Total number randomised in this trial:** 82 **Number randomised to treatment group:** 41 (56% men; mean age 56.9, SD 5.8) **Number randomised to control group:** 41 (53.6% men; mean age 57.7, SD 6.6) **Total number included in final analysis:** 82 **Number included in treatment group for final analysis:** 41 **Number included in control group for final analysis:** 41

Zhang 2013 *(Continued)*

Interventions	**Treatment:** rTMS + fluoxetine (20 mg/d) + stroke medications. Frequency: 10 Hz, intensity: 90% motor threshold, 1 stimulation lasts 4 seconds in 1 series, 20 series a day, 3 times a week, location: left DLPFC **Control:** fluoxetine + stroke medications **Duration:** 8 weeks **Follow-up:** none
Outcomes	**Primary outcome** • Depression measured using HDRS
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Comment:** random number table used for sequence generation
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** information about blinding of participants and personnel not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** information about blinding of outcome assessors not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** ITT analysis reported; no missing data
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline demographics between groups

Zhao 2004

Study characteristics

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** psychoeducation **Control arm:** usual care
Participants	**Geographical location:** China **Setting:** inpatient

Zhao 2004 *(Continued)*

	Stroke criteria: not reported **Method of stroke diagnosis:** diagnosis via CT or MRI (100%) **Time since stroke:** not reported **Inclusion criteria:** (1) cognitively competent; (2) no acute medical problems **Exclusion criteria:** (1) serious mental problems; (2) low intelligence; (3) other serious neurological condition; (4) heart failure; (5) other acute disease **Depression criteria:** HDRS score > 17 **Total number randomised in this trial:** 70 **Number randomised to treatment group:** 35 (57% men, mean age 65 years, SD 13) **Number randomised to control group:** 35 (51% men, mean age 61 years, SD 14) **Total number included in final analysis:** 70 **Number included in treatment group for final analysis:** 35 **Number included in control group for final analysis:** 35
Interventions	**Treatment:** psychoeducation, daily, less than 30 minutes **Administered by:** special personnel who received 2 weeks training before the trial started **Supervision:** not reported **Intervention fidelity:** unclear; no formal evaluation of the quality or content of therapy provided **Control:** usual care **Duration:** 4 weeks **Follow-up:** none
Outcomes	**Primary outcomes** • Depression (reduction in scores from baseline to end of treatment) measured using HDRS
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Comment:** method of sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	**Comment:** single-blind reported; participants not blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Comment:** outcome assessment blinded

Zhao 2004 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** ITT analysis reported (complete follow-up of all randomised participants)
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline demographic characteristics between groups

Zheng 2016

Study characteristics	
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** intra-low frequency (ILF)-TMS + cerebrovascular disease routine care + early rehabilitation **Control arm:** cerebrovascular disease routine care + early rehabilitation
Participants	**Geographical location:** China **Setting:** inpatient **Number of participants:** 82 **Stroke criteria:** ischaemic and haemorrhagic stroke **Method of stroke diagnosis:** complying with diagnostic criteria for cerebral infarction and cerebral haemorrhage formulated by the Fourth National Conference on Cerebrovascular Diseases **Time since stroke:** not reported **Inclusion criteria:** (1) meeting diagnostic criteria of the CCMD-3 for depression; (2) stable vital signs, ability to understand and perform rehabilitation **Exclusion criteria:** (1) history of psychiatric illness; (2) dementia; (3) severe physical illness; (4) history of epilepsy **Depression criteria:** meeting diagnostic criteria of the CCMD-3 for depression **Total number randomised in this trial:** 82 **Number randomised to treatment group:** 41 (56% men; mean age 63.8, SD 8.5) **Number randomised to control group:** 41 (60% men; mean age 64.3, SD 6.9) **Total number included in final analysis:** 82 **Number included in treatment group for final analysis:** 41 **Number included in control group for final analysis:** 42
Interventions	**Treatment:** intra-low frequency (ILF)-TMS + cerebrovascular disease routine care + early rehabilitation. Frequency: < 0.2 Hz, 20 minutes per treatment, and 1 treatment per day, at least 5 times a week, lasting for 2 successive courses **Control:** cerebrovascular disease routine care + early rehabilitation

Zheng 2016 *(Continued)*

	Duration: 4 weeks **Follow-up:** none
Outcomes	**Primary outcomes** • Depression measured using HDRS • Impairment measured using SSS
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Comment:** method of sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	**Comment:** method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** information about blinding of participants and personnel not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** information about blinding of outcome assessors not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** ITT analysis reported; no missing data
Selective reporting (reporting bias)	Unclear risk	**Comment:** all prespecified outcomes reported; no trial protocol available to compare with the publication
Other bias	Low risk	**Comment:** no differences in baseline demographics between groups

** Results for control group halved
^ Results for attention control and control group pooled
ABI: acquired brain injury
ADL: activities of daily living
AE: adverse event
AHI: Authentic Happiness Inventory
BA: Behavioural activation
BDI: Beck Depression Inventory
BI: Barthel Index
BZDs: benzodiazepines
CBT: cognitive-behavioural therapy
CCMD-2-R: Chinese Classification of Mental Disorders, Second Edition, Revised
CCMD-3: Chinese Classification of Mental Disorders, Third Edition
CGI: Clinical Global Impression Scale
CIPI: constructive integrative psychosocial intervention
CNS: central nervous system
CSI: Caregiver Strain Index
CSS: Chinese Stroke Scale
CST: Consent support tool
CT: computed tomography

CTCBI: Community Treatment Centre for Brain Injury
DASS-21: Depression Anxiety Stress Scales - 21 items
DLPFC: dorsolateral pre-frontal cortex
DSM: Diagnostic and Statistical Manual
EADL: extended activities of daily living
EEG: electroencephalogram
EFT: ecosystem focused therapy
EQ5D-5L: EuroQol 5 dimensions 5 levels version
ESD: Education on Stroke and Depression
FAC: Functional Ambulatory Category
FIM: Functional Independence Measure
FMA: Fugl-Meyer Assessment
GCS: Glasgow Coma Scale
GDS: Geriatric Depression Scale
GHQ-28: 28-item General Health Questionnaire
HADS: Hospital Anxiety Depression Scale
HAMD: Hamilton Depression Scale
HARS: Hamilton Anxiety Rating Scale
HCl: Hydrochloride
HDRS-24: 24-item Hamilton Depression Rating Scale
HDRS-17: 17-item Hamilton Depression Rating Scale
HRQoL: health-related quality of life
Hz: Hertz
ICD: International Classification of Diseases
ILF: intra-low frequency
ITT: intention-to-treat
LE: lower extremity
LOCF: last-observation-carried-forward
LTF: loss to follow-up
MADRS: Montgomery Asberg Depression Rating Scale
MBC: Modified Brunnstrom Classification
MBI: Modified Barthel Index
MI: motivational interviewing
min: minimum
MMSE: Mini Mental State Examination
MoCA: Montreal Cognitive Assessment Scale
MPAI-4: Mayo-Portland Adaptability Inventory-4
MRI: magnetic resonance imaging
n/a: not applicable
NIHSS: National Institute of Health Stroke Scale
NRI: norepinephrine reuptake inhibitor
P300: the P300 is a wave that represents a positive deflection in the human event-related potential. It is most commonly elicited when a patient detects an occasional "target" stimulus in a regular train of standard stimuli
PHQ-9: 9-item Patient Health Questionnaire
PMES: percutaneous mastoid electrical stimulation
PROBE: prospective, randomised open-blinded endpoint
PSD: post-stroke depression
PSE: Present State Examination
QoL: quality of life
RA: research assistant
RMT: resting motor threshold
rTMS: repetitive transcranial magnetic stimulation
s: seconds
SAD-Q: Stroke Aphasia Depression Questionnaire
SAH: subarachnoid haemorrhage
SAQoL: Stroke Aphasia Quality of Life Scale
SCAN: Schedules for Clinical Assessment in Neuropsychiatry
SD: standard deviation
SDS: Severity of Dependence Scale
SE: standard error
SF-36: 36-item short form survey
SNRI: selective norepinephrine reuptake inhibitor

SSEQ: Stroke Self Efficacy Questionnaire
SSRI: selective serotonin reuptake inhibitor
SSS: Scandinavian Stroke Scale
TCA: tricyclic antidepressant
tDCS: Transcranial direct current stimulation
TMS: transcranial magnetic stimulation
TMSE: Thai Mental State Examination
UE: upper extremity
VAMS: Visual Analogue Mood Scale
VAS: visual analogue scale (100 mm)
WDI: Wakefield Depression Inventory
WHO: World Health Organization
WHODAS- II: World Health Organization Disability Assessment Schedule
WHOQoL-BREF: abbreviated World Health Organization quality of life questionnaire
ZDS: Zung Depression Scale

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Aben 2014	Depression not the primary outcome of this study
ACTRN12615000840583	Not RCT
ACTRN12620001174976	Not RCT
Agnoli 1985	Unable to isolate data for stroke patients only
Bai 2017	Depression not the primary outcome of this study
Bai 2019	Not RCT
Beauchamp 2020	Intervention did not meet the criteria.
Bramanti 1989	Data were not available for depressed participants only.
Casella 1960	Depression not the primary outcome of this study
Chalmers 2019	Not RCT
Chang 2011	Data were not available for depressed participants only.
Chen 2019	Intervention did not meet the criteria.
Cheng 2016	Depression was not the primary outcome of this study.
Cheng 2020	Intervention did not meet the criteria.
ChiCTR1800016101	Intervention aimed to prevent depression.
ChiCTR1800017752	Intervention did not meet the criteria.
ChiCTR1800019366	Not RCT
ChiCTR1900021168	No sham group
ChiCTR1900026358	Not RCT

Study	Reason for exclusion
ChiCTR2000029450	No placebo control group
ChiCTR2000029554	Intervention did not meet the criteria.
ChiCTR2000035588	Intervention did not meet the criteria.
ChiCTR2000036944	Intervention did not meet the criteria.
ChiCTR2000039143	Not RCT
ChiCTR2000039459	No sham control group
ChiCTR2100042684	Depression was not the primary outcome of the study.
Choi-Kwon 2006	Data were not available for depressed participants only.
Chollet 2011	Depression was not the primary outcome of this study.
Clark 2003	Data were not available for depressed participants only.
CTRI/2021/02/031410	Intervention did not meet the criteria.
da SilvaJunior 2019	No sham control group
Delbari 2011	Data were not available for depressed participants only.
Doshi 2019	Intervention did not meet the criteria.
Downes 1995	Data were not available for depressed participants only.
EUCTR2005-005266-37-DE	Intervention aimed to prevent depression.
EUCTR2014-000846-32-ES	Depression was not the primary outcome of the study.
Evans 1997	Unable to isolate data for stroke patients only
Finkenzeller 2006	Depression assessments not available at a consistent time point
Franco 2001	Letter to the editor
Frey 2020	Not RCT
Gamberini 2021	Depression was not the primary outcome of the study.
Griffin-Musick 2020	Not RCT
Gustafsson 2020	Intervention did not meet the criteria.
Hadidi 2014	Data were not available for depressed participants only.
He 2004	Intervention aimed to prevent depression.
He 2021	No control group
Hilari 2021	Intervention did not meet the criteria.

Study	Reason for exclusion
Hill 2019	Intervention aimed to prevent depression.
Hjelle 2019	Data not available for depressed participants only.
Hu 2003	Depression not the primary outcome of this study
ISRCTN60046672	No placebo control group
ISRCTN88489864	Depression was not the primary outcome of this study.
Jiang 2004	Depression was not the primary outcome of this study.
Jorge 2004	Data were not available for depressed participants only.
Jorge 2008	Data were not available for depressed participants only.
JPRN-UMIN000013200	Not RCT
JPRN-UMIN000027051	Included a different patient population in the study
JPRN-UMIN000029117	Intervention did not meet the criteria.
Kim 2010a	Data were not available for depressed participants only.
Kim 2010b	Data were not available for depressed participants only.
Kim 2017	Data were not available for depressed participants only.
Kim 2017a	Data were not available for depressed participants only.
Kim 2019	Data were not available in a format suitable for meta-analysis.
Kok 2021	Letter to the editor
Konigsberg 2021	Depression was not the primary outcome of the study.
Kootker 2012	Data were not available in the format suitable for meta-analysis.
Laska 2005	Depression was not the primary outcome of this study.
Leijon 1989	Depression was not the primary outcome of this study.
Li 2016	Results not available in format suitable for this review
Li 2021	Intervention did not meet the criteria.
Liang 2003	No placebo control group
Lobjanidze 2010	Depression was not the primary outcome of this study.
Majumdar 2019	Intervention did not meet the criteria.
Mauri 1988	Data were not available in a format suitable for meta-analysis.
Meara 1998	Data were not available for depressed participants only.

Study	Reason for exclusion
Morariu 2019	Intervention aimed to prevent depression.
Narushima 2007	Depression was not the primary outcome of this study.
NCT00071643	Intervention aimed to prevent depression.
NCT00177424	Intervention aimed to prevent depression.
NCT02947776	Intervention aimed to prevent depression.
NCT03256305	No sham rTMS or usual care
NCT03500250	Depression was not the primary outcome of the study.
NCT03615079	No control group
NCT03750526	Intervention aimed to prevent depression.
NCT03761303	Trial was withdrawn (no eligible patients could be recruited).
NCT03826875	Intervention aimed to prevent depression.
NCT03864484	Intervention did not meet the criteria.
NCT03910855	Intervention did not meet the criteria.
NCT03956693	Intervention did not meet the criteria.
NCT04011202	Intervention did not meet the criteria.
NCT04302493	Intervention aimed to prevent depression.
NCT04318951	Intervention did not meet the criteria.
NCT04567472	No control group
NCT04655937	Depression was not the primary outcome of the study.
NCT04713020	Intervention did not meet the criteria.
NCT04776226	Depression was not the primary outcome of the study.
Niimi 2020	Intervention aimed to prevent depression.
Ohtomo 1985	Data were not available for depressed participants only.
Ostwald 2014	Data were not available for depressed participants only.
Otomo 1986	Intervention aimed to prevent depression.
Poalelungi 2020	Intervention did not meet the criteria.
Raffaele 1996	Data were not available for depressed participants only.
Rich 2016	Depression was not the primary outcome of this study.

Study	Reason for exclusion
Robinson 2000	Data were not available for depressed participants only.
Robinson 2017	Depression was not the primary outcome of this study.
Rudberg 2017	Depression was not the primary outcome of this study.
Sieger 2018	Depression was not the primary outcome of this study.
Sivenius 2001	Depression was not the primary outcome of this study.
Slenders 2019	Intervention did not meet the criteria.
Sonis 2004	Letter to the editor
Su 2004a	Depression was not the primary outcome of this study.
Sun 2000	Data were not available for depressed participants only.
Szepfalusi 2017	Depression was not the primary outcome of this study.
TCTR20181216001	Intervention was aimed at preventing depression.
Tian 2016	No placebo control group
Uchida 2020	Intervention did not meet the criteria.
Visser 2015	Depression was not the primary outcome of this study.
Vranceanu 2020	Depression was not the primary outcome of the study.
Walker-Batson 1995	Depression was not the primary outcome of this study.
Wang 2003	Intervention did not meet the criteria.
Wang 2009	Depression was not the primary outcome of this study.
Wang 2020	Intervention did not meet the criteria.
Wu 2012	Intervention did not meet the criteria.
Xie 2005	No placebo control group
Xu 2010	Not RCT
Yao 2021	No placebo control group
Ye 2004	No placebo control group
Yu 2021	Results not available in format suitable for this review
Zhang 2013a	No placebo control group
Zhou 2004	Intervention did not meet the criteria.

RCT: randomised controlled trial

Characteristics of studies awaiting classification *[ordered by study ID]*

Chen 2002a

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** paroxetine (SSRI) **Control arm:** placebo
Participants	**Geographical location:** China **Setting:** unclear **Number of participants:** 36 **Stroke criteria:** unclear **Method of stroke diagnosis:** not reported **Inclusion criteria:** not reported **Exclusion criteria:** (1) cognitive impairment (MMSE < 24); (2) depression deterioration (HDRS > 24); (3) suicidal mood; (4) drug intolerability **Depression criteria:** unclear **Total number randomised in this trial:** 36 **Number randomised to treatment group:** 24 **Number randomised to control group:** 12** **Total number included in final analysis:** 34 **Number included in treatment group for final analysis:** 24 **Number included in control group for final analysis:** 10**
Interventions	**Treatment:** paroxetine (SSRI) 200 mg once daily **Control:** placebo (guvitamine) 10 mg 3 × daily **Duration:** 8 weeks **Follow-up:** none
Outcomes	**Primary outcomes** • Depression measured using HDRS **Secondary outcomes** • Disability measured using BI • Impairment measured using CSS
Notes	Unable to obtain information on the primary outcome: whether depression or functional recovery

Chen 2002b

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** doxepin **Control arm:** placebo
Participants	**Geographical location:** China **Setting:** unclear **Number of participants:** 36 **Stroke criteria:** unclear **Method of stroke diagnosis:** not reported **Inclusion criteria:** not reported **Exclusion criteria:** (1) cognitive impairment (MMSE < 24); (2) depression deterioration (HDRS > 24); (3) suicidal mood; (4) drug intolerability **Depression criteria:** unclear **Total numbers randomised in this trial:** 36 **Numbers randomised to treatment group:** 24 **Numbers randomised to control group:** 12** **Total numbers included in final analysis:** 26 **Numbers included in treatment group for final analysis:** 16 **Numbers included in control group for final analysis:** 10**
Interventions	**Treatment:** doxepin 25 mg 3 × daily **Control:** placebo (guvitamine) 10 mg 3 × daily **Duration:** 8 weeks **Follow-up:** none
Outcomes	**Primary outcome** • Depression measured using HDRS **Secondary outcomes** • Disability measured using BI • Impairment measured using CSS
Notes	Unable to obtain information on the primary outcome: whether depression or functional recovery

Ding 2005

Methods	**Study design:** parallel design **Number of arms:** 2

Ding 2005 *(Continued)*

	Treatment arm: paroxetine (SSRI) + psychotherapy + education **Control arm:** paroxetine (SSRI)
Participants	**Geographical location:** China **Setting:** outpatient **Stroke criteria:** ischaemic and haemorrhagic stroke **Method of stroke diagnosis:** clinical diagnosis with imaging consistent with stroke using Oxford Community Stroke Project classification and structural brain CT classification (by anatomical location) **Time since stroke:** 2 to 6 months **Inclusion criteria:** (1) meeting depression diagnostic criteria of the CCMD-3 and 17-item HDRS score > 17) **Exclusion criteria:** (1) bipolar disorders; (2) drug dependence or abuse **Depression criteria:** psychiatric interview; meeting depression diagnostic criteria of the CCMD-3; 17-item HDRS score > 17; HARS score > 7; clinical impression **Total number randomised in this trial:** 68 **Number randomised to treatment group:** 34 (56% men; mean age 61.3 years, SD 9.3) **Number randomised to control group:** 34 (47% men; mean age 60.5 years, SD 10.4) **Total number included in final analysis:** 68 **Number included in treatment group for final analysis:** 34 (56% men; mean age 61.3 years, SD 9.3) **Number included in control group for final analysis:** 34 (47% men; mean age 60.5 years, SD 10.4)
Interventions	**Treatment:** combination of paroxetine (SSRI, variable dose, started from 10 mg/d, titrated up to 20 to 30 mg/d) + psychotherapy: combination of cognitive therapy targeted at beliefs about stroke depression; behavioural therapy targeted at attitudes in practice and education. Psychotherapy was delivered in 40 to 60-minute sessions, 2 to 3 sessions a week **Administered by:** a professional physician; training in psychotherapy unclear **Supervision of therapists:** not reported **Intervention fidelity:** not reported **Control:** paroxetine (SSRI, variable dose, started from 10 mg/d, titrated up to 20 to 30 mg/d) **Duration:** 8 weeks **Follow-up:** 4 months
Outcomes	**Primary outcomes** • Depression measured using HDRS **Secondary outcomes** • Anxiety measured using HARS • Activities of daily living measured using BI • Symptoms measured using Treatment Emergent Symptom Scale

Ding 2005 *(Continued)*

Notes	Unable to obtain information to determine if the psychotherapy component of the intervention met the review criteria for psychotherapy

Evans 1985

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** telephone counselling **Control arm:** usual care
Participants	**Geographical location:** USA **Setting:** outpatient **Stroke criteria:** unclear (also includes people with spinal cord injury, CNS disease, and 'other') **Method of stroke diagnosis:** not reported **Inclusion criteria:** (1) patients discharged from rehabilitation centre; (2) housebound; (3) able to hear; (4) ordinary speech; (5) sufficient cognitive ability to engage in meaningful conversation **Exclusion criteria:** not reported **Depression criteria:** score taken from the Life Satisfaction Index (LSI); unclear how scored **Total number randomised in this trial:** 38 **Number randomised to treatment group:** 19 (95% men, mean age 54.8 years, SD 11.9 years); 4 with stroke **Number randomised to control group:** 19 (95% men, mean age 54.8 years, SD 10.2 years); 5 with stroke **Total number included in final analysis:** unclear **Number included in treatment group for final analysis:** unclear **Number included in control group for final analysis:** unclear
Interventions	**Treatment:** 8-weekly hour-long counselling sessions by phone with groups of 4 patients. Formulation of behaviorally specific goals encouraged and developed with each patient, and discussion directed at finding ways to meet those goals **Administered by:** an experienced counsellor **Supervision:** not reported **Control:** usual care (no contact) **Duration:** not reported **Follow-up:** not reported
Outcomes	**Primary outcome** • Depression - unclear what measure was used

Evans 1985 *(Continued)*

Notes	Unable to obtain any more information on this trial or series of trials despite multiple attempts since 2003

Finkenzeller 2009

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** sertraline (SSRI) + psychological therapy **Control arm:** sertraline (SSRI)
Participants	**Geographical location:** Germany **Setting:** inpatient **Stroke criteria:** all subtypes **Method of stroke diagnosis:** unclear **Time since stroke:** < 3 months **Inclusion criteria:** (1) onset of stroke no longer than 3 months **Exclusion criteria:** (1) previous or current psychiatric disorder like substance abuse, borderline or antisocial personality disorder, or other prominent Axis I disorder; (2) with previous depressive disorder, only if participants were still treated with antidepressive medication for this matter; (3) stronger cognitive impairment (e.g. dementia, aphasia, delirium) (no defined criteria or cut-off) **Depression criteria:** HADS > 7 on the subscale Depression, HDRS score > 13 **Total number randomised in this trial:** 21 **Number randomised to treatment group:** 9 (39% men, mean age 64.7, SD 11.1) **Number randomised to control group:** 12 (50% men, mean age 71.7, SD 7.1) **Total number included in final analysis:** 21 **Number included in treatment group for final analysis:** 9 (39% men, mean age 64.7, SD 11.1) **Number included in control group for final analysis:** 12 (50% men, mean age 71.7, SD 7.1)
Interventions	**Treatment:** sertraline (SSRI) 50 mg/d + psychological therapy (twice a week) **Administered by:** not reported **Supervision:** not reported **Intervention fidelity:** not reported **Control:** sertraline (SSRI) **Duration:** 4 to 8 weeks **Follow-up:** none
Outcomes	**Primary outcomes** • Depression (response > 50% reduction in initial score) measured using HDRS

Finkenzeller 2009 *(Continued)*

	• Depression (remission) measured using HDRS (< 8)
Notes	Unable to obtain information to determine if the psychotherapy component of the intervention met the review criteria for psychotherapy

Hanspal 2007

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** sertraline (SSRI) **Control arm:** placebo
Participants	**Geographical location:** UK **Setting:** unclear **Stroke criteria:** unclear (also includes people with non-vascular events such as trauma, hypoxia, or encephalitis) **Method of stroke diagnosis:** not reported **Inclusion criteria:** not reported **Exclusion criteria:** not reported **Depression criteria:** unclear **Total number randomised in this trial:** unclear **Number randomised to treatment group:** unclear **Number randomised to control group:** unclear **Total number included in final analysis:** unclear **Number included in treatment group for final analysis:** unclear **Number included in control group for final analysis:** unclear
Interventions	**Treatment:** sertraline (SSRI) **Control:** placebo **Duration:** not reported **Follow-up:** not reported
Outcomes	**Primary outcome** • Depression: unclear what measure was used
Notes	Unable to obtain any more information on this trial despite multiple attempts since 2007

He 2003

Methods	**Study design:** parallel design

He 2003 *(Continued)*

	Number of arms: 2 **Treatment arm:** amitriptyline (TCA) + psychological intervention + routine drugs for cerebrovascular disease **Control arm:** amitriptyline (TCA) + routine drugs for cerebrovascular disease
Participants	**Geographical location:** China **Setting:** unclear **Stroke criteria:** cerebral infarction and haemorrhage **Method of stroke diagnosis:** stroke diagnosed according to the standards of National Fourth Cerebral Vascular Disease Meeting of Chinese Medical Association in 1995 **Inclusion criteria:** (1) score > 8 in the CCMD-2-R **Exclusion criteria:** (1) history of mental disorder; (2) patients with coma, anepia, intelligence disorder; (3) patients with severe disease of heart, liver, and lung **Depression criteria:** score > 8 in the CCMD-2-R **Total number randomised in this trial:** 67 **Number randomised to treatment group:** 35 (54.3% men, mean 64 years, SD 9) **Number randomised to control group:** 32 (percentage of men and mean age not reported for this group) **Total number included in final analysis:** unclear **Number included in treatment group for final analysis:** unclear **Number included in control group for final analysis:** unclear
Interventions	**Treatment:** amitriptyline (TCA + psychological intervention + routine drugs for cerebrovascular disease). Psychological intervention included (1) treatment of cognitive behaviour; (2) supportive psychological treatment; (3) education about hypertension, coronary heart disease, and diabetes; (4) education about psychological hygiene **Administered by:** not reported **Supervision:** not reported **Intervention fidelity:** not reported **Control:** amitriptyline (TCA) + routine drugs for cerebrovascular disease **Duration:** 6 weeks **Follow-up:** none
Outcomes	**Primary outcomes** • Depression measured using HDRS • Activities of daily living (unclear what measure was used)
Notes	Unable to obtain information on the intervention of this trial

He 2005

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** paroxetine (SSRI) **Control arm:** psychotherapy + paroxetine (SSRI)
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** ischaemic stroke and cerebral haemorrhage **Method of stroke diagnosis:** first-ever stroke with a diagnosis consistent with diagnostic criteria for cerebral infarct formulated by the Fourth National Conference on Cerebrovascular Disease and confirmation by brain CT or MRI **Time since stroke:** not reported **Inclusion criteria:** (1) first-ever stroke; (2) meeting organic depressive disorder/organic anxiety disorder diagnostic criteria of ICD-10; (3) 17-item HDRS score ≥ 17; HARS score ≥ 14 **Exclusion criteria:** (1) history of psychiatric illness; (2) taking antidepressants and neuroleptics in the previous 3 months; (3) aphasia; (4) severe cognitive impairment; (5) allergy to paroxetine; (6) suicidal behaviour; (7) in a coma **Depression criteria:** meeting organic depressive disorder/organic anxiety disorder diagnostic criteria of ICD-10 and 17-item HDRS score ≥ 17; HARS score ≥ 14 **Total number randomised in this trial:** 54 **Number randomised to treatment group:** 27 (52% men; mean age 64, SD 5.3) **Number randomised to control group:** 27 (52% men; mean age 62.4, SD 6.1) **Total number included in final analysis:** 54 **Number included in treatment group for final analysis:** 27 **Number included in control group for final analysis:** 27
Interventions	**Treatment:** combined psychotherapy (early supportive psychotherapy (1 × 30 minutes session/week) + paroxetine (SSRI) 20 mg/d **Administered by:** not reported **Supervision:** not reported **Intervention fidelity:** not reported **Control:** paroxetine (SSRI) 20 mg/d **Duration:** 6 weeks **Follow-up:** none
Outcomes	**Primary outcomes** • Depression measured using HDRS • Anxiety measured by HARS **Secondary outcomes** • Symptoms measured using Treatment Emergent Symptom Scale

He 2005 *(Continued)*

	• Disability measured using BI • Impairment measured using SSS
Notes	Unable to obtain information to determine if the psychotherapy component of the intervention met the review criteria for psychotherapy

Huang 2005

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** venlafaxine (SNRI) + cognitive therapy **Control arm:** venlafaxine (SNRI)
Participants	**Geographical location:** China **Setting:** mixed **Stroke criteria:** ischaemic stroke only **Method of stroke diagnosis:** first-ever stroke with diagnosis consistent with diagnostic criteria for cerebral infarct formulated by the Fourth National Conference on Cerebrovascular Disease and confirmation by brain CT or MRI **Time since stroke:** not reported **Inclusion criteria:** (1) first-ever stroke; (2) depression developed in the acute stage of cerebral infarct; (3) HDRS score ≥ 18 **Exclusion criteria:** (1) history of psychiatric illness; (2) dementia; (3) aphasia; (4) consciousness disturbance; (5) apraxia; (6) other organic disease; (7) systematic disease; (8) depression developed in the acute stage of cerebral infarct **Depression criteria:** HDRS score ≥ 18; depression developed in the acute stage of cerebral infarct **Total number randomised in this trial:** 82 **Number randomised to treatment group:** 41 (% men not reported, mean age 62.2 years, SD 8.3) **Number randomised to control group:** 41 (% men not reported, mean age 61.8 years, SD 8.7) **Total number included in final analysis:** 80 **Number included in treatment group for final analysis:** 40 (63% men, mean age not reported) **Number included in control group for final analysis:** 40 (61% men, mean age not reported)
Interventions	**Treatment:** venlafaxine (SNRI) 121.56 mg/d + combined cognitive therapy (more than 1 hour every session, 1 session/week initially, 1 session fortnightly 1 month later, and 1 to 2 sessions/month 2 months later) **Administered by:** not reported **Supervision:** not reported **Intervention fidelity:** not reported **Control:** venlafaxine (SNRI) 121.56 mg/d **Duration:** 3 months

Huang 2005 *(Continued)*

	Follow-up: none
Outcomes	**Primary outcomes** • Depression measured using HDRS **Secondary outcomes** • Symptoms measured using Treatment Emergent Symptom Scale
Notes	Unable to obtain information to determine if the psychotherapy component of the intervention met the review criteria for psychotherapy

IRCT201008214607N1

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** Citalopram (SSRI) 20-80 mg/d + cognitive behaviour therapy **Control arm:** Citalopram (SSRI) 20-80 mg/d
Participants	**Geographical location:** Iran **Setting:** not reported **Stroke criteria:** not reported **Method of stroke diagnosis:** not reported **Inclusion criteria:** (1) diagnosis of post-stroke depression by neurologist and DSM IV-TR criteria; (2) stroke clinical symptoms with findings of damage in brain CT scan or MRI **Exclusion criteria:** (1) severe motor or sensory deficit; (2) aphasia; (3) loss of consciousness **Depression criteria:** diagnosed according to DSM IV-TR
Interventions	**Treatment:** Citalopram (SSRI) 20-80 mg/d + cognitive behaviour therapy **Control:** Citalopram (SSRI) 20-80 mg/d **Duration:** 3 months **Follow-up:** 3 months
Outcomes	**Primary outcome** • Depression measured using BDI
Notes	Unable to locate the published results of the trial

Katz 1998

Methods	**Study design:** unclear **Number of arms:** 4 **Experimental arm 1:** group psychotherapy

Katz 1998 *(Continued)*

	Experimental arm 2: behavioural therapy **Experimental arm 3:** combined antidepressant and individual psychotherapy plus group psychotherapy **Control arm:** unclear
Participants	**Geographical location:** unclear **Setting:** unclear **Stroke criteria:** unclear **Method of stroke diagnosis:** unclear **Inclusion criteria:** not reported **Exclusion criteria:** not reported **Depression criteria:** unclear **Total number randomised in this trial:** unclear **Number randomised to treatment group:** unclear **Number randomised to control group:** unclear **Total number included in final analysis:** unclear **Number included in treatment group for final analysis:** unclear **Number included in control group for final analysis:** unclear
Interventions	**Treatment 1:** group psychotherapy **Treatment 2:** behavioural therapy **Treatment 3:** combined antidepressant and individual psychotherapy plus group psychotherapy **Control:** unclear **Duration:** not reported **Follow-up:** not reported
Outcomes	**Primary outcome** • Depression - unclear what measure was used
Notes	Unable to obtain any more information on this trial or series of trials despite multiple attempts since 2002

Kuriakose 2020

Methods	**Study design:** prospective randomised controlled study **Number of arms:** 2 **Experimental arm:** active tDCS **Control arm:** sham tDCS

Kuriakose 2020 *(Continued)*

Participants	**Geographical location:** USA **Setting:** unclear **Stroke criteria:** acute hemiplegic stroke with onset 5-15 days **Method of stroke diagnosis:** not reported **Inclusion criteria:** not reported **Exclusion criteria:** not reported **Depression criteria:** not reported **Total number randomised in this trial:** 2 **Number randomised to treatment group:** 1 **Number randomised to control group:** 1 **Total number included in final analysis:** 2 **Number included in treatment group for final analysis:** 2 **Number included in control group for final analysis:** 2
Interventions	**Treatment:** active tDCS **Control:** sham tDCS **Duration:** 5 days **Follow-up:** unclear
Outcomes	**Primary outcomes** • Unclear
Notes	Unable to obtain information on the primary outcome: whether depression or functional recovery

Latow 1983

Methods	**Study design:** unclear **Number of arms:** unclear **Experimental arm:** psychotherapy **Control arm:** unclear
Participants	**Geographical location:** unclear **Setting:** unclear **Stroke criteria:** unclear **Method of stroke diagnosis:** not reported **Inclusion criteria:** not reported **Exclusion criteria:** not reported

Latow 1983 *(Continued)*

	Depression criteria: unclear **Total number randomised in this trial:** unclear **Number randomised to treatment group:** unclear **Number randomised to control group:** unclear **Total number included in final analysis:** unclear **Number included in treatment group for final analysis:** unclear **Number included in control group for final analysis:** unclear
Interventions	**Treatment:** psychotherapy **Control:** unclear **Duration:** unclear **Follow-up:** unclear
Outcomes	**Primary outcome** • Depression - unclear what measure was used
Notes	Unable to obtain a copy of this article, which also may be a book

Lee 2005

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** rTMS **Control arm:** sham stimulation
Participants	**Geographical location:** Republic of Korea **Setting:** not reported **Stroke criteria:** ischaemic stroke **Method of stroke diagnosis:** radiological diagnosis of location of infarct was given, but it was unclear whether this was used to make the diagnosis **Inclusion criteria:** (1) patients who did not respond to conventional antidepressant medication (paroxetine 20 mg/d); (2) Rancho Los Amogos cognitive function scale more than VIIa **Exclusion criteria:** (1) history of psychiatric illness; (2) aphasia; (3) arrhythmia; (4) left pre-frontal cortical lesion; (5) seizure or internal metallic device **Depression criteria:** BDI > 17 **Total number randomised in this trial:** 20 **Number randomised to treatment group:** 10 (70% men, mean age 67.8, SD 2.3) **Number randomised to control group:** 10 (60% men, mean age 66.3, SD 3.0) **Total number included in final analysis:** unclear

Lee 2005 *(Continued)*

	Number included in treatment group for final analysis: unclear
	Number included in control group for final analysis: unclear
Interventions	**Treatment:** rTMS 10 Hz at an intensity of 110% for 1 second
	Administered by: not reported
	Control: sham stimulation
	Frequency: 10 trains separated by 60 seconds
	Duration: for 10 days during a 2-week period
	Follow-up: none
Outcomes	**Primary outcomes**
	• Depression measured using HDRS • Depression measured using BDI
	Secondary outcomes
	• Cognitive function measured using MMSE
Notes	Unable to obtain any more information on this trial despite multiple attempts since 2008

Li 2019

Methods	**Study design:** parallel design
	Number of arms: 2
	Experimental arm: antidepressant (name and class not reported) + neuron-specific enolase
	Control arm: unclear
Participants	**Geographical location:** China
	Setting: unclear
	Stroke criteria: not reported
	Method of stroke diagnosis: not reported
	Depression criteria: unclear
	Total number randomised in this trial: 119
	Number randomised to treatment group: unclear
	Number randomised to control group: unclear
	Total number included in final analysis: unclear
	Number included in treatment group for final analysis: unclear
	Number included in control group for final analysis: unclear
Interventions	**Treatment:** antidepressant (name and class not reported) + neuron-specific enolase
	Control: unclear

Li 2019 *(Continued)*

	Duration: 6 months **Follow-up:** 6 months
Outcomes	**Primary outcomes** • Neurological function measured using NIHSS • Depression measured using 24-item HDRS • Plasma levels of neuron-specific enolase
Notes	Unable to obtain information on the control group

Liu 2010

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** rTMS + routine care + physical factors treatment + acupuncture + psychotherapy **Control arm:** sham rTMS + routine care + physical factors treatment + acupuncture + psychotherapy
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** ischaemic stroke **Method of stroke diagnosis:** clinical diagnosis plus confirmation by imaging that a relevant lesion needed to be visible **Inclusion criteria:** (1) no dementia; (2) no aphasia; (3) clear consciousness; (4) age < 75 years **Exclusion criteria:** (1) cerebral haemorrhage; (2) history of epilepsy; (3) metal implant in the body; (4) other serious physical illness; (5) history of psychiatric illness or family history **Depression criteria:** meeting diagnostic criteria of ICD-10 for depression and 24-item HDRS score > 20 **Total number randomised in this trial:** 60 **Number randomised to treatment group:** 30 (36% men; mean age 59, SD 9) **Number randomised to control group:** 30 (30% men; mean age 58, SD 11) **Total number included in final analysis:** 60 **Number included in treatment group for final analysis:** 30 **Number included in control group for final analysis:** 30
Interventions	**Treatment:** rTMS + routine care (medications (sertraline or citalopram), physical factors treatment (musical therapy, high-voltage static current therapy), Chinese medicine (acupuncture), and psychotherapy (patient-centred therapy, cognitive therapy, behaviour therapy)). Frequency: 10 to 15 Hz, intensity: 90% motor threshold, 1 stimulation lasting 1 second and stop for 10 seconds, total 1200 stimulations per day, for 10 days, location: left DLPFC **Control:** sham rTMS + routine care (medications (sertraline or citalopram), physical factors treatment (musical therapy, high-voltage static current therapy), Chinese medicine (acupuncture), and

Liu 2010 *(Continued)*

	psychotherapy (patient-centred therapy, cognitive therapy, behaviour therapy)). Keeping the coils at 90-degree angle with the scalp, keeping the coils at a distance of 8 cm from treatment area **Duration:** 10 days **Follow-up:** 40 days
Outcomes	**Primary outcome** • Depression measured using HDRS
Notes	Unable to obtain information to determine if the psychotherapy component of the intervention met the review criteria for psychotherapy

Pearson 2005

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** nurse-led education intervention **Control arm:** unclear
Participants	**Geographical location:** unclear **Setting:** outpatient **Number of participants:** 41 **Stroke criteria:** unclear **Method of stroke diagnosis:** not reported **Inclusion criteria:** not reported **Exclusion criteria:** not reported **Depression criteria:** unclear **Total number randomised in this trial:** 41 **Number randomised to treatment group:** 20 **Number randomised to control group:** 21 **Total number included in final analysis:** unclear **Number included in treatment group for final analysis:** unclear **Number included in control group for final analysis:** unclear
Interventions	**Treatment:** Orem's self-care model of nursing, Knowles' principles of adult learning, nurse-led educational intervention **Control:** unclear **Duration:** 16 hours **Follow-up:** not reported
Outcomes	**Primary outcome**

Pearson 2005 *(Continued)*

	• Depression measured using BDI
Notes	Able to locate only conference abstract

Razazian 2016

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** fluoxetine (SSRI) **Control arm:** placebo
Participants	**Geographical location:** Iran **Setting:** inpatient **Stroke criteria:** acute ischaemic stroke **Method of stroke diagnosis:** documented with CT scan **Time since stroke:** not reported **Inclusion criteria:** (1) acute ischaemic stroke (documented with CT scan) that leads monoparesis, hemiparesis, or hemiplegia; (2) not in a comatose state and stable **Exclusion criteria:** (1) death due to any cause during assessment; (2) pregnancy; (3) poor compliance of drugs and physiotherapy; (4) miscarriage returning of patient for further exams and assessments; (5) any drug complication during assessment (prospected or not); (6) any metabolic disease (liver, renal, cardiac impairment, and hyperthyroidism); (7) ischaemic stroke in the territory of anterior cerebral artery (ACA) or posterior cerebral artery (PCA), using any interfering drugs with fluoxetine (such as cyproheptadine, selegiline) **Depression criteria:** none **Total number randomised in this trial:** 172 **Number randomised to treatment group:** 86 (50.6% men; mean age 63.2, SD 11.4) **Number randomised to control group:** 86 (41.3% men; mean age 64.6, SD 11.9) **Total number included in final analysis:** 150 **Number included in treatment group for final analysis:** 75 **Number included in control group for final analysis:** 75
Interventions	**Treatment:** fluoxetine (SSRI) 20 mg/d **Control:** placebo **Duration:** 45 days **Follow-up:** 90 days
Outcomes	**Primary outcomes** • Motor impairment • Depression measured using ZDS • Disability measured using BI

Razazian 2016 *(Continued)*

Notes	Unable to obtain information on the primary outcome: whether depression or functional recovery

Tang 2002

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** paroxetine (SSRI) + cognitive therapy (frequency unknown) **Control arm:** paroxetine (SSRI)
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** unclear **Method of stroke diagnosis:** diagnosis consistent with diagnostic criteria for stroke formulated by the Second National Symposium on Cerebrovascular Disease and confirmation by brain CT or MRI **Time since stroke:** 2 weeks ago **Inclusion criteria:** (1) no history of aphasia or agnosia; (2) clear consciousness; (3) stroke onset at least 2 weeks ago **Exclusion criteria:** (1) history of psychiatric illness; (2) organic or reactive depression; (3) comorbid with other severe psychiatric symptoms, or family history **Depression criteria:** psychiatric interview to confirm diagnosis meets diagnostic criteria of CCMD-2-R; ZDS score ≥ 50 **Total number randomised in this trial:** 41 **Number randomised to treatment group:** 20 (60% men; mean age 57.5, SD 5.2) **Number randomised to control group:** 21 (57% men; mean age 56.3, SD 5.7) **Total number included in final analysis:** 41 **Number included in treatment group for final analysis:** 20 **Number included in control group for final analysis:** 21
Interventions	**Treatment:** combined paroxetine (SSRI) 20 mg/d in the morning and cognitive therapy (frequency unknown). Cognitive therapy entailed guiding patients to apply cognitive remediation for negative thoughts; recognise situations causing depression; re-establish healthy ideas and attitudes; establish family co-operation **Administered by:** not reported **Supervision:** not reported **Intervention fidelity:** not reported **Control:** paroxetine (SSRI) 20 mg/d in the morning **Duration:** 1 month **Follow-up:** none
Outcomes	**Primary outcomes**

Tang 2002 *(Continued)*

	• Depression measured using ZDS **Secondary outcomes** • Cognitive functioning measured using MMSE • Evaluation of clinical status, stratifying clinical status as recovered (disappearance of symptoms, insight recovery, social function recovery), obviously improved (most symptoms disappear, insight partial recovery), improved (only slightly improved), not efficacious (no any improvement and even worse)
Notes	Unable to obtain information to determine if the psychotherapy component of the intervention meets the review criteria for psychotherapy

Wang 2015

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** rTMS + conventional drugs, rehabilitation training, and psychological counselling therapy **Control arm:** conventional drugs, rehabilitation training, and psychological counselling therapy
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** not reported **Method of stroke diagnosis:** clinical criteria only **Inclusion criteria:** (1) meeting diagnostic criteria of ICD for organic depression; (2) 17-item HDRS score ≥ 8; (3) over 65 years of age **Exclusion criteria:** not reported **Depression criteria:** meeting diagnostic criteria of ICD for organic depression and 17-item HDRS score ≥ 8 **Total number randomised in this trial:** 150 **Number randomised to treatment group:** 75 (56% men; mean age 56.7, SD 7.2) **Number randomised to control group:** 75 (53% men; mean age 57.9, SD 6.8) **Total number included in final analysis:** 150 **Number included in treatment group for final analysis:** 75 **Number included in control group for final analysis:** 75
Interventions	**Treatment:** rTMS + conventional drugs, rehabilitation training, and psychological counselling therapy. Frequency: 10 Hz, intensity: 60% motor threshold, 1 stimulation lasts 4 seconds and stops for 56 seconds, 30 stimulations for 1 series, 5 series a week, for successive 12 weeks, location: left DLFPC **Control:** conventional drugs, rehabilitation training, and psychological counselling therapy **Duration:** 12 weeks

Wang 2015 *(Continued)*

	Follow-up: none
Outcomes	**Primary outcomes** • Depression measured using HDRS • Disability measured using BI
Notes	Unable to obtain information to determine if the psychotherapy component of the intervention met the review criteria for psychotherapy

Yan 2010a

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** high-frequency rTMS + routine care + flupentixol and melitracen 10.5 mg/tablet, 1 tablet twice a day + psychotherapy **Control arm:** sham rTMS + routine care + flupentixol and melitracen 10.5 mg/tablet, 1 tablet twice a day + psychotherapy
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** not reported **Method of stroke diagnosis:** diagnosis consistent with diagnostic criteria for stroke formulated by the Fourth National Symposium on Cerebrovascular Disease in 1995 and confirmation by brain CT or MRI stated **Time since stroke:** < 6 months **Inclusion criteria:** (1) right-handedness; (2) disease course < 6 months; (3) can sign informed consent **Exclusion criteria:** (1) history of psychiatric illness or family history; (2) aphasia; (3) severe dementia; (4) severe physical illness, consciousness disturbance, or deafness, which influences the expression of depressed mood; (4) psychoactive or non-addiction-producing substance-induced depression; (5) various reasons to refuse trial or difficulty in finishing trial **Depression criteria:** depression diagnosed according to CCMD-3 **Total number randomised in this trial:** 20 **Number randomised to treatment group:** 10 (50% men; mean age 68.65, SD 7.62) **Number randomised to control group:** 10** (55% men; mean age 68.70, SD 8.94) **Total number included in final analysis:** 20 **Number included in treatment group for final analysis:** 10 **Number included in control group for final analysis:** 10**
Interventions	**Treatment:** high-frequency rTMS + routine care + flupentixol and melitracen 10.5 mg/tablet, 1 tablet twice a day + psychotherapy. High rTMS frequency: 10 Hz; intensity: 110% motor threshold; location: left DLPFC; 1 sequence included continuous stimulations for 30 minutes, frequency of treatment: 1 sequence a day during 09:00 to 10:00

Yan 2010a *(Continued)*

	Control: sham rTMS + routine care + flupentixol and melitracen 10.5 mg/tablet, 1 twice a day + psychotherapy. Sham rTMS 0 Hz; intensity: 0; location: left or right DLPFC; 1 sequence included continuous stimulations for 30 minutes, frequency of treatment: 1 sequence a day during 09:00 to 10:00 **Duration:** 7 days **Follow-up:** none
Outcomes	**Primary outcomes** • Depression measured using HDRS • Impairment measured using NIHSS **Secondary outcomes** • Adverse events • Leaving the trial early • Death
Notes	Unable to obtain information to determine if the psychotherapy component of the intervention met the review criteria for psychotherapy

Yan 2010b

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** low-frequency rTMS + routine care + flupentixol and melitracen 10.5 mg/tablet, 1 tablet twice a day + psychotherapy **Control arm:** sham rTMS + routine care + flupentixol and melitracen 10.5 mg/tablet, 1 tablet twice a day + psychotherapy
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** not reported **Method of stroke diagnosis:** diagnosis consistent with diagnostic criteria for stroke formulated by the Fourth National Symposium on Cerebrovascular Disease in 1995 and confirmation by brain CT or MRI stated **Time since stroke:** < 6 months **Inclusion criteria:** (1) right-handedness; (2) disease course < 6 months; (3) can sign informed consent **Exclusion criteria:** (1) history of psychiatric illness or family history; (2) aphasia; (3) severe dementia; (4) severe physical illness, consciousness disturbance, or deafness, which influences the expression of depressed mood; (4) psychoactive or non-addiction-producing substance-induced depression; (5) various reasons to refuse trial or difficulty in finishing trial **Depression criteria:** depression diagnosed according to the CCMD-3 **Total number randomised in this trial:** 20 **Number randomised to treatment group:** 10 (55% men; mean age 69.65 ± 5.81) **Number randomised to control group:** 10** (55% men; mean age 68.70 ± 8.94)

Yan 2010b *(Continued)*

	Total number included in final analysis: 20 **Number included in treatment group for final analysis:** 10 **Number included in control group for final analysis:** 10**
Interventions	**Treatment:** low-frequency rTMS + routine care + flupentixol and melitracen 10.5 mg/tablet, 1 tablet twice a day + psychotherapy. Low rTMS frequency: 1 Hz; intensity: 110% motor threshold; location: left DLPFC; 1 sequence included continuous stimulations for 30 minutes; frequency of treatment: 1 sequence a day during 09:00 to 10:00 **Control:** sham rTMS + routine care + flupentixol and melitracen 10.5 mg/tablet, 1 tablet twice a day + psychotherapy. Sham rTMS 0 Hz; intensity: 0; location: left or right DLPFC; 1 sequence included continuous stimulations for 30 minutes; frequency of treatment: 1 sequence a day during 09:00 to 10:00 **Duration:** 7 days **Follow-up:** none
Outcomes	**Primary outcomes** • Depression measured using HDRS • Impairment measured using NIHSS **Secondary outcomes** • Adverse events • Leaving the trial early • Death
Notes	Unable to obtain information to determine if the psychotherapy component of the intervention met the review criteria for psychotherapy

Yan 2010c

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** high-frequency rTMS + routine care + flupentixol and melitracen 10.5 mg/tablet, 1 tablet twice a day + psychotherapy **Control arm:** routine care + flupentixol and melitracen 10.5 mg/tablet, 1 tablet twice a day + psychotherapy
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** not reported **Method of stroke diagnosis:** diagnosis consistent with diagnostic criteria for stroke formulated by the Fourth National Symposium on Cerebrovascular Disease in 1995 and confirmation by brain CT or MRI stated **Time since stroke:** < 6 months **Inclusion criteria:** (1) right-handedness; (2) disease course < 6 months; (3) can sign informed consent

Yan 2010c *(Continued)*

	Exclusion criteria: (1) history of psychiatric illness or family history; (2) aphasia; (3) severe dementia; (4) severe physical illnesses, consciousness disturbance, or deafness, which influences the expression of depressed mood; (4) psychoactive or non-addiction-producing substance-induced depression; (5) various reasons to refuse trial or difficulty in finishing trial **Depression criteria:** depression diagnosed according to the CCMD-3 **Total number randomised in this trial:** 20 **Number randomised to treatment group:** 10 (50% men; mean age 68.65, SD 7.62) **Number randomised to control group:** 10** (60% men; mean age 67.25, SD 9.15) **Total number included in final analysis:** 20 **Number included in treatment group for final analysis:** 10 **Number included in control group for final analysis:** 10**
Interventions	**Treatment:** high-frequency rTMS + routine care + flupentixol and melitracen 10.5 mg/tablet, 1 tablet twice a day + psychotherapy. High rTMS frequency: 10 Hz; intensity: 110% motor threshold; location: left DLPFC; 1 sequence included continuous stimulations for 30 minutes; frequency of treatment: 1 sequence a day during 09:00 to 10:00 **Control:** routine care + flupentixol and melitracen 10.5 mg/tablet, 1 tablet twice a day + psychotherapy **Duration:** 7 days **Follow-up:** none
Outcomes	**Primary outcomes** • Depression measured using HDRS • Impairment measured using NIHSS **Secondary outcomes** • Adverse events • Leaving the trial early • Death
Notes	Unable to obtain information to determine if the psychotherapy component of the intervention met the review criteria for psychotherapy

Yan 2010d

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** low-frequency rTMS + routine care + flupentixol and melitracen 10.5 mg/tablet, 1 tablet twice a day + psychotherapy **Control arm:** routine care + flupentixol and melitracen 10.5 mg/tablet, 1 tablet twice a day + psychotherapy
Participants	**Geographical location:** China **Setting:** inpatient

Yan 2010d *(Continued)*

	Stroke criteria: not reported **Method of stroke diagnosis:** diagnosis consistent with diagnostic criteria for stroke formulated by the Fourth National Symposium on Cerebrovascular Disease in 1995 and confirmation by brain CT or MRI stated **Time since stroke:** < 6 months **Inclusion criteria:** (1) right-handedness; (2) disease course < 6 months; (3) can sign informed consent **Exclusion criteria:** (1) history of psychiatric illness or family history; (2) aphasia; (3) severe dementia; (4) severe physical illness, consciousness disturbance, or deafness, which influences the expression of depressed mood; (4) psychoactive or non-addiction-producing substance-induced depression; (5) various reasons to refuse trial or difficulty in finishing trial **Depression criteria:** depression diagnosed according to the CCMD-3 **Total numbers randomised in this trial:** 20 **Numbers randomised to treatment group:** 10 (55% men; mean age 69.65, SD 5.81) **Numbers randomised to control group:** 10** (60% men; mean age 67.25, SD 9.15) **Total numbers included in final analysis:** 20 **Numbers included in treatment group for final analysis:** 10 **Numbers included in control group for final analysis:** 10**
Interventions	**Treatment:** low-frequency rTMS + routine care + flupentixol and melitracen 10.5 mg/tablet, 1 tablet twice a day + psychotherapy. Low rTMS frequency: 1 Hz; intensity: 110% motor threshold; location: left DLPFC; 1 sequence included continuous stimulations for 30 minutes; frequency of treatment: 1 sequence a day during 09:00 to 10:00 **Control:** routine care + flupentixol and melitracen 10.5 mg/tablet, 1 tablet twice a day + psychotherapy **Duration:** 7 days **Follow-up:** none
Outcomes	**Primary outcomes** • Depression measured using HDRS • Impairment measured using NIHSS **Secondary outcomes** • Adverse events • Leaving the trial early • Death
Notes	Unable to obtain information to determine if the psychotherapy component of the intervention met the review criteria for psychotherapy

Yu 2019

Methods	**Study design:** parallel design **Number of arms:** 2

Yu 2019 *(Continued)*

	Experimental arm: intensive patient care programme (IPCP) **Control arm:** usual care, education and cognitive rehabilitation training
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** acute ischaemic stroke (AIS) **Method of stroke diagnosis:** diagnosed as primary AIS confirmed by brain CT (including perfusion CT) or MRI (including diffusion-weighted MRI and perfusion MRI) **Inclusion criteria:** (1) diagnosed as primary AIS confirmed by brain CT (including perfusion CT) or MRI (including diffusion-weighted MRI and perfusion MRI); (2) first-ever ischaemic stroke; (3) age above 18 years old; (4) able to understand the informed consent and independently complete assessment questionnaires of cognitive, anxiety and depression **Exclusion criteria:** (1) haemorrhagic stroke; (2) any type of aphasia, severe hearing impairment, serious dementia which was defined as Mini-Mental State Examination (MMSE) score < 10; (3) life expectancy was less than 12 months judged by clinician; (4) complicated with malignant tumours or uncontrolled diabetes, hypertension or heart disease; (5) unable to be regularly followed up; (6) current participation in another interventional trial **Depression criteria:** no criteria for depression at entry **Total number randomised in this trial:** 242 **Number randomised to treatment group:** 121 (59.5% men; mean age 67.3, SD 11.3) **Number randomised to control group:** 121 (63.6% men; mean age 67.5, SD 13.7) **Total number included in final analysis:** 242 **Number included in treatment group for final analysis:** 121 **Number included in control group for final analysis:** 121
Interventions	**Treatment:** IPCP (comprehensive psychoeducation and psychonursing for a total of 24 sessions were given to the patients, containing eight topics with each session for one hour in duration, and two sessions per month for up to 12 months + cognitive rehabilitation training + mobile app to spread knowledge of care, post messages, inquiry patients' current health status, maintain daily contact with patients, help patients and caregivers cope with emergency and answer patients' questions; patients could communicate with each other, ask nurses for help and make appointments for follow-up) **Administered by:** trained nurses **Supervision:** not reported **Intervention fidelity:** not reported **Control:** usual care, education and cognitive rehabilitation training **Duration:** 12 months **Follow-up:** 12 months
Outcomes	**Primary outcomes** • Depression measured using HADS-D • Cognitive functioning measured using MMSE • Anxiety measured using HADS-A

Yu 2019 *(Continued)*

Notes	Unable to obtain information to determine if the psychotherapy component of the intervention met the review criteria for psychotherapy

Zhang 2021

Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** rehabilitation nursing **Control arm:** conventional nursing
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** cerebral ischaemic stroke **Method of stroke diagnosis:** meeting the relevant content in the standard of the 4th National Academic Conference on Cerebrovascular Diseases (1995) after brain MRI and CT examinations **Inclusion criteria:** (1) meeting the relevant content in the standard of the 4th National Academic Conference on Cerebrovascular Diseases (1995) after brain MRI and CT examinations; (2) all vital signs tended to be stable; (3) all patients had not received rehabilitation nursing and other related training before **Exclusion criteria:** (1) patients who had sequelae of nervous system diseases and history of mental illness; (2) patients who were unable to participate in the completion of this as accompanied by other systemic diseases; (3) patients with disturbance of consciousness, complete impaired speech and eating function **Depression criteria:** no criteria for depression at entry **Total number randomised in this trial:** 84 **Number randomised to treatment group:** 42 (64.29% men; mean age 65.0, SD 3.7) **Number randomised to control group:** 42 (57.14 men; mean age 65.5, SD 2.7) **Total number included in final analysis:** unclear **Number included in treatment group for final analysis:** unclear **Number included in control group for final analysis:** unclear
Interventions	**Treatment:** rehabilitation nursing which included psychological intervention, lying position training, language function recovery, brain function recovery, swallowing function recovery, activity function training for one month **Control:** conventional nursing **Duration:** 1 month **Follow-up:** none
Outcomes	**Primary outcomes** • Neurological function measured using NIHSS • Depression measured using Self-rating Depression Scale (SDS)

Zhang 2021 *(Continued)*

	• Disability measured using BI
Notes	Unable to obtain information to determine if the psychotherapy component of the intervention met the review criteria for psychotherapy

** Results for control group halved
ACA: anterior cerebral artery
AIS: acute ischaemic stroke
BDI: Beck Depression Inventory
BI: Barthel Index
CCMD-2-R: Chinese Classification of Mental Disorders, Second Edition, Revised
CCMD-3: Chinese Classification of Mental Disorders, Third Edition
CNS: central nervous system
CSS: Chinese Stroke Scale
CT: computed tomography
DLPFC: dorsolateral pre-frontal cortex
DSM: Diagnostic and Statistical Manual of Mental Disorders
HADS: Hospital Anxiety Depression Scale
HARS: Hamilton Anxiety Rating Scale
HDRS-17: 17-item Hamilton Depression Rating Scale
HDRS-24: 24-item Hamilton Depression Rating Scale
Hz: hertz
ICD: International Classification of Diseases
IPCP: Intensive Patient Care Programme
LSI: Life Satisfaction Index
MMSE: Mini Mental State Examination
MRI: magnetic resonance imaging
NIHSS: National Institute of Health Stroke Scale
PCA: posterior cerebral artery
rTMS: repetitive transcranial magnetic stimulation
SD: standard deviation
SDS: Self-rating Depression Scale
SNRI: selective norepinephrine reuptake inhibitor
SSRI: selective serotonin reuptake inhibitor
SSS: Scandinavian Stroke Scale
TCA: tricyclic antidepressant
tDCS: transcranial direct current stimulation
USA: United State of America
ZDS: Zung Depression Scale

Characteristics of ongoing studies *[ordered by study ID]*

ACTRN12620000165987

Study name	Examining the efficacy of an online cognitive behaviour therapy (CBT) - based self-management program for adults with neurological disorders
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** well-being neuro course **Control arm:** waiting-list control
Participants	**Geographical location:** Australia **Setting:** not reported **Stroke criteria:** not reported

ACTRN12620000165987 *(Continued)*

	Method of stroke diagnosis: not reported **Inclusion criteria:** (1) diagnosis of multiple sclerosis, epilepsy, Parkinson's disease, stroke, traumatic brain injury or acquired brain injury by a GP or specialist; (2) reporting that the neurological disorder affects their cognitive and emotional health; (3) 18+ years of age; (4) living in Australia; (4) provide informed consent **Exclusion criteria:** (1) inability to use a computer; (2) very severe depressive symptoms indicative of > 25 on the PhQ-9; (3) significant suicidal ideation (i.e. indicated by a score > 2 to Question 9 on the PHQ-9); (4) acutely suicidal or recent history of attempted suicide or self-harm; (5) not being under medical management for their neurological disorder; (6) serious cognitive impairment (< 21 on the Telephone Interview of Cognitive Status; TICS) indicative of dementia **Depression criteria:** no criteria for depression at entry
Interventions	**Treatment:** the well-being neuro course is based on CBT principles and teaches evidence-based skills for managing the impacts of neurological conditions on day-to-day activities and overall mental health. Each lesson takes between 10 and 20 minutes to complete and it is suggested that participants read each lesson at least twice and spend approximately 4 hours, across the week, practicing the skills taught. **Administered by:** online **Supervision:** not reported **Control:** waiting-list control will receive the same treatment after the active treatment group has completed the 10-week course. **Duration:** 10 weeks **Follow-up:** 3 months
Outcomes	**Primary outcome** • Disability measured using 12-item World Health Organization Disability Assessment Schedule 2.0 (WHODAS-12) • Depression measured using PHQ-9 • Anxiety measured using 7-item Generalized Anxiety Disorder (GAD-7) **Secondary outcomes** • Quality of life measured using Neuro-QoL • Treatment satisfaction • Compensatory cognitive strategies
Starting date	February 2020
Contact information	Dr Milena Gandy, Building C3A, Department of Psychology, Balaclava Road, Macquarie University, Marsfield, NSW, 2109, Australia Email: milena.gandy@mq.edu.au
Notes	

ChiCTR1800020468

Study name	Therapeutic effect of high frequency repetitive transcranial magnetic stimulation with different frequencies on patients with post-stroke depression
Methods	**Study design:** parallel design

ChiCTR1800020468 *(Continued)*

	Number of arms: 2 **Experimental arm:** 5Hz transcranial magnetic stimulation (TMS) + antidepressant + conventional treatment **Control arm:** sham TMS + antidepressant + conventional treatment
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** acute cerebral ischaemic stroke **Method of stroke diagnosis:** not reported **Inclusion criteria:** (1) the diagnosis of the disease is in line with the guidelines for the diagnosis and treatment of acute cerebral ischaemic stroke in China in 2014 and the guidelines for the diagnosis and treatment of cerebral haemorrhage in China; (2) transcranial CT and/or MRI confirmed stroke; (3) diagnosis of depressive episodes meets Chinese classification and diagnostic criteria of mental disorders-3 (CCMD-3) or the diagnostic and statistical manual of mental disorders VI (DSM-VI) for depressive episodes; (4) Hamilton depression rating scale ≥ 8 points; (5) signing informed consent **Exclusion criteria:** (1) patients with mental diseases before stroke; (2) patients with severe disturbances of consciousness, aphasia, understanding of expression disorders and cognitive impairment (MMSE ≤ 9 points); (3) history of seizures; (4) intracranial, cardiac, etc.; have implanted metal objects **Depression criteria:Inclusion criteria:** meets Chinese classification and diagnostic criteria of mental disorders-3 (CCMD-3) or the diagnostic and statistical manual of mental disorders VI (DSM-VI) for depressive episodes and Hamilton depression rating scale ≥ 8 points
Interventions	**Treatment:** 5Hz transcranial magnetic stimulation (TMS) + antidepressant + conventional treatment **Control:** sham TMS + antidepressant + conventional treatment **Duration:** not reported **Follow-up:** not reported
Outcomes	**Primary outcome** • Depression measured using HDRS **Secondary outcomes** • Remission rate • Disability measured using Modified Barthel Index (MBI) • Activities of daily living measured using ADLS • Response rate
Starting date	January 2019
Contact information	Dr Jiali Hu, The Affiliated Hospital of Qingdao University, 1677 Wutaishan Road, Huangdao District, Qingdao, Shandong, China Email: hujialiys@163.com
Notes	

ChiCTR1900024245

Study name	The effect of repeated transcranial magnetic stimulation on post-stroke depression and the and mechanism research by functional MRI
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** transcranial magnetic stimulation (TMS) **Control arm:** sham TMS
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** subcortical stroke **Method of stroke diagnosis:** not reported **Inclusion criteria:** (1) previous history of subcortical stroke; (2) time of stroke was 3 months to 1 year for non-acute stroke; (3) aged 40 to 75 years; (4) HAMD (7-21 points), Center for Epidemiological Studies Depression CESD scale (> 20 points), FMA (50-95 points), BS stage ≥ 3, NIHSS < 12, conventional rehabilitation treatment; (5) sign the informed consent **Exclusion criteria:** (1) patients with acute stroke and cerebral trauma; (2) intracranial infection, effusion or tumour occupation; (3) intracranial metal and other foreign bodies (such as orthopaedic materials, arterial clips, etc.); (4) has pacemaker, deep brain stimulator and other electronic equipment; (5) previous seizures, including primary epilepsy and secondary epilepsy; (6) severe complications after stroke, such as pneumonia and heart disease; (7) previous history of depression and antidepressant use; (8) cognitive dysfunction or aphasia (MMSE < 17); (9) patients who cannot cooperate in neuropsychological testing; (10) not following the prescribed treatment regimen and poor compliance **Depression criteria:Inclusion criteria:** HAMD (7-21 points) and CESD scale (> 20 points)
Interventions	**Treatment:** transcranial magnetic stimulation (TMS) **Control:** sham TMS **Duration:** not reported **Follow-up:** not reported
Outcomes	**Primary outcome** • Depression measured using 17-item HDRS **Secondary outcomes** • Neurological function measured using NIHSS • Functional recovery measured using modified Rankin Scale (mRS) • Cognitive function measured using Mini Mental State Examination (MMSE) • Anxiety measured using 17-item HDRS-Anxiety • Sleep measured using Pittsburgh Sleep Scale • Depression measured using CESD scale
Starting date	June 2020
Contact information	Dr Zhou Zu, Department of Neurology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, 1095 Jiefang Avenue, Qiaokou District, Wuhan, Hubei, China

ChiCTR1900024245 *(Continued)*

	Email: zhouzhu@hust.edu.cn
Notes	

ChiCTR1900025440

Study name	Effects of transcranial direct current stimulation for the treatment of post-stroke depression
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** transcranial direct current stimulation (tDCS) + routine treatment **Control arm:** sham tDCS
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** acute cerebral ischaemic stroke **Method of stroke diagnosis:** the diagnosis of the disease is in line with the guidelines for the diagnosis and treatment of acute cerebral ischaemic stroke in China in 2014 and the guidelines for the diagnosis and treatment of cerebral haemorrhage in China **Inclusion criteria:** (1) the diagnosis of the disease is in line with the guidelines for the diagnosis and treatment of acute cerebral ischaemic stroke in China in 2014 and the guidelines for the diagnosis and treatment of cerebral haemorrhage in China; (2) transcranial CT and/or MRI confirmed stroke; (3) diagnosis of depressive episodes meets Chinese classification and diagnostic criteria of mental disorders-3 (CCMD-3) or the diagnostic and statistical manual of mental disorders VI (DSM-VI) for depressive episodes; (4) HDRS > 8 points; (5) signing informed consent **Exclusion criteria:** (1) patients with mental diseases before stroke; (2) patients with severe disturbances of consciousness, aphasia, understanding of expression disorders and cognitive impairment (MMSE ≤ 9 points); (3) the patient has a history of seizures; (4) intracranial, cardiac, etc.; have implanted metal objects **Depression criteria:Inclusion criteria:** meets Chinese classification and diagnostic criteria of mental disorders-3 (CCMD-3) or the diagnostic and statistical manual of mental disorders VI (DSM-VI) for depressive episodes and HDRS > 8 points
Interventions	**Treatment:** transcranial direct current stimulation (tdCS) + routine treatment **Control:** sham tDCS **Duration:** not reported **Follow-up:** not reported
Outcomes	**Primary outcome** • Depression measured using 17-item HDRS **Secondary outcomes** • Remission rate • Activities of daily living measured using ADLS • Disability measured using modified Barthel Index (mBI) • Adverse events

ChiCTR1900025440 *(Continued)*

Starting date	January 2021
Contact information	Dr Weiming Sun, The First Affiliated Hospital of Nanchang University, 17 Yongwai Main Street, Donghu District, Nanchang, Jiangxi, China Email: sunweiming08@126.com
Notes	

ChiCTR1900027686

Study name	The effect and mechanism of intermittent theta burst stimulation on post-stroke depression
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** intermittent theta burst stimulation (iTBS) **Control arm:** sham iTBS
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** not reported **Method of stroke diagnosis:** consistent with the western diagnostic criteria of stroke and CT or MRI showed clear signs of neurological damage **Inclusion criteria:** (1) consistent with the Western diagnostic criteria of stroke and CT or MRI showed clear signs of neurological damage; (2) Hamilton Depression Scale (HAMD) > 8 points; (3) both male and female aged 30 to 80 years old; (4) right-handed; (5) conscious; (6) understand, agree to participate in the study and sign the informed consent form **Exclusion criteria:** (1) other brain diseases; (2) severe systemic diseases; (3) severe aphasia or severe cognitive impairment, severe hearing impairment, visual impairment or severe language understanding disorder may affect the assessment due to other reasons; (4) history of depression and other mental illnesses before stroke occurs; (5) addiction to drugs, alcohol or other substances; (6) metal implants in the body; history of epilepsy or history of seizures; direct genus has a history of epilepsy and other contraindications for transcranial magnetic stimulation; (7) history of skull fractures and/or severe head injuries, head and/or brain surgery; (8) pregnancy (positive HCG test), lactating women **Depression criteria:Inclusion criteria:** HDRS > 8 points
Interventions	**Treatment:** iTBS **Control:** sham iTBS **Duration:** not reported **Follow-up:** not reported
Outcomes	**Primary outcome** • Depression measured using 17-item HDRS **Secondary outcomes** • Blood biochemical index

ChiCTR1900027686 *(Continued)*

	• Neuroimaging index
Starting date	January 2019
Contact information	Dr Meng Ren, ShangHai University of Traditional Chinese Medicine, 110 Ganhe Road, Shanghai, China Email: 1404754641@qq.com
Notes	

ChiCTR2000029809

Study name	Cognitive effects of electrical current therapy in post-stroke depression: a study protocol for a randomized controlled trial
Methods	**Study design:** parallel design **Number of arms:** 3 **Experimental arm 1:** tDCS + placebo **Experimental arm 2:** sham tDCS + escitalopram (SSRI) **Control arm:** sham tDCS + placebo
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** first or recurrent ischaemic stroke **Method of stroke diagnosis:** confirmed by brain CT or MRI **Inclusion criteria:** (1) between 18 and 75 years of age with no gender-based restriction; (2) first or recurrent ischaemic stroke that was confirmed by brain CT or MRI; (3) a minimum of 3 months and a maximum of 5-years post-stroke; (4) DSM-V diagnosis for depression due to stroke; (5) 17-item HDRS score greater than or equal to 17 points and less than 24; (6) patients willing to participate in the RCT and sign informed consent forms; (7) right-handedness **Exclusion criteria:** (1) individuals with any lifetime history of depression, anxiety, bipolar disorder, schizophrenia, etc; (2) individuals with substance abuse, panic disorder, or post-traumatic stress disorder in the past 6 months prior to admission of stroke; (3) a high risk of attempting suicide (a score of more than 2 points on the third question (Suicide) of the HDRS-17); (4) aphasia and severe cognitive impairment (MMSE scores < 10 points); (5) presence of other mental disorders (such as adaptation disorders) caused by substance abuse (such as medication, drug addiction, alcoholism); (6) current or prior any psychological intervention for any reason; (7) participation in another clinical trial; (8) currently pregnant or breastfeeding **Depression criteria:Inclusion criteria:** meets the DSM-V criteria and HDRS score greater than or equal to 17 points and less than 24
Interventions	**Treatment 1:** tDCS + placebo Treatment 2: sham tDCS + escitalopram (SSRI) **Control:** sham tDCS + placebo **Duration:** not reported **Follow-up:** not reported

ChiCTR2000029809 *(Continued)*

Outcomes	**Primary outcomes** • Depression measured using HDRS • Cognitive function measured using the MoCA and Mini Mental State Examination (MMSE) **Secondary outcome** • Depression measured using Zung Depression Scale (ZDS) • Disability measured using Modified Barthel Index (MBI)
Starting date	March 2020
Contact information	Dr Sergio R Leigue, Shanghai Seventh People's Hospital, Shanghai University of TCM, 358 Datong Road, Pudong New District, Shanghai Email: Dr.Leigue@yahoo.com
Notes	

ChiCTR2000035582

Study name	Clinical study of low intensity ultrasound nerve stimulation in the treatment of post-stroke anxiety and depression
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** low intensity ultrasound treatment **Control arm:** usual care
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** not reported **Method of stroke diagnosis:** not reported **Inclusion criteria:** (1) confirmed stroke sequelae; 2) patients with depression and anxiety were diagnosed by DSM-V; 3) aged 60-80 years old; 4) currently, there is no antidepressant and anti-anxiety medication; 5) normal renal and cardiac function was not found; 6) understand the procedure and method of the trial, voluntarily and strictly abide by the clinical trial protocol to complete the trial, and sign the informed consent; (4) able to follow the drug dosage and visit plan; (5) no serious infection, respiratory insufficiency, etc.; can actively cooperate; (6) no allergic disease, non-allergic constitution; (7) no drug abusers or addicts; (8) no clinical trial within 3 months before the trial **Exclusion criteria:** (1) cannot objectively describe their symptoms, or cannot take the initiative to cooperate; (2) patients with severe respiratory system, cardiovascular system disease, liver and kidney dysfunction, malignant tumour; (3) people with allergic diseases and allergic constitution; (4) those with suspected or had a history of drug abuse and addiction; (5) those who participated in clinical trials within 3 months before the trial; (6) sponsor or researcher directly involved in the trial or their family members; (7) any other reason why they could not be selected **Depression criteria:Inclusion criteria:** meet the DSM-V criteria
Interventions	**Treatment:** low-intensity ultrasound treatment **Control:** usual care

ChiCTR2000035582 *(Continued)*

	Duration: not reported **Follow-up:** not reported
Outcomes	**Primary outcomes** • Depression measured using PHQ-9 • Anxiety measured using GAD-7 Anxiety **Secondary outcome** • Quality of life measured using a quality of life questionnaire
Starting date	October 2020
Contact information	Dr Duan Junli, Xinhua Hospital Affiliated to Medical College of Shanghai Jiaotong University, 1665 Kongjiang Road, Yangpu District, Shanghai, China Email: duanjunlixh@163.com
Notes	

ChiCTR2100041707

Study name	Effects of rTMS on depressive state and motor function in patients with subthreshold depression after stroke
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** rTMS **Control arm:** usual care
Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** meet the 4th National Cerebrovascular Disease Conference of Chinese Medical Association 1995 **Method of stroke diagnosis:** confirmation by brain CT or MRI scan **Inclusion criteria:** (1) meet the 4th National Cerebrovascular Disease Conference of Chinese Medical Association 1995 confirmed by CT or MRI; 2) age 16-80 years old; 3) stable; 4) right-handed; 5) CES-D score ≥ 16; 6) HDRS score ≤ 17; (4) able to follow the drug dosage and visit plan; (5) no serious infection, respiratory insufficiency, etc, can actively cooperate; (6) no history of psychoactive substances **Exclusion criteria:** (1) previous mental illness or organic mental disorder; (2) people with severe cardiovascular system disease, liver and kidney dysfunction, cognitive impairment and aphasia; (3) people with depressive episode caused by psychoactive substance abuse; (4) those with history of suicide attempts; (5) those participating in other clinical trials; (6) pregnant, lactating or taking oestrogen drugs; (7) had received rTMS or ECT within one year **Depression criteria:Inclusion criteria:** CES-D score ≥ 16; 6) HDRS score ≤ 17
Interventions	**Treatment:** rTMS **Control:** usual care

ChiCTR2100041707 *(Continued)*

	Duration: not reported **Follow-up:** not reported
Outcomes	**Primary outcomes** • Depression measured using HDRS and CES-D **Secondary outcome** • Activities of daily living measured using MBI • Functional recovery measured using FMA
Starting date	January 2021
Contact information	Jiancheng Liu, General Hospital of Western War Zone of PLA, 270 Tianhui Road, Rongdu Avenue, Jinniu District, Chengdu, Sichuan, China Email: 422327057@qq.com
Notes	

Ding 2021

Study name	Clinical efficacy of Danzhi Xiaoyao Powder in the treatment of post-stroke depression: a protocol for randomized, double-blind clinical study
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** Danzhi Xiaoyao powder + SSRI (escitalopram oxalate) **Control arm:** Danzhi Xiaoyao stimulant + SSRI (escitalopram oxalate)
Participants	**Geographical location:** China **Setting:** not reported **Stroke criteria:** meet the Main Points of Diagnosis of Various Cerebrovascular Diseases **Method of stroke diagnosis:** meet the Main Points of Diagnosis of Various Cerebrovascular Diseases **Inclusion criteria:** (1) patients whose age ≥ 18 years, and < 75 years; (2) patients who meet the diagnostic criteria of stroke and depression, and HDRS > 18 points; (3) patients who have not taken antidepressants (including Traditional Chinese medicine and Western medicine) in the last 2 weeks; (4) patients who agree to participate in this study and signed informed consent **Exclusion criteria:** (1) patients with mental diseases other than depression; (2) patients who are addicted to alcohol, abuse and depend on psychoactive substances or drugs (including sleeping pills); (3) patients who cannot understand scale content due to consciousness or language barrier; (4) patients whose ALT, AST or Cr reaches 1.5 times of normal upper limit; (5) patients who are allergic to the investigational drug ingredients; (6) patients with severe mental diseases, unable to express themselves accurately or take medicine on time, or unable to complete the test **Depression criteria:Inclusion criteria:** meets CCMD criteria and HDRS > 18 points.
Interventions	**Treatment:** Danzhi Xiaoyao powder (Bai Zhu 10 g, Chai Hu, 15 g, Dang Gui 10 g, Fu Ling 15g, Gan Cao, 10 g, Dan Pi, 10 g, Zhi Zi, 10 g, Bai Shao, 15 g; made by Sichuan Neo-Green Pharmaceutical

Ding 2021 *(Continued)*

	Technology Development Co, Ltd, 1 bag at a time, 3 times a day) + SSRI (escitalopram oxalate twice a day, 5 mg for each oral administration) **Control:** Danzhi Xiaoyao stimulant (made by Sichuan Neo-Green Pharmaceutical Technology Development Co., Ltd., its appearance and taste are the same as Xiaoyao Powder, 1 bag at a time, 3 times a day) + SSRI (escitalopram oxalate twice a day, 5 mg for each oral administration) **Duration:** not reported **Follow-up:** not reported
Outcomes	**Primary outcome:** • Depression measured as the total effective rate and curative effect (reduction in HDRS score). The therapeutic criteria for depression were: recovery: reduction rate > 75%; significant effect: reduction rate > 50%; effective: reduction rate ≥ 25%; ineffective: reduction rate < 25%, total effective rate = (recovery number + significant effective number + effective number)/total number *100% and HDRS scores **Secondary outcomes:** • Activities of daily living measured by BI • Neurological recovery measured by NIHSS and the modified Edinburgh-Scandinavian stroke scale • Adverse reactions
Starting date	Not reported
Contact information	Jun Yao, No.1 Changzheng Road, Taixing 225400, Jiangsu Province, PR China E-mail: myxu1986@foxmail.com
Notes	

IRCT20090716002195N3

Study name	Efficacy of mindfulness-based intervention and transcranial direct current stimulation on cognitive disorders and emotional problems in patients with stroke: a randomized clinical trial
Methods	**Study design:** parallel design **Number of arms:** 4 **Experimental arm 1:** tDCS **Experimental arm 2:** mindfulness intervention **Experimental arm 3:** tDCS + mindfulness intervention **Control arm:** usual care
Participants	**Geographical location:** Iran **Setting:** not reported **Stroke criteria:** within 3 months of first stroke **Method of stroke diagnosis:** ICD-10 code 163 and 163.3 **Inclusion criteria:** (1) No unilateral brain involvement; (2) patients able to read and write; (3) available for follow-up; (4) able to sign the consent form

IRCT20090716002195N3 *(Continued)*

	Exclusion criteria: (1) patients with aphasia; (2) history of stroke; (3) history of psychiatric disease **Depression criteria:Inclusion criteria:** not reported
Interventions	**Treatment 1:** tDCS (2 mA electric current for 20 minutes for 10 sessions) **Treatment 2:** Mindfulness intervention (Kabat-Zinn mindfulness-based stress reduction treatment programme 2003, 2.5 hours for 8 sessions) **Treatment 3:** tDCS + mindfulness intervention **Control:** usual care **Duration:** not reported **Follow-up:** not reported
Outcomes	**Primary outcomes:** • Cognitive function measured by Addenbrooke's Cognitive Examination • Depression measured by BDI • Anxiety measured by BAI
Starting date	June 2019
Contact information	Mehdi Farhoudi, Tabriz University of Medical Sciences, Golgash Street, Tabriz, East Azerbaijan 5166614766 Email: farhoudi_m@yahoo.com/farhoudim@tbzmed.ac.ir
Notes	

IRCT2017030921965N4

Study name	Clinical trial to evaluate the efficacy of electrical stimulation of the brain with direct electrical current on depression after stroke
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm 1:** tDCS- anodal **Experimental arm 2:** tDCS-cathodal **Control arm:** sham tDCS
Participants	**Geographical location:** Iran **Setting:** inpatient **Stroke criteria:** not reported **Method of stroke diagnosis:** not reported **Inclusion criteria:** (1) patients with brain stroke; (2) people aged at least 21 years during 48 hours of their first brain stroke **Exclusion criteria:** (1) cardiac pacemaker or metal implants or instruments inside the patient's body; (2) treatment-resistant seizures; (3) using any psychoactive or stimulation drugs; (4) preg-

IRCT2017030921965N4 *(Continued)*

	nancy; (5) the existence of any neurological condition affecting sensory-motor systems, such as brain tumours, dementia, or severe substance abuse and medications and severe cognitive decline **Depression criteria:Inclusion criteria:** clinical interview with a psychiatrist and meets the criteria for depression according to DSM-V
Interventions	**Treatment 1:** tDCS- anodal. Treatment will be carried out in 15 sessions, three sessions per week and a consistent, direct and uniform current will be sent to the brain through anodal type waves for up to 30 minutes Treatment 2: tDCS- cathodal. Treatment will be carried out in 15 sessions, three sessions per week and a consistent, direct and uniform current will be sent to the brain through cathodal type waves for up to 30 minutes **Control:** sham tDCS. The control group will get electrical stimulation in the initial moments of each treatment session then the current will be switched off **Duration:** 2 weeks **Follow-up:** 15 days, 1 month and 3 months
Outcomes	**Primary outcome** • Depression measured using Beck Depressio Inventory (BDI)
Starting date	March 2017
Contact information	Dr Homa Zarrabi, Guilan University Of Medical Sciences, 15 Khordad Avenue, Shafa Hospital, Rasht, Iran Email: dr_zarrabi2000@ yahoo.com
Notes	

Kirkevold 2018

Study name	Promoting psychosocial well-being following stroke: study protocol for a randomised, controlled trial
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** dialogue-based intervention **Control arm:** usual care
Participants	**Geographical location:** Norway **Setting:** mixed **Stroke criteria:** unclear **Method of stroke diagnosis:** not reported **Inclusion criteria:** (1) adults over 18 years of age; (2) acute stroke within the last month before inclusion; (3) medically stable; (4) sufficient cognitive functioning to participate (assessed by physician/stroke team); (5) interested in participating; (6) able to understand and speak Norwegian; (7) able to give informed consent

Kirkevold 2018 *(Continued)*

	Exclusion criteria: (1) serious somatic or psychiatric disease, as these are assumed to impact ability to participate in the intervention; (2) severe dementia; (3) significant impressive aphasia or severe expressive aphasia **Depression criteria:** no criteria for depression at entry
Interventions	**Treatment:** dialogue-based intervention to promote psychosocial well-being. Intervention consists of 8 1 to 1 and a half hour dialogue-based sessions between the stroke survivor and a specially trained health professional (RN or OT). Each meeting has a guiding topical outline, which addresses significant issues described in the research literature (e.g. bodily changes, emotional challenges, personal relations, daily life issues, meaningful activities, existential issues, important values) **Administered by:** trained health professional (RN or OT) **Supervision:** not reported **Control:** usual care **Duration:** 6 months **Follow-up:** 2 weeks
Outcomes	**Primary outcome** • Depression measured using GHQ-28 **Secondary outcomes** • Coherence measured using SOC-13 • Health-related quality of life measured using SAQoL-39
Starting date	December 2014
Contact information	Dr Marit Kirkevold, Institute of Health and Society and Research Center for Rehabilitation and Rehabilitation services and models (CHARM), University of Oslo, PO Box 1130, Blindern, 0318 Oslo, Norway Email: marit.kirkevold@medisin.uio.no
Notes	

NCT03056287

Study name	Exercise and brain stimulation for post-stroke
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** rTMS **Control arm:** Sham rTMS
Participants	**Geographical location:** USA **Setting:** unclear **Stroke criteria:** unclear **Method of stroke diagnosis:** not reported

NCT03056287 *(Continued)*

	Inclusion criteria: (1) major depressive disorder (PHQ-9 > 10); (2) no antidepressant medications or clinically able to discontinue medications **Exclusion criteria:** (1) unable to ambulate at least 150 feet before stroke, or experienced intermittent claudication while walking; (2) history of congestive heart failure, unstable cardiac arrhythmias, hypertrophic cardiomyopathy, severe aortic stenosis, angina or dyspnoea at rest or during ADLs; (3) history of oxygen dependence; (4) pre-existing neurological disorders, dementia, or previous stroke; (5) history of major head trauma; (6) legal blindness or severe visual impairment; (7) history of psychosis or other Axis I disorder that is primary; (8) life expectancy < 1 year; (9) severe arthritis or other problem that limits passive range of motion; (10) history of DVT or pulmonary embolism within 6 months; (11) uncontrolled diabetes with recent weight loss, diabetic coma, or frequent insulin reactions; (12) severe hypertension with systolic > 200 mmHg and diastolic > 110 mmHg at rest; (13) suicide attempt in the last 2 years or at suicidal risk as assessed by SCID interview; (14) previous or current enrolment in a clinical trial to enhance motor recovery; (15) currently exercising ≥ 2 times per week (≥ 20 minutes); (16) presence of non-MRI compatible implants, pregnancy, or severe claustrophobia **Depression criteria:** PHQ-9 > 10 and diagnosed according to DSM-IV
Interventions	**Treatment:** rTMS **Control:** sham rTMS **Duration:** 8 weeks **Follow-up:** 8 weeks
Outcomes	**Primary outcome** • Depression measured using HDRS **Secondary outcome** • Walking speed
Starting date	1 January 2016
Contact information	Dr Chris Gregory, Medical University of South Carolina, Charleston, South Carolina, United States 29425 Email: gregoryc@musc.edu
Notes	

NCT03645759

Study name	Improving quality of life for veterans with stroke and psychological distress
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** I'm whole- behavioural health treatment **Control arm:** education + usual care
Participants	**Geographical location:** USA **Setting:** inpatient **Stroke criteria:** stroke and/or transient ischaemic attack

NCT03645759 *(Continued)*

	Method of stroke diagnosis: not reported **Inclusion criteria:** (1) a documented history of stroke and/or transient ischaemic attack within the last 30 days; (2) a modified Rankin score of > 3); (3) regular access to a computer or tablet with internet and a camera; (4) ability to give appropriate informed consent; (5) score > 5 on a measure of depression (Patient Health Questionnaire [PHQ-8]) and/or > 17 on a measure of anxiety (Generalized Anxiety Disorder-7 [GAD-7]) assessments; (6) ability to ambulate with or without assistance of a cane or walker **Exclusion criteria:** (1) cognitive impairment, as evidenced by a score of > 3 on a brief cognitive screener; (2) documented diagnosis of psychotic disorder or schizophrenia; (3) documented severe depression, anxiety (based on PHQ-8 or GAD-7 score of > 20), or hospitalisation for psychiatric illness within the past 30 days **Depression criteria:** PHQ-8 score > 5
Interventions	**Treatment:** I'm whole- 6 behavioural health treatment sessions that focus on stroke self-management, psychological distress and social re-integration. Treatments will occur weekly. **Control:** education + usual care. This arm will only receive the standard usual care for stroke self-management provided by the Michael E. Debakey VA Medical facility and will receive 6 brief health education calls unrelated to stroke or psychological distress. **Duration:** not reported **Follow-up:** 6 and 12 weeks
Outcomes	**Primary outcome** • Mood measured using Stroke Specific Quality of Life scale **Secondary outcome** • Impact of stroke measured using Stroke Impact scale • Depression measured using PHQ-8 • Anxiety measured using GAD-7
Starting date	November 2019
Contact information	Dr Gina Evans, Michael E. DeBakey VA Medical Center, Houston, Texas, United States, 77030 Email: Gina.Evans@va.gov
Notes	

NCT04941482

Study name	Intervention effectiveness towards improving physical and mental health for post-stroke patients
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** multi-intervention programme **Control arm:** usual care
Participants	**Geographical location:** Vietnam **Setting:** inpatient

NCT04941482 *(Continued)*

	Stroke criteria: not reported **Method of stroke diagnosis:** diagnosis of stroke according to WHO's definition of stroke **Inclusion criteria:** (1) diagnosis of stroke according to WHO's definition of stroke; (2) are managed at the National Geriatrics Hospital in Vietnam; (3) include 24 hours to 1 week after stroke; (4) provide informed consent; (5) willing to attend intervention therapies and follow-up evaluations for half-year; (6) have conscious, cognitive, and communication abilities **Exclusion criteria:** (1) do not agree to participate in the study; (2) are included in other experimental studies; (3) have mental disorders before stroke attack; (4) Glasgow score ≤ 8; (5) other diseases that make it difficult to complete the intervention **Depression criteria:** no criteria for depression at entry
Interventions	**Treatment:** multi-intervention programme which includes motivational interviewing. This will occur in the first three months (one time per week in the first month and one time per the second and third month). This intervention method aims to discover and resolve patient's conflicts by a standardised communication skill to improve their mental health and change negative behaviours. **Control:** usual care which involves standard health check and functional near-infrared spectroscopy (fNIRS) measure **Duration:** 3 months **Follow-up:** 6 months
Outcomes	**Primary outcomes** • Depression measured using PHQ-9 • Cognitive function measured using Mini Mental State Examination (MMSE) • Disability measured using Barthel Index • Impact of stroke measured using Stroke Impact scale **Secondary outcomes** • Fatigue measured using Fatique Severity Scale (FSS) • Sleep quality measured using Pittsburgh Sleep Quality Index (PSQI)
Starting date	August 2021
Contact information	Dr Thao TP Nguyen, National Geriatrics Hospital, Hanoi, Vietnam, 100000 Email: vuthanhhuyen11@hmu.edu.vn
Notes	

NCT04985838

Study name	Helping ease anxiety and depression following stroke stage 3 (HEADS UP)
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** HEADS UP, a group-based Mindfulness Based Stress Reduction (MBSR) course **Control arm:** no intervention
Participants	**Geographical location:** UK

NCT04985838 *(Continued)*

	Setting: inpatient **Stroke criteria:** not reported **Method of stroke diagnosis:** not reported **Inclusion criteria:** (1) aged ≥ 18 years; (2) have had ≥ 1 stroke at least 3 months previously; (3) able to speak and understand conversational English **Exclusion criteria:** (1) prior MBSR attendance in the last three years (as this may confound results); (2) current participant in another trial of a similar psychological self-management intervention; (3) currently receiving treatment for PTSD (post-traumatic stress disorder) or psychosis; (4) disclosing suicidal ideation; (5) cannot follow a 2-stage command e.g. Please spell your surname and then tell me the days of the week; Please count to six and then spell your first name; (6) scores < 25 on TICSm (modified Telephone Interview of Cognitive Status; Appendix 7); (7) scores < 3 on the PHQ-4 **Depression criteria:** no criteria for depression at entry
Interventions	**Treatment:** HEADS UP - a group-based MBSR course adapted for people affected by stroke and delivered using a video communication platform e.g. Zoom. An informal introductory session in the first week is followed by 8 weekly sessions (2.5 hours, incorporating 30-minute comfort breaks). A 6-hour silent retreat is offered in week 7. An optional follow-up session is offered six-eight weeks after completion of the 9-week course. **Control:** no intervention **Duration:** 9 weeks **Follow-up:** 20 and 32 weeks
Outcomes	**Primary outcomes** • Depression measured using Beck Depression Inventory-II • Anxiety measured using Beck Anxiety Inventory • Depression and anxiety measured using Depression Anxiety Stress Scale **Secondary outcomes** • Impact of stroke measured using Short Form Stroke Impact Scale • Quality of life measured using EQ-5D 5 Level
Starting date	
Contact information	Dr Maggie Lawrence, Glasgow Caledonian University Glasgow, Glasgow, UK, G4 0BA Email: maggie.lawrence@gcu.ac.uk
Notes	

NCT05097040

Study name	A coach-guided online acceptance and commitment therapy (ACT) intervention for stroke survivors
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** acceptance and commitment therapy **Control arm:** usual care

NCT05097040 *(Continued)*

Participants	**Geographical location:** USA **Setting:** not reported **Stroke criteria:** not reported **Method of stroke diagnosis:** not reported **Inclusion criteria:** (1) aged ≥ 18 years; (2) with a confirmed diagnosis of stroke; (3) have at least mild symptoms of psychological distress measured by DASS-21; (4) have a computer or a smart-phone with internet access at home **Exclusion criteria:** (1) living in a nursing home; (2) a diagnosis of severe cognitive impairment e.g., dementia; (3) not fluent in English; (4) severe communication difficulties e.g., aphasia; (6) with life-threatening illness e.g., cancer; (7) with other CNS disorders; (8) currently receiving a psychological therapy; (9) prior experience in ACT; (10) psychiatric hospitalisation or diagnosis of mental illness in the past 2 years; (11) taking antipsychotic medication **Depression criteria:** mild symptoms of psychological distress measured by DASS-21.
Interventions	**Treatment:** acceptance and commitment therapy (7 individual sessions guided by a trained coach through zoom videoconferencing) **Control:** usual care **Duration:** 6 weeks **Follow-up:** 4 weeks post-treatment
Outcomes	**Primary outcomes:** • Depression measured by PHQ-9 • Anxiety measured by GAD-7 • Stress measured by Perceived Stress Scale **Secondary outcomes:** • Quality of life measured by WHO-QoL Psychological health component • Self-compassion measured by Self-Compassion Scale- Short Form
Starting date	January 2022
Contact information	Areum Han, University of Alabama, Birmingham, Alabama, USA Email: ahan@uab.edu
Notes	

Tang 2017

Study name	Repetitive transcranial magnetic stimulation for depression after basal ganglia ischaemic stroke: protocol for a multicentre randomised double-blind placebo-controlled trial
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** active rTMS **Control arm:** sham rTMS

Tang 2017 *(Continued)*

Participants	**Geographical location:** China **Setting:** inpatient **Stroke criteria:** ischaemic stroke **Method of stroke diagnosis:** clinical and MRI or CT findings of basal ganglia ischaemic stroke **Inclusion criteria:** (1) first-time ischaemic stroke; (2) recent stroke (within 3 weeks to 3 months) **Exclusion criteria:** (1) prior history of depressive disorders or major trauma within 1 year, severe depression, or any other severe mental disorder; (2) current or prior antidepressant use for any reason; (3) aphasia or severe cognitive impairment, severe hearing impairment, or severe language comprehension deficit due to other causes; (4) other cerebral disease such as Parkinson's disease, encephalitis, dementia, multiple sclerosis, head injury, severe systemic disease, or ongoing neoplasia; (5) ongoing postoperative recovery **Depression criteria:** DSM-IV diagnosis of depression due to stroke (ICD-10-CM code 293.83 (F06.32))
Interventions	**Treatment:** active rTMS **Control:** sham rTMS **Duration:** not reported **Follow-up:** not reported
Outcomes	**Primary outcome** • Depression measured using 24-item HDRS **Secondary outcomes** • Impairment measured using NIHSS • Activities of Daily Living measured using ADLS • Cognitive functioning measured using MoCA • Aphasia measured using Aphasia Battery in Chinese, Social Support Revalued Scale
Starting date	20 November 2017
Contact information	Dr Lianxu Zhao Email: zhaolianxu@smu.edu.cn
Notes	

Xu 2016

Study name	Efficacy and feasibility of antidepressant treatment in patients with post-stroke depression
Methods	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** rTMS **Control arm:** sham rTMS
Participants	**Geographical location:** China

Xu 2016 *(Continued)*

	Setting: unclear **Number of participants:** unclear **Stroke criteria:** ischaemic stroke **Method of stroke diagnosis:** ischaemic brain region or infarction confirmed by CT or MRI **Inclusion criteria:** (1) 2 weeks to 3 months after acute ischaemic stroke **Exclusion criteria:** (1) all kinds of serious mental disorders other than depressive disorder; confirmed cases of various types of depression, or history of major mental trauma within 1 year; (2) verbal communication failure (aphasia, severe cognitive impairment, severe hearing loss, etc.); (3) other systemic diseases that have a serious impact on abilities of daily living; (4) brain disease other than stroke (such as Parkinson's disease, encephalitis, multiple sclerosis, brain trauma, etc.); (5) nuclear magnetic resonance or transcranial magnetic stimulation contraindications **Depression criteria:** diagnostic criteria of depression disorder caused by other somatic disease accorded with American *Diagnostic and Statistical Manual of Mental Disorders* (DSM-V, ICD-10-CM 293.83 (F06.32))
Interventions	**Treatment:** rTMS **Control:** sham rTMS **Duration:** not reported **Follow-up:** not reported
Outcomes	**Primary outcome** • Depression measured using HDRS **Secondary outcomes** • Dependence measured using Social Support Revalued Scale • Disability and impairments measured using Medical Coping Modes Questionnaire
Starting date	1 January 2016
Contact information	Dr Suiyi Xu Email: suiyixu@sina.com
Notes	**Author contact:** emailed study authors to check if there are any published results for the trial 3 December 2018; no reply received

ACT: Acceptance and Commitment Therapy
ADLs: activities of daily living
ADLS: Activities of Daily Living Scale
ALT: alanine transaminase
AST: aspartate aminotransferase
BA: behavioural activation
BAI: Beck Anxiety Inventory
BDI: Beck Depression Inventory
BI: Barthel Index
BS: Brunnstrom Stages of recovery
CBT: Cognitive Behavioural Therapy
CCMD-3: Chinese Classification of Mental Disorders
CES-D: Center for Epidemiological Studies Depression scale
CNS: Central nervous system
Cr: creatinine
CT: computed tomography

DASS-21: 21-item Depression Anxiety Stress Scale
DSM-IV: Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition
DSM-V: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
DVT: deep vein thrombosis
EADL: Extended Activities of Daily Living
ECT: electroconvulsive therapy
EQ5D: EuroQoL 5-dimensions
FMA: Fugl-Meyer Assessment
fNIRS: functional near-infrared spectroscopy
FSS: Fatique Severity Scale
GAD-7: 7-item Generalised Anxiety Disorder scale
GHQ-28: 28-item General Health Questionnaire
GP: general practitioner
HAMD: Hamilton Depression Scale
HCG test: Human chorionic gonadotropin (pregnancy) test
HDRS-24: 24-item Hamilton Depression Rating Scale
ICD: International Classification for Diseases
iTBS: intermittent theta burst stimulation
MBI: modified Barthel Index
MBSR: Mindfulness Based Stress Reduction
MMSE: Mini Mental State Examination
mRS: modified Rankin Scale
MoCA: Montreal Cognitive Assessment
MRI: magnetic resonance imaging
NIHSS: National Institutes of Health Stroke Scale
OT: occupational therapist
PHQ-9(or 4 or 8): 9-item Patient Health Questionnaire
PSQI: Pittsburgh Sleep Quality Index
PTSD: post-traumatic stress disorder
QoL: quality of life
RCT: randomised controlled trial
RN: registered nurse
rTMS: repetitive transcranial magnetic stimulation
SAD-Q: Stroke Aphasia Depression Questionnaire - hospital version
SAQoL-39: Stroke Aphasia Quality of Life Scale
SCID: severe combined immunodeficiency
SOC-13: Sense of Coherence
SSRI: selective serotonin reuptake inhibitor
tDCS: transcranial direct current stimulation
TICS: Telephone Interview of Cognitive Status
TICSm: modified Telephone Interview of Cognitive Status
TMS: transcranial magnetic stimulation
VAMS: Visual Analog Mood Scale
WHO: World Health Organisation
WHODAS-12: 12-item World Health Organisation Disability Assessment Schedule
WHO-QoL: World Health Organisation Quality of Life
ZDS: Zung Depression Scale

DATA AND ANALYSES

Comparison 1. Pharmacological interventions versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Depression: meeting study criteria for depression at end of treatment	8	1025	Risk Ratio (M-H, Random, 95% CI)	0.70 [0.55, 0.88]

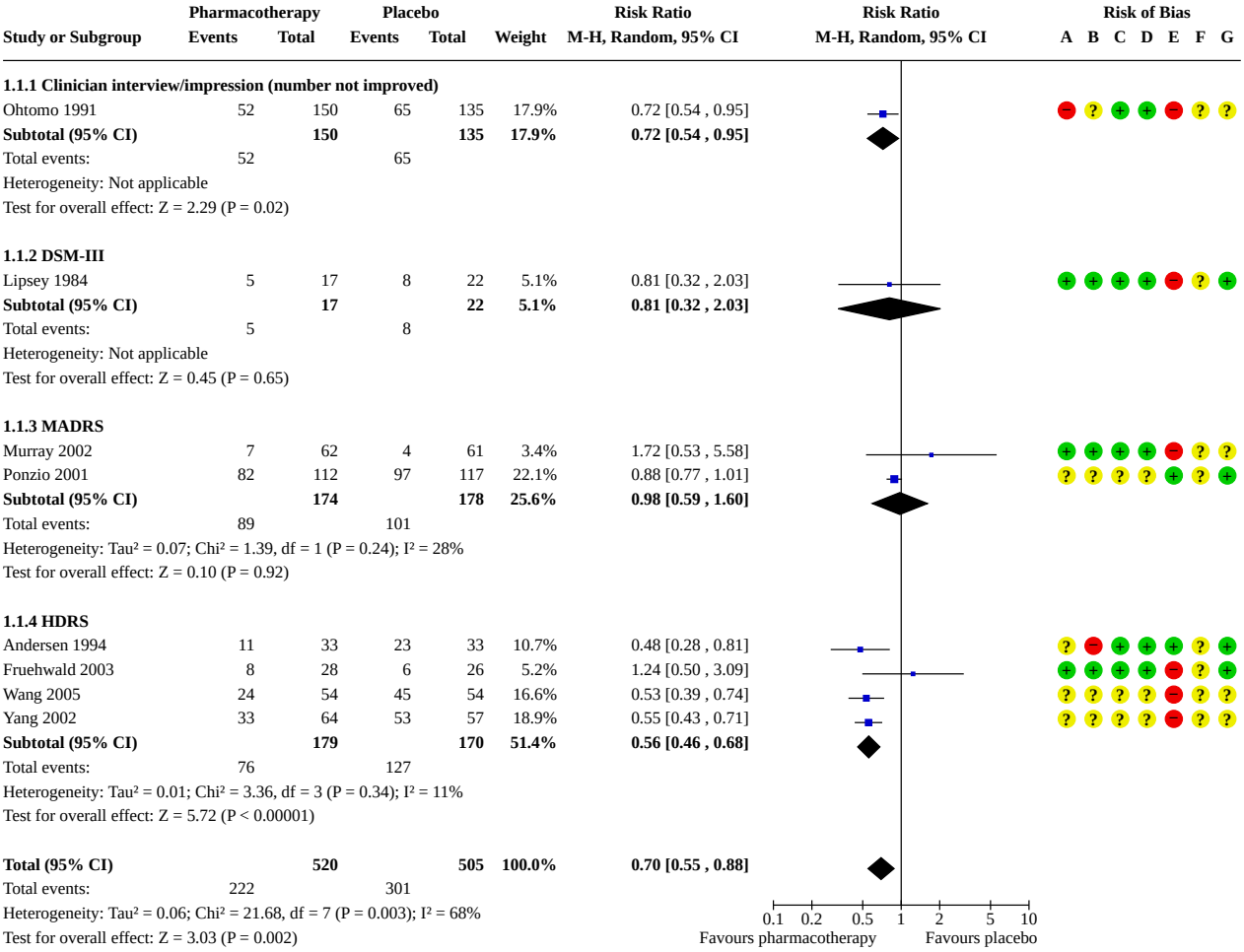
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1.1 Clinician interview/impression (number not improved)	1	285	Risk Ratio (M-H, Random, 95% CI)	0.72 [0.54, 0.95]
1.1.2 DSM-III	1	39	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.32, 2.03]
1.1.3 MADRS	2	352	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.59, 1.60]
1.1.4 HDRS	4	349	Risk Ratio (M-H, Random, 95% CI)	0.56 [0.46, 0.68]
1.2 Depression: < 50% reduction in scale scores at end of treatment	6	511	Risk Ratio (M-H, Random, 95% CI)	0.48 [0.32, 0.70]
1.2.1 HDRS	4	357	Risk Ratio (M-H, Random, 95% CI)	0.40 [0.25, 0.61]
1.2.2 MADRS	2	154	Risk Ratio (M-H, Random, 95% CI)	0.77 [0.59, 1.01]
1.3 Depression: average change in scores between baseline and end of treatment	5		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
1.3.1 BDI (high score = more depressed)	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
1.3.2 CGI (low score = improvement/high score = deterioration)	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
1.3.3 HDRS (high score = more depressed)	2		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
1.3.4 MADRS (high score = more depressed)	3		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
1.4 Depression: mean scores at end of treatment	15		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
1.4.1 BDI (high score = more depressed)	4		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
1.4.2 CGI (low score = improvement/high score = deterioration)	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
1.4.3 HDRS (high score = more depressed)	13		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
1.4.4 MADRS (high score = more depressed)	2		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
1.4.5 Melancholia scale (high score = more depressed)	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.4.6 Zung Depression Scale (high score = more depressed)	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
1.5 Anxiety: meeting study criteria for anxiety at end of treatment	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.5.1 Clinician interview/impression	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.6 Cognitive function: average change in scores between baseline and end of treatment	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.6.1 MMSE (low score = cognitive impairment)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.7 Cognitive function: mean scores at end of treatment	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.7.1 MMSE (low score = cognitive impairment)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.8 Activities of daily living: average change in scores between baseline and end of treatment	2	256	Mean Difference (IV, Random, 95% CI)	-8.00 [-24.18, 8.18]
1.8.1 Barthel Index (high score = more dependent)	2	256	Mean Difference (IV, Random, 95% CI)	-8.00 [-24.18, 8.18]
1.9 Activities of daily living: mean scores at end of treatment	3	316	Mean Difference (IV, Random, 95% CI)	3.14 [-0.97, 7.26]
1.9.1 Barthel Index (high score = more dependent)	3	316	Mean Difference (IV, Random, 95% CI)	3.14 [-0.97, 7.26]
1.10 Disability: average change in scores between baseline and end of treatment	3		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
1.10.1 Functional Independence Measure (low score = dependence)	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
1.10.2 Motoricity Index (low score = more motor impairment)	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
1.10.3 Scandinavian Stroke Scale (low score = more neurological deficit)	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
1.10.4 Rankin Scale (high score = more disability)	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
1.11 Disability: mean scores at end of treatment	3		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.11.1 Functional Independence Measure (low score = dependence)	2		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.11.2 Motoricity Index (low score = more motor impairment)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.11.3 Scandinavian Stroke Scale (low score = more neurological deficit)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.12 Neurological function: average change in scores between baseline and end of treatment	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.12.1 Chinese Stroke Scale (high score = more impairment)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.13 Neurological function: mean scores at end of treatment	4	304	Std. Mean Difference (IV, Random, 95% CI)	-0.95 [-1.44, -0.45]
1.13.1 Chinese Stroke Scale (high score = more impairment)	3	231	Std. Mean Difference (IV, Random, 95% CI)	-1.15 [-1.59, -0.72]
1.13.2 National Institutes of Health Stroke Scale (high score = more impairment	1	73	Std. Mean Difference (IV, Random, 95% CI)	-0.40 [-0.87, 0.06]
1.14 Adverse events: death	9	848	Risk Ratio (M-H, Random, 95% CI)	0.64 [0.20, 2.07]
1.14.1 At end of treatment	9	848	Risk Ratio (M-H, Random, 95% CI)	0.64 [0.20, 2.07]
1.15 Adverse events: all	10		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.15.1 Central nervous system events (e.g. confusion, sedation, tremor)	5	488	Risk Ratio (M-H, Fixed, 95% CI)	1.55 [1.12, 2.15]
1.15.2 Psychiatric events (e.g. anxiety, increased depression)	3	183	Risk Ratio (M-H, Fixed, 95% CI)	0.28 [0.05, 1.70]
1.15.3 Recurrent stroke	3	195	Risk Ratio (M-H, Fixed, 95% CI)	1.51 [0.29, 7.76]
1.15.4 Vascular events - not stroke (e.g. dizziness, palpitation)	7	587	Risk Ratio (M-H, Fixed, 95% CI)	1.44 [0.94, 2.22]
1.15.5 Gastrointestinal effects (e.g. constipation, diarrhoea)	4	473	Risk Ratio (M-H, Fixed, 95% CI)	1.62 [1.19, 2.19]
1.15.6 Other events - not listed above (e.g. dysuria, eye discomfort)	7	638	Risk Ratio (M-H, Fixed, 95% CI)	1.32 [1.00, 1.75]
1.15.7 Protocol violation (e.g. refused treatment, withdrew consent)	5	334	Risk Ratio (M-H, Fixed, 95% CI)	1.10 [0.45, 2.68]
1.16 Adverse events: leaving the study early (including death)	13		Risk Ratio (M-H, Random, 95% CI)	Subtotals only

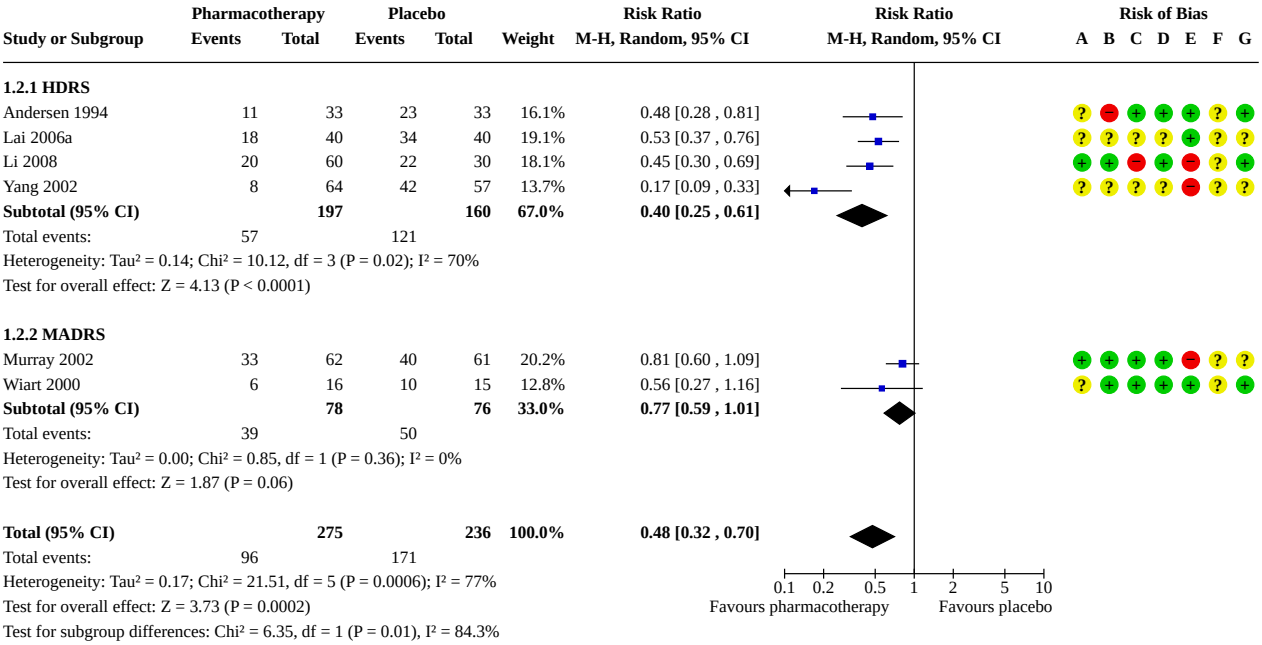
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.16.1 All dropouts and withdrawals	13	1165	Risk Ratio (M-H, Random, 95% CI)	1.07 [0.82, 1.39]

Analysis 1.1. Comparison 1: Pharmacological interventions versus placebo, Outcome 1: Depression: meeting study criteria for depression at end of treatment



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.2. Comparison 1: Pharmacological interventions versus placebo, Outcome 2: Depression: < 50% reduction in scale scores at end of treatment

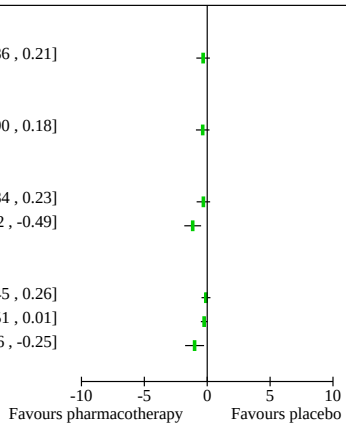


Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.3. Comparison 1: Pharmacological interventions versus placebo, Outcome 3: Depression: average change in scores between baseline and end of treatment

Study or Subgroup	Pharmacotherapy Mean	SD	Total	Placebo Mean	SD	Total	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A	B	C	D	E	F	G
1.3.1 BDI (high score = more depressed)														
Fruehwald 2003	-6.1	5.6	28	-4.1	6.48	26	-0.33 [-0.86 , 0.21]	+	+	+	+	−	?	+
1.3.2 CGI (low score = improvement/high score = deterioration)														
Fruehwald 2003	-2.7	1.6	28	-2.1	1.7	26	-0.36 [-0.90 , 0.18]	+	+	+	+	−	?	+
1.3.3 HDRS (high score = more depressed)														
Fruehwald 2003	-23.3	12	28	-19.1	15.1	26	-0.30 [-0.84 , 0.23]	+	+	+	+	−	?	+
Jiang 2001a	-20.13	6.82	30	-11.85	7.5	15	-1.15 [-1.82 , -0.49]	?	−	−	?	+	?	−
1.3.4 MADRS (high score = more depressed)														
Murray 2002	-8.5	8.9	62	-7.6	9.3	61	-0.10 [-0.45 , 0.26]	+	+	+	+	−	?	?
Ponzio 2001	-12	9.48	112	-9.9	7.47	117	-0.25 [-0.51 , 0.01]	?	?	?	?	+	?	+
Wiart 2000	-16.6	8.1	16	-8.4	7.8	15	-1.00 [-1.76 , -0.25]	?	+	+	+	+	?	+

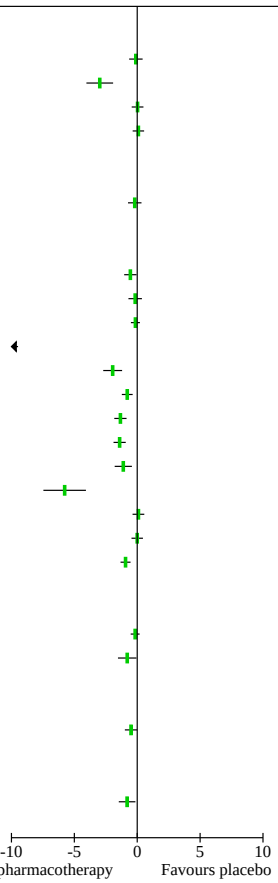


Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.4. Comparison 1: Pharmacological interventions versus placebo, Outcome 4: Depression: mean scores at end of treatment

Study or Subgroup	Pharmacotherapy Mean	SD	Total	Placebo Mean	SD	Total	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
1.4.1 BDI (high score = more depressed)								
Fruehwald 2003	6.1	5.6	28	6.8	7.4	26	-0.11 [-0.64 , 0.43]	+ + + + − ? +
Rampello 2005	8.06	3.43	16	18.4	3.33	15	-2.98 [-4.04 , -1.92]	+ + − + + ? +
Robinson 2008a	9.1	7.1	48	8.9	7.3	28	0.03 [-0.44 , 0.49]	+ + + + − − ?
Robinson 2008b	9.6	7.5	55	8.9	7.3	28	0.09 [-0.36 , 0.55]	+ + + + − − ?
1.4.2 CGI (low score = improvement/high score = deterioration)								
Fruehwald 2003	3.1	1.3	28	3.4	1.7	26	-0.20 [-0.73 , 0.34]	+ + + + − ? +
1.4.3 HDRS (high score = more depressed)								
Andersen 1994	11.4	5.1	33	14.1	4.7	33	-0.54 [-1.04 , -0.05]	? − + + + ? +
Fruehwald 2003	9.5	7.9	28	11.2	12.4	26	-0.16 [-0.70 , 0.37]	+ + + + − ? +
Gao 2017a	8.1	2.4	91	8.5	3.4	45	-0.14 [-0.50 , 0.21]	+ − − − − ? +
Huang 2002	4.76	0.6	40	16.34	1.3	40	-11.33 [-13.18 , -9.47]	? ? ? ? + ? +
Jiang 2001a	5.12	3.11	30	13.21	5.56	15	-1.95 [-2.70 , -1.20]	? − − ? + ? −
Kong 2007	12.6	5.3	48	16.3	3.7	42	-0.79 [-1.22 , -0.36]	+ + + ? − ? +
Lai 2006a	12.5	8.4	40	21.5	4.3	40	-1.34 [-1.82 , -0.85]	? ? ? ? + ? ?
Li 2008	14.5	2.4	60	18.7	3.9	30	-1.40 [-1.88 , -0.91]	+ + − + − ? +
Lipsey 1984	2.8	2.65	17	10	8.13	22	-1.11 [-1.79 , -0.42]	+ + + + − ? +
Rampello 2005	9.26	2.15	16	22.73	2.4	15	-5.77 [-7.46 , -4.08]	+ + − + + ? +
Robinson 2008a	10.2	7.5	48	9.5	6.6	28	0.10 [-0.37 , 0.56]	+ + + + − − ?
Robinson 2008b	9.5	6.6	55	9.5	6.6	28	0.00 [-0.46 , 0.46]	+ + + + − − ?
Wang 2005	11.18	4.25	54	15.3	4.56	54	-0.93 [-1.33 , -0.53]	? ? ? ? − ? ?
1.4.4 MADRS (high score = more depressed)								
Murray 2002	10.5	9.6	62	12	8.5	61	-0.16 [-0.52 , 0.19]	+ + + + − ? ?
Wiart 2000	11.8	6.7	16	18.7	10	15	-0.79 [-1.53 , -0.06]	? + + + + ? +
1.4.5 Melancholia scale (high score = more depressed)								
Andersen 1994	10.5	5.1	33	12.9	4.5	33	-0.49 [-0.98 , -0.00]	? − + + + ? +
1.4.6 Zung Depression Scale (high score = more depressed)								
Lipsey 1984	31	9.95	17	42	15.49	22	-0.81 [-1.47 , -0.15]	+ + + + − ? +

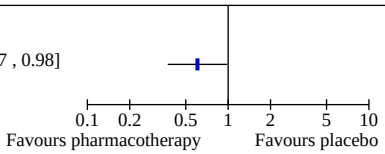


Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.5. Comparison 1: Pharmacological interventions versus placebo, Outcome 5: Anxiety: meeting study criteria for anxiety at end of treatment

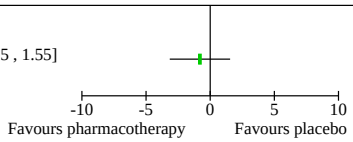
Study or Subgroup	Pharmacotherapy Events	Pharmacotherapy Total	Placebo Events	Placebo Total	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI	Risk of Bias A B C D E F G
1.5.1 Clinician interview/impression							
Ohtomo 1991	46	150	57	135	0.61 [0.37 , 0.98]		− ? + + − ? ?



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.6. Comparison 1: Pharmacological interventions versus placebo, Outcome 6: Cognitive function: average change in scores between baseline and end of treatment

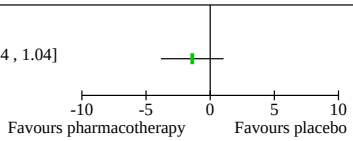
Study or Subgroup	Pharmacotherapy Mean	Pharmacotherapy SD	Pharmacotherapy Total	Placebo Mean	Placebo SD	Placebo Total	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
1.6.1 MMSE (low score = cognitive impairment)									
Wiart 2000	1.3	3.71	16	2.1	2.95	15	-0.80 [-3.15 , 1.55]		? + + + + ? +



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.7. Comparison 1: Pharmacological interventions versus placebo, Outcome 7: Cognitive function: mean scores at end of treatment

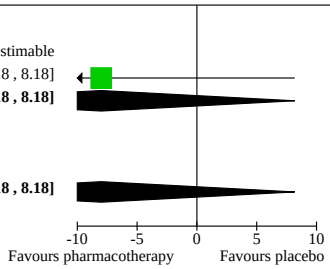
Study or Subgroup	Pharmacotherapy Mean	Pharmacotherapy SD	Pharmacotherapy Total	Placebo Mean	Placebo SD	Placebo Total	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
1.7.1 MMSE (low score = cognitive impairment)									
Wiart 2000	24.8	3.9	16	26.2	3	15	-1.40 [-3.84 , 1.04]		? + + + + ? +



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.8. Comparison 1: Pharmacological interventions versus placebo, Outcome 8: Activities of daily living: average change in scores between baseline and end of treatment

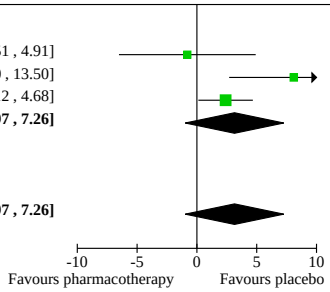
Study or Subgroup	Pharmacotherapy Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
1.8.1 Barthel Index (high score = more dependent)										
Ponzio 2001	1.7	0	112	1.8	0	117		Not estimable		? ? ? ? + ? +
Reding 1986	-28	23.22	11	-20	17.5	16	100.0%	-8.00 [-24.18 , 8.18]		+ + + + + ? ?
Subtotal (95% CI)			**123**			**133**	**100.0%**	**-8.00 [-24.18 , 8.18]**		
Heterogeneity: Not applicable										
Test for overall effect: Z = 0.97 (P = 0.33)										
Total (95% CI)			**123**			**133**	**100.0%**	**-8.00 [-24.18 , 8.18]**		
Heterogeneity: Not applicable										
Test for overall effect: Z = 0.97 (P = 0.33)										
Test for subgroup differences: Not applicable										



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.9. Comparison 1: Pharmacological interventions versus placebo, Outcome 9: Activities of daily living: mean scores at end of treatment

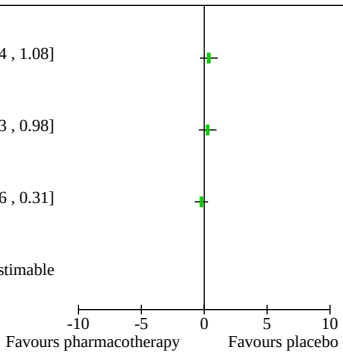
Study or Subgroup	Pharmacotherapy Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
1.9.1 Barthel Index (high score = more dependent)										
Gao 2017a	71.5	16.2	91	72.3	15.9	45	26.3%	-0.80 [-6.51 , 4.91]		+ − − − − ? +
Kong 2007	60.4	12.5	48	52.3	13.5	42	27.8%	8.10 [2.70 , 13.50]		+ + + ? − ? +
Li 2008	40.8	3.7	60	38.4	5.8	30	45.9%	2.40 [0.12 , 4.68]		+ + − + − ? +
Subtotal (95% CI)			**199**			**117**	**100.0%**	**3.14 [-0.97 , 7.26]**		
Heterogeneity: Tau² = 8.26; Chi² = 5.34, df = 2 (P = 0.07); I² = 63%										
Test for overall effect: Z = 1.50 (P = 0.13)										
Total (95% CI)			**199**			**117**	**100.0%**	**3.14 [-0.97 , 7.26]**		
Heterogeneity: Tau² = 8.26; Chi² = 5.34, df = 2 (P = 0.07); I² = 63%										
Test for overall effect: Z = 1.50 (P = 0.13)										
Test for subgroup differences: Not applicable										



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.10. Comparison 1: Pharmacological interventions versus placebo, Outcome 10: Disability: average change in scores between baseline and end of treatment

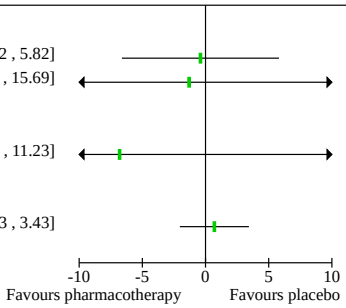
Study or Subgroup	Pharmacotherapy Mean	SD	Total	Placebo Mean	SD	Total	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
1.10.1 Functional Independence Measure (low score = dependence)								
Wiart 2000	24.7	20.37	16	16.4	23.2	15	0.37 [-0.34 , 1.08]	? + + + + ? +
1.10.2 Motoricity Index (low score = more motor impairment)								
Wiart 2000	18.9	23.81	16	11.9	26	15	0.27 [-0.43 , 0.98]	? + + + + ? +
1.10.3 Scandinavian Stroke Scale (low score = more neurological deficit)								
Fruehwald 2003	13.5	7.4	28	15.4	9.24	26	-0.22 [-0.76 , 0.31]	+ + + + − ? +
1.10.4 Rankin Scale (high score = more disability)								
Ponzio 2001	-0.4	0	112	-0.4	0	117	Not estimable	? ? ? ? + ? +



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.11. Comparison 1: Pharmacological interventions versus placebo, Outcome 11: Disability: mean scores at end of treatment

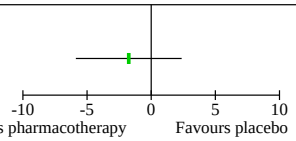
Study or Subgroup	Pharmacotherapy Mean	SD	Total	Placebo Mean	SD	Total	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
1.11.1 Functional Independence Measure (low score = dependence)								
Gao 2017a	71.1	17	91	71.5	17.6	45	-0.40 [-6.62 , 5.82]	+ − − − − ? +
Wiart 2000	87.4	22.8	16	88.7	25.3	15	-1.30 [-18.29 , 15.69]	? + + + + ? +
1.11.2 Motoricity Index (low score = more motor impairment)								
Wiart 2000	48.5	24.6	16	55.3	26.5	15	-6.80 [-24.83 , 11.23]	? + + + + ? +
1.11.3 Scandinavian Stroke Scale (low score = more neurological deficit)								
Fruehwald 2003	53.5	4.8	28	52.8	5.4	26	0.70 [-2.03 , 3.43]	+ + + + − ? +



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.12. Comparison 1: Pharmacological interventions versus placebo, Outcome 12: Neurological function: average change in scores between baseline and end of treatment

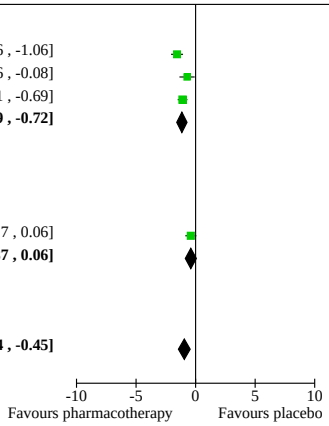
Study or Subgroup	Pharmacotherapy Mean	SD	Total	Placebo Mean	SD	Total	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
1.12.1 Chinese Stroke Scale (high score = more impairment)								
Jiang 2001a	-14.81	6.39	30	-13.06	6.78	15	-1.75 [-5.87 , 2.37]	? − − ? + ? −



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.13. Comparison 1: Pharmacological interventions versus placebo, Outcome 13: Neurological function: mean scores at end of treatment

Study or Subgroup	Pharmacotherapy Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
1.13.1 Chinese Stroke Scale (high score = more impairment)									
Huang 2002	4.02	1.86	40	8.57	3.64	40	25.0%	-1.56 [-2.06 , -1.06]	? ? ? ? + ? +
Jiang 2001a	3.23	2.37	30	5.2	3.27	15	21.6%	-0.72 [-1.36 , -0.08]	? − − ? + ? −
Wang 2005	5.83	6.57	52	13.86	7.89	54	27.4%	-1.10 [-1.51 , -0.69]	? ? ? ? − ? ?
Subtotal (95% CI)			**122**			**109**	**74.0%**	**-1.15 [-1.59 , -0.72]**	
Heterogeneity: Tau² = 0.08; Chi² = 4.34, df = 2 (P = 0.11); I² = 54%									
Test for overall effect: Z = 5.22 (P < 0.00001)									
1.13.2 National Institutes of Health Stroke Scale (high score = more impairment									
Kong 2007	8.6	6.4	37	11.2	6.4	36	26.0%	-0.40 [-0.87 , 0.06]	+ + + ? − ? +
Subtotal (95% CI)			**37**			**36**	**26.0%**	**-0.40 [-0.87 , 0.06]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 1.70 (P = 0.09)									
Total (95% CI)			**159**			**145**	**100.0%**	**-0.95 [-1.44 , -0.45]**	
Heterogeneity: Tau² = 0.19; Chi² = 11.98, df = 3 (P = 0.007); I² = 75%									
Test for overall effect: Z = 3.76 (P = 0.0002)									
Test for subgroup differences: Chi² = 5.37, df = 1 (P = 0.02), I² = 81.4%									



Risk of bias legend
(A) Random sequence generation (selection bias)
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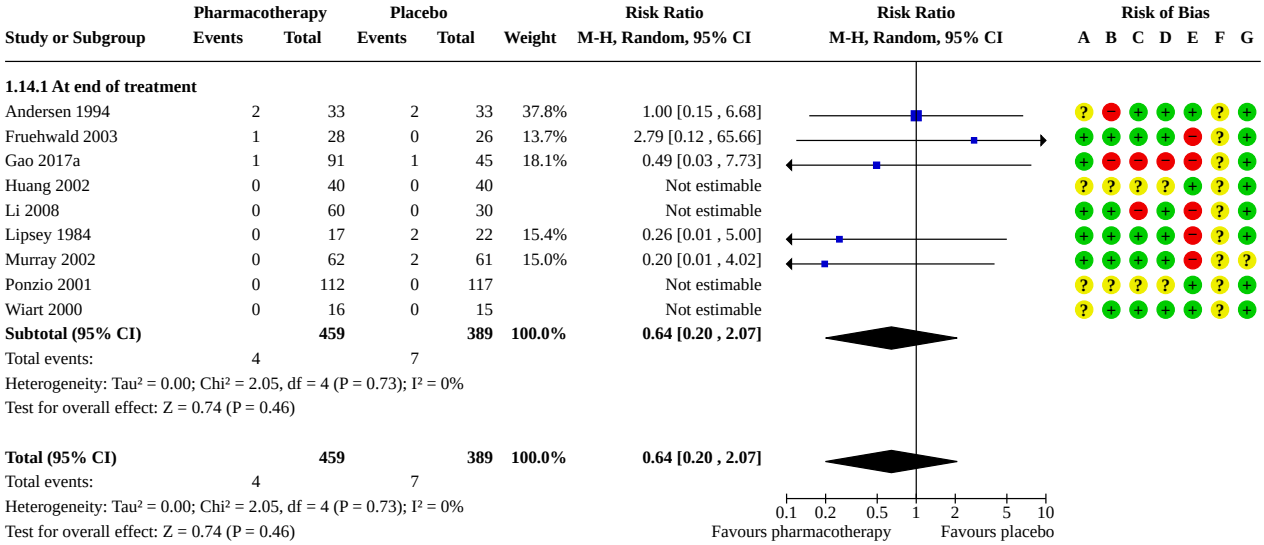
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.14. Comparison 1: Pharmacological interventions versus placebo, Outcome 14: Adverse events: death



Risk of bias legend

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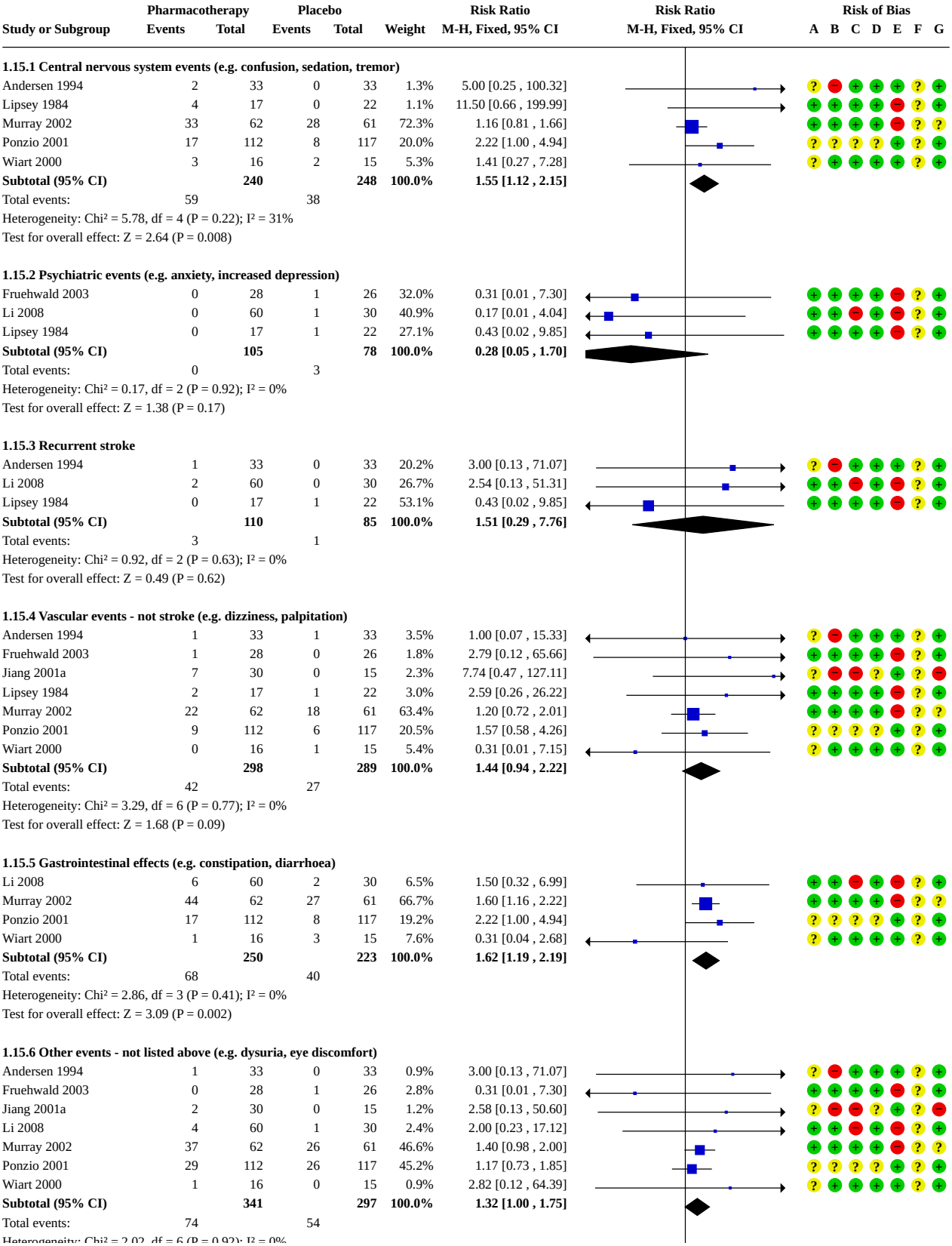
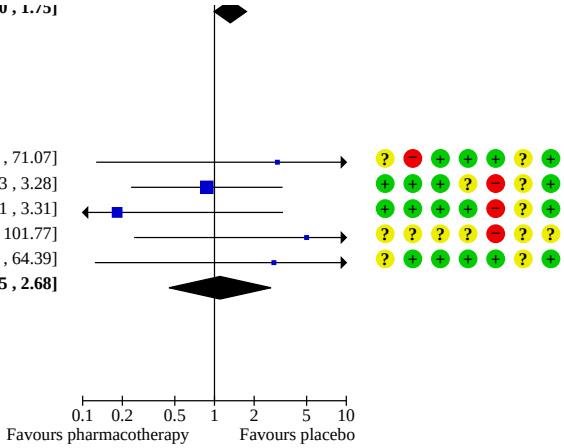
Analysis 1.15. Comparison 1: Pharmacological interventions versus placebo, Outcome 15: Adverse events: all



Analysis 1.15. (Continued)

Subtotal (95% CI)		**341**		**297**	**100.0%**	**1.32 [1.00 , 1.75]**
Total events:	74		54			
Heterogeneity: Chi² = 2.02, df = 6 (P = 0.92); I² = 0%						
Test for overall effect: Z = 1.93 (P = 0.05)						
1.15.7 Protocol violation (e.g. refused treatment, withdrew consent)						
Andersen 1994	1	33	0	33	5.6%	3.00 [0.13 , 71.07]
Kong 2007	4	48	4	42	48.2%	0.88 [0.23 , 3.28]
Lipsey 1984	0	17	3	22	34.7%	0.18 [0.01 , 3.31]
Wang 2005	2	54	0	54	5.6%	5.00 [0.25 , 101.77]
Wiart 2000	1	16	0	15	5.8%	2.82 [0.12 , 64.39]
Subtotal (95% CI)		**168**		**166**	**100.0%**	**1.10 [0.45 , 2.68]**
Total events:	8		7			
Heterogeneity: Chi² = 3.30, df = 4 (P = 0.51); I² = 0%						
Test for overall effect: Z = 0.21 (P = 0.83)						



Risk of bias legend
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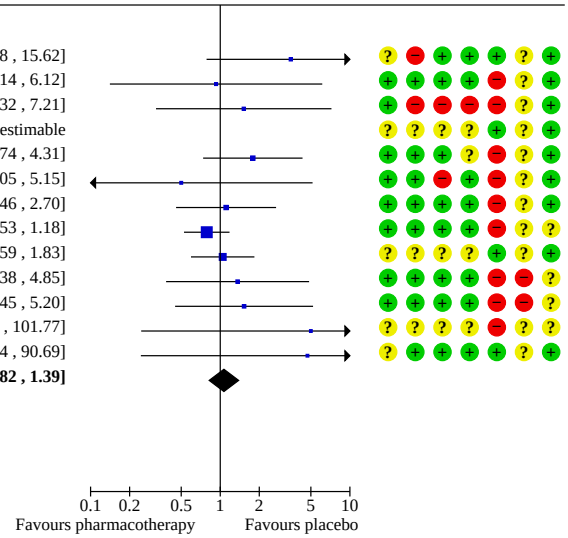
(G) Other bias

Analysis 1.16. Comparison 1: Pharmacological interventions versus placebo, Outcome 16: Adverse events: leaving the study early (including death)

Study or Subgroup	Pharmacotherapy Events	Pharmacotherapy Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
1.16.1 All dropouts and withdrawals						
Andersen 1994	7	33	2	33	3.0%	3.50 [0.78 , 15.62]
Fruehwald 2003	2	28	2	26	1.9%	0.93 [0.14 , 6.12]
Gao 2017a	6	85	2	43	2.8%	1.52 [0.32 , 7.21]
Huang 2002	0	40	0	40		Not estimable
Kong 2007	11	37	6	36	8.8%	1.78 [0.74 , 4.31]
Li 2008	2	60	1	15	1.3%	0.50 [0.05 , 5.15]
Lipsey 1984	6	17	7	22	8.6%	1.11 [0.46 , 2.70]
Murray 2002	24	62	30	61	41.8%	0.79 [0.53 , 1.18]
Ponzio 2001	20	112	20	117	21.5%	1.04 [0.59 , 1.83]
Robinson 2008a	7	48	3	28	4.2%	1.36 [0.38 , 4.85]
Robinson 2008b	9	55	3	28	4.5%	1.53 [0.45 , 5.20]
Wang 2005	2	54	0	54	0.8%	5.00 [0.25 , 101.77]
Wiart 2000	2	16	0	15	0.8%	4.71 [0.24 , 90.69]
Subtotal (95% CI)		**647**		**518**	**100.0%**	**1.07 [0.82 , 1.39]**
Total events:	98		76			
Heterogeneity: Tau² = 0.00; Chi² = 9.38, df = 11 (P = 0.59); I² = 0%						
Test for overall effect: Z = 0.49 (P = 0.62)						

Risk Ratio M-H, Random, 95% CI

Risk of Bias A B C D E F G



Risk of bias legend
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(F) Selective reporting (reporting bias)
(G) Other bias

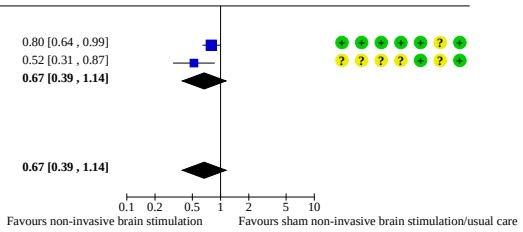
Comparison 2. Non-invasive brain stimulation versus sham non-invasive brain stimulation and/or usual care

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 Depression: meeting study criteria for depression at end of treatment	2	130	Risk Ratio (M-H, Random, 95% CI)	0.67 [0.39, 1.14]
2.1.1 HDRS (high score = more depressed)	2	130	Risk Ratio (M-H, Random, 95% CI)	0.67 [0.39, 1.14]
2.2 Depression: <50% reduction in scale scores at end of treatment	2	130	Risk Ratio (M-H, Random, 95% CI)	0.84 [0.52, 1.37]
2.2.1 HDRS (high score = more depressed)	2	130	Risk Ratio (M-H, Random, 95% CI)	0.84 [0.52, 1.37]
2.3 Depression: mean scores at end of treatment	9		Mean Difference (IV, Random, 95% CI)	Subtotals only
2.3.1 HDRS (high score = more depressed)	8	505	Mean Difference (IV, Random, 95% CI)	-6.51 [-9.64, -3.38]
2.3.2 PHQ-9 (high score = more depressed)	1	11	Mean Difference (IV, Random, 95% CI)	-4.60 [-9.89, 0.69]
2.3.3 BDI (high score = more depressed)	1	11	Mean Difference (IV, Random, 95% CI)	-10.80 [-22.38, 0.78]
2.3.4 MADRS (high score = more depressed)	1	48	Mean Difference (IV, Random, 95% CI)	3.80 [-1.13, 8.73]
2.4 Depression: mean scores at end of follow-up	4		Mean Difference (IV, Random, 95% CI)	Totals not selected
2.4.1 HDRS (high score = more depressed)	3		Mean Difference (IV, Random, 95% CI)	Totals not selected
2.4.2 PHQ-9 (high score = more depressed)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2.4.3 BDI (high score = more depressed)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2.4.4 MADRS (high score = more depressed)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2.5 Cognitive function: mean scores at the end of follow-up	1		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.5.1 MMSE (low score = cognitive impairment)	1		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.5.2 MoCA (low score = cognitive impairment)	1		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.6 Activities of daily living: mean scores at end of treatment	3	256	Std. Mean Difference (IV, Random, 95% CI)	1.31 [-0.62, 3.24]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.6.1 Barthel Index (high score = more dependent)	2	156	Std. Mean Difference (IV, Random, 95% CI)	0.22 [-0.10, 0.53]
2.6.2 ADL (high score = more impairment)	1	100	Std. Mean Difference (IV, Random, 95% CI)	3.50 [2.87, 4.13]
2.7 Activities of daily living: mean scores at the end of follow-up	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.7.1 Barthel Index (high score = more dependent)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.8 Neurological function: average change in scores between baseline and end of treatment	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.8.1 Chinese Stroke Scale (high score = more impairment)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.9 Neurological function: mean scores at end of treatment	3	290	Std. Mean Difference (IV, Random, 95% CI)	-2.21 [-3.32, -1.09]
2.9.1 Chinese Stroke Scale (high score = more impairment)	2	190	Std. Mean Difference (IV, Random, 95% CI)	-1.79 [-2.94, -0.64]
2.9.2 National Institutes of Health Stroke Scale (high score = more impairment)	1	100	Std. Mean Difference (IV, Random, 95% CI)	-3.04 [-3.63, -2.46]
2.10 Adverse events: death	4	0	Risk Ratio (M-H, Random, 95% CI)	Not estimable
2.10.1 At end of treatment	4	0	Risk Ratio (M-H, Random, 95% CI)	Not estimable
2.11 Adverse events: all	4	614	Risk Ratio (M-H, Random, 95% CI)	0.54 [0.26, 1.12]
2.11.1 Central nervous system events (e.g. confusion, headache, tremor)	4	183	Risk Ratio (M-H, Random, 95% CI)	0.61 [0.23, 1.64]
2.11.2 Gastrointestinal effects (e.g. constipation, diarrhoea)	2	0	Risk Ratio (M-H, Random, 95% CI)	Not estimable
2.11.3 Recurrent stroke	2	0	Risk Ratio (M-H, Random, 95% CI)	Not estimable
2.11.4 Other events - not listed above (e.g. dysuria, neck pain, eye discomfort)	4	183	Risk Ratio (M-H, Random, 95% CI)	0.47 [0.16, 1.39]
2.12 Adverse events: leaving the study early (including death)	2	0	Risk Ratio (M-H, Random, 95% CI)	Not estimable
2.12.1 All dropouts and withdrawals	2	0	Risk Ratio (M-H, Random, 95% CI)	Not estimable

Analysis 2.1. Comparison 2: Non-invasive brain stimulation versus sham non-invasive brain stimulation and/or usual care, Outcome 1: Depression: meeting study criteria for depression at end of treatment

Study or Subgroup	Non-invasive brain stimulation Events	Total	Sham non-invasive brain stimulation/usual care Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
2.1.1 HDRS (high score = more depressed)						
Valiengo 2017	19	24	24	24	59.0%	0.80 [0.64 , 0.99]
Zheng 2016	13	41	25	41	41.0%	0.52 [0.31 , 0.87]
Subtotal (95% CI)		**65**		**65**	**100.0%**	**0.67 [0.39 , 1.14]**
Total events:	32		49			
Heterogeneity: Tau² = 0.11; Chi² = 3.86, df = 1 (P = 0.05); I² = 74%						
Test for overall effect: Z = 1.47 (P = 0.14)						
Total (95% CI)		**65**		**65**	**100.0%**	**0.67 [0.39 , 1.14]**
Total events:	32		49			
Heterogeneity: Tau² = 0.11; Chi² = 3.86, df = 1 (P = 0.05); I² = 74%						
Test for overall effect: Z = 1.47 (P = 0.14)						
Test for subgroup differences: Not applicable						



Risk of bias legend
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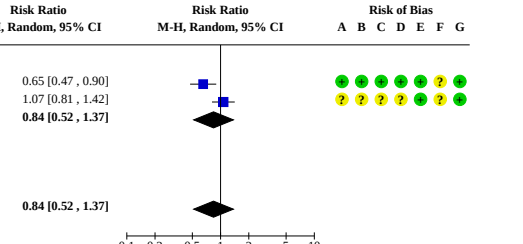
(G) Other bias

Analysis 2.2. Comparison 2: Non-invasive brain stimulation versus sham non-invasive brain stimulation and/or usual care, Outcome 2: Depression: <50% reduction in scale scores at end of treatment

Study or Subgroup	Non-invasive brain stimulation Events	Total	Sham non-invasive brain stimulation/usual care Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
2.2.1 HDRS (high score = more depressed)						
Valiengo 2017	15	24	23	24	48.7%	0.65 [0.47 , 0.90]
Zheng 2016	30	41	28	41	51.3%	1.07 [0.81 , 1.42]
Subtotal (95% CI)		**65**		**65**	**100.0%**	**0.84 [0.52 , 1.37]**
Total events:	45		51			
Heterogeneity: Tau² = 0.10; Chi² = 5.27, df = 1 (P = 0.02); I² = 81%						
Test for overall effect: Z = 0.69 (P = 0.49)						
Total (95% CI)		**65**		**65**	**100.0%**	**0.84 [0.52 , 1.37]**
Total events:	45		51			
Heterogeneity: Tau² = 0.10; Chi² = 5.27, df = 1 (P = 0.02); I² = 81%						
Test for overall effect: Z = 0.69 (P = 0.49)						
Test for subgroup differences: Not applicable						



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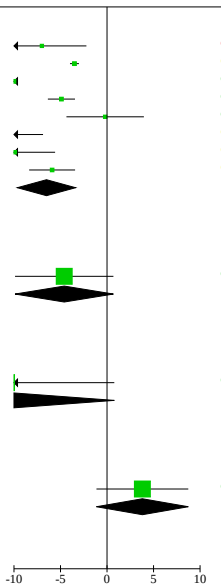
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 2.3. Comparison 2: Non-invasive brain stimulation versus sham non-invasive brain stimulation and/or usual care, Outcome 3: Depression: mean scores at end of treatment

Study or Subgroup	Non-invasive brain stimulation Mean	SD	Total	Sham non-invasive brain stimulation/usual care Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
2.3.1 HDRS (high score = more depressed)								
Chen 2005a	15.4	6.7	16	22.4	7.1	16	10.7%	-7.00 [-11.78 , -2.22]
Gu 2016	6.8	0.6	12	10.3	0.6	12	14.2%	-3.50 [-3.98 , -3.02]
Jiang 2014a	7	0.9	50	17	1.1	50	14.2%	-10.00 [-10.39 , -9.61]
Meng 2015	14.3	4.5	54	19.2	3.1	54	13.8%	-4.90 [-6.36 , -3.44]
Valiengo 2017	15.1	8.7	24	15.3	5.7	24	11.4%	-0.20 [-4.36 , 3.96]
Yang 2014a	7.43	2.76	37	18.49	9.09	19	11.4%	-11.06 [-15.24 , -6.88]
Yang 2014b	8.59	3.14	37	18.49	9.09	18	11.2%	-9.90 [-14.22 , -5.58]
Zheng 2016	13.3	5.6	41	19.2	5.8	41	13.1%	-5.90 [-8.37 , -3.43]
Subtotal (95% CI)			**271**			**234**	**100.0%**	**-6.51 [-9.64 , -3.38]**
Heterogeneity: Tau² = 17.90; Chi² = 448.37, df = 7 (P < 0.00001); I² = 98%								
Test for overall effect: Z = 4.07 (P < 0.0001)								
2.3.2 PHQ-9 (high score = more depressed)								
Hordacre 2021	4	3.85	6	8.6	4.9	5	100.0%	-4.60 [-9.89 , 0.69]
Subtotal (95% CI)			**6**			**5**	**100.0%**	**-4.60 [-9.89 , 0.69]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.71 (P = 0.09)								
2.3.3 BDI (high score = more depressed)								
Hordacre 2021	9	5.29	6	19.8	12.3	5	100.0%	-10.80 [-22.38 , 0.78]
Subtotal (95% CI)			**6**			**5**	**100.0%**	**-10.80 [-22.38 , 0.78]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.83 (P = 0.07)								
2.3.4 MADRS (high score = more depressed)								
Valiengo 2017	20.8	9.3	24	17	8.1	24	100.0%	3.80 [-1.13 , 8.73]
Subtotal (95% CI)			**24**			**24**	**100.0%**	**3.80 [-1.13 , 8.73]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.51 (P = 0.13)								



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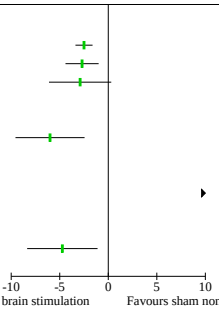
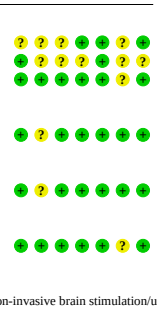
(G) Other bias

Analysis 2.4. Comparison 2: Non-invasive brain stimulation versus sham non-invasive brain stimulation and/or usual care, Outcome 4: Depression: mean scores at end of follow-up

Study or Subgroup	Non-invasive brain stimulation Mean	SD	Total	Sham non-invasive brain stimulation/usual care Mean	SD	Total	Mean Difference IV, Random, 95% CI
2.4.1 HDRS (high score = more depressed)							
Gu 2016	7.8	1.1	12	10.3	1.1	12	-2.50 [-3.38 , -1.62]
Meng 2015	9.3	2.2	54	12	6.01	54	-2.70 [-4.41 , -0.99]
Valiengo 2017	13.7	6.7	24	16.6	4.4	24	-2.90 [-6.11 , 0.31]
2.4.2 PHQ-9 (high score = more depressed)							
Hordacre 2021	4	3.22	6	10	2.8	5	-6.00 [-9.56 , -2.44]
2.4.3 BDI (high score = more depressed)							
Hordacre 2021	112	5.34	6	19.6	11.3	5	92.40 [81.61 , 103.19]
2.4.4 MADRS (high score = more depressed)							
Valiengo 2017	13.37	6.7	24	18.1	6.1	24	-4.73 [-8.36 , -1.10]





Risk of bias legend
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(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
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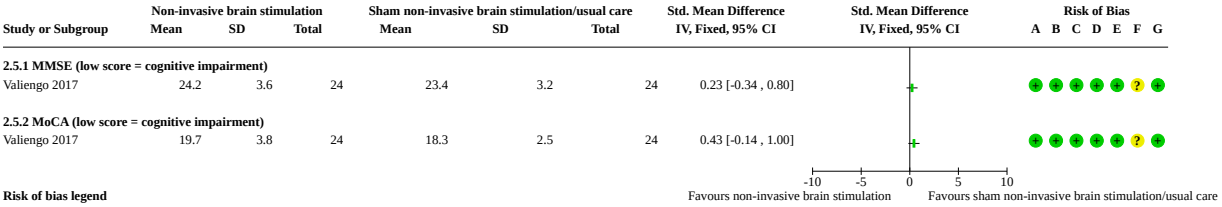
(G) Other bias

Analysis 2.5. Comparison 2: Non-invasive brain stimulation versus sham non-invasive brain stimulation and/or usual care, Outcome 5: Cognitive function: mean scores at the end of follow-up



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
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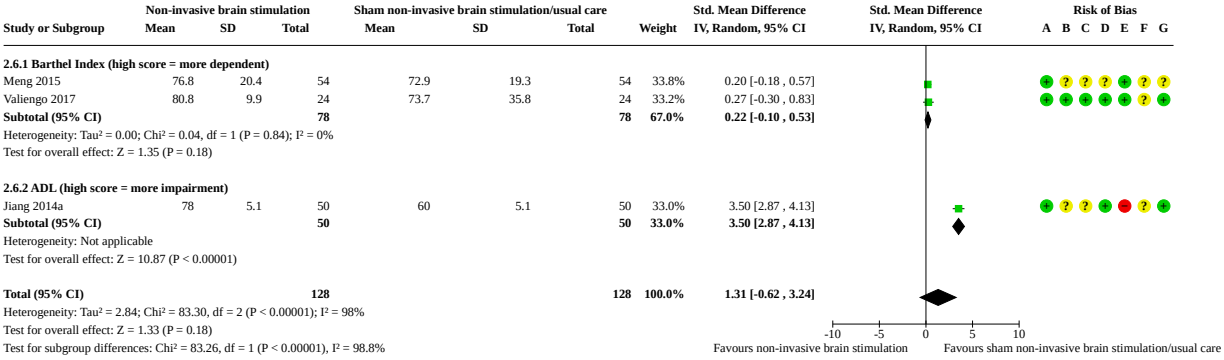
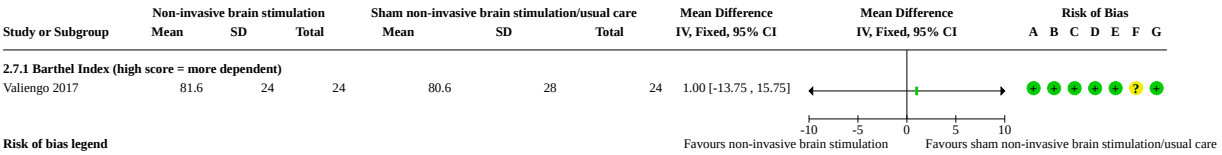
(G) Other bias

Analysis 2.6. Comparison 2: Non-invasive brain stimulation versus sham non-invasive brain stimulation and/or usual care, Outcome 6: Activities of daily living: mean scores at end of treatment



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 2.7. Comparison 2: Non-invasive brain stimulation versus sham non-invasive brain stimulation and/or usual care, Outcome 7: Activities of daily living: mean scores at the end of follow-up



Risk of bias legend
(A) Random sequence generation (selection bias)
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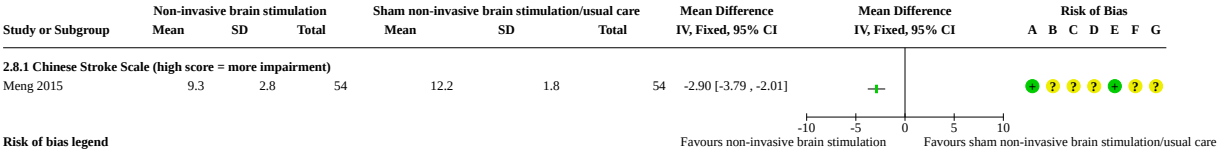
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 2.8. Comparison 2: Non-invasive brain stimulation versus sham non-invasive brain stimulation and/or usual care, Outcome 8: Neurological function: average change in scores between baseline and end of treatment

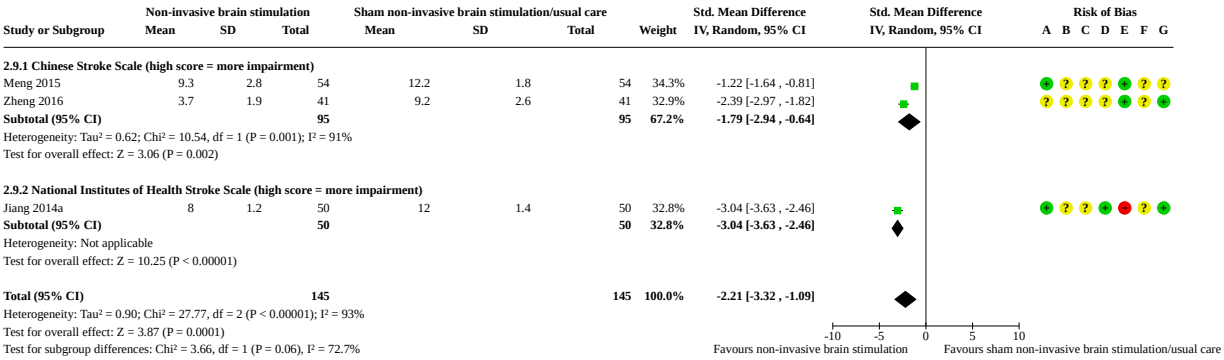


Study or Subgroup	Non-invasive brain stimulation Mean	SD	Total	Sham non-invasive brain stimulation/usual care Mean	SD	Total	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
2.8.1 Chinese Stroke Scale (high score = more impairment)									
Meng 2015	9.3	2.8	54	12.2	1.8	54	-2.90 [-3.79 , -2.01]		

-10 -5 0 5 10
Favours non-invasive brain stimulation | Favours sham non-invasive brain stimulation/usual care

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 2.9. Comparison 2: Non-invasive brain stimulation versus sham non-invasive brain stimulation and/or usual care, Outcome 9: Neurological function: mean scores at end of treatment

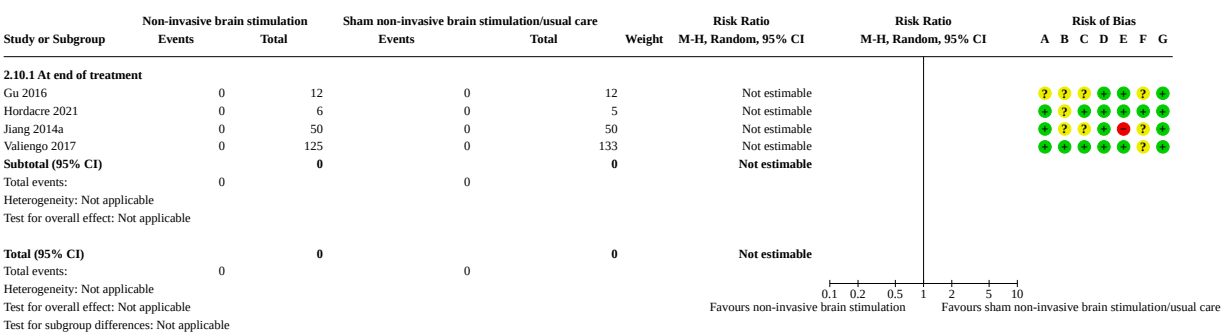


Study or Subgroup	Non-invasive brain stimulation Mean	SD	Total	Sham non-invasive brain stimulation/usual care Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
2.9.1 Chinese Stroke Scale (high score = more impairment)										
Meng 2015	9.3	2.8	54	12.2	1.8	54	34.3%	-1.22 [-1.64 , -0.81]		
Zheng 2016	3.7	1.9	41	9.2	2.6	41	32.9%	-2.39 [-2.97 , -1.82]		
Subtotal (95% CI)			**95**			**95**	**67.2%**	**-1.79 [-2.94 , -0.64]**		
Heterogeneity: Tau² = 0.62; Chi² = 10.54, df = 1 (P = 0.001); I² = 91%										
Test for overall effect: Z = 3.06 (P = 0.002)										
2.9.2 National Institutes of Health Stroke Scale (high score = more impairment)										
Jiang 2014a	8	1.2	50	12	1.4	50	32.8%	-3.04 [-3.63 , -2.46]		
Subtotal (95% CI)			**50**			**50**	**32.8%**	**-3.04 [-3.63 , -2.46]**		
Heterogeneity: Not applicable										
Test for overall effect: Z = 10.25 (P < 0.00001)										
Total (95% CI)			**145**			**145**	**100.0%**	**-2.21 [-3.32 , -1.09]**		
Heterogeneity: Tau² = 0.90; Chi² = 27.77, df = 2 (P < 0.00001); I² = 93%										
Test for overall effect: Z = 3.87 (P = 0.0001)										
Test for subgroup differences: Chi² = 3.66, df = 1 (P = 0.06), I² = 72.7%										

-10 -5 0 5 10
Favours non-invasive brain stimulation | Favours sham non-invasive brain stimulation/usual care

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 2.10. Comparison 2: Non-invasive brain stimulation versus sham non-invasive brain stimulation and/or usual care, Outcome 10: Adverse events: death

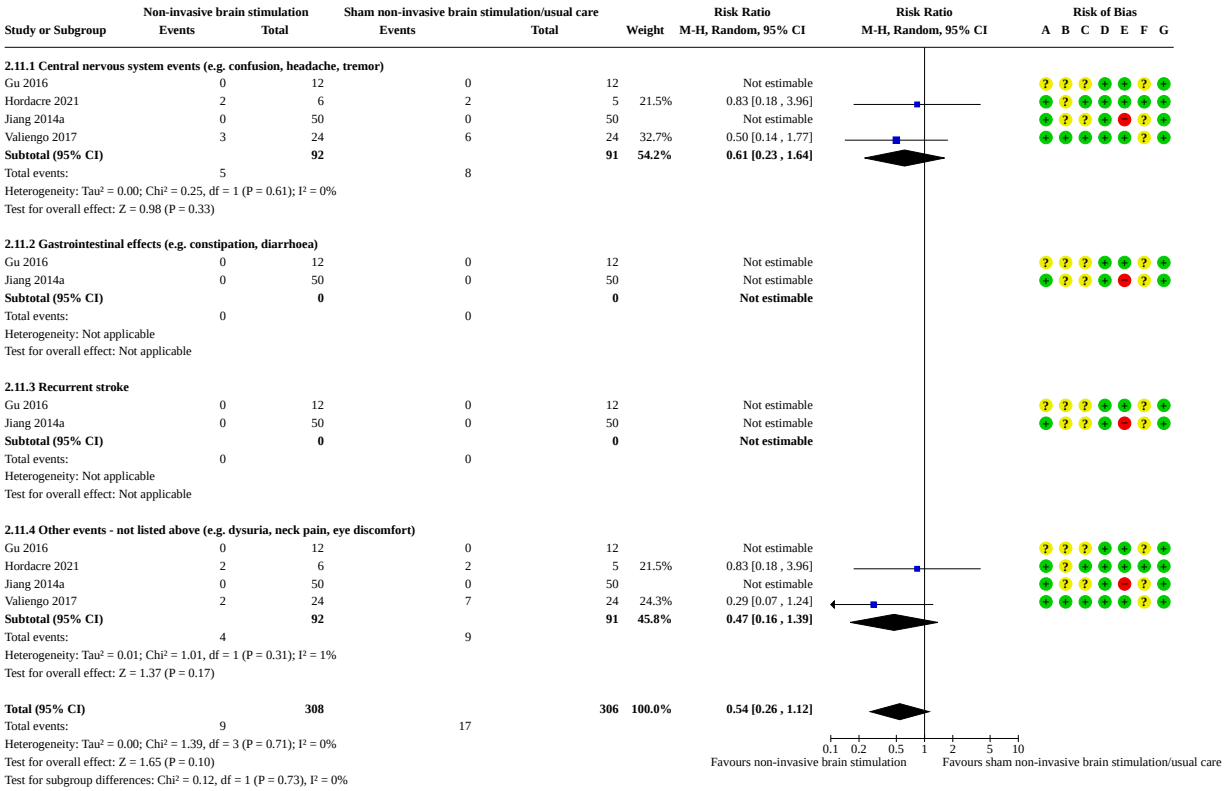


Study or Subgroup	Non-invasive brain stimulation Events	Total	Sham non-invasive brain stimulation/usual care Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI	Risk of Bias A B C D E F G
2.10.1 At end of treatment								
Gu 2016	0	12	0	12		Not estimable		
Hordacre 2021	0	6	0	5		Not estimable		
Jiang 2014a	0	50	0	50		Not estimable		
Valiengo 2017	0	125	0	133		Not estimable		
Subtotal (95% CI)		**0**		**0**		**Not estimable**		
Total events:	0		0					
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
Total (95% CI)		**0**		**0**		**Not estimable**		
Total events:	0		0					
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
Test for subgroup differences: Not applicable								

0.1 0.2 0.5 1 2 5 10
Favours non-invasive brain stimulation | Favours sham non-invasive brain stimulation/usual care

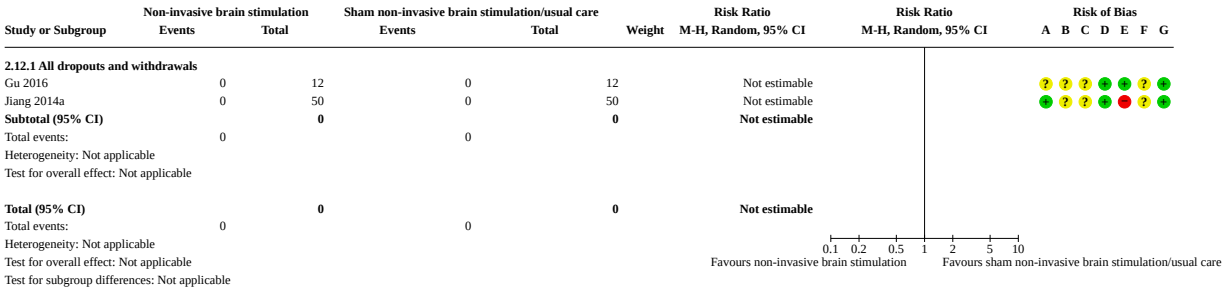
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 2.11. Comparison 2: Non-invasive brain stimulation versus sham non-invasive brain stimulation and/or usual care, Outcome 11: Adverse events: all



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 2.12. Comparison 2: Non-invasive brain stimulation versus sham non-invasive brain stimulation and/or usual care, Outcome 12: Adverse events: leaving the study early (including death)



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 3. Psychological therapy versus usual care and/or attention control

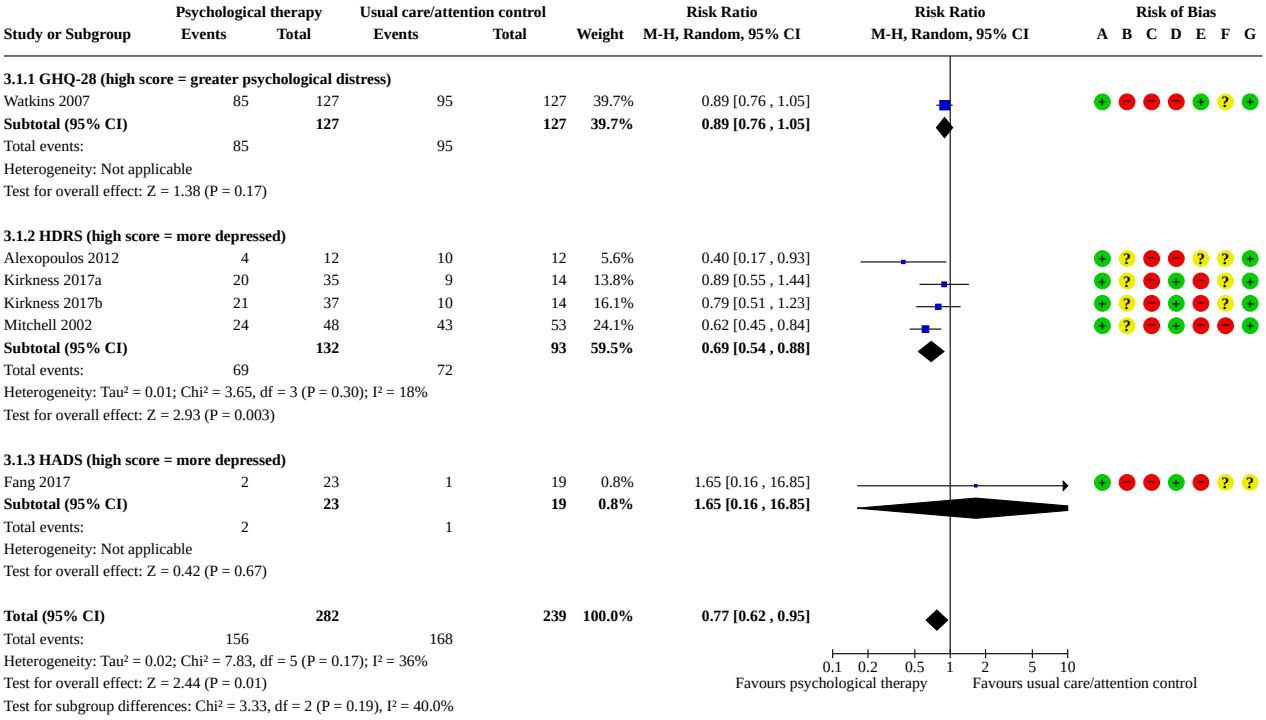
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.1 Depression: meeting study criteria for depression at end of treatment	6	521	Risk Ratio (M-H, Random, 95% CI)	0.77 [0.62, 0.95]
3.1.1 GHQ-28 (high score = greater psychological distress)	1	254	Risk Ratio (M-H, Random, 95% CI)	0.89 [0.76, 1.05]
3.1.2 HDRS (high score = more depressed)	4	225	Risk Ratio (M-H, Random, 95% CI)	0.69 [0.54, 0.88]
3.1.3 HADS (high score = more depressed)	1	42	Risk Ratio (M-H, Random, 95% CI)	1.65 [0.16, 16.85]
3.2 Depression: < 50% reduction in scale scores at end of treatment	0	0	Risk Ratio (M-H, Random, 95% CI)	Not estimable
3.3 Depression: average change in scores between baseline and end of treatment	3	189	Mean Difference (IV, Random, 95% CI)	-6.20 [-8.24, -4.16]
3.3.1 HDRS (high score = more depressed)	3	189	Mean Difference (IV, Random, 95% CI)	-6.20 [-8.24, -4.16]
3.4 Depression: mean scores at end of treatment	18		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.4.1 BDI (high score = more depressed)	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.4.2 WDI (high score = more depressed)	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.4.3 HDRS (high score = more depressed)	13		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.4.4 SAD-Q 21-item (high score = more depressed)	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.4.5 Zung SDS (high score = more depressed)	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.4.6 MADRS (high score= more depressed	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.4.7 HADS (high score = more depressed)	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.4.8 Visual Analog Mood Scale (high score = more depressed)	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.4.9 AHI (high score = more depressed	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.4.10 DASS-21 (high score = more depressed)	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.4.11 SDS (high score= more depressed)	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.5 Depression: meeting study criteria for depression at end of follow-up	3	201	Risk Ratio (M-H, Random, 95% CI)	0.85 [0.59, 1.21]
3.5.1 HDRS (high score = more depressed)	3	201	Risk Ratio (M-H, Random, 95% CI)	0.85 [0.59, 1.21]
3.6 Depression: average change in scores between baseline and end of follow-up	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3.6.1 HDRS (high score = more depressed)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3.7 Depression: mean scores at end of follow-up	7		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.7.1 BDI (high score = more depressed)	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.7.2 WDI (high score = more depressed)	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.7.3 SAD-Q 21-item (high score = more depressed)	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.7.4 HDRS (high score = more depressed)	2		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.7.5 HADS (high score = more depressed)	2		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.7.6 MADRS (high score = more depressed)	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.7.7 VAMS (high score = more depressed)	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.7.8 PHQ-9 (high score = more depressed)	2		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.8 Psychological distress: average change in scores between baseline and end of treatment	2	377	Mean Difference (IV, Random, 95% CI)	-0.21 [-1.89, 1.48]
3.8.1 GHQ-28 (high score = greater psychological distress)	2	377	Mean Difference (IV, Random, 95% CI)	-0.21 [-1.89, 1.48]
3.9 Psychological distress: mean scores at end of treatment	2	377	Mean Difference (IV, Random, 95% CI)	-0.43 [-2.17, 1.31]
3.9.1 GHQ-28 (high score = greater psychological distress)	2	377	Mean Difference (IV, Random, 95% CI)	-0.43 [-2.17, 1.31]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.10 Anxiety: meeting study criteria for anxiety at end of treatment	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
3.10.1 HADS Anxiety (high score = more anxious)	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
3.11 Anxiety: mean scores at end of treatment	4		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.11.1 HADS Anxiety (high score = more anxious)	2		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.11.2 State Trait Anxiety Inventory-Trait (high score = more anxious)	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.11.3 State Trait Anxiety Inventory-State (high score = more anxious)	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.11.4 HARS (high score= more anxious)	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.11.5 SAS (high score= more anxious)	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.12 Anxiety: mean scores at end of follow-up	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.12.1 State Trait Anxiety Inventory - Trait (high score = more anxious)	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.12.2 State Trait Anxiety Inventory - State (high score = more anxious)	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.13 Activities of daily living: average change in scores from baseline to end of treatment	2	377	Std. Mean Difference (IV, Random, 95% CI)	-0.03 [-0.24, 0.18]
3.13.1 Nottingham EADL (high score = more independent)	1	123	Std. Mean Difference (IV, Random, 95% CI)	-0.10 [-0.48, 0.28]
3.13.2 Barthel Index (high score = more dependent)	1	254	Std. Mean Difference (IV, Random, 95% CI)	0.00 [-0.25, 0.25]
3.14 Activities of daily living: mean scores at end of treatment	9		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.14.1 Barthel Index (high score = more dependent)	9		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.14.2 Nottingham EADL (high score = more independent)	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.15 Activities of daily living: mean scores at end of follow-up	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

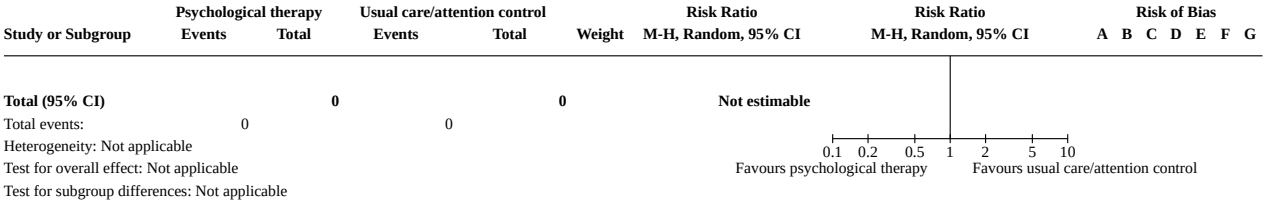
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.15.1 Modified Barthel Index (high score = more dependent)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3.16 Disability: mean scores at end of treatment	2	162	Std. Mean Difference (IV, Random, 95% CI)	-0.16 [-0.48, 0.17]
3.16.1 WHODAS-II total	1	24	Std. Mean Difference (IV, Random, 95% CI)	-0.51 [-1.33, 0.30]
3.16.2 FIM Motor	1	138	Std. Mean Difference (IV, Random, 95% CI)	-0.09 [-0.44, 0.27]
3.17 Neurological function: mean scores at end of treatment	2	158	Mean Difference (IV, Fixed, 95% CI)	-1.19 [-1.56, -0.83]
3.17.1 NIHSS (high score= more impairment)	2	158	Mean Difference (IV, Fixed, 95% CI)	-1.19 [-1.56, -0.83]
3.18 Adverse events: death	9		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
3.18.1 At end of treatment	9	889	Risk Ratio (M-H, Random, 95% CI)	0.65 [0.26, 1.66]
3.19 Adverse events: all	6		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
3.19.1 Central nervous system events (e.g. suicidal intentions)	2	126	Risk Ratio (M-H, Random, 95% CI)	0.87 [0.20, 3.90]
3.19.2 Recurrent stroke	1	254	Risk Ratio (M-H, Random, 95% CI)	5.00 [0.24, 103.12]
3.19.3 Vascular events - not stroke (e.g. transient ischaemic attack)	1	254	Risk Ratio (M-H, Random, 95% CI)	0.71 [0.23, 2.19]
3.19.4 Other events - not listed above (e.g. fall, too ill)	3	254	Risk Ratio (M-H, Random, 95% CI)	0.62 [0.13, 3.09]
3.19.5 Protocol violation (e.g. refused treatment, withdrew consent)	3	250	Risk Ratio (M-H, Random, 95% CI)	1.08 [0.21, 5.50]
3.20 Adverse events: leaving the study early (including death)	8		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
3.20.1 All dropouts and withdrawals	8	784	Risk Ratio (M-H, Random, 95% CI)	0.83 [0.42, 1.63]

Analysis 3.1. Comparison 3: Psychological therapy versus usual care and/or attention control, Outcome 1: Depression: meeting study criteria for depression at end of treatment



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

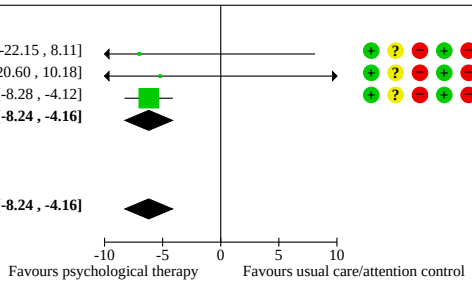
Analysis 3.2. Comparison 3: Psychological therapy versus usual care and/or attention control, Outcome 2: Depression: < 50% reduction in scale scores at end of treatment



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 3.3. Comparison 3: Psychological therapy versus usual care and/or attention control, Outcome 3: Depression: average change in scores between baseline and end of treatment

Study or Subgroup	Psychological therapy Mean	SD	Total	Usual care/attention control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
3.3.1 HDRS (high score = more depressed)									
Kirkness 2017a	-40.21	25.3	31	-33.19	22.5	13	1.8%	-7.02 [-22.15 , 8.11]	+ ? − + − ? +
Kirkness 2017b	-38.4	27.8	34	-33.19	22.5	13	1.8%	-5.21 [-20.60 , 10.18]	+ ? − + − ? +
Mitchell 2002	-9.8	4.9	45	-3.6	5.6	53	96.4%	-6.20 [-8.28 , -4.12]	+ ? − + − − +
Subtotal (95% CI)			**110**			**79**	**100.0%**	**-6.20 [-8.24 , -4.16]**	
Heterogeneity: Tau² = 0.00; Chi² = 0.03, df = 2 (P = 0.99); I² = 0%									
Test for overall effect: Z = 5.95 (P < 0.00001)									
Total (95% CI)			**110**			**79**	**100.0%**	**-6.20 [-8.24 , -4.16]**	
Heterogeneity: Tau² = 0.00; Chi² = 0.03, df = 2 (P = 0.99); I² = 0%									
Test for overall effect: Z = 5.95 (P < 0.00001)									
Test for subgroup differences: Not applicable									

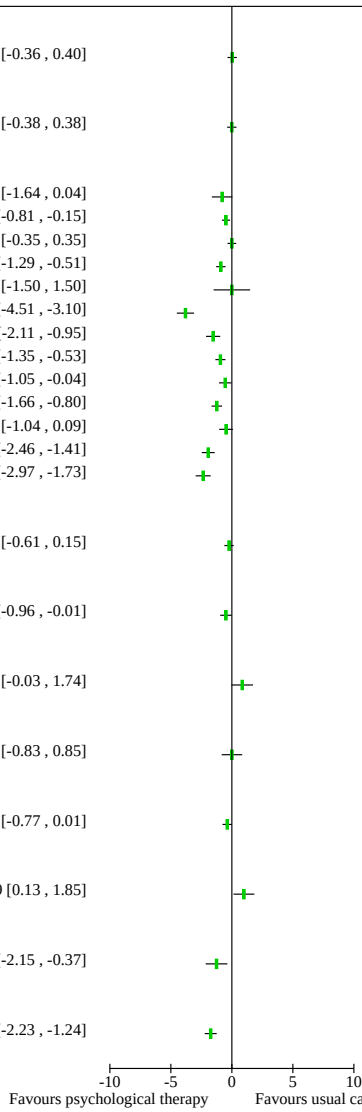


Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 3.4. Comparison 3: Psychological therapy versus usual care and/or attention control, Outcome 4: Depression: mean scores at end of treatment

Study or Subgroup	Psychological therapy Mean	SD	Total	Usual care/attention control Mean	SD	Total	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
3.4.1 BDI (high score = more depressed)								
Lincoln 2003	15.21	10.1	39	15	8.41	84	0.02 [-0.36 , 0.40]	+ − − − − ? −
3.4.2 WDI (high score = more depressed)								
Lincoln 2003	18.97	8.34	39	19	7.14	84	-0.00 [-0.38 , 0.38]	+ − − − − ? −
3.4.3 HDRS (high score = more depressed)								
Alexopoulos 2012	8.2	6.63	12	13.2	5.37	12	-0.80 [-1.64 , 0.04]	+ ? − − ? ? +
Cao 2009b	36.2	5	72	38.8	5.7	72	-0.48 [-0.81 , -0.15]	? ? ? ? − ? +
Gao 2017b	8.5	2.7	92	8.5	3.4	46	0.00 [-0.35 , 0.35]	+ − − − − ? +
Li 2009	9.26	2.74	58	11.89	3.06	56	-0.90 [-1.29 , -0.51]	? ? ? ? + ? +
Li 2019a	30	8	4	30	14	3	0.00 [-1.50 , 1.50]	? ? ? ? + ? +
Liang 2015	9.03	1.21	45	20.31	4	44	-3.80 [-4.51 , -3.10]	? ? ? ? + ? ?
Lu 2018	14.01	3.27	30	19.57	3.86	30	-1.53 [-2.11 , -0.95]	? ? ? ? + ? +
Mitchell 2002	10.29	5.29	48	16.17	6.95	53	-0.94 [-1.35 , -0.53]	+ ? − + − − +
Tao 2008	15.3	6.2	32	18.9	6.9	30	-0.54 [-1.05 , -0.04]	? ? ? ? + + ?
Tian 2010	16.74	2.94	50	20.36	2.89	50	-1.23 [-1.66 , -0.80]	? ? ? ? + ? ?
Wang 2019	11.08	4.1	25	13.28	4.98	25	-0.47 [-1.04 , 0.09]	? ? ? ? + ? +
Wei 2021	6.35	1.01	39	8.63	1.29	44	-1.94 [-2.46 , -1.41]	+ ? ? ? + ? +
Zhao 2004	14.35	3.12	35	21.07	2.5	35	-2.35 [-2.97 , -1.73]	? ? − + + ? +
3.4.4 SAD-Q 21-item (high score = more depressed)								
Thomas 2007	16.9	10.2	51	19.2	9.6	54	-0.23 [-0.61 , 0.15]	+ + − ? − − +
3.4.5 Zung SDS (high score = more depressed)								
Wang 2004a	40.23	7.62	35	44.16	8.43	35	-0.48 [-0.96 , -0.01]	? ? ? ? + ? +
3.4.6 MADRS (high score= more depressed								
Hoffmann 2015	19.39	1.202	12	18.49	0.73	10	0.85 [-0.03 , 1.74]	+ − − + + ? ?
3.4.7 HADS (high score = more depressed)								
Hoffmann 2015	8.23	1.41	12	8.22	0.89	10	0.01 [-0.83 , 0.85]	+ − − + + ? ?
3.4.8 Visual Analog Mood Scale (high score = more depressed)								
Thomas 2007	26.5	22.3	51	36.3	28.4	54	-0.38 [-0.77 , 0.01]	+ + − ? − − +
3.4.9 AHI (high score = more depressed								
Cullen 2018	2.69	0.6	12	2.1	0.55	12	0.99 [0.13 , 1.85]	+ + ? + − ? +
3.4.10 DASS-21 (high score = more depressed)								
Cullen 2018	13.5	11.5	12	28.5	11.55	12	-1.26 [-2.15 , -0.37]	+ + ? + − ? +
3.4.11 SDS (high score= more depressed)								
Liang 2015	41.32	5.42	45	51.33	6.01	44	-1.74 [-2.23 , -1.24]	? ? ? ? + ? ?

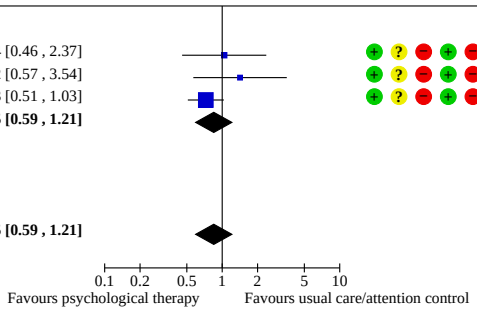


Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 3.5. Comparison 3: Psychological therapy versus usual care and/or attention control, Outcome 5: Depression: meeting study criteria for depression at end of follow-up

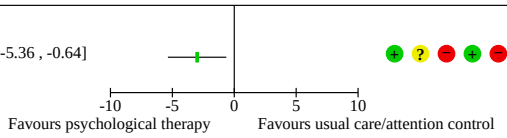
Study or Subgroup	Psychological therapy Events	Total	Usual care/attention control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Risk of Bias A B C D E F G
3.5.1 HDRS (high score = more depressed)							
Kirkness 2017a	13	35	5	14	17.0%	1.04 [0.46 , 2.37]	+ ? − + − ? +
Kirkness 2017b	15	37	4	14	14.0%	1.42 [0.57 , 3.54]	+ ? − + − ? +
Mitchell 2002	23	48	35	53	68.9%	0.73 [0.51 , 1.03]	+ ? − + − − +
Subtotal (95% CI)		**120**		**81**	**100.0%**	**0.85 [0.59 , 1.21]**	
Total events:	51		44				
Heterogeneity: Tau² = 0.02; Chi² = 2.25, df = 2 (P = 0.32); I² = 11%							
Test for overall effect: Z = 0.91 (P = 0.36)							
Total (95% CI)		**120**		**81**	**100.0%**	**0.85 [0.59 , 1.21]**	
Total events:	51		44				
Heterogeneity: Tau² = 0.02; Chi² = 2.25, df = 2 (P = 0.32); I² = 11%							
Test for overall effect: Z = 0.91 (P = 0.36)							
Test for subgroup differences: Not applicable							



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 3.6. Comparison 3: Psychological therapy versus usual care and/or attention control, Outcome 6: Depression: average change in scores between baseline and end of follow-up

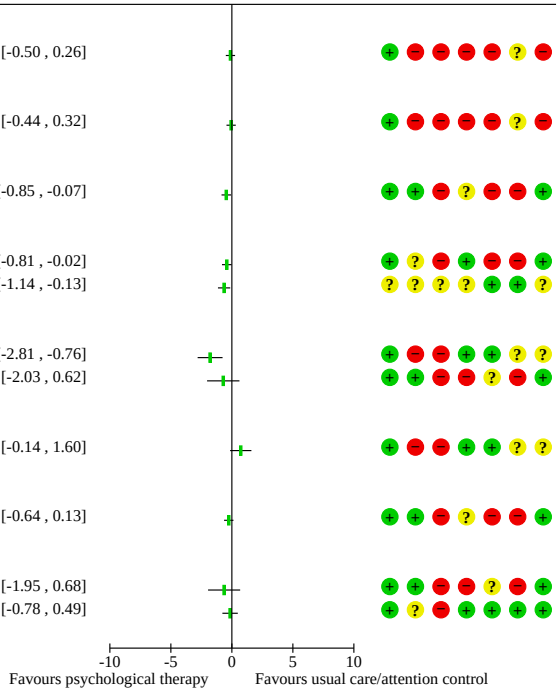
Study or Subgroup	Psychological therapy Mean	SD	Total	Usual care/attention control Mean	SD	Total	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
3.6.1 HDRS (high score = more depressed)								
Mitchell 2002	-9.2	5.7	48	-6.2	6.4	53	-3.00 [-5.36 , -0.64]	+ ? − + − − +



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 3.7. Comparison 3: Psychological therapy versus usual care and/or attention control, Outcome 7: Depression: mean scores at end of follow-up

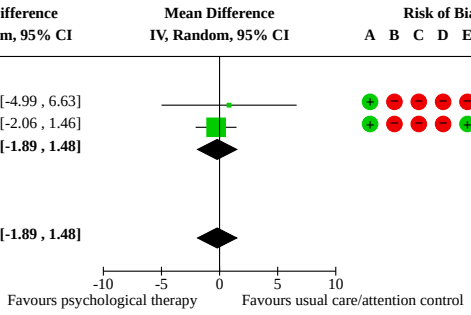
Study or Subgroup	Psychological therapy Mean	SD	Total	Usual care/attention control Mean	SD	Total	Std. Mean Difference IV, Random, 95% CI
3.7.1 BDI (high score = more depressed)							
Lincoln 2003	14.29	7.98	39	15.28	8.7	84	-0.12 [-0.50 , 0.26]
3.7.2 WDI (high score = more depressed)							
Lincoln 2003	19.18	7.29	39	19.69	8.84	84	-0.06 [-0.44 , 0.32]
3.7.3 SAD-Q 21-item (high score = more depressed)							
Thomas 2007	17.4	10	51	21.9	9.5	54	-0.46 [-0.85 , -0.07]
3.7.4 HDRS (high score = more depressed)							
Mitchell 2002	8.73	5.98	48	11.3	6.31	53	-0.41 [-0.81 , -0.02]
Tao 2008	10.6	7.2	32	14.9	6.1	32	-0.64 [-1.14 , -0.13]
3.7.5 HADS (high score = more depressed)							
Hoffmann 2015	4.64	2.68	12	8.89	1.7	10	-1.78 [-2.81 , -0.76]
Kerr 2018	4.5	3.9	4	7	2.7	6	-0.70 [-2.03 , 0.62]
3.7.6 MADRS (high score = more depressed)							
Hoffmann 2015	19.82	1.81	12	18.66	1.1	10	0.73 [-0.14 , 1.60]
3.7.7 VAMS (high score = more depressed)							
Thomas 2007	25.5	21.5	51	32.1	29.3	54	-0.25 [-0.64 , 0.13]
3.7.8 PHQ-9 (high score = more depressed)							
Kerr 2018	1.7	2.9	4	6	7.4	6	-0.64 [-1.95 , 0.68]
Thomas 2016	16.2	4.9	18	16.9	4.6	21	-0.14 [-0.78 , 0.49]



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 3.8. Comparison 3: Psychological therapy versus usual care and/or attention control, Outcome 8: Psychological distress: average change in scores between baseline and end of treatment

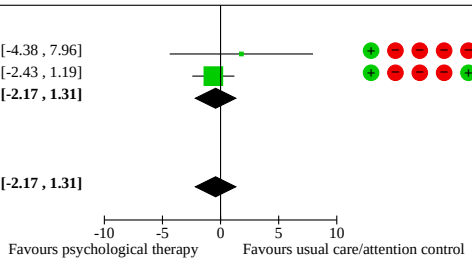
Study or Subgroup	Psychological therapy Mean	SD	Total	Usual care/attention control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
3.8.1 GHQ-28 (high score = greater psychological distress)								
Lincoln 2003	-6.18	15.31	39	-7	15.3	84	8.4%	0.82 [-4.99 , 6.63]
Watkins 2007	-1.3	7.1	127	-1	7.2	127	91.6%	-0.30 [-2.06 , 1.46]
Subtotal (95% CI)			**166**			**211**	**100.0%**	**-0.21 [-1.89 , 1.48]**
Heterogeneity: Tau² = 0.00; Chi² = 0.13, df = 1 (P = 0.72); I² = 0%								
Test for overall effect: Z = 0.24 (P = 0.81)								
Total (95% CI)			**166**			**211**	**100.0%**	**-0.21 [-1.89 , 1.48]**
Heterogeneity: Tau² = 0.00; Chi² = 0.13, df = 1 (P = 0.72); I² = 0%								
Test for overall effect: Z = 0.24 (P = 0.81)								
Test for subgroup differences: Not applicable								



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 3.9. Comparison 3: Psychological therapy versus usual care and/or attention control, Outcome 9: Psychological distress: mean scores at end of treatment

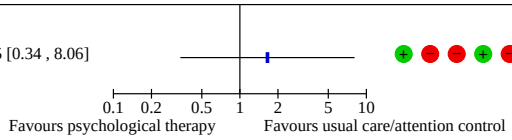
Study or Subgroup	Psychological therapy Mean	SD	Total	Usual care/attention control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
3.9.1 GHQ-28 (high score = greater psychological distress)								
Lincoln 2003	28.79	16.71	39	27	15.17	84	7.9%	1.79 [-4.38 , 7.96]
Watkins 2007	9.02	7.66	127	9.64	7.04	127	92.1%	-0.62 [-2.43 , 1.19]
Subtotal (95% CI)			**166**			**211**	**100.0%**	**-0.43 [-2.17 , 1.31]**
Heterogeneity: Tau² = 0.00; Chi² = 0.54, df = 1 (P = 0.46); I² = 0%								
Test for overall effect: Z = 0.48 (P = 0.63)								
Total (95% CI)			**166**			**211**	**100.0%**	**-0.43 [-2.17 , 1.31]**
Heterogeneity: Tau² = 0.00; Chi² = 0.54, df = 1 (P = 0.46); I² = 0%								
Test for overall effect: Z = 0.48 (P = 0.63)								
Test for subgroup differences: Not applicable								



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 3.10. Comparison 3: Psychological therapy versus usual care and/or attention control, Outcome 10: Anxiety: meeting study criteria for anxiety at end of treatment

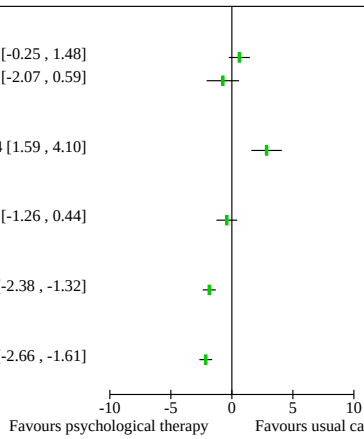
Study or Subgroup	Psychological therapy Events	Total	Usual care/attention control Events	Total	Risk Ratio M-H, Fixed, 95% CI
3.10.1 HADS Anxiety (high score = more anxious)					
Fang 2017	4	23	2	19	1.65 [0.34 , 8.06]

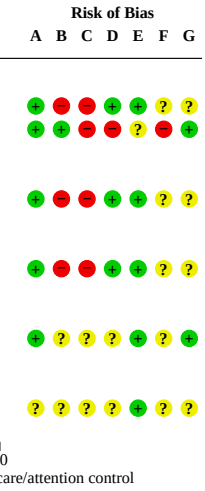


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 3.11. Comparison 3: Psychological therapy versus usual care and/or attention control, Outcome 11: Anxiety: mean scores at end of treatment

Study or Subgroup	Psychological therapy Mean	SD	Total	Usual care/attention control Mean	SD	Total	Std. Mean Difference IV, Random, 95% CI
3.11.1 HADS Anxiety (high score = more anxious)							
Hoffmann 2015	8.07	0.95	12	7.57	0.51	10	0.61 [-0.25 , 1.48]
Kerr 2018	4.5	4	4	8.2	4.8	6	-0.74 [-2.07 , 0.59]
3.11.2 State Trait Anxiety Inventory- Trait (high score = more anxious)							
Hoffmann 2015	46.24	1.05	12	43.63	0.62	10	2.84 [1.59 , 4.10]
3.11.3 State Trait Anxiety Inventory- State (high score = more anxious)							
Hoffmann 2015	45	2.26	12	45.82	1.34	10	-0.41 [-1.26 , 0.44]
3.11.4 HARS (high score= more anxious)							
Wei 2021	6.53	1.04	39	8.74	1.31	39	-1.85 [-2.38 , -1.32]
3.11.5 SAS (high score= more anxious)							
Liang 2015	40.31	5.14	45	51.23	4.98	44	-2.14 [-2.66 , -1.61]

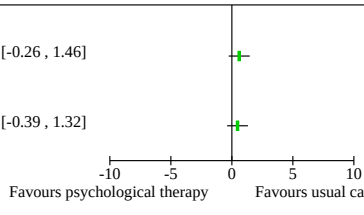


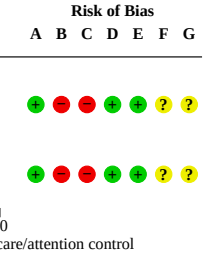


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 3.12. Comparison 3: Psychological therapy versus usual care and/or attention control, Outcome 12: Anxiety: mean scores at end of follow-up

Study or Subgroup	Psychological therapy Mean	SD	Total	Usual care/attention control Mean	SD	Total	Std. Mean Difference IV, Random, 95% CI
3.12.1 State Trait Anxiety Inventory - Trait (high score = more anxious)							
Hoffmann 2015	44.66	1.4	12	43.92	0.84	10	0.60 [-0.26 , 1.46]
3.12.2 State Trait Anxiety Inventory - State (high score = more anxious)							
Hoffmann 2015	46.25	3.25	12	44.93	1.93	10	0.46 [-0.39 , 1.32]

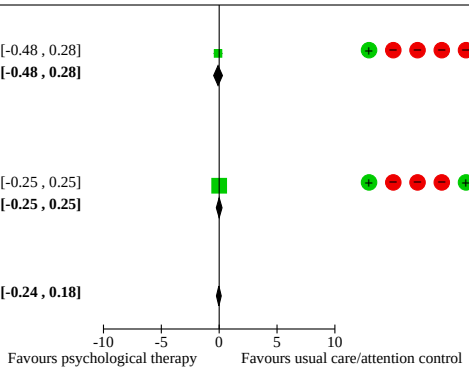




Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 3.13. Comparison 3: Psychological therapy versus usual care and/or attention control, Outcome 13: Activities of daily living: average change in scores from baseline to end of treatment

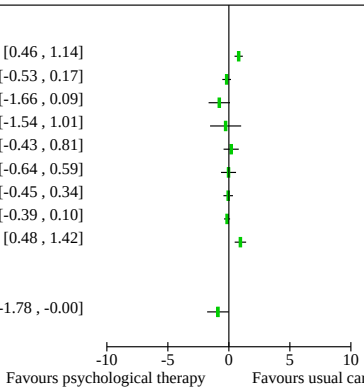
Study or Subgroup	Psychological therapy Mean	SD	Total	Usual care/attention control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
3.13.1 Nottingham EADL (high score = more independent)								
Lincoln 2003	-5.4	13.31	39	-4	14.69	84	29.5%	-0.10 [-0.48 , 0.28]
Subtotal (95% CI)			**39**			**84**	**29.5%**	**-0.10 [-0.48 , 0.28]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.50 (P = 0.62)								
3.13.2 Barthel Index (high score = more dependent)								
Watkins 2007	-1.4	3.9	127	-1.4	4.4	127	70.5%	0.00 [-0.25 , 0.25]
Subtotal (95% CI)			**127**			**127**	**70.5%**	**0.00 [-0.25 , 0.25]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (P = 1.00)								
Total (95% CI)			**166**			**211**	**100.0%**	**-0.03 [-0.24 , 0.18]**
Heterogeneity: Tau² = 0.00; Chi² = 0.18, df = 1 (P = 0.67); I² = 0%								
Test for overall effect: Z = 0.27 (P = 0.78)								
Test for subgroup differences: Chi² = 0.18, df = 1 (P = 0.67), I² = 0%								

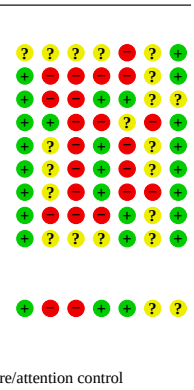


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 3.14. Comparison 3: Psychological therapy versus usual care and/or attention control, Outcome 14: Activities of daily living: mean scores at end of treatment

Study or Subgroup	Psychological therapy Mean	SD	Total	Usual care/attention control Mean	SD	Total	Std. Mean Difference IV, Random, 95% CI
3.14.1 Barthel Index (high score = more dependent)							
Cao 2009b	42.7	8.3	72	36.3	7.5	72	0.80 [0.46 , 1.14]
Gao 2017b	69.3	16.9	92	72.3	15.9	46	-0.18 [-0.53 , 0.17]
Hoffmann 2015	68.18	2.82	12	70.23	2.08	10	-0.78 [-1.66 , 0.09]
Kerr 2018	95.7	7.2	4	97.8	7.1	6	-0.27 [-1.54 , 1.01]
Kirkness 2017a	94.7	15	35	91.7	17.25	14	0.19 [-0.43 , 0.81]
Kirkness 2017b	91.2	18.2	37	91.7	17.25	14	-0.03 [-0.64 , 0.59]
Mitchell 2002	85.5	25.1	48	86.7	17.9	53	-0.06 [-0.45 , 0.34]
Watkins 2007	16.2	4.3	127	16.8	3.8	127	-0.15 [-0.39 , 0.10]
Wei 2021	74.35	9.87	39	65.63	8.32	39	0.95 [0.48 , 1.42]
3.14.2 Nottingham EADL (high score = more independent)							
Hoffmann 2015	34.69	6.5	12	39.66	3.5	10	-0.89 [-1.78 , -0.00]

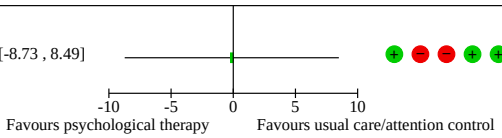




Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 3.15. Comparison 3: Psychological therapy versus usual care and/or attention control, Outcome 15: Activities of daily living: mean scores at end of follow-up

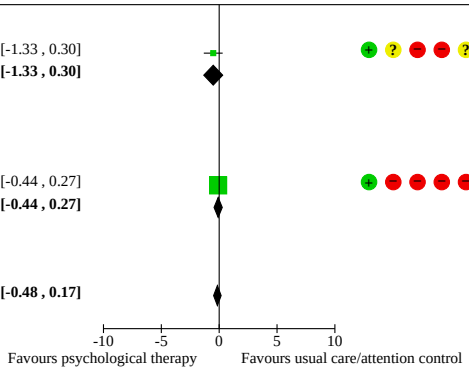
Study or Subgroup	Psychological therapy Mean	SD	Total	Usual care/attention control Mean	SD	Total	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
3.15.1 Modified Barthel Index (high score = more dependent)									
Hoffmann 2015	76.27	5.6	2	76.39	4.25	5	-0.12 [-8.73 , 8.49]		+ − − + + ? ?



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 3.16. Comparison 3: Psychological therapy versus usual care and/or attention control, Outcome 16: Disability: mean scores at end of treatment

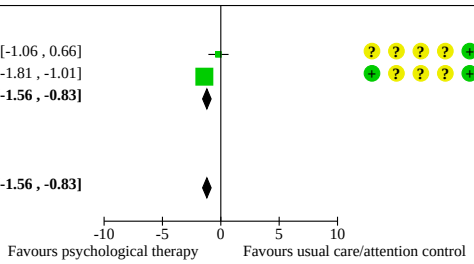
Study or Subgroup	Psychological therapy Mean	SD	Total	Usual care/attention control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
3.16.1 WHODAS-II total										
Alexopoulos 2012	24.5	8.54	12	29.5	10.16	12	15.9%	-0.51 [-1.33 , 0.30]		+ ? − − ? ? +
Subtotal (95% CI)			**12**			**12**	**15.9%**	**-0.51 [-1.33 , 0.30]**		
Heterogeneity: Not applicable										
Test for overall effect: Z = 1.24 (P = 0.22)										
3.16.2 FIM Motor										
Gao 2017b	69.9	18.1	92	71.5	17.6	46	84.1%	-0.09 [-0.44 , 0.27]		+ − − − − ? +
Subtotal (95% CI)			**92**			**46**	**84.1%**	**-0.09 [-0.44 , 0.27]**		
Heterogeneity: Not applicable										
Test for overall effect: Z = 0.49 (P = 0.62)										
Total (95% CI)			**104**			**58**	**100.0%**	**-0.16 [-0.48 , 0.17]**		
Heterogeneity: Tau² = 0.00; Chi² = 0.88, df = 1 (P = 0.35); I² = 0%										
Test for overall effect: Z = 0.94 (P = 0.35)										
Test for subgroup differences: Chi² = 0.88, df = 1 (P = 0.35), I² = 0%										



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 3.17. Comparison 3: Psychological therapy versus usual care and/or attention control, Outcome 17: Neurological function: mean scores at end of treatment

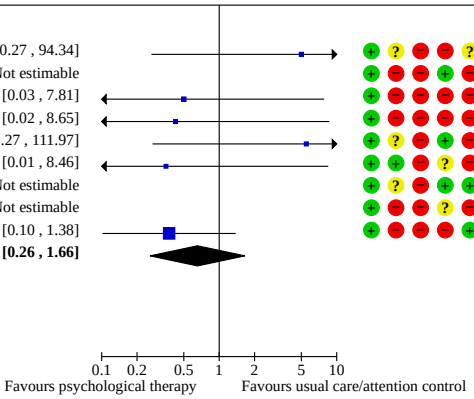
Study or Subgroup	Psychological therapy Mean	SD	Total	Usual care/attention control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
3.17.1 NIHSS (high score= more impairment)									
Liang 2015	6.4	2.11	40	6.6	1.82	40	17.8%	-0.20 [-1.06 , 0.66]	? ? ? ? + ? ?
Wei 2021	3.07	0.76	39	4.48	1.03	39	82.2%	-1.41 [-1.81 , -1.01]	+ ? ? ? + ? +
Subtotal (95% CI)			**79**			**79**	**100.0%**	**-1.19 [-1.56 , -0.83]**	
Heterogeneity: Chi² = 6.20, df = 1 (P = 0.01); I² = 84%									
Test for overall effect: Z = 6.43 (P < 0.00001)									
Total (95% CI)			**79**			**79**	**100.0%**	**-1.19 [-1.56 , -0.83]**	
Heterogeneity: Chi² = 6.20, df = 1 (P = 0.01); I² = 84%									
Test for overall effect: Z = 6.43 (P < 0.00001)									
Test for subgroup differences: Not applicable									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

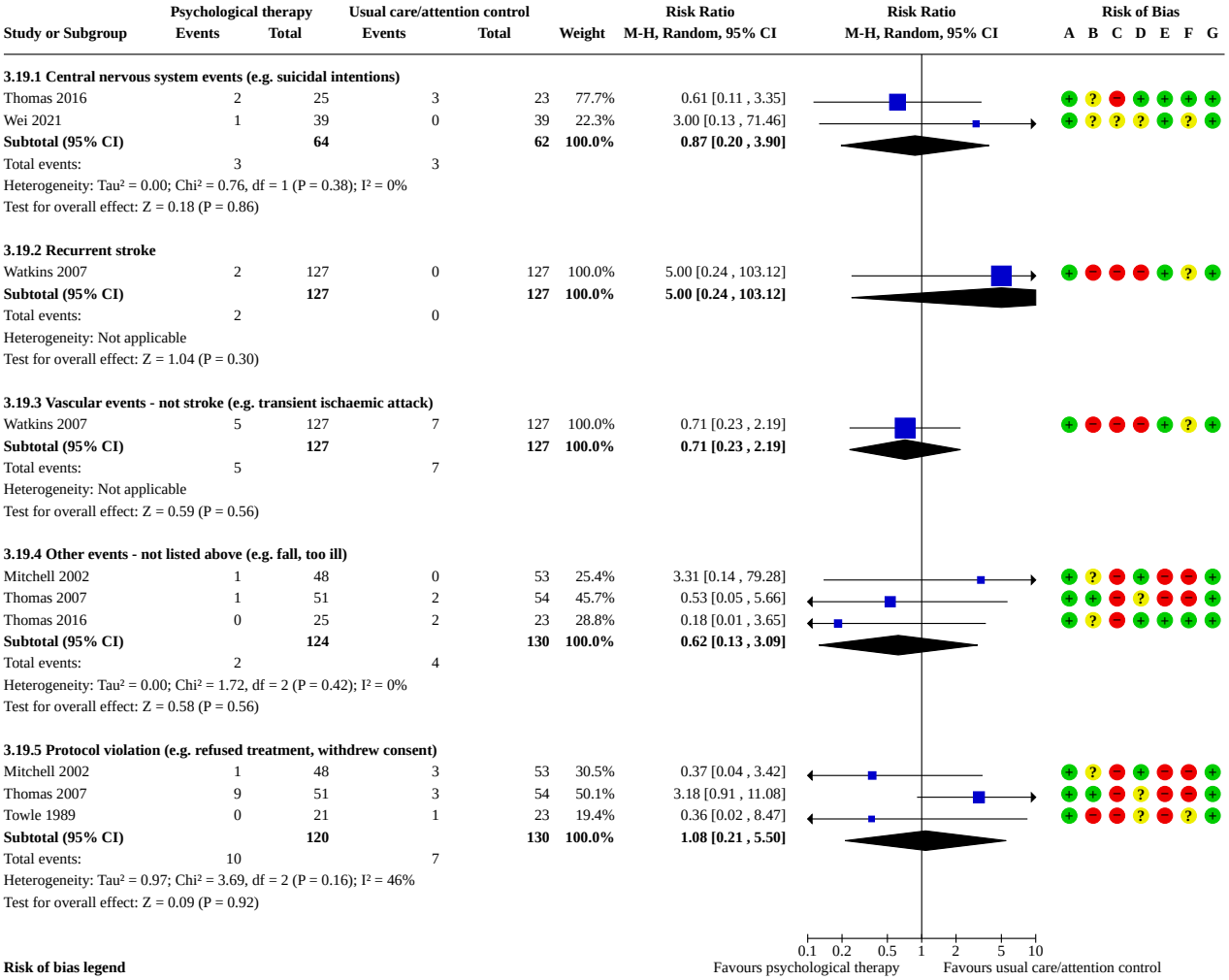
Analysis 3.18. Comparison 3: Psychological therapy versus usual care and/or attention control, Outcome 18: Adverse events: death

Study or Subgroup	Psychological therapy Events	Total	Usual care/attention control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Risk of Bias A B C D E F G
3.18.1 At end of treatment							
Alexopoulos 2012	2	12	0	12	10.0%	5.00 [0.27 , 94.34]	+ ? − − ? ? +
Fang 2017	0	23	0	19		Not estimable	+ − − + − ? ?
Gao 2017b	1	92	1	46	11.4%	0.50 [0.03 , 7.81]	+ − − − − ? +
Lincoln 2003	0	39	2	84	9.5%	0.42 [0.02 , 8.65]	+ − − − − ? −
Mitchell 2002	2	48	0	53	9.5%	5.51 [0.27 , 111.97]	+ ? − + − − +
Thomas 2007	0	51	1	54	8.6%	0.35 [0.01 , 8.46]	+ + − ? − − +
Thomas 2016	0	25	0	33		Not estimable	+ ? − + + + +
Towle 1989	0	21	0	23		Not estimable	+ − − ? − ? +
Watkins 2007	3	127	8	127	50.9%	0.38 [0.10 , 1.38]	+ − − − + ? +
Subtotal (95% CI)		**438**		**451**	**100.0%**	**0.65 [0.26 , 1.66]**	
Total events:	8		12				
Heterogeneity: Tau² = 0.00; Chi² = 4.80, df = 5 (P = 0.44); I² = 0%							
Test for overall effect: Z = 0.90 (P = 0.37)							



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 3.19. Comparison 3: Psychological therapy versus usual care and/or attention control, Outcome 19: Adverse events: all

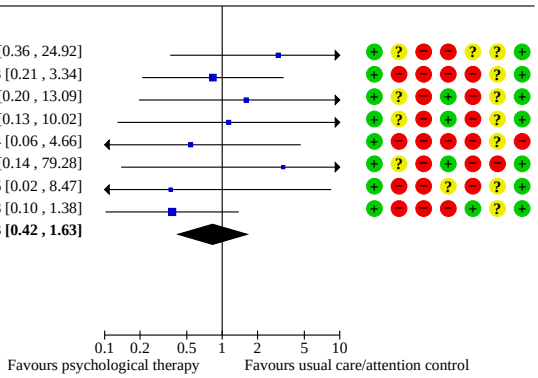


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 3.20. Comparison 3: Psychological therapy versus usual care and/or attention control, Outcome 20: Adverse events: leaving the study early (including death)

Study or Subgroup	Psychological therapy Events	Total	Usual care/attention control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
3.20.1 All dropouts and withdrawals						
Alexopoulos 2012	3	12	1	12	10.2%	3.00 [0.36 , 24.92]
Gao 2017b	5	92	3	46	23.8%	0.83 [0.21 , 3.34]
Kirkness 2017a	4	35	1	14	10.4%	1.60 [0.20 , 13.09]
Kirkness 2017b	3	37	1	14	9.7%	1.14 [0.13 , 10.02]
Lincoln 2003	1	39	4	84	9.8%	0.54 [0.06 , 4.66]
Mitchell 2002	1	48	0	53	4.5%	3.31 [0.14 , 79.28]
Towle 1989	0	21	1	23	4.6%	0.36 [0.02 , 8.47]
Watkins 2007	3	127	8	127	26.9%	0.38 [0.10 , 1.38]
Subtotal (95% CI)		**411**		**373**	**100.0%**	**0.83 [0.42 , 1.63]**
Total events:	20		19			

Heterogeneity: Tau² = 0.00; Chi² = 4.44, df = 7 (P = 0.73); I² = 0%
Test for overall effect: Z = 0.54 (P = 0.59)



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 4. Pharmacological intervention and psychological therapy (combination) versus a pharmacological intervention and usual care or attention control (single)

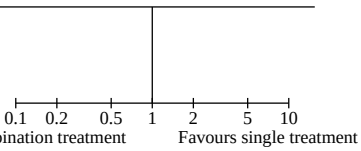
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.1 Depression: meeting study criteria for depression at end of treatment	0	0	Risk Ratio (M-H, Random, 95% CI)	Not estimable
4.2 Depression: < 50% reduction in scale scores at end of treatment	0	0	Risk Ratio (M-H, Random, 95% CI)	Not estimable
4.3 Depression: mean scores at end of treatment	3	278	Mean Difference (IV, Fixed, 95% CI)	-1.60 [-2.13, -1.08]
4.3.1 HDRS (high score = more depressed)	3	278	Mean Difference (IV, Fixed, 95% CI)	-1.60 [-2.13, -1.08]
4.4 Anxiety: mean scores at end of treatment	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4.4.1 HAMA (high score = more anxious)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4.5 Activities of daily living: mean scores at end of treatment	2	198	Mean Difference (IV, Random, 95% CI)	11.83 [0.27, 23.40]
4.5.1 Barthel Index (high score = more dependent)	2	198	Mean Difference (IV, Random, 95% CI)	11.83 [0.27, 23.40]
4.6 Neurological function: mean scores at end of treatment	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.6.1 Scandinavian Stroke Scale (low score = more neurological deficit)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4.7 Adverse events: death	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
4.7.1 At end of treatment	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
4.8 Adverse events: all	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
4.8.1 Gastrointestinal effects (e.g. constipation, diarrhoea)	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
4.9 Adverse events: leaving the study early (including death)	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
4.9.1 All dropouts and withdrawals	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

Analysis 4.1. Comparison 4: Pharmacological intervention and psychological therapy (combination) versus a pharmacological intervention and usual care or attention control (single), Outcome 1: Depression: meeting study criteria for depression at end of treatment

Study or Subgroup	Combination treatment Events	Combination treatment Total	Single treatment Events	Single treatment Total	Weight	Risk Ratio M-H, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

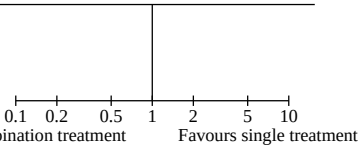
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 4.2. Comparison 4: Pharmacological intervention and psychological therapy (combination) versus a pharmacological intervention and usual care or attention control (single), Outcome 2: Depression: < 50% reduction in scale scores at end of treatment

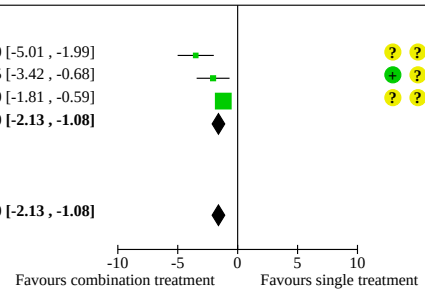
Study or Subgroup	Combination treatment Events	Combination treatment Total	Single treatment Events	Single treatment Total	Weight	Risk Ratio M-H, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

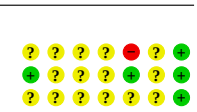
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 4.3. Comparison 4: Pharmacological intervention and psychological therapy (combination) versus a pharmacological intervention and usual care or attention control (single), Outcome 3: Depression: mean scores at end of treatment

Study or Subgroup	Combination treatment Mean	SD	Total	Single treatment Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
4.3.1 HDRS (high score = more depressed)								
Cao 2009a	26.7	5	72	30.2	4.2	72	12.1%	-3.50 [-5.01 , -1.99]
Fan 2010	10.25	3.21	40	12.3	3.05	40	14.7%	-2.05 [-3.42 , -0.68]
Wang 2005a	8.9	1.2	27	10.1	1.1	27	73.2%	-1.20 [-1.81 , -0.59]
Subtotal (95% CI)			**139**			**139**	**100.0%**	**-1.60 [-2.13 , -1.08]**
Heterogeneity: Chi² = 8.14, df = 2 (P = 0.02); I² = 75%								
Test for overall effect: Z = 5.98 (P < 0.00001)								
Total (95% CI)			**139**			**139**	**100.0%**	**-1.60 [-2.13 , -1.08]**
Heterogeneity: Chi² = 8.14, df = 2 (P = 0.02); I² = 75%								
Test for overall effect: Z = 5.98 (P < 0.00001)								
Test for subgroup differences: Not applicable								

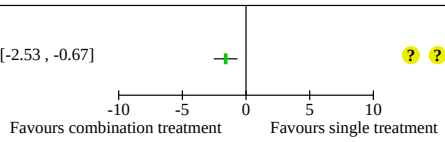




Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 4.4. Comparison 4: Pharmacological intervention and psychological therapy (combination) versus a pharmacological intervention and usual care or attention control (single), Outcome 4: Anxiety: mean scores at end of treatment

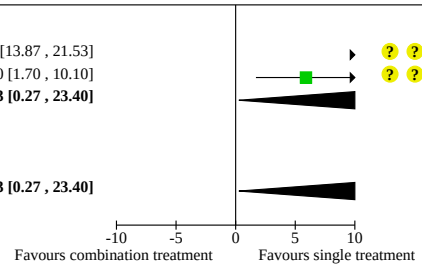
Study or Subgroup	Combination treatment Mean	SD	Total	Single treatment Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
4.4.1 HAMA (high score = more anxious)							
Wang 2005a	3.8	1.8	27	5.4	1.7	27	-1.60 [-2.53 , -0.67]



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 4.5. Comparison 4: Pharmacological intervention and psychological therapy (combination) versus a pharmacological intervention and usual care or attention control (single), Outcome 5: Activities of daily living: mean scores at end of treatment

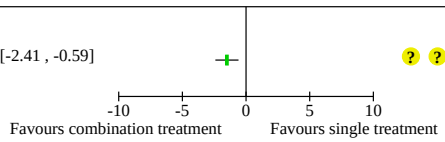
Study or Subgroup	Combination treatment Mean	SD	Total	Single treatment Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
4.5.1 Barthel Index (high score = more dependent)									
Cao 2009a	80.1	10.3	72	62.4	13	72	50.3%	17.70 [13.87 , 21.53]	? ? ? ? - ? +
Wang 2005a	90.2	7.3	27	84.3	8.4	27	49.7%	5.90 [1.70 , 10.10]	? ? ? ? ? ? +
Subtotal (95% CI)			**99**			**99**	**100.0%**	**11.83 [0.27 , 23.40]**	
Heterogeneity: Tau² = 65.42; Chi² = 16.56, df = 1 (P < 0.0001); I² = 94%									
Test for overall effect: Z = 2.01 (P = 0.04)									
Total (95% CI)			**99**			**99**	**100.0%**	**11.83 [0.27 , 23.40]**	
Heterogeneity: Tau² = 65.42; Chi² = 16.56, df = 1 (P < 0.0001); I² = 94%									
Test for overall effect: Z = 2.01 (P = 0.04)									
Test for subgroup differences: Not applicable									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 4.6. Comparison 4: Pharmacological intervention and psychological therapy (combination) versus a pharmacological intervention and usual care or attention control (single), Outcome 6: Neurological function: mean scores at end of treatment

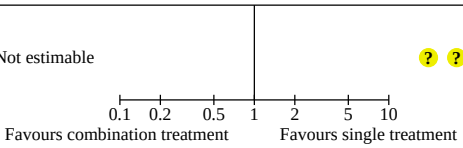
Study or Subgroup	Combination treatment Mean	SD	Total	Single treatment Mean	SD	Total	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
4.6.1 Scandinavian Stroke Scale (low score = more neurological deficit)								
Wang 2005a	5	1.8	27	6.5	1.6	27	-1.50 [-2.41 , -0.59]	? ? ? ? ? ? +



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 4.7. Comparison 4: Pharmacological intervention and psychological therapy (combination) versus a pharmacological intervention and usual care or attention control (single), Outcome 7: Adverse events: death

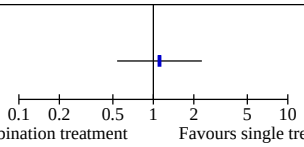
Study or Subgroup	Combination treatment Events	Total	Single treatment Events	Total	Risk Ratio M-H, Fixed, 95% CI	Risk of Bias A B C D E F G
4.7.1 At end of treatment						
Wang 2005a	0	27	0	27	Not estimable	? ? ? ? ? ? +



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 4.8. Comparison 4: Pharmacological intervention and psychological therapy (combination) versus a pharmacological intervention and usual care or attention control (single), Outcome 8: Adverse events: all

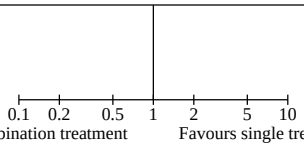
Study or Subgroup	Combination treatment Events	Total	Single treatment Events	Total	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI	Risk of Bias A B C D E F G
4.8.1 Gastrointestinal effects (e.g. constipation, diarrhoea)							
Wang 2005a	10	27	9	27	1.11 [0.54 , 2.30]		? ? ? ? ? ? +



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 4.9. Comparison 4: Pharmacological intervention and psychological therapy (combination) versus a pharmacological intervention and usual care or attention control (single), Outcome 9: Adverse events: leaving the study early (including death)

Study or Subgroup	Combination treatment Events	Total	Single treatment Events	Total	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI	Risk of Bias A B C D E F G
4.9.1 All dropouts and withdrawals							
Wang 2005a	0	27	0	27	Not estimable		? ? ? ? ? ? +



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 5. Pharmacological intervention and non-invasive brain stimulation (combination) versus a pharmacological intervention and sham stimulation or usual care (single)

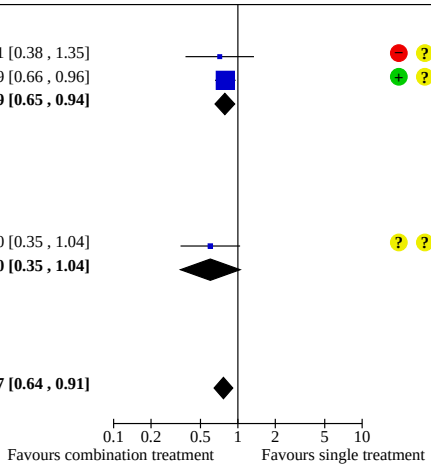
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.1 Depression: meeting the criteria for depression at end of treatment	3	392	Risk Ratio (M-H, Random, 95% CI)	0.77 [0.64, 0.91]
5.1.1 HDRS (high score = more depressed)	2	318	Risk Ratio (M-H, Random, 95% CI)	0.79 [0.65, 0.94]
5.1.2 SDS (high score= more depressed)	1	74	Risk Ratio (M-H, Random, 95% CI)	0.60 [0.35, 1.04]
5.2 Depression: <50% reduction in scale scores at end of treatment	3	392	Risk Ratio (M-H, Random, 95% CI)	0.95 [0.69, 1.30]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.2.1 HDRS (high score = more depressed)	2	318	Risk Ratio (M-H, Random, 95% CI)	0.94 [0.54, 1.66]
5.2.2 SDS (high score= more depressed)	1	74	Risk Ratio (M-H, Random, 95% CI)	0.97 [0.77, 1.22]
5.3 Depression: mean scores at end of treatment	12	1055	Std. Mean Difference (IV, Random, 95% CI)	-1.06 [-1.60, -0.52]
5.3.1 HDRS (high score = more depressed)	11	981	Std. Mean Difference (IV, Random, 95% CI)	-0.88 [-1.36, -0.39]
5.3.2 SDS (high score = more depressed)	1	74	Std. Mean Difference (IV, Random, 95% CI)	-3.11 [-3.80, -2.42]
5.4 Depression: mean scores at end of follow-up	3	147	Mean Difference (IV, Fixed, 95% CI)	-3.00 [-3.39, -2.60]
5.4.1 HDRS (high score = more depressed)	3	147	Mean Difference (IV, Fixed, 95% CI)	-3.00 [-3.39, -2.60]
5.5 Cognitive function: mean scores at end of treatment	2	318	Std. Mean Difference (IV, Fixed, 95% CI)	-0.25 [-0.48, -0.03]
5.5.1 MMSE (low score = cognitive impairment)	1	60	Std. Mean Difference (IV, Fixed, 95% CI)	0.91 [0.38, 1.44]
5.5.2 MoCA (low score = cognitive impairment)	1	258	Std. Mean Difference (IV, Fixed, 95% CI)	-0.51 [-0.75, -0.26]
5.6 Activities of daily living: mean scores at end of treatment	5	403	Std. Mean Difference (IV, Random, 95% CI)	2.03 [1.21, 2.85]
5.6.1 Barthel Index (high score = more dependent)	3	243	Std. Mean Difference (IV, Random, 95% CI)	2.49 [1.78, 3.19]
5.6.2 ADL (high score = more impairment)	2	160	Std. Mean Difference (IV, Random, 95% CI)	1.33 [-0.28, 2.94]
5.7 Activities of daily living: mean scores at the end of follow-up	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5.7.1 Barthel Index (high score = more dependent)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5.8 Disability: mean scores at end of treatment	2	180	Mean Difference (IV, Random, 95% CI)	-10.02 [-20.14, 0.11]
5.8.1 SDS (high score = more disability	2	180	Mean Difference (IV, Random, 95% CI)	-10.02 [-20.14, 0.11]
5.9 Neurological function: mean scores at end of treatment	4	280	Mean Difference (IV, Random, 95% CI)	-2.78 [-4.13, -1.44]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.9.1 NIHSS (high score = more impairment)	4	280	Mean Difference (IV, Random, 95% CI)	-2.78 [-4.13, -1.44]
5.10 Adverse events: death	5	487	Risk Ratio (M-H, Random, 95% CI)	1.06 [0.27, 4.16]
5.10.1 At end of treatment	5	487	Risk Ratio (M-H, Random, 95% CI)	1.06 [0.27, 4.16]
5.11 Adverse events: all	5		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
5.11.1 Central nervous system events (e.g. headache, seizures)	3	341	Risk Ratio (M-H, Random, 95% CI)	0.50 [0.05, 5.28]
5.11.2 Gastrointestinal effects (e.g. constipation, diarrhoea)	3	341	Risk Ratio (M-H, Random, 95% CI)	1.50 [0.46, 4.88]
5.11.3 Recurrent stroke	1	258	Risk Ratio (M-H, Random, 95% CI)	1.60 [0.46, 5.52]
5.11.4 Other events - not listed above (e.g. insomnia, discomfort, headaches)	2	120	Risk Ratio (M-H, Random, 95% CI)	7.00 [0.38, 129.93]
5.12 Adverse events: leaving the study early (including death)	6	567	Risk Ratio (M-H, Random, 95% CI)	1.81 [0.87, 3.75]
5.12.1 All dropouts and withdrawals	6	567	Risk Ratio (M-H, Random, 95% CI)	1.81 [0.87, 3.75]

Analysis 5.1. Comparison 5: Pharmacological intervention and non-invasive brain stimulation (combination) versus a pharmacological intervention and sham stimulation or usual care (single), Outcome 1: Depression: meeting the criteria for depression at end of treatment

Study or Subgroup	Combination treatment Events	Total	Single treatment Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
5.1.1 HDRS (high score = more depressed)						
Du 2005	10	30	14	30	7.4%	0.71 [0.38 , 1.35]
Lu 2020	70	125	94	133	82.8%	0.79 [0.66 , 0.96]
Subtotal (95% CI)		**155**		**163**	**90.2%**	**0.79 [0.65 , 0.94]**
Total events:	80		108			
Heterogeneity: Tau² = 0.00; Chi² = 0.10, df = 1 (P = 0.76); I² = 0%						
Test for overall effect: Z = 2.60 (P = 0.009)						
5.1.2 SDS (high score= more depressed)						
Liu 2020	12	37	20	37	9.8%	0.60 [0.35 , 1.04]
Subtotal (95% CI)		**37**		**37**	**9.8%**	**0.60 [0.35 , 1.04]**
Total events:	12		20			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.81 (P = 0.07)						
Total (95% CI)		**192**		**200**	**100.0%**	**0.77 [0.64 , 0.91]**
Total events:	92		128			
Heterogeneity: Tau² = 0.00; Chi² = 0.95, df = 2 (P = 0.62); I² = 0%						
Test for overall effect: Z = 3.04 (P = 0.002)						
Test for subgroup differences: Chi² = 0.83, df = 1 (P = 0.36), I² = 0%						

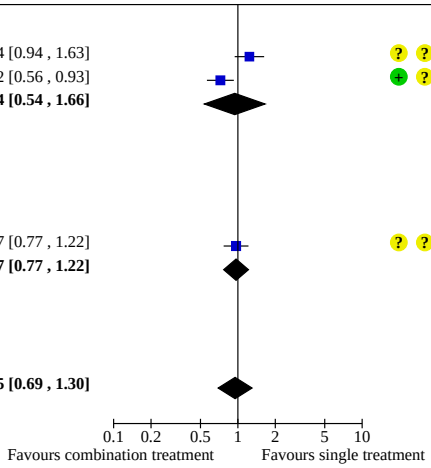


Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 5.2. Comparison 5: Pharmacological intervention and non-invasive brain stimulation (combination) versus a pharmacological intervention and sham stimulation or usual care (single), Outcome 2: Depression: <50% reduction in scale scores at end of treatment

Study or Subgroup	Combination treatment Events	Total	Single treatment Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
5.2.1 HDRS (high score = more depressed)						
Li 2013	26	30	21	30	32.1%	1.24 [0.94 , 1.63]
Lu 2020	53	125	78	133	33.4%	0.72 [0.56 , 0.93]
Subtotal (95% CI)		**155**		**163**	**65.5%**	**0.94 [0.54 , 1.66]**
Total events:	79		99			
Heterogeneity: Tau² = 0.15; Chi² = 9.28, df = 1 (P = 0.002); I² = 89%						
Test for overall effect: Z = 0.20 (P = 0.84)						
5.2.2 SDS (high score= more depressed)						
Liu 2020	29	37	30	37	34.5%	0.97 [0.77 , 1.22]
Subtotal (95% CI)		**37**		**37**	**34.5%**	**0.97 [0.77 , 1.22]**
Total events:	29		30			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.29 (P = 0.77)						
Total (95% CI)		**192**		**200**	**100.0%**	**0.95 [0.69 , 1.30]**
Total events:	108		129			
Heterogeneity: Tau² = 0.06; Chi² = 9.47, df = 2 (P = 0.009); I² = 79%						
Test for overall effect: Z = 0.32 (P = 0.75)						
Test for subgroup differences: Chi² = 0.01, df = 1 (P = 0.94), I² = 0%						

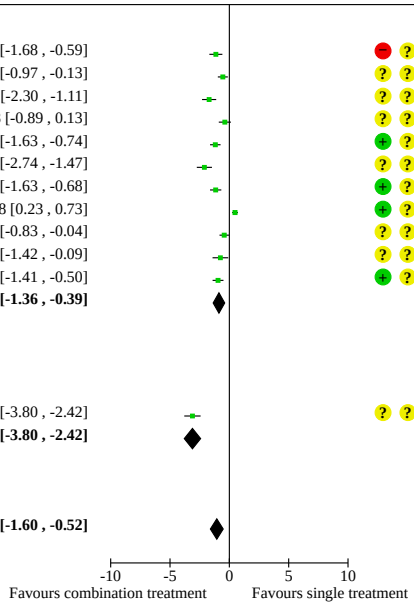


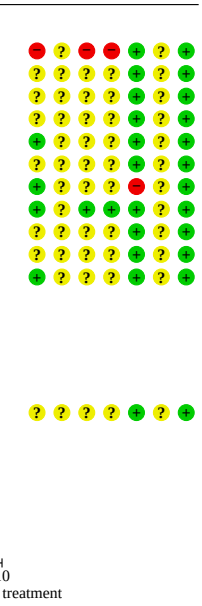
Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 5.3. Comparison 5: Pharmacological intervention and non-invasive brain stimulation (combination) versus a pharmacological intervention and sham stimulation or usual care (single), Outcome 3: Depression: mean scores at end of treatment

Study or Subgroup	Combination treatment Mean	SD	Total	Single treatment Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
5.3.1 HDRS (high score = more depressed)								
Du 2005	6	5	30	13	7	30	8.3%	-1.14 [-1.68 , -0.59]
Fan 2014	15.29	2.36	45	16.68	2.65	45	8.6%	-0.55 [-0.97 , -0.13]
Jin 2013	14.12	3.71	30	19.83	2.85	30	8.1%	-1.70 [-2.30 , -1.11]
Li 2013	13.25	3.62	30	14.69	3.87	30	8.3%	-0.38 [-0.89 , 0.13]
Li 2014	7.18	3.55	47	11.22	3.21	46	8.5%	-1.18 [-1.63 , -0.74]
Liu 2015	13.51	3.12	30	19.84	2.81	30	8.0%	-2.10 [-2.74 , -1.47]
Lu 2016	16.42	7.01	40	24.47	6.83	40	8.4%	-1.15 [-1.63 , -0.68]
Lu 2020	28.26	1.95	125	27.26	2.2	133	8.9%	0.48 [0.23 , 0.73]
Sun 2013	19.78	3.33	50	21.22	3.28	50	8.6%	-0.43 [-0.83 , -0.04]
Yang 2013	12.89	2.27	19	15.08	3.31	19	7.9%	-0.76 [-1.42 , -0.09]
Zhang 2013	9.47	3.47	41	12.8	3.45	41	8.5%	-0.95 [-1.41 , -0.50]
Subtotal (95% CI)			**487**			**494**	**92.1%**	**-0.88 [-1.36 , -0.39]**
Heterogeneity: Tau² = 0.61; Chi² = 125.92, df = 10 (P < 0.00001); I² = 92%								
Test for overall effect: Z = 3.54 (P = 0.0004)								
5.3.2 SDS (high score = more depressed)								
Liu 2020	14.25	2.11	37	23.16	3.41	37	7.9%	-3.11 [-3.80 , -2.42]
Subtotal (95% CI)			**37**			**37**	**7.9%**	**-3.11 [-3.80 , -2.42]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 8.86 (P < 0.00001)								
Total (95% CI)			**524**			**531**	**100.0%**	**-1.06 [-1.60 , -0.52]**
Heterogeneity: Tau² = 0.84; Chi² = 177.86, df = 11 (P < 0.00001); I² = 94%								
Test for overall effect: Z = 3.84 (P = 0.0001)								
Test for subgroup differences: Chi² = 27.02, df = 1 (P < 0.00001), I² = 96.3%								

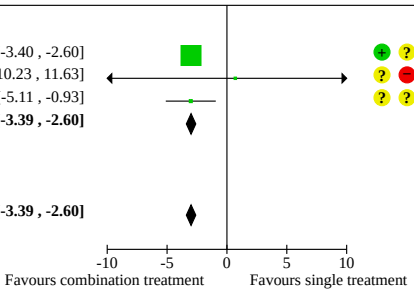


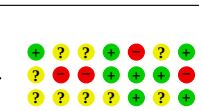


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 5.4. Comparison 5: Pharmacological intervention and non-invasive brain stimulation (combination) versus a pharmacological intervention and sham stimulation or usual care (single), Outcome 4: Depression: mean scores at end of follow-up

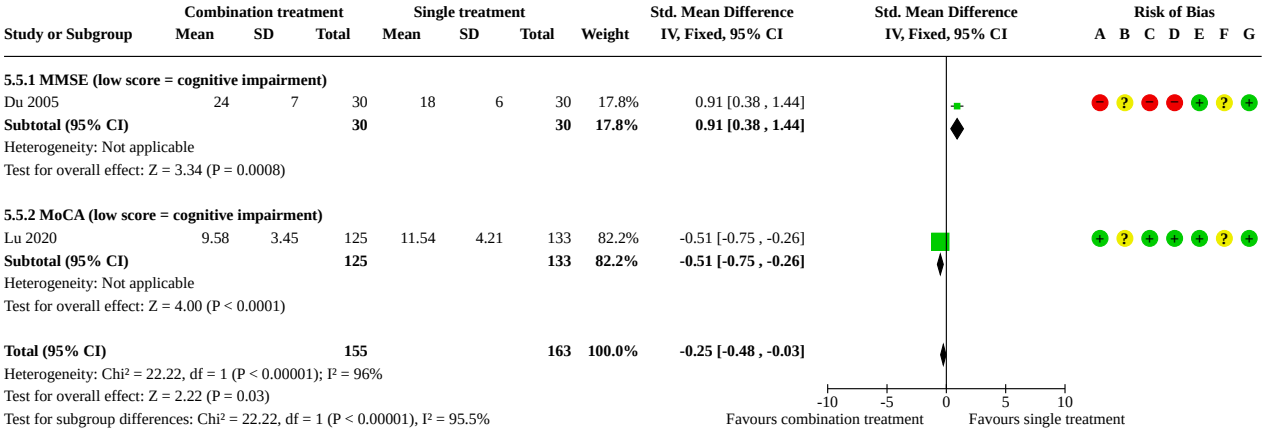
Study or Subgroup	Combination treatment Mean	SD	Total	Single treatment Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
5.4.1 HDRS (high score = more depressed)								
Jiang 2014b	5	0.8	50	8	1.2	50	96.3%	-3.00 [-3.40 , -2.60]
Terachinda 2021	8.2	7.8	5	7.5	8.7	4	0.1%	0.70 [-10.23 , 11.63]
Yang 2013	7.11	3.41	19	10.13	3.15	19	3.5%	-3.02 [-5.11 , -0.93]
Subtotal (95% CI)			**74**			**73**	**100.0%**	**-3.00 [-3.39 , -2.60]**
Heterogeneity: Chi² = 0.44, df = 2 (P = 0.80); I² = 0%								
Test for overall effect: Z = 14.97 (P < 0.00001)								
Total (95% CI)			**74**			**73**	**100.0%**	**-3.00 [-3.39 , -2.60]**
Heterogeneity: Chi² = 0.44, df = 2 (P = 0.80); I² = 0%								
Test for overall effect: Z = 14.97 (P < 0.00001)								
Test for subgroup differences: Not applicable								





Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

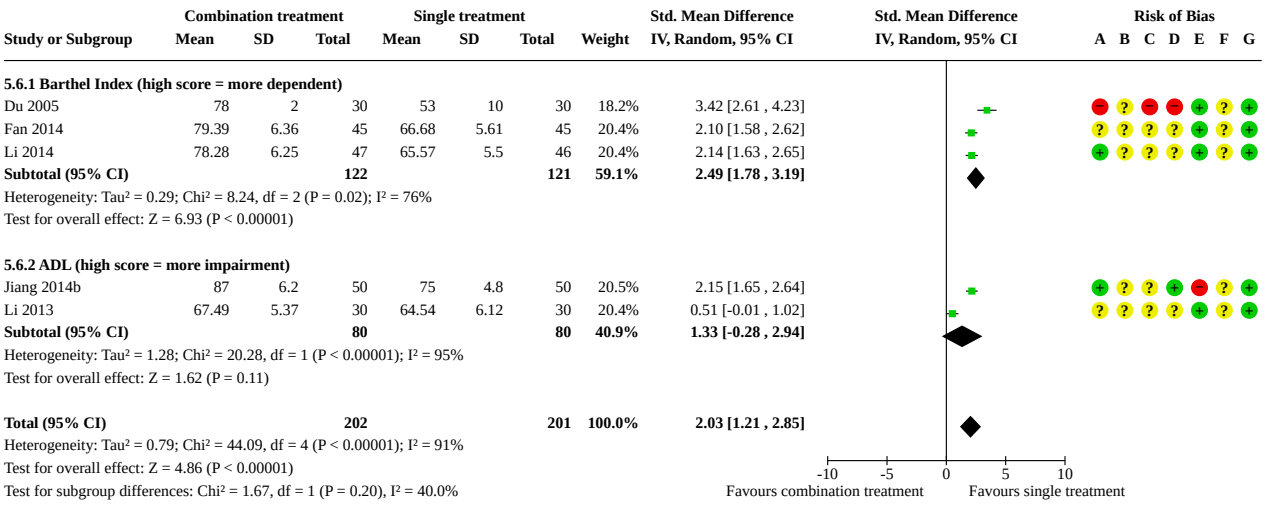
Analysis 5.5. Comparison 5: Pharmacological intervention and non-invasive brain stimulation (combination) versus a pharmacological intervention and sham stimulation or usual care (single), Outcome 5: Cognitive function: mean scores at end of treatment



Study or Subgroup	Combination treatment Mean	SD	Total	Single treatment Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI	Std. Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
5.5.1 MMSE (low score = cognitive impairment)										
Du 2005	24	7	30	18	6	30	17.8%	0.91 [0.38 , 1.44]		
Subtotal (95% CI)			**30**			**30**	**17.8%**	**0.91 [0.38 , 1.44]**		
Heterogeneity: Not applicable										
Test for overall effect: Z = 3.34 (P = 0.0008)										
5.5.2 MoCA (low score = cognitive impairment)										
Lu 2020	9.58	3.45	125	11.54	4.21	133	82.2%	-0.51 [-0.75 , -0.26]		
Subtotal (95% CI)			**125**			**133**	**82.2%**	**-0.51 [-0.75 , -0.26]**		
Heterogeneity: Not applicable										
Test for overall effect: Z = 4.00 (P < 0.0001)										
Total (95% CI)			**155**			**163**	**100.0%**	**-0.25 [-0.48 , -0.03]**		
Heterogeneity: Chi² = 22.22, df = 1 (P < 0.00001); I² = 96%										
Test for overall effect: Z = 2.22 (P = 0.03)										
Test for subgroup differences: Chi² = 22.22, df = 1 (P < 0.00001), I² = 95.5%										

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 5.6. Comparison 5: Pharmacological intervention and non-invasive brain stimulation (combination) versus a pharmacological intervention and sham stimulation or usual care (single), Outcome 6: Activities of daily living: mean scores at end of treatment

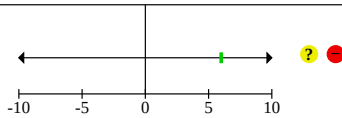


Study or Subgroup	Combination treatment Mean	SD	Total	Single treatment Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
5.6.1 Barthel Index (high score = more dependent)										
Du 2005	78	2	30	53	10	30	18.2%	3.42 [2.61 , 4.23]		
Fan 2014	79.39	6.36	45	66.68	5.61	45	20.4%	2.10 [1.58 , 2.62]		
Li 2014	78.28	6.25	47	65.57	5.5	46	20.4%	2.14 [1.63 , 2.65]		
Subtotal (95% CI)			**122**			**121**	**59.1%**	**2.49 [1.78 , 3.19]**		
Heterogeneity: Tau² = 0.29; Chi² = 8.24, df = 2 (P = 0.02); I² = 76%										
Test for overall effect: Z = 6.93 (P < 0.00001)										
5.6.2 ADL (high score = more impairment)										
Jiang 2014b	87	6.2	50	75	4.8	50	20.5%	2.15 [1.65 , 2.64]		
Li 2013	67.49	5.37	30	64.54	6.12	30	20.4%	0.51 [-0.01 , 1.02]		
Subtotal (95% CI)			**80**			**80**	**40.9%**	**1.33 [-0.28 , 2.94]**		
Heterogeneity: Tau² = 1.28; Chi² = 20.28, df = 1 (P < 0.00001); I² = 95%										
Test for overall effect: Z = 1.62 (P = 0.11)										
Total (95% CI)			**202**			**201**	**100.0%**	**2.03 [1.21 , 2.85]**		
Heterogeneity: Tau² = 0.79; Chi² = 44.09, df = 4 (P < 0.00001); I² = 91%										
Test for overall effect: Z = 4.86 (P < 0.00001)										
Test for subgroup differences: Chi² = 1.67, df = 1 (P = 0.20), I² = 40.0%										

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 5.7. Comparison 5: Pharmacological intervention and non-invasive brain stimulation (combination) versus a pharmacological intervention and sham stimulation or usual care (single), Outcome 7: Activities of daily living: mean scores at the end of follow-up

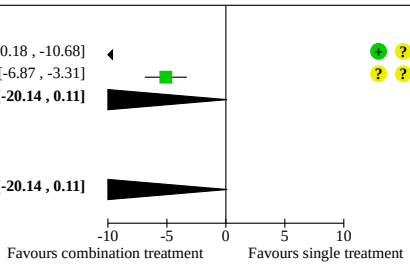
Study or Subgroup	Combination treatment Mean	SD	Total	Single treatment Mean	SD	Total	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
5.7.1 Barthel Index (high score = more dependent)									
Terachinda 2021	82	22.2	5	76	27	4	6.00 [-26.84 , 38.84]		? − − + + + −



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 5.8. Comparison 5: Pharmacological intervention and non-invasive brain stimulation (combination) versus a pharmacological intervention and sham stimulation or usual care (single), Outcome 8: Disability: mean scores at end of treatment

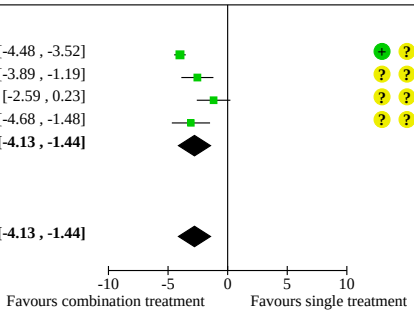
Study or Subgroup	Combination treatment Mean	SD	Total	Single treatment Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
5.8.1 SDS (high score = more disability										
Lu 2016	47.48	9.28	40	62.91	12.19	40	47.6%	-15.43 [-20.18 , -10.68]		+ ? ? ? − ? +
Sun 2013	26.56	4.15	50	31.65	4.91	50	52.4%	-5.09 [-6.87 , -3.31]		? ? ? ? + ? +
Subtotal (95% CI)			**90**			**90**	**100.0%**	**-10.02 [-20.14 , 0.11]**		
Heterogeneity: Tau² = 50.11; Chi² = 15.97, df = 1 (P < 0.0001); I² = 94%										
Test for overall effect: Z = 1.94 (P = 0.05)										
Total (95% CI)			**90**			**90**	**100.0%**	**-10.02 [-20.14 , 0.11]**		
Heterogeneity: Tau² = 50.11; Chi² = 15.97, df = 1 (P < 0.0001); I² = 94%										
Test for overall effect: Z = 1.94 (P = 0.05)										
Test for subgroup differences: Not applicable										

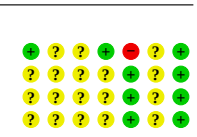


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 5.9. Comparison 5: Pharmacological intervention and non-invasive brain stimulation (combination) versus a pharmacological intervention and sham stimulation or usual care (single), Outcome 9: Neurological function: mean scores at end of treatment

Study or Subgroup	Combination treatment Mean	SD	Total	Single treatment Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
5.9.1 NIHSS (high score = more impairment)								
Jiang 2014b	5	0.9	50	9	1.5	50	30.5%	-4.00 [-4.48 , -3.52]
Jin 2013	6.08	2.14	30	8.62	3.09	30	24.1%	-2.54 [-3.89 , -1.19]
Li 2013	10.28	2.45	30	11.46	3.08	30	23.5%	-1.18 [-2.59 , 0.23]
Liu 2015	6.13	3.02	30	9.21	3.31	30	21.9%	-3.08 [-4.68 , -1.48]
Subtotal (95% CI)			**140**			**140**	**100.0%**	**-2.78 [-4.13 , -1.44]**
Heterogeneity: Tau² = 1.48; Chi² = 16.68, df = 3 (P = 0.0008); I² = 82%								
Test for overall effect: Z = 4.05 (P < 0.0001)								
Total (95% CI)			**140**			**140**	**100.0%**	**-2.78 [-4.13 , -1.44]**
Heterogeneity: Tau² = 1.48; Chi² = 16.68, df = 3 (P = 0.0008); I² = 82%								
Test for overall effect: Z = 4.05 (P < 0.0001)								
Test for subgroup differences: Not applicable								

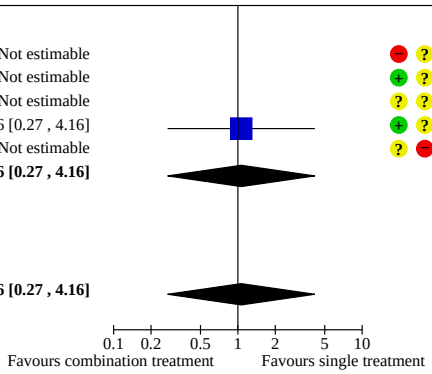


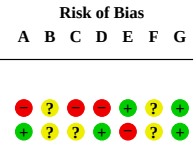


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 5.10. Comparison 5: Pharmacological intervention and non-invasive brain stimulation (combination) versus a pharmacological intervention and sham stimulation or usual care (single), Outcome 10: Adverse events: death

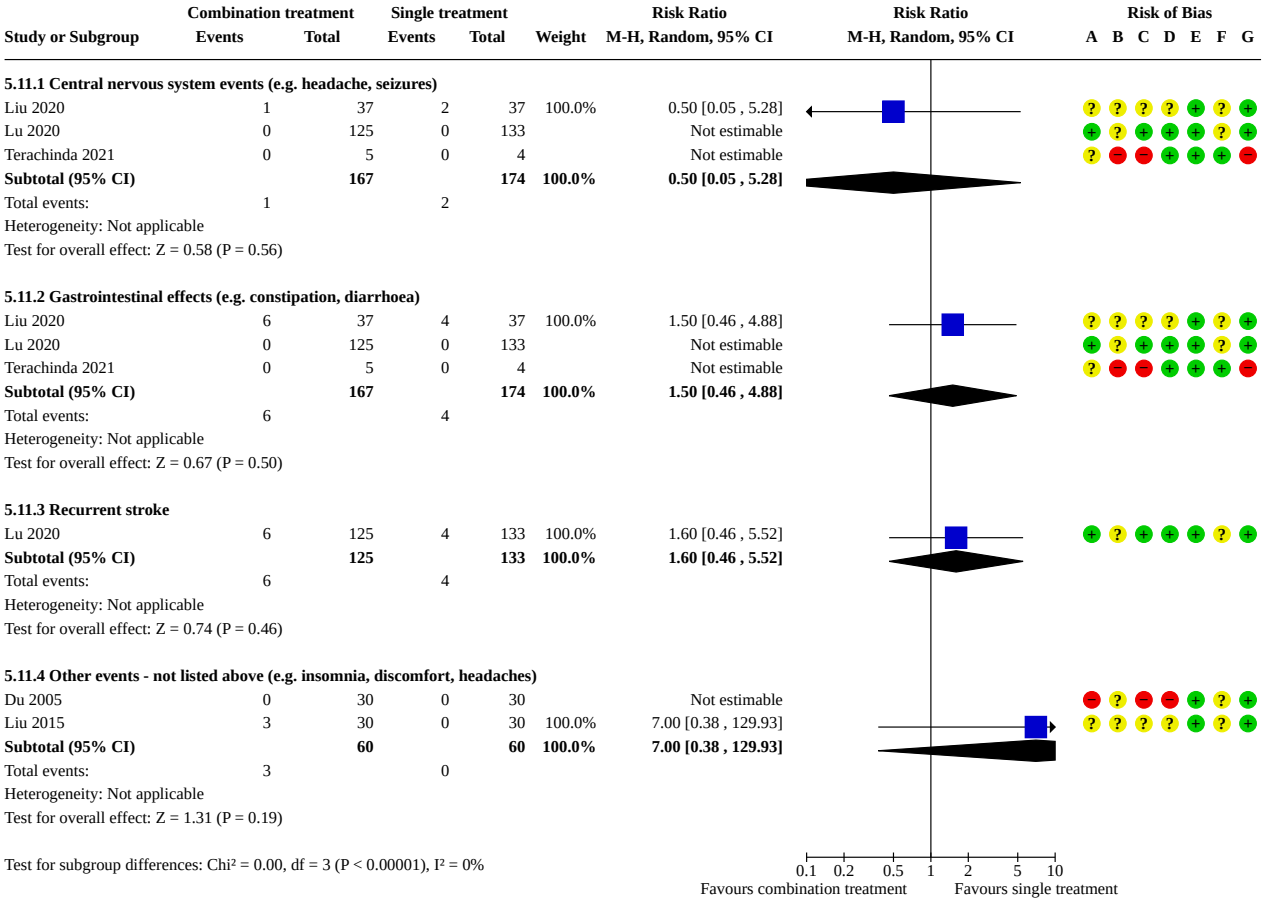
Study or Subgroup	Combination treatment Events	Total	Single treatment Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
5.10.1 At end of treatment						
Du 2005	0	30	0	30		Not estimable
Jiang 2014b	0	50	0	50		Not estimable
Liu 2015	0	30	0	30		Not estimable
Lu 2020	4	125	4	133	100.0%	1.06 [0.27 , 4.16]
Terachinda 2021	0	5	0	4		Not estimable
Subtotal (95% CI)		**240**		**247**	**100.0%**	**1.06 [0.27 , 4.16]**
Total events:	4		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.09 (P = 0.93)						
Total (95% CI)		**240**		**247**	**100.0%**	**1.06 [0.27 , 4.16]**
Total events:	4		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.09 (P = 0.93)						
Test for subgroup differences: Not applicable						





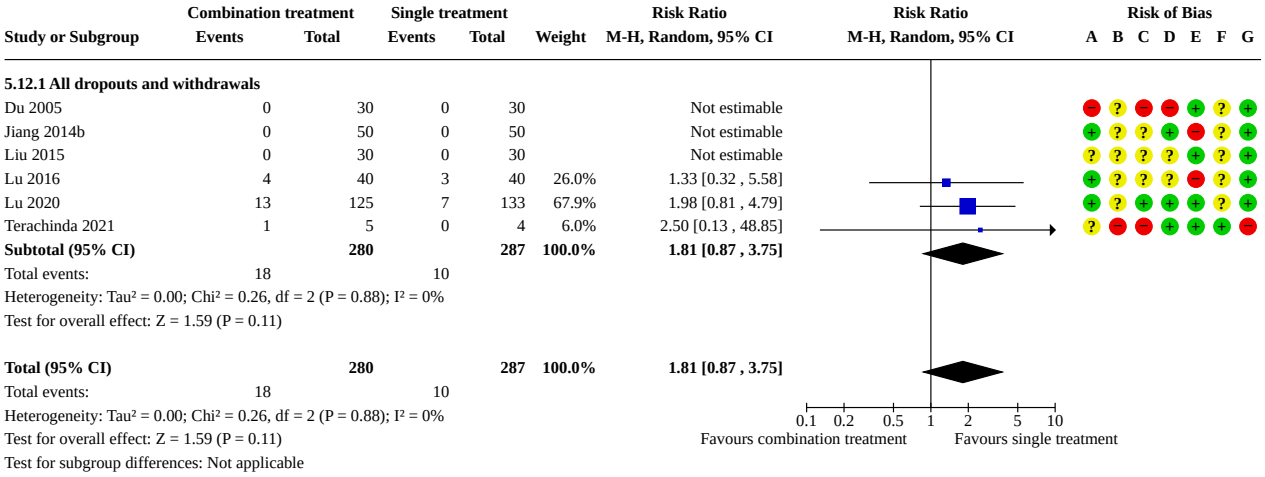
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 5.11. Comparison 5: Pharmacological intervention and non-invasive brain stimulation (combination) versus a pharmacological intervention and sham stimulation or usual care (single), Outcome 11: Adverse events: all



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 5.12. Comparison 5: Pharmacological intervention and non-invasive brain stimulation (combination) versus a pharmacological intervention and sham stimulation or usual care (single), Outcome 12: Adverse events: leaving the study early (including death)



Study or Subgroup	Combination treatment Events	Total	Single treatment Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
5.12.1 All dropouts and withdrawals						
Du 2005	0	30	0	30		Not estimable
Jiang 2014b	0	50	0	50		Not estimable
Liu 2015	0	30	0	30		Not estimable
Lu 2016	4	40	3	40	26.0%	1.33 [0.32 , 5.58]
Lu 2020	13	125	7	133	67.9%	1.98 [0.81 , 4.79]
Terachinda 2021	1	5	0	4	6.0%	2.50 [0.13 , 48.85]
Subtotal (95% CI)		**280**		**287**	**100.0%**	**1.81 [0.87 , 3.75]**
Total events:	18		10			
Heterogeneity: Tau² = 0.00; Chi² = 0.26, df = 2 (P = 0.88); I² = 0%						
Test for overall effect: Z = 1.59 (P = 0.11)						
Total (95% CI)		**280**		**287**	**100.0%**	**1.81 [0.87 , 3.75]**
Total events:	18		10			
Heterogeneity: Tau² = 0.00; Chi² = 0.26, df = 2 (P = 0.88); I² = 0%						
Test for overall effect: Z = 1.59 (P = 0.11)						
Test for subgroup differences: Not applicable						

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

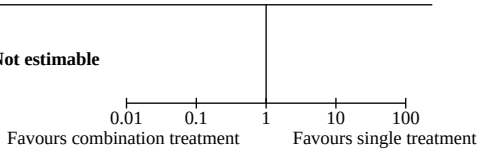
Comparison 6. Non-invasive brain stimulation and psychological therapy (combination) versus psychological therapy and usual care (single)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6.1 Depression: meeting study criteria for depression at end of treatment	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
6.2 Depression: < 50% reduction in scale scores at end of treatment	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
6.3 Depression: mean scores at end of treatment	1		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6.3.1 HDRS (high score= more depressed)	1		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6.3.2 MADRS (high score= more depressed)	1		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Analysis 6.1. Comparison 6: Non-invasive brain stimulation and psychological therapy (combination) versus psychological therapy and usual care (single), Outcome 1: Depression: meeting study criteria for depression at end of treatment

Study or Subgroup	Combination treatment Events	Total	Single treatment Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

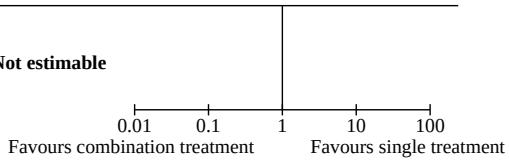
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 6.2. Comparison 6: Non-invasive brain stimulation and psychological therapy (combination) versus psychological therapy and usual care (single), Outcome 2: Depression: < 50% reduction in scale scores at end of treatment

Study or Subgroup	Experimental Events	Total	Single treatment Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 6.3. Comparison 6: Non-invasive brain stimulation and psychological therapy (combination) versus psychological therapy and usual care (single), Outcome 3: Depression: mean scores at end of treatment

Study or Subgroup	Combination treatment Mean	SD	Total	Single treatment Mean	SD	Total	Std. Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
6.3.1 HDRS (high score= more depressed)								
Wu 2019	6.42	3.3	40	8.32	2.1	40	-0.68 [-1.13 , -0.23]	+ ? + ? − ? ?
6.3.2 MADRS (high score= more depressed)								
Wu 2019	10.3	1.57	40	11.65	2.8	40	-0.59 [-1.04 , -0.14]	+ ? + ? − ? ?

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

ADDITIONAL TABLES

Table 1. Characteristics of 'dropout' studies

Study ID	Methods	Participants	Interventions	Outcomes	Notes
Bramanti 1989	**Study design:** parallel design	**Geographical location:** Italy **Setting:** unclear	**Treatment:** protirelin tartrate (TRH-T) 2 mg/d	• Depression measured using HDRS	Results not available in format suit-

Table 1. Characteristics of 'dropout' studies *(Continued)*

	Number of arms: 2 **Experimental arm:** protirelin tartrate (TRH-T) **Control arm:** placebo	**Number of participants:** 30 **Stroke criteria:** acute stroke **Method of stroke diagnosis:** not reported **Inclusion criteria:** not reported **Exclusion criteria:** not reported **Depression criteria:** not reported **Total number included in this trial:** unclear (63% men, mean age 72.2, SD not reported for the overall cohort) **Number included in treatment group:** unclear **Number included in control group:** unclear	**Control:** placebo **Duration:** 2 weeks **Follow-up:** none		able for this review
Chang 2011	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** rational emotive behaviour therapy (REBT) + usual care **Control arm:** usual care	**Geographical location:** China **Setting:** inpatient **Number of participants:** 16 **Stroke criteria:** ischaemic strokes **Method of stroke diagnosis:** diagnosis confirmed by imaging **Inclusion criteria:** not reported **Exclusion criteria:** (1) history of mental illness; (2) cognitive impairment; (3) severe aphasia; (4) > 2 weeks post-stroke **Depression criteria:** Chinese version of HDRS score ≥ 35 **Total number included in this trial:** 16 (% men and age unknown) **Number included in treatment group:** 8 **Number included in control group:** 8	**Treatment:** REBT + usual care. REBT counselling therapy (1 to 2 hour sessions/week) consisting of a knowledge component (education about health psychology and recovery from hemiplegic stroke) and a behavioural training component (belief changes, forgiveness training, anger management) **Administered by:** a trained psychology graduate (regular care administered by hospital nurses) **Supervision:** unclear **Intervention fidelity:** not reported **Control:** usual care **Duration:** 1 month	• Depression measured using Chinese version of HDRS • Anxiety measured using Chinese version of HARS • Disability measured using Chinese version of BI	Unable to isolate outcome data for those with depression at randomisation
Choi-Kwon 2006	**Study design:** parallel design **Number of arms:** 2	**Geographical location:** South Korea **Setting:** outpatients **Number of participants:** 152 **Stroke criteria:** ischaemic stroke **Method of stroke diagnosis:** diagnosis via CT and MRI scans; interview	**Treatment:** fluoxetine (SSRI) 20 mg daily **Control:** matched placebo **Duration:** 3 months	• Depression measured using BDI • Leaving the study early • Adverse events	Unable to isolate outcome data for those with depression at randomisation

Table 1. Characteristics of 'dropout' studies *(Continued)*

	Experimental arm: fluoxetine (SSRI) **Control arm:** matched placebo	performed on average of 14 months after stroke **Inclusion criteria:** not reported **Exclusion criteria:** (1) did not undergo imaging (CT/MRI) studies; (2) SAH; (3) had TIA without progression to stroke; (4) severe communication problems (aphasia, dementia, or dysarthria); (5) scored < 23 on MMSE; (6) history of depression or psychiatric illness before onset of stroke; (7) already treated with psychiatric regimens; (8) lived alone **Depression criteria:** psychiatric interview, BDI score > 13 **Total number included in this trial:** 152 **Number included in treatment group:** 76 (75% men, mean age 58 years, SD 9) **Number included in control group:** 76 (79% men, mean age 58 years, SD 9)			
Delbari 2011	**Study design:** parallel design **Number of arms:** 4 **Experimental arm A:** methylphenidate + placebo **Experimental arm B:** levodopa + placebo **Experimental arm C:** methylphenidate + levodopa **Control arm:** 2 × 10 mg placebo + 1 × 125 mg placebo	**Geographical location:** Iran **Setting:** inpatient **Number of participants:** 78 **Stroke criteria:** ischaemic stroke **Method of stroke diagnosis:** not reported **Inclusion criteria:** (1) only participants with limb (arm or leg) paresis **Exclusion criteria:** (1) unable to respond or directly consent; (2) comorbidities requiring strict blood pressure control and put at risk by the potential of hypertension from MPH therapy (history of haemorrhagic stroke, recent myocardial infarction within 4-week period, decompensated cardiac insufficiency, tachycardia, uncontrolled hypertension, unstable metabolic disease, glaucoma); (3) potential for adverse outcomes from stimulant effects of MPH, including seizure and agitation major cognitive deficits preventing adequate study participation; (4) currently taking alpha-adrenergic agonists, antagonists, neuroleptics, benzodiazepines, MAO inhibitors, or antidepressants; (5) known hypersensitivity to MPH or LD	**Treatment A:** 2 × 10 mg methylphenidate + 125 mg placebo (content unknown) **Treatment B:** 1 × 12.5 mg levodopa + 2 × 10 mg placebo **Treatment C:** 2 × 10 mg methylphenidate + 1 × 125 mg levodopa **Control:** 2 × 10 mg placebo + 1 × 125 mg placebo **Duration:** 5 days a week for a total of 15 sessions	• Depression measured using GDS • Cognitive function measured using MMSE	Unable to isolate outcome data for those with depression at randomisation

Table 1. Characteristics of 'dropout' studies *(Continued)*

		Depression criteria: GDS < 7.8 **Total number included in this trial:** 78 **Number included in Treatment A:** 19 (47% men, mean age 64.05, SD 10.8) **Number included in Treatment B:** 20 (70% men, mean age 66.3, SD 9.5) **Number included in Treatment C:** 19 (58% men, 60.2, SD 9.1) **Number included in control group:** 20 (70% men, mean age 65.3, SD 9.6)			
Downes 1995	**Study design:** parallel design **Number of arms:** 3 **Experimental arm 1:** information + counselling **Experimental arm 2:** information pack **Control arm:** standard care	**Geographical location:** UK **Setting:** outpatient **Number of participants:** 62 **Stroke criteria:** not reported **Method of stroke diagnosis:** not reported **Inclusion criteria:** (1) lived at home; (2) had an informal carer; (3) stroke increase in mRS; (4) post-stroke mRS score of 2 to 5 **Exclusion criteria:** (1) not living at home; (2) not having an informal carer; (3) having no increase in disability or change in lifestyle/dependency **Total number included in this trial:** 62 **Number included in treatment 1:** 22 (50% men, age not reported) **Number included in treatment 2:** 22 (55% men, age not reported) **Number included in control group:** 18 (44% men, age not reported)	**Treatment 1:** information plus counselling. Egan's problem-solving approach, individual is helped to explore concerns, clarify problems, set goals, and take appropriate action. Protocol discussed first and formulated into a counsellor/client contract. Information pack containing information on physical, cognitive, behavioural, and emotional effects of stroke, carer well-being, and local services **Treatment 2:** information only: information pack containing information on physical, cognitive, behavioural, and emotional effects of stroke, carer well-being, and local services **Control:** standard care, no visit(s) or information pack provided **Duration:** information session consisted of 1 visit and provision of the information pack. Counselling consisted of up to 8 counselling sessions over 4 to 6 months	• Depression measured using HADS-Depression • Anxiety measured using HADS-Anxiety	Unable to isolate outcome data for those with depression at randomisation

Table 1. Characteristics of 'dropout' studies *(Continued)*

			Delivered by: nurse counsellor		
Hadidi 2014	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** problem-solving therapy (PST) **Control arm:** weekly telephone calls	**Geographical location:** USA **Setting:** inpatient **Number of participants:** **Stroke criteria:** first-time diagnosis of ischaemic stroke < 48 hours **Method of stroke diagnosis:** not reported **Inclusion criteria:** (1) Mini-Cog score of 3; ≥ 50 years of age; (2) able to read and write in English **Exclusion criteria:** (1) previous history of mental health problems; (2) diagnosis of severe aphasia as identified by a speech pathologist; (3) haemorrhagic stroke or transient ischaemic attack; (4) medical instability requiring transfer to critical care **Depression criteria:** CES-D score measured at baseline but participants recruited regardless of their CES-D score. If CES-D score > 10, or suicidal ideation, the primary physician was notified **Total number included in this trial:** 22 **Number included in treatment group:** 11 (18% men, mean age 73) **Number included in control group:** 11 (45% men, mean age 69)	**Treatment:** 1-on-1 problem-solving therapy sessions lasting 1 to 2 hours. Therapy entails providing patient information on impact and guidance to enable the patient to identify and define the problem; brainstorm all potential solutions; select the most appropriate and feasible solution; create and implement a SMART (Specific, Measureable, Achievable, Realistic, and Timely) goal; evaluate and review progress in follow-up sessions **Administered by:** a doctoral nursing student who received PST training through a 13-module online program adapted from standard 3-day in-person training **Supervision:** principal Investigator who had undergone in-person PST training **Intervention fidelity:** not reported **Control:** weekly telephone calls to assess CES-D and FIM scores **Duration:** once per week for 10 weeks	• Depression measured using CES-D • Impairment measured using FIM • Leaving the trial early	Unable to isolate outcome data for those with depression at randomisation
Hjelle 2019	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** dialogue-based intervention + usual care	**Geographical location:** Norway **Setting:** inpatient **Number of participants:** 322 **Stroke criteria:** ischaemic stroke **Method of stroke diagnosis:** not reported **Inclusion criteria:** (1) aged > 18 years; (2) had an acute stroke with-	**Treatment:** 8 individual sessions. Interventions were delivered mainly in the participants' homes. The sessions content addressed feelings, thoughts and reflections related to the participants' expe-	• Proportion of participants with normal mood measured using General Health Question-	Unable to isolate outcome data for those with depression at randomisation

Table 1. Characteristics of 'dropout' studies *(Continued)*

	Control arm: usual care	in the past month; (3) were medically stable; (4) had sufficient cognitive functioning to provide informed consent and participate; (5) understood and spoke Norwegian **Exclusion criteria:** (1) severe dementia; (2) other serious somatic or psychiatric diseases; (3) severe aphasia **Depression criteria:** no criteria for depression at entry **Total number included in this trial:** 322 **Number included in treatment group:** 166 (59.6% men; mean age 66, SD 12.1) **Number included in control group:** 156 (58.3% men; mean age 65, SD 13.3)	riences after stroke, and were based on topics highlighted as significant issues in the stroke literature and in the development and feasibility studies. **Administered by:** registered nurse or occupational therapist **Supervised by:** not reported **Control:** acute treatment at stroke units and rehabilitation centres or in the municipality. All participants were followed up by their physicians in accordance with the Norwegian clinical guidelines for treatment and rehabilitation after stroke in addition to nursing and therapy input (e.g. through a multidisciplinary team) based on need and availability. **Duration:** 17 weeks	naire-28 (GHQ-28) • Depression measured using Yale-Brown single-item questionnaire • Health-related quality of life measured using Stroke and Aphasia Quality of Life Scale (SAQOL-39)	
Jorge 2004	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** rTMS **Control arm:** sham rTMS	**Geographical location:** USA **Setting:** outpatient **Number of participants:** 20 **Stroke criteria:** ischaemic stroke **Method of stroke diagnosis:** clinical diagnosis of ischaemic stroke confirmed by imaging **Inclusion criteria:** not reported **Exclusion criteria:** (1) haemorrhagic stroke; (2) clinical evidence of dementia MMSE scores < 23; (3) aphasia with severe language comprehension deficits; (4) alcohol or drug abuse during past 12 months; (5) severe systemic disease or ongoing neoplasia; (6) neurodegenerative disorders such as Parkinson's disease or Alzheimer's disease; (7) contraindications to rTMS including prior occurrence of induced seizures; major head trauma; or his-	**Treatment:** rTMS delivered over the left pre-frontal cortex at frequency of 10 Hz, intensity of 110% of the motor threshold, duration of 5 seconds, and total of 20 trains separated by 60-second pauses. Cumulative rTMS exposure for the 10-Hz stimuli was 5 seconds × 20 per session × 10 sessions × 1000 seconds of cumulative exposure or a total of 10,000 magnetic pulses **Control:** sham stimulation: similar stimulation parameters to the rTMS stated	• Depression clinical response (reduction in HDRS total score ≥ 50% and patient no longer meeting DSM-IV criteria for depression diagnosis) • Remission of depression (reduction in HDRS total score ≥ 50% with final HDRS score < 8)	Unable to isolate outcome data for those with depression at randomisation

Table 1. Characteristics of 'dropout' studies *(Continued)*

		tory of idiopathic epilepsy; presence of metal in the skull, cranial cavity, or brain parenchyma; cardiac pacemaker, implanted defibrillator, or intracardiac lines **Depression criteria:** psychiatric diagnosis (i.e. depression due to stroke with major depressive-like episode or research criteria for minor depression) was made using symptoms elicited by a version of the Present State Examination modified to identify DSM-IV symptoms of depression and anxiety disorder; evidence that depression was unresponsive to at least 2 treatments with antidepressants given in adequate doses; clear clinical indication of a significant change in the course or severity of depressive disorder after stroke **Total number included in this trial:** 20 **Number included in treatment group:** 10 (60% men; mean age 63.1, SD 8.1) **Number included in control group:** 10 (50% men; mean age 66.5, SD 12.2)	but with the coil angled off the head, to produce a 67% to 73% reduction in the magnetic field **Administered by:** investigators at the ECT facility in the Department of Psychiatry **Duration:** 2 weeks	• Depression measured using 17-item HDRS • Cognitive function measured using MMSE • Adverse events	
Jorge 2008	**Study design:** parallel design **Number of arms:** 4 **Experimental arm A:** 10 rTMS sessions **Experimental Arm B:** 15 rTMS sessions **Control arm A:** 10 sham rTMS **Control arm B:** 15 sham rTMS	**Geographical location:** USA **Setting:** mixed **Number of participants:** unclear **Stroke criteria:** not an entry criteria. Includes participants with clinical diagnosis of vascular depression **Inclusion criteria:** not reported **Exclusion criteria:** (1) presence of severe heart or respiratory failure or renal or hepatic failure, or occurrence of ongoing neoplastic process; (2) neurodegenerative disorders such as idiopathic Parkinson's disease or probable Alzheimer's disease and clinical evidence of dementia (Clinical Dementia Rating Scale score 0.5); (3) depressed participants who were actively suicidal, who presented with prominent psychotic features, or with comorbid alcohol or other drug abuse that was active within 2 years before the study; (4) prior occurrence of induced seizures, major head trauma, and history of epilepsy; (5) metal in the skull, cranial cavity, or brain parenchyma; cardiac pacemaker, im-	**Treatment A:** 10 rTMS sessions in the left DLPFC at frequency of 10 Hz and intensity of 110% of the motor threshold during a 6-second period, with a total of 20 trains separated by 1-minute pauses. Treatment was administered during a 10-day period for a total cumulative dose (TCD) of 12,000 pulses (i.e. TCD-12K group) **Treatment B:** 15 rTMS sessions in the left pre-frontal cortex at frequency of 10 Hz and intensity of 110% of the motor threshold during a 6-second period, with a total of 20 trains separated by 1-minute pauses. Treatment was ad-	• Depression - unclear what measure was used	Unable to obtain information about whether any participants in this study have a diagnosis of stroke and whether some participants who received treatment A are the same as those reported in Jorge 2004

Table 1. Characteristics of 'dropout' studies *(Continued)*

		planted defibrillator, or medication pump **Depression criteria:** diagnosis of major depression during current depressive episode **Total number included in this trial:** number of stroke participants unclear **Number included in treatment group:** number of stroke participants unclear **Number included in control group:** number of stroke participants unclear	ministered during a 10-day period with 2 sessions per day for 5 days to achieve a TCD of 18,000 pulses (i.e. TCD-18K group) **Control A:** 10 sham stimulation sessions with matched pulses but performed with a specially designed coil that looks exactly like the standard stimulating coil but produces scalp sensation without actual cortical stimulation **Control B:** 15 sham stimulation sessions **Duration:** 10 days		
Kim 2019	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** rTMS **Control arm:** sham stimulation	**Geographical location:** South Korea **Setting:** unclear **Number of participants:** 12 **Stroke criteria:** first-ever stroke **Method of diagnosis:** not reported **Inclusion criteria:** (1) first-ever stroke; (2) cognitive impairment **Exclusion criteria:** not reported **Depression criteria:** none **Total number included in this trial:** 12 **Number included in treatment group:** unclear **Number included in control group:** unclear	**Treatment:** rTMS; frequency: 10Hz; 80% of resting motor threshold; 10 sessions for 2 weeks; location: left DLPFC **Control:** sham stimulation **Duration:** 2 weeks **Follow-up:** 1 and 3 months	• Cognitive function measured using Montreal Cognitive Assessment (MoCA) • Motor recovery measured using Fugl-Meyer Assessment (FMA) • Disability measured using Modified Bathel Index (MBI) • Depression measured using Geriatric Depression Scale (GDS)	Results not available in format suitable for this review
Kim 2017	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** escitalopram	**Geographical location:** South Korea **Setting:** unclear **Number of participants:** 478 **Stroke criteria:** ischaemic stroke or intracerebral haemorrhage	**Treatment:** escitalopram (5 mg daily as a starting dose, dose increased to 10 mg daily from the second week and then every other day for 1 week) **Control:** placebo	• Depression measured using MADRS • Emotional incontinence measured using	Unable to isolate outcome data for those with depression at randomisation

Table 1. Characteristics of 'dropout' studies *(Continued)*

	Control arm: placebo	**Method of diagnosis:** diagnosis confirmed by MRI or CT **Inclusion criteria:** (1) acute ischaemic stroke or intracerebral haemorrhage within previous 21 days **Exclusion criteria:** (1) history of diagnosed depression or other psychiatric diseases before index stroke; (2) severe dementia, defined as requiring assistance from others to maintain activities of daily living because of cognitive dysfunction (stages 5 to 7 of the Global Deterioration Scale); (3) aphasia resulting in communication difficulties regardless of reasons; (4) exhibiting strong suicidal thoughts (combined MADRS score > 8 on ninth and tenth questions); (5) seizures; (6) history of other brain disease or head trauma within 30 days before screening; (7) abnormal blood tests such as abnormal liver function test or renal insufficiency; (8) pregnant or lactating **Depression criteria:** none **Total number included in this trial:** 478 **Number included in treatment group:** 241 (57% men, mean age 63.6, SD 12.6) **Number included in control group:** 237 (65% men, mean age 63.5, SD 12.0)	**Duration:** 12 weeks **Follow-up:** 6 months	Kim's criteria • Anger proneness measured using Spielberg Train Anger Scale • Impairment measured using NIHSS • Disability measured using mRS and BI	
Kim 2017a	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** rTMS **Control arm:** sham rTMS	**Georgraphical location:** South Korea **Setting:** inpatient **Number of participants:** 44 **Stroke criteria:** right hemisphere ischaemic or haemorrhagic stroke **Method of stroke diagnosis:** unclear **Inclusion criteria:** (1) diagnosis of right hemisphere ischaemic or haemorrhagic stroke **Exclusion criteria:** (1) severe cognitive impairment that made it difficult to understand instructions; (2) seizures; (3) severe head trauma; (4) metal skull implant; (5) pacemaker **Depression criteria:** none **Total number included in this trial:** 44	**Treatment:** rTMS. rTMS stimulus was targeted at P3, over the left parieto-occipital cortex, and at P4, over the right parieto-occipital cortex. To set the motor threshold before stimulation, a cotton cap with a grid (1×1 cm^2) was fixed to the scalp from the nasion to the inion, a magnetic stimulus was applied to the cranium, and motor-evoked potentials were measured. Low-frequency rTMS stimulation was applied to P3 on	• Depression measured using BDI • Activities of daily living measured using FIM	Unable to isolate outcome data for those with depression at randomisation

Table 1. Characteristics of 'dropout' studies *(Continued)*

		Number included in treatment group: 22 (82% men, mean age 52.6, SD 10.6) **Number included in control group:** 22 (59% men, mean age 64.3, SD 11.5)	the left, healthy side, using a 1-Hz stimulus at 90% motor threshold, 4 times, for 5 minutes at a time, separated by 1-minute intervals. High-frequency rTMS was applied to P4 on the right, affected side, using a 5-Hz stimulus at 90% motor threshold, 20 times, for 5 seconds at a time, separated by 55-second intervals **Control:** sham rTMS. Mock stimulus used the same protocol as low-frequency rTMS, except that the coil was not placed against the skull, and the stimulus was applied in the vertical direction **Duration:** 12 weeks **Follow-up:** 8 weeks		
Kootker 2012	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** tailored cognitive-behavioural therapy (CBT) **Control arm:** computer cognitive training (CCT)	**Geographical location:** The Netherlands **Setting:** outpatient **Number of participants:** 61 **Stroke criteria:** all subtypes **Method of stroke diagnosis:** clinically confirmed stroke **Inclusion criteria:** (1) sustained any type of clinically confirmed stroke at least 3 months earlier; (2) only mild cognitive impairment (MMSE score); (3) scoring positively on communication-related items of NIHSS; (4) mastered Dutch language **Exclusion criteria:** (1) pre-stroke major depression requiring psychiatric care; (2) post-stroke major depression requiring a start with medication; (3) pre-morbid disability as reflected in a BI score < 19 (out of 20); (4) severe comorbidity that might affect mood (e.g. cancer) **Depression criteria:** HADS score > 7	**Treatment:** tailored cognitive-behavioural therapy. Each session consisted of 2 × 20 to 25-minute blocks divided by a 10 to 15-minute break. Therefore, each session lasted approximately 1 hour. Goals for attaining daily life activities were primarily set together by the patient and the therapist using pictures from the Activity Card Sort. Concurrently with psychological sessions, the CBT intervention was augmented with 3 sessions of occupational therapy or movement therapy. During these sessions, an occupational or movement therapist helped partici-	• Depression measured using HADS-Depression • Anxiety measured using HADS-Anxiety • Quality of life measured using EQ5D	Results not available in format suitable for this review

Table 1. Characteristics of 'dropout' studies *(Continued)*

	Total number included in this trial: 61 **Number included in treatment group:** 31 (61.3% men, mean age 61, SD not reported) **Number included in control group:** 30 (63.3%, mean age 61, SD not reported)	pants in establishing and attaining goals aimed at meaningful activities and social participation. These goals were attuned to the content of the psychological sessions. **Administered by:** certified healthcare psychologist (therapist) **Supervision:** not reported **Intervention fidelity:** not reported **Control:** computer cognitive training. A desktop was set up with headphones and a keyboard with coloured patches attached to 2 keys. Patients could select any (or a combination) of 4 specific cognitive domains for training (i.e. attention, memory, executive functioning, visual attention). As participants improved, the Cogniplus Program adjusted the level of difficulty for each training task accordingly. In this way, each patient trained at his/her individual level and pace. **Administered by:** self-administered, but cognitive trainers or psychological assistants were present to assist participants during training. **Duration:** 4 months **Follow-up:** 12 months

Table 1. Characteristics of 'dropout' studies *(Continued)*

Li 2016	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** rTMS + fluoxetine 20 mg/day (SSRI) **Control arm:** fluoxetine 20 mg/day (SSRI)	**Geographical location:** China **Setting:** mixed **Number of participants:** 61 **Stroke criteria:** unclear **Method of stroke diagnosis:** clinical diagnosis according to the Guiding Principles of Clinical Research on the Treatment of Stroke by New Chinese Herbal Medicines published in 2002 **Inclusion criteria:** (1) meets clinical diagnosis according to the Guiding Principles of Clinical Research on the Treatment of Stroke by New Chinese Herbal Medicines; (2) meets Chinese classification of Mental Disorders-3 (CCMD-3) depression diagnostic criteria and Internal Medicine of Traditional Chinese Medicine diagnostic criteria for stagnation of Liver-Qi type post-stroke depression and HDRS score ≥ 8; (3) age between 35 and 75 y/o; (4) onset of depression in 0.5-1 months after stroke **Exclusion criteria:** (1) previous severe depression or psychiatric illness history; (2) taking antidepressants in recent 2 weeks; (3) severe aphasia and vascular dementia; (4) severe cardiovascular diseases, impaired hepatorenal functions, haematologic illness or epilepsy, and other organ dysfunction; (5) those who have implants and stimulators (metal, electronic cochlea, post-percutaneous coronary intervention (PCI), cardiac and brain pacemakers) in the body **Depression criteria:** According to the Chinese classification of Mental Disorders-3 (CCMD-3) depression diagnostic criteria and Internal Medicine of Traditional Chinese Medicine diagnostic criteria for stagnation of Liver-Qi type post-stroke depression and HDRS score ≥ 8 **Total number included in this trial:** 61 **Number included in treatment group:** 31 (55% male, mean age 56, SD 7.6) **Number included in control group:** 30 (50% male, mean age 61, SD 7.2)	**Treatment:** rTMS + fluoxetine 20 mg/day (SSRI) **Control:** fluoxetine 20 mg/day (SSRI) **Duration:** 2 weeks **Follow-up:** None	• Depression measured using 24-item HDRS	Results not available in format suitable for this review

Table 1. Characteristics of 'dropout' studies *(Continued)*

Mauri 1988	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** mianserin **Control arm:** placebo	**Geographical location:** Spain **Setting:** unclear **Number of participants:** unclear **Stroke criteria:** ischaemic stroke **Method of diagnosis:** unclear **Inclusion criteria:** not reported **Exclusion criteria:** not reported **Depression criteria:** GDS (15 item) score > 4 **Total number included in this trial:** unclear **Number included in treatment group:** unclear **Number included in control group:** unclear	**Treatment:** mianserin **Control:** placebo **Duration:** 6 weeks	• Depression - unclear what measure was used	Results not available in format suitable for this review
Meara 1998	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** sertraline **Control arm:** placebo	**Geographical location:** UK **Setting:** inpatient **Number of participants:** unclear **Stroke criteria:** ischaemic stroke **Method of stroke diagnosis:** unclear **Inclusion criteria:** not reported **Exclusion criteria:** (1) moderate to severe dementia; (2) severe aphasia, communication difficulties; (3) poorly controlled epilepsy **Depression criteria:** GDS (15 item) score > 4 **Total number included in this trial:** unclear **Number included in treatment:** unclear **Number included in control group:** unclear	**Treatment:** sertraline, 50 mg daily. Dose escalation to 100 mg for non-responders at 2 weeks **Control:** matched placebo **Duration:** 6 weeks	• Depression measured using GDS	Results not available in format suitable for this review
Ohtomo 1985	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** tiapride **Control arm:** placebo	**Geographical location:** Japan **Setting:** unclear **Number of participants:** 188 **Stroke criteria:** all subtypes **Method of stroke diagnosis:** diagnosis via clinical signs and CT **Inclusion criteria:** (1) > 40 years of age, high blood pressure (> 160/90 mmHg), and hypertensive changes on fundoscopy changes; (2) stable neuroleptic, minor tranquilliser, an-	**Treatment:** tiapride, 75 mg daily for 1 week, dose escalation to 150 to 225 mg daily for 5 weeks according to clinical response **Control:** matched placebo **Duration:** 6 weeks	• Depression - unclear what measure was used	Unable to isolate outcome data for those with depression at randomisation

Table 1. Characteristics of 'dropout' studies *(Continued)*

		tidepressant, brain metabolic activators, cerebro-vasodilators washed out for 3 to 7 days before randomisation **Exclusion criteria:** (1) severe aphasia; (2) severe dementia; (3) drug dependence; (4) inadequate conditions for the study **Depression criteria:** not reported **Total number included in this trial:** 288 **Number included in treatment group:** 141 (54% men, mean age not reported) **Number included in control group:** 147 (61% men, mean age not reported)			
Ostwald 2014	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** counselling + mailed information **Control arm:** mailed information	**Geographical location:** USA **Setting:** outpatient **Number of participants:** 159 **Stroke criteria:** not reported **Method of stroke diagnosis:** not reported **Inclusion criteria:** not reported **Exclusion criteria:** (1) history of psychopathology for patient or caregiver; (2) globally aphasic preventing communication and consent; (3) patient or caregiver has comorbidity that would take priority over stroke rehabilitation; (4) life expectancy < 6 months **Depression criteria:** depression not an entry criterion **Total number included in this trial:** 159 **Number included in treatment group:** 80 (69% men, mean age 66.98, SD 9.04) **Number included in control group:** 79 (81% men, mean age 65.75, SD 9.26)	**Treatment:** home visits from a multi-disciplinary therapy team to provide education, support, skill training, counselling, and linkages to social and community resources + mailed information. Average dose 36.7 hours **Administered by:** advanced practice nurses, occupational and physical therapists **Supervision:** not reported **Intervention fidelity:** not reported **Control:** mailed information **Duration:** 6 months	• Depression measured using GDS • Disability measured using FIM • Quality of life measured using SF-36	Unable to isolate outcome data for those with depression at randomisation
Raffaele 1996	**Study design:** parallel design **Number of arms:** 2	**Geographical location:** Italy **Setting:** outpatient **Number of participants:** 22 **Stroke criteria:** unclear	**Treatment:** trazodone 300 mg/d **Control:** placebo **Duration:** 30 to 45 days	• Depression measured using ZDS • Activities of daily living mea-	Unable to isolate outcome data for those with depression at randomisation

Table 1. Characteristics of 'dropout' studies *(Continued)*

	Experimental arm: trazodone **Control arm:** placebo	**Method of stroke diagnosis:** not reported **Inclusion criteria:** not reported **Exclusion criteria:** not reported **Depression criteria:** ZDS **Total number included in this trial:** 22 **Number included in treatment group:** 11 (45.4% men, mean age 69.5, SD 2.3) **Number included in control group:** 11 (72.7% men, mean age 70.4, SD 3.0)	**Follow-up:** unclear	sured using BI	
Robinson 2000	**Study design:** cross-over design **Number of arms:** 3 **Experimental arm 1:** nortriptyline **Experimental arm 2:** fluoxetine **Control arm:** placebo	**Geographical location:** USA **Setting:** mixed **Number of participants:** **Stroke criteria:** infarction and haemorrhage **Method of stroke diagnosis:** not reported **Inclusion criteria:** (1) acute stroke within 6 months of onset of the study; (2) taking antidepressants other than fluoxetine at the time of enrolment and allowed to stop antidepressants for a 2-week washout period before the study; (3) patient's immediate family and treating physician agree to the patient's participation **Exclusion criteria:** (1) severe comprehension deficit that precluded a verbal interview (defined as failing part 1 of the Token Test); (2) any other significant medical illness that would threaten life or recovery from stroke; (3) prior history of head injury; (4) prior history of other brain disease with the exception of prior stroke **Depression criteria:** DSM-IV and HDRS **Total number included in this trial:** unclear **Number included in treatment group 1:** unclear (74% men, mean age 65, SD 14)	**Treatment 1:** nortriptyline (SNRI). Doses of 25 mg/d gradually increased to 100 mg/d **Treatment 2:** fluoxetine (SSRI). Doses of 10 mg/d gradually increased to 40 mg/d **Control:** matched placebo **Duration:** 12 weeks **Follow-up:** none	• Depression measured using 24-item HDRS • Anxiety measured using HARS • Activities of daily living measured using FIM and John Hopkins Functional Inventory • Cognitive functioning measured using MMSE	Unable to isolate outcome data for those with depression at randomisation

Table 1. Characteristics of 'dropout' studies *(Continued)*

		Number included in treatment group 2: unclear (31% men, mean age 64, SD 10) **Number included in control group:** unclear (53% men, mean age 73, SD 8)			
Sun 2000	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** add-on psychotherapy **Control arm:** usual care	**Geographical location:** China **Setting:** not reported **Number of participants:** 60 **Stroke criteria:** all ischaemic and haemorrhagic strokes **Method of stroke diagnosis:** diagnosis consistent with diagnostic criteria for stroke reported in *Chinese Journal of Neurology and Psychiatry* in 1988 and confirmation by brain CT or MRI **Inclusion criteria:** not reported **Exclusion criteria:** (1) severe cognitive impairment; (2) obvious consciousness disturbance **Depression criteria:** none **Total number included in this trial:** 60 **Number included in treatment group:** 30 (60% men, mean age 56.5, SD 13.4, 53.3% ischaemic) **Number included in control group:** 30 (63% men, 55.9, SD 14.3, 56.7% ischaemic)	**Treatment:** add-on psychotherapy entailing understanding the patient's reaction to sudden illness and letting the patient talk about concerns in mind, to give sympathy, care, and support; inducing correct understanding of the illness by the patient, helping him/her to analyse current problems and building confidence to overcome the disease; promoting the family's help and co-operation; giving praise, encouragement, or small prizes for patient improvement **Administered by:** not reported **Supervision:** not reported **Intervention fidelity:** not reported **Control:** usual care	• Depression - unclear what measure was used	Unable to isolate outcome data for those with depression at randomisation
Yu 2021	**Study design:** parallel design **Number of arms:** 2 **Experimental arm:** fluoxetine + rTMS **Control arm:** fluoxetine	**Geographical location:** China **Setting:** inpatient **Number of participants:** 115 **Stroke criteria:** all ischaemic and haemorrhagic strokes **Method of stroke diagnosis:** met clinical diagnosis **Inclusion criteria:** (1) met the clinical diagnosis and whose related diagnosis was confirmed as stroke; (2) participants 45-65 years old; (3) participants with complete general clinical data; (4) participants who agreed	**Treatment:** fluoxetine + rTMS **Control:** fluoxetine **Duration:** not reported **Follow-up:** none	• Anxiety measured using SAS • Depression measured using SDS • Neurological function measured using NIHSS • Cognitive function measured using MMSE	Results not available in format suitable for this review

Table 1. Characteristics of 'dropout' studies *(Continued)*

	to cooperate with and assist the medical staff in our hospital to complete the investigation, and participants who signed the informed consent forms **Exclusion criteria:** (1) participants who quit the experiment halfway; (2) participants comorbid with malignancies or severe organ dysfunction, people with infectious diseases, poor treatment compliance, a physical disability, and; (3) participants who transferred from one hospital to another **Depression criteria:** none **Total number included in this trial:** 115 **Number included in treatment group:** 60 (mean age 55.91, SD 8.76 **Number included in control group:** 55 (mean 55.75, SD 9.02)	• Functional capacity measured using BI • Quality of life measured using SF-36

BDI: Beck Depression Inventory
BI: Barthel Index
CBT: cognitive behavioural therapy
CCMD-3: Chinese classification of mental disorders
CCT: computer cognitive training
CES-D: Centre for Epidemiologic Studies Depression Scale
CT: computed tomography
DLPFC: dorsolateral pre-frontal cortex
DSM- IV: Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition
ECT: electroconvulsive therapy
EQ5D: EuroQoL 5-dimension
FIM: Functional Independence Measure
FMA: Fugl-Meyer Assessment
GDS: Geriatric Depression Scale
GHQ-28: 28-item General Health Questionnaire
HADS: Hospital Anxiety and Depression Scale
HARS: Hamilton Anxiety Rating Scale
HDRS: Hamilton Depression Rating Scale
Hz: hertz
LD: levodopa
MADRS: Montgomery Asberg Depression Rating Scale
MAO: monoamine oxidase
MBI: modified Bathel Index
MINI: Mini-International Neuropsychiatry Interview
MMSE: Mini Mental State Examination
MoCA: Montreal Cognitive Assessment
MPH: methylphenidate
MRI: magnetic resonance imaging
mRS: modified Rankin Scale
NIHSS: National Institute of Health Stroke Scale
PCI: percutaneous coronary intervention
PICH: primary intracerebral haemorrhage
PHQ-9: 9-item Patient Health Questionnaire
PST: Problem-solving therapy

REBT: rational emotive behaviour therapy
rTMS: repetitive transcranial magnetic stimulation
SAH: subarachnoid haemorrhage
SAQOL-39: Stroke and Aphasia Quality of Life Scale
SAS: Self-rating Anxiety Scale
SD: standard deviation
SDS: Self-rating Depression Scale
SF-36: Short-Form 36
SMART: Specific, Measureable, Achievable, Realistic, Timely
SNRI: selective nortriptyline reuptake inhibitor
SSRI: selective serotonin reuptake inhibitor
TCD: total cumulative dose
TIA: transient ischaemic attack
tDCS: transcranial direct current stimulation
TRH-T: protirelin tartrate
ZDS: Zung Depression Scale

APPENDICES

Appendix 1. Living systematic review protocol

The methods outlined below are specific to maintaining the review as a living systematic review on the CDSR. Core review methods, such as the criteria for considering studies in the review and assessment of risk of bias, are unchanged. As such, below we outline only those areas of the Methods for which additional activities or rules apply.

Search methods for identification of trials

We will re-run electronic database and trial registry searches bi-monthly. We are incorporating new evidence rapidly after it is identified. We will search other resources (conference abstracts) manually, annually.

As additional steps to inform the living systematic review, we are contacting corresponding authors of ongoing trials as they are identified and asking them to advise when results are available, or to share early or unpublished data. We are contacting the corresponding authors of any newly included trials for advice about other relevant trials and to request additional trial data and, in some instances, additional analyses. We will manually screen the reference list of any newly-included studies and systematic reviews.

We will reconsider search methods and strategies once a year to ensure they reflect any terminology changes in the topic area or in the databases.

Selection of studies

We will immediately screen any new citations retrieved during the bi-monthly searches.

Data synthesis

Whenever we find new evidence (i.e. trials, data or information) meeting the review inclusion criteria, we will extract the data, assess risk of bias and incorporate it in the synthesis every four months, as appropriate. We will incorporate any new trial data into existing meta-analyses using the standard approaches outlined in the Data synthesis section. Formal sequential meta-analysis approaches will not be used for updated meta-analyses.

Methods for future updates

We will review scope and methods approximately annually, or more frequently if appropriate, in light of potential changes in the topic area or the evidence being included in the review (for example, additional comparisons, interventions, subgroups or outcomes, or new methods available).

We will make decisions about whether to stop updating when appropriate (e.g. if conclusions are unlikely to change with future updates; no meaningful effect is likely to be found; the review question is no longer a priority for decision-making; or no new evidence is likely), and will be guided by ongoing research in this area.

Appendix 2. Search review - 2022

Electronic searches

Cochrane Stroke Trial Register - searched February 2022; Cochrane Anxiety and Neurosis Trial Register - searched February 2022.

The remaining databases were also searched on June 2021.

- Cochrane Central Register of Controlled Trials (CENTRAL)

#1 MeSH descriptor: [Cerebrovascular Disorders]
#2 MeSH descriptor: [Basal Ganglia Cerebrovascular Disease]
#3 MeSH descriptor: [Brain Ischemia]
#4 MeSH descriptor: [Carotid Artery Diseases]
#5 MeSH descriptor: [Intracranial Arterial Diseases]
#6 MeSH descriptor: [Intracranial Arteriovenous Malformations]
#7 MeSH descriptor: [Intracranial Embolism and Thrombosis]
#8 MeSH descriptor: [Intracranial Hemorrhages]
#9 MeSH descriptor: [Stroke]
#10 MeSH descriptor: [Hemorrhagic Stroke]
#11 MeSH descriptor: [Ischemic Stroke]
#12 MeSH descriptor: [Brain Infarction]
#13 MeSH descriptor: [Stroke, Lacunar]
#14 MeSH descriptor: [Vasospasm, Intracranial]
#15 MeSH descriptor: [Vertebral Artery Dissection]
#16 MeSH descriptor: [Stroke Rehabilitation]
#17 (stroke or poststroke or post-stroke or cerebrovasc* or (cerebr$ NEAR/3 vasc*) or CVA* or apoplectic or apoplex* or (transient NEAR/3 isch?emic NEAR/3 attack) or tia* or SAH or AVM or ESUS or ICH or (cerebral small vessel NEAR/3 disease*)):ti,ab,kw
#18 ((cerebr* or cerebell* or arteriovenous or vertebrobasil* or interhemispheric or hemispher* or intracran* or intracerebral or infratentorial or supratentorial or MCA* or ((anterior or posterior) NEAR/3 circulat*) or lenticulostriate or ((basilar or brachial or vertebr*) NEAR/3 arter*)) NEAR/3 ((blood NEAR/5 clot*) or disease* or damage* or disorder* or disturbance or dissection or lesion or syndrome or arrest or accident or lesion or vasculopathy or insult or attack or injury or insufficiency or malformation or obstruct* or anomal*)):ti,ab,kw
#19 ((brain or cerebr* or cerebell* or vertebrobasil* or hemispher* or intracran* or intracerebral or infratentorial or supratentorial or middle cerebral artery or MCA* or anterior circulation or posterior circulation or basilar artery or vertebral artery or space-occupying) NEAR/5 (isch?emi* or infarct* or thrombo* or emboli* or occlus* or hypoxi*)):ti,ab,kw
#20 ((brain or cerebr* or cerebell* or intracerebral or intracran* or parenchymal or intraparenchymal or intraventricular or infratentorial or supratentorial or basal gangli* or putaminal or putamen or posterior fossa or hemispher* or subarachnoid) NEAR/5 (h?emorrhag* or h?ematoma* or bleed*)):ti,ab,kw
#21 {or #1-#20}
#22 MeSH descriptor: [Depression]
#23 MeSH descriptor: [Depressive Disorder]
#24 MeSH descriptor: [Depressive Disorder, Major]
#25 MeSH descriptor: [Depressive Disorder, Treatment-Resistant]
#26 MeSH descriptor: [Dysthymic Disorder]
#27 MeSH descriptor: [Antidepressive Agents]
#28 ((depress* or dysthymi*or dysphor*or antidepress*or anti-depress*)):ti,ab,kw
#29 {or #22-#28}
#30 #21 and #29

- MEDLINE

1. cerebrovascular disorders/ or exp basal ganglia cerebrovascular disease/ or exp brain ischemia/ or exp carotid artery diseases/ or exp intracranial arterial diseases/ or exp intracranial arteriovenous malformations/ or exp "intracranial embolism and thrombosis"/ or exp intracranial hemorrhages/ or stroke/ or hemorrhagic stroke/ or exp ischemic stroke/ or exp brain infarction/ or stroke, lacunar/ or vasospasm, intracranial/ or vertebral artery dissection/
2. stroke rehabilitation/
3. (stroke or poststroke or post-stroke or cerebrovasc$ or (cerebr$ adj3 vasc$) or CVA$ or apoplectic or apoplex$ or (transient adj3 isch?emic adj3 attack) or tia$ or SAH or AVM or ESUS or ICH or (cerebral small vessel adj3 disease$)).tw.
4. ((cerebr$ or cerebell$ or arteriovenous or vertebrobasil$ or interhemispheric or hemispher$ or intracran$ or intracerebral or infratentorial or supratentorial or MCA$ or ((anterior or posterior) adj3 circulat$) or lenticulostriate or ((basilar or brachial or vertebr$) adj3 arter$)) adj3 ((blood adj5 clot$) or disease$ or damage$ or disorder$ or disturbance or dissection or lesion or syndrome or arrest or accident or lesion or vasculopathy or insult or attack or injury or insufficiency or malformation or obstruct$ or anomal$)).tw.
5. ((cerebr$ or cerebell$ or arteriovenous or vertebrobasil$ or interhemispheric or hemispher$ or intracran$ or corpus callosum or intracerebral or intracortical or intraventricular or periventricular or posterior fossa or infratentorial or supratentorial or MCA$ or ((anterior or posterior) adj3 circulation) or basal ganglia or ((basilar or brachial or vertebr$) adj3 arter$) or space-occupying or brain ventricle$ or lacunar or cortical or ocular) adj3 (isch?emi$ or infarct$ or thrombo$ or emboli$ or occlus$ or hypoxi$ or vasospasm or obstruct$ or vasoconstrict$)).tw.
6. ((cerebr$ or cerebell$ or vertebrobasil$ or interhemispheric or hemispher$ or intracran$ or corpus callosum or intracerebral or intracortical or intraventricular or periventricular or posterior fossa or infratentorial or supratentorial or MCA$ or ((anterior or posterior)

adj3 circulation) or basal ganglia or ((basilar or brachial or vertebr$) adj3 arter$) or space-occupying or brain ventricle$ or subarachnoid $ or arachnoid$) adj3 (h?emorrhag$ or h?ematom$ or bleed$)).tw.
7. or/1-6
8. depression/
9. depressive disorder/ or depressive disorder, major/ or depressive disorder, treatment-resistant/ or dysthymic disorder/ or or exp antidepressive agents/
10. (depress$ or dysthymi$ or dysphor$ or antidepress$ or anti-depress$).tw.
11. or/8-10
12. randomized controlled trial.pt.
13. controlled clinical trial.pt.
14. randomized.ab.
15. placebo.ab.
16. clinical trials as topic.sh.
17. random$.ab.
18. trial.ti.
19. or/12-18
20. exp animals/ not humans.sh.
21. 19 not 20
22. 7 and 11 and 21

- Embase

The stroke and depression subject search terms (lines 1-6 and 7-12) has been linked to an adapted version of the Cochrane Embase Project filter for identifying RCTs in Embase Ovid (see www.cochranelibrary.com/help/central-creation-details.html for information) (or/13-34)

1. cerebrovascular disease/ or exp basal ganglion hemorrhage/ or exp brain hematoma/ or exp brain hemorrhage/ or exp brain infarction/ or exp brain ischemia/ or exp carotid artery disease/ or cerebral artery disease/ or exp cerebrovascular accident/ or exp cerebrovascular malformation/ or exp intracranial aneurysm/ or exp occlusive cerebrovascular disease/ or stroke/ or stroke unit/ or stroke patient/
2. (stroke or poststroke or post-stroke or cerebrovasc$ or (cerebr$ adj3 vasc$) or CVA$ or apoplectic or apoplex$ or (transient adj3 isch? emic adj3 attack) or tia$ or SAH or AVM or ESUS or ICH or (cerebral small vessel adj3 disease$)).tw.
3. ((cerebr$ or cerebell$ or arteriovenous or vertebrobasil$ or interhemispheric or hemispher$ or intracran$ or intracerebral or infratentorial or supratentorial or MCA$ or ((anterior or posterior) adj3 circulat$) or lenticulostriate or ((basilar or brachial or vertebr$) adj3 arter$)) adj3 ((blood adj5 clot$) or disease$ or damage$ or disorder$ or disturbance or dissection or lesion or syndrome or arrest or accident or lesion or vasculopathy or insult or attack or injury or insufficiency or malformation or obstruct$ or anomal$)).tw.
4. ((cerebr$ or cerebell$ or arteriovenous or vertebrobasil$ or interhemispheric or hemispher$ or intracran$ or corpus callosum or intracerebral or intracortical or intraventricular or periventricular or posterior fossa or infratentorial or supratentorial or MCA$ or ((anterior or posterior) adj3 circulation) or basal ganglia or ((basilar or brachial or vertebr$) adj3 arter$) or space-occupying or brain ventricle$ or lacunar or cortical or ocular) adj3 (isch?emi$ or infarct$ or thrombo$ or emboli$ or occlus$ or hypoxi$ or vasospasm or obstruct$ or vasoconstrict$)).tw.
5. ((cerebr$ or cerebell$ or vertebrobasil$ or interhemispheric or hemispher$ or intracran$ or corpus callosum or intracerebral or intracortical or intraventricular or periventricular or posterior fossa or infratentorial or supratentorial or MCA$ or ((anterior or posterior) adj3 circulation) or basal ganglia or ((basilar or brachial or vertebr$) adj3 arter$) or space-occupying or brain ventricle$ or subarachnoid $ or arachnoid$) adj3 (h?emorrhag$ or h?ematom$ or bleed$)).tw.
6. or/1-5
7. depression/ or agitated depression/ or atypical depression/ or dysphoria/ or dysthymia/ or endogenous depression/ or involutional depression/ or late life depression/ or major depression/ or masked depression/ or reactive depression/ or recurrent brief depression/ or treatment resistant depression/ or exp antidepressant agent/
8. ((depress$ or dysthymi$ or dysphor$ or antidepress$ or anti-depress$).tw.).tw.
9. 7 or 8
10. 6 and 9
11. post-stroke depression/
12. 10 or 11
13. Randomized Controlled Trial/ or "randomized controlled trial (topic)"/
14. Randomization/
15. Controlled clinical trial/ or "controlled clinical trial (topic)"/
16. control group/ or controlled study/
17. clinical trial/ or "clinical trial (topic)"/ or phase 1 clinical trial/ or phase 2 clinical trial/ or phase 3 clinical trial/ or phase 4 clinical trial/
18. crossover procedure/
19. single blind procedure/ or double blind procedure/ or triple blind procedure/
20. placebo/ or placebo effect/
21. (random$ or RCT or RCTs).tw.
22. (controlled adj5 (trial$ or stud$)).tw.

23. (clinical$ adj5 trial$).tw.
24. clinical trial registration.ab.
25. ((control or treatment or experiment$ or intervention) adj5 (group$ or subject$ or patient$)).tw.
26. (quasi-random$ or quasi random$ or pseudo-random$ or pseudo random$).tw.
27. ((control or experiment$ or conservative) adj5 (treatment or therapy or procedure or manage$)).tw.
28. ((singl$ or doubl$ or tripl$ or trebl$) adj5 (blind$ or mask$)).tw.
29. (cross-over or cross over or crossover).tw.
30. (placebo$ or sham).tw.
31. trial.ti.
32. (assign$ or allocat$).tw.
33. controls.tw.
34. or/13-33
35. 12 and 34

- CINAHL

This search strategy uses the highly sensitive search filter (S11-S32) to identify reports of controlled clinical trials within CINAHL Plus (Glanville, Dooley, Wisniewski, Foxlee, Noel-Storr 2019). Glanville J, Dooley G, Wisniewski S, Foxlee R, Noel-Storr A. Development of a search filter to identify reports of controlled clinical trials within CINAHL Plus. Health Libraries Journal. 2019 36(1):73-90. [DOI: 10.1111/hir.12251]
S33S32 NOT S31
S32S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25
S31S29 NOT S30
S30MH (human)
S29S26 OR S27 OR S28
S28MH animals+
S27TI (animal model*)
S26MH (animal studies)
S25AB (cluster W3 RCT)
S24MH (crossover design) OR MH (comparative studies)
S23AB (control W5 group)
S22PT (randomized controlled trial)
S21MH (placebos)
S20MH (sample size) AND AB (assigned OR allocated OR control)
S19TI (trial)
S18AB (random*)
S17TI (randomised OR randomized)
S16MH cluster sample
S15MH pretest-posttest design
S14MH random assignment
S13MH single-blind studies
S12MH double-blind studies
S11MH randomized controlled trials
S10S7 OR S8 OR S9
S9TI (depress* or dysthymi*or dysphor*or antidepress*or anti-depress*) OR AB (depress* or dysthymi*or dysphor*or antidepress*or anti-depress*)
S8(MH "Antidepressive Agents+")
S7(MH "Depression") OR (MH "Depression, Reactive") OR (MH "Dysthymic Disorder")
S6S1 or S2 or S3 or S4 or S5
S5TI ((brain or cerebr* or cerebell* or intracerebral or intracran* or parenchymal or intraparenchymal or intraventricular or infratentorial or supratentorial or "basal gangli*" or putaminal or putamen or "posterior fossa" or hemispher* or subarachnoid) N5 (h?emorrhag* or h?ematoma* or bleed*)) or AB ((brain or cerebr* or cerebell* or intracerebral or intracran* or parenchymal or intraparenchymal or intraventricular or infratentorial or supratentorial or "basal gangli*" or putaminal or putamen or "posterior fossa" or hemispher* or subarachnoid) N5 (h?emorrhag* or h?ematoma* or bleed*))
S4TI ((brain or cerebr* or cerebell* or vertebrobasil* or hemispher* or intracran* or intracerebral or infratentorial or supratentorial or "middle cerebral artery" or MCA* or "anterior circulation" or "posterior circulation" or "basilar artery" or "vertebral artery" or "space-occupying") N5 (isch?emi* or infarct* or thrombo* or emboli* or occlus* or hypoxi*)) or AB ((brain or cerebr* or cerebell* or vertebrobasil* or hemispher* or intracran* or intracerebral or infratentorial or supratentorial or "middle cerebral artery" or MCA* or "anterior circulation" or "posterior circulation" or "basilar artery" or "vertebral artery" or "space-occupying") N5 (isch?emi* or infarct* or thrombo* or emboli* or occlus* or hypoxi*))
S3TI ((cerebr* or cerebell* or arteriovenous or vertebrobasil* or interhemispheric or hemispher* or intracran* or intracerebral or infratentorial or supratentorial or MCA* or ((anterior or posterior) NEAR/3 circulat*) or lenticulostriate or ((basilar or brachial or vertebr*) N3 arter*)) N3 ((blood N5 clot*) or disease* or damage* or disorder* or disturbance or dissection or lesion or syndrome or arrest or accident

or lesion or vasculopathy or insult or attack or injury or insufficiency or malformation or obstruct* or anomal*)) or AB ((cerebr* or cerebell* or arteriovenous or vertebrobasil* or interhemispheric or hemispher* or intracran* or intracerebral or infratentorial or supratentorial or MCA* or ((anterior or posterior) NEAR/3 circulat*) or lenticulostriate or ((basilar or brachial or vertebr*) N3 arter*)) N3 ((blood N5 clot*) or disease* or damage* or disorder* or disturbance or dissection or lesion or syndrome or arrest or accident or lesion or vasculopathy or insult or attack or injury or insufficiency or malformation or obstruct* or anomal*))
S2TI (stroke or poststroke or post-stroke or cerebrovasc* or (cerebr* N3 vasc*) or CVA* or apoplectic or apoplex* or (transient N3 isch?emic N3 attack) or tia* or SAH or AVM or ESUS or ICH or ("cerebral small vessel" N3 disease*)) OR AB (stroke or poststroke or post-stroke or cerebrovasc* or (cerebr* N3 vasc*) or CVA* or apoplectic or apoplex* or (transient N3 isch?emic N3 attack) or tia* or SAH or AVM or ESUS or ICH or ("cerebral small vessel" N3 disease*))
S1(MH "Cerebrovascular Disorders") OR (MH "Basal Ganglia Cerebrovascular Disease+") OR (MH "Carotid Artery Diseases+") OR (MH "Cerebral Ischemia+") OR (MH "Cerebral Vasospasm") OR (MH "Intracranial Arterial Diseases+") OR (MH "Intracranial Embolism and Thrombosis") OR (MH "Intracranial Hemorrhage+") OR (MH "Stroke") OR (MH "Vertebral Artery Dissections")

- PsycINFO

1. cerebrovascular disorders/ or cerebral hemorrhage/ or exp cerebral ischemia/ or cerebral small vessel disease/ or cerebrovascular accidents/ or subarachnoid hemorrhage/
2. (stroke or poststroke or post-stroke or cerebrovasc$ or (cerebr$ adj3 vasc$) or CVA$ or apoplectic or apoplex$ or (transient adj3 isch?emic adj3 attack) or tia$ or SAH or AVM or ESUS or ICH or (cerebral small vessel adj3 disease$)).tw.
3. ((cerebr$ or cerebell$ or arteriovenous or vertebrobasil$ or interhemispheric or hemispher$ or intracran$ or intracerebral or infratentorial or supratentorial or MCA$ or ((anterior or posterior) adj3 circulat$) or lenticulostriate or ((basilar or brachial or vertebr$) adj3 arter$)) adj3 ((blood adj5 clot$) or disease$ or damage$ or disorder$ or disturbance or dissection or lesion or syndrome or arrest or accident or lesion or vasculopathy or insult or attack or injury or insufficiency or malformation or obstruct$ or anomal$)).tw.
4. ((cerebr$ or cerebell$ or arteriovenous or vertebrobasil$ or interhemispheric or hemispher$ or intracran$ or corpus callosum or intracerebral or intracortical or intraventricular or periventricular or posterior fossa or infratentorial or supratentorial or MCA$ or ((anterior or posterior) adj3 circulation) or basal ganglia or ((basilar or brachial or vertebr$) adj3 arter$) or space-occupying or brain ventricle$ or lacunar or cortical or ocular) adj3 (isch?emi$ or infarct$ or thrombo$ or emboli$ or occlus$ or hypoxi$ or vasospasm or obstruct$ or vasoconstrict$)).tw.
5. ((cerebr$ or cerebell$ or vertebrobasil$ or interhemispheric or hemispher$ or intracran$ or corpus callosum or intracerebral or intracortical or intraventricular or periventricular or posterior fossa or infratentorial or supratentorial or MCA$ or ((anterior or posterior) adj3 circulation) or basal ganglia or ((basilar or brachial or vertebr$) adj3 arter$) or space-occupying or brain ventricle$ or subarachnoid $ or arachnoid$) adj3 (h?emorrhag$ or h?ematom$ or bleed$)).tw.
6. 1 or 2 or 3 or 4 or 5
7. major depression/ or dysthymic disorder/ or endogenous depression/ or late life depression/ or reactive depression/ or recurrent depression/ or treatment resistant depression/ or atypical depression/ or "depression (emotion)"/
8. exp antidepressant drugs/
9. (depress$ or dysthymi$ or dysphor$ or antidepress$ or anti-depress$).tw.
10. 7 or 8 or 9
11. clinical trials/ or exp randomized controlled trials/
12. treatment effectiveness evaluation/ or randomized clinical trials/
13. placebo/
14. (random$ or RCT or RCTs).tw.
15. (controlled adj5 (trial$ or stud$)).tw.
16. (clinical$ adj5 trial$).tw.
17. ((control or treatment or experiment$ or intervention) adj5 (group$ or subject$ or patient$)).tw.
18. random$.tw.
19. ((control or experiment$ or conservative) adj5 (treatment or therapy or procedure or manage$)).tw.
20. ((singl$ or doubl$ or tripl$ or trebl$) adj5 (blind$ or mask$)).tw.
21. (cross-over or cross over or crossover).tw.
22. (placebo$ or sham).tw.
23. trial.ti.
24. (assign$ or allocat$).tw.
25. or/11-23
26. 6 and 10 and 25

- Science Citation Index - Expanded (SCI-EXPANDED), Social Sciences Citation Index (SSCI), and Arts & Humanities Citation Index (A&HCI) within Web of Science

#19 #5 AND #6 AND #18
#18 #7 or #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17
#17 TS=(assign* or allocat* or controls)
#16 TI=trial
#15 TS=(placebo* or sham)

#14 TS=(cross-over or cross over or crossover)
#13 TS=((singl* or doubl* or tripl* or trebl*) NEAR/5 (blind* or mask*))
#12 TS=((control or experiment* or conservative) NEAR/5 (treatment or therapy or procedure or manage*))
#11 TS=(quasi-random* or quasi random* or pseudo-random* or pseudo random*)
#10 TS=((control or treatment or experiment* or intervention) NEAR/5 (group* or subject* or patient*))
#9 TS=(clinical* NEAR/5 trial*)
#8 TS=(controlled NEAR/5 (trial* or stud*))
#7 TS=(random* or RCT or RCTs)
#6 TS=(depress* or dysthymi*or dysphor*or antidepress*or anti-depress*)
#5 #4 OR #3 OR #2 OR #1
#4 TS=((brain or cerebr* or cerebell* or intracerebral or intracran* or parenchymal or intraparenchymal or intraventricular or infratentorial or supratentorial or "basal gangli*" or putaminal or putamen or "posterior fossa" or hemispher* or subarachnoid) NEAR/5 (h?emorrhag* or h?ematoma* or bleed*))
#3 TS=((brain or cerebr* or cerebell* or vertebrobasil* or hemispher* or intracran* or intracerebral or infratentorial or supratentorial or "middle cerebral artery" or MCA* or "anterior circulation" or "posterior circulation" or "basilar artery" or "vertebral artery" or "space-occupying") NEAR/5 (isch?emi* or infarct* or thrombo* or emboli* or occlus* or hypoxi*))
#2 TS=((cerebr* or cerebell* or arteriovenous or vertebrobasil* or interhemispheric or hemispher* or intracran* or intracerebral or infratentorial or supratentorial or MCA* or ((anterior or posterior) NEAR/3 circulat*) or lenticulostriate or ((basilar or brachial or vertebr*) NEAR/3 arter*)) NEAR/3 ((blood NEAR/5 clot*) or disease* or damage* or disorder* or disturbance or dissection or lesion or syndrome or arrest or accident or lesion or vasculopathy or insult or attack or injury or insufficiency or malformation or obstruct* or anomal*))
#1 TS=(stroke or poststroke or post-stroke or cerebrovasc* or (cerebr* NEAR3 vasc*) or CVA* or apoplectic or apoplex* or (transient NEAR3 isch?emic NEAR/3 attack) or tia* or SAH or AVM or ESUS or ICH or ("cerebral small vessel" NEAR/3 disease*))

Additional searches

Online clinical trials and research registers were also searched in February 2022.

- www.ClinicalTrials.gov (https://clinicaltrials.gov/)

(depression OR low mood) AND (Brain Infarction OR Intracranial Hemorrhages OR Carotid Artery Diseases OR Brain Ischemia OR Cerebral Hemorrhage OR Cerebrovascular Disorders OR Stroke)

- WHO International Clinical Trials Registry Platform (https://www.who.int/ictrp/search/en/)

(depression OR low mood) AND AREA [StudyType] EXPAND [Term] COVER [FullMatch] "Interventional" AND AREA [ConditionSearch] (Brain Infarction OR Intracranial Hemorrhages OR Carotid Artery Diseases OR Brain Ischemia OR Cerebral Hemorrhage OR Cerebrovascular Disorders OR Stroke) AND AREA [StudyFirstPostDate] EXPAND [Term] RANGE [08/09/2018, 06/01/2021].

Reference lists

Reference lists of relevant studies and systematic reviews were searched to identify studies not already included.

Personal communication

Authors of included studies were contacted for information on published and unpublished information.

Appendix 3. Search review - 2018

Electronic searches

Cochrane Stroke Trial Register - searched August 2018; Cochrane Anxiety and Neurosis Trial Register - searched August 2018.

The remaining databases were also searched on August 2018.

- Cochrane Central Register of Controlled Trials (CENTRAL)
- MEDLINE
- Embase
- CINAHL
- PsycINFO
- Science Citation Index - Expanded (SCI-EXPANDED), Social Sciences Citation Index (SSCI), and Arts & Humanities Citation Index (A&HCI) within Web of Science

The following search strategy with a combination of controlled vocabulary and free-text terms for MEDLINE and modified to suit the other databases.

1. cerebrovascular disorders/ or exp basal ganglia cerebrovascular disease/ or exp brain ischemia/ or exp carotid artery diseases/ or exp intracranial arterial diseases/ or exp "intracranial embolism and thrombosis"/ or exp intracranial hemorrhages/ or stroke/ or exp brain infarction/ or stroke, lacunar/ or vasospasm, intracranial/ or vertebral artery dissection/
2. (stroke or poststroke or post-stroke or cerebrovasc$ or brain vasc$ or cerebral vasc$ or cva$ or apoplex$ or SAH).tw.
3. ((brain$ or cerebr$ or cerebell$ or intracran$ or intracerebral) adj5 (isch?emi$ or infarct$ or thrombo$ or emboli$ or occlus$)).tw.
4. ((brain$ or cerebr$ or cerebell$ or intracerebral or intracranial or subarachnoid) adj5 (haemorrhage$ or hemorrhage$ or haematoma$ or hematoma$ or bleed$)).tw.
5. hemiplegia/ or exp paresis/
6. (hemipleg$ or hemipar$ or paresis or paretic).tw.
7. 1 or 2 or 3 or 4 or 5 or 6
8. depressive disorder/ or depressive disorder, major/ or depressive disorder, treatment-resistant/ or dysthymic disorder/ or Depression/ or exp Antidepressive Agents/
9. (depress$ or dysthymi$ or dysphor$ or antidepress$ or anti-depress$).tw.
10. 8 or 9
11. Randomized Controlled Trials as Topic/
12. random allocation/
13. Controlled Clinical Trials as Topic/
14. control groups/
15. clinical trials as topic/ or clinical trials, phase i as topic/ or clinical trials, phase ii as topic/ or clinical trials, phase iii as topic/ or clinical trials, phase iv as topic/
16. double-blind method/
17. single-blind method/
18. Placebos/
19. placebo effect/
20. cross-over studies/
21. Therapies, Investigational/
22. Drug Evaluation/
23. Research Design/
24. randomized controlled trial.pt.
25. controlled clinical trial.pt.
26. (clinical trial or clinical trial phase i or clinical trial phase ii or clinical trial phase iii or clinical trial phase iv).pt.
27. (random$ or RCT or RCTs).tw.
28. (controlled adj5 (trial$ or stud$)).tw.
29. (clinical$ adj5 trial$).tw.
30. ((control or treatment or experiment$ or intervention) adj5 (group$ or subject$ or patient$)).tw.
31. (quasi-random$ or quasi random$ or pseudo-random$ or pseudo random$).tw.
32. ((control or experiment$ or conservative) adj5 (treatment or therapy or procedure or manage$)).tw.
33. ((singl$ or doubl$ or tripl$ or trebl$) adj5 (blind$ or mask$)).tw.
34. (cross-over or cross over or crossover).tw.
35. (placebo$ or sham).tw.
36. trial.ti.
37. (assign$ or allocat$).tw.
38. or/11-37
39. 7 and 10 and 38
40. exp animals/ not humans.sh.
41. 39 not 40

Additional searches

The following conference abstracts and proceedings were searched.

1. European Stroke Conference (2011- 2018)
2. Stroke Society of Australasia Annual Scientific Meetings (2011- 2017)
3. World Stroke Congress (2000-2016)
4. Asia Pacific Stroke Conference (2011-2017)

Online clinical trials and research registers were also searched August 2018.

- www.ClinicalTrials.gov (https://clinicaltrials.gov/)

(depression OR low mood) AND (Brain Infarction OR Intracranial Hemorrhages OR Carotid Artery Diseases OR Brain Ischemia OR Cerebral Hemorrhage OR Cerebrovascular Disorders OR Stroke)

- WHO International Clinical Trials Registry Platform (https://www.who.int/ictrp/search/en/)

Condition: stroke AND depression OR low mood
Recruitment status is: ALL
Phases are: ALL
Hide synonyms
- 9-52 DEPRESSIVE DISORDERS, BEREAVEMENT, DEPRESSED, DEPRESSED - SYMPTOM, DEPRESSED MOOD, DEPRESSED MOOD (FINDING), DEPRESSED MOOD (PHYSICAL FINDING), DEPRESSED STATE, DEPRESSIVE DIS, DEPRESSIVE DISORDER, DEPRESSIVE DISORDER (DISORDER), DEPRESSIVE DISORDER [DISEASE/FINDING], DEPRESSIVE DISORDER NOS, DEPRESSIVE DISORDER, NOS, DEPRESSIVE DISORDERS, DEPRESSIVE DISORDERS NOS, DEPRESSIVE ILLNESS, DEPRESSIVE NEUROSES, DEPRESSIVE NEUROSIS, DEPRESSIVE STATE, DEPRESSIVE STATE NOS, DEPRESSIVE; DISORDER, DEPRESSIVE; NEUROSIS, DEPRESSIVE; STATE, DISORDER, DEPRESSIVE, DISORDER; DEPRESSIVE, DISORDERS, DEPRESSIVE, DYSTHYMIC DISORDER, FEELING BLUE, FEELING DOWN, FEELING;DOWN, LOW MOOD, MELANCHOLY, MISERABLE, MOOD DEPRESSED, MOOD DISORDER OF DEPRESSED TYPE, MOOD DISORDER OF DEPRESSED TYPE (DISORDER), MOROSE MOOD, NEUROSES, DEPRESSIVE, NEUROSIS, DEPRESSIVE, NEUROSIS; DEPRESSIVE, PUSH DOWN OR DEPRESS, STATE; DEPRESSIVE, depression - DEPRESSED, DEPRESSED MOOD, DEPRESSED MOOD (FINDING), DEPRESSED MOOD (PHYSICAL FINDING), FEELING BLUE, FEELING DOWN, FEELING;DOWN, MELANCHOLY, MOOD DEPRESSED, MOOD DEPRESSION, MOOD DEPRESSIONS, MOROSE MOOD, low mood - ACCIDENT CEREBROVASCULAR, ACCIDENT; CEREBRAL, ACCIDENT; CEREBROVASCULAR, APOPLEXY, APOPLEXY, CEREBROVASCULAR, APOPLEXY; CEREBRAL, BRAIN ATTACK, BRAIN VASCULAR ACCIDENT, BRAIN VASCULAR ACCIDENTS, CEREBRAL VASCULAR ACCIDENT, CEREBRAL VASCULAR EVENTS, CEREBRAL; ACCIDENT, CEREBRAL; APOPLEXY, CEREBROVASCULAR ACCIDENT, CEREBROVASCULAR ACCIDENT (DISORDER), CEREBROVASCULAR ACCIDENT NOS, CEREBROVASCULAR ACCIDENT, NOS, CEREBROVASCULAR ACCIDENTS, CEREBROVASCULAR APOPLEXY, CEREBROVASCULAR; ACCIDENT, CVA, CVA (CEREBRAL VASCULAR ACCIDENT), CVA (CEREBROVASCULAR ACCIDENT), CVA NOS, CVAS (CEREBROVASCULAR ACCIDENT), NEURO: CEREBROVASCULAR ACCIDENT, VASCULAR ACCIDENT, BRAIN, VASCULAR ACCIDENTS, BRAIN, stroke

Reference lists

Reference lists of relevant studies and systematic reviews were searched to identify studies not already included.

Personal communication

Professional bodies, authors of included studies, and pharmaceutical companies were contacted for information on published and unpublished information.

Appendix 4. Search review - 2008

Electronic searches

Cochrane Stroke Trial Register - searched October 2007; Cochrane Anxiety and Neurosis Trial Register - searched February 2008.

The remaining databases were searched May 2006.

- Cochrane Central Register of Controlled Trials (CENTRAL)
- MEDLINE
- Embase
- CINAHL
- PsycINFO
- Applied Science and Technology Plus
- Arts and Humanities Index
- Biological Abstracts
- BIOSIS Previews
- General Science Plus
- Science Citation Index
- Social Sciences Citation Index
- ISI Web of Science
- Dissertations and Theses

The following search strategy with a combination of controlled vocabulary and free-text terms for MEDLINE and CINAHL (Ovid), and modified to suit the other databases.

1 exp cerebrovascular disorders/
2 (stroke$ or poststroke$ or cva$).tw.
3 (cerebrovascular$ or cerebral vascular).tw.
4 (cerebral or cerebellar or brain$ or vertebrobasilar).tw.

5 (infarct$ or isch?emi$ or thrombo$ or emboli$ or apoplexy).tw.
6 (cerebral or intracerebral or intracranial or brain$).tw.
7 (haemorrhage or hemorrhage or bleed$).tw.
8 4 and 5
9 6 and 7
10 1 or 2 or 3 or 8 or 9
11 Depression/
12 Depression, involutional/ or Depressive disorder/ or Dysthymic disorder/
13 (depress$ or dysthymi$).tw.
14 11 or 12 or 13
15 10 and 14
16 randomized controlled trial.pt.
17 randomized controlled trials/
18 controlled clinical trial.pt.
19 controlled clinical trials/
20 random allocation/
21 double-blind method/
22 single-blind method/
23 clinical trial.pt.
24 exp clinical trials/
25 (clin$ adj25 trial$).tw.
26 ((singl$ or doubl$ or tripl$ or trebl$) adj25 (blind$ or mask$)).tw.
27 placebos/
28 placebo$.tw.
29 random$.tw.
30 research design/
31 clinical trial phase ii.pt.
32 clinical trial phase iii.pt.
33 clinical trial phase iv.pt.
34 meta analysis.pt.
35 multicenter study.pt.
36 intervention studies/
37 cross-over studies/
38 meta-analysis/
39 control$.tw.
40 alternate treatment.tw.
41 "comparative study"/
42 exp evaluation studies/
43 Follow-up studies/
44 Prospective studies/
45 prospective.tw.
46 (versus or sham or intervention group or comparative stud$).tw.
47 or/16-46
48 15 and 47
49 limit 48 to human

Additional searches

The following conference abstracts and proceedings were searched.

- European Stroke Conferences (2000 to 2007)
- Stroke Society of Australasia Annual Scientific Meetings (1999 to 2007)

Online clinical trials and research registries were also searched August 2007.

- www.strokecenter.org/trials
- www.ClinicalTrials.gov
- www.Clinicalstudyresults.org
- www.anzctr.org.au

Reference lists

Reference lists of relevant studies were searched to identify studies not already included.

Personal communication

Professional bodies, authors of included studies, and pharmaceutical companies were contacted for information on published and unpublished information.

Appendix 5. Study flow diagram for living review update (to August 2021)

Figure 7

Figure 7. Study flow diagram for living review update (to August 2021). Details of searches for previous versions of this review are available in those reviews

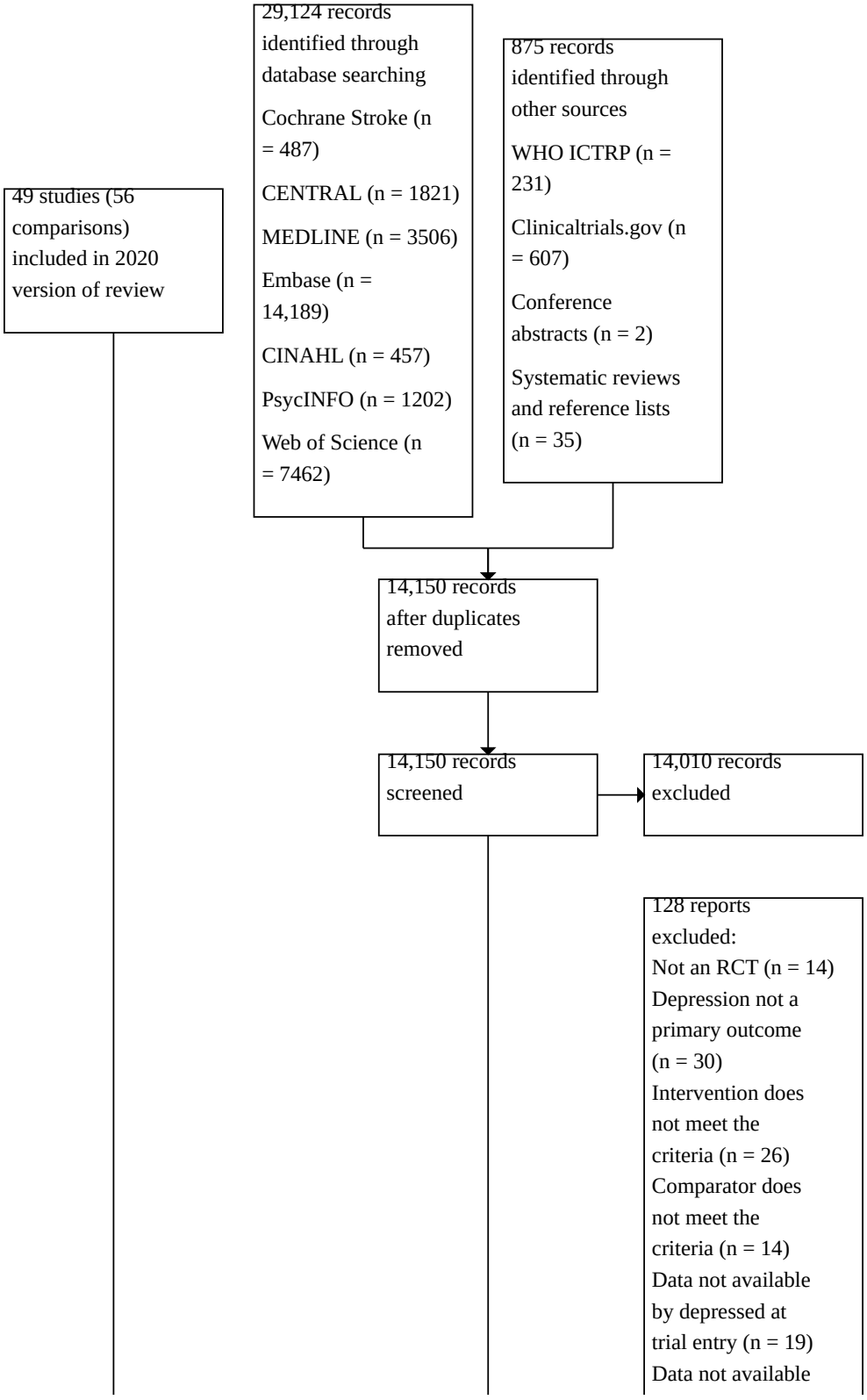


Figure 7. (Continued)

WHAT'S NEW

Date	Event	Description
5 July 2023	New search has been performed	Searches run; we identified 16 new trials (16 new comparisons) and 2489 new participants. The review now has a total of 72 included trials involving 5831 participants.
5 July 2023	New citation required but conclusions have not changed	New authors added; word order of title changed

HISTORY

Protocol first published: Issue 1, 2002
Review first published: Issue 3, 2004

Date	Event	Description
13 August 2018	New citation required and conclusions have changed	New data are included. New authors are included
13 August 2018	New search has been performed	New interventions are included: combination psychological and pharmacological interventions vs a single intervention, and non-invasive brain stimulation interventions Thirty-three new trials (39 comparisons) with 2753 participants are included in the review. A total of 49 trials (56 comparisons) with 3342 participants are included in the review. Data were available for 20 pharmacological comparisons, 8 non-invasive brain stimulation comparisons, 16 psychological therapy comparisons, and 12 combination therapy trials Covidence was used to collate and screen identified titles and abstracts MH extracted additional data from previously included trials Searches for the review were completed to 13 August 2018
28 March 2008	Amended	Review was converted to new review format
14 March 2008	New search has been performed	Searches for the review were completed to February 2008 Seven new trials have been added: 6 pharmacological interventions, making a total of 13, and 2 psychological interventions, making a total of 4 comparisons. A total of 16 trials with 1655 participants are now included Eight trials require more information before they can be assessed for inclusion in the review (down from 14 in the previous version). Nine trials appear to meet the review inclusion criteria, but information is not available in a format suitable for pooling. Three studies are ongoing (up from 0 in the previous version)
14 March 2008	New citation required and conclusions have changed	This version of the review found a small but significant effect of pharmacotherapy (not psychotherapy) on treating depression and reducing depressive symptoms in stroke patients There has been a change in authorship

CONTRIBUTIONS OF AUTHORS

SA: contributed to writing the review, completed title screening and inclusion/exclusion review, extracted data, performed meta-analyses and GRADE assessment.
KC: completed title screening and inclusion/exclusion review and data extraction.
CFH: assisted with obtaining, translating, and extracting data from Chinese studies for the current updated review.
HL: completed title screening and cross-checked data extraction.
AH: conceived the idea for the review; contributed to development, writing, and editing of the protocol; and undertook the work necessary to complete the 2004 and 2008 reviews.
MH: contributed to development, writing, and editing of the protocol; undertook the work necessary to complete the 2004 and 2008 reviews; and oversaw each version of the review updates.

All review authors read and edited this update.

DECLARATIONS OF INTEREST

SA: none known.
KC: none known.
C-FH: none known.
HL: none known.
AH: none known.
MH: none known.

SOURCES OF SUPPORT

Internal sources

- The George Institute for International Health, Australia

  Salary support

External sources

- Stroke Society of Australasia, Australia

  Overseas Study Scholarship during first version of this review
- The Academic Unit of Psychiatry, The University of Leeds, UK

  In kind support for sabbatical during first version of this review
- The Department of Clinical Neurosciences, The University of Edinburgh, UK

  In kind support for sabbatical during first version of this review
- The Clinical Trials Research Unit, The University of Auckland, New Zealand

  Salary support during first version of this review

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The title of the review changed when it was updated to a living review. Previously the review title was 'Pharmacological, psychological, and non-invasive brain stimulation interventions for treating depression after stroke'. The new title 'Pharmacological, non-invasive brain stimulation and psychological interventions, and their combination, for treating depression after stroke' better reflects the interventions included in the review and presents the interventions in the same order they are covered in the review.

In the previous update, the review was expanded to include other non-invasive brain stimulation interventions such as 1) transcranial magnetic stimulation or repetitive transcranial magnetic stimulation (TMS or rTMS, where a magnetic 'coil' is placed near the head of the person receiving treatment without making physical contact); 2) transcranial direct current stimulation (tDCS, where a constant, low current is delivered directly to the brain area of interest via small electrodes); 3) cranial electrotherapy stimulation (CES, where a small, pulsed electrical current is applied across a patient's head); and 4) magnetic seizure therapy (MST), a type of convulsive therapy that involves replacing the electrical stimulation used in ECT with a rapidly alternating strong magnetic stimulation; and 5) combinations of all included interventions compared with a single intervention plus a respective control.

This update includes some new methods relevant to living systematic reviews, which are described in the Methods and Appendix 1 (Living systematic review protocol).

Health-related quality of life was rarely reported across the included studies, so we have removed this as a secondary outcome.

We identified a duplication of text related to subgroup analyses. We have removed the sentence "We planned to undertake subgroup analyses for all outcomes when feasible to explore the influence of date of publication, sample size, duration of follow-up, treatment type, high (over 20%) number of dropouts, and blinded versus unblinded outcome assessors" and kept the sentence stating we will conduct subgroup analyses to examine the impact of treatment type and duration, and of stroke severity.

INDEX TERMS

Medical Subject Headings (MeSH)

Antidepressive Agents [*therapeutic use]; Depressive Disorder [etiology] [*therapy]; Electric Stimulation Therapy [*methods]; Psychotherapy [*methods]; Quality of Life; Randomized Controlled Trials as Topic; Stroke [*psychology]

MeSH check words

Humans