Questions 47, 48, 49 evidence tables

Question 47: What is the best treatment for post-stroke depression?
Question 48: What is the best method to prevent post-stroke depression?
Question 49: Do interventions aimed at treating anxiety after stroke improve outcome?

NB Any discrepancies between reviewers in evidence quality and comment were discussed at the corresponding evidence review meeting

SSRI = selective serotonin reuptake inhibitor, GI = gastrointestinal, QoL = quality of life, ABI = acquired brain injury, HF-rTMS = high frequency radio transcranial magnetic stimulation, TBI = traumatic brain injury, MADRS = Montgomery–Åsberg Depression Rating Scale, MMSE = Mini-mental state examination, MoCA = Montreal cognitive assessment, HADS-A = Hospital Anxiety and Depression Scale for anxiety, HADS-D =, Hospital Anxiety and Depression Scale for depression, SAS = Zung self-rating anxiety scale, and SDS = Zung self-rating depression scale, PHQ-9 = Patient Health Quetionnaire-9, GAD-7 = Generalised Anxiety Disorder-7, HRQoL = Health related quality of life, (ED-5D-5L), WEMWBS = Warwick and Edinburgh Mental Well-being Scale, TMT = Trail Making Test, DST = Digit Span Test, MAACL-R = Multiple Affect Adjective Checklist-Revised, GSE = General Self Efficacy Scale, G-ACT = Group Acceptance and Commitment Therapy, SR = systematic review, MA = meta-analysis, RCT = randomised controlled trial, IPDMA = individual patient data meta-analysis, MDT = multidisciplinary team, PICO = patient/population, intervention, comparison and outcomes, OR = odds ratio, CI = confidence interval, QoL = quality of life, ADL = activities of daily living, OR = odds ratio, RR = relative risk, aOR = adjusted odds ratio, cOR = crude odds ratio, CI = confidence interval, RoB = risk of bias, I2 = heterogeneity statistic.

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
706	L. A. Legg et al. (2021). Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery. Cochrane Database of Systematic Reviews 2021:11 CD009286	SR with MA Any stroke survivor with or without depression 63 RCTs, 9168 participants	Any SSRI, any dose (32 trials used fluoxetine)	Primary outcome was function (not relevant to guideline question) Secondary outcomes included depression and anxiety. Adverse events.	SSRI reduced depression SMD -0.11 (95%CI:-0.19 to -004) 2 RCTs, 2861 participants Increased GI adverse events RR 2.1 (95%CI: 1.00 to 4.76) 2 RCTs, 148 participants	+ Does not include AFFINITY Does not include EFFECTS Marked heterogeneity Most papers not considered in synthesis as low quality Acceptable quality SR +
706	L. A. Legg et al. (2021). Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery. Cochrane	Systematic review 63 eligible trials recruiting 9168 participants	SSRI (any type, any dose, for any duration and for any clinical indication)	Primary outcomes: disability score or independence	No reliable evidence that SSRIs should be used routinely to promote recovery after stroke (confirmed by meta-analysis	++ High quality

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
	Database of Systematic Reviews 2021:11 CD009286		Comparator: usual care or placebo	Secondary outcomes: impairment, depression, anxiety, quality of life, fatigue, healthcare cost, death, adverse events, leaving the trial early	of three trials with low risk of bias). Potential improvements in disability but not dependence (identified from trials at high risk of bias). SSRIs reduced the average depression score (SMD 0.11 lower, 0.19 lower to 0.04 lower; 2 trials, 2861 participants; moderate-quality evidence), but there was a higher observed number of gastrointestinal side effects among participants treated with SSRIs compared to placebo (RR 2.19, 95% CI 1.00 to 4.76; P = 0.05; 2 studies, 148 participants; moderate-quality evidence), with no evidence of heterogeneity (I2 = 0%). For seizures there was no evidence of a substantial Difference	High quality as only included the studies at low risk of bias. Acknowledges review will need updated when ongoing studies are completed. Presume this has not yet been undertaken.
707	M. F. Love et al. (2019). Mind-Body Interventions, Psychological Stressors, and Quality of Life in Stroke Survivors: A Systematic Review. Stroke 50:2 434-440	Systematic review 4 RCTs with depression related outcomes 2 RCTs with anxiety related outcomes	'Mind body interventions' – yoga and Tai Chi	Varied across studies	No evidence of statistical differences in those RCTs with depression or anxiety outcomes. However, individual trials all under powered.	- Low quality SR (issues with heterogeneity not adequately addressed) that includes low quality trial evidence

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
707	M. F. Love et al. (2019). Mind-Body Interventions, Psychological Stressors, and Quality of Life in Stroke Survivors: A Systematic Review. Stroke 50:2 434-440	SYSTEMATIC REVIEW Aim: To synthesize evidence of the effects of mind-body interventions on psychological stressors, quality of life, and biological outcomes for stroke survivors. Definition: Mind-body practices, a varied group of techniques derived from ancient traditions which include meditation, yoga, and tai chi.	Mind-body interventions included yoga or tai chi.	Included studies used a range of outcome measures relating to - Quality of Life Stroke impact scale Physical function (incl. balance/ motor function) Thematic analysis of qualitative data	Psychological stressors, including post stroke depression, anxiety and QoL improved over time, but statistically significant between-group differences were largely absent. The 3 included studies with a qualitative design reported themes reflecting improvement in psychological stressors and quality of life.	+ Acceptable
745	C. Cheng et al. (2021). Reminiscence therapy-based care program relieves post-stroke cognitive impairment, anxiety, and depression in acute ischemic stroke patients: a randomized, controlled study. Irish Journal of Medical Science 190:1 345-355	RTC 130 patients with acute ischemic stroke Setting: community /outpatient treatment; N=65 each group; 50-85 years; Exclusion: MMSE <10, severe cognitive impairment, aphasia, visual imp., mental health problems, premorbid depression/anxiety; tumours and haemorraghes;	DC meeting in hospital: stroke information given by nurse (60mins session); Control group: Post-DC outpatient intervention; Cognitive remediation model; Over 12 months; Led by nurses who had done a 4 week crash course in cognitive training; Group intervention of 7-10 participants; 45 mins sessions;2xmonth; Reminiscence group: Cognitive training plus Reminiscence;	Reminiscence group participants performed better on cognitive and psychological measures than the cog. Rehab. only group from month 9 onwards; Cognitive training plus reminiscence intervention are effective for improvement of cognitive scores and reduction of anxiety.	Reminiscence group results compared with control group: Sign. Improvement on MMSE & MoCA score at month 9; Number of cognitively impaired patients sign decreased at month 12; Anxiety scores on HADS sign. Decreased at months 12. Depression scores did not differ sign. Between groups at month 12. Patients' satisfaction with intervention was sign higher at month 12	High evidence quality. Comment: Excellent intervention, but very staff intensive. Long-term intensive intervention required until improvements were seen; The results indicated usefulness of patients' improvements on the measures. No info about transfer effects on their community independence re cognition, competence or quality of life.

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
			2xmonth; For 12 months; Same group format as Cognitive Rehab group. 105 mins session due to additional Reminiscence elements			
745	C. Cheng et al. (2021). Reminiscence therapy-based care program relieves post-stroke cognitive impairment, anxiety, and depression in acute ischemic stroke patients: a randomized, controlled study. Irish Journal of Medical Science 190:1 345-355	RCT; 1:1 block randomised; n= 130, aged within 50-85 years	Control Group: Post-Discharge, Multifaceted Group Cognitive Rehabilitation, x2 sessions per month for 12 months, 45 minutes per session. Intervention Group: Post-Discharge, Multifaceted Group Cognitive Rehabilitation & Reminiscence Therapy, x2 sessions per month for 12 months, 105 minutes per session (60 min per reminiscence session, with the remaining 45 min dedicated to cognitive rehabilitation	Baseline; Mini-mental state examination (MMSE), Montreal cognitive assessment (MoCA), Hospital Anxiety and Depression Scale for anxiety (HADS-A), Hospital Anxiety and Depression Scale for depression (HADS-D), Zung self-rating anxiety scale (SAS), and Zung self-rating depression scale (SDS). 3 Months, 6 Months, 9 Months, 12 Months; MMSE, MoCA, HADS-A, HADS-D, SAS, SDS, scored from 0 to 10 points (where 0 indicates the least satisfaction, and 10 indicates greatest satisfaction).	All participants 130 included in an Intention To Treat Principle. Cognitive Impairment; MMSE score was increased in the RTBC group com-pared with the control group at M9 (P = 0.014) and M12 (P = 0.034), MoCA score was increased in the RTBC group compared with the control group at M9 (P = 0.012) and M12 (P = 0.006) Anxiety; HADS-A score at M12 (P = 0.027) was lower in the RTBC group compared with the control group, the SAS score was lower in the RTBC group compared with the control group at M9 (P = 0.048) and M12 (P = 0.002)	**+/-** Participants not blinded, Assessors Not blinded, Analyst blinded,

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
					Depression; HADS-D score was numerically lower in the RTBC group compared with the control group at M9 (P = 0.077) and M12 (P = 0.063) but statistically non-significant, the SDS score was decreased in the RTBC group compared with the control group at M9 (P = 0.033) and M12 (P = 0.039). Satisfaction; The satisfaction score was higher in the RTBC group compared with the control group at M3 (P = 0.005), M6 (P = 0.015), and M12 (P = 0.036)	
746	M. H. Chun et al. (2017). The effects of forest therapy on depression and anxiety in patients with chronic stroke. International Journal of Neuroscience 127:3 199-203	RCT, South Korea, n=59, >1 year post-stroke. The majority of study participants had depression and/or anxiety at baseline (60-80%) and elevated levels of oxidative stress and reduced anti-oxidative capacity (30-50%).	Four-day (three night) program at a recreational forest area or urban group staying in a hotel NB both groups participated in meditation and walking activities	Psychological (Beck Depression Inventory, 17-item Hamilton Depression Inventory, Spielberger State-Trait Anxiety Inventory); Oxidative stress (reactive oxygen metabolite); Anti-oxidative capacity (biological antioxidant potentials), measured immediately before and after the treatment programs	Reduction in depression and anxiety and improvements in biological antioxidant potentials greater in the forest group compared to the urban group	**+** Drop-out rate unclear; issues with blinding common to most attempts to evaluate a psychosocial intervention such as this; no long-term follow-up
746	M. H. Chun et al. (2017). The effects of forest therapy on	? RCT, ?1:1, unclear method Chronic Stroke; n=59	Control; Hotel stay in an urban location; group medication and	Baseline; Beck Depression Inventory (BDI), Hamilton	Within Group; Before and After Intervention; Forest Group, the BDI, HAM-D17 and	**+/-** Participants not blinded,

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
	depression and anxiety in patients with chronic stroke. International Journal of Neuroscience 127:3 199-203		walking in an urban environment. Intervention; Recreational Forest Site, 4 days & 3 nights group program, Multifaceted group programme of meditation, experiencing the forest through the 5 senses and walking in the forest.	Depression Rating Scale (HAM-D17), Spielberger State-Trait Anxiety Inventory (STAI); Oxidative stress assessment with d-ROM values >300 U CARR indicating oxidative stress; Antioxidant capacity with <2000 µmol/L indicating reduced antioxidant capacity. Post-Intervention; Repeated baseline measures.	STAI scores after program participation were significantly lower than baseline scores (paired t-test, $p < 0.05$); Urban group, STAI scores significantly increased after program participation (paired t-test, $p < 0.05$, Table 2), but no significant changes were observed for BDI, HAM-D17 (paired t-test, $p > 0.05$) Between Group; Before and After Intervention; reductions in BDI, HAM-D17 and STAI scores were significantly greater in the forest group compared to the urban group (ANCOVA, $p < 0.05$)	Assessors Not blinded, Analyst not blinded, Allocation unclear
708	S. Majumdar et al. (2019). Brief group-based acceptance and commitment therapy for stroke survivors. The British journal of clinical psychology 58:1 70-90	RCT Stroke survivor selected by clinical teams (not selected on basis of depression or anxiety) Several years post stroke No measures of stroke severity Three centres in NHS N=53	ACTivate Your Life after Stroke', consisted of 2-hr weekly didactic PowerPoint group sessions, for four consecutive weeks	Depression (PHQ9) Primary Anxiety (GAD7) immediately post treatment	Fewer scoring above a threshold on PHQ in the intervention group	- Low quality trial evidence Did not use PROBE design No correction for baseline imbalance Limited detail on concomitant therapy No active control No economic analysis
708	S. Majumdar et al. (2019). Brief group-based acceptance and commitment therapy for stroke survivors. The British journal of	Design: Parallel group RCT Not blinded (as noted by the authors) Setting: Three NHS sites in South Wales, participants recruited through clinicians.	Acceptance and Commitment Therapy (ACT): 'ACTivate Your Life After Stroke'. 2-hr, group, weekly didactic Powerpoint sessions for 4 consecutive	Primary outcome: Depression measured using Patient Health Quetionnaire-9 (PHQ-9) Secondary outcomes: Anxiety measures using	Mixed repeated measures ANOVA, intention to treat analysis Significant time x group interaction for depression in favour of ACT over TAU at pre-	+ Evidence quality: Acceptable (+): randomised but baseline differences between groups, not blind, allocation concealment unclear.

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
	clinical psychology 58:1 70-90	Participants: Inclusion criteria: diagnosed stroke, discharged from hospital, over 18 years old, did not have severe communication difficulties or cognitive impairments Excluded if had: another acquired brain injury, diagnosed degenerative condition, severe mental illness Intervention group (ACT) n=26, mean age 65.3, 21 male (80.8%) Control group (TAU) n=27, mean age 60.0, 11 male (40.7%)	weeks. Carers were invited to the course but were not part of the study analysis. Courses run in community by at least two facilitators who were clinical psychologists, assistant psychologists or stroke care co-ordinators who had received intensive 2 day training course. At least one clinical psychologist present at each site. Treatment as usual control group (TAU): Following usual treatments available.	Generalised Anxiety Disorder-7 (GAD-7) Health related quality of life, HRQoL (ED-5D-5L) Hope (Adult Hope Scale) Mental well-being (Warwick and Edinburgh Mental Well-being Scale; WEMWBS)	treatment to post-treatment (medium effect size) and pre-treatment to 2 month follow up (medium effect size). 53.8% (n=14) of participants in ACT group exhibited clinically significant change on PHQ-9 from pre-treatment compared with 7.5% (n=2) in TAU group. Significant finding of ACT over TAU for self-reported health status and hopefulness. No significant effects for HRQoL, anxiety or mental well-being	No control of concomitant treatments. Small sample size but promising results.
709	S. Allida et al (2020). Pharmacological, psychological, and non-invasive brain stimulation interventions for treating depression after stroke. Cochrane Database of Systematic Reviews. 2020, Issue 5. Art. No.: CD003689.	Design – Systematic Review Participants - 49 trials (56 comparisons) with 3342 participants.	(1) pharmacological interventions with placebo - 20 comparisons); (2) various forms of non-invasive brain stimulation with sham stimulation or usual care (8 comparisons); (3) psychologicaltherapy with usual care and/or attention control (16 comparisons); (4)	Reduction in the prevalence of diagnosable depression or reduce levels of depressive symptoms, improve physical and neurological function and health-related quality of life, and reduce dependency a(er stroke	Pharmacological or psychological therapies can reduce the prevalence of depression. Pharmacological intervention was associated with adverse events related to the CNS and the gastrointestinal tract No trials of non-invasive brain stimulation reported on meeting study criteria for depression at end of treatment. Only one trial of non-invasive brain stimulation reported on the outcome	**++** High quality

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
			pharmacological intervention and psychological therapy (2 comparisons); and (5) non-invasive brain stimulation and pharmacological intervention (10 comparisons).		<50% reduction in depression scale scores Estimates of treatment effects were imprecise due to small numbers in most studies and recruitment of people with very different baseline characteristics. Certainty of evidence as very low.	
709	S. Allida et al (2020). Pharmacological, psychological, and non-invasive brain stimulation interventions for treating depression after stroke. Cochrane Database of Systematic Reviews. 2020, Issue 5. Art. No.: CD003689.	Meta-analysis, update to existing Cochrane review, n=3342 in people with depression after stroke, with the range covering 'within a few days' to 36 months post-stroke, from 49 RCTs (56 comparisons). Studies were from Asia (30), Europe (11), North America (6), and Australia (2). Assurances given that review includes all potentially relevant trials.	RCT studies evaluating (1) pharmacological interventions, (2) non-invasive brain stimulation, (3) psychological therapy, (4) or combinations of these interventions published up to August 2018. The study authors report on five principal comparisons (studies were lacking for certain combinations of the above named interventions).	Fewer people meeting the study criteria for depression at the end of treatment (data from 14 trials); less than 50% reduction in depression scale scores at the end of treatment (data from six trials).	Very low-certainty evidence suggesting that pharmacological or psychological therapies can reduce the prevalence of depression. Very low-certainty evidence suggests that pharmacological therapy, psychological therapy, non-invasive brain stimulation, and combined interventions can reduce depressive symptoms.	**++** Review rigorously adhered to Cochrane methods for performing systematic reviews. The study authors conclude that more evidence is required before recommendations can be made about the routine use of such treatments. Estimates of treatment effects imprecise due to small sample sizes of included trials, wide confidence intervals, and participants with very different baseline characteristics. Also, consistent methods to diagnose depression were lacking (rendering it difficult to pool outcome data for many participants).
711	C. Baker et al. (2018). A systematic review of rehabilitation	Design: Systematic review	Classified treatments as: communicative functioning	Mood/depression outcomes (primary or	People with aphasia with mild depression may benefit from psychosocial-type	**+** Acceptable quality

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
	interventions to prevent and treat depression in post-stroke aphasia. Disability and rehabilitation 40:16 1870-1892	Setting: Hospital, clinic, community, home Participants: Studies ranged from n=1-n=1042 with post-stroke aphasia. 45 studies included (22 were RCTs). Included experimental (randomised and non randomised controlled group trials and single participant designs) and non-experimental or exploratory designs (pre-post case series, mixed methods of quantitative and qualitative analysis)	treatments, psychosocial functioning, cognitive functioning, physical functioning, multidisciplinary rehabilitation and transition. Studies with pharmacological or medical interventions (e.g. antidepressant medication, electroconvulsive therapy, transcranial magnetic stimulation, neurofeedback) were excluded	secondary) using a validated tool(s)	treatments (based on 3 level ii studies with small to medium effect sizes). For those without depression, mood may be enhanced through participation in a range of interventions (based on 4 level ii studies; 1 level iii-3 study and 6 level iv studies). It is not clear which interventions may prevent depression in post-stroke aphasia. No evidence was found for the treatment of moderate to severe depression in post-stroke aphasia. Methodological limitations identified – lack of inclusion and description of people with aphasia, insufficient detail about intervention, uncertainty around cut-off in depression outcome measures, unclear detail on the timing of interventions.	Screening by one author, unclear decisions discussed with co-authors Unclear how many extracted data
711	C. Baker et al. (2018). A systematic review of rehabilitation interventions to prevent and treat depression in post-stroke aphasia. Disability and rehabilitation 40:16 1870-1892	Design – Systematic Review Setting – clinic, hospital, home, community Participants – sample size in studies ranged from 1-1042	goal setting and achievement, psychosocial support, communication partner training and narrative therapy Studies with pharmacological or medical interventions	mood/depression outcomes (primary or secondary) using a validated tools	People with aphasia with mild depression may benefit from psychosocial-type treatments (based on 3 level ii studies with small to medium effect sizes). For those without depression, mood may be enhanced through participation in a range of	- Low quality Unclear who selected the studies or who extracted the data

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
		Included both experimental (randomized and non-randomized controlled group trials and single participant designs) and non-experimental or exploratory designs (pre–post case series, mixed methods of quantitative and qualitative data	(e.g. antidepressant medication, electroconvulsive therapy, transcranial magnetic stimulation, neurofeedback) were excluded		interventions (based on 4 level ii studies; 1 level iii-3 study and 6 level iv studies). It is not clear which interventions may prevent depression in post-stroke aphasia. No evidence was found for the treatment of moderate to severe depression in post-stroke aphasia.	Independently rated for quality methodological markers by two reviewers
716	K. D. B. Vallury et al. (2015). Do family-oriented interventions reduce poststroke depression? A systematic review and recommendations for practice. Topics in Stroke Rehabilitation 22:6 453-459	Meta-analysis; 8 databases researched; 25 articles analysed; Inclusion: Stroke, Carer intervention used, Controlled or uncontrolled design;	Majority of studies reported intervention as preventative; depression symptoms were not required; Depression changes measures in relation to intervention; 12 week programmes, 1 study reported on a 12 month programme; Treatment commenced in hospital or shortly after DC; Collaborative interactions between stroke patient and carer/family as key ingredient;	5 out of 25 studies demonstrated sign. Reduction of post-stroke depression; Methodical flaw? If patients did not have to present with depression to be included in interventions, then this would reduce the likelihood of sign improvements of depression symptoms; The 5 effective studies: 'positive trend' to reduce depression in stroke patients; 'potential' of such interventions; Effectiveness	Effective interventions consisted of: - Early interventions, asap after stroke, - Regular sessions Longer programme (at least 12 weeks)	- Evidence quality: low meta-analysis; The selected studies used inconsistent baseline measures for depression. This analysis reports varied outcomes between the studies.

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
716	K. D. B. Vallury et al. (2015). Do family-oriented interventions reduce poststroke depression? A systematic review and recommendations for practice. Topics in Stroke Rehabilitation 22:6 453-459	SR Aim: To systematically review the evidence regarding the effectiveness of family-oriented interventions to prevent and manage depression after stroke and identify components of effective interventions.	Family-oriented interventions	Changes in depression	Five studies demonstrated significant reductions in depression. Four reported improved PSD outcomes in stroke survivors only; one had positive impacts on depression for both stroke survivors and their family caregivers Commonalities across effective studies included the delivery of interventions that were structured and multicomponent (including goal setting/ problem solving, skills building), actively engaged patients and families, coordinated care, and were initiated soon after a stroke.	+ Acceptable
710	O. P. Almeida et al. (2021). Depression Outcomes among Patients Treated with Fluoxetine for Stroke Recovery: The AFFINITY Randomized Clinical Trial. JAMA Neurology 78:9 1072-1079	Secondary outcomes from RCT Southern hemisphere Stroke survivors N=1221	20mg fluoxetine daily with 15 days of stroke	Incident depression defined as PHQ-9 dichotomised, clinical diagnosis depression, at 4,12,26 weeks Adverse events described in primary trial paper	No difference in incident depression 215 v 20% No difference in use of depression treatments Possible difference in clinical diagnosis of depression favouring SSRI 7% v 4%	+ Secondary analysis of large well conducted RCT Acceptable quality
710	O. P. Almeida et al. (2021). Depression Outcomes among Patients Treated with	secondary analysis - To investigate whether daily treatment with 20 mg of fluoxetine hydrochloride	Fluoxetine hydrochloride, 20 mg, or matched placebo daily for 26 weeks	PHQ-9 (9 item) score of 9 or lower was a prespecified secondary outcome of the trial.	Routine daily treatment with 20 mg of fluoxetine did not decrease the proportion of people affected by clinically	++ High quality

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
	Fluoxetine for Stroke Recovery: The AFFINITY Randomized Clinical Trial. JAMA Neurology 78:9 1072-1079	reduces the proportion of people affected by clinically significant symptoms of depression after stroke Design RCT (1:1 assignment), double-blind, placebo-controlled trial, 1221 participants in Australia, New Zealand, and Vietnam followed up for 6 months. Inclusion Adults aged 18 years or older 2 to 15 days after stroke, with modified Rankin Scale score of 1 or higher Excluded people with a history of epilepsy, bipolar disorder, hepatic or renal impairment, or hyponatremia or who had used antipsychotic medications or selective serotonin reuptake inhibitors within the last month those with a life-threatening illness who were pregnant or of childbearing potential and not taking adequate contraception or who were enrolled in another trial		Other outcomes included participant-reported clinician diagnosis of depression, prescription of a non-trial antidepressant, or nonpharmacologic treatment of depression.	significant symptoms of depression after a stroke, nor did it affect the proportion of people prescribed an antidepressant or receiving nonpharmacologic treatments compared with placebo	double-blind, placebo-controlled clinical trial of fluoxetine Excluded from the analyses participants for whom no baseline PHQ-9 data were available Web-based randomization service. A minimization algorithm was used to reduce group imbalance Groups were balanced for all baseline measures
713	C. M. Haire et al (2021). Effects of therapeutic instrumental music	Toronto, community stroke care 3 arm randomised controlled trial	Group 1 participants received 45 minutes of active TIMP training; Group 2 participants	Mental flexibility (measured using the Trail Making Test (TMT) Part B)	No significant changes were obtained for any of the groups	- Low quality

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
	performance and motor imagery on chronic post-stroke cognition and affect: A randomized controlled trial. NeuroRehabilitation. 48: 2. 195-208.	Thirty community-dwelling volunteers (14 females, mean age 55.9); 10 in each intervention arm.	received 30 minutes of TIMP followed by 15 minutes of cued motor imagery (TIMP+cMI), which involved listening to a metronome beat set to the participant's preferred tempo for each exercise while engaging in motor imagery; Group 3 participants received 30 minutes of TIMP followed by 15 minutes of motor imagery without external cues (TIMP+MI).	Short term memory capacity (measured using the Digit Span Test (DST)) Current affective state (measured using the Multiple Affect Adjective Checklist – Revised (MAACL-R) (includes anxiety, depression, hostility, dysphoria, positive affect) Self-efficacy (measured using the General Self-Efficacy Scale (GSE)) Valence, arousal & dominance (measured using the Self-Assessment Manikin (SAM))	on subscales for depression and hostility. Improvements in positive affect, reduced negative affect and anxiety.	Small sample size, single site study therefore of low quality. Blinded, randomised allocation to groups but no usual care/control group to assess differences between groups with no intervention at all. Intervention arms not particularly well described
713	C. M. Haire et al (2021). Effects of therapeutic instrumental music performance and motor imagery on chronic post-stroke cognition and affect: A randomized controlled trial. NeuroRehabilitation. 48: 2. 195-208.	RANDOMISED CONTROLLED Trial Aim: To investigate the effects of Therapeutic Instrumental Music Performance (TIMP) training with and without Motor Imagery on cognitive functioning and affective responding in chronic post-stroke individuals Hypothesis: The current study investigates the hypothesis that TIMP	3 experimental arms: 1. TIMP (n=10) 2. TIMP + cued Motor Imagery (TIMP+cMI) (n=10) 3. TIMT + motor Imagery without cue (TIMP + MI) (n=10) Training took place three times a week for three weeks, and was conducted by qualified Neurologic Music Therapists.	Trail Making Test (TMT) - Part B to assess mental flexibility Digit Span Test (DST) to determine short-term memory capacity, Multiple Affect Adjective Checklist - Revised (MAACL-R) to ascertain current affective state	The TIMP+MI group showed a statistically significant decrease in time from pre-test 2 to post-test on the TMT. The TIMP group showed a significant increase on MAACL sensation seeking scores TIMP+cMI showed respective increases and decreases in positive and negative affect on the MAACL, and increases on	- Low quality Small study - 30 participants in all/ 10 in each group No power calculation

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
		interventions, with and without motor imagery, may improve cognitive and affective outcomes relative to baseline performances in individuals at the chronic post-stroke stage. Definition: Therapeutic Instrumental Music Performance (TIMP) is a neurologic music therapy (NMT) technique which uses carefully selected and positioned acoustic and electronic instruments in upper extremity rehabilitation		General Self-Efficacy Scale (GSE) to assess perceived self-efficacy The Self-Assessment Maniqin (SAM)	the Valence, Dominance, and Arousal portions of the SAM No statistically significant association between cognitive and affective measures was obtained.	
714	J. A. Kootker et al. (2017). Augmented Cognitive Behavioral Therapy for Poststroke Depressive Symptoms: A Randomized Controlled Trial. Archives of Physical Medicine and Rehabilitation 98:4 687-694	Design: Mutlicentre, assessor-blinded randomised controlled trial Setting: Ambulatory rehabilitation setting. Netherlands. Participants: n=61 Patients with Hospital Anxiety and Depression Scale- depression subscale HADS-D) score >8 at least 3 months post-stroke	CBT: 13-16 sessions, approx. one our each over 4 months. Administered by certified health psychologist. Augmented with goal-directed, real life activity training. Or an equal period of Computerised cognitive training (CCT), largely self-administered but assistance present if needed	Primary: Hospital Anxiety and Depression Scale-depression subscale (HADS-D) Secondary: anxiety (HADS Anxiety), qualitative aspects of mood (Post Stroke Depression Rating Scale), quality of life (Stroke Specific Quality of Life Scale), social participation (Utrecht Scale for Evaluation of Rehabilitation-Participation), subjective wellbeing (Life Satisfaction Questionnaire).	No group differences between CBT and CCT for any of the primary or secondary outcomes. Both interventions improved scores on depression, anxiety, quality of life, satisfaction with life and participation. Unclear whether both interventions are better than natural history.	**+** Adequate quality Did not have a non-intervention group.

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
714	J. A. Kootker et al. (2017). Augmented Cognitive Behavioral Therapy for Poststroke Depressive Symptoms: A Randomized Controlled Trial. Archives of Physical Medicine and Rehabilitation 98:4 687-694	Multicentre, Netherlands (n=61), recruited within three months of CVE with elevated score on a depression measure (>7). Assessor-blinded, randomised controlled trial.	Four months of Cognitive behavioural therapy (CBT) (13-16 sessions of approx. one-hour duration) augmented with real-life activity training (three sessions) or an equal period of largely self-administered Computerised Cognitive Training (CCT)	Primary: Hospital Anxiety and Depression Scale depression subscale (HADS-D). Secondary: measures of anxiety, qualitative aspects of mood, coping, social participation, and subjective well-being. Measures collected at baseline, immediately posttreatment, four and eight months posttreatment.	There were no between groups differences after treatment for any of the primary or secondary outcome measures. CBT and CCT had similar effects; depression scores, anxiety symptoms, quality of life, satisfaction with life and participation improved in both groups after treatment. Both types of interventions may be considered to improve depressive symptoms (NB underlying mechanism unclear without further research).	+ There was no non-intervention control group (cannot rule out that any beneficial effect of CBT or CTT was nonspecific or that HADS-D scores improved simply because of regression to the mean). There is a need to determine if both interventions are better than natural history.
717	S. V. Kotov et al. (2020). Possibilities for Correcting Emotional and Behavioral Impairments in Stroke Patients during Rehabilitation Therapy. Neuroscience and Behavioral Physiology 50:2 156-161	Russia, acute stroke unit RCT design (n=50 in intervention, n=50 in control) 100 patients (61 men, 39 women, aged 40– 79 years, mean age 67.5 ± 0.6 years).	Intervention: daily robot mechanotherapy (for 7 mins in session 1, increasing to 30-40 mins three times a day, sessions started on days 3-5 and were delivered daily for 14 days) + tablet PC with games for exercises (first session run by Dr and then patient worked independently in the ward or in groups in 4-6 daily sessions for 20-30 mins throughout inpatient period; on	Emotional and behavioral impairments were assessed objectively using psychometric scales (the Beck Depression and Anxiety scales).	Significant improvements in depression in the intervention group. Follow-up observations of patients of the study group during treatment demonstrated a gradual decrease in the mean level of depression on the Beck scale. On discharge from hospital, by day 21, there was a statistically significant decrease in the mean score ($p = 0.0083$). By the end of the observation period (six months), there was also a statistically	- Low quality Approach to randomization not described, not clear whether blinding or forms of concealment used. Usual care for control group not described. Not reported whether there were any drop outs and intention to treat analysis conducted or not. N=100 but n=50 per group which is rather small.

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			discharge patients continued to work independently at home). Control: received standard therapy		significant decrease in the mean Beck score (p = 0.0001). Over the whole observation period (six months), there was an increase in depressive disorders in patients of the control group, apparent as a statistically significant increase in the mean Beck depression scale score (p = 0.0016).	
717	S. V. Kotov et al. (2020). Possibilities for Correcting Emotional and Behavioral Impairments in Stroke Patients during Rehabilitation Therapy. Neuroscience and Behavioral Physiology 50:2 156-161	RANDOMISED CONTROLLED TRIAL Aim: To assess the efficacy of mechanotherapy and cognitive stimulation using tablet PC technology (game apps for independent exercises by the patient) with the aim of developing memory, perception, reactions, and counting. Delivered during the acute phase of ischemic stroke	Experimental group (n=50): Daily robot mechano - therapy using a MOTOmed bedside trainer and tablet PC technology for independent exercises for patients to develop memory, perception, reactions, and counting. Control Group (n=50): Standard therapy	modified Rankin scale Beck Depression and Anxiety Scales Outcome measures completed at baseline, after 21 days (end of hospital period)/ 3 months/ 6 months	Significant reduction in emotional and behavioral impairments in the experimental group The severity of depressive disorders decreased in intervention group by the end of the in-patient period and at six months Anxiety showed statistically significant decreases during the whole of the observation period in the intervention group Functional recovery Improved in the intervention group	- Low quality 'Simple randomisation procedure' used – no further details given No concealment measures described No dropouts reported over the 6-month period (unusual?) No power calculation reported
718	Y. Lee et al. (2021). Effectiveness of non-pharmacological interventions for	Systematic review and meta-analysis. Included 22 trials in meta-synthesis (n=24 to n=411	Complementary and Alternative Therapy (CAT); [Acupuncture;	Depression symptoms, measured by any validated depression scale.	Overall beneficial effects of NPIs on depression post-intervention and at follow up. Individual beneficial effects	**++** High quality

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
	treating post-stroke depressive symptoms: Systematic review and meta-analysis of randomized controlled trials. Topics in Stroke Rehabilitation 28:4 289-320	per study), 13 of which eligible for meta-analysis. Studies of non pharmacological interventions (NPIs) for treating depression in people following stroke compared to control conditions.	Music therapy] Exercise; Psychosocial Therapy; Multifactorial Therapy; Pooled Non-Pharmacological Interventions;	Measured at post-intervention and follow up (1-12 months).	found for complementary and alternative therapy (CAT) and psychosocial therapy post-intervention. Authors concluded that CAT and psychosocial therapy appear promising strategies for post-stroke depression.	Followed JBI methodology
718	Y. Lee et al. (2021). Effectiveness of non-pharmacological interventions for treating post-stroke depressive symptoms: Systematic review and meta-analysis of randomized controlled trials. Topics in Stroke Rehabilitation 28:4 289-320	SR&MA; 13 trials (22 trials included, exclusions; 3 trials publication bias, 6 trials insufficient data), Post-Stroke Period; Acute 4 trials, subacute 3 trials, chronic 6 trials. Post-intervention; Complementary and Alternative Therapy (CAT); n=228, 5 trials, [Acupuncture; n= 154, 3 trials, Music therapy; n= 74, 2 trials] Exercise; n=263, 4 trials, Psychosocial Therapy; n=216, 2 trials, Multifactorial Therapy; n=186, 1 trial, Pooled Non-Pharmacological Interventions; n=893, 12 trials. At follow-up; (1month to 12 months post-intervention) Complementary and Alternative Therapy (CAT); n=36, 1 trial, Exercise; n=263, 4 trials, Psychosocial Therapy; n=63, 1 trial, Multifactorial Therapy; n=358, 2 trials, Pooled Non-	Complementary and Alternative Therapy (CAT); [Acupuncture; Music therapy] Exercise; Psychosocial Therapy; Multifactorial Therapy; Pooled Non-Pharmacological Interventions;	Depressive symptoms; Measured on any validated depression scale (9 Scales used, most common Hamilton Rating Scale for Depression); Measured; Post-intervention; At follow-up (1month to 12 months post-intervention).	Depressive symptoms; Post-intervention; Complementary and Alternative Therapy (CAT); Small but statistically significant effect. [Acupuncture; Medium statistically significant effect, Music therapy; Nonsignificant, non-beneficial effect] Exercise; Non significant, non-beneficial effect, Psychosocial Therapy; Small but statistically significant effect, Multifactorial Therapy; Non-significant, non-beneficial effect. Pooled Non-Pharmacological Interventions; Small but statistically significant effect. At follow-up; Complementary and Alternative Therapy (CAT); Non-significant, non-beneficial effect, Exercise; Non	++ Utilises JBI Methodology consistently Good I2 across all meta analyses, thus low heterogeneity,

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
		Pharmacological Interventions; n=720, 8 trials.			significant, non-beneficial effect, Psychosocial Therapy; Non-significant, non-beneficial effect, Multifactorial Therapy; Non-significant, non-beneficial effect, Pooled Non-Pharmacological Interventions; Small but statistically significant effect.	
719	X. X. Liang et al (2020). Hyperbaric oxygen therapy for post-stroke depression: A systematic review and meta-analysis. Clinical Neurology & Neurosurgery. 195. 105910.	SR&MA; 27 Trials, n=2250, All Studies Included conducted in China, Response Rate; 9 trials, n=# Depression Severity; [HAMD 17-items; X trials, n=XX, HAMD 24-items; 4 trials, n= XX, SDS; 1 trial, n=XX] Neurological Deficit; NIHSS; 9 trials, n= XX, CSS; 4 trials, n=XX, MESSS; 4 trials. Physical Disability; BI; 11 studies, n- xx,	Hyperbaric oxygen treatment (HBOT); providing patient with 100% pure oxygen at a pressure above normal atmosphere.	Primary Outcome; Response Rate [Defined as a 50% reduction in Hamilton Depression Rating Scale (HAMD) scores after treatment] OR Depression severity quantified by HAMD. Secondary Outcomes; de-pression severity quantified by Zung Self-Rating Depression Scale (SDS), neurological deficit quantified by National Institute of Health Stroke Scale (NIHSS), Chinese Stroke Scale (CSS) and Modified Edinburgh-Scandinavian Stroke Scale (MESSS), physical disability determined by Barthel Index (BI), and reported adverse events.	Primary Outcome; Response Rate; Statistically significant higher vs control OR Depression Severity; [HAMD 17-items & HAMD 24-items; Statistically significant reduction] Secondary Outcomes; Depression Severity; SDS; Statistically significant reduction, Neurological Deficit; NIHSS; Statistically significant reduction, CSS; Statistically significant reduction; NIHSS; Statistically significant reduction; MESSS; Statistically significant reduction, Physical Disability; BI; Statistically significant increase.	0 Variables I2 Scores across meta-analyses varying from low to high heterogeneity. All studies included score as an 'unclear risk of bias' on multiple categories.

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
719	X. X. Liang et al (2020). Hyperbaric oxygen therapy for post-stroke depression: A systematic review and meta-analysis. Clinical Neurology & Neurosurgery. 195. 105910.	Systematic review and meta-analysis, n=2250 with a diagnosis of post-stroke depression, from 27 RCTs.	Interventions evaluating hyperbaric oxygen therapy alone or in combination with other therapeutic approaches for depression (studies published up to 17th May 2019). Hyperbaric oxygen therapy versus antidepressant control; hyperbaric oxygen therapy plus antidepressant versus antidepressant monotherapy.	Response rate defined as 50% reduction in Hamilton Depression Rating Scale scores after treatment and depression severity (quantified by Hamilton Depression Rating Scale score). Other outcome measures included neurological deficit (Chinese Stroke Scale) and physical deficit (Barthel Index).	The hyperbaric oxygen therapy group showed a higher response rate and a beneficial effect on treatment severity, neurological deficit, and physical disability relative to controls.	+ Mostly appears to have been a well conducted systematic review of at least an 'acceptable' standard however the findings are limited by the low quality of included trials and small sample sizes. Only nine studies reported response rate. Applicability to the patient group targeted by this guideline questionable.
720	C. Liu et al (2019). Efficacy and Safety of High-Frequency Repetitive Transcranial Magnetic Stimulation for Poststroke Depression: A Systematic Review and Meta-analysis. Archives of Physical Medicine and Rehabilitation. 100: 10. 1964-1975.	SR with MA of 17 RCTS Eligible studies recruited stroke survivors with depression Only three studies published in peer reviewed English language journals 1171 participants in MA	High frequency repetitive transcranial magnetic stimulation at >10Hz with differing treatment periods	Hamilton depression (HAM-D) Response rate Adverse events Attrition Function	SMD of 1 point less with intervention Higher odds of remission OR 2.7 Limited data on adverse effects	- Restricted to RCTS that measure HAM-D. Included trials had issues with blinding and analysis (few used ITT) The published review deviated from the protocol in many areas Low quality SR – What do other guidelines say on TCMS?
720	C. Liu et al (2019). Efficacy and Safety of High-Frequency	SR	high-frequency repetitive transcranial magnetic stimulation	Hamilton depression (HAM-D) Adverse events	HF-rTMS had significantly positive effects on depression in patients with	-

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
	Repetitive Transcranial Magnetic Stimulation for Poststroke Depression: A Systematic Review and Meta-analysis. Archives of Physical Medicine and Rehabilitation. 100: 10. 1964-1975.	17 RCTs were included for meta-analysis. 1171 study participants (mean age 35.6-68.7 years)	alone or in combination with conventional treatment (such as vasodilators, nutritional supplements for the nervous system, and antidepressants)	Attrition BI NIHSS	stroke. The effect sizes of the SMD ranged from small to large (SMD, -1.01; 95% CI -1.36 to -0.66; P<.001; I2, 85%; n=1053), and the effect sizes of the OR were large (response rates, 58.43% vs 33.59%; OR, 3.31; 95% CI, 2.25-4.88; P<.001; I2, 0%; n=529; remission rates, 26.59% vs 12.60%; OR, 2.72; 95% CI, 1.69-4.38; P<.001; I2, 0%; N=529). In terms of treatment side effects, the HF-rTMS group was more prone to headache than the control group (OR, 3.53; 95% CI, 1.85-8.55; P<.001; I2, 0%; n=496).	double-blinding was not consider in SR or eligibility criteria when scoring the quality of studies. Low quality
721	G. E. Mead et al. (2020). Fluoxetine for stroke recovery: Meta-analysis of randomized controlled trials. International Journal of Stroke 15:4 365-376	SR with MA of 13 trials N=4145 participants Depression was not an eligibility criterion	Fluoxetine any dose	Primary outcome was function (not relevant to guideline question) Secondary outcomes included depression and anxiety. Adverse events.	6 trials, n=3113 assessed depression scores. SMD: -0.16 (955CI:-0.23 to -0.09) 2 trial assessed incident depression n=3194, RR0.77 (95%CI:0.65 to 0.90) More seizures and possibly more fractures with SSRI No anxiety data.	**++** High quality SR Does not include AFFINITY Does not include EFFECTS
723	B. Qin et al. (2018). Efficacy, acceptability, and tolerability of antidepressant treatments for patients with post-stroke depression: a network meta-analysis.	SR with NMA 14 RCTs N=949 participants Stroke with depression was eligibility criterion	Antidepressant pharmacological therapy	Depression rating scale Discontinuation Adverse events	Doxepin, paroxetine, nortiptyline all superior to placebo Doxepin and Paroxetine had more discontinuation than placebo	**-** No SR protocol Mix of open label and blinded RCTs Low quality SR – Does not add anything to

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
	Brazilian Journal of Medical & Biological Research 51:7 e7218					pairwise MA
723	B. Qin et al. (2018). Efficacy, acceptability, and tolerability of antidepressant treatments for patients with post-stroke depression: a network meta-analysis. Brazilian Journal of Medical & Biological Research 51:7 e7218	Meta-analysis; RTCs assessing any antidepressant available, 9 types; Antidepressants as monotherapy; 14 Studies selected between 1984 -2012; 949 patients; Mean age 60 years; 46% females;	Randomisation to placebo or antidepressant; Assessment: patients met DSM criteria for depression; Treatment period 8 weeks; Methods: self-reported questionnaire scores;	Few sign differences on all outcomes; Doxepin, Paroxetine, Nortryptilyne were sign. more effective than placebo; But they were not sign. more effective in comparison to other types of antidepressants	Study results provided little evidence for a preferred type of antidepressants,	- Evidence quality: low Comment: The authors listed several limitations of the study. Not all included studies were clear re randomization; durations of prescriptions of antidepressants varied; inconsistencies in efficacy outcomes noted. Generally, the effectiveness of antidepressants was not consistently proven nor was the advantage of one drug over another or over placebo. Studies analysed appeared dated.
724	A. Urech et al. (2020). An integrative neuro-psychotherapy treatment to foster the adjustment in acquired brain injury patients-a randomized controlled study. Journal of Clinical Medicine 9:6 1684	RTC: integrative neuro-psychotherapy group; Standard neuropsychological treatment; 25 patients; 80% of patients stroke	Assessment of depression (primary outcomes), emotional regulation and quality of life variables. Treatment 1:1 sessions	No difference was found in treatment outcomes between both interventions; Sign improvement of emotion regulation: between-group difference at post-treatment, this effect disappeared at 6month follow-up;	Results demonstrated difficulties re psychotherapy for ABI patients as a range of symptoms need to be addressed at the same time;	- Evidence quality low. Comment: insufficient evidence for a preferred method of neuropsychological therapy; large within-group differences make tailored treatments necessary.

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			Patient-tailored treatment plan; Delivered by trained psychotherapists and neuropsychologists; Length of treatment according to need; Average length 20.6 weeks 6-months follow-up;	large within group effect sizes; T-test outcomes: sign within-group reduction of depression symptoms in both groups; T-test outcomes: sign. Within-group improvement of awareness, emotion-regulation, fatigue, quality of life, acceptance, rumination and acceptance of social support;		Positive improvements were not maintained after 6 months; Intensive and tailored treatment delivered by qualified staff = resource intensive.
724	A. Urech et al. (2020). An integrative neuro-psychotherapy treatment to foster the adjustment in acquired brain injury patients-a randomized controlled study. Journal of Clinical Medicine 9:6 1684	RCT, outpatient setting, Switzerland, n=25 (80% with stroke), at least six months after CVE, with a diagnosis of adjustment disorder (DSM-IV)	A newly developed integrative cognitive-behavioural treatment combined with a neuropsychological therapy (average number of sessions = 20.6) or a standard neuropsychological treatment alone (average number of sessions = 18.3)	Beck Depression Inventory post-treatment and six-month follow-up; secondary outcomes included measures of quality of life, emotion regulation skills, acceptance of disability, awareness, illness coping, mental fatigue, relationship quality	Large within-groups effects on depression scores but the two groups did not differ from one another at post-treatment nor at follow-up	- Arguably the treatment and active control conditions were too similar in nature and coupled with low power there was an increased likelihood of a type II error.
725	M. M. Visser et al. (2016). Problem-solving therapy during outpatient stroke rehabilitation improves coping and	RCT; open group, n= 166, random block randomisation.	Control group; standard of care; Occupational therapy, Physiotherapy, Psychology, Speech &	Primary Outcome; Coping Inventory for Stressful Situations - Task-oriented coping subscale	Primary Outcome; Coping Inventory for Stressful Situations - Task-oriented coping subscale; Statistically significant difference favouring intervention at 6	- Unclear blinding of participant or assessors

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
	health-related quality of life: Randomized controlled trial. Stroke 47:1 135-142		Language Therapy, social work. Intervention group; Standard of care plus, Problem-Solving Therapy; Open group, 8 group sessions, 1.5 hours a week with additional homework exercises.	Secondary Outcomes; Coping Inventory for Stressful Situations [3 sub-scales task-oriented, emotion-oriented, and avoidant Coping], Social Problem Solving Inventory-Revised, Stroke-Specific Quality-of-Life Scale-12, EuroQol EQ-5D-5. Assessed at timepoints; Baseline; 3 weeks before intervention, After intervention (within 10 days); 6 months post intervention, 12 months post-intervention.	months post-intervention only, non-statistically significant difference between both groups at 12 months post stroke. Secondary Outcomes; Non statistically significant differences between intervention group and control on all measures at 6 months and 12 months post-intervention.	Enrolment of first 3 participants to PST group at each site clear risk of bias.
725	M. M. Visser et al. (2016). Problem-solving therapy during outpatient stroke rehabilitation improves coping and health-related quality of life: Randomized controlled trial. Stroke 47:1 135-142	Outpatient rehabilitation, the Netherlands RCT design, multicentre 166 stroke survivors (mean age 53.3 years, 53% men, median time post stroke 7.29 months)	Intervention group: received Problem Solving Therapy (PST) in addition to usual rehabilitation/care during the last 8 weeks of their outpatient rehabilitation. PST intervention consists of 8 group sessions of 1.5 hours a week with additional homework exercises. Delivered by a neuropsychologist. Sessions focussed on (1) defining the	Coping strategies (measured using the Coping Inventory for Stressful Situations) Problem solving skills (measured using the Social Problem Solving Inventory-Revised) HRQoL (measured using the Stroke-Specific Quality-of-Life Scale-12 and the EuroQol EQ-5D-5L)	Six months post intervention, the PST group showed significant improvement when compared with the control group in task-oriented coping (P=0.008), but not stroke-specific psychosocial HRQoL. Furthermore, avoidant coping (P=0.039) and the utility value for general HRQoL (P=0.034) improved more in the PST group than in the control after 6 months. Although depression scores improved in both groups	**++** High quality Power calculation undertaken to make sure sufficiently powered and achieved the required sample size. Multicentre, randomised design, randomisation procedure well described. Blinding of treatment allocation. Use of valid and reliable instruments

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			problem, (2) generating multiple solutions, (3) selectinga solution and (4) implementing and evaluating the solution. Control group: received standard outpatient rehabilitation only (description of this provided in the paper)	Depression (measured using the Center for Epidemiological Studies Depression Scale) Patients were assessed at the rehabilitation center or at home at 4 time points; within 3 weeks before the intervention (T0), within 10 days post intervention (T1), and 6 (T2) and 12 (T3) months post intervention.	across the intervention period there were no changes between the groups. Intervention had no observable effect on depression.	
726	X. Wang et al. (2020). The effects of mindfulness-based intervention on quality of life and poststroke depression in patients with spontaneous intracerebral hemorrhage in China. International Journal of Geriatric Psychiatry 35:5 572-580	Design: Single blind randomised controlled trial Setting: West China Hospital, Sichuan University Participants: 3-6 months post spontaneous intracerebral haemorrhage (sICH), aged 40 and older, NIHSS<20 at time 1, able to understand and speak Chinese. Exclusions: ICF due to trauma, tumour apoplexy, ruptured aneurysm, cavernous haemangioma, or AVM, recurrent SiCH and cognitive deficits. n=67 (after missing values removed) intervention group, n=67 (after missing values removed) control group	Mindfulness-based cognitive therapy (MBCT) – Eight 2-hour group sessions over consecutive weeks Control group – stress management education. Eight 2-hour group sessions in a lecture format.	Post-test questionnaires completed after 8 weeks of intervention. Depression (Centre for Epidemiological Studies Depression Scale; CES-D); train mindfulness (Mindful attention awareness scale; MAAS); quality of life (Functional assessment of cancer-therapy brain; FACT-Br); stroke severity (NIHSS).	Significant differences of depression, trait mindfulness, social well-being and QoL found in the intervention group from time 1 to time 2. During the MCBT intervention sessions 31/101 withdrew from the MCBT project. In the control group 23/101 withdrew. After missing data, analysed data for 67/101 intervention and 67/101 control so drop out about 33% in each arm.	- Low quality No details on randomisation, allocation concealment or blinding. Limited detail on process for completing post test questionnaires. No long term follow up. High attrition and missing data in both groups.

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
726	X. Wang et al. (2020). The effects of mindfulness-based intervention on quality of life and poststroke depression in patients with spontaneous intracerebral hemorrhage in China. International Journal of Geriatric Psychiatry 35:5 572-580	RCT Single centre China ICH with moderate severity 202 randomsied, 134 patients (67 in control group and 67 in intervention group) included in primary analysis	mindfulness-based cognitive therapy. eight 2-hour group sessions over consecutive weeks delivered by a therapist 'active' control	CES-D (depression) Other outcomes not relevant to guideline question Limited detail on timing of assessment	Substantial attrition from intervention (n=34) Analysis of outcomes is atypical, suggest benefit of intervention	- Low quality RCT Lacks CONSORT detail Atypical analysis
727	P. Chippala et al. (2020). Effect of very early mobilisation on symptoms of depression and anxiety following acute stroke: A randomised controlled trial. Journal of Clinical and Diagnostic Research 14:2 YC01-YC05	Setting hospital India Design RCT Subjects - 105 individuals with acute stroke (62 male and 43 female) aged 30-81 years were recruited in the study inclusion age above 18 years admitted within 24 hours of onset of symptoms, were able to comprehend and respond verbally, systolic BP between 120 and 180 mm Hg, an O2 saturation >92%, a pulse rate between 40 -100 bpm normal range of body temperature <38.5°C	Intervention group received very early mobilisation including out of bed activities such as sitting, standing upright, walking begun within 24 hours of stroke onset for 5-30 minutes (Determined by patient tolerance) at least twice a day, for seven days	Symptoms of depression and anxiety were measured using the Hospital Anxiety and Depression (HAD) rating scale on admission, at discharge and at three months follow-up. The Mann-Whitney U-test was used to compare the HAD rating scale measures between groups and the p-value <0.05 was considered as significant	Change scores (at admission-at discharge) in HADS-Anxiety scores were higher for the intervention group (median=4.5, inter quartile range=2.25-7.75) than the standard care group (median=1, inter quartile range=0.2-5) and change scores (three months follow-up at admission) in HADS-Anxiety scores were higher for the intervention group (median=5, inter quartile range=3-7) than the standard care group (median=1, inter quartile range=0-5). Mann-Whitney U test results showed that improvement in HADS Anxiety scores were statistically significant (p<0.05)	+ Acceptable single centre, small study, attrition was low, documentation of frequency, intensity, and duration of mobilisation was not done

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
727	P. Chippala et al. (2020). Effect of very early mobilisation on symptoms of depression and anxiety following acute stroke: A randomised controlled trial. Journal of Clinical and Diagnostic Research 14:2 YC01-YC05	RANDOMISED CONTROLLED TRIAL Aim: To determine the effect of very early mobilisation coupled with standard care compared with the standard care alone on symptoms of depression and anxiety following acute stroke	Intervention group (n=48) received very early mobilisation including out of bed activities such as sitting, standing upright, walking begun within 24 hours of stroke onset for 5-30 minutes (Determined by patient tolerance) at least twice a day, for seven days plus standard care Standard care group (n=47): physiotherapy x 45 minutes once a day	Hospital Anxiety and Depression (HAD) rating scale on admission, at discharge and at three months follow-up.	The intervention group (n=48) demonstrated a significant decrease in symptoms of anxiety and depression at discharge ($p<0.05$) and at three months follow-up ($p<0.05$) than the standard care group (n=47). Very early mobilisation may be potential treatment to prevent or reduce symptoms of depression and anxiety following acute stroke. No deaths reported in either group	**+** Acceptable
729	K. Hill et al. (2019). Prevention of mood disorder after stroke: A randomised controlled trial of problem solving therapy versus volunteer support. BMC Neurology 19:1 128	Leeds/Bradford, NHS, UK; 3-group, parallel RCT; n=450 community-dwelling stroke patients within 1 month of CVE	Six, fortnightly sessions (median=5) of manualised problem-solving therapy with Community Psychiatric Nurse (n=151) or six-eight visits (median=6) from a volunteer for talking (non-specific) support (median = 6; n=149)) or treatment as usual (n=150)	Psychological (General Health Questionnaire, Present State Examination: short form); Activity (Barthel, Frenchay Activities Index); Satisfaction with hospital care (medication use, contacts with health and social care services, patient satisfaction) at six and 12 months	Participants in the problem-solving group had significantly lower General Health Questionnaire scores and median Present State Examination symptom scores at 12 months; no differences detected between groups for the activity measures at 6 or 12 months Participants in the treatment condition were no less likely to have a diagnosable depressive disorder at follow-up.	**+** Randomisation procedure described and participants unaware that their treatment was being randomly allocated but not masked to their allocation (impossible given the nature of the intervention).

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
729	K. Hill et al. (2019). Prevention of mood disorder after stroke: A randomised controlled trial of problem solving therapy versus volunteer support. BMC Neurology 19:1 128	3 group parallel RCT n=450 community-dwelling stroke patients within 1 month of hospital admission of first stroke. Hospitals in Leeds and Bradford, UK.	Six, fortnightly sessions (median=5) of manualised problem-solving therapy delivered in the patient's home by Community Psychiatric Nurse (n=151) or 6-8 visits (median=6) from a volunteer to provide talking (non-specific) support (median = 6; n=149) or treatment as usual (n=150)	Mood (General Health Questionnaire-28, Present State Examination: short form); Activity (Barthel, Frenchay Activities Index); Satisfaction with hospital care (medication use, contacts with health and social care services, patient satisfaction) at 6 and 12 months after stroke.	Participants in the problem solving therapy group had lower levels of major depression and depression caseness on the GHQ at 6 and 12 months follow up but this difference was not significant. At 12 months participants in the problem-solving group had significantly lower GHQ and Present State Examination symptom scores. No significant difference between groups on activity measures at 6 and 12 months.	**+** Adequate quality Not possible for participants to be blind to allocation.
730	A. Lewin-Richter et al. (2015). Predictivity of early depressive symptoms for post-stroke depression. Journal of Nutrition, Health and Aging 19:7 754-758	3 group parallel RCT n=450 community-dwelling stroke patients within 1 month of hospital admission of first stroke. Hospitals in Leeds and Bradford, UK.	Six, fortnightly sessions (median=5) of manualised problem-solving therapy delivered in the patient's home by Community Psychiatric Nurse (n=151) or 6-8 visits (median=6) from a volunteer to provide talking (non-specific) support (median = 6; n=149) or treatment as usual (n=150)	Mood (General Health Questionnaire-28, Present State Examination: short form); Activity (Barthel, Frenchay Activities Index); Satisfaction with hospital care (medication use, contacts with health and social care services, patient satisfaction) at 6 and 12 months after stroke.	Participants in the problem solving therapy group had lower levels of major depression and depression caseness on the GHQ at 6 and 12 months follow up but this difference was not significant. At 12 months participants in the problem-solving group had significantly lower GHQ and Present State Examination symptom scores. No significant difference between groups on activity measures at 6 and 12 months.	**+** Adequate quality Not possible for participants to be blind to allocation.

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
731	Y. Niu et al (2022). The Efficacy of Group Acceptance and Commitment Therapy for Preventing Post-Stroke Depression: A Randomized Controlled Trial. Journal of Stroke and Cerebrovascular Diseases. 31: 2. 106225.	RCT, China, n=104, acute hospital setting. Participants sub-divided into mild stroke group and moderate stroke group	Group Acceptance and Commitment Therapy (G-ACT) (five sessions, 45-55 min/session) plus weekly telephone support or 'usual care'	Psychological (24-item Hamilton Depression Scale) and neurological function (National Institutes of Health Stroke Scale, Barthel Index) at baseline, two weeks, one month and three months follow-up	Improvement in depression scores at three months follow-up for mild and moderate stroke patients receiving the Group Acceptance and Commitment Therapy intervention; no difference in measures of neurological function at three months follow-up	**+** Follow-up period not adequate to establish whether there is any protective benefit against the development of post-stroke depression in the medium- to long-term. Both treatment and control groups had subclinical depression scores at three-month follow-up; difficult to judge the extent to which the intervention was preventative (even though there was an observed effect for treatment condition on depression scores)
736	H. Y. Y. Chun et al (2018). A systematic review of anxiety interventions in stroke and acquired brain injury: Efficacy and trial design. Journal of Psychosomatic Research 104. 65-75.	Review of RCTs about anxiety treatment for ABI (stroke and TBI); 14 studies (12 stroke, 1 stroke+TBI, 1 TBI); 928 participants Small sample sizes in all studies 7 community studies, 3 inpatient studies, 2 outpatient studies, 1 study from inpatient to community,	Different types of anxiety disorders targeted in different studies; Different types of psychotherapy and alternative treatments administered Outcome measures: Different time points in different studies Control condition: 'usual care' most common, 1 study was		5 psychotherapy comparisons: intervention better than control -standardized mean difference: −0.41 [−0.79, −0.03], I2 =28%); 4 pharmacotherapy comparisons: intervention better than (SMD: −2.12 [−3.05, −1.18], I2 =89%). One comparison of mixed pharmacotherapy and Psychotherapy: intervention better than just usual care (SMD:−4.79 [−5.87,−3.71]). One comparison of	Evidence quality low Studies underpowered and risk of bias (non-blinded personnel); Comment: questions arose whether some of the selected therapies were valid in view of the condition they aimed to treat (i.e. was the kind of anxiety disorder targeted which is associated with stroke and is the right kind of treatment for this type of anxiety disorder?)

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		Time since injury: 15 days to 13 years.	placebo control,, 1 study active control Variety of rating scales selected		forest therapy versus urban control (SMD: −2.00 [−2.59, −1.41]).	
737	P. Knapp et al. (2017). Interventions for treating anxiety after stroke. Cochrane Database of Systematic Reviews 2017:5 CD008860	Systematic review and meta-analysis, interventions for treating anxiety after stroke. Included 3 RCTs (total n=196).	One trial of relaxation therapy (using a CD) One trial of paroxetine One trial of buspirone	Primary outcomes – clinician diagnosis of anxiety or score on a rating scale or self-report	In all three trials the interventions had a significant effect on anxiety diagnosis or symptoms Greater adverse events reported for drug therapy trials. Adverse events not reported for relaxation CD. Insufficient evidence to guide the treatment of anxiety after stroke.	+ Acceptable quality Quality of the evidence included in the review as very low (small sample size and sources of bias).
737	P. Knapp et al. (2017). Interventions for treating anxiety after stroke. Cochrane Database of Systematic Reviews 2017:5 CD008860	SR with MA of 3 RCTs Eligible studies recruited stroke survivors with anxiety 196 participants included in MA	Mixed One trial of relaxation therapy (using a CD) One trial of paroxetine One trial of buspirone	Primary – clinical diagnosis of anxiety, anxiety score	All interventions had a significant effect on anxiety or anxiety symptoms Greater adverse effects with drug therapy, no adverse effect data for the relaxation CD	+ Acceptable quality SR Overall low quality of evidence in this review with underpowered and potentially biased RCTs
739	F. J. Aidar et al. (2018). A randomized trial of the effects of an aquatic exercise program on depression, anxiety levels, and functional capacity of people who suffered an ischemic	RCT; n=36, chronic ischaemic stroke (>1 Year),	Control Group; no intervention Intervention Group; aquatic based physical activity, twice weekly, 45-60 mins per session.	Primary outcome; none detailed Secondary Outcomes; Depression; Beck Depression Inventory (BDI), Anxiety; State-Trait Anxiety Inventory: Form Y (STAI), Timed “up and go”	Secondary Outcomes; Statistically significant difference between experimental and control groups post-treatment on all outcomes.	- No ITT No allocation concealment No blinding to intervention or assessor.

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	stroke. Journal of Sports Medicine and Physical Fitness 58:44780 1171-7			Test, Timed 7.62m (25 feet) Walk, Getting up from a sitting position, Berg Balance Scale. Before and 12 weeks post-treatment.		No attentional control
739	F. J. Aidar et al. (2018). A randomized trial of the effects of an aquatic exercise program on depression, anxiety levels, and functional capacity of people who suffered an ischemic stroke. Journal of Sports Medicine and Physical Fitness 58:44780 1171-7	RCT 19 and 17 in each group Ischaemic stroke at least one year post ictus	aquatic exercise program - two sessions per week, each lasting between 45 and 60 minutes over 12 weeks.	State- Trait Anxiety Inventory Beck Depression Inventory	Modest reduction in depression and anxiety	- Low quality RCT Lacks CONSORT detail Small sample size Atypical analysis
742	M. Le Danseur et al. (2019). Music as a Therapy to Alleviate Anxiety During Inpatient Rehabilitation for Stroke. Rehabilitation nursing : the official journal of the Association of Rehabilitation Nurses 44:1 29-34	prospective, nonblinded, randomized study in an inpatient rehabilitation setting. 50 participants	1 hour of music music intervention group listened to music of their choice (participants chose from one of five music genres: Christian/gospel, classical, classic rock, country western, or pop/modern) for 1 hour. Participants randomized to the control arm were asked to carry on with	Anxiety was measured with the State–Trait Anxiety Inventory (STAI) and the Hospital Anxiety Depression Score (HAD	After listening to music for 1 hour, participants who completed the posttest (n = 44) reported significantly less anxiety ($p < .0001$) compared to before the intervention. The control group showed no difference in their pre- and posttest anxiety scores ($p = .84$). No differences were determined among age, gender, or diagnostic groups.	- Low quality Non blinded - randomized by random number assignment - number generator – sealed envelope

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			their daily routine for 1 hour (e.g., watching TV, walking, reading, eating). At the end of 1 hour,			
742	M. Le Danseur et al. (2019). Music as a Therapy to Alleviate Anxiety During Inpatient Rehabilitation for Stroke. Rehabilitation nursing : the official journal of the Association of Rehabilitation Nurses 44:1 29-34	Non blinded RCT; Inpatient setting; Ischemic or haemorrhagic stroke; 50 participants; 44 completed the study; Group 1: 1 hour of music Group 2: 1 hour no music: people carried on with their normal activities during the hour One-time intervention; Patients chose their own music; Exclusions: hearing impairments	Anxiety and depression screening: state-trait anxiety inventory, HADS		Music group had sign less anxiety after intervention than before (p<.0001) No music group: no change in anxiety pre and post	- Evidence quality: low Comment: this study reported the outcomes of a one-off, one hour only treatment; music intervention was not standardised, intervention was only offered in one hospital setting
743	A. West et al. (2019). An exploratory investigation of the effect of naturalistic light on depression, anxiety, and cognitive outcomes in stroke patients during admission for rehabilitation: A randomized controlled trial.	Quasi-Randomised Controlled Trial; n=99, rehabilitation Unit	Control Group; 14 days Standard Indoor Lighting Intervention Group; 14 days Always on Naturalistic Lighting.	Primary Outcomes; Depression; Hamilton Depression Scale (HAM-D), Major Depression Inventory (MDI), Well-being; WHO-Five Well-being Index (WHO-5), Hospital Anxiety and Depression Scale: Depression subscale (HADS-D),Anxiety; Hospital Anxiety and	Primary Outcomes; Depression; Statistically Significant Reduction on all scales in the intervention group compared with the control group upon discharge. Secondary Outcomes; No statistically significant difference increase in MoCA scores in the intervention group compared with the control group upon discharge.	- Non-blinded randomisation Non-blinded assessment Participants not blinded

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
	NeuroRehabilitation 44:3 341-351			Depression Scale: Anxiety subscale (HADS-A) Secondary Outcomes; Cognition; Montreal Cognitive Assessment (MoCA)		
743	A. West et al. (2019). An exploratory investigation of the effect of naturalistic light on depression, anxiety, and cognitive outcomes in stroke patients during admission for rehabilitation: A randomized controlled trial. NeuroRehabilitation 44:3 341-351	Quasi-RCT Hospital rehab setting, Denmark 90 eligible but 71 stroke survivors completed the survey (44 males, 27 females, mean age 73 years)	Intervention: naturalistic light in rehab unit (24 hour naturalistic lighting scheme was implemented in all areas and rooms) Control: standard indoor lighting in rehab unit (fluorescent tubes in normal ceiling lights) Non-blinded randomisation	Depression (measured using the Depression Hamilton Depression Scale & Major Depression Inventory) Wellbeing (measured by WHO Five Well-being Index) Anxiety (Hospital Anxiety and Depression Scale (HADS)) Cognition (Montreal Cognitive Assessment MoCA) Use of anxiety and/or antidepressant prescriptions was recorded at inclusion and discharge.	Depressive mood (MDI p = 0.0005, HAM-D6 p = 0.011) and anxiety (HADS anxiety p = 0.045) was reduced, and well-being (WHO-5 p = 0.046) was increased, in the IU at discharge compared to the CU. No difference was found in cognition (MoCA p = 0.969). No difference was found in HADS depression score. Significant decrease in depressive mood & anxiety symptoms over the 14 day intervention period. Naturalistic light during admission may significantly improve mental health during rehabilitation.	- Low quality Non blinded randomisation Reasonable number discontinued because of difficulties completing the measures. Authors comment that many participants were cognitively challenged and so this may be why they struggled to complete measures. And HADS measure was only one that didn't show any change in depressive symptoms – suggested to be for this reason. Although naturalistic light was intervention, no description of what care delivery, staffing etc. was like within and between the different units. No idea of what interventions and rehab support people got so difficult to tell if results are due to the lighting alone.

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						No concealment, people knew which unit they were in but authors do not attempt to address this Power calculation for sample size is confusing and poorly described. Not sure what the actual sample size that was needed to show an effect was.
744	F. Yu et al. (2019). Effect of family education program on cognitive impairment, anxiety, and depression in persons who have had a stroke: A randomized, controlled study. Nursing & Health Sciences 21:1 44-53	RCT Acute stroke context (participants recruited within 7 days post stroke), China 114 patients recruited (n=72 in FMEP (intervention) and n=72 in control). 82% of intervention group & 79% of control group completed 12 month follow up. Mean age: 63.60 (intervention) & 63.58 (control) Sex: n=47 male and n=53 female.	Intervention: Family member education programme (FMEP). 12 month intervention focussed on education, provision of counselling and support. First two weeks consisted of 5 educational sessions. For the next 3-8 weeks, the family member was invited to join weekly workshop that provided counselling, communication and assistance to resolve any issues they were facing. Nurse or rehab specialist also visited during this time (not sure how often). Between 3-12 months, a monthly call was made to the family	Cognitive impairment (assessed using the Montreal Cognitive Assessment score (MOCA) and Minimum Mental State Examination (MMSE) Anxiety (as measured using the HADs Anxiety score) Depression (as measured using the HADs depression score)	CI scores improved based on MOCA but not MMSE instruments. Statistically significant reduction in anxiety scores in FEMP group from baseline to 12 months (−.21 _ 1.96), whereas it increased in the control group (.51 _ 1.51, P = .015). Statistically significant reduction in HADS depression score from baseline to 12 months in FEMP group (−.54 _ 2.06) and increased in the control group (.47 _ 1.60, P = .001) The results suggest that FEMP might reduce and depression in people	- Low quality Authors comment that different instruments detected different effects from the intervention and that the HADS anxiety and depression scales may not be reliable. Small sample size. Procedures for randomisation and blinding were not fully reported/clear. Aspects of how the intervention was delivered were also intervention were also unclear (e.g. input of specialist nurse/rehabilitation specialists from 3 weeks onwards, not clear what this involved and how often it occurred and when over the course of the intervention period).

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			member check on the condition of the patient and offer opportunity to raise any concerns. PLUS usual care. Control: usual care (but not described)			
744	F. Yu et al. (2019). Effect of family education program on cognitive impairment, anxiety, and depression in persons who have had a stroke: A randomized, controlled study. Nursing & Health Sciences 21:1 44-53	RANDOMISED CONTROLLED TRIAL Aim: To evaluate the effects of the family member education program (FMEP) on cognitive impairment, anxiety, and depression in persons who have had a stroke. Definition: Health education for patients' family members is considered to be a good way to increase understanding of diseases, relevant physiological management, and psychological support skills that enable them to provide better care for their relatives Hypothesis: FMEP will reduce cognitive impairment, anxiety, and depression in persons who have had a stroke.	Intervention group: FEMP (education re. understanding of stroke, influence of stroke, common issues, physical care, and mental health care and a weekly workshop that provided counselling, communication, and assistance to resolve any issues they were facing and home visits if required and monthly calls) plus conventional treatment (n=72) Control: conventional treatment alone (n=72)	Montreal Cognitive Assessment (MOCA) Hospital Anxiety and Depression Scale Minimum Mental State Examination (MMSE) score Outcomes collected at baseline, 3,6 and 12 months *No carer outcome measures collected	The FMEP decreased cognitive impairment when assessed by MOCA score, while no difference in cognitive impairment, as assessed by the MMSE score, was found between the FMEP and control groups; FMEP might reduce anxiety and decreased depression in persons who have had a stroke.	- Low quality Small sample size No power calculation No economic evaluation (this was a labour intensive intervention)

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
749	E. Lundstrom et al (2020). Safety and efficacy of fluoxetine on functional recovery after acute stroke (EFFECTS): a randomised, double-blind, placebo-controlled trial. Lancet Neurology. 19: 8. 661-669.	RCT in Sweden Post stroke (2 to 15 days post ictus) 1500 participants Recruited population were generally mild strokes NIHSS 3 (median)	Fluoxetine 20mg once daily for six months (versus matching placebo)	Primary outcome was function (mRS) Secondary outcomes included incident depression (DSM IV, clinical diagnosis) and safety measures.	Primary outcome was neutral. Fluoxetine reduced depression (54 [7·2%] patients vs 81 [10·8%]; difference -3·6% [95% CI -0·065 to -0·0071]; p=0·015) The emotion item of SIS was also less in the treatment group (data not available in primary paper) There were more fractures (28 [3·7%] vs 11 [1·5%]; difference 2·2% [95% 37 CI 0·0066 to 0·039]; p=0·0058) and more hyponatremia (11 [1·47%] patients vs 1 [0·13%]; difference 1·34% [95% CI 0·0043 to 0·022]; p=0·0038).	High quality trial Was harmonised with FOCUS and (to an extent) AFFINITY – the three should be pooled?
747	H. M. Kalbouneh et al (2022). Safety and Efficacy of SSRIs in Improving Poststroke Recovery: A Systematic Review and Meta-Analysis. 11: 13.	Meta-analysis. Included placebo-controlled study designs which reported SSRIs' effects on poststroke depression, anxiety, disability, dependence, motor abilities, and cognitive functions. Included 44 studies (total participants n= 16,164).	Of the participants,.5% were treated using SSRIs (8137/16 164), whereas 49.5% were treated using a placebo (8027/16 164).	Depression, anxiety, disability, dependence, motor ability, cognitive functions.	SSRIs had a significant effect on preventing depression and treating depression (Hamilton Rating Scale for Depression), anxiety, dependence, motor abilities (NIHSS) and cognitive function. No significant effect of SSRI on disability. Treating with SSRIs increased the risk of seizures. No difference in incidence of gastrointestinal symptoms or bleeding between SSRIs and placebo.	++ Good quality systematic review and meta-analysis

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
748	J. Tay et al (2022). Does fluoxetine reduce apathetic and depressive symptoms after stroke? An analysis of the EFFECTS trial dataset. International journal of stroke : official journal of the International Stroke Society.	Post-hoc analysis of the EFFECTS trial. EFFECTs RCT included patients ≥18 years old, 2-15 days post stroke. Randomised controlled trial.	Intervention: 20mg oral fluoxetine once daily for 6 months Control: Matching placebo for 6 months.	The Montgomery–Åsberg Depression Rating Scale (MADRS) at baseline and 6 months. Divide items on the MADRS into those reflecting apathy and those reflecting depression.	Of 1500 participants enrolled, complete MADRS data were available for 1369. The modified intention-to-treat population included 681 patients in the fluoxetine group and 688 in the placebo group. Baseline characteristics well balanced between both groups. Fluoxetine group had higher apathy scores at baseline. Apathy scores increased in both fluoxetine and placebo groups. Fluoxetine was associated with a reduction in depressive scores. Authors conclude that Post-stroke apathetic and depressive symptoms respond differently to fluoxetine. Authors suggest that fluoxetine is ineffective in preventing post-stroke apathy.	**+** This paper is post-hoc analysis of the EFFECTS trial which was a high-quality RCT. Limited by using single item measure of apathy.