CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS

MOOD, COGNITION AND FATIGUE FOLLOWING STROKE EVIDENCE TABLES

Post-Stroke Depression: Non-pharmacological Interventions

Update 2019

Lanctôt KL, Swartz RH (Writing Group Chairs) on Behalf of the Canadian Stroke Best Practice Recommendations Mood, Cognition and Fatigue following Stroke Writing Group and the Canadian Stroke Best Practice and Quality Advisory Committee, in collaboration with the Canadian Stroke Consortium

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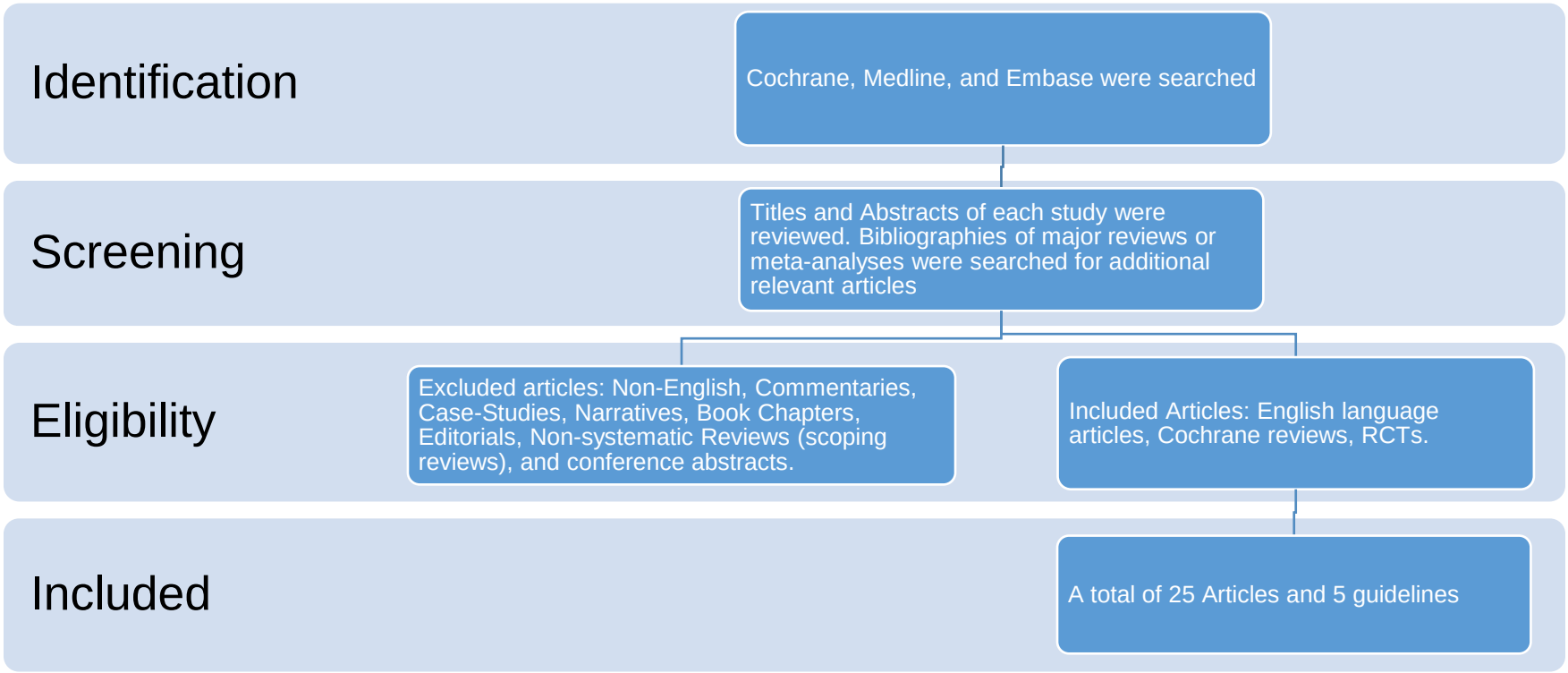
Search Strategy



The Medline, Embase, PsycInfo, and Cochrane databases were searched using the terms [stroke OR cerebrovascular disorders] and [depression OR depressive disorders OR anxiety OR anxiety disorders OR emotional incontinence]. The title and abstract of each article was reviewed for relevance. Bibliographies were reviewed to find additional relevant articles. Articles were excluded if they were: non-English, commentaries, case-studies, narrative, book chapters, editorials, non-systematic review, or conference abstracts. Additional searches for relevant best practice guidelines were completed and included in a separate section of the review. A total of 54 articles and 5 guidelines were included and were separated into categories designed to answer specific questions.

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Published Guidelines

Guideline	Recommendations
Stroke Foundation. Clinical Guidelines for Stroke Management 2017. Melbourne Australia. (Part 6)	Weak Recommendation For stroke survivors, psychological strategies (e.g. problem solving, motivational interviewing) may be used to prevent depression. Weak recommendation New For stroke survivors with depression or depressive symptoms, structured exercise programs, particularly those of high intensity, may be used. Weak recommendation New For stroke survivors with depression or depressive symptoms, acupuncture may be used. Weak recommendation AGAINST New For stroke survivors with depression, non-invasive brain stimulation (transcranial direct stimulation or repetitive transcranial magnetic stimulation) should not be used in routine practice and only used as part of a research framework.
Winstein CJ, Stein J, Arena R, Bates B, Cherney LR, Cramer SC, Deruyter F, Eng JJ, Fisher B, Harvey RL, Lang CE, MacKay-Lyons M, Ottenbacher KJ, Pugh S, Reeves MJ, Richards LG, Stiers W, Zorowitz RD; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, and Council on Quality of Care and Outcomes Research. **Guidelines for adult stroke rehabilitation and recovery: a guideline for healthcare professionals from the American Heart Association/American Stroke Association.** ***Stroke* 2016;47:e98–e169. (selected)**	Patient education about stroke is recommended. Patients should be provided with information, advice, and the opportunity to talk about the impact of the illness on their lives. Class 1; LOE B. Periodic reassessment of depression, anxiety, and other psychiatric symptoms may be useful in the care of stroke survivors. Class IIA; LOE B. Consultation by a qualified psychiatrist or psychologist for stroke survivors with mood disorders causing persistent distress or worsening disability can be useful. Class IIA; LOE C. The efficacy of individual psychotherapy alone in the treatment of poststroke depression is unclear. Class IIB; LOE B. Patient education, counseling, and social support may be considered as components of treatment for poststroke depression. Class IIB; LOE B. An exercise program of at least 4 weeks duration may be considered as a complementary treatment for poststroke depression. Class IIB; LOE B.
Intercollegiate Stroke Working Party. National clinical guideline for stroke, *5th* edition. London: Royal College of Physicians, 2016.	**Anxiety, depression and psychological distress** A People with stroke with one mood disorder (e.g. depression) should be assessed for others (e.g. anxiety). B People with or at risk of depression or anxiety after stroke should be offered brief psychological interventions such as motivational interviewing or problem-solving therapy (adapted if necessary for use with people with aphasia or cognitive problems) before considering antidepressant medication. C People with mild or moderate symptoms of psychological distress, depression or anxiety after stroke should be given information, support and advice and considered for one or more of the following interventions: – increased social interaction; – increased exercise; – other psychosocial interventions such as psychosocial education groups. D People with aphasia and low mood after stroke should be considered for individual behavioural therapy e.g. from an assistant psychologist.

	E People with depression or anxiety after stroke who are treated with antidepressant medication should be monitored for adverse effects and treated for at least four months beyond initial recovery. If the person's mood has not improved after 2-4 weeks, medication adherence should be checked before considering a dose increase or a change to another antidepressant. F People with severe or persistent symptoms of emotional disturbance after stroke should receive specialist assessment and treatment from a clinical neuropsychologist/clinical psychologist. **Emotionalism** F People with severe or persistent symptoms of emotional disturbance after stroke should receive specialist assessment and treatment from a clinical neuropsychologist/clinical psychologist.
National Stroke Foundation. Clinical Guidelines for Stroke Management 2010 Recommendations. Melbourne Australia.	**Mood disturbance** 1. All patients should be screened for depression using a validated tool (GPP) 2. Patients with suspected altered mood (e.g., depression, anxiety, emotional lability) should be assessed by trained personnel using a standardized and validated scale (B) 3. Diagnosis should only be made following clinical interview (GPP) 4. Psychological strategies (e.g., problem solving, motivational interviewing), can be used to prevent depression after stroke (B). 5. Routine use of antidepressants to prevent post-stroke depression is NOT recommended (B). 6. Antidepressants can be used for stroke patients who are depressed (following due consideration of the benefit and risk profile for the individual) and for those with emotional lability (B). 7. Psychological (cognitive-behavioural) intervention can be used for stroke patients who are depressed (B). **Behavioural change** 1. The impact of chronic behavioural changes (irritability, aggression, perseveration, adynamia/apathy, emotional lability, disinhibition, and impulsivity) on functional activities, participation and quality of life, including the impact on relationships, employment and leisure, should be assessed and addressed as appropriate over time (GPP). 2. Stroke survivors and their families/cares should be given access to individually tailored interventions for personality and behavioural changes e.g. participation in anger-management therapy and rehabilitation training and support in management of complex and challenging behaviour (GPP). **Care after hospital discharge** Stroke survivors can be managed using a care management model after discharge. If used, care manages should be able to recognize and manage depression and help to coordinate appropriate interventions via a medical practitioner (C).
Scottish Intercollegiate Guidelines Network (SIGN). Management of patients with stroke: Rehabilitation, prevention and management of complications, and discharge planning: A national clinical guideline, 2010. Edinburgh, Scotland.	**Preventing post-stroke depression** 1. Routine prescription of antidepressants is not recommended to prevent post-stroke depression (B). 2. Offering routine psychological therapies in one-to-one format following a stroke is not recommended to prevent post-stroke depression (B). 3. Psychological principles from motivational interviewing and problem solving should be incorporated into education programmes for people who have had a stroke (B). 4. Stroke rehabilitation services should consider structured, psychologically-based programmes (incorporating education and advice) to target individuals' emotional adjustment to the impact of stroke, and to increase their sense of control over their recovery. Such programmes require staff training and ongoing evaluation to ensure clinical benefit (GPP). **Treating post-stroke depression** 1. Patients with post-stroke depression should be considered for antidepressant treatment, with decisions made on an individual basis. Clinicians should monitor response to treatment, plan regular reviews and should be vigilant to the possible occurrence of unwanted side effects, issues of adherence to medication and the possibility of symptom relapse (A). 2. Clinicians need to make decisions on the choice of antidepressant on a case-by-case basis, taking into account factors such as risk of seizures, falls and delirium (GPP). 3. Patients who fail to respond to antidepressant therapy, or who do not wish to take medication, should be considered for a trial of talking-based therapy, with clinicians carefully monitoring response to treatment (GPP).

	4. Clinicians should be aware that environmental factors (eg opportunities for social interaction, noise levels) often have an impact on mood, and should consider whether it is possible to alter these factors when individuals experience post-stroke depression (GPP). **Emotional lability** 1. Patients with post-stroke emotionalism may be considered for a course of antidepressant medication (B). 2. Possible side effects of antidepressant treatment should be explained to patients prior to commencing treatment (GPP). 3. Patients and carers should be offered a clear explanation and advice about emotionalism, and considered for psychological (talking-based) support if they have a poor response to antidepressant medication and show evidence of distress about their condition. Local psychological support, education and advice should be considered on an individual basis as available. Such advice should be embedded in general education programmes. **Post-stroke emotional adjustment** 1. People who have had a stroke should be considered for workbook approaches that aim to address their beliefs and attitudes about their recovery (GPP). **Summary of Recommendations** 1. Appropriate referral to health and clinical psychology services should be considered for patients and carers to promote good recovery/adaptation and prevent and treat abnormal adaptation to the consequences of stroke (GPP). 2. All stroke patients (including those cared for in primary care) should be screened for mood disturbance (GPP). 3. Some form of screening should occur, eg using the Stroke Aphasic Depression Questionnaire (SAD-Q) or General Health Questionnaire of 12 items (GHQ-12): • as early as appropriate and definitely before discharge, and • at regular intervals thereafter 4. Clinical judgement should be used to determine how regularly mood should be re-assessed (GPP). If an individual is suspected of having a mood disorder they should be referred to an appropriately trained professional for a full assessment, or to a rehabilitation team member who has received training in the identification of psychological distress (GPP).
VA/DoD clinical practice guideline for the management of stroke rehabilitation 2010.	**Post stroke depression** 1. There are several treatment options for the patient with stroke and mild depression that can be used alone or in combination based on the patient's individual need and preference for services. Refer to VA/DoD guidelines for the management of Major Depression Disorder (MDD). 2. Patients diagnosed with moderate to severe depression after stroke should be referred to Mental Health specialty for evaluation and treatment. 3. There is conflicting evidence regarding the use of routine pharmacotherapy or psychotherapy to prevent depression or other mood disorders following stroke. 4. Patients with stroke who are suspected of wishing to harm themselves or others (suicidal or homicidal ideation) should be referred immediately to Mental Health for evaluation. 5. Recommend that patients with stroke should be given information, advice, and the opportunity to talk about the impact of the illness upon their lives. **Other Mood Disorders** 6. Patients following stroke exhibiting extreme emotional lability (i.e. pathological crying/tearfulness) should be given a trial of antidepressant medication, if no contraindication exists. SSRIs are recommended in this patient population. [A] 7. Patients with stroke who are diagnosed with anxiety related disorders should be evaluated for pharmacotherapy options. Consider psychotherapy intervention for anxiety and panic. Cognitive Behavioral Therapy has been found to be a more efficacious treatment for anxiety and panic disorder than other therapeutic interventions. 8. Recommend skills training regarding Activities of Daily Living (ADL's), and psychoeducation regarding stroke recovery with the family. 9. Encourage the patient with stroke to become involved in physical and/or other leisure activities. **Assessment of emotional and behavioral state**

	1. Initial evaluation of the patient should include a psychosocial history that covers pre-morbid personality characteristics, psychological disorders, pre-morbid social roles, and level of available social support. 2. Brief, continual assessments of psychological adjustment should be conducted to quickly identify when new problems occur. These assessments should also include ongoing monitoring of suicidal ideation and substance abuse. Other psychological factors deserving attention include: level of insight, level of self-efficacy/locus of control, loss of identity concerns, social support, sexuality, and sleep. 3. Review all medications and supplements including over the counter (OTC) medications that may affect behavior and function. 4. Inclusion of collateral information (e.g., spouse, children) is recommended to obtain a comprehensive picture of the patient's pre-morbid functioning and psychological changes since the stroke. 5. There is insufficient evidence to recommend the use of any specific tools to assess psychological adjustment. Several screening and assessment tools exist. (See Appendix B for standard instruments for psychological assessment.) 6. Post-stroke patients should be assessed for other psychiatric illnesses, including anxiety, bipolar illness, SUD, and nicotine dependence. Refer for further evaluation by mental health if indicated. **Use of standardized assessments** 1. Recommend that all patients should be screened for depression and motor, sensory, cognitive, communication, and swallowing deficits by appropriately trained clinicians, using standardized and valid screening tools. [C] If depression, or motor, sensory, cognitive, communication, or swallowing deficits are found on initial screening assessment, patients should be formally assessed by the appropriate clinician from the coordinated rehabilitation team. [C]

Evidence Tables

Non-pharmacotherapy for the Treatment of Post-Stroke Depression

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Meta-analyses					
Bell & D'Zurilla 2009 **USA** **Systematic review & meta-analysis**	NA	21 controlled studies examining problem-solving therapy (PST) among persons with depressive symptomatology, including those with major/minor depression, unipolar depression and suicidal ideation. No patients with post-stroke depression were included	Treatment contrasts included PST vs. alternative treatments (drug therapy, supportive therapy/attention control, other named therapy, or waitlist-list control). Duration of treatment was not stated. Duration of follow-up was reported in 11 studies (one month, n=2; 3 months, n=4; 6 months, n=3; and one year, n=2)	**Primary outcome:** Effect size (SMD and Hedge's g)	In post-treatment analysis, PST was associated with a small to medium effect size (d=.40). Effect sizes ranged from −1.15 to 3.80. PST was associated with small, non-significant effect sizes, compared with alternative psychosocial therapies (d= .17, p=0 .68) and medication treatment (d=−.13, p= 0.23). PST was associated with a medium, significant effect size compared with supportive therapy and attention control groups (d= .45, p<0.00). PST was associated with a large, but non-significant effect size, compared with wait-list controls (d= 2.38, p= .09). At follow-up, PST was associated with a significant medium-sized effect size, compared with all other alternative treatments (d=.48, p<0.01, n= 11 studies).
Wilson et al. 2009 **UK** **Cochrane Review**	N/A	9 RCTs of cognitive behaviour therapy or psychodynamic therapy approaches vs. controls in populations of older individuals (aged ≥55 years). Study settings included primary, secondary, community and inpatient (including nursing homes). All participants in identified studies were diagnosed with depressed according to DSM, ICD or RDC criteria or according to standardized rating scales.	All types of psychotherapeutic interventions were included and were categorized as cognitive behavioural therapies (CBT), psychodynamic therapy, interpersonal therapy, and supportive therapy.	**Primary outcome:** Reduction in the severity of symptoms of depression. **Secondary outcomes**: Dropouts and ratings of life satisfaction.	7 trials provided data pertaining to the comparison of CBT vs. controls. No trials provided data comparing psychodynamic therapy vs. control groups. Based on data from 141 participants included in 5 studies, CBT was found to be more effective than waiting list control conditions for the reduction of symptoms of depression (WMD: -9.85, 95% CI -11.97, -7.73) assessed on the Hamilton Rating Scale for Depression (HRSD). 3 small trials provided comparisons of CBT with psychodynamic therapies. However, there was no difference in effect demonstrated between these two therapeutic modalities (n=57) when assessed on the HRSD (WMD: =1.57 95% CI -5.59, 2.44) or the BDI (WMD: -2.28, 95% CI -11.14, 6.57). CBT was also superior to active controls when

					assessed using the HRSD in 3 small trials (WMD: -5.69, 95% CI -11.04, -0.35), but not when using the Geriatric Depression Scale (WMD: 0.0, 95% CI -5.31, 1.32).
Hackett et al. 2008 **Australia** **Cochrane Review**	NA	12 RCTs (n=1,121), including patients following stroke with a diagnosis of 1) depressive disorder, as defined by symptom scores on a standard screening instrument; (2 major depression, and 3) dysthymia or minor depression.	8 trials compared a pharmacotherapy vs. placebo. In 4 of the included trials, different forms of psychotherapy were evaluated including problem-solving therapy + counselling delivered by social workers (n=1), structured Cognitive Behavioural Therapy (n=1), motivational interviewing (n=1) and a supportive psychological intervention including education (n=1). The control condition was usual care in all trials. Frequency and duration of the interventions varied.	**Primary outcome:** Prevalence of diagnosable depressive disorder following treatment. **Secondary outcomes:** Scores on depression rating scale, physical function, and mortality.	Data was available from 445 participants from 3 of the identified trials. Active treatment was not associated with better outcomes compared with the control condition on any of the outcomes.
Psychotherapeutic Approaches					
Peng et al. 2016 **China** **RCT**	CA: ☑ Blinding patient: ☒ therapist ☒ assessor: ☑ ITT: ☒	180 patients recovering from aged 40 to 90 years with an ischemic stroke occurring with the previous 3 months. Mean age was 60 years, 72% were male. 58% of patients were depressed (HAM-D >7) and 55% had anxiety (HAM-A >6)	Participants were randomized 1:1 to a neuro-linguistic programming (NLP) group or usual care. Patients in the NLP group participated in 4 sessions (each lasting 60-120 minutes) over 2 weeks, initiated within 3 days of discharge from inpatient rehabilitation. NLP techniques included banishing negative thoughts or beliefs, bad moods, increasing mental energy, releasing pressure, and relaxing.	**Primary outcome:** Prevalences of depression and anxiety, remission of depressive symptoms (score ≤7 on HAM-D), assessed after the intervention and at 6-months follow-up **Secondary outcomes:** Quality of Life Index and Barthel Index scores	After the intervention, the prevalences of depression and anxiety were 17.8% (NLP) and 37.8% (usual care) for depression; and 23.3% (NLP) and 40.0% (usual care) for anxiety. At 6 months after the intervention, the prevalences of depression and anxiety were not significantly different: 6.3% (NLP) vs. 10.5% (usual care) for depression, p=0.35; and 5.1% (NLP) vs. 13.2% (usual care) for anxiety, p=0.079. After the intervention, significantly more patients in the intervention group achieved remission of depressive and anxious symptoms (HAM-D remitters: 82.2% vs. 62.2%, p=0.03); HAM-A remitters: 76.7% vs. 60%, p=0 .016). At the end of treatment, the odds of remission of depression and anxiety were significantly higher in the intervention group (OR=3.207; 95% CI 1.560-6.59 and OR=2.520, 95% CI 1.289-4.928), but were not increased significantly at 6 months post intervention.
Alexopoulos et al. 2012 **USA**	CA:☒ Blinding: patient ☒ therapist ☒	24 patients admitted for inpatient rehabilitation following stroke identified with post stroke depression, based on a Patient Health Questionnaire (PHQ-9)	Participants were randomly assigned to receive either ecosystem focused therapy (EFT) or education on stroke and depression	**Primary outcome:** Trajectories of scores over the treatment period of depression (assessed using HAM-D) and disability (assessed using	There was a trend toward greater decline in symptoms of depression associated with EFT (p=0.054). The mean HAD-D score at 12 weeks was non-significantly lower in the EFT group (8.2 vs. 13.2).

RCT	assessor ☒ ITT:☑	score >10.Individuals with mild to moderate aphasia could be included in the study. Mean age was 71 years, 58.3% of participants were male.	(ESD). EFT was provided in 12 weekly sessions of approximately 45 minutes in length. Inpatients had the first session prior to discharge; the remaining sessions were conducted in the participants' homes. EFT uses an integrated, educational, problem-solving approach to work through 5 therapy components – 1) provide an action-oriented perspective to recovery; 2) form a treatment "adherence enhancement structure" 3) provide a "problem solving structure" 4) help the family "re-engineer" to accommodate changed abilities and 5) coordinate with therapists and resources to develop a rehabilitation plan.	World Health Organization Disability Assessment Schedule-II (WHODAS-II)	The odds of remission of depression were significantly higher in the EFT group (66.7% vs. 16.7%; OR=10, 95% CI 1.44-69.26). Assignment to the EFT group was associated with greater gains in function over time (p=0.015). 7/12 patients in the EFT condition and 5/12 patients in the ESD condition were treated with antidepressants at some point during the 12-week intervention period.
Thomas et al. 2012 **UK** **RCT** ***Communication and Low Mood (CALM)***	CA: ☑ Blinding patient: ☒ therapist ☒ assessor: ☒ ITT: ☑	105 stroke patients with post stroke depression and aphasia. Low mood was assessed using the 'sad' item of the Visual Analog Mood Scales (cut-off >50) and the Stroke Aphasic Depression Questionnaire (SADQ), cutoff >6. Mean age was 67 years, 63% were male. Median time from stroke onset was 9 months.	Participants were randomized to receive behavioural therapy (n=51) or usual care (n=54). Behavioural therapy was provided by an assistant psychologist in up to 20, 1-hour sessions over the course of 3 months.	**Primary outcome**: The SADQ scores at 6 months after randomization. **Secondary outcomes**: The Visual Analogue 'sad' item, Visual Analogue Self-Esteem Scale, the Nottingham Leisure Questionnaire, and the Carer Strain Index.	At 6 months, assignment to the behavioural therapy group was a significant independent predictor of SADQ scores (p= 0.045), which remained significant when baseline values were controlled for (p = 0.022). At 6 months, assignment to the behavioural therapy group was a not significant independent predictor of SADQ scores for any of the secondary outcome measure scores. At 6 months, 28% of those in the intervention group and 27% of those in the control group were reported using medication for mood problems. Lost to follow-up: intervention group=15.7%; control group=14.8%.
Lincoln & Flannaghan 2003 **UK** **RCT**	CA: ☑ Blinding: patient ☒ therapist ☒ assessor ☑ ITT:☒	123 persons recovering from stroke, identified as depressed based on a score >10 on Beck Depression Inventory (BDI) or >18 on Wakefield Depression Inventory (WDI). Mean age of patients was 66 years, 51% were male There were 60 patients with a primary diagnosis of major depression at baseline.	Participants were randomly allocated to one of 3 conditions: 1) no intervention (n=41), 2) attention placebo (n=43) and 3) Cognitive Behavioral Therapy (CBT) (n=39). Patients in condition 1 had no further contact with the community psychiatric nurse. Patients in the	**Primary outcomes:** BDI and WDI scores at 3 and 6 months. **Secondary outcomes:** Extended Activities of Daily Living (EADL) scale, London Handicap Scale (LHS) and a rating of satisfaction with care, at 3 and 6 months.	At baseline, there were significantly more individuals with a diagnosis of major depression (ICD-10) allocated to receive CBT than either attention control or no intervention (p<0.05), although there were no significant differences in the BDI or WDI scores between groups at the time of study entry (p=0.2 and p=0.2, respectively). There were no significant differences in mean BDI or WDI scores between groups at 3 months (p=0.5, p=0.9, respectively) or at 6-month follow-up (p=0.6,

			attention placebo (2) condition received 10, 1-hour visits over 3 months by the community psychiatric nurse in which they discussed daily life, consequences and changes associated with stroke. In the CBT (3) condition, participants received 10, 1-hour sessions over 3 months by the community psychiatric nurse who used techniques such as education, graded task assignment, activity scheduling and identification and modification of unhelpful thoughts/beliefs – tailored to individual participants.		p=0.4, respectively). There were no significant differences between groups on any of the secondary outcomes, at 3 or 6 months. 34% of the patients received antidepressant therapy at some point during the study period. There was no significant between group difference in the proportion of participants receiving antidepressant therapy.
Acupuncture					
Zhang et al. 2012 **China** **Systematic Review and Meta-analysis**	NA	15 RCTs (n=1,079 participants) including participants with post-stroke depression. Mean ages ranged from 38-79.	All studies compared acupuncture vs. pharmacotherapy or "western" treatments for depression. Fluoxetine was the most commonly-used drug (n=12 trials). Duration of treatment ranged from 14 days to 2 months.	**Primary outcome:** "Curative effect" and "effective rate" (not defined) of acupuncture vs. pharmacotherapy.	Treatment with acupuncture was associated with improved odds of recovery/remission compared with pharmacotherapy (OR=1.48, 95% CI 1.10-1.97). Treatment with acupuncture was not associated with significantly increased odds of an "effective rate (OR=0.83, 95% CI 0.63- 1.09, p=0.18).
Zhang et al. 2010 **China** **Systematic Review and Meta-analysis**	N/A	53 high-quality RCTs, including participants with diagnoses of: major depressive disorder, post-stroke depression, postmenstrual depression, peri-natal depression, comorbid depression and post-traumatic depression. 20 trials evaluated the use of acupuncture in the treatment of post-stroke depression, of which 15 were included for analysis (n=1,680).	Acupuncture intervention was compared against controlled comparison conditions (pharmacotherapy, sham acupuncture and waitlist controls). 12 trials compared acupuncture monotherapy to pharmacotherapy, 3 compared it to waitlist control groups. Fluoxetine 20mg/day was the most commonly prescribed antidepressant.12 trials utilized combinations of bilateral scalp and body acupoints. 11 trials used manual stimulation only. Number of sessions ranged from 15 to 60 and length of	**Primary outcome:** Response rate, defined as ≥50% reduction in depression scores from baseline. **Secondary outcomes:** Changes in score on scales used to assess depression (usually HRSD).	Active acupuncture therapy was associated with improved response rates compared with antidepressant therapy (RR=1.31, 95% CI 1.19-1.44, p<0.0001). Pooled analysis of the 3 studies that compared acupuncture to waitlisted control groups demonstrated a significant effect in favour of acupuncture (RR=2.33, 95% CI 1.44-3.78, p=0.0006). Overall, patients treated with active or sham acupuncture reported fewer side effects than those treated with antidepressants (10.2% vs. 40.4%, p<0.001). The most commonly reported side effects associated with acupuncture included needling pain, transient dizziness and nausea.

			treatment from 4 to 8 weeks.		
Repetitive transcranial magnetic stimulation (rTMS)					
Shen et al. 2017 **China** **Systematic review & meta-analysis**	NA	22 RCTs studies (n=1764 patients), with confirmed diagnosis of depression due to stroke. Mean age of participants ranged from 52-69 years.	Trials compared treatment with rTMS +/- co-interventions vs. sham-rTMS, placebo, or active treatments (antidepressant, acupuncture or regular treatment. The duration of treatment ranged from 2 to 8 weeks (median of 4 weeks).	**Primary outcome:** Change in severity of depression measured by the Hamilton Depression Rating Scale (HAM-D) **Secondary outcomes:** Response rates, remission rates, stroke severity and ability to perform daily activities	At the end of treatment, the mean reduction in HAM-D scores was significantly greater for the rTMS group (MD=-6.09, 95% CI -7.74 to -4.45, p<0.0001). Data from 22 studies were included. The odds of responding to treatment were significantly higher in the rTMS group (OR=3.46, 95% CI 2.52-4.76, p < 0.00001). Data from 12 studies were included. The odds of achieving remission of symptoms were not significantly greater in the rTMS group (OR=0.99, 95% CI 0.56- 1.75, p=0.10). Data from 12 studies were included. The ability of persons to perform ADLs was significantly greater in the rTMS group (SMD=1.20; 95% CI 0.68-1.72, p<0.001). Data from 7 trials were included.
Gu et al. 2017 **Korea** **RCT**	CA:☒ Blinding: patient☑ assessor☑ ITT:☒	24 patients, aged 20-80 years admitted ≥6 months post stroke onset for inpatient stroke rehabilitation, with Beck Depression Inventory (BDI) scores >12 and Hamilton Depression Rating Scale (HAM-D17 scores >6. Mean age was 61 years, 58% male, mean time from stroke was 10.2 months	Patients were randomized 1:1 to receive 10 sessions of active (high-frequency, 10 Hz) or sham stimulation, 5 days a week for 2 weeks, in addition to rehabilitation therapies.	**Primary outcomes:** BDI and HAD-17 scores **Secondary outcomes:** Motricity Indices, Brunnstrom Classification and Functional Ambulatory Category	Patients who received active rTMS had significantly lowered mean BDI and HAM-D17 scores from baseline, assessed on the day before treatment to 4 weeks after the end of treatment (active 22.0 to 16.3 vs. sham 22.4 to 22.8, p<0.0001 and active 9.8 to 7.8 vs sham 10.2 to 10.3, p<0.0001, respectively). There were no significant differences in change scores between groups on any of the secondary outcomes. There were no serious adverse events.
Jorge et al. 2004 **USA** **RCT**	CA:☒ Blinding: patient ☑ therapist ☒ assessor☑ ITT:☒	20 patients with hemispheric, brainstem or cerebellar stroke and DSM-IV diagnosis of depression. Patients with MMSE ≤ 23 were excluded. All patients had failed to respond to at least 2 previous trials of antidepressants given at adequate doses. Mean age in the treatment condition was 63.1 and 66.5 in the sham condition. 45% were female.	Pretreatment: Antidepressant medication was tapered and then discontinued for at least 5 days before performing baseline evaluation. Length of time required was dependent on the half-life of the antidepressant used. Following pre-treatment, patients were randomly assigned to receive 10 sessions of active, left pre-frontal rTMS (10 Hz at 110% MT for 5 seconds for a total of 20 trains separated by 60-second pauses) or sham treatment	**Primary outcome:** Response and remission, evaluated using the Hamilton Rating Scale for Depression (HRSD-17). Response was defined as a decrease in total score of at least 50% and no longer meeting DSM-IV criteria for depression, one week post intervention. Remission was defined as reduction of HRSD scores by at least 50% and final HRSD scores <8.	Active rTMS treatment was associated with a significant reduction in depressive symptomatology, with a mean reduction of 7.3 points in HAM-D scores (p<0.0006). Percentage reduction in HAM-D scores was 38% in rTMS group vs. 13%in the control group. Results of cognitive and neuropsychological testing revealed no significant differences between sham and active treatment groups. 3 persons in the active rTMS group vs. 0 persons in the sham group experienced remission (p=>0.05). All adverse events registered during the course of treatment were mild and included mild headache (6 patients), local discomfort at the stimulation site due to cap tightness (5 patients) and exacerbation of insomnia (1 patient).

			over a 2-week period.		
Transcranial direct current stimulation (tDCS)					
Valiengo et al. 2017 **Brazil** **RCT**	CA:☑ Blinding: patient ☑ assessor☑ ITT:☑	48 patients, aged 30-90 years, within 5 years of first stroke, with Hamilton Depression Rating Scale, 17-items (HDRS-17) score ≥17, assessed within the previous 1-12 months, who had not been treated with antidepressants. Mean age was 62 years, 50% were men. Mean time post stroke was 15 months.	Patients were randomized to receive active or sham tDCS, consisting of 12 x 30 min sessions of 2 mA anodal left/cathodal right dorsolateral prefrontal tDCS, administered for 6 weeks (once daily on weekdays for 2 weeks, then 1 session every other week).	**Primary outcome:** Change in HDRS scores at 6 weeks **Secondary outcomes:** Clinical response, defined as ≥50% in baseline HDRS score, remission, defined as an end point HDRS score <8, and Montgomery-Åsberg Depression Rating Scale (MADRS) scores	43 participants completed the study. At the end of treatment, active tDCS was associated with a significantly greater reduction in HDRS-17 scores (mean difference=4.7, 95% CI 2.1 to 7.3; p<0.001) and MADRS scores (mean difference= −4.5 points, 95% CI −8.8 to −0.2, p=0.04). The response rate was significantly higher in the active group (37.5% vs 4.1%, OR=13.8, 95% CI 1.6 to 120, NNT=3). Remission was achieved significantly more often in the active group (20.8% vs. 0%, p=0.049, OR=7.9, NNT=5). There were no so serious adverse events.
Physical Activity					
Eng & Reime 2014 **Canada** **Systematic review & meta-analysis**	NA	13 RCTs (n=1,022) that included adults recovering from stroke. Age ranged from 21 to 93 years. Timing of stroke onset ranged from 30 days to 6 years. In 12/13 trials, participants did not meet criteria for depression; however, there was a substantial proportion of participants who had clinically relevant symptoms or were taking antidepressant medication	Trials compared physical exercise with usual care, or no care. Interventions included progressive resistance training (n=4), functional exercises (n=2), treadmill exercises (n=2), individual exercises with education (n=1), community-based rehabilitation (n=3) and Bobath exercises (n=1). In 11/13 trials the intervention was provided at least twice weekly for a minimal duration of 4 weeks.	**Primary outcome:** Standardized mean difference between groups in depression scores at the end of treatment or follow-up. Depression was assessed using the Hospital Anxiety and Depression Scale (n=8), the Geriatric Depression Scale (n=2), the Beck Depression Scale (n=2) and The Centre for Epidemiology Scale for Depression (n=1).	Physical exercise was associated with significantly lower depression scores (SMD=−0.13, 95% CI −0.26 to −0.01, p=0.03). In 10 trials (n=889), depression was assessed 10 weeks to 9 months after the cessation of the intervention, at which point, physical exercise was not associated with a decrease in depression scores (SMD=−0.04, 95% CI −0.17, to 0.09, p=0.53).
Sims et al. 2009 **Australia** **RCT**	CA:☒ Blinding: patient☒ therapist☒ assessor☒ ITT:☑	45 patients, > 6 months post stroke identified with post stroke depression (PSD), based on a score of ≥5 on the Patient Health Questionnaire (PHQ-9). Mean age was 67 years, 60% were male. Time from stroke onset was 13–18 months for 49% of participants.	Participants were randomized to an exercise group (n=23), which consisted of 2 sessions per week for 10 weeks of progressive resistance training, provided in small groups within the community, or the control group (n=22), who received usual care and were asked not to perform any resistance training.	**Primary outcome:** Centre for Epidemiologic Studies for Depression scale (CES-D) scores at the end of treatment (T2) and at 6-month follow-up (T3) **Secondary outcomes:** The proportion of participants not depressed at T2 and T3 (CES-D < 16)	At baseline, the mean CES-D score was significantly higher for participants in the control group (23.3 vs. 15.4, p=0.003). At the 10 week and 6 month follow, the intervention group had lower mean CES-D scores (15.13 vs. 20.62, p=0.08 and 13.78 vs. 22.70, p=0.004); however, these differences did not remain significant after controlling for baseline depression. The odds of being depressed either at T2 or T3 were not reduced significantly for participants in the intervention group.
Lai et al. 2006	CA: ☑	100 stroke patients, age >50 year, with stroke onset within 30	Patients were randomized to an exercise group (n=44)	**Primary outcome:** GDS scores	At 3 months, the mean GDS score was significantly lower in the exercise group (2.5 ± 2.5 vs. 4.4 ± 3.4,

USA **RCT**	Blinding: patient ☒ therapist ☒ assessor☑ ITT:☑	to 150 days, able to ambulate 25 ft independently, with mild to moderate stroke deficits, who had completed acute rehabilitation. The mean age was 69.8 years, 53% were male. Mean time since stroke onset was 75 days. 21% of the sample had significant depressive symptoms, based on a Geriatric Depression Scale (GDS) score ≥6.	and a usual care group (n=49). The exercise intervention consisted of 36 in-home session (3x/week) supervised by a therapist, for 9 months. The exercise protocol was based on a structured and progressive program designed to improve strength, balance, and endurance. For participants in the usual care group (n=49), a research assistant visited every 2 weeks for education and vital sign measurements. 54% of the usual care group received some form of professional in-home therapy.	**Secondary outcomes:** Proportion of participants with GDS scores >6, The SF-36 and the Stroke Impact Scale (SIS) emotion score. Assessments were conducted at before randomization (baseline), at 3 months after baseline (after the 3-month exercise intervention), and at 9 months after baseline (6 months after the intervention).	p<0.05). At 6 months post intervention, the difference was no longer significant. The proportion of participants with GDS scores >6 at 3 months was significantly higher in the usual care group (35.6% vs.14%, p=0.03), but not at 9 months (25% vs. 7.5%) Mean SIS and SF-36 emotion scores were significantly higher in the exercise group at 3 months, but not at 9 months
Support/Education					
Smith et al. 2012 **USA** **RCT**	CA: ☒ Blinding patient: ☒ therapist ☒ assessor: ☑ ITT: ☑	38 caregiver-stroke survivor dyads in which a female spouse provided care at home to a male stroke survivor. To be included, at least one dyad member had mild depression (Patient Health Questionnaire-9 score >9) and neither was medically unstable or terminally ill at the time of recruitment. Mean age of caregivers was 55 years, mean age of stroke survivors was 59 years.	Participants were randomized to a web-based intervention group (n=19) or to an information-only control group (n=19) for 11 weeks. The active intervention aimed to provide knowledge, resources and skills to caregivers through the use of professional guides, educational videos, and online components such as chat sessions and messages boards.	**Primary outcome:** Centre for Epidemiological Studies Depression Scale (CESD), the PHQ-9, the Mastery Scale, the Self-Esteem Scale, and the Social Support Survey, assessed at baseline, post-intervention, and 1-month follow-up.	Caregivers who received the active intervention reported significantly lower scores on the CESD at follow-up (p<0.01). There were no significant between group differences in mean CESD scores for stroke survivors scores at any time point. There were no significant differences in mean scores between groups at the end of treatment or 1-month follow-up.

Non-pharmacotherapy for the Treatment of Post-Stroke Anxiety

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Golding et al. 2016, 2017	CA: ☑	21 persons living in the community, recovering from	Participants were randomized 1:1 to an	**Primary outcome:** Changes in HADS-A scores,	At baseline, the mean HADS-A scores for participants in the intervention and control groups were 10.9 and

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
UK **RCT**	Blinding patient: ☒ therapist ☒ assessor: ☑ ITT: ☒	stroke, with Hospital Anxiety and Depression (HADS)-A score ≥6, who were cognitively intact. Mean age was 65 years, 50% were female. Mean time since stroke was 118 months (intervention group) and 69.9 months (control group).	intervention or control group. Persons in the intervention group received a self-help CD, with instructions to listen to it and following its instructions 5x/week for a month, at which point they could choose whether to continue using the CD. Persons in the control group received the CD after 3 months.	from baseline to 1, 2 and 3 months	10.5, respectively. At one month, mean HADS-A scores were significantly lower in the intervention group (7.4 vs. 10.6, Δ=3.5 vs. -0.10, p=0.002). At 2 months, mean HADS-A scores were significantly lower in the intervention group (7.0 vs. 11.4, Δ=4.11 vs. -0.90, p<0.001). At 3 months, mean HADS-A scores were significantly lower in the intervention group (6.9 vs. 11.0, Δ=4.22 vs. -0.50, p=0.001). At 3 months 4 participants in the intervention group no longer had clinical signs of anxiety vs. 1 in the control group. **One-year follow-up** 15 participants completed one-year assessments Mean HADS-A scores were significantly lower at one year, from baseline for participants in the intervention group (4.43 and 9.14, p=0.001), but not significantly lower from at one year from post-intervention.
Ping & Songhai 2008 **China** **RCT**	CA: ☒ Blinding patient: ☒ therapist ☒ assessor: ☒ ITT: ☒	67 inpatients and outpatients treated at a single facility following ischemic or hemorrhagic stroke with post-stroke anxiety neurosis, defined by Hamilton Anxiety Depression Scale (HAMA) score ≥20 and Self-Rating Anxiety Scale (SAS) score ≥50.	Patients were randomized to receive treatment with acupuncture, given once a day for 2 courses (15 x=1 course) or 0.4-0.8 mg Alprazolam, taken 3x/week x 4 weeks (control group)	**Primary outcome:** Anxiety status at end of treatment. I) Cured: reduction in HAMA score by 90-100%; Markedly relieved: reduction in score of 60-90%; Improved: reduction in score by 30-60%; Failed: reduction in score <30%	From baseline to end of treatment, there was a significant improvement in response rates within both groups, with no significant differences between groups (Cured: 5 in acupuncture group vs. 6 in control group; 16 in both groups who were markedly improved; 7 in acupuncture group vs. 5 in control group who were improved and 6 in both groups who failed treatment) There were no significant differences in mean HAMA or SAS scores between groups, before or after treatment.
Ryan et al. 2006 **UK** **RCT**	CA: ☑ Blinding patient: ☒ therapist ☒ assessor: ☑ ITT: ☒	165 patients, aged ≥65 years, recently discharged from hospital following a stroke (n=89) or hip fracture. Mean age of stroke patients was 77 years	Patients were randomized to receive an augmented service of ≥ 6 contacts with members of a multidisciplinary rehabilitation team in their home (maximum length of treatment time was 12 weeks) or ≤3 contacts with multidisciplinary rehab team	**Primary outcome:** HADS	At 3 months follow-up, significant differences were found for the stroke group in favor of the more intensive intervention group on anxiety (p=0.02) and depression (p=0.01). Mean change in HADS-A score over study period for more intensive and less intensive groups were -0.9 vs. 0.38, respectively.

Non-pharmacotherapy for the Treatment of Post-Stroke Apathy

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Chen et al. 2019 **China** **RCT**	CA: ☑ Blinding patient: ☒ therapist ☒ assessor: ☑ ITT: ☒	488 adult patients with first-ever ischemic stroke sustained within the previous 7 days. The study recruited patients with apathy at 6 times following stroke (baseline, and 1,3,6,9 and 12 months). A score of ≥37 on the Apathy Evaluation Scale-C (AESC/Clinical-Rated Apathy) indicated apathy. Maximum score is 72. Mean age was 65.1 years, 47.1% were women.	Participants were randomized 1:1 to a Motor Relearning Program (MRP) or Bobath approach) and received physiotherapy 5 days a week, ≥ 40 minutes for 4 weeks.	**Primary outcome:** Incidence of apathy at 12 months post stroke	The time from enrollment to onset of apathy was 3.93 months for Motor Learning Program, and 4.17 months for Bobath group (p=ns). 83 patients in the Bobath group and 57 patients in the MRP developed apathy. The risk of developing apathy was significantly higher in the Bobath group (HR=1.63, 95% CI 1.16-2.28, p=0.005). After excluding 109 patients with comorbid depression the risk of developing apathy remained significantly higher in the Bobath group (HR=1.65, 95% CI 1.13-2.42, p=0.010).

Non-pharmacotherapeutic Interventions for Prevention of Post-Stroke Depression

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Hackett et al. 2013 **Australia** **RCT** ***ImProving Outcomes after STroke (POST)***	CA: ☑ Blinding patient: ☒ therapist ☒ assessor: ☑ ITT: ☑	201 patients, aged ≥18 years, with a recent stroke (onset within the previous 8 weeks), with a Hospital Anxiety and Depression Scale (HADS) score <8. Patients with serious concomitant illness, were excluded. Mean age was 70 years, 43% were female, 28% were independent in ADLs.	Participants were to the intervention group (n=100) or to the usual care control group (n=101). Participants in the intervention group received a personalized post card at 1, 2, 3, 4, and 5 months following hospital discharge.	**Primary outcome:** Presence of depression at six months, defined as HADS>8. **Secondary outcomes:** Changes in HADS-D, HAD-A and PHQ-9, between 3 and 6 months	The proportion of participants with depression at the end of the 6-month study period did not differ significantly between the two groups (1.1% vs. 3.9%; RR= 0.29, 95% CI 0.03 to 2.71). Additionally, no significant between group differences were reported with respect to mean scores on the HADS total and subscale scores or on the PHQ-9.
Robinson et al. 2008, 2017 **Mikami et al. 2011** **USA**	CA:☑ Blinding: patient ☒ therapist ☒ assessor ☑	176 patients, aged 50-90 years recovering from ischemic or haemorrhagic stroke occurring within the previous 3 months, who were not diagnosed with depression. Depression was assessed using the DSM-IV	Patients were randomly assigned to receive 1 of 3 treatments: i) escitalopram 10 mg/d (if <65 yrs, 5 mg/d for patients ≥ 65, n=59) ii) matching placebo, n=58 or iii) problem-solving therapy	**Primary outcome:** The onset of diagnosable major or minor depression, diagnosed using DSM-IV criteria at 12 months.	At one year, in the per-protocol analysis, adjusted for previous history of mood disorders, patients assigned to the placebo condition were more likely to develop depression than individuals receiving PST (adj. HR=2.2, 95% CI 1.4-3.5, p<0.001). The result was not significant in the intention-to-treat

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
RCT	ITT:☑	criteria or a score >11 on the Hamilton Depression Scale. Mean ages across treatment groups ranged from 61-97 years, 59.7% of participants were male.	(PST), n=59, (6 treatment sessions over 12 weeks + 6 reinforcement sessions over 9 months). The problem-solving therapy used in this study was a manual-based intervention developed in the UK. All sessions were videotaped and evaluated for adherence.		analysis that included 27 patients who did not receive any treatment. (30.5% vs. 34.5%, HR=1.1, 95% CI 0.8-1.5, p=0.51). **2011 follow-up study** During the 6 months after cessation of treatment, 108 participants were available for evaluation. The incidence of new onset major depression was significantly higher for participants initially randomized to receive escitalopram (4 cases (11.8%) vs. 0 for placebo (p=0.114) and 0 for PST (p=0.038). Mean Hamilton Depression Scale scores were significantly higher for patients who received escitalopram compared with those who received placebo or PST (6.8 vs. 4.5 or 4.0, p=0.007, respectively). **2017 follow-up** A mean of 8 years following the end of treatment, 122 participants were available. Participants who received PST were significantly less likely to have died (HR= 0.4625), compared with the combined group of escitalopram + placebo. Increasing age and the development of depression were significant predictors or mortality.
Hackett et al. 2008 **Australia** **Cochrane Review**	NA	14 trials (RCTs), which included participants without a diagnosis of depression who had experienced a stroke, recruited from hospitals, outpatient clinics or from home. The mean or median age of the participants ranged from 55 to 74 years.	Among the trials, most of which examined a pharmacological agent for the prevention of post-stroke depression, 4 provided outcome data regarding the evaluation of psychotherapeutic interventions vs control groups, including problem-solving therapy (n=2), “home-based therapy” (n=1) and “motivational interviewing” (n=1). Treatment duration varied from one visit per week for four weeks to	**Primary outcome:** Proportion of patients who met the criteria for depression at the end of study (or study follow-up).	Outcome data for psychological therapy were available for 4 trials (n=902 participants). The odds of developing depression were significantly lower for participants in the active intervention group (OR= 0.64, 95% CI 0.42 to 0.98, p=0.04). Psychological interventions were associated with an improvement in mean GHQ-28 scores from baseline to end of treatment (MD= -1.37, 95% CI -2.33, -0.40, p=0.006). There was no evidence of benefit (or harm) demonstrated in ADL or social activities.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			monthly home visits over one year		

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