



HEART &  
STROKE  
FOUNDATION

CANADIAN  
**Stroke**  
**BEST PRACTICE**  
RECOMMENDATIONS

# CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS

## **Mood, Cognition and Fatigue Following Stroke Evidence Tables**

### ***Post-Stroke Depression: Non-pharmacological Interventions***

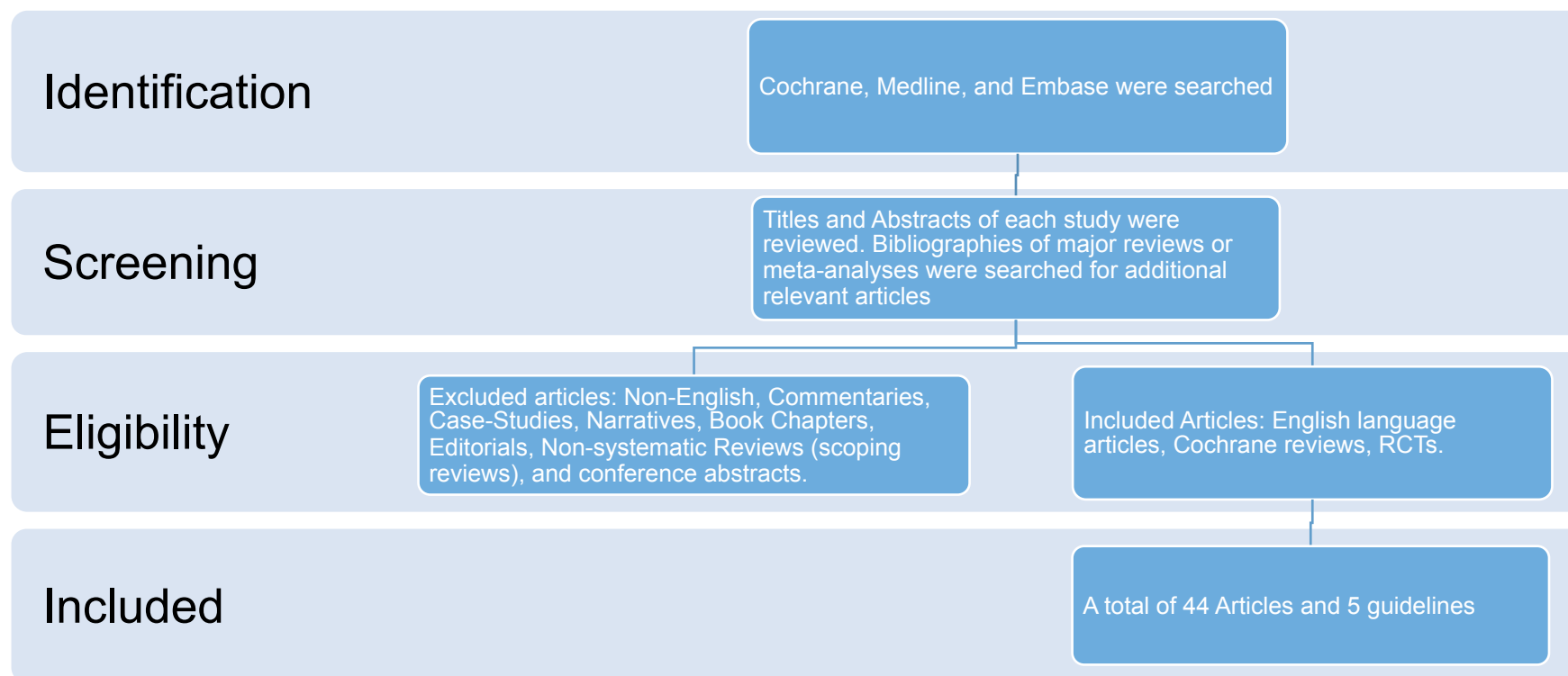
*Eskes G and Lanctot K (Writing Group Chairs)  
on Behalf of the Canadian Stroke Best Practice Recommendations  
Mood, Cognition and Fatigue Writing Group*

© 2015 Heart and Stroke Foundation

## Table of Contents

Search Strategy.....	3
Published Guidelines.....	4
Non-pharmacotherapy for the treatment of diagnosed PSD.....	9
Meta-analyses.....	9
Cognitive Behaviour Therapy (CBT).....	10
Acupuncture.....	14
Other Non-pharmacological Interventions.....	16
Specific Treatments of Mild Depression or Dysthymia.....	18
Interventions that may Improve Symptoms of Depression.....	21
Physical Exercise.....	21
Music Therapy.....	26
Prevention of Post-stroke Depression.....	29
Prophylactic Pharmacotherapy.....	29
Non-pharmacotherapeutic Interventions for Prevention of PSD.....	37
Care Management, Social Support and Post-stroke Depression.....	40
Post-stroke Anxiety and Co-morbid Depression.....	42
Post-stroke Emotionalism.....	43
Reference List.....	44

## 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 44 articles and 5 guidelines were included and were separated into categories designed to answer specific questions.

## Published Guidelines

Guideline	Recommendations
<b>National Stroke Foundation. Clinical Guidelines for Stroke Management 2010 Recommendations. Melbourne Australia.</b>	<p><b>Mood disturbance</b></p> <ol style="list-style-type: none"> <li>1. All patients should be screened for depression using a validated tool (GPP)</li> <li>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)</li> <li>3. Diagnosis should only be made following clinical interview (GPP)</li> <li>4. Psychological strategies (e.g., problem solving, motivational interviewing), can be used to prevent depression after stroke (B).</li> <li>5. Routine use of antidepressants to prevent post-stroke depression is NOT recommended (B).</li> <li>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).</li> <li>7. Psychological (cognitive-behavioural) intervention can be used for stroke patients who are depressed (B).</li> </ol> <p><b>Behavioural change</b></p> <ol style="list-style-type: none"> <li>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).</li> <li>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).</li> </ol> <p><b>Care after hospital discharge</b></p> <p>Stroke survivors can be managed using a care management model after discharge. If used, care managers should be able to recognize and manage depression and help to coordinate appropriate interventions via a medical practitioner (C).</p>
<b>Intercollegiate Stroke Working Party. National clinical guideline for stroke, 4th edition. London: Royal College of Physicians, 2012.</b>	<p><b>Depression and anxiety</b></p> <ol style="list-style-type: none"> <li>1. Any patient considered to have depression or anxiety should be assessed for other mood disorders.</li> <li>2. Patients with mild or moderate symptoms of depression should be given information, support and advice (see recommendation 6.34.1G) and considered for one or more of the following interventions: <ul style="list-style-type: none"> <li>• increased social interaction</li> <li>• increased exercise</li> <li>• goal setting</li> <li>• other psychosocial interventions.</li> </ul> </li> <li>3. Patients prescribed antidepressant drug treatment for depression or anxiety should be monitored for known adverse effects, and treatment continued for at least 4 months beyond initial recovery. If the patient's mood has not improved 2–4 weeks after initiating treatment, check that the patient is taking the medicine as prescribed. If they are, then consider increasing the dose or changing to another antidepressant.</li> <li>4. Patients receiving drug treatment for depression or anxiety should have it reviewed regularly to assess continued need.</li> <li>5. Brief, structured psychological therapy should be considered for patients with depression. Therapy will need to be adapted for use in those with neurological conditions.</li> <li>6. Antidepressant treatment should not be used routinely to prevent the onset of depression.</li> </ol>

Guideline	Recommendations
	<p><b>Emotionalism</b></p> <ol style="list-style-type: none"> <li>Any patient who persistently cries or laughs in unexpected situations or who is upset by their fluctuating emotional state should be assessed by a specialist or member of the stroke team trained in the assessment of emotionalism.</li> <li>Any patient diagnosed with emotionalism should, when they show increased emotional behaviour, be appropriately distracted from the provoking stimuli.</li> <li>Patients with severe, persistent or troublesome emotionalism should be given antidepressant drug treatment, monitoring the frequency of crying to check effectiveness. Patients should be monitored for known adverse effects. If the emotionalism has not improved 2–4 weeks after initiating treatment, check that the patient is taking the medicine as prescribed. If they are, then consider increasing the dose or changing to another antidepressant.</li> </ol> <p><b>Psychological Care</b></p> <ol style="list-style-type: none"> <li>Services should adopt a comprehensive approach to the delivery of psychological care after stroke, which should be delivered by using a ‘stepped care’ model from the acute stage to long-term management (see chapter 7).</li> <li>Interventions for individual disorders of mood or cognition should be applied within the framework of a stepped care and comprehensive model.</li> <li>Patients with continuing disorders should be considered for comprehensive interventions tailored towards developing compensatory behaviours and the learning of adaptive skills.</li> <li>Within Step 1 care all patients after stroke should be screened within 6 weeks of diagnosis, using a validated tool, to identify mood disturbance and cognitive impairment.</li> <li>Assessment measures should be adapted for use with patients with expressive or minor receptive aphasia. In patients with more severe aphasia, an assessment tool designed specifically for this purpose, such as the SAD-Q or DISCS, should be used. In patients with aphasia or other impairments that complicate assessment, careful observations over time (including response to a trial of antidepressant medication if considered necessary) should be used.</li> <li>Within Step 2 care, patients identified as having symptoms of mood disorder should be offered a more detailed assessment, seeking information on past history, potential causes and impact, and treatment preferences.</li> <li>In patients with mild or moderate symptoms of mood disorder, patients and carers should be provided with information, support and advice about the mood disorder as the first line of intervention. This may be from within the MDT by nominated staff who are suitably trained and supervised, and may also involve the voluntary sector.</li> <li>Within Step 3 care, patients with severe or persistent symptoms of mood disorder should be considered for referral to a specialist in the management of mood disorder in stroke.</li> <li>Psychological or pharmaceutical treatment (or a combination) for mood disorder should be provided if: recommended by a clinician with expertise in managing mood disorder after stroke; or, as the second line of intervention, if the patient has not responded to information, support and advice. Any treatment should be monitored for effectiveness and kept under review.</li> <li>Any patient assessed as having a cognitive impairment should be considered for referral to a specialist in cognitive aspects of stroke. Patients identified as having cognitive impairment or mood disorder should be reassessed before discharge decisions are taken.</li> </ol>
<p><b>Scottish Intercollegiate Guidelines Network (SIGN). Management of patients with stroke: Rehabilitation, prevention and</b></p>	<p><b>Preventing post-stroke depression</b></p> <ol style="list-style-type: none"> <li>Routine prescription of antidepressants is not recommended to prevent post-stroke depression (B).</li> <li>Offering routine psychological therapies in one-to-one format following a stroke is not recommended to prevent</li> </ol>

Guideline	Recommendations
<p><b>management of complications, and discharge planning: A national clinical guideline, 2010. Edinburgh, Scotland.</b></p>	<p>post-stroke depression (B).</p> <ol style="list-style-type: none"> <li>Psychological principles from motivational interviewing and problem solving should be incorporated into education programmes for people who have had a stroke (B).</li> <li>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).</li> </ol> <p><b>Treating post-stroke depression</b></p> <ol style="list-style-type: none"> <li>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).</li> <li>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).</li> <li>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).</li> <li>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).</li> </ol> <p><b>Emotional lability</b></p> <ol style="list-style-type: none"> <li>Patients with post-stroke emotionalism may be considered for a course of antidepressant medication (B).</li> <li>Possible side effects of antidepressant treatment should be explained to patients prior to commencing treatment (GPP).</li> <li>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.</li> </ol> <p><b>Post-stroke emotional adjustment</b></p> <ol style="list-style-type: none"> <li>People who have had a stroke should be considered for workbook approaches that aim to address their beliefs and attitudes about their recovery (GPP).</li> </ol> <p><b>Summary of Recommendations</b></p> <ol style="list-style-type: none"> <li>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).</li> <li>All stroke patients (including those cared for in primary care) should be screened for mood disturbance (GPP).</li> <li>Some form of screening should occur, eg using the Stroke Aphasic Depression Questionnaire (SAD-Q) or General Health Questionnaire of 12 items (GHQ-12): <ul style="list-style-type: none"> <li>as early as appropriate and definitely before discharge, and</li> <li>at regular intervals thereafter</li> </ul> </li> <li>Clinical judgement should be used to determine how regularly mood should be re-assessed (GPP).</li> </ol>

Guideline	Recommendations
	<p>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).</p>
<p><b>VA/DoD clinical practice guideline for the management of stroke rehabilitation 2010.</b></p>	<p><b>Post stroke depression</b></p> <ol style="list-style-type: none"> <li>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).</li> <li>2. Patients diagnosed with moderate to severe depression after stroke should be referred to Mental Health specialty for evaluation and treatment.</li> <li>3. There is conflicting evidence regarding the use of routine pharmacotherapy or psychotherapy to prevent depression or other mood disorders following stroke.</li> <li>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.</li> <li>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.</li> </ol> <p><b>Other Mood Disorders</b></p> <ol style="list-style-type: none"> <li>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]</li> <li>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.</li> <li>8. Recommend skills training regarding Activities of Daily Living (ADL's), and psychoeducation regarding stroke recovery with the family.</li> <li>9. Encourage the patient with stroke to become involved in physical and/or other leisure activities.</li> </ol> <p><b>Assessment of emotional and behavioral state</b></p> <ol style="list-style-type: none"> <li>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.</li> <li>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.</li> <li>3. Review all medications and supplements including over the counter (OTC) medications that may affect behavior and function.</li> <li>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.</li> <li>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.)</li> <li>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.</li> </ol>

Guideline	Recommendations
	<p><b>Use of standardized assessments</b></p> <ol style="list-style-type: none"> <li>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]</li> </ol>
<p><b>Duncan PW, Zorowitz R, Bates B, et al. Management of adult stroke rehabilitation care: a clinical practice guideline. Stroke 2005;36:e100-e143.</b></p>	<p><b>Mood Disturbance</b></p> <ol style="list-style-type: none"> <li>1. The Working Group makes no recommendation for the use of any specific diagnostic tool over another.</li> <li>2. Recommend using a structured inventory to assess specific psychiatric symptoms and monitor symptom change over time (refer to the VA/DoD Guideline for Management of Major Depressive Disorder at <a href="http://www.oqp.med.va.gov/cpg/MDD/MDD_Base.htm">http://www.oqp.med.va.gov/cpg/MDD/MDD_Base.htm</a>).</li> <li>3. Recommend assessing poststroke patients for other psychiatric illnesses, including anxiety, bipolar illness, and pathological affect.</li> <li>4. Strongly recommend that patients with a diagnosed depressive disorder be given a trial of antidepressant medication, if no contraindication exists.</li> <li>5. The Working Group makes no recommendation for the use of 1 class of antidepressants over another; however, side effect profiles suggest that SSRIs may be favored in this patient population.</li> <li>6. Recommend patients with severe, persistent, or troublesome tearfulness be given a trial on antidepressant medications.</li> <li>7. Recommend SSRIs as the antidepressant of choice in patients with severe, persistent, or troublesome tearfulness.</li> <li>8. There is insufficient evidence to recommend for or against the use of individual psychotherapy alone in the treatment of PSD.</li> <li>9. Recommend patients be given information, advice, and the opportunity to talk about the impact of the illness on their lives.</li> <li>10. Routine use of prophylactic antidepressants is not recommended in poststroke patients.</li> <li>11. Recommend that mood disorders causing persistent distress or worsening disability be managed by, or with the advice of, an experienced clinical psychologist or psychiatrist.</li> </ol> <p><b>The use of standardized assessment tools</b></p> <ol style="list-style-type: none"> <li>1. Recommend that all patients be screened for depression and motor, sensory, cognitive, communication, and swallowing deficits by appropriately trained clinicians, using standardized and valid screening tools. Recommend that if depression and motor, sensory, cognitive, communication, and swallowing deficits are found, all patients should be formally assessed by the appropriate clinician from the coordinated rehabilitation team.</li> </ol>



## Evidence Tables

### Non-pharmacotherapy for the Treatment of Diagnosed PSD

#### Meta-analyses

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
<b>Wilson et al. 2009</b>  <b>Cochrane Review &amp; Meta-analysis</b>	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 standardised rating scales.	Studies were identified via searches of electronic databases and hand searching the Journal of Geriatric Psychiatry, the Irish Journal of Psychiatry and reference lists of systematic reviews and identified articles. All types of psychotherapeutic interventions were included and were categorised as cognitive behavioural therapies (CBT), psychodynamic therapy, interpersonal therapy, and supportive therapy.	Primary outcomes for the analyses were reduction in the severity of symptoms of depression. Secondary outcomes included study dropouts and ratings of life satisfaction.	<p>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 in 5 of these studies participants, 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).</p> <p>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).</p> <p>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).</p> <p>The authors note that, given the relatively few, small trials included in the analyses, the results do not provide strong support for the use of psychotherapeutic interventions in this population.</p>
<b>Hackett et al. 2008</b>  <b>Cochrane Review &amp; Meta-analysis</b>	N/A	This review and meta-analysis included both pharmacological interventions and non-pharmacological interventions. There were <b>4 trials</b> identified that	Cochrane literature search and review. Identified randomised controlled trials comparing pharmacological trials with placebo, or various	Primary analyses investigated the prevalence of diagnosable depressive disorder following treatment. Secondary outcomes included depression rating scale	There were 16 trials in all – 12 addressed the effectiveness of pharmacotherapy, 4 examined various forms of psychotherapy. There were no trials of ECT included in the analyses. Forms of psychotherapy identified were: problem-solving therapy + counselling delivered by social workers, structured CBT, motivational

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		assessed the effectiveness of psychological interventions.	forms of psychotherapy or ECT with usual care (or attention control) in individuals with stroke for the purposes of treating PSD.	scores, physical function, and mortality.	<p>interviewing and a supportive psychological intervention including education. Frequency and duration of intervention varied. Data was available from 445 participants from 3 of the identified trials. There was no treatment effect associated with psychotherapy on any of the endpoints measured.</p> <p><b>Please note:</b> Not all of these studies were, strictly speaking, treatments for a diagnosed depressive disorder. For example in Watkins et al (2007) which described motivational interviewing and was included in this analysis, patients were not necessarily depressed at baseline and there was no diagnostic assessment of participants at study entry. Mood, not depression, was assessed at baseline using the GHQ-28 and the vast majority (197/207 and 195/204 in the control and intervention groups respectively) of participants had “normal mood”.</p>

## Cognitive Behaviour Therapy (CBT)

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
<b>Alexopoulos et al. 2012</b>  <b>RCT</b>	CA: <input checked="" type="checkbox"/>  Blinding: Patient <input checked="" type="checkbox"/> Therapist <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/>  ITT: <input checked="" type="checkbox"/>	24 individuals diagnosed with post stroke depression (via SCI for DSM-IV-TR), MMSE $\geq 20$ . Individuals with mild to moderate aphasia could be included in the study. 58.3% of participants were male. Mean age = 70.9 $\pm$ 8.5 years. Patients were recruited during inpatient rehabilitation following stroke	Participants were randomly assigned to receive either ecosystem focused therapy (EFT) or education on stroke and depression (ESD). EFT was provided in 12 weekly sessions of approximately 45 minutes in length. Inpatients had the first session prior to	Primary study outcome was the reduction of depression and disability. Severity of depression was quantified using the HRSD. The WHODAS-II was also administered as an assessment of function.  <b>Assessment Points:</b> Baseline, weekly during throughout the study.	Treatment X time analysis using a mixed effects linear model revealed an interaction suggesting that there was a trend toward greater decline in symptoms of depression associated with EFT vs. ESD or education ( $p=0.054$ ). The mean HRSD score at 12 weeks was 8.2 (sd=6.63) for individuals in the intervention group and 13.2 (sd=5.37) for individuals assigned to the education control group. In addition, remission of depression was recorded for 8/12 participants receiving EFT (66.7%) vs. 2/12 (16.7%) participants in the education group (OR = 10,

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			<p>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. Families and/or informal carers participated in sessions on an as-needed basis. Four therapists were trained in both EFT and ESD. All sessions were audiotaped.</p> <p><b>Duration of Intervention:</b> 12 weeks</p>		<p>95% CI 1.44, 69.26). The standardized between group effect size at the end of the intervention was 0.83 (95%CI =0.07, 1.72). In terms of disability, assignment to the EFT group was associated with greater gains in function over time (<math>p=0.015</math>). At 12 weeks, the standardized effect size between groups was 0.53 (95% CI -0.36, 1.43). It should be noted that 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.</p>
<p><b>Thomas et al. 2012</b></p> <p><b>UK</b></p> <p><b>RCT</b></p>	<p>CA: <input checked="" type="checkbox"/></p> <p>Blinding patient: <input checked="" type="checkbox"/></p> <p>Therapist <input checked="" type="checkbox"/></p> <p>assessor: <input checked="" type="checkbox"/></p>	<p>105 stroke patients with post stroke depression and aphasia.</p> <p>Individuals who were blind, deaf, had dementia, or received treatment for depression at the time of</p>	<p>Participants were randomized to receive behavioural therapy (<math>n=51</math>) or usual care (<math>n=54</math>). Behavioural therapy was provided by an assistant psychologist in up to 20, 1-hour</p>	<p><b>Primary outcome:</b> The Stroke Aphasic Depression Questionnaire (SADQ).</p> <p><b>Secondary outcomes:</b> The Visual Analogue ‘sad’ item, Visual Analogue Self-Esteem Scale, the</p>	<p>As compared to those in the control group, participants who received behavioural therapy reported significantly less depression on the SADQ at both the 3 (<math>p=0.05</math>) and 6 (<math>p=0.002</math>) month assessments, controlling for communication impairment SADQ scores at baseline. In an intention-to-treat sensitivity analysis, behavioural therapy was still</p>

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
	ITT: <input checked="" type="checkbox"/>	stroke were excluded.	sessions over the course of 3 months.	Nottingham Leisure Questionnaire, and the Carer Strain Index.  <b>Timing of assessment:</b> baseline and at 3 and 6 months.	significantly associated with SADQ scores at six months but not at 3 months. Scores on the visual analogue 'sad' item and the visual analogue self-esteem scale significantly favoured the intervention group at 3 months, controlling for communication impairment and SADQ at baseline, but not at six months.  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%.
<b>Chang et al. 2011</b>  <b>RCT</b>	CA: <input checked="" type="checkbox"/>  Blinding: Patient <input checked="" type="checkbox"/> Therapist <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/>  ITT: <input checked="" type="checkbox"/>	66 individuals with hemiplegic stroke and MMSE scores $\geq 24$ . Individuals with mild aphasia were included. Mean patient age = $58.86 \pm 10.4$ years. Time since stroke ranged from 28 to 264 days. Baseline HRSD scores were $26.49 (\pm 9.4)$ for male and $36.3 (\pm 9.4)$ for female participants).	Participants were randomly assigned to either a control group (n=32) or knowledge and behavioural therapy group (KBT) (n=34). Both groups received all regular inpatient rehabilitation interventions daily. KBT consisted of both knowledge and behavioural training (based on rational emotive behavioural therapy, a form of cognitive behavioural therapy). KBT was provided weekly in 1-2 hour sessions administered by a psychology graduate student over a one-month period. Behaviour training included belief change, forgiveness and anger	Primary outcome is not explicitly stated. Many variables are assessed including: Anger (State-Trait Anger Expression Inventory), Anxiety (Hamilton Anxiety Scale), Depression (Hamilton Rating Scale for Depression), Health related quality of life (Stroke Specific Quality of Life Scale), and physical function/activities of daily living (Barthel Index).  <b>Assessment Points:</b> Baseline, 1 month	At baseline, gender was strongly associated with depression. Female participants reported ( $p < 0.001$ ) more severe symptoms of depression than male participants. Group X time analyses were used to examine effects of treatment. KBT was associated with greater improvement over time when compared to the control condition in terms of symptoms of depression ( $F = 27.64$ , $p < 0.001$ ). When examining change in terms of effect sizes, the authors reported that the control group showed improvements in depression over time (within group: $t = -4$ , $p < 0.001$ , $d = -1.0$ ) while the experimental group also showed significant, though greater, improvement over the same period ( $t = -8.13$ , $p < 0.001$ , $d = -2.03$ ). Between group comparison of effect sizes was significant ( $p < 0.001$ ) in favour of the intervention. Overall, use of KBT was associated with significant improvement in anger, quality of life, and ADLs in addition to symptoms of depression.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			management training while the knowledge component addressed lifestyle risks and changes required to reduce risk for subsequent stroke.  <b>Duration of Intervention:</b> One month.		
<b>Lincoln and Flannaghan 2003</b>  <b>RCT</b>	CA: <input checked="" type="checkbox"/>  Blinding: Patient <input checked="" type="checkbox"/> Therapist <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/>  ITT: <input checked="" type="checkbox"/>	123 stroke patients identified via hospital records who were either living at home, in hospital or living in long-term care one-month post stroke with >10 score on Beck Depression Inventory (BDI) or >18 on Wakefield Depression Inventory (WDI). There were 60 patients with a primary diagnosis of major depression at baseline. Mean age of patients was 65 ±15.1 in the no intervention group, 66.1±13.2 in the attention group and 67.1±12.7 in the CBT group. 51% of participants were male. Potential participants were excluded if they scored ≤23 on the MMSE.	Participants were randomly allocated to one of 3 conditions: 1) no intervention (n=41), 2) attention placebo (n=43) and 3) CBT (n=39). Patients in condition 1 had no further contact with the community psychiatric nurse. Patients in the 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	Primary outcome measures were the BDI and the WDI. Secondary outcomes included the EADL scale, LHS and a rating of satisfaction of care.  <b>Assessment Points:</b> baseline, 3 and 6 months post-randomization.	Examination of between group differences at baseline revealed no significant differences except that 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). Mean number of CBT sessions delivered to participants was 9.85 (±2.31). Mean number of attention control sessions delivered was 10 (±0.55), but there was no significant between group difference reported in number of sessions received. For the primary study outcomes, the authors reported no significant difference on either the BDI or WDI at 3 months (p=0.5, p=0.9, respectively) or at 6 month follow-up (p=0.6, 0.4, respectively). It should be noted that 32% of the patients recruited did receive antidepressant therapy at some point during the study period. No between group differences were found in terms of the proportion of participants receiving antidepressant therapy ( $\chi^2=0.2$ , p=0.9).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			modification of unhelpful thoughts/beliefs – tailored to individual participants.  <b>Duration of Intervention:</b> 3 months.		

## Acupuncture

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
<b>Zhang, G.C. et al. 2012</b>  <b>Systematic Review and Meta-analysis</b>	N/A	15 randomized controlled trials evaluating acupuncture vs. “western medicine” where western medicine appeared to be pharmacotherapy. Overall, 1079 participants were included in the trials – ages ranged from 38-79.	Included studies all provided standardized diagnosis of PSD. Quality of RCTs was assessed using the Grade scale (though the results of this assessment were not reported clearly). Pooled analyses were conducted for dichotomous outcomes using odds ratios. Fixed effect models were used when no significant heterogeneity was identified.	“Curative effect” and “effective rate” of acupuncture vs. pharmacotherapy. While curative rate may be taken as remission of depression, the authors do not provide any definition for “effective rate” or “obvious effective rate”, which they also report.  All studies used the HRSD to evaluate outcome, so pooled analysis is based on assessment using a single tool.	All studies provided comparisons between acupuncture and pharmacotherapy or “western” treatments for depression. Duration of treatment ranged from 14 days to 2 months. On pooled analysis, the authors reported a significant effect in favour of acupuncture in terms of “curative rate”, such that treatment with acupuncture was associated with improved odds of recovery/remission when compared with pharmacotherapy (OR=1.48, 95% CI 1.10, 1.97). They also reported an “obvious effective rate” which was not defined that was also in favour of acupuncture (OR=1.39, 95% CI 1.08, 1.8); however, it was not possible to determine, from the data or figures provided, to what this might refer. The “effective rate”, which was also not defined by the authors, was not significantly in favour of either treatment (OR=0.83, 95% CI 0.63, 1.09, p=0.18).  <b>Adverse events:</b> The authors provide no assessment of adverse events.
<b>Zhang, Z.J et al. 2010</b>	N/A	53 trials were identified as high-quality RCTs (Jadad scores $\geq 3$ ). 20 of these	All studies included diagnoses of depression based on standardized	Treatment outcomes included dichotomous and continuous data.	All studies used the HRSD for evaluation of study endpoints. 12 trials compared acupuncture monotherapy to pharmacotherapy,

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
<b>Systematic Review and Meta-analysis</b>		trials evaluated the use of acupuncture in the treatment of post stroke depression. 15 were included for analysis (n=1680).	<p>classification (ICD, Chinese classification of mental disorder or DSM). For PSD, addition diagnostic criteria included verification of stroke (either ischemic or haemorrhagic). Methodological quality of studies was assessed using a modified Jadad scale.</p> <p>Acupuncture intervention was compared against controlled comparison conditions (pharmacotherapy, sham acupuncture and waitlist controls).</p> <p>On pooled analysis, dichotomous data was analysed using risk ratios, weighted mean differences for continuous data. Differences in changes between groups from baseline to end of intervention were expressed using Cohen's d effect sizes. Heterogeneity was assessed using the <math>I^2</math> statistic. High heterogeneity was defined as <math>&gt;50\%</math>.</p>	<p>Response rates (dichotomous) were defined as <math>\geq 50\%</math> reduction in scores on assessment of depression (HRSD usually) from baseline. Continuous data were baseline to endpoint changes in score on scales used to assess depression (usually HRSD). Adverse events recorded in the included studies were pooled for analysis where possible.</p>	<p>3 compared it to waitlist control groups. Fluoxetine 20mg/day was the most commonly prescribed antidepressant in these studies. 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 treatment from 4 to 8 weeks.</p> <p>On pooled analysis, active acupuncture therapy was associated with improved response rates when compared with antidepressant therapy (RR=1.43, 95% CI 0.19, 2.68, <math>p=0.02</math>). However, significant heterogeneity was associated with this analysis (<math>I^2=70\%</math>). The authors suggest that this may be attributed to wide between-study variation in number and locations of acupoints used, stimulation modes, number of treatment sessions and duration of treatment.</p> <p>Pooled analysis of the 3 studies that compared acupuncture to waitlisted control groups demonstrated a significant effect in favour of acupuncture (RR=7.24, 95% CI 5.05,9.46) and no significant heterogeneity (<math>I^2=0\%</math>).</p> <p><b>Adverse Events:</b> The authors provided a pooled analysis of all trials – those for MDD and PSD together for adverse events. Overall, patients treated with active or sham acupuncture reported fewer side effects than those treated with antidepressants (10.2% vs. 40.4%, <math>\chi^2=389.46</math>, <math>p&lt;0.001</math>). The most commonly reported side effects associated with acupuncture included needling pain, transient dizziness and nausea.</p>



## Other Non-pharmacological Interventions

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
<b>Huang et al. 2012</b>  <b>China</b>  <b>Controlled Before and After Study</b>	N/A	182 ischemic stroke patients with post-stroke depression and high-grade carotid artery stenosis.  <b>Exclusion criteria:</b> history of mental disorders, consciousness disturbances, aphasia, or dementia.	All participants were offered the choice of carotid angioplasty stent placement (CAS), of which 104 underwent the procedure. The 78 participants who refused CAS were prescribed fluoxetine titrated to 20-40mg per day.	Depression was assessed with the Hamilton Depression Rating Scale (HDRS).  <b>Timing of assessment:</b> baseline and at 1 and 3 months.	As compared to those who received fluoxetine, participants who underwent CAS reported significantly lower scores on the HDRS at 1 month ( $p=0.005$ ); however, differences between the two groups were no longer significant at the 3 month follow-up. Receipts
<b>Smith et al. 2012</b>  <b>US</b>  <b>RCT</b>	CA: <input checked="" type="checkbox"/>  Blinding patient: <input checked="" type="checkbox"/> Therapist <input checked="" type="checkbox"/> assessor: <input checked="" type="checkbox"/>  ITT: <input checked="" type="checkbox"/>	38 caregiver-stroke survivor dyads in which a spouse provided care at home to a male stroke survivor. At least one dyad member had mild or more severe depression and neither was medically unstable or terminally ill at the time of recruitment.  23.6% of those screened for eligibility were included in the study.	Participants were randomized to a web-based intervention group ( $n=19$ ) or to an information-only control group ( $n=19$ ). 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.  <b>Duration of intervention:</b> 11 weeks	Outcome measures included the Centre for Epidemiological Studies Depression Scale (CESD), the Patient Health Questionnaire (PHQ-9), the Mastery Scale, the Self-Esteem Scale, and the Social Support Survey.  <b>Timing of assessment:</b> baseline, post-intervention, and 1-month follow-up.	Caregivers who received the active intervention reported significantly lower scores on the CESD at both the post-intervention (Effect Size (ES)=-0.79) and follow-up assessments (ES=-0.52), as compared to participants in the control condition ( $p<0.01$ ). Between group comparison of stroke survivors scores on the CESD did not differ significantly at any time point. No significant between group comparisons were reported for any of the secondary outcomes for either the stroke survivors or their caregivers.  <b>Lost to follow-up:</b> intervention group = 21.1%, control group = 10.5%.
<b>Kim et al. 2010</b>  <b>RCT</b>	CA: <input checked="" type="checkbox"/>  Blinding: Patient <input checked="" type="checkbox"/> Therapist <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/>  ITT: <input checked="" type="checkbox"/>	18 individuals (10 male) with stroke at least one month prior were recruited. Mean age = 62.9 years (range: 55-70). All patients could follow simple commands, MMSE ranged from 10 – 24.	Participants were randomly assigned to one of three treatment groups; low-frequency (1 Hz), high-frequency (10Hz) or sham (control) rTMS stimulation to the left dorsolateral prefrontal cortex (DLPFC). Low frequency stimulation	No primary outcome was stipulated.  The effect of rTMS treatment on mood was assessed using the Beck Depression Inventory.  <b>Assessment Points:</b> Baseline and immediately following completion of the	50% of participants in the rTMS conditions were treated with antidepressants at baseline as were 66.7% of patients assigned to the sham condition. No changes to antidepressant medications were made during rTMS treatment. Over time, high frequency rTMS was associated with a reduction in BDI scores (Wilcoxon $Z=-11.20$ , $p=0.04$ ). In addition the post-treatment BDI score in the high frequency rTMS group was significantly lower than the post treatment BDI scores in either the low frequency rTMS group or



Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			<p>consisted of 1 HZ stimulation at 80% MT in 3 trains of 5 min duration each separated by 1 min pauses over a total of 20 minutes. High frequency stimulation was 10-HZ at 80% MT in 3 blocks each separated by a 10 minute interval. Sham stimulation mimicked the low intensity intervention except the angle of the coil was placed at 990% perpendicular to the skull.</p> <p>Patients received 10 treatment session; 5 times per week over a 2-week period). During the study period, all participants also received conventional cognitive rehabilitation 2 or 3 times per week. Evaluations included the Computerized Neuropsychological Test (digit span, visual span, verbal learning, visual learning, visual continuous performance, auditory continuous performance &amp; word-colour tests), the Tower of London Test (planning ability), the modified Barthel Index and Beck Depression Inventory.</p> <p><b>Duration of Intervention:</b> 2 weeks</p>	rTMS protocol.	<p>sham group (3.3 ±2.3 vs. 13.8±8.5 vs. 14.0±8.3, p=0.02).</p> <p>Treatment at either frequency was not associated with any significant difference on any cognitive assessment including Tower of London reaction time when compared to the control group.</p> <p><b>Side Effects:</b> No major side effects, such as seizures, were reported by patients in either treatment condition.</p>

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
<b>Jorge et al. 2004</b>  <b>RCT</b>	CA: <input checked="" type="checkbox"/>  Blinding: Patient <input checked="" type="checkbox"/> Therapist <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/>  ITT: <input checked="" type="checkbox"/>	20 patients with hemispheric, brainstem or cerebellar stroke and DSM-IV diagnosis of depression. Patients with MMSE $\leq$ 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 ( $\pm$ 8.1) and 66.5 ( $\pm$ 12.2) in the sham condition. 9/20 participants 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 over a 2-week period.	Primary outcome was response and remission rates 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. Remission was defined as reduction of HRSD scores by at least 50% and final HRSD scores $<$ 8. Adverse events were recorded on case report forms and graded on a three point scale: 1. Mild, 2. Moderate and 3. Severe.  <b>Assessment Points:</b> Baseline, 1 week post intervention.	Active rTMS treatment was associated with a significant reduction in depressive symptomatology assessed on the HRSD ( $p < 0.0006$ ). Results of cognitive and neuropsychological testing revealed no significant differences between sham and active treatment groups.  <b>Adverse events:</b> 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).

## Specific Treatments of Mild Depression or Dysthymia

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
<b>Lamers et al. 2010</b>  <b>RCT</b>	CA: <input checked="" type="checkbox"/>  Blinding: Patient <input checked="" type="checkbox"/> Therapist <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/>  ITT: <input checked="" type="checkbox"/>	This study included 361 primary care patients 60 years of age or older with both a chronic health condition (chronic obstructive pulmonary disease or type II diabetes mellitus) and minor depression or mild-moderate major depression.	Patients were randomly assigned to either the intervention group ( $n = 183$ ) or care as usual ( $n = 178$ ). The intervention, which combined cognitive behavioural therapy and self-management, was delivered by a trained	Depression was assessed with the Beck Depression Inventory (BDI), which was considered both continuously and dichotomously ( $\geq 50\%$ reduction in score). Quality of life was also assessed using the P0physical and Mental components scales	Patients in the intervention group reported significantly fewer depressive symptoms than patients in the usual care group at both 3 and 9 months (mean difference = 1.61 & 2.09, respectively, both significant at $p < .05$ ). At nine months, patients receiving the active intervention were also more likely to have experienced a 50% decrease in depressive symptoms, controlling for age, sex, education level, time, and baseline BDI (OR = 3.22; 95% CI = 1.31 –

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		Patients with severe depression (HAM-D $\geq 18$ ) were excluded.	nurse in the patient's home for a total of 2-10 1 hour visits.  <u>Study Period:</u> (at most) 3 months	of the SF-36.  <u>Time points for assessment:</u> Baseline, 1 week, 3 and 9 months.	7.89). Although no overall differences were found with respect to quality of life, in stratified analyses diabetic patients in the intervention arm reported having a significantly better quality of life scores at 9 months, as compared to diabetic patients in the control arm (mean difference = 3.85, $p < 0.05$ ).
<b>Jonkers et al. 2012</b>  <b>RCT</b>	CA: <input checked="" type="checkbox"/>  Blinding: Patient <input checked="" type="checkbox"/> Therapist <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/>  ITT: <input checked="" type="checkbox"/>	This article presents a secondary analysis of data presented in Lamers et al. (2010). Please refer to the sample description provided for Lamers et al. (above).	Please refer to the methods description provided for Lamers et al. (above).	Outcomes included the Self-Efficacy Scale, the Anxiety subscale of the SCL-90, daily functioning (assessed with the Activities of Daily Living scale & the Groningen Activity Restriction Scale), and social participation (assessed with selected items from the Impact on Participation and Autonomy questionnaire).  <u>Time points for assessment:</u> Baseline, 1 week, 3 and 9 months.	Patients in the intervention group reported better self-efficacy (Effect size [ES] = .27 & .29), daily functioning (ES = .42 & .40), and social participation (ES = .22 & .39) at both the 3 month and 9 month follow-up (respectively), all significant at $p < 0.05$ , controlling for age, sex, education level, chronic condition type, and baseline score for each respective outcome. Patients in the active treatment arm also reported significantly less anxiety than those in the control arm at 9 months (ES = .37, $p < 0.05$ ), controlling for the same variables listed above. It should be noted that differences between the two study conditions appear to reflect deterioration of outcomes in the control group and stabilization (rather than improvement) in the intervention group. No differences were found between patients with different chronic conditions.
<b>Williams et al. 2000</b>  <b>RCT</b>	CA: <input checked="" type="checkbox"/>  Blinding: Patient <input checked="" type="checkbox"/> Therapist <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/>  ITT: <input checked="" type="checkbox"/>	This study included 415 primary care patients 60 years of age or older who met the criteria for diagnosis with either dysthymia or minor depression and who scored $\geq 10$ on the HAM-D. Patients meeting the criteria for diagnosis of major depression were excluded.	Patients were randomized to one of three conditions: placebo ( $n = 140$ ), treatment with paroxetine (10-40mg/d; $n = 137$ ), or problem-solving treatment ( $n = 138$ ). The problem solving treatment, which was based on cognitive-behavioural principles, was provided for 1 hour at the first session and 30 minutes thereafter. All treatments were	The primary outcome was change on the the Hopkins Symptom Checklist Depression Scale (HSCL-D-20), with 7 additional items added to 'increase responsiveness'. The SF-36 was also assessed.  <u>Time points for assessment:</u> The primary outcome was assessed at baseline and at the 1, 2, 4, 6, 8, and 11 week follow-ups. Other outcomes were	Reduction in depression symptomatology for patients in the psychotherapy group did not differ significantly as to compared to patients in the placebo group (mean difference = 0.11, $p > 0.05$ ) or the paroxetine group (mean difference = 0.09, $p > 0.05$ ). However, patients in the pharmacotherapy condition reported a significantly greater reduction in depression symptomatology than those in the placebo condition (mean difference = 0.21, $p < 0.05$ ). Although psychotherapy did not appear to have a significant impact on mental health functioning for most of the participants in this study, for participants with minor depression who were in the lowest tertile of baseline functioning, those

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			provided for a total of 6 sessions.  Study period: 11 weeks	assessed at baseline and at 6 and 11 weeks.	randomized to problem-solving treatment improved significantly more as compared to those randomized to the placebo condition (mean difference = 4.7, $p < 0.05$ ).
<b>van't Veer-Tazelaar et al. 2009</b>  <b>RCT</b>	CA: <input checked="" type="checkbox"/>  Blinding: Patient <input checked="" type="checkbox"/> Therapist <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/>  ITT: <input checked="" type="checkbox"/>	This study included 170 primary care patients 75 years of age or older with CES-D scores $\geq 16$ . Individuals meeting diagnostic criteria for a depressive or anxiety disorder (at study entry or during the previous year) were excluded.	Participants were randomized to either a stepped-care program ( $n = 86$ ) or care as usual (which may have included pharmacotherapy or psychotherapy; $n = 84$ ). Stepped care sequentially included watchful waiting, CBT-based bibliotherapy, CBT-based problem-solving, and referral to primary care.  Study period: 1 year	The primary outcome was incidence of major depressive disorder or anxiety disorder, as determined by the Mini International Neuropsychiatric Interview (MINI). The CES-D was also assessed.  <u>Time points for assessment:</u> The MINI was assessed at baseline and at 6 and 12 month follow-ups, whereas the CES-D was assessed every 3 months.	As compared to the treatment group in which 11.6% (10/86) of participants developed a major depression or anxiety disorder, 23.8% (20/84) of those in the usual care group developed such a disorder (Relative Risk = 0.49; 95% CI 0.24 – 0.98, $p < 0.05$ ). The number needed to treat to prevent the onset of a major depression and/or anxiety disorder was 8.2.
<b>Dozeman et al. 2012</b>  <b>RCT</b>	CA: <input checked="" type="checkbox"/>  Blinding: Patient <input checked="" type="checkbox"/> Therapist <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/>  ITT: <input checked="" type="checkbox"/>	This study included 185 individuals 60 years of age or older living in a residential home who scored $\geq 8$ on the CES-D. Individuals meeting diagnostic criteria for a depressive or anxiety disorder were excluded.	Participants were randomized to either a stepped-care program ( $n = 93$ ) or care as usual (which may have included pharmacotherapy or psychotherapy; $n = 92$ ). Stepped care sequentially included watchful waiting, activity-scheduling, life review, and consultation with a general practitioner.  Study period: 1 year	The primary outcome was incidence of major depressive disorder or anxiety disorder, as determined by the Mini International Neuropsychiatric Interview (MINI). Depressive (CES-D) and anxiety (HADS-A) symptomatology and were also assessed.  <u>Time points for assessment:</u> Baseline and 1, 4, 7, 10, and 12 month follow-up.	6/93 (6.5%) participants in the intervention group and 13/92 (14.1%) participants in the usual care group developed a depressive disorder over the course of the study. This difference resulted in an adjusted incidence rate ratio (IRR) = 0.26 (95% CI = 0.12 – 0.80, $p < 0.05$ ). 8/93 (8.6%) participants in the intervention group and 4/92 (4.4%) participants in the usual care group developed an anxiety disorder: this difference in incidence was not significant (adjusted IRR = 1.32 (95% CI 0.48 – 3.62, $p > 0.05$ ). Similarly, comparison of the combined incidence of depression and anxiety disorders between the two groups was not significant (adjusted IRR = 0.50 (95% CI 0.23 – 1.12, $p > 0.05$ ).
<b>Moss et al. 2012</b>  <b>RCT</b>	CA: <input checked="" type="checkbox"/>  Blinding: Patient <input checked="" type="checkbox"/>	This study included 26 community-dwelling adults 65 years of age or older who scored $\geq 5$ on the Geriatric Depression Scale (GDS).	Participants were randomized to either a waitlist control group ( $n = 13$ ) or to behavioural activation bibliotherapy	The primary outcome measure was clinician-rated HAM-D. Participants also completed the self-report GDS.	Participants in the active treatment group were rated as having significantly fewer depressive symptoms following the 1-month treatment as compared to those in the control group, adjusting for baseline symptomatology ( $F_{(1, 23)} = 10.16$ , $p <$

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
	Therapist <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/>  ITT: <input checked="" type="checkbox"/>	Participants were not formally assessed for a depressive disorder at baseline and participants with elevated scores on the GDS were not excluded (baseline GDS scores ranged from 2-23).	(n = 13). Participants in the control condition were offered the active treatment following a 1-month delay.  <u>Study period:</u> 1 month treatment follow-up by a 1-month follow-up	Time points for <u>assessment:</u> Assessments were completed at baseline, post-treatment, and 1-month follow-up.	0.05). The treatment effect size was large ( $d = 1.08$ ). Between group comparisons based on the self-report GDS were not significant.

## Interventions that May Improve Symptoms of Depression

### Physical Exercise

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
<b>Chaipayat &amp; Kulkantrakorn 2012</b>  <b>Thailand</b>  <b>RCT</b>	CA: <input checked="" type="checkbox"/>  Blinding patient: <input checked="" type="checkbox"/> Therapist <input checked="" type="checkbox"/> assessor: <input checked="" type="checkbox"/>  ITT: <input checked="" type="checkbox"/>	60 patients with middle cerebral artery infarction.  <b>Exclusion criteria:</b> uncontrolled hypertension, severe dysphasia, severe cognitive impairment, and pre-or post-stroke residence in a nursing home.  88% of those screened for eligibility were included in the study.	Participants were randomized to receive a 6-month home-based exercise program (n=30) or standard care (n=30). The exercise program was provided once per month for six months by a physiotherapist who selected exercise sequences from a video library. Participants in the intervention group were asked to watch the videos once per day.	Depression was assessed with the Hospital Anxiety and Depression Scale (HADS), with presence of depression defined as a score >10. Other outcome measures included the Mini-Mental State Examination and the Barthel Index.  <b>Timing of assessment:</b> baseline and at 1, 2, 4, 12, and 24 months following hospital discharge.	Treatment compliance in the intervention group was reported to be 92-95%. Participants in both groups experienced significant reductions in depression severity during the study period. At the 24-month follow-up, participants in the intervention group reported a significantly lower mean score on the HADS, controlling for age, depression, and dementia at baseline ( $p=0.01$ ).
<b>Chan et al. 2012</b>  <b>RCT</b>	CA: <input checked="" type="checkbox"/>  Blinding: Patient <input checked="" type="checkbox"/> Therapist <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/>	14 outpatients with a minimum of 6 months post stroke and incidence of chronic hemiparesis where recruited. All individuals must have completed acute and post-acute stroke	Patients were randomly assigned to either the yoga/exercise group (YEX) or to the exercise group (EX). The YEX group (n=8) consisted of six 90 min yoga sessions	Self-reported symptoms of depression were assessed using the Geriatric Depression Scale (GDS15). Symptoms of anxiety and negative were measured using the State Trait	There were no significant differences in changes of depression and state and trait anxiety between groups post intervention (GDS15 $P=0.749$ , STAI-Y1, $P=0.595$ , STAI-Y2, $P=0.407$ ).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
	ITT: <input checked="" type="checkbox"/>	rehabilitation and able to ambulate 10 m with or without an assistive device. A pre-intervention diagnosis of depression was not reported. The mean age in the yoga/exercise (YEX) group was 67.1 +/- 15.4 years and 71.7 +/- 12.7 years in the exercise (EX) group. The mean time since for the YEX group was 6.4 ±3 years and 11.2 +/- 5.8 years for the EX group.	1x/week along with home practice sessions. They also participated in six 50 min exercise sessions 1x/week. The EX group (n=6) participated only in the group exercises classes which was weekly for 6 weeks.  <u>Study Period</u> = 6 week intervention	Anxiety Inventory (STAI)  <b>Assessment Points:</b> Baseline and 6 weeks	
<b>Lai et al. 2006</b>  <b>RCT</b>	CA: <input checked="" type="checkbox"/>  Blinding: Patient <input checked="" type="checkbox"/> Therapist <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/>  ITT: <input checked="" type="checkbox"/>	100 stroke patients that completed acute rehabilitation were randomized into an exercise group and a usual care group. Although depression is the major outcome for this study population, no pre-intervention diagnosis was reported. The mean age = 68.5±9 for the exercise group and 70.4±11.3 in the usual care group. Days post stroke = 77.5±28.7 for the exercise group and 74.1±27.2 for the usual care group.	The exercise group (n=44) consisted of a 36 session therapist supervised in home program. The exercise protocol was based on a structured and progressive program designed to improve strength, balance, and endurance. For 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.  <u>Study Period</u> = 9 months	Depressive symptoms were assessed using the Geriatric Depression Scale (GDS15). The SF-36 and the Stroke Impact Scale (SIS) was used to measure quality of life. The Orpington Prognostic Score was used to measure stroke severity and number of other measures where used to measure stroke related impairments: Berg Balance Scale (BBS), grip strength, functional reach, lower extremity isometric strength, gait speed, endurance, 6MWT, Wolfe motor function test  <b>Assessment Points:</b> Baseline, 3, and 9 months	Only 18% of the exercise group and 22% of the usual care group had depressive symptoms according to the GDS15 at baseline. At 3 months, 15% of the exercise group and 35.6% of the usual care group had depressive symptoms (P=0.03) and at 9 months 7.5% for the exercise group and 25% for the usual care group (P=0.07). There was a positive trend regarding the other outcome measures for the exercise group but only participants with depressive symptoms had improved quality of life.
<b>Mead et al. 2007</b>  <b>RCT</b>	CA: <input checked="" type="checkbox"/>  Blinding: Patient <input checked="" type="checkbox"/> Therapist	66 independently ambulatory stroke patients without significant dysphasia, confusion, or medical contraindications, who have completed their	Patients were randomly assigned to receive a 12-week outpatient program of progressive strength and resistance exercises (n=32) or	The study team used the following outcome measures: FIM, Nottingham extended Activities of Daily Living, Rivermead Mobility Score, TUG, SF-36,	At 3 and 7 months, the assessment for depression identified no significant within-group change over time (ES=0.008, 0.001) and no significant between group differences (p=0.49, 0.82).



Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
	<input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/> ITT: <input checked="" type="checkbox"/>	acute rehabilitation and have been discharged from hospital. The mean age and median number of days since stroke for the exercise group are: 72.0±10.4 and 171 (55-287); and for the relaxation group: 71.7±9.6 and 147.5(78.8-235.5)	relaxation (n=34). Treatment sessions were 1.5 hours, 3x/week.  <u>Study Period</u> = 7 months	Hospital Anxiety and Depression Scale (HADS), and aspects of physical fitness (gait speed, leg extensor power, and walking economy).  <u>Assessment Points:</u> Baseline, 3, and 7 months	
<b>Brittle et al. 2009</b>  <b>RCT</b>	CA: <input checked="" type="checkbox"/>  Blinding: Patient <input checked="" type="checkbox"/> Therapist <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/>  ITT: <input checked="" type="checkbox"/>	56 residents from 5 Long term care facilities with self-care dependency needs. The mean (SD) age and number of patients with a confirmed stroke for the exercise group are: 87(6.99) and n=7(25%); and for the control group: 82(9.98) and n=6(21%)	Randomization was done by facility. The exercise group (n=28) focused on flexibility, sitting balance, posture, coordination, strengthening, and cardiovascular fitness. Sessions were 40-60 min in length and were provided 2x/week for 5 weeks. The usual care group (n=28) received no physiotherapy or exercise training.  <u>Study Period</u> = 6 months	Outcome measures included the Rivermead Mobility Index, Hospital Anxiety and Depression Scale (HADS), and the Stroke aphasic Depression Scale (SADQ)  <u>Assessment Points:</u> Baseline, 3, and 6 months	There were no significant improvements were found in favor of the exercise group for any of the outcomes assessed. Participants with severe cognitive impairment had difficulty participating in the intervention.  <u>Adverse Events:</u> Although some of the more cognitively impaired subjects were disruptive in the intervention sessions, there were no reported adverse events related to the study.
<b>Harrington et al. 2010</b>  <b>RCT</b>	CA: <input checked="" type="checkbox"/>  Blinding: Patient <input checked="" type="checkbox"/> Therapist <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/>  ITT: <input checked="" type="checkbox"/>	243 community dwelling patients aged greater than 50, with a median (IQR) time post stroke of 10.3(5.4-17.1) months. The mean (SD) age for the exercise group was 70(10.2) and 71(10.5) for the standard care group.	Participants were randomly allocated to either receive standard care (n=124) or a peer-volunteer-facilitated exercise and education intervention (n=119). The exercise intervention was focused on balance, endurance, strength, flexibility, function and wellbeing. Each session consisted of 1 hour of exercise, followed by a short break and 1 hour of education.	The primary study outcomes were the Subjective Index of Physical and Social Outcome (SIPSO), the Frenchay Activities Index (FAI), the Rivermead Mobility Index (RMI).  Secondary outcomes were and the WHOQoL-Bref, The functional reach test, TUG, and Hospital Anxiety and Depression Scale (HADS).	There was a significant difference of improvement in the psychological domain of the WHOQoL-Bref at 6 months (P=0.01), there were no significant differences noted in the other secondary outcomes, including depression.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			The program ran 2x/week for 8 weeks.  Study Period = 1 year	<b>Assessment Points:</b> Baseline, 9 weeks, 6 months, and 1 year	
<b>Lennon et al. 2008</b>  <b>RCT</b>	CA: <input checked="" type="checkbox"/>  Blinding: Patient <input checked="" type="checkbox"/> Therapist <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/>  ITT: <input checked="" type="checkbox"/>	48 community dwelling ischemic stroke patients (> 1 year post stroke). The mean (SD) age and time since stroke for the intervention group was 59.0(10.3) years and 237.3(110.3) weeks. For the control group, their age was 60.5(10.0) years and time since stroke was 245.3(169.8) weeks.	Patients were random assigned to either regular physiotherapy and occupational therapy services in addition to a cardiac rehabilitation program (intervention, n=24) or to usual therapy services (control, n=24). The intervention group attended a 30 min cardiac rehabilitation program using a cycle ergometer 2x/week for 10 weeks. They exercised at 50-60% of their maximal heart rate. In addition they attended 2 life skills classes. The control group received no additional intervention beyond usual physiotherapy and occupational therapy services.  Study Period = 10 weeks	The primary outcome measures included V0 <sub>2</sub> , Cardiac Risk Score, rate of perceived exertion (RPE), resting blood pressure, and fasting lipid profiles.  Secondary outcomes included the Frenchay Activity Index (FAI), and the Hospital Anxiety and Depression Scale (HADS).  <b>Assessment Points:</b> Baseline and 10 weeks	Pre and post assessment of depression using the HADS showed improvement over time within the intervention group (5.1±3.4 to 3.0±2.8; p<0.001). However, no significant difference was noted for between group analysis (p=0.22).
<b>Sims et al. 2009</b>  <b>RCT</b>	CA: <input checked="" type="checkbox"/>  Blinding: Patient <input checked="" type="checkbox"/> Therapist <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/>	45 patients > 6 months post stroke diagnosed with post stroke depression (PSD). The PHQ-9 depression model was used to screen patients. Scores of ≥5 were identified as having PSD.	The exercise group (n=23) consisted of 2 sessions per week for 10 weeks of progressive resistance training. Sessions were provided in small groups within the community. The control group (n=22) received usual care and	The primary outcome measure was the Centre for Epidemiologic Studies for Depression scale (CES-D).  The secondary outcome measures assessed psychosocial health status. They included: the Assessment of Quality of	At baseline, the control group had significantly more severe depression based on the CES-D (p=0.003). At the 10 week and 6 month follow up measures, the intervention group had fewer symptoms of depression (p=0.08 and p=0.004); however, these between group differences were not significant when controlling for baseline depression. Almost half of each group experienced a clinically significant decrease in depressive e symptoms (>5 pts on CES-D) from



Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
	ITT:☑		<p>were asked not to perform any resistance training.</p> <p><u>Study Period</u> = 6 months</p>	<p>Life Instrument (AQoL), the Short Form-12 (SF-12), the stroke specific QOL measure, the Satisfaction with life Scale (SWLS), the Social support survey (SSS), the Life Orientation Test-Revised (LOT-R), a 10-item measure of generalized dispositional optimism, the Self-Esteem Scale, the Recovery Locus of Control Scale (RLOC), and muscle strength.</p> <p><b>Assessment Points:</b> Baseline, 10 weeks, and 6 months</p>	<p>baseline to 6 month follow up. This reduction was maintained in almost 30% of the intervention group and 16% of the control group. This difference did not reach statistical significance.</p>
<p><b>Van de Port et al. 2012</b></p> <p><b>RCT</b></p>	<p>CA: ☑</p> <p>Blinding: Patient ☑ Therapist ☑ Assessor ☑</p> <p>ITT:☑</p>	<p>250 community dwelling stroke patients that have completed their inpatient rehabilitation and are able to walk 10m unassisted. The mean (SD) age and time since stroke of the intervention group: 56(10) and 91(42); and for the control group: 58(10) and 103(51).</p>	<p>Patients randomly allocated to the intervention group (n=126) received a 90 min, graded task oriented circuit training program 2x/week for 12 weeks. The training included 8 work stations intended to improve meaningful tasks related to walking competency. Patients allocated to the control group (n=124) received usual outpatient physiotherapy (usually 1 on1 treatments).</p> <p><u>Study Period</u> = 24 weeks</p>	<p>Primary outcome measures: The mobility domain of the Stroke Impact Scale (SIS).</p> <p><b>Assessment Points:</b> Baseline, 12, and 24 weeks</p> <p>Secondary outcome measures: the remaining aspects of the SIS, Rivermead mobility index (RMI), the falls efficacy scale (FES), the Nottingham extended activities of daily living (NEADL), the Hospital Anxiety and Depression Scale (HADS), and the fatigue severity scale (FSS)</p> <p><b>Assessment Points:</b> Baseline, 6, 12, 18, and 24</p>	<p>There was no significant group X time interaction for the mood and emotions domain of the SIS from baseline to 12 weeks (p=0.41) or from 12 to 24 weeks (p=0.41). Similarly, there was no group X time interaction identified for change in the HADS from baseline to 12 weeks (p=0.86) for from 12 to 24 weeks (p=0.37).</p> <p><u>Adverse events:</u> 29 falls were reported in the intervention group and 26 falls for the control group. Two serious adverse events were reported in the intervention group: one patient fell and required a consultation with a physician and one patient experienced arrhythmias.</p>

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
<b>Graven et al. 2011</b>  <b>Systematic Review and Meta-Analysis</b>	N/A	54 RCTs were identified. All of the RCTs were grouped by intervention type. In the exercise intervention category, 10 RCTs were identified representing 512 patients	The 10 included studies were split into 2 groups. Group 1 consisted of 6 RCTs that compared exercise interventions to usual care or no intervention. Group 2 consisted of 4 RCTs with 2 interventions. Examples of comparison groups are lower intensity exercises, relaxation, unsupervised programs, range of motion programs, and usual outpatient exercise programs  In both groups, the primary exercise interventions were focused programs with an intensity of 2-3x/week over a 6 to 12 week duration (average was 9.8) with an exception of one study (7 weeks).	weeks  Outcomes of interest were separated into 3 categories: Depressed mood, participation, and HRQoL.  Specific outcomes individual RCTs used to measure depression mood included the Geriatric Depression scale (GDS), the Geriatric Depression scale 15 (GDS-15), the Hospital Anxiety and Depression Scale (HADS), and the Centre for Epidemiologic Studies for Depression scale (CES-D)	The results of the meta-analysis indicated a Level 1 evidence for exercise improving depression symptoms in the short term. This conclusion was based on 2 RCTs that provided sufficient parametric data. Individually, both studies showed no benefits for exercise in the main group comparisons. When data was pooled, they demonstrated a significant difference (n=137; standardized mean difference: -2.03, 95% CI: -3.22 to -.085). Differences in the follow up assessments precluded analysis of long term benefits.

## Music Therapy

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
<b>Jun et al. 2012</b>  <b>RCT</b>	CA:☒  Blinding: Patient	30 patients with ischemic stroke with the past 2 weeks, no previous psychiatric disease and	Consenting inpatients in a neurology unit were randomly assigned to receive either movement	Secondary hypothesis and, therefore secondary outcomes pertained to psychological function –	At baseline, it was noted that participants allocated to the control group attained significantly greater CES-D scores than individuals in the intervention condition

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
	<input checked="" type="checkbox"/> Therapist <input checked="" type="checkbox"/> Assessor ITT: <input checked="" type="checkbox"/>	MMSE >20 points. Mean age was 60.7 ( $\pm 8.6$ ) in the experimental condition and 55.1 ( $\pm 17.2$ ) in the control group. 50% of participants were female.	and music therapy (MMT; n=15) or usual care (n=15). MMT consisted of 3 phases: 1) preparatory activities for 20 minutes (stretching routine set to quiet meditational music), 2) main activities for 30 minutes (music listening, singing and playing along using a selection of instruments) and 3) finishing activities for 10 minutes (patients were asked to express difficulties and benefits of MMT, share emotions and communicate experiences). The control group received routine care only. The intervention was provided in one hour sessions, three times per week for a total of 8 weeks by a music therapist and the researchers.  <b>Duration of Intervention:</b> 8 weeks.	specifically mood and depression. Psychological state was assessed using the Korean version of the Profile of Mood States. Depression was assessed using the Center for Epidemiologic Studies Depression Scale (CES-D).  <b>Assessment Points:</b> Baseline, 8 weeks	(p=0.048). The authors did not adjust for this initial between group difference in later analyses. At the end of 8 weeks, mood state had improved in the experimental group, but deteriorated in the control group suggesting a positive effect associated with MMT (t for the comparison of mean difference = 1.82, p=0.04). However, for depression alone, this was not the case. Both groups demonstrated improvement over time – and, in fact, the control group demonstrated greater reduction in depressive symptomatology. The mean difference over time in CES-D scores within the experimental group was 6.46 ( $\pm 11.8$ ) and 9.67 ( $\pm 15.27$ ) in the control condition (t for the between group comparison of mean differences = -0.59, p=0.28).  <b>Adverse events:</b> Although there were some difficulties reported with the physical aspects of MMT at the beginning of the therapy, there were no adverse events reported. Verbal reports provided by the participants suggested that they enjoyed MMT.
<b>Sarkamo et al. 2008</b>  <b>RCT</b>	CA: <input checked="" type="checkbox"/>  Blinding: Patient <input checked="" type="checkbox"/>	55 patients with a right or left MCA stroke. Participants were recruited during their acute care hospital stay following	Participants were randomly assigned to receive either music therapy (n=19), language therapy (n=19)	Mood was a secondary outcome in this study after “cognitive function”. It was assessed using the Finnish version of Profile of Mood	There were no significant between group differences reported at baseline for any demographic or clinical variables. Groups were also equivalent for estimates of time spent in relevant leisure activities prior to stroke (music or

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
	Therapist <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/> ITT: <input checked="" type="checkbox"/>	stroke. Mean age of participants was 56.1 ( $\pm 9.6$ ), 59.3 ( $\pm 8.3$ ) and 61.5 ( $\pm 8.0$ ) years in the music, language and control groups, respectively. 29/55 participants were male.	or no intervention (control; n=17). Participants in the music group were provided with portable CD players and a selection of CDs that included their favourite music. Participants in the language group were provided with portable cassette players and narrated "books on tape" selected from the library. Both groups received instruction on how to use the players and told to listen to the material provided independently for $\geq 1$ hour/day either in the hospital or at home and asked to keep a diary of their listening activities. Music therapists kept close contact with patients for the duration of the intervention to encourage listening activities, provide new listening material and provide helpful and practical information as needed.  <b>Duration of intervention:</b> 2 months.	States (POMS), which contains a depression subscale.  <b>Assessment Points:</b> Baseline, 3 months and 6 months.	radio listening, reading). 13/55 participants reported taking an antidepressant at baseline – there were no between group differences for antidepressant use. At the 3 month assessment, there was a significant between group difference noted on the depression subscale of the POMS ( $F(2,51) = 3.7$ , $P=0.03$ ), such that, on post hoc testing, scores for participants assigned to music listening were demonstrated to be significantly lower than those in the control group ( $p=0.024$ ). At 6 months, there was still a trend toward improvement demonstrated by individuals who had participated in music listening ( $p=0.07$ ).  No adverse events were reported with either listening intervention.

## Prevention of Post-Stroke Depression

### Prophylactic Pharmacotherapy

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
<b>Salter et al. 2012</b>  <b>Systematic Review and Meta-analysis</b>	N/A	8 randomised controlled trials that examined prevention of PSD via comparison of pharmacotherapy with a control condition. Participants were limited to individuals with no clinically diagnosable PSD at study entry.	6 databases were searched; articles for inclusion were selected and confirmed by 2 researchers. Study quality and abstraction performed by 2 researchers. Pooled analysis performed using fixed effects models. Heterogeneity was assessed using the $I^2$ statistic. Publication bias assessed using funnel plot regression and egger's intercept for identification of asymmetry.	Risk for development of PSD was assessed (pooled OR) based on cases of depression recorded at end of treatment in each study. Also examined impact of duration of treatment and antidepressant class on risk for PSD.	<p>Interview-based assessments were used to determine the presence/absence of depression in all studies except one that used the HADS. Pooled analysis, based on 776 observations, demonstrated a significantly reduced risk for development of PSD associated with the use of prophylactic pharmacotherapy (OR=0.34, 95% 0.22-0.53, <math>p&lt;0.001</math>). No significant heterogeneity was identified.</p> <p>Duration of treatment ranged from 3 months to 1 year. Analysis of the 5 trials with treatment duration of 1 years revealed a significant reduction in odds for PSD (OR=0.31, 95% CI 0.18, 0.56; <math>p&lt;0.001</math>).</p> <p>All studies were of similar methodological quality; however, removal of the single open label study did not substantially alter the results. No significant publication bias was identified.</p> <p><b>Adverse events:</b> Assessment and reporting of side effects in the identified studies was generally very poor, making it difficult to provide a comprehensive evaluation of these as part of the meta-analysis. However, the most commonly reported side effects in those studies that did report them appeared to be tiredness/fatigue, dizziness and gastrointestinal upsets (most often nausea and diarrhea).</p>
<b>Yi et al. 2010</b>  <b>Systematic Review and Meta-analysis</b>	N/A	6 trials (3 English, 3 Chinese) that examined the use of fluoxetine in the prevention of PSD vs. placebo or no treatment conditions. All study participants were confirmed as having no diagnosis of depression at study entry.	2 researchers reviewed search results to identify studies for inclusion. Studies were assessed for quality using Cochrane criteria. Fixed effects models were used for pooled analyses unless significant heterogeneity was identified (in which case	OR's were calculated for outcome of incident PSD. Drop-out rates were examined in order to evaluate safety considerations of fluoxetine treatment.	<p>3/6 trials compared fluoxetine to placebo and 3/6 trials compared fluoxetine to no treatment. Duration of intervention ranged from 4 to 12 weeks.</p> <p>Only 3 studies provided data on the development of new onset depression in treatment vs. control conditions (n=176). Pooled analysis demonstrated a reduction in risk for onset of depression associated with treatment with fluoxetine (OR=0.25, 95% CI 0.11, 0.56, <math>p=0.0009</math>). In addition, analysis of symptom</p>

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			random effects analyses were used).		<p>severity suggested that treatment was associated with a non-significant reduction in symptoms (WMD=-3.97, 95% CI-9.85, 1.9). However, this analysis was associated with significant heterogeneity.</p> <p><b>Adverse Events:</b> Drop-out rates attributable to adverse events ranged from 0% to 11.1% in groups assigned to fluoxetine treatment and 0% to 14.3% in comparison groups. Pooled analysis demonstrated no significant between group difference in terms of drop-out rates.</p>
<p><b>Hackett et al. 2008</b></p> <p><b>Systematic Review and Meta-Analysis</b></p>	N/A	14 trials (RCTs) in which either a pharmaceutical agent or psychological therapy was used to prevent the onset of PSD vs. placebo or usual care. 10 of the identified trials (12 comparisons) examined the use of pharmacotherapy for the prevention of PSD.	Cochrane review – searched multiple databases as well as dissertations and theses. Authors and drug companies were also contacted. Review authors reviewed identified articles for possible inclusion, checked abstractions and reviewed quality assessments. Pooled analysis was performed using fixed effects models except in the case of unexplained heterogeneity, in which case, random effects models were used to combine data. ORs were used for dichotomous outcomes, WMDs for continuous ones. Heterogeneity was assessed using the I <sup>2</sup> statistic.	Main outcome of interest was the proportion of patients who met the criteria for depression at the end of study (or study follow-up).	<p>Treatment duration varied from 2 weeks to 12 months. A variety of antidepressant agents were used. 6/10 trials reported numbers of participants meeting the criteria for depression at the end of the study intervention. This proportion appeared to be lower in groups of individuals assigned to treatment with a prophylactic antidepressant; however, no pooled analysis was performed in view of the wide variety of study methods and assessment tools used.</p> <p>There was also no clear evidence of harm based on reporting of adverse events.</p> <p>NOTE: Not all of the studies included in this review could be considered prevention studies. Many did not exclude individuals with depression at baseline, some did not assess depression at baseline or report incidence of depression post-intervention. It is unclear if some patient-level data may have been used from some studies.</p>
<b>Chen et al. 2007</b>	N/A	10 RCTs comparing the use of a single antidepressant agent with a control	Literature search results were reviewed by 2 reviewers. Identification	Primary study outcome was the occurrence rate of new onset PSD confirmed by	Rates of new onset PSD were reported in 8 studies. Pooled rate of occurrence was 12.54% in the intervention group and 29.17% in the

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
<b>Systematic Review and Meta-Analysis</b>		condition for the prevention of PSD. All study participants were confirmed as having no diagnosis of depression at study entry. If mixed patient groups were included in a study, results for nondepressed patients had to be presented separately.	and selection of studies for inclusion were reviewed by 2 authors. Data abstraction and study evaluation was also completed by 2 reviewers. Pooled analyses were undertaken. Rate differences were calculated (RD) for dichotomous outcomes and weighted mean differences (WMD) for continuous outcomes. Fixed effects models were used except in the presence of significant statistical heterogeneity as assessed using the $I^2$ statistic.	diagnosis (DSM-IV) or use of a validated rating scale at the end of study. Secondary outcome was depression severity.	control conditions (RD=-0.17, 95% CI -0.26, -0.08). Both SSRI use and TCA use was associated with reductions in the occurrence rate of PSD. Reductions in rate did not appear to be associated with the interval between onset of stroke and the beginning of the prophylactic intervention. Calculation of Egger's intercept for assessment of publication bias demonstrated no significant bias (-2.96, 95% CI -6.64 to 0.71).
<b>Robinson et al. 2000</b>  <b>RCT</b>	CA: <input checked="" type="checkbox"/>  Blinding: Patient <input checked="" type="checkbox"/> Therapist <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/>  ITT: <input checked="" type="checkbox"/>	104 adult individuals with previous stroke (within 6 months of study baseline). 48 individuals with no diagnosis of depression were enrolled in the study in order to assess effects of antidepressant use on recovery.	This study was originally designed as a randomized crossover trial. <b>Depressed</b> patients were randomly assigned to either <b>fluoxetine</b> (10mg/d gradually increased to 40 mg/day) or <b>nortriptyline</b> (dose of 25 mg/day gradually increased to 100 mg/day) or identical <b>placebo</b> given over 12 weeks. Patients received 12 weeks of active treatments and crossed-over to 12 weeks of placebo treatment. However, as data from a significant number of participants	The Hamilton Rating Scale for Depression (HRSD-28) was used to assess depression at baseline and at each 3-week evaluation point. Successful response to treatment was defined as a >50% reduction in the HRSD scale score + failure to fulfill the criteria for major or minor depression.	There were no significant treatment effects or time X treatment interactions reported for the analysis of data gathered from participants who were "nondepressed". There were significant within group changes notes over time on functional assessments (e.g. FIM and the Johns Hopkins Functioning Inventory). However, neither depressed nor non-depressed patients in either active treatment condition demonstrated significant greater improvement in functional recover than those assigned to placebo.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			<p>assigned to the placebo condition “became ineligible for analysis” (31% response rate), an independent groups design was applied to the analysis. Nondepressed patients were simply assigned to receive 12 weeks of treatment with nortriptyline, fluoxetine or matching placebo with no crossover.</p> <p>Results for the group of individuals labelled “nondepressed” are reported following the 12-week treatment period.</p>		
<p><b>Narushima et al. 2002*</b></p> <p><b>RCT</b></p>	<p>CA: <input checked="" type="checkbox"/></p> <p>Blinding: Patient <input checked="" type="checkbox"/> Therapist <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/></p> <p>ITT: <input checked="" type="checkbox"/></p>	<p>48 individuals who had experienced stroke within the last 6 months, but who were not diagnosed with depression at baseline. Diagnosis of depression was made according to DSM-IV criteria.</p>	<p>Participants were randomly assigned to receive treatment with nortriptyline (25-100 mg/day), fluoxetine (10 – 40 mg /day) or with a matching placebo for a period of 3 months.</p>	<p>Depression and depressive symptomatology were assessed using the Hamilton Rating Scale for Depression (HRSD).</p> <p>Evaluations were completed at baseline, post-treatment and at 6, 9, 12 and 24 months follow-up.</p>	<p>During treatment, one minor depression was identified in participants assigned to nortriptyline group, three in group assigned to fluoxetine and 5 in the placebo condition. On ITT analysis of active treatment vs. placebo, there was no significant between group difference demonstrated.</p> <p>At the end of study, when treatment was discontinued, patients assigned to nortriptyline were more likely than individuals in other groups to develop depression and to experience severe symptoms of depression over the next 6 months of follow-up. However, there were no significant between group differences in terms of prevalence of depression.</p> <p>At 9 months’ follow-up, individuals who had been assigned to active treatment experienced a greater frequency of depression than individuals assigned to placebo during the study period.</p>



Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					However, at 12 and 24 month follow-up, there were no significant between group differences.
<b>Rasmussen et al. 2003*</b>  <b>RCT</b>	CA: <input checked="" type="checkbox"/>  Blinding: Patient <input checked="" type="checkbox"/> Therapist <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/>  ITT: <input checked="" type="checkbox"/>	137 individuals who had experienced stroke within the preceding 4 weeks and who were not experiencing depression at the time of study entry. Individuals with significant aphasia or cognitive impairments (dementia) were excluded.  Depression was defined as obtaining a score of >18 on the HRSD-17, or ≥9 on the HRSD-6.	Participant were randomly assigned to treatment with sertraline (50 mg/day/ n=70) or matching placebo (n=67) for a period of one year. Treatment dose could be increased in increments of 50mg to a maximum of 150 mg/day in order to achieve clinical effectiveness.	A modified version of the HRSD-17 was used to assess the primary outcome (depression) along with the GDS and CGI assessments. Side effects were evaluated using the UKU side effect rating scale.  Evaluations were conducted at 11 visits following randomization, occurring at 4-5 week intervals.	Kaplan-Meier analysis demonstrated that sertraline has a significantly superior prophylactic efficacy compared to placebo. Overall, after 52 weeks of treatment, 8.2% of the sertraline-treated group developed depression compared to 22.8% of the placebo treated group assessed on the Hamilton Rating Scale for Depression. Using assessment data obtained from the HRSD-6, statistical superiority in favour of treatment appeared at week 6; however, using the HRSD-17, significance was not established until week 21.  <u>Side effects:</u> There were no significant between group differences in terms of the frequency of reported effects. There were fewer patients in the active treatment group who reported severe cardiovascular and noncardiovascular events. Incidence of diarrhea and nausea were 5% higher among individuals treated with sertraline.
<b>Niedermaier et al. 2004*</b>  <b>RCT</b>	CA: <input checked="" type="checkbox"/>  Blinding: Patient <input checked="" type="checkbox"/> Therapist <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/>  ITT: <input checked="" type="checkbox"/>	70 patients with acute ischemic stroke with no depression (or depression diagnosed within 2 weeks prior to the index stroke event), or use of antidepressants in the immediate pre-stroke period	Participants were randomly assigned to receive treatment with mirtazapine 30 mg (qhs) (n=35) or to a control condition (n=35). Patients in the treatment condition received 30 mg.  Treatment began one day after the qualifying stroke event, and continued for a period of one year.  If a patient developed depression, and they had been assigned to the treatment condition,	Primary outcome was occurrence of depression. Depression was assessed using the HRSD administered via a semi-structured interview. Response to treatment in the case where depression emerged as was treated was defined as a reduction of >50% in the HRSD score. Criteria for the diagnosis of depression were from the DSM-IV and ≥16 score on the HRSD.  Patients were examined on day 7, 44, 90, 180 and 360.	Based on DSM-IV criteria, 40% of patients (n=14) assigned to the control group developed post-stroke depression vs. 5.7% of patients (n=2) treated with mirtazapine (p<0.001). The 14 patients originally assigned to the control group who developed depression were treated with mirtazapine – only 1 of whom required treatment at a dose of 45 mg/day. Of the 2 patients who were assigned to active treatment and developed depression, only one responded to an increased dose of mirtazapine. In all, 15/16 patients who developed PSD demonstrated remission of symptoms following treatment.  <u>Side effects:</u> No serious side effects were observed. Mild sedation was the side effect most commonly reported.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			the dose was increased to 45 mg. If, after 21 days at the increased dose, depression continued, they were excluded from the study. If a patient in the control condition was diagnosed with depression, they were given a starting dose of 30 mg mirtazapine for a minimum of 3 weeks after which it could be increased to 45 mg if required. If after an additional 3 weeks at the increased dose, depression did not improve, the patient was excluded from the study.		
<b>Almeida et al. 2006 *</b>  <b>RCT</b>	CA: <input checked="" type="checkbox"/>  Blinding: Patient <input checked="" type="checkbox"/> Therapist <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/>  ITT: <input checked="" type="checkbox"/>	111 stroke patients within 2 weeks of a recent stroke event	Participants were randomly assigned to receive either treatment with sertraline (50 mg once per day) or a matching placebo. Treatment was continued for a period of 24 weeks.	Primary study endpoint was development of significant symptoms of depression assessed on the Hospital Anxiety and Depression Scale (HADS-D) or as diagnosed through clinical examination made by the attending physician.  Evaluations were conducted at baseline, week 24 and week 52.	Post treatment (24 weeks), 21.6% of patients assigned to the placebo group and 16.7% of patients assigned to treatment with sertraline were diagnosed with depression (OR = 0.8, p=0.59). Of the patients assessed at 52 weeks, 30% in the placebo group vs. 22.7% in the active treatment group met the criteria for depression (ns). In addition, treatment with sertraline did not appear to result in improvements in terms of cognition, disability or mortality when compared to the placebo condition.
<b>Robinson et al. 2008*</b>  <b>RCT</b>	CA: <input checked="" type="checkbox"/>  Blinding: Patient <input checked="" type="checkbox"/> Therapist <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/>	176 patients with either ischemic or haemorrhagic stroke (within 3 months) were enrolled. Depression was assessed at baseline. Patients meeting the DSM-IV criteria for depression or a score >11 on the HRSD	176 patients with no depression were randomly assigned to received 1 of 3 treatments within 3 months of stroke onset; i) escitalopram 10 mg/d (if <65 yrs, 5 mg/d for	Primary study outcome was the onset of diagnosable depression. In addition, patients (and family and physicians) were asked about adverse events at 3 month intervals)	Patients assigned to placebo condition developed 11 major and 2 minor cases of depression. Those assigned to problem-solving developed 5 major and 2 minor cases while patients receiving escitalopram developed 3 major and 2 minor cases. Overall, patients with a history of mood disorders were 5.2 times more likely to develop depression than those without

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
	ITT: <input checked="" type="checkbox"/>	<input checked="" type="checkbox"/> were excluded as were patients with severe cognitive deficits. Mean age was 61.3 ( $\pm 13.7$ ), 67.3 ( $\pm 11.2$ ), 63.9 ( $\pm 13.3$ ) in the treatment conditions and control group respectively. 59.7% of participants were male.	patients $\geq 65$ ) ii) matching placebo or iii) <b>problem-solving therapy</b> (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.	<b>Timing of Assessment:</b> Patients were evaluated using the structured clinical interview for the DSM-IV at 3, 6, 9 and 12 months.	( $p < .001$ ). Adjusted for previous history of mood disorders, patients assigned to the placebo condition were more likely to develop depression than individuals receiving either therapy with escitalopram (adj. HR= 4.5, 95% CI 2.4-8.2, $p < 0.001$ ) or problem-solving therapy (adj. HR=2.2, 95% CI 1.4-3.5, $p < 0.001$ ). On intention-to-treat analysis that included 27 patients who did not receive any treatment and assumed all untreated patients developed depression, escitalopram was still associated with a significantly reduced risk for depression (23.1% vs. 34.5%, HR = 2.2 95% CI 1.2-39, $p = 0.007$ ); however, problem-solving therapy was not (30.5% vs. 34.5%, HR=1.1, 95% CI 0.8-1.5, $p = 0.51$ ).  <b>Adverse Events:</b> There were no between group differences for any of the adverse events reported. However, side effects reported did include decreased libido, fatigue, and GI symptoms. There was no evidence that patients receiving problem-solving therapy were more or less likely to be hospitalized with illness of cardiovascular origin than individuals receiving escitalopram.
<b>Tsai et al. 2011*</b>  <b>RCT</b>	CA: <input checked="" type="checkbox"/> Blinding: Patient <input checked="" type="checkbox"/> Therapist <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/> ITT: <input checked="" type="checkbox"/>	92 patients with first or recurrent ischemic stroke (within the preceding 4 weeks) and no depression. Individuals with previous depression, those taking antidepressants or with possible, undiagnosed depression (HAM-D $\geq 10$ ) were excluded from the study	Study participants were assigned to receive either 50 mg milnacipran (titrated to 100 mg by one week of treatment) per day, or matching placebo. Duration of treatment was 1 year. 56 participants completed the study.	The primary outcome appeared to be incidence of PSD. This was based on the administration of a modified version of the HRSD-17 (item 14 – sexual behaviour -- removed) and the DSM-IV criteria for major depression. The modified HRSD, BI and NIHSS scales were administered at 3, 6, 9, and 12 month follow-up visits.	60.9% of patients completed the 12-month study. Overall, 8 participants developed PSD during the treatment period – only one of whom was assigned to the active treatment condition. Incidence of depression was 2.22% in the treatment group and 15.22% in the control group. There was a statistically significant benefit associated with milnacipran over placebo ( $p = 0.048$ ).  <b>Side effects:</b> Side effects were reported by both groups – there was no significant between group difference reported for study withdrawal due to side effects ( $p = 0.73$ ). The main reason for study withdrawal was reported to be difficulty in

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					following the study protocol, not side effects associated with treatment. In total, 7/21 patients who withdrew from the active treatment group did so because of reported side effects.
<b>Chollet et al. 2011*</b>  <b>FLAME</b>  <b>France</b>  <b>RCT</b>	CA: <input checked="" type="checkbox"/>  Blinding: Patient <input checked="" type="checkbox"/>  Therapist <input checked="" type="checkbox"/>  Assessor <input checked="" type="checkbox"/>  ITT: <input checked="" type="checkbox"/>	118 patients with acute ischemic stroke.  Exclusion criteria: age <18 or >55, severe disability (NIHSS>20), premorbid or current deficits that could interfere with assessment, current diagnosis of depression, or use of antidepressants in the month prior to recruitment.	Participants were randomized 5-10 days post-stroke to receive fluoxetine (20 mg/day; n=59) or placebo (n=59) for 90 days. All participants received physiotherapy and standard inpatient stroke care during the study period.	Primary outcome: Fugl-Meyer Motor Scale (FMMS).  Secondary outcomes: National Institutes of Health Stroke Scale, modified Rankin Scale, and the Montgomery Asberg Depression Rating Scale.  <b>Timing of assessment:</b> baseline and at 30 and 90 days.	There was a significantly greater frequency of depression identified among patients assigned to placebo when compared to those assigned to active treatment (4 pts vs. 17, p=0.002). From baseline to 90 days, there was a significant between group difference reported in mean change in symptoms of depression (p=0.032). Over the treatment period, there was no change in depressive symptomatology within the treatment group (adjusted mean change = -0.1, 95% CI -2.1 to 1.9) while there was a significant increase in symptoms in the placebo group (adj. Mean change = 3.2, 95% CI 1.1-5.3). Change in symptoms of depression was adjusted for age, history of previous stroke and Fugl-Meyer score assessed at baseline.  <u>Side effects:</u> Two serious adverse events occurred in the fluoxetine group (hyponatraemia and partial seizure). Transient digestive disorders (nausea, diarrhoea, and abdominal pain) were more common in the active treatment group (25% vs. 11%).
<b>Zhang et al. 2013</b>  <b>RCT</b>		95 individuals who had experienced ischemic stroke but who were non-depressed at baseline	Participants were randomly assigned to receive either treatment with duloxetine (30 – 90 mg/day; n=47) or a placebo (n=48). Treatment was provided over a period of 12 weeks, in addition to routine therapy.	Depression was assessed using the HRSD. In addition to the HRSD, the NIHSS, the MMSE, the ADL (Chinese version) and SF-36 were administered to assess neurological, cognitive and motor function as well as quality of life.  Study follow-up was conducted at 24 weeks.	Treatment with duloxetine was associated with lower incidence of minor and MDD when compared to placebo. In addition, use of duloxetine was associated with improved cognitive function, more rapid rehabilitation and higher QOL of life scores when compared to the placebo condition. Significant higher ADL and QoL scores than placebo at endpoint  Side effects: Nausea, vomiting.

\*trial included in most recent meta-analysis

## Non-pharmacotherapeutic Interventions for Prevention of PSD

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
<b>Wu et al. 2012</b>  <b>China</b>  <b>RCT</b>	CA: <input checked="" type="checkbox"/>  Blinding patient: <input checked="" type="checkbox"/> Therapist <input checked="" type="checkbox"/> assessor: <input checked="" type="checkbox"/>  ITT: <input checked="" type="checkbox"/>	120 patients with acute stroke. Patients with previous stroke or in unstable medical condition were excluded.	Participants were randomized to receive early psychological therapy and comprehensive rehabilitation training (n=60) or usual care (n=60). Psychological therapy was provided in 20 minute sessions 5 times per week while rehabilitation training was provided in 30 minute sessions twice per week.	The Symptom Checklist 90 (SCL-90) and the Barthel Index were assessed on day 3 and day 21.	The authors reported that participants in the intervention group reported significantly fewer symptoms of depression, anxiety, hostility, fear, and somatization at day 21, as compared to those in the control group (all at p<0.05).
<b>Watkins et al. 2007</b>  <b>RCT</b>	CA: <input checked="" type="checkbox"/>  Blinding: Patient <input checked="" type="checkbox"/> Therapist <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/>  ITT: <input checked="" type="checkbox"/>	411 patients with stroke. Patient mood was assessed at baseline using the GHQ-28 and considered normal in 197/207 individuals in the control condition and 195/204 individuals in the intervention condition. Median age was 70 years in both the control and intervention conditions (ranges 61-77 and 61-78, respectively). 58.9% and 57.8% of individuals enrolled in the control and treatment conditions were male. Individuals with cognitive or communication problems that might prevent interviewing were excluded.	All patients received usual stroke care. Patients in the treatment condition also received 4 weekly, individual sessions of motivational interviewing. Sessions were conducted by the same therapist and lasted 30 – 60 minutes each. Motivational interviewing is a talk-based therapy intended to assist the patient in identifying personal goals for recovery and perceived barriers to achieving these goals. Patients are encouraged/ supported in the identification of solutions. Initial	Mood as assessed on the GHQ-28. A single item depression screen (Yale) was also administered.  <b>Timing of Assessment:</b> Baseline assessments were conducted between 5 – 28 days following the stroke event. Outcomes were assessed via mailed questionnaire at 3 months.	A significant benefit on mood was associated with the treatment condition over usual care at 3 months (OR for normal mood = 1.60, 95% CI 1.04, 2.46; p=0.03). Using a self-report, single item, screening tool for depression (Yale), a protective effect of motivational interviewing was also identified (OR = 1.65, 95% CI 1.06, 2.58; p=0.03). Motivational interviewing was not associated with reduced risk for dependency or morality.  <b>Note:</b> The only assessment pertaining to the development of depression in this study was the use of the single item Yale assessment. There was no formal assessment of depression and the primary outcome of the study was general mood or general psychiatric distress, not depression. This study, however, is included in the Hackett et al. meta-analyses evaluating interventions intended both to treat and to prevent PSD.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			appointments for motivational interviewing were set at the time of randomization. Therapists received 4 days of training in motivational interviewing followed by 10 practice sessions and were supervised by a clinical psychologist through team meetings. Individuals assigned to the control condition received usual nursing and therapy care, including regular multidisciplinary team meetings and discharge planning and a regular review assessment at 3 months post stroke.		
<b>Watkins et al. 2011</b>  <b>Follow-up Study to Watkins et al. 2007</b>	N/A	As above.	125 patients assigned to the control group and 164 assigned to the intervention participated in the 12 –month follow-up to Watkins et al. 2007). Analysis was conducted on an intention to treat basis.	Mood as assessed on the GHQ-28. A single item depression screen (Yale) was also administered.  <b>Timing of Assessment:</b> 12-month follow-up	At 12 months, the significant benefit associated with motivational interviewing appeared to be maintained (OR for normal mood = 1.66, 95% CI 1.08-2.55, p=0.02). The previously identified protective effect vs. depression (based on the Yale screening tool) was not present at 12 months (OR = 1.1, 95% CI 0.74-1.64, p=0.80).
<b>Robinson et al. 2008</b>  <b>RCT</b>	CA:☑  Blinding: Patient ☑ Therapist ☑ Assessor ☑	176 patients with either ischemic or haemorrhagic stroke (within 3 months) were enrolled. Depression was assessed at baseline. Patients meeting the DSM-IV criteria for depression or a score >11 on the HRSD were excluded as were	176 patients with no depression were randomly assigned to received 1 of 3 treatments within 3 months of stroke onset; i) escitalopram 10 mg/d (if <65 yrs, 5 mg/d for patients ≥ 65) ii)	Primary study outcome was the onset of diagnosable depression. In addition, patients (and family and physicians) were asked about adverse events at 3 month intervals)	Patients assigned to placebo condition developed 11 major and 2 minor cases of depression. Those assigned to problem-solving developed 5 major and 2 minor cases while patients receiving escitalopram developed 3 major and 2 minor cases. Overall, patients with a history of mood disorders were 5.2 times more likely to develop depression than those without (p<.001). Adjusted for previous history of mood



Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
	ITT:☑	patients with severe cognitive deficits. Mean age was 61.3 ( $\pm 13.7$ ), 67.3 ( $\pm 11.2$ ), 63.9 ( $\pm 13.3$ ) in the treatment conditions and control group respectively. 59.7% of participants were male.	matching placebo or iii) <b>problem-solving therapy</b> (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.	<b>Timing of Assessment:</b> Patients were evaluated using the structured clinical interview for the DSM-IV at 3, 6, 9 and 12 months.	disorders, patients assigned to the placebo condition were more likely to develop depression than individuals receiving either therapy with escitalopram (adj. HR= 4.5, 95% CI 2.4-8.2, $p < 0.001$ ) or problem-solving therapy (adj. HR=2.2, 95% CI 1.4-3.5, $p < 0.001$ ). On intention-to-treat analysis that included 27 patients who did not receive any treatment and assumed all untreated patients developed depression, escitalopram was still associated with a significantly reduced risk for depression (23.1% vs. 34.5%, HR = 2.2 95% CI 1.2-39, $p = 0.007$ ); however, problem-solving therapy was not (30.5% vs. 34.5%, HR=1.1, 95% CI 0.8-1.5, $p = 0.51$ ).  <b>Adverse Events:</b> There were no between group differences for any of the adverse events reported. There was no evidence that patients receiving problem-solving therapy were more or less likely to be hospitalized with illness of cardiovascular origin than individuals receiving escitalopram.
<b>Hackett et al. 2008</b>  <b>Systematic Review and Meta-Analysis</b>	N/A	14 trials (RCTs) in which either a pharmaceutical agent or psychological therapy was used to prevent the onset of PSD vs. placebo or usual care. 4 of the identified trials provided outcome data regarding the evaluation of psychotherapeutic interventions vs control groups.	Cochrane review – searched multiple databases as well as dissertations and theses. Authors and drug companies were also contacted. Review authors reviewed identified articles for possible inclusion, checked abstractions and reviewed quality assessments. Pooled analysis was performed using fixed effects models except in the case of unexplained heterogeneity, in which case, random effects	Main outcome of interest was the proportion of patients who met the criteria for depression at the end of study (or study follow-up).	Various forms of therapies were considered. Problem-solving therapy was used in 2, one used “home-based therapy” and the remainder was “motivational interviewing” (see Watkins et al. above). A small benefit was seen in the pooled analysis in favour of psychotherapy (OR=0.64, 95% CI 0.42, 0.98). However, note that the criteria for depression was not diagnostic (See Watkins et al. above, for example).  NOTE: Not all of the studies included in this review could be considered prevention studies. Many did not exclude individuals with depression at baseline, some did not assess depression at baseline or report incidence of depression post-intervention. It is unclear if some patient-level data may have been used from some studies.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			models were used to combine data. ORs were used for dichotomous outcomes, WMDs for continuous ones. Heterogeneity was assessed using the I <sup>2</sup> statistic.		

## Care Management, Social Support and Post-stroke Depression

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
<b>Hackett et al. 2013</b>  <b>T5 RCT</b>	CA: <input checked="" type="checkbox"/>  Blinding patient: <input checked="" type="checkbox"/> Therapist <input checked="" type="checkbox"/> assessor: <input checked="" type="checkbox"/>  ITT: <input checked="" type="checkbox"/>	201 patients with post stroke depression. Patients with serious concomitant illness, without a fixed address / phone access, and those >18 years of age were excluded.  36.7% of those assessed for eligibility were included in the study.	Participants were randomized within 8 weeks of stroke 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.	The primary outcome was presence of depression at six months, defined as a score of >8 on the Hospital Anxiety and Depression Scale (HADS) depression subscale. The Patient Health Questionnaire (PHQ-9) was also assessed.  <b>Timing of assessment:</b> baseline and at 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 (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.
<b>Graven et al. 2011</b>  <b>Systematic Review</b>	N/A	54 RCTs were identified. All of the RCTs were grouped by intervention type. 9 studies were classified as "care co-ordination, psycho-social and inter-disciplinary management". Seven of these studies included evaluation of depression as study outcomes.	To explore community-based interventions delivered by nurses and allied health professionals in addressing depression, participation and HRQOL. Identified articles from multiple databases. Studies were selected following search review conducted	Meta-analyses and assignment of levels of evidence where possible.  Depression assessments included the CES-D, HADS, GDS, GDS-15, and WDI. The authors list version of the GHQ, although this is, strictly speaking, not an assessment of depression.	A wide variety of approaches by various healthcare professionals (e.g. nurse practitioners, social workers, psychologists) using a variety of resources were included in the 9 identified studies. Contacts with healthcare professionals were noted to have included the following features: assessment of needs, coordination of a treatment plan, support and/or counselling, liaison with other services (e.g. general practitioner). Interventions included home visits and phone contact. There was a wide variety in timing post stroke,



Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			by 2 reviewers. Identified studies were evaluated for methodological quality. Interventions were categorised into similar types and pooled analyses conducted where possible. Levels of evidence were assigned where meta-analyses were not possible.		intensity of intervention, types and numbers of healthcare disciplines involved and assessment of outcomes. No pooled analysis was possible and no level of evidence was assigned. Overall, the authors reported that there was “insufficient evidence to support care coordination activities for reducing depression”.
<b>Salter et al. 2010</b>  <b>Systematic Review</b>	N/A	10 RCTs were identified for inclusion. 7 examined home-based support and care coordination interventions. The remaining 3 studies described a specific social support intervention, a family counselling (+information) intervention and a day service respectively.	Identified RCTs from multiple databases that evaluated the provision of a stroke-specific intervention for the provision, creation or enhancement of support for individuals with stroke and assessed depression or mood as a study outcome. Information and education or skills training studies were excluded. Lit searches were reviewed by 2 study authors. Data abstraction and quality assessment was also completed by 2 study authors. Given the heterogeneity and omissions in reported data, pooled analyses were not possible.	Psychological distress, mood or depression.  Assessment was conducted using a variety of instruments including the GHQ (psychological distress), HADS, the GDS and the BDI.  Only 4/10 studies reported assessment of mood at both baseline and one or more follow-up points.	4/7 studies examining home-based support and care coordination interventions examined the impact of the Family Support Organiser service in the UK that offered information, advice and emotional support to individuals with stroke and their carers/families. An additional 2 studies examined outreach nursing programs while the remaining program evaluated a 3-month care coordination program provided by qualified social workers. There was a great deal of variability noted in terms of timing and intensity of intervention and assessment of outcome as well.  Overall, only 1 out of the 10 studies demonstrated a significant effect in terms of mood following receipt of the intervention. Claiborne (2006) described a social worker-led care coordination intervention that was associated with a significant decrease in symptoms of depression over time. In that intervention, frequent, regular SW-initiated contact included ongoing screening for depression and provision of counselling in addition to referrals to mental healthcare services as needed.
<b>Ellis et al. 2010</b>  <b>Systematic Review and</b>	N/A	14 published RCTs and 2 unpublished trials that were discovered following contact with study trialists. All	Cochrane review using patient level data (n=4759) using a collaborative review	Primary outcomes were subjective health status and extended activities of daily living (patients).	Analysis of mental health under a single heading was not considered possible, given the use of both general (e.g. GHQ) and more specific measures (e.g. HADS or GDS).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
<b>Meta-analysis</b>		studies evaluated interventions that used a “stroke liaison worker”; that is, a worker who provided a service that included more than one of: 1) education and information, 2) social support and 3) liaison with other services as needed.	process with trialists or lead investigators from identified trials.	Secondary outcomes for the patient participants included mental health, specifically depression and anxiety.	Analysis for “mental health”, was based on 3081 participants in 15 interventions. Results did not suggest any benefit associated with participation in the stroke liaison condition vs. usual care (SMD=-0.01, 95%CI -0.08, 0.07, p=0.87). Specific analysis of depression outcomes was based on observations gained from 2743 participants in 15 interventions. Similarly, no benefit associated with the stroke liaison worker intervention was noted when compared with usual care (SMD=-0.04, 95% CI -0.12, 0.04, p=0.30).

## Post-stroke Anxiety and Co-morbid Depression

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
<b>Campbell Burton et al. 2001</b>  <b>Systematic Review (Cochrane)</b>	N/A	2 randomised controlled trials enrolling a total of 175 participants. All participants had experienced stroke and had been given a diagnosis of co-morbid depression and anxiety. Neither trial included a placebo condition.	Searches were conducted from earliest dates possible for specific electronic databases through 2010. Two review authors considered all identified articles for possible inclusion. No meta-analysis or pooling of results was possible. A narrative review was conducted.	Primary outcomes included the proportion of patients, following treatment, without a clinical diagnosis of anxiety based on the DSM (or other standard classification) and the proportion of patients scoring outside the symptom range as defined by the primary study author via anxiety rating scale or self-report.	In one trial, patients were randomly assigned to treatment with paroxetine, paroxetine + psychotherapy or usual care. Based on Hamilton-Anxiety Rating scores (HAM-A), mean anxiety scores were significantly lower in both intervention groups when compared to the control group at 6 weeks (p<0.01). A similar trend was noted for depression scale scores. Mean HAM-A scores were reduced by 58% in the paroxetine condition and 71% in the paroxetine + psychotherapy condition.  In the other trial, patients were assigned to receive either buspirone hydrochloride or usual care. At the four-week assessment point, both groups had experienced a reduction in HAM-A anxiety scores. However, reduction in anxiety was significantly greater in the intervention group when compared to the usual care group (p<0.01). Treatment was also associated with a significant reduction in depressive symptoms. There was no information available regarding the treatment of anxiety only. 8/-

## Post-stroke Emotionalism

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
<b>Hackett et al. 2010</b>  <b>Meta-analysis (Cochrane Review)</b>	N/A	A total of 7 RCTs (representing 239 patients) were identified for inclusion, 5 of which (representing 213 patients) reported sufficient data for analysis.	Included studies compared any pharmacological agent with placebo for the treatment of emotionalism post stroke. Studies in which treatment was primarily targeted stroke-associated pain syndrome or depression were excluded, even if emotionalism was assessed as a secondary outcome.	Primary outcomes included the percentage of patients achieving $\geq 50\%$ reduction in emotionalism, reduced tearfulness, clinical impression of change, and improvement on measures assessing emotional lability.	All five trials reported large treatment effects for the primary outcomes: 50% reduction in emotionalism (ES = 63, 95% CI 2.63 – 1511.41), reduced tearfulness (ES = 9.35, 95% CI 4.26 – 20.54), clinical impression of change (7.22, 95% CI 0.72 – 72.70), and improved Lability Scale score (7.22, 95% CI 0.72 – 72.70) and Pathological Laughter and Crying Scale scores (ES not estimable). However, the authors noted that many of studies were not of high methodological quality and that many of the confidence intervals were wide, suggesting that pharmacotherapy may only be associated with a small treatment effect. Drug class did not appear to impact the effectiveness of treatment.

## Reference List

- Alexopoulos GS, Wilkins VM, Marino P, Kanellopoulos D, Reding M, Sirey JA, et al. Ecosystem focused therapy in poststroke depression: a preliminary study. *Int J Geriatr Psychiatry* 2012 Oct;27(10):1053-60.
- Almeida OP, Waterreus A, Hankey GJ. Preventing depression after stroke: Results from a randomized placebo-controlled trial. *The Journal of clinical psychiatry*. 2006 Jul;67(7):1104-9.
- Brittle N, Patel S, Wright C, Baral S, Versfeld P, Sackley C. An exploratory cluster randomized controlled trial of group exercise on mobility and depression in care home residents. *Clin Rehabil* 2009 Feb;23(2):146-54.
- Campbell Burton CA, Holmes J, Murray J, Gillespie D, Lightbody CE, Watkins CL, Knapp P. Interventions for treating anxiety after stroke. *Cochrane Database of Systematic Reviews*. 2011, Issue 12. Art. No. CD008860. DOI: 10.1002/14651858.CD008860.pub2.
- Chaiyawat P, Kulkantrakorn K. Randomized controlled trial of home rehabilitation for patients with ischemic stroke: impact upon disability and elderly depression. *Psychogeriatrics: The Official Journal of the Japanese Psychogeriatric Society*. 2012;12(3):193-9.
- Chan W, Immink MA, Hillier S. Yoga and exercise for symptoms of depression and anxiety in people with poststroke disability: a randomized, controlled pilot trial. *Altern Ther Health Med* 2012 May;18(3):34-43.
- Chang K, Zhang H, Xia Y, Chen C. Testing the effectiveness of knowledge and behavior therapy in patients of hemiplegic stroke. *Top Stroke Rehabil* 2011 Sep;18(5):525-35.
- Chen Y, Patel NC, Guo JJ, Zhan S. Antidepressant prophylaxis for poststroke depression: a meta-analysis. *Int Clin Psychopharmacol* 2007 May;22(3):159-66.
- Chollet F, Tardy J, Albucher JF, Thalamas C, Berard E, Lamy C, et al. Fluoxetine for motor recovery after acute ischaemic stroke (FLAME): a randomised placebo-controlled trial. *Lancet neurology*. 2011 Feb;10(2):123-30.
- Dozeman E, van Marwijk HW, van Schaik DJ, Smit F, Stek ML, van der Horst HE, et al. Contradictory effects for prevention of depression and anxiety in residents in homes for the elderly: a pragmatic randomized controlled trial. *Int Psychogeriatr* 2012 Aug;24(8):1242-51.
- Ellis G, Mant J, Langhorne P, Dennis M, Winner S. Stroke liaison workers for stroke patients and carers: an individual patient data meta-analysis. *Cochrane Database Syst Rev* 2010;(5):CD005066.
- Graven C, Brock K, Hill K, Joubert L. Are rehabilitation and/or care co-ordination interventions delivered in the community effective in reducing depression, facilitating participation and improving quality of life after stroke? *Disabil Rehabil* 2011;33(17-18):1501-20.
- Hackett ML, Carter G, Crimmins D, Clarke T, Arblaster L, Billot L, et al. Improving Outcomes after STroke (POST): Results from the randomized clinical pilot trial. *International Journal of Stroke*. 2013;8(8):707-10.
- Hackett ML, Yang M, Anderson CS, Horrocks JA, House A. Pharmaceutical interventions for emotionalism after stroke. *Cochrane Database Syst Rev* 2010;(2):CD003690.
- Hackett ML, Anderson CS, House A, Halteh C. Interventions for preventing depression after stroke. *Cochrane Database of Systematic Reviews* 2008;(Issue No. 3):Art No. CD003689.
- Hackett ML, Anderson CS, House A, Xia J. Interventions for treating depression after stroke. *Cochrane Database of Systematic Reviews* 2008;(4):Art No. CD003437.
- Harrington R, Taylor G, Hollinghurst S, Reed M, Kay H, Wood VA. A community-based exercise and education scheme for stroke survivors: a randomized controlled trial and economic evaluation. *Clin Rehabil* 2010 Jan;24(1):3-15.
- Huang H, Chen K, Guo T, Zhang Y, Qu W, Zhou Z, et al. Treatment with carotid angioplasty stent placement for post-stroke depression compared to antidepressants. *Neurosciences*. 2012;17(1):53-6.
- Jonkers CC, Lamers F, Bosma H, Metsemakers JF, van Eijk JT. The effectiveness of a minimal psychological intervention on self-management beliefs and behaviors in depressed chronically ill elderly persons: a randomized trial. *Int Psychogeriatr* 2012 Feb;24(2):288-97.
- Jorge RE, Robinson RG, Tateno A, Narushima K, Acion L, Moser D, et al. Repetitive transcranial magnetic stimulation as treatment of poststroke depression: A preliminary study.

- Biol Psychiatry 2004;55:398-405.
- Jun EM, Roh YH, Kim MJ. The effect of music-movement therapy on physical and psychological states of stroke patients. J Clin Nurs 2012 Sep 17.
- Kim BR, Kim DY, Chun MH, Yi JH, Kwon JS. Effect of repetitive transcranial magnetic stimulation on cognition and mood in stroke patients: a double-blind, sham-controlled trial. Am J Phys Med Rehabil 2010 May;89(5):362-8.
- Lai SM, Studenski S, Richards L, Perera S, Reker D, Rigler S, et al. Therapeutic exercise and depressive symptoms after stroke. J Am Geriatr Soc 2006 Feb;54(2):240-7.
- Lennon O, Carey A, Gaffney N, Stephenson J, Blake C. A pilot randomized controlled trial to evaluate the benefit of the cardiac rehabilitation paradigm for the non-acute ischaemic stroke population. Clin Rehabil 2008 Feb;22(2):125-33.
- Lincoln NB, Flannaghan T. Cognitive behavioral psychotherapy for depression following stroke: a randomized controlled trial. Stroke 2003 Jan;34(1):111-5.
- Lamers F, Jonkers CC, Bosma H, Kempen GI, Meijer JA, Penninx BW, et al. A minimal psychological intervention in chronically ill elderly patients with depression: a randomized trial. Psychother Psychosom 2010 Jun;79(4):217-26.
- Mead GE, Greig CA, Cunningham I, Lewis SJ, Dinan S, Saunders DH, et al. Stroke: a randomized trial of exercise or relaxation. J Am Geriatr Soc 2007 Jun;55(6):892-9.
- Moss K, Scogin F, Di NE, Presnell A. A self-help behavioral activation treatment for geriatric depressive symptoms. Aging Ment Health 2012;16(5):625-35.
- Narushima K, Kosier JT, Robinson RG. Preventing poststroke depression: a 12-week double-blind randomized treatment trial and 21-month follow-up. The Journal of nervous and mental disease. 2002 May;190(5):296-303.
- Niedermaier N, Bohrer E, Schulte K, Schlattmann P, Heuser I. Prevention and treatment of poststroke depression with mirtazapine in patients with acute stroke. The Journal of clinical psychiatry. 2004 Dec;65(12):1619-23.
- Rasmussen A, Lunde M, Poulsen DL, Sorensen K, Qvitzau S, Bech P. A double-blind, placebo-controlled study of sertraline in the prevention of depression in stroke patients. Psychosomatics. 2003 May-Jun;44(3):216-21.
- Robinson RG, Schultz SK, Castillo C, Kopel T, Kosier JT, Newman RM, et al. Nortriptyline versus fluoxetine in the treatment of depression and in short-term recovery after stroke: a placebo-controlled, double-blind study. The American journal of psychiatry. 2000 Mar;157(3):351-9.
- Robinson RG, Jorge RE, Moser DJ, Acion L, Solodkin A, Small SL, et al. Escitalopram and problem-solving therapy for prevention of poststroke depression: a randomized controlled trial. JAMA 2008 May 28;299(20):2391-400.
- Salter KL, Foley NC, Zhu L, Jutai JW, Teasell RW. Prevention of Poststroke Depression: Does Prophylactic Pharmacotherapy Work? Journal of Stroke and Cerebrovascular Diseases 2012;(0).
- Salter K, Foley N, Teasell R. Social support interventions and mood status post stroke: a review. Int J Nurs Stud 2010 May;47(5):616-25.
- Sarkamo T, Tervaniemi M, Laitinen S, Forsblom A, Soinila S, Mikkonen M, et al. Music listening enhances cognitive recovery and mood after middle cerebral artery stroke. Brain 2008 Mar;131(Pt 3):866-76.
- Sims J, Galea M, Taylor N, Dodd K, Jespersen S, Joubert L, et al. Regenerate: assessing the feasibility of a strength-training program to enhance the physical and mental health of chronic post stroke patients with depression. Int J Geriatr Psychiatry 2009 Jan;24(1):76-83.
- Smith GC, Egbert N, Dellman-Jenkins M, Nanna K, Palmieri PA. Reducing depression in stroke survivors and their informal caregivers: a randomized clinical trial of a Web-based intervention. Rehabilitation Psychology. 2012;57(3):196-206.
- Thomas SA, Walker MF, Macniven JA, Haworth H, Lincoln NB. Communication and Low Mood (CALM): a randomized controlled trial of behavioural therapy for stroke patients with aphasia. Clinical Rehabil 2012;27:398-408.
- Tsai CS, Wu CL, Chou SY, Tsang HY, Hung TH, Su JA. Prevention of poststroke depression with milnacipran in patients with acute ischemic stroke: a double-blind randomized placebo-controlled trial. International clinical psychopharmacology. 2011 Sep;26(5):263-7.
- van de Port IG, Wevers LE, Lindeman E, Kwakkel G. Effects of circuit training as alternative to usual physiotherapy after stroke: randomised controlled trial. BMJ 2012;344:e2672.
- van't Veer-Tazelaar PJ, van Marwijk HW, van OP, van Hout HP, van der Horst HE, Cuijpers P, et al. Stepped-care prevention of anxiety and depression in late life: a randomized

- controlled trial. Arch Gen Psychiatry 2009 Mar;66(3):297-304.
- Watkins CL, Auton MF, Deans CF, Dickinson HA, Jack CI, Lightbody CE, et al. Motivational interviewing early after acute stroke: a randomized, controlled trial. Stroke 2007 Mar;38(3):1004-9.
- Watkins CL, Wathan JV, Leathley MJ, Auton MF, Deans CF, Dickinson HA, et al. The 12-month effects of early motivational interviewing after acute stroke: a randomized controlled trial. Stroke 2011 Jul;42(7):1956-61.
- Williams JW, Jr., Barrett J, Oxman T, Frank E, Katon W, Sullivan M, et al. Treatment of dysthymia and minor depression in primary care: A randomized controlled trial in older adults. JAMA 2000 Sep 27;284(12):1519-26.
- Wilson K, Mottram PG, Vassilas C. Psychotherapeutic treatments for older depressed people. Cochrane Database of Systematic Reviews 2009;1(Art No. CD004853):1-32.
- Wu DY, Guo M, Gao YS, Kang YH, Guo JC, Jiang XL, et al. Clinical effects of comprehensive therapy of early psychological intervention and rehabilitation training on neurological rehabilitation of patients with acute stroke. Asian Pacific Journal of Tropical Medicine. 2012;5(11):914-6.
- Yi ZM, Liu F, Zhai SD. Fluoxetine for the prophylaxis of poststroke depression in patients with stroke: a meta-analysis. Int J Clin Pract 2010 Aug;64(9):1310-7.
- Zhang LS, Hu XY, Yao LY, Geng Y, Wei LL, Zhang JH, et al. Prophylactic effects of duloxetine on post-stroke depression symptoms: an open single-blind trial. European Neurology. 2013;69(6):336-43.
- Zhang GC, Fu WB, Xu NG, Liu JH, Zhu XP, Liang ZH, et al. Meta analysis of the curative effect of acupuncture on post-stroke depression. J Tradit Chin Med 2012 Mar;32(1):6-11.
- Zhang ZJ, Chen HY, Yip KC, Ng R, Wong VT. The effectiveness and safety of acupuncture therapy in depressive disorders: systematic review and meta-analysis. J Affect Disord 2010 Jul;124(1-2):9-21.